Synthesis of A/B Ring Analogs of Territrem B and Evaluation of Their Biological Activities

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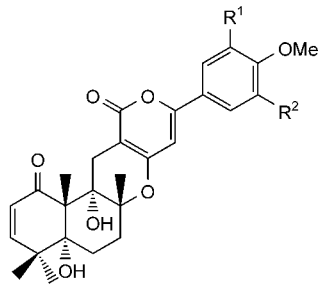
Two series of territrem B analogs, *i.e.*, **5**–**10**, containing both the 2-en-1-one-A-ring and the aromatic-E-ring pharmacophores were designed and synthesized from jujubogenin (**4a**). The anti-acetylcholinesterase (anti-AChE), anti-caspase-3, and other biological activities of these territrem-B analogs and their intermediates were assessed. Compound **9b**, **22a**, and **24f** were shown to be weak inhibitors of AChE. None of the synthesized compounds exhibited significant inhibitory activity on caspase-3. On the other hand, compounds **22e**, **24a, 7b**, and **8a** showed mild cytotoxicity on cultured KB cells, with IC_{50} values of 2.0, 3.5, 6.5, and 14 μM, respectively. In addition, compounds **23b** and **5f** were active against injury arising from oxygen-glucose deprivation.

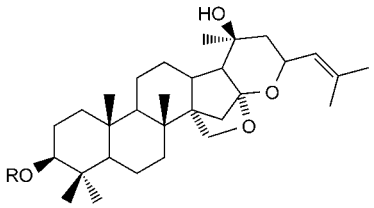
Introduction. – Diseases associated with an aging population are on the rise and becoming a serious issue around the world. *Alzheimer*'s disease (AD), a major health problem of many old people, is a disorder associated with progressive degeneration of memory and cognition functions. One of the strategies to treat this disease is the employment of acetylcholinesterase (AChE) inhibitors, a therapeutic approach based on the cholinergic deficiency hypothesis of AD [1][2]. This hypothesis rationalizes that the loss of acetylcholine (ACh) in the brain is one of the main causes of AD [2]. Consequently, inhibition of AChE has become an important treatment regimen because inhibiting the removal of ACh could improve the ACh level in the brain [3].

Arisugacin A (**1**) and B (**2**), and territrem B (**3**), which were isolated from the culture broth of *Penicillium* sp. FO-4259 and *Aspergillus terreus* 23-1, respectively, are members of the meroterpenoid family [4]. They show potent inhibitory activities against AChE with IC_{50} values in the range of 1 to 26 nM. Moreover, their inhibitory mechanism is different from the other known AChE inhibitors [5]. *Peng et al.* [6] proposed that the 2-en-1-one moiety in these compounds is essential for their inhibitory activities against AChE because modification of the A ring in territrem B resulted in a large reduction or even complete abolition of the inhibitory potency. *Zhao et al.* [7] had

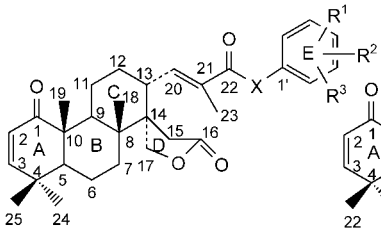
prepared A/B-ring analogs of territrem B starting from the triterpenoid jujubogenin (**4a**) and found that they possess inhibitory activity against AChE with an IC_{50} value of 10 μM. In addition, we proposed that the aromatic moiety in the E ring present in territrem B and arisugacins might be another pharmacophore apart from the 2-en-1-one moiety in the A ring. Therefore, attempts to combine the two potential pharmacophores into one molecule would constitute an extension of the structure-activity-relationship (SAR) investigation of these AChE inhibitors.



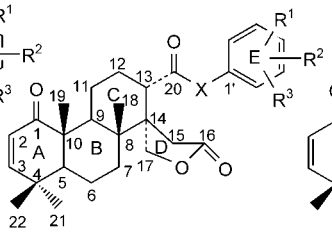
1 R^1= H, R^2= MeO; arisugacin A
2 R^1= H, R^2= H; arisugacin B
3 R^1= R^2= MeO; territrem B



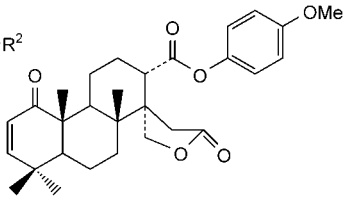
4a R=H; jujubogenin
b R=sugar; jujubogenin glycosides



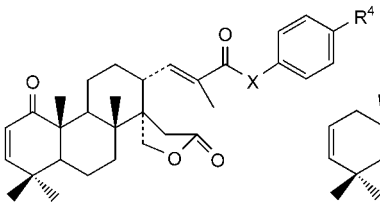
8 X=O
9 X=S
10 X=NH



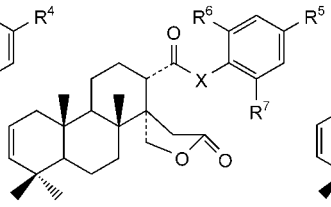
5 X=O
6 X=S
7 X=NH



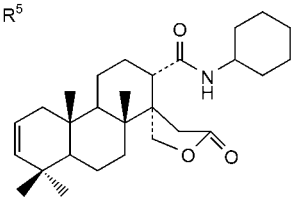
5f



7b X=NH, R^4=Cl
8a X=O, R^4=H
9b X=S, R^4=Cl



22a X=O, R^5=R^6=R^7=H
22e X=O, R^5=MeO, R^6=R^7=H
23b X=S, R^5=H, R^6=R^7=Cl
24a X=NH, R^5=R^6=R^7=H



24f

According to the prediction of a molecular-modelling study, *Chen et al.* [5] showed that the pyran and the terpenoid moieties of territrem B (**3**) bind to AChE by occupying a large portion of the AChE substrate channel (the gorge), making contacts

with 23 amino acids to block the access of ACh to the bottom of the long narrow gorge, at which the catalytic center of AChE is buried [5]. As a result of this binding, the substrate ACh is prevented from being hydrolyzed. To choke the entrance of the gorge, the molecule must adopt a suitable spatial length. This 'choking hypothesis' enspired us to design a series of molecules with different lengths as compared to the leads, *e.g.*, by preparing a molecule with an eight-bond linkage between C(1) of the 1-one function and C(1′) of the aromatic ring (see **5**–**7**), and a corresponding ten-bond-linkage molecule (see **8**–**10** in *Fig. 1*). To demonstrate the relationship between the length and bioactivity, the length of the C(1)···C(1′) distance in compounds **5**–**10** (named *Distance A*, abbreviated as Da) was also compared with that of territrem B (**3**) by means of SYBYL calculations (*Table 1*).

Table 1. *Comparison of Distances within Territrem B* (**3**) *and* **5**–**10** *by SYBYL Calculations.* See also *Fig. 1.*

	Eight-bond-linkage compounds				Ten-bond-linkage compounds		
	territrem B (**3**)	**5**	**6**	**7**	**8**	**9**	**10**
Da[a]) [Å]	11.809	12.017	12.885	11.965	14.861	15.673	14.783
Db[b]) [Å]	4.910	7.443	7.441	7.409	9.014	9.669	9.056
Dc[c]) [Å]	6.994	6.156	6.345	6.399	9.160	8.419	8.874
Dd[d]) [Å]	11.373	10.349	11.102	10.589	10.194	8.575	9.670

[a]) Da = sum of the length of bold bonds between C(1) and C(1′). [b]) Db = spatial distance between the two C=O of **5**–**10** and territrem B (**3**). [c]) Dc = spatial distance between the O-atom at C(1) and the X-atom of **5**–**10**, and the distance between the O-atom at C(1) and C(9) in territrem B (**3**). [d]) Dd = spatial distance between the geometric center of the 2-en-1-one moiety and that of the aromatic ring in territrem B (**3**) and **5**–**10**.

Furthermore, it is conceivable that the two carbonyl groups present in territrem B (**3**) might bind jointly with AChE in a cooperative manner to block the substrate channel. Therefore, the spatial distance between its two C=O groups (named *Distance B*, abbreviated as Db) might also be important; thus, the Db of **3** and **5**–**10** were also compared (*Table 1*). Based on the principle of bioisosterism, the aromatic thioesters and aromatic amides were synthesized. The two other spatial-distance factors Dc and Dd (see *Fig. 1*), *i.e.*, the spatial distances between C(1) = *O* and the X-atom of **5**–**10** (Dc) and between the geometrical center of the 2-en-1-one pharmacophore and the geometrical center of the aromatic ring of **5**–**10** (Dd), respectively, were also calculated (*Table 1*).

Since the supply of territrem B (**3**) is limited due to the low yield from fermentation, we started our semi-synthetic preparative work from the naturally abundant triterpenoid jujubogenin (**4a**), which was derived from jujubogenin glycosides **4b** isolated from the leaves of *Zizyphus jujuba* Var. *spinosa* (BUNGE) HU. With the view of looking into other potential biological activities related to the prevention and treatment of AD, these synthetic compounds were also tested for caspase-3 inhibition and protection against oxygen-glucose deprivation (OGD)-induced injury of rat primary neurons.

The synthesis and the evaluation of the biological activities of the compounds **5**–**10** are reported herein, together with a comparison of their spatial parameters Da to Dd.

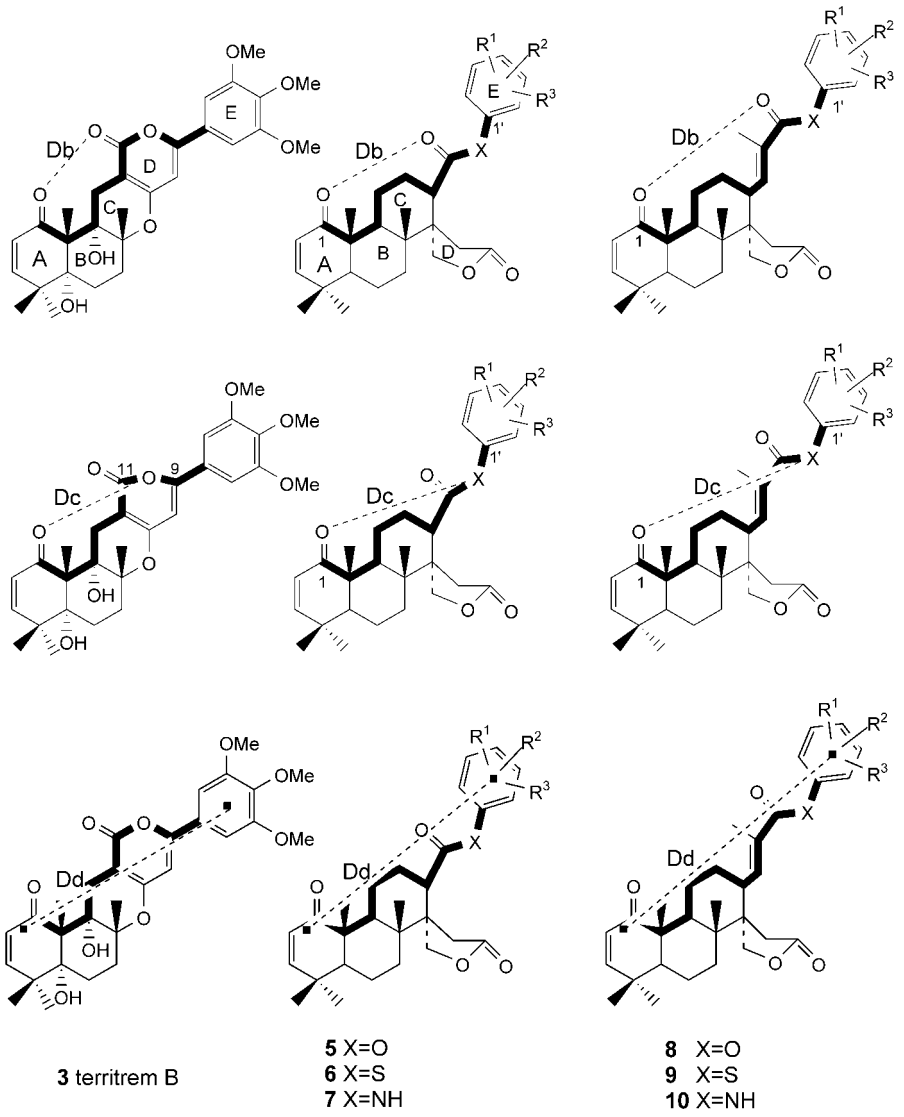
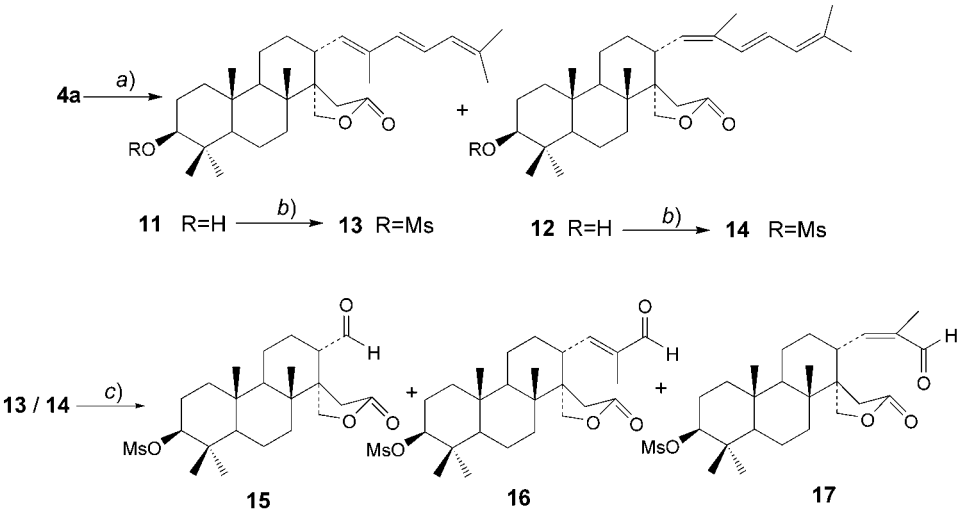


Fig. 1. *Eight-bond- and ten-bond-linked potential inhibitors* **5**–**7** *and* **8**–**10** *of acetylcholinesterase as compared to territrem B* (**3**). See also *Table 1*.

Results and Discussions. – *Synthesis.* The BuOH extract from the leaves of *Zizyphus jujuba* Var. *spinosa* (BUNGE) HU, containing jujubogenin glycosides **4b**, was treated under O_2 with NaOBu at 90° to give jujubogenin (**4a**) [7]. After acidic hydrolysis of pure jujubogenin **4a** (→ **11**/**12**) followed by mesylation, a mixture **13**/**14** of (20*E*)- and (20*Z*)-3-[(methylsulfonyl)oxy]-ebelin lactone [7] was obtained (*Scheme 1*). The crude mixture was ozonized and reduced with Me_2S [8] to afford the aldehydes **15**–**17** with yields of 44, 8, and 1%, respectively. However, when the

Scheme 1



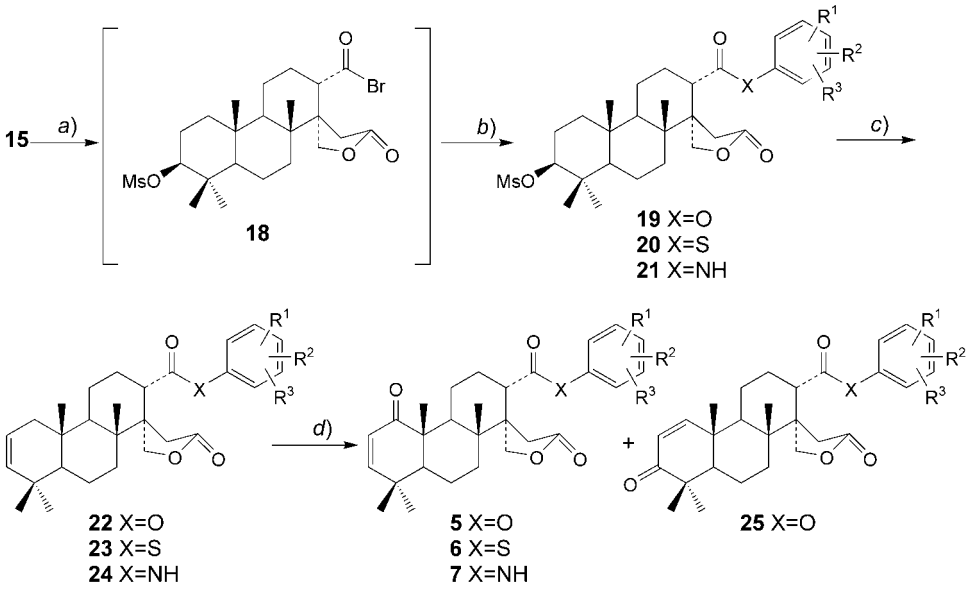
a) HCl/EtOH/H_2O 1 : 3 : 3, 80°, 5 h. *b*) MsCl, pyridine, 0°, 10 h. *c*) 1. O_3, MeOH/CH_2Cl_2 1 : 1, − 78°, 1 h; 2. Me_2S, − 10°, 1 h; 0°, 1 h; r.t., 1 h.

ozonide was reduced with Zn powder or with thiourea, the yields of aldehydes were unsatisfactory.

Oxidation of aldehyde **15** with *N*-bromosuccinimide (NBS) under irradiation [9] gave the corresponding acyl bromide **18**, which was treated directly with substituted phenols, thiophenols, or arylamines to afford the corresponding esters **19**, thioesters **20**, or amides **21** in 22.7–75.2% yield (*Scheme 2*). Compounds **19**–**21** were treated with Li_2CO_3 in refluxing *N*,*N*-dimethylacetamide (DMAC) [10] for 30 min to afford the 2-ene derivatives **22**–**24** in 28.3–83.9% yield. During the oxidation of **22** ($R^1 = R^3 = H$, $R^2 = H$, 4′-Cl or 4′-NO_2) by CrO_3 in AcOH at 80°, the yield of the corresponding target compounds **5** was not satisfactory (18–29.4%) due to formation of the 1-en-3-one by-products **25** by an unexpected radical rearrangement reaction. Furthermore, when the aromatic ring was substituted by an electron-donating group such as MeO or Me, it was difficult to obtain the expected enone products **5**–**7**, since the electron-donating aryl part was fragile under these oxidative conditions.

Alternatively, oxidation of the 2-ene compounds **22**–**24** with the mild oxidative reagent *N*-bromosuccinimide (NBS) in 1,4-dioxane in the presence of $CaCO_3$ [11] furnished the target enone compounds **5**–**7** directly in 20–37% yield as well as the 1-bromo products **26**–**28** (*Scheme 3*). The latter could be hydrolyzed to the enol derivatives, which were subsequently oxidized with pyridinium chlorochromate (PCC) to give enones **5**–**7** smoothly. As a result, the total yield of **5**–**7** was higher than that obtained from oxidation by CrO_3. Moreover, when the aromatic ring was substituted by an electron-donating group such as one or more MeO, the corresponding 2-en-1-one derivatives of **5**–**7** could also be obtained smoothly in good yield. Therefore, the preparative route of the 2-en-1-one moiety in **5**–**7** from 2-ene compounds **22**–**24** by oxidation with NBS is entirely feasible and, in fact, favorable.

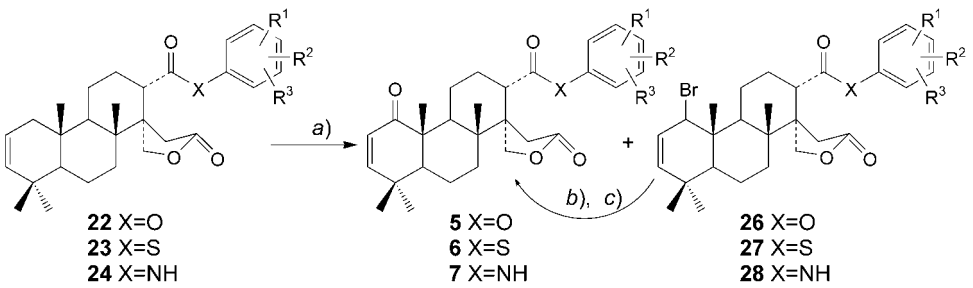
Scheme 2[a])



a) NBS, CCl_4, *hv*, reflux, 5 min. *b*) ArOH, ArSH, or $ArNH_2$, Et_3N, r.t., 1 h. *c*) Li_2CO_3, DMAC, reflux, 0.5 h. *d*) CrO_3, AcOH, 80°, 1 h.

[a]) For R^1, R^2, and R^3, see names in the *Exper. Part.*

Scheme 3[a])



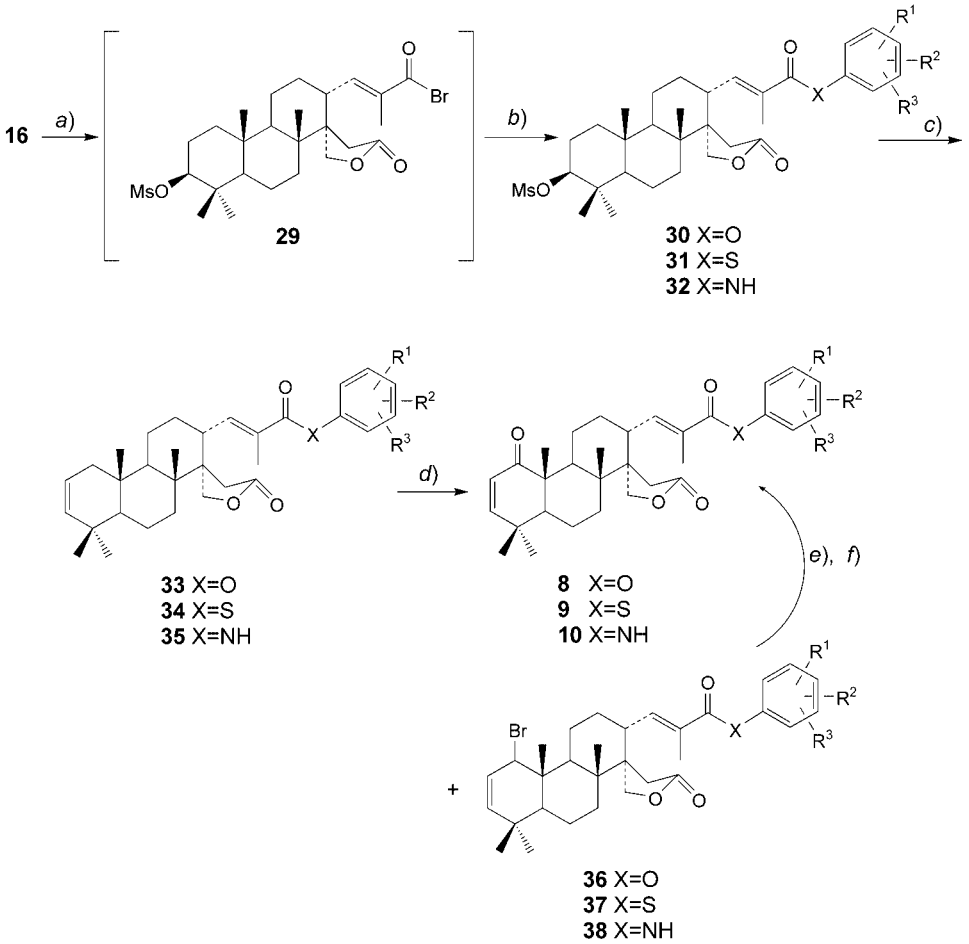
a) $CaCO_3$, NBS, dioxane, H_2O, 50°, 6 h, *hv*. *b*) $CaCO_3$, H_2O, dioxane, reflux, 5 h. *c*) PCC, CH_2Cl_2, reflux, 6 h.

[a]) For R^1, R^2, and R^3, see names in the *Exper. Part.*

By a similar method, the other series of territrem B analogs **8**–**10** and their intermediates **30**–**38** could also be prepared from the α,β-unsaturated aldehyde **16** *via* **29** (*Scheme 4*).

Evaluation of Biological Activities. All the synthesized compounds were evaluated for their AChE inhibitory activities according to the method of *Ellman et al.* [12]. However, only compounds **9b** and **24f** showed some activity against AChE with 70% inhibition at 10^{-4} M. Thus, probably some other factors apart from the 2-en-1-one and

Scheme 4[a])



a) NBS, CCl_4, *hv*, reflux, 5 min. *b*) ArOH, ArSH, or $ArNH_2$, Et_3N, r.t., 1 h. *c*) Li_2CO_3, DMAC, reflux, 0.5 h. *d*) $CaCO_3$, NBS, dioxane, H_2O, 50°, 6 h, *hv*. *e*) $CaCO_3$, H_2O, dioxane, reflux, 5 h. *f*) PCC, CH_2Cl_2, reflux, 6 h.

[a]) For R^1, R^2, and R^3, see names in the *Exper. Part.*

aromatic-E-ring pharmacophores contribute to the anti-AChE activity. The absence of the 5α-OH and 9α-OH groups in the territrem-B analogs might also affect their AChE-inhibition activity. Furthermore, it could be seen that the C(2)=C(3) moiety and the aliphatic E ring might also affect the anti-AChE activity. On the other hand, increasing the number of bonds between the two C=O groups did not improve the enzyme-inhibition activity. The superposition of compounds **5a**–**h**, **6a**–**c**, **7a**–**c**, **8a**–**d**, **9a**–**c**, and **10a** with territrem B (**3**), based on their C-atoms in the A and B rings, as calculated by the SYBYL program, showed that the aromatic E ring in these derivatives has apparently deviated from that in territrem B (*Figs. 2* and *3*). Therefore, subsequent

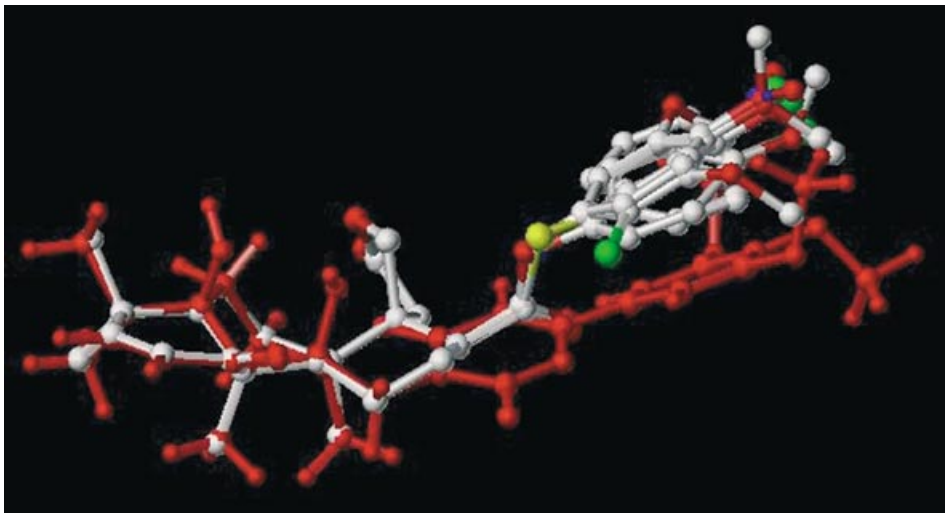


Fig. 2. *Superposition of compounds* **5a**–**h**, **6a**–**c**, **7a**–**c**, *and territrem B* (**3**; in red), *based on C-atoms in the A and B rings, obtained by SYBYL calculations*

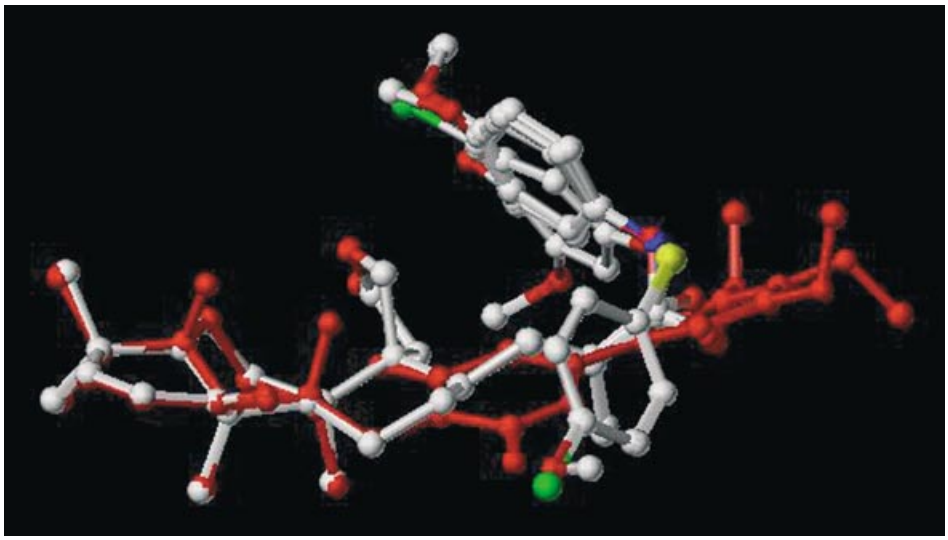


Fig. 3. *Superposition of compounds* **8a**–**d**, **9a**–**c**, **10a**, *and territrem B* (**3**; in red), *based on C-atoms in the A and B rings, obtained by SYBYL calculations*

modifications would focus on the synthesis of further analogs possessing a planar angle identical to that of territrem B, and with the enone and the aromatic rings combined in the same molecule with a suitable spatial length.

Within the caspase family, caspase-3 plays a critical role in neuronal-cell death during development and after neuronal injury [13], and has previously been shown to be relevant to memory loss [14]. However, results related to the investigation of

territrem-B analogs on this enzyme model are absent in the pertinent literature. Therefore, the two series of compounds were tested for caspase-3 inhibitory activity. However, the results showed rather weak inhibitory activities of these synthetic compounds (*Table 2*).

Table 2. *Inhibition* [%] *of Caspase-3 by Selected Compounds at 20-*μM *Concentration*

	5a	**5b**	**6b**	**22a**	**22c**	**22g**	**22h**	**33d**	**34c**	**35b**
Inhibition	0	2.0	3.5	2.7	4.2	5.4	1.6	1.8	3.3	2.4

Although, to the best of our knowledge, the cytotoxicity of territrem B (**3**) and its analogs is not described in the literature, enones quite often act as cytotoxic pharmacophores, and many natural products possess cytotoxicity against various tumor cell lines [15][16]. Since the two series of synthetic analogs contain a common 2-en-1-one moiety and were derived from natural products, it is reasonable to investigate the cytotoxicity of these compounds as well. The commonly used cultured KB cell line was employed for this screening [17]. In addition to compounds **7b** and **8a** showing cytotoxicity to KB cells at 6.5 and 14.0 μM, respectively, two 2-ene intermediates, compounds **22e** and **24a**, also exhibited cytotoxicity at 2.0 and 3.5 μM, respectively (*Table 3*). This might be due to the presence of the γ-lactone structure in these molecules.

Table 3. *Cytotoxicity of Compounds* **8a**, **7b**, **24a**, *and* **22e** *against KB Cells*

	8a	**7b**	**24a**	**22e**
Inhibition [%] at 10 μM[a])	68 ± 11	50 ± 8	56 ± 13	56 ± 6
IC_{50} [μM][a])	14.0 ± 1.3	6.5 ± 1.8	3.5 ± 0.4	2.0 ± 0.3

[a]) Values are expressed as mean ± standard deviation, $n = 3$.

It is known that the risk of AD is significantly increased after acute events of cerebrovascular diseases such as stroke or transient ischemic attacks. Furthermore, organic damage of the brain caused by OGD may also lead to dementia [18]. We have, therefore, examined the potential neuroprotective effect of these synthetic analogs on OGD-induced injury on rat primary neurons. The results showed that compounds **23b** and **5f** exhibit protective activity on rat hippocampal cell against OGD injury (*Table 4*).

Conclusions. – Two series of triterpenoid derivatives, **5**–**7** and **8**–**10**, were prepared starting from jujubogenin (**4a**). Few synthetic analogs exhibited promising inhibitory activity towards AChE. This implies that some other structural factors influencing the inhibition ratio among the territrem-B analogs remain to be elucidated. Based on the results obtained in the present study, further preparation and investigation of territrem-B analogs possessing both 5α-OH and 9α-OH groups together with the 2-en-1-one moiety and the appropriate spatial position of the aromatic E ring will be carried out in our further work. The assumption that these synthetic compounds might be cytotoxic was justified to some extent by the finding that compounds **22e**, **24a**, **7b**, and **8a** show

Table 4. *Protection of Rat Primary Neurons from OGD-Induced Injury*

	c [μM]	OD_{490} [nm][a])
OGD Control		0.094 ± 0.002
Compound **23b**	0.1	0.115 ± 0.009[b])
	1.0	0.114 ± 0.005[b])
	10.0	0.123 ± 0.018[b])
Compound **5f**	0.1	0.116 ± 0.004[b])
	1.0	0.132 ± 0.008[b])
	10.0	0.127 ± 0.004[b])

[a]) Values are expressed as mean ± standard deviation, $n = 3$. [b]) $P < 0.05$ *vs.* OGD control.

some cytotoxicity on cultured KB cells. In addition, compounds **23b** and **5f** exhibited protective activity against OGD-induced injury of rat primary neurons, indicating that further investigations of these compounds on the prevention and treatment of the complications of cerebrovascular diseases are highly warranted.

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Experimental Part

1. *General.* TLC: silica gel *60 GF-254* plates. CC = column chromatography, FC = flash CC. NMR Spectra: *Bruker Advance* at 400 MHz, *Bruker Advance DMX* at 500 (^{1}H) and 100 MHz (^{13}C); chemical shift δ in ppm with Me_4Si as an internal standard, coupling constants J in Hz. EI-MS: *HP5898B.* ESI-MS: *Bruker Esquire 3000+*. FAB-MS: *VG Autospec-3000*. Molecular calculations were carried out with the SYBYL program version 6.1, on a *Silicon-Graphics Indigo* (*SGI*) workstation.

2. *Jujubogenin* (**4a**): *General Method.* Jujubogenin (**4a**) was prepared from the jujubogenin glycoside **4b** isolated from the leaves of *Zizyphus jujuba* Var. *spinosa* (BUNGE) HU according to [7].

3. *Aldehydes* **15**–**17**: *General Method.* 3.1. The crude mixture **13**/**14** of (20*E*)- and (20*Z*)-3-*O*-(methylsulfonyl)ebelin lactones[1]) was prepared according to [7] by hydrolysis of jujubogenin (**4a**; 5.0 g, 10.6 mmol) followed by mesylation of the crude ebelin lactones **11** and **12**.

3.2. *Ozonolysis of the Crude Mixture* **13**/**14**. The colorless soln. of the crude mixture **13**/**14** in CH_2Cl_2 (10 ml) and MeOH (40 ml) was cooled to $-78°$ in a liq. N_2/EtOH bath, and O_3 containing O_2 was introduced (0.1 m^3/h) until no starting material could be detected by TLC. Me_2S (3.5 ml) was added dropwise within 1 min at $-70°$, and then the temp. was increased to $-10°$. Stirring was continued for 1 h at $-10°$ and then for 1 h at 0°. AcOH (0.5 ml) was added, and the reaction was continued for 1 h at r.t. After evaporation, the residue was taken up in CH_2Cl_2 (50 ml) and H_2O (30 ml), the aq. layer extracted with CH_2Cl_2 (3 × 50 ml), the combined org. layer washed with 10% aq. Na_2CO_3 soln. and H_2O, dried ($MgSO_4$), and evaporated, and the white solid subjected to CC (SiO_2, hexane/AcOEt 2:1): *3*-O-*(methylsulfonyl)-20-secoebelin-20-al lactone*[1]) (**15**; 2.1 g, 44% from **4a**), *(20*E*)-3*-O-*(methylsulfonyl)-22-secoebelin-22-al lactone*[1]) (**16**; 0.4 g, 8% from **4a**), and *(20*Z*)-3*-O-*(methylsulfonyl)-22-secoebelin-22-al lactone*[1]) (**17**; 0.05 g, 1% from **4a**). ^{1}H-NMR of **15**–**17**: in accordance with those reported in [19].

4. *3*-O-*(Methylsulfonyl)-20-secoebelin-20-oic Acid Lactone 20-Aryl Esters* (= *(1′*S*,2′*S*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-Tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsulfonyl)oxy]-5-oxospiro[furan-3(*2H*),1′(*2′H*)-phenanthrene]-2′-carboxylic Acid Aryl Esters*) **19**, *3*-O-*(Methylsulfonyl)-20-secoebelin-20-thioic Acid Lactone 20*-S-*Aryl Esters* (= *(1′*S*,2′*S*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-Tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsul-*

[1]) Ebelin lactone = (1′*S*,2′*R*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-2′-[(1*E*,3*E*)-2,6-dimethylhepta-1,3,5-trienyl]dodecahydro-7′-hydroxy-4′b,8′,8′,10′a-tetramethylspiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-5(4*H*)-one.

*fonyl)oxy]-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carbothioic Acid S-Aryl Esters*) **20**, *and* N-*Aryl-3*-O-*(methylsulfonyl)-20-secoebelin-20-amide Lactones* (=*(1′*S*,2′*S*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R)-N-*Aryl-tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsulfonyl)oxy]-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′carboxamides*) **21**: *General Method.* To a soln. of **15** (132 mg, 0.3 mmol) in CCl_4 (10 ml), NBS (62.3 mg, 0.35 mmol) was added under N_2. The flask was irradiated with a 100-W flood lamp, and spontaneous reflux was allowed to continue for 5 min. Then the mixture containing acyl bromide **18** was cooled to 0° and treated directly with the substituted phenol, thiophenol, or aniline (0.3 mmol each) in the presence of Et_3N (0.3 mmol). Stirring was continued for 1 h at r.t. After evaporation, the residue was diluted with CH_2Cl_2 (10 ml), the soln. washed with H_2O, dried ($MgSO_4$), and evaporated, and the crude product subjected to CC (SiO_2, hexane/AcOEt 3:1): **19**, **20**, or **21**, resp.

20-Phenyl Ester **19a**: Yield 92 mg (57.6%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.53. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 1.04 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.65 (*d*, *J* = 18.7, 1 H–C(15)); 2.68 (*d*, *J* = 18.7, 1 H–C(15)); 2.96 (*m*, H–C(13)); 3.03 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 11.8, 4.9, H–C(3)); 4.43 (*d*, *J* = 10.2, 1 H–C(17)); 4.69 (*d*, *J* = 10.3, 1 H–C(17)); 7.04 (*dd*, *J* = 1.2, 8.2, H–C(2′), H–C(6′)); 7.23 (*m*, H–C(4′)); 7.37 (*m*, H–C(3′), H–C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.0 (C(19)); 16.2 (C(21)); 17.8 (C(18)); 17.8 (C(6)); 19.4 (C(11)); 25.1 (C(12)); 26.1 (C(2)); 29.7 (C(22)); 33.4 (C(15)); 34.7 (C(7)); 36.8 (C(10)); 38.1 (C(1)); 38.7 ($MeSO_2$); 40.5 (C(4)); 46.2 (C(9)); 50.0 (C(14)); 52.2 (C(13)); 55.2 (C(5)); 69.6 (C(17)); 89.5 (C(3)); 121.4 (C(2′), C(6′)); 126.2 (C(4′)); 129.5 (C(3′), C(5′)); 150.2 (C(1′)); 172.3 (C(20)); 176.0 (C(16)). EI-MS: 532 (2, M^+), 436 (6), 393 (29), 343 (37), 315 (100), 135 (67), 121 (73), 107 (52), 94 (88).

20-(4-Chlorophenyl) Ester **19b**: Yield 73.2 mg (43.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.55. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.60 (*d*, *J* = 18.6, 1 H–C(15)); 2.71 (*d*, *J* = 18.5, 1 H–C(15)); 2.95 (*m*, H–C(13)); 3.03 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 11.5, 4.8, H–C(3)); 4.43 (*d*, *J* = 10.2, 1 H–C(17)); 4.66 (*d*, *J* = 10.2, 1 H–C(17)); 6.99 (br. *d*, *J* = 8.4, H–C(2′), H–C(6′)); 7.33 (*dd*, *J* = 8.4, H–C(3′), H–C(5′)). EI-MS: 531 (3, $[M-Cl]^+$), 485 (2), 450 (17), 435 (3), 407 (7), 343 (8), 315 (20), 108 (100).

20-(2,4-Dichlorophenyl) Ester **19c**: Yield 91.1 mg (50.7%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.58. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.60 (*d*, *J* = 18.8, 1 H–C(15)); 2.71(*d*, *J* = 18.7, 1 H–C(15)); 2.96 (*s*, $MeSO_2$); 3.08 (*m*, H–C(13)); 4.34 (*dd*, *J* = 11.7, 4.8, H–C(3)); 4.44 (*d*, *J* = 10.3, 1 H–C(17)); 4.66 (*d*, *J* = 10.3, 1 H–C(17)); 7.05 (*d*, *J* = 8.4, H–C(6′)); 7.26 (*dd*, *J* = 8.4, 2.4, H–C(5′)); 7.44 (*d*, *J* = 2.4, H–C(3′)). EI-MS: 504 (4, $[M-Me_3SO_3H+1]^+$), 359 (6), 343 (21), 315 (92), 191 (24), 162 (46), 147 (27), 121 (100).

20-[4-(Methylthio)phenyl] Ester **19d**: Yield 129.3 mg (74.6%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.58. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.92 (*s*, Me(22)); 0.94 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.47 (*s*, MeS); 2.56 (*d*, *J* = 18.6, 1 H–C(15)); 2.68 (*d*, *J* = 18.6, 1 H–C(15)); 2.95 (*m*, H–C(13)); 3.02 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 11.8, 4.6, H–C(3)); 4.45 (*d*, *J* = 10.2, 1 H–C(17)); 4.67 (*d*, *J* = 10.2, 1 H–C(17)); 7.07 (br. *d*, *J* = 8.8, H–C(2′), H–C(6′)); 7.25 (br. *d*, *J* = 8.8, H–C(3′), H–C(5′)). EI-MS: 482 (40, $[M-Me_3SO_3H]^+$), 439 (4), 407 (7), 343 (2), 315 (13), 140 (100). FAB-MS: 578 (5, M^+), 530 (17).

20-(4-Methoxyphenyl) Ester **19e**: Yield 60.9 mg (36.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.31. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.65 (*d*, *J* = 18.6, 1 H–C(15)); 2.68 (*d*, *J* = 18.5, 1 H–C(15)); 2.95 (*m*, H–C(13)); 3.03 (*s*, $MeSO_2$); 3.78 (*s*, MeO); 4.20 (*dd*, *J* = 11.8, 4.8, H–C(3)); 4.44 (*d*, *J* = 10.2, 1 H–C(17)); 4.69 (*d*, *J* = 10.2, 1 H–C(17)); 6.87 (br. *d*, *J* = 8.8, H–C(3′), H–C(5′)); 6.95 (br. *d*, *J* = 8.8, H–C(2′), H–C(6′)). FAB-MS: 564 (9, $[M+2]^+$), 466 (4), 343 (11), 315 (7), 282 (100).

20-(Naphthalen-1-yl) Ester **19f**: Yield 128.7 mg (73.7%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.48. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(22)); 0.95 (*s*, Me(19)); 1.06 (*s*, Me(21)); 1.12 (*s*, Me(18)); 2.72 (*d*, *J* = 18.7, H–C(15)); 2.75 (*d*, *J* = 18.6, H–C(15)); 3.03 (*s*, $MeSO_2$); 3.25 (*m*, H–C(13)); 4.35 (*dd*, *J* = 11.8, 4.7, H–C(3)); 4.48 (*d*, *J* = 10.3, 1 H–C(17)); 4.77 (*d*, *J* = 10.1, 1 H–C(17)); 7.20 (*d*, *J* = 8.0, H–C(2′)); 7.46 (*m*, H–C(5′)); 7.52 (*m*, H–C(3′), H–C(4′)); 7.75 (*m*, H–C(6′), H–C(7′)); 7.88 (*m*, H–C(8′)). EI-MS: 486 (8, $[M-MeSO_3H]^+$), 343 (3), 315 (16), 144 (100).

20-(Naphthalen-2-yl) Ester **19g**: Yield 39.6 mg (22.7%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.52. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(22)); 0.93 (*s*, Me(19)); 1.06 (*s*, Me(21)); 1.09 (*s*, Me(18)); 2.72 (*d*, *J* = 18.7, 1 H–C(15)); 2.74 (*d*, *J* = 18.6, 1 H–C(15)); 3.03 (*s*, $MeSO_2$); 3.08 (*m*, H–C(13)); 4.35 (*dd*, *J* = 11.7, 4.7, H–C(3)); 4.48 (*d*, *J* = 10.3, 1 H–C(17)); 4.74 (*d*, *J* = 10.1, 1 H–C(17)); 7.18 (*dd*, *J* = 2.5, 8.5, 1 H); 7.48 (*m*, 3 H); 7.80 (*m*, 3 H). EI-MS: 486 (12, $[M-MeSO_3H]^+$), 443 (10), 343 (7), 315 (27), 144 (100).

20-(4-Nitropheny) Ester **19h**: Yield 112.7 mg (65.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.65. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.59 (*d*, *J* = 18.7,

1 H–C(15)); 2.75 (*d*, *J* = 18.6, 1 H–C(15)); 3.03 (*s*, $MeSO_2$); 3.05 (*m*, H–C(13)); 4.32 (*dd*, *J* = 11.5, 4.9, H–C(3)); 4.45 (*d*, *J* = 10.2, 1 H–C(17)); 4.63 (*d*, *J* = 10.2, 1 H–C(17)); 7.24 (br. *d*, *J* = 8.8, H–C(2′), H–C(6′)); 8.26 (br. *d*, *J* = 8.8, H–C(3′), H–C(5′)). EI-MS: 481 (37, $[M - MeSO_3H]^+$), 466 (27), 451 (7), 438 (100), 343 (31), 315 (72).

20-(4-Methylphenyl) Ester **19i**: Yield 79.1 mg (48.3%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.30. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.33 (*s*, Me–C(4′)); 2.65 (*d*, *J* = 18.7, 1 H–C(15)); 2.70 (*d*, *J* = 18.6, 1 H–C(15)); 2.98 (*m*, H–C(13)); 3.03 (*s*, $MeSO_2$); 4.33 (*dd*, *J* = 11.8, 4.9, H–C(3)); 4.43 (*d*, *J* = 10.2, 1 H–C(17)); 4.63 (*d*, *J* = 10.2, 1 H–C(17)); 6.90 (br. *d*, *J* = 8.4, H–C(2′), H–C(6′)); 7.17 (br. *d*, *J* = 8.4, H–C(3′), H–C(5′)). EI-MS: 546 (5, M^+), 466 (27), 450 (45), 407 (35), 343 (15), 315 (58), 135 (57), 108 (100).

20-([1,1′-Biphenyloxy]-4-yl) Ester **19j**: Yield 93.2 mg (51.1%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.56. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 1.06 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.65 (*d*, *J* = 18.7, 1 H–C(15)); 2.58 (*d*, *J* = 18.7, 1 H–C(15)); 3.05 (*m*, H–C(13)); 3.02 (*s*, $MeSO_2$); 4.27 (*dd*, *J* = 11.8, 4.9, H–C(3)); 4.37 (*d*, *J* = 10.2, 1 H–C(17)); 4.64 (*d*, *J* = 10.3, 1 H–C(17)); 7.04 (br. *d*, *J* = 8.4, H–C(3′), H–C(5′)); 7.36 (*m*, H–C(4″)); 7.43 (*m*, H–C(2′), H–C(6′)); 7.48 (*m*, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.2 (C(19)); 16.4 (C(21)); 18.0 (C(18)); 18.0 (C(6)); 19.6 (C(11)); 25.3 (C(12)); 26.2 (C(2)); 28.3 (C(22)); 33.6 (C(15)); 34.9 (C(7)); 37.0 (C(10)); 38.3 (C(1)); 38.7 ($MeSO_2$); 40.7 (C(4)); 46.24 (C(9)); 50.3 (C(14)); 52.4 (C(13)); 55.3 (C(5)); 69.8 (C(17)); 89.6 (C(3)); 121.8 (C(3′), C(5′)); 127.3 (C(2″), C(6″)); 127.6 (C(4″)); 128.4 (C(2′), C(6′)); 128.9 (C(3″), C(5″)); 139.5 (C(1′)); 140.4 (C(1″)); 149.7 (C(4′)); 1721.9 (C(20)); 175.6 (C(16)). EI-MS: 608 (1, M^+), 512 (37), 497 (6), 469 (37), 343 (5), 315 (31), 170 (100).

20-(3,4,5-Trimethoxyphenyl) Ester **19k**: Yield 73.4 mg (40.0%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.22. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.96 (*s*, Me(19)); 1.06 (*s*, Me(21)); 1.13 (*s*, Me(18)); 2.60 (*d*, *J* = 18.7, 1 H–C(15)); 2.67 (*d*, *J* = 18.6, 1 H–C(15)); 3.07 (*m*, H–C(13)); 3.09 (*s*, $MeSO_2$); 3.69 (*s*, MeO); 3.77 (*s*, MeO–C(2′), MeO–C(6′)); 4.31 (*dd*, *J* = 11.2, 6.4, H–C(3)); 4.55 (*d*, *J* = 10.4, 1 H–C(17)); 4.61 (*d*, *J* = 10.4, 1 H–C(17)); 6.44 (br. *s*, H–C(2′), H–C(6′)).

20-S-*Phenyl Ester* **20a**: Yield 75.8 mg (46.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.68. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.90 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.04 (*s*, Me(18)); 2.64 (br. *s*, H–C(15)); 3.02 (*s*, $MeSO_2$); 3.05 (*m*, H–C(13)); 4.32 (*dd*, *J* = 11.9, 4.6, H–C(3)); 4.35 (*d*, *J* = 10.0, 1 H–C(17)); 4.82 (*d*, *J* = 10.1, 1 H–C(17)); 7.38 (*m*, H–C(2′), H–C(6′)); 7.42 (*m*, H–C(3′), H–C(5′)); 7.45 (*m*, H–C(4′)).

20-S-*(4-Chlorophenyl) Ester* **20b**: Yield 92.8 mg (53.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.76. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.85 (*s*, Me(22)); 0.88 (*s*, Me(19)); 1.01 (*s*, Me(21)); 1.03 (*s*, Me(18)); 2.59 (*d*, *J* = 18.6, 1 H–C(15)); 2.62 (*d*, *J* = 18.6, 1 H–C(15)); 3.00 (*s*, $MeSO_2$); 3.05 (*m*, H–C(13)); 4.32 (*dd*, *J* = 11.9, 4.6, H–C(3)); 4.74 (*d*, *J* = 10.1, 1 H–C(17)); 4.76 (*d*, *J* = 10.1, 1 H–C(17)); 7.20 (br. *d*, *J* = 8.4, H–C(2′), H–C(6′)); 7.42 (br. *d*, *J* = 8.4, H–C(3′), H–C(5′)). EI-MS: 545 (1, $[M - Cl]^+$), 531 (16), 516 (3), 486 (7), 471 (2), 443 (10), 383 (67), 357 (11), 343 (71), 315 (100).

20-S-*(2,6-Dichlorophenyl) Ester* **20c**: Yield 128.1 mg (69.2%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.72. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.06 (*s*, Me(18)); 2.61 (*d*, *J* = 18.6, 1 H–C(15)); 2.70 (*d*, *J* = 18.6, 1 H–C(15)); 3.02 (*s*, $MeSO_2$); 3.09 (*m*, H–C(13)); 4.38 (*dd*, *J* = 11.6, 5.2, H–C(3)); 4.38 (*d*, *J* = 10.1, 1 H–C(17)); 4.80 (*d*, *J* = 10.1, 1 H–C(17)); 7.29 (*m*, H–C(4′)); 7.42 (br. *d*, *J* = 8.0, H–C(3′), H–C(5′)).

20-S-*(4-Methoxyphenyl) Ester* **20d**: Yield 90.3 mg (52.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.58. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.90 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.04 (*s*, Me(18)); 2.64 (*s*, 2 H–C(15)); 3.02 (*s*, $MeSO_2$); 3.05 (*m*, H–C(13)); 3.81 (*s*, MeO); 4.28 (*m*, H–C(3)); 4.35 (*d*, *J* = 9.9, 1 H–C(17)); 4.87 (*d*, *J* = 9.9, 1 H–C(17)); 6.87 (br. *d*, *J* = 8.8, H–C(3′), H–C(5′)); 7.28 (br. *d*, *J* = 8.8, H–C(2′), H–C(6′)). EI-MS: 578 (0.5, M^+), 482 (20), 343 (7), 315 (56).

20-S-*(3-Methoxyphenyl) Ester* **20e**: Yield 46.3 mg (26.7%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.62. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.04 (*s*, Me(21)); 1.06 (*s*, Me(18)); 2.64 (*s*, 2 H–C(15)); 3.03 (*s*, $MeSO_2$); 3.06 (*m*, H–C(13)); 3.82 (*s*, MeO); 4.33 (*dd*, *J* = 11.6, 4.4, H–C(3)); 4.38 (*d*, *J* = 10.0, 1 H–C(17)); 4.82 (*d*, *J* = 10.0, 1 H–C(17)); 6.91 (*m*, H–C(2′)); 6.95 (br. *d*, *J* = 8.4, H–C(4′), H–C(6′)); 7.32 (*m*, H–C(5′)).

20-S-*(2-Methoxyphenyl) Ester* **20f**: Yield 104.5 mg (60.3%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.65. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.06 (*s*, Me(18)); 2.62 (*d*, *J* = 18.8, 1 H–C(15)); 2.93 (*d*, *J* = 18.8, 1 H–C(15)); 3.02 (*s*, $MeSO_2$); 3.06 (*m*, H–C(13)); 3.81 (*s*, MeO); 4.33 (*dd*, *J* = 11.6, 4.8, H–C(3)); 4.38 (*d*, *J* = 10.4, 1 H–C(17)); 4.87 (*d*, *J* = 10.4, 1 H–C(17)); 6.97 (*m*, H–C(3′), H–C(5′)); 7.34 (*dd*, *J* = 8.0, 1.6, H–C(6′)); 7.42 (*ddd*, *J* = 1.6, 7.6, 8.0, H–C(4′)).

N-*Phenyl-20-amide* **21a**: Yield 71.9 mg (46%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.50. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.79 (*s*, Me(22)); 0.84 (*s*, Me(19)); 0.97 (*s*, Me(21)); 0.97 (*s*, Me(18)); 2.25 (*d*, J = 18.6, 1 H−C(15)); 2.64 (*d*, J = 18.6, 1 H−C(15)); 2.84 (*m*, H−C(13)); 3.16 (*s*, $MeSO_2$); 4.28 (*dd*, J = 11.5, 4.7, H−C(3)); 4.39 (*d*, J = 9.6, 1 H−C(17)); 4.90 (*d*, J = 9.6, 1 H−C(17)); 7.10 (*m*, H−C(4′)); 7.28 (*m*, H−C(3′), H−C(5′)); 7.53 (br. *d*, J = 8.0, H−C(2′), H−C(6′)); 8.31 (*s*, NHCO). EI-MS: 389 (2, $[M - MeSO_3H]^+$), 357 (40), 345 (14), 329 (100).

N-*(4-Chlorophenyl)-20-amide* **21b**: Yield 98.5 mg (58%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.36. ^{1}H-NMR (400 MHz, (D_6)DMSO): 0.81 (*s*, Me(22)); 0.87 (*s*, Me(19)); 0.99 (*s*, Me(21)); 1.00 (*s*, Me(18)); 2.32 (*d*, J = 18.7, 1 H−C(15)); 2.55 (*d*, J = 18.8, 1 H−C(15)); 2.86 (*s*, $MeSO_2$); 3.05 (*m*, H−C(13)); 4.29 (*dd*, J = 11.5, 4.9, H−C(3)); 4.40 (*d*, J = 10.0, 1 H−C(17)); 5.01 (*d*, J = 10.0, 1 H−C(17)); 7.23 (br. *d*, J = 8.8, H−C(2′), H−C(6′)); 7.57 (br. *d*, J = 8.8, H−C(3′), H−C(5′)).

N-*(3,4-Dichlorophenyl)-20-amide* **21c**: Yield 135.1 mg (75.2%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.53. ^{1}H-NMR (400 MHz, $(CD_3)_2CO$): 0.84 (*s*, Me(22)); 0.90 (*s*, Me(19)); 1.02 (*s*, Me(21)); 1.03 (*s*, Me(18)); 2.38 (*d*, J = 18.6, 1 H−C(15)); 2.58 (*d*, J = 18.6, 1 H−C(15)); 2.84 (*m*, H−C(13)); 3.03 (*s*, $MeSO_2$); 4.28 (*dd*, J = 11.6, 5.5, H−C(3)); 4.46 (*d*, J = 10.0, 1 H−C(17)); 5.01 (*d*, J = 10.0, 1 H−C(17)); 7.34 (*m*, H−C(5′), H−C(6′)); 7.88 (br. *s*, H−C(2′)). EI-MS: 599 (26, M^+), 503 (18).

N-*(4-Methoxyphenyl)-20-amide* **21d**: Yield 109.4 mg (65%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.44. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 1.04 (*s*, Me(21)); 1.05 (*s*, Me(18)); 2.32 (*d*, J = 18.6, 1 H−C(15)); 2.53 (*d*, J = 18.7, 1 H−C(15)); 3.02 (*s*, $MeSO_2$); 3.78 (*s*, MeO); 4.32 (*dd*, J = 11.8, 4.6, H−C(3)); 4.38 (*d*, J = 10.3, 1 H−C(17)); 5.24 (*d*, J = 10.3, 1 H−C(17)); 6.84 (br. *d*, J = 8.0, H−C(3′), H−C(5′)); 7.37 (br. *d*, J = 8.0, H−C(2′), H−C(6′)).

N-*(1,1′-[Biphenyl]-4-yl)-20-amide* **21e**: Yield 92.9 mg (51%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.44. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.90 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.03 (*s*, Me(18)); 2.50 (*d*, J = 18.1, 1 H−C(15)); 2.62 (*d*, J = 18.0, 1 H−C(15)); 3.03 (*s*, $MeSO_2$); 4.33 (*dd*, J = 11.6, 4.7, H−C(3)); 4.42 (*d*, J = 10.0, 1 H−C(17)); 5.17 (*d*, J = 10.0, 1 H−C(17)); 7.33 (*m*, H−C(4″)); 7.42 (*m*, H−C(3″), H−C(5″)); 7.54 (*m*, 6 H). FAB-MS: 608 (26, $[M+1]^+$), 530 (50), 441 (91), 343 (5).

N-*(4-Methylphenyl)-20-amide* **21f**: Yield 60.5 mg (37%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.48. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.90 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.04 (*s*, Me(18)); 2.32 (*d*, J = 18.7, 1 H−C(15)); 2.33 (*s*, Me−C(4′)); 2.53 (*d*, J = 18.7, 1 H−C(15)); 3.03 (*s*, $MeSO_2$); 4.32 (*dd*, J = 11.8, 4.6, H−C(3)); 4.37 (*d*, J = 10.2, 1 H−C(17)); 5.14 (*d*, J = 10.2, 1 H−C(17)); 7.03 (br. *d*, J = 8.0, H−C(3′), H−C(5′)); 7.28 (br. *d*, J = 8.0, H−C(2′), H−C(6′)). FAB-MS: 546 (25, $[M+1]^+$). EI-MS: 449 (25, $[M - MeSO_3H]^+$), 434 (32), 406 (53), 107 (100).

N-*(2,4,5-Trichlorophenyl)-20-amide* **21g**: Yield 97.3 mg (51.1%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.40. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.92 (*s*, Me(22)); 0.96 (*s*, Me(19)); 1.05 (*s*, Me(21)); 1.06 (*s*, Me(18)); 2.41 (*d*, J = 18.5, 1 H−C(15)); 2.65 (*d*, J = 18.7, 1 H−C(15)); 3.03 (*s*, $MeSO_2$); 4.32 (*dd*, J = 11.6, 4.7, H−C(3)); 4.43 (*d*, J = 9.9, 1 H−C(17)); 5.14 (*d*, J = 9.8, 1 H−C(17)); 7.49 (*s*, J = 8.0, H−C(3′)); 7.58 (*s*, H−C(6′)). FAB-MS: 635 (4, M^+), 530 (64), 515 (5), 441 (20).

N-*(Cyclohexyl)-20-amide* **21h**: Yield 111.1 mg (68.7%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.30. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.90 (*s*, Me(19)); 0.99 (*s*, Me(21)); 1.03 (*s*, Me(18)); 2.37 (*d*, J = 18.0, 1 H−C(15)); 2.52 (*d*, J = 18.0, 1 H−C(15)); 3.02 (*s*, $MeSO_2$); 4.32 (*dd*, J = 11.8, 4.6, H−C(3)); 4.36 (*d*, J = 9.9, 1 H−C(17)); 5.13 (*d*, J = 9.9, 1 H−C(17)). FAB-MS: 539 (3, M^+), 441 (36).

5. *3-Deoxy-20-secoebelin-2-en-20-oic Acid Lactone 20-Aryl Esters* (= *(1′*S,*2′*S,*4′a*R,*4′b*S,*8′a*S,*10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxylic Acid Aryl Esters*) **22**, *3-Deoxy-20-secoebelin-2-en-20-oic Acid Lactone 20-*S*-Aryl Esters* (= *(1′*S,*2′*S,*4′a*R,*4′b*S,*8′a*S,*10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carbothioic Acid* S*-Aryl Esters*) **23**, *and* N*-Aryl-3-deoxy-20-secoebelin-2-en-20-amide Lactones* (= *(1′*S,*2′*S,*4′a*R,*4′b*S,*8′a*S,*10′a*R*)-*N*-Aryl-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-dodecahydro-4b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxamides*) **24**: *General Method*. To a soln. of **19**, **20**, or **21** (0.1 mmol) in *N*,*N*-dimethylacetamide (10 ml), Li_2CO_3 (0.5 mmol) was added. The mixture was refluxed for 0.5 h and cooled to r.t. The suspension was taken up with 1M aq. HCl and extracted with Et_2O (3 × 10 ml), the org. layer washed with H_2O (3 × 5 ml), dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexane/AcOEt 5:1): **22**, **23**, or **24**, resp.

20-Phenyl Ester **22a**: From **19a**, 33 mg (75.7%) of **22a**. Colorless oil. R_f (hexane/AcOEt 5:1) 0.40. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.93 (*s*, Me(22)); 0.95 (*s*, Me(19)); 1.01 (*s*, Me(21)); 1.11 (*s*, Me(18)); 2.67 (*d*, J = 18.7, 1 H−C(15)); 2.75 (*d*, J = 18.7, 1 H−C(15)); 3.06 (*dd*, J = 3.9, 13.1, H−C(13)); 4.52 (*d*, J = 10.4, 1 H−C(17)); 4.73 (*d*, J = 10.4, 1 H−C(17)); 5.44 (*m*, H−C(3)); 5.45 (*m*, H−C(2)); 7.08 (*dd*, J = 1.2, 8.5, H−C(2′), H−C(6′));

7.25 (*m*, H–C(4′)); 7.40 (*m*, H–C(3′), H–C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.2 (C(19)); 17.2 (C(21)); 18.8 (C(6)); 19.6 (C(11)); 22.6 (C(18)); 26.3 (C(12)); 31.6 (C(22)); 32.5 (C(15)); 34.6 (C(7)); 36.2 (C(10)); 38.6 (C(8)); 40.7 (C(4)); 40.8 (C(1)); 46.2 (C(9)); 50.0 (C(14)); 51.0 (C(13)); 51.7 (C(5)); 69.6 (C(17)); 120.8 (C(2)); 121.4 (C(2′), C(6′)); 126.1 (C(4′)); 129.5 (C(3′), C(5′)); 137.9 (C(3)); 150.2 (C(1′)); 172.5 (C(20)); 176.2 (C(16)). EI-MS: 436 (9, M^+), 343 (37), 315 (61), 135 (51), 121 (51), 107 (49), 94 (100).

20-(4-Chlorophenyl) Ester **22b**: From **19b**, 38 mg (81%) of **22b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.62. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.60 (*d*, J = 18.6, 1 H–C(15)); 2.74 (*d*, J = 18.5, 1 H–C(15)); 3.02 (*dd*, J = 3.8, 13.2, H–C(13)); 4.48 (*d*, J = 10.2, 1 H–C(17)); 4.65 (*d*, J = 10.2, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 6.97 (*dd*, J = 2.4, 8.8, H–C(2′), H–C(6′)); 7.33 (br. *d*, J = 8.8, H–C(3′), H–C(5′)). EI-MS: 470 (25, M^+), 343 (45), 315 (100), 301 (7), 136 (79), 107 (66).

20-(2,4-Dichlorophenyl) Ester **22c**: From **19c**, 38.4 mg (76.1%) of **22c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.88 (*s*, Me(19)); 0.97 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.61 (*d*, J = 18.7, 1 H–C(15)); 2.72 (*d*, J = 18.7, 1 H–C(15)); 3.03 (*dd*, J = 3.9, 13.1, H–C(13)); 4.49 (*d*, J = 10.3, 1 H–C(17)); 4.67 (*d*, J = 10.3, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 7.06 (*d*, J = 8.8, H–C(6′)); 7.26 (*dd*, J = 2.4, 8.8, H–C(5′)); 7.44 (*d*, J = 2.4, H–C(3′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.3 (C(19)); 17.3 (C(21)); 19.1 (C(6)); 19.8 (C(11)); 22.7 (C(18)); 26.4 (C(12)); 31.7 (C(22)); 32.6 (C(15)); 34.8 (C(7)); 36.4 (C(10)); 38.6 (C(8)); 40.8 (C(4)); 40.9 (C(1)); 46.3 (C(9)); 50.1 (C(14)); 51.1 (C(13)); 51.8 (C(5)); 69.8 (C(17)); 120.0 (C(2)); 124.7 (C(6′)); 127.7 (C(2′)); 128.3 (C(3′)); 130.2 (C(5′)); 132.4 (C(4′)); 138.1 (C(3)); 145.4 (C(1′)); 171.6 (C(20)); 176.3 (C(16)). EI-MS: 505 (8, M^+), 343 (72), 315 (100).

20-[4-(Methylthio)phenyl] Ester **22d**: From **19d**, 34.7 mg (72%) of **22d**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.57. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.46 (*s*, MeS); 2.64 (*d*, J = 18.8, 1 H–C(15)); 2.71 (*d*, J = 18.8, 1 H–C(15)); 3.04 (*dd*, J = 3.8, 13.2, H–C(13)); 4.47 (*d*, J = 10.2, 1 H–C(17)); 4.67 (*d*, J = 10.2, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.07 (br. *d*, J = 8.8, H–C(2′), H–C(6′)); 7.25 (br. *d*, J = 8.8, H–C(3′), H–C(5′)). EI-MS: 482 (12, M^+), 343 (45), 140 (100).

20-(4-Methoxyphenyl) Ester **22e**: From **19e**, 39.1 mg (83.9%) of **22e**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.41. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (*s*, Me(22)); 0.88 (*s*, Me(19)); 0.99 (*s*, Me(21)); 1.09 (*s*, Me(18)); 2.64 (*d*, J = 18.7, 1 H–C(15)); 2.72 (*d*, J = 18.6, 1 H–C(15)); 3.03 (*dd*, J = 3.9, 13.1, H–C(13)); 3.80 (*s*, MeO); 4.47 (*d*, J = 10.2, 1 H–C(17)); 4.69 (*d*, J = 10.2, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 6.87 (br. *d*, J = 8.8, H–C(3′), H–C(5′)); 6.96 (*dd*, J = 2.2, 8.8, H–C(2′), H–C(6′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.4 (C(19)); 17.3 (C(21)); 20.0 (C(6)); 19.8 (C(11)); 22.7 (C(18)); 26.4 (C(12)); 31.8 (C(22)); 32.7 (C(15)); 34.8 (C(7)); 36.4 (C(10)); 38.6 (C(8)); 40.8 (C(4)); 40.9 (C(1)); 46.3 (C(9)); 50.2 (C(14)); 51.2 (C(13)); 51.8 (C(5)); 69.8 (C(17)); 114.7 (C(3′), C(5′)); 121.0 (C(2)); 122.3 (C(2′), C(6′); 140.1 (C(3)); 143.9 (C(1′)); 157.6 (C(4′)); 173.1 (C(20)); 176.4 (C(16)). EI-MS: 466 (18, M^+), 343 (3), 315 (8), 124 (100).

20-(Naphthalen-1-yl) Ester **22f**: From **19f**, 27.2 mg (56%) of **22f**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.62. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.96 (*s*, Me(22)); 0.97 (*s*, Me(19)); 1.03 (*s*, Me(21)); 1.14 (*s*, Me(18)); 2.73 (*d*, J = 18.6, 1 H–C(15)); 2.81 (*d*, J = 18.6, 1 H–C(15)); 3.28 (*dd*, J = 3.8, 13.8, H–C(13)); 4.57 (*d*, J = 10.2, 1 H–C(17)); 4.82 (*d*, J = 10.2, 1 H–C(17)); 5.43 (*m*, H–C(3)); 5.46 (*m*, H–C(2)); 7.21 (*d*, J = 7.6, H–C(2′)); 7.48 (*m*, H–C(5′)); 7.52 (*m*, H–C(3′), H–C(4′)); 7.78 (*m*, H–C(6′), H–C(7′)); 7.88 (*m*, H–C(8′)). EI-MS: 486 (4, M^+), 343 (3), 315 (7), 144 (100).

20-(4-Nitrophenyl) Ester **22g**: From **19h**, 28.9 mg (60%) of **22g**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.42. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.10 (*s*, Me(18)); 2.62 (*d*, J = 18.8, 1 H–C(15)); 2.80 (*d*, J = 18.8, 1 H–C(15)); 3.07 (*dd*, J = 4.0, 12.8, H–C(13)); 4.50 (*d*, J = 10.2, 1 H–C(17)); 4.64 (*d*, J = 10.2, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.25 (br. *d*, J = 9.2, H–C(2′), H–C(6′)); 8.27 (br. *d*, J = 9.2, H–C(3′), H–C(5′)). EI-MS: 481 (5, M^+), 343 (40), 315 (59), 109 (100).

20-(Naphthalen-2-yl) Ester **22h**: From **19g**, 27.2 mg (56%) of **22h**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.68 (*d*, J = 18.6, 1 H–C(15)); 2.74 (*d*, J = 18.6, 1 H–C(15)); 3.08 (*dd*, J = 3.2, 12.8, H–C(13)); 4.52 (*d*, J = 10.2, 1 H–C(17)); 4.74 (*d*, J = 10.2, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 7.18 (*dd*, J = 2.4, 8.8, 1 H); 7.49 (*m*, 3 H); 7.82 (*m*, 3 H). EI-MS: 486 (7, M^+), 343 (1), 315 (3), 144 (100).

20-(4-Methylphenyl) Ester **22i**: From **19i**, 27 mg (60%) of **22i**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(22)); 0.92 (*s*, Me(19)); 0.97 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.34 (*s*, Me–C(4′)); 2.64 (*d*, J = 18.8, 1 H–C(15)); 2.71 (*d*, J = 18.8, 1 H–C(15)); 3.02 (*dd*, J = 4.0, 13.2, H–C(13)); 4.48 (*d*, J = 10.2, 1 H–C(17)); 4.69 (*d*, J = 10.2, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 6.92

(br. d, J = 8.4, H–C(3′), H–C(5′)); 7.17 (br. d, J = 8.4, H–C(2′), H–C(6′)). EI-MS: 450 (62, M^+), 343 (11), 315 (59), 135 (58), 108 (100).

20-([1,1′-Biphenyl]-4-yl) Ester **22j**: From **19j**, 31.8 mg (62.1%) of **22j**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.92 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.65 (d, J = 18.6, 1 H–C(15)); 2.75 (d, J = 18.6, 1 H–C(15)); 3.07 (dd, J = 4.0, 13.2, H–C(13)); 4.50 (d, J = 10.1, 1 H–C(17)); 4.71 (d, J = 10.1, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.04 (br. d, J = 8.4, H–C(3′), H–C(5′)); 7.35 (*m*, H–C(4″)); 7.43 (*m*, H–C(2′), H–C(6′)); 7.48 (*m*, 4 H). EI-MS: 512 (19, M^+), 343 (7), 315 (31), 170 (100).

20-S-*(4-Chlorophenyl) Ester* **23a**: From **20b**, 30.7 mg (63.2%) of **23a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.53. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.90 (*s*, Me(19)); 0.96 (*s*, Me(21)); 1.10 (*s*, Me(18)); 2.61 (d, J = 18.6, 1 H–C(15)); 2.67 (d, J = 18.6, 1 H–C(15)); 3.07 (dd, J = 4.0, 13.2, H–C(13)); 4.42 (d, J = 10.1, 1 H–C(17)); 4.77 (d, J = 10.1, 1 H–C(17)); 5.39 (*m*, H–C(3)); 5.40 (*m*, H–C(2)); 7.30 (br. d, J = 8.0, H–C(2′), H–C(6′)); 7.39 (br. d, J = 8.0, H–C(3′), H–C(5′)). EI-MS: 486 (4, M^+), 344 (11).

20-S-*(2,6-Dichlorophenyl) Ester* **23b**: From **20c**, 41.7 mg (28.3%) of **23b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.63. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.95 (*s*, Me(19)); 1.08 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.67 (d, J = 18.6, 1 H–C(15)); 2.71 (d, J = 18.6, 1 H–C(15)); 3.14 (dd, J = 4.0, 13.2, H–C(13)); 4.44 (d, J = 10.4, 1 H–C(17)); 4.81 (d, J = 10.4, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 7.31 (*m*, H–C(4′)); 7.44 (br. d, J = 8.0, H–C(3′), H–C(5′)).

N-*Phenyl-20-amide* **24a**: From **21a**, 31 mg (73%) of **24a**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.52. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.92 (*s*, Me(19)); 0.99 (*s*, Me(21)); 1.08 (*s*, Me(18)); 2.55 (d, J = 18.4, 1 H–C(15)); 2.62 (d, J = 18.4, 1 H–C(15)); 4.43 (d, J = 10.1, 1 H–C(17)); 5.10 (d, J = 10.1, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.12 (*m*, H–C(4′)); 7.29 (*m*, H–C(3′), H–C(5′)); 7.45 (*m*, H–C(2′), H–C(6′)).

N-*(3,4-Dichlorophenyl)-20-amide* **24b**: From **21c**, 34.2 mg (68%) of **24b**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.42. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.90 (*s*, Me(19)); 0.97 (*s*, Me(21)); 1.05 (*s*, Me(18)); 2.37 (d, J = 17.7, 1 H–C(15)); 2.63 (d, J = 17.6, 1 H–C(15)); 4.47 (d, J = 10.1, 1 H–C(17)); 4.55 (d, J = 10.1, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.42 (*m*, H–C(2)); 7.35 (*m*, H–C(5′), H–C(6′)); 7.71 (br. *s*, H–C(2′)).

N-*(4-Chlorophenyl)-20-amide* **24c**: From **21b**, 23.4 mg (49.8%) of **24c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.30. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.99 (*s*, Me(21)); 1.04 (*s*, Me(18)); 2.42 (d, J = 18.6, 1 H–C(15)); 2.63 (d, J = 18.6, 1 H–C(15)); 4.47 (d, J = 10.0, 1 H–C(17)); 5.11 (d, J = 10.0, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.39 (*m*, 2 H); 7.71 (*m*, 2 H).

N-*(2,4,5-Trichlorophenyl)-20-amide* **24d**: From **21g**, 29.9 mg (55.5%) of **24d**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.37. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.98 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.42 (d, J = 19.5, 1 H–C(15)); 2.65 (d, J = 19.6, 1 H–C(15)); 4.47 (d, J = 9.8, 1 H–C(17)); 4.95 (d, J = 9.7, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.48 (*s*, H–C(3′)); 7.55 (*s*, H–C(6′)).

N-*(1,1′-[Biphenyl]-4-yl)-20-amide* **24e**: From **21e**, 36.9 mg (72.3%) of **24c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.20. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 0.91 (*s*, Me(19)); 0.97 (*s*, Me(21)); 1.07 (*s*, Me(18)); 2.48 (d, J = 18.0, 1 H–C(15)); 2.62 (d, J = 18.0, 1 H–C(15)); 4.51 (d, J = 10.0, 1 H–C(17)); 5.18 (d, J = 10.0, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 7.32 (*m*, 1 H); 7.42 (*m*, 2 H); 7.55 (*m*, 6 H). EI-MS: 511 (76, M^+), 169 (100).

N-*Cyclohexyl-20-amide* **24f**: From **21h**, 32.6 mg (73.9%) of **24f**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.23. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 0.88 (*s*, Me(19)); 0.96 (*s*, Me(21)); 1.00 (*s*, Me(18)); 2.37 (d, J = 18.0, 1 H–C(15)); 2.53 (d, J = 18.0, 1 H–C(15)); 4.41 (d, J = 9.9, 1 H–C(17)); 5.12 (d, J = 9.9, 1 H–C(17)). EI-MS: 441 (M^+).

6. *Oxidation of 2-Ene Derivatives* **22** *with CrO_3: 3-Deoxy-1-oxo-20-secoebelin-2-en-20-oic Acid Lactone Aryl Esters* (= *(1′*S*,2′*S*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxylic Acid Aryl Esters*) **5**: *General Method*. To a soln. of **22** (0.1 mmol) in AcOH (1 ml), CrO_3 in AcOH (1 ml) was added dropwise at 80°, and stirring was continued for 1 h. After evaporation, the residue was taken up with H_2O and extracted with CH_2Cl_2, the org. phase evaporated, and the residue purified by CC (SiO_2, hexane/AcOEt 2:1): **5** and the by-products **25**.

20-Phenyl Ester **5a**: From **22a**, 11.7 mg (26%) of **5a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.33. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(22)); 1.11 (*s*, Me(19)); 1.13 (*s*, Me(21)); 1.15 (*s*, Me(18)); 2.69 (d, J = 18.7, 1 H–C(15)); 2.71 (d, J = 18.6, 1 H–C(15)); 3.05 (dd, J = 3.5, 13.0, H–C(13)); 4.46 (d, J = 10.6, 1 H–C(17)); 4.76 (d, J = 10.3, 1 H–C(17)); 5.71 (d, J = 10.3, H–C(2)); 6.35 (d, J = 10.2, H–C(3)); 7.06 (br. d, J = 7.3, H–C(2′), H–C(6′)); 7.26 (*m*, H–C(4′)); 7.37 (*m*, H–C(3′), H–C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.8 (C(19)); 17.9 (C(21)); 18.4 (C(6)); 21.8 (C(22)); 22.7 (C(11)); 26.3 (C(12)); 31.0 (C(18)); 32.3 (C(15)); 34.8

(C(7)); 36.4 (C(8)); 40.8 (C(4)); 43.1 (C(9)); 46.6 (C(13)); 47.4 (C(10)); 50.1 (C(14)); 50.9 (C(5)); 69.9 (C(17)); 121.4 (C(2′), C(6′)); 124.1 (C(2)); 126.1 (C(4′)); 129.5 (C(3′), C(5′)); 150.2 (C(1′)); 154.7 (C(3)); 172.4 (C(20)); 176.2 (C(16)); 206.1 (C(1)). EI-MS: 450 (27, M^+), 357 (35), 329 (100), 217 (30).

20-(2,4-Dichlorophenyl) Ester **5b**: From **22c**, 14.5 mg (27.9%) of **5b**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.82. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.93 (*s*, Me(22)); 1.09 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.14 (*s*, Me(18)); 2.65 (*d*, *J* = 18.7, 1 H−C(15)); 2.73 (*d*, *J* = 18.6, 1 H−C(15)); 3.12 (*dd*, *J* = 3.5, 13.0, H−C(13)); 4.46 (*d*, *J* = 10.0, 1 H−C(17)); 4.76 (*d*, *J* = 10.0, 1 H−C(17)); 5.70 (*d*, *J* = 10.0, H−C(2)); 6.35 (*d*, *J* = 10.1, H−C(3)); 7.03 (br. *d*, *J* = 8.4, H−C(6′)); 7.26 (*m*, H−C(5′)); 7.44 (*d*, *J* = 2.4, H−C(3′)). EI-MS: 519 (4, M^+), 373 (13), 357 (41), 329 (100), 168 (38).

20-(4-Chlorophenyl) Ester **5c**: From **22b**, 10.9 mg (22.5%) of **5c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.53. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.11 (*s*, Me(22)); 1.13 (*s*, Me(19)); 1.15 (*s*, Me(21)); 1.23 (*s*, Me(18)); 2.62 (*d*, *J* = 18.7, 1 H−C(15)); 2.70 (*d*, *J* = 18.6, 1 H−C(15)); 3.12 (*dd*, *J* = 3.5, 13.0, H−C(13)); 4.46 (*d*, *J* = 10.3, 1 H−C(17)); 4.72 (*d*, *J* = 10.3, 1 H−C(17)); 5.71 (*d*, *J* = 10.3, H−C(2)); 6.35 (*d*, *J* = 10.4, H−C(3)); 7.02 (br. *d*, *J* = 8.8, H−C(2′), H−C(6′)); 7.35 (*d*, *J* = 8.8, H−C(3′), H−C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.8 (C(19)); 18.1 (C(21)); 18.4 (C(6)); 21.9 (C(22)); 22.6 (C(11)); 26.2 (C(12)); 31.0 (C(18)); 32.4 (C(15)); 34.8 (C(7)); 36.4 (C(8)); 40.7 (C(4)); 43.1 (C(9)); 46.7 (C(13)); 47.5 (C(10)); 50.5 (C(14)); 50.9 (C(5)); 69.7 (C(17)); 122.8 (C(2′), C(6′)); 124.1 (C(2)); 129.6 (C(3′), C(5′)); 132.5 (C(4′)); 149.2 (C(1′)); 154.7 (C(3)); 171.7 (C(20)); 176.1 (C(16)); 206.1 (C(1)). EI-MS: 484 (5, M^+), 357 (30), 329 (100).

20-(4-Nitrophenyl) Ester **5d**: From **22g**, 14.5 mg (29.4%) of **5d**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.36. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.11 (*s*, Me(22)); 1.14 (*s*, Me(19)); 1.16 (*s*, Me(21)); 1.24 (*s*, Me(18)); 2.59 (*d*, *J* = 18.7, 1 H−C(15)); 2.75 (*d*, *J* = 18.6, 1 H−C(15)); 3.18 (*dd*, *J* = 3.5, 13.0, H−C(13)); 4.47 (*d*, *J* = 10.2, 1 H−C(17)); 4.71 (*d*, *J* = 10.2, 1 H−C(17)); 5.71 (*d*, *J* = 10.4, H−C(2)); 6.36 (*d*, *J* = 10.4, H−C(3)); 7.26 (*dd*, *J* = 2.4, 7.2, H−C(2′), H−C(6′)); 8.27 (*dd*, *J* = 2.4, 7.2, H−C(3′), H−C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.7 (C(19)); 18.1 (C(21)); 18.4 (C(6)); 21.8 (C(22)); 22.6 (C(11)); 26.1 (C(12)); 30.9 (C(18)); 32.5 (C(15)); 34.8 (C(7)); 36.3 (C(8)); 40.7 (C(4)); 43.1 (C(9)); 46.8 (C(13)); 47.4 (C(10)); 50.5 (C(14)); 50.9 (C(5)); 69.5 (C(17)); 122.5 (C(2′), C(6′)); 124.0 (C(2)); 125.2 (C(3′), C(5′)); 145.6 (C(4′)); 154.8 (C(1′)); 154.7 (C(3)); 171.5 (C(20)); 175.8 (C(16)); 205.9 (C(1)). EI-MS: 357 (7, $[M - NO_2C_6H_4O]^+$), 329 (18), 137 (17).

20-(4-Methylphenyl) Ester **5e**: From **22i**, 8.3 mg (18%) of **5e**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.38. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(22)); 1.09 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.13 (*s*, Me(18)); 2.34 (*s*, Me−C(4′)); 2.65 (*d*, *J* = 18.7, 1 H−C(15)); 2.72 (*d*, *J* = 18.6, 1 H−C(15)); 3.06 (*dd*, *J* = 3.5, 13.0, H−C(13)); 4.47 (*d*, *J* = 10.2, 1 H−C(17)); 4.70 (*d*, *J* = 10.2, 1 H−C(17)); 5.72 (*d*, *J* = 10.4, H−C(2)); 6.35 (*d*, *J* = 10.4, H−C(3)); 6.93 (br. *d*, *J* = 8.0, H−C(2′), H−C(6′)); 7.15 (br. *d*, *J* = 8.0, H−C(3′), H−C(5′)). EI-MS: 464 (8, M^+), 357 (4), 329 (15), 135 (17), 108 (100).

3-Deoxy-3-oxo-20-secoebelin-1-en-20-oic Acid Lactone Phenyl Ester (= *(1′*S*,2′*S*,4′a*R*,4′b*R*,8′a*R*,10′a*R*)-3′,4,4′,4′a,4′b,5,7′,8′8′a,9′10′10′a-Dodecahydro-4′b,8′,8′10′a-tetramethyl-5,7′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxylic Acid Phenyl Ester*; **25a**): From **22a**, 7.2 mg (16%) of **25a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.21. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.11 (*s*, Me(21)); 1.12 (*s*, Me(18)); 1.17 (*s*, Me(19)); 1.18 (*s*, Me(22)); 2.72 (*d*, *J* = 18.7, 1 H−C(15)); 2.74 (*d*, *J* = 18.3, 1 H−C(15)); 3.10 (*m*, H−C(13)); 4.45 (*d*, *J* = 10.7, 1 H−C(17)); 4.71 (*d*, *J* = 10.7, 1 H−C(17)); 5.89 (*d*, *J* = 10.2, H−C(2)); 7.08 (*d*, *J* = 10.2, H−C(1)); 7.06 (br. *d*, *J* = 8.4, H−C(2′), H−C(6′)); 7.27 (*m*, H−C(4′)); 7.39 (*m*, H−C(3′), H−C(5′)).

7. *Oxidation of 2-Ene Derivatives* **22**, **23**, or **24** *with* N-*Bromosuccinimide* (NBS): *20-Aryl Esters* **5**, *20-*S*-Aryl Esters* (= *(1′*S*,2′*S*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carbothioic Acid* S*-Aryl Esters*) **6**, *and* N*-Aryl-20-amides* (= *(1′*S*,2′*S*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-*N*-Aryl-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′10′a-dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxamides*) **7**: *General Method*. 7.1. To a soln. of **22**, **23**, or **24** (0.025 mmol) in 1,4-dioxane (5 ml), $CaCO_3$ (0.19 mmol) and NBS (0.15 mmol) were added. The mixture was heated at 50° for 6 h under irradiation. After neutralization with 5% aq. HCl soln., the suspension was extracted with Et_2O and the org. layer washed with H_2O, dried ($MgSO_4$), and evaporated: yellow oil **A**. This crude product could be used directly in the next step or purified by FC (hexane/AcOEt 3:1): **5**, **6**, or **7**, resp., and the 1-bromo-2-ene derivatives **26**, **27**, or **28**, resp.

7.2. To the yellow oil **A** in 1,4-dioxane (2 ml) were added $CaCO_3$ (0.026 mmol) and H_2O (20 µl). The mixture was refluxed for 5 h. After neutralization with 5% aq. HCl soln., the mixture was extracted with Et_2O and the org. layer washed with brine, dried ($MgSO_4$), and evaporated: yellowish oil **B**.

7.3. To the yellowish oil **B** in CH_2Cl_2 (5 ml) was added PCC (0.1 mmol), and the soln. was refluxed for 6 h. The mixture was diluted with CH_2Cl_2, the soln. washed with 10% aq. K_2CO_3 soln., and H_2O, dried ($MgSO_4$), and evaporated, and the obtained brown oil purified by FC (SiO_2, hexane/$CHCl_3$/Me_2CO 15:5:1): **5**, **6**, or **7**, resp.

20-(4-Methoxyphenyl) Ester **5f**: From **22e**, 6.9 mg (57.4%) of **5f**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.37. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.11 (*s*, Me(22)); 1.13 (*s*, Me(19)); 1.15 (*s*, Me(21)); 1.20 (*s*, Me(18)); 2.68 (*d*, *J* = 18.4, 1 H−C(15)); 2.71 (*d*, *J* = 18.4, 1 H−C(15)); 3.06 (*dd*, *J* = 4.4, 13.2, H−C(13)); 3.80 (*s*, MeO); 4.48 (*d*, *J* = 10.4, 1 H−C(17)); 4.77 (*d*, *J* = 10.4, 1 H−C(17)); 5.72 (*d*, *J* = 10.0, H−C(2)); 6.36 (*d*, *J* = 10.0, H−C(3)); 6.88 (br. *d*, *J* = 9.2, H−C(3′), H−C(5′)); 6.98 (br. *d*, *J* = 9.2, H−C(2′), H−C(6′)). ESI-MS: 503.3 ([*M* + Na]$^+$).

20-(Naphthalen-1-yl) Ester **5g**: From **22f**, 5.3 mg (44.7%) of **5g**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.10. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.10 (*s*, Me(22)); 1.14 (*s*, Me(19)); 1.17 (*s*, Me(21)); 1.19 (*s*, Me(18)); 2.68 (*d*, *J* = 18.4, 1 H−C(15)); 2.77 (*d*, *J* = 18.4, 1 H−C(15)); 3.09 (*dd*, *J* = 4.4, 13.2, H−C(13)); 4.49 (*d*, *J* = 10.2, 1 H−C(17)); 4.80 (*d*, *J* = 10.2, 1 H−C(17)); 5.72 (*d*, *J* = 10.4, H−C(2)); 6.37 (*d*, *J* = 10.4, H−C(3)); 7.15 (br. *d*, *J* = 7.6, H−C(2′)); 7.36 (*m*, H−C(5′)); 7.45 (*m*, H−C(3′), H−C(4′)); 7.58 (*m*, 3 H). ESI-MS: 501 ([*M* + Na]$^+$).

20-(3,4,5-Trimethoxyphenyl) Ester **5h**: 22.8 mg (14.1% based on **15**) of **5h**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.60. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.07 (*s*, Me(22)); 1.09 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.19 (*s*, Me(18)); 2.66 (*d*, *J* = 18.6, 1 H−C(15)); 2.71 (*d*, *J* = 18.6, 1 H−C(15)); 3.13 (*dd*, *J* = 3.7, 13.3, H−C(13)); 3.82 (*s*, MeO−C(4′)); 3.86 (*s*, MeO−C(3′), MeO−C(5′)); 4.47 (*d*, *J* = 10.3, 1 H−C(17)); 4.76 (*d*, *J* = 10.3, 1 H−C(17)); 5.69 (*d*, *J* = 10.1, H−C(2)); 6.35 (*d*, *J* = 10.1, H−C(3)); 6.52 (br. *s*, H−C(2′), H−C(6′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.3 (C(19)); 18.0 (C(21)); 18.4 (C(6)); 21.8 (C(22)); 22.7 (C(11)); 26.4 (C(12)); 30.9 (C(18)); 32.2 (C(15)); 34.9 (C(7)); 36.3 (C(8)); 40.7 (C(4)); 42.9 (C(9)); 46.6 (C(13)); 47.4 (C(10)); 50.1 (C(14)); 50.8 (C(5)); 56.2 (MeO−C(4′)); 61.2 (MeO−C(3′), MeO−C(5′)); 69.9 (C(17)); 102.9 (C(2′), C(6′)); 124.1 (C(2)); 141.2 (C(4′)); 151.5 (C(1′)); 153.1 (C(3′), C(5′)); 154.7 (C(3)); 171.7 (C(20)); 176.4 (C(16)); 206.2 (C(1)). ESI-MS: 565.3 ([*M* + 2 + Na]$^+$).

20-S-*Phenyl Ester* **6a**: 26.8 mg (19.2% based on **15**) of **6a**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.70. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.08 (*s*, Me(22)); 1.11 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.21 (*s*, Me(18)); 2.65 (br. *s*, 2 H−C(15)); 3.11 (*dd*, *J* = 3.6, 13.2, H−C(13)); 4.41 (*d*, *J* = 10.3, 1 H−C(17)); 4.87 (*d*, *J* = 10.3, 1 H−C(17)); 5.69 (*d*, *J* = 10.1, H−C(2)); 6.33 (*d*, *J* = 10.1, H−C(3)); 7.36 (*m*, 2 H); 7.41 (*m*, 3 H). ESI-MS: 489.3 ([*M* + Na]$^+$).

20-S-*(4-Chlorophenyl) Ester* **6b**: From **23a**, 3.8 mg (30.5%) of **6b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.33. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.06 (*s*, Me(22)); 1.11 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.21 (*s*, Me(18)); 2.60 (*d*, *J* = 18.6, 1 H−C(15)); 2.66 (*d*, *J* = 18.6, 1 H−C(15)); 3.09 (*dd*, *J* = 3.6, 13.2, H−C(13)); 4.40 (*d*, *J* = 10.3, 1 H−C(17)); 4.83 (*d*, *J* = 10.3, 1 H−C(17)); 5.69 (*d*, *J* = 10.1, H−C(2)); 6.34 (*d*, *J* = 10.1, H−C(3)); 7.29 (*dd*, *J* = 6.7, 1.8, H−C(3′), H−C(5′)); 7.39 (*dd*, *J* = 6.7, 1.8, H−C(2′), H−C(6′)). ESI-MS: 523.3 ([*M* + Na]$^+$).

20-S-*(4-Methoxyphenyl) Ester* **6c**: 63.2 mg (42.5% based on **15**) of **6c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.32. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.09 (*s*, Me(22)); 1.12 (*s*, Me(19)); 1.14 (*s*, Me(21)); 1.17 (*s*, Me(18)); 2.70 (br. *s*, 2 H−C(15)); 3.09 (*dd*, *J* = 4.4, 13.2, H−C(13)); 3.83 (*s*, MeO); 4.41 (*d*, *J* = 10.3, 1 H−C(17)); 4.88 (*d*, *J* = 10.3, 1 H−C(17)); 5.70 (*d*, *J* = 10.1, H−C(2)); 6.35 (*d*, *J* = 10.1, H−C(3)); 6.96 (br. *d*, *J* = 8.8, H−C(3′), H−C(5′)); 7.29 (*dd*, *J* = 8.8, H−C(2′), H−C(6′)). ESI-MS: 519.4 ([*M* + Na]$^+$).

N-*Phenyl-20-amide* **7a**: 45.8 mg (34.0% based on **15**) of **7a**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.45. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.08 (*s*, Me(22)); 1.10 (*s*, Me(19)); 1.11 (*s*, Me(21)); 1.18 (*s*, Me(18)); 2.57 (*d*, *J* = 18.0, 1 H−C(15)); 2.61 (*d*, *J* = 18.0, 1 H−C(15)); 4.46 (*d*, *J* = 10.1, 1 H−C(17)); 5.13 (*d*, *J* = 10.1, 1 H−C(17)); 5.69 (*d*, *J* = 10.1, H−C(2)); 6.34 (*d*, *J* = 10.1, H−C(3)); 7.13 (*m*, H−C(4′)); 7.31 (*m*, H−C(3′), H−C(5′)); 7.44 (br. *d*, *J* = 6.4, H−C(2′), H−C(6′)). ESI-MS: 472.4 ([*M* + Na]$^+$).

N-*(4-Chlorophenyl)-20-amide* **7b**: 38.4 mg (26.5% based on **15**) of **7b**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.45. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.09 (*s*, Me(22)); 1.12 (*s*, Me(19)); 1.14 (*s*, Me(21)); 1.20 (*s*, Me(18)); 2.48 (*d*, *J* = 18.3, 1 H−C(15)); 2.60 (*d*, *J* = 18.3, 1 H−C(15)); 4.45 (*d*, *J* = 10.1, 1 H−C(17)); 5.08 (*d*, *J* = 10.1, 1 H−C(17)); 5.69 (*d*, *J* = 10.1, H−C(2)); 6.34 (*d*, *J* = 10.1, H−C(3)); 7.31 (br. *d*, *J* = 8.8, H−C(3′), H−C(5′)); 7.47 (*d*, *J* = 8.8, H−C(2′), H−C(6′)). ESI-MS: 506.3 ([*M* + Na]$^+$).

N-*(4-Methoxyphenyl)-20-amide* **7c**: 25.6 mg (17.8% based on **15**) of **7c**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.48. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.04 (*s*, Me(22)); 1.08 (*s*, Me(19)); 1.12 (*s*, Me(21)); 1.15 (*s*, Me(18)); 2.60 (*d*, *J* = 18.3, 1 H−C(15)); 3.24 (*d*, *J* = 18.3, 1 H−C(15)); 3.80 (*s*, MeO); 4.45 (*d*, *J* = 10.1, 1 H−C(17)); 5.08 (*d*, *J* = 10.1, 1 H−C(17)); 5.70 (*d*, *J* = 10.1, H−C(2)); 6.33 (*d*, *J* = 10.1, H−C(3)); 6.89 (br. *d*, *J* = 8.8, H−C(3′), H−C(5′)); 7.03 (*d*, *J* = 8.8, H−C(2′), H−C(6′)).

1-Bromo-3-deoxy-20-secoebelin-2-en-20-oic Acid Lactone Phenyl Ester (= *(1′*S*,2′*S*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-5-Bromo-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthrene]-2′-carboxylic Acid Phenyl Ester*; **26a**). From **22a**, 4.9 mg (39.6%) of **26a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.35. ^{1}H-NMR (400 MHz, $(CD_3)_2CO$): 0.95 (*s*, Me(22)); 1.05 (*s*, Me(19)); 1.09 (*s*, Me(21)); 1.19 (*s*, Me(18)); 2.63 (*d*, *J* = 18.4, 1 H−C(15)); 2.78 (*d*, *J* = 18.4, 1 H−C(15)); 3.17 (*dd*, *J* = 3.7, 13.6, H−C(13));

4.54 (*d*, *J* = 10.4, 1 H–C(17)); 4.62 (*d*, *J* = 10.4, 1 H–C(17)); 4.72 (*d*, *J* = 5.6, H–C(1)); 5.48 (*d*, *J* = 9.6, H–C(3)); 5.84 (*dd*, *J* = 5.6, 9.6, H–C(2)); 7.12 (br. *d*, *J* = 8.0, H–C(2′), H–C(6′)); 7.24 (*m*, H–C(4′)); 7.39 (*m*, H–C(3′), H–C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.5 (C(19)); 17.1 (C(21)); 19.5 (C(6)); 23.4 (C(22)); 20.1 (C(11)); 26.6 (C(12)); 30.8 (C(18)); 32.3 (C(15)); 35.2 (C(7)); 35.6 (C(8)); 40.8 (C(4)); 41.3 (C(10)); 45.3 (C(13)); 46.9 (C(9)); 47.1 (C(5)); 51.3 (C(14)); 63.3 (C(1)); 70.0 (C(17)); 122.6 (C(2′), C(6′)); 124.8 (C(2)); 126.7 (C(4′)); 130.2 (C(3′), C(5′)); 140.4 (C(3)); 151.6 (C(1′)); 173.4 (C(20)); 176.3 (C(16)). EI-MS: 419 (4, $[M - Br]^+$), 406 (5), 378 (7), 341 (9), 313 (18).

8. *(20*E*)-3-*O*-(Methylsulfonyl)-22-secoebelin-22-oic Acid Lactone 22-Aryl Esters* (= *(2*E*)-2-Methyl-3-[(1′*S*,2′*R*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsulfonyl)oxy]-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl]prop-2-enoic Acid Aryl Esters*) **30**, *(20*E*)-3-*O*-(Methylsulfonyl)-22-secoebelin-22-oic Acid Lactone 22-*S*-Aryl Esters* (= *(2*E*)-2-Methyl-3-[(1′*S*,2′*R*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsulfonyl)oxy]-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl]prop-2-enethioic Acid* S*-Aryl Esters*) **31**, *or (20*E*)-*N*-Aryl-3-*O*-(Methylsulfonyl)-22-secoebelin-22-amide Lactones* (= *(2*E*)-*N*-Aryl-2-methyl-3-[(1′*S*,2′*R*,4′a*R*,4′b*R*,7′*S*,8′a*R*,10′a*R*)-tetradecahydro-4′b,8′,8′,10′a-tetramethyl-7′-[(methylsulfonyl)oxy]-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′yl]prop-2-enamides*) **32**: *General Method*. To a soln of **16** (81.6 mg, 0.17 mmol) in CCl_4 (10 ml), NBS (33.8 mg, 0.19 mmol) was added under N_2. The flask was irradiated with a 100-W flood lamp, and the spontaneous reflux was allowed to continue for 5 min. Then the mixture containing acyl bromide **29** was cooled to 0° and treated directly with the substituted phenol, thiophenol, or aniline (0.2 mmol in each case) in the presence of Et_3N (0.17 mmol). Stirring was continued for 1 h at r.t. After evaporation, the residue was diluted with CH_2Cl_2 (10 ml), the soln. washed with H_2O, dried ($MgSO_4$), and evaporated, and the crude product purified by CC (SiO_2, hexane/AcOEt (3:1): **30**, **31**, or **32**, resp.

22-Phenyl Ester **30a**: Yield 58.5 mg (60.2%). Colorless oil. R_f (hexane/AcOEt 3:1) 0.28. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.92 (*s*, Me(19)); 1.04 (*s*, Me(24)); 1.09 (*s*, Me(18)); 1.99 (br. *s*, Me(23)); 2.06 (*d*, *J* = 18.3, 1 H–C(15)); 2.56 (*d*, *J* = 18.7, 1 H–C(15)); 2.91 (*m*, H–C(13)); 3.02 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 4.5, 11.3, H–C(3)); 4.38 (*d*, *J* = 10.4, 1 H–C(17)); 4.45 (*d*, *J* = 10.6, 1 H–C(17)); 6.79 (br. *d*, *J* = 10.7, H–C(20)); 7.10 (*dd*, *J* = 1.0, 8.4, H–C(2′), H–C(6′)); 7.24 (*m*, H–C(4′)); 7.39 (*m*, H–C(3′), H–C(5′)). EI-MS: 479 (8, $[M - PhO]^+$), 476 (6), 383 (100). FAB-MS: 573 (23, $[M + 1]^+$), 479 (100), 383 (16).

22-(4-Chlorophenyl) Ester **30b**: Yield 44.4 mg (43%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.42. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (*s*, Me(25)); 0.94 (*s*, Me(19)); 1.08 (*s*, Me(24)); 1.11 (*s*, Me(18)); 2.00 (*d*, *J* = 1.2, Me(23)); 2.05 (*d*, *J* = 18.4, 1 H–C(15)); 2.58 (*d*, *J* = 18.4, 1 H–C(15)); 2.93 (*ddd*, *J* = 2.0, 3.6, 10.4, H–C(13)); 3.03 (*s*, $MeSO_2$); 4.36 (*dd*, *J* = 5.2, 12.0, H–C(3)); 4.40 (*d*, *J* = 10.4, 1 H–C(17)); 4.46 (*d*, *J* = 10.4, 1 H–C(17)); 6.79 (*dd*, *J* = 1.2, 10.4, H–C(20)); 7.07 (*dd*, *J* = 1.6, 8.2, H–C(2′), H–C(6′)); 7.36 (*dd*, *J* = 1.6, 8.4, H–C(3′), H–C(5′)).

22-(4-Methoxyphenyl) Ester **30c**: Yield 55.6 mg (54.3%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.47. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(25)); 0.91 (*s*, Me(19)); 1.03 (*s*, Me(24)); 1.07 (*s*, Me(18)); 1.97 (*d*, *J* = 1.2, Me(23)); 2.05 (*d*, *J* = 18.0, 1 H–C(15)); 2.53 (*d*, *J* = 18.4, 1 H–C(15)); 2.88 (*ddd*, *J* = 2.0, 3.6, 10.4, H–C(13)); 3.01 (*s*, $MeSO_2$); 3.78 (*s*, MeO); 4.37 (*dd*, *J* = 4.8, 11.6, H–C(3)); 4.37 (*d*, *J* = 10.8, 1 H–C(17)); 4.42 (*d*, *J* = 10.8, 1 H–C(17)); 6.75 (*dd*, *J* = 1.2, 10.8, H–C(20)); 6.89 (br. *d*, *J* = 9.2, H–C(3′), H–C(5′)); 6.99 (br. *d*, *J* = 9.2, H–C(2′), H–C(6′)).

22-(4-Nitrophenyl) Ester **30d**: Yield 78.2 mg (74.6%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.63. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.94 (*s*, Me(19)); 1.06 (*s*, Me(24)); 1.12 (*s*, Me(18)); 2.03 (*d*, *J* = 1.2, Me(23)); 2.39 (*d*, *J* = 18.8, 1 H–C(15)); 2.59 (*d*, *J* = 18.8, 1 H–C(15)); 2.94 (*ddd*, *J* = 2.0, 3.6, 10.4, H–C(13)); 3.04 (*s*, $MeSO_2$); 4.35 (*dd*, *J* = 4.8, 11.2, H–C(3)); 4.39 (*d*, *J* = 12.8, 1 H–C(17)); 4.43 (*d*, *J* = 12.8, 1 H–C(17)); 6.91 (*dd*, *J* = 1.2, 10.8, H–C(20)); 7.32 (br. *d*, *J* = 9.2, H–C(3′), H–C(5′)); 8.30 (br. *d*, *J* = 9.2, H–C(2′), H–C(6′)).

22-(3,4,5-Trimethoxyphenyl) Ester **30e**: Yield 23.7 mg (21.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.50. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(25)); 0.89 (*s*, Me(19)); 1.05 (*s*, Me(24)); 1.05 (*s*, Me(18)); 2.09 (*d*, *J* = 1.2, Me(23)); 2.41 (*d*, *J* = 18.0, 1 H–C(15)); 2.52 (*d*, *J* = 18.0, 1 H–C(15)); 3.03 (*m*, H–C(13)); 3.04 (*s*, $MeSO_2$); 3.84 (*s*, MeO–C(4′)); 3.88 (*s*, MeO–C(3′), MeO–C(5′)); 4.35 (*dd*, *J* = 4.4, 11.2, H–C(3)); 4.37 (*d*, *J* = 10.4, 1 H–C(17)); 4.41 (*d*, *J* = 10.4, 1 H–C(17)); 5.88 (*dd*, *J* = 1.2, 11.6, H–C(20)); 6.36 (br. *s*, H–C(2′), H–C(6′)).

*22-*S*-Phenyl Ester* **31a**: Yield 44.4 mg (44.4%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.36. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(25)); 0.93 (*s*, Me(19)); 1.06 (*s*, Me(24)); 1.09 (*s*, Me(18)); 1.96 (*d*, *J* = 1.2, Me(23)); 2.04 (*d*, *J* = 18.0, 1 H–C(15)); 2.58 (*d*, *J* = 18.0, 1 H–C(15)); 2.94 (*m*, H–C(13)); 3.04 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 3.2, 8.0, H–C(3)); 4.41 (*d*, *J* = 10.4, 1 H–C(17)); 4.48 (*d*, *J* = 10.4, 1 H–C(17)); 6.62 (*dd*, *J* = 1.2, 10.4, H–C(20)); 7.42 (*m*, 5 H).

N-*Phenyl-22-amide* **32a**: Yield 70.2 mg (72.3%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.43. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.92 (*s*, Me(19)); 1.05 (*s*, Me(24)); 1.11 (*s*, Me(18)); 2.00 (*d*, *J* = 1.6, Me(23)); 1.99 (*d*, *J* = 17.2, 1 H–C(15)); 2.66 (*d*, *J* = 17.2, 1 H–C(15)); 2.87 (*ddd*, *J* = 4.8, 10.8, 12.4, H–C(13)); 3.04 (*s*, $MeSO_2$); 4.35 (*dd*, *J* = 4.8, 11.6, H–C(3)); 4.42 (*d*, *J* = 10.4, 1 H–C(17)); 4.46 (*d*, *J* = 10.4, 1 H–C(17)); 5.80 (*dd*, *J* = 1.6, 10.8, H–C(20)); 7.11 (*t*, *J* = 4.8, 4.8, H–C(4′)); 7.34 (*t*, *J* = 4.8, 8.8, H–C(3′), H–C(5′)); 7.59 (*dd*, *J* = 0.8, 8.8, H–C(2′), H–C(6′)).

N-*(4-Chlorophenyl)-22-amide* **32b**: Yield 46.4 mg (45.1%). Colorless oil. R_f (hexane/AcOEt 1:1) 0.37. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(25)); 0.92 (*s*, Me(19)); 1.04 (*s*, Me(24)); 1.10 (*s*, Me(18)); 1.98 (*d*, *J* = 1.6, Me(23)); 1.96 (*d*, *J* = 17.2, 1 H–C(15)); 2.64 (*d*, *J* = 17.2, 1 H–C(15)); 2.87 (*ddd*, *J* = 4.8, 10.8, 12.4, H–C(13)); 3.04 (*s*, $MeSO_2$); 4.34 (*dd*, *J* = 4.2, 12.0, H–C(3)); 4.42 (*d*, *J* = 10.0, 1 H–C(17)); 4.47 (*d*, *J* = 10.0, 1 H–C(17)); 5.78 (br. *d*, *J* = 10.4, H–C(20)); 7.28 (*dd*, *J* = 2.0, 8.8, H–C(3′), H–C(5′)); 7.55 (*dd*, *J* = 2.0, 8.8, H–C(2′), H–C(6′)).

9. *(20*E*)-3-Deoxy-22-secoebelin-2-en-22-oic Acid Lactone 22-Aryl Esters* (= *(2*E*)-3-[(1′*S*,2′*R*,4′a*R*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl]-2-methylprop-2-enoic Acid Aryl Esters*) **33**, *(20*E*)-3-Deoxy-22-secoebelin-2-en-22-oic Acid Lactone 22-*S*-Aryl Esters* (= *(2*E*)-3-[(1′*S*,2′*R*,4′a*R*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl]-2-methylprop-2-enethioic Acid* S*-Aryl Esters*) **34**, *or (20*E*)-*N*-Aryl-3-deoxy-22-secoebelin-2-en-22-amide Lactones* (= *(2*E*)-*N*-Aryl-3-[(1′*S*,2′*R*,4′a*R*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-dodecahydro-4′b,8′,8′,10′a-tetramethyl-5-oxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl]-2-methylprop-2-enamide*) **35**: *General Method*. To a soln. of **30**, **31**, or **32** (0.1 mmol) in *N*,*N*-dimethylacetamide (10 ml), Li_2CO_3 (0.5 mmol) was added. The mixture was refluxed for 0.5 h and cooled to r.t. The suspension was taken up with 1M aq. HCl and extracted with Et_2O, the org. layer washed with brine, dried ($MgSO_4$), and evaporated, and the crude product purified by FC (hexane/AcOEt 5:1): **33**, **34**, or **35**, resp.

22-Phenyl Ester **33a**: From **30a**, 27.2 mg (57.2%) of **33a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.61. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.97 (*s*, Me(19)); 1.10 (*s*, Me(24)); 1.11 (*s*, Me(18)); 2.03 (br. *s*, Me(23)); 2.08 (*d*, *J* = 18.4, 1 H–C(15)); 2.56 (*d*, *J* = 18.4, 1 H–C(15)); 2.93 (*m*, H–C(13)); 4.39 (*d*, *J* = 10.4, 1 H–C(17)); 4.49 (*d*, *J* = 10.4, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 6.81 (br. *d*, *J* = 10.8, H–C(20)); 7.09 (br. *d*, *J* = 8.0, H–C(2′), H–C(6′)); 7.24 (*t*, *J* = 7.6, 7.6, H–C(4′)); 7.37 (*t*, *J* = 7.6, 8.0, H–C(3′), H–C(5′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 13.3 (C(23)); 16.2 (C(19)); 17.3 (C(24)); 18.9 (C(6)); 20.1 (C(11)); 22.6 (C(18)); 28.2 (C(12)); 31.6 (C(25)); 33.1 (C(15)); 34.7 (C(7)); 36.3 (C(10)); 38.6 (C(8)); 40.0 (C(9)); 40.2 (C(4)); 40.8 (C(1)); 51.2 (C(13)); 51.4 (C(14)); 51.8 (C(5)); 69.3 (C(17)); 120.9 (C(2)); 121.7 (C(2′), C(6′); 125.7 (C(4′)); 129.3 (C(3′), C(5′)); 130.3 (C(21)); 137.9 (C(3)); 142.3 (C(20)); 150.9 (C(1′)); 165.9 (C(22)); 176.4 (C(16)). EI-MS: 383 (100, $[M - PhO]^+$), 355 (1), 121 (41), 93 (60).

22-(4-Chlorophenyl) Ester **33b**: From **30b**, 21.3 mg (41.7%) of **33b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.50. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.90 (*s*, Me(25)); 0.92 (*s*, Me(19)); 0.99 (*s*, Me(24)); 1.13 (*s*, Me(18)); 2.01 (*d*, *J* = 1.6, Me(23)); 2.06 (*d*, *J* = 18.2, 1 H–C(15)); 2.60 (*d*, *J* = 18.2, 1 H–C(15)); 2.97 (*m*, H–C(13)); 4.39 (*d*, *J* = 10.4, 1 H–C(17)); 4.51 (*d*, *J* = 10.4, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 6.82 (*dd*, *J* = 1.6, 10.8, H–C(20)); 7.07 (br. *d*, *J* = 8.8, H–C(2′), H–C(6′)); 7.35 (br. *d*, *J* = 8.0, H–C(3′), H–C(5′)).

22-(4-Methoxyphenyl) Ester **33c**: From **30c**, 37.8 mg (74.7%) of **33c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.33. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.92 (*s*, Me(19)); 1.01 (*s*, Me(24)); 1.12 (*s*, Me(18)); 2.01 (*d*, *J* = 1.2, Me(23)); 1.98 (*d*, *J* = 18.2, 1 H–C(15)); 2.60 (*d*, *J* = 18.2, 1 H–C(15)); 2.98 (*m*, H–C(13)); 3.81 (*s*, MeO); 4.42 (*d*, *J* = 10.4, 1 H–C(17)); 4.54 (*d*, *J* = 10.4, 1 H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 6.30 (*dd*, *J* = 1.2, 10.4, H–C(20)); 6.91 (br. *d*, *J* = 8.2, H–C(3′), H–C(5′)); 7.02 (br. *d*, *J* = 8.2, H–C(2′), H–C(6′)).

22-(4-Nitrophenyl) Ester **33d**: From **30d**, 28 mg (53.8%) of **33d**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.53. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.93 (*s*, Me(19)); 0.99 (*s*, Me(24)); 1.12 (*s*, Me(18)); 2.03 (*d*, *J* = 1.2, Me(23)); 2.10 (*d*, *J* = 18.0, 1 H–C(15)); 2.66 (*d*, *J* = 18.0, 1 H–C(15)); 2.99 (*m*, H–C(13)); 4.41 (*d*, *J* = 10.8, H–C(17)); 4.52 (*d*, *J* = 10.8, H–C(17)); 5.42 (*m*, H–C(3)); 5.43 (*m*, H–C(2)); 6.86 (*dd*, *J* = 1.2, 10.4, H–C(20)); 7.31 (br. *d*, *J* = 9.2, H–C(3′), H–C(5′)); 8.28 (br. *d*, *J* = 9.2, H–C(2′), H–C(6′)).

22-(3,4,5-Trimethoxyphenyl) Ester **33e**: From **30e**, 15.6 mg (27.6%) of **33e**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.62. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.89 (*s*, Me(19)); 0.97 (*s*, Me(24)); 1.07 (*s*, Me(18)); 2.13 (br. *s*, Me(23)); 2.65 (*d*, *J* = 18.2, 1 H–C(15)); 2.73 (*d*, *J* = 18.2, 1 H–C(15)); 3.01 (*m*, H–C(13)); 3.80 (*s*, MeO–C(4′)); 3.82 (*s*, MeO–C(3′), MeO–C(5′)); 4.41 (*d*, *J* = 10.8, 1 H–C(17)); 4.68 (*d*, *J* = 10.8, 1 H–C(17)); 5.41 (*m*, H–C(3)); 5.40 (*m*, H–C(2)); 6.36 (br. *d*, *J* = 10.4, H–C(20)); 6.28 (br. *s*, H–C(2′), H–C(6′)).

22-S-*Phenyl Ester* **34a**: From **31a**, 13.4 mg (27.3%) of **34a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.55. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.86 (*s*, Me(25)); 0.90 (*s*, Me(19)); 0.98 (*s*, Me(24)); 1.03 (*s*, Me(18)); 2.12 (*d*, *J* = 1.6, Me(23)); 2.36 (*d*, *J* = 18.0, 1 H−C(15)); 2.56 (*d*, *J* = 18.0, 1 H−C(15)); 3.40 (*m*, H−C(13)); 4.32 (*d*, *J* = 10.4, 1 H−C(17)); 4.44 (*d*, *J* = 10.4, 1 H−C(17)); 5.42 (*m*, H−C(3)); 5.43 (*m*, H−C(2)); 5.52 (*dd*, *J* = 1.6, 10.2, H−C(20)); 7.45 (*m*, 5 H).

22-(4-Chlorophenyl) Ester **34b**: 42.1 mg (47.0% based on **16**) of **34b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.67. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.89 (*s*, Me(25)); 0.92 (*s*, Me(19)); 0.97 (*s*, Me(24)); 1.12 (*s*, Me(18)); 1.97 (*d*, *J* = 1.2, Me(23)); 2.56 (*d*, *J* = 18.2, 1 H−C(15)); 2.64 (*d*, *J* = 18.2, 1 H−C(15)); 2.92 (*m*, H−C(13)); 4.42 (*d*, *J* = 10.8, 1 H−C(17)); 4.54 (*d*, *J* = 10.8, 1 H−C(17)); 5.43 (*m*, H−C(3)); 5.44 (*m*, H−C(2)); 6.63 (*dd*, *J* = 1.2, 10.0, H−C(20)); 7.38 (br. *d*, *J* = 9.2, H−C(3′), H−C(5′)); 7.39 (br. *d*, *J* = 9.2, H−C(2′), H−C(6′)).

22-S-*(4-Methoxyphenyl) Ester* **34c**: 40.2 mg (44.9% based on **16**) of **34c**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.33. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.92 (*s*, Me(25)); 0.96 (*s*, Me(19)); 1.11 (*s*, Me(24)); 1.13 (*s*, Me(18)); 1.96 (*d*, *J* = 1.2, Me(23)); 2.08 (*d*, *J* = 18.2, 1 H−C(15)); 2.60 (*d*, *J* = 18.2, 1 H−C(15)); 2.96 (*m*, H−C(13)); 3.84 (*s*, MeO); 4.41 (*d*, *J* = 10.4, 1 H−C(17)); 4.54 (*d*, *J* = 10.4, 1 H−C(17)); 5.42 (*m*, H−C(3)); 5.43 (*m*, H−C(2)); 6.63 (*dd*, *J* = 1.2, 10.4, H−C(20)); 6.95 (br. *d*, *J* = 8.8, H−C(3′), H−C(5′)); 7.33 (br. *d*, *J* = 8.8, H−C(2′), H−C(6′)).

N-*Phenyl-22-amide* **35a**: From **32a**, 24 mg (50.5%) of **35a**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.33. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.88 (*s*, Me(25)); 0.93 (*s*, Me(19)); 0.99 (*s*, Me(24)); 1.11 (*s*, Me(18)); 1.98 (*d*, *J* = 1.6, Me(23)); 1.98 (*d*, *J* = 18.2, 1 H−C(15)); 2.66 (*d*, *J* = 18.2, 1 H−C(15)); 2.91 (*m*, H−C(13)); 4.42 (*d*, *J* = 10.8, 1 H−C(17)); 4.51 (*d*, *J* = 10.8, 1 H−C(17)); 5.42 (*m*, H−C(3)); 5.43 (*m*, H−C(2)); 5.82 (*dd*, *J* = 1.6, 10.8, H−C(20)); 7.10 (*t*, *J* = 7.6, H−C(4′)); 7.32 (*t*, *J* = 7.6, 8.4, H−C(3′), H−C(5′)); 7.33 (br. *d*, *J* = 8.4, H−C(2′), H−C(6′)).

N-*(4-Chlorophenyl-22-amide* **35b**: From **32b**, 23.4 mg (45.9%) of **35b**. Colorless oil. R_f (hexane/AcOEt 4:1) 0.37. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.87 (*s*, Me(25)); 0.89 (*s*, Me(19)); 1.01 (*s*, Me(24)); 1.14 (*s*, Me(18)); 1.98 (*d*, *J* = 1.6, Me(23)); 1.98 (*d*, *J* = 17.2, 1 H−C(15)); 2.66 (*d*, *J* = 17.2, 1 H−C(15)); 2.90 (*m*, H−C(13)); 4.42 (*d*, *J* = 10.4, 1 H−C(17)); 4.53 (*d*, *J* = 10.4, 1 H−C(17)); 5.43 (*m*, H−C(3)); 5.45 (*m*, H−C(2)); 5.80 (*dd*, *J* = 1.6, 10.4, H−C(20)); 7.28 (*dd*, *J* = 2.0, 6.8, H−C(3′), H−C(5′)); 7.56 (*dd*, *J* = 2.0, 6.8, H−C(2′), H−C(6′)).

10. *(20*E*)-3-Deoxy-1-oxo-22-secoebelin2-en-22-oic Acid Lactone 22-Aryl Esters* (=*(2*E*)-3-{(1′*S*,2′*R*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl}-2-methylprop-2-enoic Acid Aryl Esters*) **8**, *(20*E*)-3-Deoxy-1-oxo-22-secoebelin-2-en-22-oic Acid Lactone 22-*S*-Aryl Esters* (=*(2*E*)-3-{(1′*S*,2′*R*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-Dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl}-2-methylprop-2-enethioic Acid* S*-Aryl Esters*) **9**, *and (20*E*)-*N*-Aryl-3-deoxy-1-oxo-22-secoebelin-2-en-22-amide Lactones* (=*(2*E*)-*N*-Aryl-3-{(1′*S*,2′*R*,4′a*S*,4′b*S*,8′a*S*,10′a*R*)-3′,4,4′,4′a,4′b,5,5′,8′,8′a,9′,10′,10′a-dodecahydro-4′b,8′,8′,10′a-tetramethyl-5,5′-dioxospiro[furan-3(2*H*),1′(2′*H*)-phenanthren]-2′-yl}-2-methylprop-2-enamides*) **10**: *General Method*. 10.1. To a soln. of **33**, **34**, or **35** (0.025 mmol) in dioxane (5 ml), $CaCO_3$ (0.14 mmol) and NBS (0.12 mmol) were added. The mixture was heated at 50° for 6 h under irradiation. After neutralization with 5% aq. HCl soln., the mixture was extracted with Et_2O and the org. layer washed with H_2O, dried ($MgSO_4$), and evaporated: yellowish oil **C**. This crude product could be used directly in the next step or could be purified by FC (hexane/AcOEt 3:1): **8**, **9**, or **10**, resp., and the by-products **36**, **37**, or **38**, resp.

10.2. To the crude yellowish oil **C** in dioxane (5 ml), $CaCO_3$ (0.14 mmol) and H_2O (50 µl) were added. The mixture was refluxed for 5 h. After neutralization with 5% aq. HCl soln., the mixture was extracted with Et_2O (3 × 10 ml) and the org. layer washed with H_2O (10 ml), dried ($MgSO_4$), and evaporated: yellowish oil **D**.

10.3. To the yellowish oil **D** in CH_2Cl_2 (5 ml), PCC (0.1 mmol) was added and the mixture refluxed for 6 h. The mixture was diluted with CH_2Cl_2 (20 ml), the soln. washed with 10% aq. K_2CO_3 soln. and H_2O, dried ($MgSO_4$), and evaporated, and the a brown oil purified by FC (SiO_2, hexane/$CHCl_3$/Me_2CO 15:5:1): **8**, **9**, or **10**, resp.

22-Phenyl Ester **8a**: From **33a**, 4.1 mg (34%) of **8a**. Colorless oil. R_f (hexane/AcOEt 3:1) 0.42. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.10 (*s*, Me(25)); 1.13 (*s*, Me(19)); 1.18 (*s*, Me(24)); 1.24 (*s*, Me(18)); 2.01 (br. *s*, Me(23)); 2.08 (*d*, *J* = 18.4, 1 H−C(15)); 2.56 (*d*, = 18.4, 1 H−C(15)); 2.98 (*m*, H−C(13)); 4.46 (*m*, 2 H−C(17)); 5.71 (*d*, *J* = 10.0, H−C(2)); 6.34 (*m*, *J* = 10.0, H−C(3)); 6.85 (br. *d*, *J* = 10.8, H−C(20)); 7.11 (br. *d*, *J* = 7.6, H−C(2′), H−C(6′)); 7.25 (*m*, H−C(4′)); 7.38 (*m*, H−C(3′), H−C(5′)).

22-(4-Chlorophenyl) Ester **8b**: 30.2 mg (33.9% based on **16**) of **8b**. Colorless oil. R_f (hexane/AcOEt 3:1) 0.42. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.07 (*s*, Me(25)); 1.12 (*s*, Me(19)); 1.17 (*s*, Me(24)); 1.22 (*s*, Me(18)); 2.00 (br. *s*, Me(23)); 2.08 (*d*, *J* = 18.4, 1 H−C(15)); 2.56 (*d*, *J* = 18.4, 1 H−C(15)); 2.97 (*m*, H−C(13)); 4.41

(br. *s*, 2 H–C(17)); 5.69 (*d*, *J* = 10.1, H–C(2)); 6.34 (*m*, *J* = 10.1, H–C(3)); 6.84 (br. *d*, *J* = 10.6, H–C(20)); 7.10 (*dd*, *J* = 0.4, 8.1, H–C(2′), H–C(6′)); 7.38 (*dd*, *J* = 0.4, 8.1, H–C(3′), H–C(5′)). ESI-MS: 479 ([*M* + 1 + Na – Cl]$^+$).

22-(4-Methoxyphenyl) Ester **8c**: From **33c**, 4.2 mg (32.1%) of **8c**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.59. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.07 (*s*, Me(25)); 1.12 (*s*, Me(19)); 1.16 (*s*, Me(24)); 1.22 (*s*, Me(18)); 1.97 (*d*, *J* = 0.8, Me(23)); 2.06 (*d*, *J* = 18.4, 1 H–C(15)); 2.56 (*d*, *J* = 18.4, 1 H–C(15)); 2.94 (*m*, H–C(13)); 4.48 (*m*, 2 H–C(17)); 5.70 (*d*, *J* = 10.1, H–C(2)); 6.34 (*m*, *J* = 10.1, H–C(3)); 6.64 (*dd*, *J* = 1.1, 10.3, H–C(20)); 6.93 (*dd*, *J* = 1.8, 8.7, H–C(2′), H–C(6′)); 7.32 (*dd*, *J* = 1.8, 8.7, H–C(3′), H–C(5′)). ESI-MS: 559.6 ([*M* + K]$^+$).

22-(3,4,5-Trimethoxyphenyl) Ester **8d**: 19.1 mg (19.4% based on **16**) of **8d**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.55. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.09 (*s*, Me(25)); 1.12 (*s*, Me(19)); 1.17 (*s*, Me(24)); 1.22 (*s*, Me(18)); 2.03 (*d*, *J* = 1.1, Me(23)); 2.03 (*d*, *J* = 18.3, 1 H–C(15)); 2.56 (*d*, *J* = 18.3, 1 H–C(15)); 3.01 (*m*, H–C(13)); 3.83 (*s*, MeO–C(4′)); 3.87 (*s*, MeO–C(3′), MeO–C(5′)); 4.47 (br. *s*, 2 H–C(17)); 5.70 (*d*, *J* = 10.1, H–C(2)); 6.35 (*m*, *J* = 10.1, H–C(3)); 6.92 (*dd*, *J* = 1.0, 10.4, H–C(20)); 6.60 (br. *s*, H–C(2′), H–C(6′)). ^{13}C-NMR (100 MHz, $CDCl_3$): 13.3 (C(23)); 14.1 (C(19)); 18.0 (C(24)); 18.4 (C(6)); 23.1 (C(11)); 21.8 (C(18)); 28.1 (C(12)); 29.6 (C(25)); 34.7 (C(15)); 33.1 (C(7)); 36.4 (C(10)); 40.1 (C(8)); 40.4 (C(13)); 43.1 (C(9)); 47.5 (C(4)); 50.9 (C(5)); 51.4 (C(14)); 56.2 (*Me*O–C(4′)); 61.1 (*Me*O–C(3′), *Me*O–C(5′); 69.2 (C(17)); 103.4 (C(2′), C(6′)); 124.0 (C(2)); 129.6 (C(21)); 141.4 (C(4′)); 143.2(C(20)); 144.6 (C(1′)); 152.9 (C(3′), C(5′)); 154.7 (C(3)); 165.1 (C(22)); 175.8 (C(16)); 206.2 (C(1)). ESI-MS: 580.4 (10, M^+).

22-S-*Phenyl Ester* **9a**: 11.6 mg (13.5% based on **16**) of **9a**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.60. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.09 (*s*, Me(25)); 1.11 (*s*, Me(19)); 1.16 (*s*, Me(24)); 1.23 (*s*, Me(18)); 1.95 (*d*, *J* = 1.0, Me(23)); 2.04 (*d*, *J* = 18.3, 1 H–C(15)); 2.57 (*d*, *J* = 18.3, 1 H–C(15)); 2.98 (*m*, H–C(13)); 4.48 (*m*, 2 H–C(17)); 5.70 (*d*, *J* = 10.1, H–C(2)); 6.34 (*m*, *J* = 10.1, H–C(3)); 6.68 (*dd*, *J* = 1.0, 10.5, H–C(20)); 7.40–7.42 (*m*, 5 H). ESI-MS: 529 (100, [*M* + Na]$^+$).

22-S-*(4-Chlorophenyl) Ester* **9b**: 19.7 mg (21.5% based on **16**) of **9b**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.62. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.09 (*s*, Me(25)); 1.12 (*s*, Me(19)); 1.16 (*s*, Me(24)); 1.22 (*s*, Me(18)); 1.94 (br. *s*, Me(23)); 1.98 (*d*, *J* = 18.4, 1 H–C(15)); 2.58 (*d*, *J* = 18.4, 1 H–C(15)); 2.96 (*m*, H–C(13)); 4.47 (br. *s*, 2 H–C(17)); 5.70 (*d*, *J* = 10.1, H–C(2)); 6.34 (*m*, *J* = 10.1, H–C(3)); 6.59 (br. *d*, *J* = 10.3, H–C(20)); 7.33–7.36 (*m*, 4 H). ^{13}C-NMR (100 MHz, $CDCl_3$): 13.4 (C(23)); 15.7 (C(19)); 17.9 (C(24)); 18.0 (C(6)); 21.8 (C(18)); 23.0 (C(11)); 27.8 (C(12)); 31.0 (C(25)); 32.8 (C(7)); 34.8 (C(15)); 36.3 (C(10)); 39.9 (C(8)); 40.0 (C(13)); 43.1 (C(9)); 47.4 (C(4)); 50.8 (C(5)); 52.3 (C(14)); 69.4 (C(17)); 124.0 (C(2)); 129.2 (C(2′), C(6′)); 129.6 (C(21)); 135.8 (C(4′)); 136.3 (C(3′), C(5′)); 138.4 (C(20)); 141.4 (C(1′)); 151.7 (C(3)); 175.9 (C(16)); 191.4 (C(22)); 206.4 (C(1)). ESI-MS: 564.3 ([*M* + 1 + Na]$^+$).

22-S-*(4-Methoxyphenyl) Ester* **9c**: From **34c**, 8.2 mg (61.0%) of **9c**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.59. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.09 (*s*, Me(25)); 1.12 (*s*, Me(19)); 1.17 (*s*, Me(24)); 1.23 (*s*, Me(18)); 2.06 (br. *s*, Me(23)); 2.06 (*d*, *J* = 18.2, 1 H–C(15)); 2.56 (*d*, *J* = 18.2, 1 H–C(15)); 2.94 (*m*, H–C(13)); 3.80 (*s*, MeO); 4.46 (br. *s*, 2 H–C(17)); 5.70 (*d*, *J* = 10.1, H–C(2)); 6.34 (*m*, *J* = 10.1, H–C(3)); 6.82 (br. *d*, *J* = 10.5, H–C(20)); 6.88 (br. *d*, *J* = 8.7, H–C(3′), H–C(5′)); 7.02 (br. *d*, *J* = 8.7, H–C(2′), H–C(6′)). ESI-MS: 538 ([*M* + 2]$^+$).

N-*(4-Methoxyphenyl)-22-amide* **10a**: From **16**, 11.5 mg (13.1%) of **10a**. Colorless oil. R_f (hexane/AcOEt 1:1) 0.67. ^{1}H-NMR (500 MHz, $CDCl_3$): 1.06 (*s*, Me(25)); 1.09 (*s*, Me(19)); 1.12 (*s*, Me(24)); 1.22 (*s*, Me(18)); 2.05 (br. *s*, Me(23)); 2.51 (*d*, *J* = 18.2, 1 H–C(15)); 2.62 (*d*, *J* = 18.2, 1 H–C(15)); 2.94 (*m*, H–C(13)); 3.82 (*s*, MeO); 4.35 (br. *s*, 2 H–C(17)); 5.66 (*d*, *J* = 10.2, H–C(2)); 6.35 (*m*, *J* = 10.2, H–C(3)); 6.84 (br. *d*, *J* = 10.4, H–C(20)); 7.47 (*m*, 4 H). ESI-MS: 543.1 ([*M* + 1 + Na]$^+$).

11. *AChE Inhibitory Activities.* AChE activity was measured spectrophotometrically according to *Ellman et al.* [12]. Briefly, to 3 ml of 0.1M phosphate buffer at pH 8.0, 20 µl of 0.075M acetylthiocholine iodide or chloride (*Sigma*, U.S.A.) was added, followed by 100 µl of 0.1M 5,5′-dithiobis[2-nitrobenzoic acid] and 10–100 µl of the sample to be tested. At 25°, the reaction was started by addition of 20 µl of an AChE (*Sigma*, U.S.A.) stock soln. (5 units/ml), and the time course of the enzyme activity was monitored for 3 min.

12. *KB Cell Cytotoxicity Assay.* KB-Cells survival was determined by the MTT assays [17]. Briefly, the tetrazolium salt MTT (= 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide; *Sigma*, St. Louis, MO, USA) soln. was prepared at 5 mg/ml in phosphate-buffered saline freshly before use. KB Cells were diluted in fresh complete medium and seeded in 96-well plates (*Falcon*, Franklin Lakes, NJ, USA) (10^4 cells/well). After 24 h incubation, cells were treated with various concentrations of synthetic compounds for 72 h, then 10 µl of MTT soln. was added to each well. The plates were then incubated in a CO_2 incubator for 4 h. After incubation, the cells were lysed with DMSO. The plates were analyzed in a multiwell-plate reader (*Bio-Tek Instruments*, USA) at 570 nm.

13. *Caspase-3 Cleavage Assay.* The fluorogenic substrate for caspase-3 (Ac-DEVD-AMC) is labeled with the fluorochrome 7-amino-4-methyl coumarin (= 7-amino-4-methyl-2*H*-1-benzopyran-2-one; AMC). The substrate produces a blue fluorescence that can be detected by exposure to UV light at 360 nm. AMC is released from these substrates upon cleavage by caspase-3. Free AMC produces a yellow-green fluorescence that could be monitored in a fluorometer at 460 nm. The amount of yellow-green fluorescence produced upon cleavage is proportional to the amount of caspase-3 activity [14].

14. *Protection of Rat Primary Neurons Against OGD-Induced Injury.* Cortical neurons were isolated from newborn rats and cultured at 37° in a humidified atmosphere containing 5% of CO_2. Cells were seeded at a density of $2 \cdot 10^5$ per ml in phenol red-free RPMI 1640 medium, supplemented with 10% heat-inactivated fetal bovine serum, penicillin (100 units/ml), and streptomycin (100 μg/ml). Experiments were carried out 10 d after cells were seeded [18].

For OGD insult, the original media were removed, and the cells were washed with a glucose-free *Earle*'s balanced salt soln. (EBSS, pH 7.4, supplemented with penicillin (100 units/ml) and streptomycin (100 μg/ml)). The cultures were then placed in fresh glucose-free EBSS and held for 6 h in a box containing 95% (*v*/*v*) of N_2 and 5% (*v*/*v*) of CO_2 at 37°. Control cultures were maintained for the same interval of time under standard conditions.

The synthetic compounds were dissolved and diluted in a phosphate-buffered saline (PBS) and were added into the cultures 2 h before OGD treatment. After OGD for 6 h, cell viability was evaluated by the ability to reduce MTT, as an indication of metabolic activity. This viability assay was conducted in 96-well plates, and the formed formazan, the metabolite of MTT, was detected by spectrophotometric measurement at 490 nm in a microplate reader (*Bio-Tek Instruments*, USA).

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