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# CHEMICAL STUDIES OF MARINE INVERTEBRATES—XLIII[1]

## NOVEL SESQUITERPENES FROM *CLAVULARIA INFLATA* AND *CLAVULARIA KOELLIKERI* (Coelenterata, Octocorallia, Stolonifera)[2]

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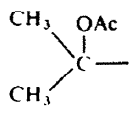
**Abstract** –Two novel sesquiterpenes, 12-acetoxycyclosinularane (**1**) and 12-acetoxysinularene (**2**), have been isolated from *Clavularia inflata*. Their structures have been determined by X-ray diffraction analysis and chemical correlation respectively. Moreover, the new aromadendrane sesquiterpene (1R*, 1aS*, 4R*, 7R*, 7aS*, 7bS*, 5Z)-4,4a,7-trihydroxyaromadendr-5-en-8-oic acid methyl ester (**19**) has been isolated from the related species *C. koellikeri*. Its structure has been established by X-ray diffraction analysis. These compounds are the first sesquiterpenes isolated from Octocorallia of the order Stolonifera.

The chemical examination of the Alcyonacea and Gorgonacea has already afforded a vast array of new sesqui- and diterpenes.[4] In contrast, only one species (*Clavularia inflata*) of the closely related order Stolonifera has been studied until now. From a sample of this species, collected near Laing Island (Papua-New Guinea), three new diterpenes (1R,4R)-dihydroxyclavular-17-ene, (4R)-hydroxyclavulara-1(15),17-diene and (3S,4S)-dihydroxyclavulara-1(15), 17-diene have been isolated.[5] A sample of *C. inflata* collected on the Great Barrier Reef yielded a rearranged dolabellane diterpene besides (3S,4S)-dihydroxyclavulara-1(15),17-diene.[6] In this paper we wish to report the isolation and structure determination of: (i) 12-acetoxycyclosinularane (**1**) and 12-acetoxysinularene (**2**) which are found together with the three aforementioned clavularane diterpenes in the $CH_2Cl_2$ extract of *C. inflata* from Laing Island; (ii) (1R*, 1aS*, 4R*, 7R*, 7aS*, 7bS*, 5Z)-4,4a,7-trihydroxyaromadendr-5-en-8-oic acid methyl ester (**19**) from *C. koellikeri*, collected in the same region.

Compounds **1** and **2** could not be separated by silica gel column chromatography and were obtained in a pure state by a combination of chromatography on $AgNO_3$ impregnated silica gel and preparative gas chromatography. The spectral properties of compound **1** (oil, $C_{17}H_{26}O_2$ by HRMS) indicate the presence of a cyclopropane ring bearing at least one hydrogen atom (1H, d at 0.5 ppm, J = 5Hz), an acetoxyl group ($\nu_{C=O}$ 1735 $cm^{-1}$; $\nu_{C-O}$ 1260 $cm^{-1}$; $^1H$ NMR: 3H singlet at 1.93 ppm), four tertiary methyl groups (3H singlets at 0.83 and 1.10 ppm and one 6H singlet at 1.50 ppm). The latter signal suggests the presence of partial structure A in **1**:




A

The $^{13}C$ NMR spectrum of **1** confirms the presence of an acetoxyl group (C = O: s at 170.34 ppm; C – O: s at 85.87 ppm) and indicates the absence of any further $sp^2$ carbon atom. This implies that **1** is a tetracyclic sesquiterpene. LAH reduction of **1** afforded the oily monohydroxy derivative **3** ($C_{15}H_{24}O$, $M^+$ at *m/e* 220, $\nu_{OH}$ at 3420 $cm^{-1}$). The $^1H$ NMR spectra of **1** and **3** are practically identical, except that the 3H singlet at 1.93 ppm in the spectrum of **1** is lacking in that of **3**, while the 6H singlet at 1.50 ppm has been shifted to 1.24 ppm. This observation confirms the presence of partial structure A in **1**.

Dehydration of **3** with oxalic acid led to a 2:1 mixture of **4** and **5** (as shown by $^1H$ NMR and GLC on a 10% SP 2330 column at 120°). The crude mixture was oxidized with $OsO_4$ affording three isomeric diols. Diol **6** ($M^+$ at *m/e* 236), originating from **4**, could be easily separated from the two other diols **7** and **8**. The latter were not separated from each other but the mass and $^1H$ NMR spectra of the mixture show that they both derive from **5** by $OsO_4$ hydroxylation of the isopropenyl group.

Since diol **6** could be crystallized easily from pentane, its structure was determined by X-ray diffraction analysis. The crystals of **6** belong to space group P $6_322$ with a = 12.82(2), c = 29.63(5) Å, Z = 12. Intensities of 1,310 independent reflections were collected on a Syntex $P2_1$ diffractometer using MoK$\alpha$ radiation (2$\theta$ max = 47°). The structure was solved using the YZARC 78 programs[7] and the refinements were realised using the SHELX 76 programs.[8] $R_{final}$ = 0.062. A computer-generated drawing of **6** (relative configuration) is depicted in Fig. 1 and the atomic coordinates are given in Table 1.

Since **6** originates from **1** by the route shown in Fig. 2, the latter must possess structure **1**. However, this reaction sequence precludes the assignment of the configuration at C-5 in **1**. Cleavage of diol **6** with $NaIO_4$ afforded ketone **9** ($M^+$ at *m/e* 176; $\nu_{C=O}$ at 1720 $cm^{-1}$) exhibiting a positive CD curve (methanol,

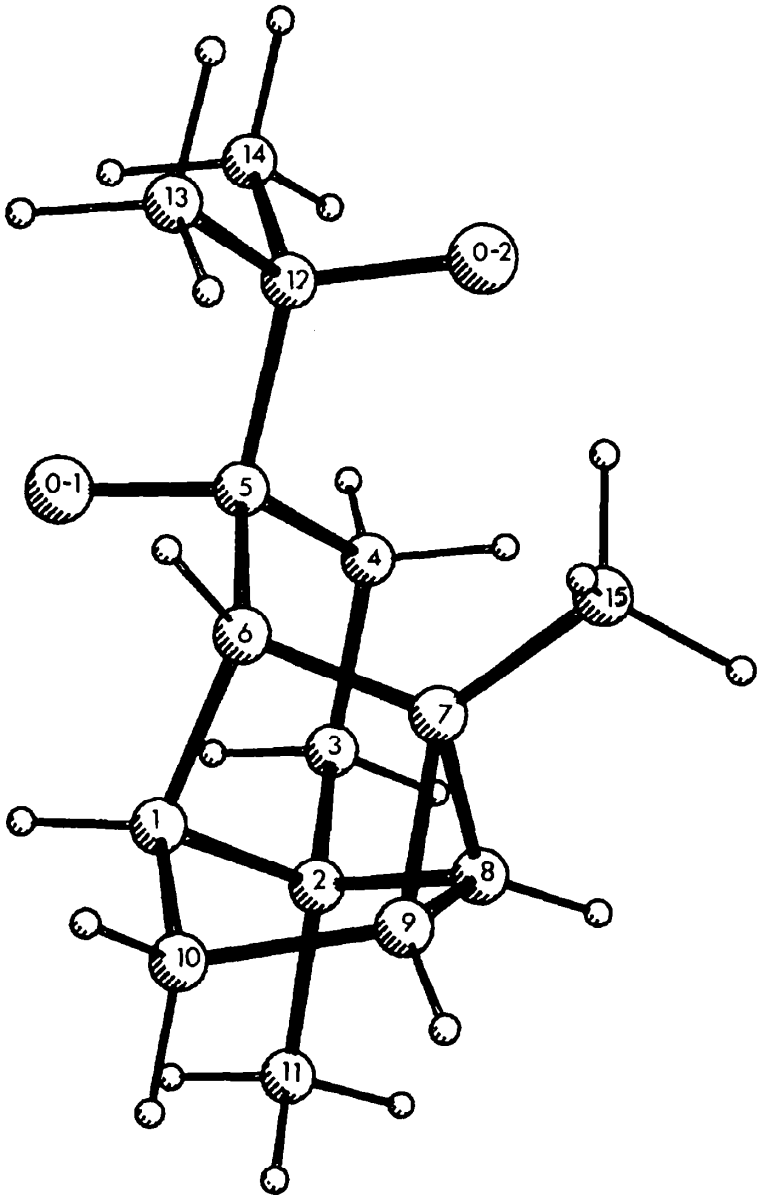
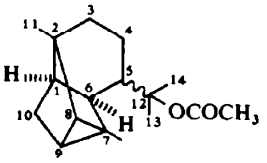
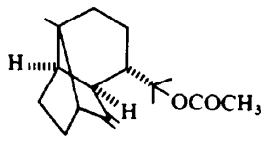



Fig. 1. Computer drawing of compound **6**.



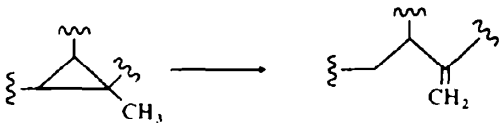

**1**




**2**

$[\theta]_{298}$ +5,102). Application of the octant rule to **9** indicates that its absolute configuration is as shown. The absolute configuration of all related compounds (**1** and **3**–**8**) follows, except at carbon atom C-5. Compound **1** is closely related to sinularene (**10**) isolated from *Sinularia mayi*.[9] If we draw the hypothesis that both **1** and **10** have the same configuration at C-5 (*vide infra*), then **1** could be named 12-acetoxycyclosinularane.

The spectral properties of compound **2** (oil, $C_{17}H_{26}O$ by HRMS) show the presence of an acetoxyl group ($\nu_{C=O}$ 1745 cm$^{-1}$; $\nu_{C-O}$ 1270 cm$^{-1}$; $^1$H NMR: 3H singlet at 1.99 ppm), an exomethylene double bond ($\nu_{C=C}$ at 1680 cm$^{-1}$; $\delta_{C=CH_2}$ at 895 cm$^{-1}$; $^1$H NMR; 1H singlets at 4.67 and 4.85 ppm) and three tertiary methyl groups (3H singlet at 0.98 ppm and 6H singlet at 1.47 ppm). Comparison of the spectral properties of **1** and **2** suggests that **2** could be derived from **1** by the opening of the cyclopropane ring as shown below:




If this is the case, **2** would be 12-acetoxysinularene. To confirm this hypothesis, **2** has been correlated with sinularene, following Fig. 3. To obtain suitable quantities of **2** from the sesquiterpene mixture, two different approaches were used: (a) the **1** + **2** mixture was treated with LAH to afford the alcohols **3** and **11**

Table 1. Atomic coordinates ( $\times 10^4$) of compound **6**

| | X | Y | Z |
|---|---|---|---|
| C-1 | 1840(10) | -559(9) | 1437(4) |
| C-2 | 2661(11) | -1129(10) | 1493(4) |
| C-3 | 3260(11) | -1122(11) | 1037(3) |
| C-4 | 3995(10) | 129(11) | 831(4) |
| C-5 | 3308(10) | 812(10) | 825(4) |
| C-6 | 2787(9) | 748(10) | 1313(4) |
| C-7 | 3614(10) | 970(10) | 1718(4) |
| C-8 | 3528(11) | -205(12) | 1834(4) |
| C-9 | 2809(10) | 218(10) | 2106(3) |
| C-10 | 1509(10) | -413(11) | 1917(4) |
| C-11 | 1991(12) | -2410(10) | 1682(4) |
| C-12 | 4104(10) | 2123(12) | 634(3) |
| C-13 | 3497(10) | 2877(10) | 691(4) |
| C-14 | 4371(9) | 2081(10) | 130(3) |
| C-15 | 4722(10) | 2172(12) | 1834(3) |
| O-1 | 2285(6) | 194(6) | 527(2) |
| O-2 | 5230(6) | 2744(6) | 860(2) |

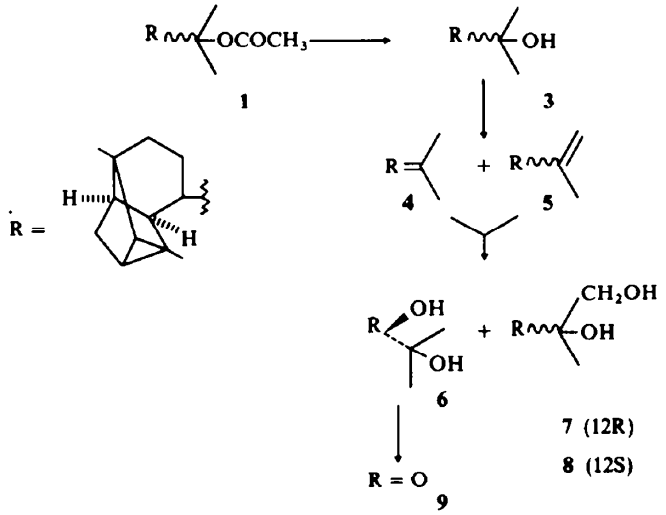



Fig. 2. Degradation of 12-acetoxycyclosinularane (1).

respectively. (In contrast with the initial mixture, the corresponding alcohols could be easily separated by $AgNO_3$ impregnated silica gel column chromatography); (b) $OsO_4$ treatment of the **1** + **2** mixture led to an easily separatable mixture of unchanged **1** and diol acetate **12**. The triol **13** is obtained either by LAH reduction of **12** or by $OsO_4$ hydroxylation of **11**.

Cleavage of the $\alpha$-glycol group of **13** afforded the ketoalcohol **14** which, on dehydration with $POCl_3$, yielded a mixture of **15** and **16** in a 4:6 ratio, as determined by GLC and $^1$H NMR.

Controlled catalytic microhydrogenation[10] of this mixture furnished the saturated ketone **17**, together with unchanged **15** and a small amount of **18**. Pure **15** and **17** were obtained by preparative GLC. Ketone **17** proved to be identical (MS, IR, NMR, CD) with the ketone obtained by Djerassi *et al.* from sinularene.[9] Consequently compound **2** is 12-acetoxysinularene.

Compound **18**, the C-5 epimer of **17** results from the hydrogenation of the isopropylidene group of **15**.

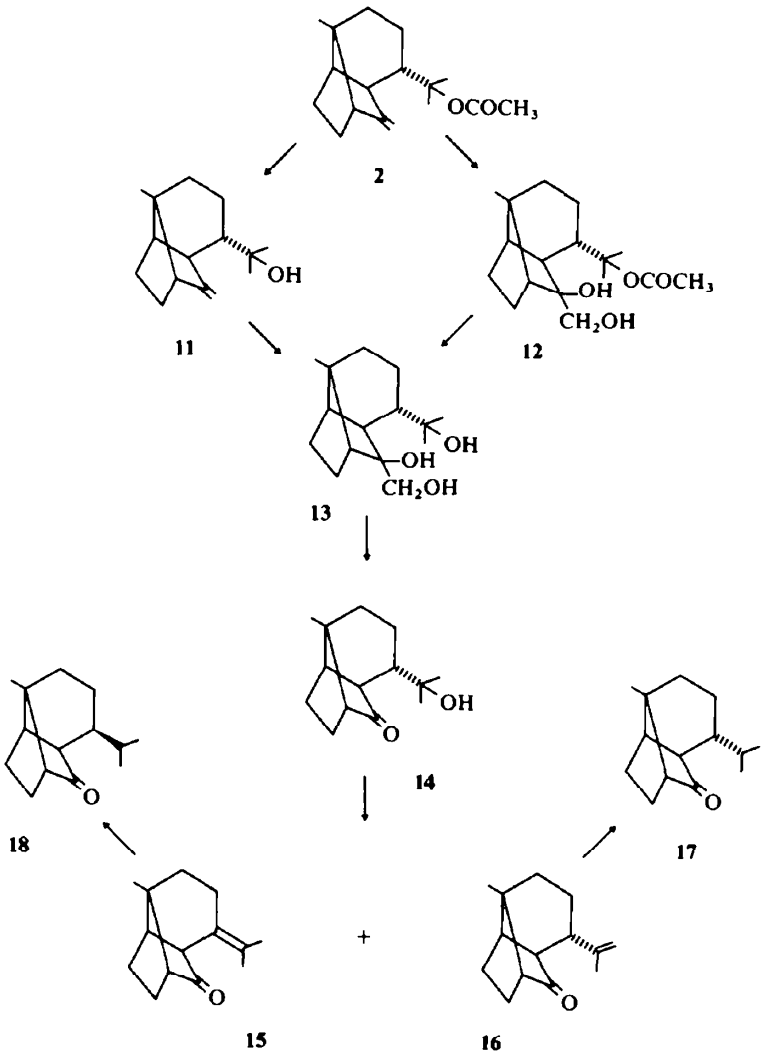
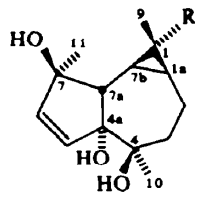


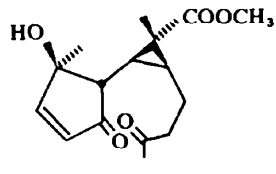

Fig. 3. Degradation of 12-acetoxysinularene (2)

Indeed, examination of molecular model suggests that hydrogenation from the re face will be preferred. Accordingly hydrogenation of pure **15** led only to **18**. Since **2** has the same C-5 configuration as sinularene, it is most likely that the configuration of this asymmetric centre in **1** is also the same.

Compound **19** ($C_{16}H_{24}O_5$ by HRMS) was isolated by repetitive silica gel column chromatography from a $CH_2Cl_2$/MeOH (9:1) extract of *C. koellikeri*, as a colourless oil, homogeneous in tlc and GLC. Its spectral properties show the presence of a methyl ester ($\nu_{C=O}$ 1725 cm$^{-1}$; $^1$H NMR: 3H s at 3.61 ppm), a Z disubstituted double bond bearing two quaternary carbon atoms ($^1$H NMR: 2H, AB system at 5.9 ppm, J = 6Hz; $^{13}$C NMR: 145.7, d and 131.3, d), three tertiary methyl groups ($^1$H NMR: 3H s at 1.25, 1.28 and 1.31 ppm) and three tertiary hydroxyl groups ($\nu_{OH}$ 3450 cm$^{-1}$; $^{13}$C NMR: s at 88.4, 82.65 and 74.7 ppm). The methyl ester and the double bond account for two of the five unsaturations of the molecule which is thus tricyclic. As expected, **19** could not be acetylated under usual conditions. It does not react with $NaIO_4$, but is cleaved by $Pb(OAc)_4$ to yield diketone **20** ($M^+$ at *m/e* 294, $C_{16}H_{22}O_5$; IR (film): $\nu_{C=O}$ 1720 cm$^{-1}$, shoulders at 1715 and 1730 cm$^{-1}$, $\nu_{OH}$ 3460 cm$^{-1}$; UV ($CH_3OH$): $\lambda_{max}$ 235 nm ($\varepsilon$ 8.300)), containing a methylketone (2.11, 3H, s) and a conjugated




**19** R = $COOCH_3$
**21** R = $CH_2OH$




**20**

cyclopentenone (UV: $\lambda_{max}$ 235 nm, ε 8.300; $^1$H NMR: 6.04 ppm, 1H, d, J = 3Hz and 7.35 ppm, 1H, d, J = 3Hz). These results indicate that **19** contains a *trans* α-glycol group.[11] LAH reduction of **19** afforded tetrol **21** ($M^+$ at *m/e* 268, $C_{15}H_{24}O_4$; IR (film): $\nu_{OH}$ 3400 cm$^{-1}$, no $\nu_{C=O}$). Since the two protons of the newly formed primary alcohol appear as an AB system (3.78 ppm, J = 5Hz), one can conclude that the carbon atom bearing the methyl ester group is quaternary.

Tetrol **21** remains unchanged on $NaIO_4$ treatment and since the chemical degradation of **19** did not seem straightforward, **21** was submitted to an X-ray diffraction analysis. The crystals of **21** belong to the monoclinic space group $P2_1$, with a = 8.625 (7), b = 11.397 (5), c = 15.320 (9) Å, $\beta$ = 105.66° (6) and Z = 4. Intensities of 2,272 independent reflections were collected on a SYNTEX $P2_1$ diffractometer using MoKα radiation ($2\theta_{max}$ = 47°). The structure was solved using the MAGIC 78[7] programs and the refinements were realized using the SHELX 76 programs.[8] $R_{final}$ = 0.047. A computer-generated drawing of **21**, showing the relative configuration, is depicted in Figure 4. The atomic coordinates are given in Table 2.

It follows that the natural compound **19** is the methyl ester of (1R*, 1aS*, 4R*, 4aR*, 7R*, 7aS*, 7bS*, 5Z)-4,4a,7-trihydroxyaromadendr-5-en-8-oic acid.

It is interesting to note, that compounds **1**, **2** and **19** are the first sesquiterpenes isolated from Octocorallia of the order Stolonifera.

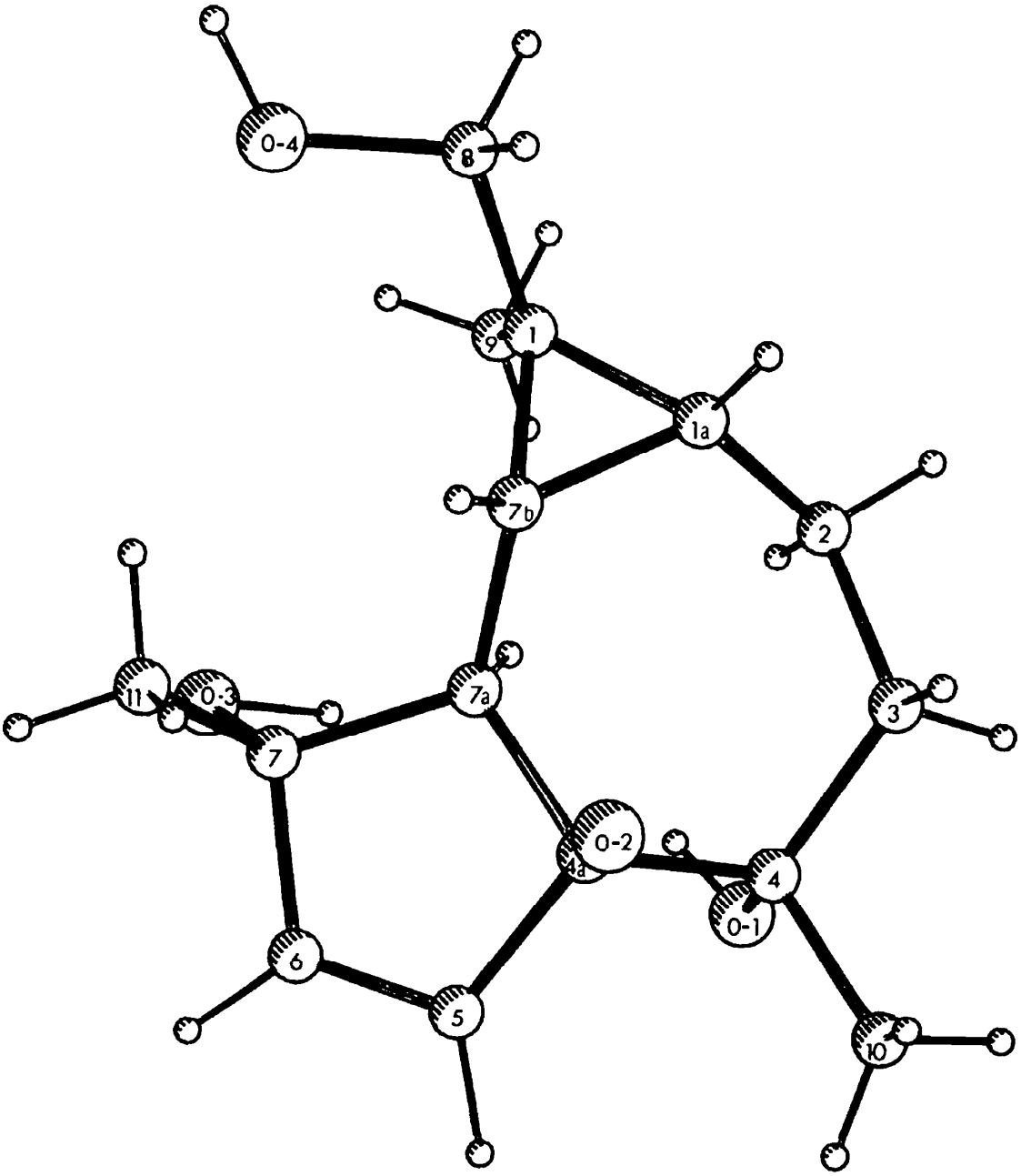



Fig. 4. Computer drawing of compound **21**.

Table 2. Atomic coordinates ( $\times 10^4$) of compound **21**

| | X | Y | Z |
|---|---|---|---|
| C-1 | 7730(7) | 5886(8) | 9717(4) |
| C-1a | 7576(7) | 4749(7) | 9186(4) |
| C-2 | 7116(8) | 4727(8) | 8155(4) |
| C-3 | 5933(8) | 3745(8) | 7761(5) |
| C-4 | 4116(8) | 3945(7) | 7659(4) |
| C-4a | 3722(7) | 4241(7) | 8561(4) |
| C-5 | 1979(7) | 4587(7) | 8443(4) |
| C-6 | 1834(7) | 5504(7) | 8929(4) |
| C-7 | 3423(7) | 5972(7) | 9493(4) |
| C-7a | 4629(7) | 5335(6) | 9053(4) |
| C-7b | 6301(7) | 5076(7) | 9649(4) |
| C-8 | 8956(8) | 5871(9) | 10628(4) |
| C-9 | 7608(6) | 7054(8) | 9241(5) |
| C-10 | 3208(9) | 2874(8) | 7220(5) |
| C-11 | 3672(8) | 5728(8) | 10484(4) |
| O-1 | 3517(5) | 4881(6) | 7021(3) |
| O-2 | 4116(5) | 3240(5) | 9161(3) |
| O-3 | 3451(5) | 7225(6) | 9340(3) |
| O-4 | 8408(5) | 6586(7) | 11248(3) |

## EXPERIMENTAL

The NMR spectra were recorded in $CDCl_3$ solution. Chemical shifts are quoted in $\delta$ values (ppm) downfield from TMS as internal standard. All the described compounds were homogeneous in tlc and GLC.

*Isolation of* **1** *and* **2**. 977 g of sun-dried specimens of *C. inflata*, collected around Laing Island, Papua-New Guinea, were finely ground and the resulting powder was then extracted in a Soxhlet during 24 h with $CH_2Cl_2$. This afforded 64.3 g of an oily extract which was chromatographed on a silica gel column (eluent $CH_2Cl_2$). The less polar fraction (8.45 g) shows a major spot by tlc (hexane–acetone 9:1). The compounds corresponding to this spot were further purified by chromatography on a second silica gel column (eluent: hexane, then hexane–acetone 95:5). This yielded 5.69 g (0.58% dry weight) of an oil homogeneous by tlc but showing two peaks by GLC (10% SP 2330, 130°): 85% of compound **1** and 15% of compound **2**, **1** and **2** could be separated by combining a chromatography on $AgNO_3$ impregnated silica gel column (eluent: hexane–acetone 98:2) and preparative GLC (10% SP 2330, 145°).

**1**: Oil; $C_{17}H_{26}O_2$ (HRMS: calculated 262.1926; measured 262.1926); $[\alpha]_D = +20.5°$ (c = 0.4, $CHCl_3$); IR (film): $\nu_{C=O}$ 1735 $cm^{-1}$, $\nu_{C-O}$ 1260 $cm^{-1}$; $^1H$ NMR (60 MHz): 0.5 (1H, d, J = 5Hz, cyclopropane CH), 0.83 and 1.10 (3H each, s, $^{11}CH_3$ and $^{15}CH_3$), 1.50 (6H, s, $^{13}CH_3$ and $^{14}CH_3$), 1.93 (3H, s, $CH_3COO$); $^{13}C$ NMR (15.08 MHz): 170.34 (s), 85.87 (s), 46.34 (d), 43.81 (s), 41.93 (q), 40.55 (d), 32.38, 31.41 (s), 27.38, 25.12, 24.98, 22.75, 22.27, 22.19, 19.95, 19.85, 13.55 (d); MS: 262 (2, $M^+$), 202 (18), 187 (21), 161 (25), 159 (50), 145 (45), 134 (30), 133 (31), 131 (50), 119 (100), 118 (42), 107 (52), 105 (75), 101 (65).

**2**: Oil; $C_{17}H_{26}O_2$ (HRMS: calculated 262.1926; measured 262.1926); $[\alpha]_D = -92.2°$ (c = 0.346, $CHCl_3$); IR (film): $\nu_{C=O}$ 1745 $cm^{-1}$, $\nu_{C=C}$ 1680 $cm^{-1}$, $\nu_{C-O}$ 1275 $cm^{-1}$, $\delta_{C=CH_2}$ 895 $cm^{-1}$; $^1H$ NMR (60 MHz): 0.98 (3H, s, $^{11}CH_3$), 1.47 (6H, s, $^{13}CH_3$ and $^{14}CH_3$), 1.99 (3H, s, $CH_3COO$), 4.67 and 4.85 (1H each, s, $^{15}CH_2$); MS: 262 (0.1, $M^+$), 202 (4), 187 (7), 174 (4), 159 (12), 146 (9), 145 (11), 131 (32), 119 (28), 117 (22), 107 (36), 106 (20), 105 (100), 101 (22).

LAH *reduction of* **1** *and* **2**. A mixture of **1** and **2** (250 mg) in anhydrous THF (10 ml) was treated with LAH (500 mg) during 24 h at room temperature under stirring. Usual work up, followed by silica gel column chromatography (hexane–ethyl acetate 95:5 and 90:10) afforded 149 mg of **3** and 32 mg of **11**.

**3**: Oil; $C_{15}H_{24}O$; IR (film); $\nu_{OH}$ 3420 $cm^{-1}$; $^1H$ NMR (60 MHz): 0.54 (1H, m, cyclopropane CH), 0.83 and 1.12 (3H each, s, $^{11}CH_3$ and $^{15}CH_3$), 1.24 (6H, s, $^{13}CH_3$ and $^{14}CH_3$); MS: 220 (2, $M^+$), 202 (1), 162 (47), 147 (34), 119 (53), 107 (37), 106 (87), 105 (100).

**11**: Oil; $C_{15}H_{24}O$; IR (film): $\nu_{OH}$ 3420 $cm^{-1}$, $\nu_{C=C}$ 1668 $cm^{-1}$; $^1H$ NMR (60 MHz): 0.97 (3H, s, $^{11}CH_3$), 1.21 (6H, s, $^{13}CH_3$ and $^{14}CH_3$), 4.67 and 4.84 (1H each, s, $^{15}CH_2$); MS: 220 (2, $M^+$), 202 (36), 187 (45), 174 (35), 159 (60), 147 (39), 119 (35), 105 (51), 93 (30), 91 (51), 59 (100).

*Treatment of* **1** *and* **2** *with* $OsO_4$. A mixture of **1** and **2** (600 mg) in pyridine (5 ml) was treated with $OsO_4$ (200 mg) at room temperature under stirring. After 72 h, 15 ml of an aqueous solution of $NaHSO_3$ 10% were added and the stirring continued for 48 h. Usual work up followed by chromatography on $SiO_2$ (eluent: hexane–acetone 9:1 then 7:3) afforded 458 mg of unchanged **1** and 114 mg of **12**.

**12**: Oil; $C_{17}H_{28}O_4$; IR (film): $\nu_{OH}$ 3450 $cm^{-1}$, $\nu_{C=O}$ 1730 $cm^{-1}$; $^1H$ NMR (60 MHz): 1.03 (3H, s, $^{11}CH_3$), 1.40 and 1.45 (3H each, s, $^{13}CH_3$ and $^{14}CH_3$), 1.97 (3H, s, $CH_3COO$), 2.93 (2H, bs, disappearing on $D_2O$ treatment), 3.98 and 3.60 (AB system, 2H, J = 11Hz); MS: 296 (small ion, $M^+$), 236 (4), 205 (7), 187 (8), 177 (14), 160 (16), 145 (70), 133 (40), 119 (50), 107 (100), 105 (50).

*LAH reduction of* **12**. LAH (200 mg) reduction of **12** (110 mg) in anhydrous THF (room temperature, 48 h) yielded

90 mg of triol **13**. The same triol **13** was obtained on treatment of **11** with $OsO_4$.

**13**: Amorphous solid ; $C_{15}H_{26}O_3$; IR (KBr): $\nu_{OH}$ 3350 $cm^{-1}$; $^1H$ NMR (60 MHz, $CD_3OD$): 1.05 (3H, s, $^{11}CH_3$), 1.15 (6H, s, $^{13}CH_3$ and $^{14}CH_3$), 3.73 (AB system, 2H, $^{15}CH_2$); MS: 254 ($M^+$, small), 236 (10), 218 (11), 205 (44), 203 (11), 187 (27), 177 (67), 165 (25), 160 (31), 145 (36), 135 (30), 121 (36), 107 (46), 59 (100).

$NaIO_4$ *treatment of* **13**. Compound **13** (90 mg) dissolved in 10 ml of $CH_3OH$ was treated with 250 mg of $NaIO_4$ dissolved in 1 ml of $H_2O$. The solution was stirred at room temp (4 h). Usual work up, followed by chromatography on silica gel column (eluent: hexane–acetone 7 : 3) afforded 50 mg of pure **14**.

**14**: Amorphous white solid; $C_{14}H_{22}O_2$; IR (film): $\nu_{OH}$ 3480 $cm^{-1}$, $\nu_{C=O}$ 1750 $cm^{-1}$; $^1H$ NMR (60 MHz): 1.06 (3H, s, $^{11}CH_3$), 1.18 and 1.24 (3H each, s, $^{13}CH_3$ and $^{14}CH_3$); MS: 222 ($M^+$, 7), 164 (59), 149 (76), 136 (45), 135 (62), 121 (37)...59 (100).

*Preparation of* **17** *from* **14**. To 29 mg of **14** dissolved in 5 ml of pyridine are added 5 drops of $POCl_3$. The resulting solution is stirred for 24 hours at room temp. Usual work up afforded 20 mg of an oil homogeneous by tlc (hexane–acetone 7 : 3) but showing 2 major peaks by GLC (10% Carbowax 20 M, 185 ). The $^1H$ NMR of the crude mixture together with the measurement of the relative peaks area in GLC indicate that the mixture contained 60% of **16** (isopropenyl) and 40% of **15** (isopropylidene). Without further purification, this mixture was submitted to a careful selective catalytic microhydrogenation (EtOH–$PtO_2$).[10] The ketone **17** was separated from unchanged **15** by preparative GLC (10% Carbowax 20 M; 180 ). The spectral properties of **17** were identical with those of the ketone obtained by Djerassi *et al.* from sinularene[9] (MS, IR, NMR, CD).

Hydrogenation of **15** ($PtO_2$–EtOH, room temp, 24 h) yielded the epimeric ketone **18**.

**15**. Oil; $C_{14}H_{20}O$; $^1H$ NMR (100 MHz): 1.02 (3H, s, $^{11}CH_3$), 1.68 and 1.73 (3H each, s, $^{13}CH_3$ and $^{14}CH_3$); MS: 204 ($M^+$, 9), 176 (6), 161 (38), 135 (51), 133 (50), 119 (41), 105 (60), 93 (66), 91 (100).

**17**: Oil; $C_{14}H_{22}O$; IR (film): $\nu_{C=O}$ 1740 $cm^{-1}$; $^1H$ NMR (100 MHz): 0.86 and 0.90 (3H, each, d, J = 6.5Hz, $^{13}CH_3$ and $^{14}CH_3$), 0.98 (3H, s, $^{11}CH_3$); MS: 206 ($M^+$, 6), 173 (8), 145 (46), 135 (66), 107 (44), 93 (100)...; CD ($CH_3OH$): $[\theta]_{288}$ −2,538, $[\theta]_{318}$ +161.

**18**: Oil; $C_{14}H_{20}O$; $^1H$ NMR (100 MHz): 0.79 and 0.92 (3 H each, d, J = 7.5Hz, $^{13}CH_3$ and $^{14}CH_3$), 0.96 (3H, s, $^{11}CH_3$); MS: identical to that of **17**.

*Oxalic acid dehydration of* **3**. Compound **3** (230 mg) was refluxed in anhydrous $C_6H_6$ (30 ml) containing oxalic acid (35 mg). 10 ml of $C_6H_6$ were distilled off and the reflux maintained for 1 h, after which tlc analyses did not show any significant progress. After cooling, 10 ml of a saturated $Na_2CO_3$ solution were added. Usual work-up and silica gel column chromatography (hexane–acetone 99 : 1, then 80 : 20), afforded 92 mg of a mixture of **4** and **5** and 105 mg of starting **3**. The latter were resubmitted to oxalic acid treatment, yielding after chromatography a further 88 mg of **4** and **5** which were joined to the previously obtained material. Ratio of **4** and **5** was 70 : 30 as shown by GLC (10%, SP 2330 column, 120 ) and $^1H$ NMR (small C = $CH_2$ singlet at 4.82 ppm). $M^+$ at *m/e* 202.

*Treatment of the* **4** + **5** *mixture with* $OsO_4$. The mixture of **4** and **5** (180 mg) was treated under stirring with $OsO_4$ (300 mg) in pyridine (8 ml) during 72 h. 15 ml of an aqueous solution of $NaHSO_3$ 10% were then added and the stirring continued during 48 h. Usual work-up and chromatography on $SiO_2$ (eluent: hexane–acetone 85 : 15) afforded 100 mg of **6** and 50 mg of a mixture of **7** and **8** ($M^+$ 236).

**6**: $C_{15}H_{24}O_2$; m.p. 63–64° (from pentane); IR: $\nu_{OH}$ 3,460 $cm^{-1}$; $^1H$ NMR: 0.6 (2H, m, cyclopropane CH), 0.87 and 1.03 (3H each, s, $^{11}CH_3$ and $^{15}CH_3$), 1.28 and 1.31 (3H each, s, $^{13}CH_3$ and $^{14}CH_3$); MS: 236 ($M^+$, 1.2), 205 (4), 177 (100), 159 (16), 133 (10), 121 (20), 119 (29), 107 (25).

$NaIO_4$ *treatment of* **6**. Diol **6** (60 mg) in MeOH (5 ml) and $H_2O$ (4 ml) was treated with $NaIO_4$ (320 mg) during 90 h. Usual work-up afforded 50 mg of oily **9**.

**9**: Oil; $C_{12}H_{16}O$; CD ($CH_3OH$): $[\theta]_{298}$ +5,102; IR (film): $\nu_{C=O}$ 1720 $cm^{-1}$; $^1H$ NMR: 0.95 and 1.17 ppm (3H each, s, $^{11}CH_3$ and $^{15}CH_3$); MS: 176 ($M^+$, 50), 161 (18), 143 (10), 132 (50), 119 (100), 108 (75), 105 (98), 91 (90).

*Isolation of* **19**. Sun-dried specimens of *C. koellikeri* were finely ground and 300 g of the resulting powder was then extracted at room temperature with $CH_2Cl_2$/MeOH (9 : 1). This afforded 20.4 g of crude extract which were chromatographed on a silica gel column (eluent: hexane–acetone 95 : 5, then 5 : 5). Repetitive silica gel column chromatography of the more polar fraction thus obtained, afforded 450 mg of **19**, as an oil homogeneous in tlc and GLC (3%, OV3, 195 ).

**19**: $C_{16}H_{24}O_5$ (HRMS: calculated 296.1623; measured 296.1624); $[\alpha]_D = -72 \pm 1$ (c = 0.52, $CHCl_3$); IR (KBr): $\nu_{C=O}$ 1715 $cm^{-1}$, $\nu_{OH}$ 3450 $cm^{-1}$; $^1H$ NMR (100 MHz): 1.25, 1.28, 1.31 (3H each, s, $^9CH_3$, $^{10}CH_3$ and $^{11}CH_3$), 3.61 (3H, s, $COOCH_3$), 5.9 (AB system, 2H, J = 6Hz, H−C=C−H); $^{13}C$ NMR: 176.7 (s), 145.7 (d), 131.3 (d), 88.4 (s), 82.65 (s), 74.7 (s), 52.1 (d), 48.45 (q), 36.5 (t), 28.45, 27.9, 26.3, 25.6 and 24.5 (multiplicities not determined), 18.2 (t), 10.4 (d); MS: 296 ($M^+$, 1), 278 (25), 246 (26), 218 (9), 203 (9), 200 (10), 188 (44), 175 (32), 161 (25), 151 (43), 147 (31)... 108 (100).

$NaIO_4$ *treatment of* **19**. Compound **19** (5 mg) was recovered unchanged after treatment with $NaIO_4$ (15 mg) in MeOH/$H_2O$ (9 : 1) for 24 h at room temp.

$Pb(OAc)_4$ *treatment of* **19**. Compound **19** (24 mg) was treated with $Pb(OAc)_4$ (250 mg) in pyridine (9 ml) for 18 h at room temperature. After destroying the excess of $Pb(OAc)_4$ with oxalic acid, usual work-up and chromatography on a silica gel column (eluent hexane–acetone 7 : 3 → 5 : 5) afforded 15 mg of **20**, homogeneous in tlc and GLC (3%OV3, 195°).

**20**: Oil; $C_{16}H_{22}O_4$; IR: $\nu_{C=O}$ 1720 $cm^{-1}$ with shoulders at 1715 and 1730 $cm^{-1}$, $\nu_{OH}$ 3460 $cm^{-1}$; $^1H$ NMR (100 MHz): 1.24, 1.30 (3H each, s), 2.11 (3H, s, $CH_3-\overset{\overset{O}{\|}}{C}-$), 3.61 (3H, s, $COOCH_3$), 6.04 (1H, d, J = 3Hz), 7.35 (1H, d, J = 3Hz, $CH=CH-\overset{\overset{O}{\|}}{C}$); UV: $\lambda_{max}$ 235 nm ($\varepsilon$ 8.300). MS: 294 ($M^+$, 2), 276 (4), 236 (10), 219 (6), 217 (7), 212 (6), 202 (6), 201 (8), 191 (7), 183 (74), 177 (19), 159 (25), 151 (100).

*LAH treatment of* **19**. Compound **19** (80 mg) was treated with LAH (400 mg) in anhydrous THF (25 ml) for 4 h at room temp. After destroying the excess of LAH with AcOEt and a saturated $MgSO_4$ solution, usual work-up followed by silica gel column chromatography (eluent: $CHCl_3$–EtOH 9 : 1 → 7 : 3) afforded 40 mg of **21** which was crystallized in $Et_2O$ containing a small amount of Reichstein's mixture.

**21**: m.p. 203.5° ; IR: $\nu_{OH}$ 3400 $cm^{-1}$, no $\nu_{C=O}$; $^1H$ NMR: 1.2 (3H, s), 1.3 (6H, s), 3.65 (2H, AB system, J = 5Hz, $-CH_2OH$), 5.83 (2H, s); MS: 268 ($M^+$, 0.2), 250 (2, $M^+ - 18$), 232 (4), 217 (2), 207 (4), 193 (4), 189 (6), 175 (30), 161 (25), 151 (40), 137 (45), 135 (50), 125 (50), 121 (60)... 95 (100).

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## REFERENCES

[1]For part XLII, see C. Charles, J. C. Braekman, D. Daloze and B. Tursch, *Tetrahedron* **36**, 2133 (1980).
[2]King Leopold III Biological Station, Laing Island, Papua-New Guinea, Contribution n 23.
[3]Chercheur qualifié du Fonds National de la Recherche Scientifique.
[4]B. Tursch, J. C. Braekman, D. Daloze and M. Kaisin in *Marine Natural Products*, Vol. II, Ed. P. Scheuer, Acad. Press (1978).

[5]J. C. Braekman, D. Daloze, R. Schubert, M. Albericci, B. Tursch and R. Karlsson, *Tetrahedron* **34**, 1551, (1978).
[6]B. F. Bowden, J. C. Braekman, J. C. Coll and S. J. Mitchell. *Austr. J. Chem.* **33**, 927 (1980).
[7]J. P. Declercq, G. Germain, M. M. Woolfson, *Acta Cryst.* **A35**, 622 (1979).
[8]G. M. Sheldrick, *SHELX* 76, University of Cambridge (U.K.) 1978.
[9]C. M. Beechan, C. Djerassi, J. S. Finer and J. Clardy, *Tetrahedron Lett.* 2395, (1977).
[10]N. Clauson-Kaas and F. Limborg, *Acta Chem. Scand.* **1**, 884, (1947).
[11]K. L. Rinehart, jr., *Oxidation and Reduction of Organic Compounds*, p. 80. Prentice-Hall, 1973.