118. The Synthesis of (±)-11-Deoxydaunomycinone *via* Regioselective Tandem *Diels-Alder* Reactions[1])

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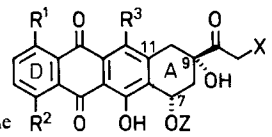
The 2,5-dimethylidene-3,6-bis[(*Z*)-(2-nitrophenyl)sulfenylmethylidene]-7-oxabicyclo[2.2.1]heptane (**13**) can be used to generate polyfunctional and multicyclic molecules with high regio- and stereoselectivity *via* two successive *Diels-Alder* additions using two different dienophiles. This principle has been applied to the synthesis of (±)-11-deoxydaunomycinone (**7**), the aglycone of an important antitumor drug. The 2,3-didehydroanisole adds to **13** and gives the monoadduct **14** with high regioselectivity. No trace of bis-adduct is observed. The 1,4-epoxy-1,2,3,4-tetrahydro-5-methoxy-3-methylidene-2-[(*Z*)-(2-nitrophenyl)sulfenylmethylidene]anthracene (**15**) obtained on treating **14** with K_2CO_3 adds to methyl vinyl ketone to give [(1*RS*,2*SR*,5*RS*,12*RS*)-5,12-epoxy-1,2,3,4,5,12-hexahydro-7-methoxy-1-(2-nitrophenyl)sulfenyl-2-naphthacenyl] methyl ketone (**16**) with high regio- and stereoselectivity. The acid-catalyzed 7-oxanorbornadiene→phenol rearrangement of **16** is regioselective and gives (5-acetoxy-3,4-dihydro-7-methoxy-2-naphthacenyl) methyl ketone (**20**) which was transformed into (±)-7,11-dideoxydaunomycinone ((±)-**24**), a known precursor of **7**.

Introduction. – The anthracyclines constitute a group of natural antibiotics isolated from cultures of various *Streptomyces* [1] spp., certain members of which possess significant antineoplastic activity. Among these, daunomycin (**1**) and adriamycin (**2**) have been the object of considerable interest in recent years because of their value in cancer chemotherapy [2] which was only limited because of their cardiotoxicity [3]. Total syntheses of the corresponding aglycone parts of daunomycinone (**3**) and adriamycinone (**4**) have been subject of intense study in the last 15 years due to the lack of an efficient biosynthetic process [4] as well as a search for more active analogs with reduced cardiotoxicity [5]. *Arcamone* and coworkers [6] isolated from *Micromonospora peucetica* the 11-deoxydaunomycine (**5**) and 11-deoxyadriamycine (**6**) which were shown to possess significant antitumor activity and to be less cardiotoxic than **1** and **2**. The potential advantages associated with these compounds have prompted interest in their preparations, and several total synthesis of the aglycone fragment (±)-11-deoxydaunomycinone

1[a]) R^1 = H, R^2 = OMe, R^3 = OH, X = H, Z = 'daunosaminyl'; daunomycin
2[a]) R^1 = H, R^2 = OMe, R^3 = OH, X = OH, Z = 'daunosaminyl'; adriamycin
3 R^1 = H, R^2 = OMe, R^3 = OH, X = Z = H; daunomycinone
4 R^1 = H, R^2 = OMe, R^3 = OH, X = OH, Z = H; adriamycinone
5 R^1 = H, R^2 = OMe, R^3 = X = H, Z = 'daunosaminyl'; 11-deoxydaunomycine
6 R^1 = H, R^2 = OMe, R^3 = H, X = OH, Z = 'daunosaminyl'; 11-deoxyadriamycine
7 R^1 = H, R^2 = OMe, R^3 = H, X = Z = H; 11-deoxydaunomycinone
8 R^1 = R^2 = H, R^3 = OH, X = Z = H
9 R^1 = R^2 = OMe, R^3 = OH, X = Z = H

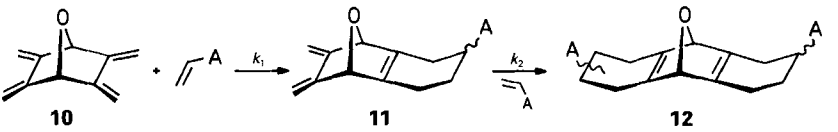


[a]) Customary numbering of this class of compounds.

[1]) Part of the Ph. D. thesis of *Jean-Marc Tornare*, University of Lausanne, March 1985.

(**7**) have been published [7–20]. *Kishi* and coworkers [21] have proposed a practical asymmetric synthesis of **7** and related compounds [22].

A few years ago we reported that 2,3,5,6-tetrakis(methylidene)-7-oxabicyclo[2.2.1]heptane (**10**), readily obtained from furan and maleic anhydride [23], can be used to prepare various anthracyclinones such as **3** [24], **8** [25], and **9** [26]. The principle of our strategy rests upon the fact that the rate constant of the *Diels-Alder* addition of **10**→**11** (k_1) is much larger than that (k_2) for the reaction of the corresponding monoadduct **11** with the same dienophile giving the corresponding bis-adduct **12** [27]. A major difficulty in the synthesis of the anthracyclinones **3**, **4**, and **7** is to control the substitution pattern of the two remote rings A and D. This cannot be realized following our strategy (see, however, [24]) **10**→**11**→**12**, unless one utilizes an analog of **10** with substituted diene



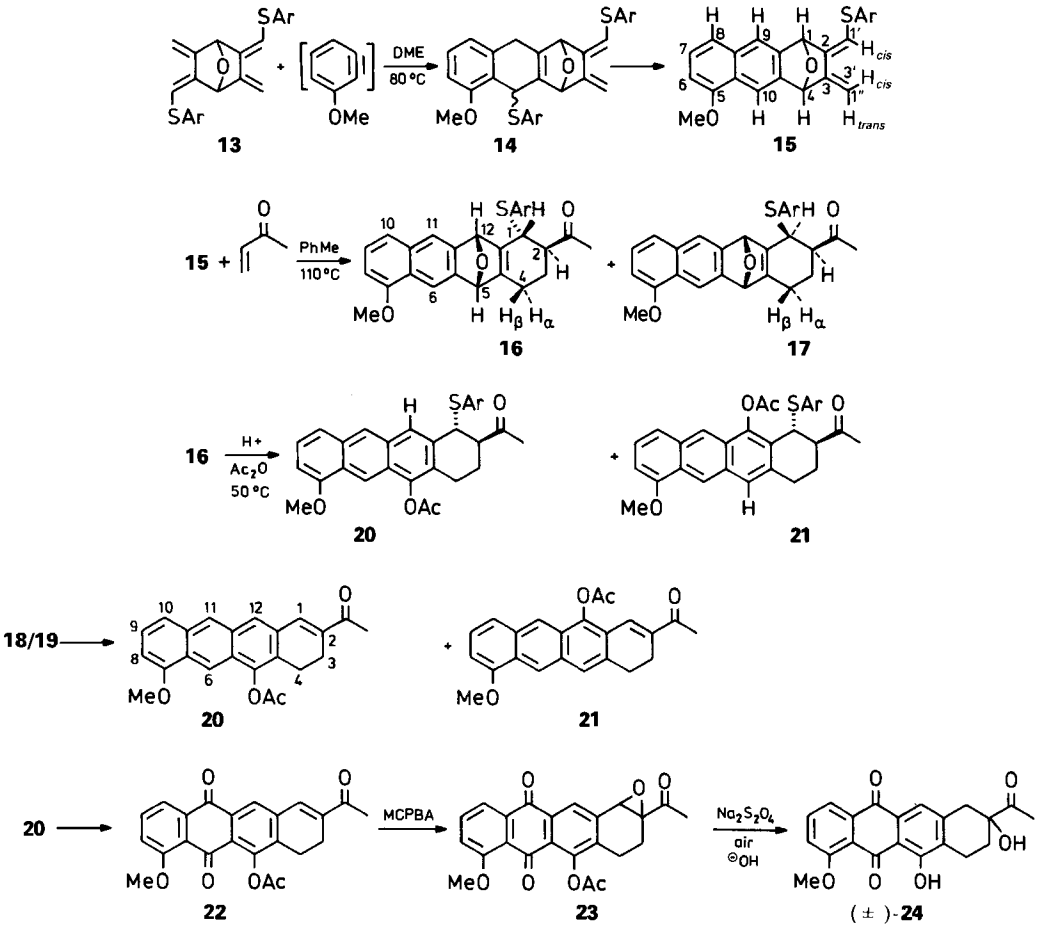
10 **11** **12**

moieties whose substituents are able to steer the regiochemistry of the two successive (tandem) cycloadditions[2]). Recently we have succeeded in preparing the tetraene **13** (Ar = 2-$NO_2C_6H_4$) [29]. Double addition of 2-nitrobenzenesulfenyl chloride to **10**, followed by elimination of two equiv. of HCl afforded **13** in a stereoselective fashion. The tetraene **13** was shown to be a versatile reagent for regio- and stereoselective tandem *Diels-Alder* reactions [29]. As for **10**, the rate of the addition of the first equiv. of a strong dienophile to **13** is much larger than the rate of the addition of the second equiv. of the same dienophile to the corresponding monoadduct. We report here on the application of tetraene **13** to the doubly-convergent regioselective synthesis of (±)-11-deoxydaunomycinone (**7**).

Results and Discussion. – The deamination of 2-amino-6-methoxybenzoic acid [30] (pentyl nitrite, dimethoxyethane (DME), 85°C [31]) in the presence of tetraene **13** gave a mixture of the adduct **14** and its product of elimination **15**. On treating this mixture with K_2CO_3 in boiling acetone, **15** was the sole product isolated in 46% yield. The reaction of the 2,3-didehydroanisole (assumed to be generated during the deamination reaction) with **13** is highly regioselective since no trace of an other regioisomer than **15** could be observed. Furthermore, the reaction of **14** or/and **15** with 2,3-didehydroanisole is much slower than with **13** as no trace of the corresponding bis-adduct could be detected. This is in contrast with the reaction of didehydrobenzene with tetraene **10** which was shown to give the corresponding mono- and bis-adducts competitively [25]. The modest yield of the transformation **13**→**15** is attributed to a certain lability of the tetraene **13** and diene **15** under the reaction conditions.

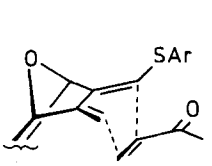
The structure of **15** was established by 360-MHz-^{1}H-NMR spectroscopy and by measurement of NOE's between adjacent protons. Irradiation of the olefinic proton at 6.43 ppm (H_{cis}–C(1'); *cis* with respect to C(2), C(3)) led to a NOE at 5.43 ppm attributed to H_{cis}–C(1''). No NOE was observed at H–C(1) (6.23 ppm), in agreement

[2]) Tetraenes substituted at a bridgehead centre such as 1-(dimethoxy)methyl-2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]heptane can also be considered as reagents for tandem regio- and stereo-selective tandem cycloadditions, see [28].

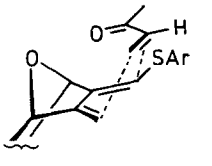


with the (*Z*)-configuration of the thioolefin moiety. Irradiation of the signal H_{cis}–C(1″) led to NOE's at 6.43 (H_{cis}–C(1′)) and 5.35 ppm (H_{trans}–C(1″)). Irradiation of the latter signal gave NOE's at 5.43 (H_{cis}–C(1″)) and 5.82 ppm (H–C(4)). Irradiations of the signals at 5.82 (H–C(4)), 8.21 (H–C(10)), and 6.23 (H–C(1)) ppm led to NOE's at 8.21 (*s*, H–C(10)), 5.82 (br. *s*, H–C(4)), and 7.73 ppm (*s*, H–C(9)), respectively. Irradiation at 7.73 ppm (H–C(9)) led to NOE's at 6.23 (H–C(1)) and 7.40 ppm (H–C(8)). The latter signal appeared as a *dd* with ^3J = 7.5 and ^4J = 2.8 Hz.

The addition of methyl vinyl ketone (MVK) to **15** in toluene (110°C) gave a 9:1 mixture of the adducts **16** and **17** (88% isolated). The major isomer **16** was isolated in pure form by recrystallization from CH_2Cl_2/Et_2O 4:1. No trace of any other isomeric adduct could be detected, thus demonstrating the completely regioselective nature and the high stereoselectivity of the *Diels-Alder* reactions **15** + MVK. Out of eight possible orientations for the cycloadducts (regio-isomers *'ortho' vs. 'meta'*, face selectivity *'exo' vs. 'endo'*, *Alder- vs. anti-Alder*-rule orientation of the dienophile), only those represented by the transition states **16′** and **17′** are favoured. In contrast with the *'exo'*-face selectivity of the cycloadditions of ethylenetetracarbonitrile and *N*-phenyltriazolinedione to 2,3-dimethylidene-7-oxabicyclo[2.2.1]heptanes substituted with a chlorine atom or a methoxy



16' (→**16**)

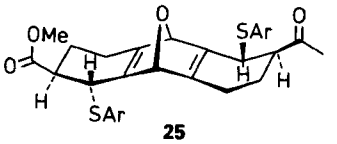


17' (→**17**)

group at the diene moiety [32], the thermal reaction **15** + MVK is 90% *'endo'*-face selective. Interestingly, the *'endo'*-face attack (giving **16**) follows the *anti-Alder*-rule of cycloaddition, whereas the *'exo'*-face attack (giving **17**) obeys the *Alder* rule [33]. Competition between a steric factor (favouring *'exo'*-face attack) and a stereoelectronic factor (favouring *'endo'*-face attack) can be invoked to interpret our observations[3]).

The structures of adducts **16** and **17** were deduced from their 360-MHz ^{1}H-NMR spectra and from double-irradiation experiments.

The α-position of the arylthio substituent at C(1) was given by the homoallylic coupling constants [32] [36] measured between the bridgehead proton H–C(5) and H–C(1) (^5J = 1.0 Hz in **16**; < 0.2 Hz in **17**[4])) and between H_β–C(1)/H_β–C(4) (^5J = 2.2 Hz in **16**) and H_β–C(1)/H_α–C(4) (^5J = 2.8 Hz in **16**). The proton H_β–C(4) of **16** was recognized by its long-range coupling with the bridgehead proton H–C(12) (^5J = 1.0 Hz) whereas H_α–C(4) does not couple with H–C(12). The β-position of the acetyl side chain at C(2) was deduced from the vicinal coupling constants measured between H–C(2) and H–C(1) (6.2 Hz in **16**, 4.1 Hz in **17**[4])), between H–C(2) and H_α–C(3) (4.0 Hz in **16**), between H–C(2) and H_β–C(3) (7.8 Hz in **16**). The structure of **16** (and **17**) was further confirmed by comparing the ^{1}H-NMR characteristics with those observed for the bis-adduct **25** whose structure was established by X-ray crystallography [34].



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On treating **16** in Ac_2O with a small amount of CF_3COOH (80°C, 1 h), a 3:1 to 4:1 mixture of the tetrahydronaphthacene derivatives **18** and **19** was obtained[5]). The crude mixture was then treated with *meta*-chloroperbenzoic acid (MCPBA; $NaHCO_3$, CH_2Cl_2, 20°C, 15 min) to afford a mixture **20**/**21** from which the major isomer **20** was obtained pure (65% based on **16**) by crystallization from CH_2Cl_2/Et_2O 5:1. The structure of **20** was given by its mode of formation and its 360-MHz ^{1}H-NMR spectra. It was confirmed by NOE measurements between the adjacent protons (see *Exper. Part*). *Jones'* oxidation (4N CrO_3 in aqueous H_2SO_4) of **20** in acetone (0°C, N_2 atmosphere, 1 h) gave the anthraquinone **22** in 64% yield. The latter was epoxidized (MCPBA, 10 molar excess, CH_2Cl_2, 15 h) to **23** (42%) at 20°C. At higher temperature, *Baeyer-Villiger*-reaction products were formed competitively. Attempts to epoxidize **22** with basic H_2O_2 led to decomposition of the product. The reduction of the epoxide **23** with $Na_2S_2O_4$ under alcaline conditions [37] yielded the known (±)-7,11-dideoxydaunomycinone ((±)-**24**) [7e] [10] [12c] which was identical (spectral data, mixed 360-MHz ^{1}H-NMR spectrum, mixed m.p.) with an authen-

[3]) Further examples of face-selective cycloadditions of **13** and related 2,3-dimethylidenebicyclo[2.2.1]heptanes will be presented in forthcoming publications [34] [35].

[4]) Measured in the ^{1}H-NMR spectrum of a mixture **16**/**17** (mother liquor of the crystallization of **16**).

[5]) In Ac_2O/CH_2Cl_2 1:1, a 1:1 mixture **18**/**19** was obtained.

tic sample of (±)-**24** furnished by Dr. *Gesson*[6]). The conversion of (±)-**24** into (±)-11-deoxydaunomycinone ((±)-**7**) has been reported [7] [11].

Conclusion. – The arylthio substituents in the tetraene **13** add further flexibility to our doubly-convergent approach[7]) to the synthesis of anthracyclinones. They render the tandem *Diels-Alder* additions completely regioselective, even with a highly reactive dienophile such as 2,3-didehydroanisole [39]. The arylthio substituents are also useful in the further transformations of the adducts and bis-adducts. For instance, base-induced elimination of arenesulfenic acid in **14** allows aromatization of the C-ring of the anthracyclinone. In the bis-adduct **16**, the arylthio substituent makes the acid-catalyzed oxanorbornadiene→phenol rearrangement [40] regioselective. In principle, and following techniques applied by us earlier [24–26], compounds **18** and **19** or/and **20** and **21** could be used to generate daunomycinone (**3**). Work is underway to prepare **3** and **7** in an optically pure form[8]).

We thank *Hoffmann-La Roche & Co., AG,* Basel, the *Swiss National Science Foundation,* and the *Fonds Herbette,* Lausanne, for generous support. We thank also Prof. *J. Lauterwein* and Mr. *M. Rey* for their help in the 360-MHz-^{1}H-NMR measurements. We are greateful also to Dr. *W. Vetter, Hoffmann-La Roche,* Basel, for measurements of absolute masses by high resolution mass spectrometry. We thank Miss *V. Pidoux* for technical assistance.

Experimental Part

General Remarks. See [25] [42]. None of the procedures described below has been optimized.

2,5-Dimethylidene-3,6-bis[(Z)-(2-nitrophenyl)sulfenylmethylidene]-7-oxabicyclo[2.2.1]heptane (**13**). LiCl (17.4 g, 0.41 mol) and 2-nitrobenzenesulfenyl chloride (17.1 g, 0.09 mol) were dissolved in anh. AcOH (200 ml) at 20°. A soln. of 2,3,5,6-tetramethylidene-7-oxabicyclo[2.2.1]heptane (5.8 g, 0.0397 mol) [23] in anh. AcOH (90 ml) was added and the mixture stirred at 20° for 4 h. The precipitate *A* (8.3 g of unstable bis-adducts, 40%) was filtered off and used directly for the elimination of HCl. The filtrate was stirred at 20° for 12 h and yielded a second precipitate *B* of bis-adducts (7 g, 34%). The precipitates were dried separately *in vacuo* at 20°. *A* and *B* were dissolved in 265 and 225 ml of anh. THF, respectively. After cooling to –78°, *t*-BuOK (3 mol-equiv.) was added portionwise under stirring and Ar. The temp. was allowed to raise slowly to 20°. After addition of H_2O (100 ml), the mixtures were extracted with CH_2Cl_2 (200 ml, 3 times). The extracts were washed with H_2O (200 ml, 3 times) and filtered through silica gel (100 g). After solvent evaporation, the residues were recrystallized from CH_2Cl_2/hexane 9:1. *A* yielded pure **13** (3.9 g, 24% based on **10**), yellow crystals, m.p. 187–188°. UV (CH_3CN): 240 (34000), 300 (20500), 382 (12500). IR (KBr): 3100, 3000, 1595, 1570, 1505, 1455, 1345, 1305, 1255, 1225, 1170, 1150, 1110, 1060, 1045, 975, 915. ^{1}H-NMR ($CDCl_3$): 8.25–7.34 (*m*, 8 arom. H); 6.49 (*s*, 2 ArSC*H*); 5.67 (br. *s*, H–C(1), H–C(4)); 5.45 (*s*, *H*CH=C(2) and *H*CH=C(5) *cis* to C(2),C(3) and C(5),C(6), resp.); 5.37 (*s*, 2H). ^{13}C-NMR ($CDCl_3$): 146.6 (*s*, C(3), C(6)); 146.0 (*s*, C(arom.)–NO_2), 143.9 (*s*, C(2), C(5)); 135.7 (*s*, C(arom.)–S); 133.7, 128.9, 125.9 (2 C) (*dd*, $^1J_{C,H}$ = 170, $^3J_{C,H}$ = 8, 4 arom.); 110.5 (*d*, $^1J_{C,H}$ = 178, ArS*C*H); 104.6 (*t*, $^1J_{C,H}$ = 164, H_2C=C(3), H_2C=C(6)); 83.6 (*dm*, $^1J_{C,H}$ = 170, C(1), C(4))[9]). MS (70 eV): 453 (11), 452 (34, M^+), 336 (12), 333 (27), 314 (30), 298 (31), 253 (16), 252 (24), 236 (15), 225 (13), 224 (29), 223 (19), 222 (16), 221 (16), 208 (14), 195 (14), 179 (23), 154 (27), 147 (37), 138 (76), 44 (100). Anal. calc. for $C_{22}H_{16}N_2O_5S_2$ (452.512): C 58.39, H 3.56; found: C 58.21, H 3.57.

Precipitate *B* yielded a mixture of **13** (35–45%), *2,5-dimethylidene-3-[(Z)-(2-nitrophenyl)-sulfenylmethylidene]-6-[(E)-(2-nitrophenyl)sulfenylmethylidene]-7-oxabicyclo[2.2.1]heptane* (**26**; 5–15%) and *2-endo-chloromethyl-3,6-dimethylidene-2-exo-(2-nitrophenyl)sulfenyl-5-[(Z)-(2-nitrophenyl)sulfenylmethylidene]-7-oxabicyclo[2.2.1]heptane* (**27**; 5–15%) separated by column chromatography on silica gel (500 g, AcOEt/hexane

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[6]) We thank Dr. *J.P. Gesson* for ^{1}H-NMR and IR spectra and an authentic sample of (±)-**24**.

[7]) It has been called a 'doubly, doubly-convergent' synthesis [38].

[8]) See *e.g.*, the techniques applied to the synthesis of (+)-4-demethoxydaunomycinone [37] [41].

[9]) The signal attributions were confirmed by 2-D (δ_C *vs.* δ_H) NMR spectroscopy. We thank Mr. *J. Wernly* for these measurements.

1:3). Characteristics of **26**: unstable, yellow oil. ^{1}H-NMR ($CDCl_3$): 8.26–7.32 (*m*, 8 arom. H); 6.55, 6.48 (2*s*, 2 ArSC*H*); 6.0, 5.61, 5.44, 5.24 (4*s*, 4 olef. H); 5.64, 5.22 (2 br. *s*, H–C(1), H–C(4)); NOE measurements confirmed the attributions and the structure.

Characteristics of **27**: yellow crystals, m.p. 192–193° (CH_2Cl_2/hexane 9:1). UV (CH_3CN): 240 (sh, 20000), 300 (12500), 376 (6000). IR (KBr): 3100, 3080, 3020, 2960, 1590, 1570, 1525, 1455, 1430, 1365, 1340, 1305, 1290, 1260, 1210, 1110, 1060, 985, 960, 915, 900. ^{1}H-NMR ($CDCl_3$): 8.25–7.35 (*m*, 8H); 6.65 (*s*, 1H); 5.42 (br. *s*, 1H); 5.35 (*s*, 1H); 5.22 (*s*, 1H); 5.13 (*s*, 1H); 5.05 (br. *s*, 1H); 5.02 (br. *s*, 1H); 3.82, 3.69 (2*d*, ^2J = 12.5, $ClCH_2$). ^{13}C-NMR (CD_3COCD_3): 156.4, 150.6, 147.4, 146.4, 144.0, 135.8 (br. *s*); 139.7, 135.1, 132.7, 131.4, 130.3, 127.5, 126.6, 124.8 (*dd*, $^1J_{C,H}$ = 170, $^3J_{C,H}$ = 8); 126.3 (*s*); 115.7 (*d*, $^1J_{C,H}$ = 180); 110.9, 104.1 (2*t*, $^1J_{C,H}$ = 164); 87.5, 86.7 (2 *dm*, $^1J_{C,H}$ = 172); 65.2 (*s*); 50.1 (*t*, $^1J_{C,H}$ = 156). MS (70 eV): 336 (7.2, $M^+ - [SC_6H_4NO_2]$), 334 (19), 298 (4), 252 (10), 236 (7), 225 (6), 224 (10), 223 (11), 208 (8), 197 (28), 196 (11), 195 (73), 179 (18), 160 (9), 147 (24), 138 (100). Anal. calc. for $C_{22}H_{17}N_2O_5S_2$ (488.970): C 54.04, H 3.50; found: C 54.25, H 3.60.

The configuration of C(2) in **27** is not established unambiguously.

When less than 2.2 mol-equiv. of 2-nitrobenzenesulfenyl chloride was used in the preparation of **13**, the treatment of precipitate *B* with *t*-BuOK gave a mixture of **13**, **26**, **27**, and *2,3,5-trimethylidene-6-[(Z)-(2-nitrophenyl)sulfenylmethylidene]-7-oxabicyclo[2.2.1]heptane* (**28**), separated by column chromatography on silica gel (AcOEt/hexane 1:3). Characteristics of **28**: yellow crystals, m.p. 138–139° (CH_2Cl_2/hexane 9:1). UV (CH_3CN): 230 (25000), 246 (19000), 308 (9500), 374 (5500). IR (KBr): 3100, 3000, 2820, 1590, 1570, 1510, 1450, 1335, 1305, 1255, 1150, 1105, 1040, 900, 850. ^{1}H-NMR ($CDCl_3$): 8.23–7.31 (*m*, 4 arom. H); 6.44 (*s*, ArSC*H*); 5.58 (br. *s*, H–C(1)); 5.41 (*s*, 1H); 5.35 (*s*, 2H); 5.24 (*s*, 2H); 5.19 (*s*, 1H); 5.16 (br. *s*, H–C(4)). ^{13}C-NMR ($CDCl_3$): 147.2, 145.8, 145.6, 145.4, 144.0, 135.9 (br. *s*); 133.6, 128.7, 125.8, 125.7 (*dd*, $^1J_{C,H}$ = 168, $^3J_{C,H}$ = 8, arom. C); 109.6 (*d*, $^1J_{C,H}$ = 176); 103.6, 103.2 (*t*, $^1J_{C,H}$ = 162); 85.7, 83.3 (*dm*, $^1J_{C,H}$ = 166, C(1), C(4)). CI-MS (CH_4): 300 (100, $M^+ + 1$), 258 (19), 156 (13), 154 (25). Anal. calc. for $C_{16}H_{16}NO_3S$ (299.346): C 64.19, H 4.37; found: C 64.09, H 4.27.

1,4-Epoxy-1,2,3,4-tetrahydro-5-methoxy-3-methylidene-2-[(Z)-(2-nitrophenyl)sulfenylmethylidene]anthracene (**15**). A soln. of 1-amino-6-methoxybenzoic acid [30] (449 mg, 2.68 mmol) in DME (5.5 ml) and a soln. of pentyl nitrite (0.472 ml, 3.54 mmol) in DME (5.5 ml) were added dropwise and simultaneously to a stirred soln. of **13** (734 mg, 1.62 mmol) in DME (13 ml) heated to 85°. The mixture was stirred at 85° for 30 min until the end of gas evolution. After cooling to 20°, CH_2Cl_2 (80 ml) was added. The soln. was washed with 10% aq. KOH soln. (30 ml) and the aq. layer extracted with CH_2Cl_2 (30 ml, 3 times). The org. phases were united and washed with H_2O (30 ml, 5 times). After drying ($MgSO_4$), the soln. was filtered through silica gel (20 g), evaporated to dryness, and the residue dried *i.v.* (P_2O_5). The oily product was dissolved in anh. acetone (30 ml). After addition of anh. K_2CO_3 (700 mg, 5 mmol), the soln. was heated under reflux for 12 h. After cooling to 20°, the mixture was filtered and the filtrate evaporated to dryness. The crude **15** was dissolved in CH_2Cl_2 (30 ml) and washed with H_2O (20 ml, 3 times). After drying ($MgSO_4$), the solv. was evaporated and the residue recrystallized from CH_2Cl_2/hexane/Et_2O 6:3:1 yielding 301 mg (46%) of yellow crystals, m.p. 186–187°. UV (CH_3CN): 216 (45000), 253 (36000), 296 (15500), 381 (4500). IR (KBr): 3000, 2960, 2920, 2840, 1730, 1710, 1595, 1570, 1520, 1505, 1450, 1435, 1335, 1300, 1280, 1260, 1255, 1215, 1190, 1180, 1130, 1100, 1075, 1060, 1030, 855. ^{1}H-NMR ($CDCl_3$): 8.26–7.32 (*m*, 6H, *Ar*S, H–C(7), H–C(8)); 8.21 (*s*, H–C(10)); 7.73 (*s*, H–C(9)); 6.86 (*dd*, ^3J(H–C(6),H–C(7)) = 5.8, ^4J(H–C(6),H–C(8)) = 2.8, H–C(6)); 6.43 (*s*, ArSC*H*); 6.23 (*s*, H–C(1)); 5.82 (*s*, H–C(4)); 5.43 (*s*, *H*CH=C(3) *cis* to C(2),C(3)); 5.35 (*s*, HC*H*=C(3) *trans* to C(2),C(3)); 4.01 (*s*, CH_3O). ^{13}C-NMR ($CDCl_3$): 155.8, 147.4, 145.8, 144.7, 141.0, 140.6, 136.2, 134.2 (*s*, C(4a), C(8a), C(9a), C(2), C(3), C(5), SAr); 133.6, 128.7, 125.9, 125.6 (*dd*, $^1J_{C,H}$ = 166, $^3J_{C,H}$ = 8, H–*C* of SAr); 126.3 (*d*, $^1J_{C,H}$ = 160, C(7)); 125.0 (*s*, C(10a)); 120.7 (*dm*, $^1J_{C,H}$ = 160, C(8)); 118.3 (*d*, $^1J_{C,H}$ = 162, C(9)); 112.8 (*d*, $^1J_{C,H}$ = 164, C(10)); 109.7 (*d*, $^1J_{C,H}$ = 176, ArS*C*H); 104.7 (*d*, $^1J_{C,H}$ = 158, C(6)); 104.2 (*t*, $^1J_{C,H}$ = 160, H_2C=C(3)); 83.9 (*d*, $^1J_{C,H}$ = 166, C(1)); 81.33 (*d*, $^1J_{C,H}$ = 166, C(4)); 55.5 (*q*, $^1J_{C,H}$ = 143, CH_3O). MS (70 eV): 404 (11), 403 (34, M^+), 341 (10), 295 (11), 282 (11), 281 (31), 266 (20), 265 (58), 264 (21), 252 (22), 250 (39), 249 (100). Anal. calc. for $C_{23}H_{17}NO_4S$ (403.453): C 68.47, H 4.24; found: C 68.53, H 4.31.

[(1RS,2RS,5RS,12RS)-5,12-Epoxy-1,2,3,4,5,12-hexahydro-7-methoxy-1-(2-nitrophenyl)sulfenyl-2-naphthacenyl] Methyl Ketone (**16**). A mixture of **15** (490 mg, 1.21 mmol) and MVK (1 ml, 12.1 mmol) in anh. toluene (6 ml) was heated to 110° for 18 h. After evaporation, the residue was purified on column chromatography (SiO_2, AcOEt/petroleum ether 1:1). The first fraction contained 55 mg (9%) of the minor adduct **17** and the second fraction the major adduct **16** which was recrystallized from CH_2Cl/Et_2O 4:1 yielding 453 mg (79%) of yellow crystals, m.p. 189–191°. UV (CH_3CN): 210 (38500), 251 (40000), 284 (14000), 316 (3300), 331 (3400). IR (KBr): 3100, 3080, 3020, 2970, 2940, 2900, 2850, 1705, 1615, 1600, 1590, 1570, 1510, 1470, 1365, 1350, 1300, 1265, 1250, 1230, 1190, 1160, 1150, 1125, 1085, 1070, 1050, 930, 850, 835, 800, 780, 760, 740, 715, 690, 650, 640. ^{1}H-NMR (CD_2Cl_2): 8.15–7.28 (*m*, 6H, Ar-S, H–C(9), H–C(10)); 8.0 (*s*, H–C(6)); 7.33 (*s*, H–C(11)); 6.9 (*dd*, ^3J(H–C(8),H–C(9)) = 7.5, ^4J(H–C(8),H–C(10)) = 1.0, H–C(8)); 5.56 (br. *s*, ^5J(H–C(12),H$_\beta$–C(4)) = 1.0,

H–C(12)); 5.53 (br. *s*, ^5J(H–C(5),H_β–C(1)) = 1.0, H–C(5)); 3.92 (*dddd*, ^3J(H_β–C(1),H–C(2)) = 6.2, ^5J(H_β–C(1),H_α–C(4)) = 2.8, ^5J(H_β–C(1),H_β–C(4)) = 2.2, ^5J(H_β–C(1),H–C(5)) = 1.0, H_β–C(1)); 4.0 (*s*, CH_3O); 2.71 (*ddd*, ^3J(H–C(2),H_β–C(3)) = 7.8, ^3J(H–C(2),H_β–C(1)) = 6.2, ^3J(H–C(2),H_α–C(3)) = 4.0, H–C(2)); 2.48 (*m*, ^2J = 18.5, ^5J(H_β–C(4),H_β–C(1)) = 2.2, ^5J(H_β–C(4),H–C(12)) = 1.0, H_β–C(4)); 2.17 (*s*, CH_3CO); 2.16–2.06 (*m*, ^2J = 18.5, ^5J(H_α–C(4),H_β–C(1)) = 2.8, H_α–C(4)); 2.02–1.88 (*m*, $H_2C(3)$). MS (70 eV): 473 (1, M^+), 318 (10), 278 (19), 277 (100), 276 (19), 275 (17), 260 (10), 259 (14), 249 (14). Anal. calc. for $C_{27}H_{23}NO_5S$ (473.544): C 68.48, H 4.89; found: C 68.32, H 4.99.

(5-Acetoxy-3,4-dihydro-7-methoxy-2-naphthacenyl) Methyl Ketone (**20**). A soln. of **16** (156 mg, 0.33 mmol) in Ac_2O (4.5 ml) containing CF_3COOH (60 µl, 0.78 mmol) was heated to 50° under N_2 for 1 h. Anh. pyridine (1 ml) was added and the mixture allowed to cool to 20°. After stirring at 20° for 20 min, CH_2Cl_2 (10 ml) was added and the soln. extracted successively with 5% aq. HCl soln. (10 ml, 3 times) and sat. aq. K_2CO_3 soln. (10 ml, 3 times). After drying ($MgSO_4$), the solvent was evaporated and the residue taken up with CH_2Cl_2 (6 ml). A 0.5M aq. soln. of $NaHCO_3$ (6 ml) and MCPBA (90 mg, 0.47 mmol) was added and the mixture stirred at 20° for 15 min. The org. layer was separated and washed with sat. aq. K_2CO_3 soln. (10 ml, 3 times). After drying ($MgSO_4$), the soln. was filtered through silica gel (5 g) and the solv. evaporated. The residue contained a 3:1 to 4:1 mixture **18**/**19**. The major isomer **18** was obtained pure by recrystallization from CH_2Cl_2/Et_2O 5:1 yielding 77 mg (65%) of yellow crystals, m.p. 199–201° (dec). UV(CH_3CN): 239 (19000), 260 (12000), 306 (30000), 319 (31000), 361 (5200), 379 (5100). IR (KBr): 3065, 3020, 2960, 2910, 2850, 1760, 1655, 1635, 1615, 1565, 1460, 1440, 1385, 1370, 1310, 1275, 1255, 1225, 1205, 1170, 1155, 1110, 1065, 980, 910, 890, 790. ^{1}H-NMR (CD_2Cl_2): 8.69 (*s*, H–C(6)); 8.41 (*s*, H–C(11)); 7.86 (*s*, H–C(12)); 7.65 (*s*, H–C(1)); 7.59 (*d*, ^3J(H–C(10),H–C(9)) = 7.5, H–C(10)); 7.42 (*dd*, ^3J = 7.5, ^3J(H–C(9),H–C(8)) = 7.4, H–C(9)); 6.82 (*d*, ^3J = 7.4, H–C(8)); 4.09 (*s*, CH_3O); 2.99–2.59 (*m*, $H_2C(3)$,$H_2C(4)$); 2.59 (*s*, $OCOCH_3$); 2.49 (*s*, 3H, $COCH_3$). Irradiation at 7.65 (H–C(1)) led to NOE's at 7.86 (H–C(12)) and 2.49 ($COCH_3$); 7.86→7.65 and 8.41; 8.41→7.86 and 7.59; 7.52→8.41 and 7.42; 4.09(CH_3O)→6.82(H–C(8)) and 8.69(H–C(6)); 2.59($OCOCH_3$)→8.69(H–C(6)); 2.49($COCH_3$)→7.65 ppm. MS (70 eV): 361 (7), 360 (32, M^+), 318 (100), 275 (24), 202 (9). MS (HR): 360.1360 ($C_{23}H_{20}O_4$, calc. 360.1361).

6-Acetoxy-9-acetyl-7,8-dihydro-4-methoxy-5,12-naphthacenequinone[10]) (**22**). A soln. of **20** (70 mg, 0.18 mmol) in acetone (8 ml) and 4N *Jones'* reagent (0.9 ml, 1.22 mmol of CrO_3; from 26.72 g of CrO_3, 23 ml of conc. H_2SO_4, diluted to 200 ml with H_2O) were added dropwise and simultaneously to stirred acetone (8 ml) maintained at 0°. After stirring at 0° for 1 h, i-PrOH (1 ml) was added and the mixture stirred for 10 min, then CH_2Cl_2 (20 ml) was added. The soln. was washed with 10% aq. $NaHCO_3$ soln. (10 ml, 2 times) and then with sat. aq. NaCl soln. (10 ml, 3 times). The aq. phase was extracted with CH_2Cl_2 (10 ml, 2 times). The org. extracts were united, dried ($MgSO_4$), and evaporated to dryness. The crude **22** was recrystallized from CH_2Cl_2/acetone/MeOH 1:4:1 yielding 42 mg (64%) of yellow crystals, m.p. 238–240° (dec). UV (CH_3CN): 233 (27000), 287 (53000), 297 (53000), 282 (12000). IR (KBr): 3100, 2950, 2850, 1750, 1670, 1590, 1475, 1455, 1440, 1390, 1370, 1355, 1335, 1320, 1300, 1280, 1265, 1250, 1235, 1210, 1195, 1180, 1120, 1105, 1050, 1020, 1010, 965, 925, 885, 795, 750. ^{1}H-NMR (CD_2Cl_2): 8.06 (*s*, H–C(11)); 7.90 (*dd*, ^3J(H–C(1),H–C(2)) = 7.7, ^4J(H–C(1),H–C(3)) = 1, H–C(1)); 7.7 (*dd*, ^3J = 8.5, 7.7, H–C(2)); 7.48 (br. *s*, H–C(10)); 7.34 (*dd*, ^3J(H–C(2),H–C(3)) = 8.5, ^4J(H–C(3),H–C(1)) = 1, H–C(3)); 4.03 (*s*, CH_3O); 2.98–2.60 (*m*, $H_2C(7)$,$H_2C(8)$); 2.55 (*s*, $OCOCH_3$); 2.51 (*s*, $COCH_3$). MS (70 eV): 390 (9, M^+), 349 (19), 348 (100), 333 (19), 332 (12), 330 (16), 315 (10), 305 (49), 291 (13), 290 (28), 289 (14), 288 (13), 287 (26). MS (HR): 390.1106 ($C_{23}H_{18}O_6$, calc. 390.1103).

(±)-6-Acetoxy-9-acetyl-9,10-epoxy-7,8,9,10-tetrahydro-4-methoxy-5,12-naphthacenequinone[10]) (**23**). A mixture of **22** (96 mg, 0.2 mmol) and MCPBA (471 mg, 2.73 mmol) in CH_2Cl_2 (5 ml) was stirred at 20° for 15 h. The precipitate was filtered off and the soln. washed with 10% aq. K_2CO_3 soln. (10 ml, 5 times). After drying ($MgSO_4$) and evaporation, the crude **23** was purified on silica gel (AcOEt/hexane 4:1) yielding 42 mg (42%) of yellow-orange crystals, m.p. 235-6° (dec.; CH_2Cl_2/Et_2O 2:1). UV (CH_3CN): 219 (33000), 260 (35000), 281 (sh, 6700), 381 (6400). IR (KBr): 2980, 2940, 2880, 1775, 1715, 1680, 1590, 1440, 1380, 1370, 1350, 1330, 1220, 1200, 1180, 1110, 1070, 1040, 840. ^{1}H-NMR ($CDCl_3$): 8.25 (*s*, H–C(11)); 7.91 (*dd*, ^3J(H–C(1),H–C(2)) = 7.2, ^4J(H–C(1),H–C(3)) = 1, H–C(1)); 7.71 (*dd*, ^3J = 7.5, 7.2, H–C(2)); 7.34 (*dd*, ^3J(H–C(3),H–C(2)) = 7.5, ^4J(H–C(3),H–C(1)) = 1, H–C(3)); 4.18 (*s*, H–C(10)); 4.02 (*s*, CH_3O); 2.75–2.65 (*m*, 2H); 2.47 (*s*, $OCOCH_3$); 2.34–2.22 (*m*, 2H); 2.17 (*s*, $COCH_3$). MS (70 eV): 406 (11, M^+), 380 (19), 364 (100), 363 (10), 362 (11), 349 (15), 348 (56), 347 (24), 346 (57), 338 (68), 328 (30), 322 (87), 321 (66), 320 (27), 304 (75). MS (HR): 406.1050 ($C_{23}H_{18}O_{17}$, calc. 406.1052).

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[10]) IUPAC names: 11-acetoxy-8-acetyl-9,10-dihydro-1-methoxy-5,12-naphthacenequinone (**22**); 11-acetoxy-8-acetyl-7,8-epoxy-7,8,9,10-tetrahydro-1-methoxy-5,12-naphthacenequinone (**23**); 8-acetyl-7,8,9,10-tetrahydro-8,11-dihydroxy-1-methoxy-5,12-naphthacenequinone ((±)-**24**).

(±)-7,11-Dideoxydaunomycinone[10]) ((±)-**24**). Air was bubbled through a soln. of NaOH (38 mg, 0.95 mmol) and $Na_2S_2O_4$ (81 mg, 0.46 mmol) in H_2O (1.3 ml) for 10 min. The epoxide **23** (9 mg, 0.022 mmol) was added and the mixture stirred at 20° for 1 h. Air was bubbled through the mixture for 10 min. The mixture was acidified with 5% aq. HCl, and air was bubbled for another 10 min. The mixture was extracted with CH_2Cl_2 (5 ml, 3 times) and the extract washed with H_2O (5 ml, 3 times). After evaporation, the crude **24** was purified by TLC (SiO_2, AcOEt/hexane 4:1) yielding 3.1 mg (38%) of yellow-orange crystals, m.p. 209–211° ([11] [12c]: 209–211°; [10]: 210–211°). ^{1}H-NMR ($CDCl_3$): 13.43 (*s*, HO–C(6)); 7.98 (*d*, ^3J = 8.3, H–C(1)); 7.76 (*t*, ^3J = 8.3, H–C(2)); 7.56 (*s*, H–C(11)); 7.36 (*d*, ^3J = 8.3, H–C(3)); 4.10 (*s*, CH_3O); 3.73 (*s*, HO–C(9)); 3.32 (*d*, ^2J = 17, H–C(10)); 3.15 (*dd*, 1H, ^2J = 18, ^5J = 2) and 2.95 (*m*, 1H, $H_2C(7)$); 2.82 (*dd*, ^2J = 17, ^5J = 2 Hz, H–C(10)); 2.38 (*s*, $COCH_3$), 2.02 (*m*, $H_2C(8)$). MS (70 eV): 366 (14, M^+), 348 (18), 323 (100), 305 (19), 293 (12), 290 (10).

REFERENCES

[1] H. Brockmann, *Fortschr. Chem. Org. Naturstoffe* **1963,** *21,* 121; S.A. Waksman, 'The Actinomycetes', The Ronald Press, New York, 1967.

[2] G. Cassinelli, P. Orezzi, P. Gior, *Microbiol.* **1963,** *11,* 167; M. Dobost, P. Gauter, M. Maral, L. Ninet, S. Pinnert, J. Preud'Homme, G.H. Werner, *C.R. Acad. Sci. Paris* **1963,** *257,* 1813; M.G. Brachnikova, N.V. Kostantinova, P.A. Pomaskova, B.M. Zacharov, *Antibiotiki* **1966,** *11,* 763; J.R. Brown, *Prog. Med. Chem.* **1978,** *15,* 126; F. Arcamone, 'Topics in Antibiotic Chemistry', Ed. P.G. Sammes, Halsted Press, New York, 1978, Vol. 2, p. 102; W.A. Remers, 'The Chemistry of Antitumor Antibiotics', Wiley-Interscience, New York, 1979, Vol. 1, p. 63; F. Arcamone, 'Doxorubicin', Academic Press, New York, 1981; F. Arcamone, 'Anthracycline Antibiotics', Ed. H.S. El Khadem, Academic Press, New York, 1982.

[3] F. Arcamone, *Lloydia* **1977,** *40,* 405; S.T. Crooke, V.H. Du Vernay, S. Mong, 'Molecular Pharmacology of Anthracyclines', in 'Molecular Actions and Targets for Cancer Chemotherapeutic Agents', Academic Press, New York, 1981, chap. 7; A. Di Marco, F. Arcamone, F. Zunio, 'Daunomycin, Adriamycin, and Structural Analogs: Biological Activity and Mechanisms of Action in Antibiotics', Eds. J.W. Corcoran, F.E. Hahn, Springer-Verlag, Berlin, 1975, Vol. 3; R. Bühner, *Beitr. Onkol. (Basel)* **1981,** *9,* 33; T. Komiyama, T. Kikuchi, Y. Sugiura, *Biochem. Pharmacol.* **1982,** *31,* 3651.

[4] F. Arcamone, G. Cassinelli, G. Fantini, A. Grein, P. Orezzi, C. Pol, C. Spalla, *Biotechnol. Bioeng.* **1969,** *11,* 1101.

[5] T.R. Kelly, Guest Ed., 'Recent Aspects of Anthracyclinone Chemistry', Tetrahedron Symposia-in-Print, No. 17, 1984, Vol. 40, p. 4537–4793.

[6] F. Arcamone, G. Cassinelli, F. Di Matteo, S. Forenza, M.C. Ripamonti, G. Rivola, A. Vigevani, J. Clardy, T. McCabe, *J. Am. Chem. Soc.* **1980,** *102,* 1462.

[7] a) J.P. Gesson, J.C. Jacquesy, M. Mondon, *Tetrahedron Lett.* **1980,** *21,* 3351; b) J.P. Gesson, J.C. Jacquesy, B. Renoux, *ibid.* **1983,** *24,* 2757; c) J.P. Gesson, J.C. Jacquesy, M. Mondon, *Nouv. J. Chim.* **1983,** *7,* 205; d) J.P. Gesson, M. Mondon, *J. Chem. Soc., Chem. Commun.* **1982,** 421; e) J.P. Gesson, J.C. Jacquesy, B. Renoux, *Tetrahedron* **1984,** *40,* 4743.

[8] J.C. Bauman, R.B. Barber, R.D. Gless, H. Rapoport, *Tetrahedron Lett.* **1980,** *21,* 4777.

[9] J. Alexander, D.L. Flynn, L.A. Mitscher, T. Veysoglu, *Tetrahedron Lett.* **1981,** *22,* 3711.

[10] J. Yadav, P. Corey, C.T. Hsu, K. Perlman, C.J. Sih, *Tetrahedron Lett.* **1981,** *22,* 811.

[11] S.D. Kimball, D.R. Walt, F. Johnson, *J. Am. Chem. Soc.* **1981,** *103,* 1561.

[12] a) A.V.R. Rao, V.H. Deshpande, N.L. Reddy, *Tetrahedron Lett.* **1982,** *23,* 775; b) A.V.R. Rao, A.R. Mehendale, K.B. Reddy, *ibid.* **1982,** *23,* 2415; c) A.V.R. Rao, K.B. Reddy, A.R. Mehendal, *J. Chem. Soc., Chem. Commun.* **1983,** 564.

[13] A.S. Kende, J.P. Rizzi, *Tetrahedron Lett.* **1981,** *22,* 1799; A.S. Kende, S.D. Boettger, *J. Org. Chem.* **1981,** *46,* 2799; A.S. Kende, J.P. Rizzi, M.L. King, in 'Anthracycline Antibiotics', Academic Press, New York, 1982, p. 141.

[14] K. Krohn, *Angew. Chem., Int. Ed.* **1981,** *20,* 576.

[15] M.E. Jung, M. Node, R.W. Pfluger, M.A. Lyster, J.A. Lowe, III, *J. Org. Chem.* **1982,** *47,* 1150; M.E. Jung, J.A. Lowe, III, M.A. Lyster, M. Node, R.W. Pfluger, R.W. Brown, *Tetrahedron* **1984,** *40,* 4751.

[16] F.M. Hauser, D. Mal, *J. Am. Chem. Soc.* **1983,** *105,* 5688; F.M. Hauser, S. Prasanna, D.W. Combs, *J. Org. Chem.* **1983,** *48,* 1328; F.M. Hauser, V.M. Baghdanov, *Tetrahedron* **1984,** *40,* 4719.

[17] E. Vedejs, W.H. Miller, J.R. Pribish, *J. Org. Chem.* **1983,** *48,* 3613.

[18] Y. Tamura, S. Akai, M. Sasho, Y. Kita, *Tetrahedron Lett.* **1984,** *25,* 1167.

[19] M. Uemura, T. Minami, Y. Hayashi, *J. Chem. Soc., Chem. Commun.* **1984,** 1193.
[20] K. A. Parker, E. A. Tallman, *Tetrahedron* **1984,** *40,* 4781.
[21] H. Sekizaki, M. Jung, J. M. McNamara, Y. Kishi, *J. Am. Chem. Soc.* **1982,** *104,* 7372.
[22] J. M. McNamara, Y. Kishi, *J. Am. Chem. Soc.* **1982,** *104,* 7371; *Tetrahedron* **1984,** *40,* 4685.
[23] C. Mahaim. P.-A. Carrupt, J.-P. Hagenbuch, A. Florey, P. Vogel, *Helv. Chim. Acta* **1980,** *63,* 1149.
[24] J. Tamariz, P. Vogel, *Tetrahedron* **1984,** *40,* 4549; J. Tamariz, L. Schwager, J. A. A. Stibbard, P. Vogel, *Tetrahedron Lett.* **1983,** *24,* 1497; J. Tamariz, P. Vogel, *Angew. Chem., Int. Ed.* **1984,** *23,* 74.
[25] Y. Bessière, P. Vogel, *Helv. Chim. Acta* **1980,** *63,* 232.
[26] P.-A. Carrupt, P. Vogel, *Tetrahedron Lett.* **1979,** *20,* 4533.
[27] O. Pilet, P. Vogel, *Helv. Chim. Acta* **1981,** *64,* 2563; see also; O. Pilet, J.-L. Birbaum, P. Vogel, *ibid.* **1983,** *66,* 19.
[28] J.-L. Métral, P. Vogel, *Helv. Chim. Acta* **1985,** *68,* 334: see also: J.-L. Métral, P. Vogel, *Tetrahedron Lett.* **1984,** *25,* 5387.
[29] J.-M. Tornare, P. Vogel, *J. Org. Chem.* **1984,** *49,* 2510.
[30] R. N. Warrener, R. A. Russell, S. M. Marcuccio, *Aust. J. Chem.* **1980,** *33,* 2777.
[31] A. S. Kende, D. P. Curran, Y. Tsay, J. E. Mills, *Tetrahedron Lett.* **1977,** 3537.
[32] C. Mahaim, P. Vogel, *Helv. Chim. Acta* **1982,** *65,* 866.
[33] K. Alder, G. Stein, *Justus Liebigs Ann. Chem.* **1933,** *504,* 22; *ibid.* **1934,** *514,* 1; R. B. Woodward, T. J. Katz, *Tetrahedron* **1959,** *5,* 70.
[34] A. A. Pinkerton, D. Schwarzenbach, J.-M. Tornare, P. Vogel, *Helv. Chim. Acta,* submitted.
[35] P.-A. Carrupt, F. Berchier, P. Vogel, *Helv. Chim. Acta,* submitted.
[36] C. Mahaim, Dissertation No. 426, Ecole Polytechnique Fédérale de Lausanne, 1981.
[37] D. Dominguez, M. P. Cava, *J. Org. Chem.* **1983,** *48,* 2820.
[38] S. H. Bertz, *J. Am. Chem. Soc.* **1982,** *104,* 5801.
[39] L. Castedo, E. Guitian, C. Saá, R. Suan, J. M. Saá, *Tetrahedron Lett.* **1983,** *24,* 2107.
[40] P. Vogel, B. Willhalm, H. Prinzbach, *Helv. Chim. Acta* **1969,** *52,* 584.
[41] A. V. R. Rao, J. S. Yadav, K. B. Reddy, A. R. Mehendale, *J. Chem. Soc., Chem. Commun.* **1984,** 453; S. Terashima, K. Tamoto, M. Sugimori, *Tetrahedron Lett.* **1982,** *23,* 4107; K. Tamoto, M. Sugimori, S. Terashima, *Tetrahedron* **1984,** *40,* 4617.
[42] A. A. Pinkerton, D. Schwarzenbach, J.-L. Birbaum, P.-A. Carrupt, L. Schwager, P. Vogel, *Helv. Chim. Acta* **1984,** *67,* 1136.