Regeneration of Δ^{18}-tabersonine from **3** also necessitates cleavage of the 1,16-bond, along with a shift of H(2), either to N(1) or to C(16).

This synthesis of scandine from the readily available Δ^{18}-tabersonine is though to mimic in a very short process one more biotransformations of the highly versatile *Aspidosperma* precursors.

Experimental Section

Melting points were taken on a Reichert Microscop and are uncorrected. ^{1}H NMR spectra were measured on a Perkin-Elmer R12B spectrometer (60 MHz) or on IEF 400, a prototype built at the University of Orsay (402 MHz), in $CDCl_3$ using Me_4Si as internal standard. Separations were done on TLC and with a Chromatotron (R) apparatus with Kieselgel 60 PF_{254} (Merck) and eluant CH_2Cl_2/MeOH.

16-Chloroindolenine 2. *t*-BuOCl (6% w/v solution in CH_2Cl_2, 6.4 mL) was added over a period of 1 h to a solution of Δ^{18}-tabersonine (**1**)[6] (720 mg) and triethylamine (0.32 mL) in methylene chloride (35 mL) under cooling at 0 °C. Evaporation of the solvent and crystallization from acetone gave **2** (564 mg, 71%): mp 150–158 °C dec; MS, *m/z* 368 ($M^{+\cdot}$), 370; UV λ_{max} 222, 275 nm; IR ν_{CO} 1735 cm^{-1}.

Aziridine 3. The 16-chloroindolenine **2** prepared from 720 mg 1 was dissolved in AcOH (20 mL) and portionwise added with $NaBH_3CN$ (1 g) over a period of 1 h at room temperature. The solution was poured into a saturated aqueous solution of K_2CO_3 and extracted with CH_2Cl_2. Purification through centrifuge TLC (Chromatotron^R, silica, 99:1 CH_2Cl_2/MeOH) afforded 382 mg aziridine **3** (53% from 1), which could not be induced to crystallize: $[\alpha]_D$ +49° (*c* 1.4, MeOH); MS, found for $M^{+\cdot}$ 334.1692 (calcd for $C_{21}H_{22}N_2O_2$ 334.1676); MS, *m/z* (relative intensity) 105 (60), 119 (80), 120 (43), 133 (100), 167 (12), 201 (13), 214 (10), 228 (28), 229 (12), 275 (6), 333 (7), 334 (11); UV λ_{max} 212, 230 (sh), 270, 280 nm; IR (film) ν_{CO} 1730 cm^{-1}; ^{1}H NMR (60 MHz) δ 0.65 (1 H, d, J = 12 Hz) and 2.67 (1 H, d, J = 12 Hz) [H-17 and H-17′], 3.8 (3 H, s, CO_2CH_3), 5–6 (5 H, m, olefinic protons), 7–7.4 (4 H, m, aromatic protons); ^{13}C NMR δ (carbon number) 26.1 (17), 37.6 (6), 41.3 (20), 45.8 (5), 49.5 (16), 53.0 (OMe), 53.4 (7), 54.5 (3), 57.4 (2), 74.6 (21), 113.7 (18), 122.0 (12), 122.6 (9), 124.7 (14), 126.9 (10), 128.1 (11), 129.8 (15), 143.9 (19), 147.9 (8), 149.1 (13), 170.9 (22).

Flow Thermolysis of Aziridine 3. Aziridine **3** (44 mg) in MeOH–PhH (2:1, 20 mL) was passed through a glass fitted column heated at 495–510 °C under a slight vacuum (water pump) while the eluant was trapped in a liquid nitrogen cooled vessel. Evaporation of the solvent and separation on TLC afforded Δ^{18}-tabersonine (**1**), 8 mg (18%), and imine **4**, 5 mg (11%), along with recovered aziridine **3**, 13 mg (29%). Imine **4**: $[\alpha]_D$ +161° (*c* 0.5 MeOH); UV λ_{max} 215, 270 nm; IR ν_{CO} 1725 cm^{-1}, ν_{CN} 1610 cm^{-1} (weak); MS, found for $M^{+\cdot}$ 334.1600 (calcd for $C_{21}H_{22}N_2O_2$ 334.1676); MS, *m/z* (relative intensity) 105 (21), 119 (28), 120 (35), 134 (100), 170 (20), 214 (29), 275 (38), 276 (16), 303 (5), 334 (75); ^{1}H NMR δ 3.61 (3 H, s, CO_2CH_3), 4.8–6 (5 H, m, olefinic protons), 7.2–7.5 (4 H, m, aromatic protons), 7.52 (1 H, s, H-2); ^{13}C NMR δ (carbon number) 40.8 (6), 45.5 (17), 47.0 (20), 48.2 (3), 52.4 (OMe), 53.9 (5), 54.6 (7), 60.3 (16), 85.1 (21), 114.8 (18), 123.4 (14), 126.3 (12*), 127.3 (10), 128.6 (9*), 128.7 (11), 131.5 (15), 133.2 (8), 140.2 (13), 142.4 (19), 159.9 (2), 170.6 (22) [*may be inverted].

Oxidation of Imine 4. Imine **4** (14 mg) in acetone (2 mL) was added with 2 equiv of Jones' reagent at −10 °C. After 30 min, the solution was placed at +4 °C for 2 more hours. The solvent was evaporated at room temperature under vacuum, and an aqueous 10% solution of $NaHSO_3$ (2 mL) was added. After basification with Na_2CO_3, the solution was extracted with CH_2Cl_2. Separation on TLC afforded imine **4**, 3.5 mg (25%), and scandine (**5**), 5 mg (35%): $[\alpha]_D$ +206–210° (*c* 0.2, MeOH) [lit.[2] $[\alpha]_D$ +254°]; the IR, UV, MS, and ^{1}H NMR spectra and the R_f were identical with those of an authentic sample.

Hydrogenation of Synthetic Scandine (5). Catalytic hydrogenation (PtO_2, 20 mg) of synthetic scandine (**5**) (2 mg) in methanol (1 mL) followed by crystallization from hexane–CH_2Cl_2 gave tetrahydroscandine **7**, which was identical with an authentic sample: mp 209–211 °C; $[\alpha]_D$ +92.4° (MeOH, *c* 0.1); IR, MS, and R_F were all identical with an authentic sample.

Meloscine (6). Saponification and decarboxylation[2] of synthetic scandine (**5**) (5 mg) afforded meloscine (**6**) (3.5 mg), which was identical [mp 177–183 °C (lit.[2] mp 181–185 °C); $[\alpha]_D$ +130° (*c* 0.04, EtOH) (lit.[2] $[\alpha]_D$ +133.8°); IR; MS; 400-MHz ^{1}H NMR) with an authentic sample.

Acknowledgment. Thanks are due to H. Bailla (Faculté des Sciences, Reims), S. K. Kan (Orsay), E. Kremp (Strasbourg), and M. Merle (ICI-Pharma, Reims) for spectral measurements and to Prof. M. Plat (Chatenay-Malabry) for a generous gift of reference samples and spectra.

Registry No. 1, 58471-12-8; **2**, 97674-39-0; **3**, 97674-40-3; **4**, 97674-41-4; **5**, 24314-59-8; **6**, 24314-51-0; **7**, 91201-55-7.

(11) **Note added in proof**: This rearrangement apparently better accounts for the configuration of scandine presented in Chart I[2] than for the revised – configuration of the COOMe later proposed.[3] Moreover, the NMR spectrum of the amine resulting from the reduction of **4** exhibited a COOMe signal at 3.61 ppm, which reflected an anisotropic effect of the benzene ring consistent with the depicted configuration.

The Total Synthesis of Optically Pure (9*R*,13*S*)- and (9*R*,13*R*)-7-Deoxy-13-dihydrodaunomycinone

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13-Dihydrodaunomycin **1** has long been recognized as the major human metabolite of the antineoplastic anthracycline daunomycin **2**.[1] Whilst **1** has been prepared by microbial[2] and chemical reduction[3] of **2**, no attempt to assign the stereochemistry at C13[4] has been reported. Recently Cassinelli et al. have reported[5] that 4-demethoxydaunomycin **3** (idarubicin) can be reduced microbially to afford an idarubicinol **4** identical with that excreted by patients treated with **3**. These authors initially assigned the 13*R* stereochemistry to this product, although this was subsequently corrected by Broadhurst et al.,[6] who showed that the totally synthetic 13*S* isomer corresponded to the biologically obtained product. As both dihydroderivatives **1** and **4** are active antineoplastic agents,[2,7] routes leading

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(2) (a) Aszalos, A. A.; Bachur, N. R.; Hamilton, B. K.; Langlukke, A. F.; Roller, P. P.; Sheikh, M. Y.; Sutphin, M. C.; Thomas, M. C.; Wareheim, D. A.; Wright, L. H. *J. Antibiot.* **1977**, *30*, 50. (b) Marshall, V. P.; McGovren, J. P.; Richard, F. A.; Richard, R. E.; Wiley, P. F. *J. Antibiot.* **1978**, *31*, 336.

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(4) The numbering used here is that commonly accepted for anthracyclines. Systematic notations C9, C11, and C13, referred to above, become C8, C10, and C11, respectively.

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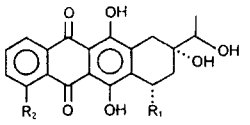
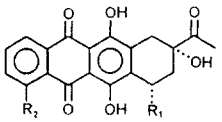


1, R_1 = O-Daunosaminyl, R_2 = OCH_3
4, R_1 = O-Daunosaminyl, R_2 = H
5, R_1 = H, R_2 = OCH_3



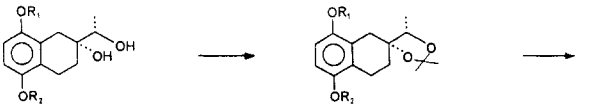
2, R_2 = O-Daunosaminyl, R_2 = OCH_3
3, R_1 = O-Daunosaminyl, R_2 = H

to their total synthesis are of considerable interest. In addition another dihydro compound, namely 7-deoxy-13-dihydrodaunomycinone **5**, has reportedly been isolated from a strain of *Streptomyces* (PD.J566) originating from Michaelmas Cay in Australia.[8] Since this product occurred together with known daunomycin derivatives, it was assumed to have the 9*R* configuration. However, subsequent attempts to synthesize **5** stereospecifically by borohydride reduction of (−)-7-deoxydaunomycinone yielded unseparated mixtures of the 9*R*,13*R* and 9*R*,13*S* isomers.[9] Consequently, the configuration of C13 of the natural product remained undefined.

It is now clearly recognized[10] that the annelation of chiral quinone monoketals with anions derived from 3-(phenylsulfonyl)phthalides **21** and **25** provides a regio and enantiospecific route to a variety of anthracycline derivatives.[10,11] The exceptionally mild conditions employed in this reaction appeared well suited to the total synthesis of 13-dihydrodaunomycin derivatives of defined stereochemistry. We now describe experiments leading to the title compounds.

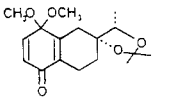
Preparation of (9*R*,13*S*)-7-Deoxy-13-dihydrodaunomycinone (24). The previously described optically pure diol **6**[12] was converted to its isopropylidene derivative **8** which underwent clean hydrogenolysis to the phenol **10** (Scheme I). Oxidation of **10** with thallium(III) nitrate in a mixture of methanol, trimethyl orthoformate, and THF afforded the required monoketal **11** in excellent yield. Condensation of **11** with the anion of **21** at −78 °C afforded the expected naphthacenedione **22** in 94% yield (Scheme II), with recovery of unreacted **11** (6%) possible after chromatography. Quantitative removal of the isopropylidene group in **22** was effected by treatment with acid resin (AG-50W-X2)[13] to give optically pure diol **23**. Since demethylation of related systems[10,11] with BCl_3 are known not to racemize the tertiary C9 alcohol, it remained only to establish that the chiral diol **23** could be demethylated without racemizing the C13 secondary alcohol. Treatment of either **22** or **23** with BCl_3 in CH_2Cl_2 at −78 °C afforded **24**, mp 245–247 °C, $[\alpha]_D$ −108°. In order to confirm the absence of racemization at either C9 or C13, a sample of **24** was exposed to an excess of BCl_3 at −78 °C and subsequently recovered. Samples subjected to analysis

Scheme I. Synthesis of Dienones 11 and 17

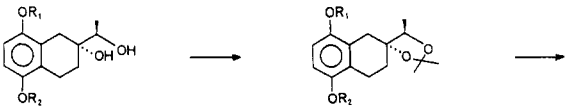


6, R_1 = CH_3, R_2 = $PhCH_2$
7, R_1 = $PhCH_2$, R_2 = CH_3

8, R_1 = CH_3, R_2 = $PhCH_2$
9, R_1 = $PhCH_2$, R_2 = CH_3
10, R_1 = CH_3, R_2 = H

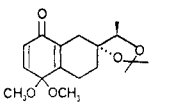


11



12, R_1 = CH_3, R_2 = $PhCH_2$
13, R_1 = $PhCH_2$, R_2 = CH_3

14, R_1 = CH_3, R_2 = $PhCH_2$
15, R_1 = $PhCH_2$, R_2 = CH_3
16, R_1 = H, R_2 = CH_3

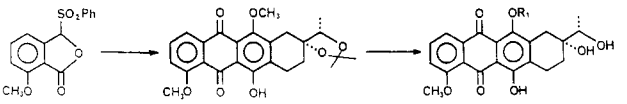


17

18, R_1 = CH_3, R_2 = $PhCH_2$
19, R_1 = $PhCH_2$, R_2 = CH_3

20

Scheme II. Synthesis of 9*R*,13*S* Isomer 24



21 22

23, R_1 = CH_3
24, R_1 = H

by HPLC[14] and NMR were identical with the initial product and showed no indication of a second diastereomer. In addition the chiroptical properties of both initial and recovered products were identical within experimental error. The results constituted the first total synthesis of **24** in optically pure form.

Preparation of (9*R*,13*R*)-7-Deoxy-13-dihydrodaunomycinone (28). Entry to the 13*R* series of compounds proved more difficult as attempts to prepare the diol **12** by inversion of the secondary center in **6** with reagents such as CsOAc or $CsOCOCF_3$ yielded mainly the epoxide **20**. Reduction of the chiral ketones **18** and **19** with sodium borohydride proceeded with total lack of diastereoselection to yield 1:1 mixtures of **6** + **12** and **7** + **13**, respectively, but a preparative separation could be achieved only in the latter case. In order to establish unequivocally the configuration of the secondary centers, the isomeric diols **7** and **13** were converted to the isopropylidene derivatives **9** and **15** and the products subjected to NOE analysis according to the method of Ogawa.[15]

An examination of molecular models reveals that the ketal **15** derived from the *R*,*R* diol should show an Over-

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(11) Russell, R. A.; Warrener, R. N.; Irvine, R. W.; Krauss, A. S. *Tetrahedron Lett.* **1984**, *25*, 1517.
(12) Russell, R. A.; Krauss, A. S.; Irvine, R. W.; Warrener, R. N. *Aust. J. Chem.* **1985**, *38*, 179.
(13) Model studies using the chiral diol **6** have shown that under these conditions no racemization of either chiral center occurs.
(14) HPLC was conducted on a Perkin-Elmer High Speed C18 column using MeOH/H_2O (3:1) as eluent. This analytical method clearly resolved the 13*R* and 13*S* isomers.
(15) Ogawa, Y.; Mori, H.; Yamada, N.; Kon, K.; *J. Antibiot.* **1984**, *37*, 44.

hauser enhancement between the side chain methyl groups and the nonbenzylic ring protons, while the corresponding effect in the *R,S* isomer involves the methyl group and the benzylic protons at C1. The NOE results justify the stereochemistry assigned to **9** and **15** and provided unequivocal support for the stereochemistry of the related chiral diol **7**.[12]

Hydrogenolysis of the benzyl ether in **15** produced the phenol **16**, which, when oxidized with thallium(III) nitrate, afforded the dienone **17**. In keeping with our earlier findings on modal selectivity[11] in (phenylsulfonyl)phthalide anion–quinone monoketal condensations, this mode B type reaction between the dienone **17** and **25** proceeded in only poor yield (12%) to afford the quinone **26**. Deketalization of **26** formed the diol **27**, which demethylated slowly with BCl_3 at −42 °C to afford (9*R*,13*R*)-7-deoxy-13-dihydrodaunomycinone (**28**) (Scheme III), mp 231 °C, $[\alpha]_D$ −62°. Analysis of isomer **28** by HPLC confirmed the absence of any of the 9*R*,13*S* isomer in this product, an observation further supported by ^1H NMR spectroscopy.

A comparison of the 270-MHz ^1H NMR spectra of the 9*R*,13*S* isomer **24** and the 9*R*,13*R* isomer **28** enabled a clear distinction to be drawn between the two synthetic products.[16] Although no sample of the authentic natural product was available for direct comparison,[17] the reported spectroscopic data matched only the 9*R*,13*S* product. Furthermore the reported[8] melting point of 243–245 °C matches within experimental error that of the synthetic 9*R*,13*S* isomer **24**. The discrepancy between our measured specific rotation ($[\alpha]_D$ −108° (*c* 0.128)) and that reported in the literature ($[\alpha]_D$ −128° (*c* 0.22)) is difficult to explain. The variation cannot be attributed to our recently described solvent induced effects,[18] since both measurement were recorded on solutions in 1:1 $CHCl_3$/MeOH. It may however be due to concentration effects, as our sample of the 9*R*,13*S* isomer **24** was too insoluble in 1:1 $CHCl_3$/MeOH to permit $[\alpha]_D$ measurements at the original concentration.

Experimental Section[19]

(4*R*,5*S*)-(−)-5′-(Benzyloxy)-8′-methoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalene] (8). The optically pure (−)-diol **6** (2.0 g, 6.1 mmol) and *p*-toluenesulfonic acid (0.04 g) were dissolved in dry DMF (20 mL). 2,2-Dimethoxypropane (2.8 mL) was then added, and the mixture was stirred at room temperature for 1 h. The reaction mixture was poured onto brine/water (1:1; 400 mL) and extracted with EtOAc (4 × 100 mL). The combined extracts were washed successively with water (3 × 200 mL), saturated sodium bicarbonate solution (200 mL), and brine (200 mL), dried, filtered, and evaporated. The *isopropylidene compound* 8 (2.2 g; 98%) crystallized slowly on standing: mp 99–101 °C; $[\alpha]_D$ −127.7°, (*c* 0.95); IR 2950, 2930, 1590, 1450, 1437, 1379, 1369, 1316, 1250, 1090, 1064, 1047 cm^{-1}; ^1H NMR δ 7.38 (m, 5 H, Ar H), 6.64 (AB q, 2 H, H6′, 7′), 5.00 (s, 2 H, Ar CH_2), 4.01 (q, 1 H, H5, *J* = 6.3 Hz), 3.77 (s, 3 H, OCH_3), 3.04 (m, 2 H, H4′), 2.76 (AB q, 2 H, H1′), 1.98 (m, 1 H, H3′), 1.79 (m, 1 H, H3′), 1.47 (s, 3 H, $C2CH_3$), 1.39 (s, 3 H, $C5CH_3$, *J* = 6.3 Hz); ^{13}C NMR δ 151.6, 150.2, 137.8, 128.5 (2 C), 127.7, 127.1 (2 C), 126.4, 125.6, 108.5, 107.3, 106.8, 80.4, 79.3, 70.2, 55.6, 32.1, 30.4, 28.9, 27.1, 21.8, 15.7.

Anal. Calcd for $C_{23}H_{28}O_4$: C, 74.97; H, 7.66. Found: C, 75.14; H, 7.83.

(4*R*,5*S*)-(+)-8′-Methoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalen]-5′-ol (10). A solution of the optically pure (−)-isopropylidene compound 8 (2.1 g, 5.7 mmol) in EtOAc (100 mL) and glacial HOAc (0.5 mL) was hydrogenated over palladium on charcoal catalyst (10%; 250 mg) for 40 h. The reaction mixture was then filtered, and the filtrate was washed successively with saturated sodium bicarbonate solution (2 × 100 mL) and brine (100 mL), dried, filtered, and evaporated. The crude product was recrystallized from Et_2O/petrol to give the *phenol* **10** as colorless prisms (1.44 g; 91%): mp 164–166 °C; $[\alpha]_D$ + 3.9° (*c* 0.925), $[\alpha]_{365}$ +23.2° (*c* 0.925); IR 3600, 2980, 2930, 1600, 1455, 1435, 1379, 1368, 1230, 1157, 1090, 1072, 1045, 1028, 995 cm^{-1}; ^1H NMR δ 6.54 (s, 2 H, H6′,7′), 4.97 (br s, 1 H, OH), 4.06 (q, 1 H, H5, *J* = 6.3 Hz), 3.76 (s, 3 H, OCH_3), 2.63–2.92 (m, 4 H, H1′,4′), 1.99 (m, 1 H, H3′), 1.82 (m, 1 H, H3′), 1.47 (s, 3 H, $C2CH_3$), 1.40 (s, 3 H, $C2CH_3$), 1.17 (d, 3 H, $C5CH_3$, *J* = 6.3 Hz); ^{13}C NMR δ 151.5, 147.0, 125.4, 123.8, 111.7, 108.1, 107.0, 80.4, 79.3, 55.8, 31.9, 30.3, 28.8, 27.2, 21.4, 15.6.

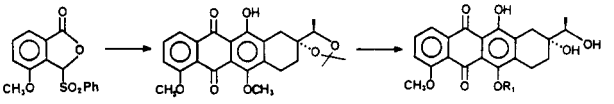
Anal. Calcd for $C_{16}H_{22}O_4$: C, 69.04; H, 7.97. Found: C, 69.39; H, 8.27.

(4*R*,5*S*)-(+)-8′,8′-Dimethoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalen]-5′(8′*H*)-one (11). A mixture of the (+)-phenol **10** (1.20 g, 4.3 mmol) and sodium bicarbonate (1.5 g) in MeOH (60 mL), THF (30 mL), and trimethyl orthoformate (40 mL) was stirred and cooled to 0 °C. Thallium(III) nitrate trihydrate (2.08 g) was then added, and the mixture was stirred at 0 °C for 1.5 h. The reaction mixture was then poured into water (500 mL) and extracted with CH_2Cl_2 (4 × 100 mL). The combined extracts were washed successively with water (200 mL) and brine (200 mL), dried, filtered, and evaporated. The residue was flash chromatographed (15% EtOAc in petrol) to give the dienone **11** as a pale yellow oil (1.26 g; 95%): $[\alpha]_D$ +18.6° (*c* 0.995); IR 2990, 2945, 2840, 1680, 1645, 1625, 1382, 1373, 1292, 1155, 1080, 1000, 971, 889 cm^{-1}; ^1H NMR δ 6.77 (d, 1 H, H6′, *J* = 10.3 Hz), 6.43 (d, 1 H, H7′, *J* = 10.3 Hz), 4.01 (q, 1 H, H5, *J* = 6.5 Hz), 3.30 (s, 3 H, OCH_3), 3.18 (s, 3 H, OCH_3), 2.56 (m, 2 H, H4′), 2.44 (dd, 1 H, H1′, *J* = 19.0 Hz, *J* = 1.3 Hz), 2.26 (ddd, 1 H, H1′, *J* = 19.0 Hz, *J* = 2.2 Hz), 1.79 (m, 1 H, H3′), 1.62 (m, 1 H, H3′), 1.44 (s, 3 H, $C2CH_3$), 1.36 (s, 3 H, $C2CH_3$), 1.27 (d, 3 H, $C5CH_3$, *J* = 6.5 Hz).

Anal. Calcd for $C_{17}H_{24}O_5$: C, 66.21; H, 7.84. Found: C, 66.12; H, 7.90.

(4*R*,5*S*)-(−)-1′,6′-Dimethoxy-11′-hydroxy-2,2,5-trimethyl-9′,10′-dihydrospiro[1,3-dioxolane-4,8′(7′*H*)-naphthacene]-5′,12′-dione (22). A solution of diisopropylamine (0.475 mL, 3.39 mmol) in THF (10 mL) at 0 °C under an argon atmosphere was treated with *n*-BuLi (2.11 mL, 1.6 M, 3.38 mmol) for 5 min. The solution was cooled to −78 °C and a solution of **21** (1.09 g, 3.58

Scheme III. Synthesis of 9*R*,13*R* Isomer 28



25 **26** **27**, $R_1 = CH_3$; **28**, $R_1 = H$

(16) At 270 MHz the 9*R*,13*S* isomer shows the H8 resonances as a poorly resolved six-line multiplet centered at δ 1.5 and an ill-defined multiplet at δ 1.88. The corresponding H8 protons in the 9*R*,13*R* isomer appear as a narrow, two-proton, multiplet at δ 1.7.

(17) Attempts to contact Drs. Kern, Bunge, French, and Dion[8] at their original address were unsuccessful.

(18) Russell, R. A.; Irvine, R. W.; Krauss, A. S. *Tetrahedron Lett.* **1984**, 5817.

(19) The following abbreviations have been used throughout the Experimental Section: *n*-butyllithium (*n*-BuLi), chloroform ($CHCl_3$), dichloromethane (CH_2Cl_2), diethyl ether (Et_2O), ethyl acetate (EtOAc), methanol (MeOH), tetrahydrofuran (THF), acetone (Me_2CO). Standardization of *n*-BuLi was performed by the method of Watson and Eashan (*J. Organomet. Chem.* **1967**, *9*, 165). Ethanol-free $CHCl_3$ was prepared by shaking with concentrated sulfuric acid, washing with water, and distilling from $CaCl_2$. Anhydrous CH_2Cl_2 was distilled from P_2O_5 under an argon atmosphere. Anhydrous THF was distilled from $LiAlH_4$ under an argon atmosphere. Dry acetone was distilled from boric anhydride. Petrol refers to a hydrocarbon fraction with bp 60–70 °C. Column chromatography was performed on Merck silica (70–230 mesh). Melting points were recorded on a Kofler micro heating stage apparatus and are uncorrected. ^1H NMR and ^{13}C NMR spectra were recorded on a Brüker HFX-270 at 270 and 67.89 MHz, respectively. Spectra were recorded in $CDCl_3$ with tetramethylsilane as an internal reference. Infrared spectra ($CHCl_3$ solutions) were recorded on a Perkin-Elmer 283 spectrophotometer. High-resolution mass measurements were performed on an A.E.I. MS 902 spectrometer. Unless otherwise stated, polarimetry was performed on solutions in $CHCl_3$ on Perkin-Elmer 241 polarimeter. Apparatus used in reactions performed under an argon atmosphere was flamed out and cooled under a stream of argon. Organic solutions were dried over magnesium sulfate and filtered through a sintered funnel prior to evaporation.

mmol) in THF (80 mL) introduced dropwise over 0.25 h. After the mixture was stirred for a further 0.25 h at −78 °C, a solution of **11** (0.315 g, 1.02 mmol) in THF (5 mL) was introduced dropwise over 1 min and the resulting mixture allowed to warm to 0 °C over 4 h. The mixture was partitioned between 50% brine/water (100 mL) and EtOAc (50 mL) and the aqueous phase extracted with EtOAc (2 × 50 mL). The combined organic phase was washed successively with water (50 mL) and brine (50 mL) and dried and the solvent evaporated. Column chromatography of the residue (25% EtOAc in petrol) afforded unreacted **11** (0.018 g, 6%) and **22** as an orange solid (0.423 g, 94%). Crystallization from Et_2O gave orange needles: mp 160–161 °C; $[\alpha]_D$ −36.7° (*c* 0.81, 1:1 $CHCl_3$/MeOH); IR 3530, 2980, 2940, 2870, 1664, 1625, 1588, 1425, 1381, 1290, 1035, 996, 979, 922, 908 cm^{-1}; ^1H NMR δ 13.81 (s, 1 H, OH), 7.95 (dd, 1 H, H4′, *J* = 7.7 Hz, *J* = 1.4 Hz), 7.71 (dd, 1 H, H3′, *J* = 7.7 Hz, *J* = 8.1 Hz) 7.30 (dd, 1 H, H2′, *J* = 8.1 Hz, *J* = 1.4 Hz), 4.10 (q, 1 H, H5, *J* = 1.6 Hz), 4.06 (s, 3 H, C1′OCH_3), 3.87 (s, 3 H, C6′OCH_3), 2.60–3.25 (m, 4 H, H7′, 10′), 1.68–2.09 (m, 2 H, H9′), 1.44 (s, 3 H, C2CH_3), 1.39 (s, 3 H, C2CH_3), 1.24 (d, 3 H, C5CH_3, *J* = 6.3 Hz); ^{13}C NMR δ 188.7, 181.8, 160.4, 157.8, 152.0, 140.7, 137.2, 135.5 (2 C), 120.5 (2 C), 119.9, 117.1, 113.7, 107.2, 79.7, 79.1, 60.9, 56.7, 30.8 (2 C), 28.7, 26.9, 21.7, 15.3.

Anal. Calcd for $C_{25}H_{26}O_7$: C, 68.48; H, 5.98. Found: C, 68.74; H, 6.19.

(8*R*,1′*S*)-(−)-8,11-Dihydroxy-1,6-dimethoxy-8-(1′-hydroxyethyl)-7,8,9,10-tetrahydro-5,12-naphthacenedione (23). A solution of **22** (0.10 g) in MeOH (25 mL) and THF (25 mL) was stirred with strong acid resin [Biorad AG 50W-X2(H)] (1.0 g) at reflux for 2.5 h. The hot solution was filtered through Celite and the residue washed with hot CH_2Cl_2 until the filtrate was colorless. Evaporation of the solvent afforded **23** as a yellow powder (0.091 g, 100%). Crystallization from CH_2Cl_2/EtOAc gave yellow needles: mp 225 °C; $[\alpha_D]$ −92.4° (*c* 0.28, 1:1 $CHCl_3$/MeOH); IR 3330, 3000, 2925, 2835, 1658, 1620, 1585, 1418, 1382, 1354, 1290, 1195, 1135, 1100, 1003, 982, 921 cm^{-1}; ^1H NMR (Me_2SO-d_6) δ 13.70 (s, 1 H, C11OH), 7.94 (dd, 1 H, H4, *J* = 7.5 Hz, *J* = 1.0 Hz), 7.74 (dd, 1 H, H3, *J* = 8.0 Hz, *J* = 7.5 Hz), 7.35 (dd, 1 H, H2, *J* = 8.0 Hz, *J* = 1.0 Hz), 4.10 (s, 3 H, C1OCH_3), 3.87 (s, 3 H, C6OCH_3), 3.85 (q, 1 H, H1′, *J* = 6.5 Hz), 2.56–3.18 (m, 4 H, H7,10), 2.85 (br s, 2 H, C8OH, C1′OH), 1.60–2.25 (m, 2 H, H9), 1.31 (d, 3 H, H2′, *J* = 6.5 Hz).

Anal. Calcd for $C_{22}H_{22}O_7$: C, 66.32; H, 5.57. Found: C, 66.21; H, 5.78.

(8*R*,1′*S*)-(−)-8-(1′-Hydroxyethyl)-1-methoxy-6,8,11-trihydroxy-7,8,9,10-tetrahydro-5,12-naphthacenedione [(9*R*,13*S*)-7-Deoxy-13-dihydrodaunomycinone] (24). To a stirred solution of the ketal **22** (200 mg) in dry CH_2Cl_2 (150 mL) under an argon atmosphere at −78 °C was added, dropwise, a solution of boron trichloride in dry CH_2Cl_2 (1.80 mL, 1 M) and the mixture stirred at −78 °C for 0.25 h. MeOH (5 mL) was added, the mixture stirred at −78 °C for a further 5 min and poured into dilute aqueous sodium bicarbonate (0.1 M, 120 mL), and the aqueous phase extracted with CH_2Cl_2 (2 × 50 mL). The combined organic phase was washed successively with water (100 mL) and brine (100 mL) and dried and the solvent evaporated. the solid residue was taken up in hot $CHCl_3$ (150 mL) and filtered through Celite and the filtrant washed with hot $CHCl_3$ (5 × 20 mL). Evaporation of solvent from the combined filtrate yielded the *title compound* as a red solid (172 mg, 98%), which upon crystallization from a mixture of $CHCl_3$ and MeOH afforded red needles: mp 245–247 °C (sweats at 230 °C); $[\alpha]_D$ −108° (*c* 0.128, 1:1 $CHCl_3$/MeOH); IR 3450, 1609, 1587, 1402, 1283, 1249, 1215, 1061, 1000, 988, 820 cm^{-1}; ^1H NMR (Me_2SO -d_6) δ 13.91 (s, 1 H, C11OH), 13.38 (s, 1 H, C6OH), 7.86 (m, 2 H, H3,4), 7.59 (m, 1 H, H2), 4.68 (d, 1 H, C1′OH, *J* = 4 Hz), 4.26 (s, 1 H, C8OH), 3.96 (s, 3 H, OCH_3), 3.55 (dq, 1 H, H1′, *J* = 10 Hz, *J* = 4 Hz), 2.51–2.95 (m, 4 H, H7,10), 1.89 (m, 1 H, H9), 1.50 (m, 1 H, H9), 1.14 (d, 3 H, H2′, *J* = 6 Hz).

Anal. Calcd for $C_{21}H_{20}O_7$: C, 65.62; H, 5.24. Found: C, 65.37; H, 5.30.

(2*R*,1′*R*)-(−)-8-(Benzyloxy)-2-(1′ hydroxyethyl)-5-methoxy-1,2,3,4-tetrahydronaphthalen-2-ol (13). To a solution of hydroxy ketone **19** (535 mg) in ethanol (50 mL) was added sodium borohydride (64 mg) and the mixture stirred at 20 °C for 1 h. The solvent was evaporated and the residue partitioned between water (50 mL) and CH_2Cl_2 (50 mL). The aqueous phase was acidified with 1 M hydrochloric acid and extracted with CH_2Cl_2 (2 × 20 mL), the combined organic phase washed successively with water (2 × 30 mL) and brine (30 mL) and dried, and the solvent evaporated. Column chromatography of the residue in very dilute solution to prevent crystallization of the mixture on the column (50% EtOAc, in hexane) afforded diol **7** (128 mg, 24%), $[\alpha]_D$ −37.9° (*c* 0.73.) [lit.[12] −38.6° (*c* 1.40)], diol **13** (158 mg, 29.5%), and a mixture of **7** and **13** (225 mg). The mixture of **7** and **13** (353 mg) was reoxidized with Fetizon's reagent (3.5 g) in benzene (50 mL) as previously described[12] and the product reduced with sodium borohydride as described above. These steps were repeated two further times to yield a total of 445 mg of diol **13** (83%). Recrystallization from Et_2O afforded colorless needles: mp 134–135 °C; $[\alpha]_D$ −17.3° (*c* 0.65); IR 3570, 2940, 2835, 1600, 1463, 1380, 1328, 1254, 1090, 950, 899, 871 cm^{-1}; ^1H NMR δ 7.22–7.41 (m, 5 H, Ar), 6.62 (AB q, 2 H, H6,7), 4.97 (s, 2 H, $PhCH_2$), 3.75 (s, 3 H, OCH_3), 3.69 (dq, 1 H, H1′, *J* = 6.4 Hz, *J* = 4.7 Hz), 2.60–2.86 (m, 4 H, H1,4), 2.51 (d, 1 H, OH, *J* = 4.7 Hz), 2.23 (s, 1 H, OH), 1.88 (m, 1 H, H3), 1.57 (ddd, 1 H, H3 *J* = 6.6 Hz, *J* = 9.8 Hz, *J* = 13.1 Hz), 1.18 (d, 3 H, H2′, *J* = 6.4 Hz); ^{13}C NMR δ 151.4 (C8 or C5), 150.9 (C5 or C8), 137.6 (Ar), 128.5 (2 C, Ar), 127.7 (Ar), 127.2 (2 C, Ar), 126.1 (C9 or C10), 124.8 (C10 or C9), 108.9 (C6 or C7), 107.0 (C7 or C6), 72.6 (C1′), 72.2 (C2), 70.4 ($PhCH_2$), 55.5 (OCH_3), 33.2 (C1), 27.2 (C4), 19.9 (C3), 17.1 (C2′).

Anal. Calcd for $C_{20}H_{24}O_4$: C, 73.1; H, 7.4. Found: C, 72.9, H, 7.6.

(4*R*,5*R*)-(−)-8′-(Benzyloxy)-5′-methoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalene] (15). A solution of the diol **13** (184 mg), 2,2-dimethoxypropane (300 μL), and *p*-toluenesulfonic acid (3 mg) in dry DMF (4 mL) was stirred at 15 °C for 6 h. The mixture was poured into water (50 mL) and extracted with Et_2O (3 × 30 mL) the combined organic phase washed with water (3 × 30 mL) and brine (30 mL) and dried, and the solvent evaporated to give the ketal **15** as a colorless solid (206 mg, 100%). Crystallization from a mixture of Et_2O and hexane afforded colorless needles: mp 157.5–158 °C; $[\alpha]_D$ −46.7° (*c* 0.93); IR 2980, 2940, 2880, 2835, 1600, 1475, 1460, 1452, 1379, 1370, 1325, 1248, 1160, 1119, 1080, 1067, 1002 cm^{-1}; ^1H NMR δ 7.28–7.42 (m, 5 H, Ar) 6.63 (AB q, 2 H, H6′,7′), 5.01 (AB q, 2 H, $PhCH_2$), 4.11 (q, 1 H, H5, *J* = 6.4 Hz), 3.78 (s, 3 H, OCH_3), 2.62–2.99 (m, 4 H, H1′,4′), 1.98 (m, 1 H, H3′), 1.94 (m, 1 H, H3′), 1.46 (s, 3 H, C2CH_3), 1.39 (s, 3 H, C2CH_3), 1.27 (d, 3 H, C5CH_3, *J* = 6.4 Hz); ^{13}C NMR δ 151.5 (C8′ or C5′), 150.9 (C5′ or C8′), 137.8 (Ar), 128.5 (2 C, Ar), 127.7 (Ar), 127.2 (2 C, Ar), 127.0 (C9′ or C10′), 124.9 (C10′ or C9′), 108.5 (C6′ or C7′), 107.2 (C7′ or C6′), 107.1 (C2), 79.8 (C4), 78.2 (C5), 70.3 ($PhCH_2$), 55.6 (OCH_3), 33.1 (C1′), 28.7 (C2CH_3), 27.1 (C2CH_3), 26.5 (C4′), 19.6 (C3′), 13.6 (C5CH_3).

Anal. Calcd for $C_{23}H_{28}O_4$ C, 75.0; H, 7.7. Found: C, 75.1; H, 7.7.

(4*R*,5*R*)-(−)-5′-Methoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalen]-8′-ol (16). A solution of the ketal **15** (193 mg) in EtOAc (30 mL) and HOAc (150 μL) was stirred with 10% palladized charcoal (40 mg) under a hydrogen atmosphere for 16 h at room temperature. The mixture was filtered through Celite, the filtrant washed with Et_2O (3 × 30 mL), the combined filtrate shaken successively with 5% aqueous sodium bicarbonate (30 mL) and brine (30 mL) and dried, and the solvent evaporated to give the *title phenol* as a colorless syrup, which crystallized upon trituration with Et_2O (144 mg, 99%). Recrystallization from a mixture of Et_2O and hexane afforded colorless prisms: mp 135–135.5 °C (sweats at 130 °C); $[\alpha]_D$ −51.8° (*c* 0.95); IR 3590, 2980, 2940, 2870, 2835, 1609, 1475, 1460, 1379, 1369, 1321, 1255, 1158, 1118, 1090, 1080, 1003, 982, 944, 859 cm^{-1}; ^1H NMR δ 6.54 (s, 2 H, H6′,7′), 4.54 (s, 1 H, OH), 4.13 (q, 1 H, H5, *J* = 6.4 Hz), 3.77 (s, 3 H, OCH_3), 2.94 (ddd, 1 H, H4′, *J* = 17.7 Hz, *J* = 5.8 Hz, *J* = 2.2 Hz), 2.60–2.78 (m, 3 H, H1′,4′), 1.97 (m, 1 H, H3′), 1.94 (m, 1 H, H3′), 1.46 (s, 3 H, C2CH_3), 1.39 (s, 3 H, C2CH_3), 1.28 (d, 3 H, C5CH_3, *J* = 6.4 Hz); ^{13}C NMR δ 151.3 (C5′), 147.5 (C8′), 126.9 (C9′), 122.7 (C10′), 111.6 (C7′), 108.0 (C6′), 107.3 (C1), 79.8 (C4), 78.3 (C5), 55.8 (OCH_3), 32.9 (C1′), 28.7 (C2CH_3), 27.0 (C2CH_3), 26.5 (C4′), 19.8 (C3′), 13.6 (C5CH_3).

Anal. (accurate mass) Calcd for $C_{16}H_{22}O_4$: 278.1518. Found: 278.1521.

(4*R*,5*R*)-(−)-5′,5′-Dimethoxy-2,2,5-trimethyl-3′,4′-dihydrospiro[1,3-dioxolane-4,2′(1′*H*)-naphthalen]-8′(5′*H*)-one (17).

A mixture of the phenol **16** (132 mg) and sodium bicarbonate (100 mg) in MeOH (6 mL), THF (3 mL), and trimethyl orthoformate (3 mL) was stirred at 0 °C. Thallium(III) nitrate trihydrate (215 mg) was added and the mixture stirred at 0 °C for 0.5 h. The reaction mixture was poured into water (50 mL) and extracted with CH_2Cl_2 (3 × 30 mL). The combined extracts were washed successively with water (3 × 20 mL) and brine (20 mL) and dried, and the solvent was evaporated. Flash column chromatography of the residue (15% EtOAc in hexane) afforded the *title dienone* as a colorless syrup (128 mg, 88%): $[\alpha]_D$ −43.0° (*c* 1.12); IR (film) 2880, 2840, 2775, 1672, 1645, 1620, 1450, 1380, 1371, 1290, 1160, 1090, 1070, 1005, 971 cm^{-1}; ^1H NMR δ 6.77 (d, 1 H, H7′, *J* = 10.2 Hz), 6.40 (d, 1 H, H6′, *J* = 10.2 Hz), 4.05 (q, 1 H, H5, *J* = 6.3 Hz), 3.22 (s, 6 H, OCH_3), 2.29–2.80 (m, 4 H, H1′,4′), 2.00 (m, 1 H, H3′), 1.82 (m, 1 H, H3′), 1.41 (s, 3 H, $C2CH_3$), 1.33 (s, 3 H, $C2CH_3$), 1.23 (d, 3 H, $C5CH_3$, *J* = 6.3 Hz).

Anal. (accurate mass) calcd for $C_{17}H_{24}O_5$: 308.1624. Found: 308.1628.

(4*R*,5*R*)-(−)-1′,11′-Dimethoxy-6′-hydroxy-2,2,5-trimethyl-9′,10′-dihydrospiro[1,3-dioxolane-4,8′(7′*H*)-naphthacene]-5′,12′-dione (26). A solution of diisopropylamine (173 μL) in THF (5 mL) under an argon atmosphere was stirred at 0 °C with *n*-BuLi (780 μL, 1.58 M) for 5 min. The solution was cooled to −78 °C and a solution of the phthalide **25** (400 mg) in THF (15 mL) added dropwise over 5 min. After the mixture was stirred for 0.25 h at −78 °C a solution of the dienone **17** (115 mg) in THF (3 mL) was added. The vessel was removed from the cold bath and the reaction mixture stirred until ambient temperature (18 °C) was attained (0.5 h). The reaction mixture was poured into water (70 mL) and extracted with EtOAc (2 × 20 mL), and the combined extracts were washed successively with water (20 mL) and brine (20 mL) and dried, and the solvent evaporated. The residue was dissolved in CH_2Cl_2 (1 mL), Et_2O added (5 mL), and the solution allowed to stand until precipitation of unreacted **25** was complete. The solid material was removed by filtration, the filtrant washed well with Et_2O, and the combined filtrate concentrated and flash column chromatographed (20% EtOAc in petrol) to give unreacted **17** (93 mg, 81%) and the *title compound* (19 mg, 12%). Crystallization from MeOH afforded orange plates: mp 236–238 °C (sweats at 230 °C); $[\alpha]_D$ −62.0° (*c* 0.18, 1:1 MeOH/$CHCl_3$); IR 3520, 2990, 2945, 2850, 1779, 1725, 1670, 1630, 1588, 1450, 1409, 1385, 1368, 1278, 1166, 1121, 1098, 1085, 1070, 1020, 1005, 989, 948, 875 cm^{-1}; ^1H NMR δ 13.34 (s, 1 H, OH), 7.90 (dd, 1 H, H4′, *J* = 8.2 Hz, *J* = 0.8 Hz), 7.67 (dd, 1 H, H3′, *J* = 8.4 Hz, *J* = 8.2 Hz), 7.32 (dd, 1 H, H2′, *J* = 8.4 Hz, *J* = 0.8 Hz), 4.03 (s, 3 H, C1′OCH_3), 3.93 (s, 3 H, C11′OCH_3), 3.20 (ddd, 1 H, H10′, *J* = 17.9 Hz, *J* = 4.2 Hz, *J* = 1.4 Hz), 2.65–2.97 (m, 3 H, H7′,10′), 2.04 (m, 1 H, H9′), 1.99 (m, 1 H, H9′), 1.48 (s, 3 H, $C2CH_3$), 1.41 (s, 3 H, $C2CH_3$), 1.30 (d, 3 H, $C5CH_3$, *J* = 6.4 Hz).

Anal. (accurate mass) calcd for $C_{25}H_{26}O_7$: 438.1679. Found: 438.1673.

(8*R*,1′*R*)-(−)-8-(1′-Hydroxyethyl)-1-methoxy-6,8,11-trihydroxy-7,8,9,10-tetrahydro-5,12-naphthacenedione [(9*R*,13*R*)-7-Deoxy-13-dihydrodaunomycinone] (28). A solution of the ketal **26** (30 mg) in dry CH_2Cl_2 (20 mL) was stirred at −42 °C under an argon atmosphere. Boron trichloride (1.02 M in CH_2Cl_2, 805 μL, 12 equiv) was added and stirring maintained at −42 °C for 2 h. MeOH (2 mL) was added and the mixture stirred for 3 min at −42 °C and then poured into water (50 mL) containing saturated sodium bicarbonate solution (1 mL). The aqueous phase was extracted with $CHCl_3$ (2 × 20 mL), the combined organic phase washed successively with water (2 × 20 mL) and brine (30 mL) and dried, and the solvent evaporated. Column chromatography of the residue (acid washed silica; 10% MeOH in CH_2Cl_2) afforded diol **27** (8 mg, 29%) and the *title diol* (17.3 mg, 66%). Recrystallization from a mixture of CH_2Cl_2 and hexane gave red prisms: mp 245–247 °C; $[\alpha]_D$ −61° (*c* 0.14, 1:1 MeOH/$CHCl_3$); IR 3580, 2920, 1615, 1587, 1580, 1450, 1408, 1284, 1268, 1067, 988 cm^{-1}; ^1H NMR δ (Me_2SO-d_6) 13.89 (s, 1 H, C11OH), 13.38 (s, 1 H, C6OH), 7.82–7.89 (m, 2 H, H3,4), 7.58 (dd, 1 H, H2, *J* = 5.9 Hz, *J* = 3.7 Hz), 4.68 (d, 1 H, C1′OH, *J* = 5.2 Hz), 4.28 (s, 1 H, C8OH), 3.96 (s, 3 H, OCH_3), 3.48 (dq, 1 H, H1′, *J* = 6.3 Hz, *J* = 5.2 Hz), 2.51–2.79 (m, 4 H, H7,10), 1.69 (m, 2 H, H9), 1.17 (d, 3 H, H2′, *J* = 6.3 Hz).

Anal. (accurate mass) Calcd for $C_{21}H_{20}O_7$: 384.1209. Found: 384.1248.

Registry No. (−)-**6**, 100939-58-0; (−)-**7**, 90744-27-7; (−)-**8**, 100939-59-1; (+)-**10**, 100939-60-4; (+)-**11**, 100939-61-5; (−)-**13**, 100992-84-5; (−)-**15**, 101052-85-1; (−)-**16**, 100992-85-6; (−)-**17**, 100939-63-7; **19**, 81504-96-3; **21**, 65131-09-1; (−)-**22**, 95496-08-5; (−)-**23**, 100939-62-6; (−)-**24**, 40940-87-2; **25**, 74724-81-5; (−)-**26**, 100939-64-8; (−)-**27**, 100939-65-9; (−)-**28**, 100992-86-7.

Oxidative Cleavage of 1,2-Diols to Carboxylic Acids by Hydrogen Peroxide

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While a number of oxidants have been described in combination with a metal catalyst for oxidative cleavage of 1,2-diols to carboxylic acids,[1] almost no attention has been devoted to the employment of hydrogen peroxide for this reaction, and the few results that have appeared so far[2] are fragmentary and of little preparative value.

We now report that aqueous hydrogen peroxide in conjunction with catalytic amounts of tungstate and phosphate (or arsenate) ions,[3] under acidic conditions, provides a synthetically useful procedure for the highly selective oxidative cleavage of water-soluble 1,2-diols to carboxylic acids. The method, which utilizes a rather inexpensive catalyst and a cheap nonpolluting oxidant, is particularly suitable when large-scale reactions are considered. Primary–secondary and secondary–secondary as well as secondary–tertiary 1,2-diols (open chain and cyclic) can satisfactorily be oxidized.

The reaction is conveniently conducted by simply stirring at 90 °C an acidic (pH 2) aqueous solution containing the diol, hydrogen peroxide (in a 10% molar excess over the stoichiometric amount required[4]), and the catalyst until the charged oxidant has almost completely disappeared (usually 5 h). A molar ratio for diol/WO_4^{2-}/PO_4^{3-}(AsO_4^{3-}) of 50:2:1 is commonly used. Conventional workup of the reaction mixture affords monobasic, dibasic, and keto acids of satisfactory purity in good to excellent yields (Table I).

The efficiency of the oxidation is dependent upon the pH of the reaction solution. The best results were obtained at pH 2. An increase in pH considerably reduces the activity of the catalytic system. The use of tungstate ions alone as well as replacement of tungsten by molybdenum in the above system also leads to a significant decrease of the yield. It should be pointed out that in the absence of the catalyst oxidation proceeds to only a negligible extent.

Some aspects of the present method are worth mentioning. The reaction appears to be relatively insensitive to geometric constraints. Indeed, *cis*- and *trans*-1,2-cyclohexanediol were both oxidized to adipic acid at nearly similar rates. By contrast, the presence of electron-with-

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(2) (a) Choe, S.; Tsutsumi, S. *Nippon Kagaku Zasshi* **1960**, *81*, 785; *Chem. Abstr.* **1962**, *56*, 9987*b*. (b) Trost, B. M.; Masuyama, Y. *Isr. J. Chem.* **1984**, *24*, 134.

(3) Such a catalytic association has successfully been applied to the epoxidation of unactivated olefins by H_2O_2 under phase-transfer conditions: Venturello, C.; Alneri, E.; Ricci, M. *J. Org. Chem.* **1983**, *48*, 3831.

(4) Oxidation of secondary–tertiary and secondary–secondary 1,2-diols to acids obeys a 1:2 and 1:3 stoichiometry of substrate to H_2O_2, respectively. With primary–secondary 1,2-diols, a 1:4 molar ratio is required as the coproduced formic acid is further oxidized to carbon dioxide under the reaction conditions.

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