Charles University in Prague

Faculty of Science

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MODIFICATION OF ISOPRENOIDS

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PhD Thesis

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Prohlašuji, že jsem tuto práci vypracovala samostatně pod vedením školitele Prof. RNDr. Martina Kotory, CSc. a řádně ocitovala všechny použité prameny. Dále prohlašuji, že jsem tuto práci ani její část nepředložila k získání stejného nebo jiného akademického titulu.

V Praze dne 24. srpna 2010 ……

Barbara Eignerová

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1. Introduction

This PhD work is focused on the development of a new methodology aiming at the introduction of the perfluoroalkylated side-chains into various types of molecules. Synthesis of perfluoroalkylated compounds, owing to their biological properties, is a frequent target of organic chemistry.[1] During the last couple of decades a number of different methods enabling perfluoroalkylation have been developed. Among the classical methods belong procedures based on nucleophilic, electrophilic, or radical reactions.[2] Interestingly, only a few examples of a transition metal catalyzed perfluoroalkylation reactions have been reported.[3] Despite the fact that many of these methods have wide synthetic applicability, they are not general and search for new procedures is a desirable target.

One of the possible and hitherto unexplored methods for the synthesis of perfluoroalkylated compounds is a ruthenium-complex catalyzed alkene cross-metathesis. Potentially, a reaction of a suitable terminal alkene reactant bearing a perfluoroalkylated moiety with the second terminal alkene could give rise to a new and more complex internal alkene. Regarding perfluoroalkylated alkenes suitable for the cross-metathesis reactions, (perfluoroalkyl)propenes can be considered as convenient substrates that can be easily prepared from the commercially available starting material.

Interestingly and luckily, prior to this work, the above mentioned strategy has not been pursued and thus it constituted an ideal opportunity for the exploratory research in this area. The work is focused on the scope and the limits of the cross-metathesis between perfluoroalkylated propenes with various terminal alkenes and its application in the synthesis of biologically active compounds.

2. Current State of Art

2.1. Cross-metathesis

2.1.1. General Aspects of Alkene Metathesis

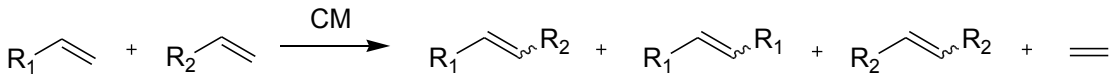
Alkenes constitute an important group of compounds. The structural motive containing the carbon-carbon double bond is widespread in natural products and commonly used in the organic synthesis. The relevance of alkenes in the organic synthesis lies in the possibility of further modifications of the double bond. The double bond can be either functionalized or transformed into a variety of different functional groups.

There are a number of diverse methods for the construction of the substituted C-C double bond and they could be roughly divided into three major groups. The first group of such reactions consists of olefination methods. They are usually based on the nucleophilic attack on a carbonyl group by a carbon nucleophile (Wittig, Horner-Wadsworth-Emmons, Julia reactions, etc.). The second is represented by cross coupling reactions between substituted vinyl derivatives with suitable reactants (Suzuki, Stille, Negishi couplings, Heck reaction, etc.). The third group encompasses elimination reactions.

Although many of these reactions are reliable and of wide synthetic use, there are still opportunities to develop a new methodology. This is caused by the fact that the aforementioned methods may rely on reaction partners that could be difficult to prepare, or may not be stable enough, or a reaction may require rather harsh conditions (like a strongly basic environment) that are not compatible with the attached functional groups. Their protection and subsequent deprotection add reaction steps, which result in lower yields and lengthier syntheses.

The alkene metathesis is a conceptually different method for the synthesis of new substituted C–C double bonds. It was discovered in the 1950s, but for the following forty years it was struggling to become a common synthetic tool mainly because of severe reaction conditions. Only during the last two decades developments in the area of metathesis catalysts have resulted in fruitful discoveries that enabled this methodology to become one of standard synthetic tools for the construction of substituted double bonds. The metathesis reactions can be classified into several groups: i) ring closing metathesis (RCM), ii) ring opening metathesis polymerization (ROMP), and iii) enyne metathesis (EM). All of them have become reliable routine methods used widely in both academic and industrial area.[4]

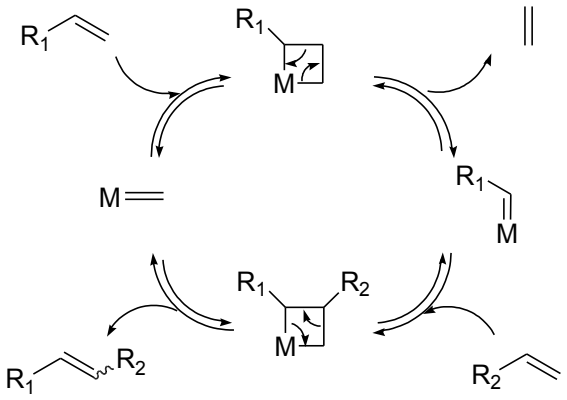
There is also another olefin metathesis: the cross-metathesis (CM), which represents an elegant method for the formation of a new substituted internal C–C double bond directly from two terminal alkenes (Scheme 1).[5] Despite the considerable synthetic interest, it is problematic in some aspects. The unpredictable reaction scope, the hardly definable alkene stereoselectivity, and occasional low yields sometimes complicate its application in organic synthesis. On the other hand, among considerable advantages of the CM in comparison to other C–C bond forming reactions belong:[6] i) easier preparation of the starting terminal or internal alkenes (in comparison with the preparation of compounds commonly used in the C–C coupling reactions such as unsaturated boranes, stannanes, halides, triflates), ii) it is carried out under mild reaction conditions (low reaction temperatures 40-60 °C and neutral environment), iii) a broad functional group tolerance, and finally, iv) in case of monosubstituted alkenes ethene is formed as the side-product.



Scheme 1

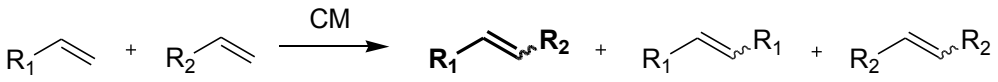
Owing to the reactivity of the double bond, alkenes are in general suitable for further modification, such as hydrogenation, halogenation, epoxidation, or cycloaddition. Therefore, every new method of their synthesis is still valuable for organic chemistry.

Cross-metathesis mechanism, selectivity, and catalysts. The alkene metathesis concept is based on the redistribution of double bonds. The widely accepted mechanism, which was originally proposed by Hérisson and Chauvin in 1971,[7] is assumed to proceed by a [2+2] cycloaddition of an alkene with a metal alkylidene complex forming a metallocyclobutane intermediate, which subsequently undergoes a [2+2] cycloreversion to generate ethylene and a substrate-loaded metal carbene (Scheme 2). This intermediate reacts with the second alkene in the same fashion to release a product and regenerate the catalyst. Although reversible, the catalytic cycle is a thermodynamically controlled process and the reaction is driven forward by evolution of ethylene gas.



Scheme 2

If two alkenes of a similar reactivity are subjected to CM conditions, assuming a full conversion, a maximum of 50% yield of the desired product will be obtained while 25% of both homocoupling products will be formed (Scheme 3). To achieve a synthetically efficient yield of 91%, again theoretically assuming a full conversion, 10 equivalents of one reacting partner should be used. Fortunately, this statement is not valid in general. Many examples demonstrate that even the 1:1 ratio of reacting alkenes can result in a high selectivity for the cross-metathesis product. A rationale for the observed selectivity is not often clear and it is assumed that it could be a combination of electronic and/or steric effects of the involved C-C double bonds as well as properties of the catalysts used.



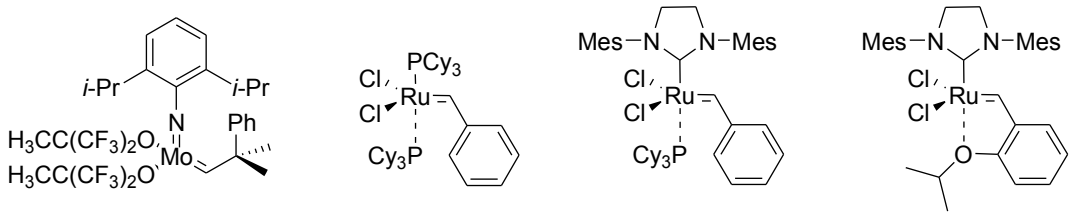
R_1 :	R_2	selectivity
1	1	50%
2	1	67%
4	1	80%
10	1	91%
20	1	95%

Scheme 3

A further issue in the cross-metathesis is the stereoselectivity of the product's substituted C-C double bond. Although the thermodynamically favored *trans*-alkenes are usually the major products, a mixture of *E*/*Z* isomers can be obtained especially when the energy difference between them is small.

Despite all these objections, the CM can be the very efficient way to conjoin two molecules. Studies in this field yielded various options how to reduce or overcome the

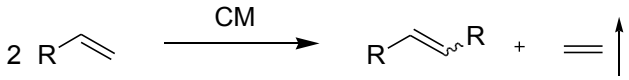
limitations presented above. The development of the increasingly active molybdenum and ruthenium based catalysts (Figure 1) extended significantly the potential application of cross-metatheses in organic synthesis. These catalysts are characterized by a high stability and a wide functional group tolerance.



Schrock | Grubbs 1st generation (G I) | Grubbs 2nd generation (G II) | Hoveyda-Grubbs 2nd generation (H-G II)

Figure 1

Classification of alkenes. Due to the multitude of factors influencing alkene reactivity in CM, a more straightforward, empirical ordering or categorization is required. The most convenient way to rank the alkene reactivity is to examine their ability to homodimerize (Scheme 4).



Scheme 4

Alkenes can be classified into four groups according to their tendency to undergo the homodimerization in the presence of other alkenes (Table 1).[8] These data are based on the reactions carried out in the presence of Grubbs 2nd generation catalyst. Type I alkenes are categorized as those able to undergo a rapid homodimerization and can participate in CM as well as their terminal alkene counterpart. Type II alkenes homodimerized slowly, and unlike Type I alkenes, their homodimers can only be sparingly consumed in subsequent metathesis reactions. Type III alkenes are essentially unable to be homodimerized by the catalyst but are still able to undergo CM with Type I and II alkenes. Type IV alkenes are not able to participate in CM with a particular catalyst but do not inhibit the catalyst activity toward other alkenes. Outside these categories are alkenes that deactivate the catalyst. In general, a reactivity gradient exists from most active Type I to least active Type IV. To avoid the statistical product distribution in inefficient reactions, the selective CM reaction can be

designed by using olefins from two different types, whose rates of dimerization are significantly distinct and/or slower than the CM product formation according to the Table 1.

Table 1. Alkene Categories according to the Selectivity in CM.

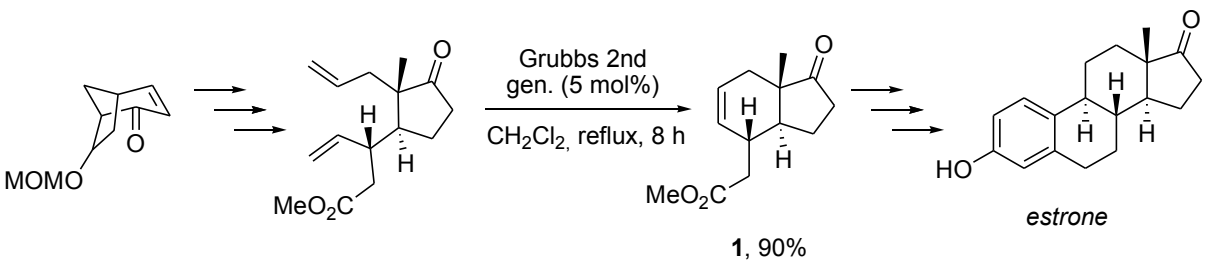
Alkenes	Typical structural motives	Homodimerization	Cross-metathesis with
Type I	terminal alkenes primary allylic alcohols or esters allyl halides styrenes (no large ortho subst.) allyl phosphonates allyl silanes allyl sulfides protected allyl amines	rapid	Type I - statistical Type II - selective Type III - selective Type IV - no reaction
Type II	styrenes (large ortho subst.) acrylates acrylamides acrylic acid acrolein vinyl ketones unprotected tert. allylic alcohols secondary allylic alcohols (perfluoroalkyl)ethenes	slow	Type II - non selective Type III - slow reaction Type IV - no reaction
Type III	1,1-disubst. alkenes trisubst. alkenes phenylvinyl sulfones protected tert. allylic alcohols	no	Type III - non selective Type IV - no reaction
Type IV	vinyl nitro alkenes protected trisubst. allyl alcohols	no	Type IV - no reaction

2.1.2. Examples of Metathesis in Syntheses of Isoprenoids

Different kinds of metathesis reactions are commonly used in organic synthesis. In this regard, also the synthesis of steroids and terpenes provides a great opportunity to successfully apply this methodology. Generally, the application of the metathesis reaction can be divided into two groups: i) ring closing metathesis and ii) cross-metathesis. The former is most often used to synthesize the basic isoprenoid frameworks (polycyclic systems), whereas the latter is usually used for the construction or modification of side-chains.

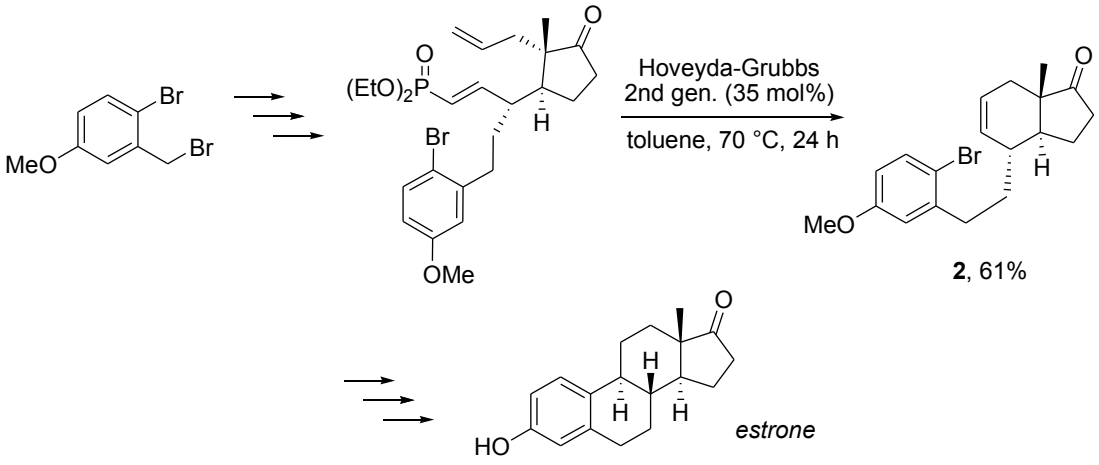
Syntheses of estrone. Estrone, because of its molecular complexity and the presence of several contiguous stereocenters, has been for a long period of time a favorable synthetic target. In this respect, also several syntheses based on the exploitation of the metathesis methodology have been reported. As a typical example may serve the approach of Ogasawara *et al.*[9] starting from a bicyclo[3.2.1]octane (Scheme 5). The key step in the synthesis was the

construction of a bicyclo[4.3.0]nonane building block (precursor of the estrone C and D rings) by ring closing metathesis of a suitably substituted 1,7-octadiene. The reaction catalyzed by Grubbs 2nd generation catalyst proceeded in excellent yield of 90%.



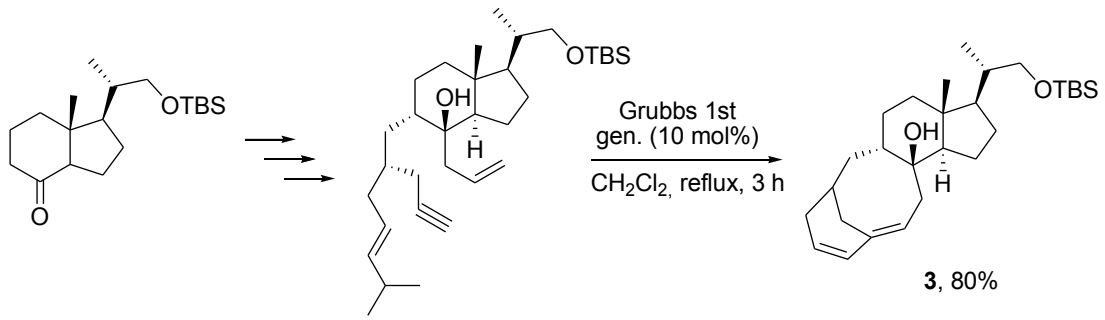
Scheme 5

The second example presented by Linclau *et al.*[10] is based again on the ring closing metathesis that resulted in the formation of a bicyclo[4.3.0]nonane building block. Although similarities with the above mentioned approach could be noticed, there are considerable differences. Firstly, the substrate already bears a side-chain with a benzene ring and secondly, it contains the substituted double bond. The presence of the side-chain with the benzene ring serves for the construction of the estrone A and B rings. The importance of the phosphonate group grounds in its influence on the required stereochemistry at C14 that determines the *trans* connection of the C and D rings. The subsequent metathesis reaction of a suitably substituted 1,7-octadiene catalyzed by Hoveyda-Grubbs 2nd generation catalyst gave rise to the desired product **2** in good 61% yield (Scheme 6).



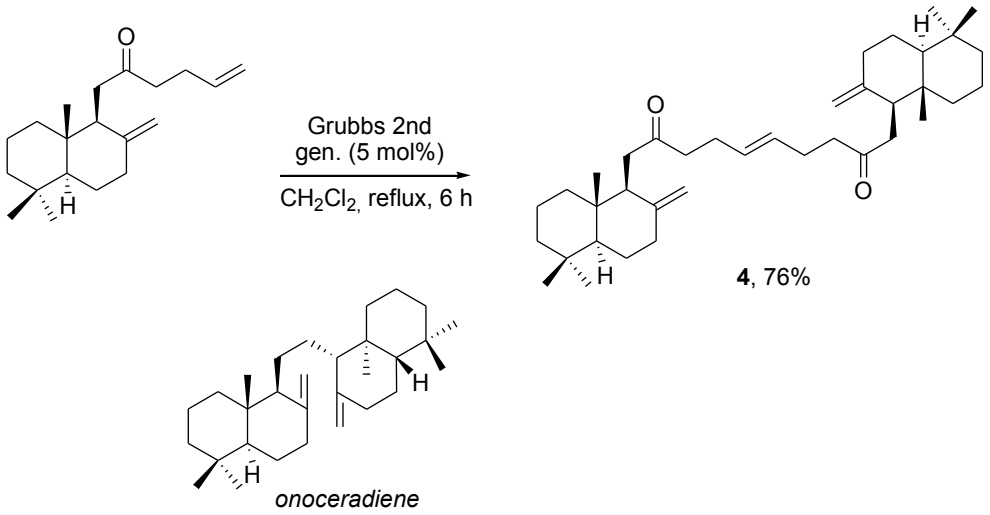
Scheme 6

Synthesis of taxosteroidal skeleton.[11] Taxosteroids are a new class of compounds that combine the [5.3.1] carbocyclic system of taxanes with steroid C and D rings, and the steroid side-chain. Granja *et al.*[11] have shown that a molecule possessing a part of the taxane and steroid framework can be synthesized by using a tandem ring closing metathesis of a suitably substituted dienyne (Scheme 7). The proper order of the tandem RCM was secured by the introduction of *i*-Pr group on one of the alkene moieties, ensuring its lower reactivity (steric reason) and thus reacting only in the last step. The impressive 80% yield of the product **3** was achieved by using Grubbs 1st generation catalyst after the optimization of the reaction conditions (catalyst, substituents attached to one of the double bonds).



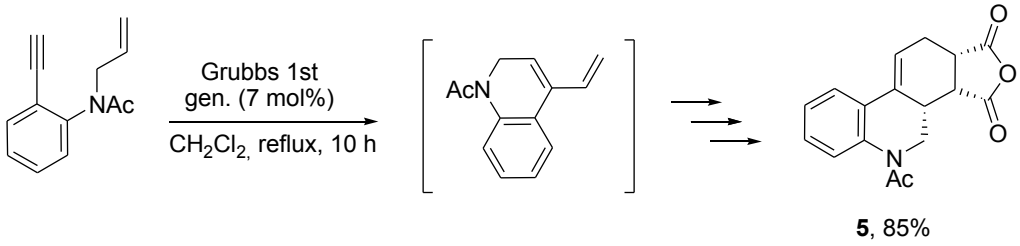
Scheme 7

Synthesis of onocerane skeleton.[12] Onoceranes constitute a family of triterpenes isolated from plants belonging to *Lycopodium* genus. Some onoceranoids have been found to exhibit the acetylcholinesterase activity having the therapeutic potential in the treatment of Alzheimer's disease. De la Torre *et al.*[12] synthesized a series of onoceradiene-like structures, which contained different linkers between C11 and C13. These compounds were accessible by the homodimerization of a bicyclic diene (Scheme 8). The homodimerization was preferred instead of a possible ring closing metathesis because of a higher reactivity of the monosubstituted double bond. The cross-metathesis was catalyzed by Grubbs 2nd generation catalyst and yielded the compound **4** in 76%.



Scheme 8

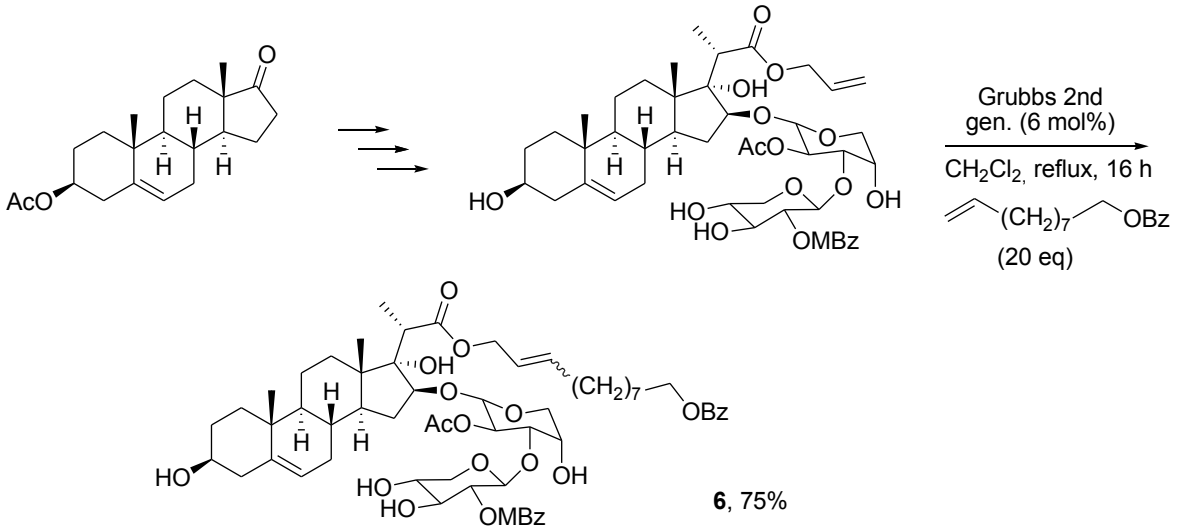
Synthesis of azasteroids.[13] A new entry to the azasteroid framework has been developed by Pérez-Castells *et al.*[13] The procedure was based on the tandem one pot enyne metathesis/Diels–Alder reactions (Scheme 9). The aromatic enyne (obtained by the Sonogashira coupling) succumbed to the intramolecular enyne metathesis catalyzed by using Grubbs 1st generation catalyst to yield a compound with the 1,3-diene moiety that instantaneously reacted by the Diels-Alder reaction with maleic acid anhydride present in the reaction mixture to furnish the tetracyclic compound **5** with the azasteroid framework in excellent 85% yield.



Scheme 9

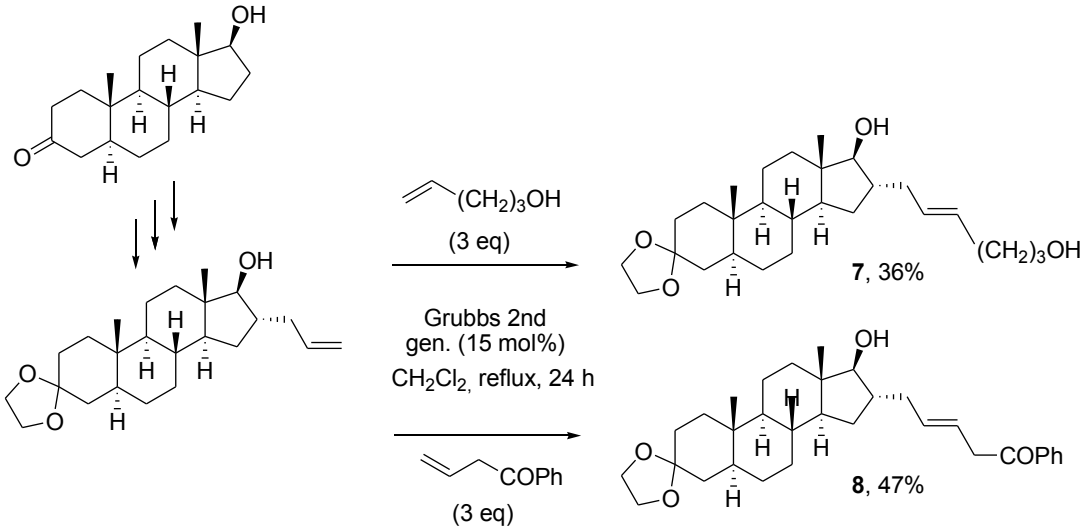
Derivatization of saponins.[14] Saponins, featuring a 16β,17α-dihydroxycholest-22-one aglycon and an acylated β-D-xylopyranosyl-(1→3)-α-L-arabinopyranosyl residue attached to the 16-hydroxyl group, have recently been isolated from a group of lily plants *Ornithogalum* genus. They show a potent antitumor activity, especially against leukemia HL-60. Yu *et al*.[14] synthesized a series of saponin derivatives bearing different side-chains and screened their activities. The derivatives were synthesized by CM with alkenols catalyzed by Grubbs 2nd generation catalyst. As a typical example may serve the synthesis of the derivative **6**, which

was accomplished in 75% yield. The prepared derivative **6** exhibited promising antitumor activities.



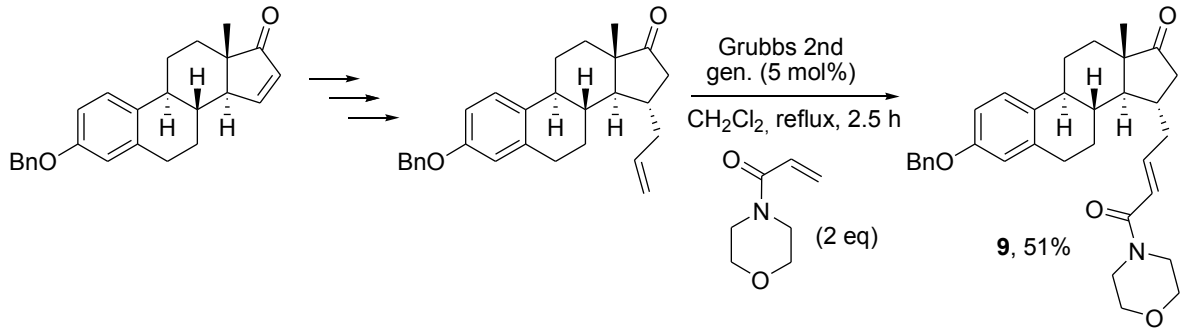
Scheme 10

Derivatization of androstane skeleton.[15] Compounds with an androstane skeleton exhibit therapeutic potential in the treatment of prostate cancer and search for their new derivatives with a higher activity is still desirable. Poirier *et al*.[15] used the CM for the elongation of the side-chain attached to C16 of the steroidal D ring. Starting from commercial dihydrotestosterone, the 16α-allylated precursor was synthesized (Scheme 11). Then the cross-metathesis of the 16α-allylated precursor with various terminal alkenes catalyzed by Grubbs 2nd generation catalyst yielded different derivatives. The syntheses of **7** and **8** in 36 and 47% yield, respectively, may serve as typical examples.



Scheme 11

Synthesis of estrone derivatives.[16] The attractive target in the treatment of estradiol dependent diseases such as breast cancer or endometriosis are compounds, which influence the conversion of estrone to the potent estrogen estradiol in body tissues. It has been shown that substitution of the estrone framework leads to compounds that are able to inhibit this conversion and therefore attract the attention of chemists. One of the possible derivatizations of the estrone skeleton constitutes a modification of the steroidal D ring. Grela *et al.*[16] described the synthesis of such derivatives by using the CM of a 15α-allylated precursor with substituted acrylates catalyzed by Grubbs 2nd generation catalyst (Scheme 12). The desired product **9** was obtained in mediocre 51% yield.



Scheme 12

2.2. Fluorinated Compounds

2.2.1. Pharmacochemical Properties of Fluorinated Compounds[17,18]

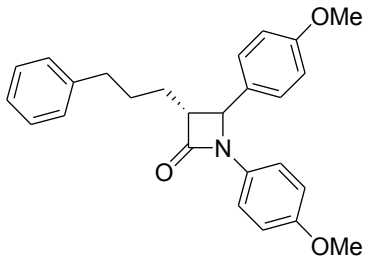
Carbon-bound fluorine atoms are unique in organic chemistry and often determine the properties of the whole compound. High electronegativity and a small size of the fluorine atom[19] as well as a very different chemical reactivity with respect to the hydrogen atom make syntheses of fluorine substituted compounds attractive. With the van der Waals radius of 1.47 Å,[20] covalently bound fluorine occupies a smaller volume than the methyl, amino, or hydroxyl groups, but is larger than a hydrogen atom (van der Waals radius of 1.2 Å). Numerous examples can be found, where fluorine has effectively replaced either hydrogen or oxygen and retained the comparable activities albeit different properties.

Despite the low occurrence of fluorine-containing compounds in Nature, synthetic fluoro-organic chemistry has made a considerable progress over recent decades. Still, until the 1970s, fluorinated compounds were rarely used in medicinal chemistry. This has changed

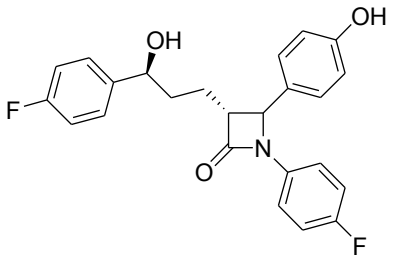
quite dramatically over the last 20 years and fluorinated compounds are nowadays synthesized in the pharmaceutical industry on a routine basis.[21-23]

The importance of the fluorine introduction stems from the following findings: i) metabolic stability is one of the key factors in the determination of the bioavailability of a compound and the presence of fluorine can prevent the undesirable degradation, ii) fluorine can change the acido-basic properties of a compound, and iii) fluorine substituents are introduced to increase the binding affinity of a compound.

Improving metabolic stability with fluorine. The low metabolic stability is the frequent limiting factor of many potentially active drugs. A rapid oxidative metabolism by the liver enzymes, in particular the P450 cytochromes, is often found to limit the bioavailability for an organism. An usual strategy to circumvent this problem is to make the molecule more polar or to block the reactive site by the introduction of a fluorine atom. The discovery of the cholesterol-absorption inhibitor Ezetimibe (Figure 2) is an illustrative example.[24-25] Starting from the moderately potent compound SCH 48461, the blockade of two metabolically labile sites in the molecule by fluorine substituents contributed significantly to the discovery of SCH 58235 (Ezetimibe). Furthermore, the introduction of fluorine atoms prevents oxidation of the monosubstituted benzene ring to phenol and the dealkylation of the methoxy group.



SCH 48461
ED_{50} (hamster) = 2.2 mg kg^{-1}



SCH 58235, Ezetimibe
oral cholesterol absorption inhibitor
ED_{50} (hamster) = 0.04 mg kg^{-1}

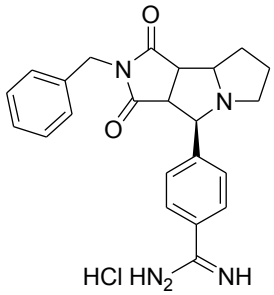
Figure 2

Effect of fluorine on physicochemical properties. As the most electronegative atom, fluorine has a very strong effect on the acidity or basicity of nearby functional groups. Depending on the position of the fluorine substituent relative to the acidic or basic group in the molecule, a pK_a shift of several log units can be observed. For example, the pK_a's of acetic acid and its fluorinated analogues are 4.76 (CH_3COOH), 2.59 (CH_2FCOOH), 1.24

(CHF_2COOH), and 0.23 (CF_3COOH).[26] This capability strongly effects also the bioavailability. Furthermore, a fluorine atom introduced close to a basic group reduces its basicity, what results in a better membrane permeation of such compound and improves its bioavailability.

The next aspect, the lipophilicity, is often the key molecular parameter in medicinal chemistry. Typically, compounds bearing lipophilic groups (ligands) are required to obtain a good binding affinity to the target protein.[27] On the other hand, it should be taken into account that high lipophilicity usually results in reduced solubility and may cause other undesirable properties of the compound. The investigation of the replacement of a hydrogen by a fluorine atom and its effect on the overall lipophilicity were carried out.[17] Unfortunately, this study showed that the concept of increased lipophilicity due to the H/F exchange does not appear to hold in general and should therefore be used with care.

Role of fluorine in protein-ligand interactions. The presence of fluorine can have significant effects on the binding affinity in protein-ligand complexes. This effect can be direct by an interaction of fluorine with a protein, or it can be indirect by the polarity modulation of other ligand groups that interact with the protein. Frequently, it is found that the introduction of a fluorine atom leads to a slight enhancement of binding affinity due to an increased lipophilicity. Probably the strongest indirect effect of fluorine on binding affinity is through the change of acidity or basicity of the ligand molecule. Fluorine also has a significant importance to polar interactions. Olsen *et al*.[28] have presented a set of fluorine-substituted thrombin inhibitors, where C–F···C=O interactions play an important role in protein-ligand interactions. A fluorine scan of thrombin inhibitors led to the discovery of a 4-monofluorinated compound **11** that binds 5.4-fold more strongly to thrombin than the nonfluorinated parent compound **10** (Figure 3). Moreover, the compound **11** exhibits 4.5-fold improvement in the selectivity. The binding mode of the fluorinated compound **11** was determined by X-ray structure analysis and shows that the F atom is in remarkably close contact with the H–C_α–C=O moiety of Asn98 of thrombin. The authors suggest that this H–C_α–C=O fragment should be considered fluorophilic because it offers several favorable polar interactions with fluorine.



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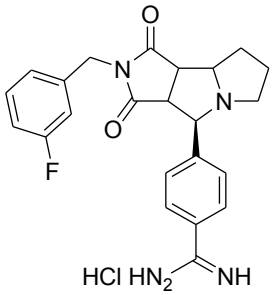


11

thrombin inhibitors

Figure 3

In general, the importance of fluorine in medicinal chemistry is crucial. It is worth summarizing the main beneficial effects - it enhances the duration of action and potency, improves pharmacokinetics by the attenuation of biliary clearance, increases the binding affinity, reduces the plasma protein binding leading to a higher free fraction of a drug, and finally facilitates the cell penetration. It is evident that all above mentioned facts led to the contemporary expansion of fluorine-focused chemistry.

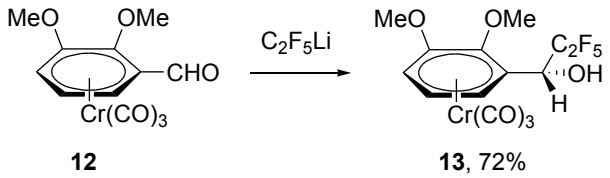
2.2.2. Methods of Preparation of Perfluoroalkylated Compounds

Various fluorinating and trifluoromethylating methods are known and have been widely used in organic synthesis. Regarding the related process – perfluoroalkylation – a considerably smaller number of methods is available. The development of simple procedures for the straightforward introduction of a perfluoroalkyl group into a molecule has been the subject of continuous investigations in recent years. These methods can be divided into following groups according to the reaction mechanism.[2]

Perfluoroalkylation *via* nucleophilic reactions. This method is based on the nucleophilic addition reaction, in which a perfluoroalkylated nucleophile (perfluoroalkylorganometallic reagent) adds to an electrophile – usually the carbon of the carbon-heteroatom double bond (aldehydes, ketones, imines). A variety of organometallic compounds such as Li, Mg, Zn, etc. can be exploited in this process. Some examples are listed below.[2]

The addition of perfluoroethyllithium to the chiral arenechromium tricarbonyl aldehyde **12** was carried out by Solladie´-Cavallo *et al.* (Scheme 13).[29] The addition of the perfluoroethyl group proceeded *trans* to the $Cr(CO)_3$ tripod and the compound **13** was

obtained in 72% yield. The decomplexation by UV irradiation afforded the optically active perfluoroethylcarbinol.



12 **13**, 72%

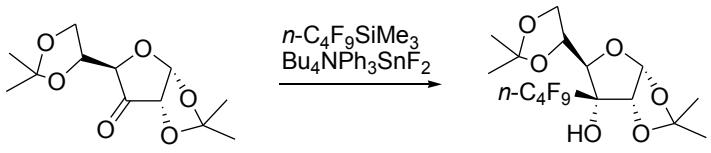
Scheme 13

Perfluorohexyllithium, generated in situ from the reaction of primary perfluorohexyl iodide and MeLi-LiCl in the presence of boron trifluoride, reacted with chiral imine **14** to give chiral benzylamine **15** in 75% yield (Scheme 14). This reaction proceeded with the good yield and diastereospecificity (dr = 96/4). Interestingly, the diastereofacial selectivity observed in the reaction did not agree with Cram's chelation model; thus, the authors (Suzuki *et al.*[30]) proposed a chelation model involving an interaction of BF_3 with the perfluoroalkyllithium.

14 **15**, 75%

Scheme 14

Portella *et al.*[31] described the perfluoroalkylation of the carbohydrate **16** with the perfluorobutyltrimethylsilane. The reaction with the silyl reagent proceeded with complete stereoselectivity, giving the D-*allo* derivative **17** in 70% yield as the unique observable product (Scheme 15).[31]



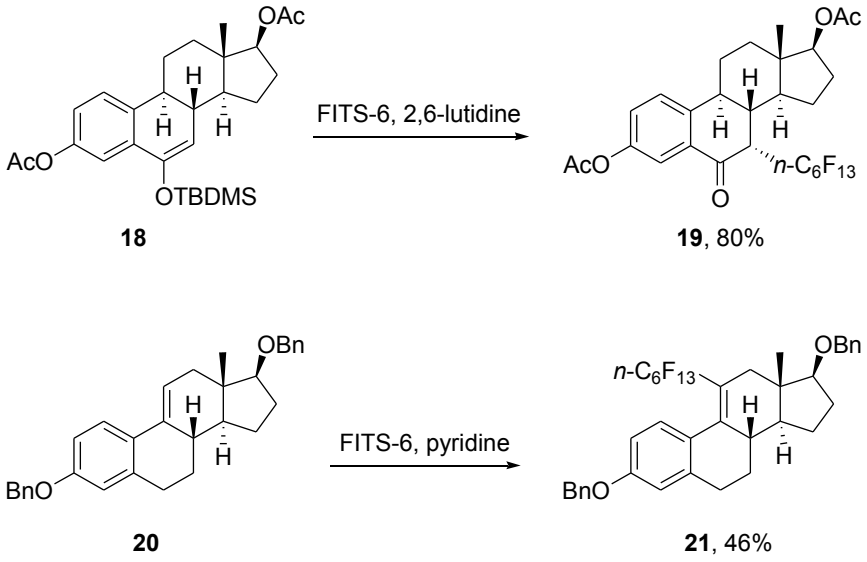
16 **17**, 70%

Scheme 15

Perfluoroalkylation *via* electrophilic reactions.[32] The high electronegativity of fluorine (4.0) or R_F groups (CF_3; 3.45) prevents an easy formation of perfluoroalkyl cations,

which complicates the electrophilic perfluoroalkylation. The reaction itself proceeds through the reaction of a perfluoroalkylated electrophile with the electrons of a double bond. It may also be inhibited by steric effects. (Perfluoroalkyl)aryliodonium salts and (perfluoroalkyl)chalcogen salts are the usually used perfluoroalkylation agents.[32]

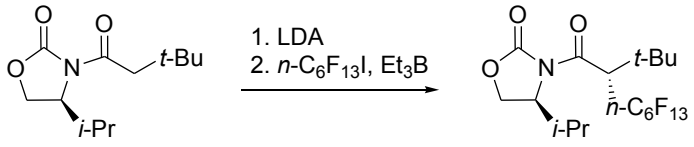
Blazejewski *et al.*[33] described the syntheses of perfluorohexylestradiols. The reaction of FITS-6 (perfluorohexylphenyliodonium trifluoromethanesulfonate) with the silyl enol ether **18** or the alkene **20** provided the perfluorohexyl steroids **19** and **21** in 80 and 46% yield, respectively (Scheme 16). The first reaction of the protected enolate **18** was highly diastereoselective giving the product **19** in α/β = 10/1.[33] In the second one the product **21** with the substituted double bond was formed.



Scheme 16

Perfluoroalkylation *via* radical reactions.[34] The fundamentally most important reactions of free radicals (species with odd number of electrons) are those involving their addition to multiple bonds, particularly their additions to alkenes, and their hydrogen abstraction reactions.[34]

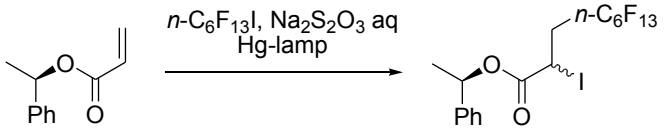
Triethylborane is an effective radical initiator for the generation of perfluoroalkyl radicals from perfluoroalkyl iodides reported by Kobayashi *et al.*[35] As a typical example of the radical perfluoroalkylation may serve the triethylborane initiated perfluoroalkylation of lithium enolate of *N*-acyloxazolidinone **22** with perfluorohexyl iodide (Scheme 17). The reaction proceeded with high diastereoselectivity (93%) and in acceptable yield (57%) of the target compound **23**.



22 **23**, 57%

Scheme 17

Nagano *et al.*[36] published a reaction of the acrylic acid derivative **24** bearing a chiral auxiliary, which was perfluoroalkylated by perfluorohexyl iodide in the presence of an aqueous solution of $Na_2S_2O_3$ under UV irradiation. The reaction was found to be regioselective yielding exclusively the compound **25** in 80% yield (Scheme 18).[36] The obtained product **25** is the direct precursor for the synthesis of chiral fluorine-containing amino acids.



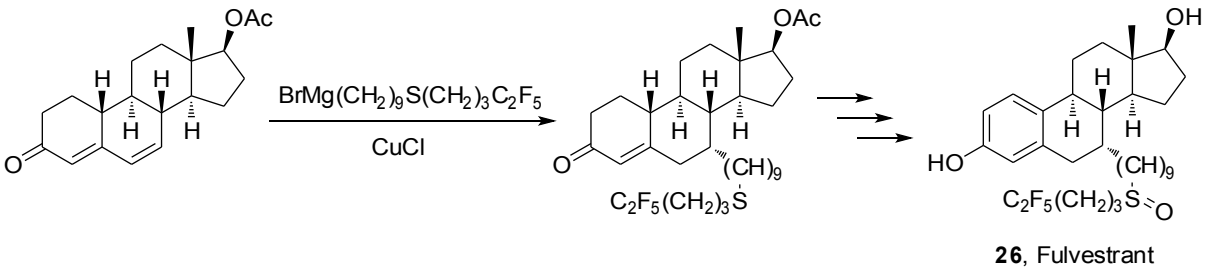
24 **25**, 80%

Scheme 18

2.2.3. Perfluoroalkylated Compounds in Pharmaceuticals and Agrochemicals[1]

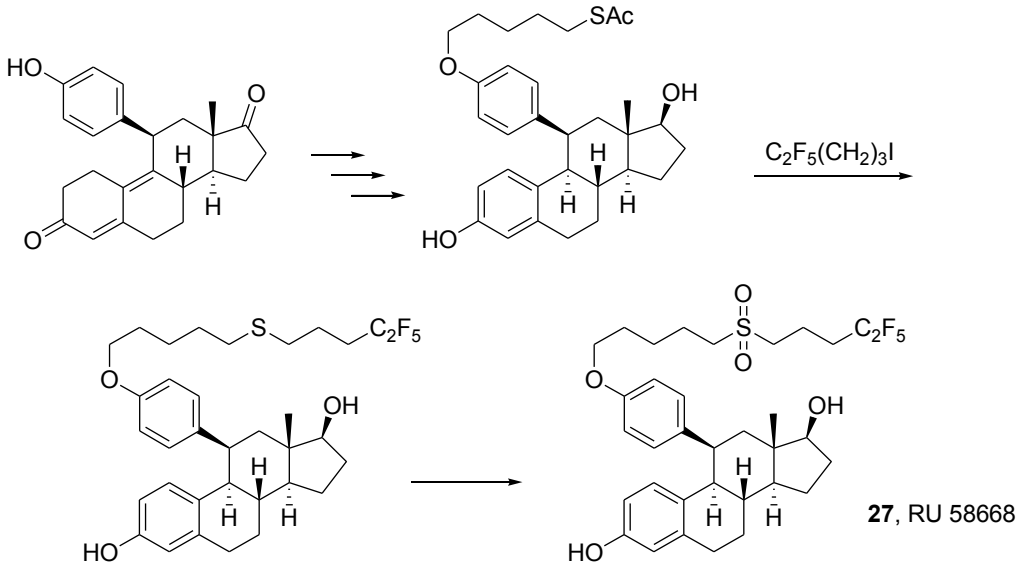
Following examples should demonstrate the diversity of biological effects of perfluoroalkylated compounds. Some of the presented compounds belong to the group of important marketed pharmaceuticals, the others are potential agrochemicals or disinfectants.

Probably the most crucial representative belonging to the substituted estrogen derivatives is Fulvestrant **26**.[37] This compound is an estrogen receptor antagonist, which binds to the receptors in the competitive manner with an affinity similar to that of estradiol. Fulvestrant **26** down regulates the estrogen receptor (ER) in human breast cancer cells. It is marketed for the treatment of hormone-dependent breast cancer. The synthesis involves a perfluoroalkylating step based on the reaction of the fluorinated Grignard reagent with the conjugated C–C bond (Scheme 19).



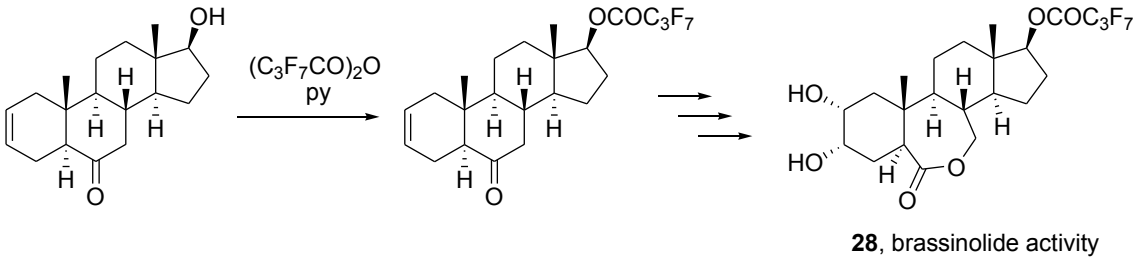
Scheme 19

The pure anti-estrogen RU 58668 **27** has been reported to cause a protein synthesis dependent paralysis of ER in the particulate fractions of the cytoplasm that depends entirely on an intact ligand-binding domain. The therapeutic potential of the compound **27** in breast cancer treatment has been reported.[38] These studies suggest that RU 58668 **27** may be used for the treatment of ER+ patients, which are primarily resistant to the usually used tamoxifen treatment and as an adjuvant to prevent the development of metastases (Scheme 20).



Scheme 20

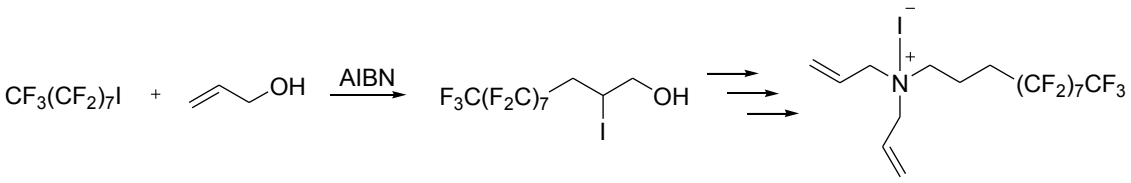
The androstane brassinosteroid **28** with 17β-perfluoroalkylated ester group was synthesized by the esterification of 17β-hydroxyl group with perfluoropropane acid anhydride and evaluated for the brassinolide activity by using the bean second-internode bioassay (Scheme 21).[39]



28, brassinolide activity

Scheme 21

The perfluoroalkyl-containing diallyl quaternary ammonium salt **29** was prepared from perfluorooctyl iodide. It exhibits good antimicrobial activities against both gram-positive *Staphylococcus aureus* and gram-negative *Escherichia coli*. The character of the compound **29** also enables its application for a textile and its utilization in protective fabrics[40] (Scheme 22).

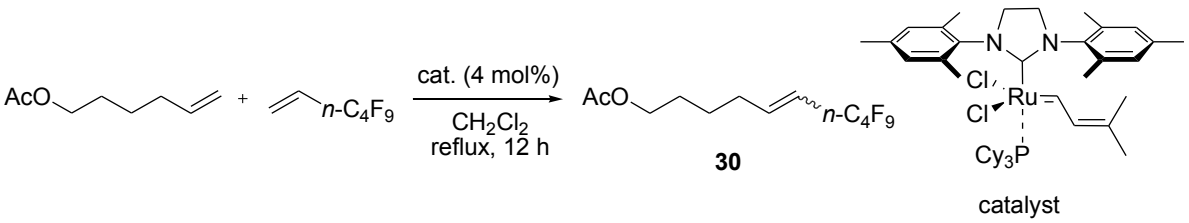


29, antimicrobial activity

Scheme 22

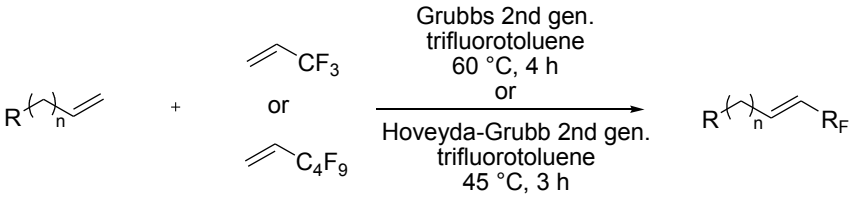
2.3. Perfluoroalkylation *via* Cross-metathesis

The perfluoroalkylation *via* cross-metathesis of alkenes is a rather unexplored area. Only a few publications have been reported in the last decade. The first reference to this topic came from Grubbs's laboratories in 2000.[41] During this work they screened the ability of a newly prepared ruthenium based catalyst (Scheme 23) in syntheses of functionalized olefins by using CM. For example, an acetoxyhexene underwent the cross-metathesis with an electron-deficient (perfluorobutyl)ethene and afforded the CM product **30** in moderate 34% yield (Scheme 23). The above mentioned reaction was carried out in refluxing dichloromethane, catalyzed by modified Grubbs 2nd generation catalyst (4 mol%), and two equivalents of the fluorinated reagent were used. The poor *E*/*Z* selectivity was observed in this case, the CM product **30** was isolated as a mixture of *E*/*Z* isomers in ratio 2.3/1.



Scheme 23

The detailed study of the perfluoroalkylation *via* CM by using (perfluoroalkyl)ethenes was carried out by Blechert *et al.* in 2001 (Scheme 24).[3] They compared the activity of three commercially available catalysts Grubbs 1st, Grubbs 2nd, and Hoveyda-Grubbs 2nd generation in the cross-metatheses of (trifluoromethyl)- or (perfluorobutyl)ethenes with various terminal olefins (different chain length and substituents – alkyl, alkenyl, aryl, etc.). It was found that the Grubbs 1st generation catalyst was completely inactive in these types of reactions. On the other hand, Grubbs 2nd and Hoveyda-Grubbs 2nd generation were both efficient. Nevertheless, the use of the Hoveyda-Grubbs 2nd generation catalyst resulted in higher yields of products and a lower (or no) amount of the homodimers.



Scheme 24

Furthermore, it was inevitable to use 10 equivalents of the (perfluoroalkyl)ethene in all reactions to achieve good yields of the perfluoroalkylated products. In addition, the reactions had to be run in trifluorotoluene to overcome the insolubility of the catalyst in excess of (perfluoroalkyl)ethene. Also the reaction conditions necessary for both catalysts were different. The Grubbs 2nd generation catalyst required harsher conditions to obtain reasonable yields in comparison with Hoveyda-Grubbs 2nd generation. In the first case the reactions were carried out at 60 °C for 4 h, in the second one 45 °C and 3 h were sufficient. The loading of catalysts Grubbs 2nd generation and Hoveyda-Grubbs 2nd generation differed in case of (trifluoromethyl)ethene from (nonafluorobutyl)ethene. The shorter perfluoroalkylated chain was more reactive and 5 mol% of Grubbs 2nd generation and Hoveyda-Grubbs 2nd generation

catalysts were used, the longer required 10 mol%. Despite the previous observation concerning a moderate *E*-selectivity, all prepared CM products had an *E*/*Z* ratio of ≥ 20/1.

Grubbs *et al.*[8] summarized the above mentioned results from the point of view of the classification of alkenes. (Perfluoroalkyl)ethenes were categorized as Type II alkenes that slowly homodimerize. They thus should react selectively with Type I, non-selectively with Type II, and slowly with Type III alkenes.

3. Aims of Work

The first aim of this work is the development of a new methodology, which would enable to introduce pefluoroalkylated chains to various types of compounds under mild reaction conditions. The underlying strategy is to explore the scope and the limits of a ruthenium complex catalyzed cross-metathesis (CM) between a suitable olefinic substrate and easily accessible (perfluoroalkyl)propenes.

The second aim is to specifically apply the developed methodology in syntheses of:

a) perfluoroalkylated carboranes

b) perfluoroalkylated brassinosteroids

c) perfluoroalkylated derivatives of estrone

The majority of the prepared compounds should be subjected to the biological tests. It is expected that the prepared perfluoroalkylated compounds – analogues or derivatives of natural or biologically active compounds – will exhibit interesting and perhaps desirable biological properties (e.g. metabolic stability, increased lipophilicity, etc.).

4. Results and Discussion

4.1. Perfluoroalkylation *via* Cross-metathesis

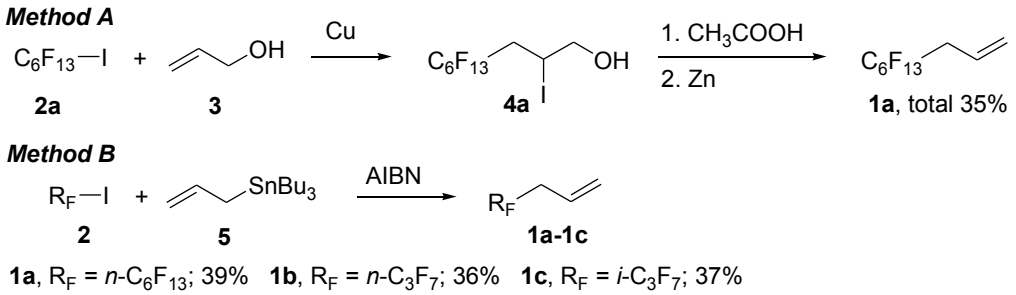
The presence of fluorine or fluorinated functional groups is often a crucial feature of widely used drugs and agrochemicals. Therefore, the introduction of fluorine or a fluorinated functional group is now a target of many research teams. In preceding decades different synthetic approaches have been reported but there is still a demand for the development of new methodologies in this area of chemistry. Among widely exploited methods in organic synthesis belongs alkene metathesis, which enables to couple double bonds under neutral and mild reaction conditions.[6] The cross-metathesis was applied in organofluorine chemistry as a useful synthetic tool in many cases.[42,43] Moreover, Blechert *et al.*[3] reported that (perfluoroalkyl)*ethenes* could be used as substrates in the ruthenium-catalyzed cross-metathesis reactions for the synthesis of perfluoroalkylated compounds. Since it has been demonstrated that the inductive effect of a perfluoroalkyl group profoundly changes with the distance from the reaction centre (e.g. different reactivity of $R_FCH{=}CH_2$ and $R_FCH_2CH{=}CH_2$,[44] and $R_F(CH_2)_nCH_2I$[45]), an exploration of the reactivity and scope of the reaction of (perfluoroalkyl)*propenes* in cross-metathesis reaction was tempting. This method was expected to allow the attachment of various fluorinated side-chains to the C–C double bonds starting from terminal alkenes and (perfluoroalkyl)propenes.[46]

4.1.1. Preparation of (Perfluoroalkyl)propenes

(Perfluoroalkyl)propenes can be easily prepared from a simple starting material – from perfluoroalkyl iodides. As representatives of (perfluoroalkyl)propenes were chosen 4,4,5,5,6,6,7,7,8,8,9,9,9-tridecafluorononon-1-ene **1a** ((perfluorohexyl)propene), 4,4,5,5,6,6,6-heptafluorohex-1-ene **1b** ((perfluoropropyl)propene), and 4-(trifluoromethyl)-4,5,5,5-tetrafluoropent-1-ene **1c** ((*iso*-perfluoropropyl)propene). Initially, the compound **1a** was synthesized by a two-step procedure (Scheme 25). The first step was based on the copper catalyzed addition of perfluorohexyl iodide **2a** to allyl alcohol **3**,[47] which afforded the intermediate **4a** in 65% yield, followed by elimination promoted by zinc under acidic conditions (54%).[48] The (perfluorohexyl)propene **1a** was obtained in overall 35% yield.

Later, a more convenient one-step procedure based on the radical reaction of perfluoroalkyl iodides **2** with allyltributylstannane **5** was used (Scheme 25).[49] (Perfluoroalkyl)propenes **1a**, **1b**, and **1c** were obtained in 39, 36, and 37% yields, respectively. This procedure provided multigram quantities of the starting material; moreover,

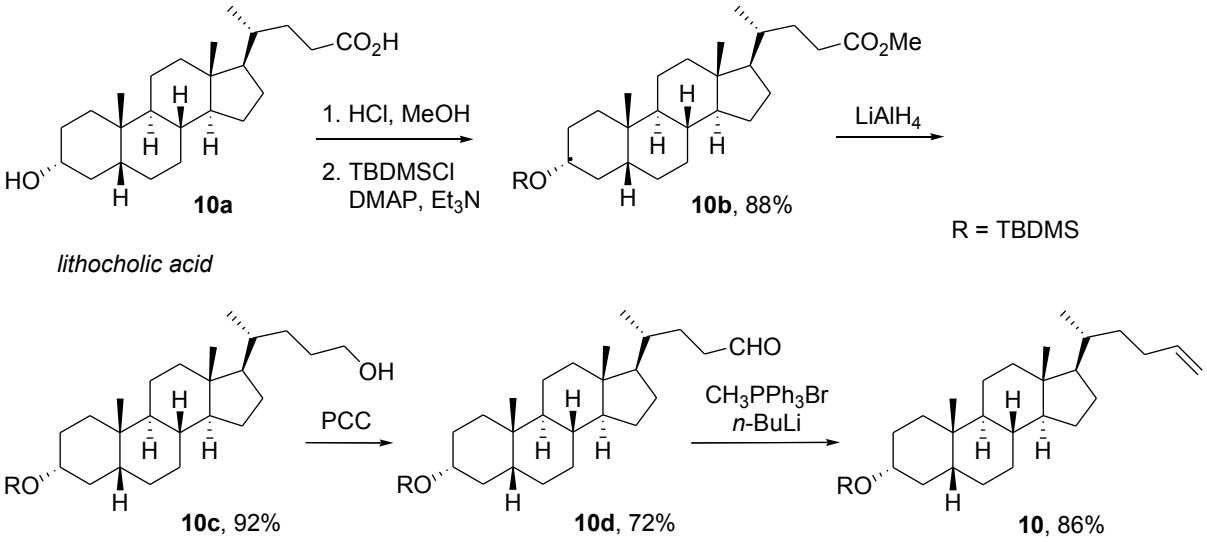
this approach had the added benefit of an easy removal of the pure product from the reaction mixture by distillation.



Scheme 25

4.1.2. Model Compounds with Terminal Double Bond

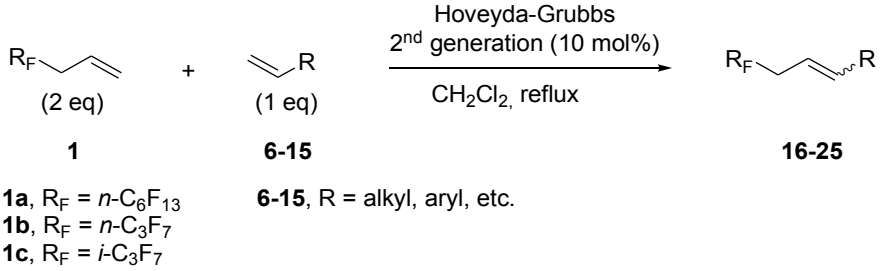
Cross-metatheses of the prepared (perfluoroalkyl)propenes with a wide range of alkene substrates were carried out to assess the scope of the reaction. Firstly, the commercially available naphthalene derivatives **6** and **7** served as representatives of aromatics. Vinylferrocene **8**[50] was chosen as a representative of metallocenes. Then the terminal alkene **9** was prepared according to the described strategy.[51] Subsequently, a steroid derivative with the terminal double bond was synthesized from lithocholic acid **10a** (Scheme 26). The first two steps involved quantitative esterification of carboxyl group and an inevitable protection of hydroxyl group in A-ring of the steroidal skeleton (**10b**). Then followed the reduction of methyl ester by using $LiAlH_4$ to primary alcohol **10c** in 92% yield, finally oxidation with PCC yielded the aldehyde **10d** in acceptable 72% yield. The last step of this reaction sequence was the Wittig olefination,[52] which afforded the terminal alkene **10** in 86% yield. This synthetic route was concluded in 5 steps in total yield 57%. The derivative **11** was isolated as a minor side-product in 5% yield during the preparation of **10**. The compound **12** was obtained by the deprotection of **10** by using TBAF in 84% yield. The last representative of the steroid derivatives – the alkene **13** – was synthesized according to the known procedure.[53] Finally, the selection was completed by the allylglucose derivative **14** and β-allylcyclodextrin **15**.[54]



Scheme 26

4.1.3. Reaction Conditions

It was shown previously that CM are conveniently catalyzed by ruthenium based catalysts.[5,6,8] Hoveyda-Grubbs 2nd generation[55] was chosen as the catalyst of choice because of its high catalytic activity. In general, it was found that cross-metatheses of (perfluoroalkyl)propenes with the terminal alkenes **6-15** carried out in the presence of a catalytic amount of Hoveyda-Grubbs 2nd generation catalyst (10 mol%) in dichloromethane under reflux proceeded well to give the expected products (Scheme 27). The replacement of dichloromethane by toluene or trifluorotoluene gave rather lower yields. All reactions were carried out until the disappearance of the starting materials **6-15** or until the progress of the reaction was not observed any more (usually 3 h). Also the (perfluoroalkyl)propene/substrate ratio 2/1 was sufficient to achieve reasonable yields of the target compounds (Table 2). The analyses of the resulting reaction mixtures showed the presence of the fluorinated homodimer ***dim*-1a** in isolable amount. A homodimerization of substrates **6-15** was not observed in the presence of Hoveyda-Grubbs 2nd generation catalyst.



Scheme 27

4.1.4. Results of Cross-metathesis

Initially, cross-metatheses were carried out with substrates **6-15** and (perfluorohexyl)propene **1a**. The reactions of 1- and 2-vinylnaphthalene **6** and **7** afforded rather low yields of the corresponding perfluoroalkylated alkenes **16** (17%) and **17** (15%). The low yields could be attributed to the propensity of **6** and **7** for the polymerization (entries 1 and 2). Considerably better result was obtained with vinylferrocene **8**, where the product **18** was obtained in reasonable 48% yield (entry 3). The metathesis reaction proceeded very well also with the alkene **9** and the corresponding product **19** was obtained in 66% yield (entry 4). Subsequently, the reaction was carried out with the alkene **10** obtained from lithocholic acid and the product **20a** was isolated in very good 75% yield (entry 5). Then the metathesis was also accomplished with the compound **11** giving the expected product **21** in good 64% yield (entry 7). Gratifyingly, the metathesis proceeded with the compound **12** having a free hydroxyl group to yield the desired product **22a** in 70% yield (entry 8). Under the same conditions the reaction of the compound **13** was run to give the product **23a** in good yield of 79% (entry 11). In an analogical manner, the metathesis reaction was carried out with the 1-allylglucose derivative **14** and yielded the expected compound **24** in 64% yield (entry 13). Finally, the reaction with β-allylcyclodextrin **15** was carried out and yielded 48% of the target product **25** (entry 14).[54]

In addition, the metathesis reactions with **1b** and **1c** were carried out with the selected substrates. The reaction of **10** with **1c** gave **20c** in 63% yield (entry 6). Also the metathesis of **12** with **1b** and **1c** yielded the corresponding products **22b** and **22c** in good yields of 71 and 75%, respectively (entries 9 and 10). The similar result was observed in reaction of **1b** with **13** affording the corresponding product **23b** in 81% yield (entry 12).

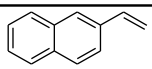
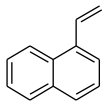
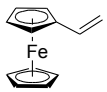
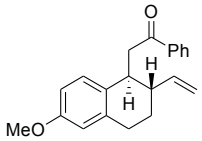
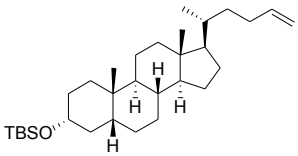
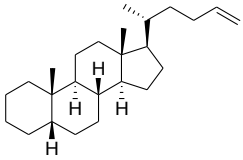
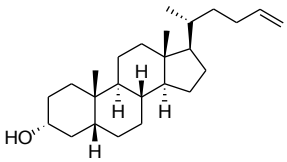
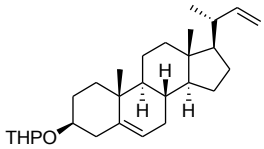
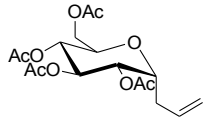
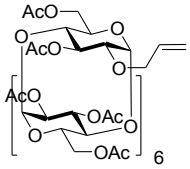
The metathesis with substrate **10** was also carried out in the presence of 5 and 2 mol% of Hoveyda-Grubbs 2nd generation catalyst to demonstrate the possibility of decreasing of the catalyst amount. In the former case (5 mol%) the conversion of the starting material was quantitative and in the latter 80% (according to ^{1}H NMR analysis of the reaction mixtures).

The metathesis of **10** with **1a** was also carried out in the presence of Grubbs 2nd generation catalyst to compare catalytic activity and selectivity of both catalysts. It proceeded to give rise to the expected product **20a** in 59% yield; however, the formation a minor amount of homodimer ***dim*-10** (10%) was observed (entry 5).

The *E/Z* selectivity in cross-metatheses can be a critical issue, especially when the double bond of the obtained alkene should be further elaborated. The reactions mentioned

above proceeded in general with high degree of *E* selectivity. In fact, there were observed no signals that could be attributed to *Z* isomers in NMR spectra. An exception from the general trend was the metathesis of the protected alkene derivative **10** with *iso*-(perfluoropropyl)propene **1c**, which gave product **20c** as a mixture of *E/Z* isomers in 7/1 ratio. Interestingly, the reactions of alkenes bearing free hydroxyl group **12** with **1a**-**1c** gave the corresponding products **22a**-**22c** as mixtures of double bond isomers with low *E/Z* ratio (1.5-2/1).

Table 2. Synthesis of Perfluoroalkylated Compounds by Cross-metathesis.[a]

Entry	**1**	Substrate		Product	*E*/*Z*	Yield [%][b]
1	**1a**		**6**	**16**	*E*	17
2	**1a**		**7**	**17**	*E*	15
3	**1a**		**8**	**18**	*E*	48
4	**1a**		**9**	**19**	*E*	66
5	**1a**		**10**	**20a**	*E*	75 (59)[c]
6	**1c**			**20c**	7/1	63
7	**1a**		**11**	**21**	4/1	64
8	**1a**		**12**	**22a**	2/1	70
9	**1b**			**22b**	1.5/1	71
10	**1c**			**22c**	1.5/1	75
11	**1a**		**13**	**23a**	*E*	79
12	**1b**			**23b**	*E*	81
13	**1a**		**14**	**24**	*E*	64
14	**1a**		**15**	**25**	*E*	48

[a] All reactions were catalyzed by Hoveyda-Grubbs 2nd generation catalyst (10 mol%) unless otherwise noted.

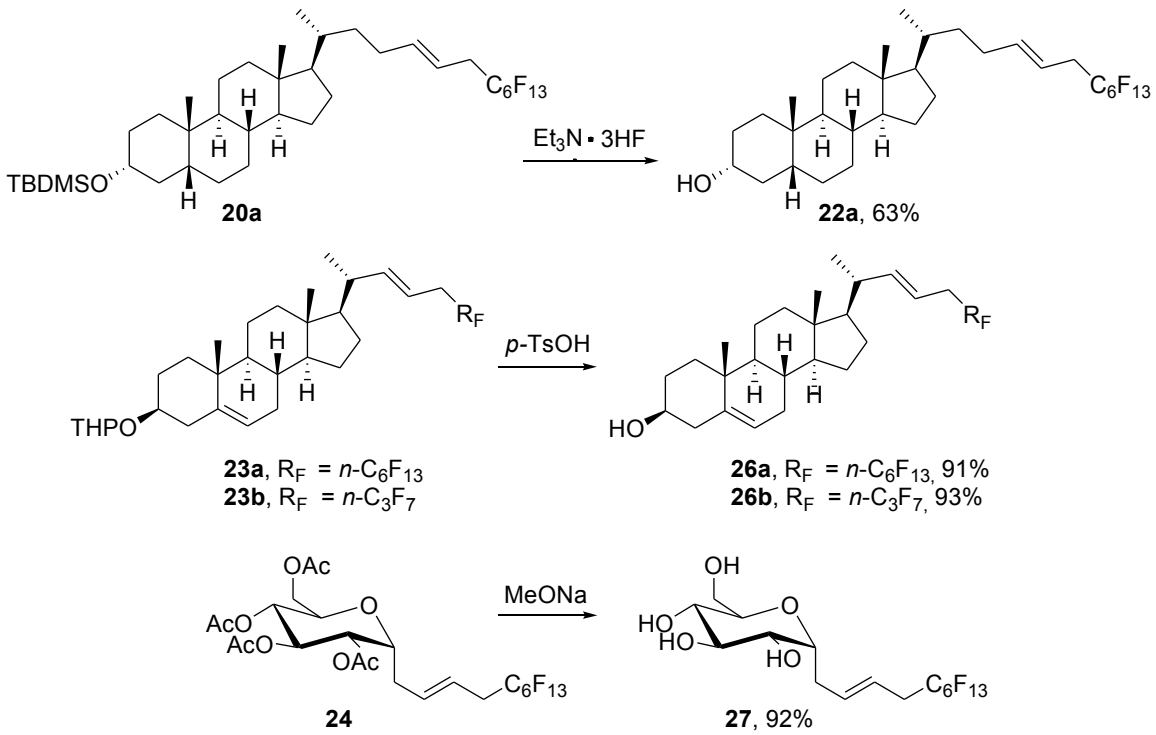
[b] Isolated yields.

[c] Grubbs 2nd generation catalyst (10 mol%) was used.

4.1.5. Removal of Protecting Groups

The deprotection of TBDMS group from **20a** with $Et_3N{\bullet}3HF$[56] in THF afforded the compound **22a** in 63% yield. The removal of the THP protective group from **23a** and **23b**

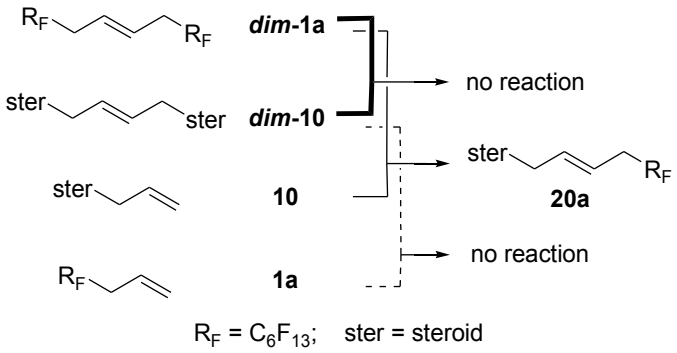
with *p*-TsOH in MeOH proceeded quantitatively and substances **26a** and **26b** were obtained in 91 and 93% isolated yields, respectively. Analogically, the deprotection of the saccharide derivative **24** under basic conditions (MeONa/MeOH) afforded **27** in 92% yield (Scheme 28).



Scheme 28

4.1.6. Reaction of Dimers

Since the homodimer of (perfluorohexyl)propene ***dim*-1a** was the major side-product in cross-metathesis reactions, it was studied whether this compound could participate in CM as well. A larger amount of steroidal homodimer ***dim*-10** was synthesized by using Grubbs 2nd generation catalyst (Hoveyda-Grubbs 2nd generation catalyst did not promote the reaction) in 52% yield. Then three cross-metathesis reactions were carried out. In the first case the reaction of two homodimers ***dim*-1a** and ***dim*-10** did not proceed. In the second case the smooth reaction of the fluorinated homodimer ***dim*-1a** and the olefin **10** was observed affording the desired cross-metathesis product **20a** in quantitative yield (^{1}H NMR yield). In the last case, i.e. the reaction of the steroidal homodimer ***dim*-10** and the (perfluorohexyl)propene **1a**, again no reaction was observed (Scheme 29).



Scheme 29

4.1.7. Summary

The metathesis reaction of (perfluoroalkyl)propenes and various terminal alkenes including terpenes and saccharides proceeded in all cases from good to excellent yields under mild reaction conditions (reflux in dichloromethane) and favorable (perfluoroalkyl)propene/substrate ratio 2/1. The reaction conditions as well as the known tolerance of the catalyst used for a wide range of functional groups enabled to carry out the metathesis also with substrates having unprotected hydroxyl groups, thus allowing the direct perfluoroalkylation avoiding the often lengthy and problematic protection/deprotection reaction sequence. Thus the developed methodology constitutes a simple pathway for introducing of the perfluoroalkyl side-chains into structurally various compounds and can be use as a powerful synthetic tool in further projects.

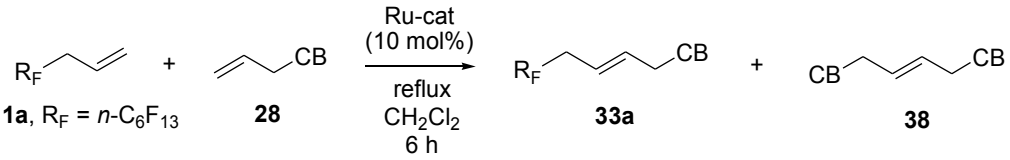
4.2. Synthesis of Fluorinated Carboranes

Carboranes (CB) are artificial aromatic polyhedral clusters composed of boron and carbon atoms. Due to the unique bonding system within the molecule they are exceptionally stable compounds and this property has opened numerous perspectives to their practical use.[57,58] CB are widely used in the radionuclide diagnostics, therapy, and related fields.[57-60] Probably the best known example of their application is boron neutron capture therapy,[59] which is binary radiation therapy for the treatment of cancer. It entails the capture of thermal neutrons by boron-10 (^{10}B) nuclei that have been selectively delivered to tumor cells. Among the other utilizations belong the carborane based super acids[60] and using metallacarborane anions of $(C_2B_9H_{11})_2Co^-$ type for solvent extraction of radionuclides from spent nuclears fuels.[59] The cobalt bis(dicarbollide) anion, $[3,3'\text{-}Co(1,2\text{-}C_2B_9H_{11})_2]^-$, was also proposed for a use in medicinal chemistry because of an exceptional stability of this compound.[61] Recently, metallacarboranes derivatives were found to have antiviral (anti-HIV activity).[62-65] The

preparation of biologically active CB is mainly based either on an attachment of a carborane fragment to other molecules or making it a part of the molecular framework. One of the possible methods how to achieve this goal is the use of the cross-metathesis reaction of carboranes bearing the terminal alkene moiety with other alkenes. However, this area of chemistry is rather unexplored and only a few papers have been reported so far. Among them belongs Sneddon's fundamental study regarding the cross-metathesis of alkenylcarboranes with various alkenes[66] and synthesis of amphiphilic carborane-containing copolymers.[67] This terra incognita represented a good opportunity for the demonstration of the versatility of our perfluoroalkylating methodology.

4.2.1. Screening of the Catalytic Activity

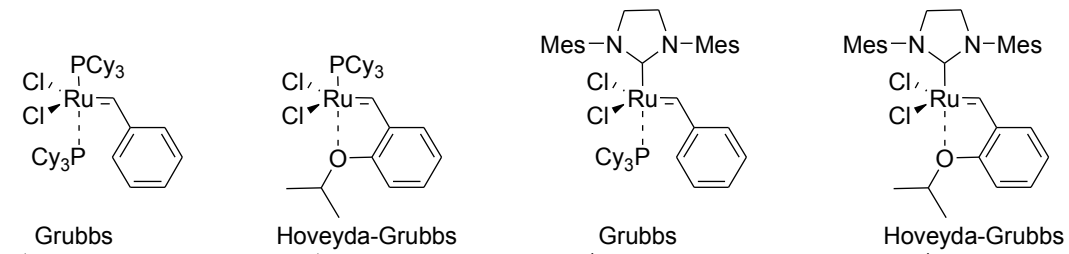
At the beginning, the catalytic activity of various Ru-based complexes in CM of (perfluorohexyl)propene **1a** with 1-allyl-1,2-dicarbadodecaborane **28** (Scheme 30) was screened on the analytical scale and the results are summarized in Table 3.



1a, R_F = *n*-C_6F_{13} **28** **33a** **38**

Scheme 30

Four catalysts were chosen - Grubbs 1st generation (G I), Hoveyda-Grubbs 1st generation (H-G I), Grubbs 2nd generation (G II), and Hoveyda-Grubbs 2nd generation (H-G II) (Figure 4). The first two of above mentioned catalysts did not promote the reaction (entries 1 and 2). On the other hand, G II and H-G II catalysts had comparable activity providing the perfluoroalkylated carborane **33a** in 63 and 68% yields along with dimer **38**[66] in 10 and 14% yields, respectively (entries 3 and 4). The highest catalytic activity of H-G II catalyst is consistent with the previous observations (Table 3).[46]



Grubbs 1st generation | Hoveyda-Grubbs 1st generation | Grubbs 2nd generation | Hoveyda-Grubbs 2nd generation

Figure 4

Table 3. Reaction of **28** with **1a** Catalyzed by Various Metathesis Catalysts.

Entry	Catalyst	**33**, Yield (%)[a,b]	**38**, Yield (%)[a]
1	G I	0 (100)	0
2	H-G I	0 (100)	0
3	G II	63 (16)	10
4	H-G II	68 (8)	14

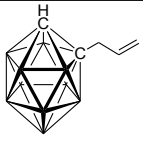
[a] ^{1}H NMR yield.

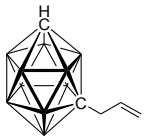
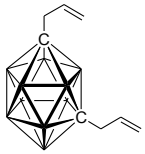
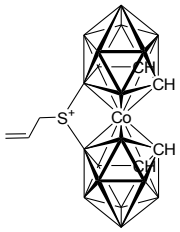
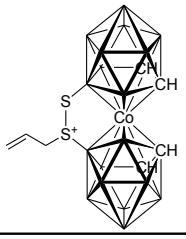
[b] In parentheses is an amount of the unreacted **28**.

4.2.2. Results of Cross-metathesis

H-G II catalyst was chosen as the catalyst of choice for metathesis reactions on the preparative scale on the basis of the results presented in Table 3. All starting compounds **28-32** were prepared according to the previously published procedures.[68-70] Firstly, the reactions were carried out with (perfluorohexyl)propene **1a** (Table 4). Thus the metathesis of *ortho*- and *meta*-allylcarboranes **28** and **29** gave rather mediocre isolated yields of the desired perfluoroalkylated carboranes **33a** and **34a** (34 and 31%, isolated) (entries 1 and 3). Subsequently, the carborane bearing two terminal double bonds **30** underwent the two-fold CM with **1a** and the compound **35a** was isolated in 38% yield (entry 5). The reaction proceeded also with the sulfur-bridged carboranyl Co-complexes **31** and **32** bearing the allyl sulphide moiety. In this regard, it is noteworthy that yields were higher than with other carborane derivatives. The reaction of the compound **31** furnished the corresponding product **36a** in good 53% isolated yield (entry 6). Analogically, the reaction with the disulfane derivative **32** gave rise to the carborane **37a**, which was isolated in 44% yield (entry 7). Then the metathesis reactions of the selected carboranes with **1b** and **1c** were carried out. The metathesis of **28** with **1c** gave **33c** in acceptable 32% isolated yield (entry 2). Also the reaction of **29** with **1b** yielded the corresponding product **34b** in the isolated yield of 34% (entry 4). Finally, the similar result was observed in the reaction of **32** with **1b**, which afforded the product **37b** in the reasonable 41% isolated yield (entry 8).[71]

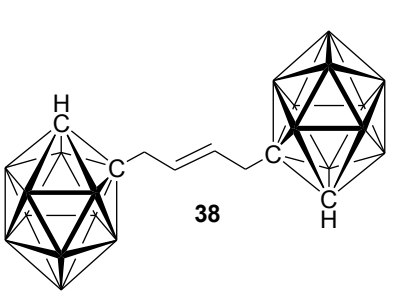
Table 4. Synthesis of Perfluoroalkylated Carboranes.

Entry	**1**	Carborane	Product	Yield (%)[a]
1	**1a**	 **28**	**33a**	34
2	**1c**		**33c**	32

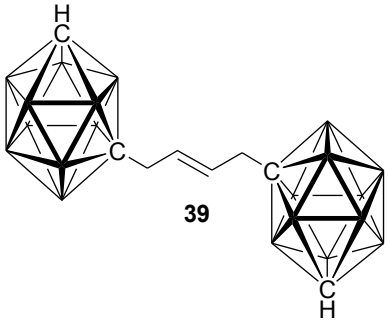
3	**1a**		**29**	**34a**	31
4	**1b**			**34b**	34
5	**1a**		**30**	**35a**	38
6	**1a**		**31**	**36a**	53
7	**1a**		**32**	**37a**	44
8	**1b**			**37b**	41

[a] Isolated yields.

In some cases the lower yields could be attributed to the formation of carborane dimers and to the low conversion (unreacted starting material was recovered often in more than 20%). For example, during the metathesis of **28** or **29** with **1a** the dimers **38** and **39** (Figure 5) were isolated in 23 and 27% yields, respectively. The observed discrepancy in the isolated yields of the carborane dimers resulted from the different concentrations of the reactants on the analytical and preparative scales. It should be added that either prolongation of the reaction time or adding the catalyst in small portions during the course of the reaction or a change of a solvent (e.g. to toluene) did not substantially affect the overall yields of the CM products. Also the reaction of carborane dimer **38** with **1a** was tried and no traces of the CM product were detected in the reaction mixture. Another complication was the separation of products from the substrates and dimers, because all compounds are extremely non-polar.



38



39

Figure 5

4.2.3. Spectroscopic Properties

In NMR spectra, some interesting effects were observed. It was shown previously[70] that metallacarboranes bridged with one sulfur atom can assume only *e*-1,1',2,2' conformation with two planes of symmetry passing through the central Co atom. In this conformation all four carbon atoms of the dicarbollide cages are equivalent. In agreement with this assumption it was possible to observe in ^{13}C NMR spectrum of the compound **36a** only one signal of the carborane carbon atoms. On the other hand, compounds with two-atom S_2 bridge can have a zig-zag character[70] (*s*-1,1',2,2' conformation) with no plane of symmetry and thus two enantiomeric forms are possible. In ^{13}C NMR spectra of compounds **37a** and **37b** four signals belonging to the carborane carbon atoms were found, which indicates not only a non-equivalency of both dicarbollide moieties but also a loss of a plane of symmetry in them that is in agreement with the proposed "frozen" *s*-1,1',2,2'conformation. Two enantiomeric forms of the S_2 bridged carborane are equally possible; this is manifested in non-equivalency of hydrogen atoms in the positions 1 and 4 of the compound **37a**, which became diastereotopic.

4.3. Synthesis of Fluorinated Brassinosteroids

Brassinosteroids belong to a family of natural plant hormones with many potential applications in agrochemistry. They are able to stimulate the growth of plants under unsuitable conditions (e.g. lack of irradiation, nutrients, inadequate temperature, etc.).[72,73] Moreover, some exert unexpected antiviral and cancerostatic activity.[74-77] Unfortunatelly, their duration of action in organisms is often insufficient. They are easily inactivated, among other reactions, by the conversion to more hydroxylated derivatives.[78] The hydroxylation proceeds mainly in the side-chain, e.g. in the position 26. Several papers describe metabolic accumulation of C-26-, C-28-hydroxylated, or further oxidized products.

One of the approaches to suppress the oxidation constitutes a substitution of a hydrogen atom to other elements. Since the biodegradability of the C–F bond is very low, fluorine-containing brassinosteroids could have a wide practical application because of a higher metabolic stability in target organisms. This assumption has been confirmed by the synthesis and metabolic stability studies of the monofluororinated brassinosteroids[79] and their derivatives bearing perfluoroalkylated ester side-chain instead of the classical sterol one.[39]

The most active brassinosteroid – brassinolide **40** (Figure 6) – was for the first time isolated and identified from the pollen of *Brassica napus*, but it is found there in the extremely low concentration.[80] Therefore, an efficient laboratory synthesis is still the desirable issue. The aim of this project was the development of a suitable synthetic strategy for the preparation of fluorinated analogues of brassinosteroids and the evaluation of their biological activities.

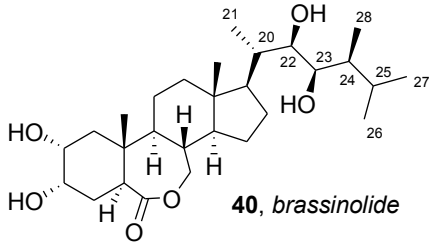
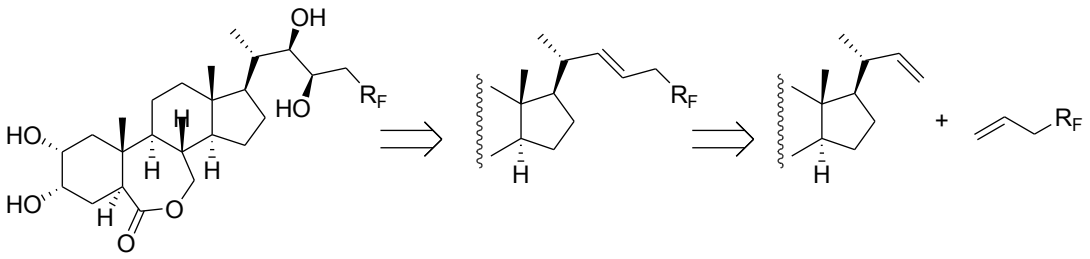


Figure 6

4.3.1. Retrosynthesis

The retrosynthetic analysis of a perfluoroalkylated brassinosteroid was based on two following assumption: a) the 1,2-diol moiety could be conveniently synthesized by dihydroxylation of a suitable intermediate bearing the internal C–C double bond and b) the fluorinated side-chain containing the double bond could be easy to obtain by using CM of a terminal alkene with the appropriate (perfluoroalkyl)propene (Scheme 31).



Scheme 31

4.3.2. Synthesis

The suitable substrate **42** was prepared by the standard synthetic methodology in six steps from the commercially available carboxylic acid **41** according to the reported procedure (Scheme 32).[81] The ester **42** was reduced by using $LiAlH_4$ to primary alcohol **43** in 88% yield, which was oxidized by using Dess-Martin periodinane reagent to the aldehyde **44** (76%).[82] Then the Wittig olefination afforded the terminal alkene **45** in 93% yield.[52] The deprotection

of its carbonyl group under acidic conditions afforded the required alkene **46** in good 96% isolated yield.

With the alkene **46** on hand, CM with (perfluorohexyl)- **1a**, (perfluoropropyl)- **1b**, and (perfluoroisopropyl)propene **1c** could be carried out. Fortunately, it was found that our conditions[46,71] were also suitable for the CM with the substrate **46**. The cross-metathesis was effectively catalyzed by Hoveyda-Grubbs 2nd generation catalyst (10 mol%) in refluxing dichloromethane and moreover, only 2 equivalents of (perfluoroalkyl)propenes **1a-1c** were sufficient for achieving reasonable yields. The reactions were stopped after 4 h, when no further progress was observed according to the TLC analysis. In all cases the cross-metathesis proceeded smoothly to give the corresponding perfluoroalkylated products **47a-47c** in good 67, 71, and 59% isolated yields, respectively. According to the NMR analysis compounds **47a** and **47b** were obtained as pure *trans* double bond isomers, only in case of **47c** a 19/1 *trans*/*cis* mixture was obtained. All compounds **47a-47c** were crystalline and the structure of *trans*-**47c** was unequivocally confirmed by a single crystal X-ray analysis (Figure 7).

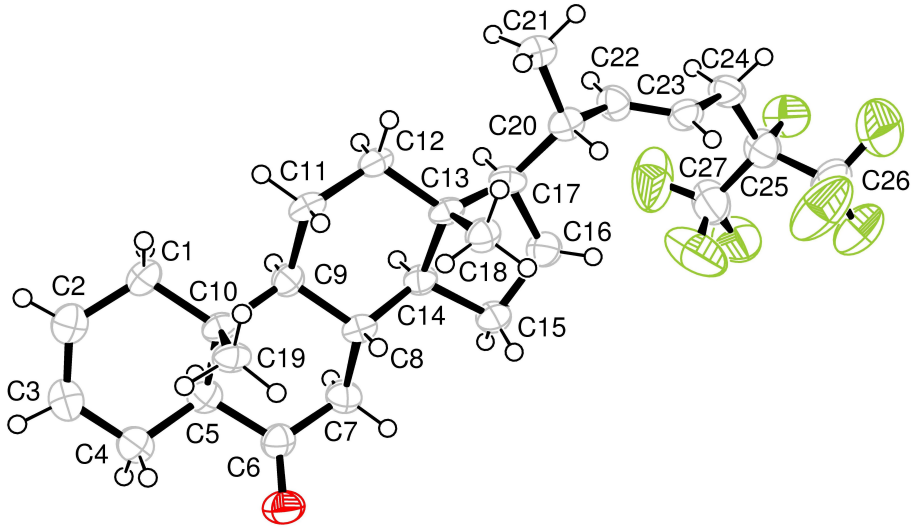
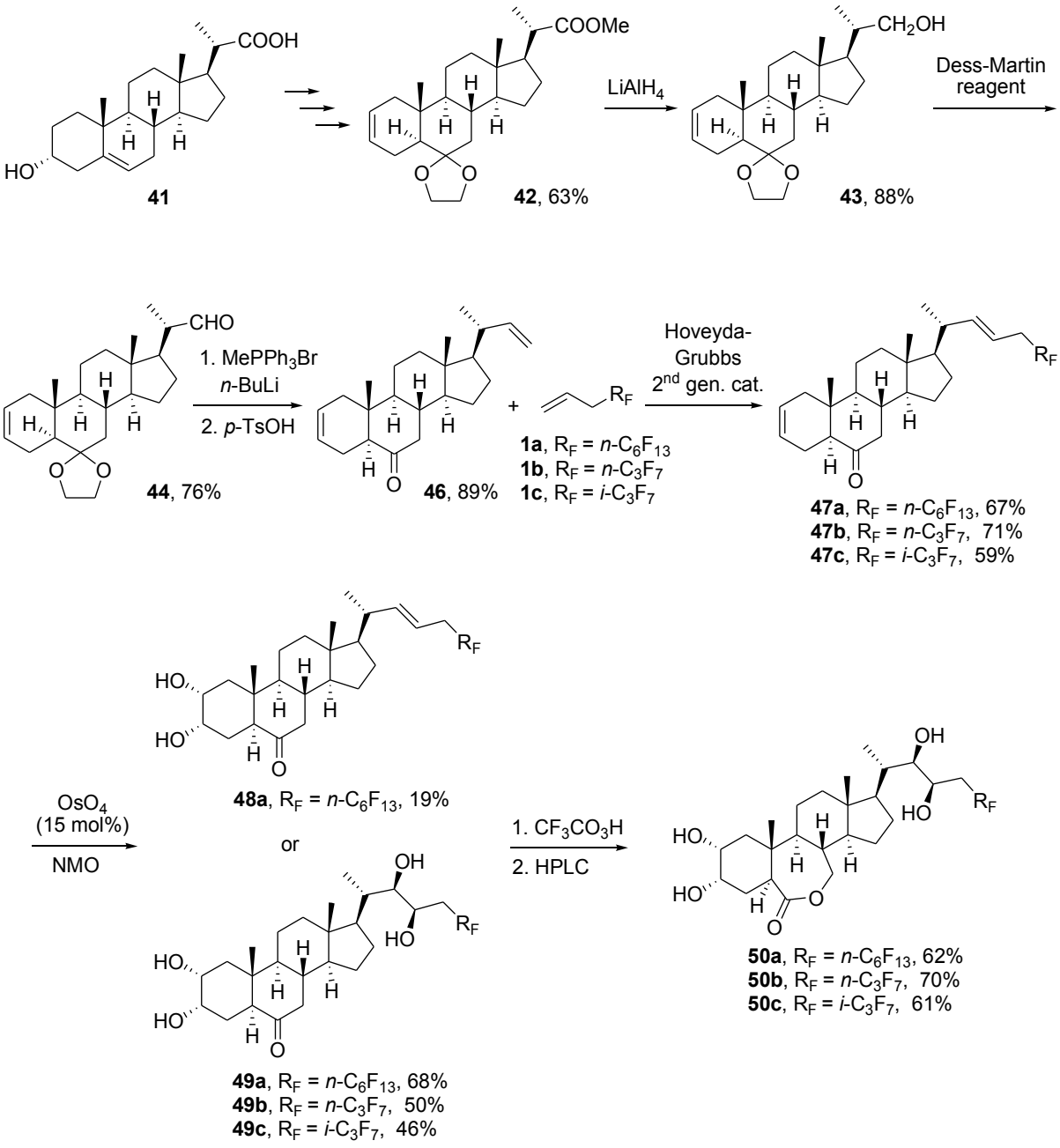


Figure 7

Since compounds **47a-47c** possess two double bonds within the molecule, a simultaneous dihydroxylation was attempted. The hydroxylation of the double bonds was carried out by a catalytic amount of OsO_4 (15 mol%) and excess *N*-methyl morpholine *N*-oxide (3.5 fold excess). Initially, the hydroxylation of **47a** for 2 h led only to a 1/1.5 mixture of **48a** and **49a** in 50% isolated yield. This finding clearly demonstrated that dihydroxylation takes place preferentially on the more electron-rich double bond in the cyclohexene ring. In

order to achieve full conversion the hydroxylation time was prolonged to 16 h. Under these conditions **47a-47c** were fully converted to tetraols **49a-49c** as single diastereoisomers in good isolated yields of 68, 50 and 46%, respectively. The diastereoselectivity was controlled by the molecular scaffold of **47**. The dihydroxylation of the cyclohexene ring proceeded from the sterically less hindered side, i.e., the oxidizing agent approached from the bottom side of the molecule. The diastereoselectivity in the side-chain was controlled by the presence of the centre of chirality on C20. No other isomers were detected in the reaction mixtures.

Finally, the synthesis was accomplished by Baeyer-Villiger oxidation of **49a-49c** by using trifluoroperacetic acid (prepared by mixing trifluoroacetic anhydride and hydrogen peroxide in dichloromethane) under ambient conditions. In each case the oxidation afforded a mixture of two regioisomeric lactones in 4/1 ratio in favor of the desired regioisomers **50a-50c** with natural configuration of the diol moiety in the side-chain. The desired brassinosteroids **50a-50c** were isolated by preparative HPLC in 62, 70, and 61% yields, respectively (Scheme 32).[83]



Scheme 32

4.3.3. Biological Evaluation

Subsequently, the newly prepared brassinosteroids with perfluoroalkylated side-chains were tested in collaborating laboratories for biological activities in various assays, e.g. $GABA_A$ activity,[79,84] cytotoxicity,[74,77] and brassinolide activity.[39,85]

$GABA_A$ receptors activity (Prague Psychiatric Centre, Dr. Krištofíková): γ-Aminobutyric acid (GABA) is a major inhibitory neurotransmitter in the mammalian brain that is involved in controlling of the muscle tone. The binding of the prepared compounds **50a-50c** to $GABA_A$ receptors was tested *in vitro* using neural membranes of male rat brains.

The specific steroid binding was detected by the decrease of the [^{35}S]-*tert*-butylbicyclo-[2.2.2] phosphorothionate (TBPS) binding after the application of the tested compounds. The results could be summarized as follows: the heptafluoro derivative **50c** compares favorably to the natural hormone allopregnanolone **51** (Figure 8) and its higher metabolic stability should more than compensate for its slightly lower GABA-like activity. The compound **50a**, which does not contain the steroidal *i*-octyl side-chain, is active at a higher concentration only and the compound **50b** is inactive (Table 5).[83]

Table 5. Modulatory Effect on $GABA_A$ Receptors.

Compound	[^{35}S]-TBPS (%)[a]	I_{max}(%)[b]	IC_{50} (nM)[c]
allopregnanolone **51**	56.2 ± 6.0	79.0	80
50a	47.2 ± 15.1	57.9	900
50b	95.1 ± 14.8	–[d]	–[d]
50c	56.6 ± 14.6	59.4	100

[a] For 100 nM concentration of the tested compounds.

[b] The maximal suppression of the binding.

[c] The steroid concentration producing a half-maximal inhibition.

[d] Not determined.

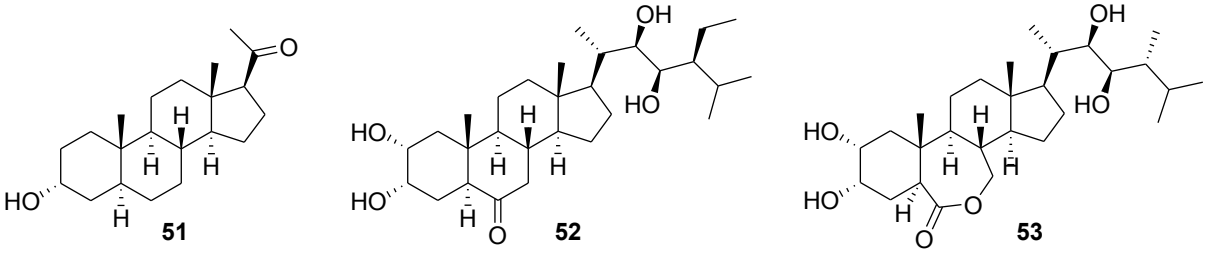


Figure 8

Anticancer activity (Laboratory of Growth Regulators, Palacky University Olomouc, Dr. Oklešťková-Swaczynová). The cytotoxic activities of **49a-49c** and **50a-50c** were determined by comparing human normal (fibroblast BJ) and cancer cell lines (T-lymphoblastic leukemia CEM and breast carcinoma MCF 7). These were exposed to six serial 4-fold dilutions of each drug for 72 h, the proportions of surviving cells were then estimated, and IC_{50} values were calculated (28-homocastasterone **52** was used as a positive control, Figure 8). Unfortunately, only **49b** exhibited a slight activity against CEM cell line (IC_{50} = 34.7 μM). The other tested compounds such as **50a-50c**, **49a**, and **49c** had extremely weak or no detectable activity (IC_{50} > 50 μM). However, it is important to emphasize that tested compounds are not toxic towards normal human cells at all (Table 6).[83]

Table 6. Cytotoxic Activity of Brassinosteroids Determined by Calcein-AM Assays.[a]

Compound	CEM[b] (μM)	MCF 7[c] (μM)
28-homocastasterone **52**	13 ± 2.8	> 50
50a	> 50	> 50
50b	> 50	> 50
50c	> 50	> 50
49a	> 50	> 50
49b	35.3 ± 1.6	48.2 ± 0.6
49c	> 50	> 50

[a] The IC_{50} values are expressed as mean ±SD values of three independent experiments performed in triplicate.

[b] T-lymphoblastic leukemia cell line CEM.

[c] Breast carcinoma cell lines MCF 7.

Brassinolide-type activity (Laboratory of Growth Regulators, Palacky University Olomouc, Dr. Oklešťková-Swaczynová). Finally, the brassinolide activity was measured by the bean second-internode bioassay.[39,85] The length of the second internodes was measured 5 days after the application of tested compounds in lanoline and the difference in length between treated and control plants provided a measure of the activity. It was found that the compound **50b** exhibited an expressive swelling of the bean second-internode at the concentration 10^{-7} mol·L^{-1}. Moreover, the compound **50c** exhibited surprising activity at lower and higher concentrations differing by 5 orders (10^{-7} and 10^{-12} mol·L^{-1}, +15.9 and +10.7 mm, respectively) (Table 7).[83]

Table 7. Activity in the Bean Second-Internode Bioassay.

Compound	PSI[a]	SD
24-epibrassinolide **53**	32.3	±5.7
50a	3.1	±1.1
50b	11.0	±3.7
50c	0.9	±0.3
49a	14.1	±4.1
49b	9.6	±3.1

49c	11.6	±4.9

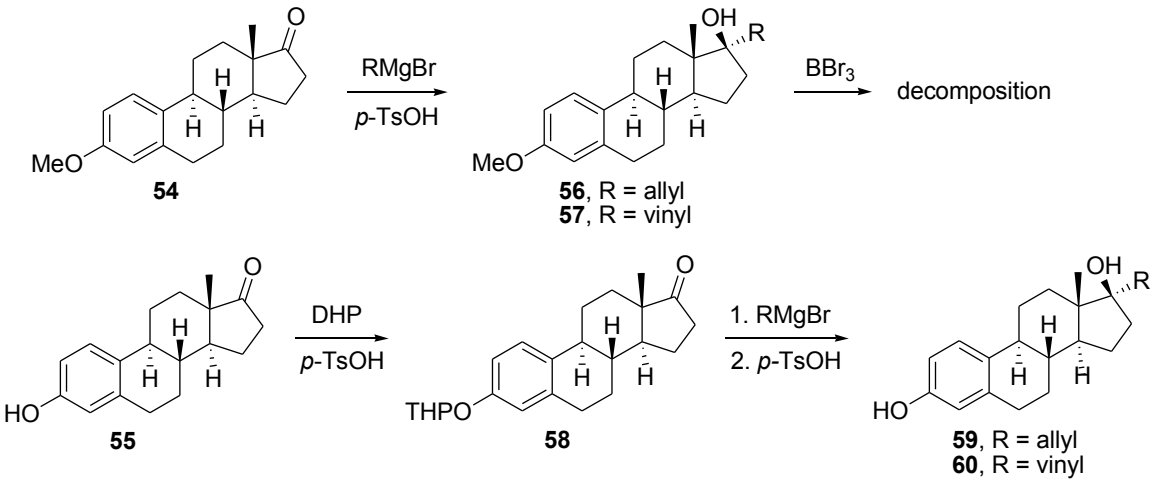
[a] PSI – Difference of prolongation of the Second Internode SD (mm) at concentration 10^{-10} mol·L^{-1} to control.

4.4. Synthesis of Fluorinated Derivates of Estrone

Estrogen receptor α (ERα), estrogen receptor β (ERβ), glucocorticoid receptor (GR), and mineralocorticoid receptor (MR) belong to a steroid hormone receptor family of ligand inducible transcription factors. Hydrophobic ligands bind to these receptors and modulate the transcription of target genes. ERα and ERβ are products of two separate genes and mediate the effect of the main and the most potent natural estrogen - 17β-estradiol (E2). E2 binds to both receptors with a similar affinity that means it is unselective.[86] Although ERα and ERβ are very similar proteins, the expression distribution is different in various tissues. ERα mediates the action of estrogens in classical tissues like uterus and mammary gland. ERα is also an important marker and traditional target for the therapy of breast cancer[87] and it promotes a proliferation of certain healthy and cancer tissues. On the other hand, the role of ERβ was established in the brain, ovary, cardiovascular system,[88] prostate, and in several animal models of inflammation.[89] Numerous studies report about antiproliferative effect of the increasing expression level of ERβ on the prostatic tissue[90,91] or cell-lines derived from different cancerous tissues like breast[92] or colon cancer.[93,94] The distinct biological roles of both estrogen receptors, ERα and ERβ, are despite intensive research efforts not fully understood. Therefore ligands selective for either of two isotypes are useful research tools as they allow for exerting a desired subset of biological effects mediated by only one of the receptor. One contribution to this research topic comes also from our laboratory and shows that the 17α-arylestradiols bearing a lipophilic indanyl moiety have an unusual selectivity for ERβ or ERα.[95] Also the attachment of highly lipophilic aliphatic side-chains onto the steroid framework has various beneficial effects. In 2000 Poirier *et al*. synthesized a series of 17α-alkyl- and 17α-alkenylestradiol derivatives and studied their properties as inhibitors for steroid sulfatase.[96] Regarding all the above mentioned effects of estradiol or its derivatives, the aim was to synthesize compounds retaining the ability to bind to ERs while exhibiting decrease in estrogenic potency. One possible way how to achieve this goal constitutes the introduction of a perfluoroalkylated side-chain into estradiol derivatives.

4.4.1. Synthesis of Starting Compounds

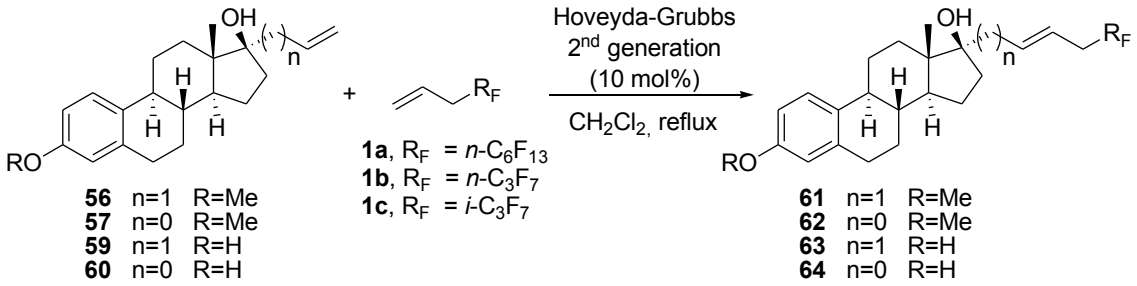
Initially, the 3-methoxyestrone **54** was chosen as a starting compound for the syntheses of estrone derivatives. The starting 17α-alkenyl compounds were prepared *via* standard procedure with Grignard reagents – allylmagnesium and vinylmagnesium bromides (Scheme 33).[97] Since the methyl-18 on the β-face of the steroid directs the nucleophilic attack of an alkenyl at the less hindered steroidal α-face, these alkenylations of C17-keto steroid should be stereoselective.[98] Indeed, it was confirmed that all compounds **56**, **57**, **59**, and **60** were obtained as the 17α-alkylation products exclusively. The reaction of the 3-methoxyestrone **54** with allylmagnesium bromide proceeded exceptionally cleanly and afforded the compound **56** in high 94% yield. That one using vinylmagnesium bromide was sluggish and gave rise to the vinyl derivative **57** in mediocre yield of 45%. Moreover, the course of the reaction was accompanied by the formation of the non-alkylated product of the reduction and by the presence of the unreacted starting material. The effort to deprotect the methoxy group by using BBr_3[99] to obtain derivatives **59** and **60** with the free hydroxyl group was not successful. The analysis of the reaction mixture showed only an extensive decomposition and no formation of any major product. Finally, switching to a different protective group resolved this issue. The 3-hydroxyl group of estrone **55** was readily converted into THP ether **58** in high 92% yield. Subsequently, two reactions with Grignard reagents (allyl- and vinylmagnesium bromides) were carried out and followed by the deprotection under acidic conditions. This procedure furnished compounds **59** and **60** in 82 and 47% yields, respectively (Scheme 33).[100]



Scheme 33

4.4.2. Results of Cross-metathesis with Estrone Derivatives

The CM was accomplished *via* our previously reported procedure.[46,71,83] The reaction was carried out with the estradiol derivatives **56**, **57**, **59**, and **60** and the (perfluoroalkyl)propenes **1a-1c**. It was catalyzed by using Hoveyda-Grubbs 2nd generation catalyst (10 mol%) in refluxing dichloromethane (Scheme 34).

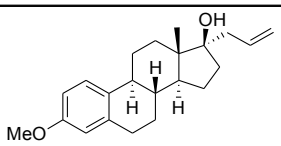
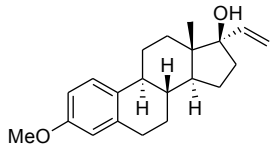
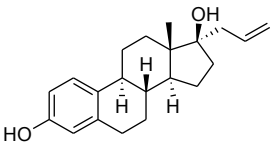
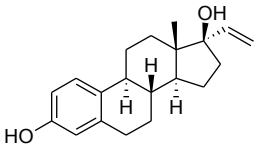


Scheme 34

Thus a series of estrone derivatives **61-64** was obtained and the results are summarized in Table 8. Initially, the metathesis of the substrate **56** and (perfluorohexyl)propene **1a** afforded the derivative **61a** in acceptable 53% yield (entry 1). Then the reaction between **1b** and **56** was carried out and the compound **61b** was obtained in good 68% yield (entry 2). Considerably lower yields were achieved with the substrate **57**, where products **62a** and **62b** were prepared in 36 and 29% yield, respectively (entries 3 and 4). This fact could be attributed to a larger sterical hindrance of the double bond in the vinyl-derivative **57**. The same conditions were used also for the reaction of the compound **59** with three (perfluoroalkyl)propenes **1a**, **1b**, and **1c**. In this case similar results were observed and the metathesis products **63a**-**63c** were isolated in reasonable yields of 58-67% (entries 5, 6, and 7). The metathesis of the substrate **60** with **1a**, **1b**, and **1c** repetitively afforded the corresponding products **64a**-**64c** in rather low yields for similar reasons like in case of the compound **57**. The product **64a** was obtained in 39% yield (entry 8). The synthesis of **64b** and **64c** was even less effective and gave corresponding compounds in 25 and 12% isolated yields, respectively (entries 9 and 10).[100] The polarity of starting materials was very similar to products and this fact hindered the separation of the reaction mixtures. The problem was finally solved by using the fluorinated silica gel. This special technique uses the silica gel with a fluorocarbon bonded phase, coupled with an organic solvent. A mixture of organic and fluorous-tagged compounds is loaded onto fluorous silica gel. Primarily, the system is eluted with a "fluorophobic" solvent. Polar organic solvents (e.g. 80-100% aqueous methanol or acetonitrile) are the most common fluorophobic solvents. During this first elution, the

nontagged organic compound is rapidly washed from the column, while the fluorous-tagged compound is retained. The second elution with a "fluorophilic" solvent (usually Et_2O or THF) then washes the fluorous fraction from the column.[49] This method enabled the clean separation of fluorinated products from non-fluorinated substrates in the above mentioned synthesis.

Table 8. Synthesis of 17α-perfluoroalkylated Estradiols.

Entry	**1**	**2**	Product	Yield [%][a]
1	**1a**	 **56**	**61a**	53
2	**1b**		**61b**	68
3	**1a**	 **57**	**62a**	36
4	**1b**		**62b**	29
5	**1a**	 **59**	**63a**	62
6	**1b**		**63b**	58
7	**1c**		**63c**	67
8	**1a**	 **60**	**64a**	39
9	**1b**		**64b**	25
10	**1c**		**64c**	12

[a] Isolated yields.

4.4.3. Biological Evaluation

The prepared estradiol derivatives with perfluoroalkylated side-chains **61-64** were subjected to the biochemical testing in both agonistic and antagonistic mode by using a panel of stable steroid receptor reporter cell-lines established in U2OS cells and consisting of ERα-LBD, ERβ-LBD, GR-LBD, and MR-LBD reporters **(**Institute of Molecular Genetics AS CR, Prague, Dr. Sedlák).[100] It was measured the ability to induce a transactivation or a transrepression by these receptors. Some of the derivatives showed high activity on ERα and ERβ and in addition, some compounds were selective for ERα (**63b**, **63c**, **64b**). It was also displayed that the presence of the hydroxyl group in the position 3 is essential for the biological activity. The most ERα selective compounds were **63c** and **64b** (Figure 9) that not only strongly activate ERα but also inhibit ERβ. Only few other compounds showing similar properties were described recently.[101] Furthermore, **64a** and **64b** have unique properties. **64b** has the highest potency from all tested compounds for ERα. It activates ERα with almost full

efficacy and in the same time and together with **64a** shows mixed partial agonistic/antagonistic properties on ERβ, which is often observed in selective estrogen receptor modulators (SERMs). Interestingly and unlike to what we observe in **64a** and **64b**, classical SERMs only act both as agonists and antagonists on ERα while they are mostly full antagonists on ERβ. From this perspective, further study of **63c, 64b**, and related derivatives can bring a new light to our understanding of how the specific ligand-induced conformational changes of ERs translate into the transcription of target genes.

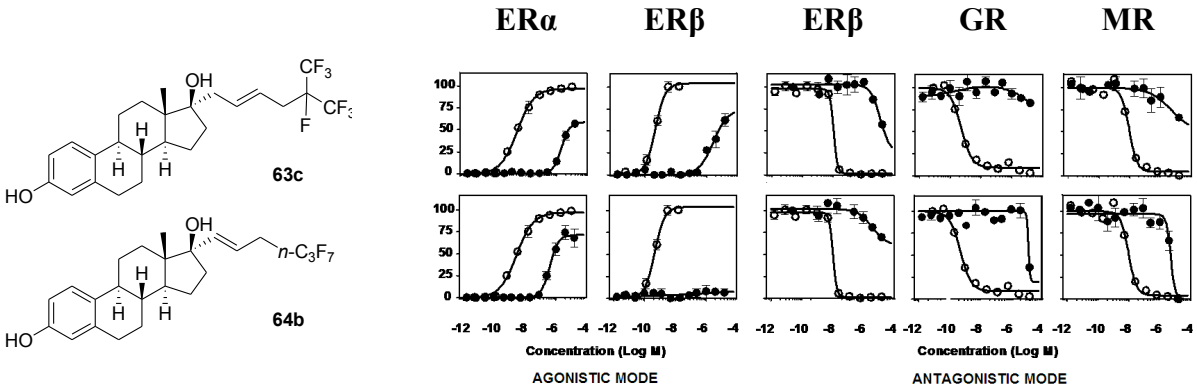


Figure 9

4.5. Synthesis of Carboranylated Derivates of Estrone

A study of ERα and ERβ has been recently reported because both receptors play an crucial role in female and male reproductive systems. They regulate essential processes during the development and are important factors in certain types of cancer.[102,103] The preparation of new ligands modulating the activity of ERα and/or ERβ is an important goal in the current steroid receptor research as they enable controlling processes, which are driven by these receptors. To give an example, selective ligands for ERβ were synthesized recently and their promising role was recognized in various animal models of inflammation, prostate cancer, chronic myeloid leukemia, and neurodegenerative diseases.[89,104] During the last decade it has been shown also in our research group that 17α-substituted arylestradiols bearing liphophilic aromatic moiety have interesting properties regarding binding to ERα and ERβ.[95,96,98,100,105-110] The introduction of a large group to 17α position of E2 does not suppress binding to ERs and transactivation by these receptors. On the contrary, these compounds surprisingly retain

estrogenic properties and in addition they exhibit some other intriguing characteristics such as selectivity for either ER or agonist effect on ERα and antagonist effect on ERβ. In other cases, mixed agonist/antagonist profile on ERβ are observed. These results suggest that ERs tolerate surprisingly large and diverse substituents in the 17α position and these modifications can lead to the compounds with interesting biological effects. Because carboranes exhibit various potential applications in medicinal chemistry (Chapter 3.2.), it was proposed that 17α-carboranylated derivatives of estradiol could constitute a new and perspective contribution to this area of medicinal chemistry.

4.5.1. Synthesis of Starting Compounds

The easiest and most flexible approach to the synthesis of estradiols bearing the carborane moiety in the side chain would be based on the CM of terminal olefins. For this purpose, the 17α-alkenylestradiols **59** and **60** (allyl- and vinyl-) were synthesized according to the same procedure as in Chapter 3.4.[100] All starting allylcarboranes **28**, **29**, **31**, and **32** were prepared by the previously reported procedures (Figure 10).[68-70]

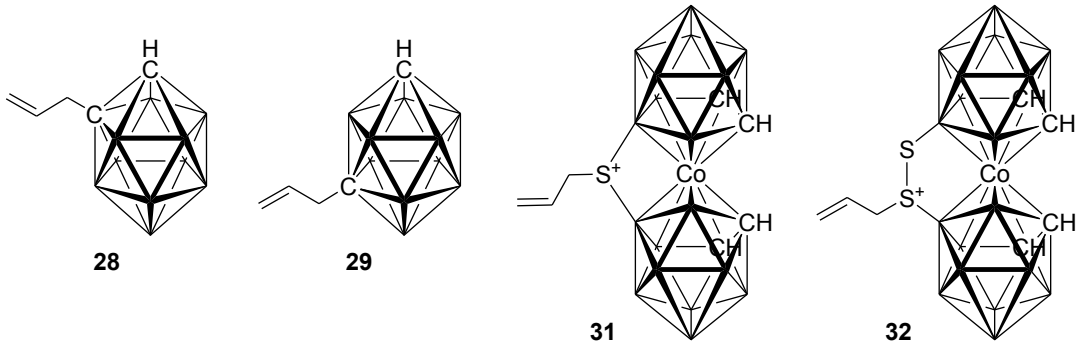
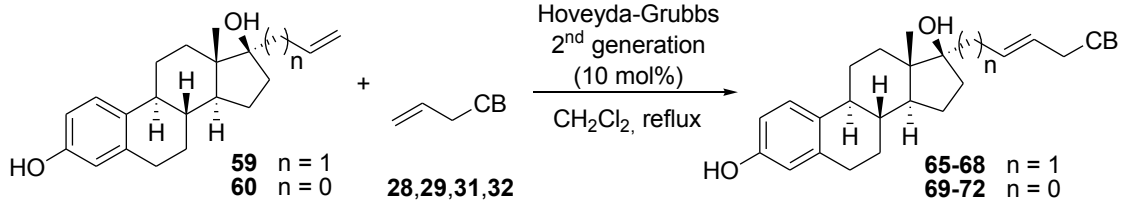


Figure 10

4.5.2. Results of Cross-metathesis between Estradiols and Carboranes

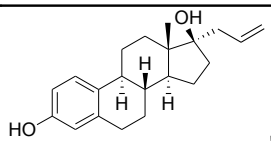
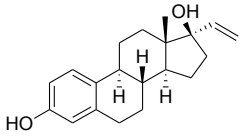
The cross-metatheses of **59** or **60** with carboranes **28**, **29**, **31**, and **32** were carried out in the presence of Hoveyda-Grubbs 2nd generation catalyst (10 mol%) under standard conditions (CH_2Cl_2, 42 °C, 4 h) (Scheme 35).[46]



Scheme 35

In all cases the expected carboranylestradiols **65-72** were obtained as the major products; the results summarized in Table 9. Initially, the metathesis of 17α-allylestradiol **59** and *ortho*-allylcarborane **28** afforded the derivative **65** in good 57% yield (entry 1). Then the reaction between **59** and **29** was carried out and the *meta*-allylcarborane derivative **66** was obtained in acceptable 55% yield (entry 2). Similar efficiency was achieved with the substrate **59** and compounds **31** and **32**, where products **67** and **68** were obtained in 44 and 52% yields, respectively (entries 3 and 4). The same conditions were used also for cross-metathesis of 17α-vinylestradiol **60** with allylcarborane derivatives **28**, **29**, **31**, and **32** and the corresponding metathesis products **69-72** were isolated in reasonable yields of 29-41% (entries 5-8). Again the higher sterical hindrance of the vinylestradiol **60** was observed, which caused a lower efficiency of CM. The derivative **71** was recrystalized from EtOH and its structure was unequivocally confirmed by a single crystal X-ray analysis (Figure 11).[111]

Table 9. Synthesis of 17α-carbonylated Estradiols.

Entry	Estradiol	Carborane	Product	Yield [%][a]
1	 **59**	**28**	**65**	57
2		**29**	**66**	55
3		**31**	**67**	44
4		**32**	**68**	52
5	 **60**	**28**	**69**	37
6		**29**	**70**	38
7		**31**	**71**	41
8		**32**	**72**	29

[a] Isolated yields

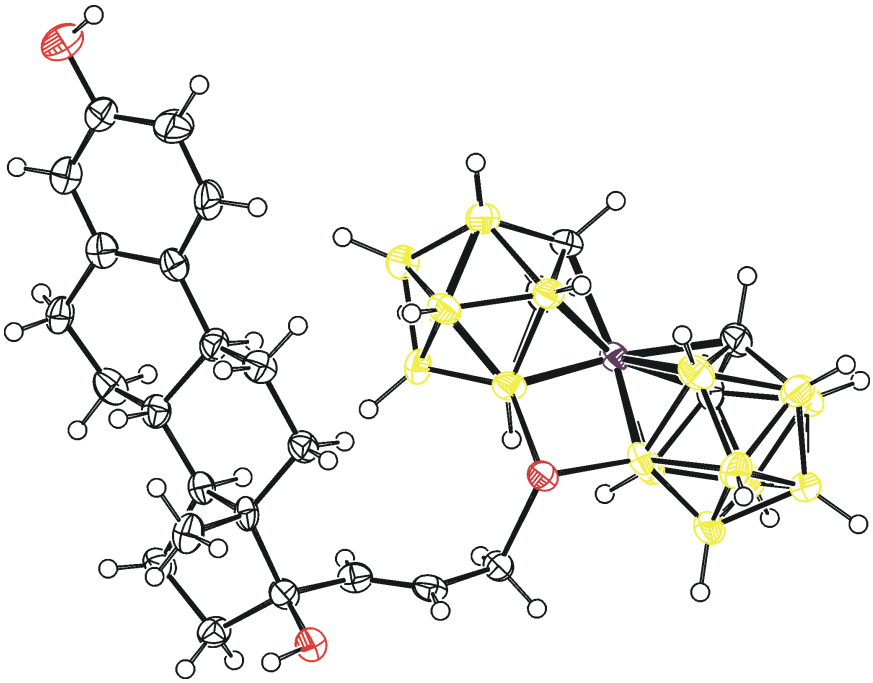


Figure 11

4.5.3. Biological Evaluation

The ability of newly synthesized compounds to modulate the activity of different steroid receptors was examined by using previously described U2OS reporter cell-lines (Institute of Molecular Genetics AS CR, Prague, Dr. Sedlák).[111] As a first step the capacity of new compounds to activate ERα and ERβ was measured. None of the tested compounds was able to fully activate any of the ERs in the wide concentration range (0.05 nM to 15 nM) that was used for testing. However, the efficacy of the most compounds falls in the range of 50-75 % of 17β-estradiol. The potency of new ligands extends from 0.12 to 2.73 % for ERα and 0.01 to 0.16 % for ERβ compared to E2. These values suggest that subset of compounds bearing substituents consisting of two carborane cages (**67**, **68**, **71**, **72**) are slightly poorer agonists of both ERs than compounds with smaller substituents consisting of one carborane cage. In agreement with this observation, **67** was found to be the least potent agonist for both ERs from the tested compounds. On the other hand, **68** acts as a rather potent and surprisingly efficient agonist of ERα and the most potent agonist of ERβ from the tested compounds.[111]

5. Experimental Section

All solvents were used as obtained unless otherwise noted. THF was distilled from sodium and benzophenone, and MeOH from Mg under an argon atmosphere. Vinylferrocene **8** was prepared by M. Sobociková (Charles University in Prague). Olefin **9** was synthesized by P. Herrmann (Charles University in Prague). Steroidal aldehyde **13'** and substrate **42** were prepared by B. Slavíková (Institute of Organic Chemistry and Biochemistry, Prague). Glucose derivative **14** was kindly donated by L. Kniežo (Institute of Chemical Technology, Prague). Cyclodextrin derivative **15** was synthesized by M. Řezanka (Charles University in Prague). All allylated carboranes **28-32** were prepared by Z. Janoušek (Institute of Inorganic Chemistry, Prague). All other reagents were obtained from commercial sources. The NMR spectra were measured on Bruker AVANCE 400, 500, and 600 instruments (^{1}H at 400, 500, or 600 MHz; ^{13}C at 100.6, 125.7, or 150.9 MHz) as solutions in $CDCl_3$ at 27 °C. The ^{11}B NMR and ^{19}F NMR were measured at 160.4 MHz and at 470.3 MHz. Chemical shifts are given in δ-scale (^{1}H NMR spectra were referenced to TMS as an internal standard and ^{13}C NMR spectra to $CDCl_3$ at δ 77.0) unless otherwise noted, coupling constants *J* are given in Hz. Melting points (uncorrected) were determined by using a Kofler apparatus. Infrared spectra were recorded as $CHCl_3$ solutions or as KBr tablets on Nicolet 750 FT-IR and are reported in wave numbers (cm^{-1}). FAB mass spectra (ionization by Xe, accelerating voltage 8 kV, thioglycerol-glycerol 3:1 matrix) and EI mass spectra were measured on a ZAB-EQ (VG Analytical) spectrometer. ESI mass spectra were measured on a Q-TOF micro (Waters) spectrometer in positive mode. Optical rotations were recorded in $CHCl_3$ at 25 °C and are given in 10^{-1} deg cm^2 g^{-1} unless otherwise noted. Fluka 60 silica gel or fluorinated silica gel Fluoro*Flash* 40 μm were used for flash chromatography. TLC was performed on silica gel 60 F_{254}-coated aluminum sheets or Fluoro*Flash* HPTLC F_{254}-coated glass sheets and spots were detected by UV illumination and spraying with 10% aqueous H_2SO_4 solution or 3% aq. $KMnO_4$ solution. All metathesis reactions were carried out under an argon atmosphere using Schlenk-tube technique. Used HPLC system consisted of High Pressure Pump (model 361, Gilson) Valve Rheodyne, Preparative Column (10 x 250 mm) with silica gel filling (Biosher PSI 200 7micro-m, Labio), preparative ELSD Detector (Gilson) connected with PC (software Trilution LC, Gilson), and Automatic Fraction Collector (model 346, Gilson).

General Procedure for Preparation of (Perfluoroalkyl)propenes 1 by using Allyltributylstannane 5.[49]

Perfluoroalkyl iodide **2** (1 mmol), allyltributylstannane **5** (2 mmol), and AIBN (0.1 mmol) were placed in a flask under an argon atmosphere, and the mixture was stirred at 70 °C for 5 h. The product was distilled from the reaction mixture under atmospheric pressure.

4,4,5,5,6,6,7,7,8,8,9,9,9-Tridecafluorononon-1-ene (1a). The reaction was carried out with perfluorohexyl iodide **2a** (25 g, 56 mmol) and allyltributylstannane **5** (37.12 g, 112 mmol) according to the general procedure. The distillation under atmospheric pressure yielded 7.86 g (39%) of the title compound **1a** as a colorless liquid: bp 109-112 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.86 (td, $J_{3,F}$ = 18.0 Hz, $J_{3,2}$ = 6.8 Hz, 2H, H-3a and H-3b), 5.34 (m, 2H, H-1a and H-1b), 5.81 (m, 1H, H-2). Spectral characteristics are in agreement with the previously reported data.[112]

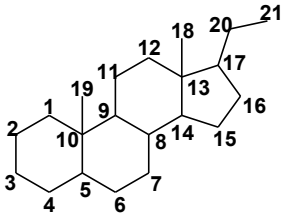
4,4,5,5,6,6,6-Heptafluorohex-1-ene (1b). The reaction was carried out with perfluoropropyl iodide **2b** (25 g, 85 mmol) and allyltributylstannane **5** (56 g, 170 mmol) according to the general procedure. The distillation under atmospheric pressure yielded 6.43 g (36%) of the title compound **1b** as a colorless liquid: bp 57-58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.84 (tdt, $J_{3,F}$ = 18.2 Hz, $J_{3,2}$ = 7.1 Hz, $J_{3,1}$ = 1.3 Hz, 2H, H-3a and H-3b), 5.34 (m, 2H, H-1a and H-1b), 5.80 (m, 1H, H-2). Spectral characteristics are in agreement with the previously reported data.[113]

4-(Trifluoromethyl)-4,5,5,5-tetrafluoropent-1-ene (1c). The reaction was carried out with *iso*-perfluoropropyl iodide **2c** (25 g, 85 mmol) and allyltributylstannane **5** (56 g, 170 mmol) according to the general procedure. The distillation under atmospheric pressure yielded 6.6 g (37%) of the title compound **1c** as a colorless liquid: bp 51-52 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85 (dd, $J_{3,F}$ = 20.0 Hz, $J_{3,2}$ = 7.2 Hz, 2H, H-3a and H-3b), 5.30 (m, 2H, H-1a and H-1b), 5.79 (m, 1H, H-2). Spectral characteristics are in agreement with the previously reported data.[114]

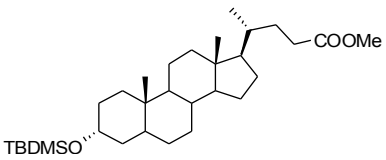
Procedure for Preparation of (Perfluorohexyl)propene 1a by using Allylalcohol 3.[47,48] A 10 mL glass ampule was charged with perfluorohexyl iodide **2a** (4.5 g, 10 mmol), 2-propen-1-ol (1.2 g, 20 mmol), and fine copper powder (63 mg, 1

mmol). The reaction mixture was stirred for 2 h at 120° C. After this period, the reaction mixture was dissolved in 10 mL of Et_2O, the catalyst was filtered off, and the solvent evaporated to obtain 3.3 g (65%) of the crude **4**. This compound was mixed with a 30% aqueous solution of acetic acid (3.9 g) and the resulting mixture was heated at 85° C with stirring. Powdered zinc (624 mg, 9.5 mmol) was added in small portions over a 4 h period and the reaction mixture was stirred for further 2 h. Aqueous HCl (50 µl) was added and the mixture was stirred for 4 h at 80° C to dissolve excess of zinc. The two resulting phases were separated and the organic phase was distilled obtaining 1.27 g (54%) of the compound **2a** as a colorless liquid.

Numbering of Steroidal Skeleton.

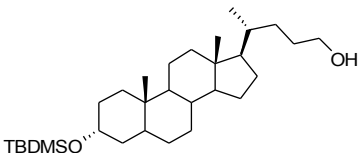


3-(*tert*-Butyl-dimethyl-silyl)-methyl lithocholate (10b). To a solution of lithocholic acid **10a**

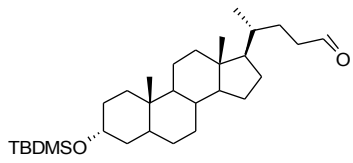


(10.17 g, 27 mmol) in distillated MeOH (40 mL) was added 10 mL of $CHCl_3$ and 0.5 mL of 35% HCl dissolved in 3 mL of MeOH at 40 °C. The reaction mixture was refluxed for 1 h and stirred overnight. Then the volatiles were evaporated, the crude dissolved in 50 mL of $CHCl_3$, washed with water, saturated solution of $NaHCO_3$, and the filtrate was dried over $MgSO_4$. Crystallization (MeOH) gave 10.2 g (97%) of the methyl ester as white crystals. To a solution of methyl ester (10 g, 26 mmol) in CH_2Cl_2 (40 mL) was added TBDMSCl (4.63 g, 30 mmol) and DMAP (0.32g, 2.6 mmol). The reaction mixture was cooled to 0 °C and Et_3N (5.44 mL, 39 mmol) was added dropwise. The course of the reaction was monitored by TLC (10/1 hexane/EtOAc). Then volatiles were removed under reduce pressure, and crude product was chromatographed on silica gel (10/1 hexane/EtOAc) to give 11.39 g (88%) of the title compound **10b** as a white powder: ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.63 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 2.22 (m, 1H, H-23b), 2.35 (m, 1H, H-23a), 3.58 (m, 1H, H-3), 3.66 (s, 3H, OCH_3).

3-(*tert*-Butyl-dimethyl-silyl)-cholan-24-ol (10c).[115] Protected methyl ester **10b** (2.8 g, 5.55 mmol was dissolved in dried Et_2O (50 mL). To this mild stirred and cooled solution was cautiously added $LiAlH_4$ (253 mg, 6.6 mmol). The suspension was further stirred at 25 °C under an argon atmosphere, the course of the reaction was monitored by TLC (10/1 hexane/EtOAc). After 2 h, the reaction was finished and excess of $LiAlH_4$ was carefully eliminated by addition of the mixture (2/1 EtOAc/H_2O). The resulting suspension was filtred, washed with EtOAc, and the filtrate was dried over $MgSO_4$. Crystallization (EtOH) gave 2.42 g (92%) of the compound **10c** as white needles: mp 167-169 °C; $[\alpha]_D$ +33.7 (*c* 0.45, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.63 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.92 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 3.58 (m, 1H, H-3), 3.61 (m, 2H, H-24). ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.63 (Si-$(CH_3)_2$), 11.99 (CH_3-18), 18.34 (**C**-$(CH_3)_3$), 18.60 (CH_3-21), 20.78 (CH_2-11), 23.37 (CH_3-19), 24.20 (CH_2-15), 25.96 (C-(**C**$H_3)_3$), 26.38 (CH_2-7), 27.28 (CH_2-6), 28.31 (CH_2-16), 29.40 (CH_2-23), 30.98 (CH_2-2), 31.78 (CH_2-22), 34.56 (C-10), 35.55 (CH_2-1), 35.58 (CH-20), 35.83 (CH-8), 36.88 (CH_2-4), 40.12 (CH_2-12), 40.17 (CH-9), 42.26 (CH-5), 42.65 (C-13), 56.14 (CH-14), 56.38 (CH-17), 63.60 (CH_2-24), 72.82 (CH-3); IR ($CHCl_3$) ν 3624, 1472, 1390, 1375, 1054 cm^{-1}; MS (FAB, m/z (rel.%)) 477 (M^++H, 5), 345 (34), 327 (5), 257 (8), 215 (14), 185 (50); HR-MS (FAB) calcd. for $C_{30}H_{57}O_2Si$ [M^++H] 477.4127, found 477.4128. R_f (10/1 hexane/EtOAc) = 0.27.



3-(*tert*-Butyl-dimethyl-silyl)-cholan-24-al (10d).[115] Alcohol **10c** (5 g, 10.5 mmol) was dissolved in dried CH_2Cl_2 (40 mL) and pyridiniumchlorochromate (2.69 g, 12.5 mmol) was added. The mixture was stirred under an argon atmosphere and the course of the reaction was monitored by TLC (9/1 hexane/EtOAc). After 16 h Et_2O (40 mL) was added to the reaction mixture. The suspension was filtered over the column of silica gel and the column was further washed (1/1 CH_2Cl_2/Et_2O). Evaporation of volatiles, chromatography on silica gel (45/1 toluene/EtOAc), and crystallization (Et_2O) yielded 3.58 g (72%) of the compound **10d** as a colorless oil: $[\alpha]_D$ +29.6 (*c* 0.39, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.64 (s, 3H, 3 × H-18), 0.90 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 2.35 (dddd, J_{gem} = 16.8, $J_{23b,22a}$ = 9.6, $J_{23b,22b}$ = 6.3, $J_{23b,24}$ = 1.7 Hz, 1H, H-23b), 2.46 (dddd, J_{gem} = 16.8, $J_{23a,22a}$ = 9.9,

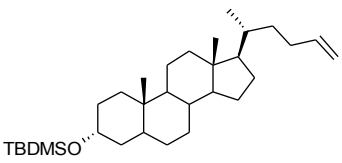


$J_{23a,22b}$ = 5.3, $J_{23a,24}$ = 1.7 Hz, 1H, H-23a), 3.58 (m, 1H, H-3), 9.77 (t, $J_{24,23}$ = 2.0 Hz, 1H, H-24). ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.63 (Si-$(CH_3)_2$), 12.00 (CH_3-18), 18.32 (CH_3-21), 18.34 (**C**-$(CH_3)_3$), 20.76 (CH_2-11), 23.36 (CH_3-19), 24.18 (CH_2-15), 25.96 (C-(**C**$H_3)_3$), 26.36 (CH_2-7), 27.25 (CH_2-6), 27.92 (CH_2-22), 28.24 (CH_2-16), 30.99 (CH_2-2), 34.55 (C-10), 35.31 (CH-20), 35.54 (CH_2-1), 35.81 (CH-8), 36.87 (CH_2-4), 40.08 (CH_2-12), 40.14 (CH-9), 40.90 (CH_2-23), 42.24 (CH-5), 42.70 (C-13), 55.93 (CH-14), 56.35 (CH-17), 72.80 (CH-3), 203.31 (CH_2-24); IR ($CHCl_3$) ν 2726, 1722, 1472, 1376, 1254 cm^{-1}; MS (FAB, m/z (rel.%)) 474 (M^+, 1), 435 (4), 373 (5), 325 (4), 257 (14), 185 (35). R_f(9/1 hexane/EtOAc) = 0.57.

General Procedure for Wittig Olefination.[52]

To a suspension of methyl triphenylphosphonium bromide (6 mmol) in THF (16 mL) was added *n*-BuLi (1.59 M solution in *n*-hexane, 6 mmol) at 0 °C, and stirred for 1 h. To the resultant red solution was added a solution of a substrate (4 mmol) in THF (8 mL) and stirred for 4.5 h at 25 °C. The reaction mixture was quenched by water and extracted with Et_2O (3 × 10 mL). The combined organic fractions were washed with brine, dried over anhydrous $MgSO_4$, and the filtrate was concentrated under reduced pressure. Column chromatography of the residue afforded products with terminal double bond.

(1'',1''-Dimethylethyl)dimethyl[[(3α)-20-(1'-buten-4'-yl)pregnan-3-yl]oxy]silane (10).

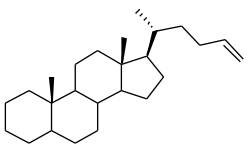


The reaction was carried out with **10d** (2 g, 4 mmol) and methyl triphenylphosphonium bromide (2.2 g, 6 mmol). Column chromatography on silica gel (heptane) afforded 1.71 g (86%) of **10** and 102 mg (5%) of a side product **11** as colorless oils.

10: $[\alpha]_D$ +31.7 (*c* 0.31, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.63 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 2.11 (m, 1H, H-23a), 3.58 (m, 1H, H-3), 4.91 (ddt, $J_{25t,24}$ = 10.2 Hz, $J_{25t,25c}$ = 2.1 Hz, $J_{25t,23}$ = 1.0 Hz, 1H, H-25 *trans*), 4.99 (ddt, $J_{25c,24}$ = 17.1 Hz, $J_{25c,25t}$ = 2.0 Hz, $J_{25c,23}$ = 1.5 Hz, 1H, H-25 *cis*), 5.80 (m, 1H, H-24); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.59 (Si-$(CH_3)_2$), 12.01 (CH_3-18), 18.39 (**C**-$(CH_3)_3$), 18.47 (CH_3-21), 20.82 (CH_2-11), 23.40 (CH_3-19), 24.23 (CH_2-15), 25.98 (C-(**C**$H_3)_3$), 26.42 (CH_2-7), 27.32 (CH_2-6), 28.30 (CH_2-16), 30.55 (CH_2-23), 31.03 (CH_2-2), 34.59 (C-10), 35.22 (CH_2-22), 35.41 (CH-20), 35.60 (CH_2-1), 35.87 (CH-8), 36.93 (CH_2-4), 40.18 (CH_2-12), 40.23 (CH-9), 42.31 (CH-5), 42.72 (C-13), 56.25 (CH-14), 56.43 (CH-17), 72.85 (CH-3), 113.85 (CH_2-25), 139.69 (CH-24); IR ($CHCl_3$) ν 3078, 2859, 1639,

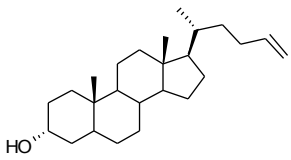
1472, 1408, 1374, 1254, 1093, 996, 913 cm^{-1}; MS (FAB, m/z (rel.%)) 472 (M^+, 1), 457 (4), 415 (5), 339 (8), 255 (4), 147 (20). R_f(heptane) = 0.63.

20-(1'-Buten-4'-yl)pregnane (11): $[\alpha]_D$ +25.2 (*c* 0.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$)



δ 0.65 (s, 3H, H-18a, H-18b and H-18c), 0.93 (s, 3H, H-19a, H-19b and H-19c), 0.93 (d, $J_{21,20}$ = 6.6, 3H, H-21a, H-21b and H-21c), 2.12 (m, 1H, H-23a), 4.92 (ddt, $J_{25t,24}$ = 10.2, $J_{25t,25c}$ = 2.2, $J_{25c,23}$ = 1.2, 1H, H-25 *trans*), 5.00 (ddt, $J_{25c,24}$ = 17.1, $J_{25c,25t}$ = 2.0, $J_{25c,23}$ = 1.5, 1H, H-25 *cis*), 5.81 (m, 1H, H-24); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.04 (CH_3-18), 18.48 (CH_3-21), 20.82 (CH_2-11), 21.33 (CH_2-2), 24.25 (CH_2-15), 24.28 (CH_3-19), 26.57 (CH_2-7), 27.02 (CH_2-6), 27.25 (CH_2-3), 27.52 (CH_2-4), 28.31 (CH_2-16), 30.53 (CH_2-23), 35.24 (CH_2-22), 35.35 (C-10), 35.40 (CH-20), 35.87 (CH-8), 37.58 (CH_2-1), 40.30 (CH_2-12), 40.51 (CH-9), 42.74 (C-13), 43.73 (CH-5), 56.25 (CH-14), 56.63 (CH-17), 113.84 (CH_2-25), 139.72 (CH-24); IR ($CHCl_3$) ν 3078, 2978, 1639, 1415, 1376, 997, 912 cm^{-1}; MS (FAB, m/z (rel.%)) 342 (M^+, 2), 341 (9), 257 (6), 217 (7), 109 (51); HR-MS (FAB) calcd. for $C_{25}H_{43}$ [M^++H] 343.3366, found 343.3364. R_f(heptane) = 0.75.

(3α,5β)-20-(1'-Buten-4'-yl)pregnan-3-ol (12). TBAF•$3H_2O$ (83 mg, 0.32 mmol) was added



to a solution of **10** (150 mg, 0.32 mmol) in THF (10 mL), and the mixture was stirred at 60 °C for 12 h. The course of the reaction was monitored by TLC (toluene). Then volatiles were removed under reduced pressure and crude product was chromatographed on silica gel (toluene) to give 96 mg (84%) of the title compound **12** as a colorless oil: $[\alpha]_D$ +33.0 (*c* 0.20, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.64 (s, 3H, 3 × H-18), 0.92 (s, 3H, 3 × H-19), 0.92 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.11 (m, 1H, H-23a), 3.62 (m, 1H, H-3), 4.91 (dm, $J_{25t,24}$ = 10.2 Hz, 1H, H-25 *trans*), 4.99 (dm, $J_{25c,24}$ = 17.1 Hz, 1H, H-25 *cis*), 5.80 (m, 1H, H-24); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 12.02 (CH_3-18), 18.46 (CH_3-21), 20.81 (CH_2-11), 23.37 (CH_3-19), 24.21 (CH_2-15), 26.42 (CH_2-7), 27.19 (CH_2-6), 28.27 (CH_2-16), 30.53 (2C, CH_2-2 and CH_2-23), 34.55 (C-10), 35.20 (CH_2-22), 35.33 (CH_2-1), 35.38 (CH-20), 35.83 (CH-8), 36.44 (CH_2-4), 40.19 (CH_2-12), 40.43 (CH-9), 42.09 (CH-5), 42.71 (C-13), 56.21 (CH-14), 56.50 (CH-17), 71.86 (CH-3), 113.85 (CH-25), 139.67 (CH-24); IR ($CHCl_3$) ν 3609, 3457, 3078, 2867, 1639, 1415, 1377, 1030, 996, 913 cm^{-1}; MS (FAB, m/z (rel.%)) 357 (M^+-H, 2), 341 (14), 285 (1), 155 (15); HR-MS (FAB) calcd. for $C_{25}H_{41}O$ [M^+-H] 357.3157, found 357.3162. R_f(toluene) = 0.26.

Tetrahydro-2-[[(3β)-24-norchola-5,22-dien-3-yl]oxy]-2H-pyran (13). The reaction was carried out with aldehyde **13'**[53] (319 mg, 0.77 mmol) and methyl triphenylphosphonium bromide (411 g, 1.15 mmol) according to the general procedure.[52] Column chromatography on silica gel (hexane) afforded 207 g (65%) of **13** as a colorless oil: $[\alpha]_D$ –55.6 (*c* 0.14, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 1.01 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 3.50 (m, 2H, H-6'a and H-3), 3.91 (m, 1H, H-6'b), 4.71 (m, 1H, H-2'), 4.81 (dd, $J_{23t,22}$ = 10.2 Hz, J_{gem} = 2.0 Hz, 1H, H-23 *trans*), 4.90 (ddd, $J_{23c,22}$ = 17.1 Hz, J_{gem} = 2.0 Hz, $J_{23c,20}$ = 0.9 Hz, 1H, H-23 *cis*), 5.34 (m, 1H, H-6), 5.66 (ddd, $J_{22,23c}$ = 17.1 Hz, $J_{22,23t}$ = 10.2 Hz, $J_{22,20}$ = 8.4 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.01 (CH_3-18), 19.37 (CH_3-19), 20.01 (CH_2-4'a), 20.08 (CH_2-4'b), 20.10 (CH_3-21), 21.02 (CH_2-11), 24.25 (CH_2-15), 25.46 (CH_2-5'), 27.95 (CH_2-2a), 28.38 (CH_2-16), 29.66 (CH_2-2b), 31.24 (CH_2-3'a), 31.27 (CH_2-3'a), 31.85 (CH-8), 31.87 (CH_2-7), 36.74 (C-10a), 36.78 (C-10b), 37.17 (CH_2-1a), 37.42 (CH_2-1b), 38.73 (CH_2-4a), 39.63 (CH_2-12), 40.21 (CH_2-4b), 41.21 (CH-20), 42.28 (C-13), 50.12 (CH-9a), 50.15 (CH-9b), 55.38 (CH-17), 56.73 (CH-14), 62.81 (CH_2-6'a), 62.92 (CH_2-6'b), 75.97 (CH-3), 96.80 (CH-2'a), 96.97 (CH-2'b), 111.51 (CH_2-23), 121.45 (CH-6a), 121.53 (CH-6b), 140.86 (C-5a), 141.03 (C-5b), 145.28 (CH-22); IR ($CHCl_3$): 3076, 1829, 1668, 1637, 1476, 1379, 1113, 992, 912 cm^{-1}; MS (FAB, m/z (rel.%)) 435 (M^++Na, 4), 387 (1), 343 (12), 311 (13), 217 (12), 153 (31); HR-MS (FAB) calcd for $C_{28}H_{44}O_2Na$ [M^++Na] 435.3239, found 435.3253. R_f(15/1 hexane/Et_2O) = 0.28.

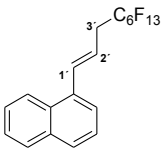
General Procedure for Cross-metathesis of Terminal Alkenes with (Perfluoroalkyl)propenes.[46]

To a mixture of terminal alkene (1 mmol) and (perfluoroalkyl)propenes **1a-1c** (2 mmol) in CH_2Cl_2 was added Hoveyda-Grubbs 2nd generation catalyst (63 mg, 0.1 mmol) under an argon atmosphere. The resulting solution was stirred at 42 °C for 4 h. Removal of the solvent *in vacuo* gave a brown oil, which was purified by flash chromatography.

2-((*E*)-4',4',5',5',6',6',7',7',8',8',9',9',9'-Tridecafluorononon-1'-enyl)naphthalene (16). The reaction was carried out with **6** (154 mg, 1 mmol) and (perfluorohexyl)propene **1a** (720 mg, 2 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/heptane) afforded 81 mg (17%) of the compound **16** as a white foam: $[\alpha]_D$ +3.0 (*c* 0.26, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$)

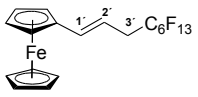
δ 3.07 (btd, $J_{3',F}$ = 18.1 Hz, $J_{3',2'}$ = 7.2 Hz, 2H, 2 × H-3'), 6.26 (dt, $J_{2',1'}$ =15.8 Hz, $J_{2',3'}$ = 7.3 Hz, 1H, H-2'), 6.78 (bd, $J_{1',2'}$ = 15.8 Hz, 1H, H-1'), 7.47 (m, 2H, H-6 and H-7), 7.60 (dd, $J_{3,4}$ = 8.6 Hz, $J_{3,1}$ = 1.8 Hz, 1H, H-3), 7.74 (d, $J_{1,3}$ = 1.7 Hz, 1H, H-1), 7.81 (m, 3H, H-4, H-5 and H-8); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 35.27 (t, $J_{3',F}$ = 22.6 Hz, CH_2-3´), 116.31 (t, $J_{2',F}$ = 4.4 Hz, CH-2´), 123.29 (CH-3), 126.17 and 126.41 (CH-6 and CH-7), 126.64 (CH-1), 127.68, 128.05 and 128.36 (CH-8, CH-4 and CH-5), 133.18, 133.45 and 133.61 (C-2, C-4a and C-8a), 137.33 (CH-1'); IR ($CHCl_3$) ν 3061, 3010, 1657, 1628, 1599, 1509, 1364, 1347, 1243, 1145, 969 cm^{-1}; MS (FAB, m/z (rel.%)) 487 (M^++H, 12), 361 (7), 312 (3), 233 (5), 207 (46), 156 (32); HR-MS (FAB) calcd for $C_{19}H_{12}F_{13}$ [M^+ + H] 487.0731, found 487.0717. R_f(hexane) = 0.53.

1-((*E*)-(4',4',5',5',6',6',7',7',8',8',9',9',9'-Tridecafluorononon-1'-enyl)naphthalene (17). The



reaction was carried out with **7** (154 mg, 1 mmol) and **1a** (720 mg, 2 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/heptane) afforded 75 mg (15%) of the compound **17** as a white foam: $[\alpha]_D$ +10.9 (*c* 0.21, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.14 (m, 2H, 2 × H-3'), 6.16 (dt, $J_{2',1'}$ =15.6 Hz, $J_{2',3'}$ = 7.2 Hz, 1H, H-2'), 7.37 (dt, $J_{1',2'}$ = 15.7 Hz, $J_{1',3'}$ = 1.5 Hz, 1H, H-1'), 7.45 (m, 1H, H-3), 7.51 (m, 2H, H-6 and H-7), 7.58 (m, 1H, H-2), 7.81 (m, 1H, H-4), 7.86 (m, 1H, H-5), 8.06 (m, 1H, H-8); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 35.48 (t, $J_{3',F}$ = 22.5 Hz, CH_2-3'), 119.37 (t, $J_{2',F}$ = 4.4 Hz, CH-2'), 123.61 (CH-8), 124.24 (CH-2), 125.58 (CH-3), 125.91 (CH-6), 126.27 (CH-7), 128.49 (CH-4), 128.58 (CH-5), 130.98 (C-8a), 133.55 (C-4a), 134.09 (C-1), 134.88 (CH-1'); IR ($CHCl_3$) ν 3064, 3050, 1592, 1510, 1344, 1344, 1267, 1243, 1145, 969 cm^{-1}; MS (FAB, m/z (rel.%)) 486 (M^+, 22), 467 (4), 196 (3), 167 (32), 153 (23); HR-MS (FAB) calcd for $C_{19}H_{11}F_{13}$ [M^+] 486.0653, found 486.0631. R_f(hexane) = 0.53.

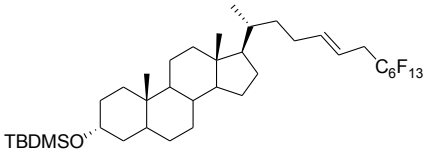
1-((*E*)-4',4',5',5',6',6',7',7',8',8',9',9',9'-Tridecafluorononon-1'-enyl)ferrocene (18). The



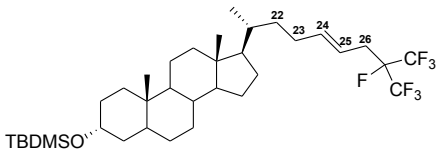
reaction was carried out with **8** (106 mg, 0.5 mmol) and **1a** (360 mg, 1 mmol) according to the general procedure. Column chromatography on silica gel (toluene) and crystallization (CH_2Cl_2/hexane) yielded 130 mg (48%) of the compound **18** as orange crystals: mp 91 °C; $[\alpha]_D$ +6.9 (*c* 0.17, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.87 (dt, $J_{3',F}$ = 18.0 Hz, $J_{3',2'}$ = 7.3 Hz, 2H, H-3'), 4.11 (s, 5H, Cp), 4.23 (m, 2H, H-3 and H-4), 4.35 (m, 2H, H-2 and H-5), 5.70 (dt, $J_{2',1'}$ = 15.6 Hz, $J_{2',3'}$ = 7.3 Hz, 1H, H-2'), 6.37 (bd, $J_{1',2'}$ = 15.7 Hz, 1H, H-1'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 35.25 (t, $J_{3',F}$ =

45.3 Hz, CH_2-3'), 66.85 (CH-2 and CH-5), 68.95 (CH-3 and CH-4), 69.18 (Cp), 81.74 (CH-1), 112.46 (t, $J_{2',F}$ = 4.3 Hz, CH-2'), 135.20 (CH-1'); IR ($CHCl_3$) ν 3099, 3011, 1657, 1412, 1347, 1243, 1145, 1106, 962 cm^{-1}; MS (FAB, m/z (rel.%)) 544 (M^+, 28), 274 (17), 256 (13), 232 (12), 181 (76), 149 (22); HR-MS (FAB) calcd for $C_{19}H_{13}F_{13}Fe_1$ [M^+] 544.0159, found 544.0154. R_f(hexane) = 0.31.

(*E*)-2-(6'-Methoxy-2'-(4'',4'',5'',5'',6'',6'',7'',7'',8'',8'',9'',9'',9''-tridecafluorononon-1''-enyl)-1',2',3',4'-tetrahydronaphthalen-1'-yl)-1-phenylethanone (19). The reaction was carried out with **9** (100 mg, 0.33 mmol) and **1a** (238 mg, 0.66 mmol) according to the general procedure. Column chromatography on silica gel (20/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 4/1 MeOH/water-washing of the non-fluorinated starting material, 2nd elution Et_2O-washing of the product) yielded 144 mg (66%) of the compound **19** as an yellowish oil: $[\alpha]_D$ +2.0 (*c* 0.30, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.73 (m, 1H, H-3'b), 1.99 (dtd, J_{gem} = 13.5 Hz, $J_{3'a,4'}$ = 6.7 Hz, $J_{3'a,2'}$ = 3.5 Hz, 1H, H-3'a), 2.52 (m, 1H, H-2'), 2.73 (td, $J_{3'',F}$ = 18.1 Hz, $J_{3'',2''}$ = 7.0 Hz, 2H, H-3''), 2.80 (t, $J_{4',3'}$ = 6.5 Hz, 2H, 2 × H-4'), 3.25 (dd, J_{gem} = 17.7 Hz, $J_{2a,1'}$ = 5.2 Hz, 1H, H-2a), 3.36 (dd, J_{gem} = 17.7 Hz, $J_{2b,1'}$ = 7.0 Hz, 1H, H-2b), 3.50 (m, 1H, H-1'), 5.47 (dtd, $J_{2'',1''}$ = 15.4 Hz, $J_{2'',3''}$ = 7.1 Hz, $J_{2'',2''}$ = 0.8 Hz, 1H, H-2''), 5.72 (ddt, $J_{1'',2''}$ = 15.4 Hz, $J_{1'',2'}$ = 8.2 Hz, $J_{1'',3''}$ = 1.3 Hz, 1H, H-1''), 6.62 (d, $J_{5',7'}$ = 2.8 Hz, 1H, H-5'), 6.68 (dd, $J_{7',8'}$ = 8.5 Hz, $J_{7',5'}$ = 2.8 Hz, 1H, H-7'), 7.00 (d, $J_{8',7'}$ = 8.5 Hz, 1H, H-8'), 7.45 (m, 2H, Ph), 7.56 (m, 1H, Ph), 7.95 (m, 2H, Ph); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 26.07 (CH_2-3'), 27.09 (CH_2-4'), 34.82 (t, $J_{3'',F}$ = 22.6 Hz, CH_2-3''), 37.35 (CH-1'), 41.95 (CH-2'), 45.76 (CH_2-2), 55.14 (OCH_3), 112.55 (CH-7'), 113.36 (CH-5'), 117.07 (t, $J_{2'',F}$ = 4.2 Hz, CH-2''), 128.01 (Ph), 128.60 (Ph), 129.61 (CH-8'), 130.96 (C-8'a), 133.07 (Ph), 137.13 (Ph), 137.59 (C-4'a), 141.79 (CH-1''), 157.61 (C-6'), 199.11 (C-1); IR ($CHCl_3$) ν 3088, 3061, 3028, 2839, 1685, 1609, 1598, 1449, 1352, 1242, 1145, 1120, 974, 598 cm^{-1}; MS (FAB, m/z (rel.%)) 639 (M^++H, 3), 595 (2), 519 (21), 262 (8), 253 (9), 155 (22); HR-MS (FAB) calcd for $C_{28}H_{24}F_{13}O_2$ [M^++H] 639.1569, found 639.1562. R_f(20/1 hexane/Et_2O) = 0.25.

3'-(*E*)-(1'',1''-Dimethylethyl)dimethyl[[(3α)-20-(6',6',7',7',8',8',9',9',10',10',11',11',11'-tridecafluoroundec-3'-en-1'-yl)pregnan-3-yl]oxy]silane (20a). 

The reaction was carried out with **10** (95 mg, 0.2 mmol) and **1a** (144 mg, 0.4 mmol) according to the general procedure. Column chromatography on silica gel (20/1 hexane/toluene) yielded 121 mg (75%) of the compound **20a** as a colorless oil: $[\alpha]_D$ +21.0 (*c* 0.27, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.62 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.91 (d, $J_{21,20}$ = 6.4 Hz, 3H, 3 × H-21), 2.13 (m, 1H, H-2'a), 2.78 (dt, $J_{5',F}$ = 18.2 Hz, $J_{5',4'}$ = 6.8 Hz, 2H, 2 × H-5'), 3.58 (m, 1H, H-3), 5.38 (m, 1H, H-4'), 5.69 (m, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.62 (Si-$(CH_3)_2$), 11.92 (CH_3-18), 18.36 (**C**-$(CH_3)_3$), 18.38 (CH_3-21), 20.79 (CH_2-11), 23.38 (CH_3-19), 24.20 (CH_2-15), 25.97 (C-(**C**$H_3)_3$), 26.40 (CH_2-7), 27.29 (CH_2-6), 28.29 (CH_2-16), 29.33 (CH_2-2'), 31.01 (CH_2-2), 34.58 (C-10), 34.82 (t, $J_{5',F}$ = 22.6 Hz, CH_2-5'), 35.13 (CH_2-1'), 35.28 (CH-20), 35.57 (CH_2-1), 35.84 (CH-8), 36.91 (CH_2-4), 40.15 (CH_2-12), 40.18 (CH-9), 42.29 (CH-5), 42.70 (C-13), 56.17 (CH-14), 56.41 (CH-17), 72.85 (CH-3), 115.85 (t, $J_{4',F}$ = 4.0 Hz, CH-4'), 139.64 (CH-3'); IR ($CHCl_3$) ν 2931, 2859, 1672, 1471, 1373, 1243, 1071, 972 cm^{-1}; MS (FAB, m/z (rel.%)) 804 (M^+, 2), 672 (4), 654 (3), 630 (1), 315 (9), 280 (20). R_f(10/1 hexane/toluene) = 0.42.

A mixture of 3'-(*E*)- and 3'-(*Z*)-(1'',1''-dimethylethyl)dimethyl[[(3α)-20-(6'-(trifluoromethyl)-6',7',7',7'-tetrafluorohept-3'-en-1'-yl)pregnan-3-yl]oxy]silane (20c). 

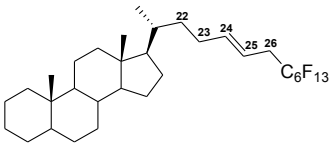
The reaction was carried out with **10** (80 mg, 0.17 mmol) and **1c** (72 mg, 0.34 mmol) according to the general procedure. Column chromatography on silica gel (heptane) afforded 69 mg (63%) of the title compound **20c** (inseparable 7/1 mixture of E/Z isomers) as a colorless oil: $[\alpha]_D$ +31.5 (*c* 0.21, $CHCl_3$); IR ($CHCl_3$) ν 2931, 2859, 1671, 1471, 1374, 1244, 1091, 974 cm^{-1}; MS (FAB, m/z (rel.%)) 653 (M^+-H, 2), 521 (5), 463 (2), 413 (1), 337 (9), 236 (4); HR-MS (FAB) calcd. for $C_{35}H_{56}OF_7Si$ [M^+-H] 653.3989, found 653.3971. R_f(heptane) = 0.45.

(*E*)-20c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.62 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.89 (d, $J_{21,20}$ = 6.8 Hz, 3H, 3 × H-21), 0.90 (s, 3H, 3 × H-19), 2.13 (m, 1H, H-2'a), 2.79 (bdd, $J_{5',F}$ = 20.0 Hz, $J_{5',4'}$ = 7.2 Hz, 2H, 2 × H-5'), 3.58 (m, 1H, H-3), 5.36 (dm, $J_{4',3'}$ = 15.2 Hz, 1H, H-4'), 5.65 (dm, $J_{3',4'}$ = 15.2 Hz, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.62 (Si-$(CH_3)_2$), 11.92 (CH_3-18), 18.32 (CH_3-21), 18.36 (**C**-$(CH_3)_3$), 20.79 (CH_2-

11), 23.38 (CH_3-19), 24.21 (CH_2-15), 25.97 (C-(**C**H_3)$_3$), 26.40 (CH_2-7), 27.29 (CH_2-6), 28.27 (CH_2-16), 29.20 (CH_2-2**'**), 31.00 (CH_2-2), 34.58 (d, $J_{5',F}$ = 20.9 Hz, CH_2-5**'**), 34.58 (C-10), 35.07 (CH_2-1**'**), 35.19 (CH-20), 35.57 (CH_2-1), 35.84 (CH-8), 36.90 (CH_2-4), 40.14 (CH_2-12), 40.17 (CH-9), 42.28 (CH-5), 42.70 (C-13), 56.16 (CH-14), 56.40 (CH-17), 72.85 (CH-3), 116.97 (d, $J_{4',F}$ = 5.6 Hz, CH-4**'**), 138.93 (CH-3**'**).

(*Z*)-20c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-(CH_3)$_2$), 0.63 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-(CH_3)$_3$), 0.89 (d, $J_{21,20}$ = 6.8 Hz, 3H, 3 × H-21), 0.90 (s, 3H, 3 × H-19), 2.13 (m, 1H, H-2'a), 2.86 (bdd, $J_{5',F}$ = 19.6 Hz, $J_{5',4'}$ = 7.6 Hz, 2H, 2 × H-5'), 3.58 (m, 1H, H-3), 5.36 (dm, $J_{4',3'}$ = 15.2 Hz, 1H, H-4'), 5.65 (dm, $J_{3',4'}$ = 15.2 Hz, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.62 (Si-(CH_3)$_2$), 11.92 (CH_3-18), 18.32 (CH_3-21), 18.36 (**C**-(CH_3)$_3$), 20.79 (CH_2-11), 23.38 (CH_3-19), 24.21 (CH_2-15), 25.97 (C-(**C**H_3)$_3$), 26.40 (CH_2-7), 27.29 (CH_2-6), 28.27 (CH_2-16), 29.20 (CH_2-2'), 31.00 (CH_2-2), 34.58 (d, $J_{5',F}$ = 20.9 Hz, CH_2-5'), 34.58 (C-10), 35.07 (CH_2-1'), 35.19 (CH-20), 35.57 (CH_2-1), 35.84 (CH-8), 36.90 (CH_2-4), 40.14 (CH_2-12), 40.17 (CH-9), 42.28 (CH-5), 42.70 (C-13), 56.16 (CH-14), 56.40 (CH-17), 72.85 (CH-3), 116.05 (d, $J_{4',F}$ = 5.6 Hz, CH-4'), 136.84 (CH-3').

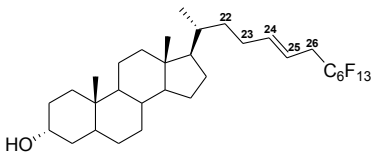
A mixture of 3'-(*E*)- and 3'-(*Z*)-20-(6',6',7',7',8',8',9',9',10',10',11',11',11'-tridecaflouroundec-3´-en-1´-yl)pregnane (21). The reaction was carried out with **11** (75 mg, 0.22 mmol) and **1a** (158 mg, 0.44 mmol) according to the general procedure. Column chromatography on silica gel (heptane) and then on silica gel (undecane) afforded 95 mg (64%) of the title compound **21** (inseparable 4/1 mixture of E/Z isomers) as a colorless oil: $[\alpha]_D$ +39.6 (*c* 0.11, $CHCl_3$); IR ($CHCl_3$) ν 2931, 2863, 1673, 1375, 1363, 1242, 1145, 973 cm^{-1}; MS (APCI, m/z (rel.%)) 674 (M^+, 1), 607 (65), 551 (52), 495 (36), 439 (9), 391 (7), 278 (4). R_f(undecane) = 0.75.



(*E*)-21: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (s, 3H, 3 × H-18), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 0.91 (s, 3H, 3 × H-19), 2.78 (td, $J_{5',F}$ = 18.7 Hz, $J_{5',4'}$ = 7.1 Hz, 2H, 2 × H-5'), 5.38 (m, 1H, H-4'), 5.69 (dtt, $J_{3',4'}$ = 15.4 Hz, $J_{3',2'}$ = 6.8 Hz, $J_{3',5'}$ = 1.4 Hz, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 11.97 (CH_3-18), 18.41 (CH_3-21), 20.82 (CH_2-11), 21.33 (CH_2-2), 24.23 (CH_2-15), 24.27 (CH_3-19), 27.03, 27.25 and 27.52 (CH_2-3, CH_2-4 and CH_2-6), 28.30 (CH_2-16), 29.32 (CH_2-2'), 34.82 (t, $J_{5',F}$ = 22.4 Hz, CH_2-5'), 35.17 (CH_2-1'), 35.29 (CH-20), 35.36 (C-10), 35.88 (CH-8), 37.58 (CH_2-1), 40.30 (CH_2-12), 40.51 (CH-9), 42.74 (C-13), 43.73 (CH-5), 56.20 (CH-14), 56.63 (CH-17), 115.85 (CH-4'), 139.65 (CH-3').

(*Z*)-21: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (s, 3H, 3 × H-18), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 0.91 (s, 3H, 3 × H-19), 2.78 (td, $J_{5',F}$ = 18.7 Hz, $J_{5',4'}$ = 7.1 Hz, 2H, 2 × H-5'), 5.38 (m, 1H, H-4'), 5.69 (dtt, $J_{3',4'}$ = 15.4 Hz, $J_{3',2'}$ = 6.8 Hz, $J_{3',5'}$ = 1.4 Hz, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 11.97 (CH_3-18), 18.41 (CH_3-21), 20.82 (CH_2-11), 21.33 (CH_2-2), 24.23 (CH_2-15), 24.27 (CH_3-19), 27.03, 27.25 and 27.52 (CH_2-3, CH_2-4 and CH_2-6), 28.30 (CH_2-16), 29.32 (CH_2-2'), 34.82 (t, $J_{5',F}$ = 22.4 Hz, CH_2-5'), 35.17 (CH_2-1'), 35.29 (CH-20), 35.36 (C-10), 35.88 (CH-8), 37.58 (CH_2-1), 40.30 (CH_2-12), 40.51 (CH-9), 42.74 (C-13), 43.73 (CH-5), 56.12 (CH-17), 56.20 (CH-14), 115.10 (CH-4'), 137.70 (CH-3').

A mixture of 3'-(*E*)- and 3'-(*Z*)-(3α,5β)-20-(6',6',7',7',8',8',9',9',10',10',11',11',11'-tridecafluoroundec-3'-en-1'-yl)pregnan-3-ol (22a). The reaction was carried out with **12** (100 mg, 0.28 mmol) and **1a** (180 mg, 0.5 mmol) according to the general procedure. Column chromatography on silica gel (20/1 toluene/Et_2O) and on fluorinated silica gel (1st elution 7/1 MeOH/water-washing of the non-fluorinated starting material, 2nd elution Et_2O-washing of the product) afforded 135 mg (70%) of the title compound **22a** (inseparable 2/1 mixture of *E*/*Z* isomers) as a colorless oil: $[\alpha]_D$ +14.0 (*c* 0.19, $CHCl_3$); IR ($CHCl_3$) ν 3609, 2938, 2867, 1672, 1471, 1377, 1365, 1242, 1145, 1031, 1012, 973 cm^{-1}; MS (ESI, m/z (rel.%)) 690 (M^+, 1), 663 (14), 610 (3), 648 (10), 426 (100), 316 (43), 288 (98); HR-MS (FAB) calcd for $C_{32}H_{42}F_7$ [M^+-OH] 673.3079, found 673.3089. R_f(20/1 toluene/Et_2O) = 0.25.

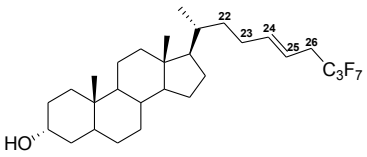


(*E*)-22a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (s, 3H, 3 × H-18), 0.91 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.78 (dt, $J_{5',F}$ = 18.2 Hz, $J_{5',4'}$ = 6.8 Hz, 2H, H-5'), 3.63 (m, 1H, H-3), 5.38 (m, 1H, H-4'), 5.69 (m, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 11.95 (CH_3-18), 18.39 (CH_3-21), 20.81 (CH_2-11), 23.36 (CH_3-19), 24.19 (CH_2-15), 26.41 (CH_2-7), 27.18 (CH_2-6), 28.26 (CH_2-16), 30.53 (2C, CH_2-2 and CH_2-2'), 34.55 (C-10), 34.82 (t, $J_{5',F}$ = 22.7 Hz, CH_2-5'), 35.13 (CH_2-1'), 35.26 (CH-20), 35.32 (CH_2-1), 35.83 (CH-8), 36.44 (CH_2-4), 40.19 (CH_2-12), 40.42 (CH-9), 42.08 (CH-5), 42.71 (C-13), 56.16 (CH-14), 56.51 (CH-17), 71.88 (CH-3), 115.89 (t, $J_{4',F}$ = 4.1 Hz, CH-4'), 139.61 (CH-3').

(*Z*)-22a: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (s, 3H, 3 × H-18), 0.91 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.78 (dt, $J_{5',F}$ = 18.2 Hz, $J_{5',4'}$ = 6.8 Hz, 2H, H-5'), 3.63 (m, 1H, H-3), 5.38 (m, 1H, H-4'), 5.69 (m, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 12.01 (CH_3-18), 18.52 (CH_3-21), 20.81 (CH_2-11), 23.36 (CH_3-19), 24.19 (CH_2-15), 26.41 (CH_2-7),

27.18 (CH_2-6), 28.26 (CH_2-16), 29.31 (t, $J_{5',F}$ = 22.7 Hz, CH_2-5'), 30.53 (CH_2-2), 34.55 (C-10), 35.13 (CH_2-1'), 35.26 (CH-20), 35.32 (CH_2-1), 35.83 (CH-8), 36.44 (CH_2-4), 39.26 (CH_2-2'), 40.19 (CH_2-12), 40.42 (CH-9), 42.08 (CH-5), 42.71 (C-13), 56.16 (CH-14), 56.51 (CH-17), 71.88 (CH-3), 117.49 (t, $J_{4',F}$ = 4.0 Hz, CH-4'), 137.54 (CH-3').

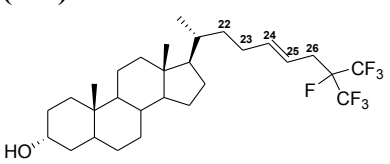
A mixture of 3'-(*E*)- and 3'-(*Z*)-(3α,5β)-20-(6',6',7',7',8',8',8'-heptafluorooct-3'-en-1'-yl)pregnan-3-ol (22b). The reaction was carried out with **12** (80 mg, 0.22 mmol) and **1b** (105 mg, 0.5 mmol) according to the general procedure. Column chromatography on silica gel (toluene) afforded 80 mg (71%) of the title compound **22b** (inseparable 1.5/1 mixture of E/Z isomers) as a white powder: $[\alpha]_D$ +25.6 (*c* 0.23, $CHCl_3$); IR ($CHCl_3$) ν 3609, 2935, 2867, 1672, 1377, 1353, 1276, 1031, 1012, 972 cm^{-1}; MS (EI, m/z (rel.%)) 540 (M^+, 1), 522 (8), 493 (3), 301 (3), 285 (31), 257 (12), 215 (36); HR-MS (EI) calcd for $C_{29}H_{43}OF_7$ [M^+] 540.3202, found 540.3228. R_f(toluene) = 0.29.



(*E*)-22b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.64 (s, 3H, 3 × H-18), 0.90 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.78 (m, 2H, H-5'), 3.63 (m, 1H, H-3), 5.37 (m, 1H, H-4'), 5.68 (m, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 11.99 (CH_3-18), 18.38 (CH_3-21), 20.81 (CH_2-11), 23.36 (CH_3-19), 24.20 (CH_2-15), 26.41 (CH_2-7), 27.19 (CH_2-2), 28.27 (CH_2-16), 30.54 (2C, CH_2-2 and CH_2-2'), 34.56 (m, CH_2-5'), 35.13 (CH_2-1'), 35.25 (CH-20), 35.33 (CH_2-1), 35.84 (CH-8), 36.44 (CH_2-4), 40.19 (CH_2-12), 40.43 (CH-9), 42.09 (CH-5), 42.71 (C-13), 56.17 (CH-14), 56.51 (CH-17), 71.86 (CH-3), 115.87 (CH-4'), 139.56 (CH-3').

(*Z*)-22b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.65 (s, 3H, 3 × H-18), 0.91 (d, $J_{21,20}$ = 6.4 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.78 (m, 2H, H-5'), 3.63 (m, 1H, H-3), 5.37 (m, 1H, H-4'), 5.68 (m, 1H, H-3'); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 12.04 (CH_3-18), 18.52 (CH_3-21), 20.81 (CH_2-11), 23.36 (CH_3-19), 24.20 (CH_2-15), 26.41 (CH_2-7), 27.19 (CH_2-2), 28.27 (CH_2-16), 29.31 (m, CH_2-5'), 30.54 (CH_2-2), 35.13 (CH_2-1'), 35.25 (CH-20), 35.33 (CH_2-1), 35.84 (CH-8), 36.44 (CH_2-4), 39.34 (CH_2-2'), 40.19 (CH_2-12), 40.43 (CH-9), 42.09 (CH-5), 42.71 (C-13), 56.17 (CH-14), 56.45 (CH-17), 71.86 (CH-3), 117.43 (CH-4'), 137.50 (CH-3').

(3α,5β)-20-(6'-(Trifluoromethyl)-6',7',7',7'-tetraafluorooct-3'-en-1'-yl)pregnan-3-ol (22c). The reaction was carried out with **12** (150 mg, 0.42 mmol) and **1c** (168 mg, 0.80 mmol) according to the general procedure. Column chromatography on silica gel (5/1 hexane/Et_2O) afforded 171 mg (75%) of the

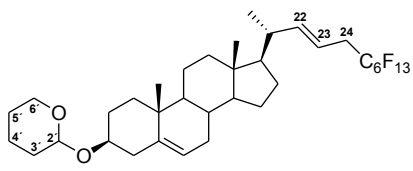


title compound **22c** (inseparable 1/1 mixture of E/Z isomers) as a colorless oil. $[\alpha]_D$ +19.6 (*c* 0.16, $CHCl_3$); IR ($CHCl_3$) ν 3610, 2937, 2867, 1671, 1376, 1365, 1286, 1030, 1012, 974 cm^{-1}; MS (FAB, m/z (rel.%)) 563 (M^++Na, 2), 523 (5), 507 (12), 337 (8), 263 (9), 233 (4), 179 (8). R_f(4/1 hexane/Et_2O) = 0.26.

(*E*)-22c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.63 (s, 3H, 3 × H-18), 0.90 (d, $J_{21,20}$ = 6.3 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.80 (m, 2H, H-5'), 3.63 (m, 1H, H-3), 5.36 (m, 1H, H-4'), 5.65 (m, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 11.92 (CH_3-18), 18.29 (CH_3-21), 20.76 (CH_2-11), 23.34 (CH_3-19), 24.18 (CH_2-15), 26.38 (CH_2-7), 27.14 (CH_2-6), 28.24 (CH_2-16), 29.17 (CH_2-2'), 30.45 (CH_2-2), 32.62 (d, $J_{5',F}$ = 20.9 Hz, CH_2-5'), 34.52 (C-10), 35.02 (CH_2-1'), 35.15 (CH-20), 35.28 (CH_2-1), 35.78 (CH-8), 36.35 (CH_2-4), 40.13 (CH_2-12), 40.35 (CH-9), 42.01 (CH-5), 42.67 (C-13), 56.10 (CH-14), 56.45 (CH-17), 71.85 (CH-3), 116.95 (d, $J_{4',F}$ = 5.4 Hz, CH-4'), 138.89 (CH-3').

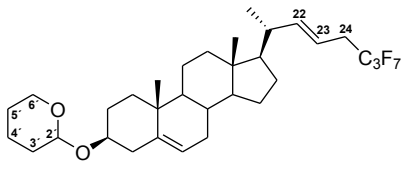
(*Z*)-22c: ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.64 (s, 3H, 3 × H-18), 0.89 (d, $J_{21,20}$ = 6.3 Hz, 3H, 3 × H-21), 0.92 (s, 3H, 3 × H-19), 2.80 (m, 2H, 2 × H-5'), 3.63 (m, 1H, H-3), 5.36 (m, 1H, H-4'), 5.65 (m, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.00 (CH_3-18), 18.47 (CH_3-21), 20.76 (CH_2-11), 23.34 (CH_3-19), 24.18 (CH_2-15), 26.38 (CH_2-7), 27.14 (CH_2-6), 28.24 (CH_2-16), 30.45 (CH_2-2), 32.54 (d, $J_{5',F}$ = 20.9 Hz, CH_2-5'), 34.52 (C-10), 35.02 (CH_2-1'), 35.15 (CH-20), 35.28 (CH_2-1), 35.78 (CH-8), 36.35 (CH_2-4), 39.12 (CH_2-2'), 40.13 (CH_2-12), 40.35 (CH-9), 42.01 (CH-5), 42.64 (C-13), 55.60 (CH-14), 56.39 (CH-17), 71.85 (CH-3), 118.49 (d, $J_{4',F}$ = 5.6 Hz, CH-4'), 136.79 (CH-3').

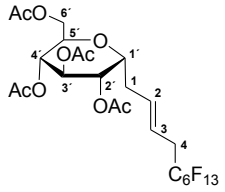
22-(*E*)-Tetrahydro-2'-[[(3β)-25,25,26,26,27,27,28,28,29,29,30,30,30-tridecafluoro-chola-5,22-dien-3-yl]oxy]-2H-pyran (23a). The reaction was carried out with **13** (82 mg, 0.2 mmol) and **1a** (144 mg, 0.4 mmol) according to the general procedure. Column chromatography on silica gel (20/1 hexane/Et_2O) and crystallization from acetone yielded 115 mg (79%) of the compound **23a** as white crystals: mp 144 °C; $[\alpha]_D$ -25.2 (*c* 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 1.01 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.75 (m, 2H, 2 × H-24), 3.48 (m, 1H, H-6'a), 3.53 (m, 1H, H-3), 3.92 (m, 1H, H-6'b), 4.72 (m, 1H, H-2'), 5.30 (bdt, $J_{23,22}$ = 15.2 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.34 (m, 1H, H-6), 5.55 (ddt, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, $J_{22,24}$ = 1.3 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.02 (CH_3-18), 19.37 (CH_3-19), 20.02 (CH_2-4'a), 20.10 (CH_2-4'b), 20.14 (CH_3-21), 21.00 (CH_2-11), 24.24 (CH_2-15), 25.46



(CH_2-5'), 27.95 (CH_2-2a), 28.24 (CH_2-16), 29.67 (CH_2-2b), 31.25 (CH_2-3'a), 31.28 (CH_2-3'a), 31.84 (CH-8), 31.87 (CH_2-7), 34.74 (t, $J_{24,F}$ = 22.6 Hz, CH_2-24), 36.75 (C-10a), 36.78 (C-10b), 37.18 (CH_2-1a), 37.42 (CH_2-1b), 38.73 (CH_2-4a), 39.60 (CH_2-12), 40.22 (CH-20 and CH_2-4b), 42.32 (C-13), 50.11 (CH-9a), 50.15 (CH-9b), 55.36 (CH-17), 56.70 (CH-14), 62.83 (CH_2-6'a), 62.95 (CH_2-6'b), 75.96 (CH-3), 96.81 (CH-2'a), 96.99 (CH-2'b), 113.58 (CH-23), 121.43 (CH-6a), 121.51 (CH-6b), 140.87 (C-5a), 141.04 (C-5b), 145.36 (CH-22); IR ($CHCl_3$): 3005, 2944, 2870, 1668, 1379, 1361, 1242, 975 cm^{-1}; MS (FAB, m/z (rel.%)) 745 (M^++H, 1), 663 (4), 341 (12), 207 (18); HR-MS (FAB) calcd for $C_{35}H_{46}O_2F_{13}$ [M^++H] 745.3290, found 745.3276. R_f(15/1 hexane/Et_2O) = 0.27.

22-(*E*)-Tetrahydro-2'-[[(3β)-25,25,26,26,27,27,27-heptafluoro-chola-5,22-dien-3-yl]oxy]-2H-pyran (23b). The reaction was carried out with **13** (82 mg, 0.2 mmol) and **1b** (84 mg, 0.4 mmol) according to the general procedure. Column chromatography on silica gel (20/1 hexane/Et_2O) and crystallization from EtOH/$CHCl_3$ yielded 96 mg (81%) of the compound **23b** as white crystals: mp 159 °C; $[\alpha]_D$ –42.3 (*c* 0.24, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 1.01 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.74 (m, 2H, H-24), 3.48 (m, 1H, H-6'a), 3.53 (m, 1H, H-3), 3.92 (m, 1H, H-6'b), 4.72 (m, 1H, H-2'), 5.30 (bdt, $J_{23,22}$ = 15.2 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.34 (m, 1H, H-6), 5.55 (ddt, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, $J_{22,24}$ = 1.3 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.02 (CH_3-18), 19.36 (CH_3-19), 20.01 (CH_2-4'a), 20.10 (CH_2-4'b), 20.14 (CH_3-21), 20.98 (CH_2-11), 24.24 (CH_2-15), 25.46 (CH_2-5'), 27.94 (CH_2-2a), 28.24 (CH_2-16), 29.66 (CH_2-2b), 31.24 (CH_2-3'a), 31.28 (CH_2-3'a), 31.84 (CH-8), 31.87 (CH_2-7), 34.48 (t, $J_{24,F}$ = 22.6 Hz, CH_2-24), 36.74 (C-10a), 36.78 (C-10b), 37.17 (CH_2-1a), 37.42 (CH_2-1b), 38.73 (CH_2-4a), 39.60 (CH_2-12), 40.21 (CH-20 and CH_2-4b), 42.32 (C-13), 50.11 (CH-9a), 50.14 (CH-9b), 55.35 (CH-17), 56.69 (CH-14), 62.82 (CH_2-6'a), 62.94 (CH_2-6'b), 75.95 (CH-3), 96.81 (CH-2'a), 96.98 (CH-2'b), 113.56 (CH-23), 121.43 (CH-6a), 121.50 (CH-6b), 140.86 (C-5a), 141.04 (C-5b), 145.31 (CH-22); IR ($CHCl_3$) ν 3005, 2944, 2870, 1668, 1378, 1353, 1274, 976, 956 cm^{-1}; MS (FAB, m/z (rel.%)) 617 (M^++Na, 7), 571 (2), 529 (3), 507 (4), 309 (12), 253 (14); HR-MS (FAB) calcd for $C_{32}H_{45}O_2F_7Na$ [M^++Na] 617.3205, found 617.3189. R_f(15/1 hexane/Et_2O) = 0.27.





2-(*E*)-1-(2′,3′,4′,6′-Tetra-*O*-acetyl-α-D-glucopyranosyl)-5,5,6,6,7,7,8,8,9,9,10,10,10-trideca-fluorodec-2-ene (24). The reaction was carried out with **14** (93 mg, 0.25 mmol) and **1a** (180 mg, 0.5 mmol) according to the general procedure. Column chromatography on silica gel (5/1 hexane/EtOAc) and crystallization from pentane/Et_2O yielded 112 mg (64%) of the compound **24** as white crystals: mp 66 °C; $[\alpha]_D$ +52.8 (*c* 0.17, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.04 (s, 6H), 2.06 (s, 3H), 2.08 (s, 3H) (4× CH_3CO), 2.36 (dt, J_{gem} = 15.8 Hz, $J_{1b,1'}$ = $J_{1b,2}$ = 4.9 Hz, 1H, H-1b), 2.62 (ddd, J_{gem} = 15.8 Hz, $J_{1a,1'}$ = 11.1 Hz, $J_{1a,2}$ = 7.3 Hz, 1H, H-1a), 2.83 (td, $J_{4,F}$ = 18.2 Hz, $J_{4,3}$ = 6.9 Hz, 2H, H-4), 3.85 (ddd, $J_{5',4'}$ = 9.3 Hz, $J_{5',6'b}$ = 5.0 Hz, $J_{5',6'a}$ = 2.7 Hz, 1H, H-5'), 4.04 (dd, J_{gem} = 12.3 Hz, $J_{6'b,5'}$ = 2.6 Hz, 1H, H-6'b), 4.27 (m, 2H, H-1' and H-6'a), 5.00 (t, $J_{4',3'}$ = $J_{4',5'}$ = 9.1 Hz, 1H, H-4'), 5.10 (dd, $J_{2',3'}$ = 9.4 Hz, $J_{2',1'}$ = 5.7 Hz, 1H, H-2'), 5.32 (t, $J_{3',2'}$ = $J_{3',4'}$ = 9.1 Hz, 1H, H-3'), 5.58 (m, 1H, H-3), 5.70 (m, 1H, H-2); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 20.60, 20.62, 20.65, 20.67 (4× **C**H_3CO), 29.29 (CH_2-1), 34.75 (t, $J_{4,F}$ = 22.3 Hz, CH_2-4), 62.01 (CH_2-6'), 68.56 (CH-4'), 68.94 (CH-5'), 70,05 (CH-2'), 70.21 (CH-3'), 71.81 (CH-1'), 119.86 (t, $J_{3,F}$ = 4.1 Hz, CH-3), 133.05 (CH-2), 169.49, 169.58, 170.11, 170.61 (4× CH_3**C**O); IR ($CHCl_3$) ν 2957, 1751, 1650, 1455, 1431, 1348, 1245, 1145, 972 cm^{-1}; MS (ESI, m/z (rel.%)) 704 (M^+, 3), 667 (2), 645 (23), 525 (4), 483 (6), 314 (3), 288 (6); HR-MS (ESI) calcd for $C_{24}H_{26}O_9F_{13}$ [M^++H] 705.1369, found 705.1395. R_f (2/1 hexane/Et_2O) = 0.21.

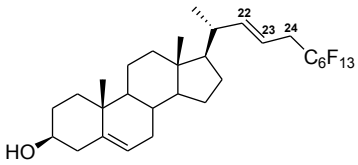
Per-*O*-acetyl-6^I-*O*-(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluorodec-2-en-1-yl)-β-cyclodextrin (25). The reaction was carried out with **15** (72 mg, 36 μmol) and **1a** (27 mg, 74 μmol) according to the general procedure. Column chromatography on silica gel (EtOAc) and on fluorinated silica gel (1st elution 4/1 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) yielded 40 mg (48%) of the compound **25** as a white powder: mp 115–117 °C; $[\alpha]_D$ +100 (*c* 0.27, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) *δ* 1.98-2.10 (m, 60 H, 20 × CH_3), 2.85 (td, $J_{H,F}$ = 18.9 Hz, $J_{H,H}$ = 6.7 Hz, 2H, 2 × H-4'), 3.56-4.61 (m, 30H, 2 × H-1', 7 × H-4, 7 × H-5, 14 × H-6), 4.67-4.86 (m, 7H, 7 × H-2), 5.02–5.11 (m, 6H, 6 × H-1), 5.14 (d, *J* = 3.9 Hz, 1H, H-1), 5.18–5.41 (m, 7H, 7 × H-3), 5.60–5.72 (m, 1H, H-3'), 5.81 (dt, *J* = 15.8 Hz, 5.4 Hz, 1H, H-2'); ^{13}C NMR (101 MHz, $CDCl_3$) *δ* 20.62-20.86 (20 × CH_3), 34.35 (t, $J_{C,F}$ = 22.6 Hz, C-4'), 62.39-62.71 (6 × C-6), 67.82 (C-6^I), 71.11 (C-1'), 69.22-77.22 (7 × C-2, 7 × C-3, 7 × C-4, 7 × C-5), 96.34 (C-1), 96.48 (C-

1), 96.48 (C-1), 96.77 (C-1), 96.86 (C-1), 96.94 (C-1), 97.14 (C-1), 119.97 (t, $J_{C,F}$ = 4.1 Hz, C-3'), 134.11 (C-2'), 169.28-170.90 (20 × C=O); IR (KBr) ν 1750, 1370, 1241, 1052 cm^{-1}; MS (ESI, *m/z* (rel.%)) 2370.2 (M^+ + Na, 80). R_f(EtOAc) = 0.38.

General Procedure for Removal of THP Protective Group.

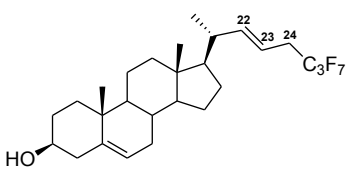
4-Methylbenzenesulfonic acid (1 mmol) was added to a solution of protected compound (1 mmol) in MeOH (10 ml), and the mixture was stirred at 25 °C for 2 h. After completion of the reaction, volatiles were evaporated under reduced pressure, a crude product was dissolved in CH_2Cl_2, washed with water, and dried over sodium sulfate.

22-(*E*)-25,25,26,26,27,27,28,28,29,29,30,30,30-Tridecafluoro-chola-5,22-diene-3β-ol (26a).



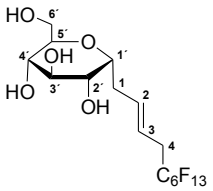
The reaction was carried out with **23a** (50 mg, 0.07 mmol) and 4-methylbenzenesulfonic acid (12 mg, 0.07 mmol) according to the general procedure. Crystallization from MeOH yielded 40 mg (91%) of the title compound **26a** as a colorless oil: $[\alpha]_D$ – 25.5 (*c* 0.21, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 1.01 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.24 (m, 1H, H-4b), 2.30 (ddd, J_{gem} = 13.1 Hz, $J_{4a,3}$ = 5.0 Hz, $J_{4a,6}$ = 2.2 Hz, 1H, H-4a), 2.75 (m, 2H, H-24), 3.53 (m, 1H, H-3), 5.31 (bdt, $J_{23,22}$ = 15.3 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.35 (m, 1H, H-6), 5.55 (bdd, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.02 (CH_3-18), 19.38 (CH_3-19), 20.14 (CH_3-21), 21.02 (CH_2-11), 24.25 (CH_2-15), 28.24 (CH_2-16), 31.61 (CH_2-2), 31.82 (CH_2-7), 31.85 (CH-8), 34.75 (t, $J_{24,F}$ = 22.7 Hz, CH_2-24), 36.48 (C-10), 37.22 (CH_2-1), 39.60 (CH_2-12), 40.21 (CH-20), 42.25 (CH_2-4), 42.32 (C-13), 50.07 (CH-9), 55.36 (CH-17), 56.71 (CH-14), 71.78 (CH-3), 113.60 (CH-23), 121.65 (CH-6), 140.71 (C-5), 145.34 (CH-22); IR ($CHCl_3$) ν 3609, 3477, 2941, 1668, 1380, 1349, 1242, 1047, 975, 961 cm^{-1}; MS (FAB, m/z (rel.%)) 660 (M^+, 1), 643 (21), 471 (2), 387 (8) 341 (11), 253 (4), 155 (27); HR-MS (FAB) calcd for $C_{30}H_{36}F_{13}$ [M^+-OH] 643.2609, found 643.2599. R_f(10/1 hexane/Et_2O) = 0.13.

22-(*E*)-25,25,26,26,27,27,27-Heptafluoro-chola-5,22-diene-3β-ol (26b). The reaction was carried out with **23b** (40 mg, 0.07 mmol) and 4-methylbenzenesulfonic acid (12 mg, 0.07 mmol) according to the general procedure. Crystallization from MeOH yielded 32 mg (93%) of the title compound **26b** as white crystals: mp 122



°C; $[\alpha]_D$ –21.1 (*c* 0.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 1.01 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.24 (m, 1H, H-4b), 2.30 (ddd, J_{gem} = 13.1 Hz, $J_{4a,3}$ = 5.1 Hz, $J_{4a,6}$ = 2.2 Hz, 1H, H-4a), 2.74 (m, 2H, 2 × H-24), 3.53 (m, 1H, H-3), 5.30 (bdt, $J_{23,22}$ = 15.3 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.35 (m, 1H, H-6), 5.55 (bdd, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.03 (CH_3-18), 19.38 (CH_3-19), 20.14 (CH_3-21), 21.02 (CH_2-11), 24.25 (CH_2-15), 28.24 (CH_2-16), 31.61 (CH_2-2), 31.82 (CH_2-7), 31.84 (CH-8), 34.48 (t, $J_{24,F}$ = 22.8 Hz, CH_2-24), 36.47 (C-10), 37.22 (CH_2-1), 39.60 (CH_2-12), 40.20 (CH-20), 42.25 (CH_2-4), 42.32 (C-13), 50.07 (CH-9), 55.35 (CH-17), 56.70 (CH-14), 71.77 (CH-3), 113.59 (CH-23), 121.64 (CH-6), 140.71 (C-5), 145.29 (CH-22); IR ($CHCl_3$) ν 3609, 3471, 2939, 1669, 1379, 1379, 1353, 1273, 1047, 976, 956 cm^{-1}; MS (FAB, m/z (rel.%)) 511 (M^++H, 1), 509 (9), 493 (34), 329 (7), 303 (4), 237 (40), 207 (22); HR-MS (FAB) calcd for $C_{27}H_{36}OF_7$ [M^+-H] 509.2654, found 509.2676. R_f(10/1 hexane/Et_2O) = 0.13.

2-(*E*)-1-(α-D-Glucopyranosyl)-5,5,6,6,7,7,8,8,9,9,10,10, 10-tridecafluorodec-2-ene (27). A



solution of **24** (30 mg, 0.04 mmol) in MeOH (4 mL) was treated with 1M methanolic sodium methoxid (10 µL, 0.01 mmol) at 25 °C for 1 h. After the consumption of the starting material (TLC-1/1 MeOH/$CHCl_3$), the Dowex (100 µl) was added to the reaction mixture. Then filtration, evaporation of volatiles, and column chromatography on silica gel (1/1 MeOH/$CHCl_3$) afforded 21 mg (92%) of the title compound **27** as a colorless oil: $[\alpha]_D$ +44.7 (*c* 0.18, $CHCl_3$); ^1H NMR (500 MHz, CD_3OD) δ 2.47 (m, 2H, H-1), 2.92 (td, $J_{4,F}$ = 18.8 Hz, $J_{4,3}$ = 7.2 Hz, 2H, H-4), 3.28 (dd, $J_{4',5'}$ = 9.6 Hz, $J_{4',3'}$ = 8.5 Hz, 1H, H-4'), 3.43 (ddd, $J_{5',4'}$ = 9.6 Hz, $J_{5',6'b}$ = 5.2 Hz, $J_{5',6'a}$ = 2.6 Hz, 1H, H-5'), 3.53 (dd, $J_{3',2'}$ = 9.5 Hz, $J_{3',4'}$ = 8.5 Hz, 1H, H-3'), 3.59 (dd, $J_{2',3'}$ = 9.4 Hz, $J_{2',1'}$ = 5.8 Hz, 1H, H-2'), 3.65 (dd, J_{gem} = 11.8 Hz, $J_{6'b,5'}$ = 5.2 Hz, 1H, H-6'b), 3.74 (dd, J_{gem} = 11.7 Hz, $J_{6'a,5'}$ = 2.6 Hz, 1H, H-6'a), 3.95 (ddd, $J_{1',1a}$ = 11.1 Hz, $J_{1',2'}$ = 5.7 Hz, $J_{1',1b}$ = 4.1 Hz, 1H, H-1'), 5.54 (m, 1H, H-3), 5.85 (dtt, $J_{2,3}$ = 15.3 Hz, $J_{2,1}$ = 6.9 Hz, $J_{2,4}$ = 1.3 Hz, 1H, H-2); ^{13}C NMR (125.7 MHz, CD_3OD) δ 29.39 (CH_2-1), 35.62 (t, $J_{4,F}$ = 22.1 Hz, CH_2-4), 62.83 (CH_2-6'), 72.10, 72.87, 74.51, 75.17, 76.86 (CH-4', CH-5', CH-2', CH-3', CH-1'), 119.54 (t, $J_{3,F}$ = 4.3 Hz, CH-3), 136.73 (CH-2); IR ($CHCl_3$) ν 3391, 2927, 1455, 1433, 1368, 1352, 1245, 1095, 1064, 972 cm^{-1}; MS (FAB, m/z (rel.%)) 559 (M^++Na, 23), 413 (7), 308 (6), 252 (4), 230 (26), 176 (93), 153 (100); HR-MS (FAB) calcd for $C_{16}H_{17}O_5F_{13}Na$ [M^++Na] 559.0766, found 559.0769. R_f(1/1 MeOH/$CHCl_3$) = 0.36.

Dimer of 1a. The reaction was carried out with **1a** (360 mg, 1 mmol) according to the general procedure for cross-metathesis and Grubbs 2nd generation catalyst (10 mol%) was used. Column chromatography on silica gel (hexane) yielded 263 mg (76%) of the compound ***dim*-1a** as colorless liquid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (td, $J_{2,F}$ = 18.0 Hz, $J_{2,1}$ = 4.0 Hz, 2H, H-3), 5.74 (m, 1H, H-1); ^{13}C NMR (125.7 MHz, $CDCl_3$) δ 34.85 (t, $J_{C\text{-}F}$ = 22.7 Hz, 2C, 2 × CH_2-2), 125.03 (t, $J_{C\text{-}F}$ = 5.1 Hz, 2C, 2 × CH-1); IR ($CHCl_3$) ν 2928, 2855, 1363, 1350, 1243, 1170, 1146, 1121, 974 cm^{-1}.

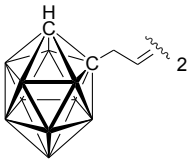
Dimer of 10. The reaction was carried out with **10** (47 mg, 0.1 mmol) according to the general procedure for cross-metathesis. Column chromatography on silica gel (5/1 hexane/toluene) yielded 24 mg (52%) of the compound ***dim*-10** as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.06 (s, 6H, Si-$(CH_3)_2$), 0.63 (s, 3H, 3 × H-18), 0.89 (s, 9H, C-$(CH_3)_3$), 0.90 (s, 3H, 3 × H-19), 0.91 (d, $J_{21,20}$ = 6.5 Hz, 3H, 3 × H-21), 3.58 (m, 1H, H-3), 5.33 (m, 1H, H-24); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ -4.61 (4C, 2 × Si-$(CH_3)_2$), 11.98 (2C, 2 × CH_3-18), 18.32 (2C, 2 × **C**-$(CH_3)_3$), 18.64 (2C, 2 × CH_3-21), 20.75 (2C, 2 × CH_2-11), 23.37 (2C, 2 × CH_3-19), 24.22 (2C, 2 × CH_2-15), 25.95 (6C, 2 × C-(**C**$H_3)_3$), 26.38 (2C, 2 × CH_2-7), 27.28 (2C, 2 × CH_2-6), 28.24 (2C, 2 × CH_2-16), 29.35 (2C, 2 × CH_2-2**'**), 30.98 (2C, 2 × CH_2-2), 34.56 (4C, 2 × C and 2 × CH_2), 35.55 (2C, 2 × CH_2), 35.83 (2C, 2 × CH), 36.15 (2C, 2 × CH), 36.88 (2C, 2 × CH_2), 40.02 (2C, 2 × CH_2), 40.16 (2C, 2 × CH), 42.27 (2C, 2 × CH), 42.63 (2C, 2 × C), 55.86 (2C, 2 × CH), 56.37 (2C, 2 × CH), 72.83 (2C, 2 × CH-3), 129.88 (2C, 2 × CH-3**'**); IR ($CHCl_3$) ν 2930, 2859, 1463, 1407, 1374, 1254, 1070, 969 cm^{-1}.

1-(5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluorodecen-2-en-1-yl)-1,2-dicarbadodecaborane (33a). The reaction was carried out with **28** (90 mg, 0.50 mmol) and **1a** (360 mg, 1.00 mmol) according to the general procedure. Column chromatography on silica gel (heptane) afforded **33a** (85 mg, 34%) as a colorless oil and the carborane homodimer **38** (20 mg, 23%) as a colorless oil.

33a: ^{1}H NMR (600 MHz $CDCl_3$) δ 1.59-2.81 (m, 10H, B-H), 2.87 (btd, $J_{4',F}$ = 18.0 Hz, $J_{4',3'}$ = 7.0 Hz, 2H, H-4'), 2.99 (dm, $J_{1',2'}$ = 7.4 Hz, 2H, H-1'), 3.52 (bs, 1H, H-2), 5.55 (dtm, $J_{3',2'}$ = 15.3 Hz, $J_{3',4'}$ = 7.0 Hz, 1H, H-3'), 5.66 (dtt, $J_{2',3'}$ = 15.3 Hz, $J_{2',1'}$ = 7.4 Hz, $J_{2',4'}$ = 1.1 Hz, 1H,

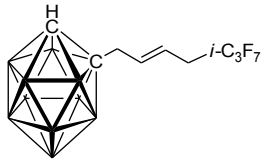
H-2'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.77 (t, $J_{4',F}$ = 22.8 Hz, CH_2-4'), 40.52 (CH_2-1'), 59.69 (CH-2), 73.08 (C-1), 123.21 (t, $J_{3',F}$ = 4.4 Hz, CH-3'), 131.40 (CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -1.35 (d, *J* = 150 Hz, 1B, B-9), -4.70 (d, *J* = 150 Hz, 1B, B-12), -8.23 (d, *J* = 153 Hz, 2B, B-8 and B-10), -10.40 (d, *J* = 160 Hz, 2B, B-4 and B-5), -11.80 (d, *J* = ~100 Hz, 2B, B-7 and B-11), -12.10 (d, *J* = 155 Hz, 2B, B-3 and B-6); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -76.99 (m, 3F), -109.17 (m, 2F), -118.11 (m, 2F), -119.07 (m, 2F), -119.21 (m, 2F), -122.33 (m, 2F); IR ($CHCl_3$) ν 3068, 2929, 2597, 1362, 1243, 1020, 997 cm^{-1}; MS (ESI, m/z (rel.%)) 518 (M^+, 8), 495 (100), 475 (45), 435 (17), 416 (5); HR-MS (ESI) calcd. for $C_{12}H_{16}B_{10}F_{13}$ [M^+-H] 517.1980, found 517.1987. R_f(hexane) = 0.63.

38: ^{1}H NMR (600 MHz, $CDCl_3$) δ 3.15 (m, 4H, H-1'), 4.61 (bs, 2H, H-2), 5.66 (m, 2H, H-2');



^{13}C NMR (150.9 MHz, $CDCl_3$) δ 40.52 (2C, CH_2-1'), 62.71 (2C, CH-2), 75.68 (2C, C-1), 130.45 (2C, CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -2.07 (d, *J* = 151 Hz, 2B, B-9), -5.21 (d, *J* = 150 Hz, 2B, B-12), -8.71 (d, *J* = 153 Hz, 4B, B-8 and B-10), -10.59 (d, *J* = 160 Hz, 4B, B-4 and B-5), -11.41 (d, *J* = ~110 Hz, 4B, B-7 and B-11), -12.21 (d, *J* = 158 Hz, 4B, B-3 and B-6); IR ($CHCl_3$) ν 3067, 2929, 2598, 1433, 1018, 979 cm^{-1}; MS (EI, m/z (rel.%)) 344 (M^+, 7), 181 (47), 153 (15); HR-MS (EI) calcd. for $C_8H_{28}B_{20}$ [M^+] 344.4052, found 344.4068. R_f(hexane) = 0.60.

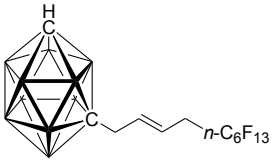
1-(5-Trifluoromethyl-5,6,6,6-tetrafluorohexen-2-en-1-yl)-1,2-dicarbadodecaborane (33c).



The reaction was carried out with **28** (90 mg, 0.50 mmol) and **1c** (210 mg, 1.00 mmol) according to the general procedure. Column chromatography on silica gel (hexane) afforded **33c** (57 mg, 32%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.53-2.83 (bm, 10H, B-H), 2.86 (ddm, $J_{4',F}$ = 20.0 Hz, $J_{4',3'}$ = 7.0 Hz, 2H, H-4'), 2.98 (d, $J_{1',2'}$ = 7.4 Hz, 2H, H-1'), 3.51 (bs, 1H, H-2), 5.53 (dm, $J_{3',2'}$ = 15.2 Hz, 1H, H-3'), 5.62 (dtt, $J_{2',3'}$ = 15.2 Hz, $J_{2',1'}$ = 7.4 Hz, $J_{2',4'}$ = 1.2 Hz, 1H, H-2'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 32.02 (d, $J_{4',F}$ = 21.0 Hz, CH_2-4'), 40.45 (CH_2-1'), 59.67 (CH-2), 73.04 (C-1), 124.14 (d, $J_{3',F}$ = 5.7 Hz, CH-3'), 130.61 (CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -1.36 (d, *J* = 151 Hz, 1B, B-9), -4.68 (d, *J* = 150 Hz, 1B, B-12), -8.23 (d, *J* = 153 Hz, 2B, B-8 and B-10), -10.42 (d, *J* = 160 Hz, 2B, B-4 and B-5), -11.85 (d, *J* = 100 Hz, 2B, B-7 and B-11), -12.14 (d, *J* = 150 Hz, 2B, B-3); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -72.22 (d, $J_{F\text{-}C\text{-}C\text{-}F}$ = 7.0 Hz, 6F), -178.61 (m, 1F); IR ($CHCl_3$) ν 3068, 2928, 2597, 1353, 1249, 1019, 997 cm^{-1}; MS (EI, m/z (rel.%)) 368 (M^+, 28),

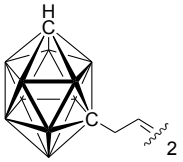
278 (21), 216 (45), 202 (77), 154 (35); HR-MS (EI) calcd. for $C_9H_{17}B_{10}F_7$ [M^+] 368.2149, found 368.2160. R_f(hexane) = 0.45.

1-(5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluorodecen-2-en-1-yl)-1,7-dicarbadodecaborane (34a). The reaction was carried out with **29** (100 mg, 0.54 mmol) and **1a** (390 mg, 1.08 mmol) according to the general procedure. Column chromatography on silica gel (hexane) afforded **34a** (86 mg, 31%) as a colorless oil and the carborane homodimer **39** (25 mg, 27%) as a colorless oil.

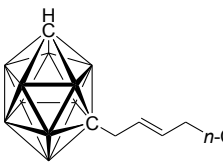


34a: ^{1}H NMR (600 MHz, d_6-acetone) δ 2.81 (bd, $J_{1',2'}$ = 7.5 Hz, 2H, H-1'), 3.07 (btd, $J_{4',F}$ = 19.0 Hz, $J_{4',3'}$ = 7.3 Hz, 2H, H-4'), 5.56 (m, 1H, H-3'), 5.79 (dtt, $J_{2',3'}$ = 15.2 Hz, $J_{2',1'}$ = 7.5 Hz, $J_{2',4'}$ = 1.3 Hz, 1H, H-2'); ^{13}C NMR (150.9 MHz, d_6-acetone) δ 34.57 (t, $J_{4',F}$ = 22.0 Hz, CH_2-4'), 40.04 (CH_2-1'), 56.99 (CH-7), 76.10 (C-1), 121.58 (t, $J_{3',F}$ = 4.6 Hz, CH-3'), 134.97 (CH-2'); ^{11}B NMR (160.4 MHz, d_6-acetone, $BF_3{\cdot}Et_2O$) δ -3.56 (d, J = 161, 1B, B-5), -9.06 (d, J = 160, 1B, B-12), -10.18 (d, J = 155, 4B, B-4, B-6, B-9, and B-10), -12.64 (d, J = 172, 2B, B-8 and B-11), -14.34 (d, J = 180, 2B, B-2,3); ^{19}F NMR (470.3 MHz, d_6-acetone, C_6F_6) δ -77.87 (m, 3F), -109.57 (m, 2F), -118.68 (m, 2F), -119.64 (m, 2F), -119.77 (m, 2F), -122.96 (m, 2F); IR ($CHCl_3$) ν 3069, 2929, 2603, 1361, 1243, 1005, 977 cm^{-1}; MS (EI, m/z (rel.%)) 518 (M^+, 41), 495 (4), 247 (45), 202 (64), 181 (75); HR-MS (EI) calcd. for $C_{12}H_{17}B_{10}F_{13}$ [M^+] 518.2053, found 518.2067. R_f(hexane) = 0.52.

39: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.74 (m, 4H, H-1'), 3.67 (bs, 2H, H-2), 5.42 (m, 2H, H-2'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 39.99 (2C, CH_2-1'), 56.91 (2C, CH-7), 76.47 (2C, C-1), 130.43 (2C, CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -3.55 (d, J = 161 Hz, 2B, B-5), -9.09 (J = 160 Hz, 2B, B-12), -10.17 (d, J = 155 Hz, 8B, B-4, B-6, B-9, and B-10), -12.68 (d, J = 172 Hz, 4B, B-8 and B-11), -14.32 (d, J = 180 Hz, 4B, B-2 and B-3); IR ($CHCl_3$) ν 3068, 2929, 2597, 1434, 1018, 979 cm^{-1}; MS (EI, m/z (rel.%)) 344 (M^+, 12), 181 (36), 153 (26); HR-MS (EI) calcd. for $C_8H_{28}B_{20}$ [M^+] 344.4052, found 344.4066. R_f(hexane) = 0.60.

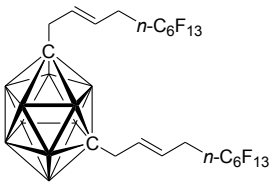


1-(5,5,6,6,7,7,8,8,8-Heptafluorohept-2-en-1-yl)-1,7-dicarbadodecaborane (34b). The reaction was carried out with **29** (50 mg, 0.27 mmol) and **1b** (113 mg, 0.54 mmol) according to the general procedure. Column chromatography on silica gel (hexane) afforded **34b** (33 mg, 34%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.69 (bd, $J_{1',2'}$ = 7.5 Hz, 2H, H-1'), 2.82 (tdm, $J_{4',F}$



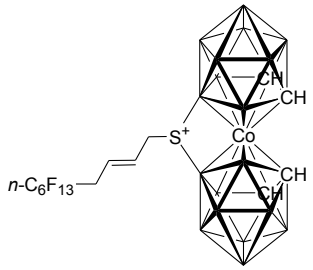
= 18.0 Hz, $J_{4',3'}$ = 7.1 Hz, 2H, H-4'), 2.93 (bs, 1H, H-7), 5.42 (dm, $J_{3',2'}$ = 15.2 Hz, 1H, H-3'), 5.60 (dtt, $J_{2',3'}$ = 15.2 Hz, $J_{2',1'}$ = 7.5 Hz, $J_{2',4'}$ = 1.3 Hz, 1H, H-2'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.16 (t, $J_{4',F}$ = 22.6 Hz, CH_2-4'), 39.61 (CH_2-1'), 55.12 (CH_{carb}-7), 74.44 (C_{carb}-1), 120.58 (t, $J_{3',F}$ = 4.3 Hz, CH-3'), 133.76 (CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -3.26 (d, J = 160 Hz, 1B, B-5), -8.92 (J = 160 Hz, 1B, B-12), -9.79 (d, J = 155 Hz, 4B, B-9 and B-10), -10.12 (d, J = 150 Hz, 4B, B-4 and B-6), -12.62 (d, J = 170 Hz, 2B, B-8 and B-11), -14.65 (d, J = 180 Hz, 2B, B-2 and B-3); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -76.77 (m, 3F), -110.28 (m, 2F), -123.58 (m, 2F); IR ($CHCl_3$) ν 3069, 2926, 2603, 1353, 1231, 1006, 977 cm^{-1}; MS (EI, m/z (rel.%)) 368 (M^+, 21), 314 (34), 247 (15), 202 (64), 182 (100); HR-MS (EI) calcd. for $C_9H_{17}B_{10}F_7$ [M^+] 368.2149, found 368.2154. R_f(hexane) = 0.68.

1,7-Di(5,5,6,6,7,7,8,8,9,9,10,10,10-tridecafluorodecen-2-en-1-yl)-1,7-dicarbadodecabora-



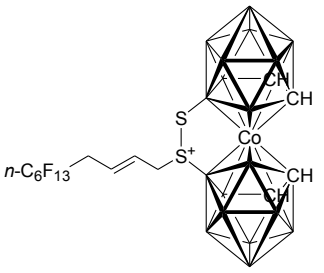
ne (35a). The reaction was carried out with **30** (100 mg, 0.45 mmol) and **1a** (646 mg, 1.80 mmol) according to the general procedure. Column chromatography on silica gel (hexane) afforded **35a** (152 mg, 38%) as a colorless oil: ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.66 (bd, $J_{1',2'}$ = 7.5 Hz, 4H, H-1'), 2.82 (btd, $J_{4',F}$ = 18.3 Hz, $J_{4',3'}$ = 6.9 Hz, 4H, H-4'), 5.41 (m, 2H, H-3'), 5.59 (dtt, $J_{2',3'}$ = 15.2 Hz, $J_{2',1'}$ = 7.5 Hz, $J_{2',4'}$ = 1.3 Hz, 2H, H-2'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.37 (t, $J_{4',F}$ = 22.7 Hz, 2C, CH_2-4'), 39.66 (2C, CH_2-1'), 74.38 (2C, C-1 and C-7), 120.65 (t, $J_{3',F}$ = 4.3 Hz, 2C, CH-3'), 133.78 (2C, CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ -5.31 (d, J = 160 Hz, 2B, B-5 and B-12), -10.07 (d, J = 160 Hz, 2B, B-9 and B-10), -12.65 (d, J = 160 Hz, 2B, B-4, B-6, B-8, and B-11), -13.19 (d, J = 160 Hz, 2B, B-2 and B-3); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -77.02 (m, 3F), -109.40 (m, 2F), -118.15 (m, 2F), -119.10 (m, 2F), -119.34 (m, 2F), -122.37 (m, 2F); IR ($CHCl_3$) ν 2926, 2598, 1361, 1243, 997 cm^{-1}; MS (EI, m/z (rel.%)) 890 (M^+, 48), 830 (4), 618 (40), 569 (45), 305 (7), 238 (12); HR-MS (EI) calcd. for $C_{22}H_{22}B_{10}F_{26}$ [M^+] 890.2237, found 890.2251. R_f(hexane) = 0.65.

8,8'-μ-(5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluorodecen-2-en-1-ylthiolato)]-[3,3'-como-cobalt(III)-bis-(1,2-dicarbaundecaborate)] (36a). The reaction was carried out with **31** (115 mg, 0.29 mmol) and **1a** (209 mg, 0.58 mmol) according to the general procedure. Column chromatography on silica gel (5/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 3/1 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded **36a** (112 mg, 53%) as an orange solid: mp 186-188 °C; ^{1}H NMR (600



MHz, $CDCl_3$) δ 1.43-4.51 (bm, 16H, B-H), 2.81-2.96 (m, 2H, H-4'), 3.15 (bs, 2H, C_{carb}-H), 3.45 (bs, 2H, C_{carb}-H), 3.74 (d, $J_{1',2'}$ = 6.7 Hz, 1H, H-1'), 5.72-5.88 (m, 2H, H-2' and H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.50 (t, $J_{4',F}$ = 22.7 Hz, CH_2-4'), 42.03 (CH_2-1'), 48.87 (4C, CH_{carb}), 125.57 (t, $J_{3',F}$ = 4.4 Hz, CH-3'), 128.04 (CH-2'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ 2.99 (d, J = 146 Hz, 2B, B-10 and 10'), -2.94 (s, 2B, B-8 and B-8'), -4.86 (d, J = 153 Hz, 2B, B-4 and B-4'), -7.05 (d, J = ~160 Hz, 6B, B-7, B-7', B-9, B-9', B-12, and B-12'), -13.25 (d, J = 160 Hz, 4B, B-5, B-5', B-11, and B-11'), -20.95 (d, J = 155 Hz, 2B, B-6 and B-6'); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -76.95 (m, 3F), -109.01 (m, 2F), -118.09 (m, 2F), -119.06 (m, 2F), -119.15 (m, 2F), -122.29 (m, 2F); IR ($CHCl_3$) ν 2617, 2586, 1670, 1360, 1243, 973 cm^{-1}; MS (ESI, m/z (rel.%)) 729 (M^+-H, 4), 385 (3), 352 (9); HR-MS (ESI) calcd. for $C_{14}H_{25}B_{18}CoF_{13}S$ [M^+-H] 729.2482, found 729.2476. R_f(5/1 hexane/Et_2O) = 0.33.

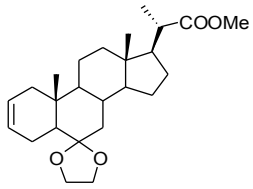
8,8'-μ-(5,5,6,6,7,7,8,8,9,9,10,10,10-Tridecafluorodecen-2-ene-1-yldithiolato)-[3,3'-como-cobalt(III)-bis-(1,2-dicarbaundecaborate)] (37a). The reaction was carried out with **32** (115 mg, 0.27 mmol) and **1a** (194 mg, 0.54 mmol) according to the general procedure. Column chromatography on silica gel (5/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 3/1 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded **37a** (89 mg, 44%) as a dark yellow solid: mp 174-175 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ 1.40-4.37 (bm, 16H, B-H), 2.88-3.01 (m, 2H, H-4'), 3.28 (bs, 1H, C_{carb}-H), 3.45 (bs, 1H, C_{carb}-H), 3.63 (bs, 1H, C_{carb}-H), 3.70 (bs, 1H, C_{carb}-H), 4.02 (dd, J_{gem} = 12.7 Hz, $J_{1'b,2'}$ = 6.8 Hz, 1H, H-1'b), 4.44 (dd, J_{gem} = 12.7 Hz, $J_{1'a,2'}$ = 8.9 Hz, 1H, H-1'a), 5.76 (m, 1H, H-2'), 6.00 (dm, $J_{3',2'}$ = 15.4 Hz, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.59 (t, $J_{4',F}$ = 22.7 Hz, CH_2-4'), 48.77 (CH_2-1'), 48.61, 50.47, 51.49, 51.93 (4C, CH_{carb}), 126.60 (CH-2'), 128.81 (t, $J_{3',F}$ = 4.3 Hz, CH-3'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ 23.35 (s, 1B, B-8 or 8'), 21.27 (s, 1B, B-8 or 8'), 2.54 (d, J = 146 Hz, 2B, B-10 and B-10'), -0.46 (d, 1B), -2.80 (d, 5B), -3.45, (d, 1B), -4.16 (d, 1B), -6.63 (d, 1B), -11.25 (d, 1B), -13.01 (d, 1B), -14.18 (d, 1B) coincidence of 12 dublets of B atoms 4,5,7,9,11,12,4'5',7', 9',11',12', -22.44 (d, 1B, B-6 or B-6'), -23.67 (d, 1B, B-6 or B-6'); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -76.92 (m, 3F), -108.93 (m, 2F), -118.04 (m, 2F), -119.02 (m, 2F), -119.13 (m, 2F), -122.27 (m, 2F); IR ($CHCl_3$) ν 2595,



1667, 1360, 1243, 973 cm^{-1}; MS (ESI, m/z (rel.%)) 761 (M^+-H, 7), 386 (6); HR-MS (ESI) calcd. for $C_{14}H_{25}B_{18}CoF_{13}S_2$ [M^+-H] 761.2203, found 761.2199. R_f(5/1 hexane/Et_2O) = 0.33.

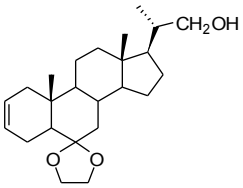
8,8'-μ-(5,5,6,6,7,7,7-Heptafluorohept-2-ene-1-yldithiolato)-[3,3'-como-cobalt(III)-bis-(1,2-dicarbaundecaborate)] (37b). The reaction was carried out with **32** (100 mg, 0.23 mmol) and **1b** (98 mg, 0.46 mmol) according to the general procedure. Column chromatography on silica gel (5/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 3/1 MeOH/water – washing of the non-fluorinated starting material, 2nd elution Et_2O – washing of the product) and the crystallization (heptane/CH_2Cl_2) yielded **37b** (58 mg, 41%) as orange crystals: mp 210-212 °C (heptane/CH_2Cl_2); ^{1}H NMR (600 MHz, $CDCl_3$) δ 2.88-2.99 (m, 2H, H-4'), 3.28 (bs, 1H, C_{carb}-H), 3.45 (bs, 1H, C_{carb}-H), 3.64 (bs, 1H, C_{carb}-H), 3.70 (bs, 1H, C_{carb}-H), 4.02 (ddm, J_{gem} = 12.7 Hz, $J_{1'b,2'}$ = 6.6 Hz, 1H, H-1'b), 4.43 (dd, J_{gem} = 12.7 Hz, $J_{1'a,2'}$ = 8.8 Hz, 1H, H-1'a), 5.76 (dm, $J_{2',3'}$ = 15.3 Hz, 1H, H-2'), 6.00 (dm, $J_{3',2'}$ = 15.3 Hz, 1H, H-3'); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 34.33 (t, $J_{4',F}$ = 23.0 Hz, CH_2-4'), 48.78 (CH_2-1'), 48.57, 50.46, 51.47, 51.91 (4C, CH_{carb}), 126.58 (CH-2'), 128.78 (t, $J_{3',F}$ = 4.3 Hz, CH-3'); ^{11}B NMR (160.4 MHz, $CDCl_3$, $BF_3{\cdot}Et_2O$) δ 23.26 (s, 1B, B-8 or 8'), 21.11 (s, 1B, B-8 or 8'), 2.44 (d, J = 146 Hz, 2B, B-10 and 10'), -0.59 (d, 1B), -2.89 (d, 5B), -3.56, (d, 1B), -4.16 (d, 1B), -7.04 (d, 1B), -11.26 (d, 1B), -13.41 (d, 1B) , -14.44 (d, 1B) coincidence of 12 dublets of B atoms 4,5,7,9,11, 12,4',5',7',9',11',12', -22.44 (d, 1B, B-6 or B-6'), -24.07 (d, 1B, B-6 or B-6'); ^{19}F NMR (470.3 MHz, $CDCl_3$, C_6F_6) δ -76.67 (m, 3F), -109.95 (m, 2F), -123.46 (m, 2F); IR ($CHCl_3$) ν 3048, 2596, 1668, 1353, 1229, 972 cm^{-1}; MS (EI, m/z (rel.%)) 612 (M^+, 7), 448 (16), 382 (91), 338 (34), 223 (75); HR-MS (ESI) calcd. for $C_{11}H_{26}B_{18}CoF_7S_2$ [M^+] 612.2371, found 612.2368. R_f(5/1 hexane/Et_2O) = 0.52.

Methyl (20*S*)-6,6-ethylenedioxy-5α-pregn-2-ene-20-carboxylate (42). A mixture of methyl (20*S*)-6-oxo-5α-pregn-2-ene-20-carboxylate **41**[81] (2.7 g, 7.5 mmol), ethylene glycol (7.0 mL, 126 mmol), *p*-toluenesulfonic acid monohydrate (26 mg, 0.14 mmol), triethoxymethane (8.2 mL, 49.3 mmol), and benzene (80 mL) was stirred at 40 °C for 4 days. The mixture was poured into of EtOAc (50 mL), washed with saturated aqueous solution of $KHCO_3$ (50 mL), water (50 mL), and dried over anhydrous $MgSO_4$. Evaporation of the volatiles under reduced pressure afforded 2.58 g (85%) of the title compound **42** as white crystals: mp 158-160 °C

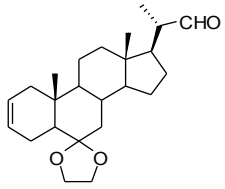


(acetone/heptane); $[\alpha]_D^{20}$ +47.6 (*c* 0.25, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 0.88 (s, 3H, 3 × H-19), 1.19 (d, $J_{21,20}$ = 6.8 Hz, 3H, 3 × H-21), 2.43 (dq, $J_{20,17}$ = 10.5 Hz, $J_{20,21}$ = 6.8 Hz, 1H, H-20), 3.64 (s, 3H, OCH_3), 3.78, 3.90, 3.93, and 3.98 (m, 4H, 2 × H-1' and 2 × H-2'), 5.54 (m, 1H, H-2), 5.66 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.14 (CH_3-18), 13.58 (CH_3-19), 17.08 (CH_3-21), 20.79 (CH_2-11), 21.41 (CH_2-4), 24.19 (CH_2-15), 27.05 (CH_2-16), 33.34 (CH-8), 35.89 (C-10), 39.53 (CH_2-12), 41.16 (CH_2-1), 41.19 (CH_2-7), 42.46 (CH-20), 42.60 (C-13), 48.04 (CH-5), 51.34 (OCH_3), 52.89 (CH-17), 53.37 (CH-9), 55.53 (CH-14), 64.10 (CH_2-1'), 65.57 (CH_2-2'), 109.94 (C-6), 124.74 (CH-2), 126.67 (CH-3), 177.34 (C(=O)-O); IR ($CHCl_3$) ν 3065, 3026, 1727, 1657, 1472, 1436, 1168, 1083, 1042, 949; MS (ESI, m/z (rel.%)) 403.1 (M^++1, 100), 311 (8); HR-MS (ESI), calc. for $C_{25}H_{39}O_4$ [M^++1] 403.2843; found 403.2842.

(20*S*)-6,6-Ethylendioxy-5α-pregn-2-en-20-yl-methanol (43). Methyl ester **42** (2.9 g, 7.2 mmol) was dissolved in dried THF (25 mL). To this mildly stirred and ice-cooled solution was cautiously added $LiAlH_4$ (7.9 mL of 1M solution in Et_2O, 7.9 mmol). The suspension was further stirred at 25 °C under an argon atmosphere and the course of the reaction was monitored by TLC (1/1 hexane/Et_2O). After 2 h (the reaction was finished) an excess of $LiAlH_4$ was decomposed by addition of 2/1 mixture of EtOAc/H_2O (6 mL). The resulting suspension was filtered, washed with EtOAc, and the filtrate was dried over anhydrous $MgSO_4$. Evaporation of the volatiles under reduced pressure followed by column chromatography on silica gel (1/1 hexane/Et_2O) yielded 2.37 g (88%) of the title compound **43** as white crystals: mp 113-114 °C; $[\alpha]_D^{20}$ +72.1 (*c* 0.16, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.71 (s, 3H, 3 × H-18), 0.88 (s, 3H, 3 × H-19), 1.05 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 3.36 (dd, J_{gem} = 10.5 Hz, $J_{22b,20}$ = 6.9 Hz, 1H, H-22b), 3.63 (dd, J_{gem} = 10.5 Hz, $J_{22a,20}$ = 3.3 Hz, 1H, H-22a), 3.74-4.02 (m, 4H, 2 × H-1'and 2 × H-2'), 5.54 (m, 1H, H-2), 5.66 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.02 (CH_3-18), 13.57 (CH_3-19), 16.71 (CH_3-21), 20.82 (CH_2-11), 21.40 (CH_2-4), 24.22 (CH_2-15), 27.60 (CH_2-16), 33.35 (CH-8), 35.86 (C-10), 38.71 (CH-20), 39.59 (CH_2-12), 41.19 (2 × C, CH_2-1 and CH_2-7), 42.60 (C-13), 48.04 (CH-5), 52.42 (CH-17), 53.40 (CH-9), 55.67 (CH-14), 64.08 (CH_2-1'), 65.55 (CH_2-2'), 67.94 (CH_2-22), 110.01 (C-6), 124.77 (CH-2), 125.65 (CH-3); IR ($CHCl_3$) ν 3629, 3492, 3067, 1657, 1388, 1306, 1185, 999 cm^{-1}; MS (EI, m/z (rel. %)) 374 (M^+, 32), 359 (6), 259 (5), 237 (100), 165 (19); HR-MS (EI) calcd. for $C_{24}H_{38}O_3$ [M^+] 374.2821, found 374.2825. R_f(1/1 hexane/ Et_2O) = 0.29.

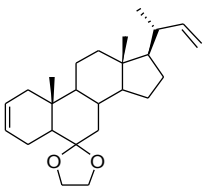


(20*S*)-6,6-Ethylendioxy-5α-pregn-2-en-20-yl-formaldehyd (44).[82] A solution of the compound **43** (2.0 g, 5.34 mmol) in CH_2Cl_2 (20 mL) was added to a stirred solution of Dess-



Martin reagent (2.49 g, 5.87 mmol) in CH_2Cl_2 (10 mL) over 2 min. After 20 min the solution was diluted with of Et_2O (30 mL) and poured into saturated aqueous solution of $NaHCO_3$ (30 mL) containing $Na_2S_2O_3$ (7 g). The mixture was stirred for 5 min, after that Et_2O (30 mL) was added, and the ether layers were separated. Then it was extracted with saturated aqueous solution of $NaHCO_3$ (30 mL), water (30 mL), and dried over $MgSO_4$. Evaporation of the volatiles under reduced pressure followed by column chromatography on silica gel (4/1 hexane/Et_2O) afforded 1.52 g (76%) of the title compound **44** as a colorless oil: $[\alpha]_D^{20}$ +28.9 (*c* 0.13, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.74 (s, 3H, 3 × H-18), 0.90 (s, 3H, 3 × H-19), 1.13 (d, $J_{21,20}$ = 6.8 Hz, 3H, 3 × H-21), 2.36 (m, 1H, H-20), 3.63 (dd, J_{gem} = 10.5 Hz, $J_{22a,20}$ = 3.3 Hz, 1H, H-22a), 3.79 (m, 1H, H-1'a), 3.91 (m, 1H, H-1'b), 3.94 (m, 1H, H-2'a), 3.98 (m, 1H, H-2'b), 5.54 (m, 1H, H-2), 5.66 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.36 (CH_3-18), 13.42 (CH_3-21), 13.58 (CH_3-19), 20.79 (CH_2-11), 21.40 (CH_2-4), 24.51 (CH_2-15), 26.94 (CH_2-16), 33.32 (CH-8), 35.90 (C-10), 39.45 (CH_2-12), 41.15 (CH_2-1), 41.18 (CH_2-7), 43.15 (C-13), 48.04 (CH-5), 49.48 (CH-20), 51.00 (CH-17), 53.40 (CH-9), 55.20 (CH-14), 64.11 (CH_2-1'), 65.58 (CH_2-2'), 109.90 (C-6), 124.70 (CH-3), 125.68 (CH-2), 205.20 (C-22); IR ($CHCl_3$) ν 1725, 1658, 1388, 1472, 1306, 1185, 950 cm^{-1}; MS (APCI, m/z (rel.%)) 373 (M^++1, 42), 359 (56), 343 (70), 315 (15), 281 (21); HR-MS (APCI) calcd. for $C_{24}H_{36}O_3$ [M^++1] 373.2737, found 373.2732. R_f(4/1 hexane/Et_2O) = 0.36.

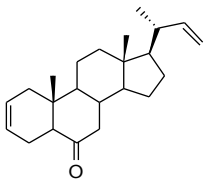
(20*S*)-6,6-Ethylendioxy-20-ethenyl-5α-pregn-2-en-6-one (45).[52] The reaction was carried



out with **44** (1.6 g, 4.3 mmol) and methyl triphenylphosphonium bromide (2.3 g, 6.44 mmol) according to the general procedure (page 59). Column chromatography on silica gel (5/1 hexane/Et_2O) afforded 1.52 g (93%) of the title compound **45** as a colorless oil: $[\alpha]_D^{20}$ +52.6 (*c* 0.22, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.71 (s, 3H, 3 × H-18), 0.88 (s, 3H, 3 × H-19), 1.03 (d, $J_{21,20}$ = 6.7 Hz, 3H, 3 × H-21), 3.74-4.02 (m, 4H, 2 × H-1'and 2 × H-2'), 4.81 (bdd, $J_{23b,22}$ = 10.2 Hz, J_{gem} = 2.1 Hz, 1H, H-23b), 4.90 (ddd, $J_{23a,22}$ = 17.1 Hz, J_{gem} = 2.1 Hz, $J_{23a,20}$ = 1.0 Hz, 1H, H-23a), 5.54 (m, 1H, H-2), 5.66 (m, 1H, H-3), 5.66 (ddd, $J_{22,23a}$ = 17.1 Hz, $J_{22,23b}$ = 10.2 Hz, $J_{22,20}$ = 8.4 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.14 (CH_3-18), 13.58 (CH_3-19), 20.09

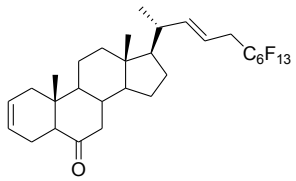
(CH_3-21), 20.83 (CH_2-11), 21.41 (CH_2-4), 24.13 (CH_2-15), 28.30 (CH_2-16), 33.32 (CH-8), 35.88 (C-10), 39.65 (CH_2-12), 41.19 (CH_2-7), 41.21 (CH-20), 41.23 (CH_2-1), 42.50 (C-13), 48.06 (CH-5), 53.46 (CH-9), 55.43 (CH-17), 55.96 (CH-14), 64.06 (CH_2-1'), 65.55 (CH_2-2'), 110.01 (C-6), 111.53 (CH_2-23), 124.78 (CH-2), 125.67 (CH-3), 145.23 (CH-22); IR ($CHCl_3$) ν 3067, 3028, 1657, 1637, 1472, 1380, 1001, 914 cm^{-1}; MS (EI, m/z (rel.%)) 370 (M^+, 47), 355 (6), 259 (5), 233 (100), 165 (29); HR-MS (EI) calcd. for $C_{25}H_{38}O_2$ [M^+] 370.2871, found 370.2870. R_f(10/1 hexane/Et_2O) = 0.48.

(20*S*)-20-Ethenyl-5α-pregn-2-en-6-one (46). 4-Methylbenzenesulfonic acid (57 mg, 0.33 mmol) was added to a solution of **45** (1.22 g, 3.29 mmol) in acetone (40 mL) and the mixture was stirred at 25 °C for 24 h. After completion of the reaction (TLC 10/1 hexane/Et_2O), volatiles were evaporated under reduced pressure. The residue was dissolved in EtOAc (100 mL), washed with a saturated aqueous solution of $NaHCO_3$ (100 mL), water (3 × 100 mL), and dried over anhydrous $MgSO_4$. Evaporation of the volatiles under reduced pressure followed by column chromatography on silica gel (5/1 hexane/Et_2O) and crystallization (MeOH) yielded 1.03 g (96%) of the title compound **46** as a white needles: mp 102-105 °C; $[\alpha]_D^{20}$ +14.7 (*c* 0.20, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 0.71 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.24 (m, 1H, H-4a), 2.35 (m, 1H, H-5), 2.35 (dd, J_{gem} = 13.3 Hz, $J_{7a,8}$ = 4.2 Hz, 1H, H-7a), 4.83 (bdd, $J_{23b,22}$ = 10.2 Hz, J_{gem} = 2.0 Hz, 1H, H-23b), 4.91 (ddd, $J_{23a,22}$ = 17.1 Hz, J_{gem} = 2.0 Hz, $J_{23a,20}$ = 1.0 Hz, 1H, H-23a), 5.57 (m, 1H, H-2), 5.66 (ddd, $J_{22,23a}$ = 17.1 Hz, $J_{22,23b}$ = 10.2 Hz, $J_{22,20}$ = 8.4 Hz, 1H, H-22), 5.69 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.09 (CH_3-18), 13.49 (CH_3-19), 20.05 (CH_3-21), 21.07 (CH_2-11), 21.69 (CH_2-4), 23.91 (CH_2-15), 28.16 (CH_2-16), 37.66 (CH-8), 39.32 (CH_2-12), 39.34 (CH_2-1), 40.02 (C-10), 41.11 (CH-20), 42.77 (C-13), 46.96 (CH_2-7), 53.37 (CH-9), 53.80 (CH-5), 55.33 (CH-17), 56.73 (CH-14), 111.80 (CH_2-23), 124.49 (CH-2), 124.93 (CH-3), 144.91 (CH-22), 212.04 (C-6); IR ($CHCl_3$) ν 3067, 3027, 1702, 1657, 1637, 1389, 998 cm^{-1}; MS (EI, m/z (rel.%)) 326 (M^+, 100), 311 (96), 298 (25), 277 (10), 149 (29); HR-MS (EI) calcd. for $C_{23}H_{34}O$ [M^+] 326.2610, found 326.2608. R_f(20/1 hexane/EtOAc) = 0.29.



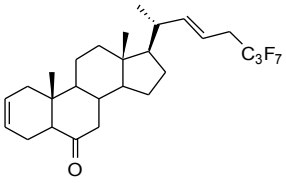
(20*S*)-20-(4',4',5',5',6',6',7',7',8',8',9',9',9'-Tridecafluorononon-1'-en-1'-yl)-5α-pregn-2-en-6-one (47a). The reaction was carried out with **46** (250 mg, 0.77 mmol) and **1a** (551 mg, 1.53 mmol) according to the general procedure. Column chromatography on silica gel (50/1

hexane/EtOAc) and crystallization (MeOH) yielded 338 mg (67%) of the title compound **47a**



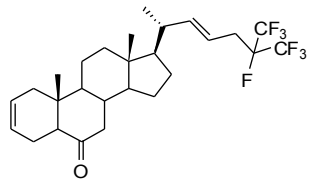
as white needles: mp 101-102 °C; $[\alpha]_D^{20}$ +6.4 (*c* 0.22, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 0.72 (s, 3H, 3 × H-19), 1.05 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.75 (m, 2H, H-24), 5.32 (dt, $J_{23,22}$ = 15.2 Hz, $J_{23,24}$ = 7.2 Hz, 1H, H-23), 5.55 (ddt, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, $J_{22,24}$ = 1.3 Hz, 1H, H-22), 5.57 (m, 1H, H-2), 5.69 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.11 (CH_3-18), 13.49 (CH_3-19), 20.10 (CH_3-21), 21.07 (CH_2-11), 21.70 (CH_2-4), 23.91 (CH_2-15), 28.04 (CH_2-16), 37.65 (CH-8), 37.72 (t, $J_{24,F}$ = 21.6 Hz, CH_2-24), 39.33 (CH_2-12), 39.34 (CH_2-1), 40.02 (C-10), 40.13 (CH-20), 42.81 (C-13), 46.94 (CH_2-7), 53.37 (CH-9), 53.82 (CH-5), 55.32 (CH-17), 56.71 (CH-14), 113.89 (CH-23), 124.49 (CH-2), 124.95 (CH-3), 145.93 (CH-22), 211.99 (C-6); IR ($CHCl_3$) ν 3030, 1702, 1657, 1388, 1364, 1351, 973 cm^{-1}; MS (EI, m/z (rel.%)) 658 (M^+, 100), 643 (86), 630 (25), 413 (7), 387 (13), 326 (8), 229 (7); HR-MS (EI) calcd. for $C_{30}H_{35}OF_{13}$ [M^+] 658.2480, found 658.2485. R_f(20/1 hexane/EtOAc) = 0.24.

(20*S*)-20-(4',4',5',5',6',6',6'-Heptafluorohex-1'-en-1'-yl)-5α-pregn-2-en-6-one (47b). The



reaction was carried out with **46** (360 mg, 1.1 mmol) and **1b** (463 mg, 2.2 mmol) according to the general procedure. Column chromatography on silica gel (50/1 hexane/EtOAc) and crystallization (MeOH) yielded 397 mg (71%) of the title compound **47b** as white crystals: mp 117-119 °C; $[\alpha]_D^{20}$ +12.9 (*c* 0.20, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.70 (s, 3H, 3 × H-18), 0.72 (s, 3H, 3 × H-19), 1.05 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.75 (m, 2H, H-24), 5.32 (dt, $J_{23,22}$ = 15.3 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.55 (ddt, $J_{22,23}$ = 15.3 Hz, $J_{22,20}$ = 8.8 Hz, $J_{22,24}$ = 1.2 Hz, 1H, H-22), 5.57 (m, 1H, H-2), 5.69 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.11 (CH_3-18), 13.49 (CH_3-19), 20.10 (CH_3-21), 21.07 (CH_2-11), 21.70 (CH_2-4), 23.91 (CH_2-15), 28.03 (CH_2-16), 37.48 (t, $J_{24,F}$ = 22.5 Hz, CH_2-24), 37.65 (CH-8), 39.33 (CH_2-12), 39.34 (CH_2-1), 40.02 (C-10), 40.11 (CH-20), 42.81 (C-13), 46.94 (CH_2-7), 53.38 (CH-9), 53.83 (CH-5), 55.34 (CH-17), 56.71 (CH-14), 113.91 (t, $J_{23,F}$ = 4.2 Hz, CH-23), 124.48 (CH-2), 124.95 (CH-3), 144.97 (CH-22), 211.93 (C-6); IR ($CHCl_3$) ν 3028, 1703, 1657, 1382, 1353, 1351, 974 cm^{-1}; MS (ESI, m/z (rel.%)) 509 (M^++1, 18), 335 (8), 310 (5), 256 (7), 234 (37); HR-MS (ESI) calcd. for $C_{27}H_{36}OF_7$ [M^++1] 509.2649, found 509.2650. R_f (20/1 hexane/EtOAc) = 0.24.

22-(*E*)-(20*S*)-25,26,26,26,27,27,27-Heptafluoro-cholesta-2,22-dien-6-one (47c). The



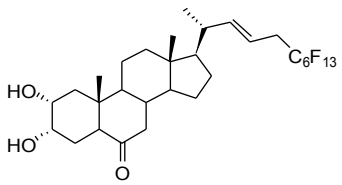
reaction was carried out with **46** (340 mg, 1.04 mmol) and **1c** (440 mg, 2.0 mmol) according to the general procedure. Column chromatography on silica gel (50/1 hexane/EtOAc) and crystallization (MeOH) yielded 315 mg (59%) of the title compound **47c** as white crystals: mp 125-126 °C; $[\alpha]_D^{20}$ +19.5 (*c* 0.17, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.69 (s, 3H, 3 × H-18), 0.71 (s, 3H, 3 × H-19), 1.03 (d, $J_{21,20}$ = 6.7 Hz, 3H, 3 × H-21), 2.77 (bdd, $J_{24,F}$ = 20.0 Hz, $J_{24,23}$ = 7.0 Hz, 2H, H-24), 5.30 (bdt, $J_{23,22}$ = 15.1 Hz, $J_{23,24}$ = 7.0 Hz, 1H, H-23), 5.52 (bdd, $J_{22,23}$ = 15.1 Hz, $J_{22,20}$ = 8.8 Hz, 1H, H-22), 5.57 (m, 1H, H-2), 5.69 (m, 1H, H-3); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.07 (CH_3-18), 13.48 (CH_3-19), 20.06 (CH_3-21), 21.06 (CH_2-11), 21.70 (CH_2-4), 23.93 (CH_2-15), 27.98 (CH_2-16), 32.54 (t, $J_{24,F}$ = 20.7 Hz, CH_2-24), 37.63 (CH-8), 39.33 (CH_2-12), 39.34 (CH_2-1), 40.01 (C-10), 40.07 (CH-20), 42.81 (C-13), 46.93 (CH_2-7), 53.37 (CH-9), 53.82 (CH-5), 55.35 (CH-17), 56.68 (CH-14), 91.29 (dsept., $J_{25,F}$ = 203.0 Hz, $J_{C\text{-}C\text{-}F}$ = 30.5 Hz, CF-25), 114.96 (d, $J_{23,F}$ = 5.9 Hz, CH-23), 124.47 (CH-2), 124.94 (CH-3), 144.31 (CH-22), 211.92 (C-6); IR ($CHCl_3$) ν 3027, 1703, 1657, 1382, 1353, 1305, 975 cm^{-1}; MS (ESI, m/z (rel.%)) 509 (M^++1, 10), 437 (3), 392 (4), 335 (18), 256 (7), 234 (36); HR-MS (ESI) calcd. for $C_{27}H_{36}OF_7$ [M^++1] 509.2649, found 509.2649. R_f(20/1 hexane/EtOAc) = 0.24.

General Procedure for Dihydroxylation.[39] A solution of OsO_4 (13 mg, 0.05 mmol) in 2-methyl-propan-2-ol (0.12 mL) was added to a solution of olefins **47a-47c** (0.35 mmol) in acetone (8 mL) and THF (8 mL). Next, *N*-methylmorpholine *N*-oxide (140 mg, 1.2 mmol) in water (0.2 mL) was added. The mixture was stirred under an argon atmosphere for 16 h at room temperature. A solution of sodium sulfite (5 mL, 10%) was then added and the mixture was stirred for 30 min, poured into water, and extracted with chloroform. Column chromatography on silica gel (1/2 hexane/EtOAc) yielded compounds **49a-49c** as colorless oils and crystallization (heptane/acetone) yielded compounds **49a-49c** as white crystals.

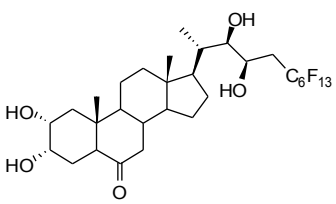
22-(*E*)-(20*S*)-2α,3α-Dihydroxy-20-(4',4',5',5',6',6',7',7',8',8',9',9',9'-tridecafluorononen-1'-en-1'-yl)-5α-pregnan-6-one (48a) and (20*S*,1'*R*,2'*R*)-2α,3α,1',2'-tetrahydroxy-20-(4',4',5',5',6',6',7',7',8',8',9',9',9'-tridecafluorononen-1'-yl)-5α-pregnan-6-one (49a). The reaction was carried out with **47a** (100 mg, 0.15 mmol) according to the general procedure for

2 h. Column chromatography on silica gel (1/2 hexane/EtOAc) afforded 21 mg (19%) of the compound **48a** as a colorless oil and 34 mg (31%) of the compound **49a** as white crystals.

48a: $[\alpha]_D^{20}$ –83.3 (*c* 0.08, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.68 (s, 3H, 3 × H-18), 0.76 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.68 (bdd, $J_{5,4a}$ = 12.5 Hz, $J_{5,4b}$ = 3.0 Hz, 1H, H-5), 2.75 (m, 2H, H-24), 3.78 (m, 1H, H-2), 4.06 (m, 1H, H-3), 5.31 (dt, $J_{23,22}$ = 15.2 Hz, $J_{23,24}$ = 7.1 Hz, 1H, H-23), 5.54 (bdd, $J_{22,23}$ = 15.2 Hz, $J_{22,20}$ = 8.8 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.18 (CH_3-18), 13.53 (CH_3-19), 20.08 (CH_3-21), 21.13 (CH_2-11), 23.89 (CH_2-15), 26.20 (CH_2-4), 28.03 (CH_2-16), 34.71 (t, $J_{24,F}$ = 22.4 Hz, CH_2-24), 37.62 (CH-8), 39.20 (CH_2-12), 40.02 (CH_2-1), 40.12 (CH-20), 42.58 (C-10), 42.92 (C-13), 46.67 (CH_2-7), 50.68 (CH-5), 53.65 (CH-9), 55.24 (CH-17), 56.60 (CH-14), 68.27 (CH-2), 68.34 (CH-3), 113.92 (CH-23), 144.97 (CH-22), 212.24 (C-6); IR ($CHCl_3$) ν 3612, 3579, 1706, 1382, 1363, 1242, 974 cm^{-1}; MS (ESI, m/z (rel.%)) 692 (M^+, 16), 578 (76), 413 (45), 301 (53), 279 (38); HR-MS (ESI) calcd. for $C_{30}H_{36}O_3F_{13}$ [M^+-1] 691.2462, found 691.2464. R_f(2/3 toluene/EtOAc) = 0.30.



49a: mp 220-221 °C (acetone/heptane); $[\alpha]_D^{20}$ –1.9 (*c* 0.11, MeOH); ^{1}H NMR (600 MHz, CD_3OD) δ 0.70 (s, 3H, 3 × H-18), 0.76 (s, 3H, 3 × H-19), 1.06 (d, $J_{21,20}$ = 6.8 Hz, 3H, 3 × H-21), 2.48 (m, 1H, H-24a), 2.69 (ddd, $J_{5,4a}$ = 12.6 Hz, $J_{5,4b}$ = 3.4 Hz, $J_{5,7a}$ = 0.8 Hz, 1H, H-5), 3.52 (dd, $J_{22,20}$ = 4.6 Hz, $J_{22,23}$ = 1.7 Hz, 1H, H-22); 3.77 (ddd, $J_{2,1b}$ = 11.8 Hz, $J_{2,1a}$ = 4.8 Hz, $J_{2,3}$ = 3.2 Hz, 1H, H-2), 4.06 (q, $J_{3,2} \sim J_{3,4a} \sim J_{3,4b}$ = 3.3 Hz, 1H, H-3), 4.30 (ddd, $J_{23,24b}$ = 8.0 Hz, $J_{23,24a}$ = 3.8 Hz, $J_{23,22}$ = 1.7 Hz, 1H, H-23); ^{13}C NMR (150.9 MHz, CD_3OD) δ 11.94 (CH_3-18), 13.54 (CH_3-19), 14.14 (CH_3-21), 21.15 (CH_2-11), 24.08 (CH_2-15), 26.42 (CH_2-4), 27.45 (CH_2-16), 36.89 (t, $J_{24,F}$ = 20.1 Hz, CH_2-24), 37.60 (CH-20), 39.32 (CH_2-12), 40.15 (CH_2-1), 41.36 (CH-8), 42.52 (C-13), 43.52 (C-10), 46.64 (CH_2-7), 50.69 (CH-5), 53.03 (CH-9), 53.61 (CH-17), 56.11 (CH-14), 64.03 (CH-23), 68.25 (CH-2), 68.35 (CH-3), 74.98 (CH-22), 211.92 (C-6); IR (KBr) ν 3439, 1711, 1699, 1364, 1241, 1046 cm^{-1}; MS (ESI, m/z (rel.%)) 726 (M^+, 6), 590 (18), 493 (4), 416 (9), 316 (47), 288 (100); HR-MS (ESI) calcd. for $C_{30}H_{39}O_5F_{13}Na$ [M^++Na] 749.2482, found 749.2476. R_f (2/3 toluene/EtOAc) = 0.23.



(20*S*,1'*R*,2'*R*)-2α,3α,1',2'-Tetrahydroxy-20-(4',4',5',5',6',6',7',7',8',8',9',9',9'-trideca-fluoronon-1'-yl)-5α-pregnan-6-one (49a). The reaction was carried out with **47a** (115 mg,

0.17 mmol) and the reaction time was prolonged for 16 h. Column chromatography on silica gel (1/2 hexane/EtOAc) afforded 86 mg (68%) of the title compound **49a** as white crystals.

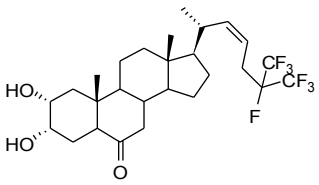
(20*S*,1'*R*,2'*R*)-2α,3α,1',2'-Tetrahydroxy-20-(4',4',5',5',6',6',6'-heptafluorohex-1'-yl)-5α-pregnan-6-one (49b). The reaction was carried out with **47b** (190 mg, 0.37 mmol) and the reaction time was prolonged for 16 h. Column chromatography on silica gel (1/2 hexane/EtOAc) afforded 107 mg (50%) of the title compound **49b** as white crystals: mp 176-178 °C; $[\alpha]_D^{20}$ –23.9 (*c* 0.13, $CHCl_3$); ^{1}H NMR (600 MHz, CD_3OD) δ 0.75 (s, 3H, 3 × H-18), 0.77 (s, 3H, 3 × H-19), 1.10 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.40 (m, 2H, H-24), 2.74 (bdd, $J_{5,4a}$ = 11.5 Hz, $J_{5,4b}$ = 3.4 Hz, 1H, H-5), 3.44 (dd, $J_{22,20}$ = 4.9 Hz, $J_{22,23}$ = 1.5 Hz, 1H, H-22), 3.66 (ddd, $J_{2,1a}$ = 11.8 Hz, $J_{2,1b}$ = 4.8 Hz, $J_{2,3}$ = 3.0 Hz, 1H, H-2), 3.95 (bq, $J_{3,2}$ = 3.0, 1H, H-3), 4.22 (ddd, $J_{23,24a}$ = 7.8 Hz, $J_{23,24}$ = 3.9 Hz, $J_{23,22}$ = 1.5 Hz, 1H, H-23); ^{13}C NMR (150.9 MHz, CD_3OD) δ 12.33 (CH_3-18), 13.87 (CH_3-19), 14.78 (CH_3-21), 22.35 (CH_2-11), 25.16 (CH_2-15), 27.86 (CH_2-4), 28.62 (CH_2-16), 34.70 (t, $J_{24,F}$ = 20.0 Hz, CH_2-24), 39.16 (CH-8), 40.76 (CH_2-12), 40.98 (CH_2-1), 42.72 (CH-20), 43.61 (C-10), 44.70 (C-13), 47.48 (CH_2-7), 52.07 (CH-5), 54.52 (CH-17), 55.05 (CH-14), 57.44 (CH-9), 65.02 (CH-23), 69.13 (CH-2), 69.48 (CH-3), 75.93 (CH-22), 215.05 (C-6); IR (KBr) ν 3432, 1703, 1630, 1388, 1354, 1198, 999 cm^{-1}; MS (ESI, m/z (rel.%)) 576 (M^+, 22), 559 (8), 533 (25), 515 (7), 496 (6); HR-MS (ESI) calcd. for $C_{27}H_{40}O_5F_7$ [M^++1] 577.2758, found 577.2759. R_f(20/1 toluene/EtOAc) = 0.23.

(20*S*,22*R*,23*R*)-2α,3α,22,23-Tetrahydroxy-25,26,26,26,27,27,27-heptafluoro-cholestan-6-one (49c) and 22-(*Z*)-(20*S*)-2α,3α-dihydroxy-25,26,26,26,27,27,27-heptafluoro-cholesta-22-en-6-one (48c). The reaction was carried out with **47c** (190 mg, 0.37 mmol). Column chromatography on silica gel (1/2 hexane/EtOAc) afforded 98 mg (46%) of the title compound **49c** as white crystals and 11 mg (5%) of the compound *cis*-**48c** as a colorless oil.

49c: mp 153-154 °C; $[\alpha]_D^{20}$ –12.0 (*c* 0.16, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.74 (s, 3H, 3 × H-18), 0.77 (s, 3H, 3 × H-19), 1.09 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.42 (m, 2H, H-24), 2.74 (ddd, $J_{5,4a}$ = 12.5 Hz, $J_{5,4b}$ = 3.4 Hz, $J_{5,7a}$ = 1.0 Hz, 1H, H-5), 3.41 (dd, $J_{22,20}$ = 5.0 Hz, $J_{22,23}$ = 1.5 Hz, 1H, H-22), 3.66 (ddd, $J_{2,1a}$ = 11.8 Hz, $J_{2,1b}$ = 4.8 Hz, $J_{2,3}$ = 3.0 Hz, 1H, H-2), 3.95 (bq, $J_{3,2} \sim J_{3,4a} \sim J_{3,4b}$ = 3.0, 1H, H-3), 4.16 (bd, $J_{23,24a}$ = 7.8 Hz, 1H, H-

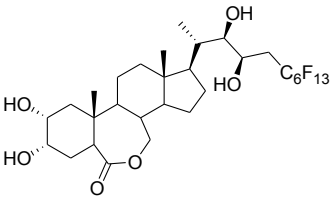
23); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.34 (CH_3-18), 13.88 (CH_3-19), 14.70 (CH_3-21), 22.34 (CH_2-11), 25.15 (CH_2-15), 27.85 (CH_2-4), 28.57 (CH_2-16), 36.18 (d, $J_{24,F}$ = 18.7 Hz, CH_2-24), 39.14 (CH-8), 40.74 (CH_2-12), 40.97 (CH_2-1), 42.71 (CH-20), 43.61 (C-10), 44.71 (C-13), 47.48 (CH_2-7), 52.06 (CH-5), 54.48 (CH-17), 55.02 (CH-14), 57.43 (CH-9), 65.61 (CH-23), 69.13 (CH-2), 69.47 (CH-3), 76.61 (CH-22), 215.04 (C-6); IR ($CHCl_3$) ν 3624, 3574, 1705, 1383, 1353, 1160, 998 cm^{-1}; MS (ESI, m/z (rel.%)) 575 (M^+-1, 8), 554 (12), 515 (7), 411 (6); HR-MS (ESI) calcd. for $C_{27}H_{40}O_5F_7$ [M^++1] 577.2758, found 577.2759. R_f (20/1 toluene/EtOAc) = 0.23.

48c: $[\alpha]_D^{20}$ –19.2 (*c* 0.12, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.71 (s, 3H, 3 × H-18), 0.77 (s, 3H, 3 × H-19), 0.99 (d, $J_{21,20}$ = 6.6 Hz, 3H, 3 × H-21), 2.69 (ddd, $J_{5,4a}$ = 12.6 Hz, $J_{5,4b}$ = 3.4 Hz, $J_{5,7a}$ = 1.0 Hz, 1H, H-5), 2.85 (m, 2H, H-24), 3.77 (m, 1H, H-2), 4.05 (bq, $J_{3,2}$ = 3.0 Hz, 1H, H-3), 5.26 (m, 1H, H-23), 5.47 (tt, $J_{22,20} \sim J_{22,23}$ = 10.6 Hz, $J_{22,24a} \sim J_{22,24b}$ = 1.3 Hz, 1H, H-22); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 12.28 (CH_3-18), 13.56 (CH_3-19), 19.95 (CH_3-21), 21.13 (CH_2-11), 23.85 (CH_2-15), 26.25 (CH_2-4), 27.15 (t, $J_{24,F}$ = 21.0 Hz, CH_2-24), 27.69 (CH_2-16), 34.37 (CH-20), 37.59 (CH-8), 39.25 (CH_2-12), 40.15 (CH_2-1), 42.56 (C-10), 42.90 (C-13), 46.67 (CH_2-7), 50.68 (CH-5), 53.70 (CH-9), 55.61 (CH-17), 56.57 (CH-14), 68.25 (CH-2), 68.36 (CH-3), 113.49 (CH-23), 142.00 (CH-22), 212.04 (C-6); IR ($CHCl_3$) ν 3615, 3578, 1705, 1382, 1352, 1246, 973 cm^{-1}; MS (ESI, m/z (rel.%)) 542 (M^+, 9), 507 (1), 411 (7), 386 (2); HR-MS (ESI) calcd. for $C_{27}H_{38}O_3F_7$ [M^++1] 543.2704, found 543.2706. R_f (20/1 toluene/EtOAc) = 0.30.



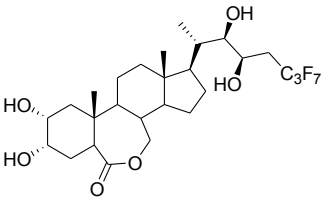
General Procedure for Baeyer-Villiger Oxidation.[116] A solution of trifluoroperoxyacetic acid in CH_2Cl_2 (20 mL), prepared from trifluoroacetic anhydride (3.23 g, 8.24 mmol) and 30% H_2O_2 (0.5 mL, 4.8 mmol), was added to a solution of ketones **49a-49c** (2 mmol) in dichloromethane (16 mL) and stirred for 4 h. Then the reaction mixture was poured into a 10% $KHCO_3$ solution (200 mL), extracted with $CHCl_3$ (3 × 150 mL), the combined organic extracts were washed with water (200 mL), and dried over anhydrous $MgSO_4$. Evaporation of the volatiles followed by column chromatography on silica gel (6/1 EtOAc/hexane) afforded 4/1 mixture of regioisomeric lactones **50/50'**. Further preparative HPLC (6/1 EtOAc/hexane) yielded target compounds **50a-50c**.

(20*S*,1'*R*,2'*R*)-2α,3α,1',2'-Tetrahydroxy-7-oxa-7a-homo-20-(4',4',5',5',6',6',7',7',8',8',9',9',9'-tridecafluorononon-1'-yl)-5α-pregnan-6-one (50a). The



reaction was carried out with **49a** (95 mg, 0.13 mmol) and trifluoroperoxyacetic acid (2 mL). Column chromatography followed by HPLC afforded 60 mg (62%) of the title compound **50a** as a colorless oil: $[\alpha]_D^{20}$ +7.5 (*c* 0.11, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.73 (s, 3H, 3 × H-18), 0.92 (s, 3H, 3 × H-19), 1.05 (d, $J_{21,20}$ = 7.0 Hz, 3H, 3 × H-21), 2.48 (m, 1H, H-24a), 3.12 (dd, $J_{5,4a}$ = 12.3 Hz, $J_{5,4b}$ = 4.5 Hz, 1H, H-5), 3.51 (dd, $J_{22,20}$ = 4.7 Hz, $J_{22,23}$ = 1.6 Hz, 1H, H-22), 3.72 (ddd, $J_{2,1b}$ = 12.1 Hz, $J_{2,1a}$ = 4.7 Hz, $J_{2,3}$ = 2.8 Hz, 1H, H-2), 4.03 (bq, $J_{3,2} \sim J_{3,4a} \sim J_{3,4b}$ = 3.0 Hz, 1H, H-3), 4.08 (m, 2H, H-7), 4.28 (ddd, $J_{23,24b}$ = 7.9 Hz, $J_{23,24a}$ = 3.9 Hz, $J_{23,22}$ = 1.6 Hz, 1H, H-23); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 11.72 (CH_3-18), 14.12 (CH_3-21), 15.44 (CH_3-19), 22.18 (CH_2-11), 24.96 (CH_2-15), 27.42 (CH_2-16), 30.96 (CH_2-4), 36.85 (t, $J_{24,F}$ = 21.1 Hz, CH_2-24), 38.28 (C-10), 39.11 (CH-8), 39.49 (CH_2-12), 40.86 (CH-5), 40.35 (CH-20), 41.40 (CH_2-1), 43.18 (C-13), 50.88 (CH-14), 52.99 (CH-17), 58.11 (CH-9), 64.01 (CH-23), 68.02 (CH-2), 68.08 (CH-3), 70.38 (CH_2-7), 74.92 (CH-22), 176.26 (C-6); IR ($CHCl_3$) ν 3623, 3578, 1721, 1388, 1363, 1164 cm^{-1}; MS (ESI, m/z (rel.%)) 741 (M^+-1, 32), 724 (8), 397 (25), 302 (7); HR-MS (ESI) calcd. for $C_{30}H_{38}O_6F_{13}$ [M^+-1] 741.2466, found 741.2446. R_f(6/1 EtOAc/hexane) = 0.16.

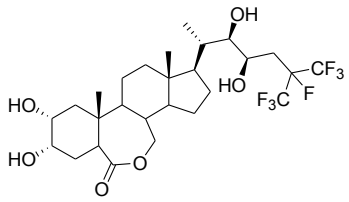
(20*S*,1'*R*,2'*R*)-2α,3α,1',2'-Tetrahydroxy-7-oxa-7a-homo-20-(4',4',5',5',6',6',6'-heptafluorohex-1'-yl)-5α-pregnan-6-one (50b). The reaction was carried out with **49b** (70



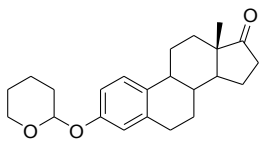
mg, 0.12 mmol) and trifluoroperoxyacetic acid (2 mL). Column chromatography followed by HPLC afforded 51 mg (70%) of the title compound **50b** as a colorless oil: $[\alpha]_D^{20}$ +7.0 (*c* 0.14, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.73 (s, 3H, 3 × H-18), 0.92 (s, 3H, 3 × H-19), 1.05 (d, $J_{21,20}$ = 7.0 Hz, 3H, 3 × H-21), 2.48 (m, 1H, H-24a), 3.12 (dd, $J_{5,4a}$ = 12.3 Hz, $J_{5,4b}$ = 4.5 Hz, 1H, H-5), 3.51 (dd, $J_{22,20}$ = 4.7 Hz, $J_{22,23}$ = 1.6 Hz, 1H, H-22), 3.72 (ddd, $J_{2,1b}$ = 12.1 Hz, $J_{2,1a}$ = 4.7 Hz, $J_{2,3}$ = 2.8 Hz, 1H, H-2), 4.03 (bq, $J_{3,2} \sim J_{3,4a} \sim J_{3,4b}$ = 3.0 Hz, 1H, H-3), 4.08 (m, 2H, H-7), 4.28 (ddd, $J_{23,24b}$ = 7.9 Hz, $J_{23,24a}$ = 3.9 Hz, $J_{23,22}$ = 1.6 Hz, 1H, H-23); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 11.72 (CH_3-18), 14.12 (CH_3-21), 15.44 (CH_3-19), 22.18 (CH_2-11), 24.96 (CH_2-15), 27.42 (CH_2-16), 30.96 (CH_2-4), 36.85 (t, $J_{24,F}$ = 21.1 Hz, CH_2-24), 38.28 (C-10), 39.11 (CH-8), 39.49 (CH_2-12), 40.86 (CH-5), 40.35 (CH-20), 41.40 (CH_2-1), 43.18 (C-13), 50.88 (CH-14), 52.99 (CH-17), 58.11 (CH-9), 64.01 (CH-23), 68.02 (CH-2), 68.08

(CH-3), 70.38 (CH_2-7), 74.92 (CH-22), 176.26 (C-6); IR ($CHCl_3$) ν 3623, 3578, 1721, 1386, 1353, 1182 cm^{-1}; MS (ESI, m/z (rel.%)) 591 (M^+-1, 16), 549 (8), 397 (5), 386 (7), 172 (6); HR-MS (ESI) calcd. for $C_{27}H_{38}O_6F_7$ [M^+-1] 591.2562, found 591.2550. R_f(6/1 EtOAc/hexane) = 0.16.

(20*S*,22*R*,23*R*)-2α,3α,22,23-Tetrahydroxy-7-oxa-7a-homo-25,26,26,26,27,27,27-heptafluoro-cholestan-6-one (50c). The reaction was carried out with **49c** (85 mg, 0.15 mmol) and trifluoroperoxyacetic acid (2 mL). Column chromatography followed by HPLC afforded 54 mg (62%) of the title compound **50c** as a colorless oil: $[\alpha]_D^{20}$ +29.4 (*c* 0.07, MeOH); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.73 (s, 3H, 3 × H-18), 0.92 (s, 3H, 3 × H-19), 1.04 (d, $J_{21,20}$ = 7.0 Hz, 3H, 3 × H-21), 2.75 (m, 1H, H-24a), 3.12 (dd, $J_{5,4a}$ = 12.3 Hz, $J_{5,4b}$ = 4.5 Hz, 1H, H-5), 3.46 (dd, $J_{22,20}$ = 4.7 Hz, $J_{22,23}$ = 1.7 Hz, 1H, H-22), 3.72 (ddd, $J_{2,1b}$ = 12.1 Hz, $J_{2,1a}$ = 4.7 Hz, $J_{2,3}$ = 2.7 Hz,1H, H-2), 4.03 (bq, $J_{3,2} \sim J_{3,4a} \sim J_{3,4b}$ = 3.0 Hz, 1H, H-3), 4.09 (m, 2H, H-7), 4.21 (m, 1H, H-23); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 11.72 (CH_3-18), 14.07 (CH_3-21), 15.44 (CH_3-19), 22.18 (CH_2-11), 24.95 (CH_2-15), 27.38 (CH_2-16), 30.96 (CH_2-4), 35.11 (d, $J_{24,F}$ = 19.0 Hz, CH_2-24), 38.28 (C-10), 39.11 (CH-8), 39.47 (CH_2-12), 40.85 (CH-5), 41.30 (CH-20), 41.40 (CH_2-1), 43.20 (C-13), 50.86 (CH-14), 52.99 (CH-17), 58.08 (CH-9), 64.64 (CH-23), 68.02 (CH-2), 68.07 (CH-3), 70.37 (CH_2-7), 75.59 (CH-22), 176.25 (C-6); IR ($CHCl_3$) ν 3621, 3578, 1722, 1385, 1340, 1182, 1067 cm^{-1}; MS (ESI, m/z (rel.%)) 591 (M^+-1, 16), 549 (8), 397 (5), 386 (7), 172 (6); HR-MS (ESI) calcd. for $C_{27}H_{38}O_6F_7$ [M^+-1] 591.2562, found 591.2547. R_f(6/1 EtOAc/hexane) = 0.16.



Estrone 3-tetrahydropyranyl ether (58). 4-Methylbenzenesulfonic acid (42 mg, 0.24 mmol) was added to a solution of estrone **55** (1.6 g, 5.93 mmol) and dihydropyran (6.4 mL, 70 mmol) in 38 mL of anhydrous THF. The reaction mixture was stirred for 1 h at 25 °C. After neutralization with saturated aqueous solution of $NaHCO_3$, the reaction mixture was evaporated to dryness under reduced pressure below 30 °C. The residue was extracted with CH_2Cl_2 and washed with water. The organic layer was evaporated and the crude product was purified by column chromatography (3/1 hexane/EtOAc) to give 1.93 g of the compound **58** (92%) as a colorless oil: ^{1}H NMR (400 MHz, d_6-acetone) δ 0.90 (s, 3H, 3 × H-18), 2.85 (m, 2H, 2 × H-6), 3.55 (m, 1H, H-6'b), 3.84 (m, 1H, H-6'a), 5.39 (m, 1H, H-2'), 6.75 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.81

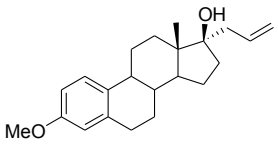


(dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.19 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1). Spectral characteristics are in agreement with the previously reported data.[117]

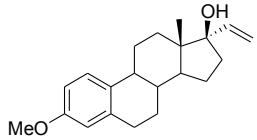
General Procedure for the Addition of Grignard Reagents.[97]

A solution of **54** or **58** (1 mmol) in dry benzene (6 mL) was added dropwise to an ice-cooled and stirred suspension of Grignard reagents – allylmagnesium bromide (3 mL of 1M solution in THF, 3 mmol) under an argon atmosphere. After addition, the stirring was continued for 3 h, then the reaction mixture was poured into saturated aqueous solution of NH_4Cl (30 mL), extracted with Et_2O, dried (Na_2SO_4), and evaporated. Column chromatography of the residue on silica gel afforded alkenylated products **56** and **59**.

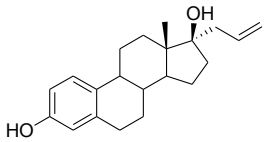
3-Methoxy-19,21,24-trinor-17β*H*-chola-1,3,5(10),22-tetraen-17-ol (56). The reaction was carried out with 3-methoxyestrone **54** (150 mg, 0.53 mmol) and allylmagnesium bromide (1.6 mL, 1.6 mmol) according to the general procedure. Column chromatography on silica gel (10/3 hexane/Et_2O) and crystallization (heptane/Et_2O) afforded 162 mg (94%) of the product **56** as white crystals: mp 89-91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 2.86 (m, 2H, H-6), 3.78 (s, 3H, OCH_3), 5.20 (m, 2H, H-23), 6.02 (m, 1H, H-22), 6.63 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.71 (dd, $J_{2,1}$ = 8.6 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H-2), 7.21 (d, $J_{1,2}$ = 8.7 Hz, 1H, H-1). Spectral characteristics are in agreement with the previously reported data.[118]



17β-Hydroxy-3-methoxy-17α-vinylestra-1,3,5(10)-triene (57). The reaction was carried out with 3-methoxyestrone **54** (500 mg, 1.76 mmol) and vinylmagnesium bromide (5.3 mL, 5.3 mmol) according to the general procedure. Column chromatography on silica gel (10/3 hexane/Et_2O) and crystallization (heptane/Et_2O) afforded 247 mg (45%) of the product **57** as white crystals: mp 96-98 °C; mp 96-98 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 3H, 3 × H-18), 2.85 (m, 2H, 2 × H-6), 3.78 (s, 3H, OCH_3), 5.15 (dd, $J_{22a,20}$ = 11.2 Hz, $J_{22a,22b}$ = 1.2 Hz, 1H, H-22a), 5.20 (dd, $J_{22b,20}$ = 17.2 Hz, $J_{22b,22a}$ = 1.2 Hz, 1H, H-22b), 6.11 (dd, $J_{20,22b}$ = 17.2 Hz, $J_{20,22a}$ = 11.2 Hz, 1H, H-20), 6.63 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.70 (dd, $J_{2,1}$ = 8.6 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H-2), 7.19 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1). Spectral characteristics are in agreement with the previously reported data.[119]

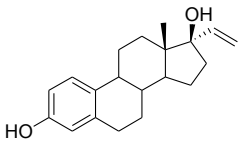


17α-(2'-Propen-1'-yl)-estra-1,3,5(10)-trien-3,17β-diol (59). The reaction was carried out with estrone 3-tetrahydropyranyl ether **58** (600 mg, 1.69 mmol) and allylmagnesium bromide



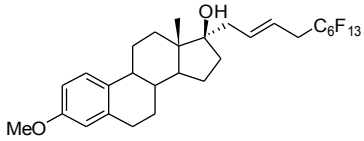
(5.1 mL, 5.1 mmol) according to the general procedure. The crude product was dissolved in MeOH (20 mL) and 4-methylbenzenesulfonic acid (26 mg, 0.15 mmol) was added. The mixture was stirred at 25 °C for 1 h. After completion of the reaction (TLC – 2/1 hexane/Et_2O), volatiles were evaporated under reduced pressure, a crude product was dissolved in CH_2Cl_2, washed with saturated aqueous solution of $NaHCO_3$, water, and dried over sodium sulfate. Column chromatography (7/3 hexane/Et_2O) and crystallization (acetone-heptane) afforded 432 mg (82%) of the title compound **59** as white crystals: mp 85-87 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (s, 3H, 3 × H-18), 2.82 (m, 2H, 2 × H-6), 5.19 (dm, $J_{3'a,2'}$ = 10.0 Hz, 1H, H-3'a), 5.22 (dm, $J_{3'b,2'}$ = 17.2 Hz, 1H, H-3'b), 6.02 (m, 1H, H-2'), 6.57 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.63 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.16 (d, $J_{1,2}$ = 8.2 Hz, 1H, H-1). Spectral characteristics are in agreement with the previously reported data.[120]

19-Nor-17β*H*-pregna-1,3,5(10),20-tetraene-3,17-diol (60). The reaction was carried out with estrone 3-tetrahydropyranyl ether **58** (1.5 g, 4.23 mmol) and



vinylmagnesium bromide (12.7 mL, 12.7 mmol) according to the general procedure. The crude product was dissolved in MeOH (30 mL) and 4-methylbenzenesulfonic acid (120 mg, 0.70 mmol) was added. The mixture was stirred at 25 °C for 1 h. After completion of the reaction (TLC – 2/1 hexane/Et_2O), volatiles were evaporated under reduced pressure, a crude product was dissolved in CH_2Cl_2, washed with saturated aqueous solution of $NaHCO_3$, water, and dried over sodium sulfate. Column chromatography (10/1 toluene/acetone) afforded 593 mg (47%) of the title compound **60** as a white foam**:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 3H, 3 × H-18), 2.82 (m, 2H, 2 × H-6), 5.15 (dd, $J_{21a,20}$ = 10.8 Hz, $J_{21a,21b}$ = 1.2 Hz, 1H, H-21a), 5.20 (dd, $J_{21b,20}$ = 17.2 Hz, $J_{21b,21a}$ = 1.2 Hz, 1H, H-21b), 6.11 (dd, $J_{20,21b}$ = 17.2 Hz, $J_{20,21a}$ = 10.8 Hz, 1H, H-20), 6.56 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.61 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.14 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1). Spectral characteristics are in agreement with the previously reported data.[119]

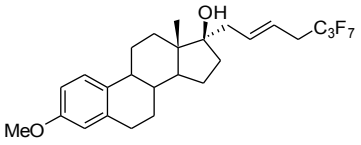
2'-(*E*)-[(3-Methoxy-17-(5',5',6',6',7',7',8',8',9',9',10',10',10'-tridecafluorodec-2'-en-1'-yl)estra-17β-ol] (61a). The reaction was carried out with **56** (140 mg, 0.43 mmol) and



(perfluorohexyl)propene **1a** (280 mg, 0.80 mmol) according to the general procedure for cross-metathesis.[46] Column

chromatography on silica gel (20/3 toluene/Et_2O) afforded 148 mg (53%) of the compound **61a** as a pale foam: $[\alpha]_D$ +43.8 (*c* 0.16, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 1.89 (m, 1H, H-7b), 1.99 (m, 1H, H-16a), 2.17 (m, 1H, H-9), 2.27 (ddd, J_{gem} = 14.0 Hz, $J_{1'a,2'}$ = 7.9 Hz, $J_{1'a,3'}$ = 0.9 Hz, 1H, H-1'a), 2.34 (m, 1H, H-11b), 2.41 (ddm, J_{gem} = 14.0 Hz, $J_{1'b,2'}$ = 6.3 Hz, 1H, H-1'b), 2.88 (m, 4H, 2 × H-6 and 2 × H-4'), 3.78 (s, 3H, OCH_3), 5.56 (dm, $J_{3',2'}$ = 15.4 Hz, 1H, H-3'), 5.95 (dddt, $J_{2',3'}$ = 15.4 Hz, $J_{2',1'a}$ = 7.9 Hz, $J_{2',1'b}$ = 6.4 Hz, $J_{2',4'}$ = 1.4 Hz, 1H, H-2'), 6.63 (dm, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.72 (dd, $J_{2,1}$ = 8.6 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H-2), 7.21 (dd, $J_{1,2}$ = 8.7 Hz, $J_{1,9}$ = 1.1 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.26 (CH_3-18), 23.39 (CH_2-15), 26.26 (CH_2-11), 27.47 (CH_2-7), 29.82 (CH_2-6), 31.69 (CH_2-12), 34.82 (CH_2-16), 34.97 (t, $J_{4',F}$ = 22.3 Hz, CH_2-4'), 39.58 (CH-8), 40.43 (CH_2-1'), 43.78 (CH-9), 46.53 (C-13), 49.58 (CH-14), 55.18 (OCH_3), 82.78 (C-17), 111.44 (CH-2), 113.77 (CH-4), 120.32 (CH-3'), 126.28 (CH-1), 132.50 (C-10), 135.31 (CH-2'), 137.95 (C-5), 157.44 (C-3); IR ($CHCl_3$) ν 3620, 3592, 3030, 2839, 1670, 1608, 1432, 1380, 1280, 976 cm^{-1}; MS (FAB, m/z (rel.%)) 658 (M^+, 12), 640 (11), 601 (5), 285 (78), 267 (39), 227 (62), 121 (19); HR-MS (FAB) calcd. for $C_{29}H_{31}O_2F_{13}$ [M^+] 658.2116, found 658.2107. R_f (5/2 hexane/Et_2O) = 0.30.

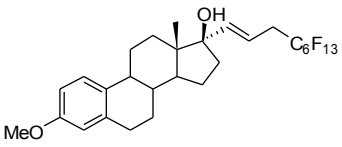
2'-(*E*)-[(3-Methoxy-17-(4',4',5',5',6',6',6'-heptafluorohept-2'-en-1'-yl)estra-17β-ol] (61b). The reaction was carried out with **56** (150 mg, 0.46 mmol) and



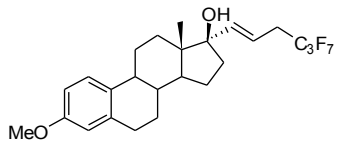
(perfluoropropyl)propene **1b** (190 mg, 0.90 mmol) according to the general procedure. Column chromatography on silica gel (20/3 toluene/Et_2O) and crystallization (heptane/acetone) afforded 158 mg (68%) of the title compound **61b** as white crystals: mp 89-90 °C; $[\alpha]_D$ +34.8 (*c* 0.29, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 1.89 (m, 1H, H-7b), 1.99 (m, 1H, H-16a), 2.16 (m, 1H, H-9), 2.27 (bdd, J_{gem} = 14.1 Hz, $J_{1'a,2'}$ = 8.0 Hz, 1H, H-1'a), 2.33 (m, 1H, H-11b), 2.40 (ddm, J_{gem} = 14.1 Hz, $J_{1'b,2'}$ = 6.3 Hz, 1H, H-1'b), 2.88 (m, 4H, 2 × H-6 and 2 × H-4'), 3.78 (s, 3H, OCH_3), 5.55 (dm, $J_{3',2'}$ = 15.4 Hz, 1H, H-3'), 5.95 (dddt, $J_{2',3'}$ = 15.4 Hz, $J_{2',1'a}$ = 7.8 Hz, $J_{2',1'b}$ = 6.4 Hz, $J_{2',4'}$ = 1.3 Hz, 1H, H-2'), 6.63 (dm, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.71 (dd, $J_{2,1}$ = 8.6 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H-2), 7.21 (dd, $J_{1,2}$ = 8.8 Hz, $J_{1,9}$ = 1.1 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.25 (CH_3-18), 23.38 (CH_2-15), 26.25 (CH_2-11), 27.46 (CH_2-7), 29.81 (CH_2-6), 31.68 (CH_2-12), 34.70 (t, $J_{4',F}$ = 22.4 Hz, CH_2-4'), 34.80 (CH_2-16), 39.57 (CH-8), 40.41 (CH_2-1'), 43.77 (CH-9), 46.52 (C-13), 49.57 (CH-14), 55.17 (OCH_3), 82.77 (C-17), 111.43 (CH-2), 113.77 (CH-4), 120.29 (t, $J_{3',F}$ = 4.0 Hz, CH-3'), 126.27 (CH-1), 132.50 (C-10), 135.27 (CH-2'), 137.94 (C-5), 157.43 (C-3); IR ($CHCl_3$) ν

3621, 3593, 2839, 1671, 1609, 1432, 1380, 1280, 975 cm^{-1}; MS (FAB, m/z (rel.%)) 509 (M^+ +H, 46), 491 (84), 309 (7), 285 (19), 223 (18), 173 (92); HR-MS (FAB) calcd. for $C_{26}H_{32}O_2F_7$ [M^++H] 509.2291, found 509.2283. R_f(5/2 hexane/Et_2O) = 0.30.

1'-(*E*)-[(3-Methoxy-17-(4',4',5',5',6',6',7',7',8',8',9',9',9'-tridecafluoronon-1'-en-1'-yl)estra-17β-ol] (62a). The reaction was carried out with **57** (180 mg, 0.58 mmol) and (perfluorohexyl)propene **1a** (415 mg, 1.15 mmol) according to the general procedure. Column chromatography on silica gel (20/3 toluene/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded 126 mg (36%) of the title compound **62a** as a pale foam: $[\alpha]_D$ +30.3 (*c* 0.07, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.94 (s, 3H, 3 × H-18), 1.74 (m, 1H, H-15a), 1.89 (m, 2H, H-7a and H-16b), 2.00 (m, 1H, H-16a), 2.12 (m, 1H, H-9), 2.29 (m, 1H, H-11a), 2.88 (m, 4H, 2 × H-6 and 2 × H-3'), 3.77 (s, 3H, OCH_3), 5.63 (dt, $J_{2',1'}$ = 15.5 Hz, $J_{2',3'}$ = 7.2 Hz, 1H, H-2'), 6.01 (dt, $J_{1',2'}$ = 15.6 Hz, $J_{1',3'}$ = 1.4 Hz, 1H, H-1'), 6.63 (dm, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.70 (dd, $J_{2,1}$ = 8.6 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.18 (dd, $J_{1,2}$ = 8.7 Hz, $J_{1,9}$ = 1.1 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.01 (CH_3-18), 23.24 (CH_2-15), 26.28 (CH_2-11), 27.45 (CH_2-7), 29.80 (CH_2-6), 32.25 (CH_2-12), 34.71 (t, $J_{3',F}$ = 22.7 Hz, CH_2-3'), 36.91 (CH_2-16), 39.48 (CH-8), 43.73 (CH-9), 46.96 (C-13), 49.22 (CH-14), 55.20 (OCH_3), 83.86 (C-17), 111.48 (CH-2), 113.84 (CH-4), 114.53 (t, $J_{2',F}$ = 4.1 Hz, CH-2'), 126.28 (CH-1), 132.52 (C-10), 137.90 (C-5), 143.37 (CH-1'), 157.50 (C-3); IR ($CHCl_3$) ν 3601, 2840, 1676, 1608, 1575, 1381, 1281, 979 cm^{-1}; MS (FAB, m/z (rel.%)) 644 (M^+, 92), 627 (74), 510 (7), 415 (11), 387 (16), 173 (100); HR-MS (FAB) calcd. for $C_{28}H_{30}O_2F_{13}$ [M^++H] 645.2038, found 645.2054. R_f(5/2 hexane/Et_2O) = 0.32.

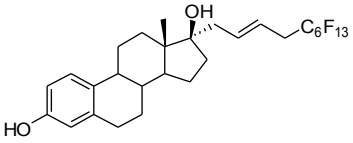


1'-(*E*)-[(3-Methoxy-17-(4',4',5',5',6',6',6'-heptafluorohept-1'-en-1'-yl)estra-17β-ol] (62b). The reaction was carried out with **57** (80 mg, 0.26 mmol) and (perfluoropropyl)propene **1b** (109 mg, 0.52 mmol) according to the general procedure. Column chromatography on silica gel (20/3 toluene/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded 37 mg (29%) of the title compound **62b** as an yellowish oil: $[\alpha]_D$ +38.2 (*c* 0.17, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.94 (s, 3H, 3 × H-18), 1.74 (m, 1H, H-15a), 1.89 (m, 2H, H-7a and H-16b), 2.00 (m, 1H, H-16a), 2.12 (m, 1H, H-9), 2.29 (m, 1H, H-11a), 2.89 (m, 4H, 2 × H-6 and 2 × H-3'), 3.77 (s, 3H, OCH_3), 5.62 (dm, $J_{2',1'}$ = 15.5

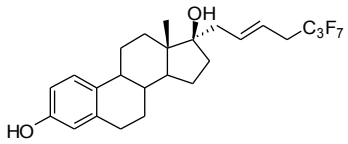


Hz, 1H, H-2'), 6.01 (dt, $J_{1',2'}$ = 15.5 Hz, $J_{1',3'}$ = 1.3 Hz, 1H, H-1'), 6.63 (dm, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.71 (dd, $J_{2,1}$ = 8.7 Hz, $J_{2,4}$ = 2.9 Hz, 1H, H-2), 7.19 (dd, $J_{1,2}$ = 8.7 Hz, $J_{1,9}$ = 1.0 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.00 (CH_3-18), 23.21 (CH_2-15), 26.24 (CH_2-11), 27.43 (CH_2-7), 29.79 (CH_2-6), 32.19 (CH_2-12), 34.41 (t, $J_{3',F}$ = 22.6 Hz, CH_2-3'), 36.83 (CH_2-16), 39.42 (CH-8), 43.70 (CH-9), 46.91 (C-13), 49.13 (CH-14), 55.18 (OCH_3), 83.85 (C-17), 111.45 (CH-2), 113.79 (CH-4), 114.51 (t, $J_{2',F}$ = 4.4 Hz, CH-2'), 126.29 (CH-1), 132.48 (C-10), 137.90 (C-5), 143.31 (CH-1'), 157.45 (C-3); IR ($CHCl_3$) ν 3601, 2840, 1677, 1609, 1575, 1381, 1281, 979 cm^{-1}; MS (FAB, m/z (rel.%)) 694 (M^+, 47), 477 (39), 391 (7), 301 (8), 237 (40), 173 (77); HR-MS (FAB) calcd. for $C_{25}H_{30}O_2F_7$ [M^++H] 495.2134, found 495.2145. R_f (5/2 hexane/Et_2O) = 0.32.

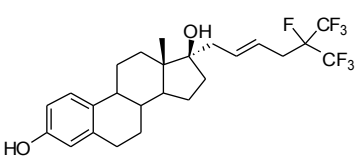
2'-(*E*)-[17-(5',5',6',6',7',7',8',8',9',9',10',10',10'-Tridecafluorodec-2'-en-1'-yl)estra-3,17β-diol] (63a). The reaction was carried out with **59** (92 mg, 0.29 mmol) and (perfluorohexyl)propene **1a** (209 mg, 0.58 mmol) according to the general procedure. Column chromatography on silica gel (7/3 hexane/EtOAc) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) and crystallization (4/1 hexane/CH_2Cl_2) afforded 118 mg (62%) of the title compound **63a** as white crystals: mp 138-140 °C; $[\alpha]_D$ +26.8 (*c* 0.23, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 1.88 (m, 1H, H-7b), 1.99 (m, 1H, H-16a), 2.14 (m, 1H, H-9), 2.27 (dd, J_{gem} = 14.1 Hz, $J_{1'a,2'}$ = 8.0 Hz, 1H, H-1'a), 2.32 (m, 1H, H-11b), 2.42 (dd, J_{gem} = 14.1 Hz, $J_{1'b,2'}$ = 6.3 Hz, 1H, H-1'b), 2.85 (m, 4H, 2 × H-6 and 2 × H-4'), 4.87 (bs, 1H, 3-OH), 5.56 (dm, $J_{3',2'}$ = 15.4 Hz, 1H, H-3'), 5.95 (dm, $J_{2',3'}$ = 15.6 Hz, 1H, H-2'), 6.56 (d, $J_{4,2}$ = 2.7 Hz, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.7 Hz, 1H, H-2), 7.14 (d, $J_{1,2}$ = 8.6 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.28 (CH_3-18), 23.39 (CH_2-15), 26.26 (CH_2-11), 27.40 (CH_2-7), 29.61 (CH_2-6), 31.69 (CH_2-12), 34.83 (CH_2-16), 34.98 (t, $J_{4',F}$ = 22.6 Hz, CH_2-4'), 39.56 (CH-8), 40.44 (CH_2-1'), 43.77 (CH-9), 46.55 (C-13), 49.60 (CH-14), 82.88 (C-17), 112.65 (CH-2), 115.23 (CH-4), 120.38 (CH-3'), 126.47 (CH-1), 132.58 (C-10), 135.25 (CH-2'), 138.25 (C-5), 153.36 (C-3); IR ($CHCl_3$) ν 3599, 1610, 1585, 1500, 1380, 1354, 1243, 976 cm^{-1}; MS (EI, m/z (rel.%)) 644 (M^+, 46), 626 (31), 651 (5), 312 (10), 271 (84), 213 (72), 159 (100); HR-MS (EI) calcd. for $C_{28}H_{29}O_2F_{13}$ [M^+] 644.1960, found 644.1965. R_f(1/1 hexane/Et_2O) = 0.33.



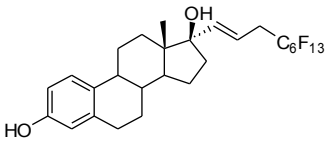
2'-(*E*)-[17-(5',5',6',6',7',7',7'-Heptafluorohept-2'-en-1'-yl)estra-3,17β-diol] (63b). The reaction was carried out with **59** (130 mg, 0.42 mmol) and (perfluoropropyl)propene **1b** (176 mg, 0.84 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded 122 mg (58%) of the title compound **63b** as a white foam: $[\alpha]_D$ +29.7 (*c* 0.20, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 1.88 (m, 1H, H-7b), 1.99 (m, 1H, H-16a), 2.14 (m, 1H, H-9), 2.27 (dd, J_{gem} = 14.1 Hz, $J_{1'a,2'}$ = 8.1 Hz, 1H, H-1'a), 2.32 (m, 1H, H-11b), 2.41 (dd, J_{gem} = 14.2 Hz, $J_{1'b,2'}$ = 6.4 Hz, 1H, H-1'b), 2.83 (m, 2H, 2 × H-6), 2.86 (td, $J_{4',F}$ = 18.4 Hz, $J_{4',3'}$ = 7.0 Hz, 2H, 2 × H-4'), 4.94 (bs, 1H, 3-OH), 5.55 (dm, $J_{3',2'}$ = 15.4 Hz, 1H, H-3'), 5.94 (dm, $J_{2',3'}$ = 15.4 Hz, 1H, H-2'), 6.56 (d, $J_{4,2}$ = 2.7 Hz, 1H, H-4), 6.63 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.15 (d, $J_{1,2}$ = 8.6 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.28 (CH_3-18), 23.39 (CH_2-15), 26.25 (CH_2-11), 27.40 (CH_2-7), 29.60 (CH_2-6), 31.68 (CH_2-12), 34.71 (t, $J_{4',F}$ = 22.6 Hz, CH_2-4'), 34.80 (CH_2-16), 39.56 (CH-8), 40.41 (CH_2-1'), 43.76 (CH-9), 46.55 (C-13), 49.59 (CH-14), 82.94 (C-17), 112.67 (CH-2), 115.24 (CH-4), 120.37 (t, $J_{3',F}$ = 4.2 Hz, CH-3'), 126.45 (CH-1), 132.52 (C-10), 135.19 (CH-2'), 138.23 (C-5), 153.40 (C-3); IR ($CHCl_3$) ν 3598, 3388, 1610, 1585, 1499, 1380, 1353, 1228, 975 cm^{-1}; MS (EI, m/z (rel.%)) 494 (M^+, 86), 476 (5), 312 (10), 294 (11), 271 (94), 213 (53), 159 (67); HR-MS (EI) calcd. for $C_{25}H_{29}O_2F_7$ [M^+] 494.2056, found 494.2048. R_f(1/1 hexane/Et_2O) = 0.33.



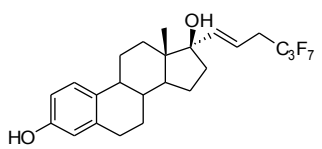
2'-(*E*)-[17-(5'-(Trifluoromethyl)-5',6',6',6'-tetrafluorohex-2'-en-1'-yl)estra-3,17β-diol] (63c). The reaction was carried out with **59** (150 mg, 0.48 mmol) and (perfluoro*iso*propyl)propene **1c** (210 mg, 1.00 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) and crystallization (4/1 hexane/CH_2Cl_2) afforded 158 mg (67%) of the title compound **63c** as white crystals: mp 180-181 °C; $[\alpha]_D$ +32.2 (*c* 0.17, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 1.88 (m, 1H, H-7b), 1.97 (m, 1H, H-16a), 2.14 (m, 1H, H-9), 2.25 (dd, J_{gem} = 14.2 Hz, $J_{1'b,2'}$ = 8.0 Hz, 1H, H-1'b), 2.31 (m, 1H, H-11a), 2.39 (dd, J_{gem} = 14.3 Hz, $J_{1'a,2'}$ = 6.2 Hz, 1H, H-1'a), 2.83 (m, 2H, 2 × H-6), 2.88 (dd, $J_{4',F}$ = 20.0 Hz, $J_{4',3'}$ = 7.0 Hz, 2H, 2 × H-4'), 4.80 (bs, 1H, 3-OH), 5.54 (dm, 1H, $J_{3',2'}$ = 15.1 Hz, H-3'), 5.92 (dm, $J_{2',3'}$ = 15.3 Hz, 1H, H-2'), 6.56 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.63 (dd,



$J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.15 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.26 (CH_3-18), 23.38 (CH_2-15), 26.25 (CH_2-11), 27.40 (CH_2-7), 29.61 (CH_2-6), 31.67 (CH_2-12), 32.68 (d, $J_{4',F}$ = 20.9 Hz, CH_2-4'), 34.77 (CH_2-16), 39.55 (CH-8), 40.32 (CH_2-1'), 43.76 (CH-9), 46.53 (C-13), 49.59 (CH-14), 82.93 (C-17), 112.65 (CH-2), 115.23 (CH-4), 121.39 (d, $J_{3',F}$ = 5.8 Hz, CH-3'), 126.47 (CH-1), 132.56 (C-10), 134.56 (CH-2'), 138.25 (CH-5), 153.36 (C-3); IR ($CHCl_3$) ν 3598, 3370, 1611, 1585, 1500, 1380, 1353, 1163, 979 cm^{-1}; MS (EI, m/z (rel.%)) 494 (M^+, 89), 476 (7), 271 (100), 253 (61), 228 (24), 213 (82); HR-MS (EI) calcd. for $C_{25}H_{29}O_2F_7$ [M^+] 494.2056, found 494.2062. R_f (1/1 hexane/Et_2O) = 0.33.

1'-(*E*)-[17-(5',5',6',6',7',7',8',8',9',9',10',10',10'-Tridecafluoronon-1'-en-1'-yl)estra-3,17β-diol] (64a). 

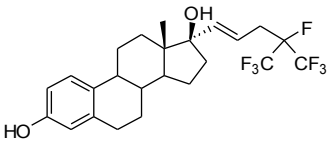
The reaction was carried out with **60** (100 mg, 0.34 mmol) and (perfluorohexyl)propene **1a** (242 mg, 0.68 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) and crystallization (4/1 hexane/CH_2Cl_2) afforded 39 mg (19%) of the title compound **64a** as white crystals: mp 167-168 °C; $[\alpha]_D$ +32.1 (*c* 0.08, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.94 (s, 3H, 3 × H-18), 1.74 (m, 1H, H-15a), 1.89 (m, 2H, H-7a and H-16b), 2.01 (m, 1H, H-16a), 2.11 (m, 1H, H-9), 2.27 (m, 1H, H-11a), 2.83 (m, 2H, 2 × H-6), 2.91 (dt, $J_{3',F}$ = 18.2 Hz, $J_{3',2'}$ = 7.2 Hz, 2H, 2 × H-3'), 4.58 (s, 1H, 3-OH), 5.62 (dt, $J_{2',1'}$ = 15.6 Hz, $J_{2',3'}$ = 7.1 Hz, 1H, H-2'), 6.01 (bd, $J_{1',2'}$ = 15.7 Hz, 1H, H-1'), 6.56 (bd, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.13 (d, $J_{1,2}$ = 8.5 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.01 (CH_3-18), 23.22 (CH_2-15), 26.25 (CH_2-11), 27.35 (CH_2-7), 29.58 (CH_2-6), 32.20 (CH_2-12), 34.67 (t, $J_{3',F}$ = 23.1 Hz, CH_2-3'), 36.86 (CH_2-16), 39.40 (CH-8), 43.68 (CH-9), 46.92 (C-13), 49.15 (CH-14), 83.89 (C-17), 112.65 (CH-2), 114.54 (t, $J_{2',F}$ = 4.0 Hz, CH-2'), 115.21 (CH-4), 126.50 (CH-1), 132.60 (C-10), 138.22 (C-5), 143.32 (CH-1'), 153.29 (C-3); IR ($CHCl_3$) ν 3600, 1611, 1585, 1499, 1381, 1357, 1243, 979 cm^{-1}; MS (EI, m/z (rel.%)) 630 (M^+, 38), 612 (33), 597 (17), 437 (9), 387 (10), 213 (100); HR-MS (EI) calcd. for $C_{27}H_{27}O_2F_{13}$ [M^+] 630.1803, found 630.1800. R_f(1/1 hexane/Et_2O) = 0.35.

1'-(*E*)-[17-(4',4',5',5',6',6',6'-Heptafluorohex-1'-en-1'-yl)estra-3,17β-diol] (64b). 

The reaction was carried out with **60** (150 mg, 0.50 mmol) and (perfluoropropyl)propene **1b** (210 mg, 1.0 mmol) according to the

general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) and crystallization (4/1 hexane/CH_2Cl_2) afforded 61 mg (25%) of the title compound **64b** as white crystals: mp 185-186 °C; $[\alpha]_D$ +26.3 (*c* 0.17, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.94 (s, 3H, 3 × H-18), 1.74 (m, 1H, H-15a), 1.89 (m, 2H, H-7a and H-16b), 2.01 (m, 1H, H-16a), 2.10 (m, 1H, H-9), 2.27 (m, 1H, H-11a), 2.81 (m, 2H, 2 × H-6), 2.89 (td, $J_{3',F}$ = 17.6 Hz, $J_{3',2'}$ = 7.1 Hz, 2H, 2 × H-3'), 4.70 (bs, 1H, 3-OH), 5.62 (dt, $J_{2',1'}$ = 15.5 Hz, $J_{2',3'}$ = 7.2 Hz, 1H, H-2'), 6.00 (bd, $J_{1',2'}$ = 15.6 Hz, 1H, H-1'), 6.56 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.13 (bd, $J_{1,2}$ = 8.5 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.01 (CH_3-18), 23.21 (CH_2-15), 26.23 (CH_2-11), 27.35 (CH_2-7), 29.58 (CH_2-6), 32.17 (CH_2-12), 34.40 (t, $J_{3',F}$ = 22.3 Hz, CH_2-3'), 36.79 (CH_2-16), 39.38 (CH-8), 43.68 (CH-9), 46.90 (C-13), 49.10 (CH-14), 83.91 (C-17), 112.65 (CH-2), 114.56 (t, $J_{2',F}$ = 4.4 Hz, CH-2'), 115.22 (CH-4), 126.50 (CH-1), 132.56 (C-10), 138.20 (C-5), 143.26 (CH-1'), 153.31 (C-3); IR ($CHCl_3$) ν 3599, 3399, 1611, 1585, 1499, 1353, 1232, 979 cm^{-1}; MS (FAB, m/z (rel.%)) 680 (M^+, 65), 462 (9), 265 (17), 228 (38), 213 (100); HR-MS (EI) calcd. for $C_{24}H_{27}O_2F_7$ [M^+] 480.1899, found 480.1905. R_f (1/1 hexane/Et_2O) = 0.35.

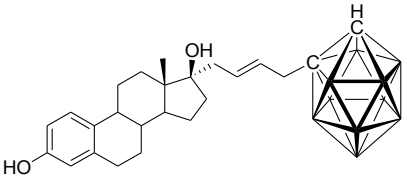
1'-(*E*)-[17-(4'-(Trifluoromethyl)-4',5',5',5'-tetrafluoropent-1'-en-1'-yl)estra-3,17β-diol] (64c). The reaction was carried out with **60** (150 mg, 0.50 mmol) and



(perfluoro*iso*propyl)propene **1c** (210 mg, 1.0 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/diethyl ether) and on fluorinated silica gel (1st elution 7/3 MeOH/water–washing of the non-fluorinated starting material, 2nd elution Et_2O–washing of the product) afforded 29 mg (12%) of the title compound **64c** as a pale foam: $[\alpha]_D$ +58.3 (*c* 0.05, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.94 (s, 3H, 3 × H-18), 1.72 (m, 1H, H-15a), 1.88 (m, 2H, H-16a and H-7b), 1.98 (m, 1H, H-16b), 2.10 (m, 1H, H-9), 2.27 (m, 1H, H-11a), 2.84 (m, 2H, 2 × H-6), 2.91 (bdd, $J_{3',F}$ = 20.1 Hz, $J_{3',2'}$ = 7.9 Hz, 2H, 2 × H-3'), 4.75 (bs, 1H, 3-OH), 5.60 (m, 1H, H-2'), 5.97 (bd, $J_{1',2'}$ = 15.4 Hz, 1H, H-1'), 6.56 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.13 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.99 (CH_3-18), 23.14 (CH_2-15), 26.21 (CH_2-11), 27.33 (CH_2-7), 29.57 (CH_2-6), 32.07 (CH_2-12), 32.43 (d, $J_{3',F}$ = 21.1 Hz, CH_2-3'), 36.65 (CH_2-16), 39.66 (CH-8), 43.65 (CH-9), 46.89 (C-13), 48.92 (CH-14), 83.83 (C-17), 112.66 (CH-2), 115.22 (CH-4), 115.76 (d, $J_{2',F}$ = 5.6 Hz, CH-2'), 126.49 (CH-1), 132.54 (C-10), 138.20 (CH-5), 142.51 (C-

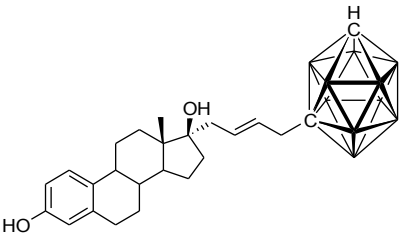
1'), 153.33 (C-3); IR ($CHCl_3$) ν 3600, 3394, 1611, 1585, 1499, 1381, 1163, 982 cm^{-1}; MS (EI, m/z (rel.%)) 480 (M^+, 52), 462 (7), 264 (5), 237 (10), 228 (34), 213 (100); HR-MS (EI) calcd. for $C_{24}H_{27}O_2F_7$ [M^+] 480.1899, found 480.1905. R_f(1/1 hexane/Et_2O) = 0.35.

2'-(*E*)-17[4'-(1'',2''-Dicarbadodecaboran-1''-yl)but-2'-en-1'-yl)]estra-3,17β-diol (65).



The reaction was carried out with **59** (80 mg, 0.26 mmol) and *ortho*-allylcarborane **28** (48 mg, 0.26 mmol) according to the general procedure. Column chromatography on silica gel (3/2 hexane/Et_2O) afforded 68 mg (57%) of the compound **65** as a pale solid: mp 130-133 °C; $[\alpha]_D$ +36.0 (*c* 0.11, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.87 (s, 3H, 3 × H-18), 2.68-2.77 (m, 2H, 2 × H-6), 2.95 (m, 2H, 2 × H-4'), 3.69 (bs, 1H, H-2''), 5.04 (bs, 1H, 3-0H), 5.43 (m, 1H, H-3'), 5.77 (m, 1H, H-2'), 6.50 (d, $J_{4,2}$ = 2.6 Hz, 1H, H-4), 6.56 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.6 Hz, 1H, H-2), 7.04 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.29 (CH_3-18), 23.35 (CH_2-15), 26.22 (CH_2-11), 27.38 (CH_2-7), 29.58 (CH_2-6), 31.67 (CH_2-12), 34.98 (CH_2-16), 39.54 (CH-8), 39.84 (CH_2-1'), 40.76 (CH_2-4'), 43.74 (CH-9), 46.55 (C-13), 49.55 (CH-14), 59.68 (CH-2''), 76.67 (C-1'')**,** 83.17 (C-17), 112.66 (CH-2), 115.24 (CH-4), 126.45 (CH-1), 126.75 (CH-3'), 132.36 (C-10), 133.57 (CH-2'), 138.19 (C-5), 153.43 (C-3); IR ($CHCl_3$) ν 3598, 2595, 1610, 1586, 1500, 1380, 1079, 978 cm^{-1}; MS (ESI, m/z (rel.%)) 469 (M^+-H, 28), 455 (11), 385 (5), 359 (8), 269 (19), 198 (12); HR-MS (ESI) calcd. for $C_{24}H_{39}O_2B_{10}$ [M^+-H] 469.3886 found 469.3886. R_f(1/1 hexane/Et_2O) = 0.20.

2'-(*E*)-17-[4'-(1'',7''-Dicarbadodecaboran-1''-yl)but-2'-en-1'-yl)]estra-3,17β-diol (66).



The reaction was carried out with **59** (80 mg, 0.26 mmol) and *meta*-allylcarborane **29** (48 mg, 0.26 mmol) according to the general procedure. Column chromatography on silica gel (3/2 hexane/Et_2O) afforded 66 mg (55%) of the title compound **66** as a white solid: mp 112-115 °C; $[\alpha]_D$ +50.9 (*c* 0.11, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.92 (s, 3H, 3 × H-18), 2.21-2.34 (m, 2H, 2 × H-1'), 2.67 (d, $J_{4',3'}$ = 7.5 Hz, 2H, 2 × H-4'), 2.78-2.87 (m, 2H, 2 × H-6), 2.90 (bs, 1H, H-2''), 4.84 (s, 1H, 3-0H), 5.44 (dm, $J_{3',2'}$ = 15.2 Hz, 1H, H-3'), 5.62 (dm, $J_{2',3'}$ = 15.2 Hz, 1H, H-2'), 6.56 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.63 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.15 (dd, $J_{1,2}$ = 8.6 Hz, $J_{1,4}$ = 1.1 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 14.30 (CH_3-18), 23.40 (CH_2-15), 26.25 (CH_2-11), 27.40 (CH_2-7), 29.61 (CH_2-6), 31.72 (CH_2-12), 34.89 (CH_2-16), 39.51

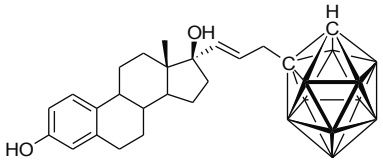
(CH-8), 40.07 (CH_2-1'), 40.08 (CH_2-4'), 43.76 (CH-9), 46.47 (C-13), 49.54 (CH-14), 55.01 (CH-2''), 77.69 (C-1''**),** 82.94 (C-17), 112.64 (CH-2), 115.22 (CH-4), 126.47 (CH-1), 130.00 (CH-3'), 130.48 (CH-2'), 132.56 (C-10), 138.24 (C-5), 153.33 (C-3); IR ($CHCl_3$) ν 3597, 2602, 1611, 1585, 1500, 1380, 1080, 979 cm^{-1}; MS (ESI, m/z (rel.%)) 469 (M^+-H, 28), 452 (11), 343 (15), 301 (8), 269 (19), 232 (12); HR-MS (ESI) calcd. for $C_{24}H_{39}O_2B_{10}$ [M^+-H] 469.3886 found 469.3886. R_f(1/1 hexane/Et_2O) = 0.26.

2'-(*E*)-17-[4'-(8,8'-μ-(Thiolato)-3,3'-como-cobalt(III)-bis-(1'',2''-dicarbadodecaboratyl))but-2'-en-1'-yl]estra-3,17β-diol (67). The reaction was carried out with **59** (78 mg, 0.25 mmol) and allylcarborane complex **31** (100 mg, 0.25 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) afforded 75 mg (44%) of the title compound **67** as a red solid: mp 134-137 °C; $[\alpha]_D$ +12.0 (*c* 0.04, $CHCl_3$); ^{1}H NMR (600 MHz, d_6-acetone) δ 0.91 (s, 3H, 3 × H-18), 1.83-1.92 (m, 2H, H-16a and H-7β), 2.13 (m, 1H, H-9), 2.25 (dd, J_{gem} = 14.0 Hz, $J_{1'b,2'}$ = 8.9 Hz, 1H, H-1'b), 2.30 (m, 1H, H-11α), 2.38 (dd, J_{gem} = 14.0 Hz, $J_{1'a,2'}$ = 4.9 Hz, 1H, H-1'a), 2.70-2.81 (m, 2H, 2 × H-6), 3.85 (m, 2H, 2 × H-4'), 4.13 (bs, 2H, H-1''), 4.18 (bs, 2H, H-2''), 5.63 (dm, $J_{3',2'}$ = 15.3 Hz, 1H, H-3'), 6.17 (dm, $J_{2',3'}$ = 15.3 Hz, 1H, H-2'), 6.51 (bs, 1H, H-4), 6.58 (bd, $J_{2,1}$ = 8.5 Hz, 1H, H-2), 7.08 (d, $J_{1,2}$ = 8.5 Hz, 1H, H-1), 8.03 (s, 1H, 3-OH); ^{13}C NMR (150.9 MHz, d_6-acetone) δ 14.93 (CH_3-18), 24.10 (CH_2-15), 27.23 (CH_2-11), 28.31 (CH_2-7), 30.34 (CH_2-6), 32.40 (CH_2-12), 34.77 (CH_2-16), 40.81 (CH-8), 41.20 (CH_2-1'), 43.78 (CH_2-4'), 44.58 (CH-9), 47.54 (C-13), 50.35 (CH-14), 51.37 (2C, CH-1''), 51.62 (2C, CH-2''), 83.14 (C-17), 113.53 (CH-2), 115.91 (CH-4), 123.42 (CH-3'), 126.98 (CH-1), 132.00 (C-10), 138.31 (CH-2'), 138.40 (C-5), 155.90 (C-3); IR ($CHCl_3$) ν 3599, 2617, 2584, 1663, 1585, 1500, 1380, 1081, 974 cm^{-1}; MS (ESI, m/z (rel.%)) 727 (M^+-H, 8), 678 (100), 506 (3), 354 (15), 283 (9); HR-MS (ESI) calcd. for $C_{27}H_{50}O_4B_{18}CoS$ [M^+-H] 727.4442 found 727.4420. R_f(1/1 hexane/Et_2O) = 0.26.

2'-(*E*)-17-[4'-(8,8'-μ-(Dithiolato)-3,3'-como-cobalt(III)-bis-(1'',2''-dicarbadodecaboratyl))but-2'-en-1'-yl]estra-3,17β-diol (68). The reaction was carried out with **59** (19 mg, 0.06 mmol) and allylcarborane complex **32** (25 mg, 0.06 mmol) according to the general procedure. Column chromatography on silica

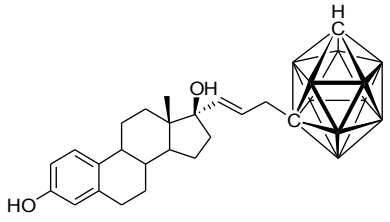
gel (1/1 hexane/Et_2O) afforded 22 mg (52%) of the title compound **68** as a red solid: mp 163-166 °C; $[\alpha]_D$ +42.2 (*c* 0.17, $CHCl_3$); ^1H NMR (600 MHz, d_6-acetone) δ 0.93 (s, 3H, 3 × H-18), 3.33 and 3.34 (s, 1H, 17-OH), 3.40-4.80 (bm, 12H, 2 × H-4' and B-H), 5.68 (m, 1H, H-3'), 6.36 (dm, $J_{2',3'}$ = 15.1 Hz, 1H, H-2'), 6.52 (d, $J_{4,2}$ = 2.6 Hz, 1H, H-4), 6.58 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.6 Hz, 1H, H-2), 7.09 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, d_6-acetone) δ 14.93 and 14.94 (CH_3-18), 24.13 (CH_2-15), 27.23 (CH_2-11), 28.31 and 28.33 (CH_2-7), 30.34 (CH_2-6), 32.43 and 32.50 (CH_2-12), 34.98 and 35.02 (CH_2-16), 40.81 (CH-8), 41.44 and 41.46 (CH_2-1'), 44.60 and 44.61 (CH-9), 47.52 and 47.57 (C-13), 50.36 and 50.39 (CH-14), 50.92 and 51.17 (CH_2-4'), 50.78 and 52.33 (CH-1''), 53.06 and 53.55 (CH-2''), 83.08 (C-17), 113.52 (CH-2), 115.90 (CH-4), 122.09 and 122.23 (CH-3'), 126.99 (CH-1), 132.01 (C-10), 138.42 (C-5), 141.80 and 141.91 (CH-2'), 155.87 (C-3); IR ($CHCl_3$) ν 3597, 2593, 1659, 1611, 1585, 1500, 1381, 1084, 977 cm^{-1}; MS (ESI, m/z (rel.%)) 710 (M^+-H, 100), 518 (3), 386 (15); HR-MS (ESI) calcd. for $C_{26}H_{48}O_2B_{18}CoS_2$ [M^+-H] 710.4217 found 710.4176. R_f (1/1 hexane/Et_2O) = 0.26

1'-(*E*)-17-[3'-(1'',2''-Dicarbadodecaboran-1''-yl)prop-1'-en-1'-yl)]estra-3,17β-diol (69).



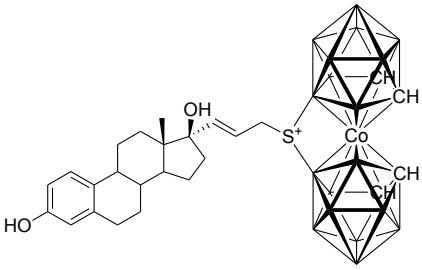
The reaction was carried out with **60** (55 mg, 0.18 mmol) and *ortho*-allylcarborane **28** (33 mg, 0.18 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) afforded 31 mg (37%) of the title compound **69** as a red solid: mp 121-123 °C; $[\alpha]_D$ +31.1 (*c* 0.10, $CHCl_3$); ^1H NMR (600 MHz, d_6-acetone) δ 0.94 (s, 3H, 3 × H-18), 3.09-3.18 (m, 2H, 2 × H-3'), 4.59 (bs, 1H, H-2''), 5.61 (dt, $J_{2',1'}$ = 15.3 Hz, $J_{2',3'}$ = 7.6 Hz, 1H, H-2'), 5.97 (dt, $J_{1',2'}$ = 15.3 Hz, $J_{1',3'}$ = 1.2 Hz, 1H, H-1'), 6.52 (dm, $J_{4,2}$ = 2.7 Hz, 1H, H-4), 6.58 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.7 Hz, 1H, H-2), 7.07 (d, $J_{1,2}$ = 8.5 Hz, 1H, H-1), 8.04 (s, 1H, 3-OH); ^{13}C NMR (150.9 MHz, d_6-acetone) δ 14.58 (CH_3-18), 23.92 (CH_2-15), 27.23 (CH_2-11), 28.21 (CH_2-7), 30.31 (CH_2-6), 33.24 (CH_2-12), 37.12 (CH_2-16), 40.64 (CH-8), 41.02 (CH_2-3'), 44.72 (CH-9), 47.81 (C-13), 49.80 (CH-14), 62.48 (CH-2''), 76.68 (C-1''**),** 83.73 (C-17), 113.60 (CH-2), 115.96 (CH-4), 121.55 (CH-2'), 126.98 (CH-1), 131.98 (C-10), 138.39 (C-5), 143.12 (CH-1'), 153.43 (C-3); IR ($CHCl_3$) ν 3068, 2596, 1612, 1585, 1500, 1380, 1081, 1019, 984 cm^{-1}; MS (ESI, m/z (rel.%)) 455 (M^+-H, 55), 366 (1), 182 (2); HR-MS (ESI) calcd. for $C_{23}H_{37}O_2B_{10}$ [M^+-H] 455.3730 found 455.3738. R_f (1/1 hexane/Et_2O) = 0.26.

1'-(*E*)-17-[3'-(1'',7''-Dicarbadodecaboran-1''-yl)prop-1'-en-1'-yl)]estra-3,17β-diol (70).



The reaction was carried out with **60** (55 mg, 0.18 mmol) and *meta*-allylcarborane **29** (33 mg, 0.18 mmol) according to the general procedure. Column chromatography on silica gel (5/1 toluene/EtOAc) and afforded 32 mg (38%) of the title compound **70** as a red solid: mp 233-235 °C; $[\alpha]_D$ +16.4 (*c* 0.11, $CHCl_3$); ^{1}H NMR (600 MHz, d_6-acetone) δ 0.94 (s, 3H, 3 × H-18), 2.70-2.83 (m, 4H, 2 × H-6 and 2 × H-3'), 3.66 (bs, 1H, H-2''), 5.49 (dd, $J_{2',1'}$ = 15.3 Hz, $J_{2',3'}$ = 8.0 Hz, 1H, H-2'), 5.81 (bd, $J_{1',2'}$ = 15.3 Hz, 1H, H-1'), 6.52 (dm, $J_{4,2}$ = 2.7 Hz, 1H, H-4), 6.58 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.6 Hz, 1H, H-2), 7.08 (d, $J_{1,2}$ = 8.7 Hz, 1H, H-1), 8.10 (s, 1H, 3-OH); ^{13}C NMR (150.9 MHz, d_6-acetone) δ 14.54 (CH_3-18), 23.85 (CH_2-15), 27.19 (CH_2-11), 28.39 (CH_2-7), 30.31 (CH_2-6), 33.09 (CH_2-12), 36.72 (CH_2-16), 40.56 (CH_2-3'), 40.62 (CH-8), 44.68 (CH-9), 47.69 (C-13), 49.41 (CH-14), 56.84 (CH-7''), 77.34 (C-1''**),** 83.65 (C-17), 113.55 (CH-2), 115.93 (CH-4), 123.72 (CH-2'), 126.97 (CH-1), 131.94 (C-10), 138.38 (C-5), 140.99 (CH-1'), 155.97 (C-3); IR ($CHCl_3$) ν 3068, 2602, 1614, 1585, 1499, 1379, 1080, 1007, 983 cm^{-1}; MS (ESI, m/z (rel.%)) 455 (M^+-H, 35), 383 (3), 283 (40), 255 (11); HR-MS (ESI) calcd. for $C_{23}H_{37}O_2B_{10}$ [M^+-H] 455.3730 found 455.3729. R_f(5/1 toluene/EtOAc) = 0.30.

1'-(*E*)-17-[3'-(8,8'-μ-(Thiolato)-3,3'-como-cobalt(III)-bis-(1'',2''-dicarbadodecaboratyl))prop-1'-en-1'-yl]estra-3,17β-diol (71).



The reaction was carried out with **60** (60 mg, 0.20 mmol) and allylcarborane complex **31** (80 mg, 0.20 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) afforded 55 mg (41%) of the title compound **71** as a red solid: 165-167 °C; $[\alpha]_D$ –7.0 (*c* 0.10, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ 0.91 (s, 3H, 3 × H-18), 1.60-2.70 (bm, 10H, B-H), 1.74 (m, 1H, H-15a), 1.82-1.90 (m, 2H, H-16a and H-7β), 1.95 (m, 1H, 16a), 2.14 (m, 1H, H-9), 2.26 (m, 1H, H-11α), 2.78-2.84 (m, 2H, 2 × H-6), 3.14-4.56 (bm, 10H, B-H), 3.70-3.81 (m, 2H, 2 × H-3'), 4.72 (bs, 1H, 3-OH), 5.72 (dt, $J_{2',1'}$ = 15.4 Hz, $J_{2',3'}$ = 7.1 Hz, 1H, H-2'), 6.10 (bd, $J_{1',2'}$ = 15.3 Hz, 1H, H-1'), 6.55 (d, $J_{4,2}$ = 2.8 Hz, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.4 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.14 (d, $J_{1,2}$ = 8.5 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.99 (CH_3-18), 23.21 (CH_2-15), 26.23 (CH_2-11), 27.18 (CH_2-7), 29.58 (CH_2-6), 32.20 (CH_2-12), 36.87 (CH_2-16), 39.40 (CH-8), 42.33 (CH_2-3'), 43.37 (CH-9), 47.21 (C-13), 48.76 (4C, CH-1'' and CH-2''), 49.14 (CH-14), 83.84 (C-17), 112.61 (CH-2), 115.15

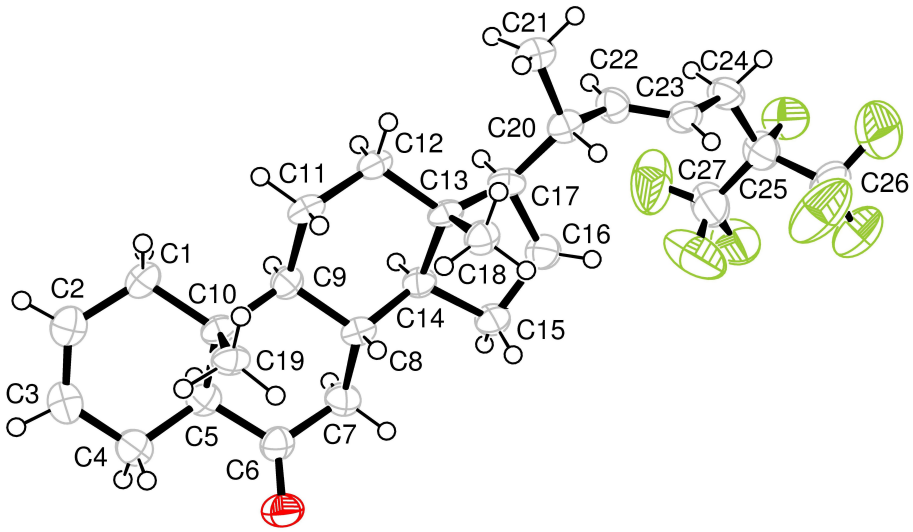
(CH-4), 118.05 (CH-2'), 126.58 (CH-1), 132.72 (C-10), 138.24 (C-5), 143.50 (CH-1'), 153.20 (C-3); IR ($CHCl_3$) ν 3599, 2617, 2585, 1627, 1585, 1499, 1381, 1081, 975 cm^{-1}; MS (ESI, m/z (rel.%)) 668 (M^+, 8), 353 (25), 283 (9), 255 (4); HR-MS (ESI) calcd. for $C_{25}H_{47}O_2B_{18}CoS$ [M^+] 668.4304 found 668.4311. R_f(1/1 hexane/Et_2O) = 0.15.

1'-(*E*)-17-[3'-(8,8'-μ-(Dithiolato)-3,3'-como-cobalt(III)-bis-(1'',2''-dicarbadodecaboratyl))prop-1'-en-1'-yl]estra-3,17β-diol (72). The reaction was carried out with **60** (24 mg, 0.08 mmol) and allylcarborane complex **32** (35 mg, 0.08 mmol) according to the general procedure. Column chromatography on silica gel (1/1 hexane/Et_2O) afforded 16 mg (29%) of the title compound **72** as a red solid: 146-148 °C; $[\alpha]_D$ +24.0 (*c* 0.17, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 0.93 (s, 3H, 3 × H-18), 0.94 (s, 3H, 3 × H-18), 2.28 (m, 1H, 11α), 2.28-2.88 (m, 2H, 2 × H-6), 3.20-4.40 (bm, 10H, B-H), 4.05 and 4.44 (m, 2H, 2 × H-3'), 6.62 (bs, 1H, 17-OH), 5.63-5.75 (m, 1H, H-2'), 6.25 and 6.29 (d, $J_{1',2'}$ = 15.4 Hz, 1H, H-1'), 6.56 (m, 1H, H-4), 6.62 (dd, $J_{2,1}$ = 8.5 Hz, $J_{2,4}$ = 2.8 Hz, 1H, H-2), 7.14 (d, $J_{1,2}$ = 8.4 Hz, 1H, H-1); ^{13}C NMR (150.9 MHz, $CDCl_3$) δ 13.99 and 14.02 (CH_3-18), 23.21 and 23.27 (CH_2-15), 26.20 (CH_2-11), 27.28 (CH_2-7), 29.54 and 29.55 (CH_2-6), 32.40 and 32.45 (CH_2-12), 37.26 and 37.28 (CH_2-16), 39.38 and 39.41 (CH-8), 43.49 and 43.54 (CH-9), 47.15 and 47.17 (C-13), 49.23 and 49.30 (CH-14), 49.56 and 49.62 (CH_2-3'), 48.60 and 50.44 (CH-1''), 51.29 and 51.73 (CH-2''), 84.17 and 84.19 (C-17), 112.63 (CH-2), 115.16 and 115.18 (CH-4), 116.36 (CH-2'), 126.53 and 126.57 (CH-1), 132.55 and 132.60 (C-10), 138.19 and 138.23 (C-5), 147.14 and 147.45 (CH-1'), 153.23 and 153.24 (C-3); IR ($CHCl_3$) ν 3598, 2594, 1659, 1611, 1585, 1499, 1380, 1081, 978 cm^{-1}; MS (ESI, m/z (rel.%)) 696 (M^+-H, 100), 386 (12); HR-MS (ESI) calcd. for $C_{25}H_{46}O_2B_{18}CoS_2$ [M^+-H] 696.4061 found 696.4038. R_f(1/1 hexane/Et_2O) = 0.13.

X-ray Crystallography

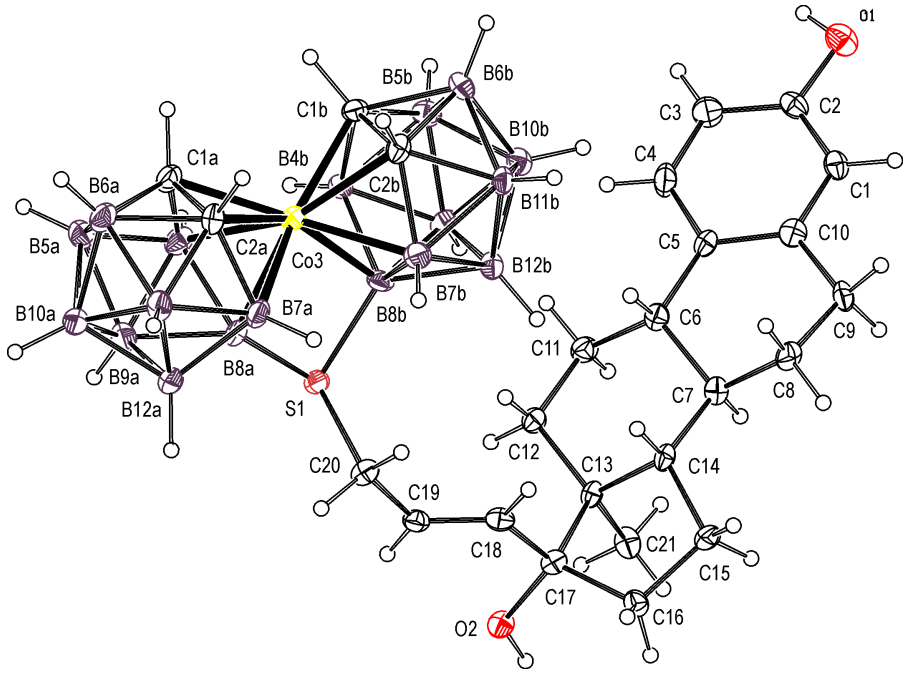
Single crystal X-ray structure analysis of *trans*-47c. The diffraction data of single crystal of *trans*-**47c** (colorless, 0.10 × 0.37 × 0.54 mm) were collected on Xcalibur X-ray diffractometer with CuKα (λ=1.54180 Å) at 150 K. The structure was solved by direct methods with SIR92[121] and refined by full-matrix least-squares on F with CRYSTALS.[122] All hydrogen atoms were located in a difference map but later were repositioned geometrically and then refined with riding constraints, while all other atoms were refined anisotropically.

Crystal data for *trans*-47c: $C_{27}H_{35}F_7O$, triclinic, space group *P1*, a = 6.0049(5) Å, b = 12.4363(10) Å, c = 16.8427(13) Å, α = 84.981(6)°, β = 88.317(7)°, γ = 87.102(6)°, V = 1250.97(17) Å3, Z = 2, M = 508.56, 27070 reflections measured, 4930 independent reflections. Final R = 0.1105, wR = 0.1072, GoF = 0.9983 for 3850 reflections with $I > 2\sigma(I)$ and 631 parameters. CCDC 720898.



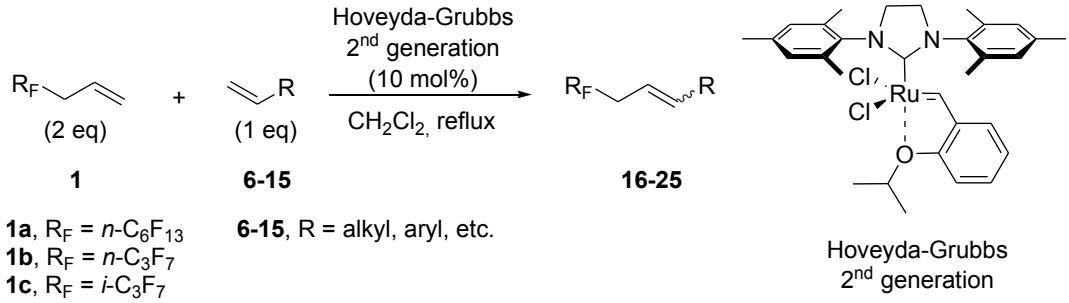
Single crystal X-ray structure analysis of 71. The crystal of compounds of **71**, was mounted on glass fibre with epoxy cement and measured on four-circle diffractometer KappaCCD with CCD area detector by monochromatized MoK_α radiation (λ = 0.71073 Å) at 150(2)K. The structures were solved by the direct method (SIR97)[121] and refined by a full matrix least squares procedure based on F^2 (SHELXL97).[123] The most of hydrogen atoms were fixed into idealized positions (riding model) and assigned temperature factors $H_{iso}(H) = 1.2\ U_{eq}$(pivot atom), for the methyl moiety multiple of 1.5 was chosen. The hydrogen connected to oxygen atoms were found on difference Fourier map and refined as riding on pivot atom. The final difference maps displayed no peaks of chemical significance.

Crystal data for 71: $C_{25}H_{47}B_{18}CoO_2S$, 3(CH_4O), orthorhombic, space group $P2_12_12_1$, a = 7.6980(4) Å, b = 24.5590(15) Å, c = 21.2290(12) Å, V = 4013.5(4) Å3, Z = 4, M = 761.32, 15459 reflections measured, 5522 independent reflections. Final R = 0.0533, wR = 0.1137, GoF = 0.99 for 3890 reflections with $I > 2\sigma(I)$ and 482 parameters.



6. Conclusion

A new perfluoroalkylation method that enables to introduce perfluoroalkylated chains into various types of molecules under mild reaction conditions was developed. The underlying strategy is based on a ruthenium complex catalyzed cross-metathesis of terminal alkenes with easily accessible (perfluoroalkyl)propenes (Scheme 36). The reaction conditions as well as the mechanism and limits of this reaction were studied.[46]



Scheme 36

Subsequently, the developed methodology was tested with a wide range of various substrates to assess its synthetic scope. This was demonstrated in the synthesis of

a) monoperfluoroalkylated cyclodextrin (Figure 12);[54]

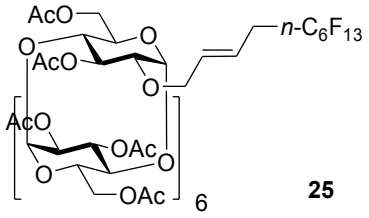
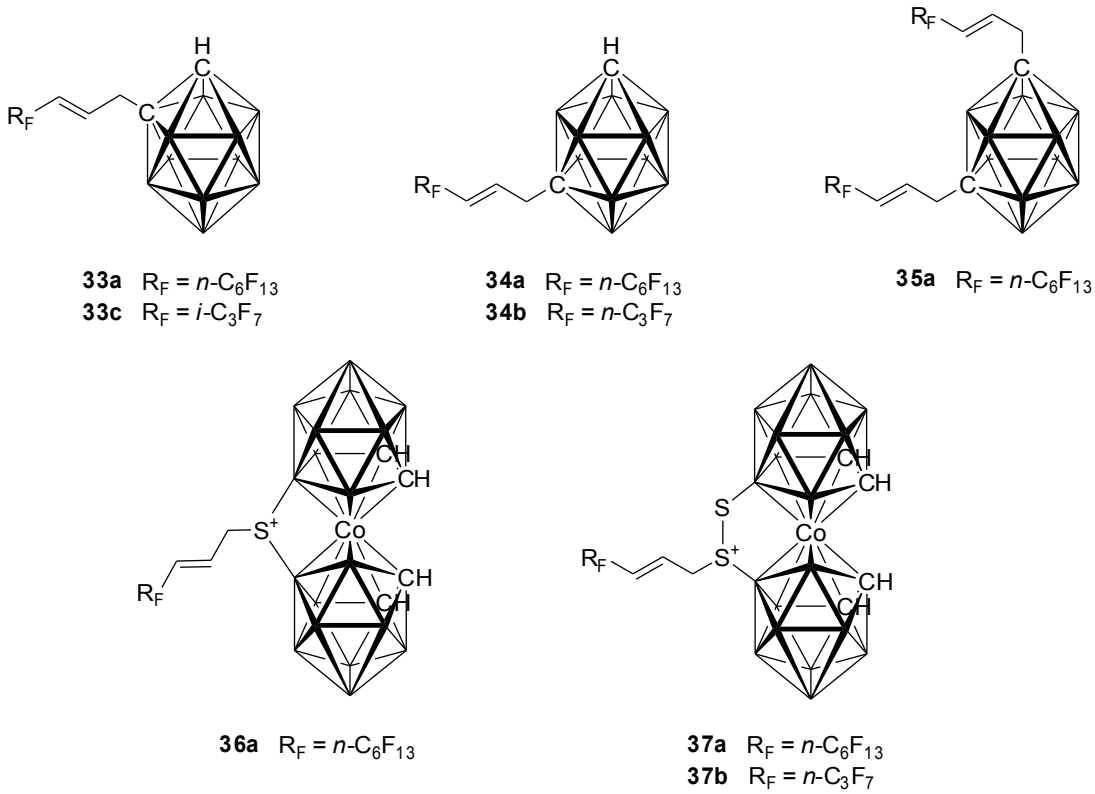


Figure 12

b) 8 mono- and diperfluoroalkylated carboranes (Figure 13);[71]



33a $R_F = n\text{-}C_6F_{13}$
33c $R_F = i\text{-}C_3F_7$

34a $R_F = n\text{-}C_6F_{13}$
34b $R_F = n\text{-}C_3F_7$

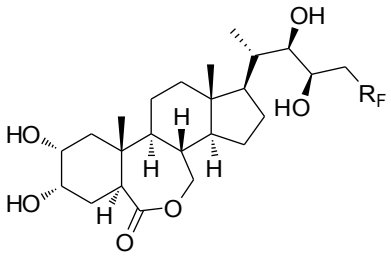
35a $R_F = n\text{-}C_6F_{13}$

36a $R_F = n\text{-}C_6F_{13}$

37a $R_F = n\text{-}C_6F_{13}$
37b $R_F = n\text{-}C_3F_7$

Figure 13

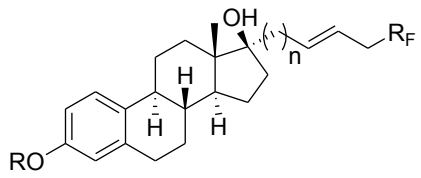
c) 3 fluorinated analogues of the natural growth hormone brassinolide that exhibited promising results in biological tests ($GABA_A$ and brassinolide activity) (Figure 14);[83]



50a $R_F = n\text{-}C_6F_{13}$
50b $R_F = n\text{-}C_3F_7$
50c $R_F = i\text{-}C_3F_7$

Figure 14

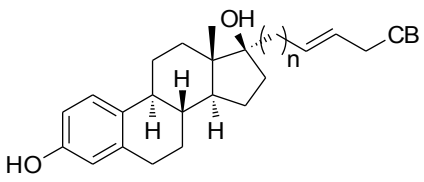
d) 10 perfluoroalkylated derivatives of estradiol that exhibited promising selectivities for ERα or ERβ (Figure 15);[100]



61a n=1 R=Me R_F = *n*-C_6F_{13}
61b n=1 R=Me R_F = *n*-C_3F_7
62a n=0 R=Me R_F = *n*-C_6F_{13}
62a n=0 R=Me R_F = *n*-C_3F_7
63a n=1 R=H R_F = *n*-C_6F_{13}
63b n=1 R=H R_F = *n*-C_3F_7
63c n=1 R=H R_F = *i*-C_3F_7
64a n=0 R=H R_F = *n*-C_6F_{13}
64b n=0 R=H R_F = *n*-C_3F_7
64c n=0 R=H R_F = *i*-C_3F_7

Figure 15

e) 8 carboranylalkyl derivatives of estradiols that also exhibited interesting selectivities for ERα or ERβ (Figure 16).[111]



65 n=1 CB = *o*-allylcarborane
66 n=1 CB = *m*-allylcarborane
67 n=1 CB = S-bridged carboranyl-Co-complex
68 n=1 CB = S_2-bridged carboranyl-Co-complex
69 n=0 CB = *o*-allylcarborane
70 n=0 CB = *m*-allylcarborane
71 n=0 CB = S-bridged carboranyl-Co-complex
72 n=0 CB = S_2-bridged carboranyl-Co-complex

Figure 16

7. References

1. (a) Isanbor, C.; O'Hagan, D. *J. Fluorine Chem.* **2006**, *127*, 303–319. (b) Bégué, J.-P.; Bonnet-Delpon, D. *J. Fluorine Chem.* **2006**, *127*, 992–1012. (c) Kirk, K. L. *J. Fluorine Chem.* **2006**, *127*, 1013–1029.
2. Ma, J.-A.; Cahard, D. *Chem. Rev*. **2008**, *108*, 1–43.
3. Imhof, S.; Randl, S.; Blechert, S. *Chem. Commun*. **2001**, 1692–1693.
4. Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005***, 44*, 4490–4527.
5. Reviews on olefin metathesis: (a) Grubbs, R. H. *Tetrahedron* **2004**, *60*, 7117–7140; (b) Trnka, T. M., Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18–29; (c) Fürstner, A. *Angew. Chem. Int. Ed.* **2000**, *39*, 3012–3043; (d) Grubbs, R. H.; Chang, S. *Tetrahedron* **1998**, *54*, 4413–4450; (e) Schuster, M., Blechert, S. *Angew. Chem. Int. Ed.* **1997**, *36*, 2036–2056.
6. Connon, S. J., Blechert, S. *Angew. Chem. Int. Ed.* **2003**, *42*, 1900–1923.
7. Hérisson, J. L.; Chauvin, Y. *Makromol. Chem.* **1971***, 141*, 161–176.
8. Chatterjee, A. K.; Choi, T.; Sanders, D. P.; Grubbs, R. H. *J. Am. Chem. Soc.* **2003***, 125*, 11360–11370.
9. Hanada, K.; Miyazawa, N.; Ogasawara, K. *Chem. Pharm. Bull.* **2003**, *51*, 104–106.
10. Foucher, V.; Guizzardi, B.; Groen, M. B.; Light, M.; Linclau, B. *Org. Lett.* **2010**, *12*, 680–683.
11. García-Fandino, R.; Codesido, E. M.; Sobarzo-Sánchez, E.; Castedo, L.; Granja, J. R. *Org. Lett.* **2004**, *6*, 193–196.
12. de la Torre, M. C.; Deometrio, A. M.; Álvaro, E.; Garcia, I.; Sierra, M. A. *Org. Lett.* **2006**, *8*, 593–596.
13. (a) Rosillo, M.; Casarrubios, L.; Dominguez, G.; Pérez-Castells, J. *Tetrahedron Lett*. **2001**, *42*, 7029–7031. (b) Dragutan, V.; Dragutan, I. *J. Organomet. Chem.* **2006**, *691*, 5129–5147.
14. Shi, B.; Tang, P.; Hu, X.; Liu, J. O.; Yu, B. *J. Org. Chem.* **2005**, *70*, 10354–10367.
15. Roy, J.; Breton, R.; Martel, C.; Labrie, F.; Poirier, D. *Bioorg. Med. Chem.* **2007**, *15*, 3003–3018.
16. Kirschning, A.; Harmrolfs, K; Mennecke, K.; Messenger, J.; Schön, U.; Grela, K. *Tetrahedron Lett.* **2008**, *49*, 3019–3022.

17. Böhm, H.-J.; Banner, D.; Bendels, S.; Kansy, M.; Kuhn, B.; Müller, K.; Obst-Sander, U.; Stahl, M. *ChemBioChem* **2004**, *5*, 637–643.
18. Hagmann, W. K. *J. Med. Chem.*, **2008**, 51, 4359–4369.
19. Pauling, L. *The Nature of the Chemical Bond*, Cornell University Press, Ithaca, 1960.
20. Bondi, A. *J. Phys. Chem*. **1964**, *68*, 441–451.
21. Park, B. K.; Kitteringham, N. R.; O'Neill, P. M. *Annu. Rev. Pharmacol. Toxicol.* **2001**, *41*, 443–470.
22. O'Hagan, D.; Rzepa, H. S. *Chem. Commun*. **1997**, 645–652.
23. Smart, B. E. *J. Fluorine Chem.* **2001**, *109*, 3–11.
24. van Heek, M.; France, C. F.; Compton, D. S.; McLeod, R. L.; Yumibe, N. P.; Alton, K. B.; Sybertz, E. J.; Davies, H. R. *J. Pharmacol. Exp. Therap.* **1997**, *283*, 157–163.
25. Clader, J. W. *J. Med. Chem.* **2004**, *47*, 1–9.
26. Swain, C.; Rupniak, N. M. J. *Ann. Rep. Med. Chem*. **1999**, *34*, 51–60.
27. Böhm, H.-J.; Schneider, G. *Protein-Ligand Interactions*, Wiley-VCH, Weinheim, 2003.
28. (a) Müller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881–1886. (b) Olsen, J. A.; Banner, D. W.; Seiler, P.; Sander, U. O.; D'Arcy, A.; Stihle, M.; Müller, K.; Diederich, F. *Angew. Chem.Int. Ed.* **2003**, *42*, 2507–2511.
29. Solladie´-Cavallo, A.; Suffert, J. *Synthesis* **1985**, 659–662.
30. Uno, H.; Okada, S.-I.; Ono, T.; Shiraishi, Y.; Suzuki, H. *J. Org. Chem.* **1992**, *57*, 1504–1513.
31. Lavaire, S.; Plantier-Royon, R.; Portella, C. *Tetrahedron: Asymmetry* **1998**, *9*, 213–226.
32. Umemoto, T. *Chem. Re*v. **1996**, *96*, 1757–1777.
33. Agouridas, V.; Blazejewski, J.-C.; Magnier, E.; Popkin, M. E. *J. Org. Chem.* **2005**, *70*, 8907–8912.
34. Dolbier, W. R. *Chem. Rev*. **1996**, *96*, 1557–1584.
35. Iseki, K.; Takahashi, M.; Asada, D.; Nagai, T.; Kobayashi, Y. *J. Fluorine Chem.* **1995**, *74*, 269–271.
36. Yajima, T.; Nagano, H. *Org. Lett.* **2007**, *9*, 2513–2515.
37. Stevenson, R.; Kerr, F.W.; Anthony, R.; Brazier, E.J.; Hogan, P.J.; David, D.D.P. PCT Int. Appl. 2002032922, **2002**.

38. Van de Velde, P. F.; Nique, F.; Bouchoux, F.; Bremaud, J.; Hameau, M. C.; Lucas, D.; Moratille, C.; Viet, S.; Philibert, D.; Teutsch, G. *J. Steroid Biochem. Mol. Biol.* **1994**, *48*, 187–196.
39. Šíša, M.; Hniličková, J.; Swaczynová, J.; Kohout, L. *Steroids* **2005**, *70*, 755–762.
40. Shao, H.; Jiang, L.; Meng, W.-D.; Qing, F.-L. *J. Fluorine Chem.* **2003**, *124*, 89–91.
41. Chatterjee, A. K.; Morgan, J. P.; Scholl, M.; Grubbs, R. H. *J. Am. Chem. Soc.* **2000**, *122*, 3783–3784.
42. Audouard, C.; Fawcett, J.; Griffiths, G. A.; Percy, J. M.; Pintat, S.; Smith, C. A. *Org. Biomol. Chem.* **2004**, *2*, 528–541.
43. Trnka, T. M.; Day, M. W.; Grubbs, R. H. *Angew. Chem. Int. Ed.* **2001**, *40*, 3441–3444.
44. Delest, B.; Shtarev, A. B.; Dolbier Jr, W. R. *Tetrahedron* **1998**, *54*, 9273-9280.
45. Brace, N. O.; Marschall, L. W.; Pinson, C. J.; van Wingerden, G. *J. Org. Chem.* **1984**, *49*, 2361-2368.
46. Eignerová, B.; Dračínský, M.; Kotora, M. *Eur. J. Org. Chem.* **2008**, *26*, 4493–4499.
47. Kotora, M.; Hájek, M.; Ameduri, B.; Boutevin, B. *J. Fluorine Chem.* **1994**, *68*, 49–56.
48. Gambaretto, G.; Coute, L.; Fornasieri, G.; Zarantonello, C.; Tonei, D.; Sassi, A.; Bertani, R. *J. Fluorine Chem.* **2003**, *121*, 57–63.
49. Matsugi, M.; Curran, D. P. *Org. Lett.* **2004**, *6*, 2717–2720.
50. Lo Strezo, C.; Ortaggi, G. *J. Chem. Soc., Perkin Trans 2* **1984**, 345–348.
51. Herrmann, P.; Buděšínský, M.; Kotora, M. *Chem. Lett.* **2007**, 1268–1269.
52. Ikeuchi, Y.; Taguchi, T.; Hanzawa, Y. *J. Org. Chem*., **2005**, *70*, 756–759.
53. Pouzar, V.; Chodounská, H.; Sameš, D.; Drašar, P.; Havel, M. *Collect. Czech. Chem. Commun.* **1990**, *55*, 1243–1256.
54. Řezanka, M.; Eignerová, B.; Jindřich, J.; Kotora, M. *Eur. J. Org. Chem.* **2010**, Manuscript accepted.
55. (a) Garber, S. B.; Kingsbury, J. S.; Gray, B. L.; Hoveyda, A., H. *J. Am. Chem. Soc.* **2000**, *122*, 8168–8179. (b) Gessler, S.; Randl, S.; Blechert, S. *Tetrahedron Lett.* **2000**, *41*, 9973-9976.
56. Čapek, P.; Pohl, R.; Hocek, M. *J. Org. Chem.* **2005**, *70*, 8001–8008.
57. Plešek, J. *Chem. Rev*. **1992**, *92*, 269–278.
58. Sivaev, I. B.; Bregadze, V. V. *Eur. J. Inorg. Chem.* **2009**, 1433–1450.

59. (a) Soloway, A. H.; Tjarks, W.; Barnum, B. A.; Rong, F.-G.; Barth, R. F.; Codogni, I. M.; Wilson, J. G. *Chem. Rev.* **1998**, *98*, 1515–1562; (b) Hawthorne, M. F.; Maderna, A. *Chem. Rev.* **1999**, *99*, 3421–3434.
60. Reed, C. A. *Chem. Commun.* **2005**, 1669–1677.
61. Sivaev, I. B.; Bregadze, V. I. *Collect. Czech. Chem. Commun.* **1999**, *64*, 783–805.
62. Cígler, P.; Kožíšek, M.; Řezáčová, P.; Brynda, J.; Otwinowski, Z.; Pokorná, J.; Plešek, J.; Grüner, B.; Dolečková-Marešová, L.; Máša, M.; Sedláček, J.; Bodem, J.; Krausslich, H. G.; Král, V.; Konvalinka, J. *Proc. Nat. Acad. Sci.* **2005**, *102*, 15394–15399.
63. Kožíšek, M.; Cígler, P.; Lepšík, M.; Fanfrlík, J.; Řezáčová, P.; Brynda, J.; Pokorná, J.; Plešek, J.; Grüner, B.; Grantz-Šašková, K.; Václavíková, J.; Král, V.; Konvalinka, J. *J. Med. Chem.* **2008**, *51*, 4839–4843.
64. Pokorná, J.; Brynda, J.; Kožíšek, M.; Cígler, P.; Lepšík, M.; Plešek, J.; Grüner, B.; Oberwinkler, H.; Krausslich, H. G.; Král, V.; Konvalinka, J.; Řezáčová, P. *FEBS J.* **2009**, *276*, 78–78.
65. Řezáčová, P.; Pokorná, J.; Brynda, J.; Kožíšek, M.; Lepšík, M.; Cígler, P.; Fanfrlík, J.; Řezáč, J.; Grantz-Šašková, K.; Sieglová, I.; Plešek, J.; Šícha, V.; Grüner, B.; Oberwinkler, H.; Sedláček, J.; Krausslich, H. G.; Hobza, P.; Král, V.; Konvalinka, J. *J. Med. Chem.* **2009**, *52*, 7132–7141.
66. Wei, X.; Carroll, P. J.; Sneddon, L. G. *Organometallics* **2006**, *25*, 609–621.
67. Simon, Y. C.; Ohm, C.; Zimmy, M. J.; Coughlin, E. B. *Macromolecules* **2007**, *40*, 5628–5630.
68. Plešek, J.; Štíbr, B.; Drdácká, E.; Plzák, Z.; Heřmánek, S. *Chem. Ind.* **1982**, 778–779.
69. Zakharkin, L. I.; Kazantsev, A. V. *Zh.Obshch. Khim*. **1967**, *37*, 1211–1216.
70. Janoušek, Z.; Plešek, J.; Heřmánek, S.; Baše, K.; Todd, L. J.; Wright, W. F. *Collect. Czech. Chem. Commun.* **1981**, *46*, 2818–2833.
71. Eignerová, B.; Janoušek, Z.; Dračínský, M.; Kotora, M. *Synlett* **2010**, *6*, 885–888.
72. Hayat, S.; Ahmad, A. *Brassinosteroids. Bioactivity and Crop Productivity*, Kluwer Academic Publishers, Dordrecht, 2003.
73. Kagale, S.; Divi, U. K.; Krochko, J. E.; Keller, W. A.; Krishna, P. *Planta* **2007**, *225*, 353–364.
74. Swaczynová, J.; Šíša, M.; Hniličková, J.; Kohout, L.; Strnad, M. *Pol. J. Chem.* **2006**, *80*, 629–635.
75. Wu, Y. D.; Lou, Y. J. *Pharmazie* **2007**, *62*, 392–395.

76. Michelini, F. M.; Ramirez, J. A.; Berra, A.; Galagovsky, L. R.; Alché, L. E. *Steroids* **2004**, *69,* 713–720.
77. Maliková, J.; Swaczynová, J.; Kolář, Z.; Strnad, M. *Phytochemistry* **2008**, *69*, 418–426.
78. Hai, T.; Schneider, B.; Adam, G. *Phytochemistry* **1995**, *40*, 443–448.
79. Slavíková, B.; Kohout, L.; Buděšínský, M.; Swaczynová, J.; Kasal, A. *J. Med. Chem.* **2008**, *51*, 3979–3984.
80. Khripach, V. A.; Zhabinskii, V. N.; de Groot, A. E. *Brassinosteroids: A New Class of Plant Hormones*, Academic Press, San Diego, 1999.
81. Kohout, L.; Chodounská, H.; Macek, M.; Strnad, M. *Collect. Czech. Chem. Commun.* **2000**, *65*, 1754–1761.
82. Dess, D. B.; Martin, J. C. *J. Am.Chem.Soc.* **1991**, *113*, 7277–7287.
83. Eignerová, B.; Slavíková, B.; Buděšínský, M.; Dračínský, M.; Klepetářová, B.; Šťastná, E.; Kotora, M. *J. Med. Chem.* **2009**, 5753–5757.
84. B. Slavíková, A. Kasal, L. Uhlířová, M. Kršiak, H. Chodounská, L. Kohout, *Steroids* **2001**, *66,* 99–105.
85. Mitchell, J. W.; Livingstone, G. A. *Bean second internode method.* In Agricultural Handbook, No. 336; U.S. Government Printing Office, Washington, DC, 1968, 26–28.
86. Gustafsson, J. A. *J Endocrinol* **1999**, *163*, 379–383.
87. Palmieri, C.; Cheng, G. J.; Saji, S.; Zelada-Hedman, M.; Warri, A.; Weihua, Z.; Van Noorden, S.; Wahlstrom, T.; Coombes, R. C.; Warner, M.; Gustafsson, J. A. *Endocr Relat Cancer* **2002**, *9*, 1–13.
88. Zhu, Y.; Bian, Z.; Lu, P.; Karas, R. H.; Bao, L.; Cox, D.; Hodgin, J.; Shaul, P. W.; Thoren, P.; Smithies, O.; Gustafsson, J. A.; Mendelsohn, M. E. *Science* **2002**, *295*, 505–508.
89. Harris, H. A. *Mol Endocrinol* **2007**, *21*, 1–13.
90. Weihua, Z.; Makela, S.; Andersson, L. C.; Salmi, S.; Saji, S.; Webster, J. I.; Jensen, E. V.; Nilsson, S.; Warner, M.; Gustafsson, J. A. *Proc. Natl. Acad. Sci. U. S. A* **2001,** 98, 6330–6335.
91. Neubauer, B. L.; McNulty, A. M.; Chedid, M.; Chen, K.; Goode, R. L.; Johnson, M. A.; Jones, C. D.; Krishnan, V.; Lynch, R.; Osborne, H. E.; Graff, J. R. *Cancer Res* **2003**, *63*, 6056–6062.
92. Omoto, Y.; Inoue, S.; Ogawa, S.; Toyama, T.; Yamashita, H.; Muramatsu, M.; Kobayashi, S.; Iwase, H. *Cancer Lett* **2001**, *163*, 207–212.

93. Campbell-Thompson, M.; Lynch, I. J.; Bhardwaj, B. *Cancer Res* **2001**, *61*, 632–640.

94. Foley, E. F.; Jazaeri, A. A.; Shupnik, M. A.; Jazaeri, O.; Rice, L. W. *Cancer Res* **2000**, *60*, 245–248.

95. (a) Novák, P.; Sedlák, D.; Bartůněk, P.; Kotora, M. CZ 300 376, **2009**. (b) Sedlák, D.; Novák, P.; Kotora, M.; Bartůněk, P. *J. Med. Chem.* **2010**, *53*, 4290–4294.

96. Boivin, R. P.; Luu-The, V.; Lachance, R.; Labrie, F.; Poirier, D. *J. Med. Chem.* **2000**, *43*, 4465–4478.

97. Gupta, A. K.; Yadav, K. M.; Patro, B.; Ila, H.; Junjappa H. *Synthesis* **1995**, 841–844.

98. (a) Salman, M.; Reddy, B. R.; Suprabhat, R.; Stotter, P. L.; Chamness, G. C. *J. Steroid. Biochem.* **1986**, *24*, 539−548. (b) Salman, M.; Reddy, B. R.; Delgado, P.; Stotter, P. L.; Fulcher, L. C.; Chamness, G. C. *Steroids* **1991**, *56*, 375−385. (c) Anstead, G. M.; Carlson, K. E.; Katzenellenbogen, J. A. *Steroids* **1997**, *62*, 268−303.

99. Aloui, F.; El Abed, R.; Marinetti, A.; Ben Hassine, B. *Tetrahedron Lett.* **2007**, *48*, 2017–2020.

100. Eignerová, B.; Sedlák, D.; Dračínský, M.; Bartůněk, P.; Kotora, M. *J. Med. Chem.* **2010**, Manuscript accepted.

101. Harrington, W. R.; Sheng, S.; Barnett, D. H.; Petz, L. N.; Katzenellenbogen, J. A.; Katzenellenbogen, B. S. *Mol. Cell. Endocrinol* **2003,** 206, 13-22.

102. Heldring, N.; Pike, A.; Andersson, S.; Matthews, J.; Cheng, G.; Hartman, J.; Tujague, M.; Strom, A.; Treuter, E.; Warner, M.; Gustafsson, J. A. *Physiol. Rev.* **2007,** *87*, 905–931.

103. Cheskis, B. J.; Greger, J. G.; Nagpal, S.; Freedman, L. P. *J. Cell. Physiol.* **2007,** *213*, 610–617.

104. Gustafsson, J. A. *Trends Pharmacol. Sci.* **2003,** 24, 479–485.

105. Peters, R. H.; Crowe, D. F.; Avery, M. A.; Chong, W. K.; Tanabe, M. *J. Med. Chem.* **1989,** *32*, 1642–1652.

106. el Amouri, H.; Vessieres, A.; Vichard, D.; Top, S.; Gruselle, M.; Jaouen, G. *J. Med. Chem.* **1992**, *35*, 3130–3135.

107. Vichard, D.; Gruselle, M.; Amouri, H.; Jaouen, G.; Vaissermann, J. *Organometallics* **1992**, *11*, 2952–2956.

108. Foy, N.; Stephan, E.; Jaouen, G. *Tetrahedron Lett.* **2000,** *41*, 8089–8092.

109. Foy, N.; Stephan, E.; Vessieres, A.; Salomon, E.; Heldt, J. M.; Huche, M.; Jaouen, G. *ChemBioChem* **2003,** *4*, 494–503.

110. Napolitano, E.; Fiaschi, R.; Carlson, K. E.; Katzenellenbogen, J. A. *J. Med. Chem.* **1995,** *38*, 429–434.
111. Eignerová, B.; Sedlák, D.; Dračínský, M.; Janoušek, Z.; Bartůněk, P.; Kotora, M. Manuscript in preparation.
112. von Werner, K.; Gendorf, W.; Wrackmeyer, B. *J. Fluorine Chem.* **1981**, *19*, 163–180.
113. Fuchikami, T.; Ojima, I. *Tetrahedron Lett.* **1986**, *25*, 307–308.
114. Knell, M.; Brace, N. DE 2 241 252, **1972**.
115. Zelenka, K. Ph.D. Thesis, Charles University, Prague, Czech Republic, 2007.
116. Kohout, L. *Collect. Czech. Chem. Commun.* **1994**, *59*, 457–460.
117. Boucheau, V.; Renaud, M.; Ravel, M. R. de; Mappus, E.; Cuilleron, C. Y. *Steroids* **1990**, *55*, 209–221.
118. Colton, F. B.; Nysted, L. N.; Riegel, B.; Raymond, A. L. *J. Am. Chem. Soc.* **1957**, *79*, 1123–1127.
119. Djerassi, C.; Scholz, C. R. *J. Am. Chem. Soc.*, **1949**, *71*, 3962–3966.
120. Counsell, R. E.; Klimstra, P. D.; Elton, R. L.; Nutting, E. F. *J. Med. Chem.* **1966**, *9*, 689–692.
121. Altomare, A.; Cascarano, G.; Giacovazzo, G.; Guagliardi, A.; Burla, M. C.; Polidori, G.; Camalli, M. *J. Appl. Cryst.* **1994,** *27*, 435–435.
122. Betteridge, P. W.; Carruthers, J. R.; Cooper, R. I.; Prout, K.; Watkin, D. J. *J. Appl. Cryst.* **2003**, *36*, 1487–1487.
123. Sheldrick, G. M. SHELXL97. University of Göttingen, Germany, 1997.

8. List of Abbreviations

AIBN azoisobutyronitril
aq. aqueous
Ac acetyl
b broad
Bn benzyl
Bz benzoyl
CB carborane
calcd calculated
CM cross-metathesis
Cy cyclohexyl
d dublet
δ chemical shift
DHP dihydropyran
DMAP dimethylaminopyridine
DMF *N*,*N*-dimethylformamid
E2 17β-estradiol
EI-MS electron impact mass spectrometry
EM enyne metathesis
ER estrogen receptor
ESI-MS electrospray ionization mass spectrometry
eq equivalent
Et ethyl
FAB fast atom bombardment
FITS-6 perfluorohexylphenyliodonium trifluoromethanesulfonate
GABA γ-aminobutaric acid
h hour
HR-MS high resolutin mass spectrometry
HPLC high pressure liquid chromatography
i-Pr isopropyl
IR infrared spectroscopy
J coupling constant
m multiplet

mp	melting point
Me	methyl
MBz	*p*-methoxybenzyol
Mes	mesityl
MOM	methoxymethyl
NMO	*N*-methyl morpholine *N*-oxide
NMR	nuclear magnetic resonance
PCC	pyridiniumchlorochromate
Ph	phenyl
Py	pyridine
q	quartet
r.t.	room temperature
RCM	ring closing metathesis
R_F	perfluoroalkyl
s	singlet
sept	septet
t	triplet
t-Bu	*t*-butyl
TBDMSCl	*t*-butyldimethylsilyl chloride
THF	tetrahydrofuran
THP	tetrahydropyranyl
TLC	thin layer chromatography
TMS	tetramethylsilane
Ts	*p*-toluensulfonyl
UV	ultraviolet

9. List of Publications

1. Eignerová, B.; Dračínský, M.; Kotora, M. Perfluoroalkylation via Cross-metathesis of Alkenes with (Perfluoroalkyl)propenes. *Eur. J. Org. Chem.* **2008**, *26*, 4493–4499.

2. Auvinet, A.-L.; Eignerová, B.; Alexandre Guy, A.; Kotora, M.; Durand, T. Total Synthesis of 4-F_{3t}-Neuroprostane and its 4-Epimer. *Tetrahedron Lett*. **2009**, *50*, 1498–1500.

3. Eignerová, B.; Slavíková, B.; Buděšínský, M.; Dračínský, M.; Klepetářová, B.; Šťastná, E.; Kotora, M. Synthesis of Fluorinated Brassinosteroids Based on Alkene Cross-metathesis and Preliminary Biological Assessment. *J. Med. Chem.* **2009**, 5353–5357.

4. Eignerová, B.; Janoušek, Z.; Dračínský, M.; Kotora, M. Synthesis of Perfluoroalkylated Carboranes by Cross-metathesis of Allylcarboranes and Perfluoroalkylpropenes. *Synlett* **2010**, *6*, 885–888.

5. Eignerová, B.; Sedlák, D.; Dračínský, M.; Bartůněk, P.; Kotora, M. Synthesis and Biochemical Characterization of a Series of 17α-Perfluoroalkylated Estradiols as Selective Ligands for ERα. *J. Med. Chem.* **2010**, Manuscript accepted.

6. Řezanka, M.; Eignerová, B.; Jindřich, J.; Kotora, M. Synthesis of Mono(perfluoroalkyl) Cyclodextrins via Cross-metathesis *Eur. J. Org. Chem.* **2010**, Manuscript accepted.

7. Biedermann, D., Eignerová, B.; Hajdúch, M.; Šarek, J. Synthesis and Evaluation of Biological Activity of the Quaternary Ammonium Salts of Lupane, Oleanane and Ursane Type Acids. *Synthesis* **2010**, Manuscript accepted.

8. Eignerová, B.; Dračínský, M.; Kotora, M. Diels-Alder Reaction of Nitroacrylate with Alkoxydiene: an Alternative Synthesis Oseltamavir-like Scaffold. Manuscript submitted.