E. *O*-Ethylboranediyl Derivative (10) of 6-Deoxy-2,3-isopropylidene-L-mannofuranose (9). 6-Deoxy-1,5-*O*-ethylboranediyl-2,3-*O*-isopropylidene-β-L-mannofuranose (10) from 9 and Ethylboroxine. Ethylboroxine (5 g, 16.7 mmol) was added to **9** (2.9 g, 14.2 mmol) in toluene (20 mL) and the azeotropic mixture of water/toluene was distilled off. The remaining toluene was removed in vacuo (10^{-3} Torr) and the residue was distilled to give **10** (2.6 g, 77%): bp 68 °C (10^{-3} Torr), $[\alpha]^{20}_D$ 39.7° (*c* 3.7, CCl_4); 0.8 g residue; MS (70 eV) M^+ 242 (B_1, rel intensity ~ 1), 227 (B_1, 16), 138 (B_1, 37), 111 (B_1, 100); ^1H NMR (100 MHz, CCl_4) τ 4.99 (br s, half-width = 2.5 Hz, H^1), 5.35 (ddd, $J_{2,3}$ = 7.5, $J_{3,4}$ = 3.5, $J_{3,5}$ = 1.5 Hz, H^3), 5.73 (dd, $J_{1,2}$ = 1.5, $J_{2,3}$ = 7.5, H^2), 5.75 (dq, $J_{3,5}$ = 1.5, $J_{5,Me}$ = 7, H^5), 6.00 (d, $J_{3,4}$ = 3.5 Hz, H^4), 8.55 (s, CMe), 8.65 (d, $J_{5,Me}$ = 7 Hz, $C^5{}_{Me}$), 8.70 (s, CMe), 9.16–9.34 (m, BEt) in the ratio 1:1:2:1:9:5.

Anal. Calcd for $C_{11}H_{19}BO_5$ (242.0): B, 4.47. Found: B, 4.38.

9 from 10 with Methanol. Two 5-mL portions of methanol were added to **10** (1.8 g, 7.4 mmol) and the dimethoxyethylborane/methanol mixture was removed in vacuo (0.1 Torr), leaving **9** (1.45 g, 96%) as residue: mp (from ether/hexane) 87 °C, $[\alpha]^{20}_D$ 17.8° (*c* 2.9, H_2O); found HZ^{20} = 3.19.

F. Determinations of Hydride Numbers (HZ). The hydride numbers (HZ) were obtained by heating the compounds, listed in Table II, to 130 °C for ~3 h with an excess of propyldiborane(6) having 11–15‰ H^-.[20] The volume of hydrogen, evolved after each determination, was measured after cooling to room temperature, and the excess >BH remaining after reaction was then determined volumetrically by addition of 2-ethylhexanol.

Registry No.—2a, 62930-56-7; **3b,** 62930-57-8; **3c,** 62930-58-9; **3d,** 62930-59-0; **6,** 62930-60-3; **8b,** 62930-61-4; **10,** 62962-24-7; ethylboroxine, 3043-60-5; triethylborane, 97-94-9; diboron trioxide, 1303-86-2; ethyldiborane, 12081-54-8; dimethoxyethylborane, 7318-82-3; ethane-1,2-diol, 107-21-1; benzoyl chloride, 98-88-4.

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Diterpenes from *Dolabella californica*

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Fourteen diterpenes have been isolated from the digestive gland of the opisthobranch mollusc *Dolabella californica*. Twelve of the diterpenes have been related through a series of chemical conversions to a compound whose structure was previously determined by x-ray analysis. The structure of the remaining compound was determined by analysis of spectroscopic data. The configurations of ten of the new diterpenes were determined by the LIS method. The compounds are all based on the dolabellane skeleton, which contains an 11-membered ring fused to a five-membered ring.

We have previously shown[1] that the digestive gland of the sea hare *Aplysia californica* contained a variety of interesting halogenated metabolites which were found to be of dietary origin.[2] Two collections of *Dolbella californica* (Sterns),[3] a related anaspidean opisthobranch mollusc, have yielded a number of diterpenes, all of which have the same novel carbon skeleton. One of the diterpenes was shown by x-ray analysis[4] to have the structure **2** and was named 10-acetoxy-18-hydroxy-2,7-dolabelladiene. We wish to report the structural determinations of the remaining diterpenes isolated from the digestive gland of *D. californica*.

The two collections of *D. californica* were made at Isla Espiritu Santo in April 1975 and March 1976. The acetone extracts of the digestive glands were chromatographed on Florisil. Rechromatography of selected fractions on silica gel gave 6 compounds from the first collection and 12 compounds from the second collection, four compounds being found in both collections. Details of the composition of the two collections, together with the molecular formulas and melting points, are shown in Table I.

An initial examination of the molecular formulas, infrared spectra, and ^1H NMR spectra (Table II) revealed that we had isolated a series of very similar compounds which differed primarily in the numbers and positions of acetate and hydroxyl groups. By reduction of the acetates to alcohols using lithium aluminum hydride in ether, we were able to relate each compound to one of four alcohols. The diacetate **1** and monoacetate **2** were both converted to the diol **3**; the triacetate **4**, three diacetates **5–7**, and a monoacetate **8** were all reduced to triol **9**; the diacetate **10** and two monoacetates **11** and **12** were related to an isomeric triol **13**; the remaining compound was an alcohol **14**.

The monoacetate **2** was the major crystalline constituent of the first collection. The molecular formula $C_{22}H_{36}O_3$, to-

Table I. Diterpenes Isolated from *Dolabella californica*

Collection					1975	1976
No. of animals					40	100
Total weight of digestive gland extracts					16 g	65 g
Registry no.	Compd	Molecular formula	Mp, °C	$[\alpha]^{20}_D$, deg	Wt, g	Wt, g
62861-12-5	1	$C_{24}H_{38}O_4$		−80.5	0.25	1.69
60259-77-0	2	$C_{22}H_{36}O_3$	78	−101	0.5	6.0
60259-76-9	3	$C_{20}H_{34}O_2$	152–153	−71.8		0.4
62861-13-6	4	$C_{26}H_{40}O_6$		−33.6		0.6
62861-14-7	5	$C_{24}H_{38}O_5$	136–137	−56.7		1.94
62861-15-8	6	$C_{24}H_{38}O_5$		−33.3	1.5	
62861-16-9	7	$C_{24}H_{38}O_5$		−26.4		0.4
62861-17-0	8	$C_{22}H_{36}O_4$		−45	1.75	7.0
62861-18-1	9	$C_{20}H_{34}O_3$	168–169	−86	1.3	
62861-19-2	10	$C_{24}H_{38}O_5$		−4.7		0.5
62861-20-5	11	$C_{22}H_{36}O_4$	153–154	−0.4		1.5
62861-21-6	12	$C_{22}H_{36}O_4$		+21.2		1.0
62861-22-7	13	$C_{20}H_{34}O_3$	157–158	−29		1.5
62861-23-8	14	$C_{20}H_{34}O$		−75.1	0.1	0.95
				Total recovery	5.4 (34%)	23.5 (36%)

Table II. ^{1}H NMR Spectra (Selected Signals) of the Diterpenes 1–14

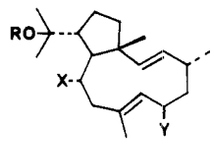
	H at C									
Compd	2	3	6	7	10	15	16	17	19	20
1	5.09	5.26		5.11	4.75	0.84	0.95	1.66	1.42	1.59
2	5.07	5.22		5.10	4.81	0.82	0.94	1.62	1.18	1.25
3	5.02	5.18		4.98	3.41	0.95	0.93	1.59	1.20	1.25
4						0.81	1.09	1.58	1.36	1.49
5	4.92	5.09	5.59	5.23	4.77	0.77	1.08	1.13	1.39	1.59
6	4.95	5.23	5.23	5.51	3.77	0.95	1.05	1.50	1.55	1.55
7	5.30	5.16	5.30	5.44	5.09	0.90	1.06	1.51	1.18	1.26
8	5.00	5.18	5.18	5.48	3.94	0.95	1.05	1.20	1.50	1.55
9	4.92	5.32	5.09	5.75	3.89	0.95	1.05	1.16	1.23	1.25
10	4.97	5.47	5.60	5.27	4.81	0.85	1.10	1.79	1.18	1.27
11	4.98	5.48	4.50	5.30	4.80	0.84	1.06	1.70	1.16	1.26
12	4.95	5.40	4.53	5.16	3.51	0.98	1.06	1.68	1.54	1.58
13	4.90	5.33	4.50	5.08		0.98	1.05	1.70	1.20	1.27
14	5.16	5.16		5.02		0.89	0.92	1.45	1.22	1.22

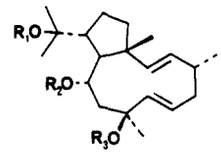
gether with an acetate signal in the ^{1}H NMR at δ 2.05 ppm and infrared bands at 3500 and 1740 cm^{-1}, strongly suggested that **2** was a monoacetate of a diol. The presence of two signals in the ^{1}H NMR at δ 1.18 and 1.25 ppm, together with a signal in the ^{13}C NMR spectrum at 72.7 ppm due to a quaternary carbon, indicated the presence of an isopropyl alcohol moiety. The ^{1}H NMR spectrum also contained signals due to methyl groups at δ 0.82 (s), 0.94 (d, J = 7 Hz), and 1.62 (bs), an α-acetoxy proton at 4.81, and vinyl protons at 5.07 (d, J = 16 Hz), 5.10 (t, J = 7 Hz), and 5.22 (dd, J = 16, 9 Hz). Irradiation at δ 2.32 caused the doublet at δ 0.94 to collapse to a singlet and the double doublet at δ 5.22 to become a doublet (J = 16 Hz). The ^{13}C NMR spectrum confirmed the presence of disubstituted and trisubstituted double bonds and contained a quaternary carbon signal at 20.8 ppm. From these data we deduced that **2** was bicyclic, containing the partial structure **15** where the quaternary carbon was at the bridgehead or at a side-chain junction. Since the coupling constant indicated a trans-disubstituted olefin, the partial structure must be in a large ring or in a side chain. Since we could not find a known carbon skeleton which contained this feature,[5] the structure of the monoacetate **2** was determined by single-crystal x-ray analysis[4].

The diacetate **1** was isolated as an oil. The ^{1}H NMR spectrum contained two acetate methyl signals at δ 2.04 and 1.91 and two signals at 1.59 and 1.42 ppm due to the methyl groups on a carbon atom bearing acetoxy. The diol **3** could be prepared from either **1** or **2** and was also a natural product. The ^{1}H NMR spectrum of **3** indicated the presence of the isopropyl alcohol side chain (δ 1.20 and 1.25) and the secondary alcohol functionality (δ 3.41).

The second group of compounds, a triacetate **4**, three diacetates **5–7**, a monoacetate **8**, and a triol **9**, all have the same carbon skeleton. All acetates **4–8** were converted into the triol **9** by reduction with lithium aluminum hydride in diethyl ether. Since the monoacetate of **8** was the major constituent in both collections, we first confined our studies to the structural elucidation of **8** and the corresponding triol **9**.

The monoacetate **8**, obtained as an oil, had the molecular formula $C_{22}H_{36}O_4$. On reduction with lithium aluminum hydride in ether, the monoacetate gave the triol **9** having a molecular formula $C_{20}H_{34}O_3$. The ^{1}H NMR spectrum of the monoacetate contained many signals which could be assigned to functional groups found in compounds **1–3**. The partial structure **15** was identified from signals at δ 0.95 (s, 3 H), 1.05 (d, 3 H, J = 7 Hz), 5.00 (d, 1 H, J = 16 Hz), and 5.18 (m, 1 H), the α-hydroxy proton gave rise to a multiplet at δ 3.94, and the isopropyl acetate side chain was represented by methyl signals at 2.02, 1.55, and 1.50 ppm. The major difference was that the trisubstituted olefin signal and the accompanying methyl signal in **2** were replaced by a methyl signal at δ 1.20, typical of a methyl group on a carbon atom bearing oxygen, and signals due to a trans-disubstituted olefinic bond at δ 5.48 (d, 1 H, J = 16 Hz) and 5.18 (m, 1 H). By careful decoupling of the ^{1}H NMR spectrum of the triol **9**, we were able to establish the presence of the 1,5-diene system. Irradiation at δ 2.57 collapsed the double doublet at δ 5.32 to a doublet, the doublet at δ 1.05 (3 H) to a singlet, and a two-proton multiplet at δ 2.16 to a broad doublet. Irradiation at δ 2.16 collapsed the multiplet at δ 5.09 to a sharp doublet and altered the multiplicity of the signal at δ 2.57. We therefore concluded that the trisubstituted olefin in **2** was replaced by an allylic tertiary alcohol in **8**.





1 R = Ac X = OAc Y = H

2 R = H X = OAc Y = H

3 R = H X = OH Y = H

10 R = H X = OAc Y = OAc

11 R = H X = OAc Y = OH

12 R = Ac X = OH Y = OH

13 R = H X = OH Y = OH

14 R = H X = H Y = H

16 R = Ac X = OAc Y = Br

4 R_1 = Ac R_2 = Ac R_3 = Ac

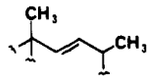
5 R_1 = Ac R_2 = Ac R_3 = H

6 R_1 = Ac R_2 = H R_3 = Ac

7 R_1 = H R_2 = Ac R_3 = Ac

8 R_1 = Ac R_2 = H R_3 = H

9 R_1 = H R_2 = H R_3 = H



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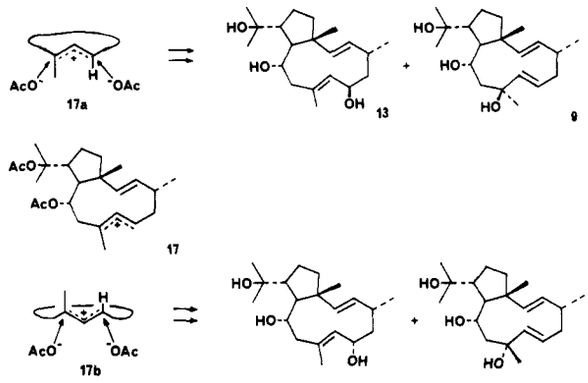
Acetylation of the secondary alcohol substituent in **8** with acetic anhydride in pyridine gave the diacetate **5**, identical in all respects with the natural material. Treatment of the diacetate with phosphorus tribromide and pyridine in hexane at −40 °C[6] gave the rearranged allylic secondary bromide **16** in 70–80% yield. The bromide **16** proved to be quite unstable and was therefore used without purification. Reduction of the bromide **16** with sodium in tetrahydrofuran containing *tert*-butyl alcohol gave the diol **3**, identical in all respects with an authentic sample, as the major product, albeit in low yield. An attempted reduction of the bromide **16** with lithium aluminum hydride gave no recognizable products, suggesting that the geometry of the medium-sized ring prevented the concerted displacement of bromide by hydride. The conversion of **8** to **3** established the structures of **4–9** with the exception of the stereochemistry at C-8, which was determined from a lanthanide-induced shift study (see below).

The triacetate **4** was obtained as an oil. The ^{1}H NMR spectrum contained three acetoxy methyl signals at δ 2.07, 1.98, and 1.95 and three signals due to methyl on a carbon atom bearing acetoxy at 1.58, 1.49, and 1.36 ppm. The diacetate **6**, obtained as an oil, contained a secondary alcohol substituent, as indicated by the ^{1}H NMR signal at δ 3.77 (m, 1 H) and three methyl groups on carbon atom bearing acetoxy which gave rise to signals at δ 1.55 (6 H) and 1.50 (3 H). The remaining diacetate **7** contained the isopropyl alcohol side chain, which gave rise to two methyl signals at δ 1.26 and 1.18 in the ^{1}H NMR spectrum.

A third group of compounds, a diacetate **10**, two monoacetates **11** and **12**, and a triol **13**, was found only in the second collection. The acetates **10–12** were all converted into the triol **13** by reduction with lithium aluminum hydride in ether. The ^{1}H NMR spectrum of the triol **13** was similar to that of the diol **3**, except in the low-field region, which contained signals at δ 4.90 (d, J = 16 Hz) and 5.33 (dd, J = 16, 7 Hz) due to a trans-disubstituted olefin and a doublet at δ 5.08 (J = 9 Hz) coupled to a multiplet at 4.50 ppm. In the diacetate **10**, the corresponding multiplet was at δ 5.60, suggesting that the multiplets were due to allylic α-hydroxy and allylic α-acetoxy protons, respectively. The similarity between the ^{1}H NMR spectra of **10–13** and that of the bromide **16** led to the hypothesis that all compounds had the same carbon skeleton and substitution pattern. The bromide **16** was therefore treated with silver acetate in aqueous tetrahydrofuran containing acetic acid at 0 °C to obtain an inseparable mixture of two triacetates, which were reduced directly with lithium aluminum hydride in ether to obtain a 3:2 mixture of triols **9** and **13**.

Scheme I. Possible Configurations of the Triols **9** and **13** Arising from the Solvolysis of Bromide **16**



The solvolysis proceeded by way of the carbonium ion intermediate **17**, which reacted with acetate to give the expected mixture of a secondary and tertiary allylic acetates. Depending on the geometry of the carbonium ion intermediate **17a** or **17b**, either of two possible pairs of triacetates might have been formed (Scheme I). Since the conformation of the acetate **2**, as determined by x-ray analysis, closely resembled intermediate **17a**, we expected the diols **9** and **13** to have the configurations shown.

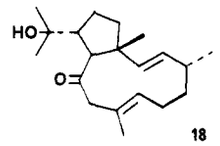
The diacetate **10** was obtained as an oil and could be prepared by acetylation of the diol **13** with acetic anhydride in pyridine at room temperature. The ^{1}H NMR spectrum of **10** contained two α-acetoxy proton signals at δ 4.81 and 5.60 and two methyl signals at δ 1.18 and 1.27 due to the isopropyl alcohol side chain. The monoacetate **11** contained an allylic secondary alcohol group which could be acetylated at room temperature to give the diacetate **10**. The ^{1}H NMR spectrum of **11** contained an α-acetoxy proton signal at δ 4.80 and an α-hydroxy proton signal at δ 4.50 which was coupled to an olefinic proton signal at δ 5.30 (d, J = 9 Hz). The ^{1}H NMR spectrum of the remaining monoacetate **12** contained two methyl signals at δ 1.54 and 1.58, due to the isopropyl acetate side chain, and α-hydroxy proton signals at δ 3.51 and 4.53.

Since we had obtained only two of four possible isomers from the solvolysis of the bromide **16**, we had predicted that the configuration at C-8 in compounds **4–9** and at C-6 in compounds **10–13** was as drawn. In order to confirm the assignments, we measured lanthanide-induced shifts[7] in the ^{1}H NMR spectra of compounds **5** and **11**. A solution of each compound in $CDCl_3$ was treated with aliquots of $Eu(fod)_3$ reagent and the induced shifts were measured. Because of the lack of rigidity in the 11-membered ring, we did not attempt a quantitative treatment of the LIS data. In the case of diacetate **5**, the proton at C-6 experienced the greatest shift, indicating that the europium atom was associated with the hydroxyl group. Examination of molecular models revealed that the relative shifts of the bridgehead methyl and the secondary methyl group would indicate whether the hydroxyl group, and therefore the europium atom, were above or below the plane of the 11-membered ring. Since the induced shift of the bridgehead methyl (49% of C-6 proton shift) was much greater than that of the secondary methyl (12% of C-6 proton shift), the configuration of **5** must be as shown. In the spectra of monoacetate **11**, the α-hydroxy proton at C-6 experienced the greatest induced shift, indicating that the europium was associated with the secondary alcohol. The induced shift of the bridgehead methyl (15.1% of C-6 proton shift) was again greater than that of the secondary methyl (12.8% of C-6 proton shift) but the difference was less pronounced. However, had the secondary hydroxyl and secondary methyl groups been on the same face of the 11-membered ring, we predicted that the induced shift of the secondary methyl signal would be

considerably greater than that of the bridgehead methyl. The configuration of **11** must therefore be as shown.

The alcohol **14** has a single hydroxyl group. The ^{1}H NMR spectrum of **14** contained a six-proton singlet at δ 1.22 due to the isopropyl alcohol side chain, together with signals at δ 0.89 (s, 3 H), 0.92 (d, 3 H, J = 7 Hz), and 5.16 (m, 2 H) due to fragment **15** and at δ 1.45 (s, 3 H) and 5.02 (t, J = 7 Hz) due to a trisubstituted olefinic group. On the basis of the spectral evidence, we proposed that **14** had the same carbon skeleton and configuration as the diol **3** but lacked the C-10 hydroxyl group. Our attempts to interconvert **3** and **14** have all failed. The diol was converted into a ketone **18** with Jones reagent, but the ketone could not be converted into the corresponding thioketal. The ketone **18** was converted into the corresponding *p*-toluenesulfonylhydrazone, but this derivative could not be reduced[8] to the alcohol **14**.

During the course of these experiments, we made some observations which implied that the 11-membered ring was more rigid than predicted from examination of molecular models. The ketone **18** did not undergo rearrangement to give a conjugated ketone, even in the presence of strong acids and bases. When the ketone **19**, obtained by Jones oxidation of **9**, was treated with *p*-toluenesulfonic acid in dry benzene, the expected dienone **20** was not formed. These results indicated that the 11-membered ring cannot accommodate a third olefinic bond, although examination of molecular models suggested that this should be possible.



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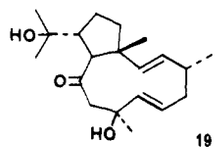

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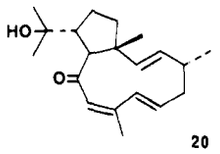

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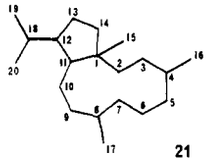
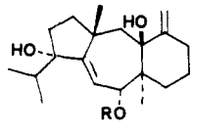


21



22 R = H

23 R = Ac

The dolabellane carbon skeleton **21** has not been encountered previously. However, at the same time that we communicated the structure of the monoacetate **2**, Pettit et al.[9] published the structures of dolatriol **22** and its acetate **23**, which were obtained from a related opisthobranch, *Dolabella auricularia*. The tricyclic skeleton of dolatriol **22** is formally related to the dolabellane skeleton by addition of a bond between carbons 3 and 8. Addition of a bond between carbons 4 and 10 in the dolabellane skeleton would give the cyathane skeleton.[10]

The dietary origin of the dolabellanes, if, like all other known opisthobranch metabolites,[11] they are indeed of dietary origin, remains a mystery. *Dolabella californica* is a nocturnal feeder. We did not observe any obvious food source while collecting the animals and concluded that *D. californica* must graze on the small algae which form a mat on the substratum. The isolation of diterpenes from two geographically separated *Dolabella* species suggests that *Dolabella* may be feeding on a specific genus of algae. Since *D. californica* produced copious quantities of purple ink, we suspect that it must eat predominantly red algae.[12,13]

Experimental Section

^{1}H NMR spectra were recorded on a Varian HR-220 spectrometer, ^{13}C NMR spectra were recorded on a Varian CFT-20 spectrometer, infrared spectra were recorded on a Perkin-Elmer Model 700 spectrophotometer, and optical rotations were measured on a Perkin-Elmer Model 141 polarimeter, using a 10-cm microcell. Low-resolution mass spectra were recorded on a Hewlett-Packard 5930A mass spectrometer. High-resolution mass measurements were supplied by the Analytical Facility at California Institution of Technology. Melting points were measured on a Fisher-Johns apparatus and are reported uncorrected. All solvents used were either spectral grade or distilled from glass prior to use.

Collection and Extraction of *Dolabella californica*. *Dolabella californica* were collected using scuba at night at Isla Espiritu Santo in the Gulf of California (24°31'N, 110°23'W) in April 1975 and March 1976. Each collection was extracted separately. The sea hares were anesthetized by injection of a saturated aqueous magnesium sulfate solution (20 mL) between the rhinophores. The digestive glands were removed by dissection, and the combined material was homogenized in acetone. The resulting suspension was filtered, and the solids were rehomogenized in acetone, allowed to stand at 5 °C for 20 h, and again filtered. The combined extracts were evaporated in vacuo to obtain an aqueous suspension of organic materials. The aqueous residue was extracted with the ether (3 × 1 L). The combined ether extracts were dried over sodium sulfate and evaporated in vacuo to obtain a brown, viscous oil.

First Collection (April 1975). Forty *Dolabella californica* gave 20 g of ether-soluble material. The brown oil (18 g) was chromatographed on a column of Florisil (40 × 6 cm diameter). The material was eluted with solvent mixtures of increasing polarity from hexane to ethyl acetate. Elution with 100% benzene gave a fraction (500 mg) which was rechromatographed on silica gel, using 25% ether in hexane as eluent, to obtain the diacetate **1** (250 mg) and the alcohol **14** (100 mg). The material which was eluted with 20% ether in benzene was crystallized from hexane to give the monoacetate **2** (500 mg). The fraction (3.0 g) which was eluted with 50% ether in benzene was rechromatographed on silica gel, using 50% ether in hexane as eluent, to obtain the diacetate **6** (1.5 g). The material (3.0 g) eluted with 10% ethyl acetate in ether was rechromatographed on silica gel, using ether as eluent, to obtain the monoacetate **8** (1.75 g). The fraction (2.0 g) eluted with 50% ethyl acetate in ether was crystallized from hexane to yield the triol **9** (1.30 g).

Second Collection (March 1976). One hundred *Dolabella* gave 70 g of ether-soluble material. The oil (65 g) was chromatographed on a column of Florisil (90 × 6 cm diameter). Material (14 g) eluted with benzene was rechromatographed on silica gel to obtain the diacetate **1** (1.5 g), the alcohol **14** (900 mg), and the monoacetate **2** (4.5 g). The fraction (19 g) eluted with 20% ether in benzene was rechromatographed on silica gel to separate the monoacetate **2** (2.0 g), the triacetate **4** (600 mg), the diacetate **5** (1.9 g), the diacetate **10** (500 mg), the diol **3** (400 mg), and the diacetate **7** (400 mg). The material (15 g) eluted with 50% ether in benzene was rechromatographed on silica gel to obtain the monoacetate **8** (7.0 g), the monoacetate **11** (1.5 g), and the monoacetate **12** (1.0 g). The material eluted with 10% ethyl acetate in ether recrystallized from ether to give the triol **13** (1.5 g).

(1*R,2*E*,4*R**,7*E*,10*S**,11*S**,12*R**)-10,18-Diacetoxy-2,7-dolabelladiene (1):** $[\alpha]^{20}_D$ −80.5° (*c* 2.6, $CHCl_3$); IR ($CHCl_3$) 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.84 (s, 3 H), 0.95 (d, 3 H, J = 7 Hz), 1.42 (s, 3 H), 1.59 (s, 3 H), 1.66 (s, 3 H), 1.91 (s, 3 H), 2.04 (s, 3 H), 3.05 (m, 1 H), 4.75 (m, 1 H), 5.09 (d, 1 H, J = 16 Hz), 5.11 (t, 1 H, J = 7 Hz), 5.26 (dd, 1 H, J = 16, 9 Hz); ^{13}C NMR ($CDCl_3$) δ 170.1, 169.0, 135.4, 134.4, 130.5, 127.3, 84.9, 70.7, 55.3, 47.2, 45.0, 38.9, 37.3, 36.0, 26.8, 26.3, 26.1, 25.7, 25.5, 23.4, 22.8, 21.0, 19.1, 18.0; mass spectrum *m/e* 390 (M^+·), 330 (M^+· − AcOH), 288, 271, 256, 228, 174, 43 (base peak); high-resolution mass measurement, observed 390.2766 ($C_{24}H_{38}O_4$ requires 390.2770).

(1*R,2*E*,4*R**,7*E*,10*S**,11*S**,12*R**)-10-Acetoxy-18-hydroxy-2,7-dolabelladiene (2):** mp 78 °C; $[\alpha]^{20}_D$ −101° (*c* 1.32, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.82 (s, 3 H), 0.94 (d, 3 H, J = 7 Hz), 1.18 (s, 3 H), 1.25 (s, 3 H), 1.62 (s, 3 H), 2.05 (s, 3 H), 4.81 (dt, 1 H, J = 9, 1, 1 Hz), 5.07 (d, 1 H, J = 16 Hz), 5.10 (t, 1 H, J = 7 Hz), 5.22 (dd, 1 H, J = 16, 9 Hz); ^{13}C NMR (C_6D_6) δ 168.9, 135.8, 131.2, 128.3, 127.4, 73.0, 71.9, 56.1, 50.0, 47.7, 46.1, 40.1, 38.3, 36.4, 32.5, 27.9, 27.3, 23.9, 22.0, 20.0, 18.8; mass spectrum *m/e* 346 (M^+·), 328, 287, 269. Anal. Calcd for $C_{22}H_{36}O_3$: C, 75.83; H, 10.4. Found: C, 75.90; H, 10.51.

(1*R,2*E*,4*R**,7*E*,10*S**,11*S**,12*R**)-10,18-Dihydroxy-2,7-dolabelladiene (3):** mp 152–153 °C; $[\alpha]^{20}_D$ −71.8° (*c* 0.92, $CHCl_3$); IR ($CHCl_3$) 3500 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.93 (d, 1 H, J = 7 Hz), 0.95 (s, 3 H), 1.20 (s, 3 H), 1.25 (s, 3 H), 1.59 (s, 3 H), 2.55 (m, 1 H), 4.98

(t, 1 H, J = 7 Hz), 5.02 (d, 1 H, J = 16 Hz), 5.18 (dd, 1 H, J = 16, 9 Hz); mass spectrum m/e 306 (M^+·) 288, 270, 255, 227, 163; high-resolution mass measurement, observed 306.2560 ($C_{20}H_{34}O_2$ requires 306.2558).

(1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-8,10,18-Triacetoxy-2,6-dolabelladiene (4):** $[\alpha]^{20}_D$ −33.6° (c 1.1, $CHCl_3$); IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.81 (s, 3 H), 1.09 (d, 3 H, J = 7 Hz), 1.36 (s, 3 H), 1.49 (s, 3 H), 1.58 (s, 3 H), 1.96 (s, 3 H), 1.98 (s, 3 H), 2.07 (s, 3 H), 2.67 (dd, 1 H, J = 15, 4 Hz), 3.07 (m, 1 H), 5.18 (m, 3 H), 5.45 (m, 2 H); mass spectrum m/e 448 (M^+·); high-resolution mass measurement, observed 448.2819 ($C_{26}H_{40}O_6$ requires 448.2824).

(1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-10,18-Diacetoxy-8-hydroxy-2,6-dolabelladiene (5):** mp 136–137 °C; $[\alpha]^{20}_D$ −56.7° (c 0.94, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.77 (s, 3 H), 1.08 (d, 3 H, J = 7 Hz), 1.18 (s, 3 H), 1.39 (s, 3 H), 1.59 (s, 3 H), 1.91 (s, 3 H), 2.05 (s, 3 H), 2.25 (m, 1 H), 4.20 (s, 1 H), 4.77 (d, 1 H, J = 8 Hz), 4.92 (d, 1 H, J = 16 Hz), 5.09 (dd, 1 H, J = 16, 9 Hz), 5.59 (m, 1 H). Anal. Calcd for $C_{24}H_{38}O_5$: C, 70.90; H, 9.42. Found: C, 71.00; H, 9.64.

(1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-8,18-Diacetoxy-10-hydroxy-2,6-dolabelladiene (6):** $[\alpha]_D$ −33.3° (c 0.40, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.05 (d, 3 H, J = 7 Hz), 1.50 (s, 3 H), 1.55 (s, 6 H), 2.00 (s, 3 H), 2.07 (s, 3 H), 2.50 (m, 2 H), 2.77 (dd, 1 H, J = 14, 8 Hz), 3.77 (m, 1 H), 4.95 (d, 1 H, J = 16 Hz), 5.23 (m, 2 H), 5.51 (d, 1 H, J = 16 Hz); ^{13}C NMR ($CDCl_3$) δ 170.5, 169.9, 139.5, 138.4, 131.9, 125.5, 86.1, 83.5, 65.8, 58.6, 53.7, 49.4, 46.8, 38.9, 38.0, 34.6, 25.8, 25.4, 23.0, 22.6, 20.3, 17.4, 17.3, 16.9; mass spectrum m/e 406 (M^+·), 287, 206, 187; high-resolution mass measurement, observed 460.2719 ($C_{24}H_{38}O_5$ requires 406.2719).

1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-8-10-Diacetoxy-18-hydroxy-2,6-dolabelladiene (7):** $[\alpha]^{20}_D$ −26.4° (c 0.36, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.06 (d, 3 H, J = 7 Hz), 1.18 (s, 3 H), 1.26 (s, 3 H), 1.51 (s, 3 H), 1.99 (s, 3 H), 2.05 (s, 3 H), 2.66 (dd, 1 H, J = 16, 6 Hz), 5.09 (m, 1 H), 5.16 (d, 1 H, J = 16 Hz), 5.30 (m, 2 H), 5.44 (d, 1 H, J = 16 Hz); high-resolution mass measurement, observed 406.2719 ($C_{24}H_{38}O_5$ requires 406.2719).

(1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-18-Acetoxy-8,10-dihydroxy-2,6-dolabelladiene (8):** $[\alpha]^{20}_D$ −45° (c 1.9, $CHCl_3$); IR 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.05 (d, 3 H, J = 7 Hz), 1.20 (s, 3 H), 1.50 (s, 3 H), 1.55 (s, 3 H), 2.02 (s, 3 H), 2.50 (m, 1 H), 2.89 (br s, 1 H), 3.94 (br s, 1 H), 5.00 (d, 1 H, J = 16 Hz), 5.18 (m, 2 H), 5.48 (d, 1 H, J = 16 Hz); ^{13}C NMR ($CDCl_3$) δ 169.5, 142.1, 138.6, 132.8, 126.4, 86.6, 74.1, 66.8, 58.0, 56.5, 49.5, 46.9, 39.2, 37.3, 35.1, 30.1, 26.1, 25.9, 23.2, 20.1, 18.0; mass spectrum m/e 364 (M^+·), 286, 206; high-resolution mass measurement, observed 364.2619 ($C_{22}H_{36}O_4$ requires 364.2613).

(1*R,2*E*,4*R**,6*E*,8*S**,10*S**,11*S**,12*R**)-8,10,18-Trihydroxy-2,6-dolabelladiene (9):** mp 168–169 °C; $[\alpha]^{20}_D$ −86° (c 0.5, $CHCl_3$); IR ($CHCl_3$) 3500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (s, 3 H), 1.05 (d, 3 H, J = 7 Hz), 1.16 (s, 3 H), 1.23 (s, 3 H), 1.25 (s, 3 H), 1.95 (m, 2 H), 2.16 (m, 2 H), 2.34 (m, 2 H), 2.57 (br s, 1 H), 3.89 (d, 1 H, J = 9 Hz), 4.92 (d, 1 H, J = 16 Hz), 5.09 (m, 1 H), 5.32 (dd, 1 H, J = 16, 10 Hz), 5.75 (d, 1 H, J = 16 Hz); ^{13}C NMR ($CDCl_3$) δ 143.1, 137.4, 132.4, 125.5, 75.0, 72.7, 67.0, 57.1, 56.8, 49.4, 47.1, 38.2, 37.9, 34.1, 31.5, 29.3, 26.0, 23.2, 16.6, 16.4. Anal. Calcd for $C_{20}H_{34}O_3$: C, 74.49; H, 10.63. Found: C, 74.70; H, 10.63.

(1*R,2*E*,4*R**,6*R**,7*E*,10*S**,11*S**,12*R**)-6,10-Diacetoxy-18-hydroxy-2,7-dolabelladiene (10):** $[\alpha]^{20}_D$ −4.7° (c 0.17, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.85 (s, 3 H), 1.10 (d, 3 H, J = 7 Hz), 1.18 (s, 3 H), 1.27 (s, 3 H), 1.78 (s, 3 H), 2.00 (s, 3 H), 2.07 (s, 3 H), 2.32 (d, 1 H, J = 7 Hz), 4.81 (m, 1 H), 4.97 (d, 1 H, J = 16 Hz), 5.27 (d, 1 H, J = 10 Hz), 5.47 (dd, 1 H, J = 16, 7 Hz), 5.60 (m, 1 H); high-resolution mass measurement, observed 406.2715 ($C_{24}H_{38}O_5$ requires 406.2719).

(1*R,2*E*,4*R**,6*R**,7*E*,10*S**,11*S**,12*R**)-10-Acetoxy-6,18-dihydroxy-2,7-dolabelladiene (11):** $[\alpha]^{20}_D$ −0.4° (c 0.7, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.84 (s, 3 H), 1.06 (d, 3 H, J = 7 Hz), 1.16 (s, 3 H), 1.26 (s, 3 H), 1.70 (s, 3 H), 2.05 (s, 3 H), 4.50 (m, 1 H), 4.80 (m, 1 H), 4.98 (d, 1 H, J = 16 Hz), 5.30 (d, 1 H, J = 9 Hz), 5.48 (dd, 1 H, J = 16, 7 Hz); high-resolution mass measurement, observed 364.2623 ($C_{22}H_{36}O_4$ requires 364.2613).

(1*R,2*E*,4*R**,6*R**,7*E*,10*S**,11*S**,12*R**)-18-Acetoxy-6,10-dihydroxy-2,7-dolabelladiene (12):** mp 153–154 °C; $[\alpha]^{20}_D$ +21.2° (c 1.06, $CHCl_3$); IR ($CHCl_3$) 3500, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3 H), 1.06 (d, 3 H, J = 7 Hz), 1.54 (s, 3 H), 1.58 (s, 3 H), 1.68 (s, 3 H), 2.02 (s, 3 H), 2.70 (m, 1 H), 2.98 (d, 1 H, J = 10 Hz), 3.51 (m, 1 H), 4.53 (m, 1 H), 4.95 (d, 1 H, J = 16 Hz), 5.16 (d, 1 H, J = 9 Hz), 5.40 (dd, 1 H, J = 16, 7 Hz); ^{13}C NMR ($CDCl_3$) δ 169.0, 135.6, 134.1, 133.0, 130.2, 86.8, 71.5, 65.3, 54.2, 47.5, 46.2, 43.1, 39.8, 31.2, 26.0, 21.9, 20.0, 18.9, 16.9, 16.0. Anal. Calcd for $C_{22}H_{36}O_4$: C, 72.49; H, 10.04. Found: C, 72.30; H, 10.04.

(1*R,2*E*,4*R**,6*R**,7*E*,10*S**,11*S**,12*R**)-6,10,18-Trihydroxy-2,7-dolabelladiene (13):** mp 157–158 °C; $[\alpha]_D$ −29° (c 0.9, $CHCl_3$); IR 3500 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (s, 3 H), 1.05 (d, 1 H, J = 7 Hz), 1.20 (s, 3 H), 1.27 (s, 3 H), 1.70 (s, 3 H), 1.93 (m, 1 H), 2.14 (d, 1 H, J = 11 Hz), 2.41 (m, 1 H), 2.53 (m, 1 H), 4.50 (m, 1 H), 4.90 (d, 1 H, J = 16 Hz), 5.08 (d, 1 H, J = 9 Hz), 5.33 (dd, 1 H, J = 16, 7 Hz). Anal. Calcd for $C_{20}H_{34}O_3 \cdot CH_3OH$: C, 71.15; H, 10.80. Found: C, 71.43; H, 10.73. (Sample for analysis was recrystallized from methanol.)

(1*R,2*E*,4*R**,7*E*,11*S**,12*R**)-18-Hydroxy-2,7-dolabelladiene (14):** $[\alpha]^{20}_D$ −75.1° (c 1.35, $CHCl_3$); IR ($CHCl_3$) 3550 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.89 (s, 3 H), 0.92 (d, 3 H, J = 7 Hz), 1.22 (s, 6 H), 1.45 (s, 3 H), 1.82 (m, 3 H), 2.09 (m, 4 H), 5.02 (t, 1 H, J = 7 Hz), 5.16 (m, 2 H); mass spectrum m/e 290 (M^+·), 272, 257, 229, 175; high-resolution mass measurement, observed 290.258 ± 0.010 ($C_{20}H_{34}O$ requires 290.261).

Reduction of Acetates with Lithium Aluminum Hydride. A solution of the diacetate **1** (20 mg, 0.05 mmol) in anhydrous tetrahydrofuran (1 mL) was added to a stirred suspension of lithium aluminum hydride (20 mg, 0.53 mmol) in anhydrous tetrahydrofuran (9 mL) at room temperature. The reaction mixture was stirred at reflux for 1 h, cooled to 0 °C, and quenched with water (3 mL), followed by 15% sodium hydroxide solution (3 mL). The inorganic salts were removed by filtration and the tetrahydrofuran was evaporated in vacuo. The aqueous residue was extracted with ether (3 × 20 ml), and the combined ether extracts were dried over sodium sulfate and evaporated in vacuo to obtain the diol **3** (12 mg, 79% theoretical) identical in all respects with the natural material.

Using identical reaction conditions and workup procedures: **2** (30 mg, 0.08 mmol) gave **3** (20 mg, 85% theoretical); **4** (24 mg, 0.054 mmol) gave **9** (15 mg, 85% theoretical); **5** (20 mg, 0.05 mmol) gave **9** (12 mg, 74% theoretical); **6** (30 mg, 0.073 mmol) gave **9** (19 mg, 81% theoretical); **7** (15 mg, 0.037 mmol) gave **9** (10 mg, 84% theoretical); **8** (25 mg, 0.065 mmol) gave **9** (17 mg, 80% theoretical); **10** (15 mg, 0.037 mmol) gave **13** (9 mg, 73% theoretical); **11** (35 mg, 0.092 mmol) gave **13** (23 mg, 77% theoretical); **12** (15 mg, 0.039 mmol) gave **13** (9 mg, 72% theoretical).

Acetylation of Monoacetate 8. Acetic anhydride (1 mL) was added to a solution of the monoacetate **8** (80 mg, 0.21 mmol) in pyridine (3 mL), and the reaction mixture was stirred under a nitrogen atmosphere for 24 h. The excess reagents were removed in vacuo, and the residue was partitioned between water and ether. The ether extracts were dried over sodium sulfate and the solvent was evaporated to yield a solid which was recrystallized from hexane to obtain the diacetate **5** (70 mg, 81% theoretical), identical in all respects with the natural material.

6-Bromo-10,18-diacetoxy-2,7-dolabelladiene (16). A solution of phosphorus tribromide (150 μL, 1.5 mmol) in hexane (5 mL) was added dropwise over 10 min to a cooled solution of the diacetate **5** (30 mg, 0.079 mmol) and pyridine (50 μL, 0.62 mmol) in hexane (10 mL) at −30 °C. The reaction mixture was stirred for 1 h at −30 °C, then quenched with water (5 mL). The mixture was extracted with ether (3 × 20 mL), the combined ether extracts were dried over the sodium sulfate, and the solvent was evaporated to yield the bromide **16** (25 mg, 67% theoretical). All attempts to purify the bromide **16** by chromatography resulted in extensive degradation. ^1H NMR ($CDCl_3$) δ 0.80 (s, 3 H), 1.05 (d, 3 H, J = 7 Hz), 1.35 (s, 3 H), 1.59 (s, 3 H), 1.70 (s, 3 H), 1.89 (s, 3 H), 2.02 (s, 3 H), 3.12 (m, 1 H), 4.70 (d, 1 H, J = 10 Hz), 4.82 (d, 1 H, J = 16 Hz), 4.98 (m, 1 H), 5.48 (dd, 1 H, J = 16, 8 Hz), 5.59 (d, 1 H, J = 10 Hz).

Reduction of Bromide 16. Sodium (30 mg, 1.3 mmol) was added to a solution of the bromide **16** (26 mg, 0.054 mmol) in tetrahydrofuran (10 mL) containing *tert*-butyl alcohol (50 μL, 0.7 mmol) and the reaction mixture was boiled under reflux for 3 h. The product was cooled and quenched with water (5 mL). The organic material was extracted with ether (3 × 15 mL), and the combined extracts were dried over sodium sulfate and evaporated in vacuo to yield an oil (8 mg). Chromatography of the oil on silica gel gave the diol **3** as the major product (4 mg, 24% theoretical).

Solvolysis of Bromide 16. A solution of silver acetate (50 mg, 0.33 mmol) in aqueous acetic acid [50 μL (0.87 mmol) in 1 mL] was added to the bromide **16** (40 mg, 0.083 mmol) in tetrahydrofuran (5 mL) at 0 °C, and the mixture was stirred for 2 h. The mixture was partitioned between water (5 mL) and ether (3 × 10 mL). The combined ether extracts were dried over sodium sulfate and the solvent was evaporated to yield a mixture of triacetates (28 mg). The product was treated with lithium aluminum hydride according to the established procedures to yield a mixture of triols (20 mg). Chromatography of the triols on silica gel gave the triols **9** (12 mg, 44% theoretical) and **13** (8 mg, 29% theoretical), both identical with authentic samples.

Jones Oxidation of the Diol 3. One equivalent of Jones reagent

(24 μL, 0.025 mmol) was added dropwise to a solution of the diol **3** (7 mg, 0.023 mmol) in anhydrous acetone (5 mL) at 0 °C. The reaction mixture was stirred for 10 min, then quenched with excess 2-propanol (1 drop) and water (5 mL). The acetone was removed in vacuo and the aqueous residue extracted with ether (3 × 10 mL). The combined ether extracts were dried over sodium sulfate and the solvent was evaporated to yield the ketone **18** (4 mg, 57% theoretical) as an oil: IR ($CHCl_3$) 3500, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.95 (d, 3 H, J = 7 Hz), 0.96 (s, 3 H), 1.18 (s, 6 H), 1.44 (s, 3 H), 2.62 (m, 1 H), 2.80 (d, 1 H, J = 10 Hz), 2.93 (d, 1 H, J = 10 Hz), 3.23 (d, 1 H, J = 10 Hz), 5.20 (m, 2 H).

Jones Oxidation of Triol 9. One equivalent of Jones reagent was added to a solution of the triol **9** (14 mg, 0.043 mmol) in acetone (5 mL) and the reaction was allowed to proceed according to the procedure above to give the ketone **19** (8 mg, 58% theoretical): IR ($CDCl_3$) 3500, 1710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.99 (d, 3 H, J = 7 Hz), 1.09 (s, 3 H), 1.13 (s, 3 H), 1.14 (s, 3 H), 1.23 (s, 3 H), 1.50 (m, 4 H), 1.93 (m, 2 H), 2.16 (m, 1 H), 2.59 (m, 2 H), 2.48 (m, 2 H), 2.83 (d, 1 H, J = 10 Hz), 5.16 (d, 1 H, J = 16 Hz), 5.23 (m, 1 H), 5.30 (m, 1 H), 5.47 (d, 1 H, J = 16 Hz).

Jones Oxidation of Triol 13. One equivalent of Jones reagent was added to a solution of the triol **13** (20 mg, 0.062 mmol) in acetone (5 mL) and the reaction was allowed to proceed according to the procedure above to give the dione (11 mg, 56% theoretical): IR ($CHCl_3$) 3500, 1710, 1680 cm^{-1}; λ_{max} 247 nm; ^1H NMR ($CDCl_3$) δ 1.03 (s, 3 H), 1.10 (d, 3 H, J = 7 Hz), 1.21 (s, 3 H), 1.91 (s, 3 H), 2.46 (br s, 2 H), 2.70 (m, 1 H), 2.95 (d, 1 H, J = 11 Hz), 3.05 (d, 1 H, J = 11 Hz), 3.39 (d, 1 H, J = 11 Hz), 5.19 (d, 1 H, J = 16 Hz), 5.49 (dd, 1 H, J = 16, 7 Hz), 5.98 (s, 1 H).

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Registry No.—**13** dione, 62861-24-9; **16**, 62861-25-0; **18**, 62861-26-1; **19**, 62861-27-2.

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A Convenient Synthesis of γ-Lactams via Michael Addition

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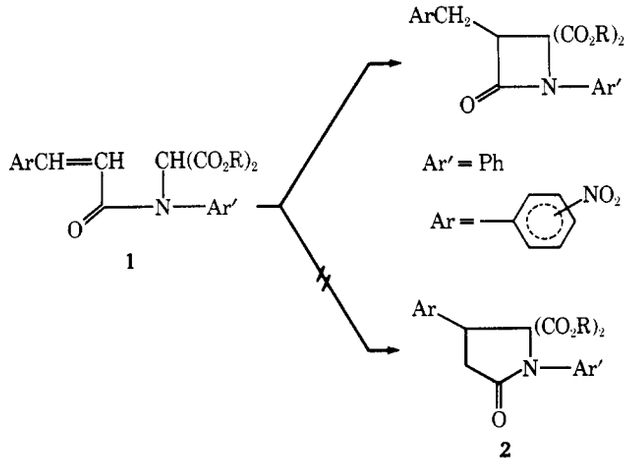
A convenient synthesis of 1-aryl-2,2-dicarboalkoxy-5-pyrrolidinones from substituted anilinomalonates by way of intermolecular Michael addition followed by amidification has been developed. This is probably the first report on a Michael addition involving an acid chloride as a Michael acceptor. The mechanism suggested has been convincingly established. A large number of γ-lactam derivatives have been prepared in good to excellent yields.

It has been demonstrated by Bose et al.[1] that *N*-acryloylanilinomalonate does not undergo intramolecular Michael addition to yield γ-lactam because the acrylic amide moiety is a poor Michael acceptor. A strong electron-withdrawing substituent in the β position of the acrylamide, however, does activate the double bond to such an extent as to lead to the formation of β- and γ-lactams[2] from suitable substrates by way of Michael addition.



Though much work has not been reported on the formation of β- or γ-lactams by intramolecular Michael addition, many γ-lactams have been conveniently synthesized by intermolecular Michael addition. Cocolas and Hartung[3] have reported that the Michael adduct between diethyl acetamidomalonate and ethyl acrylate or crotonate in ethanol gave 2-pyrrolidinones at reflux temperature. The formation of γ-lactams from the simple Michael adduct has been explained on the basis that the conformation of the molecule places the groups in question in very close proximity with each other for the attack of nitrogen on the γ-carbonyl carbon.

A detailed and exhaustive study on the synthesis of γ-lactams has been made by Pachaly et al.[4] It has been shown that *N*-acetylglycine esters also undergo similar intermolecular Michael addition provided that a strong base such as sodium hydride is used. The reaction follows a stereoselective path leading to the formation of the trans isomer of the γ-lactam.

An attempt to throw some light on the intramolecular Michael addition leading to γ-lactam formation led us to work on amide **1e** (Ar = Ph; Ar' = *p*-nitrophenyl).