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A DOUBLY-CONVERGENT AND REGIOSELECTIVE SYNTHESIS OF (±)-DAUNOMYCINONE†

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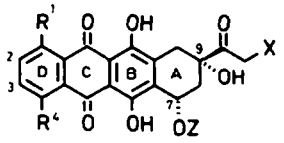
Abstract—The monoadduct of benzoquinone to 2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]heptane (**7**) was transformed into (1*RS*,4*RS*,4a*SR*)-2,3-dimethylidene-1,4-epoxy-1,2,3,4,4a,10-hexahydro-8-methoxyanthracene (**28**).‡ The exocyclic diene added to methyl vinyl ketone with high stereoselectivity and good regioselectivity, giving a 9 : 1 mixture of the naphthacenyl derivatives **38**β and **39**β which was transformed in 5 steps into (±)-7,9-dideoxydaunomycinone (**54**), a known precursor of (±)-daunomycinone.

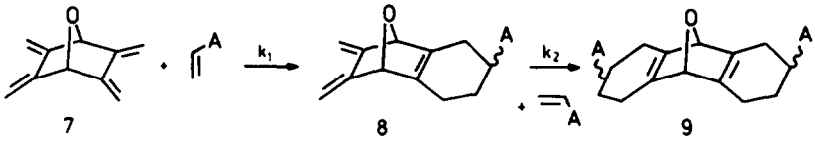
The anthracycline antibiotics[1] Daunomycin (or Daunorubicin) **1**[2] and especially Adriamycin or (Doxorubicin) **2**[3] are clinically useful drugs for the treatment of a broad spectrum of human cancers.[4] Total syntheses of the corresponding aglycone parts of daunomycinone (**3**) and adriamycinone (**4**) have been subject of intense study in the last fifteen years due to the lack of an efficient biosynthetic process[3] as well as the search for more active analogs with reduced cardiotoxicity.[5,6] We have reported a few years ago that 2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]-



R^1 = H, R^4 = OCH_3, X = H, Z = daunosaminyl **1**
R^1 = H, R^4 = OCH_3, X = OH, Z = daunosaminyl **2**
R^1 = H, R^4 = OCH_3, X = H, Z = H **3**
R^1 = H, R^4 = OCH_3, X = OH, Z = H **4**
R^1 = R^4 = X = Z = H **5**
R^1 = R^4 = OCH_3, X = Z = H **6**

heptane (**7**), readily obtained from the inexpensive furan and maleic anhydride,[7] can be used to prepare various anthracycline precursors.[8,9] The principle of our strategy (Scheme 1) rests upon the fact that the rate constant of the Diels-Alder addition of **7** → **8** (k_1) is much larger than that (k_2) for the reaction of the corresponding monoadduct **8** with the same dienophile giving the corresponding bis-adduct **9**.[10] This is true for strong dienophiles such as benzoquinone,[8] methyl acetylene-dicarboxylate, ethylenetetracarbonitrile[10] and methyl vinyl ketone[9] for which the rate constant ratio k_1/k_2 can be higher than 100.[10] With benzyne, k_1/k_2 is no greater than 5.[9]

A very short and efficient synthesis of (±)-4-demethoxydaunomycinone (**5**), the aglycone of a promising synthetic antitumor antibiotic,[5,11] was realized by applying this principle. Cycloaddition of one mol. equiv. of methylvinylketone to **7**, followed by addition of benzyne generated the skeleton of **5** in two steps.[9] By using benzoquinone and then methyl vinyl ketone as dienophiles, the tetraene **7** was transformed readily into a precursor of (±)-1-methoxydaunomycinone (**6**).[8] The syntheses of **5** and **6** were quite simple since they did not require one to control the regioselectivity of the two successive Diels-Alder additions **7** → **8** and **8** → **9**. A major difficulty in the synthesis of the natural derivatives **3** and **4** is to control the substitution pattern of the two remote rings A and D. In recent years, a great number of total syntheses have been reported to solve this synthetic challenge (for strategies using ionic cyclization reactions, see,[12] for



Scheme 1.

syntheses involving Diels-Alder additions, see[13]). Efficient asymmetric syntheses of daunomycinone and derivatives have also been realized.[14]

The Diels-Alder reactivity of an exocyclic s-cis-butadiene moiety grafted onto bicyclo[2.2.1]heptane and bicyclo[2.2.2]octane can be affected by remote substitution of the bicyclic skeleton. For instance, 5,6-dimethylidene-2-bicyclo[2.2.1]heptanone (**11**) is less reactive than the parent diene **10** toward strong dienophiles,[15] perhaps because of the electron withdrawing effect of the homoconjugated carbonyl group (inductive effect). Nevertheless, the "para" regioselectivity of the cycloaddition of **11** to methyl vinyl ketone and methyl propynoate suggested that the carbonyl may also act as an electron donating group because of a favorable hyperconjugative interaction of the type n(CO), σC(1,2) ↔ πC(5,6).[16] This interpre-

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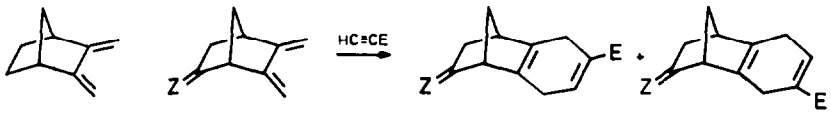
‡ IUPAC numbering; does not correspond to the atom numbering shown in scheme 2.



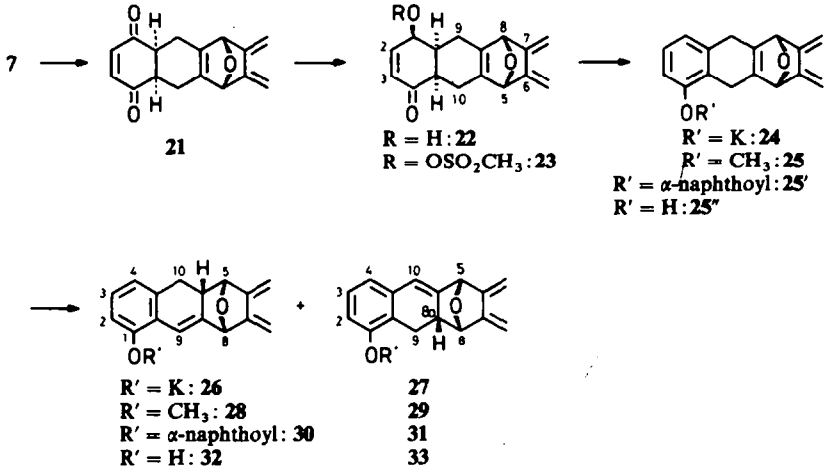
10	Z = O: 11 Z = $(NC)_2C$: 14 Z = H_2C: 18 E = $COOCH_3$	12 (major) 16 (minor) 19 (major)	13 (minor) 17 (major) 20 (minor)

tation was confirmed by the regioselectivity of the electrophilic additions of the C—C double bonds in bicyclo[2.2.1]hept-5-ene-2-one and bicyclo[2.2.2]oct-5-ene-2-one,[17] and was supported by MO calculations.[16,18] As expected for an electron withdrawing substituent such as the dicyanomethylidene group which lacks the n electrons that can interact with the σC(1,2) bond, the cycloadditions of triene **14** to methyl propynoate was "meta" regioselective. Contrastingly, that of the simpler triene **18** showed good "para" regioselectivity.[19] This result has been exploited in the development of a highly versatile synthesis of (±)-daunomycinone **3** which is reported here.

RESULTS AND DISCUSSIONS

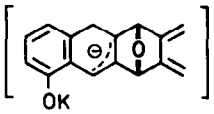
The monoadduct **21** of tetraene **7** and benzoquinone[8,20] can be reduced selectively to the alcohol **22** (94%) whose structure has been established by X-ray crystallography.[20] The corresponding methanesulfonate **23** (obtained in 94% yield from **22** by treatment with CH_3SO_2Cl in pyridine, 20°, 2 h) eliminated an equivalent of methanesulfonic acid in the presence of two mol. equiv. of t-BuOK in anh. tetrahydrofuran (THF, 0°C) giving the potassium phenolate **24** that reacted with methyl iodide to yield the corresponding substituted anisole **25** in good yield (99%).[19,20] When an excess of base was used (4.3 mol. equiv. of tBuOK) and the reaction mixture allowed to stand at 25° for 2 hr, the phenolate **24** was rearranged into the mixture of isomers **26** + **27**. Although the endocyclic double bond of the 7-oxabicyclo[2.2.1]hept-2-ene derivative **24** is a tetra-substituted one, it was expected to be more strained (because of repulsive hyperconjugative interactions)[10,20] than that in the dihydronaphthalene derivatives **26** and **27**. Quenching of these phenolates with methyl iodide gave a 7 : 3 mixture of **28** and **29**. Reaction with α-naphthoylchloride gave a 7 : 3 mixture (62%) of the esters **30** and **31**. Similarly, reaction with 10% aqueous HCl gave a 7 : 3 mixture of phenols **32** and **33**. Only the α-naphtoates **30** and **31** could be separated in good yields by preparative HPLC. Pure **28** and **29** were thus derived from the separated **30** and **31**, respectively. The minor derivative **31** could be recycled into a mixture of **26** + **27** after saponification (MeOH, K_2CO_3) and treatment with an excess of tBuOK (boiling THF). One pot transformations of **30** and **31** into **28** and **29**, respectively (K_2CO_3 in anh. MeOH + THF followed by quenching with methyl iodide) could be achieved with reasonable yields (75–80%). Better yield of **28** (96%) was obtained following a two step procedure that involved isolation of the phenol **32** (after saponification with K_2CO_3 in anh. THF/MeOH, 25°, 12 hr) followed by formation of the corresponding sodium phenolate (NaH, THF, 25°, 15 min) and reaction with methyl iodide (25°, 15 min). Under these conditions double bond isomerization and tertiary H-epimerization at C(4a) (C(5a) in scheme 2) in **28** was not observed.

The absence of *exo*-alkyl derivatives of **26** and **27** can be explained by invoking kinetic control in the formation of these phenolates that implies the selective *exo* face protonation of the hypothetical allyl anion intermediates **34** and **35**. The latter selectivity could be

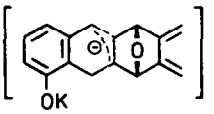


Scheme 2.

attributed to the π-anisotropy (polarization of the π-electrons of the endocyclic double toward the exo face in 7-oxabicyclo[2.2.1]hept-2-ene systems;[20] see also the face-selective, base-catalysed, keto-enol isomerizations of related systems).[21] The regioselectivity of the isomerization **24** → **26** + **27** is more difficult to explain.



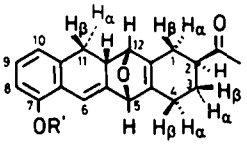
34



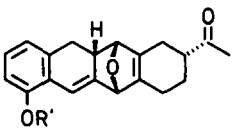
35

It is possible that the potassium counter-ion in phenolate **24** assists somehow the double bond isomerization process either because of kinetic control which would favor the formation of intermediate **34** or because of control by the relative stability of **34** and **35**. These hypotheses are supported by the following experiment. When the anisole derivative **25** was treated with an excess of tBuOK (THF, 25°) a 1 : 1 mixture of **28** and **29** was obtained. The potassium phenolate is thus required for observing a regioselective double bond isomerization. The *exo* position of the tertiary H-atom at C(10a) in **28**, **30** and **32**, and at C(8a) in **29**, **31** and **33** (1-anthryl numbering) was established by observing a vicinal coupling constant of *ca* 5 Hz between these protons and the adjacent bridgehead H-atoms. For *endo* hydrogens, the corresponding coupling constant would be near zero.[22] As expected,[22b,23] a coupling constant of *ca* 3 Hz was measured between protons H—C(9) and H—C(10a) of **28**, **30** and **32**, and between protons H—C(10) and H—C(8a) of **29**, **31** and **33**. The distinction between the isomeric pair **30** and **31** was based on their proton coupled ^{13}C-NMR spectra. In the case of the major isomer **30**, the signal at $\delta_C = 110.6$ ppm attributed to the olefinic C atom C(9) appeared as a doublet of doublets with $^1J_{C,H} \simeq 162$ Hz and $^3J_{C,H} \simeq 3.5$ Hz. The latter coupling was due to proton H—C(8). With the minor isomer **31**, the corresponding signal at $\delta_C = 116.4$ ppm (C(10)) appeared as a doublet of triplets with $^1J_{C,H} \simeq 160$ Hz and $^3J_{C,H} \simeq 4$–5 Hz, the latter coupling being due to protons H—C(4) and H—C(5) (coupling constant with H—C(8a) is expected to be near zero as the dihedral angle between the C(10)–C(10a) and C(8a)-H bonds approaches 90°).[24] The structures and spectral assignations retained for **30** and **31** were confirmed by the multiplicity of the signals of the benzylic carbons. In **30**, the signal of C(10) at $\delta_C = 30.9$ ppm appeared as a triplet of triplets with $^1J_{C,H} \simeq 128$ Hz and $^3J_{C,H} \simeq 4$ Hz whereas in **31**, the corresponding signal of C(9) at $\delta_C = 23.7$ ppm appeared as a triplet of doublets with $^1J_{C,H} \simeq 128$ Hz and $^3J_{C,H} \simeq 6$ Hz.

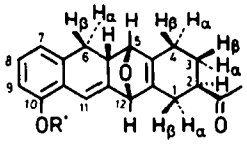
In a manner analogous to that of the simple triene **18**, the exocyclic s-cis-butadiene moieties in **30** and **31** added to methyl vinyl ketone with "para" regioselectivity giving the adducts **36** + **37** and **40** + **41**, respectively (Table 1). The additions were also stereoselective in the sense that the adducts with the acetyl side chain in the β (or *exo*) position were the major products. The same type of stereoselectivity was also observed for the cycloadditions of tetraene **7** to benzoquinone[20] and to methyl vinyl ketone.[9] This fact does not tell whether the dienophile has attacked the diene preferentially onto its *exo* or its *endo* face. From related studies, we expected the *exo* face to be preferred.[22b] The mixtures of β- and α-isomers were easily separated by column chromatography on silica gel whereas the pair of regioisomers resisted our attempts to separate them by HPLC.



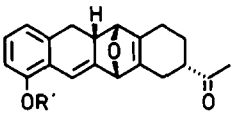
R' = α-naphthoyl: **36β**
R' = CH_3: **38β**
R' = H: **42β**



36α
38α
42α



R' = α-naphthoyl: **37β**
R' = CH_3: **39β**
R' = H: **43β**

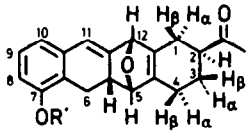


37α
39α
43α

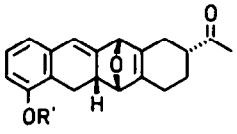
Table 1. Product distribution of the Diels–Alder additions of **28**, **30** and **31** to methyl vinyl ketone (MVK)

Triene	Mol. equiv. of MVK	Solvent	Mol. equiv. of catalyst	Temperature [°C]	Reaction time [hr]	Yield of the isolated adduct mixture	Ratio of β-acetyl vs. α-acetyl adducts†	Ratio of "para" vs. "meta" regioisomers‡	
28	20	CH_2Cl_2	5.6 $BF_3.Et_2O$	−78	2.25	80%	>98:2	**38β/39β**	9:1
30	50	toluene	—	90	20	55%	68:32	**36β/37β**	9:1
								36α/37α	3:2
30	15	CH_2Cl_2	1.0 $ZnCl_2$	25	26	56%	>98:2	**36β/37β**	7:3
30	100	toluene	4.0 $AlCl_3$	5	72	31%	>98:2	**36β/37β**	6:4
30	40	CH_2Cl_2	7.0 $BF_3.Et_2O$	−60	1	51%	>98:2	**36β/37β**	81:19
30	20	CH_2Cl_2	4.0 $BF_3.Et_2O$	−78	5	83%	>98:2	**36β/37β**	84:16
30	20	CH_2Cl_2	14.0 $BF_3.Et_2O$	−85	5	81%	>98:2	**36β/37β**	86:14
31	70	toluene	—	100	18	51%	72:28	**41β/40β**	9:1
								41α/40α	63:37
31	20	CH_2Cl_2	3.0 $ZnCl_2$	25	15	23%	>98:2	**41β/40β**	67:33
31	20	CH_2Cl_2	4.0 $BF_3.Et_2O$	−78	5	86%	>98:2	**41β/40β**	81:19

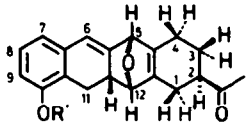
† Evaluated by preparative column chromatography on silica gel or by ^{1}H-NMR (360 MHz).
‡ Evaluated by ^{1}H-NMR (360 MHz) of the mixture of regioisomers.



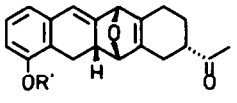
R' = α-naphthoyl: **40β**



40α



R' = α-naphthoyl: **41β**



41α

The "para" regioselectivity (9:1), the β-acetyl stereoselectivity (>98:2), and the isolated yield (80%) were the best when the methoxy derivative **28** was employed and when the addition of methyl vinyl ketone was carried out at −78° in the presence of an excess of $BF_3 \cdot Et_2O$ in CH_2Cl_2 (see Table 1). It is interesting to note a slight regioselectivity increase when going from the α-naphthoate derivative **30** (**36β/37β** 84:16, CH_2Cl_2, −78°) to **28**. This appears to be consistent with the difference in electron donating power between the α-naphthoate and methoxy groups which is transmitted to the remote diene via the homoconjugated C(8a,9) double bond in **30** and **28**. This hypothesis is consistent also with the observation of somewhat lower "para" regioselectivity for the cycloadditions of **31** compared with those of **30** under the same conditions. The effects discussed here are minute and no generalization should be advanced at this moment.

Acetylvinyl paranitrobenzoate (a dienophile almost as reactive as methyl vinyl ketone[25] and that would introduce the acetyl side chain and the oxyfunction of the anthracyclinones in one single synthetic step) added to **30** (140°, 20 hr) giving a mixture of four adducts with less stereoselectivity (β vs. α acetyl group 7:3) and regioselectivity ("para" vs. "meta" regioisomers 54:46 to 2:3) than the cycloaddition of methyl vinyl ketone to **30**.

The distinction between α- and β-acetyl adducts was confirmed by isomerization in alkaline medium. When a 7:3 mixture of adducts **36β/37β** was treated with K_2CO_3 in MeOH/THF (25°, 2 hr) a 38:16:32:14 mixture of phenols **42β/43β/42α/43α** was obtained. The isomeric mixtures **42β**+**43β** and **42α**+**43α** could be separated by TLC and analysed by ^{1}H-NMR (360 MHz). Similarly, a 3:2 mixture of **36α/37α** was transformed into a 33:22:27:18 mixture of **42β/43β/42α/43α**.†

The structures of adducts **36β** and **37β** were given by their ^{1}H-NMR (360 MHz) spectra and with the help of double irradiation experiments: they were confirmed by their transformation into the known (±)-7,9-dideoxydaunomycinone (**54**) and (±)-7,9-dideoxyisodaunomycinone (**55**), respectively (see below). The distinction between the bridgehead protons H—C(5) and H—C(12) (naphtacenyl numbering) of the 7-oxabicyclo[2.2.1]heptane rings in **36–43** was straightforward from their multiplicity. For instance with **36β**, the H—C(12) signal at $\delta_H = 5.00$ ppm was coupled ($^3J_{H,H} = 3.9$ Hz) with the adjacent tertiary proton at C(11a) ($\delta_H = 3.2$ ppm) whereas no such coupling was recorded for H—C(5) at $\delta_H = 4.95$ ppm. Similarly, H—C(5) of the minor **37β** was coupled with H—C(5a) whereas H—C(12) ($\delta_H = 4.96$ ppm) appears as a broad singlet. In the ^{1}H-NMR spectrum of **36β** (Table 2), homoallylic coupling constants $^5J_{H,H}$ of *ca* 0.7 Hz were observed between bridgehead protons H—C(5) and H—C(12) and the "*exo*" allylic protons H—C(1β) and H—C(4β), respectively. The corresponding long range coupling constant between the bridgehead protons and H—C(1α) and H—C(4α) were absent (<0.2 Hz). The isopropylidenic coupling constants $^4J_{H,H}$ between H—C(5), H—C(12) and the adjacent allylic protons were larger (0.2–0.4 Hz) for the "*exo*" protons H—C(1β) and H—C(4β) than for the "*endo*" protons H—C(1α) and H—C(4α) (<0.2 Hz). We observed also that the β allylic protons at C(1) and C(4) were more deshielded than the corresponding α protons. These features are typical for cyclohexene and cyclohexadiene rings annulated to the 7-oxabicyclo[2.2.1]hept-2-ene system.[22b,26] The proton H—C(2) at $\delta_H = 2.45$ ppm of **36β** was coupled with H—C(3β) ($^3J_{H,H} = 10$ Hz) and with H—C(3α) ($^3J_{H,H} = 2.5$ Hz). No coupling (<0.2 Hz) was detected between H—C(2) and H—C(4β) (Table 2). This suggested that H—C(3) is in an axial position in agreement with a chair conformation of the cyclohexane ring and the acetyl substituent at C(2) in an equatorial position as shown in Fig. 1.

The absence of coupling between H—C(1β) and H—C(3β) as well as the observation of a coupling constant of 5.5 Hz between H—C(3β) and H—C(4β)

† Side chain epimerization was observed neither with anh. K_2CO_3 in acetone, DMF or HMPT at 25°, nor with NaH/THF, 25° or DBN/THF, 25–50°.

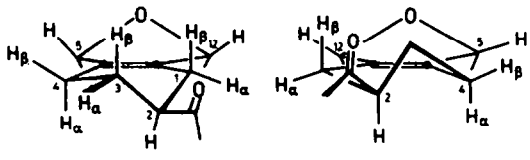
Table 2. Coupling constants (±0.1 Hz) in the ^{1}H-NMR spectra (360 MHz, $CDCl_3$) of the cyclohexane moieties annulated to 7-oxabicyclo[2.2.1]hept-2-ene rings in the major adducts **36β** and **41β**†

$J_{H-C(k),H-C(l)}$‡:	1α, 1β	1α, 2	1β, 2	1β, 4α	1β, 4β	1β, 5	1β, 12	2, 3α	2, 3β
36β:	13.0	4.5	9.0	4.0	2.5	0.7	0.2	2.5	10.0
41β:	15.0	4.0	11.0	*ca.* 3	*ca.* 2	0.4	0.2	3.0	10.0
	3α, 3β	3α, 4α	3α, 4β	3β, 4α	3β, 4β	4α, 4β	4β, 5	4β, 12§	
36β:	18.5	*ca.* 5	*ca.* 2	12.5	5.5	17.5	0.4	0.7	
41β:	13.0	5.5	2.3	12.5	5.5	17.5	0.2	0.4	

† Measured on 9:1 mixtures of **36β/37β** and **41β/40β**.

‡ IUPAC numbering, see Fig. 1.

§ No other long-range coupling constants were detected (<0.2 Hz). Double irradiation experiments were required to extract the data reported here from the ^{1}H-NMR spectra; see exp. part for other data.

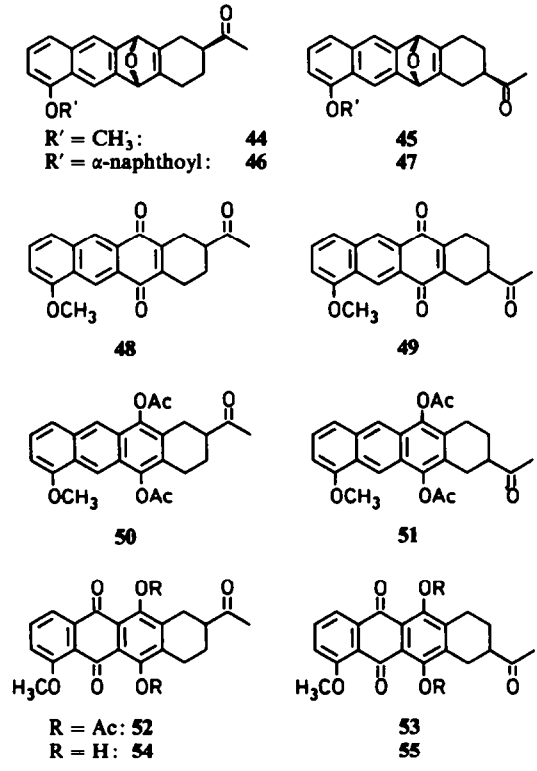


36β **41β**

Fig. 1.

confirmed the structure of **36β**. The "cisoïd" homoallylic coupling constants measured between the allylic protons (H—C(1β)/H—C(4α): $^5J_{H,H} = 4.0$ Hz; H—C(1β)/H—C(4β): $^5J_{H,H} = 2.5$ Hz) were also consistent with our signal attributions and confirmed the conformations represented in Fig. 1.[22b,26,27] The structures and NMR signal attributions of the other adducts **37–43** were established by applying the same criteria as those described for **36β** (Experimental).

The 9:1 mixture of adducts **38β/39β** was treated with dichlorodicyanobenzoquinone[28] (4 mol. equiv. of DDQ, benzene, 80°, 24 hr) and yielded a 9:1 mixture of the corresponding naphtacene derivatives **44/45** (52%).



R′ = CH$_3$: **44** **45**
R′ = α-naphthoyl: **46** **47**

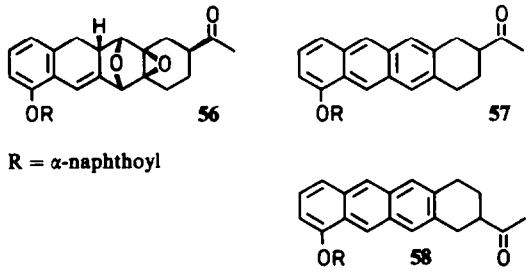
48 **49**

50 **51**

R = Ac: **52** **53**
R = H: **54** **55**

The major product was obtained pure by simple recrystallization form ether/AcOEt 1:1. The dehydrogenations of the α-naphthoates **36β** and **37β** were more difficult (large excess of DDQ, benzene, 90°, 72 hr) and gave a lower yield (<40%) of the corresponding derivatives **46** and **47** respectively.

Epoxidation of a 84:16 mixture of **36/37** with metachloroperbenzoic acid in CH_2Cl_2 at 0° afforded epoxide **56** (59% isolated). No product arising from oxidation of the C(5a)–C(6) double bond could be isolated. The enhanced reactivity of the tetrasubstituted C(1a)–C(4a) double bond in **36β** can be attributed to the "extra" strain of the 7-oxabicyclo[2.2.1]hept-2-ene double bond.[10,20] Treatment of a 84:16 mixture of **36β/37β** with CF_3COOH in $CHCl_3$ (25°, 3 hr) gave a 85:15 mixture of antracene derivatives **57/58** (48.5%). The same products were isolated (50%) by treatment with $(CH_3)_3SiI$ in anh.



56 **57**

R = α-naphthoyl

58

C_6H_6 (0°, 1 hr). Acid rearrangements of the 7-oxabicyclo[2.2.1]hepta-2,5-diene moieties[29] in **44–47** gave mixtures of air-sensitive phenols with little regioselectivity. Treatment of a 9:1 mixture of **44/45** with degassed (Ar) CF_3COOH/CH_2Cl_2 at 0° followed by addition of pyridinium chlorochromate (PCC[30]) furnished a 9:1 mixture of naphtacenequinones **48/49** (60%). The major isomer **48** was obtained pure by simple recrystallization. Reduction of a 9:1 mixture of **48/49** with zinc in acetic anhydride containing triethylamine (better than pyridine, *cf* ref. 13*b*, at 110° 1 hr; longer reaction times led to decomposition) afforded a 9:1 mixture of **50/51** (86%). Again, simple recrystallization delivered pure isomer **50**. Jones oxidation of a 9:1 mixture of **50/51** gave a 9:1 mixture of **52/53** (51%) from which **52** could be obtained pure by recrystallization. When treated with 3% HCl in methanol at 70° (12 hr),[31] there was obtained a 9:1 mixture of the known **54/55** which could be separated by TLC followed by recrystallization. The spectral characteristics and the melting point (243–4°) of the major isomer **54** were identical with those reported for (±)-7,9-dideoxydaunomycinone.[12b,d,f,k,j,k,m] The data for the minor compound **55** were identical with those reported for (±)-7,9-dideoxyisodaunomycinone.[12b] The structures of **44–53** were deduced from their mode of formation, their reactivity and spectral data. Transformation of **54** into (±)-daunomycinone (**3**)[12b,f,k,m,13b,32] as well as the conversion of **3** into adriamycinone (**4**)[32a,33] has already been achieved.

CONCLUSION

Remote substitution can control the regioselectivity of Diels-Alder additions of s-*cis*-butadiene moieties grafted onto bicyclic skeletons. Homoconjugative interactions between the C(8a)–C(9) double bond and the exocyclic diene at C(6), C(7) in **28** and **30** made these compounds add to methyl vinyl ketone with good "*para*" regioselectivity as in the case of 2,3,5-trimethylidenebicyclo[2.2.1]heptane (**18**). This principle has been exploited in the development of a doubly convergent synthesis[34] of (±)-daunomycinone starting from the readily available 2,3,4,5-tetramethylidene-7-oxabicyclo[2.2.1]heptane. Our synthesis strategy is a highly flexible one since one can, in principle, vary the structure of the three synthetic blocks (tetraene **7** and two dienophiles) that are joined together via Diels-

Alder additions. These reactions can be regioselective and thus allow one to control the substitution patterns of rings A and D. It is versatile also because the skeleton of the anthracyclinones can be obtained selectively at various oxidation levels.

EXPERIMENTAL

General remarks. Mps and bps not corrected, Tottoli apparatus; IR spectra (ν [cm^{-1}]), Beckman IR-20A and Beckman IR-4230 spectrometers; UV spectra, Carl Zeiss RPQ 20 A/C, Philips Pye-Unicam SP 8/100 or Perkin-Elmer Hitachi 340 instruments (λ_{max} [nm] (ε[$dm^3 mol^{-1} cm^{-1}$]) ^{1}H-NMR spectra, Bruker WP-80 CW (80 MHz) or Bruker WH-360 FT (360 MHz) spectrometers, the latter equipped with an Aspect 2000 computer with 32K memory space, deuterium signals of solvent as lock signal, TMS as internal reference δ_H = 0.0 ppm (δ ppm, apparent multiplicity, apparent coupling constants J in Hz, number of protons, tentative attribution [relative lanthanide complex induced shifts]); ^{13}C-NMR spectra, Bruker WP 60 FT (15.08 MHz, spectral width: 3750 Hz, 4096 points) or Bruker WH-360 FT (90.55 MHz), deuterium signal of $CDCl_3$ as lock signal, δ_C of $CDCl_3$ (76.9 ppm) as internal reference (δ ppm, apparent multiplicity, apparent coupling constants, tentative attribution [relative lanthanide induced shifts); s = singlet, d = doublet, t = triplet, qa = quadruplet, qi = quintuplet, m = multiplet, br = broad. Sometimes the NMR spectra of aromatic compounds were dependent upon the concentration of the sample measured. The solutions were degassed on a vacuum line and stored in sealed tubes or under Ar. Mass spectra (MS) in electron ionization mode, CEC 21-490 Bell-Howell or Hewlett-Packard HP 5980A; in chemical ionization mode (CI), HP 5980A or Finnigan 1020 (GC-MS systems) (m/z [amu] (% base peak). Elementary analyses were performed by the microanalytical laboratory of the University of Geneva (Dr. K. Eder) or of the University of Basel (Dr. E. Thommen), by the Rob. Ehrisman AG Laboratory in Windish, or by the laboratory Ilse Beetz in Kronach (Germany). Preparative HPLC separations, Dupont 830003-904, UV detector (254 nm), silical gel (Zorbax Sil, 7 μm; 21.2 mm × 25 cm); medium pressure chromatography separations, Lobar-Merck (lichroprep. Si60, 63–125 μm, 2.5 cm × 30 cm or 40–63 μm, 1.5 cm × 25 cm); thick layer chromatography (TLC), "Chromatotron" of Harrison Research (Palo Alto, Cal., USA), mod. 7924. Abbreviations: MVK = methyl vinyl ketone, DDQ = dichlorodicyanobenzoquinone, RT = room temperature, i.V. = in vacuo, sh = shoulder, dec = decomposition, THF = tetrahydrofuran, DMF = dimethylformamide, DMSO = dimethylsulfoxide, HMPT = hexamethylphosphortriamide, anh = anhydrous, atm = atmosphere, aq = aqueous, sat = saturated.

The procedures reported have not been optimized.

(1RS,4aSR,5SR,8RS,9aRS)-6,7-*Dimethylidene*-1,4,4a,5,6,7,8,9,9a,10-*decahydro*-5,8-*epoxy*-4-*oxo*-1-*anthryl methanesulfonate* (**23**)

Alcohol **22**[20] (0.932 g, 3.6 mmol) was dissolved in anh. pyridine (9 ml, 0.11 mol). After cooling to 0°, methanesulfonic chloride (0.85 ml, 10.9 mmol) was added dropwise under N_2 atm and vigorous stirring. The mixture was allowed to warm to RT and stand for 2 hr. It was then poured onto a mixture of ice/water (50 ml) and stirred for 20 min. The ppt was collected by filtration and washed with ice-cold water (20 ml), then with MeOH (10 ml, 2 times) and ether (10 ml), yield: 1.145 g (94.1%) of white powder, m.p. 110° (dec). UV(CH_3CN): 258 (sh, 2900), 244 (sh, 7700), 234 (sh, 11,500), 212 (24,400). IR(KBr): 3090, 3040, 3010, 2930, 2900, 2870, 2850, 1690, 1368, 1345, 1175, 950, 905, 890, 854. ^{1}H-NMR (80 MHz, $CDCl_3$): 6.8 (m, 1H); 6.2 (m, 1H); 5.9 (m, 1H); 5.3 (s, 2H); 5.1 (s, 2H); 4.9 (br.s, 1H); 5.0 (br.s, 1H); 3.2 (s, 3H); 3.1 (m, 1H); 2.8–2.2 (m, 4H); 2.0 (m, 1H). ^{13}C-NMR($CDCl_3$): 195.65 (m, C(4)); 143.65 (d, C(2)); 143.95 (s, C(6) or C(7)); 143.45 (s, C(6) or C(7)); 140.55 (s, C(8a) or C(4a)); 138.7 (s, C(4a) or C(8a)); 130.75 (d, C(3)); 101.2 (t, 2C, CH_2 = C(6) and CH_2 = C(7)); 84.55 (d, C(5) or C(8)); 84.4 (d, C(8) or C(5)); 77.75 (d, C(1)); 44.2 (d, C(4a)); 39.8 (d, C(9a)); 38.5 (qa, CH_3O)); 20.6 (t, C(10)); 18.15 (t, C(9)). MS(70 eV): 334 (22, M^+), 306 (20), 305 (15), 238 (22), 210 (100), 209 (90), 195 (66), 181 (36), 158 (49), 144 (40), 129 (20), 117 (15), 115 (18).

2,3-*Dimethylidene*-1,4-*epoxy*-1,2,3,4,9,10-*hexahydro*-5-*methoxy-anthracene* (**25**) (prepared the first time in our laboratory by Dr. J. H. A. Stibbard[19]).

Methanesulfonate **23** (1.145 g, 3.42 mmol) in anh THF (40 ml) was added dropwise to a stirred soln of tBuOK (7.51 mmol) in anh THF (12 ml) under N_2 atm. After stirring at RT for 2 hr, MeI (0.85 ml, 13.6 mmol) was added and the mixture stirred for 1½ hr at RT. The mixture was then diluted with ether (40 mol) and washed with $NaHSO_3$aq (20 ml, 2 times), then with a 10% $NaHCO_3$aq (20 ml, 2 times), and a sat NaClaq (30 ml, 3 times). After drying (Na_2SO_4), the solvent was evaporated i.V. and yielded 0.86 g (99.6%) of a crystalline, slightly beige product, pure enough for the subsequent synthetic steps, m.p. 145–47°. UV(CH_3CN): 278 (2000), 270 (2600), 244 (sh, 6600), 224 (15,600). IR(KBr): 3080, 3040, 3010, 3000, 2980, 2940, 2890, 2840, 1585, 1474, 1260, 1100, 1045, 890, 850, 770. ^{1}H-NMR (80 MHz, $CDCl_3$): 7.10 (d, J = 8.0 Hz, 1H); 6.72 (m, 2H); 5.30 (s, 2H); 5.15 (s, 4H); 3.85 (s, 3H); 3.55 (m, 4H). ^{13}C-NMR($CDCl_3$): 157.4 (s, C(5)); 144.0 (s, 2C, C(2) or C(3)); 139.1 (s, C(9a) or C(4a)); 138.25 (s, C(4a) or C(9a)); 134.3 (s, C(10a)); 126.6 (d, $^1J_{C,H}$ = 160 Hz, C(7)); 122.3 (s, C(8a)); 121.2 (dd, $^1J_{C,H}$ = 159, $^3J_{C,H}$ = 7.0 Hz, C(6)); 107.3 (dd, $^1J_{C,H}$ = 160, $^3J_{C,H}$ = 8.0 Hz, C(8)); 100.9 (t, $^1J_{C,H}$ = 159 Hz, 2C, H_2C = C(2) & H_2C = C(3)); 84.8 (d, $^1J_{C,H}$ = 170 Hz, C(1) or C(4)); 84.55 (d, $^1J_{C,H}$ = 170 Hz, C(4) or C(1)); 55.1 (qa, $^1J_{C,H}$ = 144 Hz, CH_3O); 26.6 (t, $^1J_{C,H}$ = 130 Hz, C(9)); 21.65 (t, $^1J_{C,H}$ = 130 Hz, C(10)). MS (70 eV): 252 (25, M^+), 224 (36), 223 (100), 209 (25), 208 (43), 191 (27), 178 (29), 171 (20), 169 (27), 165 (36), 152 (20), 141 (17), 139 (19), 129 (12), 128 (26), 127 (16), 115 (23). (Found: C, 80.75; H, 6.36. Calc for $C_{17}H_{16}O_2$ (252.313): C, 80.92; H, 6.39%.)

6,7-*Dimethylidene*-5,8-*epoxy*-5,6,7,8,9,10-*hexahydro*-1-*anthryl* α-*naphthoate* (**25'**)

Product of trapping of phenolate **25** *with* α-*naphthoyl chloride.* A soln of tBuOK (0.279 g, 2.5 mmol) in anh THF (5 ml) was added dropwise (in 15 min) to a stirred soln of **23** (0.253 g, 0.75 mmol) in anh THF (10 ml) under N_2 atm. and cooled to 0°. After stirring at RT for 2 hr, a soln of α-naphthoyl chloride (0.46 g, 2.4 mmol) in anh THF (2 ml) was added dropwise. After vigorous stirring at RT for 2 hr, ether (30 ml) and ice-water (10 ml) were added successively. The organic layer was washed with a sat NaClaq (10 ml, 3 times) and the aqueous phase was extracted with ether (20 ml, 2 times). After drying (Na_2SO_4) the united organic phases were concentrated i.V. The residue was taken with a minimum of $CHCl_3$/MeOH 2:1. The white crystals (α-naphthoic anhydride) were removed by filtration and the soln purified on a column of Florisil (15 g, petroleum ether/AcOEt 9:1). After recrystallization from AcOEt, 0.257 g (86.5%) of white crystals were obtained, m.p. 200–201°. UV(CH_3CN): 310 (sh, 6600), 296 (8600), 235 (sh, 31,500), 217 (47,800), 213 (49,100). IR(KBr): 3080, 3000, 2920, 2880, 1730, 1450, 1280, 1220, 1180, 1110, 990, 890, 770. ^{1}H-NMR (80 MHz, $CDCl_3$): 9.03 (m, 1H); 8.51 (dd, J = 1.3; 7.0 Hz, 1 H); 8.3–6.9 (m, 8H); 5.18 (s, 2H); 5.03 (s, 2H); 4.96 (s, 2H); 3.86 (m, 1H) 3.43 (m, 3H). MS (70 eV): 392 (1.0, M^+), 237 (1.5), 220 (4.5), 165 (7.5), 155 (100), 128 (14), 127 (84), 115 (5.3), 101 (6), 77 (6), 71 (10), 69 (13), 57 (23), 55 (21), 44 (28), 43 (30).

Trapping with water yielded the corresponding anthrol derivatives (**25"**), after purification on a column of silica gel (hexane/AcOEt 8:2), yield 82.5%, white crystals, m.p. 199.5–200.5° (AcOEt). UV(CH_3CN): 280 (1950), 274 (sh, 2300), 244 (sh, 6500), 232 (sh, 11,900), 225 (14,500). IR(KBr): 3300, 3000, 1580, 1470, 1270, 980, 895, 850, 770. ^{1}H-NMR (360 MHz, CD_3OD): 6.95 (dd, J = 7.6; 8.0 Hz, 1H, H—C(3)); 6.65 (d, J = 7.6 Hz, 1H, H—C(2)); 6.59 (d, J = 8.0 Hz, 1H, H—C(4)); 5.23 (s, 2H); 5.11 (s, 1H); 5.1 (s, 1H); 5.08 (s, 1H); 5.05 (s, 1H);

3.61 (dt, J = 6.0; 21.5 Hz, 1H); 3.51 (dt, J = 6.0; 21.5 Hz, 1H); 3.27 (dt, J = 6.0; 21.5, 1H); 3.11 (dt, J = 6.0; 21.5 Hz, 1H). MS (70 eV): 238 (22, M^+), 223 (11), 221 (6), 220 (7), 210 (39), 209 (100), 195 (30), 181 (30), 165 (42), 157 (39), 128 (25), 115 (22), 69 (14), 43 (16). (Found: C, 80.52; H, 5.90%. Calc. for $C_{16}H_{14}O_2$ (238.286): C, 80.65; H, 5.92%.)

6,7-Dimethylidene-5,8-epoxy-5,6,7,8-tetrahydro-1-anthryl α-naphthoate (DDQ oxidation of **25**)

A soln of DDQ (0.146 g, 0.643 mmol) in anh benzene (6 ml) was added to a soln of **25** (0.236 g, 0.6 mmol) in anh C_6H_6 (8 ml). After stirring at RT for 8 hr in the dark, the mixture was filtered and the ppt washed with benzene (5 ml, 4 times). The benzenic soln was washed with a sat $NaHSO_3$aq (20 ml, 4 times), then with a 10% $NaHCO_3$aq and finally with a sat NaClaq (30 ml, 2 times). The aqueous phases were extracted with benzene. The organic layers were united and dried ($MgSO_4$). After solvent evaporation i.V., the residue was purified by filtration on a short column of Florisil (3 g, hexane/AcOEt 9:1), yielding 0.177 g (75%) of colourless crystals after recrystallization from hexane/AcOEt 1:4, m.p. 134–135°. UV(CH_3CN): 300 (9600), 238 (58,500), 222 (66,800), 211 (sh, 55,000). IR(KBr): 3080, 3000, 2920, 2880, 1720, 1500, 1460, 1270, 1220, 1180, 1110, 1000, 950, 890, 840, 770. ^{1}H-NMR (80 MHz, C_6D_6): 9.35 (m, 1H); 8.5 (dd, J = 13.0; 7.0 Hz, 1H); 7.9 (s, 1H); 7.7–6.9 (m, 9H); 5.4 (s, 1H); 5.25 (s, 1H); 5.07 (s, 1H); 5.0 (s, 1H); 4.91 (s, 1H); 4.72 (s, 1H). MS (70 eV): 290 (5, M^+), 346 (3.3), 178 (5.5), 155 (100), 127 (58), 97 (14), 85 (21), 83 (22), 77 (15), 71 (38), 69 (37), 57 (84), 55 (54), 44 (46), 43 (38). Saponification (K_2CO_3/MeOH) of this compound gave the corresponding anthrol as white crystals, m.p. 194–5° ($CHCl_3$/AcOEt 7:3). UV(CH_3CN): 302 (3500), 252 (47,300), 218 (42,200). IR(KBr): 3280, 3010, 2915, 1615, 1595, 1470 1360, 1280, 1000, 940, 900, 830. ^{1}H-NMR (360 MHz, CD_3COCD_3): 8.13 (s, 1H); 7.72 (s, 1H); 7.34 (br.d, J = 8.0 Hz, 1H); 7.26 (dd, J = 7.5; 8.0 Hz, 1H); 6.9 (dd, J = 1.0; 7.5 Hz, 1H); 5.8 (br.s, 1H); 5.75 (br.s, 1H); 5.35 (s, 2H); 5.29 (s, 1H); 5.27 (s, 1H). MS (70 eV): 236 (100, M^+), 219 (16); 207 (94), 178 (50), 165 (50), 152 (41), 57 (37), 55 (36), 43 (43). (Found: C, 81.35; H, 5.09%. Calc. for $C_{16}H_{12}O_2$ (236.27): C, 81.33; H, 5.11%.)

(5RS,8RS,10aSR)-*6,7-Dimethylidene-5,8-epoxy-5,6,7,8,10,10a-hexahydro-1-anthryl α-naphthoate* (**30**)

A soln of tBuOK (0.8 g, 7.1 mmol) in anh THF (8 ml) was added dropwise to a soln of methanesulfonate **23** (0.55 g, 1.64 mmol) in anh THF (17 ml) cooled to 0° and stirred under N_2 atm. After stirring at RT for 2 hr, the mixture (containing phenolates **26** + **27**) was cooled to 0° and a soln of α-naphthoyl chloride (0.625 g, 3.2 mmol) in anh THF (15 ml) was added. After stirring at RT for 2 hr, ether (60 ml) and then water (20 ml) were added. The organic layer was washed with a sat NaClaq (20 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated i.V. and the residue purified by filtration on a column of Florisil (50 g, petroleum ether/AcOEt 9:1) yielding 0.4 g (62%) of a 7:3 mixture of α-naphthoates **30**/**31** as white powder. The major isomer **30** (second fraction) was separated from **31** (first fraction) by preparative HPLC (SiO_2, hexane/AcOEt 95:5), as white crystals, m.p. 183–4° (AcOEt/petroleum ether 2:1). UV(CH_3CN): 320 (sh, 5900), 300 (sh, 13,800), 287 (17,000), 244 (sh, 22,000), 241 (sh, 27,200), 228 (sh, 45,600), 219 (57,700), 212 (61,600), 203 (sh, 51,600). IR(KBr): 3060, 3000, 1735, 1570, 1460, 1225, 1210, 1180, 1110, 990, 890, 780. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.98 (d, J = 9.0 Hz, 1H); 8.46 (dd, J = 1.5; 7.5 Hz, 1H); 8.05 (d, J = 8.0, 1H); 7.85 (dd, J = 1.0; 8.0 Hz, 1H); 7.5 (m, 3H); 7.12 (dd, J = 7.0; 8.0 Hz, 1H, H—C(3)); 6.99 (d, J = 8.0 Hz, 2H, H—C(2) & H—C(4)); 6.4 (d, J = 3.0 Hz, 1H, H—C(9)); 5.37 (s, 1H); 5.08 (s, 1H, H—C(8)); 5.06 (s, 1H); 4.98 (s, 1H); 4.9 (d, J = 5.0 Hz, 1H, H—C(5)); 4.89 (s, 1H); 2.86 (dddd, J = 3.0; 5.0; 6.3; 16.0 Hz; 1H, H—C(10a)); 2.75 (dd, J = 6.3, 14.5 Hz, 1H, H—C(10β)); 2.46 (dd, J = 14.5; 16.0 Hz, 1H, H—C(10α)). ^{13}C-NMR (90 MHz, $CDCl_3$ of 7:3 mixture of **30**/**31**): 165.7 (m, COO of **30**); 165.5 (m, COO of **31**); 148.8 (m); 147.6 (m); 147.4 (m); 147.2 (m); 146.9 (m); 145.7 (m); 143.2 (m); 143 (m); 137 (m); 134.4 (dm, $^1J_{C,H}$ = 159.6 Hz, **30**); 134.3 (dm, $^1J_{C,H}$ = 160 Hz, **31**); 134.0 (m, 2C); 131.7 (m); 131.1 (ddd, $^1J_{C,H}$ = 162; $^3J_{C,H}$ = 8.0; 1.9 Hz, **30**); 130.9 (idem, **31**); 128.6 (dd, $^1J_{C,H}$ = 158.4 Hz, $^3J_{C,H}$ = 4.8 Hz, **30**); 128.6 (idem, **31**); 128.5 (dd, $^1J_{C,H}$ = 160.8, $^3J_{C,H}$ = 8.0 Hz, **30**); 128.0 (idem, **31**); 127.6 (m); 127.2 (d, $^1J_{C,H}$ = 162.4, C(3) of **30**); 126.9 (idem, C(3) of **31**); 126.3 (dd, $^1J_{C,H}$ = 160.8, $^3J_{C,H}$ = 8.0 Hz, 2C); 125.5 (dd, $^1J_{C,H}$ = 164.8, $^3J_{C,H}$ = 6.4 Hz, **31**); 125.4 (m); 124.3 (d, $^1J_{C,H}$ = 162.4 Hz, 2C); 120.8 (dd, $^1J_{C,H}$ = 162; $^3J_{C,H}$ = 8.0 Hz, C(2) of **31**); 120.6 (idem, C(2) of **30**); 116.4 (dt, $^1J_{C,H}$ = 160, $^3J_{C,H}$ = 4.8 Hz, C(10) of **31**); 110.6 (dd, $^1J_{C,H}$ = 162.4, $^3J_{C,H}$ = 3.5 Hz, C(9) of **30**); 105.4 (t, $^1J_{C,H}$ = 160 Hz, H_2C=C(6) or H_2C=C(7) of **31**); 105.0 (idem, of **30**); 100.7 (t, $^1J_{C,H}$ = 160 Hz, H_2C=C(7) or H_2C=C(6) of **30**); 100.4 (idem, of **31**); 84.3 (dm, $^1J_{C,H}$ = 162 Hz, C(5) of **30** & C(8) of **31**); 82.9 (idem, C(8) of **30**); 82.7 (idem, C(5) of **31**); 42.2 (dm, $^1J_{C,H}$ = 134 Hz, C(10a) of **30**); 41.9 (idem, C(8a) of **31**); 30.9 (tt, $^1J_{C,H}$ = 128.4; $^3J_{C,H}$ ≃ 4 Hz, C(10) of **30**); 23.7 (td, $^1J_{C,H}$ = 128; $^3J_{C,H}$ ≃ 6 Hz, C(9) of **31**). MS (70 eV): 155 (85); 69 (100). MS (CI, i-C_4H_{10}): 393 (0.4 M^+ + 1), 365 (0.36), 213 (1.8), 211 (3.5), 155 (1.4), 57 (100). (Found: C, 82.37; H, 5.05. Calc for $C_{27}H_{20}O_3$ (392.454): C, 82.63; H, 5.13%.)

(5RS,8RS,8aSR)-*6,7-Dimethylidene-5,8-epoxy-5,6,7,8,8a,9-hexahydro-1-anthryl α-naphthoate* (**31**)

The first fraction from the above preparative HPLC was recrystallized from AcOEt/petroleum ether 2:1, yielding white crystals, m.p. 139–40°. UV(CH_3CN): 300 (sh, 13800), 287 (16700), 244 (sh, 20800), 240 (sh, 26200), 227 (sh, 45800), 217 (58400), 212 (60300), 205 (sh, 51800). IR(KBr): 3060, 3000, 1735, 1510, 1460, 1230, 1190, 1120, 985, 780. ^{1}H-NMR (360 MHz, $CDCl_3$): 8.96 (d, J = 8.5 Hz); 8.45 (dd, J = 1.2; 7.5 Hz, 1H); 8.06 (d, J = 8.3 Hz, 1H); 7.87 (dd, J = 1.3; 8.0 Hz, 1H); 7.44 (m, 3H); 7.17 (ddd, J = 1.0; 7.5; 8.4 Hz, 1H); 6.99 (dd, J = 1.0; 8.4 Hz, 1H); 6.92 (dd, J = 1.0; 7.5 Hz, 1H); 6.39 (d, J = 3.0 Hz, 1H); 5.36 (d, J = 1.5 Hz, 1H); 5.17 (s, 1H); 5.09 (s, 1H); 4.96 (s, 1H); 4.92 (s, 1H); 4.5 (d, J = 5.0, 1H); 2.92 (dd, J = 6.5; 15.0 Hz, 1H, H—C(9β)); 2.81 (dddd, J = 3.0; 5.0; 6.5; 15.8 Hz, 1H, H—C(8a)); 2.18 (dd, J = 15.0; 15.8 Hz, 1H, H—C(9α)). ^{13}C-NMR, see above. MS (CI, i-C_4H_{10}), 393 (0.65, M^+ + H), 155 (0.6), 57 (100). (Found: C, 82.51; H, 5.17. Calc for $C_{27}H_{20}O_3$ (392.454); C, 82.63; H, 5.13%.)

(5RS,8RS,10aSR)-*6,7-Dimethylidene-5,8-epoxy-5,6,7,8,10,10a-hexahydro-1-anthrol* (**32**)

A sat soln of anh K_2CO_3 in MeOH (1 ml) was added to a soln of α-naphthoate **30** (0.5 g, 1.27 mmol) in anh THF/MeOH 6:4 (15 ml). After stirring at RT under N_2 atm for 45 min, the solvent was evaporated i.V. and the residue dissolved in AcOEt or Et_2O (60 ml). The organic soln was washed with sat NH_4Claq (30 ml, 3 times), then with sat NaClaq (30 ml, 3 times). The aq layers were extracted with AcOEt (30 ml, 2 times). After drying ($MgSO_4$) the solvent was evaporated i.V. The residue was purified by filtration on a column of silicagel (9 g, petroleum ether/AcOEt 8:2) and yielded 0.17 g (93.3%) of white crystals, m.p. 179–80° (AcOEt/petroleum ether 6:1). UV(CH_3CN): 326 (sh, 6800), 317 (8000), 302 (8900), 291 (sh, 8000), 267 (sh, 7900), 248 (sh, 12300), 226 (27200). IR(KBr): 3300, 3000, 1580, 1470, 1280, 970, 890, 870, 815, 780. ^{1}H-NMR (360 MHz, CD_3OD): 6.9 (dd, J = 7.2; 7.8 Hz, 1H, H—C(3)); 6.69 (d, J = 2.8 Hz, 1H, H—C(9)); 6.62 (d, J = 7.2 Hz, 1H, H—C(2)); 6.6 (d, J = 7.8 Hz, 1H, H—C(4)); 5.48 (d, J = 0.75 Hz, 1H); 5.22 (br.s, 1H, H—C(8)); 5.16 (d, J = 0.5 Hz, 1H); 5.07 (s, 1H); 5.04 (s, 1H); 4.98 (d, J = 4.0 Hz, 1H, H—C(5)); 2.77 (m, 1H, H—C(10a)); 2.73 (dd, J = 6.2; 14.2 Hz, 1H, H—C(10β)); 2.38 (dd, J = 14.2; 15.5 Hz, 1H, H—C(10α)). MS (70 eV): 238 (100, M^+), 223 (18), 209 (95), 195 (39), 181 (25), 165 (32), 149 (29), 115 (16), 77 (24), 69 (20), 57 (41), 55 (30), 43 (31). (Found: C, 80.57; H, 5.96. Calc for $C_{16}H_{14}O_2$ (238.286): C, 80.65; H, 5.92%.)

(5RS,8RS,8aSR)-*6,7-Dimethylidene-5,8-epoxy-5,6,7,8,8a-9-hexahydro-1-anthrol* (**33**)

Same procedure as for the preparation of **32**, starting with **31** (0.5 g, 1.27 mmol). Yield: 0.3 g (98.8%), white crystals, m.p. 162–

3° (AcOEt/petroleum ether 6:1). UV(CH_3CN): 288 (11100), 256 (7900), 238 (sh, 10000), 215 (28000). IR(KBr): 3360, 2960, 1570, 1465, 1290, 1280, 1270, 970, 905, 890, 880, 820, 775. ^{1}H-NMR (360 MHz, CD_3OD): 6.93 (dd, J = 7.3; 8.0 Hz, 1H, H—C(3)); 6.63 (dd, J = 1.0; 8.0 Hz, 1H, H—C(2)); 6.59 (d, J = 7.3 Hz, 1H, H—C(4)); 6.34 (d, J = 2.8 Hz, 1H, H—C(10)); 5.5 (s, 1H); 5.22 (br.s, 1H); 5.18 (s, 1H); 5.1 (s, 1H); 5.05 (s, 1H); 5.0 (d, J = 5.0, 1H, H—C(8)); 3.2 (dd, J = 6.6; 15.3 Hz, 1H, H—C(9β)); 2.72 (dddd, J = 2.8; 5.0; 6.6; 16.0 Hz, 1H, H—C(8a)); 1.96 (dd, J = 15.3; 16.0 Hz, 1H, H—C(9α)). MS (70 eV): 238 (87, M^+), 223 (16), 209 (100), 195 (42), 181 (27), 165 (40), 152 (13), 149 (40), 115 (23), 77 (19), 65 (15), 55 (24), 44 (56). (Found: C, 80.54; H, 5.88. Calc for $C_{16}H_{14}O_2$ (238.286): C, 80.65; H, 5.92%.)

(1RS,4RS,4aSR)-2,3-*Dimethylidene*-1,4-*epoxy*-1,2,3,4,4a,10-*hexahydro*-8-*methoxyanthracene* (**28**)[2]

The crude anthrol **32** obtained above (before purification on silicagel) was dissolved in THF/HMPT 5:1 (6 ml). A suspension of NaH (40 mg, 1.33 mmol, freshly washed with hexane (1 ml, 3 times)) in anh THF (3 ml) was added at RT under N_2 atm. After stirring at RT for 15 min, MeI (0.37 ml, 6 mmol) was added and the mixture stirred at RT for 15 min. The solvent was evaporated i.V. and the residue taken in ether (70 ml). The ethereal soln was washed with a 10% $Na_2S_2O_5$aq (20 ml, 2 times), then with a 10% $NaHCO_3$aq (20 ml, 2 times) and finally with a sat NaClaq (30 ml, 2 times). After drying ($MgSO_4$) the solvent was evaporated i.V. and the residue purified by filtration through Florisil (40 g, petroleum ether/AcOEt 95:5) and recrystallization from AcOEt/pentane 2:1 yielding 0.308 g (95.8%) of white crystals, m.p. 134–5°. UV(CH_3CN): 312 (sh, 8700), 304 (9200), 292 (9160), 280 (sh, 8100), 254 (sh, 8600), 236 (14,500), 212 (27,000). IR(CH_2Cl_2): 3020, 1580, 1480, 1135, 1090, 900, 780. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.07 (t, J = 8.0 Hz, 1H); 6.72 (m, 3H); 5.44 (s, 1H); 5.22 (s, 1H); 5.13 (s, 1H); 5.05 (s, 1H); 5.01 (s, 1H); 4.97 (d, J = 5.0, 1H, H—C(4)); 3.82 (s, 3H, CH_3O); 2.90 (dddd, J = 2.8; 5.0; 6.2; 16.4 Hz, 1H, H—C(4a)); 2.76 (dd, J = 6.2; 14.7 Hz, 1H, H—C(10β)); 2.47 (dd, J = 14.7; 16.4 Hz, H—C(10α)). MS (70 eV): 252 (92, M^+), 236 (14), 224 (22), 223 (100), 209 (35), 208 (44), 191 (26), 178 (28), 165 (37), 85 (34), 83 (64), 50 (43), 48 (98). (Found: C, 80.70; H, 6.42. Calc for $C_{17}H_{16}O_2$ (252.313): C, 80.92; H, 6.39%.)

(1RS,4RS,4aSR)-2,3-*Dimethylidene*-1,4-*epoxy*-1,2,3,4,4a,10-*hexahydro*-5-*methoxyanthracene* (**29**)[2]

A suspension of anh K_2CO_3 (0.5 g) in anh MeOH (2 ml) was added to a soln of α-naphthoate **31** (50 mg, 0.127 mmol) in anh THF (2 ml). After stirring at RT for 30 min, MeI (0.39 ml, 6.3 mmol) was added and the mixture stirred at RT for 6 hr under N_2 atm. Ether (30 ml) was added and the mixture was washed successively with a 10% $NaHSO_3$aq (10 ml, 2 times), a 10% $NaHCO_3$aq (10 ml, 2 times) and a sat NaClaq (20 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated i.V. The crude oil was filtered through Florisil (3 g, petroleum ether/AcEOt 9:1) and crystallized from AcOEt/hexane 3:1. Yield: 26 mg (79%), white crystals, m.p. 112–13°. UV(CH_3CN): 286 (10700), 256 (7750), 237 (sh, 12500), 217 (29900). IR(CH_2Cl_2): 3020, 1580, 1475, 1440, 1250, 1100, 960, 900, 820. ^{1}H-NMR (360 MHz, $CDCl_3$): 7.11 (ddd, J = 0.8; 7.5; 8.0 Hz, 1H, H—C(7)); 6.75 (d, J = 8.0 Hz, 1H); 6.73 (d, J = 7.5 Hz, 1H); 6.36 (d, J = 3.0 Hz, 1H, H—C(9)); 5.47 (s, 1H); 5.22 (s, 1H); 5.15 (s, 1H); 5.07 (s, 1H); 5.02 (s, 1H); 4.98 (d, J = 5.0 Hz, 1H, H—C(4)); 3.82 (s, 3H, CH_3O); 3.26 (dd, J = 6.8; 15.5 Hz, 1H, H—C(10β)); 2.83 (dddd, J = 3.0; 5.0; 6.8; 16.2 Hz, 1H, H—C(4a)); 2.07 (dd, J = 15.5; 16.2 Hz, 1H, H—C(10α)). MS (70 eV): 252 (87, M^+), 237 (15), 223 (100), 209 (36), 208 (47), 193 (22), 191 (20), 178 (26), 165 (33), 152 (16), 149 (58), 128 (12), 115 (23), 89 (15), 76 (22), 65 (15), 57 (30). (Found: C, 81.04; H, 6.55. Calc for $C_{17}H_{16}O_2$ (252.313): C, 80.92; H, 6.39%.)

(2RS,5RS,11aRS,12SR)-(5,12-*Epoxy*-7-α-*naphthoyloxy*-1,2,3,4,5,11,11a,12-*octahydro*-2-*naphthacenyl*)*methyl ketone* (**36β**), (2RS,5SR,11aSR,12RS)-(**36α**) *and* (2RS,5RS,5aSR,12SR)-(5,12-*epoxy*-10-α-*naphthoyloxy*-1,2,3,4,5,5a,6,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**37β**), (2RS,5SR,5aRS,12RS)-(**37α**) (*Diels–Alder adducts of* **30** *to MVK*)

(A) *Without catalyst.* A mixture of **30** (26 mg, 0.066 mmol) MVK (232 mg, 3.3 mmol) and hydroquinone (3 mg) in anh toluene (0.8 ml) was heated to 90° for 20 hr. After solvent evaporation i.V., the residue was purified by column chromatography (4 g Florisil, petroleum ether/AcOEt 4:1) and furnished 23 mg (75%) of a mixture of adducts. TLC (silical gel, hexane/AcOEt 3:2) allowed separation into two fractions, the first one contained 11.4 mg (37.2%) of a 9:1 mixture of **36β/37β**, the second, 5.5 mg (18%) of a 3:2 mixture of **36α/37α**.

(B) *With* $BF_3.Et_2O$. A degassed soln of MVK (1.48 g, 21 mmol), **30** 0.415 g, 1.058 mmol) in anh CH_2Cl_2 (30 ml) was cooled to −78°. Freshly distilled $BF_3.Et_2O$ (0.6 g, 4.2 mmol) was added dropwise under N_2 atm and the mixture was stirred at −78° for 5 hr. The cold mixture was poured at once in a separatory funnel containing ether (200 ml) and an ice-cold 10% aq solution of $NaHCO_3$. After vigorous shaking, the organic layer was separated and washed successively with a 10% $NaHCO_3$aq (30 ml) and a sat NaClaq (50 ml, 3 times). After drying ($MgSO_4$) the solvent was evaporated. The residue was purified by column chromatography (20 g Florisil, petroleum ether/AcOEt 85:15) yielding 408 mg (83.4%) of a 84:16 mixture of adducts **36β/37β**, white powder. Pure **36β** was obtained in low yield (< 10%) by recrystallization of this mixture from AcOEt, m.p. 170–171.5°. UV(CH_3CN): 326 (sh, 3000), 298 (sh, 12,000), 284 (14,200), 238 (sh, 24,000), 228 (sh, 43,200), 218 (54,100), 212 (54,800). IR(KBr: 3060, 3000, 2930, 1735, 1710, 1460, 1280, 1230, 1190, 1120, 985, 780. ^{1}H-NMR (360 MHz, $CDCl_3$ of the major isomer **36β**): 9.04 (d, J = 8.5 Hz, 1H)); 8.51 (dd, J = 1.2; 7.3 Hz, 1H); 8.11 (d, J = 8.0 Hz, 1H); 7.91 (dd, J = 1.0; 8.0, 1H); 7.66 (ddd, J = 1.6; 7.0; 8.5 Hz, 1H); 7.61 (dd, J = 7.3, 8.0 Hz, 1H); 7.58 (ddd, J = 1.0; 7.0; 8.0 Hz, 1H); 7.2 (dd, J = 6.8; 7.6 Hz, 1H, H—C(9)); 7.1 (d, J = 7.6 Hz, 1H, H—C(8)); 7.03 (d, J = 6.8 Hz, 1H, H—C(10)); 6.43 (d, J = 1,2 Hz, 1H, H—C(6)); 5.0 (dm, J = 3.9 Hz, 1H, H—C(12)); 4.95 (m, J = 0.2; 0.4; 0.7 Hz, 1H, H—C(5)); 3.2 (dm, J = 3.9; 15.5 Hz, 1H, H—C(11a)); 3.02 (dd, J = 5.5; 14.0 Hz, 1H, H—C(11β)); 2.55 (ddm, 1H, H—C(1β)); 2.45 (ddm, 1H, H—C(2)); 2.33 (dm, 1H, H—C(4β)); 2.18 (dd, 14.0; 15.5 Hz, 1H, H—C(11α)); 2.18 (s, 3H, CH_3CO); 2.17 (m, 1H, H—C(4α)); 2.02 (m, 1H, H—C(3α)); 1.97 (m, 1H, H—C(1α)); 1.64 (m, 1H, H—C(3β)); for further coupling constants, see Table 2. Further ^{1}H-NMR data attributed to the minor regioisomer **37β**: 6.44 (d, J = 1.2 Hz, 1H, H—C(11)); 4.96 (br.s, 1H, H—C(12)); 2.17 (s, CH_3CO). The other signals were completely or partially covered by those of **36β**. MS (70 eV) of **36β/37β**: 462 (5, M^+), 460 (1), 444 (2.3), 434 (4), 419 (0.5), 263 (1), 235 (1), 189 (1), 178 (1.5), 165 (2.5), 155 (100), 127 (29), 115 (1.0), 91 (0.5), 77 (1). (Found: C, 80.35; H, 5.67. Calc for $C_{31}H_{26}O_4$ (462.545): C, 80.49; H, 5.66%.)

Data of the 3:2 *mixture of regioisomers* **36α/37α**

^{1}H-NMR (360 MHz, $CDCl_3$) data of **36α**: 9.05 (d, J = 8.4 Hz, 1H); 8.52 (dd, J = 1.5; 7.5 Hz, 1H); 8.12 (d, J = 8.0 Hz, 1H); 7.93 (d, J = 8.0 Hz, 1H); 7.68–7.53 (m, 3H); 7.16 (dd, J = 7.5; 8.0 Hz, 1H, H—C(9)); 7.06 (d, J = 8.0 Hz, 1H); 7.01 (d, J = 7.5 Hz, 1H); 6.40 (d, J = 1.8 Hz, 1H, H—C(6)); 4.93 (m, 2H, H—C(5) & H—C(12)); 3.06 (dm, J = 15.0 Hz, 1H, H—C(11a)); 2.96 (dd, J = 5.0; 14.4 Hz, 1H, H—C(10β)); 2.66 (m, 1H); 2.55–1.91 (m, 5H); 2.18 (s, 3H, CH_3CO); 1.61–1.16 (m, 2H). Further signals attributed to isomer **37α**: 8.53 (d, J = 8.0 Hz, 1H); 6.98 (d, J = 7.5 Hz, 1H); 6.42 (d, J = 1.8 Hz, 1H, H—C(11)); 2.14 (s, CH_3CO).

(2RS,5RS,11aRS,12SR)-(5,12-*Epoxy*-7-*methoxy*-1,2,3,4,5,11,11a,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**38β**), (2RS,5SR,11aSR,12RS) (**38α**), (2RS,5RS,5aSR,12SR)-(5,12-*epoxy*-10-*methoxy*-1,2,3,4,5,5a,6,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**39β**) *and* (2RS,5SR,5aRS,12RS) (**39α**)

Method A, by cycloaddition. BF_3Et_2O (0.6 g, 4.2 mmol) was

added dropwise under N_2 atm to a stirred solution of MVK (1.04 g, 14.9 mmol) and **28** (188 mg, 0.746 mmol) in anh CH_2Cl_2 maintained at −78°. After stirring at −78° for 135 min, the mixture was poured at once in a separatory funnel containing ether (80 ml) and an ice-cold 10% $NaHCO_3$aq (30 ml). After vigorous shaking, the organic layer was separated and washed with a sat NaClaq (40 ml, 3 times), dried ($MgSO_4$) and evaporated i.V. The residue was purified by filtration on Florisil (23 g, petroleum ether/AcOEt 9:1) yielding 193 mg (80.3%) of a 9:1 mixture of adducts **38β/39β**, white crystals, m.p. 136–40°.

Method B, via saponification of the α-naphthoates. A sat soln of K_2CO_3 in anh MeOH (2 ml) was added to a soln of **36β/37β** 84:16 (0.2 g, 0.432 mmol) in anh THF. After stirring at RT for 12 hr, the corresponding mixture of phenols **42β/43β** were obtained as described hereafter. The crude product was then dissolved in THF/HMPT 3:1 (4 ml) and NaH (14.2 mg) was added as a suspension in THF (3 ml). After stirring at RT for 10 min methyl iodide (0.14 ml, 2.16 mmol) was added and the mixture was stirred under N_2 atm at RT for 15 min. Ether (60 ml) was added and the solution was washed successively with a 10% $NaHSO_3$aq (20 ml, 2 times), a 10% $NaHCO_3$aq (20 ml, 2 times) and a sat NaClaq (30 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated i.V. The residue was purified by medium pressure column chromatography (SiO_2 63–125 μm, petroleum ether/AcOEt 7:3). The first fraction contained 78 mg (56%) of a 84:16 mixture of **38β/39β**, white crystals. The second fraction contained 52 mg (37%) of a 84:16 mixture of **38α/39α**. Characteristics of a 9:1 mixture of **38β/39β**: UV(CH_3CN): 312 (6900), 302 (7800), 284 (9400), 276 (9350), 226 (sh, 19,000), 216 (19,800). IR($CHCl_3$): 3010, 1710, 1575, 1470, 1260, 1080. ^{1}H-NMR (360 MHz, $CDCl_3$) signals of **38β**: 7.07 (dd, J = 7.5; 8.4 Hz, 1H, H—C(9)); 6.75 (d, J = 8.4 Hz, 1H); 6.69 (d, J = 7.5 Hz, 1H); 6.66 (d, J = 2.0 Hz, 1H, H—C(6)); 4.98 (br.s, 1H, H—C(5)); 4.95 (dm, J = 4.0 Hz, 1H, H—C(12)); 3.83 (s, 3H, CH_3O); 3.02 (dm, J = 16.0 Hz, 1H, H—C(11a)); 2.90 (dd, J = 5.6; 14.4 Hz, 1H, H—C(11β)); 2.50–2.34 (m, 3H, H—C(1β), H—C(2) & H—C(4β)); 2.21 (m, 1H); 2.15 (s, 3H, CH_3CO); 2.12 (dd, J = 14.4; 16.0 Hz, 1H, H—C(11α)); 2.0 (m, 2H); 1.68 (m, 1H). Further signals of the minor isomer **39β**: 5.01 (br.s, 1H, H—C(12)); 4.93 (dm, J = 4.0 Hz, 1H, H—C(5)). MS (70 eV): 322 (31, M^+), 294 (43), 293 (84), 261 (29), 251 (17), 249 (19), 223 (100), 171 (41), 165 (29), 158 (23), 115 (31), 91 (27), 71 (30), 43 (70). (Found: C, 78.25; H, 6.94. Calc for $C_{21}H_{22}O_3$ (322.404): C, 78.23; H, 6.87%.)

Characteristics of a 84:16 mixture of **38α/39α**: UV(CH_3CN): 312 (6500), 302 (7300), 284 (9000), 276 (9100), 226 (sh, 16900), 216 (17400). IR($CHCl_3$): 3000, 1710, 1570, 1470, 1260, 1080. ^{1}H-NMR (360 MHz, $CDCl_3$) signals of **38α**: 7.05 (dd, J = 8.0; 9.0 Hz, 1H, H—C(9)); 6.72 (d, J = 9.0 Hz, 1H); 6.69 (d, J = 8.0 Hz, 1H); 6.65 (br.s, 1H, H—C(6)); 4.98 (br.s, 1H, H—C(5)); 4.91 (dm, J = 4.0 Hz, 1H, H—C(12)); 3.83 (s, 3H, CH_3O); 3.0 (dm, J = 16.0 Hz, 1H, H—C(11a)); 2.85 (dd, J = 6.0; 15.0 Hz, 1H, H—C(11β)); 2.66 (m, 1H); 2.52 (dm, J = 16.6 Hz, 1H); 2.40–2.20 (m, 4H); 2.3 (dd, J = 15.0, 16.0 Hz, 1H, H—C(11α)); 2.18 (s, 3H, CH_3CO); 1.3 (m, 1H); signals of **39α**: 4.95 (br.s, H—C(12)); 4.94 (br.s, H—C(5)); 2.89 (dd, J = 6.0; 15.0 Hz, H—C(6β)); 2.15 (s, CH_3CO). MS (70 eV): 322 (44, M^+), 304 (13), 293 (100). (Found: C, 78.24; H, 7.03. Calc for $C_{21}H_{22}O_3$ (322.404): C, 78.23; H, 6.87%.)

(2RS,5SR,11aRS,12RS)-(5,12-*Epoxy*-10-α-*naphthoyloxy*-1,2,3,4,5,11,11a,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**41β**) *and* (2RS,5SR,5aSR,12RS)-(5,12-*epoxy*-7-α-*naphthoyloxy*-1,2,3,4,5,5a,6,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**40β**)

Same procedure as for the preparation of adducts **36β/37β** using **31** (0.415 g, 1.058 mmol), MVK (1.48 g, 21 mmol) and BF_3Et_2O (0.6 g, 4.23 mmol) at −78°. Yield: 0.42 g (86%) of a 81:19 mixture of **41β/40β**, white crystalline powder. Pure **41β** could be obtained in low yield (*ca* 10%) by recrystallization from pentane/ether 1:3, m.p. 159–160°. UV(dioxane): 325 (sh, 4400), 298 (sh, 12,800), 283 (14,500), 243 (sh, 22,400), 230 (sh, 41,900), 219 (54,600). IR(KBr): 3060, 3000, 1735, 1710, 1510, 1460, 1280, 1220, 1190, 1125, 840. ^{1}H-NMR (360 MHz, $CDCl_3$), signals of the major adduct **41β**: 9.01 (d, J = 9.0 Hz, 1H); 8.51 (dd, J = 1.5; 7.5 Hz, 1H); 8.13 (d, J = 8.0 Hz, 1H); 7.94 (d, J = 8.0 Hz, 1H); 7.6 (m, 3H); 7.25 (t, J = 8.0 Hz, 1H); 7.02 (m, 2H); 6.39 (d, J = 2.0 Hz, 1H, H—C(6)); 5.01 (br.s, 1H, H—C(5)); 4.9 (dm, J = 4.0 Hz, 1H, H—C(12)); 3.12 (dd, J = 6.0; 14.5 Hz, 1H, H—C(11β)); 3.0 (dm, J = 15.0 Hz, 1H, H—C(11a)); 2.45 (m, 3H, H—C(1β), H—C(2) & H—C(4β)); 2.21 (m, 1H); 2.13 (s, 3H, CH_3CO); 2.03 (m, 1H); 1.86 (m, 2H); 1.66 (m, 1H); further signals attributed to the minor adduct **40β**: 9.03 (d, J = 9.0 Hz, 1H); 5.02 (br.s, 1H, H—C(12)); 4.88 (dm, J = 4.0 Hz, 1H, H—C(5)); 2.17 (s, 3H, CH_3CO). MS (70 eV): 462 (1, M^+), 434 (2), 290 (4), 247 (2), 155 (100). (Found: C, 80.45; H, 5.66. Calc for $C_{31}H_{26}O_4$ (462.545): C, 80.49; H, 5.66%.)

(2RS,5RS,11aRS,12SR)-(5,12-*Epoxy*-7-*hydroxy*-1,2,3,4,5,11,11a,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**42β**), (2RS,5SR,11aSR,12RS) (**43β**), (2RS,5RS,5aSR,12SR)-5,12-*epoxy*-10-*hydroxy*-1,2,3,4,5,5a,6,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**42α**) *and* (2RS,5SR,5aRS,12RS) (**43α**)

A sat soln of K_2CO_3 in anh MeOH (1 ml) was added to a soln of a 9:1 mixture of adducts **36β/37β** (130 mg, 0.28 mmol) in THF/MeOH 1:1 (1 ml). After stirring at RT for 90 min, the solvent was evaporated i.V. and the residue taken with ether (30 ml). The ethereal soln was washed successively with a sat NH_4Claq (20 ml, 2 times) and a sat NaClaq (20 ml, 2 times). After drying ($MgSO_4$), the solvent was evaporated and the residue purified by TLC (SiO_2, hexane/AcOEt 3:2). The first fraction contained 33 mg (38%) of a 9:1 mixture of **42β/43β**. UV(CH_3CN): 312 (sh, 2600), 302 (3000), 270 (4500), 212 (12,000). IR(CH_2Cl_2): 3700, 3600–3400, 2940, 1715, 1710, 1465, 1080, 960. ^{1}H-NMR (360 MHz, $CDCl_3$), signals attributed to the major isomer **42β**: 6.97 (dd, J = 7.5; 8.0 Hz, 1H, H—C(9)); 6.67 (d, J = 7.5 Hz, 1H, H—C(8)); 6.62 (d, J = 8.0 Hz, 1H, H—C(10)); 6.58 (dd, J = 0.75; 2.0 Hz; 1H, H—C(6)); 5.26 (br.s, 1H, OH); 5.01 (br.s, 1H, H—C(5)); 4.98 (dm, J = 4.0 Hz, 1H, H—C(12)); (3.01 (m, 1H, H—C(11a)); 2.89 (dd, J = 6.0; 14.4 Hz, 1H, H—C(11β)); 2.57–1.94 (m, 7H); 2.16 (s, 3H, CH_3CO); 1.66 (m, 1H, H—C(3)); further signals attributed to **43β**: 5.03 (br.s, 1H, H—C(12)); 4.95 (dm, J = 4.0 Hz, 1H, H—C(5)); 2.15 (s, 3H, CH_3CO). MS (70 eV): 308 (59, M^+), 290 (66), 279 (100). (Found: C, 77.79; H, 6.51. Calc for $C_{20}H_{20}O_3$ (308.377): C, 77.89; H, 6.53%.)

The second fraction (smaller *Rf* value) contained 28 mg (32%) of a 9:1 mixture of the isomers **42α/43α**. UV(CH_3CN): 314 (sh, 4200), 302 (5000), 284 (sh, 6200), 274 (7000), 216 (17,100). IR(CH_2Cl_2): 3600, 3060, 1715, 1710, 1465, 1170, 1090. ^{1}H-NMR (360 MHz, $CDCl_3$), signals of **42α**: 6.94 (dd, J = 7.5; 8.0 Hz, 1H, H—C(9)); 6.65 (dm, J = 7.5 Hz, 1H); 6.62 (dm, J = 8.0 Hz, 1H); 6.56 (dm, J = 2.3 Hz, 1H, H—C(6)); 5.02 (br.s, 1H, H—C(5)); 4.94 (dm, J = 4.0 Hz, 1H, H—C(12)); 4.83 (br.s, 1H, OH); 3.0 (dm, J = 15.3 Hz, 1H, H—C(11a)); 2.85 (dd, J = 6.0; 14.4 Hz, 1H, H—C(11β)); 2.60 (m, 1H, H—C(4β)); 2.51 (dm, J = 18.0 Hz, H—C(1β)); 2.43–1.9 (m, 5H); 2.18 (s, 3H, CH_3CO); 1.3 (m, 1H); further signal of the minor isomer **43α**: 2.16 (s, CH_3CO). MS (70 eV): 308 (62, M^+), 279 (100), 264 (40), 248 (50), 210 (95), 157 (64), 43 (90). (Found: C, 77.76; H, 6.58. Calc for $C_{20}H_{20}O_3$ (308.377): C, 77.89; H, 6.53%.)

(2RS,5SR,12RS)-(5,12-*Epoxy*-1,2,3,4,5,12-*hexahydro*-7-*methoxy*-2-*naphtacenyl*)*methyl ketone* (**44**)

A mixture of **38β/39β** 9:1 (250 mg, 0.776 mmol), DDQ (0.707 g, 3.11 mmol), cyclohexene oxide (0.5 g) and anh benzene (40 ml) was heated to 80° for 24 hr under N_2 atm and in the dark. After cooling to RT, the ppt was removed by filtration and washed with C_6H_6 (5 ml, 2 times). The solvent was evaporated i.V. and the residue purified on a column of Florisil (45 g, petroleum ether/AcOEt 8:2) yielding 129 mg (52%) of a 9:1 mixture of **44/45**, colourless crystals. Recrystallization from ether/AcOEt 1:1 furnished pure **44**, white crystals, m.p. 158–59°. UV(CH_3CN): 328 (790), 314 (1200), 280 (7400), 272 (sh, 7800), 250 (31100), 226 (32700), 212 (sh, 26400). IR(KBr):

3020, 2940, 1710, 1600, 1470, 1370, 1265, 1120, 1150, 840, 795, 755. ^{1}H-NMR (360 MHz, CD_2Cl_2): 7.99 (s, 1H, H—C(6)); 7.55 (s, 1H, H—C(11)); 7.36 (dd, J = 7.5; 8.0 Hz, 1H, H—C(9)); 7.32 (dm, J = 8.0 Hz, 1H, H—C(10)); 6.88 (dd, J = 1.6; 7.5 Hz, 1H, H—C(8)); 5.51 & 5.50 (2br.s, 2H, H—C(5) & H—C(12)); 4.05 (s, 3H, CH_3O); 2.15 (m, 2H); 2.27–2.13 (m, 2H); 2.08 (s, 3H, CH_3CO); 2.03–1.86 (m, 2H); 1.67 (m, 1H). MS (70 eV): 320 (100, M^+), 304 (32), 277 (45), 259 (40), 249 (32), 222 (25), 215 (19), 202 (19), 165 (11), 71 (10), 57 (9). (Found: C, 78.66; H, 6.28. Calc for $C_{21}H_{20}O_3$ (320.388): C, 78.72; H, 6.29%.)

(±)-2-*Acetyl*-7-*methoxy*-1,2,3,4-*tetrahydro*-5,12-*naphthacenequinone* (**48**)

CF_3COOH (25 drops) was added to a stirred soln of **44/45** 9:1 (0.108 g, 0.33 mmol) in CH_2Cl_2 (15 ml) and cooled to 0° under N_2 atm. After stirring at 0° for 3 hr, pyridinium chlorochromate (0.145 g, 0.67 mmol) was added portionwise at 0° under N_2 atm. After vigorous stirring at 0° for 75 min, the mixture was diluted with CH_2Cl_2 (80 ml) and extracted with a 10% $NaHCO_3$aq (30 ml, 2 times), and then with a sat NaClaq (40 ml, 2 times). After drying ($MgSO_4$) the solvent was evaporated i.V. and the residue purified on a column of silica gel (20 g, ether/CH_2Cl_2/AcOEt 9:1:1) yielding 68 mg (60%) of a 9:1 mixture of **48/49**. Recrystallization from acetone/hexane/CH_2Cl_2 3:2:1 furnished pure **48**, yellow crystals, m.p. 226–227.5°. UV(CH_3CN): 320 (2900), 296 (10,900), 284 (sh, 16,200), 272 (18,300), 246 (56,000), 202 (26,200). IR(KBr): 1700, 1665, 1620, 1390, 1290, 1270, 1250, 1140, 925, 745. ^{1}H-NMR (360 MHz, CD_2Cl_2): 9.13 (s, 1H, H—C(6)); 8.69 (s, 1H, H—C(11)); 7.76 (m, 2H, H—C(9) & H—C(10)); 7.15 (dd, J = 2.0; 7.2 Hz, 1H, H—C(8)); 4.13 (s, 3H, CH_3O); 2.98 (dm, J = 8.0 Hz, 1H); 2.92 (dm, J = 10.0 Hz, 1H); 2.85–2.56 (m, 3H); 2.3 (s, 3H, CH_3CO); 2.21 (m, 1H); 1.7 (m, 1H). MS (70 eV): 334 (57, M^+), 316 (5), 291 (100), 289 (27), 274 (19), 259 (10), 231 (11), 202 (15), 133 (25), 77 (11). (Found: C, 75.59; H, 5.50. Calc for $C_{21}H_{18}O_4$ (334.371): C, 75.43; H, 5.42%.)

(±)-(5,12-*Diacetoxy*-7-*methoxy*-1,2,3,4-*tetrahydro*-2-*naphtacenyl*)*methyl ketone* (**50**)

To a soln of **48/49** 9:1 (46 mg, 0.137 mmol) in Ac_2O (2 ml) cooled to 0°, Et_3N (0.2 ml) and Zn powder (0.09 g, 1.37 mmol) were added. The mixture was stirred at 0° for 45 min and then heated to 110° for 1 hr under N_2 atm. The ppt was removed by filtration and washed with AcOEt (5 ml, 3 times). The solvent was evaporated i.V. (Büchi, Kugelrohr). The residue was taken with CH_2Cl_2 (40 ml) and the soln was washed with a 5% HClaq (20 ml), then with a 10% $NaHCO_3$aq (20 ml) and a sat NaClaq (30 ml, 2 times). After drying ($MgSO_4$), the solvent was evaporated i.V. and the residue purified on a column of Florisil (4.5 g, petroleum ether/AcOEt 4:1) yielding 50 mg (86.4%) of a 9:1 mixture of **50/51**. Recrystallization from benzene/pentane 1:1 gave pure **50** yellowish crystals, m.p. 203–4°. UV(CH_3CN): 400 (2100), 380 (3500), 363 (1800), 262 (13,200), 244 (sh, 35,300), 222 (17,900). IR(KBr): 1760, 1720, 1470, 1375, 1240, 1210, 1110. ^{1}H-NMR (360 MHz, CD_2Cl_2): 8.87 (s, 1H, H—C(6)); 8.41 (s, 1H, H—C(11)); 7.74 (d, J = 8.8 Hz, 1H, H—C(10)); 7.55 (dd, J = 7.6; 8.8 Hz, 1H, H—C(9)); 6.63 (d, J = 7.6 Hz, 1H, H—C(8)); 4.15 (s, 3H, CH_3O); 3.35–2.71 (m, 5H); 2.61 (s, 6H, CH_3COO); 2.3 (s, 3H, CH_3CO); 2.26 (m, 1H); 1.78 (m, 1H). MS (70 eV): 420 (8, M^+), 378 (17), 336 (100), 292 (23), 278 (9), 231 (6), 202 (8), 185 (8), 133 (19), 60 (17), 55 (18). (Found: C, 71.51; H, 5.71. Calc for $C_{25}H_{24}O_6$ (420.461): C, 71.41; H, 5.75%.)

(±)-2-*Acetyl*-5,12-*diacetoxy*-7-*methoxy*-1,2,3,4-*tetrahydro*-6,11-*naphthacene-quinone* (**52**)

Under N_2 atm a soln of **50/51** 9:1 (48 mg, 0.114 mmol) in acetone (5 ml) and a soln of 4N Jones reagent (0.5 ml, 0.68 mmol CrO_3; made from 26.72 g of CrO_3, 23 ml H_2SO_4 diluted with H_2O to 200 ml) were added simultaneously and dropwise to stirred acetone (4.8 ml) cooled to 0°. The mixture was stirred at 0° for 3 hr under N_2 atm. Isopropanol (1 ml) was added and the stirring continued for 10 more min. After addition of CH_2Cl_2 (50 ml), the soln was washed with a 10% $NaHCO_3$aq (30 ml, 2 times), and then with sat NaClaq (40 ml, 3 times). The aq layers were extracted with CH_2Cl_2 (30 ml, 2 times). The organic solutions were united, dried ($MgSO_4$) and evaporated i.V. The residue was filtered through a short column of Florisil (2g, CH_2Cl_2/AcOEt 7:3) and then purified by column chromatography on silicagel (Lobar, CH_2Cl_2/AcOEt 85:15), yielding 26 mg (50.5%) of a 9:1 mixture of **52/53**. Recrystallization from benzene/pentane 2:1 gave pure **52**, yellow crystals, m.p. 227–8°. UV(CH_3CN): 370 (6900), 260 (37,100), 218 (33,800). IR(KBr): 1760, 1700, 1680, 1590, 1430, 1370, 1340, 1270, 1230, 1200, 1020, 980. ^{1}H-NMR (360 MHz, CD_2Cl_2): 7.71 (dd, J = 1.2; 7.8 Hz, 1H); 7.64 (dd, J = 7.8; 8.4 Hz, 1H, H—C(9)); 7.28 (dd, J = 1.2; 8.4, 1H); 3.96 (s, 3H, CH_3O); 3.05–2.58 (m, 5H); 2.45 (s, 3H, CH_3COO); 2.44 (s, 3H, CH_3COO); 2.22 (s, 3H, CH_3CO); 2.2 (m, 1H); 1.68 (m, 1H). MS (70 eV): 450 (1, M^+), 408 (8), 366 (100), 323 (65), 321 (34), 305 (29), 290 (12), 262 (3), 217 (6), 189 (4), 149 (4), 135 (3), 105 (4), 71 (5), 57 (9). (Found: C, 66.51; H, 4.88. Calc for $C_{25}H_{22}O_8$ (450.443): C, 66.66; H, 4.92%.)

(±)-7,9-*Dideoxydaunomycinone* (**54**) *and* (±)-7,9-*dideoxyisodaunomycinone* (**55**)

A soln of **52/53** 9:1 (190 mg, 0.422 mmol) in MeOH (20 ml) containing 3% HCl was heated to 70° for 12 hr under N_2 atm. The mixture was stirred at 0° for 2 hr. The red crystals were collected by filtration and washed with MeOH (5 ml, 3 times) yielding 115 mg (74.4%) of a 9:1 mixture of **54/55**. These two compounds were separated by TLC (silica gel, $CHCl_3$) and purified by recrystallization from CH_2Cl_2/MeOH 2:1. Characteristics of **54**: (larger *Rf*), red needles, m.p. 243–244°, litt.: 243–245°,[12b] 244–245°,[12d] 245–247°,[12j] 234–239°.[12a] UV($CHCl_3$): 536 (6500), 500 (10,900), 472 (9700), 364 (2100), 292 (7700), 252 (30,000). IR(KBr): 3600–3400 (weak), 1705, 1610, 1575, 1440, 1410, 1260, 1060, 980, 860. ^{1}H-NMR (360 MHz, $CDCl_3$): 13.84 (s, 1H, OH); 13.49 (s, 1H, OH); 8.04 (d, J = 7.5 Hz, 1H); 7.76 (dd, J = 7.5; 8.8 Hz, 1H, H—C(9)); 7.36 (d, J = 8.8 Hz, 1H); 4.08 (s, 3H, CH_3O); 3.2–3.04 (m, 2H); 2.87–2.68 (m, 3H); 2.3 (s, 3H, CH_3CO); 2.25 (m, 1H); 1.76 (m, 1H). MS (70 eV): 366 (100), 323 (86), 321 (51), 305 (55), 290 (20), 217 (10), 189 (6), 121 (5), 105 (5), 57 (5). Characteristics of the minor isomer **55** (smaller *Rf*), red needles, m.p. 215–216°, litt. 217–217°.[12b] UV($CHCl_3$): 536 (7200), 500 (11,900), 472 (sh, 10,400), 372 (7800), 284 (16,700), 256 (37,300). IR(KBr): 3600–3400 (weak), 1715, 1610, 1575, 1445, 1410, 1280, 1210, 980. ^{1}H-NMR (360 MHz, $CDCl_3$): 13.88 (s, 1H, OH); 13.43 (s, 1H, OH); 8.02 (d, J = 7.6 Hz, 1H); 7.73 (dd, J = 7.6; 8.8 Hz, 1H, H—C(8)); 7.35 (d, J = 8.8 Hz, 1H); 4.07 (s, 3H, CH_3O); 3.14 (m, 1H); 3.04 (ddd, J = 4.0; 5.0; 19.0 Hz, 1H); 2.86–2.63 (m, 3H); 2.29 (s, 3H, CH_3CO); 2.22 (m, 1H); 1.75 (m, 1H). MS (70 eV): 366 (85, M^+), 323 (71), 321 (100), 305 (33), 290 (18), 252 (14), 235 (7), 105 (12), 97 (11), 77 (16), 69 (18), 60 (13), 57 (23), 55 (21).

(2RS,4aRS,5RS,11aRS,12SR,12aSR)-(4a,12a-*Epoxy*-5,12-*epoxy*-7-α-*naphthoyloxy*-1,2,3,4,5,11,11a,12-*octahydro*-2-*naphtacenyl*)*methyl ketone* (**56**)

A soln of metachloroperbenzoic acid (26 mg, 0.15 mmol) and **36β/37β** 84:16 (70 mg, 0.15 mmol) in CH_2Cl_2 (8 ml) was stirred at 0° for 4 hr. CH_2Cl_2 (60 ml) and 10% $NaHCO_3$aq (20 ml) were added. The organic layer was washed with a sat NH_4Claq (20 ml, 2 times) and then with a sat NaClaq (30 ml, 2 times). After drying ($MgSO_4$), the solvent was evaporated i.V. and the residue purified by TLC ("Chromatotron", silica gel, petroleum ether/AcOEt 7:3) yielding 43 mg (59.3%), white crystals, m.p. 208–9° (AcOEt/hexane 3:1). UV(CH_3CN): 324 (sh, 4200), 300 (sh, 7400), 284 (sh, 9600), 270 (12,300), 238 (sh, 22,000); 224 (sh, 41,000). IR(CH_2Cl_2): 3070, 2960, 1740, 1720, 1470, 1230, 1190, 1120, 990. ^{1}H-NMR (360 MHz, $CDCl_3$): 9.09 (d, J = 9.0 Hz, 1H); 8.59 (dd, J = 1.2; 7.3 Hz, 1H); 8.19 (d, J = 8.0 Hz, 1H); 7.98 (d, J = 8.4 Hz, 1H); 7.65 (m, 3H); 7.3 (dd, J = 7.2; 8.0 Hz, 1H, H—C(9)); 7.18 (d, J = 7.2 Hz, 1H, H—C(8)); 7.15 (d, J = 8.0 Hz, 1H, H—C(10)); 6.60 (d, J = 2.4 Hz, H—C(6)); 4.73 (s, 1H, H—C(5)); 4.59 (d, J = 4.5 Hz, 1H, H—C(12)); 3.05 (dd, J = 6.0; 14.4 Hz, 1H, H—C(11β)); 2.95

(dm, J = 16.8 Hz, 1H, H—C(11a)); 2.54 (dd, J = 14.4; 16.8 Hz, 1H, H—C(11α)); 2.35–1.81 (m, 5H); 2.13 (s, 3H, CH_3CO); 1.74 (dm, J = 13.0 Hz, 1H); 1.35 (m, 1H). MS (70 eV): 478 (1.7, M^+), 460 (0.2), 450 (0.2), 435 (0.2), 366 (0.1), 263 (0.3), 155 (100), 127 (100). (Found: C, 77.78; H, 5.60. Calc for $C_{31}H_{26}O_5$ (478.544): C, 77.80; H, 5.47%.)

(7-α-Naphthoyloxy-1,2,3,4-tetrahydro-2-naphtacenyl)methyl ketone (**57**) *and* (*10-α-naphthoyloxy-1,2,3,4-tetrahydro-2-naphtacenyl)methyl ketone* (**58**)

Method A. CF_3COOH (10 drops) was added slowly to a soln of a 84:16 mixture of adducts **36β/37β** (45 mg, 0.097 mmol) in anh $CHCl_3$ (5 ml). After stirring at RT for 3 hr, the mixture was poured into a mixture of ether (50 ml) and 5% $NaHCO_3$aq (20 ml). The organic layer was washed with 5% $NaHCO_3$aq (30 ml) and then with a sat NaClaq (30 ml, 3×). After drying ($MgSO_4$), the solvent was evaporated i.V. and the residue purified by TLC (silica gel, hexane/AcOEt 4:1) yielding 21 mg (48.5%) a 84:16 mixture of **57/58**, yellowish oil.

Method B. A soln of $(CH_3)_3SiI$ (23 mg, 1.18 mmol) in anh C_6H_6 (4 ml) was added dropwise to a stirred soln of **36β/37β** 84:16 (50 mg, 0.108 mmol) in anh C_6H_6 (5 ml), cooled to 0° and under N_2 atm. After stirring at 0° for 1 hr, ether (50 ml) and a sat $Na_2S_2O_5$aq was added. The organic layer was washed with a sat $Na_2S_2O_5$aq (20 ml) and then with 5% $NaHCO_3$aq (20 ml, 2 times) and sat NaClaq (20 ml, 2 times). After drying ($MgSO_4$), the solvent was evaporated i.V. and the residue purified by TLC yielding 24 mg (50%) of a 84:16 mixture of **57/58**. UV(CH_3CN): 392 (4300), 370 (5400), 352 (4300), 296 (9400), 260 (16,000), 218 (50,000), 212 (48,600). IR (film): 3060, 2940, 1740, 1710, 1240, 1180, 1120. ^{1}H-NMR (360 MHz, $CDCl_3$) of **57**: 9.15 (d, J = 8.8 Hz, 1H); 8.79 (dd, J = 1.3; 7.5 Hz, 1H); 8.42 & 8.40 (2s, 2H); 8.12 (d, J = 8.4 Hz, 1H); 8.0 (dd, J = 1.3; 8.1 Hz, 1H); 7.94 (d, J = 8.8 Hz, 1H); 7.78 (s, 1H); 7.70 (dd, J = 7.5; 8.4 Hz, 1H); 7.68 (s, 1H); 7.67 (ddd, J = 1.3; 7.1; 8.1 Hz, 1H); 7.61 (ddd, J = 1.1; 7.1; 8.8 Hz, 1H); 7.48 (dd, J = 7.3; 8.8 Hz, 1H); 7.39 (dd, J = 0.7; 7.3 Hz, 1H); 3.26–2.94 (m, 4H); 2.87 (m, 1H); 2.28 (s, 3H, CH_3CO); 2.21 (m, 1H); 1.87 (m, 1H). Further signals attributed to the minor isomer **58**: 8.43 & 8.39 (2s, 2H); 7.75 (br.s, 1H); 2.25 (s, 3H, CH_3CO). MS (70 eV): 444 (2, M^+), 442 (2), 215 (5), 155 (100). MS (CI, CH_4): 445 (53, $M^+ + 1$), 155 (100).

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