mm, ethyl acetate:hexane (1:1), $\alpha = 5$) into major and minor *p*-chlorobenzoate positional isomers as oils.

cis-(1*S*)-Hydroxy-(2*R*)-[(*p*-chlorobenzoyl)oxy]-1,2,3,4-tetrahydrobenz[*a*]anthracene (**10a**): $k' = 0.2$ (17 mg, 54%); NMR δ (100 MHz, $CDCl_3$) 2.10–2.70 (2 H, m, 3-H), 3.04–3.24 (2 H, m, 4-H), 5.42 (1 H, m, $J_{2,3} = 12$ Hz, $J_{1,2} = 3$ Hz, $J_{2,3} = 3$ Hz, 2 H), 5.80 (1 H, d, $J_{1,2} = 3$ Hz, 1-H), 7.12–8.18 (10 H, m, aryl H), 8.36 (1 H, s, 7-H), 8.84 (1 H, s, 12-H); mass spectrum (CI, isobutane), *m/z* M^+ 402 (31%), $M^+ + 2$ 404 (11%), $M^+ - (p\text{-}ClC_6H_5CO_2)$ 247 (100%); UV (MeOH) λ_{max} (ϵ) 247 (72 900), 256 (109 000), 358 (5730), 377 (5450). The CD spectrum (MeOH:$CHCl_3$) is shown in Figure 2.

cis-(1*S*)-[(*p*-chlorobenzoyl)oxy]-(2*R*)-hydroxy-1,2,3,4-tetrahydrobenz[*a*]anthracene (**10b**): $k' = 1$ (1.4 mg, 5%); NMR δ (100 MHz, $CDCl_3$) 2.10–2.70 (2 H, m, 3-H), 3.04–3.28 (2 H, m, 4-H), 4.10 (1 H, m, 2-H), 7.16–8.04 (11 H, m, aryl and 1-H), 8.38 (1 H, s, 7-H), 8.50 (1 H, s, 12-H); mass spectrum (CI, isobutane), *m/z* $M^+ - (p\text{-}ClC_6H_5CO_2)$ 247 (100%).

Synthesis of (−)-*cis*-(8*R*,9*S*)-8,9-Dihydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene (2b) from (−)-(8*R*,9*R*)-6b. A mixture of (−)-**6b** (100 mg) and silver acetate (100 mg) in glacial acetic acid (20 mL) containing water (0.1 mL) was refluxed for 3 h. After cooling, the reaction mixture was filtered and the residue was washed with ethyl acetate. The organic phases were combined. Removal of solvent yielded a product which was dissolved in THF (10 mL) and hydrolyzed using 1 M KOH in methanol (10 mL, 1:1) over 1 h. A saturated solution of NH_4Cl (5 mL) was added to the reaction mixture, and the organic solvent was removed under vacuum. Dilution of the product mixture with water precipitated the required product **2b**, which was filtered, washed with water, and dried.

The *cis*-tetrahydrodiol **2b** was separated from a small proportion of the trans isomer by preparative TLC (silica gel, $CHCl_3$:MeOH, 19:1, 3 elutions, upper band is **2b**). Recrystallization of the *cis*-tetrahydrodiol **2b** from MeOH yielded 15 mg (30%), mp 186–188 °C, $[\alpha]_D$ −19° (THF), with identical spectral characteristics to the enantiomer obtained from the resolved diester **3b**.

Synthesis of (+)-*cis*-(10*S*,11*R*)-10,11-Dihydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene (2c) from (−)-(10*R*,11*R*)-6c. Reaction of (−)-(10*R*,11*R*)-**6c** (100 mg) with silver acetate (100 mg) in glacial acetic acid, using similar conditions and workup to that indicated for the synthesis of (−)-**2b**, gave the *cis*-tetrahydrodiol **2c** (12 mg, 25%). Recrystallization from acetone gave crystals, mp 208–210 °C, $[\alpha]_D$ +136° (THF), which had identical spectra to the (+)-enantiomeric form of **2c** derived from (+)-**3c**.

Synthesis of (−)-(10*R*)-(Benzoyloxy)-5,6,8,9,10,11-hexahydrobenz[*a*]anthracene (13) from (−)-4c. A mixture of (−)-*cis*-(10*R*,11*S*)-**4c**, 10% Pd on charcoal (35 mg), and ethyl acetate (7 mL) was stirred under an atmosphere of hydrogen at room temperature for 96 h. The catalyst was removed by filtration and washed with acetone. The combined solvent was removed under vacuum and the residue purified by preparative TLC (silica gel, hexane:dichloromethane (1:1) to yield (−)-(10*R*)-(benzoyloxy)-5,6,8,9,10,11-hexahydrobenz[*a*]anthracene **13** (7 mg, 28%): $[\alpha]_D$ −35.8° ($CHCl_3$); UV (MeOH:$CHCl_3$) $\lambda_{max}(\epsilon)$ 226 (25 500), 268 (13 800), 305 (5100); CD (MeOH/dioxane, 9:1) $\Delta\epsilon_{237}$ −13.6, $\Delta\epsilon_{229}$ 0, $\Delta\epsilon_{221}$ +10.6.

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Registry No. **1a**, 91423-01-7; **1b**, 91423-02-8; **1c**, 91423-03-9; (+)-(1*R*,2*S*)-**2a**, 91422-90-1; (−)-(1*S*,2*R*)-**2a**, 91423-71-1; (+)-(8*S*,9*R*)-**2b**, 91423-72-2; (−)-(8*R*,9*S*)-**2b**, 91423-73-3; (+)-(10*S*,11*R*)-**2c**, 91384-62-2; (+)-(1*R*,2*S*)-**3a**, 91365-97-8; (−)-(1*S*,2*R*)-**3a**, 91422-87-6; (−)-(8*S*,9*R*)-**3b**, 91365-98-9; (−)-(8*R*,9*S*)-**3b**, 91422-88-7; (+)-(10*S*,11*R*)-**3c**, 91365-99-0; (−)-(10*R*,11*S*)-**3c**, 91422-89-8; (+)-(1*R*,2*S*)-**4a**, 91422-91-2; (+)-(8*S*,9*R*)-**4b**, 91422-92-3; (+)-(10*S*,11*R*)-**4c**, 91422-93-4; (−)-(10*R*,11*S*)-**4c**, 91423-00-6; *cis*-(1*R*,2*S*)-**5a**, 91422-94-5; (−)-(8*S*,9*R*)-**5b**, 91422-95-6; (+)-(10*S*,11*R*)-**5c**, 91422-96-7; (−)-(1*R*,2*R*)-**6a**, 90997-20-9; (+)-(1*S*,2*S*)-**6a**, 91050-74-7; (−)-(8*R*,9*R*)-**6b**, 77550-50-6; (−)-(10*R*,11*R*)-**6c**, 79298-97-8; (−)-(1*R*,2*R*)-**7a**, 91422-97-8; (+)-(1*S*,2*S*)-**7a**, 91422-98-9; (+)-(1*R*,2*S*)-**8a**, 89618-16-6; (−)-(1*S*,2*R*)-**8a**, 89618-15-5; (+)-(1*S*,2*S*)-**9a**, 91422-99-0; (1*S*,2*R*)-**10a**, 91366-00-6; (1*S*,2*R*)-**10b**, 91366-01-7; **13**, 91365-96-7; benz[*a*]anthracene, 56-55-3; 1,2-dihydrobenz[*a*]anthracene, 60968-08-3; 8,9-dihydrobenz[*a*]anthracene, 60968-17-4; 10,11-dihydrobenz[*a*]anthracene, 34501-50-3.

Application of 1-*tert*-Butoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene in the Preparation of Functionalized β-Hydroxycyclohexanone Derivatives, Including Valuable Precursors of Daunomycinone Analogues

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The usefulness of 1-*tert*-butoxy-3-[(trimethylsilyl)oxy]buta-1,3-diene as a valuable precursor for the synthesis of 3-hydroxycyclohexanone derivatives has been demonstrated. With a variety of electron-poor alkenes high yields of Diels–Alder adducts were obtained which were transformed into 3-*tert*-butoxycyclohexanones by mild acid hydrolysis. After protection of the keto group by acetalization with ethylene glycol the *tert*-butoxy group was converted into a hydroxy group in high yield with trifluoroacetic acid. Also with quinone dienophiles the cycloadducts were formed in a high yield. In this case the keto group, obtained by hydrolysis of the cycloadduct, was transformed by reaction with ethynylmagnesium bromide, after which the *tert*-butoxy group again was removed with trifluoroacetic acid. A short and efficient synthesis of 4-demethoxydaunomycinone along this route has been given.

Among the large variety of 1,3-dioxygenized butadienes[1] the 1-alkoxy-3[(trimethylsilyl)oxy]buta-1,3-dienes **1a** and **1b** have been extensively investigated[2,3] in the reactions with electron-poor double bond systems (**2**). Acid hy-

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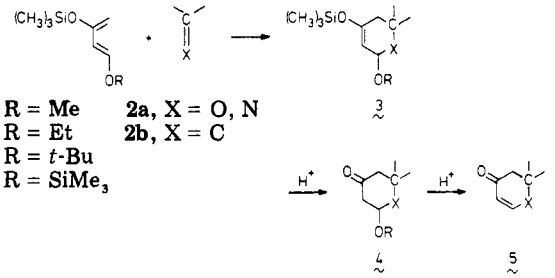
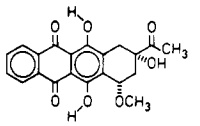
Scheme I



1a, R = Me **2a**, X = O, N
1b, R = Et **2b**, X = C
1c, R = *t*-Bu
1d, R = $SiMe_3$

drolysis of the cycloadducts leads to cycloenone products (**5**) according to Scheme I, because, in general, the primary products of the hydrolysis (**4**) are rather unstable to the applied reaction conditions. Maintenance of the alkoxy group in **4** has been reported only occasionally.[4] The reaction sequence **1** → **4** of Scheme I is a promising procedure for the synthesis of anthracycline antitumor antibiotics[5] of the doxorubicine family. The anthracyclinone precursor, racemic 7-*O*-methyl-4-demethoxydaunomycinone[6] (**6**) has been obtained in this way via a tetracyclic



6

intermediate comparable to **4** (X = CH_2, R = Me) by starting with **1a** and a proper tricyclic quinone. The keto function in the intermediate could be used for the introduction of the substituents at C(9) in **6**. In a subsequent step the 7-methoxy group had to be converted into a free hydroxy group, necessary for the conjugation with a sugar residue as found in biologically active anthracyclines. The demethylation required, however, rather drastic conditions,[7] leading to low yields. Moreover, this step restricted the whole procedure to compounds which do not contain other methoxy groups.

We envisaged that the procedure might be improved, by starting with a 1-alkoxy-3[(trimethylsilyl)oxy]butadiene in which the dealkylation in a later stage can be performed more easy and selectively, and which resists sufficiently elimination (conversion **4** → **5**) during the hydrolysis of primary cycloadducts (conversion **3** → **4**).

1-*tert*-Butoxy-3-[(trimethylsilyl)oxy]butadiene[8] (**1c**) appeared a good choice. In this paper we describe its synthesis, several examples of the preparation of 3-

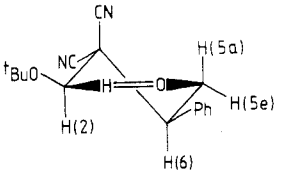
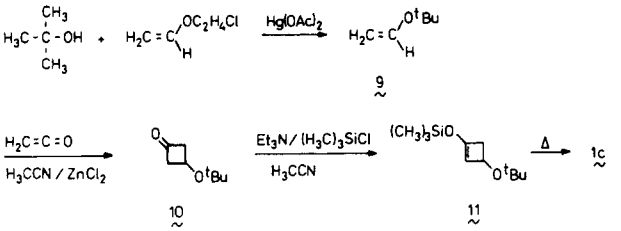
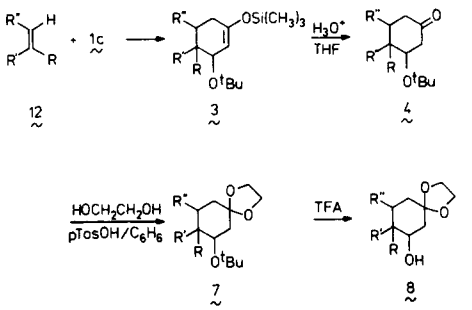


Figure 1. Structure of cycloadduct **3a**. O is the oxygen of the (trimethylsilyl)oxy group.

Scheme II. Synthesis of Butadiene 1c



Scheme III[a]



[a] **a**, R,R′ = CN, R″ = Ph; **b**, R′,R″ = C(O)OC(O), R = H; **c**, R,R″ = CO_2Me, R′ = H; **d**, R′ = CO_2Me, R,R″ = H; **e**, R = CN, R,R″ = H.

hydroxycyclohexanones (**4**) from **1c**, and the use of **1c** in the synthesis of anthracyclinones. 1,3-Bis[(trimethylsilyl)oxy]butadiene[9] (**1d**) which may also fulfil the requirements, is less reactive than **1a–c** and yielded in our hands under a variety of acidic conditions mostly **5** during the hydrolysis of **3** or during the functionalization of the carbonyl function of **4**. Probably, the (trimethylsilyl)oxy group is a better leaving group than the *tert*-butoxy group, due to the higher acidity of silanols[10] compared with the corresponding carbon alcohols.

Synthesis of Butadiene 1c. Butadiene **1c** was prepared according to a method[2a] developed previously in our laboratory for the synthesis of 1-alkoxy-substituted butadienes (Scheme II). *tert*-Butyl vinyl ether (**9**) was prepared by an improved mercury acetate catalyzed transvinylation[11] between 2-methyl-2-propanol and 2-chloroethyl vinyl ether in 95% yield. Cyclobutanone **10** was obtained in 60% yield by reaction of the vinyl ether **9** in acetonitrile containing $ZnCl_2$ as a catalyst with ketene, generated by thermolysis of acetone. The product **10** was silylated in acetonitrile with chlorotrimethylsilane and triethylamine. Distillation of **11** accomplished ring opening leading to the butadiene **1c** in 86% yield (49% overall). The butadiene could thus be prepared in quantities of 50 g.

Reaction of Butadiene 1c with Electron-Poor Ethylenes 12. Butadiene **1c** was brought into reaction with several mono-, di-, and trifunctionalized, electron-poor

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(2) Reactions of 1-alkoxy-3-[(trimethylsilyl)oxy]butadienes with alkenes. (a) Aben, R. W.; Scheeren, J. W. *J. Chem. Soc. Perkin Trans. 1* **1979**, 3132. (b) Danishefsky, S. *Acc. Chem. Res.* **1981**, *14*, 400. (c) Danishefsky, S.; Kitahara, T.; Yan, C.-F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996.
(3) Reactions of 1-alkoxy-3-[(trimethylsilyl)oxy]butadienes with aldehydes: (a) Aben, R. W.; Scheeren, J. W. *Synthesis* **1982**, 779 (b) Bednarksy, M.; Maring, C.; Danishefsky, S. *Tetrahedron Lett.* **1983**, *24*, 3451. (c) Larson, E.; Danishefsky, S. *J. Am. Chem. Soc.* **1982**, *104*, 6458.
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(8) (a) During this study butadiene **1c** was used by Danishefsky (ref 3b) in a cyclocondensation with aldehydes to measure the influence of the size of the alkoxy substituent at C(1) of the diene on the extent of asymmetric induction with chiral lanthanide complexes. It was synthesized from *trans*-1-methoxy-1-buten-3-one. (b) The butadiene has previously been used in our laboratory. Agarwal, N. L.; Scheeren, J. W. *Chem. Lett.* **1982**, 1059.
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Table I. Cycloaddition Products from 1c and Electron-Poor Olefins (12a–e)

compd[a]	^{1}H NMR, δ	reactn conditns time/temp/solvent	yield, %	mp, °C	elemental anal.[h]
3a	7.4 (5 H, bs, phenyl), 4.87 (1 H, d, $J_{2,3}$ = 1.5 Hz, H(2)), 4.78–4.62 (1 H, m, H(3)), 3.31 (1 H, dd, $J_{6a,5a}$ = 11.2 and $J_{6a,5e}$ = 5.40 Hz, H(6)), 2.86 (1 H, B of ABC with long-range coupling, $J_{6a,5a}$ = 11.2 and $J_{5a,5e}$ = 17 Hz, H(5a)), 2.48 (1 H, A of ABC, $J_{6a,5e}$ = 5.40 and $J_{5a,5e}$ = 17 Hz, H(5e)), 1.3 (9 H, s, $C(CH_3)_3$), 0.3 (9 H, s, $Si(CH_3)_3$)	2 h/40 °C/THF	83[b]	117 (from diisopropyl ether/pentane)	Found: C, 68.7; H, 7.6; N, 7.4. $C_{21}H_{28}N_2O_2Si$ requires: C, 68.44; H, 7.66; N, 7.60.
3b	5.10 (1 H, dd, $J_{3,4}$ = 6.45 and $J_{4,6}$ = 2.65 Hz, H(4)), 4.56 (1 H, dd, $J_{3,4}$ = 6.45 and $J_{2,3}$ = 4.0 Hz, H(3)), 3.73–2.13 (4 H, m), 1.11 (9 H, s, $C(CH_3)_3$), 0.22 (9 H, s, $Si(CH_3)_3$)	4 h/40 °C/THF	91[b]	oil, bp 85 °C (0.5 torr)	not determined
3c	endo/exo mixture: 5.01 (0.8 H, d, $J_{3,4}$ = 5.9 Hz, H(4) (endo)), 4.84 (0.2 H, d, $J_{3,4}$ = 3.0 Hz, H(4) (exo)), 4.55–4.30 (1 H, m, H(2)), 3.70 (3 H, s, OCH_3), 3.66 (3 H, s, OCH_3), 3.55–1.78 (4 H, m), 1.14 (1.8 H, s, $C(CH_3)_3$ (exo)), 1.11 (7.2 H, s, $C(CH_3)_3$ (endo)), 0.20 (9 H, s, $Si(CH_3)_3$). endo adduct: 5.01 (1 H, d, $J_{3,4}$ = 5.9 Hz, H(4)), 4.43 (1 H, dd, $J_{3,4}$ = 5.9 and $J_{2,3}$ = 3.5 Hz, H(3)), 3.70 (3 H, s, OCH_3), 3.66 (3 H, s, OCH_3), 3.27 (1 H, dd, $J_{1,2}$ = 12 and $J_{1,6}$ = 6.25 Hz, H(1)), 2.83 (1 H, dd, $J_{2,3}$ = 3.5 and $J_{1,2}$ = 12 Hz, H(2)), 2.47–1.84 (2 H, m, 2 H(6)), 1.11 (9 H, s, $C(CH_3)_3$), 0.20 (9 H, s, $Si(CH_3)_3$)	16 h/40 °C/THF	86[c]	oil, bp 120 °C (0.5 torr)	Found: C, 56.64; H, 7.92. $C_{17}H_{30}O_6Si$ requires: C, 56.95; H, 8.43.
3d	4.97 (0.63 H, d, J = 5.4 Hz, H(3) (endo)), 4.82 (0.36 H, d, J = 3 Hz, H(3) (exo)), 4.52–4.32 (1 H, m, H(2)), 3.68 (1.12 H, s, OCH_3 (exo)), 3.66 (1.88 H, s, OCH_3 (endo)), 2.65–1.63 (5 H, m), 1.20 (3.24 H, s, $C(CH_3)_3$ (exo)), 1.16 (5.76 H, s, $C(CH_3)_3$ (endo)), 0.23 (9 H, s, $Si(CH_3)_3$)	16 h/80 °C/neat	75[d]	oil[f]	Found: C, 59.99; H, 9.40. $C_{15}H_{28}O_4Si$ requires: C, 59.96; H, 9.39.
3e	4.88–4.72 (1 H, m, H(3)), 4.34–4.10 (1 H, m, H(2)), 2.92–1.76 (5 H, m), 1.23 (9 H, s, $C(CH_3)_3$), 0.21 (9 H, s, $Si(CH_3)_3$)	16 h/80 °C/neat	93[e]	oil[g]	not determined

[a] All products showed a characteristic IR absorption at 1660 cm^{-1} (C=CO). [b] Only endo isomer. [c] Exo:endo = 1:4. [d] Exo:endo = 1:3. [e] The endo–exo ratio could not be determined from the NMR spectrum. [f] Purified by chromatography, $CHCl_3$/diisopropyl ether 4/1. [g] Purified by chromatography, $CHCl_3$/*n*-hexane 9/1. [h] M + 1/e **3b** calcd 313.1471, found 313.1475; **3c** calcd 359.1890, found 359.1878; **3d** calcd 301.1835, found 301,1830; **3e** calcd 268.1733, found 268.1732.

ethylenes (Scheme III). In all cases the cycloadduct (**3**) was obtained in a yield between 80% and 95% (see Table I). The unsymmetrically substituted ethylenes gave only one regioisomer, as is predicted by the frontier orbital theory of Fukui[12] and is found in related reactions with other 1-alkoxy-3-[(trimethylsilyl)oxy]buta-1,3-dienes.[2]

With dicyanostyrene (**12a**) only endo addition was found. The small coupling of H(2) with H(3) ($J_{2,3}$ = 1.5 Hz) and the large coupling of H(6) with H(5a) ($J_{6,5a}$ = 11.5 Hz) in **3a** indicate equatorial positions of both the *tert*-butoxy and the C_6H_5 group (Figure 1). Broekhuis et al.[13] found a similar stereoselectivity in cycloadditions of other 1-alkoxybutadienes with **12a** and argued that the stereoselectivity is more due to steric requirements of large substituents (C_6H_5) than to secondary overlap in the transition state, in which the two reactants approach each other in nonparallel planes.

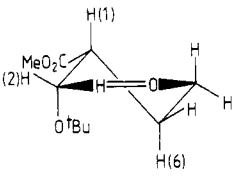

Figure 2. Structure of cycloadduct **3c**. O is the oxygen of the (trimethylsilyl)oxy group.

Maleic anhydride (**12b**) gave also endo addition (cf. ref 2c and 4). With dimethyl fumarate (**12c**) and methyl acrylate (**12d**) the stereoselectivity was less complete. According to the NMR spectra the endo adducts were formed for 75% and 70%, respectively, and had the *tert*-butoxy group in an axial position and the carbomethoxy group(s) in an equatorial position (Figure 2). The endo/exo ratio of the cycloaddition product from acrylonitrile (**12e**) could not be established because of insufficient resolution of the NMR spectrum at 90 MHz, but the mixture gave in the next step a cis/trans mixture of **4** in the ratio 2:7.

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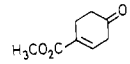
Table II. Cyclohexanones 4 from the Acid Hydrolysis of the Cycloadducts 3

product[a]	^{1}H NMR, δ	yield, %	mp, °C	peak match	elemental anal.
4a	7.4 (5 H, bs, phenyl), 4.2 (1 H, t, J = 12 Hz, HCO), 3.2–2.5 (5 H, m), 1.30 (9 H, s, $C(CH_3)_3$)	77	154 ($CHCl_3$/diisopropyl ether)	not determined	Found: C, 72.42; H, 6.74; N, 9.28. $C_{18}H_{20}N_2O_2$ requires: C, 72.95; H, 6.80; N, 9.45.
4b	4.63 (1 H, m, HCO), 3.9–1.7 (6 H, m), 1.13 (9 H, s, $C(CH_3)_3$)	91	oil[c]	calcd 241.1076 (M + 1) found 241.1079	Found: C, 59.75; H, 6.71. $C_{12}H_{16}O_5$ requires: C, 59.99; H, 6.71.
4c	4.60–4.40 (1 H, m, HCO), 3.68 (3 H, s, OCH_3), 3.29 (3 H, s, OCH_3), 3.70–3.0 (2 H, m, CH), 2.95–2.05 (4 H, m, CH_2), 1.04 (9 H, s, $C(CH_3)_3$)	96	oil[c]	calcd 287.1495 (M + 1) found 287.1486	Found: C, 58.82; H, 7.69. $C_{14}H_{22}O_6$ requires: C, 58.72; H, 7.75.
4d	4.33–4.04 (1 H, m, HCO), 3.58 (3 H, s, OCH_3), 3.11–1.67 (7 H, m), 1.11 (9 H, s, $C(CH_3)_3$)	60[b]	oil[d]	calcd 229.1440 (M + 1) found 229.1429	not determined
4e	mixture of cis/trans isomers, 4.33–4.04 (1 H, m, HCO), 3.18–1.76 (7 H, m), 1.23 (2 H, s, $C(CH_3)_3$), 1.20 (7 H, s, $C(CH_3)_3$)	83	oil[e]	calcd 196.1338 (M + 1) found 196.1336	Found: C, 67.45; H, 8.83; N, 6.94. $C_{11}H_{17}O_2N$ requires: C, 67.66; H, 8.78; N, 7.17.

[a] All products showed a characteristic IR absorption at 1720 cm^{-1} (C=O). [b] According to NMR only one isomer has been isolated, explaining the rather low yield. [c] No further purification necessary. [d] Purified by chromatography: $CHCl_3$/diisoporpyl ether 4/1. [e] Purified by chromatography: $CHCl_3$/diisopropyl ether 3/1.

All products, except **3a**, were obtained as oils, which could not always be purified completely; they were identified decisively, however, by NMR, IR, and high-resolution mass spectroscopy.

The primary cycloadducts (**3**) were hydrolyzed (by a standard procedure) in 0.1 N HCl/THF (1/25) to the β-functionalized ketones (**4**) in yields between 75% and 95% (Table II). A lower yield (60%) was only obtained with the cycloadduct of methyl acrylate (**4d**), because about 25% of the elimination product (**13**) had been



13

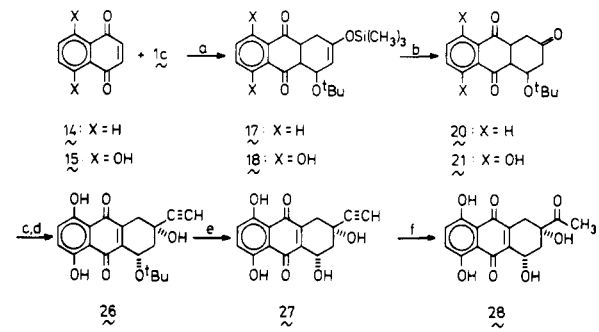
formed. This is partly due to the higher acid lability of **4d**, which caused more contamination with side products. In addition a more tedious purification was necessary. The nitrile **3b** gave ca. 10% of the elimination product. All products (**4**) were pure according to NMR, and most of them gave correct elemental analyses, in spite of their restricted stability. The *tert*-butoxycyclohexanones (**4**) were transformed into the acetals **7** (Table III) by reflux in benzene for 16 h with ethylene glycol and *p*-toluenesulfonic acid as a catalyst and separation of water with a Dean–Stark apparatus. The yields (50–80%) were lowered in some cases by considerable (10–25%) elimination during the reaction. Other ketalization methods did not give better results or did not proceed at all. The products **7** were purified by crystallization (**7a,b**) or chromatography (**7c–e**).

Finally, the hydroxy function was deprotected by stirring the compounds **7** with dry trifluoroacetic acid for 15 min. Elimination during this procedure was always small (<5%). After purification the products gave correct elemental analysis and spectral data. The results demonstrate that butadiene **1c** has attractive properties for the synthesis of 3-hydroxycyclohexanone derivatives.

Reaction of Butadiene 1c with Quinones. Butadiene **1c** was brought into reaction with the quinones **14**, **15**, and **16** (Schemes IV and V) by stirring a mixture of these compounds and the diene in THF at room temperature for 16 h. The epoxide function in **16**[14] is necessary to avoid cycloaddition on the internal double bond of quinizarin-

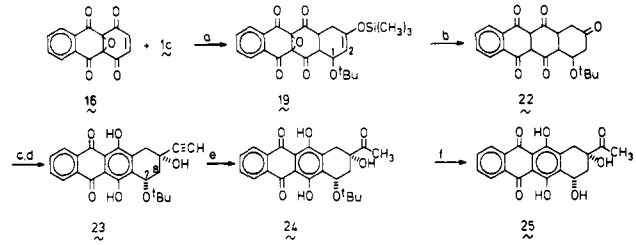
(14) Chandler, M.; Stoodley, R. J. *J. Chem. Soc., Perkin Trans. 1*, 1980, 1007; *J. Chem. Soc., Chem. Commun.* 1978, 997.

Scheme IV[a]



[a] (a) THF; (b) HCl/THF; (c) BrMgC≡CH; (d) O_2/OH^-; (e) TFA; (f) HgO/H_2SO_4/acetone.

Scheme V. Synthesis of 4-Demethoxydaunomycinone[a]



[a] (a) THF; (b) Zn/HOAc, (c) BrMgC≡CH; (d) O_2/OH^-; (e) HgO/H_2SO_4/acetone; (f) TFA.

diquinone. The cycloadducts **17** and **18** could not be isolated in a simple way because of their solubility in organic solvents and their easy hydrolysis. The NMR spectra of the crude cycloadducts showed only one isomer, probably the endo adduct. Hydrolysis of the cycloadducts **17** and **18** as described above gave, however, the crystalline ketones **20** and **21** in 81% and 85% yield, respectively. Cycloadduct **19** was isolated, in 84% yield after crystallization. It appeared from the NMR spectrum that only the endo adduct was formed, because of the large (5.4 Hz) coupling of H(1) with H(2).

The compounds **20** and **21** could not be transformed as indicated in Scheme III, because the ketalization reaction led mostly to elimination of butanol and subsequent oxidation. The compounds **19** and **21** were tested, however, as precursors in the synthesis of anthracyclinones. To this purpose the epoxide function of **19** was reduced[6] with zinc in acetic acid under simultaneous hydrolysis of the enol

Table III. Acetals 7 Obtained from the Ketones 4

product[a]	^{1}H NMR, δ	yield, %	mp, °C	peak match	elemental anal.
7a	7.40 (5 H, bs, phenyl), 4.21 (1 H, dd, J = 7 Hz and 9 Hz, HCO), 4.0 (4 H, bs, OCH_2CH_2O), 3.31 (1 H, dd, J = 3.5 Hz and 13.5 Hz, HC), 2.5–1.8 (4 H, m), 1.45 (9 H, s, $C(CH_3)_3$)	84	135 (THF/ n-hexane)	not determined	Found: C, 70.3; H, 7.1; N, 8.1. $C_{20}H_{24}N_2O_3$ requires: C, 70.57; H, 7.11; N, 8.23.
7b	4.33 (1 H, m, HCO), 3.89 (4 H, m, OCH_2CH_2O), 3.5–3.0 (2 H, m, HC), 2.5–1.8 (4 H, m, CH_2), 1.13 (9 H, s, $C(CH_3)_3$)	69	138 ($CHCl_3$/ diisopropyl ether)	not determined	Found: C, 59.36; H, 7.06. $C_{14}H_{20}O_6$ requires: C, 59.15; H, 7.09.
7c	4.24 (1 H, m, HCO), 3.96 (4 H, bs, OCH_2CH_2O), 3.84 (1 H, m, HC), 3.67 (3 H, s, OCH_3), 3.62 (3 H, s, OCH_3), 3.07 (1 H, m, HC), 2.3–1.5 (4 H, m), 1.13 (9 H, s, $C(CH_3)_3$)	67	oil[b]	not determined	Found: C, 58.03; H, 7.91. $C_{16}H_{26}O_7$ requires: C, 58.17; H, 7.93.
7d	4.11–3.96 (1 H, m, HCO), 3.84 (4 H, bs, OCH_2CH_2O), 3.64 (3 H, s, OCH_3), 2.60–1.42 (7 H, m), 1.20 (9 H, s, $C(CH_3)_3$)	50	oil[c]	calcd 273.1702 (M + 1) found 273.1705	not determined
7e	3.91 (4 H, bs, OCH_2CH_2O), 3.71 (1 H, m, HCO), 2.6–1.3 (7 H, m), 1.24 (9 H, s, $C(CH_3)_3$)	74	oil[d]	calcd 239.133 (M + 1) found 239.152	Found: C, 65.25; H, 8.67; N, 5.91. $C_{13}H_{21}O_3N$ requires: C, 65.25; H, 8.85; N, 5.85.

[a] All products showed an IR absorption at 1060 cm^{-1} (COC). [b] Purified by chromatography $CHCl_3$/diisopropyl ether 1/1. [c] Purified by chromatography $CHCl_3$/diisopropyl ether 4/1. [d] Purified by chromatography $CHCl_3$/diisopropyl ether 3/1.

ether to **22**. The product, could, however, not be isolated well and was directly converted into **23** by treatment with ethynylmagnesium bromide,[15] air oxidation, and subsequent destroying of the formed magnesium complexes by acidification of the solution with dilute acetic acid. Extraction with chloroform, evaporation of the solvent, and short column chromatography of the residue gave in 40% yield the product **23** having the 9-hydroxy and the 7-*tert*-butoxy functions in the cis position, and only 2% of the corresponding trans isomer. The cis isomer shows the smaller coupling of H(7) with H(8).[15] The high stereoselectivity of the Grignard reaction may be ascribed to steric hindrance of the *tert*-butoxy group during the attack of the nucleophile.

Treatment of **23** with mercury (II) oxide in a dilute solution of sulfuric acid in acetone gave **24** in 85% yield, from which racemic 4-demethoxydaunomycinone **25** could be obtained quantitatively by dissolution in dry trifluoroacetic acid. Ketone **21** was converted similarly into **26**. Unlike a previous preparation of this compound[15] in which the 7-hydroxy analogue of **21** was subjected to the Grignard reaction, it now proceeded again highly stereoselectively (29% cis, 2% trans product). Separation of the cis and trans isomers is less difficult for **26** than for **27**. The very low solubility of **27** restricts its chromatographic purification to very small quantities.

Dissolution of **26** in trifluoroacetic acid gave **27** in 94% yield, which can be converted to **28** by a literature method.[15] Compound **28** has been used in the synthesis of daunomycinone analogues.[15]

The results demonstrate that butadiene **1c** is an attractive parent compound in the preparation of anthracyclinones.[16] It has a high reactivity in the primary cycloaddition; it resists well undesired elimination during the hydrolysis of the cycloadducts and subsequent steps; it induces a high stereoselectivity in the Grignard reaction, necessary for the introduction of the C(9) substituents and can easily be converted into a hydroxy function under mild conditions, without isomerization of the cis to the trans isomer.

(15) Krohn, K.; Tohlkiehn, K. *Chem. Ber.* **1979**, *112*, 3453.

(16) During the last experiments of this study a similar approach to 4-demethoxydaunomycinone was reported, starting from a chiral 1-alkoxybutadiene. A high optical yield of the desired isomer was reported. Gupta, R. C.; Harland, P. A.; Stoodley, R. J. *J. Chem. Soc., Chem. Commun.* **1983**, 754.

Experimental Section

^{1}H NMR spectra were measured on a Bruker WH-90 spectrometer with Me_4Si as an internal standard. $CDCl_3$ was used as the solvent unless stated otherwise. IR spectra were measured with a Perkin-Elmer spectrophotometer Model 997. Mass spectra were obtained with a double-focussing VG M-M 7070 E mass spectrometer (peak matching) or a Finigan 3100 GCMS apparatus. Melting points were taken on a Kofler hot stage (Leitz-Wetzlar) and are uncorrected. For column chromatography Merck silica gel H (type 60) was used. The Miniprep LC (Jobin Yvon) was used for preparative HPLC.

Preparation of the Diels–Alder Adducts 3. A suitable dienophile (**12**, 20 mmol) was stirred with 25 mmol of **1c** in 50 mL of THF or neat (see Table I) at the temperature and for the time given in the Table. The solvent was evaporated. Product **3a** was crystallized from n-pentane/diisopropyl ether (1/9); **3b** and **3c** were distilled at low pressure, and **3d** and **3e** were purified by column chromatography.

Preparation of the *tert*-Butoxy Ketones 4. An adduct (**3**, 20 mmol) was dissolved in 100 mL of THF and supplied with 4 mL of 0.1 N HCl. The mixture was stirred for 15 min at room temperature and neutralized with 0.1 N $NaHCO_3$. The solvent was evaporated and the residue dissolved in $CHCl_3$. Extraction with 1 N $NaHCO_3$ and brine, followed by evaporation of the chloroform gave the crude product, which was purified by preparative HPLC; **4a** could be crystallized from chloroform/diisopropyl ether.

Preparation of the Acetals 7. A ketone (**4**, 11 mmol) was dissolved in 150 mL of benzene. After addition of 25 mmol (1.55 g) of ethylene glycol and 25 mg of p-toluenesulfonic acid the mixture was refluxed for 16 h, whereas water was separated with the aid of a Dean–Stark apparatus. The mixture was allowed to cool and extracted three times with 50 mL of 1 N $NaHCO_3$ and two times with brine. After drying over Na_2SO_4 the solvent was evaporated leaving the crude product as an oil. It was purified by HPLC or crystallization (Table III).

Deprotection of the Hydroxyl Function in 7. Synthesis of 8. An acetal (**7**, 1 mmol) was dissolved in 5 mL of dry trifluoroacetic acid. The mixture was stirred for 15 min, after which the acid was evaporated in vacuo. The products were purified by preparative HPLC or crystallization (Table IV).

***tert*-Butyl Vinyl Ether (9) (Improved Method[11]).** 2-Chloroethyl vinyl ether (1 mol = 112 g) was mixed with 300 g of

Table IV. Products 8 from Treatment of 7 with CF_3COOH

product[a]	^1H NMR, δ	yield, %	mp, °C	peak match	elemental anal.
8a	7.42 (5 H, bs, phenyl), 4.36 (1 H, dd, J = 13 Hz and 6 Hz, HCO), 4.07–3.89 (4 H, m, OCH_2CH_2O), 3.44–1.80 (5 H, m), 2.53 (1 H, bs, OH, exchanges with MeOD)	96	133 ($CHCl_3$/diisopropyl ether)	not determined	Found: C, 67.64; H, 5.84; N, 9.64. $C_{16}H_{16}N_2O_3$ requires: C, 67.59; H, 5.67; N, 9.85.
8b	5.13–5.00 (1 H, m, HCO), 4.04–3.73 (4 H, m, OCH_2CH_2O), 3.11–2.98 (1 H, m, CH), 2.91 (1 H, bs, CH), 2.60–1.87 (4 H, m, CH_2) (spectrum in CD_3COCD_3/MeOD)	78	155–157 (acetone/diisopropyl ether)	calcd 229.0712 (M + 1) found 229.0721	*e*
8c	4.56–4.31 (1 H, m, HCO), 3.89 (4 H, bs, OCH_2CH_2O), 3.67 (1 H, bs, OH, exchanges with MeOD), 3.62 (3 H, s, OCH_3), 3.60 (3 H, s, OCH_3), 3.44–2.93 (1 H, m, CH), 2.73 (1 H, dd, J = 3 Hz and J = 12 Hz), 2.49–1.33 (4 H, m)	73	oil[b]	calcd 275.1131 (M + 1) found 275.1131	Found: C, 52.79; H, 6.41. $C_{12}H_{18}O_7$ requires: C, 52.55; H, 6.62.
8d	4.49–4.16 (1 H, m, HCO), 3.87 (4 H, bs, OCH_2CH_2O), 3.78 (1 H, bs, OH, exchanges with MeOD), 3.71 (3 H, s, OCH_3), 2.58–1.24 (7 H, m)	67	oil[c]	calcd 217.1076 (M + 1) found 217.1074	Found: C, 55.57; H, 7.42. $C_{10}H_{16}O_5$ requires: C, 55.55; H, 7.46.
8e	4.28–4.04 (1 H, m, HCO), 3.91 (4 H, bs, OCH_2CH_2O), 3.60–3.24 (1 H, bs, OH, exchanges with MeOD), 2.93–2.51 (1 H, m, HCCN), 2.24–1.42 (6 H, m)	78	oil[d]	calcd 184.0974 (M + 1) found 184.0980	Found: C, 59.04; H, 7.14; N, 7.44. $C_9H_{13}NO_3$ requires: C, 59.00; H, 7.15; N, 7.65.

[a] All products showed IR absorptions at 3600 and 1040 cm^{-1} (OH). [b] Purified by chromatography: $CHCl_3$/MeOH 21/1. [c] Purified by chromatography: $CHCl_3$/diisopropyl ether 9/1. [d] Purified by chromatography: $CHCl_3$/diisopropyl ether 5/1. [e] No good elemental anayses could be obtained due to the hygroscopy of the product.

2-methyl-2-propanol and 0.5 g of mercury(II) acetate. Slow distillation through a Vigreux column (150 × 2.5 cm) equipped with a magnetic valve (60 s closed, 1 s open) yielded 95 g of **9** (95%): bp 75 °C (lit.[11] bp 77–78 °C; yield 45%).

3-*tert*-Butoxycyclobutanone (10). The vinyl ether **9** (30 g, 300 mmol) was stirred with 40 mL of dry acetonitrile containing zinc chloride (0.4 g). Ketene, generated from acetone with a ketene lamp (ca. 0.5 mol/h), was passed into the solution. The weakly exothermic reaction was stopped after disappearance of the vinyl ether signals in the NMR spectrum. The acetonitrile was evaporated in vacuo and the brown residue was distilled through a Vigreux column (30 × 1.5 cm): bp 65–67 °C (14 torr) (lit.[17] bp 74 °C (15 torr)); yield 25.5 g (60%).

1-*tert*-Butoxy-3-[(trimethylsilyl)oxy]butadiene (1c). Cyclobutanone **10** (43.0 g, 301 mmol) was stirred overnight at 50 °C with 900 mmol (91.1 g) of triethylamine and 437 mmol (47.5 g) of chlorotrimethylsilane in 200 mL of dry acetonitrile. The solvent was evaporated and the residue was dissolved in *n*-pentane. After filtration and washing of the precipitate with *n*-pentane, the solvent was evaporated and the brown residue distilled in vacuo. The product was obtained in 86% yield (55.4 g): bp 50–53 °C (0.25 torr); NMR δ 7.17 (1 H, AB, J = 12 Hz), 5.81 (1 H, AB, J = 12 Hz), 4.34 (2 H, bs), 1.63 (9 H, s), 0.53 (9 H, s).

3,4,4a,9a-Tetrahydro-4-*tert*-butoxy-2,9,10(1*H*)-anthracenetrione[2] (20). Freshly sublimed 1,4-naphthoquinone (1.58 g, 10 mmol) was dissolved in 100 mL of CH_3CN and 3.09 g (1.40 mmol) of butadiene **1c** was added to the solution. The mixture was stirred for 16 h at room temperature. The solvent was evaporated leaving **17** as an oil, which was not purified: ^1H NMR (60 MHz) δ 8.28–7.21 (4 H, m, ArH), 5.44–5.29 (1 H, m, HC=C), 4.53–4.33 (1 H, m, HCO), 3.84–2.06 (4 H, m), 0.75 (9 H, s, $C(CH_3)_3$), 0.31 (9 H, s, $Si(CH_3)_3$).

The crude **17** was dissolved in 30 mL of THF and 1 mL of 0.1 N HCl was added. After stirring for 15 min at room temperature the mixture was neutralized with 1 mL of 1 N $NaHCO_3$, dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was crystallized from ethanol: yield 2.4 g (81%); mp 134 °C; MS, m/e 300, 285, 244 (b), 227, 216, 200; IR (KBr) 1720 cm^{-1} (C=O); ^1H NMR δ 8.14–8.01 (2 H, m, ArH), 7.83–7.69 (2 H, m, ArH), 4.62–4.40 (1 H, m, HCO), 3.73–3.42 (3 H, m), 2.62 (2 H, J = 3 Hz, CH_2), 2.41 (1 H, dd, J = 7.5 Hz and J = 16 Hz), 0.67 (9 H, s, $C(CH_3)_3$). Anal. Found: C, 71.90; H, 6.71. $C_{18}H_{20}O_4$ requires: C, 71.98; H, 6.71.

3,4,4a,9a-Tetrahydro-4-*tert*-butoxy-5,8-dihydroxy-2,9,10-(1*H*)-anthracenetrione (21). A solution of 4 g (21 mmol) of 5,8-dihydroxy-1,4-naphthoquinone in 50 mL of THF was stirred with 4.92 g (23 mmol) of butadiene **1c** for 2 h at room temperature. Without isolation of the cycloadduct[18] (**18**) 2 mL of 0.1 N HCl was added to the reaction mixture. After 15 min the solvent was evaporated and the residue crystallized from $CHCl_3$/*n*-hexane: yield 6 g (85%); mp 180 °C; MS, m/e 333 (M + 1), 294, 277 (b), 259, 232, 204; $M^+ + 1/e$ calcd 333.1338, found 333.1339; IR (KBr) 1720 (C=O), 1635 (C=O, chelated) cm^{-1}; ^1H NMR δ 12.3 (1 H, s, ArOH), 12.1 (1 H, s, ArOH), 7.31 (1 H, AB, J = 8.5 Hz, ArH), 7.25 (1 H, AB, J = 8.5 Hz, ArH), 4.50–4.42 (1 H, m, HCO), 3.73–3.33 (3 H, m), 2.58 (2 H, d, J = 2.5 Hz, CH_2), 2.37 (1 H, dd, J = 7.5 Hz and J = 15.6 Hz, CH_2), 0.75 (9 H, s, $C(CH_3)_3$). Anal. Found C, 65.01; H, 6.04; $C_{18}H_{20}O_6$ requires C, 65.05; H, 6.07%.

3-Ethynyl-1,2,3,4-tetrahydro-1-*tert*-butoxy-3,5,8-trihydroxy-9,10-anthraquinone (26). A mixture of 60 mmol (1.44 g) of magnesium in 16 mL of dry THF was supplied with 6.8 g (4.66 ml) of bromoethane and stirred until all the magnesium had reacted. The solution was added to 100 mL of THF, which had been saturated with acetylene at 0 °C. Acetylene was passed through the solution for half an hour. Then 0.66 g (2 mmol) of **21** in 20 mL of THF was added.

The mixture was stirred again at 0 °C for half an hour and then added to 250 mL of 0.5% NaOH. Air was passed through the solution for 0.5 h. The mixture was acidified with acetic acid until its color turned red and extracted several times with chloroform. The combined organic layers were extracted with brine and dried over Na_2SO_4. The solvent was evaporated in vacuo leaving a red oil, which was purified by preparative HPLC (silica gel, $CHCl_3$/MeOH/HOAc (22/1/0.4)): yield 210 mg (29%); mp 158

(17) Sieja, J. B. *J. Am. Chem. Soc.* **1971**, *93*, 130.

(18) A sample of **18** was isolated in at least 90% purity by evaporation of the solvent, ^1H NMR (60 MHz) δ 12.1 (1 H, s, OH), 11.6 (1 H, s, OH), 7.2 (2 H, bs, ArH), 5.1 (1 H, m, HC=C), 4.35 (1 H, m, HCO), 3.6–2.0 (4 H, m), 0.75 (9 H, s, $C(CH_3)_3$), 0.25 (9 H, s, $Si(CH_3)_3$).

°C; MS, *m/e* 357 (M + 1), 325, 301, 300, 283, 265; M^+ + 1/e calcd 357.1338, found 357.1344. Anal. Found: C, 67.47; H, 5.63. $C_{20}H_{20}O_6$ requires: C, 67.41; H, 5.66. ^1H NMR δ 12.66 (1 H, s, ArOH), 12.55 (1 H, s, ArOH), 7.25 (1 H, AB, *J* = 28 Hz, ArH), 7.22 (1 H, AB, *J* = 28 Hz, ArH), 5.64 (1 H, 3-OH), 5.28 (1 H, m, X of ABX, H(1)), 3.81 (1 H, AB, J_{gem} = 22 Hz, H(4e)), 2.49 (1 H, AB, J_{gem} = 22 Hz, $H(4_a)$), 2.80 and 2.62 (1 H, A of ABX, J_{gem} = 15 Hz, H(2)), 2.0 and 1.84 (1 H, B of ABX, J_{gem} = 15 Hz), 2.53 (1 H, s, C≡CH), 1.38 (9 H, s, $C(CH_3)_3$).

3-Ethynyl-1,2,3,4-tetrahydro-1,3,5,8-tetrahydroxy-9,10-anthraquinone (27). 36 mg (0.11 mmol) of **26** was stirred with 1 mL of trifluoroacetic acid. After 15 min the acid was evaporated in vacuo and the crude product crystallized from acetone: yield 30 mg of **27** (94%); mp 185–190 °C dec, MS, *m/e* 301 (M + 1), 285, 284, 264, 266, 265; M + 1/e calcd 301.0712, found 301.0720.

Anal. Found: C, 60.20; H, 4.12. $C_{16}H_{12}O_6 \cdot 1H_2O$ requires: C, 60.37; H, 4.43. ^1H NMR ref 13.

5α,11α-Epoxy-1,4,4a,5a,11a,12a-hexahydro-1-*tert*-butoxy-3-[(trimethylsilyl)oxy]naphthacene-5,6,11,12-tetrone (19). To a suspension of 6 g (23.6 mmol) of 4a,9a-epoxy-4a,9a-dihydroanthracene-1,4,9,10-tetraone in 50 mL of THF was added 6 g (28 mmol) of butadiene **1c**. The mixture was stirred at room temperature for 2 h and then concentrated in vacuo. The residue was crystallized from $CHCl_3$/*n*-hexane yielding 9.2 g (84%) of the off-white product: mp 158–160 °C; MS, *m/e* 469 (M + 1), 453, 413, 396, 369; M + 1/e calcd 469.1683, found 469.1700.

Anal. Found: C, 63.82; H, 5.99. $C_{25}H_{28}O_7Si$ requires: C, 64.08; H, 6.02. ^1H NMR δ 8.15–7.60 (4 H, m, ArH), 4.98 (1 H, d, *J* = 5.4 Hz, H(2)), 4.53 (1 H, dd, $J_{1,2}$ = 5.4 and $J_{1,12a}$ = 3.4 Hz, H(1)), 3.59 (1 H, dd, $J_{4a,12a}$ = 5.4, $J_{4a,4ax}$ = 6.5 Hz, H(4a)), 2.91 (1 H, dd, $J_{4a,12a}$ = 5.4, $J_{1,12a}$ = 3.4 Hz, H(12a)), 2.71 (1 H, d, J_{gem} = 18 Hz, $H(4_{eq})$), 2.05 (1 H, dd, J_{gem} = 18 Hz, $J_{4ax,4a}$ = 6.5 Hz, $H(4_{ax})$), 0.96 (9 H, s, $C(CH_3)_3$), 0.27 (9 H, s, $Si(CH_3)_3$).

1,2,3,4-Tetrahydro-1-*tert*-butoxy-3-ethynyl-3,5,12-trihydroxynaphthacene-6,11-dione (23). Epoxide **19** (400 mg, 0.85 mmol) was added to a well stirred suspension of 0.65 g of zinc in 10 mL of acetic acid. After 24 h the reaction mixture was diluted with water (50 mL) and extracted several times with $CHCl_3$. The chloroform layers were collected and extracted with 1 N $NaHCO_3$ and brine. After drying over Na_2SO_4 the solvent was evaporated leaving crude **22**, which was used directly in the next reaction.

The crude **22** was dissolved in 10 mL of THF and added to an ice cold solution of 60 mmol of bromomagnesium acetylide in 100 mL of THF (prepared from 1.4 g of magnesium, 6.5 g of ethyl bromide, and acetylene). The mixture was stirred at 0 °C for 30 min, and then added to 400 mL of an ice-cold 0.5% NaOH solution. Air was passed through the solution for 30 min, after which the mixture was acidified with acetic acid until its color turned orange. The mixture was extracted several times with $CHCl_3$. The organic layers were combined and washed with saturated brine and dried. Evaporation of the solvent yielded a crude product which was purified by short column chromatography (silica gel, $CHCl_3$/MeOH (22/1)) to give 140 mg (39%) of the light orange compound **23**: mp 178 °C dec, melts again at 220 °C. The compound is hydroscopic; it influenced the correctness of the elemental analyses. Anal. Found: C, 70.09; H, 5.30. $C_{24}H_{22}O_6$ requires: C, 70.93; H, 5.46. MS, *m/e* (CI) 407 (M + 1), 350, 333, 317, 315, 229; M + 1/e calcd 407.1495, found 407.1491; ^1H NMR δ 13.37 (1 H, s, ArOH), 12.75 (1 H, s, ArOH), 8.44–8.20 (2 H, m, ArH), 7.93–7.44 (2 H, m, ArH), 5.95 (1 H, bs, OH(3)), 5.35 (1 H, m, H(1)), 3.69 (1 H, d, J_{gem} = 21 Hz, H(4e)), 2.99 (1 H, d, J_{gem} = 21 Hz, H(4a)), 2.80 (1 H, d, J_{gem} = 14.7 Hz, with long-range coupling, H(2e)), 2.56 (1 H, s, C≡CH), 2.06 (1 H, dd, J_{gem} = 14.7 Hz, $J_{1,2}$ = 2.9 Hz, H(2a)), 1.40 (9 H, s, $C(CH_3)_3$).

4-Demethoxy-7-*O*-*tert*-butyldaunomycinone (24). A solution of 30 mg (0.74 mmol) of compound **23** in 8 mL of acetone was added to a solution of 100 mg of yellow mercury(II) oxide in 4 mL of H_2O and 0.16 mL of concentrated sulfuric acid at 60 °C. After 10 min the mixture was diluted with 20 mL of 1 N HCl (cold) and extracted with chloroform. The extract was dried and evaporated. The residue was purified by preparative HPLC (silica gel, THF/*n*-hexane (3/1)), yielding 28 mg (85%) of light red **24**: mp 195 °C dec; MS, *m/e* 425 (M + 1), 424, 368, 353 (b); M + 1/e calcd 425.1600, found 425.1593; ^1H NMR δ 13.85 (1 H, s, ArOH), 13.52 (1 H, s, ArOH), 8.36–8.20 (2 H, m, ArH), 7.86–7.59 (2 H, m, ArH), 5.89 (1 H, s, OH(9)), 5.33 (1 H, m, H(7)), 3.25 (1 H, A of AB, J_{gem} = 19 Hz, H(10)), 2.89 (1 H, B of AB, J_{gem} = 19 Hz, H(10)), 2.36 (3 H, s, CH_3), 2.30 (1 H, d, J_{gem} = 14.5 Hz, with long-range coupling, H(8e)), 1.80 (1 H, dd, J_{gem} = 14.5 Hz, $J_{7,8}$ = 3.0 Hz, H(8a)), 1.33 (9 H, s, $C(CH_3)_3$).

4-Demethoxydaunomycinone (25). Compound **24** (20 mg) was dissolved in 1 mL of trifluoroacetic acid. After 15 min the acid was evaporated. The residue was crystallized from $CHCl_3$/ether yielding quantitatively 4-demethoxydaunomycinone.

The NMR spectrum was in accordance with data from the literature.[15]

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Registry No. **1c**, 83352-53-8; **3a**, 91281-48-0; **3b**, 91294-46-1; *endo*-**3c**, 91281-49-1; *exo*-**3c**, 91326-95-3; *exo*-**3d**, 91281-50-4; *endo*-**3d**, 91281-51-5; **3e** (isomer 1), 91294-47-2; **3e** (isomer 2), 91294-48-3; **4a**, 91281-52-6; **4b**, 91294-49-4; **4c**, 91281-53-7; **4d**, 91281-54-8; *cis*-**4e**, 91281-55-9; *trans*-**4e**, 91281-56-0; **7a**, 91281-57-1; **7b**, 91281-58-2; **7c**, 91281-59-3; **7d**, 91294-50-7; **7e**, 91365-71-8; **8a**, 91281-60-6; **8b**, 91281-61-7; **8c**, 91281-62-8; **8d**, 91281-63-9; **8e**, 91281-64-0; **9**, 926-02-3; **10**, 91281-65-1; **12a**, 2700-22-3; **12b**, 108-31-6; **12c**, 624-49-7; **12d**, 96-33-3; **12e**, 107-13-1; **14**, 130-15-4; **15**, 475-38-7; **16**, 69448-06-2; **17**, 91281-66-2; **18**, 91294-51-8; **19**, 91294-52-9; **20**, 91281-67-3; **21**, 91281-68-4; **22**, 91281-69-5; **23**, 91281-70-8; **24**, 91281-71-9; **25**, 58924-49-5; **26**, 91281-72-0; **27**, 72473-58-6; 2-chloroethyl vinyl ether, 110-75-8; 2-methyl-2-propanol, 75-65-0; ketene, 463-51-4; acetylene, 74-86-2.