107. Total Synthesis with a Chirogenic Opening Move Demonstrated on Steroids with Estrane or 18a-Homoestrane Skeleton[1][2])

by **Gerhard Quinkert***, **Michael Del Grosso, Astrid Döring, Wolfgang Döring, Ralf I. Schenkel, Markus Bauch, Gernot T. Dambacher, Jan W. Bats, Gottfried Zimmermann**, and **Gerd Dürner**

Institut für Organische Chemie der Universität Frankfurt am Main,
Marie-Curie-Str. 11, D-60439 Frankfurt am Main

Dedicated to *Albert Eschenmoser* on the occasion of his 70th birthday

(12.VI.95)

A concept of first choice for the synthesis of the title compounds had been proposed by *Dane* in the late 1930s. It was soon turned down, because the opening move – a chirogenic *Diels-Alder* reaction – did not work. With *Lewis* acids as mediators, however, a successful start has been achieved now. With Ti complexes of chelating ligands (*Seebach*'s TADDOLs (= α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols)), enantioselective formation of the desired adducts does occur. Efficient total syntheses of **2** and **3a** have been accomplished.

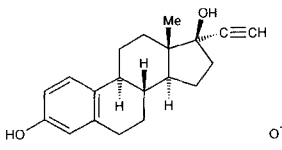
1. Introduction. – 17α-Ethynylestradiol (**1**), norgestrel (**2**), and estrone (**3a**) are representative examples of steroids containing the estrane or 18a-homoestrane skeleton. The first two of these compounds play an important role, as components of oral contraceptives, both in the welfare of individual human beings and for the benefit of all mankind. Compound **1** is readily accessible from the naturally occuring **3a**, compound **2** from the methyl ether of non-natural 18a-homoestrone (**3d**; or from either of the constitutionally isomeric dehydro derivatives **4b** or **5b**). Compounds **3a** and **3d** may, therefore, be regarded as attractive target compounds for the total synthesis of **1** and **2**, respectively. The strategy of the synthesis to be employed here, however, must be sufficiently flexible to permit incorporation of an angular Me group, as well as an angular Et group. The biosynthesis of **3a**[3]) is certainly not the appropriate model. As is often the case with compounds which perform biologically important functions, the synthetic pathway, which was found in the course of the early period of material evolution, is too convoluted to be useful for synthetic practice. Structural changes invented in the laboratory, and thus belonging to the later period of cultural evolution, are of particular value for synthetic chemistry, when they permit frequently desired structural modifications to be effected in a straightforward way. The *Diels-Alder* reaction is one such transformation, playing no role in biosynthesis, but, in contrast, occupying a prominent position in abiotic chemistry.

---

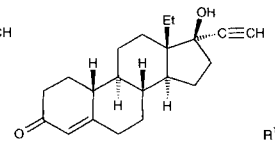
[1]) From the Ph.D. theses of *M.D.G.* [1], *A.D.* [2], *W.D.* [3], *R.I.S.* [4], *M.B.* [5], and the Diploma thesis of *G.T.D.* [6].

[2]) Abbreviations used: BHT: 2,6-Di(*tert*-butyl)-4-methylphenol; HMDS: 1,1,1,3,3,3-hexamethyldisilazane; HMPT: hexamethylphosphoric triamide.

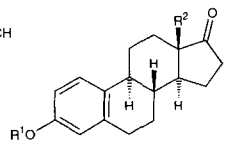
[3]) The biosynthesis of **3a** contains that one of cholesterol and includes degradation of the side chain and aromatization of ring *A*.



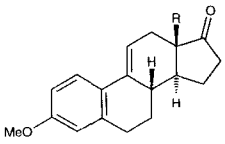
1



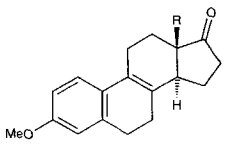
2



3a R^1 =H, R^2 = Me
3b R^1 = H, R^2 = Et
3c R^1 = R^2 = Me
3d R^1 = Me, R^2 = Et

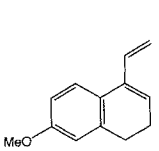


4a R = Me
4b R = Et



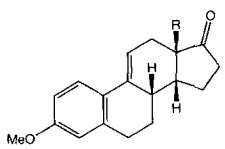
5a R = Me
5b R = Et

2. Constitutional Construction *AB* + *D* → *ABCD'* → *ABCD*. – 2.1. *With Dienophiles of Type* **7** *as the* D-*Ring Building Blocks*. It is no longer possible to ponder on the synthesis of steroids with the various basic skeletons known without thinking of intermolecular *Diels-Alder* reactions as the opening move[4]). However, unlike intramolecular *Diels-Alder* reactions[5]), they have not especially proved their worth in pellucid syntheses, particularly of steroids with the estrane skeleton[6]). As early as the late 1930s, *Dane* and *Eder* [10] were to make the discovery that the at first sight very promising cycloaddition of 1-vinyl-6-methoxy-3,4-dihydronaphthalene (**6**) with 2-methylcyclopent-2-en-1-one (**7a**) does not in fact take place. The relatively late observation that *Diels-Alder* reactions in which a *Lewis* base acted as the dienophile could be accelerated using *Lewis* acids [11] was to give a new impetus to efforts to finally make *Dane*'s concept a reality.

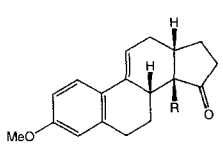


6

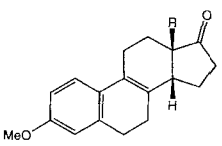
7a R = Me
7b R = Et



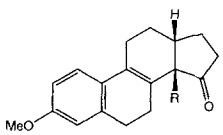
8a R = Me
8b R = Et



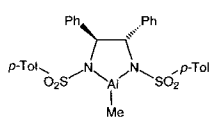
9a R = Me
9b R = Et



10a R = Me
10b R = Et



11a R = Me
11b R = Et



12a R=CF_3
12b R=1-Naphthyl
12c R=2,4,6-Triisopropylphenyl
12d R=*p*-Tol

---

[4]) See the section 'Intermolecular *Diels-Alder* reactions' in [7] [8].

[5]) See the section 'Intramolecular *Diels-Alder* reactions' in [7] [8].

[6]) The stereoselective synthesis of **3a** [9] provides an early example what optimization may achieve; the overall pathway, however, is too lengthy.

2.1.1. Diels-Alder Reactions Mediated by Lewis *Acids*[7]). Naphthalene derivative **6** does indeed react with **7a** or **7b** in the presence of *Lewis* acids (s. *Table 1*). The respective acidity (the nature of the central atom and its ligands) of the *Lewis* acid employed determines the chemical yield in which the constitutional isomers of the primary adduct (of type *rac*-**8** or *rac*-**9**[8])) or those of the derived secondary adduct (of type *rac*-**10** or *rac*-**11**) are produced.

Table 1. Diels-Alder *Reactions of Diene* **6** *with Dienophiles of Type* **7**

Dienophile	Reaction conditions	Adduct	*Exper.*
7a	[a]		–
7a	[b], 59%	*rac*-**8a** (96) + *rac*-**9a** (4)	*1.1.1*
7a	[c], 86%	*rac*-**8a** (91) + *rac*-**9a** (9)	*1.1.2*
7a	[d]		–
7a	[e], 89%	*rac*-**10a**	*1.1.4*
7b	[e], 90%	*rac*-**10b**	*1.2*

[a]) Dioxane, reflux. [b]) Et_2AlCl, CH_2Cl_2, 0°→r.t. [c]) *rac*-**12d**, $(CH_2Cl)_2$, 0°→r.t. [d]) $(i\text{-}PrO)_2TiCl_2$, CH_2Cl_2, r.t. [e]) $TiCl_4$, –80°.

Lewis acids with Al as the central atom (Et_2AlCl or *rac*-**12**[9])) lead, in moderate-to-good yields, to primary adducts, mainly consisting of *rac*-**8**. Of *Lewis* acids with Ti as the central atom, $(i\text{-}PrO)_2TiCl_2$ is insufficiently acidic (no cycloaddition), while $TiCl_4$, on the other hand, is so acidic that secondary adducts (exclusively of type *rac*-**10**) are isolated.

X-Ray crystal-structure analyses (*Fig. 1*) of *rac*-**8a**[10]), *rac*-**10a**[11]), and *rac*-**10b**[12]) establish the *cis*-fusion of the *C* and *D* rings and the location of the respective C=C bonds, as well as the favored formation of that adduct arising through an *endo* transition structure, still demonstrable in the case of *rac*-**8a**.

2.1.2. *Stereostructural Correction of the Fusion of Rings* C *and* D. Mechanism controls that rings *C* and *D* are fused in a *cis*-configuration in *Diels-Alder* adducts of type **8** or **10**. It is known that steroids of type **14** may be partially and stereoselectively hydrogenated

[7]) The essential facts were reported in [12] and a review article [13]. An overview of the influence of *Lewis* acids on the course of *Diels-Alder* reactions may be found in [14].

[8]) Compounds *rac*-**8a** and *rac*-**9a** *a priori* could be constitutional or configurational (H–C(8)/H–C(14): *cis* or *trans*) isomers. In the latter case, *rac*-**8a** and *rac*-**9a**, on treatment with HCl/MeOH, would give one and the same product, namely *rac*-**10a**, which is not true (see *Exper. 2.2*).

[9]) For preparation and use of **12** or of *ent*-**12**, see [15].

[10]) See *Exper. 1.1.1* as well as Fig. 15A in [13].

[11]) See Ref. 7 in [12] and Fig. 15B in [13].

[12]) See Ref. 7 in [12] and Fig. 15C in [13].

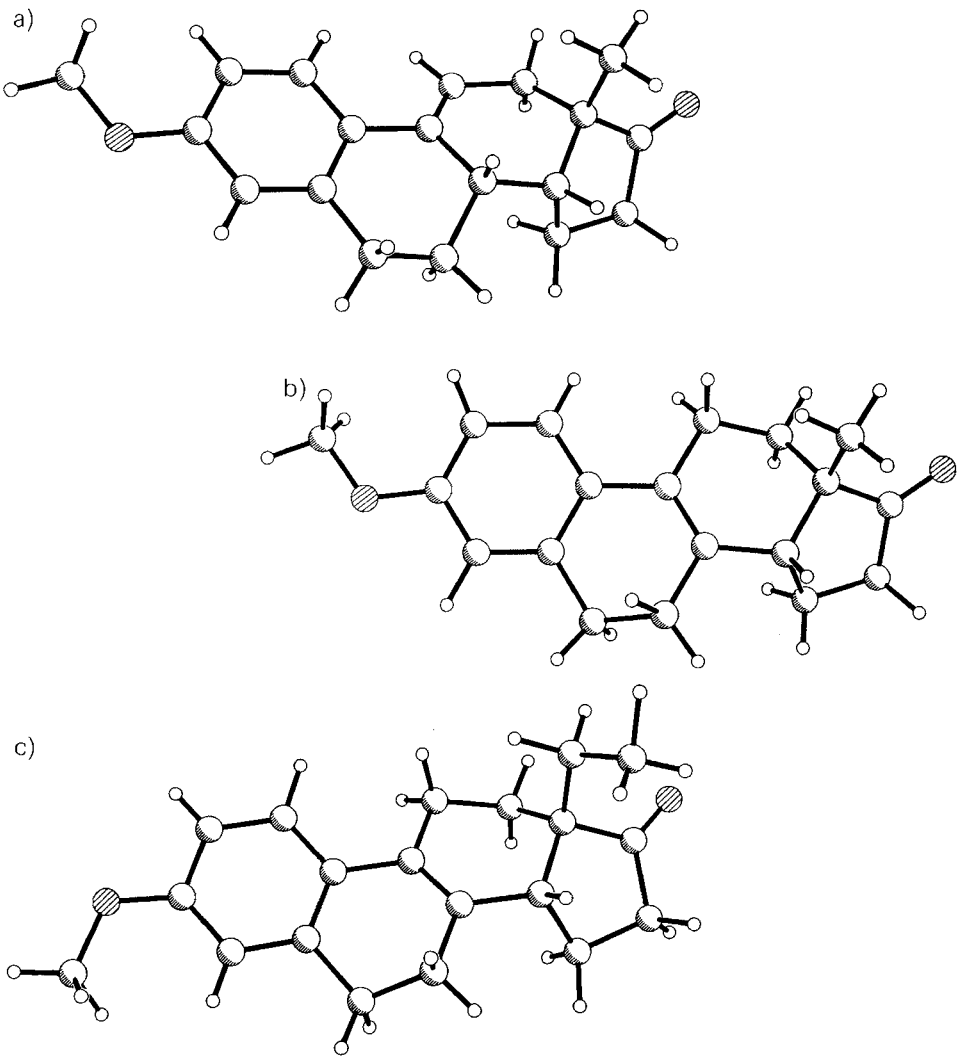
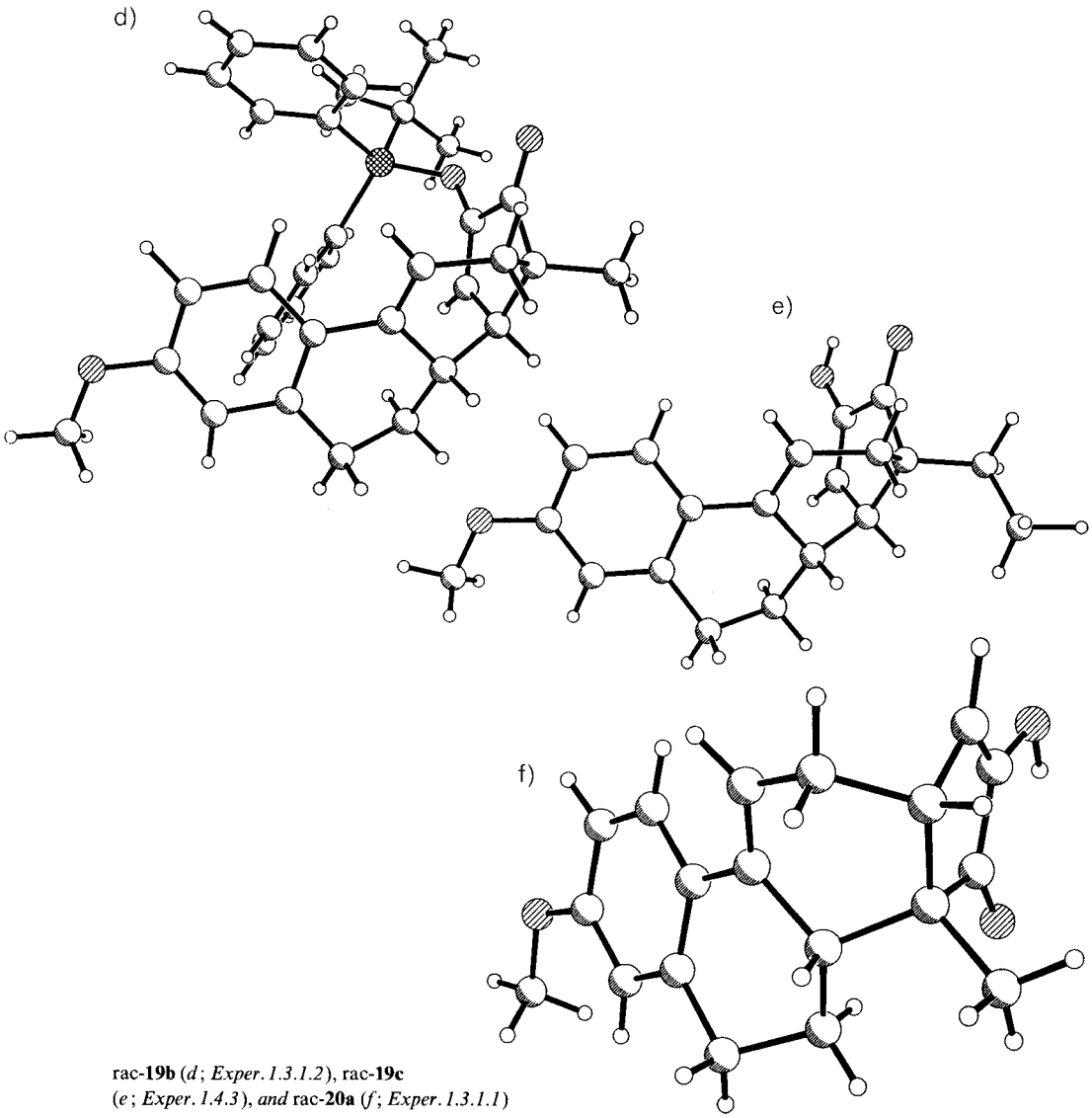


Fig. 1. *Representations of single-crystal X-ray structures of compounds* rac-**8** (*a*; *Exper. 1.1.1*), rac-**10a** (*b*; *Exper. 1.1.4*), rac-**10b** (*c*; *Exper. 1.2.1*),

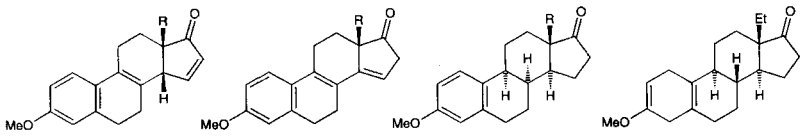
[16] to give steroids of type **5**, with *C* and *D* rings fused in a *trans*-manner. The pathway from *rac*-**8a**, *via rac*-**10a**, *rac*-**13a**, *rac*-**14a**, and thence to *rac*-**5a**, together with that one from *rac*-**10b**, *via rac*-**13b**, and *rac*-**14b** to *rac*-**5b** is outlined below.

The decisive reaction step in the sequence of transformations which begins with secondary adducts of type *rac*-**10** and ends with C(14)-isomers of type *rac*-**5** is the conversion of compounds of type *rac*-**10** into those ones of type *rac*-**13**. The majority of known literature procedures makes use of a reaction pair: bromination/dehydrobromination, sulfide oxidation/sulfoxide elimination, or selenide oxidation/selenoxide elimina-

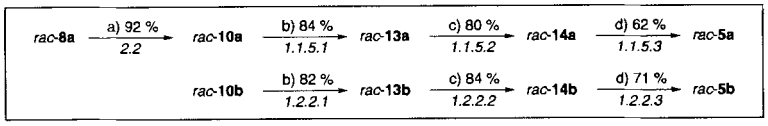


rac-**19b** (*d*; *Exper. 1.3.1.2*), rac-**19c** (*e*; *Exper. 1.4.3*), *and* rac-**20a** (*f*; *Exper. 1.3.1.1*)

tion. In the case to hand, however, these methods have all shown themselves to be unsuitable, as they lead to complex mixtures, and consequently to unsatisfactory yields of the desired dehydrogenation product. We have essentially followed a modification of a procedure reported by *Tsuji* and coworkers [17], which chemists at *Schering AG* [18] have already exploited in the preparation, with good yields, of conjugated, unsaturated 17-keto steroids. This procedure makes use of silyl enol ethers, accessible from ketones of type *rac*-**10**, which may be oxidized with equivalent quantities of $Pd(OAc)_2$ in MeCN at r.t.



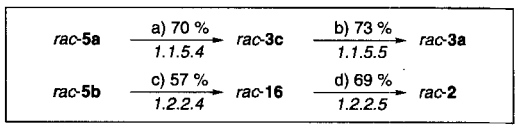
13a R = Me **13b** R = Et **14a** R = Me **14b** R = Et **15a** R = Me **15b** R = Et **16**



a) CH_2Cl_2/MeOH, HCl, r.t. b) 1. LDA, TMS-Cl, THF, −80°, 2. $Pd(OAc)_2$, MeCN, r.t. c) 1. LiHMDS, THF/HMPT, −80°, 2. AcOH, −80°. d) H_2, $Pd/CaCO_3$, r.t.

Conversion of compounds of type *rac*-**13** into compounds of type *rac*-**14** proceeded in 80% yield, by means of vinylogous deprotonation and subsequent protonation. Maximum stereostructural simplicity is achieved arriving at *Torgov*'s pentaenone[13]) of type *rac*-**14** [19]: the necessary ensuing introduction of the stereogenic centers C(14), C(9), and C(8) is initially directed by the angular Me (or Et)group. The *trans*-relationship of the *C* and *D* rings was achieved in a known manner [16] using catalytic hydrogenation[14]).

2.1.3. *Completion of the Synthesis of* rac-**3a** *and* rac-**2a**. Ionic hydrogenation [20] affords *rac*-**3c**[15]) in 70% yield from *rac*-**5a**; cleavage of the ether then gives (±)-estrone (*rac*-**3a**)[16]) in 73% yield. A series of reaction steps – reduction of the styrene derivative *rac*-**5b** with $LiAlH_4$, *Birch* reduction of the mixture of epimeric alcohols thus obtained, followed by *Oppenauer* oxidation and ethynylation of the resulting ketone *rac*-**16**[17]) – affords *rac*-**2** in an overall yield of 39% from *rac*-**5b**.



a) Et_3SiH, CF_3CO_2H, benzene, r.t. b) BBr_3, CH_2Cl_2, 0°. c) 1. $LiAlH_4$, Et_2O, ultrasound, r.t.; 2. K, aniline, NH_3(l), then Li, EtOH; 3. $(i\text{-}PrO)_3Al$, butan-1-one, benzene, reflux. d) 1. $LiC{\equiv}CH$, $H_2N(CH_2)_2NH_2$, THF, r.t.; 2. MeOH, HCl, 40–45°.

2.1.4. *Enantioselective Realization of the Chirogenic*[18]) *Opening Move*. The total synthesis of steroids with the estrane skeleton discussed here begins with a chirogenic *Diels-Alder* reaction. The first step, not possible in the absence of a catalyst, offers the oppor-

[13]) Besides *Dane*'s concept, that one of *Torgov* belongs to the simplest conceivable strategies for the synthesis of the title compounds.

[14]) Hydrogenation of *rac*-**14a** affords *rac*-**5a** (66%), *rac*-**10a** (9%), and *rac*-**15a** (5%). On hydrogenation of *rac*-**14b**, the product components *rac*-**5b** (74%), *rac*-**10b** (4%), and *rac*-**15b** (4%) were observed.

[15]) See [21] for the ionic hydrogenation of **8a** to **3a**, and [22] for that one of *rac*-**5b** to *rac*-**3b**.

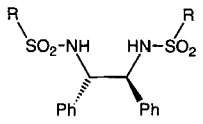
[16]) See [23] for the cleavage of the methyl ether of **3a** with BBr_3.

[17]) The reaction sequence commencing with *rac*-**5b** and ending with *rac*-**2** has already been employed in a previous total synthesis of **2** and *rac*-**2** [24].

[18]) See [25] for the meaning of the term 'chirogenic reaction step' and the usefulness of its application.

Table 2. *Enantioselective* Diels-Alder *Reactions of Diene* **6** *with Dienophile* **7a** *Mediated by Chiral, Non-racemic* Lewis *Acids, Formed by Reactions between Ligands of Type* **B** *with the Indicated Al Compounds* (for details, see *Exper. 1.1.3*)

Ligand	*Lewis* acid	Temp. [°C]	Time	Yield [%]	$[\alpha]_{589}^{20}$	Optical purity [%]
Ba	$AlMe_3$	0 to 25	15 h	92	+34	13
Ba	$AlMe_3$	−25	2.5 d	93	+32	12
Ba	$AlMe_3$	−80	7 d	85	+25	10
Ba	DIBAH	−25	15 h	26	0	0
Ba	DIBAH	−80	7 d	75	−36	13
Bb	$AlMe_3$	0 to 25	15 h	82	+3	1
Bb	$AlMe_3$	−25	2 d	68	+6	2
Bb	$AlMe_3$	−80	14 d	9	0	0
Bd	DIBAH	−25	2 d	32	+67	25
Bb	DIBAH	−80	14 d	0	–	–
Bc	$AlMe_3$	0 to 25	15 h	83	−46	17
Bc	$AlMe_3$	−25	2 d	76	−47	18
Bc	$AlMe_3$	−80	7 d	0	–	–
Bc	DIBAH	−25	2 d	9	+7	3
Bc	DIBAH	−80	14 d	0	–	–
Bd	$AlMe_3$	0 to 25	15 h	80	+41	15



B

Ba R = CF_3
Bb R = Naphthalen-1-yl
Bc R = 2,4,6-Triisopropylphenyl
Bd R = 4-Methylphenyl

tunity of achieving enantioselection with the aid of a chiral, non-racemic *Lewis* acid. Using the *Lewis* acid **12**[19]), reported by *Corey et al.*, the conversion of **6** into **7** proceeds in 80% chemical yield but with an enantiomeric excess of only 15% (see *Table 2*).

Because $(i\text{-PrO})_2TiCl_2$ was ineffective as a reaction mediator (*Sect.* 2.1.1), chiral dialkoxytitanium compounds were initially left out of consideration. These compounds were only to enter into the picture, after interest in dienophiles of type **7** had markedly declined. The fact that interest in these monodentate ligands had so diminished is due to the structure of the complex between $TiCl_4$ and ketone **7a**. The conformational space of the ligand is only negligibly restricted in the complex, a situation not very conducive to stereoselection – which requires some degree of preference for interaction with a reaction partner in one half space or the other, above or beneath the (imagined) molecular plane of the ligand. This is illustrated by the X-ray crystal-structure analysis of the dimeric 1:1 adduct $[(\mathbf{7a}\cdot TiCl_4)]$ (**17A**; see *Fig. 2*[20])). Bidentate ligands of type **18** should, therefore, be better suited for the enantioselective execution of chirogenic *Diels-Alder* reactions than monoketones of type **7**.

[19]) See *Footnote 9* regarding the complex **12** of $AlMe_3$ and (1*S*,2*S*)-1,2-bis{[(4-methylphenyl)sulfonyl]amino}-1,2-diphenylethane [15].

[20]) See Fig. 1 in [26] for a representation of **17** with the program SCHAKAL 88B (Kristallographisches Institut der Universität Freiburg) and Fig. 17 in [13] for a polytube representation (MacroModel V2.5) [27].

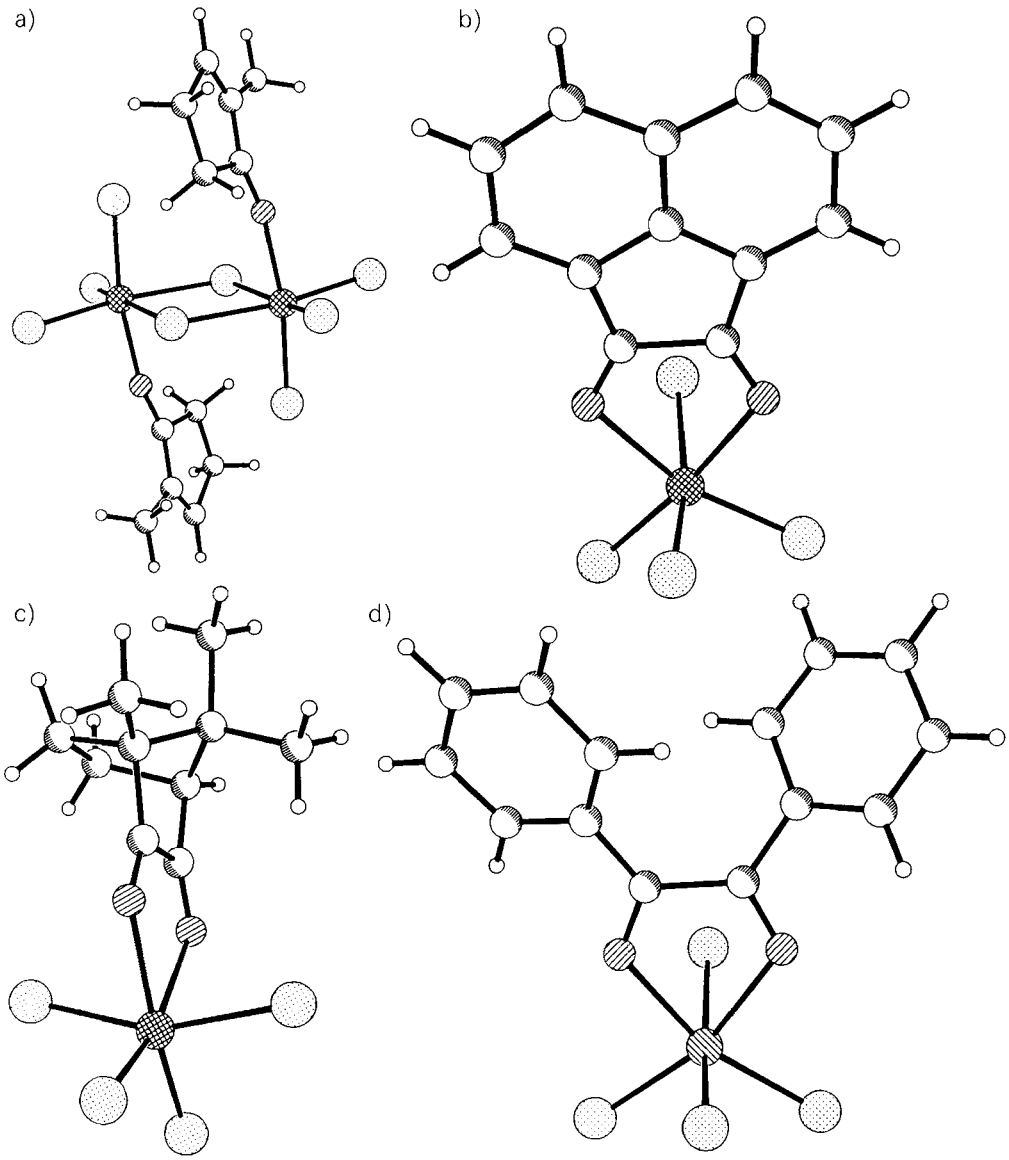
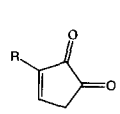


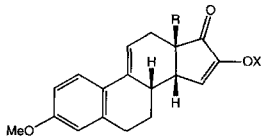
Fig. 2. *Representations of single-crystal X-ray structures of compounds* **17A** (*a*; *Exper. 5.1*), **17B** (*b*; *Exper. 5.2*), **17C** (*c*; *Exper. 5.3*), and **17D** (*d*; *Exper. 5.4*)

2.2. *With Dienophiles of Type* **18** *as the Ring-*D *Building Blocks.* 2.2.1. *By Means of* Lewis-*Acid-Mediated* Diels-Alder *Reactions*[7]). After the negative experience with **7a**, *Dane* attempted to remedy the problem using **18a** [28]. Unlike in the first case, a reaction with **6** did indeed occur in this instance. It was only twenty years later that a thorough investigation [29] established that the adduct, not unambiguously identified by *Dane*, had in fact contained two components, to which formulae *rac*-**21** (for the minor component)

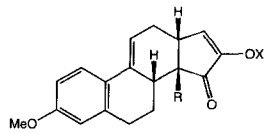
and *rac*-**22a** (for the major component) were assigned. A repetition of the experiment, however (see *Exper. 1.3.1*), revealed that, in reality, the two constitutional isomers *rac*-**19a** and *rac*-**20a** had been formed in 82% yield. It was possible to isolate the major component (with substantial losses) and identify it as *rac*-**20a** by X-ray crystal-structure analysis. For quantitative examination of the adduct, it is expedient to use the (*t*-Bu)Ph_2Si derivatives *rac*-**19b** and *rac*-**20b** rather than the parent enols; these are formed in a 1:3 ratio under the conditions stated. Although **6** had reacted with **18a** (and – as was found out later – could also do the same with **18b**; see *Exper. 1.4.1*), *Dane*, together with a whole generation of synthetic chemists, was forced to abandon this first and in its simplicity very convincing strategy: the chemical yield with which the adduct component showing the constitution of the steroid skeleton could be produced was simply too small.



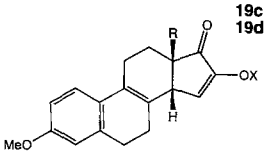
18a R = Me
18b R = Et



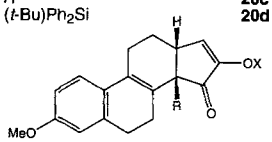
19a R = Me, X = H
19b R = Me, X = (*t*-Bu)Ph_2Si
19c R = Et, X = H
19d R = Et, X = (*t*-Bu)Ph_2Si



20a R = Me, X = H
20b R = Me, X = (*t*-Bu)Ph_2Si
20c R = Et, X = H
20d R = Et, X = (*t*-Bu)Ph_2Si



21a R = Me, X = H
21b R = Me, X = (*t*-Bu)Ph_2Si
21c R = Et, X = H
21d R = Et, X = (*t*-Bu)Ph_2Si



22a R = Me, X = H
22b R = Me, X = (*t*-Bu)Ph_2Si
22c R = Et, X = H
22d R = Et, X = (*t*-Bu)Ph_2Si

After the catalyzability of a whole class of *Diels-Alder* reactions had been established (see *Sect. 2.1*), we examined the question[21]) of whether *Lewis* acids are capable not only of accelerating adduct formation from **6** and dienophiles of type **18**, but of also affecting the relative proportions of the two components of type *rac*-**19** and *rac*-**20**. The results summarized in *Table 3* answer this question in the affirmative, offering a synthetically

Table 3. Diels-Alder *Reactions of Diene* **6** *with Dienophiles of Type* **18** (ratio of adduct components determined after silylation)

Entry	Dienophile	Reaction conditions	Adduct	Yield [%]	*Exper.*
1	**18a**	Dioxane/reflux	*rac*-**19a** (1) + *rac*-**20a** (3)	82	*1.3.1*
2	**18b**	Dioxane/reflux	*rac*-**19c** (1) + *rac*-**20c** (1.9)	40	*1.4.1*
3	**18a**	$BF_3 \cdot OEt_2/Et_2O/-20°$	*rac*-**19a** (49) + *rac*-**20a** (1)	75	*1.3.2*
4	**18b**	$BF_3 \cdot OEt_2/Et_2O/-20°$	*rac*-**19c** (32) + *rac*-**20c** (1)	53	*1.4.2*
5	**18a**	(i-PrO)$_2TiCl_2$, CH_2Cl_2, −30°; CH_2Cl_2, conc. HCl, r.t.	*rac*-**21a**	80	*1.3.3*
6	**18b**	(i-PrO)$_2TiCl_2$, CH_2Cl_2, −30°; CH_2Cl_2, conc. HCl, r.t.	*rac*-**21c**	80	*1.4.4*
7	**18b**	(i-PrO)$_3TiCl$, CH_2Cl_2, −20°	*rac*-**19c**	70	*1.4.3*

[21]) This question was raised on the occasion of a lecture in honor of *Russell E. Marker*; see [30].

valuable finding because of the pronounced reversal in the proportions of the adduct components relative to the uncatalyzed *Diels-Alder* reaction.

X-Ray crystal-structure analyses (see *Fig. 1*) of *rac*-**19b**[22]), *rac*-**19c** (see *Exper. 1.4.3*), and *rac*-**20a**[23]) lead to the conclusion, from the position of the angular Me or Et group and from the relative *syn*/*anti*-orientation of the angular ligands on C(8), C(14), and C(13), that diene and dienophile have preferentially come together *via* an *endo* transition state. Furthermore, the styrenic and enolic C=C bonds in rings *C* and *D* can be seen. As the chirogenic *Diels-Alder*s reactions of dienophiles of type **18**, unlike that one of **7a**, with diene **6** may be catalyzed by dialkoxytitanium compounds, it is to be hoped that enantioselective cycloaddition is possible, provided that **18a** or **18b** participates as a bidentate ligand in a chiral, non-racemic complex.

2.2.2. *Enantioselective Realization of the Chirogenic Opening Move*[24]). With the diketone **18a**, unlike with the monoketone **7a**, we were not succesfull in isolating a crystalline adduct with $TiCl_4$. Efforts were made to provide alternative solutions, with the isolation of complexes of $TiCl_4$ and acenaphthoquinone (**17B**) or camphorquinone (**17c**), as well as from $SnCl_4$ and benzil (**17D**), and the solving of their X-ray crystal structures (see *Fig. 2* [31]. These analyses should answer the question of whether α-diketones function as bidentate ligands to form a chelate ring with the central atom.

In the monomeric complexes **17B**, **17C**, and **17D** (see *Fig. 2*), and also in the case of the dimeric complex **17A**, the Ti- or Sn-atoms are sixfold coordinated in a distorted octahedron. Two types of Ti–Cl or Sn–Cl bonds may be identified. The longer of these may be described as axial, the shorter ones as equatorial. Such a characterization fits with the two O-atoms of the chelated α-diketone lying in a plane with the two equatorially oriented Cl-atoms and the central atom.

In order for chirogenic *Diels-Alder* reactions with α-diketones serving as dienophiles to proceed in an enantioselective manner, it is desirable to make use, if possible, of chiral, non-racemic *Lewis* acids to control not only the constitutional and relative configuration, but, additionally, the absolute configuration of the demanded adduct components.

By 1989, when we began to revive *Dane*'s concept of a simple steroid synthesis, the α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs) introduced by *Seebach et al.* [32] had already achieved considerable fame for their ability, complexed with Ti, to cause enantioselection in the prime example of *Diels-Alder* reactions – cycloaddition between cyclopentadiene and acrylic-acid derivatives [33] [34]. Since the results of, for example, the addition of cyclopentadiene to 3-[(*E*)-but-2-enyl)-1,3-oxazolidin-2-one [33] [35] [36] cannot automatically be applied to the reaction of **6** with dienophiles of type **18**, we made this last reaction, performed in the presence of various TADDOLs of type **T** complexed with Ti, the centerpiece of our own investigations on the enantioselective formation of adducts of type **21** (see *Table 4*).

With the exception of the TADDOL ligand containing 3,5-di(*tert*-butyl)phenyl residues, all the other TADDOL ligands with (*S,S*)-configuration of *Table 4* lead to adducts showing the absolute configuration of the naturally occuring steroids. When four phenanthren-9-yl residues are present in the TADDOL ligand, the cycloaddition of **6** and

---

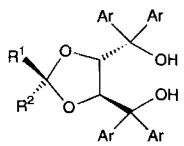
[22]) See Footnote 7 in [12] and Fig. 19B in [13] (this refers not to the enol, but to its (*t*-Bu)Ph_2Si derivative).

[23]) See Footnote 7 in [12] and Fig. 19A in [13].

[24]) The essential facts were reported in [26] and in a review article [13].

Table 4. *Enantioselective* Diels-Alder *Reactions of Diene* **6** *with Dienophiles of Type* **18** *Mediated by Ti-TADDOLate Complexes, Formed by Reaction of the Indicated TADDOL's with (i-Pro)$_2$TiCl$_2$*
(for details, see *Exper. 1.3.4* and *4.1*)

Entry	Dieno-phile	Ligand	Abs. conf.	Equiv.	Temp [°C]	Time	Yield [%]	$[\alpha]_{589}^{20}$	e.e. [%]
1	**18a**	**Ta**	(*S*,*S*)	2	−30	2 h	64	+92	45
2	**18a**	**Tb**	(*S*,*S*)	2	−50	3 h	76	+144	72[a])
3	**18a**	*ent*-**Tc**	(*R*,*R*)	2	−30	3 h	60	−162	80[a])
4	**18a**	*ent*-**Td**	(*R*,*R*)	2	−30	2 h	71	−102	51[a])
5	**18a**	**Te**	(*S*,*S*)	2	−25	15 h	54	+94	46[a])
6	**18a**	**Tf**	(*S*,*S*)	2	−50	3 h	77	+164	79
7	**18a**	**Tf**	(*S*,*S*)	0.5	−30	2 h	76	+142	71[a])
8	**18a**	**Tf**	(*S*,*S*)	2	−25	15 h	73	+174	86
9	**18a**	**Tf**	(*S*,*S*)	2	−50	5 h	64	+152	74
10	**18a**	**Tg**	(*S*,*S*)	2	−25	15 h	67	+171	81
11	**18a**	**Th**	(*S*,*S*)	2	−25	15 h	88	+27	14[a])
12	**18a**	**Ti**	(*S*,*S*)	2	−25	15 h	60	+164	79
13	**18a**	**Tk**	(*S*,*S*)	2	−25	15 h	35	+191	92
14	**18a**	**Tk**	(*S*,*S*)	2	−80	2 d	65	+194	93
15	**18a**	**Tk**	(*S*,*S*)	0.25	−80	7 d	78	+172	85
16	**18b**	**Te**	(*S*,*S*)	2	−80	7 d	60	+105	48
17	**18b**	**Tf**	(*S*,*S*)	2	−80	7 d	53	+184	80
18	**18b**	**Tl**	(*S*,*S*)	2	−80	7 d	67	−16	8
19	**18b**	**Ti**	(*S*,*S*)	2	−80	7 d	56	+171	80
20	**18b**	**Tk**	(*S*,*S*)	2	−80	7 d	50	+193	88
21	**18b**	**Tk**	(*S*,*S*)	0.2	−80	7 d	77	+196	89



T

Ta $R^1 = R^2$ = Me, Ar = Ph [32b]
Tb $R^1 = R^2$ = Me, Ar = 3,5-Dimethylphenyl *[38]*[b])
Tc $R^1 = R^2$ = Me, Ar = Naphthalen-1-yl *[32b]*[b])
ent-**Td** R^1 = Me, R^2 = Ar = Ph [38] *[41]*[b])
Te $R^1 = R^2$ = Et, Ar = Ph [35]
Tf $R^1 = R^2$ = Et, Ar = 3,5-Dimethylphenyl [35] *[38]*[b])
Tg $R^1 = R^2$ = Et, Ar = 2,5-Dimethylphenyl
Th $R^1 = R^2$ = Et, Ar = 3,4-Dimethoxyphenyl
Ti $R^1 = R^2$ = Et, Ar = Naphthalen-1-yl
Tk $R^1 = R^2$ = Et, Ar = Phenanthren-9-yl
Tl $R^1 = R^2$ = Et, Ar = 3,5-Di(*tert*-butyl)phenyl

[a]) Optical purity.
[b]) Procedures in references indicated in italics lead to enantiomeric TADDOLs.

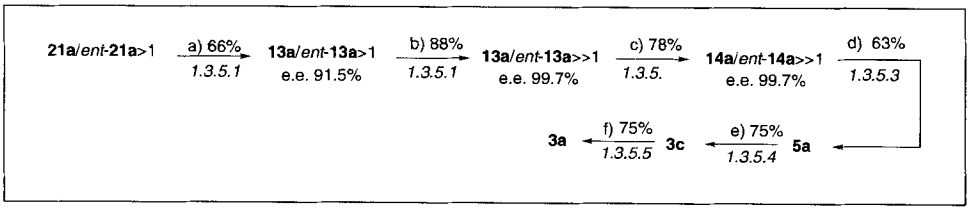
18a attains a chemical yield of 65% and an e.e. value of 93% (run with 2 equiv. of *Lewis* acid; *Entry 14*). With **18b** as the dienophile instead of **18a**, the corresponding values are 77% and 89% (run with 0.2 equiv. of *Lewis* acid; *Entry 21*).

Attempts were of course made to set up a rule in enantioselection [37] in this multitude of Ti-TADDOLate-mediated *Diels-Alder* reactions, visualizing the outcome in a particular case with the aid of a generalized model for the adduct-determining transition structure [35–39]. It became apparent that the cycloaddition of **6** with dienophiles of type **18** represent *the* exception to the rule.

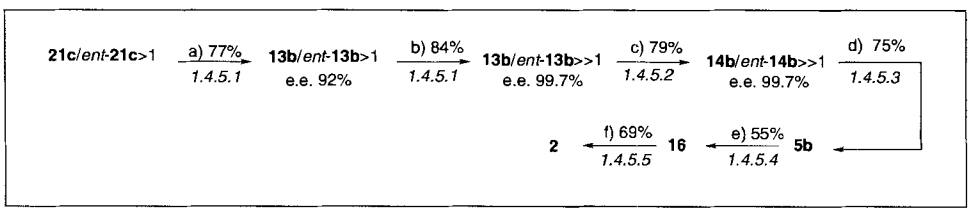
Enantioselection was initiated by suitably chosen reaction conditions for the chirogenic reaction (e.e. 93% in the Me series, 89% in the Et series) and completed by fractional crystallization (e.e. > 99.7%).

2.2.3. *Stereostructural Correction of Ring Fusion.* While secondary adducts of type **10**, resulting from the use of monoketonic dienophiles of type **7**, may be converted into compounds of type **13** by dehydrogenation, secondary adducts of type **21**, originating from diketonic dienophiles of type **18**, allow access to compounds of type **13** through deoxygenation. *Stille*'s procedure for the deoxygenation of enols [40] is the method of choice: enol triflates, forming complexes in the presence of LiCl with a $Pd(PPh_3)_4$ catalyst, can then be reduced in good yield with Bu_3SnH.

The pathway from the chiral, non-racemic *Diels-Alder* adducts to the target compounds **3a** and **2** is shown below.



a) 1. $(CF_3SO_2)_2O$, 2,6-Lutidine, CH_2Cl_2, 0°, 2. $Pd(PPh_3)_4$, Bu_3SnH, THF. b) MeOH. c) 1. BuLi, HMDS, HMPT, THF, −80°, 2. AcOH. d) H_2, 5% $Pd/CaCO_3$, C_6H_6, r.t. e) Et_3SiH, TFA, C_6H_6, r.t. f) BBr_3, CH_2Cl_2, 0°.

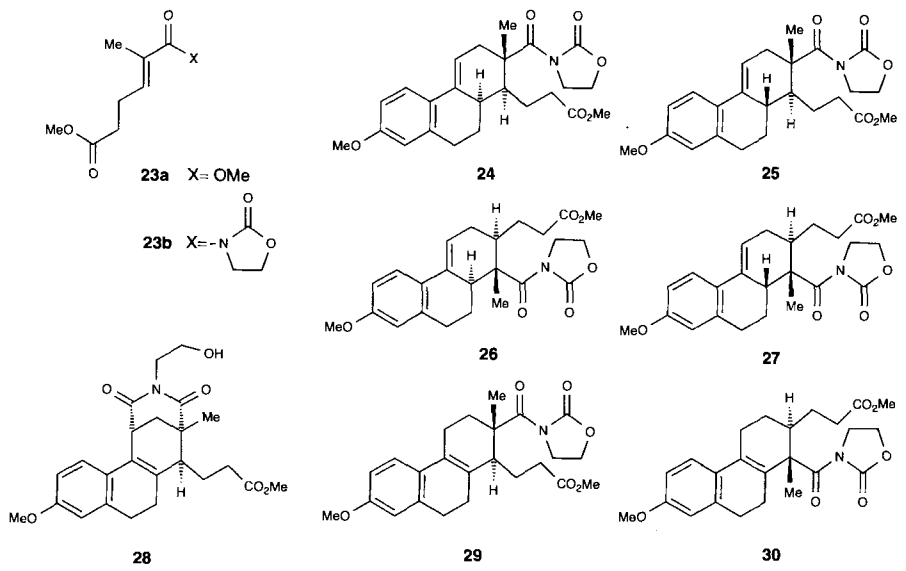


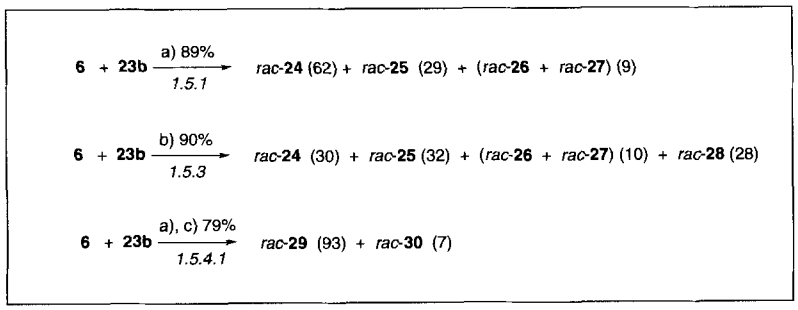
a) 1. $(CF_3SO_2)_2O$, 2,6-Lutidine, CH_2Cl_2, 0°, 2. $Pd(PPh_3)_4$, Bu_3SnH, THF. b) MeOH. c) 1. BuLi, HMDS, HMPT, THF, −80°, 2. AcOH. d) H_2, 5% $Pd/CaCO_3$, C_6H_6, r.t. e) 1. $LiAlH_4$, ultrasound, Et_2O, r.t., 2. K, aniline, $NH_3(l)$, then Li, EtOH, 3. $(i\text{-}PrO)_3Al$, butan-1-one, reflux. f) 1. $LiC{\equiv}CH \cdot H_2N(CH_2)_2NH_2$, THF, r.t.; 2. MeOH, HCl, 40–45°.

3. Constitutional Construction *AB* → *ABC* → *ABCD*. – The use of cyclic dienophiles of type **7** or **18** (of necessity with (*Z*)-configuration in the C=C bond) makes it possible to smoothly construct the steroid skeleton, at least as far as the constitution is concerned. However, the configurationally inevitable *cis*-fusion of rings *C* and *D* in the resulting adducts is highly inconvenient. It can be corrected, as shown above, by a sequence of reaction steps. The question of whether an acyclic dienophile with (*E*)-configuration of the C=C bond might not be preferable will, after all, not go away. A dienophile of type **23a** would merit consideration[25]). A successful *Diels-Alder* reaction would establish ring *C* and a *Dieckmann* condensation ring *D*. Above all, the (*E*)-configurated C_6-dienophile would ensure the thermodynamically unfavored *trans*-fusion in the sequentially arising *C* and *D* rings.

---

[25]) The suggestion to use **23a** as dienophile was included in a research proposal put forward by *M.D.G.* in April 1992 during his membership of the graduate course 'Chemical and Biological Synthesis of Active Compounds' at the Institut für Organische Chemie der Universität Frankfurt am Main.





a) Me_2AlCl, CH_2Cl_2, −25°. b) Me_2AlCl, CH_2Cl_2, 5°. c) TFA, CH_2Cl_2, 0° → r.t.

3.1. *With Dienophiles of Type* **23** *to the* ABC *System.* 3.1.1. Via Lewis-*Acid-Mediated* Diels-Alder *Reactions.* No reaction between **6** and **23a** was observed, even in the presence of *Lewis* acids. However, if instead of the monodentate ligand **23a**, the bidentate **23b** was used as the dienophile[26]), an adduct (85%) containing the components *rac*-**24**, *rac*-**25**, and (*rac*-**26** + *rac*-**27**)[27]) in the ratio 62:29:9 could be obtained after 14 d in the presence of 3 equiv. of Me_2AlCl in CH_2Cl_2. HPLC permitted separation of this mixture into its components.

The main component *rac*-**24** was identified by X-ray crystal-structure analysis (see *Fig. 3*). Constitutionally (angular Me group on C(13), C=C bond between C(9) and

[26]) α,β-Unsaturated *N*-acyloxazolidinones have been used by *Narasaka et al.* [33] [36], *Chapuis* and *Jurczak* [41], *Evans et al.* [42], *Corey* and *Matsumura* [35], and *Seebach et al.* [37] [38] as bidentate ligands, forming reactive dienophiles with chiral, non-racemic *Lewis* acids in chirogenic *Diels-Alder* reactions.

[27]) The adduct components *rac*-**26** and *rac*-**27**, constitution isomers of *rac*-**24** and *rac*-**25**, were obtained in a 3:1 ratio after HPLC separation.

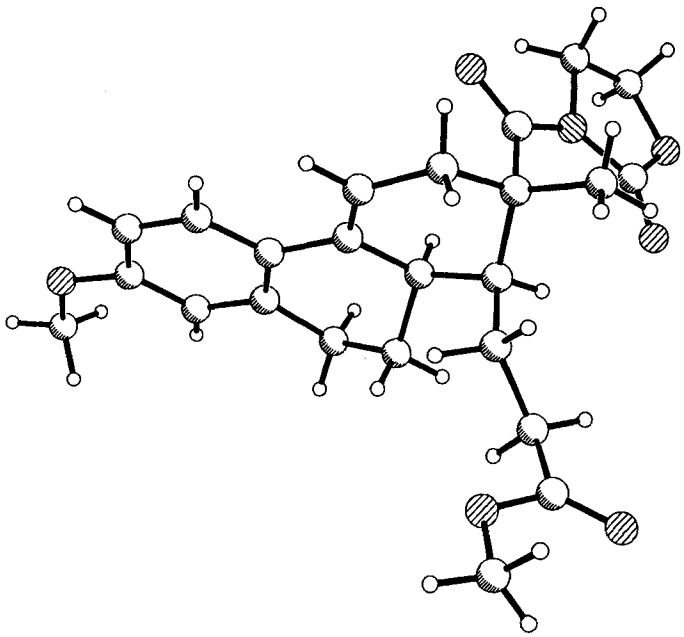


Fig. 3. *Representation of single-crystal X-ray structure of compound* rac-**24** (*Exper. 1.5.1*)

C(11)) and configurationally (*trans*-arrangement of the functional group necessary for later ring closure in ring *C*), the *Diels-Alder* reaction has taken place in the desired manner, but, however, *via* the *exo* transition structure (*syn*-arrangement of the H-atoms on C(8) and C(14)).

3.1.2. *Stereostructural Simplification.* The *Diels-Alder* reaction between **6** and **23b** did only proceed with the mediation of Al *Lewis* acids (see *Table 5*).

Table 5. Diels-Alder *Reactions of Diene* **6** *with Dienophile* **23b** *Mediated by Various* Lewis *Acids*

Entry	*Lewis* acid	Temp. [°C]	Time	Yield[a]) [%]	*rac*-**24**/*rac*-**25**/ (*rac*-**26** + *rac*-**27**)[a])
1	Me_2AlCl	−25	7 d	66	57:31:12
2	Me_2AlCl	−25	10 d	77	54:34:12
3	Me_2AlCl	−25	14 d	89	62:29:9
4	$MeAlCl_2$	−25	14 d	82	60:30:10
5	Et_2AlCl	−25	14 d	65	53:31:16
6	$EtMeAlCl_2$	5	40 h	15	69:24:7
7	$AlCl_3$	−25	7 d	2[b])	8:16:77
8	$AlMe_3$	5	40 h	5[c])	51:38:11

[a]) Overall yield determined by HPLC.

[b]) In addition to primary adduct, secondary components *rac*-**29** and *rac*-**30** were present in an overall yield of 16%.

[c]) In addition to primary adduct, *rac*-**28** was isolated in 12% yield.

$SiCl_4$, $SnCl_4$, $(i\text{-}PrO)_2TiCl_2$ $TiCl_4$, and $ZrCl_4$ did not bring about reaction; **23b** could be recovered almost quantitatively. Use of $AlCl_3$, $TiCl_4$, $(i\text{-}PrO)_2TiCl_2$, or $ZrCl_4$ led to partial or complete polymerization of diene **6**. The *Lewis* acid Me_2AlCl, which gave the highest yields, was used in various molar equivalents relative to dienophile **23b** in steps from 1 to 4 (see *Table 6*).

Table 6. Diels-Alder *Reactions of Diene* **6** *with Dienophile* **23b** *in the Presence of* Me_2AlCl *at* $-25°$

Entry	Mol.-equiv. of Me_2 AlCl	Time	Yield[a]) [%]	*rac*-**24**/*rac*-**25**/(*rac*-**26** + *rac*-**27**)
1	1 equiv.	14 d	2	54:13:33
2	2 equiv.	14 d	8	56:21:23
3	3 equiv.	14 d	89	62:29:9
4	4 equiv.	14 d	84	51:35:14

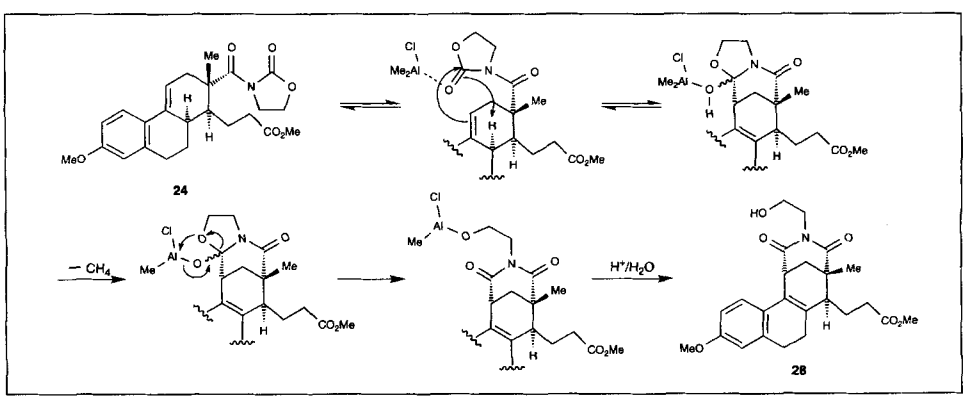
[a]) Determined by HPLC.

Table 7. Diels-Alder *Reactions of Diene* **6** *with Dienophile* **23b** *Mediated by Methylaluminium Chlorides at 5°*

Entry	*Lewis* acid	Time [h]	Yield[a])[b]) of adduct [%]	*rac*-**24**/*rac*-**25**/(*rac*-**26** + *rac*-**27**)	Yield of *rac*-**28**
1	Me_2AlCl	12	62	39:45:16	11
2	Me_2AlCl	24	65	41:45:14	25
3	Me_2AlCl	48	48	30:50:20	46
4	$MeAlCl_2$	24	72	58:20:22	7
5	$MeAlCl_2$	50	75[c])	47:38:15	15

[a]) Determined by HPLC.
[b]) Overall yield.
[c]) Conducted in the presence of 5 mol-% galvanoxyl.

Scheme 1. *Outline, How the* Diels-Alder *Adduct Component* rac-**24** *Is Converted into* rac-**28** *by a* Lewis-*Acid-Mediated Ene Reaction*

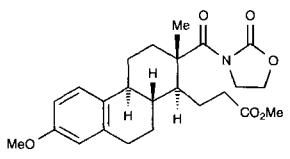


With constant temperature and reaction time, the highest yields, and also the best constitutional isomer ratios, were obtained with 3 mol-equiv. of Me_2AlCl. With 4 equiv. of *Lewis* acid, the results were less good. This may possibly be due to a change in the nature of complexation.

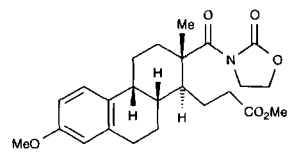
The question of whether the reaction time may be reduced by using a higher temperature can be answered in the negative (see *Table 7*). Diene **6** polymerizes more quickly at elevated temperatures. An additional reaction component also appears in the shape of the tetracyclic *rac*-**28**, which can be explained as the product of sequential intermolecular *Diels-Alder* reaction and intramolecular ene reaction (see *Scheme 1*).

3.2. *Completion of the* ABCD *System.* For a successful opening step in the total synthesis of *rac*-**3**, it seemed appropriate to constitutionally modify, and at the same time simplify, the crude product of the *Diels-Alder* reaction to fit the aim of the synthesis. This was achieved using CF_3COOH in CH_2Cl_2, the four *Diels-Alder* adduct components being transformed pairwise into the two components *rac*-**29** and *rac*-**30** and isolated in 74% and 5% yields.

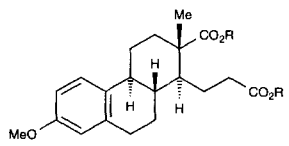
The *trans*-fusion of rings *B* and *C* was established by means of ionic hydrogenation of the C=C bond between C(8) and C(9), following essentially a procedure developed by *Posner* and *Switzer* [21]. The mixture *rac*-**29** was transformed into the components *rac*-**31** and *rac*-**32** (in ratio of *ca.* 5:1) in 68% yield. The oxazolidine group, which had proved to be essential, was removed hydrolytically in a manner based on the work of *Evans et al.* [42]. With the (±)-*O*-methylhomomarrianolic acid obtained (in yields up to 85%), the



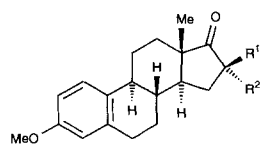
31



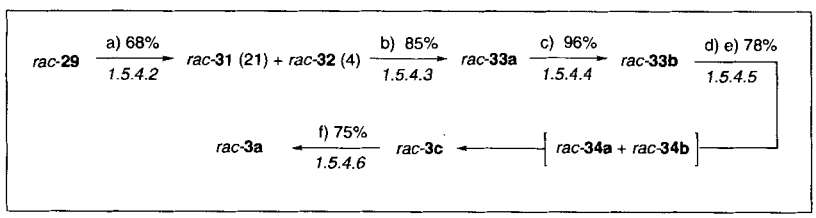
32



33a R = H
33b R = Me



34a R^1 = H, R^2 = CO_2Me
34b R^1 = CO_2Me, R^2 = H

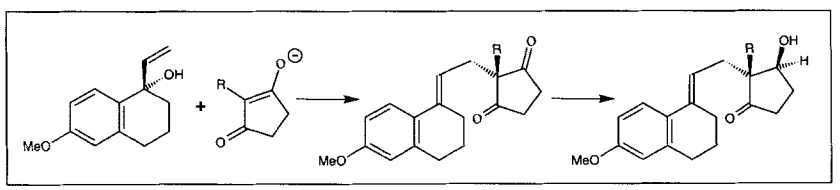


a) Et_3SiH, TFA, CH_2Cl_2, 0° → r.t. b) LiOOH, THF/H_2O, 0° → r.t. c) CH_2N_2, Et_2O/MeOH. d) *t*-BuOK, C_6H_6, reflux. e) Triethyleneglycol/H_2O, 180°. f) BBr_3, CH_2Cl_2, 0°.

historical ground for estrone total synthesis, developed by *Anner* and *Miescher* [43], and *Johnson et al.* [44a–c] in the middle of this century, was reached. Using knowledge gained then, it was possible to complete the steroid skeleton in 84% yield by means of a *Dieckmann* condensation. The mixture of *rac*-**34a** and *rac*-**34b** obtained provided (±)-estrone methyl ether (*rac*-**3c**; 93%) after sequential hydrolysis and decarboxylation: the latter was converted into (±)-estrone (*rac*-**3a**) using known methodology [44d] in 75% yield.

4. Conclusion. – When, in the 1930s, chemists began to think about the total synthesis of steroids at all, *Dane*'s concept, to build up the steroidal *ABCD* system by *Diels-Alder* reaction between an appropriate *AB* system as diene and a five-membered unsaturated ketone as dienophile, was taken for choice. But soon, when it turned out that initial hopes had been raised too much, *Dane*'s concept was superseded by *Torgov*'s idea [19] how to build up a steroidal *ABD* system (*Scheme 2*). This was definitely the case after the regio- and enantioselective reduction of the resulting achiral diketone intermediate had been succeeded.

Scheme 2. *Opening Move in* Torgov's *Concept Leading to an Achiral Diketone Which Can Be Reduced Regio- and Enantioselectively*

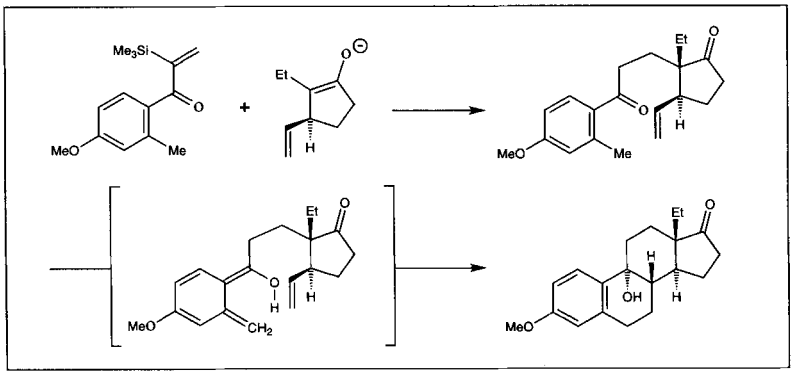


After *Valenta*'s observation [45] that, on *Diels-Alder* reaction between **6** and 2-Me-substituted 1,4-benzoquinones as dienophiles, the adduct component close to steroid constitution can be made to predominate, provided an achiral *Lewis* acid had been used as a mediator, caused some doubt, whether *Dane*'s concept, which in the meantime was lost sight of, had not been given up too early. That this doubt is justified was supported by the enantioselective verification of the chirogenic *Diels-Alder* reaction between **6** and dienophiles of type **18**, carried out in the presence of chiral, non-racemic *Lewis* acids. The prevailing opinion that *Dane*'s concept did fall out of favor has to be abandoned.

Ten years ago, we have already reported a total synthesis of **2** [24] following the constitutional construction scheme $AB \rightarrow ABD \rightarrow ABCD$. Here, an intramolecular *Diels-Alder* reaction [46] played a key role. Does the new total synthesis of **2** employing an intermolecular *Diels-Alder* reaction successfully compete with the old one making use of an intramolecular *Diels-Alder* reaction?

As far as the constitutional build-up of the steroid skeleton is concerned, the latter synthesis is chemically more innovative than the former one: by photoenolization a short-lived dienol is produced which, after deprotonation, reacts even with a rather unreactive dienophile, hereby making an *ABCD* out of an *AD* system. The precursor of the photoenol, being a 1,5-diketone, is easily formed by *Michael* addition of a chiral, non-racemic ring-*D* donor to an achiral *AB* acceptor. The required *trans*-fusion of rings *C* and *D* does not cause any worry here (*Scheme 3*).

Scheme 3. *Ring*-A Michael *Acceptor and Ring*-D Michael *Donor Afford a 1,5-Diketone, Which on Photoenolization Undergoes an Intramolecular* Diels-Alder *Reaction Completing the Steroid Skeleton*



If the way generating chirality becomes the crucial test for evaluation, the synthesis of **2** which includes an intermolecular *Diels-Alder* reaction is better than that one with an intramolecular *Diels-Alder* reaction. While a chiral, non-racemic auxiliar, in order to induce enantioselection, has to be covalently bound in the latter case, transient formation of a coordination complex suffices in the former one.

Financial support by *Deutsche Forschungsgemeinschaft* (project Qu 15/26), *Fonds der Chemischen Industrie*, Ministry of Research and Technology (project No. 0318801B), and *Hoechst AG* is gratefully acknowledged.

Experimental Part

General [47]. Solvents before use were distilled: Et_2O, THF (Na; benzophenone); toluene (Na); MeCN (CaH_2), or filtered: CH_2Cl_2 and DMF (alumina B, act. I; *ICN*). All reactions were carried out under N_2, unless otherwise stated. For reactions in CH_2Cl_2 or $(CH_2Cl)_2$), CH_2Cl_2, for reactions in Et_2O, THF, or i-BuOH, Et_2O was used for distribution of the particular product between org. solvent and sat. aq. $NaHCO_3$ soln. (*basic workup*), aq. HCl soln. (*acidic workup*) or sat. aq. NH_4Cl soln. (*usual workup*). The org. layer was washed with brine, dried ($MgSO_4$), filtered (silica gel), and evaporated. Single-crystal structure determination at r.t. with *Enraf Nonius CAD4* diffractometer (CuK_α) by direct methods. Further details of the crystal-structure determinations may be obtained from the *Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information m.b.H.*, D-76344 Eggenstein-Leopoldshafen on quoting the deposit number *CSD 58994* (if not indicated otherwise), the names of the authors, and the journal citation.

1. Preparative Investigation and Synthetic Appalication of *Diels-Alder* Reactions of Diene 6. – 1.1. *With Dienophile* **7a**. 1.1.1. *In the Presence of Et_2AlCl.* In a dry, 100-ml, three-necked, round-bottomed flask, **7a** (300 mg, 3.12 mmol; see *Exper. 3.2*) was dissolved in dry CH_2Cl_2 (50 ml). The soln. was cooled to 0°, and a 1M soln. of Et_2AlCl in toluene (1.73 ml, 3.12 mmol) was added. After stirring at 0° for 30 min, a soln. of **6** (870 mg, 4.68 mmol, 1.5 equiv.; see *Exper. 3.1*) in dry CH_2Cl_2 (3 ml) was introduced. The mixture was kept at 0–25° for 15 h. Basic workup afforded 523 mg of *rac*-**8a**/*rac*-**9a**. After FC (hexane/AcOEt 15:1) on silica gel (150 g) and crystallization (Et_2O/pentane), 482 mg (55%) of *(±)-3-methoxy-14β-estra-1,3,5(10),9(11)-tetraen-17-one* (*rac*-**8a**) were obtained. M.p. 111–112° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.21. UV (MeO): λ_{max} 263.5 (19938). IR (KBr): 1740*s* (C=O); 1065*m*, 1576*m*, 1498*m* (C=C, arom.). ^{1}H-NMR 1.12 (*s*, Me); 1.50–2.26 (*m*, 8 cycloaliph. H); 2.47–2.60 (*m*, H–C(8), H–C(16)); 2.82–2.95 (*m*, 2 H–C(6)); 3.80 (*s*, MeO); 6.11–6.15 (*m*, H–C(11)); 6.62 (*d*, J(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.74 (*dd*, J(H–C(2),H–C(4)) = 2.7, J(H–C(2),H–C(1)) = 8.8, H–C(2)); 7.56 (*d*, J(H–C(1),H–C(2)) = 8.8, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 1.50–2.26/2.47–2.60, 1.50–2.26/2.82–2.95, 2.47–2.60/6.11–6.15, 2.82–2.95/6.62, 6.62/6.74, 6.74/7.56. ^{13}C-NMR: 19.6 (C(18)); 20.6, 26.8, 29.3 (C(7), C(12), C(15)); 30.6 C(6)); 33.6 (C(14)); 35.6 (C(16)); 46.4 (C(13));

46.6 (C(8)); 55.2 (MeO); 112.8 (C(2)); 113.4 (C(4)); 113.7 (C(11)); 124.5 (C(1)); 126.8, 132.4, 138.0 (C(5), C(9), C(10)); 158.6 (C(3)); 221.0 (C(17)). Signals were assigned using a $^1H,^{13}C$-COSY spectrum. Cross peaks between 1.12/19.6, 1.50–2.26/20.6, 1.50–2.26/26.8, 1.50–2.26/29.3, 2.82–2.95/30.6, 2.47–2.60/33.6, 1.50–2.26/35.6, 2.47–2.60/35.6, 1.50–2.26/46.4, 3.80/55.2, 6.11–6.15/113.4, 6.62/113.4, 6.74/112.8, 7.56/124.5. *Crystal-structure analysis of* rac-**8a** (*Fig. 1a*): monoclinic crystals, $P2_1/a$ (No. 14); $a = 13.956$ (4), $b = 7.475$ (2), $c = 15.051$ (3) Å, $\beta = 100.60$ (2)°; $V = 1543$ (1) Å^3; $Z = 4$; $\rho = 1.215$ g/cm^3; quadrant through $2\theta = 120°$; 2227 indep. reflect. with $I > \sigma(I)$; 279 variables; $R(F) = 0.042$; $R_w(F) = 0.033$. The ratio *rac*-**8a**/*rac*-**9a** was determined as 96:4 by HPLC (hexane/AcOMe 10:1 +20% CH_2Cl_2, *MN Nucleosil 50-10*, 1.5 ml/min, 254 nm) from an experiment carried out under similar conditions. Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.89, H 7.77.

The minor component had been separated by prep. HPLC (hexane/AcOEt 10:1.5) from *rac*-**8a**/*rac*-**9a** obtained from *Exper. 1.1.2*: *(±)-3-methoxy-14β-methylgona-1,3,5(10),9-tetraen-15-one* (*rac*-**9a**): M.p. 67° (Et_2O). TLC (hexane/AcOEt 4:1): R_f 0.6. UV (MeOH): λ_{max} 264 (16784). IR (KBr): 3031*s* (=CH); 2955*s*, 2917*m*, 2810*m* (C–H); 1722*s* (C=O); 1604*m*, 1572*m*, 1493*m* (C=C, arom.). ^{1}H-NMR: 1.08 (*s*, Me); 1.27–1.36 (*m*, H–C(17)); 1.45–1.55 (*m*, H′–C(17)); 1.68–1.75 (*m*, H–C(13)); 1.68–1.81 (*m*, H–C(7)); 1.85–2.02 (*m*, H′–C(7), 2 H–C(16)); 2.19 (*dddd*, J(H′–C(12),H–C(12)) = 17.3, J(H′–C(12),H′–C(11)) = 3.0, J(H′–C(12),H–C(13)) = 7.0, J(H′–C(12),H–C(8)) = 3.0, H′–C(12)); 2.42–2.53 (*m*, 2 H–C(6)); 3.35 (*s*, MeO); 5.98–6.01 (*m*, H–C(11)); 6.53 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.75 (*dd*, J(H–C(2),H–C(4)) = 2.6, J(H–C(2),H–C(1)) = 8.7, H–C(2)); 7.41 (*d*, J(H–C(1),H–C(2)) = 8.7, H–C(1)). Signals were assigned using a $^1H,^1H$-COSY spectrum. Cross peaks between 1.27–1.36/1.45–1.55, 1.27–1.36/1.68–1.75, 1.27–1.36/1.85–2.02, 1.45–1.55/1.68–1.75, 1.45–1.55/1.85–2.02, 1.68–1.75/1.85–2.02, 1.68–1.75/2.19, 1.68–1.81/1.85–2.02, 1.68–1.81/2.42–2.53, 1.85–2.02/2.19, 1.85–2.02/2.42–2.53, 1.85–2.02/5.98–6.01, 2.19/5.98–6.01, 2.42–2.53/6.53, 6.53/6.75, 6.75/7.41. ^{13}C-NMR: 23.4 (Me); 26.2 (C(17)); 26.5, 38.0 (C(7), C(16)); 27.8 (C(12)); 31.2 (C(6)); 42.3 (C(7)); 42.5 (C(8)); 50.5 (C(14)); 54.7 (MeO); 113.1 (C(4)); 113.1 (C(4)); 113.2 (C(2)); 117.2 (C(11)); 125.2 (C(1)); 128.9, 136.1, 138.2, 159.3 (C(3), C(5), C(9), C(10)); 219.8 (C(15)). Signals were assigned using a $^1H,^{13}C$-COSY spectrum. Cross peaks between 23.4/1.08, 26.2/1.27–1.36, 26.2/1.45–1.55, 26.5/1.85–2.02, 27.8/1.85–2.02, 27.8/2.19,, 31.2/2.42–2.53, 38.0/1.85–2.02, 42.3/1.68–1.75, 42.5/1.85–2.02, 54.7/3.35, 113.1/6.53, 113.2/6.75, 117.2/5.98–6.01, 125.2/7.41. Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.69, H 7.85.

1.1.2. *In the Presence of* rac-**12a**. In a dry 1000-ml, three-necked, round-bottomed flask, bis-sulfonamide *rac*-**Ba** (16.3 g, 31.2 mmol; see *Table 2* and *Exper. 4.2.1*) was dissolved in dry $(CH_2Cl)_2$ (500 ml) at 40–50°. After cooling to 0°, a 2M soln. of $AlMe_3$ (15.6 ml, 31.2 mmol) in toluene was added dropwise within 2 min. The soln. was heated to 80° for 2 h, cooled to 0°, and a soln. of **7a** (3.00 g, 31.2 mmol) in dry $(CH_2Cl)_2$ (10 ml) was introduced. After stirring at 0° for 30 min, a soln. of **6** (8.70 g, 46.8 mmol, 1.5 equiv.) in dry $(CH_2Cl)_2$ (15 ml) was added. The mixture was stirred at 0–25° for 15 h. Basic workup left 150 ml of org. soln. to which 1 l Et_2O was added. The mixture was set aside for 2–3 h at r.t. for crystallization. Filtration and washing of the crystals with Et_2O gave *rac*-**Ba** (14.0 g, 86%). The filtrate was concentrated and the residue subjected to filtration (hexane/AcOEt 10:1) on silica gel (150 g) to give a mixture *rac*-**8a**/*rac*-**9a** (7.55 g, 86%). Separation by prep. HPLC (hexane/AcOEt 20:3) furnished *rac*-**8a** (6.17 g, 70%) as a colorless solid. Recrystallization (Et_2O/hexane) afforded *rac*-**9a** (0.52 g, 6%). The ratio of *rac*-**8a**/*rac*-**9a** was determined as 91:9 by HPLC (hexane/AcOMe 20:1 + 20% CH_2Cl_2, *MN Nucleosil 50-10*, 1.5 ml/min, 254 nm) from an experiment carried out under similar conditions on a 3.12 mM scale. Anal. data were identical with those ones under *Exper. 1.1.1*.

1.1.3. *In the Presence of a* Lewis *Acid of Type* **12** (see *Table 2*). In a dry, three-necked, round-bottomed flask, 1.25 equiv. of ligand of type **B** was dissolved in $(CH_2Cl)_2$. A soln. of DIBAH (1.2 equiv.) in CH_2Cl_2, or of $AlMe_3$ (1.2 equiv.) in toluene was added at r.t. The mixture was stirred at 80° for 3 h and cooled to r.t. For reactions at −80°, the solvent was removed and the residue dissolved in dry CH_2Cl_2. A soln. of **7a** (96 mg, 1.0 mmol) in dry CH_2Cl_2 or $(CH_2Cl)_2$ (2 ml) was added at the given reaction temp. (see *Table 2*). After stirring for 30 min, a soln. of **6** (450 mg, 2.4 mmol, 2.4 equiv.) in dry CH_2Cl_2 or $(CH_2Cl)_2$ (2 ml) was added and the mixture kept for 15 h to 14 d at the temp. mentioned. The product obtained after basic workup was filtered on silica gel (hexane/AcOEt 8:1). Optical purity was determined using **8a** as a reference (see *Exper. 2.1.1*).

1.1.4. *In the Presence of $TiCl_4$*. In a 100-ml, three-necked, round-bottomed flask, a soln. of $TiCl_4$ (0.91 ml, 8.32 mmol) in dry CH_2Cl_2 (10 ml) was added to a soln. of **7a** (320 mg, 3.33 mmol) in CH_2Cl_2 (30 ml) at −80°. The yellow mixture was stirred for 15 min, and a soln. of **6** in CH_2Cl_2 was added dropwise, until **7a** could not be detected any longer by GC (altogether 1.57 g (8.4 mmol) of diene **6**). The mixture was stirred for 1 h at −80° and warmed up to 0°. Basic workup gave a crude product which was purified by filtration (hexane/AcOEt 2:1) on silica gel (20 g), prep. HPLC (hexane/AcOEt 10:1, *MN Nucleosil 50-10*) and crystallization from Et_2O/hexane to furnish (841 mg, 89%) of *(±)-3-methoxy-14β-estra-1,3,5(10),8-tetraen-17-one* (*rac*-**10a**). M.p. 88–90° (Et_2O/hexane). TLC (hexane/AcOEt 4:1): R_f 0.54. UV (MeOH): λ_{max} 272.8 (17079). IR (KBr): 1724*s* (C=O); 1614*m* (C=C, olef.); 1570*m*,

1498*m* (C=C, arom.); 866*m*, 802*m* (trisubst. arom.). ^{1}H-NMR: 1.07 (*s*, Me); 1.44–1.53 (*m*, H–C(12)); 1.71–1.86 (*m*, H′–C(12), H–C(11)); 2.08–2.47 (*m*, 2 H–C(7), H′–C(11), H–C(14), 2 H–C(15), 2 H–C(16)); 2.66–2.85 (*m*, 2 H–C(6)); 3.80 (*s*, MeO); 6.69–6.74 (*m*, H–C(2), H–C(4)); 7.11 (*d*, *J*(H–C(1),H–C(2)) = 8.1, H–C(1)). The signals were assigned using at ^{1}H,^{1}H-COSY spectrum. Cross peaks between 1.44–1.53/1.71–1.86, 1.44–1.53/2.08–2.47, 1.71–1.86/2.08–2.47, 2.08–2.47/2.66–2.85, 6.69–6.74/7.11. ^{13}C-NMR: 20.5 (C(18)); 21.9 (C(11)); 25.4 (C(15)); 26.8 (C(12)); 27.4 (C(7)); 28.7 (C(6)); 36.6 (C(16)); 47.1 (C(13)); 48.5 (C(14)); 55.2 (MeO); 110.8 (C(2)); 113.4 (C(4)); 123.0 (C(1)); 126.3 (C(9)); 128.9 (C(8)); 131.7 (C(10)); 137.0 (C(5)); 223.0 (C(17)). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 20.5/1.07, 21.87/2.08–2.47, 25.4/1.71–1.86, 25.4/2.08–2.47, 26.8/1.44–1.53, 26.8/1.71–1.86, 27.4/2.08–2.47, 28.7/2.66–2.85, 36.6/2.08–2.47, 48.5/2.08–2.47, 110.8/6.69–6.74, 113.4/6.69–6.74, 123.0/7.11. Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.68, H 7.92. Crystal-structure analysis of *rac*-**10a**: *cf. Fig. 1, b* (depository number *CSD-55302*; CSD refcode: VIYSIF) [12].

1.1.5. *From* Diels-Alder *Adduct* rac-**10a** *to* rac-**3a**. 1.1.5.1. *Preparation of* rac-**13a**. In a three-necked, 100-ml flask equipped with internal thermometer, BuLi (3.18 ml, 1.6M soln. in hexane, 5.10 mmol, 1.2 equiv.) was added to a stirred soln. of $(i\text{-Pr})_2$NH (0.84 ml, 5.93 mmol, 1.4 equiv.) in dry THF (30 ml) at −20°. The soln. was kept for 45 min at −5 to 0° and then cooled to −80°. A soln. of *rac*-**10a** (1.20 g, 4.25 mmol) in dry THF (6 ml) was introduced avoiding the internal temp. to raise above −70°. After stirring for 1 h at −80°, Me_3SiCl (1.08 ml, 8.49 mmol, 2.0 equiv.) was added. The cooling bath was removed instantly and the temp. allowed to raise to r.t. The soln. was stirred for 1 h and then transferred to a 100-ml, one-necked, round-bottomed flask (using Et_2O). The solvent was evaporated and the resulting suspension filtered through alumina (50 g; bas. act. III; hexane/AcOEt 4:1). After removing the solvent, the remaining crude silyl enol ether (1.6 g) was dissolved in dry and O_2-free MeCN (25 ml). After addition of $Pd(OAc)_2$ (935 mg, 4.25 mmol, 1.0 equiv.), the mixture was stirred for 5 h at r.t. under Ar and then filtered through *Celite*. The filtrate was concentrated and the residue purified by FC (hexane/AcOEt 10:1; 150 g silica gel). Crystallization from MeOH gave 0.998 g (84%) of *(±)-3-methoxy-14-estra-1,3,5(10),8,15-pentaen-17-one* (*rac*-**13a**). M.p. 133–135° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.35. UV (MeOH): λ_{max} 268.5 (15510); 302 (sh). IR (KBr): 3064*w*, 3042*w* (C=C–H); 1706*s* (C=O); 1604*m*, 1583*m*, 1500*m* (arom. C=C). ^{1}H-NMR: 1.20 (*s*, Me–C(13)); 1.55–1.64 (*m*, H–C(12)); 1.88–1.96 (*m*, H′–C(12)); 2.16–2.44 (*m*, 2 H–C(7)); 2.70–2.90 (*m*, 2 H–C(6)); 3.15 (*s*, H–C(14)); 3.79 (*s*, MeO); 6.12 (*dd*, *J*(H–C(16),H–C(15)) = 5.8, *J*(H–C(16),H–C(14)) = 2.2, H–C(16)); 6.70–6.73 (*m*, H–C(2), H–C(4)); 7.07–7.10 (*m*, H–C(1)); 7.64 (*dd*, *J*(H–C(15),H–C(16)) = 5.8, *J*(H–C(15),H–C(14)) = 2.6, H–C(15)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 7.64/6.12, 7.64/3.15, 7.07–7.10/6.70–6.73, 6.12/3.15, 2.70–2.90/2.16–2.44, 1.88–1.96/2.16–2.44, 1.88–1.96/1.55–1.65. ^{13}C-NMR: 22.47 (*q*, C(18)); 22.29, 27.43 (2*t*, C(7), C(11)); 28.63 (*t*, C(6)); 31.53 (*t*, C(12)); 55.23 (*q*, MeO); 55.51 (*d*, C(14)); 110.95 (*d*, C(2)); 113.55 (*d*, C(4)); 123.37 (*d*, C(1)); 128.34 (*s*, C(9)); 128.62 /*s*, C(8)); 129.55 (*s*, C(10)); 130.53 (*d*, C(16)); 136.53 (*s*, C(5)); 158.30 (*s*, C(3)); 162.53 (*d*, C(15)); 214.36 (*s*, C(17)). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks were found between: 162.53/7.64, 130.53/6.12, 123.37/7.07–7.10, 113.55/6.70–6.73, 110.95/6.70–6.73; 110.95/6.70–6.73, 55.51/3.15, 55.23/3.79, 31.53/1.55–1.64, 31.53/1.88–1.96, 28.63/2.70–2.90, 22.43/2.16–2.44, 27.43/2.16–2.44, 22.47/1.20. Anal. calc. for $C_{19}H_{20}O_2$ (280.37): C 81.40, H 7.19; found: C 81.34, H 7.36.

1.1.5.2. *Preparation of* rac-**14a**. In a 25-ml, three-necked flask, BuLi (3.85 ml, 1.6M soln. in hexane, 6.16 mmol, 1.8 equiv.) was added to a soln. of HMDS (0.91 ml, 6.87 mmol, 2.0 equiv.) in dry THF (6 ml) and HMPT (3 ml) at −20 to −30°. After stirring for 1 h at 0–4° a soln. of *rac*-**13a** (0.960 g, 3.42 mmol) in dry THF (10 ml) was added during 1–2 min at −70 to −80°. The dark brown mixture was stirred for 1 h at −70 to −80°, and then AcOH (4 ml, 87 mmol, 20 equiv.) was added during 1–2 s. The temp. was raised to 0°. After acidic workup, the crude product was purified by FC (hexane/AcOH 20:1; 150 g silica gel) and crystallization from MeOH to give 0.768 g (80%) of *(±)-3-methoxyestra-1,3,5(10),8,14-pentaen-17-one* (*rac*-**14a**). M.p. 115–116° (MeOH) ([48]: 115–116° (MeOH); [49]: 112° (EtOH); [19]: 108–109° (MeOH)). TLC (hexane/AcOEt 4:1): R_f 0.62. UV (EtOH): λ_{max} 233.6 (12932), 311 (28827), 323.5 (22226). IR (KBr): 3059*w* (C=C–H); 1740*s* (C=O); 1598*m*, 1559*m*, 1497*m* (arom. C=C). ^{1}H-NMR: 1.14 (*s*, Me–C(13)); 1.54–1.65 (*m*, H–C(12)); 2.00–2.07 (*m*, H′–C(12)); 2.28–2.37 (*m*, H–C(7)); 2.55–2.66 (*m*, H′–C(7), 2 H–C(11)); 2.77–2.83 (*m*, 2 H–C(6)); 2.93 (*dd*, *J*(H–C(16),H′–C(16)) = 23.4, *J*(H–C(16),H–C(15)) = 3.1, H–C(15)); 3.32 (*d*, *J*(H′–C(16),H–C(16)) = 23.4, H′–C(16)); 3.81 (*s*, MeO); 5.86 (*t*, *J* = 2.5, H–C(15)); 6.73–6.77 (*m*, H–C(2), H–C(4)); 7.23–7.27 (*m*, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 7.23/6.73–6.77, 5.86/3.32, 5.86/2.93, 2.28–2.37/2.55–2.66, 2.28–2.37/2.77–2.83, 2.00–2.07/2.55–2.66, 2.00–2.07/1.54–1.65, 1.54–1.65/2.55–2.66. ^{13}C-NMR: 22.56 (*q*, C(18)); 22.73, 22.93 (2*t*, C(7), C(11)); 27.33 (*t*, C(12)); 28.42 (*t*, C(6)); 41.92 (*t*, C(16)); 49.02 (*s*, C(13)); 55.25 (*q*, MeO); 111.14 (*d*, C(2), C(4)); 114.66 (*d*, C(15)); 124.11 (*d*, C(1)); 125.32, 128.59, 129.85 (3*s*, C(8), C(9), C(10)); 138.17 (*d*, C(5)); 146.93 (*s*, C(14)); 158.68 (*s*, C(3)); 219.91 (*s*, C(17)). Anal. calc. for $C_{19}H_{20}O_2$ (280.37): C 81.40, H 7.19; found: C 81.21, H 7.13.

1.1.5.3. *Preparation of* rac-**5a**. In a 50-ml, three-necked flask, 5% Pd/$CaCO_3$ (150 mg) in C_6H_6 (20 ml) was heavily stirred under H_2 for 1 h. After *rac*-**14a** (1.0 g, 3.57 mmol) and C_6H_6 (15 ml) had been added, the flask was evacuated and filled with H_2 (80 ml, 1.0 equiv.); 45 min later, the mixture was filtrated through *Celite* and washed with Et_2O. Evaporation of the solvent gave 1.03 g of product. Anal. HPLC (hexane/AcOEt 10:1; *MN Nucleosil 50-10*, UV 254 nm) revealed the presence of *rac*-**5a** (66%), *rac*-**10a** (9%), and *rac*-**15a** (5%; for preparation and identification of *rac*-**15a**, see *Exper. 2.4.2*). Prep. HPLC (hexane/AcOEt 10:1; *MN Nucleosil 50.10*, refractom.) afforded *rac*-**10a** (69 mg, 7%) and a predominantly *rac*-**5a**-containing fraction (269 mg); crystallization from MeOH/Et_2O gave *rac*-**5a** (513 mg, 51%). Semiprep. HPLC (hexane/dioxane 10:0.7; *MN Nucleosil 50-10*, refractom.) of combined mother liquors and combined product mixtures gave additional *rac*-**5a** (112 mg, 11%). A total yield of isolated *(±)-3-methoxyestra-1,3,5(10),8-tetraen-17-one* (*rac*-**5a**) of 62% (625 mg) was obtained. M.p. 120–123° (MeOH/Et_2O 3:1) ([46a]: 120–123° (MeOH/Et_2O/petroleum ether); [48]: 118–119° (MeOH); [49]: 123° (AcOEt); [19]: 120–121° (AcOEt); [51]: 128° (hexane)). TLC (hexane/AcOEt 4:1): R_f 0.58. UV (MeOH): λ_{max} 278 (16787). IR (KBr): 3061*w* (C=C–H); 1734*s* (C=O); 1609*m*, 1568*m*, 1491*m* (C=C). IR (CCl_4): 1742*s* (C=O); 1607*m*, 1570*m*, 1555*m*, 1499*m* (C=C). ^{1}H.NMR: 0.89 (*s*, Me–C(13)); 1.60–1.85 (*m*, H–C(12), H–C(5)); 1.99–2.08 (*m*, H′–C(12)); 2.11–2.17 (*m*, H′–C(15)); 2.19–2.31 (*m*, 2 H–C(7), 2 H–C(14)); 2.51–2.81 (*m*, 2 H–C(6), 2 H–C(11), 2 H–C(16)); 3.80 (*s*, MeO); 6.70–6.74 (*m*, H–C(2), H–C(4)); 7.14 (*dd*, *J*(H–C(1),H–C(2)) ≈ 7.3, *J*(H–C(1), H–C(4)) ≈ 1.9, H–C(1)). ^{13}C-NMR: 13.22 (C(18)); 21.14 (C(15)); 23.79 (C(11)); 24.30 (C(7)); 28.48 (C(6)); 28.83 (C(12)); 36.48 (C(16)); 47.22 (C(14)); 47.58 (C(13)); 55.23 (MeO); 110.80 (C(2)); 113.66 (C(4)); 123.07 (C(1)); 126.49 (C(9)); 128.60 (C(8)); 130.58 (C(10)); 137.11 (C(5)); 158.06 (C(3)); 219.67 (C(17)). IR, ^{1}H-NMR, and ^{13}C-NMR data are identical with those in [46a]. Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.71, H 7.94.

1.1.5.4. *Preparation of* rac-**3c**. In a three-necked, 25-ml flask, Et_3SiH (1.03 ml, 6.47 mmol, 10 equiv.) and CF_3COOH (1.0 ml, 13 mmol, 20 equiv.) were added to a soln. of *rac*-**5a** (182 mg, 0.645 mmol) in dry C_6H_6 (12 ml). After stirring the mixture for 12 h at r.t. and usual workup, the residue obtained was purified by FC (hexane/AcOEt 10:1; 50 g silica gel). Crystallization from MeOH gave 128 mg (70%) of *(±)-estronemethyl ether* (*rac*-**3c**). M.p. 144–145° (MeOH) ([51]: 142–144° (MeOH); [48] [19]: 143–144° (MeOH); [23c]: 144–145° (MeOH/Aceton); [49]: 142° (MeOH); [52]: 139–141°; [44b]: 143.2–144° (MeOH)). TLC (hexane/AcOEt 2:1): R_f 0.70. UV (MeOH): λ_{max} 277.8 (2010); 286.2 (1900) ([51]: UV (MeOH): λ_{max} 276 (1900), 286 (2000)). IR (KBr): 1737*s* (C=O); 1608*m*, 1579*w*, 1504*m* (arom. C=C). ^{1}H-NMR: 0.91 (*s*, Me–C(13)); 1.39–1.67 (*m*, 6 cycloaliph. H); 1.92–2.55 (*m*, 7 cycloaliph. H); 2.87–2.93 (*m*, 2 H–C(16)); 3.78 (*s*, MeO); 6.64 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.72 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1),H–C(2)) = 8.6, H–C(2)); 7.20 (*d*, *J*(H–C(1),H–C(2)) = 8.4, H–C(1)). ^{13}C-NMR: 13.81 (C(18)); 21.54 (C(15)); 25.89 (C(11)); 26.52 (C(7)); 29.63 (C(6)); 31.56 (C(12)); 35.82 (C(16)); 38.35 (C(8)); 43.93 (C(9)); 47.96 (C(13)); 50.39 (C(14)); 55.16 (MeO); 111.54 (C(2)); 113.86 (C(4)); 126.30 (C(1)); 133.00 (C(10)); 137.71 (C(5)); 157.59 (C(3)); 220.81 (C(17)). Anal. calc. for $C_{19}H_{24}O_2$ (284.40): C 80.24, H 8.51; found: C 80.24, H 8.27.

1.1.5.5. *Preparation of* rac-**3a**. In a 25-ml flask, BBr_3 (0.70 ml, 8.85 mmol, 18 equiv.) was added to a stirred soln. of *rac*-**3c** (140 mg, 0.49 mmol) in dry CH_2Cl_2 (7 ml) at –30°. The soln. was left at 0–4° for 2 h. The orange soln. was cooled to –30°, and MeOH (2 ml) was added dropwise under stirring. The mixture was poured into $CHCl_3$ (200 ml)/H_2O (100 ml). The org. layer was washed with H_2O (2 × 100 ml), the combined aq. layers were extracted with $CHCl_3$ (100 ml), and the combined org. layers were dried ($MgSO_4$). After evaporating of the solvent *in vacuo* and dissolving the crude product in DMSO (1 ml), further purification was undertaken by FC (hexane/AcOEt 4:1; 70 g silica gel). Crystallization from EtOH afforded 97 mg (73%) of *(±)-estrone* (*rac*-**3a**). M.p. 254–255° (EtOH) ([46a]: 254–254.5° (EtOH); [44b]: 252.8–254.7° (acetone); [23c]: 254.5–256° (acetone); [43a]: 251–254°). TLC (hexane/AcOEt 2:1): R_f 0.62. UV (MeOH): λ_{max} 281 (2118); 287 (sh, 1920) ([46a]: UV: λ_{max} 280 (2110), 287 (sh, 1930)). IR (KBr): 3327*s* (OH); 1718*s* (C=O); 1619*m*, 1581*w*, 1498*m* (arom. C=C). ^{1}H-NMR: 0.90 (*s*, Me–C(13)); 1.41–1.67 (*m*, 6 cycloaliph. H); 1.88–2.55 (*m*, 7 cycloaliph. H); 2.83–2.89 (*m*, 2 H–C(16)); 5.49 (br. *s*, OH, D_2O exchange); 6.58 (*d*, *J*(H–C(2),H–C(4)) = 2.5, H–C(4)); 6.64 (*dd*, *J*(H–C(2),H–C(4)) = 2.6, *J*(H–C(1),H–C(2)) = 8.4, H–C(2)); 7.10 (*d*, *J*(H–C(1),H–C(2)) = 8.4, H–C(1)). Anal. calc. for $C_{18}H_{22}O_2$ (270.37): C 79.96, H 8.20; found: C 79.95, H 8.04.

1.2. *With Dienophile* **7b** *in the Presence of* $TiCl_4$. 1.2.1. *Preparation of* rac-**10b**. In a 250-ml, three-necked, round-bottomed flask, a soln. of $TiCl_4$ (1.12 ml, 10.2 mmol) in dry CH_2Cl_2 (20 ml) was added to a soln. of **7b** (450 mg, 4.1 mmol; see *Exper. 3.2.2*) in dry CH_2Cl_2 (50 ml) at –80°. The yellow mixture was stirred for 15 min, and a soln. of **6** (see *Exper. 3.1*) in dry CH_2Cl_2 was introduced dropwise (760 mg, 4.1 mmol, then 3 × 380 mg, 2.1 mmol), until **7b** could not be detected any longer by GC (altogether 1.9 g (10.2 mmol) of **6**). The mixture was warmed up to 0°. Basic workup gave crude *rac*-**10b**. Chromatography (hexane/AcOEt 10:1) on silica gel (60 g) and crystallization from MeOH afforded 1.109 g (90%) of *(±)-13-ethyl-3-methoxy-14β-gona-1,3,5(10),8-tetraen-17-one* (*rac*-**10b**).

M.p. 82–83° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.40. UV (MeOH): λ_{max} 272.0 (16960). IR (KBr): 3060*w* (=C–H); 2932*m*, 2830*m* (–C–H); 1732*s* (C=O); 1648*w* (C=C, olef.); 1605*m*, 1570*m*, 1499*m* (C=C, arom.). ^{1}H-NMR: 0.86 (*t*, *J*(*Me*CH$_2$,MeC*H*$_2$) = 7.4, MeCH$_2$); 1.43–1.61 (*m*, H–C(12),CH$_2$Me); 1.64–1.87 (*m*, 2 H–C(7), H–C(15), 2 H–C(11), 2 H–C(16)); 2.61–2.68 (*m*, H–C(14)); 2.71–2.82 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 6.69–6.73 (*m*, H–C(2),H–C(4)); 7.08 (m_c, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.86/1.43–1.61, 1.43–1.61/1.64–1.87, 1.43–1.61/2.07–2.41, 1.64–1.87/2.07–2.41, 1.64–1.87/2.61–2.68, 2.07–2.41/2.61–2.68, 2.07–2.41/2.71–2.82, 6.69–6.73/7.08. ^{13}C-NMR: 8.5 (C(19)); 22.0, 27.5 (C(7), C(11)); 25.4 (C(15)); 25.8 (C(12)); 26.3 (C(18)); 28.8 (C(6)); 37.8 (C(16)); 44.9 (C(14)); 51.0 (C(13)); 55.2 (MeO); 110.9, 113.4 (C(2), C(4)); 123.0 (C(1)); 126.6, 129.1, 132.0, 137.0 (C(5), C(10), C(8), C(9)); 229.9 (C(17)). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.5/0.86, 22.0/2.07–2.41, 25.4/1.64–1.87, 25.4/2.07–2.41, 25.8/1.43–1.61, 25.8/1.64–1.87, 26.3/1.43–1.61, 27.5/2.07–2.41, 28.8/2.71–2.82, 37.8/2.07–2.41, 44.9/2.61–2.68, 55.2/3.79, 110.9/6.69–6.73, 113.4/6.69–6.73, 123.0/7.08. Anal. calc. for $C_{20}H_{24}O_2$ (296.39): C 81.05, H 8.16; found: C 80.82, H 8.07. Crystal-structure analysis of *rac*-**10b**: *cf. Fig. 1, c* (depository number *CSD 55302*; CSD refcode VIYSOL) [12].

1.2.2. *From* rac-**10b** *to* rac-**2**. 1.2.2.1. *Preparation of* rac-**13b**. 1.6M BuLi soln. in toluene (2.34 ml, 3.7 mmol, 1.1 equiv. was added to a soln. of (i-Pr)$_2$NH (575 µl, 4.1 mmol, 1.2 equiv.) in dry THF (20 ml) at –80°. The mixture was warmed up to 0° and stirred for 1 h. After cooling to –80°, a soln. of *rac*-**10b** (1.0 g, 3.4 mmol) in dry THF (20 ml) was added dropwise and the mixture stirred for 1 h at –80°. Me$_3$SiCl (773 µl, 6.1 mmol, 1.8 equiv.) was added and the mixture warmed up to 0° during 1 h (TLC, hexane/AcOEt 10:1). After evaporation and chromatography (hexane/AcOEt 4:1) on alumina (B, act. III 80 g), a colorless foam (1.28 g) was obtained. A soln. of the foam in MeCN (5 ml) was added to a suspension of Pd(OAc)$_2$ (763 mg) in MeCN (10 ml). The mixture was stirred for 16 h at r.t. (TLC, hexane/AcOEt 4:1). After filtration through *Celite* and evaporation *in vacuo*, the crude product was subjected to FC (hexane/AcOEt 20:1) on silica gel (80 g). Crystallization from MeOH afforded *(±)-13-ethyl-3-methoxy-14β-gona-1,3,5(10),8,15-pentaen-17-one* (*rac*-**13b**; 820 mg, 82%). M.p. 77–78° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.32. UV (MeOH): λ_{max} 268.7 (15280). IR (KBr): 3070*w* (=C–H); 2932*m*, 2835*m* (–C–H); 1704*s* (C–O); 1662*w* (C=C, olef.); 1609*m*, 1568*m*, 1497*m* (C=C, arom.). ^{1}H-NMR: 0.85 (*t*, *J*(CH$_2$*Me*,C*H*$_2$Me) = 7.4, *Me*CH$_2$); 1.49–1.77 (*m*, MeC*H*$_2$, H–C(12)); 1.95–2.08 (*m*, H′–C(12), H–C(11)); 2.19–2.51 (*m*, 2 H–C(7), H′–C(11)); 2.68–2.91 (*m*, 2 H–C(6)); 3.25 (*ψs*, H–C(14)); 3.77 (*s*,MeO); 6.10 (*dd*, *J*(H–C(16),H–C(15)) = 5.8, *J*(H–C(16),H–C(14)) = 2.1, H–C(16)); 6.68–6.72 (*m*, H–C(2), H–C(4)); 7.03–7.06 (*m*, H–C(1)); 7.62 (*dd*, *J*(H–C(15),H–C(16)) = 5.8, *J*(H–C(15),H–C(14)) = 2.7, H–C(15)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.85/1.49–1.77, 1.49–1.77/1.95–2.08, 1.49–1.77/2.19–2.51, 1.95–2.08/2.19–2.51, 2.19–2.51/2.67–2.91; 3.25/6,10, 3.25/7.62, 6.10/7.62, 7.03–7.06/6.68–6.72. ^{13}C-NMR: 8.6 (C(19)); 22.1, 27.7, 28.6, 29.5, 31.0 (C(18), C(6), C(7), C(11), C(12)); 50.9 (C(13), 52.6 (C(14)); 55.1 (MeO); 110.9, 113.5, 123.5, 131.6 (C(1), C(2), C(4), C(16)); 128.3, 128.6, 129.9, 136.5 (C(5), C(8), C(9), C(19)); 158.2 (C(3)); 163.3 (C(15)); 214.4 (C(17)). Anal. calc. for $C_{20}H_{22}O_2$ (294.4): C 81.60, H 7.53; found: C 81.62, H 7.56.

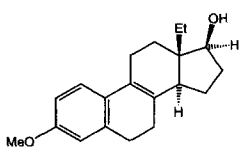
1.2.2.2. *Preparation of* rac-**14b**. 2.5M BuLi soln. in toluene (1.45 ml, 4.60 mmol, 1.8 equiv.) was added to a soln. of HMDS (1.09 ml, 5.11 mmol, 2.0 equiv.) in dry THF/HMPA (1:1, 14 ml) at –20°. The mixture was stirred for 1 h at 0°, cooled to –80° and a soln. of *rac*-**13b** (750 mg, 2.55 mmol) in dry THF (7 ml) added dropwise. After stirring for 1 h at –80°, AcOH (6 ml) was added and the mixture warmed up to 0°. Acidic workup gave a crude product which was subjected to FC (hexane/AcOEt 10:1) on silica gel (150 g). Crystallization from Et$_2$O afforded *(±)-13-ethyl-3-methoxygona-1,3,5(10),8,14-pentaen-17-one* (*rac*-**14b**; 630 mg, 84%). M.p. 77–79° (Et$_2$O) ([53]: 71–73° (MeOH/AcOEt)). TLC (hexane/AcOEt 4:1): R_f 0.42 UV (MeOH): λ_{max} 311.7 (28469) ([53]: UV: 311 (28000)). IR (KBr): 3072*w*, 3050*w* (=C–H); 1740*s* (C=O); 1620*w* (C=*C* olef.); 1602*w*, 1563*w*, 1499*s* (C=C, arom.). ^{1}H-NMR: 0.84 (*t*, *J*(MeC*H*$_2$,*Me*CH$_2$) = 7.5, *Me*CH$_2$); 1.49–1.69 (*m*, *J*(MeC*H*$_2$,*Me*CH$_2$) = 7.5, MeC*H*$_2$, H–C(12)); 2.12–2.20 (*m*, H′–C(12)); 2.28–2.38 (*m*, H–C(7)); 2.59–2.68 (*m*, H′–C(7), 2 H–C(11)); 2.77–2.83 (*m*, 2 H–C(6)); 2.92 (*dd*, *J*(H–C(16),H′–C(16)) = 23.5, *J*(H–C(16),H–C(15)) = 2.9, H–C(16)); 3.14 (*d*, *J*(H′–C(16),H–C(16)) = 23.5, H′–C(16)); 3.81 (*s*, MeO); 5.93 (*t*, *J*(H–C(15),H–C(16)) = 2.4, H–C(15)); 6.72–6.76 (*m*, H–C(2), H–C(4)); 7.20–7.24 (*m*, H–C(1)). Anal. calc. for $C_{20}H_{22}O_2$ (294.39): C 81.60, H 7.53; found: C 81.51, H 7.65.

1.2.2.3. *Preparation of* rac-**5b**. In a 50-ml *Schlenk* flask, a suspension of 5% Pd/CaCO$_3$ (43.4 mg, 5 mol-%) in dry benzene (5 ml) was evacuated and filled with H_2. The suspension was stirred under H_2 for 1 h. *rac*-**14b** (150 mg, 0.51 mmol) was added, and subsequently H_2 (18.8 ml, 0.8 mmol) was introduced through a gas bourette (TLC, hexane/AcOEt 4:1). The mixture was filtered through *Celite*, washed (Et$_2$O) and evaporated in *vacuo*. The crude product contained 129 mg (86%) of *rac*-**5b**, 2 mg (1%) of *rac*-**10b**, and 5 mg (3%) *rac*-**15b** according to anal. HPLC (hexane/AcOEt 10:1, *MN Nucleosil 50–10*, 2 ml/min, 254 nm) and was purified by semiprep. HPLC (hexane/AcOEt 10:1) to give *(±)-13-ethyl-3-methoxygona-1,3,5(10),8-tetraen-17-one* (*rac*-**5b**; 112 mg, 74%).

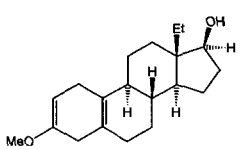
Crystallization from MeOH afforded *rac*-**5b** (107 mg, 71%). M.p. 121–123° (MeOH) ([53]: 120–122.5° (MeOH)). TLC (hexane/AcOEt 4:1): R_f 0.36. UV (MeOH): λ_{max} 279.0 (16599) ([53]: UV: λ_{max} 280 (16000)). IR (KBr): 3030*w* (=C–H); 2920*m*, 2890*m*, 2833*m* (–C–H); 1731*s* (C=O)); 1608*m*, 1568*m*, 1496*s* (C=C, arom.). ^{1}H-NMR: 0.85 (*t*, *J*(*CH*$_2$*Me*,*CH*$_2$Me) = 7.5, *Me*CH$_2$); 1.22–1.66 (*m*, *J*(*CH*$_2$Me,CH$_2$*Me*) = 7.4, MeC*H*$_2$, H–C(12)); 1.75–1.91 (*m*, H′–C(12)); 2.05–2.30 (*m*, H–C(7), 2 H–C(15), 2 H–C(16)); 2.42–2.62 (*m*, H′–C(7), 2 H–C(11)); 2.73–2.83 (*m*, 2 H–C(6), H–C(14)); 3.80 (*s*, MeO); 6.70–6.74 (*m*, H–C(2), H–C(4)); 7.11–7.15 (*m*, H–C(1)). ^{13}C-NMR: 7.8 (C(19)); 17.4, 20.6, 23.7, 24.3, 24.8, 28.5, 36.5 (C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 48.0 (C(14)); 50.8 (C(13)); 55.2 (MeO); 110.8, 113.6, 123.0 (C(1), C(2), C(4)); 126.9, 128.6, 130.5, 137.0 (C(5), C(8), C(9), C(10)); 158.0 (C(3)); 218.7 (C(17)). Anal. calc. for $H_{20}H_{24}O_2$ (296.41): C 81.04, H 8.16; found: C 80.85, H 8.07.

(±)-13-Ethyl-3-methoxy-8α-gona-1,3,5(10)-trien-17-one (*rac*-**15b**). M.p. 94–97° (MeOH) ([54]: 96–100° (MeOH/H_2O); [55]: 93–96°). TLC (hexane/AcOEt 4:1). R_f 0.36. UV (MeOH): λ_{max} 277.5 (2095). IR (KBr): 3082*w* (=C–H), 2940*m*, 2856*m* (–C–H), 1727*s* (C=O), 1608*m*, 1575*m*, 1497*m* (C=C, arom.). ^{1}H-NMR: 0.74 (*t*, *J*(*Me*CH$_2$,*CH*$_2$Me) = 7.5, *Me*CH$_2$); 1.22–2.48 (*m*, 2 H–C(7), H–C(8), 2 H–C(11), 2 H–C(12), H–C(14), 2 H–C(15), 2 H–C(16), MeC*H*$_2$); 2.60–2.85 (*m*, H–C(6), H–C(9)); 3.76 (*s*, MeO), 6.60 (*d*, *J*(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.71 (*dd*, *J*(H–C(2),H–C(1)) = 8.45, *J*(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.03 (*d*, *J*(H–C(1), H–C(2)) = 8.48, H–C(1)). Anal. calc. for $C_{20}H_{28}O_2$ (298.43): C 80.44, H 8.78; found: C 80.71, H 8.81.

1.2.2.4. *Preparation* of rac-**16**. $LiAlH_4$ (97 mg, 2.55 mmol, 0.75 equiv.) was added to a soln. of *rac*-**5b** (1.007 g, 3.40 mmol) in dry Et_2O. The mixture was subjected to ultrasound for 5 min (TLC, hexane/AcOEt 4:1). H_2O was added (ice-cooling), until a fine precipitate appeared. After decantation and washing of the residue with Et_2O (4×), the combined org. phases were dried ($MgSO_4$) and evaporated to yield *(±)-13-ethyl-3-methoxygona-1,3,5(10),8-tetraen-17β-ol* (*rac*-**35**; 994 mg, 98%) as a colorless solid. M.p. 106–108° ([53]: 102–105° (MeCN)). TLC (hexane/AcOEt 4:1): R_f 0.25. IR (KBr): 3506*s* (br., OH); 3021*w* (=C–H); 2947*s*, 2874*s*, 2832*s* (–C–H); 1610*s*, 1570*s*, 1494*s* (C=C, arom.). ^{1}H-NMR: 1.06 (*t*, *J*(CH$_2$*Me*,*CH*$_2$Me) = 7.5, *Me*CH$_2$); 1.32–1.77 (*m*, MeC*H*$_2$, H–C(12), H–C(15), 2 H–C(16), OH); 2.14.2.28 (*m*, 2 H–C(7), H′–C(15)); 2.30–2.51 (*m*, 2 H–C(11), H–C(14)); 2.69–2.76 (*m*, 2 H–C(6)); 3.80 (*s*, MeO); 3.89–3.96 (*m*, H–C(17)); 6.69–6.74 (*m*, H–C(2), H–C(4)); 7.13 (*d*, *J*(H–C(1),H–C(2)) = 8.2, H–C(1)). ^{13}C-NMR: 10.3 (C(19)); 18.0, 22.1, 24.3, 24.7, 28.6, 30.0, 31.3 (C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 44.3 (C(13)); 48.5 (C(14)); 55.3 (MeO); 82.5 (C(17)); 110.7, 113.6, 122.8 (C(1), C(2), C(4)); 125.8, 129.1, 132.2, 137.0 (C(5), C(8), C(9), C(10)); 157.7 (C(3)). Anal. calc. for $C_{20}H_{26}O_2$ (298.43): C 80.49, H 8.78; found: C 80.47, H 8.86.



35



36

A 100-ml, three-necked, round-bottomed flask equipped with an acetone/N_2-cooled *Städeler* condenser was charged with dry NH_3. (40 ml) at *ca.* –60°. Aniline (440 µl) and potassium (250 mg, 6.37 mmol, 5 equiv.) were added. A soln. of *rac*-**35** (382 mg, 1.27 mmol) in dry THF (5 ml) was added to the dark-blue soln., and the mixture was stirred for 1 h at –40°. Li (355 mg, 50.9 mmol, 40 equiv.) was added in small portions, the mixture stirred for 30 min, and EtOH (3.0 ml) added dropwise during 1 h. The mixture was warmed up to r.t. to remove the NH_3, and AcOH (10%, 70 ml) was added dropwise (ice-cooling). After basic workup, a residue was obtained which was purified by prep. HPLC (hexane/AcOEt 5:1; *MN Nucleosil 50–10*, 0.1 l/min) to give *(±)-13-ethyl-3-methoxygona-2,5(10)-dien-17-ol* (*rac*-**36**; 282 mg, 73%) as a colorless solid. A sample was crystallized from MeOH. M.p. 117–119° (MeOH) ([53]: 117–121° (MeOH)). TLC (hexane/AcOEt 4:1): R_f 0.29. IR (KBr): 3300*s* (br., OH); 2939*s*, 2818*s* (–C–H); 1697*m*, 1668*m*, (C=C, enol ether). ^{1}H-NMR: 0.98 (*t*, *J*(CH$_2$*Me*,*CH*$_2$Me) = 7.5, *Me*CH$_2$); 0.86–1.74 (*m*, 12 aliph. H, OH); 1.82–1.93 (*m*, 2 aliph. H); 2.03–2.17 (*m*, 2 aliph. H); 2.25 (*dt*, *J* = 12.6, 3.1, aliph. H); 2.47–2.87 (*m*, 4 aliph. H); 3.55 (*s*, MeO); 4.63–4.65 (*m*, H–C(2)). ^{13}C-NMR: 9.5 (C(19)); 17.8, 22.5, 25.4, 26.7, 28.3, 30.5, 31.0, 33.1, 34.1 (C(1), C(4), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 38.8, 45.2, 51.2 (C(8), C(14)); 44.9 (C(13)); 53.8 (MeO); 84.0, 90.6 (C(2), C(17)); 124.9, 128.0 (C(5), C(10)); 157.7 (C(3)). Anal. calc. for $C_{20}H_{30}O_2$ (302.46): C 79.42, H 9.99; found: C 79.33, H 9.91.

Alcohol *rac*-**36** (185 mg, 0.61 mmol), by *Oppenauer* oxidation carried out as described in [24], gave *(±)-13-ethyl-3-methoxygona-2,5(10)-dien-17-one* (*rac*-**16**; 146 mg, 79%). A sample was crystallized from MeOH. M.p.

158–161° (MeOH) ([53]: 152–160° (MeOH); [24]: 158–163° (MeOH); [56]: 160–162° (MeOH)). TLC (hexane/AcOEt 4:1): R_f 0.47. IR (KBr): 3047*w* (=C–H); 2941*s*, 2906*s*, 2846*s*, 2812*s* (–C–H); 1738*s* (C=O); 1698*s*, 1666*m* (C=C, enol ether). ^{1}H-NMR: 0.77 (*t*, J(CH$_2$*Me*,C*H*$_2$Me) = 7.5, *Me*CH$_2$); 1.13–1.37 (*m*, 4 aliph. H); 1.48–2.16 (*m*, 12 aliph. H); 2.38–2.88 (*m*, 5 aliph. H); 3.55 (*s*, MeO); 4.63–4.65 (*m*, H–C(2)). ^{13}C-NMR: 7.4 (C(19)); 17.6, 20.8, 24.6, 26.1, 27.4, 28.3, 30.4, 34.1, 35.9 (C(1), C(4), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 38.2, 45.4, 51.1 (C(8), C(9), C(14)); 53.8 (MeO); 90.2 (C(2)); 125.1, 127.6 (C(5), C(10)); 152.6 (C(3)); 219.7 (C(17)). Anal. calc. for $C_{20}H_{28}O_2$ (300.44): C 79.96, H 9.39; found: C 79.75, H 9.46.

1.2.2.5. *Preparation* of rac-**2** *from* rac-**16**. It was carried out as described in [24] to afford *(±)-norgestrel* (*rac*-**2**; 58 mg, 69%) as colorless crystals. M.p. 207–209° (MeOH) ([53]: 205–207° (MeOH); [24]: 206–208° (MeOH); [58]: 204–206° (acetone/hexane)). TLC (hexane/AcOEt 4:1): R_f 0.11. UV (MeOH): λ_{max} 240 (17089) ([53]: UV: λ_{max} 241 (16700, EtOH); [58]: UV: λ_{max} 239 (17350, EtOH)). IR (KBr): 3347*m* (OH); 3267*s* (C≡C–H); 3037*w* (=C–H); 2933*s*, 2868*m*, 2854*m* (–C–H); 1654*s* (C=O, α,β-unsat. ketone); 1616*s* (C=C, α,β-unsat. ketone). ^{1}H-NMR: 0.86–1.18 (*m*, 6 aliph. H), beneath: 1.01 (*t*, J(CH$_2$*Me*,C*H*$_2$Me) = 7.5, *Me*CH$_2$); 1.30–1.73 (*m*, 8 aliph. H); 1.78–2.53 (*m*, 12 aliph. H), beneath: 1.89 (*s*, OH); 2.59 (*s*, C≡C–H); 5.83 (*s*, H–C(4)): ^{13}C-NMR: 9.6 (C(19)); 18.9, 22.4, 26.2, 26.6, 28.4, 30.7, 35.5, 36.5, 39.6 (C(1), C(2), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 40.9, 42.5, 48.9, 50.8 (C(8), C(9), C(10), C(14)); 48.0 (C(13)); 74.2, 81.4, 87.8 (C(17), C(20), C(21)); 124.6 (C(4)); 166.5 (C(5)); 199.0 (C(3)). Anal. calc. for $C_{21}H_{28}O_2$ (312.45): C 80.73, H 9.03; found: C 80.94, H 9.20.

1.3. *With Dienophile* **18a**. 1.3.1. *Uncatalyzed Reaction*. 1.3.1.1. *Preparation of* rac-**20a**. A soln. of **18a** (500 mg, 4.54 mmol) and **6** (1.00 g, 5.36 mmol, 1.2 equiv.) in dioxane (60 ml) was heated under reflux for 50 h. After cooling to r.t., the solvent was removed *in vacuo* and the residue was subjected to chromatography (hexane/AcOEt 2:1) on silica gel (80 g). A portion (290 mg, 22%) of the main product *(±)-16-hydroxy-3-methoxy-14β-methylgona-1,3,5(10),9,16-pentaen-15-one* (*rac*-**20a**) was obtained after crystallization from Et$_2$O/pentane. M.p. 180–182° (MeOH) ([28a]: 170° (MeOH); [29]: 178–179° (MeOH/benzene)). TLC (hexane/AcOEt 4:1): R_f 0.25. UV (MeOH): λ_{max} 254.8 (20973). IR (KBr): 3340*s* (OH); 3040*w* (=C–H); 1685*s* (C=O); 1650*s* (C=C, olef.); 1605*m*, 1580*m*, 1490*s* (C=C, arom.). ^{1}H-NMR (250 MHz): 1.34 (*s*, Me); 2.09–2.17 (*m*, 2 H–C(7)); 2.35–2.41 (*m*, H–C(8), 2 H–C(12)); 2.46–2.56 (*m*, H–C(6)); 2.65–2.73 (*dt*, J(H–C(6),H′–C(6)) = 15.1, H′–C(6)); 2.76 (*dd*, J(H–C(13),H–C(12)) = 6.9, J(H–C(13),H–C(17)) = 3.7, H–C(13)); 3.76 (*s*, MeO); 5.21 (*s*, OH); 6.01 (*m*$_c$, H–C(11)); 6.19 (*d*, J(H–C(17),H–C(13)) = 3.1, H–C(17)); 6.60 (*dd*, J(H–C(2),H–C(1)) = 8.8, J(H–C(2),H–C(4)) = 2.5, H–C(2)); 7.31 (*d*, J(H–C(1),H–C(2)) = 8.6, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 2.09–2.17/2.35–2.41, 2.09–2.17/2.46–2.56, 2.09–2.17/2.65–2.73, 2.35–2.41/6.01, 2.46–2.56/2.65–2.73, 2.76/6.19, 6.60/6.68, 6.68/7.31. ^{13}C-NMR: 21.6 (C(7)); 22.5 (Me); 27.5, 30.3 (C(6), C(12)); 44.5, 45.4 (C(13), C(8)); 48.9 (C(14)); 55.2 (MeO); 112.4, 112.5, 117.8, 124.8, 130.0 (C(1), C(2), C(4), C(11), C(17)); 127.3, 137.4, 139.2, 152.6, 158.4 (C(3), C(5), C(9), C(10), C(16)); 206.4 (C(15)). Anal. calc. for $C_{19}H_{20}O_3$ (296.37): C 77.00, H 6.80; found: C 76.83, H 6.85. Crystal-structure analysis of *rac*-**20a**: *cf. Fig. 1,f* (depository number *CSD-55302*; CSD refcode VIYSEB) [12].

1.3.1.2. *Preparation of* rac-**19b** *and* rac-**20b**. Enedione **18a** (150 mg, 1.36 mmol) and diene **6** (300 mg, 1.61 mmol, 1.2 equiv.) were heated under reflux in dioxane (20 ml) for 48 h. After evaporation *in vacuo*, the residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (60 g) to give the mixture *rac*-**19a**/*rac*-**20a** (330 mg, 82%) as a yellowish solid. The solid was dissolved in dry DMF (1 ml), imidazole (184 mg, 2.67 mmol, 2.4 equiv.), (*t*-Bu)Ph$_2$SiCl (350 ml, 1.33 mmol, 1.2 equiv.) was added and the mixture stirred for 2 h at r.t. Filtration (hexane/AcOEt 10:1) of the crude product on silica gel (20 g) and purification by prep. HPLC (hexane/AcOEt 20:1 + 20% CH$_2$Cl$_2$, *MN Nucleosil 50-10*, 2 ml/min, 254 nm) afforded *rac*-**19b** (124 mg, 21% from *rac*-**19a**/*rac*-**20a**) and *rac*-**20b** (376 mg, 64% from *rac*-**19a**/*rac*-**20a**) as colorless solids. The ratio of *rac*-**19b**/*rac*-**20b** was determined to be 1:3 by HPLC (hexane/AcOMe 20:1, *MN Nucleosil 50-10*, 2 ml/min, 254 nm) from an experiment carried out under similar conditions.

*(±)-16-{[(*tert*-Butyl)diphenylsilyl]oxy}-3-methoxy-14β-estra-1,3,5(10),9,15-pentaen-17-one* (*rac*-**19b**): M.p. 138–139° (Et$_2$O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.48. UV (MeOH): λ_{max} 258.5 (18610). IR (KBr): 3090*w*, 3030*w* (=C–H); 1710*s* (C=O); 1627*m* (C=C, olef.); 1604*m*, 1580*w*, 1495*m* (C=C, arom.). ^{1}H-NMR (300 MHz): 0.84–1.03 (*m*, H–C(7)); 1.03 (*s*, *t*-Bu); 1.10 (*s*, Me); 1.67–1.74 (*m*, H′–C(7)); 1.87 (*m*$_c$, H–C(12)); 2.48–2.61 (*m*, 2 H–C(6), H–C(8), H–C(12), H–C(14)); 3.80 (*s*, MeO); 5.83 (*d*, J(H–C(15),H–C(14)) = 2.5, H–C(15)); 5.99 (*m*$_c$, H–C(11)); 6.58 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.67 (*dd*, J(H–C(2),H–C(4)) = 2.7, J(H–C(2),H–C(1)) = 8.6, H–C(2)); 7.00–7.05 (*m*, 2 arom. H); 7.13 (*d*, J(H–C(1),H–C(2)) = 8.6, H–C(1)); 7.19–7.27 (*m*, 3 arom. H); 7.33–7.48 (*m*, 1 arom. H); 7.51–7.54 (*m*, 4 arom. H). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.84–1.03/1.67–1.74, 1.67–1.74/2.48–2.61, 1.87/2.48–2.61, 1.87/5.99, 2.48–2.61/5.83, 6.58/6.67, 6.67/7.13, 7.00–7.05/7.19–7.27, 7.00–7.05/7.33–7.48, 7.19–7.27/7.33–7.48, 7.19–7.27/

7.51–7.54, 7.33–7.48/7.51–7.54. ^{13}C-NMR: 19.3 (Me_3C); 23.8 (Me); 25.3 (C(7)); 26.4 (Me_3C); 30.3 (C(6)); 34.2 (C(12)); 37.8, 48.2 (C(8), C(14)); 47.0 (C(13)); 55.3 (MeO); 112.4 (C(2)); 112.8 (C(4)); 118.4 (C(11)); 124.8, 127.5, 127.7, 129.7, 129.9, 135.3, 135.5, 135.8 (Ph); 136.3 (C(15)); 131.8, 32.2, 139.0, 153.4, 158.4 (C(3), C(5), C(9), C(10), C(16)); 208.0 (C(17)). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 23.8/1.03, 25.3/0.84–1.03, 25.3/1.67–1.74, 26.4/1.03, 30.3/2.48–2.61, 32.2/1.87, 32.2/2.48–2.61, 37.8/2.48–2.61, 48.2/2.48–2.61, 55.3/3.8, 112.4/6.67, 112.8/6.58, 118.4/5.99, 136.3/5.83. Anal. calc. for $C_{35}H_{38}O_3Si$ (534.77): C 78.61, H 7.16, Si 5.25; found: C 78.54, H 7.03, Si 5.09. Crystal-structure analysis of *rac*-**19b**: *cf. Fig. 1, d* (depository *number CSD-55302*; CSD refcode VIYSAX) [12].

*(±)-16-{[(*tert*-Butyl)diphenylsilyl]oxy}-3-methoxy-14β-methylgona-1,3,5(10),9(11),16-pentaen-15-one* (*rac*-**20b**): M.p. 101–102° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.48. UV (MeOH): λ_{max} 253.0 (16780). IR (KBr): 3070*w*, 3030*w* (=C–H); 2930*m*, 2860*m* (–C–H); 1710*s* (C=O); 1627*s* (C=C, olef.); 1604*m*, 1576*w*, 1496*m* (C=C, arom.). ^{1}H-NMR: 1.01 (*s*, *t*-Bu); 1.22 (*s*, Me); 2.02–2.26 (*m*, 2 H–C(7), H–C(8), 2 H–C(12)); 2.43–2.52 (*m*, H–C(6), H–C(13)); 2.67 (m_c, H′–C(6)); 3.79 (*s*, MeO); 5.78 (*d*, *J*(H–C(17),H–C(13)) = 3.1, H–C(17)); 5.85 (m_c, H–C(11)); 6.60 (*d*, *J*(H–C(4),H–C(2)) = 2.5, H–C(4)); 6.68 (*dd*, *J*(H–C(2),H–C(1)) = 8.5, *J*(H–C(2),H–C(4)) = 2.4, H–C(2)); 7.24–7.46 (*m*, 7 arom. H); 7.60–7.66 (*m*, 4 arom. H). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 2.02–2.26/2.43–2.52, 2.02–2.26/2.67, 2.02–2.26/5.85, 2.43–2.52/2.67, 2.43–2.52/5.78, 6.60/6.68, 6.68/7.24–7.46. ^{13}C-NMR: 19.4 (Me_3C); 21.6, 27.4 (C(7), C(12)); 22.9 (Me); 26.5 (Me_3C); 30.4 (C(6)); 44.5 (C(8)); 44.7 (C(13)); 48.3 (C(14)); 55.3 (MeO); 112.5 (C(2), C(4)); 117.7 (C(11)); 138.0 (C(17)); 124.7, 127.7, 135.4, 137.8, 139.4, 158.5 (C(1), C(3), C(5), C(9), C(10), C(16), arom. C). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 21.6/2.02–2.26, 22.9/1.22, 26.5/1.02, 27.4/2.02–2.26, 30.4/2.67, 44.5/2.02–2.26, 44.7/2.43–2.52, 55.3/3.79, 112.5/6.60, 112.5/6.68, 117.7/5.85, 138.0/5.78. Anal. calc. for $C_{35}H_{38}O_3Si$ (534.77): C 78.61, H 7.16, Si 5.25; found: C 78.37, H 7.29, Si 5.36.

1.3.2. *In the Presence of $BF_3 \cdot OEt_2$.* $BF \cdot OEt_2$ (1.0 ml, 6.14 mmol, 2.6 equiv.) was added to a soln. of **18a** (260 mg, 2.36 mmol) in dry Et_2O (15 ml) under N_2 at −20°. After stirring at −20° for 30 min, a soln. of **6** (520 mg, 2.74 mmol, 1.2 equiv) in dry Et_2O (5 ml) was added, and the mixture was stirred at −15° for 4 h. After warming up to 0° and basic workup, the resulting residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (80 g) to give the mixture *rac*-**19a**/*rac*-**20a** (530 mg, 75%) as a yellowish solid. Silylation according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_2SiCl (380 ml, 2.15 mmol) and imidazole (292 mg, 4.3 mmol) gave the mixture *rac*-**19b**/*rac*-**20b** as a colorless solid. Crystallization from Et_2O/pentane gave *rac*-**19b** (911 mg, 90% from *rac*-**19a**/*rac*-**20a**) as colorless crystals. The ratio *rac*-**19b**/*rac*-**20b** was determined to 98:2 by anal. HPLC (hexane/AcOMe 20:1, *MN Nucleosil 50-10*, 2 ml/min, 254 nm) from an experiment conducted under similar conditions. Anal. data identical with those ones under *Exper. 1.3.1.2*.

1.3.3. *In the Presence of $(i\text{-}PrO)_2TiCl_2$.* A soln. of $(i\text{-}PrO)_2TiCl_2$ (5.9 g, 25 mmol, 2.5 equiv.) in dry CH_2Cl_2 (30 ml) was added dropwise to a soln. of **18a** (1.10 g, 10 mmol) in dry CH_2Cl_2 (30 ml) under N_2 at −30°. After stirring for 30 min, a soln. of **6** (2.40 g, 13 mmol, 1.3 equiv.) in dry CH_2Cl_2 (10 ml) was added and the mixture stirred for 2 h at −30°. After warming up to r.t. and basic workup to leave a volume of *ca.* 20 ml, conc. aq. HCl soln. (10 drops) was added, and the mixture was stirred vigorously for 30 min at r.t. After filtration over $MgSO_4$ and evaporation *in vacuo*, the residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (200 g) to give *rac*-**21** (2.36 g, 80%) as a yellowish solid.

(±)-16-Hydroxy-3-methoxy-14β-estra-1,3,5(10),8,15-pentaen-17-one (*rac*-**21a**): M.p. 125–128° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.2. UV (MeOH): λ_{max} 270.0 (18960). IR (KBr): 3335*s* (OH); 3063*w*, 3025*w* (=C–H); 1695*s* (C=O); 1652*w* (C=C, olef.); 1606*m*, 1570*w*, 1490*m* (C=C, arom.). ^{1}H-NMR: 1.23 (*s*, Me); 1.57–1.68 (*m*, H–C(12)); 1.88–1.98 (*m*, H′–C(12)); 2.08–2.25 (*m*, H–C(7), H–C(11)); 2.37–2.44 (*m*, H′–C(7), H′–C(11)); 2.70–2.83 (*m*, 2 H–C(6)); 3.00 (*d*, *J*(H–C(14), H–C(15)) = 2.5, H–C(14)); 3.78 (*s*, MeO); 5.84 (*s*, OH); 6.55 (*d*, *J*(H–C(15),H–C(14)) = 3.0, H–C(15)); 6.69–6.73 (*m*, H–C(2), H–C(4)); 7.04–7.08 (*m*, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 1.57–1.68/1.88–1.98, 1.57–1.68/2.08–2.25, 1.57–1.68/2.37–2.44, 1.88–1.98/2.08–2.25, 1.88–1.98/2.37–2.44, 2.08–2.25/2.37–2.44, 2.08–2.25/2.70–2.83, 2.37–2.44/2.70–2.83, 3.00/6.55, 6.69–6.73/7.04–7.08. ^{13}C-NMR: 22.3 (C(7)); 22.8 (Me); 28.6 (C(6)); 31.9 (C(12)); 45.8 (C(13)); 49.2 (C(14)); 55.2 (MeO); 111.0, 113.5 (C(2), C(4)); 123.1 (C(1)); 128.9 (C(15)); 128.7, 129.7, 136.7 (C(5), C(8), C(9), C(10)); 150.3 (C(16)); 158.3 (C(3)); 208.8 (C(17)). Anal. calc. for $C_{19}H_{20}O_3$ (296.37): C 77.00, H 6.80; found: C 76.96, H 6.80.

Silylation according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_2SiCl (100 ml, 0.41 mmol) and imidazole (55 mg, 0.82 mmol) gave *rac*-**21b** as a colorless solid. *rac*-**21b** was the only steroidal compound that could be detected by anal. HPLC (hexane/AcOMe 10:0.3, *MN Nucleosil 50-10*, 2 ml/min, 254 nm). Crystallization from Et_2O/pentane gave *rac*-**21b** (154 mg, 85% from *rac*-**21a**).

(±)-16-{[(tert-Butyl)diphenylsilyl]oxy}-3-methoxy-14β-estra-1,3,5(10),8,15-pentaen-17-one (*rac*-**21b**): M.p. 125–128° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.2. UV (MeOH): λ_{max} 270.0 (17230). IR (KBr): 3070*w*, 3042*w* (=C–H); 2931*m*, 2857*m* (–C–H); 1712*s* (C=O); 1673*w*, 1654*w* (C=C, olef.); 1613*m*, 1590*m*, 1490*m* (C=C, arom.). ^{1}H-NMR: 1.09 (*s*, *t*-Bu, Me); 1.39–1.50 (*m*, H–C(12)); 1.85–1.96 (*m*, 2 H–C(7), H–C(11), H′–C(12)); 2.22–2.30 (*m*, H′–C(11)); 2.43–2.55 (*m*, H–C(6)); 2.59–2.69 (*m*, H′–C(6)); 2.76 (*d*, *J*(H–C(14),H–C(15)) = 2.8, H–C(14)); 3.79 (*s*, MeO); 6.15 (*d*, *J*(H–C(15),H–C(14)) = 3.1, H–C(15)); 6.64 (*d*, *J*(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.71 (*dd*, *J*(H–C(2),H–C(1)) = 8.4, *J*(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.02 (*d*, *J*(H–C(1),H–C(2)) = 8.4, H–C(1)); 7.14–7.25 (*m*, 3 arom. H); 7.31–7.43 (*m*, 3 arom. H); 7.58–7.69 (*m*, 4 arom. H). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 1.39–1.50/1.85–1.96, 1.39–1.50/2.22–2.30, 1.85–1.96/2.22–2.30, 1.85–1.96/2.43–2.55, 1.85–1.96/2.59–2.69, 2.43–2.55/2.59–2.69, 2.76/6.15, 6.64/6.71, 6.71–7.02, 7.14–7.25/7.58–7.69, 7.31–7.43/7.58–7.69. ^{13}C-NMR: 19.4 (Me_3C); 22.3, 27.3, 28.5, 31.6 (C(6), C(7), C(11), C(12)); 24.2 (Me); 26.7 (Me_3C); 45.6 (C(13)); 49.1 (C(14)); 55.3 (MeO); 110.8, 113.4, 123.4 (C(1), C(2), C(4)); 127.6, 127.8, 130.0, 135.5, 137.0 (C(15), arom. C); 128.2, 128.9, 131.8, 132.3, 136.7, 150.7, 158.1 (C(3), C(5), C(8), C(9), C(10), arom. C); 208.2 (C(17)). Anal. calc. for $C_{35}H_{38}O_3Si$ (534.77): C 78.61, H 7.16, Si 5.25; found: C 78.38, H 7.14, Si 5.10.

Without acidic isomerization, two products were obtained, which were identified, after silylation, as the double-bond isomers *rac*-**19b** and *rac*-**21b**.

1.3.4. *Li-TADDOLate-Mediated Reaction with Dienophiles* **18a** *or* **18b**. 1.3.4.1. *General Procedure for the Preparation of the Individual Ti-TADDOLates.* In a dry, round-bottomed flask, 2.0 equiv. of $(i\text{-PrO})_2TiCl_2$ and 2.2 equiv. of chiral, non-racemic TADDOL (see *Exper. 4.1*) were stirred under Ar in dry toluene (conc. *ca.* 50 mmol/l) for 1 h at r.t. The solvent was removed under reduced pressure (15 Torr, bath temp. *ca.* 50°) and the residue was dried under reduced pressure (0.1 Torr, r.t.).

1.3.4.2. *General Procedure for the Enantioselective* Diels-Alder *Reactions.* Dienophile **18a** or **18b** (1.0 mmol) was dissolved under N_2 in dry CH_2Cl_2 (20 ml) and cooled to the reaction temp. (see *Table 4*). The soln. of the chiral, non-racemic *Lewis* acid (prepared according to *General Procedure 1.3.4.1*) in dry CH_2Cl_2 (20 ml) was added dropwise and the mixture stirred for 30 min. The soln. of **6** (279 mg, 1.50 mmol, 1.5 equiv.) in dry CH_2Cl_2 (10 ml) was added and the mixture left at the reaction temp. for 2 h to 7 d (see *Table 4*). The residue obtained after acidic workup was subjected to FC (hexane/AcOEt 4:1; in case of ligand **Tk**, $CHCl_3$/acetone 50:1) on silica gel (50 g). The crude product was dissolved in CH_2Cl_2 (10 ml) and conc. aq. HCl soln. (10 drops) was added. The mixture was stirred for 30 min at r.t., filtered through $MgSO_4$, and evaporated *in vacuo*. FC (hexane/AcOEt 4:1) of the residue on silica gel (20 g) gave the adducts **21a**/*ent*-**21a** ≠ 1 or **21c**/*ent*-**21c** ≠ 1 as yellowish to colorless solids. Silylation according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_2SiCl (1.2 equiv.) and imidazole (2.4 equiv.) afforded the silyl enol ethers **21b**/*ent*-**21b** ≠ 1 or **21d**/*ent*-**21d** ≠ 1 as colorless solids. The enantiomeric excess (e.e.) of the predominant silyl enol ether was determined by ^{1}H-NMR shift experiment using (+)-[Eu(hfc)$_3$]. The optical purity of the predominant silyl enol ether was determined by comparison of the specific optical rotation with an optically pure reference (for preparation, see *Exper. 2.5.1* and *2.5.2*).

1.3.5. *From* Diels-Alder *Adduct* **21a**/ent-**21a** ≫ *1 to* **3a**. 1.3.5.1. *Preparation of* **13a**. In a dry, 50-ml three necked, round-bottomed flask, **21a**/*ent*-**21a** ≫ 1 (407 mg, 1.37 mmol; *cf. Exper. 1.3.4* and *Entry 14* of *Table 4*) was dissolved under N_2 in dry CH_2Cl_2 (20 ml). At 0°, 2,6-lutidine (0.37 ml, 3.2 mmol, 2.3 equiv.) and $(CF_3SO_2)_2O$ (0.5 ml, 3.0 mmol, 2.2 equiv.) were added simultaneously. The mixture was stirred for 1 h at 0°, the solvent was removed and the residue filtered (hexane/AcOEt 4:1) over silica gel (30 g). The resulting yellow oil was dissolved under N_2 in dry THF (100 ml) in a 250-ml, three-necked, round-bottomed flask. LiCl (176 mg, 4.15 mmol, 3 equiv.) and $Pd(PPh_3)_4$ (32 mg, 0.028 mmol, 0.02 equiv.) were added, and the mixture was heated to 40–45°. A soln. of Bu_3SnH (0.44 ml, 1.66 mmol, 1.2 equiv.) in dry THF (50 ml) was introduced dropwise during 2 h (TLC, hexane/AcOEt 4:1). After cooling to r.t. and basic workup, the crude product was subjected to FC (hexane/AcOEt 4:1) on silica gel (30 g) and prep. HPLC (hexane/AcOEt 10:3 + 30% CH_2Cl_2) to afford **13a**/*ent*-**13a** 22.5:1 (91.5% e.e., 256 mg, 66%). $[\alpha]_{589}^{20}$ = +606.3 (*c* = 1.024, $CHCl_3$); $[\alpha]_{578}^{20}$ = +638.5; $[\alpha]_{546}^{20}$ = +747.5; $[\alpha]_{436}^{20}$ = +1541.3; $[\alpha]_{365}^{20}$ = imperm.; 91% opt. purity. The e.e. of **13a** was determined to be 91.5% by anal. HPLC (hexane/i-PrOH 5:2, *Daicel Chiralcel OJ*, 0.8 ml/min, 254 nm) from an experiment carried out under similar conditions. Crystallization from MeOH gave 224 mg (88%) of **13a**/*ent*-**13a** 221:1, 99.1% e.e. TLC, UV, IR and ^{1}H-NMR data are identical with those ones in *Exper. 1.1.5.1.* M.p. 160° (MeOH). $[\alpha]_{589}^{20}$ = +671.6 (*c* = 0.9483, $CHCl_3$); $[\alpha]_{578}^{20}$ = +707.5; $[\alpha]_{546}^{20}$ = +828.2; $[\alpha]_{436}^{20}$ = +1707.9; see reference sample of **13a**: *Exper. 2.3.1.* Anal. calc. for $C_{19}H_{20}O_2$ (280.37): C 81.40, H 7.19; found: C 81.43, H 7.26.

Enrichment of a sample **13a**/*ent*-**13a** 285:1 (99.3% e.e.; 148 mg, 0.53 mmol) was possible by two successive crystallizations from MeOH to give **13a**/*ent*-**13a** 666:1 (99.7%, e.e.; 89 mg, 60%).

1.3.5.2. *Preparation of* **14a**. In a 50-ml, three-necked flask, BuLi (0.56 ml, 2.5M soln. in hexane, 1.4 mmol, 1.8 equiv.) was added to a soln. of HMDS (0.33 ml, 1.58 mmol, 2.0 equiv.) in dry THF (2 ml) and HMPT (2ml) at −20°. After stirring for 1 h at −20°, the mixture was cooled to −80° and a soln. of **13a**/*ent*-**13a** 221:1 (99.1% e.e.; 220 mg, 0.79 mmol) in dry THF (10 ml) was added. The dark mixture was stirred for 1 h at −80°. Then, AcOH (1.5 ml) was added and the temp. raised to r.t. The crude product obtained after acidic workup was purified by FC (hexane/AcOEt 10:1) on silica gel (50 g). Crystallization from MeOH gave **14a**/*ent*-**14a** 666:1 (99.7% e.e.; 171 mg; 78%). M.p. 145–146° (MeOH) ([19]: 143° (i-Pr)$_2$O). $[\alpha]_{589}^{20} = -102.6$ ($c = 0.904$, $CHCl_3$); $[\alpha]_{578}^{20} = -107.8$, $[\alpha]_{546}^{20} = -125.9$; $[\alpha]_{436}^{20} = -259.9$; $[\alpha]_{365}^{20}$ = imperm. ([19]: $[\alpha]_{589}^{20} = -143$ ($c = 0.6\%$, $CHCl_3$)). IR and ^{1}H-NMR data are identical with data in *Exper. 1.1.5.2*. Anal. calc. for $C_{19}H_{20}O_2$ (280.37): C 81.40, H 7.19; found: C 81.24, H 7.30.

1.3.5.3. *Preparation of* **5a**. In a 50-ml, three-necked flask, 5% Pd/$CaCO_3$ (110 mg) in C_6H_6 (20 ml) was heavily stirred under H_2 for 1 h; **14a** (0.589 g, 2.13 mmol) and C_6H_6 (5 ml) were added. The flask was evacuated and filled with H_2 (50 ml, 2.1 mmol, 1.0 equiv.). 45 min later the reaction mixture was filtered through *Celite* and washed with Et_2O. The solvent was removed and the resulting residue (600 mg) purified by prep. HPLC (hexane/AcOEt 10:1.2; *MN Nucleosil 50-10*, refractom.) and crystallization from MeOH to give **5a** (349 mg, 58%). Semiprep. HPLC (hexane/dioxane 10:0.7; *MN Nucleosil 50–10*, refractom.) of a predominantly **5a**-containing fraction (47 mg) afforded additional **5a** (29 mg, 5%) resulting in a total yield of 63% (378 mg) of **5a**. Ketones **10a** and **15a** of two similar experiments were collected and purified by semiprep. HPLC (hexane/AcOEt 10:1, *MN Nucleosil 50–10*, 10 ml/min, refractom.). For the preparation of **15a**, see *Exper. 2.4.1*.

Data of **5a**. M.p. 123–125° (MeOH). ([46b]: 123–125° (MeOH/AcOEt); [50]: 128° (hexane); [52]: 116–119° (Et_2O/petroleum ether)). $[\alpha]_{589}^{20} = +32.2$ ($c = 0.917$, dioxane), $[\alpha]_{578}^{20} = +34.4$; $[\alpha]_{546}^{20} = +42.5$; $[\alpha]_{436}^{20} = +116.2$; $[\alpha]_{365}^{20} = 359.8$. $[\alpha]_{589}^{20} = +30.3$ ($c = 0.991$, $CHCl_3$); $[\alpha]_{578}^{20} = +32.6$; $[\alpha]_{546}^{20} = +40.8$; $[\alpha]_{436}^{20} = +117.1$; $[\alpha]_{365}^{20} = +373.9$ ([46b]: $[\alpha]_{589}^{20} = +33.4$ ($c = 0.513$, dioxane); [52]: $[\alpha]_D = 30.4$ ($CHCl_3$); [51]: $[\alpha]_D = +29$ ($c = 1\%$, $CHCl_3$)). CD ($c = 0.0367$, dioxane): −2708 (245); +13249 (292 ([50]: $[\Delta\varepsilon]_{290} = +4.1$, $[\Delta\varepsilon]_{245}$−0.9, $[\Delta\varepsilon]_{230} = +0.7$, calc. of $[\theta]$ ($[\theta] = 3300 \times [\Delta\varepsilon]$) gives: +13530 (290); −2970 (245)). UV (MeOH): λ_{max} 278 (16640). IR, ^{1}H-NMR and ^{13}C-NMR data are identical with data in *Exper. 1.1.5.3*. Anal. calc. for $C_{19}H_{20}O_2$ (282.38): C 80.82, H 7.85; found: C 80.96, H 7.85.

Compound **10a**. Non-chiroptical data identical with those ones under *Exper. 1.1.5.3*.

1.3.5.4. *Preparation of* **3c**. In a three-necked, 25-ml, flask, Et_3SiH (1.09 ml, 6.84 mmol, 10 equiv. and CF_3COOH (1.05 ml, 13.6 mmol, 20 equiv.) were added to a soln. of **5a** (192 mg, 0.68 mmol) in dry C_6H_6 (12 ml) at r.t. After stirring for 12 h at r.t. and usual workup, a residue was obtained, which was filtered through flash silica gel (30 g; hexane/AcOEt 4:1) and purified by sempiprep. HPLC (hexane/AcOEt 10:1; *MN Nucleosil 50-10*, refractom.) and crystallization from MeOH/AcOEt 1:1 to give **3c** (142 mg, 73%). M.p. 174–175° (MeOH/AcOEt 1:1 ([46b]: 172–173° (MeOH/AcOEt 1:1); [60]: 164–167° (MeCN); [52]: 164–166° (MeOH); [61]: 174–175.5°; [21]: 165–167.5°; [43a]: 164–165° (MeOH)). $[\alpha]_{589}^{20} = +161.1$ ($c = 0.781$, dioxane); $[\alpha]_{578}^{20} = +169.2$; $[\alpha]_{546}^{20} = +196.8$; $[\alpha]_{436}^{20} = +390.7$; $[\alpha]_{365}^{20} = +838.3$ ([52]: $[\alpha]_D = +156°$ (dioxane); [46b]: $[\alpha]_{589}^{20} = 159.4$ ($c = 0.501$, dioxane); [60]: $[\alpha]_{589}^{20} = +154.0$ (dioxane); [61]: $[\alpha]_D^{33} + 159.2$ ($c = 0.72$, $CHCl_3$); [21]: $[\alpha]_D = +156.7$ ($c = 0.102$, dioxane)). CD ($c = 0.114$, dioxane): +11240 (303); +10739 (sh, 297); +8110 (sh, 312). ([62]: CD ($c = 0.167$, dioxane): +11120 (303); +10820 (sh, 297); +7700 (sh, 312) ([61]: CD ($c = 0.0003$, dioxane): +11080 (300); +9400 (268–271)). UV (MeOH+1% CH_2Cl_2): λ_{max} 278.6 (2011), 287.2 (1902). IR and ^{1}H-NMR data are identical with data in *Exper. 1.1.5.4*. Anal. calc. for $C_{19}H_{24}O_2$ (284.40): C 80.24, H 8.51; found: C 80.27, H 8.53.

1.3.5.5. *Preparation of* **3a**. In a 25-ml flask, BBr_3 (0.70 ml, 8.85 mmol, 18 equiv.) was added to a stirred soln. of **3c** (150 mg, 0.53 mmol) in dry CH_2Cl_2 (7 ml) at −30°. The soln. was left at 0–4° for 2 h, cooled to −30°. After dropwise addition of MeOH (2 ml) to the stirred soln. and usual workup, the crude product obtained was dissolved in DMSO (1 ml) and purified by FC (hexane/AcOEt 4:1; 60 g silica gel). Crystallisation from EtOH afforded **3a** (107 mg, 75%; by anal. HPLC (hexane/AcOEt 10:4.3 +10% Et_2O; *Merck Superspher Si 60*, refractom.; or hexane/AcOEt 10:4.3, *MN Nucleosil 50–10*, refractom.), no other products were determined). M.p. 259–260° (EtOH) ([46b]: 259–260.5° (EtOH); [62]: 266–267.5°; [43a]: 254–255.5° (acetone); [61]: 254–255°)). $[\alpha]_{589}^{20} = +163.6$ ($c = 0.486$, dioxane); $[\alpha]_{578}^{20} = +172.1$; $[\alpha]_{546}^{20} = +200.0$; $[\alpha]_{436}^{20} = +396.8$; $[\alpha]_{365}^{20} = +852.8$ ([46b]: $[\alpha]_{589}^{20} = +163.6$ ($c = 0.509$, dioxane); [61]: $[\alpha]_D^{32} = +153.2$ ($c = 0.31$, $CHCl_3$); [43a]: $[\alpha]_D^{21} + 149.4$ ($c = 0.6295$, $CHCl_3$); [63]: $[\alpha]_D = +160$ (dioxane)). CD ($c = 0.157$, dioxane): +11037 (303) [46b]: CD ($c = 0.157$, dioxane): +11130 (303)). UV (MeOH): λ_{max} 281 (2103); 287 (sh, 1901) ([46b]: UV (MeOH): 280 (2110); 287 (sh, 1940)). IR and ^{1}H-NMR data are identical with data in *Exper. 1.1.5.5*. Anal. calc. for $C_{18}H_{22}O_2$ (270.37): C 79.96, H 8.20; found: C 80.02, H 8.34.

1.4. *With Dienophile* **18b**. 1.4.1. *Uncatalyzed Reaction*. Compound **18b** (510 mg, 4.1 mmol); see *Exper. 3.2.2.4*) and **6** (920 mg, 4.9 mmol, 1.2 equiv.; see *Exper. 3.1*) were heated under reflux in dioxane (60 ml) for 48 h. After

evaporation *in vacuo*, the residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (80 g) to give a mixture *rac*-**19c**/*rac*-**20c** (510 mg, 40%) as a yellowish solid. Silylation according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_2SiCl (510 µl, 1.97 mmol) and imidazole (268 mg, 3.94 mmol) gave a mixture *rac*-**19d**/*rac*-**20d** as 35:65 (by anal. HPLC, hexane/Et_2O 10:1, *MN Nucleosil 50–10*, 2 ml/min, 254 nm). Separation by prep. HPLC (hexane/Et_2O 10:1.2) yielded *rac*-**19d** (252 mg, 28%) and *rac*-**20d** (469 mg, 52%) as colorless solids. Samples were crystallized from Et_2O/pentane.

*(±)-13-Ethyl-3-methoxy-16-{[(*tert*-butyl)diphenylsilyl]oxy}-14β-gona-1,3,5(10),9(11),15-pentaen-17-one* (*rac*-**19d**): M.p. 117–119° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.45. UV (MeOH): λ_{max} 258.5 (18901). IR (KBr): 3070*w*, 3046*w*, 3030*w* (=C–H); 1713*s* (C=O); 1619*s* (C=C, olef.); 1607*m*, 1569*w*, 1490*m* (C=C, arom.). ^{1}H-NMR: 0.77 (*t*, $J(MeCH_2,MeCH_2)$ = 7.4, $MeCH_2$); 0.95–1.07 (*m*, *t*-Bu, H–C(7)); 1.43–1.75 (*m*, $J(MeCH_2,MeCH_2)$ = 7.4, $MeCH_2$, H′–C(7)); 1.90 (ψ*dt*, J(H–C(12),H′–C(12)) = 15.0, J(H–C(12),H–C(11)) = 2.8, H–C(12)); 2.46–2.56 (*m*, 2 H–C(6), H–C(8), H′–C(12)); 2.65 (*dd*, J(H–C(14),H–C(8)) = 5.7, J(H–C(14),H–C(15)) = 3.1, H–C(14)); 3.81 (*s*, MeO); 5.83 (*d*, J(H–C(15),H–C(14)) = 3.1, H–C(15)); 6.01 (*m*$_c$, H–C(11)); 6.59 (*d*, J(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.68 (*dd*, J(H–C(2),H–C(1)) = 8.6, J(H–C(2),H–C(4)) = 2.7, H–C(2)); 6.97–7.03 (*m*, 2 arom. H); 7.16–7.27 (*m*, H–C(1), (3 arom. H); 7.33–7.40 (*m*, 1 arom. H); 7.45–7.55 (*m*, 4 arom. H). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.77/1.43–1.75, 0.95–1.07/1.43–1.75, 1.43–1.75/2.46–2.56, 1.90/6.01, 2.46–2.56/2.65, 2.46–2.56/6.01, 2.65/5.83, 6.59/6.68, 6.68/7.16–7.27, 6.97–7.03/7.16–7.27, 6.97–7.03/7.45–7.55, 7.16–7.27/7.33–7.40, 7.16–7.27/7.45–7.55. ^{13}C-NMR: 8.6 (C(19)); 19.3 (Me_3C); 25.4 (C(7)); 26.4 (Me_3C); 30.1 (C(18)); 30.3 (C(6)); 32.9 (C(12)); 38.1 (C(8)); 45.2 (C(14)); 51.4 (C(13)); 55.3 (MeO); 112.4 (C(2)); 112.8 (C(4)); 118.1 (C(11)); 124.8 (C(1)); 127.6, 127.7, 129.7, 129.9, 135.3, 135.5 (arom. C); 131.8, 132.1, 135.9, 139.0 (C(5), C(9), C(10), arom. C); 137.0 (C(15)); 154.5 (C(16)); 158.4 (C(3)); 208.0 (C(17)). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.6/0.77, 25.4/0.95–1.07, 25.4/1.43–1.75, 26.4/0.95–1.07, 30.1/1.43–1.75, 30.3/2.46–2.56, 32.9/1.90, 32.9/2.46–2.56, 38.1/2.46–2.56, 45.2/2.65, 55.3/3.81, 112.4/6.68, 112.8/6.59, 118.1/6.01, 124.8/7.16–7.27, 127.6, 127.7/6.97–7.03, 129.7, 129.9/7.16–7.27, 129.7, 129.9/7.33–7.40, 135.3, 135.5/7.43–7.55, 137.0/5.83. Anal. calc. for $C_{36}H_{40}O_3Si$ (548.80): C 78.39, H 7.35, Si 5.11; found: C 78.61, H 7.36, Si 5.18.

*(±)-14β-Ethyl-3-methoxy-16-{[(*tert*-butyl)diphenylsilyl]oxy}gona-1,3,5(10),9(11),16-pentaen-15-one* (rac-**20d**): M.p. 118° (Et_2O/pentane). TLC (hexane/AcOEt): R_f 4:1. 0.47 UV (MeOH); λ_{max} 254.1 (17671). IR (KBr): 3072*w*, 3044*w*, 3030*w* (=C–H); 1710*s* (C=O); 1628*s* (C=C, olef.); 1606*m*, 1570*w*, 1493*m* (C=C, arom.). ^{1}H-NMR: 0.80 (*t*, $J(MeCH_2,MeCH_2)$ = 7.4, $MeCH_2$); 1.01 (*s*, *t*-Bu); 1.68 (*m*$_c$, $J(MeCH_2,MeCH_2)$ = 7.4, $MeCH_2$); 1.96–2.20 (*m*, 2 H–C(7), 2 H–C(12)); 2.33–2.42 (*m*, H–C(8)); 2.50 (*dd*, J(H–C(6),H′–C(6)) = 12.3, J(H–C(6),H–C(7)) = 3.7, H–C(6)); 2.62–2.70 (*m*, H′–C(6), H–C(13)); 3.79 (*s*, MeO); 5.80 (*d*, J(H–C(17),H–C(13)) = 3.1, H–C(17)); 5.83–5.87 (*m*, H–C(11); 6.60 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.69 (*dd*, J(H–C(2),H–C(1)) = 8.6, J(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.26–7.47 (*m*, H–C(1), 6 arom. H); 7.60–7.65 (*m*, 4 arom. H). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.80/1.68, 1.96–2.20/2.32–2.42, 1.96–2.20/2.50, 1.96–2.20/2.62–2.70, 1.96–2.20/5.83–5.87, 2.50/2.62–2.70, 2.62–2.70/5.80, 6.60/6.69, 6.69/7.26–7.47, 7.26–7.47/7.60–7.65. ^{13}C-NMR: 8.9 (C(19)); 19.4 (Me_3C); 21.1 (C(7)); 26.5 (Me_3C); 27.7 (C(18)); 27.8 (C(12)); 30.4 (C(6)); 40.7 (C(13)); 41.8 (C(8)); 52.6 (C(14)); 55.2 (MeO); 112.4, 112.5 (C(2), C(4)); 117.5 (C(11)); 124.7 (C(1)); 127.6, 127.7, 129.8, 129.9, 135.3 (arom. C); 132.4, 137.5, 139.4 (C(5), C(9), C(10)); 138.7 (C(17)); 154.1 (C(16)); 158.5 (C(3)); 205.9 (C(15)). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.9/0.80, 21.1/1.96–2.20, 26.5/1.01, 27.7/1.68, 27.8/1.96–2.20, 30.4/2.50, 30.4/2.62–2.70, 40.7/2.62–2.70, 41.8/2.32–2.42, 55.2/3.79, 112.4, 112.4/6.60, 6.69, 117.5/5.83–5.87, 124.7/7.26–7.47, 127.6, 127.7/7.26–7.47, 128.8, 128.9/7.26–7.47, 135.3/7.60–7.65. Anal. calc. for $C_{36}H_{40}O_3Si$ (548.80): C 78.39, H 7.35; found: C 5.11, H 78.56. 7.32, 5.02.

1.4.2. *In the Presence of $BF_3 \cdot Et_2O$.* Compound **18b** (308 mg, 2.48 mmol) was dissolved in dry Et_2O (10 ml) and cooled to −15°. $BF_3 \cdot Et_2O$ (770 µl, 6.20 mmol, 2.5 equiv.) was added, and the soln. was stirred for 30 min. A soln. of **6** (555 mg, 2.98 mmol, 1.2 equiv.) in dry Et_2O (10 ml) was added dropwise and the mixture stirred for 4 h at −15°. After warming up to r.t. and basic workup, the resulting residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (50 g) to give a mixture *rac*-**19c**/*rac*-**20c** (408 mg, 53%) as a yellowish solid. Silylation according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_3SiCl (410 µl, 1.58 mmol) and imidazole (215 mg, 3.15 mmol) gave the mixture *rac*-**19d**/*rac*-**20d** 97:3 (by anal. HPLC, hexane/Et_2O 10:1, *MN Nucleosil 50–10*, 2 ml/min, 254 nm). Purification by prep. HPLC (hexane/Et_2O 10:1.2) yielded *rac*-**19d** (560 mg, 78%). A sample was crystallized from Et_2O/pentane. Anal. data identical with those ones under *Exper. 1.4.1.*

1.4.3. *In the Presence of (i-PrO)$_3$TiCl.* A 1.0M soln. of (i-PrO)$_3$TiCl in hexane (6.43 ml, 6.43 mmol, 2.5 equiv.) was added to a soln. of **18b** (319 mg, 2.57 mmol) in dry CH_2Cl_2 (20 ml) at −20°. After stirring for 30 min a soln. of **6** (575 mg, 3.08 mmol, 1.2 equiv.) in dry CH_2Cl_2 (10 ml) was added, and the mixture was stored at −20° for 16 h.

Basic workup gave a crude product, which was subjected to FC (hexane/AcOEt 4:1) on silica gel (40) to give *(±)-13-ethyl-3-methoxy-16-hydroxy-14β-gona-1,3,5(10),9,15-pentaen-17-one* (*rac*-**19c**, 559 mg, 70%) as a yellowish solid. A sample was crystallized from Et_2O. M.p. 138–140° (Et_2O). TLC (hexane/AcOEt 4:1): R_f 0.21. UV (MeOH): λ_{max} 260.7 (23279). IR (KBr): 3337*s*, 3291*m* (OH); 3034*w*, 3014*w* (=C–H); 1686*s* (C=O); 1650*s*, 1604*m*, (C=C, olef.); 1627*w*, 1571*w*, 1498*m* (C=C, arom.). ^{1}H-NMR: 0.84 (*t*, *J*(*Me*CH_2,MeCH_2) = 7.4, *Me*CH_2); 1.52–1.75 (*m*, *J*(MeCH_2,*Me*CH_2) = 7.4, MeCH_2, H–C(7)); 1.99–2.11 (*m*, H′–C(7), H–C(12)); 2.53 (*dd*, *J*(H′–C(12),H–C(12)) = 15.0, *J*(H′–C(12),H–C(11)) = 7.4, H′–C(12)); 2.61–2.78 (*m*, 2 H–C(6), H–C(8)); 2.91 (*dd*, *J*(H–C(14),H–C(8)) = 5.5, *J*(H–C(14),H–C(15)) = 3.1, H–C(14)); 3.78 (*s*, MeO); 5.40 (*s*, OH); 6.04 (m_c, *J*(H–C(11),H′–C(12)) = 7.5, H–C(11)); 6.40 (*d*, *J*(H–C(15),H–C(14)) = 3.0 H–C(15)); 6.62 (*d*, *J*(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.69 (*dd*, *J*(H–C(2),H–C(1)) = 8.6, *J*(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.36 (*d*, *J*(H–C(1),H–C(2)) = 8.6, H–C(1)). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.84/1.52–1.75, 1.52–1.75/1.99–2.11, 1.52–1.75/2.61–2.78, 1.99–2.11/2.53, 1.99–2.11/2.61–2.78, 1.99–2.11/6.04, 2.53/6.04, 2.61–2.78/2.91, 2.91/6.40, 6.62/6.69, 6.69/7.36. ^{13}C-NMR: 8.6 (C(19)); 25.8 (C(7)); 29.8 (C(18)); 30.4 (C(6)); 32.8 (C(12)); 38.1 (C(8)); 45.9 (C(14)); 52.0 (C(13)); 55.2 (MeO); 112.6 (C(2)); 112.9 (C(4)); 117.3 (C(11)); 127.3, 136.1, 139.0 (C(5), C(9), C(10)); 128.9 (C(15)); 154.1 (C(16)); 158.5 (C(3)); 208.0 (C(17)). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.6/0.84, 25.8/1.52–1.75, 25.8/1.99–2.11, 29.8/1.52–1.75, 30.4/2.61–2.78, 32.8/1.99–2.11, 32.8/2.53, 38.1/2.61–2.78, 45.9/2.91, 55.2/3.78, 112.6/6.69, 112.9/6.62, 117.3/6.04, 124.9/7.36, 128.9/6.40. Anal. calc. for $C_{20}H_{22}O_2$ (310.39): C 77.39, H 7.14; found: C 77.31, H 7.20.

Crystal-Structure Analysis of rac-**19c** (see *Fig. 1e*). Suitable crystals (orthorhombic) were obtained from Et_2O at +4°: space group *Pbca*; cell: a = 13.1265 (9) Å; b = 19.332 (1) Å; c = 25.979 (2) Å; V = 6593 (1) Å^3; Z = 16 (two independent molecules); D_c = 1.251 g·cm^{-3}. Octant up to $2\theta_{max}$ = 120°. 6109 reflections, 4879 independent reflections, 4733 reflections with $I > 0$ of a colorless, transparent crystal (size 0.3 × 0.4 mm). Number of variables: 592. The final difference density was less than 0.15 e·Å^{-3}, $R(F)$ = 0.043, $R_w(F)$ = 0.038.

Compound *rac*-**19c** (529 mg, 1.70 mmol) was silylated similar to *Exper. 1.3.1.2* using (*t*-Bu)Ph_2SiCl (530 µl, 2.05 mmol) and imidazole (279 mg, 4.09 mmol). The C(14)-ethylated isomer *rac*-**20d** could not be detected by anal. HPLC (hexane/Et_2O 10:1, *MN Nucleosil 50–10*, 2 ml/min, 254 nm). The crude product was purified by prep. HPLC (hexane/Et_2O 10:1) to give *rac*-**19d** (748 mg, 80%) as a colorless solid. A sample was crystallized from Et_2O/pentane. Anal. data identical with those under *Exper. 1.4.1.*

1.4.4. *In the Presence of (i-PrO)$_2$TiCl$_2$.* A soln. of (i-PrO)$_2$$TiCl_2$ (4.31 g, 18.2 mmol, 2.5 equiv.) in dry CH_2Cl_2 (30 ml) was added to a soln. of **18b** (902 mg, 7.3 mmol) in dry CH_2Cl_2 (20 ml) at −20°. After stirring at −20° for 30 min, a soln. of **6** (1.625 g, 8.72 mmol, 1.2 equiv.) in dry CH_2Cl_2 (25 ml) was added dropwise. The mixture was stirred for 2 h at −20° and then warmed up to r.t. After basic workup, a volume of *ca.* 50 ml was left. After addition of conc. aq. HCl soln. (10 drops), the mixture was stirred vigorously for 30 min. The mixture was dried ($MgSO_4$), evaporated *in vacuo*, and subjected to FC (hexane/AcOEt 4:1) on silica gel (150 g) to give *(±)-13-ethyl-16-hydroxy-3-methoxy-14β-gona-1,3,5(10),8,15-pentaen-17-one* (*rac*-**21c**; 1.805 g, 80%) as a yellowish solid. M.p. 143–147°. TLC (hexane/AcOEt 4:1): R_f 0.21. UV (MeO): λ_{max} 271.4 (18434). IR (KBr): 3323*s* (OH); 3064*w*, 3025*w*, 3007*w* (=C–H); 1687*s* (C=O); 1649*m* (C=C, olef.); 1606*m*, 1570*w*, 1499*m* (C=C, arom.). ^{1}H-NMR: 0.84 (*t*, *J*(MeCH_2,*Me*CH_2) = 7.4, *Me*CH_2); 1.57–1.78 (*m*, *J*(*Me*CH_2,MeCH_2) = 7.7, MeCH_2, H–C(12)); 2.00–2.11 (*m*, H–C(11), H′-C(12)); 2.17–2.26 (*m*, H–C(7)); 2.38–2.44 (*m*, H′–C(7), H′–C(11)); 2.70–2.84 (*m*, 2 H–C(6)); 3.10 (*ψs*, H–C(14); 3.79 (*s*, MeO); 5.74 (*s*, OH); 6.56 (*d*, *J*(H–C(15),H–C(14)) = 3.0, H–C(15)); 6.69–6.71 (*m*, H–C(2), H–C(4)); 7.04 (*d*, *J*(H–C(1),H–C(2)) = 9.1, H–C(1)). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.84/1.57–1.78, 1.57–1.78/2.00–2.11, 1.57–1.78/2.38–2.44, 2.00–2.11/2.38–2.44, 2.17–2.26/2.38–2.44, 2.17–2.26/2.70–2.84, 2.38–2.44/2.70–2.84, 3.10/6.56, 6.69–6.71/7.04. ^{13}C-NMR: 8.6 (C(19)); 22.2 (C(11)); 27.7 (C(7)); 28.7 (C(6)); 30.0 (C(18)); 31.4 (C(12)); 46.5 (C(14)); 49.9 (C(13)); 55.2 (MeO); 110.9, 113.5 (C(2), C(4)); 123.3 (C(1)); 128.7, 129.1, 129.8, 136.7 (C(5), C(8), C(9), C(10)); 129.6 (C(15)); 151.3 (C(16)); 158.2 (C(3)); 208.7 (C(17)). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.6/0.84, 22.2/2.00–2.11, 22.2/2.38–2.44, 27.7/2.17–2.26, 27.7/2.38–2.44, 28.7/2.70–2.84, 30.0/1.57–1.78, 31.4/1.57–1.78, 31.4/2.00–2.11, 46.5/3.10, 55.2/3.79, 110.9/6.67–6.71, 123.3/7.04, 129.6/6.56. Anal. calc. for $C_{20}H_{22}O_3$ (310.39): C 77.39, H 7.14; found: C 77.09, H 7.04.

Compound *rac*-**21c** (458 mg, 1.56 mmol) was silylated similar to *Exper. 1.3.1.2* using (*t*-Bu)Ph_2SiCl (490 µl, 1.86 mmol) and imidazole (255 mg, 3.75 mmol). *(±)-16-{[(*tert*-Butyl)diphenylsilyl]oxy}-13-ethyl-3-methoxy-14β-gona-1,3,5(10),8,15-pentaen-17-one* (*rac*-**21d**; 677 mg, 80%) was obtained as a colorless solid. A sample was crystallized from Et_2O/pentane. M.p. 120° (Et_2O/pentane). UV (MeOH): λ_{max} 271.4 (17699). IR (KBr): 3072*w*, 3054*w*, 3031*w*, (=C–H); 2931*m*, 2903*m*, 2857*m*, 2827*m* (C–H); 1716*s* (C=O); 1646*m* (C=C, olef.); 1610*s*, 1572*m*, 1498*m* (C=C, arom.). ^{1}H-NMR: 0.74 (*t*, *J*(MeCH_2,*Me*CH_2) = 7.5, *Me*CH_2); 1.09 (*s*, *t*-Bu); 1.41–1.65 (*m*,

MeCH_2, H–C(12)); 1.86–2.01 (*m*, 2 H–C(7), H–C(11), H'–C(12)); 2.25–2.31 (ψdt, H'–C(11)); 2.47–2.67 (*m*, 2 H–C(6)); 2.84 (*d*, *J*(H–C(14),H–C(15)) = 2.8, H–C(14)); 3.79 (*s*, MeO); 6.17 (*d*, *J*(H–C(15),H–C(14)) = 3.2, H–C(15)); 6.64 (*d*, *J*(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.71 (*dd*, *J*(H–C(2), H–C(1)) = 8.4, *J*(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.01 (*d*, *J*(H–C(1),H–C(2)) = 8.4, H–C(1)); 7.13–7.43 (*m*, 6 arom. H); 7.58–7.69 (*m*, 4 arom. H). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between 0.74/1.41–1.65, 1.41–1.65/1.86–2.01, 1.41–1.65/2.25–2.31, 1.86–2.01/2.25–2.31, 1.86–2.01/2.47–2.67, 2.84/6.17, 6.64/6.71, 6.71/7.01, 7.13–7.43/7.58–7.69. ^{13}C-NMR: 8.5 (C(19)); 19.4 (Me$_3$*C*), 22.2 (C(11), 26.5 (*Me*$_3$C); 27.4 (C(7)); 28.5 (C(6)); 30.7 ((C(18), C(12)); 46.4 (C(14)); 49.4 (C(13)); 55.2 (MeO); 110.7 (C(2)); 113.4 (C(4)); 123.3 (C(1)); 127.6, 127.7, 129.9, 135.4 (arom. C); 128.6, 128.9, 131.9, 132.3, 136.6 (C(5), C(8), C(9), C(10), arom. C); 137.8 (65)); 151.6 (C(16)); 158.1 (C(3)); 208.0 (C(17)). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between 8.5/0.74, 22.2/1.86–2.01, 22.2/2.25–2.31, 26.5/1.09, 27.4/1.86–2.01, 28.5/2.47–2.67, 30.7/1.41–1.65. 30.7/1.86–2.01, 46.4/2.84, 55.2/3.79, 110.7/6.71, 113.4/6.64, 123.3/7.01, 127.6/7.13–7.43, 127.7/7.13–7.43, 129.9/7.13–7.43, 135.4/7.58–7.69, 137.8/6.17. Anal. calc. for $C_{36}H_{40}O_3Si$ (548.80): C 78.79, H 7.35; Si 5.11; found: C 78.80, H 7.43, Si 5.10.

1.4.5. *From* Diels-Alder *Adduct* **21c**/ent-**21c** ≫ *1 to* **2**. 1.4.5.1. *Preparation of* **13b**. $(CF_3SO_2)_2O$ (1.96 ml, 11.96 mmol, 2.0 equiv.) and 2,6-lutidine (1.53 ml, 13.16 mmol, 2.2 equiv.) were added simultaneously to a stirred soln. of **21c**/*ent*-**21c** ≫ 1 (1.856 g, 5.98 mmol; *cf. Exper. 1.3.4* and *Entry 21* of *Table 4*) in dry CH_2Cl_2 (100 ml) at 0°. The mixture was stirred for 1 h at 0°, evaporated, and the resulting residue was subjected to FC (hexane/AcOEt 4:1) on silica gel (150 g). The obtained yellow oil (2.482 g) was dissolved in dry THF (130 ml) and the soln. added to a mixture of LiCl (690 mg, 16.24 mmol, 3.0 equiv.) and $Pd(PPh_3)_4$ (125 mg, 0.18 mmol, 2 mol-%) in dry THF (20 ml). After warming to 45°, a soln. of Bu_3SnH (1.50 ml, 5.68 mmol, 1.05 equiv.) in dry THF (80 ml) was added within 2.5 h at 45–50° (TLC, hexane/AcOEt 4:1). The residue obtained after basic workup was subjected to FC (hexane/AcOEt 10:1) on silica gel (250 g): **13b**/*ent*-**13b** 24:1 (1.532 g, 77%) was obtained as a colorless solid. $[\alpha]_{589}^{20}$ = +617.1 (*c* = 0.84, $CHCl_3$); $[\alpha]_{578}^{20}$ = +649.9; $[\alpha]_{546}^{20}$ = +761.1; $[\alpha]_{436}^{20}$ = +1512.2; $[\alpha]_{365}^{20}$ = imperm., 89% opt. purity; see reference sample of **13b**: *Exper. 2.3.2*. The e.e. of **13b** was determined to be 92% by anal. HPLC (*Daicel Chiralcel OJ*; hexane/i-PrOH 10:2; 1 ml/min; 254 nm).

Mixture **13b**/*ent*-**13b** 24:1 (1.290 g) was crystallized from MeOH twice to give **13b**/*ent*-**13b** 666:1 (1.084 g, 84%). M.p. 88–89° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.32. $[\alpha]_{589}^{20}$ = +699.2 (*c* = 1.10, $CHCl_3$); $[\alpha]_{578}^{20}$ = +736.5; $[\alpha]_{546}^{20}$ = +862.6; $[\alpha]_{436}^{20}$ = +1781.8; $[\alpha]_{365}^{20}$ = imperm.; opt. pure. UV (MeOH): λ_{max} 270 (15599). CD (*c* = 0.016, MeOH): +72733 (223), +50274 (209). IR (KBr): 3064*w* (=C–H); 2956*m*, 2936*m*, 2914*m*, 2874*m* (C–H); 1701*s* (C=O); 1640*w* (C=C, olef.); 1602*m*, 1570*m*, 1500*m* (C=C, arom.). ^{1}H-NMR: 0.83 (*t*, *J*(CH$_2$*Me*,C*H*$_2$Me) = 7.4, MeCH$_2$); 1.51–1.77 (*m*, MeCH_2, H–C(12)); 1.98–2.08 (*m*, H–C(11), H'–C(12)); 2.20–2.52 (*m*, 2 H–C(7), H'–C(11)); 2.69–2.92 (*m*, 2 H–C(6)); 3.27 (ψs, H–C(14)); 3.79 (*s*, MeO); 6.12 (*dd*, *J*(H–C(16),H–C(15)) = 5.8, *J*(H–C(16),H–C(14)) = 2.1, H–C(16)); 6.69–6.73 (*m*, H–C(2), H–C(4)); 7.04–7.08 (*m*, H–C(1)); 7.63 (*dd*, *J*(H–C(15),H–C(16)) = 5.8, *J*(H–C(15),H–C(14)) = 2.7, H–C(15)). ^{13}C-NMR: 8.8 (C(19)); 22.3, 27.8, 28.7, 29.6, 31.2 (C(6), C(7), C(8), C(11), C(12)); 51.1 (C(13)); 52.7 (C(14)); 55.3 (MeO); 111.0, 113.6, 123.4, 131.8 (C(1), C(2), C(4), C(16)); 128.4, 128.7, 130.1, 136.7 (C(5), C(8), C(9), C(10)); 158.3 (C(3)); 163.4 (C(15)); 214.6 (C(17)). Anal. calc. for $C_{20}H_{22}O_2$ (294.39): C 81.60, H 7.53; found: C 81.60, H 7.65.

The e.e. of **13b** was determined to be 99.7% by anal. HPLC (*Daicel Chiralcel*; hexane/i-PrOH 10:2; 1 ml/min; 254 nm).

1.4.5.2. *Preparation of* **14b**. A 2.5M BuLi soln. in hexane (2.46 ml, 6.15 mmol, 1.8 equiv.) was added to a soln. of HMDS (1.44 ml, 6.84 mmol, 2.0 equiv.) in dry THF/HMPA 1:1 (24 ml) at –20°. The mixture was stirred for 1 h at 0°, cooled to –80° and a soln. of **13b**/*ent*-**13b** 666:1 (1.006 g, 3.42 mmol) in dry THF (12 ml) added dropwise. After stirring for 1 h at –80°, AcOH (5 ml) was added and the mixture warmed up to 0° within 1 h. The crude product obtained after basic workup was subjected to FC (hexane/AcOEt 10:1) on silica gel (250 g). Filtration ($CHCl_3$/acetone 100:1) through flash silica gel (40 g) and crystallization from MeOH afforded **14b**/*ent*-**14b** 666:1 (792 mg, 79%) as colorless crystals. M.p. 67–68° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.43. $[\alpha]_{589}^{20}$ = –123.9 (*c* = 0.92, $CHCl_3$); $[\alpha]_{578}^{20}$ = –130.9; $[\alpha]_{546}^{20}$ = –154.0; $[\alpha]_{436}^{20}$ = –330.6; $[\alpha]_{365}^{20}$ = imperm. UV (MeOH): λ_{max} 311.8 (28844). CD (*c* = 0.017, MeOH): –27823 (232), +6977 (293), –12763 (319). IR (KBr): 3066*w*, 3056*w* (=C–H); 2936*m*, 2835*m* (C–H); 1740*s* (C=O); 1598*m*, 1560*m*, 1496*s* (C=C, arom.). ^{1}H-NMR: 0.84 (*t*, *J*(CH$_2$*Me*,C*H*$_2$Me) = 7.5, *Me*CH$_2$); 1.47–1.69 (*m*, *J*(C*H*$_2$Me,CH$_2$*Me*) = 7.7, MeCH_2, H–C(12)); 2.12–2.19 (*m*, H'–C(12)); 2.28–2.38 (*m*, H–C(7)); 2.59–2.68 (*m*, H'–C(7), 2 H–C(11)); 2.77–2.83 (*m*, 2 H–C(6)); 2.92 (*dd*, *J*(H–C(16),H'–C(16)) = 23.5, *J*(H–C(16),H–C(15)) = 3.0, H–C(16)); 3.14 (*d*, *J*(H'–C(16),H–C(16)) = 23.5, H'–C(16)); 3.81 (*s*, MeO); 5.93 (*t*, *J*(H–C(15),H–C(16)) = 2.5, H–C(15)); 6.72–6.76 (*m*, H–C(2), H–C(4)); 7.21–7.24 (*m*, H–C(1)). ^{13}C-NMR: 8.3 (C(19)); 22.9, 23.0, 25.8, 26.4, 28.5 (C(6), C(7), C(11), C(12), C(18)); 43.6 (C(16)); 53.0 (C(13)); 55.3 (MeO); 111.1, 113.6, 115.7, 124.0 (C(1), C(2), C(4), C(15)); 125.5, 128.6, 129.8, 138.1,

146.1 (C(5), C(8), C(9), C(10), C(14)); 158.6 (C(3)); 220.0 C(17)). Anal. calc. for $C_{20}H_{22}O_2$ (294.39): C 81.60, H 7.53; found: C 81.43, H 7.65.

The e.e. of **14b** was determined to be 99.7% by anal. HPLC (*Daicel Chiralcel OJ*; hexane/i-PrOH 10:2; 1 ml/min; 254 nm).

1.4.5.3. *Preparation of* **5b**. In a 50-ml *Schlenk* flask, a suspension of 5% Pd/$CaCO_3$ (193 mg, 4 mol-%) in dry benzene (10 ml) was evacuated and filled with H_2. The suspension was stirred under H_2 for 1 h. Mixture **14b**/*ent*-**14b** 666:1 (668 mg, 2.27 mmol) was added, and subsequently H_2 (68.7 ml, 3.1 mmol) introduced through a gas burette (TLC, hexane/AcOEt 4:1). After filtration through *Celite*, washing (Et_2O), and evaporation *in vacuo*, the crude product was purified by prep. HPLC (hexane/AcOEt 10:1, *MN Nucleosil 50-10*, 2 ml/min, 254 nm) to give a mixture of **5b** (532 mg, 79%), **10b** (11 mg, 2%), and **15b** (14 mg, 2%). Crystallization from MeOH afforded **5b** (504 mg, 75%) as colorless crystals. M.p. 128–130° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.36. UV (MeOH): λ_{max} 279.0 (16625). $[\alpha]_{589}^{20} = -31.5$ ($c = 0.89$, $CHCl_3$); $[\alpha]_{578}^{20} = 32.2$; $[\alpha]_{546}^{20} = -34.3$; $[\alpha]_{436}^{20} = -28.5$; $[\alpha]_{365}^{20} = +96.8$. CD ($c = 0.017$, dioxane): +4539 (229), −4921 (251), −5064 (268), +12231 (300). IR (KBr): 3030*w* (=C−H); 2920*m*, 2890*m*, 2833*m* (C−H); 1731*s* (C=O); 1608*m*, 1568*m*, 1496*s* (C=C, arom.). ^{1}H-NMR: 0.85 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 1.22–1.66 (*m*, $J(CH_2Me,CH_2Me) = 7.4$, $MeCH_2$, H−C(12)); 1.75–1.91 (*m*, H′−C(12)); 2.05–2.30 (*m*, H−C(7), 2 H−C(15), 2 H−C(16)); 2.42–2.62 (*m*, H′−C(7), 2 H−C(11)); 2.73–2.83 (*m*, 2 H−C(6), H−C(14)); 3.80 (*s*, MeO); 6.70–6.74 (*m*, H−C(2), H−C(4)); 7.11–7.15 (*m*, H−C(1)). ^{13}C-NMR: 7.8 (C(19)); 17.4, 20.6, 23.7, 24.3, 24.8, 28.5, 36.5 (C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 48.0 (C(14)); 50.8 (C(13)); 55.2 (MeO); 110.8, 113.6, 123.0 (C(1), C(2), C(4)); 126.9, 128.6, 130.5, 137.0 (C(5), C(8), C(9), C(10)); 158.0 (C(3)); 218.7 (C(17)). Anal. calc. for $C_{20}H_{24}O_2$ (296.41): C 81.04, H 8.16; found: C 80.83, H 8.27.

No trace of *ent*-**5b** could be detected by anal. HPLC (*Daicel Chiralcel OJ*; hexane/i-PrOH 10:4; 0.8 ml/min; 254 nm).

The by-products **10b** and **15b** of two identical experiments were collected and further purified by semiprep. HPLC (hexane/AcOEt 10:1, *MN Nucleosil 50-10*, 2 ml/min, 254 nm). **10b**: TLC, IR, ^{1}H-NMR and ^{13}C-NMR data were identical with those ones of *rac*-**10b** (*Exper. 1.2*). $[\alpha]_{589}^{20} = +177.8$ ($c = 0.83$, $CHCl_3$); $[\alpha]_{578}^{20} = +187.2$; $[\alpha]_{546}^{20} = +217.0$; $[\alpha]_{436}^{20} = +416.9$; $[\alpha]_{365}^{20} = +760.8$.

Data of **15b**: TLC (hexane/AcOEt 4:1): R_f 0.36. $[\alpha]_{589}^{20} = +54.9$ ($c = 0.95$, $CHCl_3$); $[\alpha]_{578}^{20} = +57.0$; $[\alpha]_{546}^{20} = +68.3$; $[\alpha]_{436}^{20} = +149.0$; $[\alpha]_{365}^{20} = +387.8$ ([57b]: $[\alpha]_{589}^{20} = +62$). IR (KBr): 3009*s* (=C−H); 2927*s*, 2854*s* (C−H); 1732*s* (C=O); 1609*m*, 1574*w*, 1492*m* (C=C, arom.). ^{1}H-NMR: 0.75 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 1.21–1.35 (*m*, 1 H, $MeCH_2$); 1.50–2.24 (*m*, 1 H, $MeCH_2$, 11 aliph. H); 2.36–2.49 (*m*, aliph. H); 2.61–2.86 (*m*, 3 aliph. H); 3.77 (*s*, MeO); 6.61 (*d*, J(H−C(4),H−C(2)) = 2.7, H−C(4)); 6.72 (*dd*, J(H−C(2),H−C(1)) = 8.4, J(H−C(2),H−C(4)) = 2.7, H−C(2)); 7.07 (*d*, J(H−C(1),H−C(2)) = 8.5, H−C(1)). ^{13}C-NMR: 8.8 (C(19)); 19.9, 20.8, 22.3, 28.3, 31.5, 35.7 (C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 38.9, 41.2, 49.4 (C(8), C(9), C(14)); 50.8 (C(13)); 55.2 (MeO); 112.2, 113.3, 130.2 (C(1), C(2), C(4)); 133.3, 137.6 (C(5), C(10)); 157.5 (C(3)); 218.9 (C(17)).

1.4.5.4. *Preparation of* **16**. $LiAlH_4$ (46 mg, 1.21 mmol) was added to a soln. of **5b** (480 mg, 1.62 mmol) in dry Et_2O (25 ml). The mixture was subjected to ultrasound for 5 min (TLC, hexane/AcOEt 4:1). H_2O was added under ice-cooling, until a fine precipitate appeared. After decantation and washing of the residue with Et_2O (4 ×), the combined org. phases were dried ($MgSO_4$) and evaporated *in vacuo* to yield **35** (475 mg, 98%) as a colorless solid. M.p. 114–116° ([57a]: 112–114° (MeOH/H_2O); [64]: 118°). TLC (hexane/AcOEt 4:1): R_f 0.25. $[\alpha]_{589}^{20} = -64.2$ ($c = 0.96$, $CHCl_3$); $[\alpha]_{578}^{20} = -67.2$; $[\alpha]_{546}^{20} = -77.4$; $[\alpha]_{436}^{20} = -144.1$; $[\alpha]_{365}^{20} = 262.8$ ([57a]: $[\alpha]_{589}^{20} = -66$; [64]: $[\alpha]_{589}^{20} = -64$). IR (KBr): 3506*s* (br., OH); 3021*w* (=C−H); 2947*s*, 2874*s*, 2832*s* (−C−H); 1610*s*, 1570*s*, 1494*s* (C=C, arom.). ^{1}H-NMR: 1.06 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 1.32–1.77 (*m*, $MeCH_2$, 2 H−C(12), H−C(15), 2 H−C(16), OH); 2.14–2.28 (*m*, 2 H−C(7), H′−C(15)); 2.30–2.51 (*m*, 2 H−C(11), H−C(14)); 2.69–2.76 (*m*, 2 H−C(6)); 3.80 (*s*, MeO); 3.89–3.96 (m_c, H−C(17)); 6.69–6.74 (*m*, H−C(2), H−C(4)); 7.13 (*d*, J(H−C(1),H−C(2)) = 8.2, H−C(1)). ^{13}C-NMR: 10.3 (C(19)); 18.0, 22.1, 24.3, 24.7, 28.6, 30.0, 31.3 (C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 44.3 C(13)); 48.5 (C(14)); 55.3 (MeO); 82.5 (C(17)); 110.7, 113.6, 122.8 (C(1), C(2), C(4)); 125.8, 129.1, 132.2, 137.0 (C(5), C(8), C(9), C(10)); 157.7 (C(3)). Anal. calc. for $C_{20}H_{26}O_2$ (298.43): C 80.49, H 8.78; found: C 80.36, H 8.79.

A 100-ml, three-necked, round-bottomed flask equipped with an acetone/N_2-cooled *Städeler* condenser was charged with dry NH_3 (30 ml) at *ca.* −60°. Aniline (410 µl) and K (136 mg, 3.35 mmol, 5 equiv.) were added. A soln. of **35** (200 mg, 0.67 mmol) in dry THF (5 ml) was introduced into the dark-blue soln., and the mixture was stirred for 1 h at −40°. Li (190 mg, 26.8 mmol, 40 equiv.) was added in small portions, the mixture stirred for 30 min, and EtOH (3.0 ml) added dropwise during 1 h. The mixture was warmed up to r.t. to remove the NH_3, and AcOH (10%, 40 ml) was added dropwise under ice-coolig. The resulting residue obtained after basic workup was purified by prep. HPLC (hexane/AcOEt 5:1, *MN Nucleosil 50-10*, 0.1 l/min) to give **36** (155 mg, 76%) as a colorless solid. A sample was crystallized from MeOH. M.p. 158–161° (MeOH) ([57a]: 159–161° (EtOH), 158–159° (petroleum

ether); [24]: 152–155° (petroleum ether/AcOEt 10:3); [65] [66]: 160–161° (MeOH)). TLC (hexane/AcOEt 4:1): R_f 0.29. $[\alpha]_{589}^{20} = +95.6$ ($c = 0.52$, dioxane); $[\alpha]_{578}^{20} = +100.0$; $[\alpha]_{546}^{20} = +114.0$; $[\alpha]_{436}^{20} = +198.7$; $[\alpha]_{365}^{20} = +323.5$ ([57a]: $[\alpha]_{589}^{20} = +95$, from petroleum ether +99° ($c = 1$, $CHCl_3$); [24]: $[\alpha]_{589}^{20} = +92.9$ ($c = 0.504$, dioxane); [65] [66]: $[\alpha]_{589}^{20} = +96$ ($c = 0.55$, dioxane)). IR (KBr): 3300*s* (br., OH); 2939*s*, 2818*s* (C–H); 1697*m*, 1668*m* (C=C, enol ether). ^{1}H-NMR: 0.98 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 0.86–1.74 (*m*, 12 aliph. H, OH); 1.82–1.93 (*m*, 2 aliph. H); 2.03–2.17 (*m*, 2 aliph. H); 2.25 (*dt*, $J = 12.6, 3.1$, aliph. H); 2.47–2.87 (*m*, 4 aliph. H); 3.55 (*s*, MeO); 4.63–4.65 (*m*, H–C(2)). ^{13}C-NMR (62.90 MHz, $CDCl_3$): 9.5 (C(19)); 17.8, 22.5, 25.4, 26.7, 28.3, 30.5, 31.0, 33.1, 34.1 (C(1), C(4), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 38.8, 45.2, 51.2 (C(8), C(9), C(14)); 44.9 (C(13)); 53.8 (MeO); 84.0, 90.6 (C(2), C(17)); 124.9, 128.0 (C(5), C(10)); 157.7 (C(3)). Anal. calc. for $C_{20}H_{30}O_2$ (302.46): C 79.42, H 9.99; found: C 78.97, H 10.17.

Compound **36** (270 mg, 0.89 mmol), $(i\text{-PrO})_3Al$ (77 mg, 0.37 mmol), and butan-1-one (500 µl) were refluxed in dry benzene (30 ml) for 24 h. The mixture was cooled to r.t., aq. 5% NaOH soln. (3.5 ml) and 2,6-Di(*tert*-butyl)-3-methylphenol (trace) were added, and the soln. was stirred for 5 min. The crude product obtained after usual workup was subjected to FC (hexane/AcOEt 4:1) on silica gel (30 g) to give **16** (221 mg, 82%). M.p. 187–189° (MeOH) ([57a]: 184–185° (MeOH); [24]: 181–184° (MeOH); [65] [66]: 189–191°). TLC (hexane/AcOEt 4:1): R_f 0.47. $[\alpha]_{589}^{20} = +160.0$ ($c = 0.94$, $CHCl_3$); $[\alpha]_{578}^{20} = +167.9$; $[\alpha]_{546}^{20} = +194.8$; $[\alpha]_{436}^{20} = +379.1$; $[\alpha]_{365}^{20} = +779.9$; ([57a]: $[\alpha]_{589}^{20} = +158$ ($c = 1$, $CHCl_3$); [24]: $[\alpha]_{589}^{20} = +156.2$ ($c = 0.45$, $CHCl_3$); [65] [66]: $[\alpha]_{589}^{20} = +159.5$ ($c = 0.45$, $CHCl_3$)). CD ($c = 0.24$, dioxane): +9250 (304) ([24]: CD: +9211 (304), ($c = 0.198$, dioxane). IR (KBr): 3047*w* (=C–H); 2941*s*, 2906*s*, 2846*s*, 2812*s* (C–H); 1738*s* (C=O); 1698*s*, 1666*m* (C=C, enol ether). ^{1}H-NMR: 0.77 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 1.13–1.37 (*m*, 4 aliph. H); 1.48–2.16 (*m*, 12 aliph. H); 2.38–2.88 (*m*, 5 aliph. H); 3.55 (*s*, MeO); 4.63–4.65 (*m*, H–C(2)). ^{13}C-NMR: 7.4 (C(19)); 17.6, 20.8, 24.6, 26.1, 27.4, 28.3, 30.4, 34.1, 35.9 (C(1), C(4), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 38.2, 45.4, 51.1 (C(8), C(9), C(14)); 53.8 (MeO); 90.2 (C(2)); 125.1, 127.6 (C(5), C(10)); 152.6 (C(3)); 219.7 (C(17)). Anal. calc. for $C_{20}H_{28}O_2$ (300.44): C 79.96, H 9.39; found: C 79.77, H 9.46.

1.4.5.5. *Preparation of* **2**. Li (41 mg, 5.93 mmol) was dissolved in stirred ethylenediamine (5 ml) under Ar. Acetylene (passed through KOH and activated charcoal) was bubbled through the dark-blue soln. for 1 h. A soln. of **16** (81 mg, 0.27 mmol) in dry THF (10 ml) was added to the white suspension, and acetylene was passed through the mixture for 2 additional h (TLC, hexane/AcOEt 4:1). 1.0 ml aq. 20% H_2SO_4 soln., 2.0 ml H_2O, 1.0 ml aq. 20% H_2SO_4 soln. and, finally, 2.0 ml H_2O were added under stirring and ice-cooling. A white solid (90 mg) obtained after basic workup, which was dissolved in MeOH (5 ml) and treated with aq. 6% HCl soln. (1.0 ml) was added and the mixture stirred at 45–50° for 45 min (TLC, hexane/AcOEt 2:1). The residue, obtained after basic workup, was subjected to chromatography (hexane/AcOEt 4:1) on flash silica gel (15 g) to give **2** (67 mg, 80%). Crystallization from MeOH afforded **2** (58 mg, 69%). M.p. 240–242° (MeOH) ([57a]: 229–231° (crude product), 228–229° (EtOH); [24]: 235–237° (MeOH); [53]: 238–242°; [65] [66]: 226–228° (crude product), 230–233° (MeOH), [67]: 240°). TLC (hexane/AcOEt 4:1): R_f 0.11. $[\alpha]_{589}^{20} = -34.0$ ($c = 0.94$, $CHCl_3$); $[\alpha]_{578}^{20} = -36.2$; $[\alpha]_{546}^{20} = -43.6$; $[\alpha]_{436}^{20} = 117.2$; $[\alpha]_{365}^{20} = -603.8$ ([57a]: $[\alpha]_{589}^{20} = -34$ ($c = 1$, $CHCl_3$); [24]: $[\alpha]_{589}^{20} = -32.4$ ($c = 0.496$, $CHCl_3$); [53]: $[\alpha]_{589}^{20} = -40.7$ ($CHCl_3$); [65] [66]: $[\alpha]_{589}^{20} = -34$ ($c = 0.94$, $CHCl_3$); [67]: $[\alpha]_{589}^{20} = -26 \pm 0.5$ ($c = 0.5$, $CHCl_3$)). CD ($c = 0.231$, dioxane): −2141 (sh, 309), −3633 (319), −4653 (332), −3714 (345), −1371 (sh, 360) ([24]: CD: −2115 (sh, 309), −3570 (320), −4525 (332), −3610 (344), −1325 (sh, 361)). UV (MeOH): λ_{max} 241 (16911) ([57a]: UV: 239 (17000); [24]: UV: 241 (16770); [65] [66]: UV: 240 (18400)). IR (KBr): 3347*m* (OH); 3267*s* (C≡C–H); 3037*w* (=C–H); 2933*s*, 2868*m*, 2854*m* (C–H); 1654*s* (C=O, α,β-unsat. ketone); 1616*s* (C=C, α,β-unsat. ketone). ^{1}H-NMR: 0.86–1.18 (*m*, 6 aliph. H), beneath: 1.01 (*t*, $J(CH_2Me,CH_2Me) = 7.5$, $MeCH_2$); 1.30–1.73 (*m*, 8 aliph. H); 1.78–2.53 (*m*, 12 aliph. H), beneath: 1.89 (*s*, OH); 2.59 (*s*, C≡CH); 5.83 (*s*, H–C(4)). ^{13}C-NMR: 9.6 (C(19)); 18.9, 22.4, 26.2, 26.6, 28.4, 30.7, 35.5, 36.5, 39.6 (C(1), C(2), C(6), C(7), C(11), C(12), C(15), C(16), C(18)); 40.9, 42.5, 48.8, 50.8 (C(8), C(9), C(10), C(14)); 48.0 (C(13)); 74.2, 81.4, 87.8 (C(17), C(20), C(21)); 124.6 (C(4)); 166.5 (C(5)); 199.9 (C(3)). Anal. calc. for $C_{21}H_{28}O_2$ (312.45): C 80.73, H 9.03; found: C 80.62, H 8.96.

No trace of *ent*-**2** could be detected by anal. HPLC (*Daicel Chiralcel OJ*; hexane/i-PrOH 5:3; 0.6 ml/min; 254 nm).

1.5. *With Dienophile* **23b**. 1.5.1. *In the Presence of Me_2AlCl at Low Temp.* In a 30-ml *Schlenk* flask, Me_2AlCl (2.74 ml, 1M in hexane, 2.74 mmol, 3 equiv.) was added to a soln. of **23b** (220 mg, 0.912 mmol; for preparation, see *Exper. 3.2.3*) in dry CH_2Cl_2 (12 ml) under dry Ar at –60°. After stirring for 30 min at –60°, a soln. of **6** (1.27 g, 6.84 mmol, 7.5 equiv., for preparation see *Exper. 3.1*) in dry CH_2Cl_2 (3 ml) was added. After stirring for 1 additional h at −60°, the temp. was raised to −30°, and the mixture stored at −30° to −25° for 14 d. The red soln. was poured into sat aq. NH_4Cl soln. and worked up in the usual way. The resulting residue was subjected to chromatography (hexane/AcOEt 4:1) on flash silica gel (150 × 30 mm column) to afford a colorless solid. Anal. HPLC (hexane/AcOMe/CH_2Cl_2 38:12:50, *MN Nucleosil 50–10*, 2 ml/min, 254 nm) showed the presence of four product compo-

nents in a total yield of 348.9 mg (89%) and a ratio of *rac*-**24**/*rac*-**25** + *rac*-**27**) of 62:29:9. Semiprep. HPLC (hexane/AcOEt/CH_2Cl_2 49:21:30; *MN Nucleosil 50–10*, 2 ml/min refraktom.) gave *rac*-**24** (212.7 mg, 55%), *rac*-**25** (97.7 mg, 25%), *rac*-**26** (23.8 mg, 6%), and *rac*-**27** (7.4 mg, 2%) as colorless solids. Crystallization of *rac*-**24** from Et_2O/CH_2Cl_2 (5°) afforded *(±)-3-[3-methoxy-16-(methoxycarbonyl)-13,16-seco*-D*-nor-8-estra-1,3,5(10),9(11)-tetraene-13-carbonyl]oxazolidin-2-one* (*rac*-**24**). M.p. 147–149°. TLC (hexane/AcOEt 1:1): R_f 0.42. UV (MeOH + 1% CH_2Cl_2): λ_{max} 264.8 (19630); 273.0 (sh); 300.0; 310.0 (sh). IR (KBr): 3032*w* (arom. CH); 2955*w* (aliph. CH); 1775*s*, 1730*s*, 1677*s* (C=O); 1607*m*, 1576*w* (arom. C=C); 1235*s*, 1038*s*. ^{1}H-NMR: 1.46 (*s*, Me–C(18)); 1.59–1.62 (*m*, 2 H–C(7)); 1.66–1.83 (*m*, 2 H–C(15)); 2.09–2.11 (*m*, H–C(12)); 2.17–2.1 (*m*, H–C(8)); 2.45–2.51 (*t*, (*t*, *J*(H–C(15),H–C(16)) = 8, 2 H–C(16)); 2.77 (*m*, 2 H–C(6)); 2.79–2.80 (*m*, H–C(14)); 2.86–2.87 (*m*, H′–C(12)); 3.67 (*s*, MeO); 3.77 (*s*, MeO); 3.99–4.08 (*m*, CH_2O), 4.35–4.42 (*m*, CH_2N); 6.24–6.26 (*m*, H–C(11)); 6.56 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.70 (*dd*, *J*(H–C(2),H–C(4)) = 2.70, *J*(H–C(1),H–C(2)) = 8.8, H–C(2)); 7.58 (*d*, *J*(H–C(1),H–C(2)) = 8.8, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.59–1.62/2.77; 1.66–1.83/2.45–2.51; 1.66–1.83/2.79–2.80; 2.79–2.80/2.17–2.18; 2.17–2.18/6.24–6.26; 3.99–4.08/4.35–4.42; 6.56/6.70; 6.70/7.5. ^{13}C-NMR: 20.4 (C(18)); 21.18 (C(7)); 27.44 (C(15)); 35.42 (C(12)); 39.94 (C(8)); 35.30 (C(16)); 31.05 (C(6)); 39.52 (C(14)); 48.82 (C(13)); 51.52 (*Me*CO_2); 55.21 (ArO*Me*); 45.31 (CH_2N); 62.08 (CH_2O); 116.91 (C(11)); 113.12 (C(4)); 112.71 (C(2)); 124.42 (C(1)); 126.89 (C(9); 131.27 (C(10)); 137.58 (C(5)); 158.20 (C(3)); 152.43, 173.83, 176.69 (3 C=O). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.46/20.42; 1.59–1.62/21.18; 1.66–1.83/27.44; 2.09–2.11/35.42; 2.17–2.18/39.94; 2.45–2.51/35.30; 2.77/31.05; 2.79–2.80/39.52; 3.67/51.52; 3.77/55.21; 4.35–4.42/45.31; 3.99–4.08/62.08; 6.24–6.26/116.91; 6.56/113.12; 6.70/112.71; 7.58/142.42. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84, N 3.28; found: C 67.48, H 6.77, N 3.31.

Crystal-Structure Analysis of rac-**24** (see *Fig. 3*). Triclinic crystal system; space group $P\bar{1}$; cell: a = 8.361 (1) Å; b = 11.003 (2) Å; c = 12.170 (2) Å; V = 1048.9 (4) Å^3; Z = 2 (two independent molecules), D_c = 1.354 g·cm^{-3}. Octant up to $2\Theta_{max}$ = 120°; 3125 independent reflections, 3060 reflections, with $I > 0$ of a colorless, transparent crystal (size 0.15 × 0.20 × 0.50 mm^3) were measured at r.t. Number of variables: 397. Structure refinement based on F values using unit weights. The final difference density was less than 0.15 e Å^{-3}, $R(F)$ = 0.038; $R(F)$ = 0.036.

(±)-3-[3-Methoxy-16-(methoxycarbonyl)-13,16-seco-D*-norestra-1,3,5(10),9(11)-tetraene-13-carbonyl]oxazolidin-2-one* (*rac*-**25**): M.p. 67° ($Et_{12}O/CH_2Cl_2$). TLC (hexane/AcOEt 1:1): R_f 0.42 UV (MeOH + 1%CH_2Cl_2): λ_{max} 262.5 (17521); 294.0. IR (KBr): 3006*w*, (arom. CH); 2948*w* (aliph. CH); 1775*s*, 1734*s*, 1677*s* (C=O); 1607*m*, 1570*w* (arom. C=C); 1257*s*; 1044*s*. ^{1}H-NMR: 1.29 (*s*,Me–C(13)); 1.63–1.69 (*m*, 2 H–C(15)); 1.96–2.04 (*m*, H–C(8)); 2.16–2.21 (*m*, 2 H–C(7)); 2.35 (*m*, H–C(12)); 2.40 (*m*, 2 H–C(16)); 2.49 (*m*, 2 H–C(14)); 2.85–2.88 (*m*, 2 H–C(6)); 3.03–3.10 (*m*, H′–C(12)); 3.66 (*s*, MeO); 3.78 (*s*, ArOMe); 4.33–4.40 (*m*, CH_2O); 4.41–4.47 (*m*, CH_2N); 6.05–6.07 (*m*, H–C(11)); 6.58 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.70 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(1),H–C(2)) = 8.8, H–C(2)); 7.45 (*d*, *J*(H–C(1), H–C(2)) = 8.8, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.63–1.69/2.40; 1.63–1.69/2.49; 2.49/1.96–2.04; 3.03–3.10/2.35; 4.33–4.40/4.41–4.47; 6.05–6.07/3.03–3.10; 6.58/6.70; 6.70/7.45. ^{13}C-NMR: 17.30 (C(18)); 27.52 (C(15)); 28.51 (C(7)); 30.35 (C(6)); 33.98 (C(12)); 34.69 (C(16)); 40.67 (C(14)); 40.70 (C(8)); 45.56 (CH_2N); 48.42 (C(13); 51.53 (MeO); 55.20 (ArOMe); 62.30 (CH_2O); 112.65 (C(2)); 112.96 (C(4)); 115.30 (C(11)); 125.15 (C(1)); 127.56 (C(9)); 134.36 (C(10); 137.00 (C(5)); 158.48 (C(3)); 152.61, 173.95, 178.75 (3 C=O). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.29/17.30; 1.63–1.69/27.52; 2.16–2.21/28.51; 2.85–2.88/30.35; 2.35/33.98; 2.40/34.69; 2.49/40.67; 1.96–2.04/40.70; 4.41–4.47/45.56; 3.66/51.53; 3.78/55.20, 4.33–4.40/62.30; 6.70/112.65; 6.58/112.96; 6.05–6.07/115.30; 7.45/125.15. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84, N 3.28; found: C 67.43, H 6.80, N 3.30.

(±)-3-[3-Methoxy-16-(methoxycarbonyl)-14,15-seco-D*-nor-8,13,14-methylgona-1,3,5(10),9(11)-tetraene-14-carbonyl]oxazolidin-2-one* (*rac*-**26**): M.p. 84–85° (Et_2O/CH_2Cl_2). TLC (hexane/AcOEt 1:1): R_f 0.42. UV (MeOH + 1% CH_2Cl_2): λ_{max} 264.5 (13449). IR (KBr): 3054*w* (arom. CH); 2925*w* (aliph. CH); 1774*s* (C=O); 1734*s* (C=O); 1676*s* (C=O); 1607*m*, 1574*w* (arom. C=C); 1234*s*. ^{1}H-NMR: 1.11 (*s*, Me–C(14)); 1.40–1.48 (*m*, 2 H–C(16)); 1.49–1.59 (*m*, 2 H–C(7)); 1.75–1.90 (*m*, H–C(12)); 2.29–2.37 (*m*, 2 H–C(15)); 2.39–2.53 (*m*, H′–C(12)); 2.75 (*m*, 2 H–C(6)); 2.95 (*m*, H–C(13)); 3.65 (*s*, MeO); 3.77 (*s*, ArOMe, and sh at 3.72, *m*, H–C(8)); 4.10–4.19 (*m*, CH_2O); 4.37–4.56 (*m*, CH_2N); 6.22 (*m*, H–C(11)); 6.55 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.70 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(1),H–C(2)) = 8.8, H–C(2)); 7.57 (*d*, *J*(H–C(1),H–C(2)) = 8.8, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.40–1.48/2.29–2.37; 1.40–1.48/2.95; 6.22/2.39–2.53. ^{13}C-NMR: 11.89 (Me–C(14)); 27.66 (C(16)); 25.12 (C(7)); 29.07 (C(12)); 31.48 (C(15)); 30.81 (C(6)); 33.51 (C(13)); 38.82 (C(8)); 51.58 (MeO); 55.14 (ArOMe); 45.97 (CH_2O); 53.62 (C(14)); 62.17 (CH_2N); 115.61 (C(11)); 112.97 (C(4)); 112.65 (C(2)); 124.75 (C(1)); 127.29 (C(9)); 132.49 (C(19)); 137.56 (C(5)); 158.24 (C(3)); 152.57, 174.08, 177.75 (3 C=O). The signals were assigned using a ^{1}H^{13}C-COSY spectrum. Cross peaks

between: 1.11/11.89; 1.40–1.48/27.66; 1.49–1.59/25.12; 1.75–1.90 and 2.39–2.53/29.07; 2.29–2.37/31.48; 2.75/30.81; 2.95/33.51; 3.7–3.8/38.82; 3.65/51.58; 3.77/55.14; 4.10–4.19/45.97; 4.37–4.56/62.17; 6.22/115.6; 6.55/112.97; 6.70/112.65; 7.57/124.75. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49) C 67.43, H 6.84, N 3.28; found: C 67.48, H 6.79, N 3.43.

The relative configuration of H–C(8) was assigned by NOE measurements (irradiated signal/NOE [%]): H–C(13)/H–C(8) (2.6%); H–C(13)/H–C(12) (2.3%); H–C(8)/H–C(13) (0.4%); H–C(8)/H–C(6) (0.3%); Me–C(14)/H–C(12) (0.5%).

*(±)-3-[3-Methoxy-16-(methoxycarbonyl)-14,15-seco-*D*-nor-13,14-methylgona-1,3,5(10),9(11)-tetraene-14-carbonyl]oxazolidin-2-one* (*rac*-**27**): M.p. 119–120° (Et_2O/CH_2Cl_2). TLC (hexane/AcOEt 1:1): R_f 0.42. UV(MeOH + 1%CH_2Cl_2): λ_{max} 264.5 (7295). IR (KBr): 3005*w* (arom. CH); 2927*m* (aliph. CH); 1774*s*, 1734*s*, 1684*s* (C=O); 1607*m*, 1570*w* (arom. C=C); 1255*s*; 1039*s*. ^{1}H-NMR: 1.48 (*s*, Me–C(14)); 1.32–1.49 (*m*, 2 H–C(7)); 1.59–1.86 (*m*, 2 H–C(16)); 1.89–2.10 (*m*, H–C(12)); 2.21–2.30 (*m*, H′–C(12)); 2.31–2.39 (*m*, H–C(13)); 2.40–2.51 (*m*, 2 H–C(15)); 2.80 (*m*, H–C(6)); 2.96 (*m*, H–C(8)); 3.65 (*s*, MeO); 3.77 (*s*, ArOMe); 3.92–4.19 (*m*, CH_2O); 4.31–4.51 (*m*, CH_2N); 5.94 (*m*, H–C(11)); 6.55 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.67 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(1),H–C(2)) = 8.8, H–C(2)); 7.38 (*d*, *J*(H–C(1),H–C(2)) = 8.8, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.32–1.49/2.80; 1.59–1.86/2.31–2.39; 2.21–2.30/2.31–2.39; 5.94/2.21–2.30. ^{13}C-NMR: 16.19 (Me–C(14)); 27.20 (C(7)); 27.04 (C(16)); 28.09 (C(12)); 35.26 (C(13)); 33.03 (C(15)); 30.58 (C(6)); 42.28 (C(8)); 51.49 (MeO); 55.17 (ArOMe); 45.39 (CH_2O); 52.17 (C(14)); 62.36 (CH_2N); 115.43 (C(11)); 112.36 (C(2)); 112.87 (C(4)); 124.85 (C(1)); 129.36 (C(9)); 135.58 (C(10)); 176.72 (3 C=O). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.48/16.19; 1.32–1.49/27.20; 1.59–1.86/27.04; 1.89–2.10 and 2.21–2.30/28.09; 2.31 –2.39/35.26; 2.40–2.51/33.03; 2.80/30.58; 2.96/42.28; 3.65/51.49; 3.77/55.17; 3.92–4.19/45.39; 4.31–4.51/62.36; 5.94/115.43; 6.67/112.36; 6.55/112.87; 7.38/124.85. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84, N 3.28; found: C 67.21, H 6.87, N 3.02.

1.5.2. *In the Presence of Various* Lewis *Acids*. The reactions were conducted according to *Exper. 1.5.1.* The results are summarized in *Table 5* and *6* (see *Sect. 3*).

1.5.3. *In the Presence of Me_2AlCl at Elevated Temp.* (see *Table 7*). Me_2AlCl (3.66 ml, 1M in hexane, 3.66 mmol, 3 equiv.) was added to soln. of **23b** (294 mg, 1.22 mmol) in dry CH_2Cl_2 (25 ml) under Ar at –60°. A soln. of **6** (1.70 g, 9.15 mmol, 7.5 equiv.) in dry CH_2Cl_2 (4 ml) was added. The mixture was left for 24 h at 5°. Usual workup followed by FC (hexane/AcOEt 4:1; 180 × 30 column) furnished two fractions. After complete elution of the first fraction, the polarity of the eluent was changed to hexane/AcOEt 1:1. The first fraction contained the four components of the *Diels-Alder* adduct (339 mg, 65%) in ratio of *rac*-**24**/*rac*-**25**/(*rac*-**26** + *rac*-**27**) 41:45:14 (determined by anal. HPLC (hexane/AcOMe/CH_2Cl_2 38:12:50; *MN Nucleosil 50–10*, 254 nm). Separation by semiprep. HPLC (hexane/AcOMe/CH_2Cl 38:12:50; *MN Nucleosil 50–10*, refractom.) afforded *rac*-**24** (133.8 mg, 26%), *rac*-**25** (149.7 mg, 29%), *rac*-**26** (40.5 mg, 8%), and *rac*-**27** (5.9 mg, 1%) as colorless solids. The second fraction contained 128.6 mg (25%) of *(±)-*N*-(2-hydroxymethyl)-3-methoxy-16-(methoxycarbonyl)-13,16-seco-*D*-norestra-1,3,5(10),8-tetraene-11,13-dicarboxiamide* (*rac*-**28**). M.p. 141–144°. TLC (hexane/AcOEt 1:1): R_f 0.15. UV (MeOH + 1%CH_2Cl_2): λ_{max} 267.5 (9646); 287.0. IR (KBr): 3382*m* (br., OH); 3003*w* (arom. CH); 2950*w* (aliph. CH); 1732*s* (ester C=O); 1674*s* (imide C=O); 1607*m*, 1574*w* (C=C); 1255*s*; 1042*s*. ^{1}H-NMR: 1.46 (*s*, Me–C(13)); 1.59–1.62 (*m*, 2 H–C(7)); 1.66–1.83 (*m*, 2 H–C(15)); 2.09–2.11 (*m*, H–C(12)); 2.17–2.18 (*m*, H–C(8)); 2.45–2.51 (*m*, 2 H–C(16)); 2.77 (*m*, 2 H–C(6)); 2.79–2.80 (*m*, H–C(14)); 2.86–2.87 (*m*, H′–C(12)); 3.67 (*s*, MeO); 3.77 (*s*, MeO); 3.99–4.08 (*m*, CH_2O); 4.35–4.42 (*m*, CH_2N); 6.66 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.75 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(1),H–C(2)) = 8.6, H–C(2)); 7.61 (*d*, *J*(H–C(1),H–C(2)) = 8.6, H–C(1)). ^{13}C-NMR: 20.42 (C(18)); 21.18 (C(7)); 27.44 (C(15)); 35.42 (C(12)); 39.94 (C(8)); 35.30 (C(16)); 31.05 (C(6)); 39.52 (C(14)); 35.42 (C(12)); 51.52 (CO_2Me); 55.21 (ArO*Me*); 45.31 (CH_2O); 62.08 (CH_2N); 113.12 (C(4)); 112.71 (C(2)); 124.42 (C(1)). Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84; N 3.28; found: C 67.38, H 6.82, N 3.43.

1.5.4. *From the Complex* Diels-Alder *Adduct to* rac-**3a**. 1.5.4.1. *Cycloaddition with Acid Treatment of the* Diels-Alder *Adduct*. In a 30-ml *Schlenk* flask, Me_2AlCl (1.74 ml, 1M in hexane, 1.74 mmol, 3 equiv.) was added to a soln. of **23b** (140 mg, 0.580 mmol) in dry CH_2Cl_2 (8 ml) under Ar at –60°. After stirring for 30 h, a soln. of **6** (0.81 g, 4.35 mmol; 7.5 equiv.) in dry CH_2Cl_2 (2 ml) was added. The mixture was stored at –30° to –25° for 14 d. The red soln. was worked up in the usual way and the resulting residue subjected to FC (hexane/AcOEt 4:1; 180 × 30 mm column). Yield (215.3 mg, 87%) and ratio of product components (*rac*-**24**/*rac*-**25**/(*rac*-**26** + *rac*-**27**) 61:32:7) were determined by anal. HPLC (hexane/AcOMe/$CH_2Cl_2$2; 38:12:50, *MN Nucleosil 50–10*, 2 ml/min, 254 nm). In a 100-ml *Schlenk* flask the colorless solid was dissolved in dry CH_2Cl_2 (30 ml) and treated with CF_3COOH (2 ml). After stirring for 15 min at 0° and for 15 min at r.t., CH_2Cl_2 (20 ml) was added. After basic workup, the obtained residue was subjected to FC (hexane/AcOEt 2:1; 150 × 30 mm column) and semiprep. HPLC (hexane/AcOEt/CH_2Cl_2 49:21:30; *MN Nucleosil 50–10*, refractom.) to give *rac*-**29** (182.7 mg, 74%) and *rac*-**30** (12.2 mg, 5%).

*(±)-3-[3-Methoxy-16-(methoxycarbonyl)-13,16-seco-*D*-norestra-1,3,5(10),8-tetraene-13-carbonyl]oxazolidin-2-one* (*rac*-**29**): M.p. 106° (Et_2O/pentane). TLC (hexane/AcOEt 1:1): R_f 0.46. UV (MeOH + 1%CH_2Cl_2) λ_{max} 273.3 (15860). IR (KBr): 3030*w* (arom. CH); 2947*m* (aliph. CH); 1779*s*, 1734*s*, 1684*s* (C=O); 1607*m*, 1570*w* (arom. C=C); 1194*s*; 1040*s*. ^{1}H-NMR: 1.46 (*s*, Me–C(13)); 1.68–1.88 (*m*, 2 H–C(15), H–C(11)); 2.09–2.18 (*m*, 2 H–C(12)); 2.20–2.42 (*m*, 2 H–C(6), H′–C(11)); 2.50 (*t*, *J*(H–C(15),H–C(16)) = 8, 2 H–C(16)); 2.60–2.77 (*m*, 2 H–C(7)); 3.01 (*t*, *J*(H–C(14),H–C(15)) = 5.7, H–C(14)); 3.67 (*s*, MeO); 3.78 (*s*, MeO); 3.94–4.18 (*m*, CH_2O); 4.24–4.39 (*m*, CH_2N); 6.66 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.69 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1),H–C(2)) = 8.3, H–C(2)); 7.10 (*d*, *J*(H–C(1),H–C(2)) = 8.3, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.68–1.88/3.01; 1.68–1.88/2.20–2.42; 2.20–2.42/2.60–2.77; 2.50/1.68–1.88; 3.01/2.20–2.42; 3.94–4.18/4.24–4.39; 6.66/6.69; 7.10/6.69. ^{13}C-NMR: 20.63 (C(18)); 23.20 (C(12)); 26.76 (C(15)); 28.67 (C(11)); 29.03 (C(7)); 30.01 (C(6)); 33.67 (C(16)); 42.98 (C(14)); 48.25 (C(13)); 51.51 (CO_2Me); 55.18 (ArO*Me*); 45.28 (CH_2N); 62.31 (CH_2O); 110.84 (C(2)); 113.26 (C(4)); 123.20 (C(1)); 126.34 (C(8)); 128.67 (C(9)); 134.44 (C(10)); 137.32 (C(5)); 158.48 (C(3)); 152.82, 173.91, 177.46 (3 C=O). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.46/20.63; 2.09–2.18/23.20; 1.68–1.88/26.76; 1.68–1.88/28.67; 2.20–2.42/28.67; 2.60–2.77/29.03; 2.20–2.42/30.01; 2.50/33.67; 3.01/42.98, 4.24–4.39/48.2; 3.67/51.51; 3.78/55.18; 3.94–4.18/62.31; 6.69/110.84; 6.66/113.26; 7.10/123.20. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84, N 3.28; found: C 67.44, H. 6.70; N 3.12.

*(±)-3-[3-Methoxy-15-(methoxycarbonyl)-14,15-seco-*D*-nor-13,14-methylgona-1,3,5(10),8-tetraen-14-carbonyl]oxazolidin-2-one* (*rac*-**30**). TLC: (hexane/AcOEt 1:1): R_f 0.46. UV (MeOH + 1%CH_2Cl_2): λ_{max} 273.5 (12256). IR (KBr): 3007*w* (arom. CH); 2923*m* (aliph. CH); 1784*s*, 1734*s*, 1676*s* (C=O); 1608*m*, 1570*w* (arom. C=C); 1195*s*; 1039*s*. ^{1}H-NMR: 1.35 (*s*, Me–C(14)); 1.42–1.72 (*m*, 2 H–C(16), H–C(11)); 1.89–2.01 (*m*, 2 H–C(12), H′–C(11)); 2.31–2.40 (*m*, 2 H–C(15)); 2.40–2.49 (*m*, H–C(13)); 2.50–2.69 (*m*, 2 H–C(6), 2 H–C(7)); 3.63 (*s*, MeO); 3.77 (*s*, MeO); 4.04–4.16 (*m*, CH_2O); 4.24–4.43 (*m*, CH_2N); 6.63 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.69 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1),H–C(2)) = 8.3, H–C(2)); 7.13 (*d*, *J*(H–C(1),H–C(2)) = 8.3, H–C(1)). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.42–1.72/1.89–2.01; 1.42–1.72/2.31–2.40; 1.89–2.01/2.40–2.49; 4.04–4.16/4.24–4.43; 6.69/6.63; 6.69/7.13. ^{13}C-NMR: 19.76 (*Me*–C(14)); 23.59 (C(11)); 25.53 (C(7)); 25.70 (C(12)); 26.37 (C(16)); 29.27 (C(6)); 31.34 (C(15)); 35.42 (C(13)); 44.91 (CH_2O); 51.42 (CO_2*Me*); 54.81 (C(14)); 55.18 (ArO*Me*); 62.07 (CH_2N); 110.97 (C(2)); 113.09 (C(4)); 123.42 (C(1)); 127.25 (C(9)); 130.7 (C(5)); 137.01 (C(10)); 157.99 (C(3)); 151.64, 174.08 and 176.38 (3 C=O). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.35/19.76; 1.42–1.72/23.59; 1.89–2.01/23.59; 2.50–2.69/25.53; 1.89–2.01/25.70; 1.42–1.72/26.37; 2.50–2.69/29.27; 2.31–2.40/31.34; 2.40–2.49/35.4; 4.24–4.43/44.91; 3.6/51.42; 4.04–4.16/62.07; 6.69/110.97; 6.63/113.09; 7.13/123.42. Anal. calc. for $C_{24}H_{29}NO_6$ (427.49): C 67.43, H 6.84, N 3.28; found: C 67.23, H 6.87, N 3.31.

1.5.4.2. *Preparation of* rac-**31**. In a three-necked, 25-ml flask, Et_3SiH (2.00 ml, 12.60 mmol, 20 equiv.) and CF_3COOH (2.17 ml, 28 mmol, 45 equiv.) were added to a soln. of *rac*-**29** (269 mg, 0.629 mmol) in dry CH_2Cl_2 (8 ml) at 0°. After stirring for 20 h and the usual workup, the obtained residue was filtered through flash silica gel (hexane/AcOEt 2:1; 150 × 25 mm column) and purified by semiprep. HPLC (at first: hexane/AcOMe/CH_2Cl_2 54:16:30; *MN Nucleosil 50-10*, refractom, and then: hexane/dioxane 10:3; *MN Nucleosil 50-10*, refractom.) to give *rac*-**31** (154.3 mg, 57%) and *rac*-**32** (29.4 mg, 11%).

*(±)-3-[3-Methoxy-16-(methoxycarbonyl)-13,16-seco-*D*-norestra-1,3,5(10)-triene-13-carbonyl]oxazolidin-2-one* (*rac*-**31**): TLC (hexane/AcOEt 1:1): R_f 0.52. UV (MeOH + 1%CH_2Cl_2): λ_{max} 278.3 (2052); 287.0. IR (KBr): 3012*w* (arom. CH); 2949*m* (aliph. CH); 1764*s*, 1731*s*, 1684*s* (C=O); 1609*m*, 1576*w* (arom. C=C); 1254*s*, 1045*s*. ^{1}H-NMR: 1.32 (*s*, H–C(18)); 1.36–1.46 (*m*, H–C(8)); 1.47–1.56 (*m*, H–C(11)); 1.58–1.61 (*m*, 2 H–C(15)); 2.01–2.10 (*m*, 2 H–C(7)); 2.12–2.16 (*m*, 2 H–C(12)); 2.25–2.37 (*m*, H–C(14), H′–C(11)); 2.39–2.54 (*m*, H–C(9), 2 H–C(16)); 2.84–2.86 (*m*, 2 H–C(6)); 3.66 (*s*, MeO); 3.77 (*s*, ArOMe); 3.99–4.22 (*m*, CH_2O); 4.33–4.47 (*m*, CH_2N); 6.61 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.71 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1),H–C(2)) = 8.6, H–C(2)); 7.19 (*d*, *J*(H–C(1),H–C(2)) = 8.5, H–C(1)). The signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.36–1.46/2.01–2.10, 2.25–2.37, 2.39–2.54; 1.47–1.56/2.25–2.37, 2.12–2.16; 1.58–1.61/2.25–2.37, 2.39–2.54; 2.01–2.10/1.36–1.46, 2.84–2.86; 3.99–4.22/4.33–4.47; 6.71/7.19, 6.61. ^{13}C-NMR: 15.99 (C(18)); 26.40 (C(11)); 26.93 (C(15)); 27.02 (C(7)); 30.34 (C(6)); 32.15 (C(12)); 34.94 (C(16)); 41.79 (C(9)); 42.06 (C(8)); 43.41 (C(14)); 45.72 (CH_2N); 50.78 (C(13)); 51.41 (MeO); 55.14 (ArOMe); 62.27 (CH_2O); 111.79 (C(2)); 113.33 (C(4)); 126.73 (C(1)); 131.99 (C(10)); 137.53 ((5)); 157.45 (C(3)); 152.61, 174.16, 179.07 (3 C=O). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 15.99/1.32; 26.40/1.47–1.56, 2.25–2.37; 26.93/1.58–1.61; 27.02/2.01–2.10; 30.34/2.84–2.86; 32.15/2.12–2.16; 41.79, 34.94/2.39–2.54; 42.06/1.36–1.46; 43.41/2.25–2.37; 45.72/4.33–4.47; 51.41/3.66; 55.14/3.71; 62.27/3.99–4.22; 111.79/6.71; 113.33/6.61; 126.73/6.61. Anal. calc. for $C_{24}H_{31}NO_6$ (429.50): C 67.11, H 7.27, N 3.26; found: C 67.05, H 7.31, N 3.01.

*(±)-3-[3-Methoxy-16-(methoxycarbonyl)-13,16-seco-*D*-nor-9β-estra-1,3,5(10)-triene-13-carbonyl]oxazolidin-2-one* (*rac*-**32**): TLC (hexane/AcOEt 1:1): R_f 0.52. UV (MeOH + 1%CH_2Cl_2): λ_{max} 278.2 (2132); 287.0. IR (KBr): 3023*w* (arom. CH); 2930*m* (aliph. CH); 1778*s*, 1733*s*, 1683*s* (C=O); 1609*m*, 1578*w* (arom. C=C); 1198*w*, 1041*s*. ^{1}H-NMR: 1.39 (*s*, H–C(18)); 1.47–1.88 (*m*, 2 H–C(7), 2 H–C(12), H–C(11)); 1.93–2.08 (*m*, H–C(8), 2 H–C(15)); 2.41–2.47 (*m*, 2 H–C(16)); 2.68–2.86 (*m*, H–C(9), 2 H–C(6), H′–C(11), H–C(14)); 3.65 (*s*, MeO); 3.75 (*s*, ArOMe); 3.90–4.19 (*m*, CH_2O); 4.35–4.44 (*m*, CH_2N); 6.55 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.68 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1),H–C(2)) = 8.6, H–C(2)); 7.00 (*d*, *J*(H–C(1),H–C(2)) = 8.5, H–C(1)). Signals were assigned using a ^{1}H,^{1}H-COSY spectrum. Cross peaks between: 1.47–1.81/2.68–2.86, 1.93–2.08; 1.93–2.08/2.41–2.47, 2.68–2.86; 3.90–4.19/4.35–4.44; 6.61/6.55, 7.00. ^{13}C-NMR: 22.05 (C(18)); 24.49 (C(11)); 24.87 (C(7)); 28.79 (C(15)); 30.02 (C(6)); 33.15 (C(12)); 34.39 (C(14)); 38.06 (C(8)); 40.94 (C(9)); 45.35 (CH_2N); 45.79 (C(13)); 51.44 (MeO); 55.10 (ArO*Me*); 62.00 (CH_2O); 112.05 (C(2)); 123.23 (C(4)); 129.71 (C(1)); 133.30 (C(10)); 136.59 ((5)); 157.40 (C(3)); 152.32, 174.08, 178.30 (3 C=O). The signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 24.87/1.47–1.88; 28.79/1.93–2.08; 30.02/2.68–2.86; 33.15/1.47–1.88; 34.39/2.68–2.86; 38.06/1.93–2.08; 40.94/2.68–2.86; 45.35/4.35–4.44; 51.44/3.65; 55.10/3.75; 62.00/3.90–4.19; 112.05/6.68; 123.23/123.23; 129.71/7.00. Anal. calc. for $C_{24}H_{31}NO_6$ (429.50): C 67.11, H 7.27, N 3.26; found: C 67.03, H 7.32, N 3.08.

The relative configuration of H–C(9) was assigned by NOE measurements (irradiated signal/NOE [%]): H–C(18)/H–C(9) (0.7%), H–C(18)/H–C(8) (1.3%); H–C(8)/H–C(9) (1.6%); H–C(8)/H–C(18) (1.6%).

1.5.4.3. *Preparation of* rac-**33a**. In a three-necked, 50-ml flask, H_2O_2 (0.82 ml of a 30% aq. soln.) was added to a stirred soln. of (*rac*-**31** (286 mg, 0.660 mmol) and LiOH(H_2O) (124.4 mg, 2.96 mmol, 4.5 equiv.) in THF (stab. with 0.025% BHT (10.5 ml)/H_2O (3.33 ml) at 0°). Stirring at 0° was continued for 30 min, then the temp. was allowed to rise. After 4.5 h at r.t. (TLC control), $NaHSO_3$ (1.2 ml of a 38% aq. soln.) was added slowly at 0°. After stirring for 1 h at 0°, Et_2O (20 ml) was added and the mixture worked up in the usual way. Crystallization of the residue from AcOEt gave 194.3 mg (85%) of *(±)-3-methoxy-17,17a-seco-*D*-homoestra-1,3,5(10)-triene-17,17a-dioic acid* (= *(±)-Homomarrianolic acid methyl ether*; *rac*-**33a**): M.p. 228–229° (AcOEt) ([9]: 226–228° (AcOEt); [43]: 225–227° (Aceton)). UV (MeOH): λ_{max} 278.2 (2194); 287.0. IR (KBr): 3080*s* (br.), 2627*m* (br., COOH); 1702*s* (br., C=O): 1610*s*, 1576*w*, 1500*s* (arom. C=C); 1253*s*. ^{1}H-NMR ($CDCl_3$ + 10% (D_6)DMSO): 1.14 (*s*, H–C(18)); 1.19–1.49 (*m*, 2 H–C(7), 2 H–C(12), H–C(11)); 1.51–1.88 (*m*, H–C(8), 2 H–C(15)); 1.92–2.20 (*m*, 2 H–C(16)); 2.28–2.51 (*m*, H–C(9), 2 H–C(6), H′–C(11), H–C(14)); 3.77 (*s*, ArOMe); 6.61 (*d*, *J*(H–C(2),H–C(4)) = 2.7, H–C(4)); 6.69 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(1),H–C(2)) = 8.6, H–C(2)); 7.20 (*d*, *J*(H–C(1), H–C(2)) = 8.6, H–C(1)); 11.69 (br. *s*, CO_2H, D_2O exchange. Anal. calc. for $C_{20}H_{26}O_5$ (346.42): C 69.34, H 7.56, found: C 69.36, H 7.62.

1.5.4.4. *Preparation of* rac-**33b**. In a 50-ml flask, CH_2N_2 (soln. in Et_2O) was added dropwise to a stirred soln. of *rac*-**33a** (235 mg, 0.67 mmol) in MeOH (9 ml)/H_2O (1 ml), until a light yellow color appeared. After stirring for 1 h at r.t., a stream of N_2 was bubbled through the soln. The mixture was extracted with CH_2Cl_2, the combined org. layers were dried ($MgSO_4$) and evaporated to give 242 mg (96%) of *dimethyl (±)-3-methoxy-17,17a-seco-*D*-homoestra-1,3,5(10)-triene-17,17a-dioate* (= *(±)-O-methylhomomarrianolic acid dimethyl ester*; *rac*-**33b**): M.p. 86°. TLC: (hexane/AcOEt 1:1): R_f 0.76. UV (MeOH): λ_{max} 278.3 (2018); 287.0. IR (KBr): 3010*w* (arom. CH); 2948*m* (aliph. CH); 1732*s* (C=O); 1610*m*, 1579*w*, 1502*s* (arom. C=C); 1237*s*. ^{1}H-NMR ($CDCl_3$ + 10% (D_6)DMSO): 1.16 (*s*, H–C(18)); 1.34–1.56 (*m*, H–C(8), H–C(11), 2 H–C(15)); 1.58–1.92 (*m*, 2 H–C(7), 2 H–C(12)); 2.05–2.11 (*m*, H–C(14)); 2.28–2.41 (*m*, H′–C(11), H–C(9), 2 H–C(16)); 2.86 (*m*, 2 H–C(6)); 3.66 (*s*, MeO); 3.71 (*s*, MeO); 3.77 (*s*, ArOMe); 6.62 (*d*, *J*(H–C(2),H–C(4)) = 2.8, H–C(4)); 6.71 (*dd*, *J*(H–C(2),H–C(4)) = 2.8, *J*(H–C(1), H–C(2)) = 8.6, H–C(2)); 7.18 (*d*, *J*(H–C(1),H–C(2)) = 8.5, H–C(1)). ^{13}C-NMR: 15.08 (C(18)); 25.91 (C(11)); 26.58 (C(15)); 27.05 (C(7)); 30.25 (C(6)); 34.79 (C(12)); 37.14 (C(16)); 41.11 (C(9)); 42.97 (C(8)); 45.64 (C(14)); 47.66 (C(13)); 51.48 (MeO); 51.85 (MeO); 55.18 (ArO*Me*); 111.82 (C(2)); 113.41 (C(4)); 26.42 (C(1)); 131.90 (C(10)); 137.64 ((5)); 157.59 (C(3)); 173.82, 178.84 (2 C=O). Anal. calc. for $C_{22}H_{30}O_5$ (374.47): C 70.56, H 8.07; found: C 70.61, H 8.06.

1.5.4.5. *Preparation of* rac-**3c**. In a three-necked, 25-ml flask, equipped with a reflux condenser, a soln. of *t*-BuOK (48 mg, 0.427 mmol, 1.5 equiv.) in dry C_6H_6 (0.4 ml) was added to a stirred soln. of (*rac*-**33b** (107 mg, 0.285 mmol, 1 equiv. in dry C_6H_6 (6 ml) at r.t. The mixture was heated under reflux for 5 h, cooled to 0°, and worked up in the usual way. The residue was subjected to FC (hexane/AcOEt 2:1; 100 × 25 mm column) to give 82.7 mg (84%) *methyl (±)-3-methoxy-17-oxoestra-1,3,5(10)-triene-16-carboxylate* (*rac*-**34a**/*rac*-**34b**) as amorphous solid. TLC (hexane/AcOEt 4:1): R_f 0.23. FT-IR ($CHCl_3$): 3020*w* (arom. CH); 2933*m* (aliph. CH); 1754*s*, 1727*s* (C=O); 1609*m*, 1576*w*, 1504*m* (arom. C=C).

In a three-necked, 25-ml flask, equipped with a reflux condenser, a suspension of *rac*-**34a**/*rac*-**34b** (82.7 mg, 0.240 mol) in triethyleneglycol (4 ml) and H_2O (0.2 ml) was left in an ultrasonic bath for 15 min. Then, the heavily

stirred mixture was heated to 180° for 30 min. After cooling to r.t., the mixture was worked up in the usual way. Crystallization of the residue from MeOH afforded 63 mg (78%) of *rac*-**3c**. Anal. calc. for $C_{19}H_{24}O_2$ (284.40): C 80.324, H 8.51; found: C 80.33, H 8.44. Physical data identical with those ones under *Exper. 1.1.5.4.*

1.5.4.6. *Preparation of* rac-**3a**. In a three-necked, 25-ml flask, BBr_3 (8.85 ml, 1M soln. in CH_2Cl_2, 8.85 mmol, 18 equiv.) was added to a stirred soln. of *rac*-**3c** (140 mg, 0.49 mmol, 1 equiv.) in dry CH_2Cl_2 (1.5 ml) at −30°. The mixture was stirred for 2 h at 0°. Then, MeOH (3 ml) was added dropwise at −30°. The mixture was worked up in the usual way. The residue was dissolved in DMSO (1 ml) and subjected to chromatography (hexane/AcOEt 4:1) with flash silica gel (130 × 25 mm column). Crystallization from EtOH afforded 99 mg (75%) of *rac*-**3a**. Anal. calc. for $C_{18}H_{22}O_2$ (270.37): C 79.96, H 8.20; found: C 79.79, H 8.22. Physical data identical with those under *Exper. 1.1.5.5.*

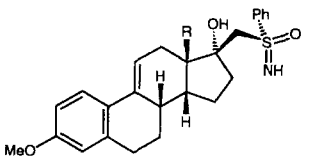
2. Preparation of Reference Compounds. – 2.1. *By Resolution.* 2.1.1. *Preparation of* **8a**. In a 250-ml, three-necked, round-bottomed flask, a 2.5M BuLi soln. in hexane (15.8 ml, 39.5 mmol, 1.80 equiv.) was added at −30° to a soln. of (*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[28]) (6.69 g, 39.5 mmol, 1.80 equiv.) in dry THF (100 ml). The mixture was stirred for 1 h at r.t. After cooling to −80°, a soln. of *rac*-**8a** (6.20 g, 39.5 mmol) in dry THF (50 ml) was added dropwise. The mixture was stirred at −80° for 1 h and warmed up to r.t. during 1 h. After usual workup, the diastereoisomers were separated by FC (2 × ; hexane/AcOEt 2:1) on silica gel (250 g) to give **37a** (4.46 g, 45%) and **38a** (4.26 g, 43%).

3-Methoxy-17β-[(S)-(phenylsulfinimidoyl)methyl]-14β-estra-1,3,5(10),9(11)-tetraen-17α-ol (**37a**). TLC (hexane/AcOEt 2:1): R_f 0.6. $[\alpha]_{589}^{20} = +72.1$ ($c = 1.117$, $CHCl_3$); $[\alpha]_{578}^{20} = +75.8$; $[\alpha]_{546}^{20} = +86.7$; $[\alpha]_{436}^{20} = +152.9$; $[\alpha]_{365}^{20} = +245.4$. UV (MeOH): λ_{max} 264 (20870); 271.5 (17665); 299 (3260); 310 (2460). IR (KBr): 3255*m* (br., OH); 3059*w* (=C–H); 1644*w* (C=C, olef.); 1607*m*, 1569*w*, 1497*s* (C=C, arom.); 1236*s*, 1152*s* (O=S=N). ^{1}H-NMR: 0.83 (*s*, Me); 1.49–2.11 (*m*, 7 cycloaliph. H); 2.32–2.37 (*m*, 1 cycloaliph. H); 2.50–3.02 (*m*, 4 cycloaliph. H); 2.62 (*s*, MeN); 3.07 (*d*, J(H–C(1'),H'–C(1')) = 13.5, H–C(1')); 3.37 (*dd*, J(H'–C(1'),H–C(1')) = 13.5, $J \approx 1.0$, H'–C(1')); 3.77 (*s*, MeO); 6.16–6.20 (*m*, H–C(11)); 6.58 (*d*, J(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.71 (*dd*, J(H–C(2),H–C(4)) = 2.8, J(H–C(2),H–C(1)) = 8.8, H–C(2)); 7.11 (br. *s*, OH, D_2O exchange); 7.56–7.68 (*m*, 4 arom. H); 7.88–7.93 (*m*, 2 arom. H). ^{13}C-NMR: 19.1 (C(18)); 22.7, 27.3, 30.2, 30.7, 33.1 (C(6), C(7), C(12), C(15), C(16)); 28.9 (MeN); 34.7 (C(14)); 46.1 (C(8)); 46.2 (C(13)); 55.2 (MeO); 62.7 (C(1')); 83.0 (C(17)); 112.6, 113.283, 116.0 (C(2), C(4), C(11)); 124.4 (C(1)); 129.0, 129.7 (C(2) (Ph), C(3) (Ph), C(5) (Ph), C(6) (Ph)); 127.3, 130.6, 137.7, 139.3 (C(5), C(9), C(10), C(1) (Ph)); 133.1 (C(4), (Ph)); 158.2 (C(3)). The relative configuration at C(17) and C(13) was determined by NOE (irradiated signal/NOE [%]): Me/CH_2S (0.8%); Me/CH_2S (2.1%); CH_2S/Me (1.3%); CH_2S/Me (3.7%). Anal. calc. for $C_{27}H_{33}SO_3N$ (451.63): C 71.81, H 7.37, N 3.10, S 7.10; found: C 71.93, H 7.41, N 3.04, S 7.21.

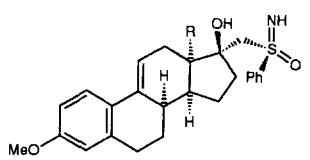
In a 250-ml, round-bottomed flask equipped with a condenser, a soln. of **37** (4.36 g, 9.65 mmol) in i-BuOH (150 ml) was heated under reflux for 5 h. After basic workup and FC (hexane/AcOEt 4:1) on silica gel (150 g), the crude product was crystallized from Et_2O/hexane to give 1.91 g (70%) of **8a**. M.p. 144–145° (Et_2O/hexane) ([68]: 143–144° (EtOH)). UV (MeOH): λ_{max} 263.5 (19621), 297 (sh, 3708), 308 (sh, 1850). $[\alpha]_{589}^{20} = +265.2$ ($c = 1.096$, $CHCl_3$); $[\alpha]_{578}^{20} = +278.9$; $[\alpha]_{546}^{20} = +325.5$; $[\alpha]_{436}^{20} = +662.1$; $[\alpha]_{365}^{20} = +1451.0$. CD ($c = 0.01297$, MeOH): +30689 (285); −23506 (263). IR, ^{1}H- and ^{13}C-NMR data are identical with data of *rac*-**8a** (*Exper. 1.1.1*). Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.90, H 7.75.

The e.e. of **8a** was determined to be > 98% (^{1}H-NMR analysis with (+)-[Pr(hfc)$_3$] as a chiral, non-racemic shift reagent).

3-Methoxy-17α[(S)-(phenylsulfinimidoyl)methyl]-8α,13α-estra-1,3,5(10),9(11)-tetraen-17β-ol (**38a**). M.p. 155–156°. TLC (hexane/AcOEt 2:1): R_f 0.4. UV (MeOH): λ_{max} 264 (21950); 271.2 (18620); 298.5 (3330); 308.5 (2605). $[\alpha]_{589}^{20} = -57.9$ ($c = 1.093$, $CHCl_3$); $[\alpha]_{578}^{20} = -60.8$; $[\alpha]_{446}^{20} = -70.2$; $[\alpha]_{436}^{20} = -134.2$; $[\alpha]_{365}^{20} = -255.7$. IR



37a R = Me
37b R = Et



38a R = Me
38b R = Et

[28]) Prepared according to [69].

(KBr): 3463*m* (br. OH); 3053*w* (=C–H); 1642*w* (C=C, olef.); 1606*m*, 1576*w*, 1498*s* (C=C, arom.); 1237*s*, 1150*s* (O=S=N). ^{1}H-NMR: 0.93 (*s*, Me); 1.37–1.56 (*m*, 3 cycloaliph. H); 1.65–1.89 (*m*, 4 cycloaliph. H); 2.02–2.14 (*m*, 1 cycloaliph. H); 2.33–2.54 (*m*, 2 cycloaliph. H); 2.72 (*s*, MeN); 2.75–2.84 (*m*, 2 cycloaliph. H); 3.35 (*d*, J(H–C(1′), H′–C(1′)) = 14.1, H–C(1′)); 3.48 (*d*, J(H′–C(1′),H–C(1′)) = 13.6, H′–C(1′)); 3.77 (*s*, MeO); 6.03 (br. *s*, OH, D_2O exchange); 6.15–6.19 (*m*, H–C(11)); 6.57 (*d*, J(H–C(4),H–C(2)) = 2.8, H–C(4)); 6.71 (*dd*, J(H–C(2),H–C(4)) = 2.8, J(H–C(2),H–C(1)) = 8.8, H–C(2)); 7.55–7.67 (*m*, 4 arom. H); 7.87–7.92 (*m*, 2 arom. H). ^{13}C-NMR: 19.9 (C(18)); 22.7, 27.1, 30.6, 30.7, 34.7 (C(6), C(7), C(12), C(15), C(16)); 29.4 (MeN); 34.7 (C(14)); 46.5 (C(13)); 46.6 (C(8)); 55.2 (MeO); 63.8 (C(1′)); 81.9 (C(17)); 112.6, 113.3, 116.2 (C(2), C(4), C(11)); 124.4 (C(1)); 129.2, 129.2 (C(2) (Ph), C(3) (Ph), C(5) (Ph), C(6) (ph)); 127.3, 130.6, 137.7, 139.8 (C(5), C(9), C(10), C(1) (Ph)); 133.1 (C(4) (Ph)); 158.2 (C(3)). The relative configuration at C(17) and C(13) was determined by NOE (irradiated signal/NOE [%]): Me/CH_2S (0.7%); Me/CH_2S (1.7%); CH_2S/Me (1.8%); CH_2S/Me (6.5).

2.1.2. *Preparation of* **10b**. Similar to *Exper. 2.1.1*, a resolution was executed. On reaction of (*S*)-*N*,*S*-dimethyl-*S*-phenylsulfoximine[28]) (2.018 g, 11.92 mmol), BuLi (4.17 ml of a 2.5M hexane soln.; 10.43 mmol), and *rac*-**10b**, a product was obtained, which, after chromatography, gave **10b**/*ent*-**10b** ≠ 1 (835 mg; 38%), **37b** (1.371 g; 40%), and **38b** (566 mg; 16%).

13-Ethyl-3-methoxy-17-[(S)-(phenylsulfinimidoyl)methyl]-14β-gona-1,3,5(10),8-tetraen-17-ol (**37b**): TLC (hexane/AcOEt): R_f 0.28. $[\alpha]_{589}$ = +46.5 (c = 1.05, $CHCl_3$); $[\alpha]_{578}$ = +49.0; $[\alpha]_{546}$ = +56.9; $[\alpha]_{436}$ = +110.2. IR (KBr): 3265 (br., OH); 3060*w* (=C–H); 2962*s*, 2933*s*, 2875*s*, 2833*s* (C–H); 1607*s*, 1572*m*, 1499*s* (C=C, arom.). ^{1}H-NMR: 0.84–1.00 (*m*, *Me*CH_2, 1 cycloaliph. H); 1.41–1.71 (*m*, 3 cycloaliph. H); 1.83 (*ψt*, 1 cycloaliph. H); 1.96–2.43 (*m*, 7 cycloaliph. H); 2.62 (*s*, MeN); 2.64–2.75 (*m*, 2 H–C(6)); 2.94–3.05 (*m*, H–C(14)); 3.12 (*d*, J(SCH_2,SCH_2) = 13.6, SCH_2); 3.46 (*dd*, J(SCH_2,SCH_2) = 13.9, J' = 2.2, CH_2S); 3.78 (*s*, MeO); 6.66 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.71 (*dd*, J(H–C(2),H–C(1)) = 8.4, J(H–C(2),H–C(4)) = 2.7, H–C(2)); 6.83 (*s*, exchangeable by D_2O, OH); 7.12 (*d*, J(H–C(1),H–C(2)) = 8.4, H–C(1)); 7.57–7.68 (*m*, 3 arom. H); 7.89–7.94 (*m*, 2 arom. H). Anal. calc. for $C_{28}H_{35}NO_3S$ (465.66): C 72.22, H 7.58, N 3.01; found: C 72.10, H 7.85, N 2.98.

Sulfoximine **37b** (1.331 g, 2.86 mmol) was cleaved by refluxing for 3 h in i-BuOH (40 ml). The product (805 mg; 95%) obtained was crystallized (MeOH) and gave 758 mg (89%) of **10b**: M.p. 102–103°. UV (MeOH): λ_{max} 273 (16960). $[\alpha]_{589}$ = +178.6 (c = 0.90, $CHCl_3$); $[\alpha]_{578}$ = +187.2; $[\alpha]_{546}$ = +217.3; $[\alpha]_{436}$ = +415.2; $[\alpha]_{365}$ = +767.7. CD (MeOH; c = 0.018): +39615 (273). IR (KBr): 3019*w* (=C–H); 2966*m*, 2930*m*, 2884*m*, 2856*m*, 2829*m* (C–H); 1736*s* (C=O); 1646*w* (C=C, olef.); 1609*m*, 1573*m*, 1498*s* (C=C, arom.). ^{1}H-NMR: 0.86 (*t*, J(CH_2Me,CH_2Me) = 7.5, MeCH_2); 1.47–1.65 (*m*, *Me*CH_2, H–C(12)); 1.70–1.87 (*m*, H′–C(12), H–C(15)); 2.11–2.40 (*m*, 2 H–C(7), 2 H–C(11), H′–C(15), 2 H–C(16)); 2.61–2.66 (*m*, H–C(14)); 2.72–2.79 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 6.69–6.74 (*m*, H–C(2), H–C(4)); 7.09 (m_c, H–C(1)). ^{13}C-NMR: 8.5 (C(19)); 22.1, 27.5 (C(7), C(11)); 25.4 (C(15)); 25.8 (C(12)); 26.3 (C(18)); 28.8 (C(6)); 37.8 (C(16)); 44.9 (C(14)); 51.0 (C(3)); 55.2 (MeO); 110.9, 113.4 (C(2), C(4)); 123.0 (C(1)); 126.6, 129.1, 131.9, 137.0 (C(5), C(8), C(9), C(10)); 158.1 (C(3)); 222.9 (C(17)). Anal. calc. for $C_{20}H_{24}O_2$ (296.41): C 81.05, H 8.16; found: C 81.12, H 8.20.

By HPLC (*Daicel Chiralcel*; hexane/i-PrOH 5:2; 0.7 ml/min; 254 nm) the e.e. was shown to be > 99.8%.

13a-Ethyl-3-methoxy-17-[(S)-(phenylsulfinimidoyl)methyl]gona-1,3,5(10),8-tetraen-17-ol (**38b**): TLC (hexane/AcOEt 4:1): R_f 0.15. $[\alpha]_{589}$ = +13.4 (c = 1.18, $CHCl_3$); $[\alpha]_{578}$ = +13.9; $[\alpha]_{546}$ = +15.6; $[\alpha]_{436}$ = +17.9. IR (KBr): 3488*m*, 3253*m* (br., OH); 3060*w* (=C–H); 2960*s*, 2932*s*, 2875*s*, 2834*s* (C–H); 1647*w* (C=C, olef.); 1607*s*, 1572*m*, 1499*s* (C=C, arom.). ^{1}H-NMR: 0.48–1.11 (*m*, 4 aliph. H; underneath: 0.94 (*t*, J(CH_2Me,CH_2Me) = 7.3, *Me*CH_2); 1.43–2.35 (*m*, 12 cycloaliph. H); 2.65–2.71 (*m*, 2 H–C(6)); 2.76 (*s*, MeN); 3.42 (*d*, J(SCH_2,SCH_2) = 14.2, CH_2S); 3.55 (*dd*, J(SCH_2,SCH_2) = 14.2, J' = 1.6, CH_2S); 3.78 (*s*, MeO); 5.63 (*s*, exchangeable by D_2O, OH); 6.65 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.70 (*dd*, J(H–C(2),H–C(1)) = 8.4, J(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.11 (*d*, J(H–C(1),H–C(2)) = 8.4, H–C(1)); 7.55–7.67 (*m*, 3 arom. H); 7.88–7.92 (*m*, 2 arom. H). Anal. calc. for $C_{28}H_{35}NO_3S$ (465.66): C 72.22, H 7.58, N 3.01; found: C 72.24, H 7.84, N 2.99.

Sulfoximine **38b** (534 mg, 1.15 mmol) was cleaved by refluxing for 3 h in i-BuOH (15 ml). The product (317 mg; 93%) was crystallized (MeOH) and gave 307 mg (90%) of *ent*-**10b**: M.p. 102–103°. TLC (hexane/AcOEt 4:1): R_f 0.40. UV (MeOH): λ_{max} 274 (17075). IR (KBr): 3019*w* (=C–H); 2966*m*, 2930*m*, 2884*m*, 2856*m*, 2829*m* (C–H); 1736*s* (C=O); 1646*w* (C=C, olef.); 1609*m*, 1573*m*, 1498*s* (C=C, arom.). ^{1}H-NMR: 0.86 (*t*, J(CH_2Me,CH_2Me) = 7.5, Me_2CH); 1.47–1.65 (*m*, MeCH_2, H–C(12)); 1.70–1.87 (*m*, H′–C(12), H–C(15)); 2.11–2.40 (*m*, 2 H–C(7), 2 H–C(11), H′–C(15), 2 H–C(16)); 2.61–2.66 (*m*, H–C(14)); 2.72–2.79 (*m*, H–C(6)); 3.79 (*s*, MeO); 6.69–6.74 (*m*, H–C(2), H–C(4)); 7.09 (m_c, H–C(1)). ^{13}C-NMR: 8.5 (C(19)); 22.1, 27.5 (C(7), C(11)); 25.4 (C(15)); 25.8 (C(12)); 26.3 (C(18)); 28.8 (C(6)); 37.8 (C(16)); 44.9 (C(14)); 51.0 (C(13)); 55.2 MeO); 110.9, 113.4 (C(2), C(4)); 123.0 (C(1)); 126.6, 129.1, 131.9, 137.0 (C(5), C(8), C(9), C(10)); 158.1 (C(3)); 222.9 (C(17)). Anal. calc. for $C_{20}H_{24}O_2$ (296.41): C 81.05, H 8.16; found: C 80.83, H 7.99.

2.2. By Acid-Mediated Isomerization. 2.2.1. *Preparation of* **10a**. In a 250-ml, round-bottomed flask, aq. conc. HCl (4 ml) was added to a soln. of **8a** (1.78 g, 6.30 mmol) in CH_2Cl_2 (15 ml) and MeOH (125 ml). After stirring for 2 h at r.t., basic workup, FC (hexane/AcOEt 4:1) on silica gel (50 g), and crystallization from Et_2O/hexane 1.64 g (92%) of **10a** were obtained. M.p. 126–127° (Et_2O) ([62] [70]: 121–122° (MeOH); [45]: 107–109° (MeOH)). UV (MeOH): λ_{max} 272 (16984). $[\alpha]_{589}^{20}$ = +216.0 (*c* = 1.104, $CHCl_3$); $[\alpha]_{578}^{20}$ = +226.9; $[\alpha]_{546}^{20}$ = +262.8; $[\alpha]_{436}^{20}$ = +502.6; $[\alpha]_{365}^{20}$ = +933.3. CD (*c* = 0.01313, MeOH); −5915 (224); +47637 (273); −8603 (300). IR, ^{1}H-NMR and ^{13}C-NMR data are identical with those of *rac*-**10a** (*Exper. 1.1.4*). Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.82, H 7.68.

2.2.2. Preparation of rac-**11a**. Similar to *Exper. 2.2*, *rac*-**9a** (113 mg, 0.40 mmol) was transformed to (*rac*-**11a** (82 mg, 73%) with aq. conc. HCl (0.3 ml) in MeOH (7.5 ml).

(±)-3-Methoxy-14β-methylgona-1,3,5(10),8-tetraen-15-one (*rac*-**11a**). M.p. 69° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.64. UV (MeOH): λ_{max} 280 (14170). IR (KBr): 2924*s*, 2834*m* (C–H); 1732*s* (C=O); 1606*s*, 1560*w*, 1500*s* (C=C). ^{1}H-NMR: 1.24 (*s*, Me); 1.78–2.04, 2.11–2.50 (2*m*, 2 H–C(7), 2 H–C(11), 2 H–C(12), H–C(13), 2 H–C(16), 2 H–C(17)); 2.61–2.67 (*m*, 2 H–C(6)); 3.79 (*s*, MeO); 6.68 (*d*, *J*(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.72 (*dd*, *J*(H–C(2),H–C(4)) = 2.7, *J*(H–C(2),H–C(1)) = 8.5, H–C(2)); 7.17 (*d*, *J*(H–C(1),H–C(2)) = 8.4, H–C(1)). ^{13}C-NMR: 21.7, 21.9, 23.3, 35.8 (C(7), C(11), C(16), C(17)); 22.0 (Me); 29.0 (C(6)); 42.6 (C(13)); 52.7 (C(14)); 55.3 (MeO); 111.1 (C(2)); 113.1 (C(4)); 123.3 (C(1)); 128.6, 129.2, 129.7, 137.8, 158.3 (C(3), C(5), C(8), C(9), C(10)); 220.2 (C(15)). Signals were assigned using a ^{1}H,^{13}C-COSY spectrum. Cross peaks between: 1.78–2.04/21.69, 1.78–2.04/21.92, 1.24/22.01, 2.11–2.50/23.27, 2.61–2.67/29.04, 2.11–2.50/35.81, 2.11–2.50/42.64, 3.79/55.25, 6.72/111.05, 6.68/113.07, 7.17/123.32. Anal. calc. for $C_{19}H_{22}O_2$ (282.38): C 80.82, H 7.85; found: C 80.89, H 7.89.

2.2.3. Preparation of rac-**29**. In a three-necked, 50-ml flask, *rac*-**24** (110 mg, 0.257 mmol) was dissolved in dry CH_2Cl_2 (20 ml). CF_3COOH (2 ml) was added at 0°. The mixture was stirred for 15 min at 0°, then for 15 min at r.t. CH_2Cl_2 (20 ml) was added to the mixture, and the org. layer was washed with sat. aq. $NaHCO_3$ (3×). The combined aq. layers were extracted with CH_2Cl_2. The combined org. layers were dried ($MgSO_4$) and evaporated *in vacuo*. Chromatography of the residue (hexane/AcOEt 2:1) with flash silica gel (120 × 30 mm column) afforded *rac*-**29** (98.6 mg, 90%) as colorless solid. Anal. data of *rac*-**29**, see *Exper. 1.5.4*.

2.3. By Dehydrogenation. 2.3.1. *Preparation of* **13a**. In a 100-ml, three-necked, round-bottomed flask, a 1.6M soln. of BuLi in hexane (4.21 ml, 6.74 mmol, 1.2 equiv.) was added to a stirred soln. of $(i\text{-Pr})_2NH$ (1.11 ml, 7.83 mmol, 1.4 equiv.) in dry THF (40 ml) at −20. The soln. was stirred for 45 min at −5° to 0°, cooled to −80°, and treated with a soln. of **10a** (1.586 g, 5.62 mmol) in dry THF (6 ml). After stirring for 1 h at −80°, Me_3SiCl (1.45 ml, 11.44 mmol, 2.0 equiv.) was added. The mixture was warmed up to r.t. and stirred for 1 h. The soln. was transferred to a 100-ml, round-bottomed flask with Et_2O and evaporated. The resulting suspension was filtered through 50 g alumina B (act. III; hexane/AcOEt 4:1). The crude product obtained after evaporation was dissolved in dry MeCN (30 ml). $Pd(OAc)_2$ (1.26 g, 5.62 mmol, 1.0 equiv.) was added, and the mixture was stirred under Ar for 5 h at r.t. Filtration through *Celite* and evaporation of the solvent gave a residue, which was purified by (hexane/AcOEt 10:1) on silica gel (200 g) and crystallization from MeOH: 1.327 g (84%) of **13a**. M.p. 133–135° (MeOH). TLC (hexane/AcOEt 4:1): R_f 0.35. $[\alpha]_{589}^{20}$ = +668.7 (*c* = 1.005, $CHCl_3$); $[\alpha]_{578}^{20}$ = +704.2; $[\alpha]_{546}^{20}$ = +824.7; $[\alpha]_{436}^{20}$ = +1700.7; $[\alpha]_{365}^{20}$ = imperm. CD (*c* = 0.1558, MeOH): +63401 (223); +47498 (269). IR and ^{1}H-NMR data are identical with those of (*rac*-**13a** (*Exper. 1.1.5.1*). Anal. calc. for $C_{19}H_{20}O_2$ (280.37): C 81.40, H 7.19; found: C 81.31, H 7.23.

2.3.2. Preparation of **13b**. Following essentially the procedure of *Exper. 2.3.1*, a 2.5M soln. of BuLi in hexane (475 µl; 1.18 mmol) was added to a soln. of $(i\text{-Pr})_2NH$ (180 µl, 1.27 mmol) in dry THF (10 ml). A soln. of **10b** (250 mg, 0.84 mmol) in THF (10 ml), and later on a soln. of Me_3SiCl (215 ml) were added. The residue (310 mg) obtained after evaporation and filtration (hexane/AcOEt 4:1) on alumina (30 g; basic, act. III) was dissolved in dry MeCN (5 ml) and dropwise to a suspension of $Pd(OAc)_2$ (191 mg, 0.84 mmol) in MeCN (5 ml). After stirring for 15 h at r.t. and workup as described before, **13b** was obtained: M.p. 88–89° (MeOH). UV (MeOH): λ_{max} 270 (15375). IR: 3064*w* (=C–H); 2956*m*, 2936*m*, 2914*m*, 2874*m* (C–H); 1701*s* (C=O); 1640*w* (C=C, olef.); 1602*m*, 1570*m*, 1500*m* (C=C, arom.). $[\alpha]_{589}$ = +695.7 (*c* = 0.96; $CHCl_3$); $[\alpha]_{578}$ = +732.4; $[\alpha]_{546}$ = +857.6; $[\alpha]_{436}$ = +1772.2. ^{1}H-NMR: 0.83 (*t*, $J(CH_2Me,CH_2Me)$ = 7.4, $MeCH_2$); 1.51–1.77 (*m*, $MeCH_2$, H–C(12)); 1.98–2.08 (*m*, H–C(11), H′–C(12)); 2.20–2.52 (*m*, 2 H–C(7), H′–C(11)); 2.69–2.92 (*m*, 2 H–C(6)); 3.27 (*ψs*, H–C(14); 3.79 (*s*, MeO); 6.12 (*dd*, *J*(H–C(16),H–C(15)) = 5.8, *J*(H–C(16),H–C(14)) = 2.1, H–C(16)); 6.69–6.73 (*m*, H–C(2), H–C(4)); 7.04–7.08 (*m*, H–C(1)); 7.63 (*dd*, *J*(H–C(15),H–C(16)) = 5.8, *J*(H–C(15),H–C(14)) = 2.7, H–C(15)). ^{13}C-NMR: 8.8 (C(19)); 22.3, 27.8, 28.7, 29.6, 31.2 (C(6), C(7), C(8), C(11), C(12)); 51.1 (C(13)); 52.7 (C(14)); 55.3 (MeO); 111.0, 113.6, 123.4, 131.8 (C(1), C(2), C(4), C(16)); 128.4, 128.7, 130.1, 136.7 (C(5), C(8), C(9), C(10)); 158.3 (C(3)); 163.4 (C(15)); 214.6 (C(17)). Anal. calc. for $C_{20}H_{22}O_2$ (294.39): C 81.60, H 7.53; found: C 81.60, H 7.65.

By HPLC (*Daicel Chiralcel OJ*; (hexane/PrOH 5:1; 1 ml/min; 254 nm), e.e. was found > 99.8%.

2.4. *By Hydrogenatioan.* 2.4.1. *Preparation of* **15a**. In a 25-ml, three-necked, rond-bottomed flask, **14a** (215 mg, 0.767 mmol) and 5% Pd/$CaCO_3$ (50 mg) were stirred under H_2 in C_6H_6 (15 ml) for 15 h at r.t. After workup according to *Exper. 1.1.5.3*, the residue was purified by semi-prep. HPLC (hexane/dioxane 10:0.7; *MN Nucleosil 50–10*, refractom.) and crystallization (MeOH) to give 145 mg (67%) of *3-methoxy-8α-estra-1,3,5(10)-trien-17-one* (**15a**). M.p. 95° (MeOH) [72]: 93–94° (MeOH); [59]: 96° (i-Pr_2O)). $[\alpha]_{589}^{20} = 98.2$ ($c = 0.549$, $CHCl_3$); $[\alpha]_{578}^{20} = +102.8$; $[\alpha]_{546}^{20} = +120.5$; $[\alpha]_{436}^{20} = +251.1$; $[\alpha]_{365}^{20} = +587.3$; [72]: $[\alpha]_{589}^{20} = +100$ ($c = 1$, $CHCl_3$) ([59]: $[\alpha]_{589}^{20} = +104$ ($c = 0.6$, MeOH)). UV (MeOH): λ_{max} 278 (2053), 286.5 (1997). IR, ^{1}H-NMR, and ^{13}C-NMR data identical with those of *rac*-**15a** in *Exper. 1.1.5.3*. Anal. calc. for $C_{19}H_{24}O_2$ (284.40): C 80.24, H 8.51; found: C 80.20, H 8.61.

2.4.2. *Preparation of* rac-**15a**. Similar to *Exper. 2.4.1*, *rac*-**14a** (300 mg, 1.07 mmol) was transformed to *rac*-**15a** (194 mg, 64%) with 5% Pd on $CaCO_3$ (150 mg) and H_2.

Data of rac-**15a**: M.p. 154–155° (MeOH) ([48]: 151–153° (EtOH); [19] [49]: 151–152° (MeOH); [73]: 152.5–154.5°). TLC (hexane/AcOEt 1:1): R_f 0.58. UV (MeOH): λ_{max} 277 (2085), 285.5 (2010). IR (KBr): 1731*s* (C=O); 1607*m*, 1584*m*, 1500*m* (C=C). ^{1}H-NMR: 1.00 (*s*, Me–C(13)); 1.38–2.24 (*m*, 2 H–C(7), H–C(8), H–C(9), H–C(11), 2 H–C(12), H–C(14), 2 H–C(15)); 2.43–2.87 (*m*, 2 H–C(6)); 3.77 (*s*, MeO); 6.62 (*d*, J(H–C(4),H–C(2)) = 2.6, H–C(4)); 6.72 (*dd*, J(H–C(2),H–C(1)) = 8.4, J(H–C(2),H–C(4)) = 2.6, H–C(2)); 7.06 (*d*, J(H–C(1),H–C(2)) = 8.5, H–C(1)). ^{13}C-NMR: 16.21 (*q*, C(18)); 21.42, 21.61, 28.51, 31.36, 32.29, 35.72 (6*t*, C(6), C(7), C(11), C(12), C(15), C(16)); 38.71, 41.15, 18.73 (3*d*, C(8), C(9), C(14)); 47.10 (*s*, C(13)); 112.16, 113.32, 130.21 (3*d*, C(1), C(2), C(4)); 133.27, 137.52 (2*s*, C(5), C(10)); 157.47 (*s*, C(3)); 220.60 (*s*, C(17)). Anal. calc. for $C_{19}H_{24}O_2$ (284.40): C 80.24, H 8.51; found: C 80.10, H 8.50.

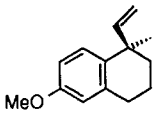
2.5. *By Oxidation.* 2.5.1. *Preparation of* **21b**. In a dry, three-necked, round-bottomed flask, equipped with a condenser, K (1.1 g, 28 mmol, 11 equiv.) was dissolved in dry *t*-BuOH (60 ml). Ketone **10a** (0.70 g, 2.48 mmol; see *Exper. 2.2.1*) was added, while the soln. was warmed to 45°. The mixture was stirred at r.t. for 2.5 h and 3-methylbutyl nitrite (0.81 ml, 6.1 mmol, 2.5 equiv.) was added. After stirring for 2 h at r.t., for 3 h at 50°, and for 15 h at r.t., usual workup gave a residue which was filtered (hexane/AcOEt 4:1) over silica gel (20 g). The crude product obtained after evaporation was dissolved in CH_2Cl_2 (70 ml) and stirred vigorously with aq. 37% HCHO soln. (40 ml) and aq. conc. HCl (14 ml) for 1.5 d at r.t. After basic workup and FC (hexane/AcOEt 4:1) on silica gel (80 g), the resulting brown oil (0.78 g) was dissolved in DMF (10 ml) and silylated according to *Exper. 1.3.1.2* with (*t*-Bu)Ph_2SiCl (0.87 ml, 3.39 mmol, 1.3 equiv.) and imidazole (0.44 g, 0.65 mmol, 2.5 equiv.) to give a product (472 mg), which, after filtration (hexane/AcOEt 10:1) over silica gel (25 g), FC (hexane/Et_2O/CH_2Cl_2 20:1:2) on silica gel (85 g), and crystallization from Et_2O/pentane, afforded 380 mg (29%) of **21b**. M.p. 65–66° (Et_2O/pentane). TLC (hexane/AcOEt 4:1): R_f 0.49. $[\alpha]_{589}^{20} = +201.5$ ($c = 1.060$, $CHCl_2$); $[\alpha]_{578}^{20} = +213.0$; $[\alpha]_{546}^{20} = +252.3$; $[\alpha]_{436}^{20} = +561.8$; $[\alpha]_{365}^{20}$ = imperm. UV (MeOH + 1% CH_2Cl_2): λ_{max} 270 (16840). CD ($c = 0.0029$, MeOH): +91950 (271); −32900 (246). IR, ^{1}H-NMR, and ^{13}C-NMR data are identical with those of *rac*-**21b** (*Exper. 1.3.3*). Anal. calc. for $C_{35}H_{38}O_3Si$ (534.77): C 78.61, H 7.16, Si 5.25; found: C 78.52, H 7.10, Si 5.07.

The e.e. of **21b** was determined to be > 97.6% by ^{1}H-NMR using (+)-[Eu(hfc)$_3$] as chiral, non-racemic shift reagent.

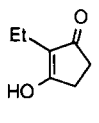
2.5.2. *Preparation of* **21d**. Compound **10b** (702 mg, 2.37 mmol; see *Exper. 2.1.2*) was added to a soln. of K (1.40 g, 35.8 mmol) in *t*-BuOH (40 ml). Then, isopentyl nitrite (800 ml, 5.92 mmol) was introduced. Usual workup furnished a residue which was chromatographed (hexane/AcOEt) on silica gel (60 g). The residue obtained was dissolved in CH_2Cl_2 (50 ml) and treated with conc. aq. HCl (14 ml) and aq. soln. of HCOH (37%). To a soln. of the isolated product (656 mg) in dry DMF (6 ml), imidazole (350 mg, 5.15 mmol) and (*t*-Bu)Ph_2SiCl (655 ml, 2.57 mmol) were added. Final workup afforded 393 mg (30%) of *16-{[(*tert*-butyl)diphenylsilyl]oxy}-13-ethyl-3-methoxy-14β-gona-1,3,5(10),8,15-pentaen-17-one* (**21d**): M.p. 102–103° (Et_2O). UV: λ_{max} 271 (17155). $[\alpha]_{589} = +222.4$ ($c = 1.12$, $CHCl_3$); $[\alpha]_{578} = +235.1$; $[\alpha]_{546} = +278.4$; $[\alpha]_{436} = +620.2$. CD (MeOH; $c = 0.039$): +95856 (271). IR: 3072*w*, 3054*w*, 3031*w* (=C–H); 2931*m*, 2903*m*, 2857*m*, 2827*m* (C–H); 1716*s* (C=O); 1646*s* (C=C, olef.); 1610*s*, 1572*m*, 1498*m* (C=C, arom.). ^{1}H-NMR: 0.74 (*t*, J(CH_2Me,CH_2Me) = 7.5, *Me*CH_2); 1.08 (*s*, *t*-Bu); 1.41–1.65 (*m*, MeCH_2, H–C(12)); 1.81–2.02 (*m*, 2 H–C(7), H–C(11), H′–C(12)); 2.25–2.31 (ψ*dt*, H′–C(11)); 2.44–2.70 (m_c, 2 H–C(6)); 2.84 (*d*, J(H–C(14),H–C(15)) = 3.1, H–C(14)); 3.80 (*s*, MeO); 6.17 (*d*, J(H–C(15),H–C(14)) = 3.2, H–C(15)); 6.64 (*d*, J(H–C(4),H–C(2)) = 2.7, H–C(4)); 6.71 (*dd*, J(H–C(2),H–C(1)) = 8.1, J(H–C(2),H–C(4)) = 2.7, H–C(2)); 7.01 (*d*, J(H–C(1),H–C(2)) = 8.4, H–C(1)). ^{13}C-NMR: 8.6 (C(19)); 19.4; 22.2; 26.5; 27.5; 28.6; 30.7; 46.4; 49.5; 55.3; 110.7; 113.4; 123.3; 127.6; 127.7; 128.6; 129.0; 130.0; 131.9; 132.3; 135.4; 136.7; 137.8; 151.6; 158.1; 208.0. Anal. calc. for $C_{36}H_{40}O_3Si$ (548.80): C 78.79, H 7.35, Si 5.12; found: C 78.62, H 7.29, Si 4.94.

The e.e. was determined by NMR spectroscopically (> 97.2%) using [Eu(hfc)$_3$] as chiral-nonracemic shift reagent and using the two *s* of the Me_3C signal as a molecular informant.

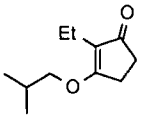
3. Preparation of Educt Components. – 3.1. *Preparation of Diene* **6**. 3.1.1. *Preparation of* rac-**39** (using the route by *Nazarov*, following a procedure described by *Robins* and *Walker* [74]). A soln. of vinyl bromide (20 ml, 278 mmol, 4.2 equiv.) in dry THF (50 ml) was added dropwise to a suspension of Mg (6 g, 247 mmol, 3.6 equiv.) in dry THF (50 ml) at max. 50°. The mixture was stirred for 1 h at r.t., and a soln of 6-methoxytetralone (12 g, 68 mmol) in dry THF (70 ml) was added at max. 35°. After stirring overnight at r.t., the mixture was refluxed for 30 min. and cooled to r.t. After usual workup, the residue was subjected to FC (hexane/AcOEt 8:1) on 200 g silica gel. *(1RS)-1-Hydroxy-6-methoxy-1-vinyl-1,2,3,4-tetrahydronaphthalene* (*rac-***39**; 12 g, 86%) was obtained as a yellow oil. TLC (hexane/AcOEt 4:1): R_f 0.30. IR (film): 3448*s* (br., OH); 3058*m*, 3000*m* (=C–H); 1640*w* (C=C, olef.); 1607*m*, 1574*m*, 1498*m* (C=C, arom.). ^{1}H-NMR: 1.72–2.02 (*m*, 2H–C(2), 2H–C(3), OH); 2.65–2.82 (*m*, 2H–C(4)); 3.75 (*s*, MeO); 5.18 (*dd*, J_{cis} = 10.5, J_{gem} = 1.5, H_{cis} of CH_2=CH); 5.26 (*dd*, J_{trans} = 16.8, J_{gem} = 1.5, H_{trans} of CH_2=CH); 6.00 (*dd*, J_{trans} = 17.1, J_{cis} = 10.5, CH_2=C*H*); 6.59 (*d*, *J*(H–C(5),H–C(7)) = 2.7, H–C(5)); 6.71 (*dd*, *J*(H–C(7),H–C(8)) = 8.6, *J*(H–C(7),H–C(5)) = 2.7, H–C(7)); 7.27 (*d*, *J*(H–C(8),H–C(7)) = 8.6, H–C(8)). Anal. calc. for $C_{13}H_{16}O_2$ (204.27): C 76.44, H 7.89; found: C 76.47, H 7.85.



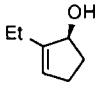
39



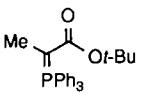
40



41

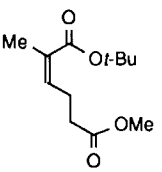


42

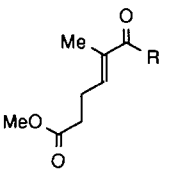


43

44



45



46a R = O*t*-Bu
46b R = OH
46c R = Cl

3.1.2. *Preparation of* **6** (essentially by the method of *Robins* and *Walker* [74]). Compound *rac-***39** (2.0 g, 9,8 mmol) was heated under weak reflux in toluene (50 ml) in the presence of TsOH·H_2O (trace) and *p*-hydroquinone (trace) for 30 min (TLC, hexane/AcOEt 2:1). After cooling and usual workup, the residue was subjected to FC (hexane/AcOEt 100:1) on silica gel (30 g). *6-Methoxy-1-vinyl-3,4-dihydronaphthalene* (**6**; 1.6 g, 88%) was obtained as a colorless oil. TLC (hexane/AcOEt 2:1): R_f 0.80. IR (film): 3082*w*, 3027*w* (=C–H); 2935*m*, 2883*m*, 2830*m* (–C–H); 1638*w* (C=C, olef.); 1607*m*, 1567*m*, 1496*m* (C=C, arom.). ^{1}H-NMR: 2.18–2.25 (*m*, 2 H–C(3)); 2.66 (*t*, *J*(H–C(4),H–C(3)) = 7.7, 2 H–C(4)); 3.71 (*s*, MeO); 5.13 (*dd*, J_{cis} = 10.9, J_{gem} = 1.9, H_{cis} of CH_2=CH); 5.48 (*dd*, J_{trans} = 17.2, J_{gem} = 1.9, H_{trans} of CH_2=CH); 6.00 (*td*, *J*(H–C(2),H–C(3)) = 4.8, *J*(H–C(2),CH_2=CH) = 0.8,H–C(2)); 6.56 (*ddd*, *J*(CH_2=C*H*,H–C(2)) = 1.1, J_{cis} = 10.9, J_{trans} = 17.4, CH_2=C*H*); 6.64–6.69 (*m*, H–C(5), H–C(7)); 7.23 (*d*, *J*(H–C(8),H–C(7)) = 8.1, H–C(8)). Anal. calc. for $C_{13}H_{14}O$ (186.35): C 83.83, H 7.58; found: C 83.84, H 7.59.

For use in *Diels-Alder* reactions, **6** was prepared freshly and stored max. 2 d at –20°.

3.2. *Preparation of the Dienophiles*. 3.2.1. *Preparation of* **7a** *and* **18a**. Compound **7a** was prepared essentially by the method described earlier ([75]: Exper. 7.2.2). Final purification was achieved by spinning band distillation. The distillate was stored at –30° unless used immediately. Compound **18a** was prepared essentially by the method of *Dane et al.* [76].

3.2.2. *Preparation of* **7b** *and* **18b**. 3.2.2.1. *Preparation of* **41**. In a 500-ml, round-bottomed flask, equipped with a *Dean-Stark* trap and a condenser, the soln. of *2-ethylcyclopent-2-en-1-one* (**40**, 30.0 g, 237 mmol) [77], i-BuOH (65 ml, 702 mmol, 3 equiv.), and TsOH·H_2O (trace) in toluene (160 ml) was refluxed overnight (16 h) with separation of H_2O. The mixture was cooled to r.t. and poured into sat. aq. $NaHCO_3$ soln./Et_2O. After separation of the org. phase, the aq. layer was extracted with Et_2O (3 ×), and the combined org. phases were washed with brine

and dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the crude product was distilled under reduced pressure (Kugelrohr, bath temp. 130°, 0.1 Torr). *2-Ethyl-3-(isobutyloxy)cyclopent-2-en-1-one* (**41**) (36.7 g, 85%) was obtained as a yellowish oil, which solidified at +4°. M.p. 37–39°. IR (film): 2965*m*, 2933*m*, 2876*w* (–C–H); 1688*s* (C=O); 1630*s* (C=C, olef.). ^{1}H-NMR: 0.99–1.03 (*m*, *Me*CH_2, *Me*$_2$CH); 2.05 (m_c, Me$_2$*CH*); 2.16 (*q*, *J*(MeCH_2,CH_2*Me*) = 7.6, MeCH_2); 2.40–2.44 (*m*, 2 H–C(4)); 2.62–2.66 (*m*, 2 H–C(5)); 3.92 (*d*, *J*(OCH_2,Me$_2$*CH*) = 6.5, CH_2O). Anal. calc. for $C_{11}H_{18}O_2$ (182.3): C 72.47, H 9.95; found: C 72.56, H 9.98.

3.2.2.2. *Preparation of* rac-**42**. A soln. of **41** (18.5 g, 0.1 mol) in dry Et_2O (30 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (4.6 g, 120 mmol, 1.2 equiv.) in dry Et_2O (150 ml) during 1 h (ice-cooling). The mixture was stirred overnight at r.t., and AcOEt (15.7 ml) was added under ice-cooling. Then, H_2O (4.2 ml), aq. 10% NaOH soln. (4.2 ml), and, finally, H_2O (6.7 ml) were added during 20 min. The stirred suspension was heated under reflux for 30 min, filtered and the residue washed with Et_2O several times. The solvent was evaporated *in vacuo*, and the crude product was subjected to FC (hexane/AcOEt 10:1) on silica gel (150 g). After evaporation of the solvent and bulb-to-bulb distillation under reduced pressure (bath temp. 100°/13 Torr), *(1RS)-2-ethylcyclopent-2-en-1-ol* (*rac*-**42**; 8.2 g, 73%) was obtained as a colorless oil. TLC (hexane/AcOEt 4:1): R_f 0.32. IR (film): 3334*s* (OH); 3049*w* (=C–H); 2963*s*, 2853*s* (C–H); 1459*m*, 1045*s*. ^{1}H-NMR: 1.09 (*t*, *J*(CH_2*Me*$_3$,*CH*$_2$Me) = 7.4, *Me*CH_2); 1.65–1.75 (*m*, H–C(5)); 2.03–2.45 (*m*, OH), 2 H–C(4), H′–C(5), MeCH_2); 4.61–4.65 (*m*, H–C(1)); 5.50–5.52 (*m*, H–C(3)). Anal. calc. for $C_7H_{12}O$ (112.17): C 74.93, H 10.78; found: C 74.95, H 10.76.

3.2.2.3. *Preparation of* **7b**. A soln. of *rac*-**42** (4.0 g, 35.6 mmol) in dry CH_2Cl_2 (10 ml) was added dropwise to a stirred suspension of pyridinium dichromate (16.9 g, 45 mmol) at r.t. After stirring for 5 h (TLC, hexane/AcOEt 4:1), the dark mixture was filtered through *Celite*, and the solvent was evaporated *in vacuo*. The residue was subjected to chromatography (hexane/AcOEt 10:1) on silica gel (80 g). After bulb-to-bulb distillation under reduced pressure (bath temp. 70°; 12 Torr), *2-ethylcyclopent-2-en-1-one* (**7b**, 3.14 g, 80%) was obtained as a colorless oil. TLC (hexane/AcOEt 4:1): R_f 0.38. IR (film): 3046*w* (=C–H); 2955*s*, 2875*s* (C–H); 1702*s* (C=O); 1631*w* (C=C, olef.). ^{1}H-NMR: 1.09 (*t*, *J*(CH_2*Me*,*CH*$_2$Me) = 7.5, *Me*CH_2); 2.14–2.23 (*m*, MeCH_2); 2.37–2.40 (*m*, 2H–C(4)); 2.51–2.60 (*m*, 2H–C(5)); 7.32–7.35 (*m*, H–C(3)). Anal. calc. for $C_7H_{10}O$ (110.16): C 76.32, H 9.01; found: C 76.08, H 9.15.

3.2.2.4. *Preparation of* **18b**[29]). A soln. of previously powdered SeO_2 (8.26 g, 74.4 mmol) in dioxane/H_2O 10:1 (60 ml) was added dropwise to a soln. of **7b** (8.20 g, 74.4 mmol) in dioxane (20 ml) at 10°. The mixture was heated to 90° for 2.5 h. The black precipitate was separated by filtration through *Celite*. After washing with CH_2Cl_2 (3 ×), the combined filtrates were dried ($MgSO_4$) and evaporated *in vacuo*. The crude product was dried *in vacuo* overnight over $CaCl_2$ and further purified by fractional distillation under reduced pressure (96–100°; 1.3 Torr) to give *3-ethylcyclopent-3-ene-1,2-dione* (**18b**) (4.67 g, 50%) as an orange-colored oil, solidifying at low temp. (below 0°). UV (MeOH): λ_{max} 234.2 (6800). IR (film): 3063*w* (=C–H); 1765*s*, 1712*s* (C=O); 1613*s* (C=C). ^{1}H-NMR: 1.17 (*t*, *J*(CH_2*Me*,*CH*$_2$$CH_3$) = 7.5, *Me*$CH_2$); 2.33–2.43 (*m*, MeC$H_2$); 3.04–3.06 (*m*, 2H–C(5)); 7.73–7.75 (*m*, H–C(4)). Anal. calc. for $C_7H_8O_2$ (124.14): C 67.73, H 6.50; found: C 67.46, H 6.72. Enedione **18b** was stored at –20°.

3.2.3. *Preparation of* **23b**. 3.2.3.1. Wittig *Reaction of* **43** *with Methyl 3-Formylpropanoate* **44**. In a three-necked, 1000-ml flask, a soln. of **44** (21.45 g, 185 mmol, 1 equiv.) [79] in dry THF (50 ml) was added slowly to a soln. of ylide **43** (72.13 g, 185 mmol, 1 equiv.) [80] in dry THF (700 ml) at 0°. After stirring for 12 h at r.t., the mixture was warmed to 55° for 1.5 h. Then, the solvent was evaporated *in vacuo*. The residue was subjected to a filtration with flash silica gel (hexane/AcOEt 2:1; 250 × 55 mm column). Bulb-to-bulb distillation of the crude product (120°/0.2 Torr) gave a mixture of **45** and **46a** as colorless liquid (35.39 g, 84%). ^{1}H-NMR revealed the ratio **45**/**46a** to 4:96 (integr. ratio of the signals 1.81 ppm/1.83 ppm, and 6.58 ppm/5.81 ppm). Separation of **45** and **46a** by prep. HPLC (hexane/AcOMe 20:1, *MN Nucleosil*, Refractom.) afforded **46a** (29.56 g, 70%) and **45** (1.28 g, 3%) as colorless liquids.

*1-(*tert*-Butyl) 6-Methyl (*E*)-2-Methylhex-2-enedioate* (**46a**): UV(TFE): λ_{max} 217.5 (12690). IR (NaCl): 2977*m*, 2954*m* (CH); 1744*s*, 1708*s* (C=O); 1651*m* (C=C); 1256*s* (C–O). ^{1}H-NMR (250 MHz): 1.48 (*s*, *t*-Bu); 1.81 (*s*, Me); 2.42–2.49 (*m*, CH_2CH_2); 3.69 (*s*, MeO); 6.58 (*m*, H–C(3)). Anal. calc. for $C_{12}H_{20}O_4$ (228.29): C 63.14, H 8.83; found: C 63.01, H 8.82.

The configuration of the C=C bond was assigned by NOE (irradiated signal/NOE [%]): Me/CH_2CH_2 (0.70%); H–C(3)/Me (–); H–C(3)/CH_2CH_2 (5.9).

*1-(*tert*-Butyl) 6-Methyl (Z)-2-Methylhex-2-enedioate* (**45**): UV (TFE): λ_{max} 217.5 (8825). IR (NaCl): 2978*m*, 2954*m* (CH); 1742*s*, 1711*s* (C=O); 1648*m* (C=C); 1249*s* (C–O). ^{1}H-NMR (250 MHz): 1.48 (*s*, *t*-Bu); 1.83 (*s*, Me); 2.37–2.44 (*m*, 2H–C(4)); 2.67–2.71 (*m*, 2H–C(5)); 3.66 (*s*, MeO); 5.81 (*m*, H–C(3)). Anal. calc. for $C_{12}H_{20}O_4$

[29]) *B. Scharf*, diploma thesis, Universität Frankfurt am Main, 1993.

(228.29): C 63.14, H 8.83; found: C 62.91, H 8.71. The configuration of the C=C bond was assigned by NOE (irradiated signal/NOE [%]): Me/H–C(3) (2.0%); H–C(3)/Me (2.6%).

3.2.3.2. *Preparation of* **46b**. In a three-necked, 250-ml flask, CF_3COOH (22 ml, 286 mmol, 7 equiv.) was added to a stirred soln. of **46a** (9.32 g, 40.83 mmol, 1 equiv.) in dry CH_2Cl_2 (100 ml) at r.t. After stirring for 5 h at r.t., toluene (80 ml) was added and the solvent evaporated *in vacuo* to leave a volume of *ca.* 30 ml. The procedure was repeated (3 × 50 ml toluene). The residual oil was crystallized in a cooling bath (liq. N_2) and washed with pentane. Acid **46b** (6.26 g, 89%) was isolated as colorless crystalline solid.

*Hydrogen 6-Methyl (*E*)-2-Methyl-2-hexenedioate* (**46b**): m.p. 62°. IR (KBr): 3300–2500*m* (br., COOH); 1732*s*, 1692*s* (C=O); 1638*m* (C=C); 1435*s*, ^{1}H-NMR (250 MHz): 1.74 (*s*, Me); 2.34–2.51 (*m*, CH_2CH_2); 3.59 (*s*, MeO); 6.57–6.62 (*m*, H–C(3)); 12.16 (br., D_2O exchange, COOH). Anal. calc. for $C_8H_{12}O_4$ (172.18): C 55.81, 7.02; found: C 55.60, H 6.85.

3.2.3.3. *Preparation of* **46c**. In a 100-ml flask, equipped with a reflux condenser, **46b** (6.45 g, 37.5 mmol) and $SOCl_2$ (10 ml, 139 mmol, 3.7 equiv.) were dissolved in benzene (20 ml). The mixture was stirred for 4 h at 70°. The solvent and residual $SOCl_2$ was removed by distillation *in vacuo* (12 Torr). Bulb-to-bulb distillation (80°/0.15 Torr) of the residue gave **46c** (6.72 g, 94%) as colorless liquid.

*Methyl (*E*)-5-(Chloroformyl)-5-methyl-4-pentenoate* (**46c**): IR (NaCl): 2998*w*, 2954*m* (aliph. CH); 1741*s* (br., COCl and COOMe); 1642*m* (C=C); 1438*m*; 1365*m*; 1176*w*.

3.2.3.4. *Preparation of* **23b**. In a three-necked, 250-ml flask, BuLi (22.8 ml, 1.53N soln. in hexane (titr. according to [81]) 33.3 mmol, 1 equiv.) was added to a soln. of oxazolidin-2-one (3.07 g, 33.3 mmol, 1 equiv.) in dry CF_3COOH (120 ml) at −60°. After stirring for 20 min at −60°, a soln. of **46c** (6.72 g, 35 mmol, 1.05 equiv.) in dry THF (10 ml) was added to the mixture. After 1 h at −60°, 30 min at 0°, and usual workup, a residue was obtained, which, on chromatography (hexane/AcOEt 4:1; 150 × 50 mm column; flash silica gel), gave *3-[(*E*)-2-methyl-5-(methoxycarbonyl)pent-2-enoyl]oxazolidin-2-one* (**23b**) as a colorless oil (7.1 g, 88%). TLC (hexane/AcOEt 1:1): R_f 0.29. UV (TFE): λ_{max} 211.5 (9010). IR (KBr): 2957*m*; 2924*m* (C–H); 1786*s*, 1736*s*, 1682*s* (C=O); 1384*s*; 1359*s*, 1323*s*; 1197*s*; 1039*s*. ^{1}H-NMR: 1.91 (*s*, Me); 2.43–2.51 (*m*, CH_2CH_2); 3.68 (*s*, MeO); 4.17 (*t*, J = 8, CH_2O); 4.65 (*t*, J = 8, CH_2N); 5.95 (*m*, H–C(3)). ^{13}C-NMR: 13.15, 23.16, 32.17 (Me, C(4), C(5)); 42.88 (CH_2N); 51.28 (MeO); 61.95 (CH_2O); 131.11 (C(3)); 135.74 (C(2)); 152.67, 171.10, 172.64 (3 C=O). Anal. calc. for $C_{11}H_{15}NO_5$ (241.24): C 54.76, H 6.26, N 5.80; found: C 54,65, H 6.27, N 5.75. The configuration of the C=C bond was assigned by NOE (irradiated signal/NOE [%]): Me/CH_2CH_2 (2.5%); H–C(3)/CH_2CH_2 (2.5%); H–C(3)/CH_2N (1.0%); CH_2N/H–C(3) (0.2%).

4. Preparation of Chiral, Non-racemic Ligands. – 4.1. *Preparation of TADDOLs.* The procedure published by *Seebach et al.* [32] [34] [37] [38] was followed. *Table 4* reveals the respective sources in the literature.

4.1.1. *(4*S*,5*S*)-2,2-Diethyl-α,α,α′,α′-tetrakis(2′,5′-dimethylphenyl)-1,3-dioxolane-4,5-dimethanol* (**Tg**). Yield: 42%. M.p. 194–196° (hexane). TLC (hexane/AcOEt 4:1): R_f 0.55. $[\alpha]_{589}^{20}$ = +2.4 (*c* = 1.000, $CHCl_3$); $[\alpha]_{578}^{20}$ = +2.2; $[\alpha]_{546}^{20}$ = +1.2; $[\alpha]_{436}^{20}$ = −13.0; $[\alpha]_{365}^{20}$ = −56.3. IR (KBr): 3489*s*, 3219*s* (O–H); 3020*m* (=C–H); 2969*s*, 2922*s*, 2879*s* (C–H); 1887*w*; 1845*w*; 1752*w*; 1612*m*; 1497*s*; 1462*s*; 1380*m*; 1343*m*; 1297*m*; 1253*m*; 1200*s*; 1077*s*; 1021*s*; 944*s*; 804*s*; 771*m*. ^{1}H-NMR: 0.63 (br. *s*, 2 *Me*CH_2); 1.16 (br. *s*, 2 MeCH_2, 2 OH); 1.70, 1.76 (2*s*, 4 *Me*$_2C_6H_3$); 2.29, 2.33 (2*s*, 4 *Me*$_2C_6H_3$); 5.15 (br. *s*, H–C(4), H–C(5)); 6.85–6.99 (*m*, 8 arom. H); 7.57 (*m*, 4 arom. H). Anal. calc. for $C_{41}H_{50}O_4$ (606.84): C 81.15, H 8.30; found: C 81.13, H 8,50.

4.1.2. *(4*S*,5*S*)-2,2-Diethyl-α,α,α′,α′-tetrakis(3′,4′-dimethoxyphenyl)-1,3-dioxolane-4,5-dimethanol* (**Th**). Yield: 32%. TLC ($CHCl_3$/acetone 8:1): R_f 0.39. $[\alpha]_{589}^{20}$ = +49.4 (*c* = 0.927, $CHCl_3$); $[\alpha]_{578}^{20}$ = +51.6; $[\alpha]_{546}^{20}$ = +58.5; $[\alpha]_{436}^{20}$ = +97.1; $[\alpha]_{365}^{20}$ = imperm. IR (KBr): 3318*m*, 3086*w* (=C–H); 2935*s*, 2834*m* (C–H); 1606 *m*; 1511*s*; 1257*s*; 1141*s*; 1012*s*. ^{1}H-NMR: 0.71 (*t*, J(*Me*CH_2,C*H*$_2$Me) = 7.3, 2 *Me*CH_2); 1.34 (*q*, J(MeC*H*$_2$,*Me*CH_2) = 7.3, 2 MeC*H*$_2$); 3.72 (*s*, 2, MeO); 3.79 (*s*, 2 MeO); 3.85 (*s*, 2 MeO); 3.90 (*s*, 2 MeO; beneath, 2 OH); 4.39 (*s*, H–C(4), H–C(5)); 6.75–7.13 (*m*, 12 arom. H). Anal. calc. for $C_{41}H_{50}O_{12}$ (734.84): C 67.02, H 6.86; found: C 66.74, H 6,93.

4.1.3. *(4*S*,5*S*)-2,2-Diethyl-α,α,α′,α′-tetra(naphthalene-1-yl)-1,3-dioxolane-4,5-dimethanol* (**Ti**). Yield: 60%. TLC (hexane/AcOEt 4:1): R_f 0.37. $[\alpha]_{589}^{20}$ = +237.4 (*c* = 1.00, $CHCl_3$); $[\alpha]_{578}^{20}$ = +248.9; $[\alpha]_{546}^{20}$ = +287.8; $[\alpha]_{436}^{20}$ = +544.0; $[\alpha]_{365}^{20}$ = +997.4. IR (KBr): 3556*s* (OH); 3379*s* (br., OH); 3089*w*, 3048*m* (=C–H); 2968*m*, 2938*m*, 2880*w* (C–H); 1599*s*, 1509*s* (C=C, arom.). ^{1}H-NMR (270 MHz, $CDCl_2$–$CDCl_2$, 370 K): 0.38 (br. *s*, *Me*CH_2); 0.85–1.14 (br. *m*, MeCH_2, OH); 5.66 (*s*, H–C(4), H–C(5)); 6.96–8.21 (br. *m*, 28 arom. H). Anal. calc. for $C_{49}H_{42}O_4$ (694.87): C 84.69, H 6.09; found: C 84.41, H 6,26.

4.1.4. *(4*S*,5*S*)-2,2-Diethyl-α,α,α′,α′-tetra(phenanthrene-9-yl)-1,3-dioxolane-4,5-dimethanol* (**Tk**). (The *Grignard* reagent from 9-bromophenanthrene was prepared in refluxing THF.) Yield: 59%. TLC (hexane/AcOEt 1:1): R_f 0.61. $[\alpha]_{589}^{20}$ = −57.4 (*c* = 0.86, $CHCl_3$); $[\alpha]_{578}^{20}$ = −61.7; $[\alpha]_{546}^{20}$ = −77.9; $[\alpha]_{436}^{20}$ = −233.5; $[\alpha]_{365}^{20}$ = imperm. IR (KBr): 3556*m*, 3370*s* (br., OH); 3058*w* (=C–H); 2968*s*, 2936*s*, 2879*m* (C–H); 1597*m*, 1494*s* (C=C, arom.).

H-NMR: 0.01–0.56 (br. *m*, *Me*CH_2, MeCH_2, H–C(4), H–C(5)); 5.71 (br. *s*, OH); 6.07 (br. *s*, OH); 6.77–8.83 (br. *m*, 36 arom. H). Anal. calc. for $C_{65}H_{50}O_4$ (895.11): C 87.22, H 5.63; found: C 87.30, H 5.83.

4.1.5. *(4S,5S)-2,2-Diethyl-α,α,α′,α′-tetrakis[3′,5′-di(* tert*-butyl)phenyl]-1,3-dioxolane-4,5-dimethanol* (**Tl**). Yield: 78%. TLC (hexane/AcOEt 20:1): R_f 0.53. $[\alpha]_{589}^{20} = +1.5$ (c = 1.06, $CHCl_3$); $[\alpha]_{578}^{20} = +1.5$; $[\alpha]_{546}^{20} = +1.1$; $[\alpha]_{436}^{20} = -3.4$; $[\alpha]_{365}^{20} = -18.5$. IR (KBr): 3553*s* (OH); 3428*s*, 3274*s* (br., OH); 3075*m* (=C–H); 2963*s*, 2904*s*, 2867*s* (C–H); 1598*s* (C=C, arom.). ^{1}H-NMR: 0.54 (*t*, J(MeCH_2, CH_2Me) = 7.4, *Me*CH_2); 1.04–1.28 (*m*, MeCH_2); 1.21 (*s*, 4 *t*-Bu); 1.28 (*s*, 4 *t*-Bu); 3.68 (*s*, OH); 4.65 (*s*, H–C(4), H–C(5)); 7.24 (*s*, 6 arom. H); 7.29 (*d*, J = 1.7, 2 arom. H); 7.35 (*d*, J = 1.8, 4 arom. H). Anal. calc. for $C_{65}H_{98}O_4$ (943.49): C 82.75, H 10.47; found: C 82.69, H 10,60.

4.2. *Preparation of the Bis-sulfonamides of Type* **B**. The bis-sulfonamides **Ba–d** were prepared according to [15].

4.2.1. *(1S,2S)-1,2-Diphenyl-*N,N′*-bis(trifluoromethanesulfonyl)ethane-1,2-diamine* (**Ba**). Yield: 88%. M.p. 216–217° (toluene/hexane). TLC (hexane/AcOEt 1:1): R_f 0.46. $[\alpha]_{589}^{20} = -8.8$ (c = 1.643, $CHCl_3$); $[\alpha]_{578}^{20} = -9.5$; $[\alpha]_{546}^{20} = -11.2$; $[\alpha]_{436}^{20} = -23.3$; $[\alpha]_{365}^{20} = -47.4$ ([15]: *ent*-**Ba**: $[\alpha]_{589}^{20} = +8.35$ (c = 1.5, $CHCl_3$)). IR (KBr): 3328*s*, 3280*s* (N–H); 3976*w*, 3039*w* (=C–H); 2895*w* (C–H); 1946*w*; 1876*w*; 1804*w*; 1558*s*; 1439*s*; 1371*s*. ^{1}H-NMR: 1.61, 5.68 (2 br. *s*, 2 NH); 4.78 (*s*, H–C(1), H–C(2)); 6.94–7.00 (*m*, 4 arom. H); 7.23–7.33 (*m*, 6 arom. H). Anal. calc. for $C_{16}H_{14}F_6N_2S_2O_4$ (476.41): C 40.33, H 2.96, N 5.88; found: C 40.54, H 3.14, N 6.08.

4.2.2. *(1S,2S)-*N,N′*-Bis(naphthalene-1-sulfonyl)-1,2-diphenylethane-1,2-diamine* (**Bb**). Yield: 60%. M.p. 265° (acetone/hexane). TLC (hexane/AcOEt 1:1): R_f 0.56. $[\alpha]_{589}^{20} = -319.6$ (c = 0.747, acetone); $[\alpha]_{578}^{20} = -336.3$; $[\alpha]_{546}^{20} = -392.9$; $[\alpha]_{436}^{20} = -792.5$; $[\alpha]_{365}^{20} = -1628.9$. IR (KBr): 3456*w*, 3307*w* (N–H); 3059*w*, 3034*w* (=C–H); 2950*w*, 2927*w* (C–H); 1709*w*; 1594*w*; 1507*m*; 1456*m*; 1438*m*; 1322*s*; 1160*s*; 1131*s*; 768*s*; 696*s*; 593*s*. ^{1}H-NMR (270 MHz, (D_6)DMSO): 4.50–4.54 (*m*, H–C(1), H–C(2)); 6.44–6.73 (*m*, 10 arom. H); 7.23–7.28 (*m*, 2 arom. H); 7.54–7.71 (*m*, 6 arom. H); 7.86–7.91 (*m*, 4 arom. H); 8.32–8.35 (*m*, 2 NH); 8.46 (*d*, J = 8.5, 2 arom. H). Anal. calc. for $C_{34}H_{28}N_2S_2O_4$ (592.73): C 68.90, H 4.76, N 4.73, S 10.82; found: C 68.76, H 4.87, N 4.65, S 10.86.

4.2.3. *(1S,2S)-1,2-Diphenyl-*N,N′*-bis[(2,4,6-triisopropylphenyl)sulfonyl]ethane-1,2-diamine* (**Bc**). Yield: 93%. TLC (hexane/AcOEt 1:1): R_f 0.74. $[\alpha]_{589}^{20} = -97.9$ (c = 1.084, $CHCl_3$); $[\alpha]_{578}^{20} = -103.0$; $[\alpha]_{546}^{20} = -119.6$; $[\alpha]_{436}^{20} = -231.3$; $[\alpha]_{365}^{20} = -434.9$. IR (KBr): 3300*m* (N–H); 3064*w*, 3033*w* (=C–H); 2960*s*, 2869*m* (C–H); 1741*w*; 1601*s*; 1458*s*; 1152*s*. ^{1}H-NMR: 1.04 (*d*, J(Me$_2$CH,Me$_2$C*H*) = 6.8, 2 *Me*$_2$CH); 1.14–1.21 (*m*, 4 *Me*$_2$CH); 2.77–2.85 (*m*, 2 Me$_2$C*H*); 3.95–4.11 (*m*, 4 Me$_2$C*H*); 4.46–4.49 (*m*, H–C(1), H–C(2)); 5.68–5.70 (*m*, 2 NH); 6.56–6.60 (*m*, 4 arom. H); 6.86–7.01 (*m*, 10 arom. H). Anal. calc. for $C_{44}H_{60}N_2S_2O_4$ (745.09): C 70.93, H 8.12, N 3.76, S 8.61; found: C 70.86, H 8.01, N 3.69, S 8.62.

4.2.4. *(1S,2S)-*N,N′*-Bis[(4-methylphenyl)sulfonyl]-1,2-diphenylethane-1,2-diamine* (**Bd**). Yield: 77%. M.p. 210–211° ($CHCl_3$/hexane) ([15]: *ent*-**Bd**: 202° ($CHCl_3$/hexane)). TLC (hexane/AcOEt 2:1): R_f 0.42. $[\alpha]_{589}^{20} = -50.1$ (c = 1.821, $CHCl_3$); $[\alpha]_{578}^{20} = -52.7$; $[\alpha]_{546}^{20} = -61.6$; $[\alpha]_{436}^{20} = -123.0$; $[\alpha]_{365}^{20} = -238.7$ ([15]: *ent*-**Bd**: $[\alpha]_D^{25} = +43.9$ (c = 1.74, $CHCl_3$)). IR (KBr): 3340*w*, 3316*w* (N–H); 3066*w*, 3031*w* (=C–H); 1598*m*, 1496*m* (C=C, arom.); 1328*s*, 1156*s* (SO–N); 813*m*, 699*s*, 670*s*. ^{1}H-NMR: 2.30 (*s*, 2 Me); 4.68–4.71 (*m*, H–C(1), H–C(2)); 6.63–6.65 (*m*, 2 NH). Anal. calc. for $C_{28}H_{28}N_2S_2O_4$ (520.67): C 64.59, H 5.42, N 5.38; found: C 64.51, H 5.53, N 5.59.

5. Preparation of Complexes between Ketones and $TiCl_4$ or $SnCl_4$. – 5.1. *Preparation od Di-μ-chlorobis[trichloro(2-methylcyclopent-2-en-1-one)titanium]* (**17A**). A 100-ml, round-bottomed flask, equipped with a rubber septum, was charged with **7a** (250 mg) in anh. CH_2Cl_2 (40 ml). At −40 to −50°, a soln. of $TiCl_4$ (285 μl) in CH_2Cl_2 (10 ml) was added dropwise *via* syringe over 5 min. After 15 h at −30°, yellow crystals had precipitated. M.p. 115–120° (dec.). IR: 1638 (C=C); 1590 (C=O). ^{1}H-NMR: 1.98–2.00 (*m*, Me); 2.89–2.91 (*m*, 2 H–C(4)); 3.21–3.23 (*m*, 2 H–C(5)); 8.00 (*ψs*, H–C(3)). ^{13}C-NMR: 10.34 (Me); 29.96 (C(4)); 36.04 (C(5)); 143.15 (C(2)); 172.94 (C(3)); 222.86 (C(1)). Anal. calc. for $C_{12}H_{16}Cl_8O_2Ti_2$ (571.68): C 25.21, H 2.82; found: C 25.17, H 2.94. A crystal of suitable size (0.25 × 0.30 × 0.80 mm) was used for X-ray structure analysis (see *Fig. 2, a*; depository number *CSD-56301*; CSD refcode: JOXWAU).

5.2. *Preparation of Tetrachloro(acenaphthene-1,2-dione-*O^1,O^2*)titanium* (**17B**). A 250-ml, two-necked, round-bottomed flask was equipped with a magnetic stirring bar, a rubber septum, and an Ar inlet adapter. The flask was charged with acenaphthenequinone (910 mg) in anh. CH_2Cl_2 (125 ml). At −20°, a soln. of $TiCl_4$ (950 mg) in CH_2Cl_2 (5 ml) was added dropwise *via* syringe. The soln., the color of which had turned from yellow to red, was replaced into one of the arms of a *Schlenk* flask. Crystals were grown by slow diffusion of hexane, which had been filled into the other arm of the *Schlenk* flask, into the CH_2Cl_2 soln. M.p. (in glass capillary) 177–178° (dec.). IR: 1689*s*, 1644 (C=O). ^{13}C-NMR: 123.78; 128.99; 130.68; 131.72; 138.28; 155.42; 192.98 (C=O). An isolated crystal was mantled with perfluorated paraffin oil and mounted in a glass capillary under N_2 for X-ray structure determination (see *Fig. 2, b*; depository number: *CSD-57702*; CSD refcode: WECZOT).

5.3. *Preparation of Tetrachloro[(1R)-1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dione-*O^1,O^2*]titanium* (**17C**). Following essentially the procedure under *Exper. 5.2*, lemon-yellow crystals were obtained, after a soln. of

(±)-1,7,7-trimethylbicyclo[2.2.1]heptane-2,3-dione (= (±)-campherquinone) in $CHCl_3$ (5 ml) had been added dropwise *via* syringe at 0° into a soln. of $TiCl_4$ (379 mg) in $CHCl_3$ (50 ml) and kept for 7 d at −25°. M.p. 63–64° (dec.). IR: 1755*w*, 1734*s* (C=O). ^{13}C-NMR: 8.06 (Me); 17.43 (Me); 22.57 (Me); 23.85; 30.26; 47.88 (C(7)); 56.67 (C(4)); 59.89 (C(1)); 209.13, 211.87 (C=O). An isolated crystal was mantled with perfluorated paraffin oil and mounted in a glass capillary under N_2 for X-ray structure determination. The crystal proved to be formed out of the (1*R*)-enantiomer (see *Fig. 2, c*; depository number: *CSD-57702*; CSD refcode: WEDBAI).

5.4. *Preparation of Tetrachloro(diphenylethandione-O^1,O^2)tin* (**17D**). A 100-ml, round-bottomed flask, equipped with a rubber septum, was charged with benzil (1.0 g) in anh. CH_2Cl_2 (20 ml). A soln. of $SnCl_4$ (0.56 ml) was slowly added *via* syringe. The yellow soln. was carefully overlaid by hexane and set aside for 15 h at −25°. M.p. (in glass capillary) 92°. IR: 1683*s*, 1673*s* (C=O); 1596*s*, 1581*m*, 1450*s* (C=C, arom.). ^{13}C-NMR: 129.04 (*d*, C(4), C(6)); 129.94 (*d*, C(3), C(7)); 132.97 (*s*, C(2)); 134.86 (*d*, C(5)); 194.63 (*s*, C(1)). For X-ray crystal-structure determination, see *Fig. 2, d* (depository number: *CSD-57702*; CSD refcode: WECZUZ).

REFERENCES

[1] M. Del Grosso, Dissertation, Univ. Frankfurt am Main, 1992.
[2] Astrid Bucher, Dissertation, Univ. Frankfurt am Main, 1992.
[3] Wolfgang Döring, Dissertation, Univ. Frankfurt am Main, 1994.
[4] Ralf I. Schenkel, Dissertation, Univ. Frankfurt am Main, 1995.
[5] Markus Bauch, Dissertation, Univ. Frankfurt am Main, 1993.
[6] Gernot T. Dambacher, Diplomarbeit, Univ. Frankfurt am Main, 1993.
[7] F. J. Zeelen, *Natural Product Reports* **1994,** *11,* 607.
[8] M. B. Groen, F. J. Zeelen, *Recl. Trav. Chim. Pay-Bas* **1986,** *105,* 465.
[9] J. E. Cole, W. S. Johnson, P. A. Robins, J. Walker, *J. Chem. Soc.* **1962,** 244.
[10] G. Becker, Dissertation, Univ. München, 1935; E. Dane, K. Eder, *Liebigs Ann. Chem.* **1939,** *539,* 207.
[11] P. Yates, P. Eaton, *J. Am. Chem. Soc.* **1960,** *82,* 4436; G. I. Fray, R. Robinson, *ibid.* **1961,** *83,* 249.
[12] G. Quinkert, M. Del Grosso, A. Bucher, J. W. Bats, G. Dürner, *Tetrahedron Lett.* **1991,** *32,* 3357.
[13] G. Quinkert, M. Del Grosso, in 'Stereoselective Synthesis', Eds. E. Ottow, K. Schöllkopf and B.-G. Schulz, Springer-Verlag, Berlin, 1993.
[14] W. Oppolzer, in 'Comprehensive Organic Synthesis', Eds. B. M. Trost and I. Fleming, Vol. 5 (Ed. L. A. Paquette), Pergamon Press, Oxford, 1991; H. B. Kagan, O. Riant, *Chem. Rev.* **1992,** *92,* 1007.
[15] E. J. Corey, R. Imwinkelried, S. Pikul, Y. B. Xiang, *J. Am. Chem. Soc.* **1989,** *111,* 5493; E. J. Corey, *Pure Appl. Chem.* **1990,** *62,* 1209.
[16] G. A. Hughes, H. Smith, *Chem. Ind. (London)* **1960,** 1022.
[17] I. Minami, K. Takahashi, I. Shimizu, T. Kimura, J. Tsui, *Tetrahedron* **1986,** *42,* 4143; J. Tsui, I. Minami, I. Shimizu, H. Kataoka, *Chem. Lett.* **1984,** 1133.
[18] S. Scholz, H. Hofmeister, G. Neef, E. Ottow, C. Scheidges, R. Wiechert, *Liebigs Ann. Chem.* **1989,** 151.
[19] S. N. Ananchenko, I. V. Torgov, *Tetrahedron Lett.* **1963,** *3,* 1553.
[20] D. N. Kursanov, Z. N. Parnes, G. I. Basova, N. M. Loim, V. I. Zdanovich, *Tetrahedron* **1967,** *23,* 2235; D. N. Kursanov, Z. N. Parnes, N. M. Loim, *Synthesis* **1974,** 633.
[21] G. H. Posner, C. Switzer, *J. Am. Chem. Soc.* **1986,** *108,* 1239.
[22] a) A. N. Chekhov, S. P. Ionov, M. V. Dodonov, S. N. Ananchenko, *Bioorg. Khim.* **1983,** *9*(7), 978; b) T. A. Serebryakova, R. N. Chigir, A. V. Zakharychev, S. N. Ananchenko, I. V. Torgov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1973,** *8,* 1917.
[23] a) K. Ponsold, H. Wagner, *Z. Chem.* **1977,** *17,* 61; b) E. H. Vickery, L. F. Pahler, E. J. Eisenbraun, *J. Org. Chem.* **1979,** *44,* 4444; c) P. A. Grieco, T. Takigava, W. J. Schillinger, *J. Org. Chem.* **1980,** *45,* 2247.
[24] H. Baier, G. Dürner, G. Quinkert, *Helv. Chim. Acta* **1985,** *68,* 1054.
[25] S. Drenkard, J. Ferris, A. Eschenmoser, *Helv. Chim. Acta* **1990,** *73,* 1373.
[26] G. Quinkert, M. Del Grosso, A. Bucher, M. Bauch, W. Döring, J. W. Bats, G. Dürner, *Tetrahedron Lett.* **1992,** *33,* 3617.
[27] F. Mohamadi, N. G. J. Richards, W. C. Guida, R. Liskamp, M. Lipton, C. Caufield, G. Chang, T. Hendrickson, W. C. Still, *J. Comput. Chem.* **1990,** *11,* 440.
[28] E. Dane, J. Schmitt, *Liebigs Ann. Chem.* a) **1938,** *536,* 197; b) **1939,** *537,* 207.

[29] G. Singh, *J. Am. Chem. Soc.* **1956,** *78,* 6109.
[30] G. Quinkert, Five Decades of Steroid Synthesis, Heft 19, Vorlesungsreihe Schering, Berlin, 1988.
[31] G. Quinkert, H. Becker, M. Del Grosso, G. Dambacher, J.W. Bats, G. Dürner, *Tetrahedron Lett.* **1993,** *34,* 6885.
[32] D. Seebach, A.K. Beck, M. Schiess, L. Widler, A. Wonnacott, *Pure Appl. Chem.* **1983,** *55,* 1807; A.K. Beck, B. Bastani, D.A. Plattner, W. Petter, D. Seebach, H. Braunschweiger, P. Gysi, L. La Vecchia, *Chimia* **1991,** *45,* 238.
[33] K. Narasaka, M. Inoue, N. Okada, *Chem. Lett.* **1986,** 1109; K. Narasaka, N. Iwasawa, M. Inoue, T. Yamada, M. Nakashima, J. Sugimori, *J. Am. Chem. Soc.* **1989,** *111,* 5340.
[34] D. Seebach, A.K. Beck, R. Imwinkelried, S. Roggo, A. Wonnacott, *Helv. Chim. Acta* **1987,** *70,* 954.
[35] E.J. Corey, Y. Matsumura, *Tetrahedron Lett.* **1991,** *32,* 6289.
[36] K. Nasaka, H. Tanaka, F. Kanai, *Bull. Chem. Soc. Jpn.* **1991,** *64,* 387.
[37] D. Seebach, D.A. Plattner, A.K. Beck, Y.M. Wang, D. Hunziker, W. Petter, *Helv. Chim. Acta* **1992,** *75,* 2171.
[38] D. Seebach, R. Dahinden, R.E. Marti, A.K. Beck, D.A. Plattner, F.N.M. Kühnle, *J. Org. Chem.* **1995,** *60,* 1788.
[39] C. Haase, C.R. Sarko, M. DiMare, *J. Org. Chem.* **1995,** *60,* 1777.
[40] W.J. Scott, J.K. Stille, *J. Am. Chem. Soc.* **1986,** *108,* 3033.
[41] C. Chapuis, J. Jurczak, *Helv. Chim. Acta* **1987,** *70,* 436.
[42] D.A. Evans, K.T. Chapman, J. Bisaha, *J. Am. Chem. Soc.* **1988,** *110,* 1238.
[43] G. Anner, K. Miescher, *Helv. Chim. Acta* a) **1948,** *31,* 2173; b) **1949,** *32,* 1957; c) **1950,** *33,* 1379.
[44] a) W.S. Johnson, D.K. Banerjee, W.P. Schneider, C.D. Gutsche, *J. Am. Chem. Soc.* **1950,** *72,* 1426; b) W.S. Johnson, D.K. Banerjee, W.P. Schneider, C.D. Gutsche, W.E. Shelberg, L.J. Chin, *ibid.* **1952,** *74,* 2832; c) W.S. Johnson, R.G. Christiansen, *ibid.* **1951,** *73,* 5511; d) W.S. Johnson, B. Bannister, R. Pappo, *ibid.* **1956,** *78,* 6331.
[45] J. Das, R. Kubela, A. MacAlpine, Z. Stojanac, Z. Valenta, *Can. J. Chem.* **1979,** *57,* 3308.
[46] a) G. Quinkert, W.-D. Weber, U. Schwartz, H. Stark, H. Baier, G. Dürner, *Liebigs Ann. Chem.* **1981,** 2335; b) G. Quinkert, U. Schwartz, H. Stark, W.-D. Weber, F. Adam, H. Baier, G. Frank, G. Dürner, *Liebigs Ann. Chem.* **1982,** 1999; c) G. Quinkert, H. Stark, *Angew. Chem.* **1983,** *95,* 651; *ibid. Int. Ed.* **1983,** *22,* 637.
[47] a) G. Quinkert, U.-M. Billhardt, H. Jakob, G. Fischer, J. Glenneberg, P. Nagler, V. Autze, N. Heim, M. Wacker, T. Schwalbe, Y. Kurth, J.W. Bats, G. Dürner, G. Zimmermann, H. Kessler, *Helv. Chim. Acta* **1987,** *70,* 771; b) G. Quinkert, N. Heim, J. Glennerberg, U. Döller, M. Eichhorn, U.-M. Billhardt, C. Schwarz, G. Zimmermann, J.W. Bats, G. Dürner, *ibid.* **1988,** *71,* 1719.
[48] G.H. Douglas, J.M. Graves, D. Hartley, G.A. Hughes, B.J. McLoughlin, J. Siddal, H. Smith, *J. Chem. Soc.* **1963,** 5072.
[49] T.B. Windholz, *J. Org. Chem.* **1963,** *28,* 1092.
[50] D. Hainout, R. Bucourt, *Bull. Soc. Chim. Fr.* **1978,** *126,* 119.
[51] W.-D. Weber, Dissertation, Univ. Frankfurt am Main, 1978.
[52] C.H. Kuo, D. Taub, N.L. Wendler, *J. Org. Chem.* **1968,** *33,* 3126.
[53] H. Smith, G.A. Hughes, G.H. Douglas, G.R. Wendt, G.C. Butzby, jun., R.A. Edgren, J. Fisher, T. Forli, B. Gadsby, D. Hartley, D. Herbst, A.B.A. Jansen, K. Ledig, B.J. McLoughlin, J. McMenamin, T.W. Pattison, P.C. Phillips, R. Rees, J. Siddal, J. Studa, L.L. Smith, J. Tokolics, D.H.P. Watson, *J. Chem. Soc.* **1964,** 4472.
[54] K. Junghans, *Chem. Ber.* **1974,** *107,* 3191.
[55] G.A. Hughes, H. Smith, 1968, U.S. Pat.; s. *Chem. Abstr.* **1968,** *70,* 88089q.
[56] E. Oskay, *Chim. Acta Turc.* **1974,** *2,* 181.
[57] a) C. Rufer, H. Kosmol, E. Schröder, K. Kiesslich, H. Gibian, *Liebigs Ann. Chem.* **1967,** *702,* 141; b) C. Rufer, E. Schröder, H. Gibian, *ibid.* **1971,** *752,* 1.
[58] M. Rosenberger, T.P. Fraher, G. Saucy, *Helv. Chim. Acta* **1971,** *54,* 2857.
[59] R. Bucourt, L. Nedelec, J.C. Grasc, J. Weill-Raynal, *Bull. Soc. Chim. Fr.* **1967,** *115,* 561.
[60] N. Cohen, B.L. Banner, W.F. Eichel, D.R. Parrish, G. Saucy, J.M. Casal, W. Meier, A. Fürst, *J. Org. Chem.* **1975,** *40,* 681.
[61] S. Takano, M. Moriya, K. Ogasawara, *Tetrahedron Lett.* **1992,** *33,* 1909.
[62] P. Crabbé, A. Cruz, J. Iriarte, *Can. J. Chem.* **1950,** *187,* 557.
[63] S. Danishefsky, P. Chain, *J. Am. Chem. Soc.* **1976,** *98,* 4975.
[64] K. Hiraga, *Chem. Pharm. Bull.* **1965,** *13,* 1289.
[65] H. Smith, 1963; a) Belg. Pat. 623,844; b) Brit. Pat. 1,041,280.

[66] Shanghai Institute, Hua Hsueh Hsueh Pao (*Acta Chim. Sinica*) **1976,** 279.
[67] Roussel-UCLAV, 1965; Neth. Pat. 6,414,702 (*CA:* **1965,** *63,* 1822).
[68] D. Banes, J. Carol, E.O. Haenni, *J. Biol. Chem.* **1950,** *187,* 557.
[69] C.R. Johnson, J.R. Zeller, *Tetrahedron* **1984,** *40,* 1225; C.R. Johnson, *Aldrichim. Acta* **1985,** *18,* 3.
[70] P.S. Jogdeo, M.S. Chada, G.V. Bhide, *Steroids* **1980,** *35,* 9.
[71] W.S. Johnson, W.F. Johns, *J. Am. Chem. Soc.* **1957,** *79,* 2005.
[72] C. Rufer, E. Schröder, H. Gibian, *Liebigs Ann. Chem.* **1976,** *705,* 211.
[73] W.S. Johnson, I.A. David, H.C. Dehm, R.J. Highet, E.W. Warnhoff, W.D. Wood, E.T. Jones, *J. Am. Chem. Soc.* **1958,** *80,* 661.
[74] P.A. Robins, J. Walker, *J. Chem. Soc.* **1956,** *3249.*
[75] G. Quinkert, H.-G. Schmalz, E. Walzer, S. Gross, T. Kowalczyk-Przewloka, C. Schierloh, G. Dürner, J.W. Bats, H. Kessler, *Liebigs Ann. Chem.* **1988,** 283.
[76] E. Dane, J. Schmitt, C. Rautenstrauch, *Liebigs Ann. Chem.* **1937,** *532,* 29; H.H. Inhoffen, H. Krämer, *Chem. Ber* **1954,** *87,* 488.
[77] H. Schick, G. Lehmann, G. Hilgetag, *Chem. Ber.* **1969,** *102,* 3238.
[78] A.M. Bernard, P.P. Piras, P. Toriggia, *Synthesis* **1990** 527; T. Pham, W.D. Lubell, *J. Org. Chem.* **1994,** *59,* 3676; M.A. Drinan, T.D. Lash, *J. Heterocycl. Chem.* **1994,** *31,* 255.
[79] A.W. Burgstahler, L.O. Weigel, C.G. Shaefer, *Synthesis* **1990,** 527.
[80] P. Stotter, K. Hill, *Tetrahedron Lett.* **1975,** *21,* 1679.
[81] G. Kofron, *J. Org. Chem.* **1976,** *41,* 1879.