Preparation and Application of Iron-substituted (*Z*)-Enals: Synthesis of 5-Substituted α,β-Butenolides

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Dedicated with Best Wishes to Professor Horst Kunz on the Occasion of his 60th Birthday

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Abstract. A reaction sequence furnishing cyclic β-[η^5-$C_5H_5(CO)_2Fe$]-substituted enals **5** starting from β-keto esters **1** is described. Organolithiums were found to react smoothly with the iron-substituted enals yielding α,β-butenolides **6** by an intramolecular cyclocarbonylation of the lithiumalkoxide initially formed. The influence of *e.g.* the reaction temperature and the solvent on the reaction cascade is discussed. A reaction mechanism is proposed.

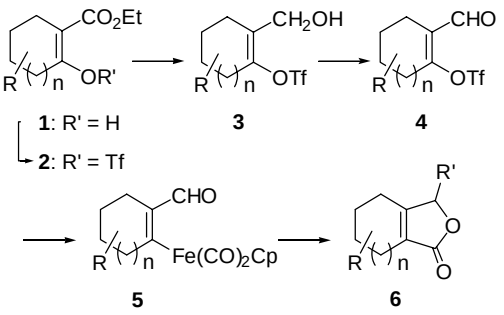
Among the reaction sequences for the synthesis of terpene lactones and derivatives the functionalization of an existing ring system with appropriate functional groups is less explored [1–7]. Whereas syntheses based on intramolecular Diels–Alder reactions [1] or cascade radical processes [2] starting from a functionalized acyclic molecular ensemble bearing an ester functional group or a butenolide are well established, minor attention has been turned to annelative ring expansion strategies. However, starting from cyclic ketones syntheses of annulated butenolides have been accomplished [3], *e.g.* by Pummerer reaction of γ-(phenylsulfinyl)-α,β-unsaturated aldehydes [4] or group transfer cyclization reactions [5]. In addition lithiation-carboxylation strategies [6] and palladium-catalyzed, carbonylative intramolecular coupling reactions [7] with hydroxy vinylbromides or hydroxy trifluoromethanesulfonates have been applied.

Our approach is based on the application of cyclic dicarbonyl(cyclopentadienyl)iron-substituted enals **5** synthesized from an existing ring system with a ketone functionality, for the construction of either lactones or lactams by one-pot procedures [8–12]. Recently, we reported on the synthesis of α,β-butenolides **6** from β-[η^5-$C_5H_5(CO)_2Fe$]-substituted enals **5** and organolithium or Grignard reagents [11, 12].

We herein wish to report full details on observations with organolithium compounds. Moreover, the experimental procedures for the synthesis of cyclic β-[η^5-$C_5H_5(CO)_2Fe$]-substituted enals **5** from β-keto esters **1** are described [12].

Synthesis of Cyclic Iron-substituted Enals

We recently turned our attention to β-keto esters and derivatives as starting materials for the construction of cyclic β-[η^5-$C_5H_5(CO)_2Fe$]-substituted enals **1** with aliphatic substitution pattern (Scheme 1). The cyclohexene carbaldehyde complexes **5a** and **5b** and the 5α-cholestan-3-one-derived compound **5c** were synthesized by this route. Major limitations of the halo Vilsmeier reaction of ketones, a method conveniently employed in the synthesis of iron-substituted enals when starting from β-halovinyl aldehydes, became obvious when applied to cyclic annelated ketones with aliphatic substitution pattern, especially steroidal ketones [13]. For example, starting from 5α-cholestan-3-one by dropwise addition of the Vilsmeier–Haack reagent prepared from $POCl_3$ and DMF (molar ratio 7:8) at 0 °C and subsequent heating to reflux for 3–4 hours a separable 2:1 mixture of the regioisomeric β-chloro enals described in the experimental section was only obtained in 54% overall yield [14].



Scheme 1 Synthesis of α,β-butenolides from iron-substituted enals derived from β-keto esters

For the synthesis of the iron complexes **5a**,**b** the β-keto esters **1a**,**b** were prepared by enamine acylation according to Stork [15]. Treatment of 5α-cholestan-3-one with NaH and diethyl carbonate in benzene gave **1c**

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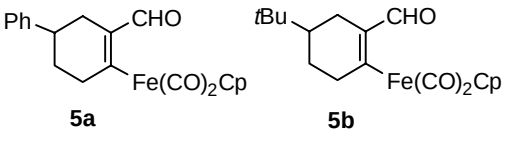
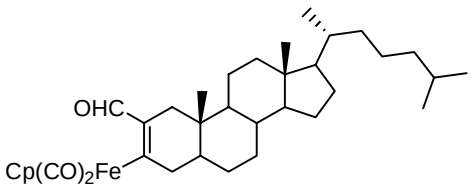
in 56% yield [16]. Using sodium hydride and trifluoromethanesulfonic anhydride, **1a** and **1b** were converted to the 2-ethoxycarbonyl vinyl trifluoromethanesulfonates **2a** and **2b** in a yield of 84% and 92%, respectively [17]. Deprotonation of the β-keto ester **1c** with *tert*-butyllithium and subsequent addition of trifluoromethanesulfonic anhydride afforded **2c** in 52% yield. Treatment with DIBAH in toluene gave the corresponding alcohols **3a**–**c** (79–99%), which were then oxidized to the aldehydes using perruthenate (TPAP) in dichloromethane in the presence of NMO in 87% up to quantitative yield [18]. From the β-trifluoromethyl(sulfonyloxy)-substituted cyclic enals **4a**–**c** and the sodium ferrate [η^5-$C_5H_5(CO)_2Fe$]Na the iron compounds **5a**–**c** were synthesized in 48–63% yield [9].



5a **5b**



5c

Suitable crystals for X-ray crystal structure analysis were obtained of compound **5b**. In the solid state a distorted 1,2-diplanar conformation of the cyclohexene ring and a *s-trans* conformation of the alkenal moiety is observed, similar to compound **5a** studied before [10, 12, 20].

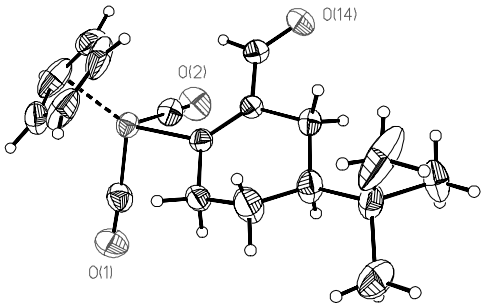
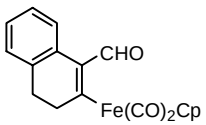
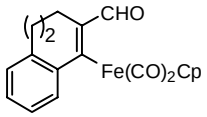


Fig. 1 X-ray structure of iron complex **5b**; ellipsoids: 50% probability

With the iron complex **5b** and **5c** at hand and the model compounds **5d** and **5e** described previously [9], reactions with organolithium compounds RLi (R = Me, *n*Bu) were examined.



5d



5e

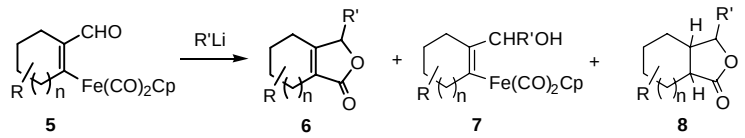
Addition of Organolithiums to Iron-substituted Enals

Addition of *n*BuLi to **5d** at –78 °C in THF led to a 40:60 mixture of **6a** and **7a** isolated in 51% yield (Table 1, entry 1). A somewhat better yield of the α,β-butenolide **6a** could be realized by raising the temperature and stirring of the solution for prolonged time at room temperature (Table 1, entry 2). Using MeLi and the reaction conditions given in Table 1, entry 3, surprisingly the γ-lactone **8a** was obtained from **5d** besides the α,β-butenolide **6b** and the mixture isolated in 40% yield. The corresponding 1,2-adduct **7** was not isolated. Similarly, treatment of **5b** with MeLi yielded α,β-butenolide **6c** besides the γ-lactone **8b** as a 60:40 product mixture in 53% overall yield (Table 1, entry 6). In an alternative procedure (Table 1, entry 7), the reaction of **5b** with MeLi in THF was hydrolyzed with D_2O to furnish **6c** in 20% yield in addition to the deuterated γ-lactone **8c** (30%). Obviously, the γ-lactone derivative is formed during hydrolysis of reaction intermediates, presumably under participation of an ironhydrido species [9, 10]. The reaction of **5b** with MeLi was studied under various conditions to improve the yield of **6c**. The choice of solvent had remarkable influence on the product ratio. With dichloromethane, a solvent usually avoided in reactions with organolithiums due to side reactions [21], the α,β-butenolide was solely obtained after hydrolysis and isolated in 42% yield (Table 1, entry 11). The yield could be further improved by the application of dichloromethane/dioxane 3:1 and compound **6c** was isolated in 59% yield (Table 1, entry 12). For reactions carried out in THF the influence of proton sources as additives was investigated, too. Remarkably, the addition of MeOH after 30 min reaction time at –78 °C afforded solely the α,β-butenolide **6c**, isolated in 41% yield (Table 1, entry 9). However, for compound **5d** a similar effect was not observed (see Table 1, entry 5).

Diisopropylamine as an additive (Table 1, entry 10) afforded the α,β-butenolide **6c** in 32% yield along with the γ-lactone **8b** (26%).

An influence of the reaction times at –78 °C and at room temperature on the product ratio was also observed. Interestingly, for reactions of compound **5d** conducted in THF by prolongation of the reaction times at –78 °C and room temperature the α,β-butenolide **6b** was solely obtained and isolated in 45% yield (Table 1, entry 4). In a series of experiments under similar reac-

Table 1 Reactions of iron-substituted (*Z*)-enals **5** with organolithium reagents



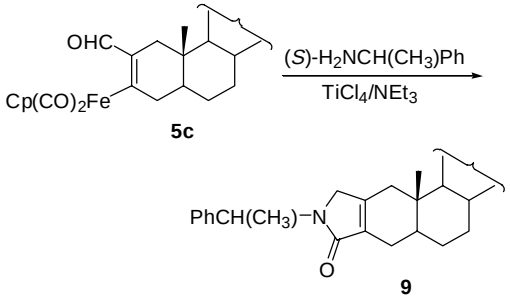
5 **6** **7** **8**

	5	solvent [a])	R'	conditions –78 °C	conditions RT	ratio 6 : 7 : 8	yield (%) [b])
1	**5d**	THF	*n*Bu	4h	–	40 : 60 : 0 (**6a**) (**7a**)	51
2	**5d**	THF	*n*Bu	1.5h	4.5h	100 : 0 : 0 (**6a**)	39
3	**5d**	THF	Me	0.75h	1.25h	79 : 0 : 21 (**6b**) (**8a**)	40
4	**5d**	THF	Me	2.75h	3.75h	100 : 0 : 0 (**6b**)	45
5	**5d**	THF/MeOH	Me	1.5h	1h	75 : 0 : 25 (**6b**) (**8a**)	45
6	**5b**	THF	Me	0.5h	1.2h	60 : 0 : 40 (**6c**) (**8b**)	53
7	**5b**	THF (D_2O) [c])	Me	0.75h	1.15h	40 : 0 : 60 (**6c**) (**8c**)	50 [d])
8	**5b**	THF/AcOH	Me	2.5h	2h	100 : 0 : 0 (**6c**)	37
9	**5b**	THF/MeOH	Me	1.75h	1h	100 : 0 : 0 (**6c**)	41
10	**5b**	THF/iPr_2NH	Me	1.5h	3.5h	55 : 0 : 45 (**6c**) (**8c**)	58 [d])
11	**5b**	CH_2Cl_2	Me	1 h	3.5h	100 : 0 : 0 (**6c**)	42
12	**5b**	CH_2Cl_2/dioxane	Me	1.15h	21h	100 : 0 : 0 (**6c**)	59
13	**5c**	THF	Me	1.5h	5h	100 : 0 : 0 (**6d**)	53
14	**5c**	THF	*n*Bu	1.5h	5h	100 : 0 : 0 (**6e**)	31
15	**5e**	THF	Me	1.5h	3.5h	100 : 0 : 0 (**6f**)	46
16	**5e**	THF	*n*Bu	1.5h	1h	100 : 0 : 0 (**6g**)	40
17	**5e**	THF	Me	0.75h	–	0 : 100 : 0 (**7b**)	72
18	**5e**	THF	*n*Bu	4h	–	0 : 100 : 0 (**7c**)	55

[a]) Additives were added after 30 min at –78°C; [b]) Isolated yield. [c]) Hydrolysis with D_2O. [d]) Products separated by chromatography

tion conditions the α,β-butenolides **6d**,**e** (Table 1, entries 13, 14) and **6f**,**g** (Table 1, entries 15, 16) were obtained exclusively from the iron compounds **5c** and **5e** and were isolated in 31–53% yield. On the other hand, treatment of the less reactive iron complex **5e** with organolithiums at –78 °C in THF and subsequent hydrolysis exclusively yielded the 1,2-adducts **7b** (Table 1, entry 17) and **7c** (Table 1, entry 18), isolated in 72% and 55% yield. Generally, 1.05–1.1 equivalents of the organolithium reagents were applied under argon atmosphere. Remarkably, saturated γ-lactones **8** could not be observed in reactions of the iron complexes with *n*BuLi.

From the experiments presented in Table 1 a strong temperature-dependence of the cyclocarbonylation step is concluded. During the formation of the α,β-butenolide framework prior aqueous workup two new absorptions at 1860–1835cm^{-1} and 1670–1650cm^{-1} are observed initially, attributed to a ferrilactone intermediate being involved in the carbonylation step. For the reaction of iron-substituted enals **5** with K-Selectride similar conclusions were drawn based on IR data. The mechanism of the formation of the saturated γ-lactones during hydrolysis is yet unknown. However, based on the labeling studies involvement of a hydridoiron intermediate formed during hydrolysis seems to be reasonable.



5c **9**

Scheme 2 Synthesis of the α,β-unsaturated γ-lactam **9**

Solvent effects in organic chemistry are ubiquitous, especially in organolithium chemistry [22]. The influence of the solvents and additives on the reaction of **5** with MeLi is remarkable. Whereas the yield of the α,β-butenolides **6** could be improved additional experiments have to be carried out to develop reaction conditions for the exclusive formation of the saturated γ-lactones **8**. Therefore, the role of the solvent and the additives remains to be further clarified.

With the iron complex **5c** in hand, we turned our attention on annelative ring expansion strategy for the synthesis of a lactam derivative. The reaction of **5c** with (*S*)-phenylethylamine in dichloromethane in the presence of $TiCl_4$/triethylamine as previously described furnished the α,β-unsaturated γ-lactam derivative **9** in 77% isolated yield (Scheme 2).

In summary, we developed an efficient synthetic route to 5-substituted α,β-butenolides starting from cyclic iron-substituted enals derived from β-keto esters. These iron compounds are useful precursor molecules for the synthesis of either lactone or lactam derivatives.

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Experimental

Melting points were measured on a Büchi apparatus and are uncorrected. IR spectra were recorded on a Perkin Elmer FT-IR spectrometer 1760X; NaCl cells were used for IR monitoring. ^{1}H NMR and ^{13}C NMR were recorded on Bruker instruments AC 200 (200 and 50.3 MHz for ^{1}H and ^{13}C, respectively), AM 400 and ARX 400 (400 and 100.6 MHz for ^{1}H and ^{13}C, respectively). The calibration of spectra was carried out by means of solvent peaks ($CDCl_3$: δ ^{1}H = 7.24, δ ^{13}C = 77.0; DMSO-d_6: δ ^{1}H = 2.49, δ ^{13}C = 39.7; pyridine-d_5: δ ^{1}H = 8.71, δ ^{13}C = 149.5). The signal multiplicities were determined by means of DEPT 135 or the APT technique. For some signal assignments, standard techniques, such as homo- and heteronuclear decoupling, 2D COSY or HETCOR, were employed. Low-resolution electron-impact mass spectra were recorded at 70 eV with a Varian MAT CH7A. HRMS and FD mass spectra were recorded on a Finnigan MAT 95. Thin-layer chromatography (TLC) was performed on silica gel 60 F_{254} (Merck) with detection by UV light (λ = 254 nm) or by treatment with either a solution of $KMnO_4$ (1.25 g) and Na_2CO_3 (6.25 g) in water (250 ml) or a solution of phosphomolybdic acid (2.5 g), cerium(IV)sulfate (1 g) and H_2SO_4 (6 ml) in water (96 ml). The products were purified by column chromatography on Baker silica gel 60 (230 – 400 mesh) or Florisil (140 – 200 mesh, supplied by Aldrich or Fluka) as previously described [9]. Elemental analyses were carried out by the Microanalytical Division of the Institute of Organic Chemistry at the University of Mainz (Germany). Petroleum ether with a boiling range of 40–70 °C was used; THF was distilled from sodium benzophenone, dichloromethane from CaH_2 immediately before use. Sodium amalgam (2%) was purchased from Lancaster, triflic anhydride, $[C_5H_5(CO)_2Fe]_2$ and methyllithium (1.6M solution in ether) from Fluka, $TiCl_4$ (1M solution in dichloromethane), *n*-butyllithium (1.6M solution in hexane) and DIBAH (1M solution in toluene) from Aldrich.

3-Chloro-5α-cholest-2-en-2-carbaldehyde

To a solution of DMF (4.0 ml, 51.8 mmol) in dichloromethane (50 ml) was added $POCl_3$ (4.1 ml, 45.3 mmol) dropwise at 0 °C, and the mixture stirred for 90 min at this temperature. 5α-Cholestan-3-one (2.5 g, 6.5 mmol) in dichloromethane (50 ml) was added at 0 °C and the reaction mixture was refluxed for three hours (TLC monitoring). The solution was cooled to 0 °C and then hydrolyzed by the careful addition of water and solid $NaHCO_3$ until no CO_2 was evolved. The aqueous layer was separated and extracted with dichloromethane (3 × 200 ml). The combined organic phases were dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography on silica gel (petroleum ether/ether 25:1) gave a mixture of regioisomers (1.51 g, 54%). Flash chromatography on silica gel with petroleum ether/ether (65:1) gave i) *3-Chloro-5α-cholest-2-en-2-carbaldehyde* (993 mg, 35.4%) and ii) *3-Chloro-5α-cholest-3-en-4-carbaldehyde* (504 mg, 18%).

3-Chloro-5α-cholest-2-en-2-carbaldehyde

Colourless crystalline solid. – TLC (petroleum ether/ether 30:1): R_f = 0.46. – IR (KBr): $\tilde{\nu}$ /cm^{-1} = 2980, 2929, 2870, 2851, 2754, 1731, 1679 (C=O), 1640, 1604, 1466, 1444, 1418. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 10.16 (s, 1H, CHO), 2.50 (d, ^2J = 17.2 Hz, 1H, H-1a), 2.39 (ddd, ^2J = 19.8 Hz, ^3J = 5.5 Hz, ^3J = 2.0 Hz, 1H, H-4a), 2.29 (dddd, ^2J = 19.9 Hz, ^3J = 11.3 Hz, ^3J = 3.3 Hz, ^3J = 1.1 Hz, 1H, H-4b), 1.96 (ddd, ^2J = 12.7 Hz, $^3J_{H\text{-}12a,H\text{-}11a}$ = $^3J_{H\text{-}12a,H\text{-}11b}$ = 3.4 Hz, 1H, H-12a), 1.83–1.63 (m, 3H, H-1b, H-7a, H-16a), 1.57–1.43 (m, 5H, H-5, H-6a, H-11a, H-15a, H-25), 1.40–0.79 (m, together with CH_3-groups, 16H, H-6b, H-7b, H-8, H-11b, H-12b, H-14, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b), 0.88 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.7 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.76–0.68 (m, together with 19-CH_3, 1H, H-9), 0.69 (s, 3H, 19-CH_3), 0.63 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 191.5 (d, CHO), 149.9 (s, C-3), 132.2 (s, C-2), 56.20 and 56.15 (2 × d, C-14 and C-17), 53.3 (d, C-9), 42.5 (s, C-13), 42.4 (d, C-5), 40.4 (t, C-4), 39.7 (t, C-12), 39.5 (t, C-24), 37.8 (t, C-1), 36.1 (t, C-22), 35.7 (d, C-20), 35.3 (d, C-8), 34.0 (s, C-10), 31.3 (t, C-7), 28.1 (t, C-16), 28.0 (d, C-25), 27.7 (t, C-6), 24.1 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.1 (t, C-11), 18.6 (q, C-21), 11.9 (q, C-18), 11.6 (q, C-19). – MS (EI): *m/z* (%) = 434.5 (16), 432.5 (43), 330.1 (12), 328.1 (13), 279.2 (17), 278.2 (35), 277.3 (36), 246.0 (45), 244 (46), 215.0 (16), 214.0 (92), 213.0 (16), 212.0 (92), 206.0 (25), 105.3 (12), 99.3 (13), 95.4 (14).

$C_{28}H_{45}ClO$	Calcd.:	C 77.65 H 10.47
(433.1)	Found:	C 77.73 H 10.29.

3-Chloro-5α-cholest-3-en-4-carbaldehyde

Colourless amorphous solid. – TLC (petroleum ether/ether 30:1): R_f = 0.54. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1678 (C=O), 1603. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 10.16 (s, 1H, CHO), 2.67–2.56 (m, 1H, H-2a), 2.50–2.44 (m, 1H, H-2b), 2.42–2.37 (m, 1H, H-6a), 2.20–2.15 (m, 1H, H-5), 1.96 (ddd, ^2J = 12.3 Hz, $^3J_{H\text{-}12a,H\text{-}11a} = {}^3J_{H\text{-}12a,H\text{-}11b}$ = 3.5 Hz, 1H, H-12a), 1.88–1.75 (m, 2H, H-1a, H-16a), 1.71–1.66 (m, 1H, H-7a), 1.59–0.73 (m, together with CH_3-groups, 30H, H-1b, H-6b, H-7b, H-8, H-9, H-11a, H-11b, H-12b, H-14, H-15a, H-15b, H-16b, H-17, 19-CH_3, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b, H-25, 26-CH_3, 27-CH_3), 0.87 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.64 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 193.2 (d, CHO), 149.5 (s, C-3), 134.8 (s, C-4), 56.22 and 56.16 (2 × d, C-14 and C-17), 52.7 (d, C-9), 47.2 (d, C-5), 42.6 (s, C-13), 39.9 (t, C-12), 39.4 (t, C-24), 36.1 (t, C-22), 35.7 (d, C-20), 35.3 (s, C-10), 35.0 (d, C-8), 34.1 (t, C-1), 33.7 (t, C-2), 31.6 (t, C-7), 28.2 (t, C-16), 28.0 (d, C-25), 24.0 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 22.3 (t, C-6), 21.3 (t, C-11), 18.6 (q, C-21), 12.9 (q, C-19), 12.1 (q, C-18).

$C_{28}H_{45}ClO$	Calcd.:	C 77.65	H 10.47
(433.1)	Found:	C 77.99	H 9.98.

2-Carboethoxy-5α-cholestan-3-one (**1c**)

5α-Cholestan-3-one (9.67 g, 25 mmol) was added to a boiling suspension of sodium hydride (3.0 g, 125 mmol) and diethyl carbonate (5.91 g, 50 mmol) in benzene (100 ml) over a period of four hours [23]. After the reaction mixture was refluxed for an additional 90 min it was cooled and, when reaching room temperature, hydrolyzed by the careful addition of glacial acetic acid (20 ml) and ice-water (60 ml). The aqueous layer was separated and extracted with benzene (40 ml). The combined organic phases were washed twice with water (40 ml) and dried (Na_2SO_4). Solvent and excess diethyl carbonate were evaporated under reduced pressure. The residue was purified by repeated column chromatography on silica gel using petroleum ether/methyl *tert*-butylether (12:1) and petroleum ether/dichloromethane (1:1), respectively. Yield 6.47 g (56%), colourless solid, *m.p.* 116 °C. – TLC (petroleum ether/dichloromethane 1:1): R_f = 0.39. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1653 (C=O), 1615 (C=C). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3436 (br, OH), 2959, 2944, 2867, 2849, 1647 (C=O), 1615 (C=C), 1467, 1445, 1418, 1409, 1384, 1371, 1363, 1356, 1310, 1294, 1275, 1259, 1250, 1222, 1206, 1053. – ^{1}H NMR (400 MHz, $CDCl_3$; 100% enolic form): δ/ppm = 12.16 (s, 1H, OH), 4.19 (dq, ^2J = 16.0 Hz, ^3J = 7.2 Hz, 1H, OCH_2-a), 4.16 (dq, ^2J = 16.1 Hz, ^3J = 7.1 Hz, 1H, OCH_2-b), 2.27 (d, ^2J = 15.6 Hz, 1H, H-1a), 2.09 (dd, ^2J = 18.8 Hz, $^3J_{H\text{-}4a,H\text{-}5}$ = 4.5 Hz, 1H, H-4a), 2.02–1.94 (m, 2H, H-4b, H-12a), 1.84–1.73 (m, 2H, H-1b, H-16a), 1.65 (m, 1H, H-7a), 1.59–0.64 (m, together with CH_3-groups, 22H, H-5, H-6a, H-6b, H-7b, H-8, H-9, H-11a, H-11b, H-12b, H-14, H-15a, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b, H-25), 1.28 (t, ^3J = 7.0 Hz, 3H, $OCH_2C\underline{H}_3$), 0.88 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.7 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.72 (s, 3H, 19-CH_3), 0.64 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$; 100% enolic form): δ/ppm = 173.0 (s, C=O), 170.8 (s, C-3), 96.5 (s, C-2), 60.1 (t, OCH_2), 56.42 and 56.35 (d, C-14 and C-17), 53.7 (d, C-9), 42.5 (s, C-13), 40.9 (d, C-5), 40.0 (t, C-12), 39.5 (t, C-24), 36.8 (t, C-1), 36.2 (t, C-22), 35.8 (d, C-20), 35.4 (d, C-8), 34.7 (s, C-10), 33.4 (t, C-4), 31.5 (t, C-7), 28.2 (t, C-16), 28.1 (t, C-6), 28.0 (d, C-25), 24.2 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.2 (t, C-11), 18.7 (q, C-21), 14.3 (q, $OCH_2\underline{C}H_3$), 12.0 (q, C-18), 11.6 (q, C-19). – MS (FD): *m/z* (%) = 459.5 (44.8, M^+ + 1), 458.5 (100, M^+).

$C_{30}H_{50}O_3$	Calcd.:	C 78.55	H 10.99
(458.7)	Found:	C 78.53	H 10.92.

Synthesis of Ethoxycarbonyl-substituted Vinyl Triflates 2 (General Procedure)

A solution of the β-ketoester **1** (10 mmol) in 30 ml of dry ether was added slowly to an ice-cooled, stirred suspension of sodium hydride (0.26 g, 11 mmol) in 50 ml of dry ether. After being stirred for 10 min at 0 °C, trifluoromethanesulfonic anhydride (1.81 ml, 11 mmol) was added and stirring was continued at 0 °C for one hour [17]. The cold reaction mixture was poured into saturated aqueous ammonium chloride solution/ether (1:2.5, 70 ml) and stirred for 5 min at room temperature. The organic layer was washed with water (50 ml) and subsequently with brine (50 ml) and dried ($MgSO_4$). After evaporation of the solvent under reduced pressure the products were purified by column chromatography (silica gel, petroleum ether/dichloromethane 1:1).

Ethyl 5-phenyl-2-[(trifluoromethyl)sulfonyloxy]-1-cyclohexene-1-carboxylate (**2a**)

Compound **2a** was prepared from 4.93 g (20 mmol) of the β-ketoester **1a** [24]. Yield 6.34 g (84%), bright yellow oil which solidified to a colourless solid, *m.p.* 48 °C. – TLC (petroleum ether/dichloromethane 1:1): R_f = 0.57. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1723 (C=O), 1216, 1141. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.37–7.19 (m, 5H), 4.26 (q, ^3J = 7.3 Hz, 2H, OCH_2), 2.95–2.80 (m, 2H), 2.70–2.42 (m, 3H), 2.13–1.90 (m, 2H), 1.30 (t, ^3J = 7.3 Hz, 3H, CH_3). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 164.4 (s, C=O), 151.1 (s, C-2), 143.7 (s, C-*i*), 128.7 (d, C-*m*), 126.8 (d, C-*p*), 126.7 (d, C-*o*), 122.9 (s, C-1), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 61.7 (t, OCH_2), 38.6 (d, C-5), 33.5 (t), 29.0 (t), 28.8 (t), 14.0 (q, CH_3). – MS (EI): *m/z* (%) = 379.1 (2, M^+ + 1), 378.2 (8, M^+), 332.9 (4), 244.9 (4), 199.0 (7), 104.0 (100, $C_8H_8^+$), 91.0 (17, $C_7H_7^+$).

$C_{16}H_{17}F_3O_5S$	Calcd.:	C 50.79	H 4.53	S 8.47
(378.4)	Found:	C 50.70	H 4.52	S 8.54.

Ethyl5-(tert-butyl)-2-[(trifluoromethyl)sulfonyloxy]-1-cyclohexene-1-carboxylate (**2b**)

Yield 3.30 g (92%), bright yellow oil. – TLC (petroleum ether/dichloromethane 1:1): R_f = 0.84. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 2963, 2909, 2872, 1723 (C=O), 1674 (C=C), 1479, 1471, 1423, 1398, 1370, 1355, 1313, 1256, 1210, 1178, 1160, 1140, 1113, 1084, 1066, 1046, 1026, 1018. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.25 (q, ^3J = 7.3 Hz, 2H, OCH_2), 2.61–2.32 (m, 3H), 2.20–2.03 (m, 1H), 1.97–1.85 (m, 1H), 1.39–1.19 (m, 2H), 1.30 (t, ^3J = 7.3 Hz, 3H, CH_3), 0.88 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 164.9 (s, C=O), 151.2 (s, C-2), 123.2 (s, C-1), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 61.6 (t, OCH_2), 42.8 (d, C-5), 32.1 (s, $\underline{C}(CH_3)_3$), 29.4 (t), 27.6 (t), 27.1 (q, $C(\underline{C}H_3)_3$), 23.6 (t), 13.9 (q, CH_3). – MS (EI): *m/z* (%) = 358.9 (1.3, M^+), 343.7 (1.5, $M^+ - CH_3$),

313.7 (9), 225.5 (9), 210.4 (5), 179.3 (4), 169.4 (48), 123.2 (46), 69.1 (12.5, CF_3^+), 57.4 (100, $C_4H_9^+$). $C_{14}H_{21}F_3O_5S$ (358.4).

Ethyl 3-[(trifluoromethyl)sulfonyloxy]-5α-cholest-2-en-2-carboxylate (**2c**)

Yield 0.56 g (9%). An improvement can be achieved by deprotonating the β-ketoester **1c** (2.89 g, 6.3 mmol) with *tert*-butyllithium (6.93 ml of 1.5N solution in pentane) at –78 °C followed by addition of trifluoromethanesulfonic anhydride (1.14 ml, 6.93 mmol). Stirring was continued at –78 °C for one hour, then the reaction mixture was warmed to room temperature and worked-up as described above. Yield 1.95 g (52%), colourless crystalline solid, *m.p.* 108 °C. – TLC (petroleum ether/dichloromethane 1:1): R_f = 0.70. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1721 (C=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2925, 2869, 2850, 1717 (C=O), 1471, 1444, 1425, 1398, 1386, 1374, 1348, 1305, 1290, 1271, 1249, 1213, 1156, 1139, 1079. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 4.25 (dq, ^2J = 12.3 Hz, ^3J = 7.1 Hz, 1H, OCH_2-a), 4.22 (dq, ^2J = 12.3 Hz, ^3J = 7.1 Hz, 1H, OCH_2-b), 2.49 (d, ^2J = 17.0 Hz, 1H, H-1a), 2.18–1.96 (m, 4H, H-1b, H-4a, H-4b, H-12a), 1.80 (m, 1H, H-16a), 1.67 (m, 1H, H-7a), 1.53-0.79 (m, together with CH_3-groups, 21H, H-5, H-6a, H-6b, H-7b, H-8, H-11a, H-11b, H-12b, H-14, H-15a, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b, H-25), 1.30 (t, ^3J = 7.0 Hz, 3H, $OCH_2C\underline{H}_3$), 0.88 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.7 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.77 (s, 3H, 19-CH_3), 0.72 (m, 1H, H-9), 0.64 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 165.0 (s, C=O), 149.5 (s, C-3), 122.1 (s, C-2), 118.4 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 61.6 (t, OCH_2), 56.32 and 56.27 (d, C-14 and C-17), 53.3 (d, C-9), 42.5 (s, C-13), 41.8 (d, C-5), 40.5 (t, C-1), 39.8 (t, C-12), 39.5 (t, C-24), 36.2 (t, C-22), 35.8 (d, C-20), 35.3 (d, C-8), 34.4 (s, C-10), 32.8 (t, C-4), 31.3 (t, C-7), 28.2 (t, C-16), 28.0 (d, C-25), 27.8 (t, C-6), 24.2 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.3 (t, C-11), 18.7 (q, C-21), 13.9 (q, $OCH_2\underline{C}H_3$), 12.0 (q, C-18), 11.4 (q, C-19). – MS (FD): *m/z* (%) = 590.4 (100, M^+).

$C_{31}H_{49}F_3O_5S$	Calcd.: C 63.03	H 8.39	S 5.43
(590.8)	Found: C 63.50	H 8.29	S 5.41.

Reduction of Ethoxycarbonyl-substituted Vinyl Triflates 2 with DIBAH (General Procedure)

To a solution of the ester (**2**, 6 mmol) in THF (40 ml) was added dropwise DIBAH (13.5 ml, 1.0M in toluene) at –78 °C. The reaction mixture was stirred overnight while reaching room temperature. The reaction was quenched by the careful addition of 2N HCl (15 ml) and water (20 ml) at 0 °C, then diluted with EtOAc (100 ml). The organic layer was washed with 2N HCl (20 ml), water (20 ml), saturated aqueous $NaHCO_3$ solution (20 ml), brine (20 ml) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the crude product was purified by flash chromatography (silica gel, petroleum ether/EtOAc-mixtures).

2-(Hydroxymethyl)-4-phenyl-1-cyclohexenyl trifluoromethanesulfonate (**3a**)

Compound **3a** was prepared from 1.89 g (5 mmol) of ester **2a**. Yield 1.54 g (92%), yellow oil. – TLC (petroleum ether/EtOAc 5:1): R_f = 0.44. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 3368 (br, OH), 3087, 3064, 3030, 2931, 1700, 1604, 1495, 1455, 1413, 1352, 1247, 1212, 1141, 1034, 1011. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.36–7.20 (m, 5H), 4.28 (d, ^2J = 12.7 Hz, 1H, OCH_2-a), 4.19 (d, ^2J = 12.2 Hz, 1H, OCH_2-b), 2.89 (m, 1H), 2.70–2.35 (m, 4H), 2.11–1.79 (m, 3H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 144.4 (s, C-1), 143.6 (s, C-*i*), 129.6 (s, C-2), 128.6 (d, C-*m*), 126.7 (d, C-*o*), 126.6 (d, C-*p*), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 59.5 (t, CH_2OH), 38.9 (d, C-4), 33.9 (t), 29.7 (t), 27.8 (t). – MS (EI): *m/z* (%) = 337.2 (1, M^+ + 1), 336.2 (9, M^+), 319.2 (2), 318.3 (12), 203.0 (3), 186.1 (19), 185.0 (32), 103.9 (100, $C_8H_8^+$), 90.9 (22, $C_7H_7^+$). $C_{14}H_{15}F_3O_4S$ (336.3).

4-(tert-Butyl)-2-(hydroxymethyl)-1-cyclohexenyl trifluoromethanesulfonate (**3b**)

Yield 1.88 g (99%), bright yellow oil. – TLC (petroleum ether/EtOAc 5:1): R_f = 0.54. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 3367 (br, OH), 2964, 2872, 1702, 1479, 1471, 1414, 1369, 1352, 1249, 1207, 1140, 1101, 1071, 1044. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.23 (d, ^2J = 12.2 Hz, 1H, OCH_2-a), 4.11 (d, ^2J = 12.7 Hz, 1H, OCH_2-b), 2.43–2.26 (m, 3H), 2.06–1.83 (m, 3H), 1.43–1.19 (m, 2H), 0.88 (s, 9H, $C(C\underline{H}_3)_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 144.0 (s, C-1), 129.8 (s, C-2), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 59.8 (t, $\underline{C}H_2OH$), 43.2 (d, C-4), 32.1 (s, $\underline{C}(CH_3)_3$), 28.5 (t), 27.9 (t), 27.1 (q, $C(\underline{C}H_3)_3$), 24.3 (t). – MS (EI): *m/z* (%) = 317.4 (0.4, M^+ + 1), 316.4 (3, M^+), 183.2 (7), 109.0 (19), 69.1 (11, CF_3^+), 57.3 (100, $C_4H_9^+$). $C_{12}H_{19}F_3O_4S$ (316.3).

2-(Hydroxymethyl)-5α-cholest-2-en-3-yl trifluoromethanesulfonate (**3c**)

Compound **3c** was prepared from 4.73 g (8 mmol) of ester **2c**. Yield 3.43 g (78%), colourless crystalline solid, *m.p.* 116 °C. – TLC (petroleum ether/EtOAc 10:1): R_f = 0.49. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3408 (br, OH), 2930, 2870, 2851, 1707, 1469, 1444, 1417, 1386, 1367, 1346, 1247, 1214, 1141, 1103, 1036, 1010, 1002. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 4.21 (d, ^2J = 12.6 Hz, 1H, OCH_2-a), 4.08 (d, ^2J = 12.3 Hz, 1H, OCH_2-b), 2.30 (d, ^2J = 17.3 Hz, 1H, H-1a), 2.18–2.03 (m, 2H, H-4a, H-4b), 2.00–1.92 (m, 2H, H-1b, H-12a), 1.79 (m, 1H, H-16a), 1.66 (m, 1H, H-7a), 1.61 (s, 1H, OH), 1.56–1.42 (m, 5H, H-5, H-11a, H-11b, H-15a, H-25), 1.40–0.64 (m, together with CH_3-groups, 17H, H-6a, H-6b, H-7b, H-8, H-9, H-12b, H-14, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b), 0.88 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.5 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.77 (s, 3H, 19-CH_3), 0.64 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 142.5 (s, C-3), 128.5 (s, C-2), 118.4 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 59.8 (t, CH_2OH), 56.3 (2 × d, C-14 and C-17), 53.4 (d, C-9), 42.49 (s, C-13), 42.46 (d, C-5), 41.0 (t, C-1), 39.8 (t, C-12), 39.5 (t, C-24), 36.2 (t, C-22), 35.8 (d, C-20), 35.4 (d, C-8), 34.7 (s, C-10), 32.1 (t, C-4), 31.4 (t, C-7), 28.2 (t, C-16), 28.02 (t, C-6), 27.99 (d, C-25), 24.2 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.3 (t, C-11), 18.7 (q, C-21), 12.0 (q, C-18), 11.6 (q, C-19). – MS (FD): *m/z* (%) = 551.4 (1.5, $M^+(^{34}S)$ + 1), 550.4 (8, $M^+(^{34}S)$), 549.4 (28, $M^+(^{32}S)$ + 1), 548.4 (100, $M^+(^{32}S)$).

$C_{29}H_{47}F_3O_4S$	Calcd.: C 63.48	H 8.63	S 5.84
(548.7)	Found: C 63.62	H 9.02	S 6.25.

Oxidation of Hydroxy Vinyl Triflates 3 with TPAP (General Procedure)

To a colourless suspension of the alcohol (**3**, 8 mmol), *N*-methylmorpholine-*N*-oxide (1.41 g, 12 mmol) and molecular sieves (4 Å, 4 g) in dichloromethane (100 ml) was added TPAP (141 mg, 5 mol%) at room temperature [18]. The green suspension was stirred for three hours (TLC monitoring) and then filtered through a plug of silica gel. The residue was washed with dichloromethane and the filtrate concentrated *in vacuo*. Purification could be achieved by flash chromatography (silica gel, petroleum ether/EtOAc-mixtures).

2-Formyl-4-phenyl-1-cyclohexenyl trifluoromethanesulfonate (**4a**)

Oxidation was performed on a 2 mmol scale according to the General Procedure (0.67 g alcohol). Yield 0.63 g (94%), yellow oil. – TLC (petroleum ether/EtOAc 5:1): R_f = 0.82. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 3087, 3064, 3031, 2934, 2874, 2763, 1690 (C=O), 1664 (C=C), 1604, 1495, 1455, 1423, 1359, 1301, 1249, 1212), 1136, 1109, 1076, 1054, 1027. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 10.12 (s, 1H, CHO), 7.38–7.18 (m, 5H), 2.93–2.58 (m, 4H), 2.43–2.27 (m, 1H), 2.21–1.86 (m, 2H). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 187.2 (d, CHO), 160.0 (s, C-1), 143.4 (s, C-*i*), 129.5 (s, C-2), 128.7 (d, C-*m*), 126.9 (d, C-*p*), 126.6 (d, C-*o*), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 37.9 (d, C-4), 29.3 (t), 29.1 (2 × t). – MS (EI): *m/z* (%) = 335.1 (2, M^+ + 1), 334.3 (15, M^+), 201.1 (2), 104.0 (100, $C_8H_8^+$), 91.0 (25, $C_7H_7^+$). $C_{14}H_{13}F_3O_4S$ (334.3).

4-(tert-Butyl)-2-formyl-1-cyclohexenyl trifluoromethanesulfonate (**4b**)

Compound **4b** was prepared from 1.48 g (4.7 mmol) of alcohol **3b**. Yield 1.47 g (quant.), bright yellow oil. – TLC (petroleum ether/ether 2:1): R_f = 0.95. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 2964, 2909, 2872, 2761, 1688 (C=O), 1666 (C=C), 1479, 1472, 1420, 1369, 1359, 1249, 1216, 1138, 1115, 1099, 1068, 1043, 1003. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 10.04 (s, 1H, CHO), 2.60–2.51 (m, 3H), 2.05–1.82 (m, 2H), 1.39–1.18 (m, 2H), 0.89 (s, 9H, C(C$\underline{H}_3$)$_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 187.8 (d, $^1J_{C,H}$ = 183 Hz, CHO), 160.6 (s, C-1), 129.9 (s, C-2), 118.3 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 42.5 (d, $^1J_{C,H}$ = 124 Hz, C-4), 32.1 (s, $\underline{C}$(CH$_3$)$_3$), 29.9 (t, $^1J_{C,H}$ = 130 Hz, CH_2), 27.1 (q, $^1J_{C,H}$ = 123 Hz, C($\underline{C}$H$_3$)$_3$), 23.7 (t), 23.4 (t). – MS (EI): *m/z* (%) = 314.2 (1, M^+), 258.1 (7), 181.1 (2), 125.1 (34), 69.1 (8, CF_3^+), 57.3 (100, $C_4H_9^+$). $C_{12}H_{17}F_3O_4S$ (314.3).

3-[(Trifluoromethyl)sulfonyloxy]-5α-cholest-2-en-2-carbaldehyde (**4c**)

Compound **4c** was prepared from 3.29 g (6 mmol) alcohol **3c**. Yield 2.85 g (87%), colourless solid, *m.p.* 100 °C. – TLC (petroleum ether/dichloromethane 1:1): R_f = 0.73. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2943, 2868, 2851, 1684 (C=O), 1664 (C=C), 1469, 1425, 1387, 1367, 1249, 1227, 1138, 1087, 1032, 1013. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 10.06 (s, 1H, CHO), 2.53 (d, ^2J = 17.6 Hz, 1H, H-1a), 2.38–2.32 (m, 2H, H-4a, H-4b), 1.99 (ddd, ^2J = 12.6 Hz, $^3J_{H\text{-}12a,H\text{-}11a}$ = $^3J_{H\text{-}12a,H\text{-}11b}$ = 3.2 Hz, 1H, H-12a), 1.82–1.76 (m, 2H, H-1b, H-16a), 1.68 (m, 1H, H-7a), 1.58–1.46 (m, 5H, H-5, H-6a, H-11a, H-15a, H-25), 1.40–0.90 (m, 15H, H-6b, H-8, H-11b, H-12b, H-14, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b), 0.89–0.80 (m, together with CH_3-groups, 1H, H-7b), 0.88 (d, ^3J = 6.5 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.7 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.78–0.69 (m, together with 19-CH_3, 1H, H-9), 0.73 (s, 3H, 19-CH_3), 0.64 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 187.8 (d, CHO), 159.1 (s, C-3), 128.7 (s, C-2), 118.4 (q, $^1J_{C,F}$ = 320 Hz, CF_3), 56.30 and 56.24 (2 × d, C-14 and C-17), 53.3 (d, C-9), 42.5 (s, C-13), 42.1 (d, C-5), 39.8 (t, C-12), 39.5 (t, C-24), 36.2 (2 × t, C-1 and C-22), 35.8 (d, C-20), 35.4 (d, C-8), 34.1 (s, C-10), 33.3 (t, C-4), 31.3 (t, C-7), 28.2 (t, C-16), 28.0 (d, C-25), 27.9 (t, C-6), 24.2 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.3 (t, C-11), 18.7 (q, C-21), 12.0 (q, C-18), 11.5 (q, C-19). – MS (FD): *m/z* (%) = 549.5 (2, M^+(^{34}S) + 1), 548.5 (9, M^+(^{34}S)), 547.5 (28, M^+(^{32}S) + 1), 546.5 (100, M^+(^{32}S)).

$C_{29}H_{45}F_3O_4S$	Calcd.:	C 63.71	H 8.30	S 5.86
(546.7)	Found:	C 64.18	H 7.59	S 6.18.

Synthesis of Iron-substituted (*Z*)-Enals 5 (General Procedure)

A solution of [$C_5H_5(CO)_2Fe$]Na, prepared from [$C_5H_5(CO)_2Fe$]$_2$ (0.35 g) and sodium amalgam (2.41 g) in THF (50 ml), was added slowly at –78 °C by means of a cannula to a solution of the appropriate formylvinyltriflate (**4**, 2 mmol) in THF (20 ml). The reaction mixture was stirred at –78 °C for one hour and then allowed to warm to room temperature over a period of one hour. The solvent was evaporated under reduced pressure and the residue dissolved in dichloromethane and subsequently purified by column chromatography on silica gel. With petroleum ether/ether (2:1) [$C_5H_5(CO)_2Fe$]$_2$ was separated, whereas with ether the iron complexes **5** were obtained. The solvent was evaporated and the residue was dried *in vacuo*.

2-[Cyclopentadienyl(dicarbonyl)iron]-5-phenyl-1-cyclohexene-1-carbaldehyde (**5a**)

Compound **5a** was prepared from 1.55 g (4.64 mmol) of aldehyde **4a**. Yield 0.81 g (48%), yellow crystals from dichloromethane/*n*-hexane [12], *m.p.* 127 °C (decomp.). – TLC (petroleum ether/EtOAc 2:1): R_f = 0.70. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 2019 and 1966 (CO-ligands), 1642 (C=O), 1602 (arom. C=C), 1548 (C=C). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3105, 3087, 2928, 2916, 2853, 2001 and 1939 (CO-ligands), 1641 (C=O), 1553 and 1543 (C=C), 1492, 1454, 1432, 1424, 1375, 1219, 1200. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 9.85 (s, 1H, CHO), 7.32–7.17 (m, 5H), 4.88 (s, 5H, C_5H_5), 2.95–2.75 (m, 4H), 2.37–2.23 (m, 1H), 1.84–1.71 (m, 2H). – ^{1}H NMR (200 MHz, DMSO-d_6): δ/ppm = 9.76 (s, 1H, CHO), 7.32–7.13 (m, 5H), 5.21 (s, 5H, C_5H_5), 3.05–2.53 (m, 4H), 2.15–1.98 (m, 1H), 1.79–1.72 (m, 2H). – ^{1}H NMR (200 MHz, pyridine-d_5): δ/ppm = 10.24 (s, 1H, CHO), 7.38–7.22 (m, 5H), 4.95 (s, 5H, C_5H_5), 3.09 (dd, ^2J = 16.1 Hz, ^3J = 4.4 Hz, 1H, H-6a), 2.92–2.85 (m, 2H, H-3a, H-3b), 2.79–2.64 (m, 1H, H-5), 2.54–2.41 (m, 1H, H-6b), 1.78–1.67 (m, 2H, H-4a, H-4b). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 214.7 (s, CO-ligands), 197.5 (d, CHO), 188.6 (s, =$\underline{C}$Fp), 146.4 (2 × s, $\underline{C}$=CFp and C-*i*), 128.3 (d, C-*m*), 126.8 (d, C-*o*), 126.0 (d, C-*p*), 86.2 (d, C_5H_5), 51.9 (t, C-3), 39.7 (d, C-5), 35.5, 33.4 (t, C-4 and C-6). – ^{13}C NMR (50.3 MHz, DMSO-d_6): δ/ppm = 216.4,

216.0 (s, CO-ligands), 196.8 (d, CHO), 189.4 (s, =CFp), 146.9, 145.8 (2 × s, C=CFp and C-*i*), 128.4 (d, C-*m*), 126.8 (d, C-*o*), 126.0 (d, C-*p*), 87.5 (d, C_5H_5), 51.1 (t, C-3), 39.4 (d, C-5), 35.8, 33.0 (t, C-4 and C-6). – ^{13}C NMR (50.3 MHz, pyridine-d_5): δ/ppm = 216.0, 215.6 (s, CO-ligands), 196.7 (d, CHO), 186.7 (s, =CFp), 147.1, 146.5 (2 × s, C=CFp and C-*i*), 128.5 (d, C-*m*), 127.0 (d, C-*o*), 126.0 (d, C-*p*), 86.9 (d, C_5H_5), 51.3 (t, C-3), 40.0 (d, C-5), 36.3, 33.3 (t, C-4 and C-6). – MS (FD): *m/z* (%) = 333.8 (100, M^+–CO).

$C_{20}H_{18}FeO_3$	Calcd.:	C 66.32	H 5.01
(362.2)	Found:	C 65.97	H 5.91.

5-(tert-Butyl)-2-[cyclopentadienyl(dicarbonyl)iron]-1-cyclohexene-1-carbaldehyde (**5b**) [10]

Compound **5b** was prepared from 1.51 g (4.8 mmol) of aldehyde **4b**. Yield 0.87 g (53%), yellow-brown crystalline solid, *m.p.* 103–104 °C (decomp.). – TLC (petroleum ether/EtOAc 2:1): R_f = 0.63. – ^{1}H NMR (200 MHz, pyridine-d_5): δ/ppm = 10.23 (s, 1H, CHO), 4.93 (s, 5H, C_5H_5), 2.96–2.63 (m, 3H), 2.15–1.98 (m, 1H), 1.57–1.52 (m, 1H), 1.22–0.96 (m, 2H), 0.81 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (50.3 MHz, pyridine-d_5): δ/ppm = 216.1, 215.7 (s, CO-ligands), 197.1 (d, CHO), 186.7 (s, =CFp), 147.1 (s, C=CFp), 86.8 (d, C_5H_5), 52.4 (t, C-3), 43.9 (d, C-5), 32.0 (s, $C(CH_3)_3$), 29.8, 27.8 (t, CH_2), 26.8 (q, CH_3). $C_{18}H_{22}FeO_3$ (342.2).

3-[Cyclopentadienyl(dicarbonyl)iron]-5α-cholest-2-en-2-carbaldehyde (**5c**)

Yield 0.66 g (57%), gold-yellow amorphous solid, decomposes above 160 °C. – TLC (petroleum ether/ether 2:1): R_f = 0.15. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 2018 and 1965 (CO-ligands), 1639 (C=O), 1546 (C=C). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2929, 2868, 2846, 2014 and 1962 (CO-ligands), 1643 (C=O), 1546 (C=C), 1467, 1443, 1375, 1212. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 4.86 (s, 5H, C_5H_5), 2.66 (dd, ^2J = 15.8 Hz, $^3J_{H\text{-}4a,H\text{-}5}$ = 3.8 Hz, 1H, H-4a), 2.53–2.37 (m, 2H), 1.94 (m, 1H, H-12a), 1.82–1.72 (m, 2H), 1.65–1.43 (m, 4H), 1.37–0.77 (m, together with CH_3-groups, 18H), 0.87 (d, ^3J = 6.5 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.5 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.5 Hz, 3H, 27-CH_3), 0.69–0.62 (m, together with 18-CH_3, 1H, H-9), 0.62 (s, 3H, 18-CH_3), 0.59 (s, 3H, 19-CH_3). – ^{1}H NMR (400 MHz, pyridine-d_5): δ/ppm = 10.25 (s, 1H, CHO), 4.97 (s, 5H, C_5H_5), 2.94 (d, ^2J = 16.5 Hz, 1H, H-1a), 2.85 (dd, ^2J = 19.9 Hz, $^3J_{H\text{-}4a,H\text{-}5}$ = 5.2 Hz, 1H, H-4a), 2.59 (dd, ^2J = 20.2 Hz, $^3J_{H\text{-}4b,H\text{-}5}$ = 12.0 Hz, 1H, H-4b), 2.01 (br d, ^2J = 16.5 Hz, 1H, H-1b), 1.94 (dt, ^2J = 12.7 Hz, ^3J = 3.4 Hz, 1H, H-12a), 1.86–1.76 (m, 1H), 1.65–1.46 (m, 4H), 1.43–1.30 (m, 6H), 1.28–0.98 (m, 9H), 0.95 (d, ^3J = 6.5 Hz, 3H, 21-CH_3), 0.92–0.82 (m, together with CH_3-groups, 2H), 0.88 (d, ^3J = 6.5 Hz, 6H, 26- and 27-CH_3), 0.78–0.61 (m, together with CH_3-groups, 2H), 0.73 (s, 3H, 18- or 19-CH_3), 0.63 (s, 3H, 18- or 19-CH_3). – ^{13}C NMR (100.6 MHz, pyridine-d_5): δ/ppm = 216.1, 215.8 (s, CO-ligands), 197.2 (d, CHO), 184.2 (s, =CFp), 146.4 (s, C=CFp), 86.7 (d, C_5H_5), 56.4 (t, C-4), 56.2, 56.1 (d, C-14 and C-17), 54.0 (d, C-9), 45.1 (d, C-5), 42.7 (t, C-1), 42.4 (s, C-13), 39.9 (t, C-12), 39.3 (t, C-24), 36.1 (t, C-22), 35.6, 35.4 (d, C-8 and C-20), 33.8 (s, C-10), 31.6 (t, C-7), 28.1, 28.0 (t, C-6 and C-16), 27.8 (d, C-25), 24.0 (t, C-15), 23.7 (t, C-23), 22.5, 22.2 (q, C-26 and C-27), 20.9 (t, C-11), 18.5 (q, C-21), 11.8 (q, C-18), 11.6 (q, C-19). – MS (FD): *m/z* (%) = 547.5 (26, M^+ + 1–CO), 546.5 (86, M^+ – CO), 426.5 (100).

$C_{35}H_{50}FeO_3$	Calcd.:	C 73.16	H 8.77
(574.6)	Found:	C 72.92	H 8.79.

Reactions of Iron Complexes 5 with Organolithiums (General Procedure)

To the iron complex **5** dissolved in THF were added 1.05–1.1 equivalents of RLi at –78 °C. The solution was stirred at –78 °C and then at room temperature until TLC monitoring indicated that the reaction was complete. Buffer and ether were added, and the reaction mixture then vigorously stirred for 5 min. The aqueous layer was separated and washed with ether (3 × 50 ml). The combined organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by chromatography.

1-(n-Butyl)-4,5-dihydronaphtho[1,2-c]furan-3(1H)-one (**6a**)

Table 1, entry 1: By following the general procedure 600 mg (1.8 mmol) **5d** dissolved in 30 ml THF were treated with 1.2 ml *n*BuLi. After having been stirred for 3h at –78 °C additional 1.2 ml of *n*BuLi were added because of incomplete consumption of the starting material. Stirring was continued for 1h at –78 °C. Then the mixture was worked-up with 80 ml buffer (pH = 6) and 100 ml ether. Purification by column chromatography on silica gel with petroleum ether/ethyl acetate afforded a product mixture of the α,β-butenolide **6a** and the 1,2-adduct **7a** in a ratio of 40:60 according to ^{1}H NMR spectroscopy. The product mixture was separated by flash chromatography on Florisil with petroleum ether/EtOAc 8:1 as eluent to yield 144 mg (20%) of **7a** and 63 mg (14%) of **6a** analytically pure.

Table 1, entry 2: By following the general procedure 450 mg (1.35 mmol) **5d** dissolved in 30 ml THF were treated with 0.9 ml *n*BuLi. Stirring was continued for 20 min at –78 °C and at room temperature for 90 min. Work-up was carried out with 100 ml buffer pH = 6 and 100 ml ether. Purification by flash chromatography on florisil with petroleum ether/EtOAc gave **6a** (126 mg, 39%) as a pale yellow-brown oil.

1-(n-Butyl)-4,5-dihydronaphtho[1,2-c]furan-3(1H)-one (**6a**)

Pale yellow oil. – TLC (petroleum ether/EtOAc 4:1): R_f = 0.44. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1745 (C=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2936, 2894, 2875, 1733 (C=O), 1652, 1452, 1394, 1341, 1316. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.33–7.21 (m, 2H, arom CH and solvent), 7.17–7.12 (m, 2H, arom CH), 5.37–5.31 (m, 1H, OC<u>H</u>CH_2), 2.98–2.90 (m, 2H), 2.72–2.58 (br m, 1H), 2.52–2.36 (br m, 1H), 2.14–2.02 (br m, 1H), 1.70–1.55 (br m, 1H), 1.47–1.23 (br m, 4H), 0.89–0.82 (t, ^3J = 6.8 Hz, 3H, CH_3). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 172.9 (C=O), 158.9, 137.9, 130.7, 128.8, 128.1, 127.0, 125.5, 124.1, 80.6, 33.4, 28.1, 26.7, 22.4, 18.2, 13.9. – MS (FD): *m/z* (%) = 242.9 (17, M^+ + 1), 241.9 (100, M^+).

$C_{16}H_{18}O_2$	Calcd.:	C 79.31	H 7.49
(242.3)	Found:	C 79.34	H 7.51.

3-[Cyclopentadienyl(dicarbonyl)iron]-4-(1-hydroxy-pentyl)-1,2-dihydronaphthalene (**7a**)

Yellow oil which solidified on standing to a yellow amorphous solid, *m.p.* 47–48 °C. – TLC (petroleum ether/EtOAc

2:1): R_f = 0.36. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 2012 and 1956 (CO-ligands). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3478, 2954, 2939, 2930, 2871, 2861, 2006 and 1948 (CO-ligands), 1532, 1479, 1467, 1457, 1447, 1431, 1272, 1251, 1040, 1016. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.92 (d, ^3J = 7.3 Hz, 1H, arom CH), 7.29–7.03 (m, 3H, arom CH and solvent), 4.92 (s, 5H, C_5H_5), 2.56–2.50 (m, 4H), 2.00 (br m, 1H), 1.66 (br m, 2H, OH* and CH_2), 1.40–1.21 (m, 4H), 0.86–0.83 (m, 3H, CH_3). * Determined by D_2O-exchange. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 216.6, 214.6 (s, CO-ligands), 153.6 (s), 145.5 (s), 137.0 (s), 134.8 (s), 126.5 (d), 125.7 (d), 124.9 (d), 123.2 (d), 85.5 (d, C_5H_5), 81.2 (d, C<u>H</u>(OH)), 47.3 (t, =C(Fp)C<u>H</u>$_2$), 34.8 (t), 31.2 (t), 29.4 (t), 22.9 (t), 14.1 (q, CH_3). – MS (FD): *m/z* (%) = 393.0 (28, M^+ + 1), 392.0 (100, M^+).
$C_{22}H_{24}FeO_3$ (392.3).

1-Methyl-4,5-dihydronaphtho[1,2-c]furan-3(1H)-one (**6b**)

Table 1, entry 3: By following the general procedure 505 mg (1.5 mmol) **5d** dissolved in 30 ml THF were treated with 1.0 ml MeLi. Stirring was continued for 45 min at –78 °C and at room temperature for 70 min. Then the reaction mixture was worked-up with 100 ml buffer pH = 6 and 100 ml ether. Purification by flash chromatography on Florisil with petroleum ether/ether (gradient, 20:1 to 15:1 to 10:1) gave a product mixture of the α,β-butenolide **6b** and the γ-lactone **8a** (120 mg, 40%) in a ratio of 79:21.

Table 1, entry 4: By following the general procedure 290 mg (0.87 mmol) **5d** dissolved in 15 ml THF were treated with 0.6 ml MeLi. Stirring was continued for 2h 45 min at –78 °C and at room temperature for 3h 45 min. Then the reaction mixture was worked-up with the following mixture: 30 ml buffer pH = 7, 50 ml saturated ammonium chloride solution and 50 ml ether. Purification by flash chromatography on silica gel with petroleum ether/EtOAc (gradient, 10:1 to 5:1, then EtOAc, 1% triethylamine) afforded **6b** (75 mg, 45%) as an amorphous solid.

1-Methyl-4,5-dihydronaphtho[1,2-c]furan-3(1H)-one (**6b**)

Yellow-brown oil which solidified to a beige amorphous solid on standing. – TLC (petroleum ether/ether 1:1): R_f = 0.36. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 3059, 2984, 2937, 2899, 1746 (C=O), 1655, 1569, 1453, 1428, 1393, 1375, 1338, 1316, 1304, 1280, 1247, 1202, 1185, 1165, 1092, 1077, 1041. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.38–7.23 (m, 3H, arom CH), 7.16–7.12 (m, 1H, arom CH), 5.40 (m, 1H, C<u>H</u>(CH_3)), 3.01–2.93 (m, 2H), 2.73–2.34 (m, 2H), 1.59 (d, ^3J = 6.8 Hz, 3H, CH_3). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 172.8 (s, C=O), 160.3 (s), 137.9 (s), 130.8 (d), 128.8 (d), 127.8 (s), 127.0 (d), 124.9 (s), 124.2 (d), 76.9 (d, O<u>C</u>H(CH_3)), 28.0 (t), 19.9 (q, CH_3), 18.1 (t). – MS (FD): *m/z* (%) = 199.9 (100, M^+). $C_{13}H_{12}O_2$ (200.2).

Selected Data of the γ-lactone **8a**: – TLC (petroleum ether/ether 1:1): R_f = 0.32. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1770 (C=O). – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.22–7.00 (m, 4H, arom CH), 5.02 (m, 1H), 3.92 (t, J = 9.0 Hz, 1H), 3.16–3.02 (m, 1H), 2.73–2.62 (m, 2H), 2.23–2.08 (m, 1H), 1.99–1.81 (m, 1H), 1.08 (d, ^3J = 6.8 Hz, 3H, CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 178.8 (C=O), 138.2, 131.9, 130.2, 129.1, 126.9, 126.1, 79.3, 41.2, 40.2, 27.7, 23.7, 18.6. $C_{13}H_{14}O_2$ (202.2).

5-(tert-Butyl)-4,5,6,7-tetrahydro-3-methyl-1(3H)isobenzofuranone (**6c**)

Table 1, entry 6: By following the general procedure 1.32 g (3.9 mmol) **5b** dissolved in 60 ml THF were treated with 2.7 ml MeLi. Stirring was continued at –78 °C for 35 min and at room temperature for 1h 10 min. The reaction mixture was worked-up with 50 ml buffer pH = 7, 50 ml water and 50 ml ether. Purification by flash chromatography on Florisil with petroleum ether/EtOAc (gradient, 10:1 to 8:1 to 6:1) gave a product mixture of **6c** and the γ-lactone **8b** (425 mg, 53%) in a ratio of 60:40 according to ^{1}H NMR spectroscopy.
Table 1, entry 7: According to the general procedure 1.04 g (3.04 mmol) **5b** dissolved in 50 ml THF were treated with 2.4 ml MeLi. Stirring was continued at –78 °C for 45 min and at room temperature for 75 min. The reaction mixture was worked-up with 5 ml D_2O and stirred vigorously prior addition of 100 ml buffer pH = 6, 50 ml brine and 50 ml ether. The crude product mixture was purified by flash chromatography on Florisil with petroleum ether/ EtOAc (30:1 to 20:1) to yield 125 mg (20%) of the α,β-butenolide **6c** and 193 mg (30%) of the deuterated γ-lactone **8c**.
Table 1, entry 10: According to the general procedure 0.61 g (1.78 mmol) **5b** dissolved in 30 ml THF were treated with 1.2 ml MeLi. After having been stirred for 30 min at –78 °C 505 µl (3.56 mmol, 2 equiv) diisopropylamine were added *via* syringe. Stirring was continued at –78 °C for additional 70 min and at room temperature for 50 min. The reaction mixture was worked-up with the following mixture: 50 ml buffer pH = 7, 50 ml brine and 50 ml ether. The combined organic layer was washed with saturated ammonium chloride solution. The crude product mixture was purified by flash chromatography on Florisil with petroleum ether/EtOAc (30:1) to separate **8b** (98 mg, 26%), whereas with petroleum ether/EtOAc 20:1 the α,β-butenolide **6c** (118 mg, 32%) was obtained.

Table 1, entry 12: According to the general procedure 1.26 g (3.68 mmol) **5b** dissolved in a mixture of 70 ml dichloromethane and 20 ml dioxane were treated with 2.9 ml MeLi. After having been stirred at –78 °C for 80 min and at room temperature for 21 h the reaction mixture was hydrolyzed with 100 ml buffer pH = 7 and worked-up as described above. The combined organic layer was washed with brine (100 ml), 1N HCl (100 ml) and water (100 ml). Purification by flash chromatography on silica gel with petroleum ether/EtOAc (gradient, 50:1 to 25:1 to 10:1, 1% triethylamine) provided **6c** (450 mg, 59%) as a colourless liquid.

5-(tert-Butyl)-4,5,6,7-tetrahydro-3-methyl-1(3H)isobenzofuranone (**6c**)

Colourless liquid. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.58. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 3305, 2961, 2869, 1752 (C=O), 1683, 1471, 1452, 1438, 1424, 1396, 1367, 1332, 1313, 1295, 1256, 1226, 1180, 1163, 1126, 1102, 1083, 1039, 1016. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.84 (q, ^3J = 6.8 Hz, 1H, H-3), 2.44–2.20 (m, 2H), 2.04–1.93 (m, 2H), 1.48–1.31 (m, 1H), 1.37 (d, ^3J = 6.8 Hz, 3H, CH_3), 1.21–1.10 (m, 1H), 0.95–0.82 (m, 1 H), 0.91 (s, 9H, C(CH_3)$_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 173.2 (s, C=O), 165.7 (s), 125.8 (s), 78.9 (d, C-3), 44.0 (d, C-5), 32.3 (s, <u>C</u>(CH_3)$_3$), 27.2 (q, C(<u>C</u>H$_3$)$_3$), 24.4 (t), 23.3 (t), 20.8 (t), 18.4 (q, CH_3). –

MS (EI): *m/z* (%) = 208 (18, M^+), 193 (6, $M^+ - CH_3$), 165 (78, $M^+ - CH_3$, CO), 152 (28), 107 (13), 81 (14), 79 (14), 57 (100), 43 (31).

$C_{13}H_{20}O_2$ (208.3)	Calcd.:	C 78.48	H 6.59
$C_{17}H_{20}O_2 \cdot 0.6\ H_2O$	Calcd.:	C 71.26	H 9.75
(219.1)	Found:	C 71.21	H 9.87.

5-(tert-Butyl)-perhydro-3-methyl-isobenzofuranone (**8b**)

Colourless liquid. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.58. – IR (film, NaCl): $\tilde{\nu}$/cm^{-1} = 2952, 2870, 1765 (C=O), 1476, 1471, 1388, 1366, 1344, 1325, 1296, 1281, 1241, 1225, 1203, 1185, 1145, 1138, 1125, 1067, 1045. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 4.64 (dq, ^3J = 6.9 Hz, 1H, H-3), 2.75–2.54 (m, 2H), 2.03–1.90 (m, 1H), 1.78–1.49 (m, 3H), 1.43–1.22 (m, 2 H), 1.36 (d, ^3J = 6.8 Hz, 3H, CH_3), 0.91–0.79 (m, 3H), 0.83 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 179.8 (s, C=O), 78.9 (d, C-3), 41.2 (d), 39.8 (d), 36.2 (d), 33.3 (s, $\underline{C}(CH_3)_3$), 27.1 (q, $C(\underline{C}H_3)_3$), 22.8 (t), 22.3 (t), 21.4 (t), 17.0 (q, CH_3). – MS (EI): *m/z* (%) = 210 (6, M^+), 195 (3, $M^+ - CH_3$), 154 (29), 136 (9), 109 (38), 81 (15), 79 (14), 67 (20), 57 (100), 43 (16).

$C_{13}H_{22}O_2$	Calcd.:	C 74.24	H 10.54
(210.3)	Found:	C 73.89	H 9.72.

5-(tert-Butyl)-3a,7a-dideutero-4,5,6,7-tetrahydro-3-methyl-1(3H)isobenzofuranone (**8c**)

Colourless liquid. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.58. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1764 (C=O). – ^{1}H NMR (400 MHz, $CDCl_3$, deuteration rate 94%): δ/ppm = 4.61 (q, ^3J = 6.7 Hz, 1H, H-3), 1.94 (dt, ^3J = 13.8 Hz, ^3J = 5.8 Hz, 1H), 1.72–1.64 (m, 1H), 1.57–1.49 (m, 2H), 1.34 (d, ^3J = 6.5 Hz, 3H, CH_3), 1.24–1.19 (m, 1H), 1.14–1.05 (m, 2H), 0.81 (s, 9H, $C(CH_3)_3$). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 179.5 (C=O), 78.7 (C-3), 41.3, 39.2 (t, $^1J_{C,D}$ = 20.3 Hz), 35.6 (t, $^1J_{C,D}$ = 20.3 Hz), 33.2 ($\underline{C}(CH_3)_3$), 27.0 ($C(\underline{C}H_3)_3$), 22.8, 22.3, 21.3, 17.0. $C_{13}H_{20}D_2O_2$ (212.3).

Methyl-substituted steroidal α,β-Butenolide (**6d**)

Table 1, entry 13: Following the general procedure, the iron complex **5c** (240 mg, 0.42 mmol) dissolved in THF (10 ml) was treated with MeLi (0.28 ml, 1.6N solution in ether). The crude product was purified by flash chromatography on silica gel with petroleum ether/methyl *tert*-butylether (12:1, 0.1% triethylamine). Yield 98 mg (53%), colourless amorphous solid, *m.p.* 95–98 °C; mixture of diastereomers: 50:50 (^{1}H NMR). – TLC (petroleum ether/EtOAc 4:1): R_f = 0.69. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1747 (C=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 2932, 2868, 1762, 1687, 1467, 1446, 1383, 1320, 1056, 1034. – ^{1}H NMR (400 MHz, $CDCl_3$, * = diastereomer): δ/ppm = 4.85–4.76 (m, 1H, $OC\underline{H}CH_3$), 2.23–2.12 (m, 2H, H-1a, H-4a), 1.99 (dt, ^2J = 12.6 Hz, ^3J = 3.2 Hz, 1H, H-12a), 1.91/1.89* (br m, 1H, H-1b), 1.85–1.74 (m, 2H, H-4b, H-16a), 1.69 (m, 1H, H-7a), 1.61–0.92 (m, together with CH_3-groups, 20H, H-5, H-6a, H-6b, H-8, H-11a, H-11b, H-12b, H-14, H-15a, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b, H-25), 1.35/1.34* (d, ^3J = 6.7 Hz, 3H, $OCHC\underline{H}_3$), 0.91–0.83 (m, together with CH_3-groups, 1H, H-7b), 0.89 (d, ^3J = 6.7 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.5 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.82–0.76 (m, 1H, H-9), 0.71/0.70* (s, 3H, 19-CH_3), 0.65 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$, * = diastereomer): δ/ppm = 173.1 (s, C=O), 164.30/164.27* (s, C-2), 124.67/124.64* (s, C-3), 79.4/78.7* (d, $O\underline{C}HCH_3$), 56.3 (d, C-14 and C-17), 53.68/53.63* (d, C-9), 42.4 (s, C-13), 41.66/41.58* (d, C-5), 39.8 (t, C-12), 39.5 (t, C-24), 37.44/37.38* (t, C-1), 36.1 (t, C-22), 35.82 (s, C-10), 35.76 (d, C-20), 35.70 (d, C-8), 31.5 (t, C-7), 28.6 (t, C-6), 28.1 (t, C-16), 27.9 (d, C-25), 24.72/24.68* (t, C-4), 24.2 (t, C-15), 23.8 (t, C-23), 22.7 and 22.5 (q, C-26 and C-27), 21.2 (t, C-11), 18.7 (q, C-21), 18.3/18.1* (q, $OCH\underline{C}H_3$), 12.05/12.01* (q, C-19), 11.93 (q, C-18). – MS (EI): *m/z* (%) = 441.2 (34, M^+ + 1), 440.3 (100, M^+), 424.9 (8, $M^+ - CH_3$), 326.8 (8), 315.0 (8), 285.0 (46), 175.7 (14), 161.7 (11), 148.6 (10). – MS (FD): *m/z* (%) = 441.5 (32, M^+ + 1), 440.5 (100, M^+). – HRMS ($C_{30}H_{48}O_2$): calcd. 440.3642, found 440.3639. $C_{30}H_{48}O_2$ (440.7).

n-Butyl-substituted steroidal α,β-Butenolide (**6e**)

Table 1, entry 14: Following the general procedure, the iron complex **5c** (210 mg, 0.36 mmol) dissolved in THF (10 ml) was treated with *n*-butyllithium (0.24 ml, 1.6N solution in hexane). The crude product was purified by flash chromatography on silica gel with petroleum ether/methyl *tert*-butylether (12:1, 0.1% triethylamine). Due to an impurity a second flash chromatography was necessary (Florisil, petroleum ether/EtOAc 10:1). Yield 54 mg (31%), colourless amorphous solid, *m.p.* 105–108 °C; mixture of diastereomers: 50:50 (^{1}H NMR). – TLC (petroleum ether/ether 4:1, * = diastereomer): R_f = 0.38/0.31*. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1747 (C=O). – ^{1}H NMR (400 MHz, $CDCl_3$, * = diastereomer): δ/ppm = 4.76*/4.70 (m, 1H, $OC\underline{H}CH_2$), 2.22–2.13 (m, 2H, H-1a, H-4a), 1.99 (dt, ^2J = 12.6 Hz, ^3J = 3.2 Hz, 1H, H-12a), 1.88–1.76 (m, 4H, H-1b, H-4b, H-16a, $OCHC\underline{H}_2CH_2$/H-a), 1.68 (m, 1H, H-7a), 1.60–0.75 (m, together with CH_3-groups, 30H, H-5, H-6a, H-6b, H-7b, H-8, H-9, H-11a, H-11b, H-12b, H-14, H-15a, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b, H-25, $OCHC\underline{H}_2CH_2$/H-b, $OCHCH_2C\underline{H}_2$/H-a and H-b, $C\underline{H}_2CH_3$, $CH_2C\underline{H}_3$), 0.88 (d, ^3J = 6.5 Hz, 3H, 21-CH_3), 0.84 (d, ^3J = 6.7 Hz, 3H, 26-CH_3), 0.83 (d, ^3J = 6.7 Hz, 3H, 27-CH_3), 0.71 (s, 3H, 19-CH_3), 0.65 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$, * = diastereomer): δ/ppm = 173.4 (s, C=O), 163.1 (s, C-2), 125.3*/125.2 (s, C-3), 83.3/82.5* (d, $O\underline{C}HCH_2$), 56.39 and 56.36 (d, C-14 and C-17), 53.7 (d, C-9), 42.5 (s, C-13), 41.7 (d, C-5), 39.9 (t, C-12), 39.5 (t, C-24), 37.9/37.8* (t, C-1), 36.2 (t, C-22), 35.9 (s, C-10), 35.8 (d, C-20), 35.7 (d, C-8), 32.1/32.0* (t, $OCH\underline{C}H_2CH_2$), 31.6 (t, C-7), 28.6 (t, C-6), 28.2 (t, C-16), 28.0 (d, C-25), 26.7/26.4* (t, $OCHCH_2\underline{C}H_2$), 24.83/24.77* (t, C-4), 24.2 (t, C-15), 23.9 (t, C-23), 22.78 and 22.54 (q, C-26 and C-27), 22.46 (t, $\underline{C}H_2CH_3$), 21.36*/21.29 (t, C-11), 18.7 (q, C-21), 13.8 (q, $CH_2\underline{C}H_3$), 12.2*/12.1 (q, C-19), 12.0 (q, C-18). – MS (EI): *m/z* (%) = 483.3 (37, M^+ + 1), 482.6 (100, M^+), 467.2 (15, $M^+ - CH_3$), 426.1 (4, $M^+ - C_4H_8$), 397.1 (27, $M^+ - C_6H_{13}$), 369.0 (15), 342.9 (11), 341.9 (14), 327.2 (79), 256.7 (18), 56.4 (23, $C_4H_8^+$). – MS (FD): *m/z* (%) = 483.6 (41, M^+ + 1), 482.6 (100, M^+). – HRMS ($C_{33}H_{54}O_2$): calcd. 482.4110, found 482.4128. $C_{33}H_{54}O_2$ (482.8).

3,4,5,6-Tetrahydro-3-methyl-1H-benzo[3,4]cyclohepta[1,2-c]furan-1-one (**6f**)

Table 1, entry 15: By following the general procedure 800 mg (2.3 mmol) **5e** dissolved in 30 ml THF were treated with 1.5 ml MeLi. Stirring was continued for 90 min at

–78 °C and at room temperature for 3.5 h. Then the reaction mixture was worked-up with 100 ml buffer (pH = 6) and 130 ml ether. Purification by flash chromatography on Florisil with petroleum ether/EtOAc (gradient 18:1 to 2:1, 1% triethylamine) gave **6f** (226 mg, 46%) as pale yellow-green crystals, *m.p.* 118–119 °C. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.37. – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3079, 3055, 2984, 2976, 2950, 2935, 2929, 2885, 2868, 1739 (C=O), 1642, 1492, 1456, 1448, 1414, 1375, 1328, 1315, 1303, 1167, 1144, 1100, 1087, 1067, 1047, 1042. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 8.16 (d, ^3J = 8.3 Hz, 1H, arom CH), 7.28–7.08 (m, 3H, arom CH), 4.86 (q, ^3J = 6.7 Hz, 1H, H-3), 2.76–2.71 (m, 2H), 2.65–2.49 (m, 2H), 2.07–1.96 (m, 2H), 1.45 (d, ^3J = 6.8 Hz, 3H, CH_3). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 172.4 (C=O), 166.0, 142.9, 128.94, 128.92, 128.8, 128.4, 126.2, 123.5, 78.4 (C-3), 34.7, 29.4, 26.4, 19.2. – MS (EI): *m/z* (%) = 214 (76, M^+), 171 (91, $M^+ - CH_3$, CO), 143 (100), 128 (48), 115 (32), 91 (7), 83 (7), 69 (8), 55 (11), 43 (12).

$C_{14}H_{14}O_2$	Calcd.:	C 78.48	H 6.59
(214.3)	Found:	C 78.41	H 6.62.

3-n-Butyl-3,4,5,6-tetrahydro-1H-benzo[3,4]cyclohepta[1,2-c]furan-1-one (**6g**)

Table 1, entry 16: In accordance with the general procedure 800 mg (2.3 mmol) **5e** dissolved in 30 ml THF were treated with 1.5 ml *n*BuLi. Stirring was continued for 90 min at –78 °C and at room temperature for 1h. Then the reaction mixture was worked-up (100 ml buffer pH = 6, 130 ml ether). Purification by flash chromatography on Florisil with petroleum ether/EtOAc (gradient, 22:1 to 3:1, then EtOAc, 1% triethylamine) gave **6g** (235 mg, 40%) as a yellow-brown oil, which solidified to a beige solid, *m.p.* 52 °C. – TLC (petroleum ether/EtOAc 4:1): R_f = 0.61. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 1745 (C=O). – IR (THF): $\tilde{\nu}$/cm^{-1} = 1754 (C=O). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3449, 2952, 2932, 2871, 1735 (C=O), 1693, 1643, 1494, 1469, 1451, 1409, 1339, 1301, 1172, 1148, 1107, 1081, 1018. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 8.18 (d, ^3J = 6.8 Hz, 1H, arom CH), 7.31–7.11 (br m, 3H, arom CH and solvent), 4.83 (t, ^3J = 6.8 Hz, 1H, OC<u>H</u>CH_2), 2.77–2.74 (m, 2H), 2.59–2.55 (m, 2H), 2.08–1.94 (m, 3H), 1.64–1.38 (br m, 5H), 0.91 (br t, 3H, CH_3). – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 172.7 (CO), 164.6, 142.8, 129.0, 128.8, 128.4, 126.3, 124.3, 82.0, 34.7, 32.5, 29.4, 26.6, 26.2, 22.5, 13.9. – MS (FD): *m/z* (%) = 257.9 (6, $M^+ + 2$), 256.9 (20, $M^+ + 1$), 255.9 (100, M^+).

$C_{17}H_{20}O_2$ (256.3)	Calcd.:	C 78.48	H 6.59
$C_{17}H_{20}O_2 \cdot ½\ H_2O$	Calcd.:	C 76.95	H 7.98
(265.4)	Found:	C 76.80	H 7.95.

9-[Cyclopentadienyl(dicarbonyl)iron]-6,7-dihydro-5H-2-[1-hydroxyethyl]-benzocycloheptene (**7b**)

Table 1, entry 17: To the iron complex **5e** (800 mg, 2.3 mmol) dissolved in 30 ml THF was added 1.5 ml MeLi dropwise *via* syringe. The solution was stirred at –78 °C until complete consumption of the starting material (TLC and IR monitoring). Then the solution was added under vigorous stirring to buffer solution (100 ml, pH = 6). Subsequently 130 ml ether were added and stirring was continued for 5 min. Work-up as described above for the synthesis of **6** afforded the crude product. Purification by column chromatography on silica gel with petroleum ether/EtOAc (10:1 to 4:1 to 1:1) as eluent gave **7b**. The solvent was evaporated and the yellow-brown solid was dissolved in dichloromethane, dried ($MgSO_4$), and the solution concentrated *in vacuo* to yield 598 mg (72%) of **7b** as a yellow amorphous solid, *m.p.* 43–44 °C. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.46. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 2013 and 1959 (CO-ligands). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3428, 2932, 2850, 2008 and 1953 (CO-ligands), 1595, 1472, 1450, 1432, 1420, 1365, 1327, 1265, 1221, 1162, 1146, 1101, 1086, 1056, 1018. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.15–7.05 (m, 2H, arom CH), 6.97–6.94 (m, 2H, arom CH), 5.05/4.96$^{\#}$ (s, 5H, C_5H_5), 4.83 (q, ^3J = 7.3 Hz, 1H, C<u>H</u>(CH_3)), 2.43–2.35 (m, 2H), 2.21–2.13 (m, 1H), 1.85–1.74 (m, 3H), 1.62 (br s, 1H, OH*), 1.45/1.31$^{\#}$ (d, ^3J = 6.4 Hz, 3H, CH_3). * Determined by D_2O-exchange; $^{\#}$ due to diastereotopic groups two signals were observed. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 217.4, 216.3 (CO-ligands), 155.3, 151.2, 149.9, 135.9, 129.5, 127.2, 125.6, 124.5, 85.7/85.4$^{\#}$ (C_5H_5), 75.4/75.3$^{\#}$ (<u>C</u>HOH), 35.1/35.0$^{\#}$, 31.9/31.7$^{\#}$, 26.6/26.4$^{\#}$, 22.4/21.8$^{\#}$. $^{\#}$ Due to diastereotopic groups two signals were observed. – MS (FD): *m/z* (%) = 365.1 (19, $M^+ + 1$), 364.1 (100, M^+), 214.0 (27).

$C_{20}H_{20}FeO_3$	Calcd.:	C 65.95	H 5.53
(364.2)	Found:	C 66.08	H 5.48.

9-[Cyclopentadienyl(dicarbonyl)iron]-6,7-dihydro-5H-2-[1-hydroxypentyl]-benzocycloheptene (**7c**)

Table 1, entry 18: A solution of **5e** (800 mg, 2.3 mmol) dissolved in 30 ml THF was treated with 1.5 ml *n*BuLi as described above. After having been stirred for four hours at –78 °C (TLC and IR monitoring) the reaction mixture was worked-up. Purification by chromatography on silica gel with petroleum ether/ether (2:1) and then with petroleum ether/EtOAc (4:1) gave **7c** (520 mg, 55%), slightly impure as a golden-yellow amorphous solid. Analytically pure material was obtained by flash chromatography on silica gel with petroleum ether/EtOAc (10:1 to 6:1) as eluent. Yellow amorphous solid, *m.p.* 47–48 °C. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.65. – IR (CH_2Cl_2): $\tilde{\nu}$/cm^{-1} = 2013 and 1959 (CO-ligands). – IR (THF): $\tilde{\nu}$/cm^{-1} = 2010 and 1957 (CO-ligands). – IR (KBr): $\tilde{\nu}$/cm^{-1} = 3428, 2932, 2856, 2008 and 1953 (CO-ligands), 1595, 1450, 1433, 1420, 1379, 1360, 1340, 1301, 1266, 1217, 1193, 1159, 1141, 1103, 1043, 1016. – ^{1}H NMR (200 MHz, $CDCl_3$): δ/ppm = 7.11 (br m, 2H, arom CH), 6.96 (br m, 2H, arom CH), 5.04/4.94$^{\#}$ (s, 5H, C_5H_5), 4.65–4.51 (br m, 1H, C<u>H</u>OH), 2.38 (br m, 2H), 2.11 (br m, 1H), 1.83–1.70 (br m, 5H), 1.62 (br s, 1H, OH*), 1.41 (br m, 4H), 0.95 (br m, 3H, CH_3). * Determined by D_2O-exchange; $^{\#}$ due to diastereotopic groups two signals were observed. – ^{1}H NMR (200 MHz, CD_2Cl_2): δ/ppm = 7.21–7.12 (m, 2H, arom CH), 7.01–6.91 (m, 2H, arom CH), 5.09/5.00$^{\#}$ (s, 5H, C_5H_5), 4.67–4.58/4.54–4.47$^{\#}$ (br m, 1H, C<u>H</u>OH), 2.51–2.30 (br m, 2H), 2.18–2.07 (m, 1H), 1.88–1.64 (br m, 5H), 1.58 (br s, 1H, OH), 1.46–1.39 (m, 4H), 0.97 (t, ^3J = 6.8 Hz, 3H, CH_3). $^{\#}$ Due to diastereotopic groups two signals were observed. – ^{13}C NMR (50.3 MHz, $CDCl_3$): δ/ppm = 216.3, 214.3 (s, CO-ligands), 155.4 (s), 151.0 (s), 149.8 (s), 136.0/135.7$^{\#}$ (s), 129.6 (d), 127.1 (d), 125.6 (d), 124.4/124.3$^{\#}$ (d), 85.8/85.5$^{\#}$ (d, C_5H_5), 80.0/79.8$^{\#}$ (d, O<u>C</u>HCH_2), 36.4 (t), 34.9 (t), 31.8 (t), 29.4/29.1$^{\#}$

(t), 27.0/26.9[#] (t), 23.2/23.0[#] (t), 14.3 (q). [#] Due to diastereotopic groups two signals were observed. – MS (FD): *m/z* (%) = 407.3 (6, $M^+ + 1$), 406.3 (100, M^+).

$C_{23}H_{26}FeO_3$	Calcd.:	C 67.99	H 6.45
(406.3)	Found:	C 66.75	H 6.01.

1-(1,5-Dimethylhexyl)-10a,12a-dimethyl-8-[(1S)-phenylethyl]-1,2,3,3a,3b,4,5,5a,6,7,8,9,10,10a,10b,11,12,12a-octadeca-hydrocyclopenta[5,6]naphtho[1,2-f]isoindol-7-on (**9**)

To the iron complex **5c** (0.66 g, 1.15 mmol) dissolved in dichloromethane (20 ml) was added (*S*)-phenylethylamine (0.15 ml, 1.21 mmol) at 0 °C in the dark followed by triethylamine (0.37 ml, 2.65 mmol). After one hour the reaction mixture was treated with $TiCl_4$ (1.15 ml, 1N solution in dichloromethane) and stirred for one hour at 0 °C. The solution was warmed to room temperature and stirred in the dark until IR monitoring indicated that the reaction was complete (13 hours). The reaction mixture was hydrolyzed by the addition of saturated aqueous ammonium chloride solution (50 ml), diluted with dichloromethane (50 ml) and 2N HCl (30 ml). This two-layer mixture was vigorously stirred for 5 min. The separated aqueous layer was extracted with dichloromethane (50 ml). The combined organic phases were washed with 2N HCl (2×50 ml), water (50 ml) and brine (50 ml), dried ($MgSO_4$), and then concentrated *in vacuo*. The concentrate was purified by flash chromatography (silica gel, petroleum ether/EtOAc 8:1 to 2:1). Yield 472 mg (77%), beige crystalline solid, *m.p.* 134–136 °C. – TLC (petroleum ether/EtOAc 2:1): R_f = 0.68. – IR (CH_2Cl_2): $\tilde{\nu}/cm^{-1}$ = 1667 (C=O). – IR (KBr): $\tilde{\nu}/cm^{-1}$ = 3439 (OH), 3086, 3061, 1684 (C=O), 1495, 1466, 1446, 1404, 1384, 1141, 1028. – ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.31–7.19 (m, 5H), 5.54 (q, ^3J = 7.0 Hz, 1H, C<u>H</u>(CH_3)), 3.60 (d, ^2J = 18.5 Hz, 1H, NCH_2-a), 3.38 (d, ^2J = 18.8 Hz, 1H, NCH_2-b), 2.20 (br d, ^2J = 17.3 Hz, 1H, H-4a), 2.11 (d, ^2J = 16.4 Hz, 1H, H-1a), 1.96 (dt, ^2J = 12.6 Hz, ^3J = 3.2 Hz, 1H, H-12a), 1.86-1.74 (m, 3H, H-1b, H-4b, H-16a), 1.66 (m, 1H, H-7a), 1.59-1.43 (m, 3H, H-6a, H-15a, H-25), 1.40–0.91 (m, 17H, H-5, H-6b, H-8, H-11a, H-11b, H-12b, H-14, H-15b, H-16b, H-17, H-20, H-22a, H-22b, H-23a, H-23b, H-24a, H-24b), 0.89–0.81 (m, together wtih 21-CH_3, 1H, H-7), 0.87 (d, ^3J = 6.8 Hz, 3H, 21-CH_3), 0.83 (d, ^3J = 6.8 Hz, 3H, 26-CH_3), 0.82 (d, ^3J = 6.5 Hz, 3H, 27-CH_3), 0.75–0.69 (m, together with 19-CH_3, 1H, H-9), 0.71 (s, 3H, 19-CH_3), 0.63 (s, 3H, 18-CH_3). – ^{13}C NMR (100.6 MHz, $CDCl_3$): δ/ppm = 171.2 (s, C=O), 149.3 (s, C-2), 141.6 (s, C-*i*), 130.5 (s, C-3), 128.5 (d, C-*m*), 127.2 (d, C-*p*), 127.0 (d, C-*o*), 56.4 and 56.3 (d, C-14 and C-17), 53.8 (d, C-9), 49.0 (t, NCH_2), 48.8 (d, Ph<u>C</u>H(CH_3)), 42.5 (s, C-13), 41.7 (d, C-5), 40.0 (t, C-12), 39.5 (t, C-24), 39.0 (t, C-1), 36.2 (t, C-22), 36.0 (s, C-10), 35.7 (2 × d, C-8 and C-20), 31.7 (t, C-7), 28.7 (t, C-6), 28.2 (t, C-16), 28.0 (d, C-25), 25.3 (t, C-4), 24.2 (t, C-15), 23.8 (t, C-23), 22.8 and 22.5 (q, C-26 and C-27), 21.2 (t, C-11), 18.7 (q, C-21), 17.7 (q, PhCH(<u>C</u>H_3)), 12.1 (q, C-19), 12.0 (q, C-18). – MS (FD): *m/z* (%) = 530.7 (100, $M^+ + 1$), 529.7 (49.3, M^+).

$C_{37}H_{55}NO$ (529.8)	Calcd.:	C 83.87	H 8.30	N 5.86
$C_{37}H_{55}NO \cdot ½\ H_2O$	Calcd.:	C 82.47	H 10.48	N 2.60
(538.8)	Found:	C 82.86	H 10.32	N 2.62.

References

[1] a) D. J. Hart, W.-L. Wu, A. P. Kozikowski, J. Am. Chem. Soc. **1995**, *117*, 9369; b) D. J. Hart, J. Li, W.-L. Wu, A. P. Kozikowski, J. Org. Chem. **1997**, *62*, 5023; c) S. Chackalmannil, R. J. Davies, T. Asberon, D. Doller, D. Leone, J. Am. Chem. Soc. **1996**, *118*, 9812; d) J. E. Baldwin, R. Chesworth, J. S. Parker, A. T. Russell, Tetrahedron Lett. **1995**, *36*, 9551

[2] G. Pattenden, L. Roberts, Tetrahedron Lett. **1996**, *37*, 4191

[3] G. Quinckert, H.-G. Schmalz, E. Walzer, T. Kowalczyk-Przewloka, G. Dürner, J. W. Bats, Angew. Chem. **1987**, *99*, 82; Angew. Chem. Int. Ed. Engl. **1987**, *26*, 61

[4] B. J. M. Jansen, C. T. Bouwman, A. de Groot, Tetrahedron Lett. **1994**, *35*, 2977

[5] R. N. Saicic, S. Z. Zard, Chem. Commun. **1996**, 1631

[6] R. M. Coates, J. W. Muskopf, P. A. Senter, J. Org. Chem. **1985**, *50*, 3541

[7] a) A. Cowell, J. K. Stille, Tetrahedron Lett. **1979**, 133; b) G. T. Crisp, A. G. Meyer, J. Org. Chem. **1992**, *57*, 6972; c) D. Yang, X.-Y. Ye, M. Xu, K.-W. Pang, N. Zou, R. M. Letcher, J. Org. Chem. **1998**, *63*, 6446

[8] K. Rück-Braun, Angew. Chem. **1997**, *109*, 526; Angew. Chem. Int. Ed. Engl. **1997**, *36*, 509

[9] K. Rück-Braun, T. Martin, M. Mikulás, Chem. Eur. J. **1999**, *5*, 1028

[10] K. Rück-Braun, C. Möller, Chem. Eur. J. **1999**, *5*, 1038

[11] C. Möller, M. Mikulás, F. Wierschem, K. Rück-Braun, Synlett **2000**, 182

[12] M. Mikulás, S. Rust, D. Schollmeyer, K. Rück-Braun, Synlett **2000**, 185

[13] The synthesis of β-halovinyl aldehydes from steroidal ketones has been reported in the past with modest success in low to moderate yield. a) G. W. Moersch, W. A. Neuklis, J. Chem. Soc. **1965**, 788; b) J. Schmitt, J. J. Panouse, P. J. Cornu, H. Pluchet, A. Hallot, P. Comoy, Bull. Soc. Chim. **1964**, 2760; c) J. Schmitt, J. J. Panouse, A. Hallot, P. J. Cornu, H. Pluchet, P. Comoy, Bull. Soc. Chim. **1964**, 2753

[14] Predominantly the β-chloro enal derived from the enolate at C-2 is formed due to preferred enolization of 3-keto-5α-steroids toward C-2. V. Kumar, S. J. Daum, M. R. Bell, M. A. Alexander, R. G. Christiansen, J. H. Ackerman, M. E. Krolski, G. M. Pilling, J. L. Herrmann Jr., R. C. Winneker, M. M. Wagner, Tetrahedron **1991**, *47*, 5099

[15] a) G. Stork, R. Terrell, J. Szmuszkovicz, J. Am. Chem. Soc. **1954**, *76*, 2029; b) G. Stork, A. Brizzolara, H. Landesman, J. Szmuszkovicz, R. Terrell, J. Am. Chem. Soc. **1963**, *85*, 207

[16] For syntheses of steroidal β-keto esters, see: a) S. Giacopello, M. E. Deluca, A. M. Seldes, Tetrahedron Lett. **1994**, *35*, 6643; b) L. N. Mander, S. P. Sethi, Tetrahedron Lett. **1983**, *24*, 5425

[17] E. Piers, H. L. Tse, Can. J. Chem. **1993**, *71*, 983

[18] S. V. Ley, N. Norman, W. P. Griffith, S. P. Marsden, Synthesis **1994**, 639

[19] R. Bucourt in Topics in Stereochemistry: E. L. Eliel, N. L. Allinger (Eds); Wiley, New York 1974, 159

[20] Details of the Crystal Structure Analysis: For the X-ray structure determination crystals of **5b** were obtained by crystallization from CH_2Cl_2 and petroleum ether. The data collections were performed in routine ω-scan, the structure was solved by direct methods (program: SIR 92) and refined by the full matrix least-squares method of SHELXL-97 (G. M. Sheldrick, Universität Göttingen 1997). All non-hydrogen atoms were refined anisotropically. The H-atoms were put into theoretical positions and refined using the riding model.

Diffractometer: Turbo-CAD4 (Enraf-Nonius); radiation: Cu-K_α with graphite monochromator. Further Details for **5b**: Crystal size: 0.064 × 0.192 × 0.320 mm^3; formula $C_{18}H_{22}FeO_3$; formula weight: 342.21; temperature: 298 K; crystal system: monoclinic; space group: $P2_1/c$; unit cell dimensions: a = 17.926 (2) Å, b = 6.3292 (5) Å, c = 16.571 (2) Å, β = 113.520 (5)°; volume: 1723.9 (3) $Å^3$; Z = 4; density (calculated): 1.319 g/cm^3; absorption coefficient: 7.09 mm^{-1}; F(000): 720; θ range for data collection: 1.5° to 75°; index ranges: $0 \le h \le 22$, $-7 \le k \le 0$, $-20 \le l \le 18$; reflections collected: 3541; independent reflections: 3541 (R_{sigma} = 0.060); reflections observed: 3226; parameters refined: 217; goodness-of fit on F^2: 1.029; final R indices [$I > 2\sigma(I)$]: R1 = 0.0631 for observed reflections; wR2 = 0.1880; R index (all data): 0.1293; largest diff. Peak and hole: 0.37/−0.32 e/$Å^3$. Crystallographic data (excluding structure factors) for the structure **5b** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no CCDC 147749. Copies of the data can be obtained, free of charge on application to the director, CCDC; 12 Union Road, Cambridge CB2 1EZ, UK, (fax: Int.code + (1223) 336-033; e-mail: deposit@ccdc.cam.ac.uk).

[21] K. Maruoka in Synthesis of Organometallic Compounds: S. Komiya (Ed); Wiley, New York 1997, 323
[22] D. Seebach, A. K. Beck, A. Studer in Modern Synthetic Methods: B. Ernst, C. Leumann (Eds.); Verlag Helvetica Chimica Acta, Basel/VCH, Weinheim 1995, 1
[23] C. Huynh, S. Julia, Bull. Soc. Chim. Fr. **1972**, 1794
[24] A. F. Casy, E. S. C. Wu, B. D. Whelton, Can. J. Chem. **1972**, *50*, 3998

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