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A SYNTHESIS OF EXALTOLIDE

1,15-PENTADECANOLIDE

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Abstract—A synthesis of exaltolide[1,4] (IV) is described and a preliminary study made of the products from hydrogenation of the intermediate 1,15-pentadec-10,12-diynolide (III) under various conditions. The effect of ring strain on the carbonyl absorption frequency of various lactones has also been examined.

THE macrocyclic lactone of 15-hydroxypentadecanoic acid, exaltolide (IV), was first synthesized by Kerschbaum[2] from the parent acid, which had been isolated from the roots of *Angelica archangelica officinalis.*[3] Recently, proof was presented for the existence of the lactone in nature.[4] The musk-like odour and strong fixative power of the lactone give it some commercial importance and consequently, several attempts have been made to devise practical syntheses.[5] However, since most involved long reaction times and the preparation and cyclization of ω-hydroxy fatty acid derivatives, the overall yields were generally low.

Recently Bhatthacharyya *et al.*[6] succeeded in synthesizing exaltolide and other macrocyclic musk compounds utilizing aleuritic acid, erucyl alcohol and kamlolenic acid, all comparatively readily available.

In a preliminary announcement, a new synthesis of exaltolide which broke away from these traditional procedures was reported.[4] A brief note describing a similar synthesis was published simultaneously by Bergel'son *et al.*[7] and further elaborated in a subsequent paper.[8] The present paper gives more extensive data which indicate the potential of the process as a method for synthesizing other macrocyclic systems.

The formation of macrocyclic rings by the intramolecular oxidative coupling of α,ω-diacetylenes has received extensive attention in recent years and a variety of mild conditions have been defined for performing the reaction.[9] With such a reaction as

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[1] British Patent Application No. 12626/60.

[2] M. Kershbaum, *Ber. Dtsch. Chem. Ges.* **60,** 902 (1927).

[3] G. Ciamician and P. Silber, *Ber. Dtsch. Chem. Ges.* **29,** 1811 (1896).

[4] J. Carnduff, G. Eglinton, W. McCrae and R. A. Raphael, *Chem. & Ind.* 559 (1960).

[5] M. Stoll and L. Ruzicka, *Helv. Chim. Acta* **11,** 1159 (1928); M. Stoll and A. Rouvé, *Ibid.* **17,** 1283 (1936); M. Stoll, *Ibid.* **30,** 1393 (1947); M. Stoll and P. Bolle, *Ibid.* **31,** 98 (1948); H. Hunsdiecker and H. Erlbach, *Ber. Dtsch. Chem. Ges.* **80,** 129 (1947).

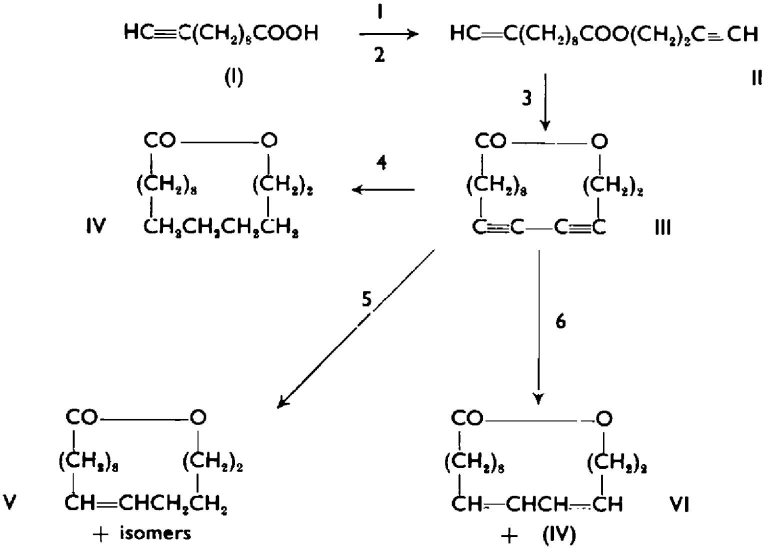
[6] H. H. Mathar and S. C. Bhattacharyya, *J. Chem. Soc.* 3505 (1963) and earlier papers.

[7] L. D. Bergel'son, Yul. G. Molotovskii and M. M. Shemaykin, *Chem. & Ind.* 558 (1960).

[8] L. D. Bergel'son, Yul. G. Molotovskii and M. M. Shemyakin, *J. Gen. Chem. U.S.S.R.* **32,** 57 (1962).

[9] G. Eglinton and W. McCrae, *Advances in Organic Chemistry* (Edited by Raphael, Taylor and Wynberg), Vol. 4, p. 225. J. Wiley, New York (1963).

the key step, a synthesis of the C_{15} lactone exaltolide (IV) was devised in which a C_{11} fragment, undec-10-ynoic acid (1) and a C_4 fragment, but-1-yn-4-ol, were first joined by esterification then cyclized by intramolecular coupling and the resultant macrocyclic diyne lactone (III) was hydrogenated.



Reagents: 1. Oxalyl chloride. 2. But-1-yn-4-ol; pyridine-ether; 20°. 3. Pyridine-ether-benzene (6:1:1); $Cu(OAc)_2$; 50°. 4. H_2–Pt. 5. H_2–Pd. 6. Lindlar's catalyst.

The starting materials for this sequence are readily available. Undec-10-ynoic acid (1) can be prepared from undec-10-enoic acid,[10] available in quantity from the pyrolysis of castor oil[11] whilst but-1-yn-4-ol is easily synthesized from sodium acetylide and ethylene oxide.[12] The oxidative cyclization of but-4-ynyl undec-10-ynoate (II) proceeded extremely smoothly, resulting in an 88% yield of crystalline 1,15-pentadec-10,12-diynolide (III). Hydrogenation of this lactone over platinum yielded the saturated lactone (IV), shown by m.p., IR spectrum and gas-liquid chromatography (GLC) to be identical to an authentic sample of exaltolide. Thus, the macrocyclic lactone exaltolide (IV) was synthesized from undec-10-enoic acid in an overall yield of 43%.

The further syntheses of other macrocyclic musk compounds now seemed possible through the specific reduction or hydration of the key intermediate, 1,15-pentadec-10,12-diynolide (III). Hydrogenation of the conjugated diyne system in dimethyl docos-10,12-diynoate had been investigated earlier by Riley who used Raney nickel at 100°.[13] Under these conditions he found that one or other of the triple bonds was first almost completely saturated before the remaining triple bond was attacked. In order to obtain some idea of the possible products from the catalytic hydrogenation of 1,15-pentadec-10,12-diynolide (III), a parallel investigation using Riley's diyne-diester was initiated. Since the site of unsaturation could best be located by cleavage

[10] H. K. Black and B. C. L. Weedon, *J. Chem. Soc.* 1785 (1953).

[11] F. Kraft, *Ber. Dtsch. Chem. Ges.* 10, 2034 (1877).

[12] A. L. Henne and K. W. Greenlee, *J. Amer. Chem. Soc.* 67, 484 (1945).

[13] J. P. Riley, *J. Chem. Soc.* 2193 (1953).

into identifiable fragments, the following procedure was generally adopted in the examination of the reduction products. These were subjected to von Rudloff oxidation[14] followed by treatment with excess ethereal diazomethane. The resultant diesters were then examined by GLC and the results interpreted on the basis of a standard curve obtained as follows. Under exactly the same conditions as those to be used in the examination of the diesters from the von Rudloff oxidation, the retention times of dimethyl suberate, azelate and sebacate were determined. The retention time of dimethyl tridecamethylenedioate, obtained by a hydrolysis of exaltolide followed by oxidation and esterification, was also utilized. The retention volumes (V_R) of the four standards were calculated and a graph of log V_R *versus* the number of methylenes (n) in each diester plotted. Since log V_R is a linear function of the number of carbons for the members of a homologous series, it was possible to estimate the number of methylenes in each diester obtained from the oxidation reactions and thence the type and proportions of double bond isomers obtained on hydrogenation of dimethyl docos-10,12-diynoate. These results are summarized in Table 1. Although some double bond migration occurred with the Pd–C catalyst, an almost statistical 1,2- and 1,4-reduction of the diyne system was obtained. Chemical reduction with sodium in liquid ammonia gave largely 1,4-reduction, but the results were not sufficiently encouraging to consider this procedure practical. Double bond migration and a lack

TABLE 1. PROPORTIONS OF ISOMERS OBTAINED ON REDUCTION OF DIMETHYL DOCOS-10,12-DIYNOATE AND 1,15-PENTADEC-10,12-DIYNOLIDE

Peak retention time (min)	Number of methylenes in chain of diesters	Percentage of each diester	Method of reduction	Percentage of double bond isomers
2·0	6	Standards		
3·1	7			
4·8	8			
43·5	13			
Dimethyl docos-10,12-diynoate				
3·1	7	1	10% Pd-C	Approximately 60% Δ^{10} and 35% Δ^{11} mono-enes.
4·8	8	26		
7·2	9	35		
11·2	10	33		
17·3	11	5		
4·8	8	30	Na/NH_3	Approximately 50% Δ^{10} and 50% Δ^{11} mono-enes.
7·2	9	47		
11·2	10	23		
1,15-Pentadec-10,12-diynolide				
3·1	7	7	10% Pd–C	27% Δ^{10}; 10% Δ^{11}; 20% Δ^{12} mono-enes and 32% of exaltolide
4·8	8	27		
7·2	9	10		
11·2	10	20		
17·3	11	4		
43·5	13	32		

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[14] E. von Rudloff, *J. Amer. Oil Chemist's Soc.* **33**, 126 (1956).

of specificity was also noted in the hydrogenation of 1,15-pentadec-10,12-diynolide with the 10% Pd–C catalyst. The reduction product, an oil, was shown by GLC to contain no starting material and, by a microhydrogenation of a sample, to contain 68% double bond material but it was not possible to distinguish fully saturated material *viz.* exaltolide, from any unsaturated products by GLC. The crude reduction product was subjected to von Rudloff oxidation followed by hydrolysis, to cleave the ester linkage, to give a mixture of dicarboxylic and hydroxy acids. The latter were further oxidized, without isolation, by an aqueous acetone solution of chromic acid and the resultant mixed acids methylated and examined by GLC. By using the same graphical procedure outlined for dimethyl docos-10,12-diynoate, the proportions of double bond isomers obtained from catalytic reduction of 1,15-pentadec-10,12-diynolide (III)were estimated (Table 1).

This lack of specificity observed for both compounds is not too surprising on consideration of the generally accepted mechanism for the catalytic reduction of triple bonds.[15] In the case of the diyne lactone (III), however, one interesting result is the low proportion of the Δ^{11} isomer and the surprisingly high yield of the saturated compound, exaltolide (IV). These results could possibly be due to a facile stereomutation of the partially formed *cis* Δ^{11} isomer with a resultant fast saturation of the *trans* oriented double bond, a mechanism in accord with Dobson's findings in the catalytic reduction of a disubstituted triple bond.[16] Why this phenomenon should be observed with 1,15-pentadec-10,12-diynolide (III) and not with dimethyl docos-10,12-diynoate is not clear though the molecular environment of the diyne system may be a factor. The attempted chemical reduction of 1,15-pentadec-10,12-diynolide (III) with sodium in liquid ammonia failed due to opening of the lactone ring and reaction of the products with the traces of sodamide inevitably formed. A more satisfactory result was obtained using Lindlar's catalyst.[17] The resultant oil was shown, by microhydrogenation of a sample, to contain 1.9 double bond equivalents, its IR spectrum showed a strong *cis* double bond peak (720 cm^{-1}) whilst the UV spectrum had one main peak at 234 $m\mu$ (ε 13,600). This latter is in keeping with the observation that the absorption maximum for monocyclic dienes increases in ring size beyond C_{10} eg. a C_{13} ring gives λ_{max} 232 $m\mu$.[18] It would also be expected that as ring size increases, the intensity values should approach those of the straight chain dienes, *viz.* ε 15,000. Since GLC of the product showed only one peak, it would seem that Lindlar's catalyst yielded the *cis-cis* $\Delta^{9,11}$ isomer with high specificity. Bergel'son *et al.* also synthesized 1,15-pentadec-10,12-dienolide (VI) and also concluded that the Lindlar catalyst produced the *cis-cis* configuration since Diels-Alder reaction with maleic anhydride was readily obtained.[8]

The unsaturated macrocyclic lactones and lactone mixtures described above, all had pleasant and tenacious odors. That of 1,15-pentadec-10,12-diynolide (III) was particularly potent, even in very small concentrations, and had a distinctly different nuance from that of exaltolide.

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[15] G. C. Bond, *Catalysis by Metals* p. 281. Butterworths, London (1962).

[16] N. A. Dobson, G. Eglinton, M. Krishnamurti, R. A. Raphael and R. G. Willis, *Tetrahedron* **16**, 16 (1961).

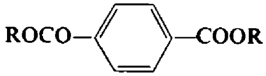
[17] H. Lindlar, *Helv. Chim. Acta* **35**, 446 (1952).

[18] A. E. Gillam and E. S. Stern, *Electronic Absorption Spectroscopy in Organic Chemistry* p. 96. E. Arnold, London (1958).

Several attempts were made to hydrate the conjugated diyne system of 1,15-pentadec-10,12-diynolide using the $Hg(OAc)_2$–HOAc–H_2SO_4 reagent and also the HgO-BF_3–ether complex.[19] All such attempts produced a complex mixture of products which were not further examined.

One of the most interesting aspects of the class of compounds exemplified by 1,15-pentadec-10,12-diynolide (III), is the stereochemistry and effect of ring strain on absorption maxima. The carbonyl stretching frequency in small ring lactones is raised by ring strain but the reverse effect may hold in larger rings, due to conformational effects and steric interaction. To determine such effects, if any, a study was made of the carbonyl absorption frequencies in the IR of available esters and lactones, the results of which are summarized in Table 2.

TABLE 2*

R	ν	$\Delta\nu_{1/2}$	ε_a per C=O
A. CARBONYL ABSORPTION FREQUENCIES FOR ESTERS OF TYPE			ROCO——COOR
1. —CH_3	1731	14	665
2. —CH_2CH_3	1725	15·5	635
3. —$CH_2C\equiv CH$	1735	15	640
4. —$(CH_2)_2C\equiv CH$	1730	14·5	735
5. —$(CH_2)_3C\equiv CH$	1727·5	14·5	655
6. —$(CH_2)_4C\equiv CH$	1726	14·5	630
7. Cyclic dimer of compound 6	1726	16	Saturated solution
B. CARBONYL ABSORPTION FREQUENCIES FOR ESTERS OF TYPE			$ROCO(CH_2)_8COOR$
8. —CH_3	1743	16	480
9. —CH_2CH_3	1738	15·5	550
10. —$(CH_2)_3CH_3$	1736	16·5	480
11. —$CH_2C\equiv CH$	1749·5	20	505
12. —$(CH_2)_2C\equiv CH$	1744	17	480
13. Cyclic dimer of compound 12	1741	16	660
14. $(CH_2)_8$ (cyclic)	1737	15	530
C. MISCELLANEOUS ESTERS			
15. $[MeO_2C(CH_2)_8C\equiv C]_2$	1743	16	540
16. Ester II	1744	17	480
17. Lactone III	1742	17·5	685
18. Exaltolide (IV)	1736	15·5	610

* All spectra were recorded linearly in cm^{-1} as percentage transmission with a Unicam S.P. 100 double beam IR spectrophotometer equipped with an S.P. 130 NaCl prism, −1500 lines per inch grating, double monochromator (vacuum). CCl_4 was used as solvent.

In all the series of esters[20] 1–2, 3–6, 8–10 and 11–12, small but fairly uniform shifts occur, presumably due to the changing inductive effect of the alkyl groups. In the series 3–6, the effect of the ethynyl group on the carbonyl frequency is zero when the two groups are separated by four methylenes but an increase in frequency occurs as the two groups are brought closer together. This follows the well-known pattern of

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[19] R. A. Raphael, *Acetylenic Compounds in Organic Synthesis* p. 203. Butterworths, London (1955).

[20] A. T. James and A. J. P. Martin, *Biochem. J.* **50**, 679 (1952).

the inductive effect as evaluated by acidity changes in substituted acids, etc. The carbonyl stretching frequency of the saturated cyclic esters, 14 and 18, and the acyclic ester, 10, are almost identical and it would seem therefore, that ring formation has no effect when the ring size is of this order. Whilst dimerization of compound 6 to 7 gave no shift in the frequency, the cyclization of the terminal diynes, 12 and 16, caused a slight decrease, probably due to the increased inductive effect of the conjugated diyne group through the two methylenes.

EXPERIMENTAL

M.ps were measured on a Kofler hot stage and are corrected. Routine IR spectra were determined as liquid films or Nujol mulls with Perkin-Elmer spectrophotometers, Models 13 or 137 (NaCl prisms). UV spectra were determined with a Unicam S.P. 500 spectrophotometer.

Dimethyl docos-10,12-*diynoate*. Undecynoic acid was prepared from undecenoic acid in 80% yield by the method of Black and Weedon[10] and its methyl ester obtained by treatment with excess ethereal diazomethane. The methyl undec-10-ynoate (9·6 g) in ethanol (72 ml) was added dropwise with stirring to a solution of CuCl (12·8 g), NH_4Cl (22·4 g) and conc. HCl (2 drops) in water (120 ml). The mixture was heated to 55–60° and air bubbled through for 5 hr. After cooling, the mixture was diluted with water (100 ml) and ether extracted (3 × 250 ml). The combined ether extract (650 ml) was filtered to remove Cu salts, washed several times with water, dried over $MgSO_4$ and evaporated. The residual solid crystallized from ether at −50° to give pure dimethyl docos-10,12-diynoate (8·0 g, 84%) m.p. 41–42° (lit. 42·5°).[13] (Found: C, 73·8; H, 9·8. Calc. for $C_{24}H_{34}O_4$: C, 73·8; H, 9·8%). $\Delta_{\text{max}}^{\text{EtOH}}$ 226, 230, and 254 mμ (ε 464, 390 and 229 respectively).

Catalytic hydrogenation of dimethyl docos-10,12-*diynoate*. The diyne-diester (780 mg) in ethyl acetate (30 ml) was shaken in a H_2 atm. over 10% Pd–C catalyst (100 mg) at room temp and press. The hydrogenation was stopped when 3 molar equiv. H_2 had been absorbed. Removal of the catalyst and evaporation of the solvent gave a colourless semi-crystalline solid (700 mg) $\bar{\nu}_{\text{max}}$ 966 (s), 720 (s) cm^{-1}.

von Rudloff oxidation of the reduction product. Sodium metaperiodate (2·24 g) and $KMnO_4$ (66 mg) were dissolved in water (150 ml). The reduction product (540 mg) was dissolved in t-butanol (100 ml) and a solution of K_2CO_3 (550 mg) in water (50 ml) added. The aqueous and alcoholic solutions were then mixed and shaken for 10 hr at room temp. The reaction was stopped by addition of sufficient solid $Na_2S_2O_6$ to remove free I_2 and the t-butanol then removed at 60° on a rotary evaporator. The aqueous solution was then acidified to pH 1·0 and continuously ether extracted over 10 hr. On drying the extract and evaporation of the solvent a white solid residue was obtained (500 mg) $\bar{\nu}_{\text{max}}$ 1690 (s) cm^{-1}.

Examination of the oxidation product by GLC. The acidic oxidation products, dissolved in ether, were treated with excess ethereal diazomethane till an IR spectrum of the crude product showed only the typical ester peak at 1740 cm^{-1}. The following general procedure was adopted for the examination of the crude mixture of diesters. A few milligrams of the material to be examined were dissolved in decalin (0·1 ml) and 0·01 microlitres of this solution placed on the GLC column by means of a micropipette. The column, with a stationary phase of 5% Apiezon on 100–120 mesh Celite, was maintained at 185° with an argon flow rate of 30 ml/min and a chart speed of 45 ins/hr.

The standards, dimethyl suberate, azelate and sebacate were obtained by treatment of the corresponding acids with ethereal diazomethane. Dimethyl tridecamethylenedioate was prepared as follows. A small authentic sample of exaltolide was hydrolysed and the resultant hydroxy acid esterified with diazomethane. Treatment of this material in acetone solution with 9·7N chromic acid aq over 12 hr followed by esterification as before yielded the required dimethyl tridecamethylenedioate.

Both the standards and the oxidation products gave symmetrical peaks, the retention time of each peak being measured from the air peak to its vertical line of symmetry. Calculation of the retention columns as detailed earlier thence yields the amount and type of double bond isomer obtained on reduction.

Reduction of dimethyl docos-10,12-*diynoate with sodium in ammonia*. The diyne-diester (500 mg) in dry tetrahydrofuran (10 ml) was added with stirring to liquid ammonia (200 ml) at −35°. No reaction between the ester and the liquid ammonia was detected on examination of a sample of the mixture. Sodium (200 mg) was added to the mixture in small pieces during 10 min and, shortly thereafter, excess solid NH_4Cl added.

The ammonia was allowed to evaporate over a period of 2 hr and the residue was diluted with water, and ether extracted (3 × 100 ml). The combined extracts were dried and evaporated to give a yellow solid (180 mg) $\bar{\nu}_{max}$ 1735 (s), 1710 (s), 960 (s), 720 (s) cm^{-1}.

von Rudloff oxidation of sodium in ammonia reduction product. Potassium carbonate (300 mg) in water (10 ml) was added to a solution of the above reduction products (180 mg) in t-butanol (70 ml). To this was added 100 ml of stock oxidant solution (14·0 g $NaIO_4$ and 250 ml 0·01M $KMnO_4$ made up to 1 l.) and the mixture shaken for 15 hr. The product was isolated as before, however, in this case 5 ml of 10M KOH was added, after the treatment with $Na_2S_2O_5$, to hydrolyse any amide. A white solid (150 mg) was obtained $\bar{\nu}_{max}$ 1690 (s) cm^{-1}. This material was esterified and examined by GLC as described previously.

But-4-*ynyl undec*-10-*ynoate* (II).[*] Undecynoyl chloride (30 g freshly prepared by reacting oxalyl chloride with the acid I) was dissolved in anhydrous ether (200 ml) and but-1-yn-4-ol (10·5 g) added. Anhydrous pyridine (12 ml) was then added with stirring at such a rate that no rise in temp occurred. After removal of the precipitated pyridine hydrochloride the neutral filtrate was isolated as an ethereal solution and filtered through a column of alumina (Brockman, Grade 1, 100 g). The ester (30·8 g, 88%) crystallized from ether in plates, m.p. 32·5–33·0° (lit. 33·8–34·2°).[7] Found: C, 76·6; H, 9·6. Calc. for $C_{15}H_{22}O_2$: C, 76·8; H, 9·5%).

1,15-*Pentadec*-10,12-*diynolide* (III). A solution of but-4-ynyl undec-10-ynoate (II, 2·5 g) in ether–pyridine (1:8, 90 ml) was added over 8 hr to a refluxing solution of anhydrous cupric acetate (12 g) in ether–benzene–pyridine (1:1:6, 800 ml), the drops of ester solution being continuously entrained by the refluxing solvent in a high dilution apparatus.[21] After a further 1·5 hr at reflux, the green solution was cooled and added slowly, with stirring to 0·05 M, H_2SO_4 (5 l.) at 0°. The neutral fraction was isolated by ether extraction and, in benzene solution, passed down a column of alumina (Brockman, Grade 1, 7 g). Concentration of the eluate gave a white crystalline solid (2·18 g, 88%) m.p. 53–54°, which crystallized from pet ether (b.p. 60–80°) as long white platelets, m.p. 55–56° (lit. 55·5–56°).[7] (Found: C, 77·7; H, 8·8. Calc. for $C_{15}H_{20}O_2$: C, 77·5; H, 8·7%). λ_{max}^{EtOH} 227·5, 238 and 254 mμ (ε 815, 677 and 290 respectively).

1,15-*Pentadecanolide* (IV) (*exaltolide*). The diyne lactone (III, 450 mg) was hydrogenated in ethyl acetate solution (50 ml) over Pt (50 mg) at room temp and press. Uptake of H_2 ceased after 4 molar equiv (180 ml) had been absorbed. Filtration and evaporation yielded a yellow oil which, on molecular distillation (100°/10^{-2} mm) gave exaltolide as colourless crystals (330 mg, 71%), m.p. and mixed m.p. 32–33° (lit. 31–32°).[6] (Found: C, 75·2; H, 11·7. Calc. for $C_{15}H_{28}O_2$: C, 74·95; H, 11·7%).

1,15-*Pentadec*-10,12-*dienolide* (VI). The diyne lactone (III, 232 mg) was hydrogenated in ethyl acetate solution (50 ml) with Lindlar's catalyst (26 mg) at room temp and press. Uptake of H_2 had considerably slowed after 40 min when the equivalent of 2 moles (47·5 ml) had been absorbed. Filtration and evaporation gave the dienolide (VI) which distilled as a colourless oil (120°/10^{-2} mm) (200 mg, 86%). (Found: C, 76·2; H, 10·0. Calc. for $C_{15}H_{24}O_2$: C, 76·2; H, 10·2%). λ_{max}^{EtOH} 234 mμ (ε 13,600).

A small sample of this dienolide (16·3 mg) was fully hydrogenated over PtO_2 (1 mg) in ethyl acetate (5 ml) at room temp and press. A total uptake of 3·06 ml H_2 was recorded, equiv to 1·9 double bonds.

Hydrogenation of 1,15-*pentadec*-10,12-*diynolide with Pd catalyst.* The diyne lactone (III, 150 mg) was hydrogenated in ethyl acetate solution (25 ml) with 10% Pd–C (30 mg) at room temp and press. After 3 molar equiv H_2 had been absorbed the reaction slowed markedly. Filtration and evaporation left the reduction product as a semi-crystalline white solid (V, 138 mg) which was not further purified prior to oxidative degradation. Initial examination by GLC (column temp 202° and argon flow rate 45 ml/min) gave the following retention time compared with those for exaltolide and the diynolide.

Compound	Reduced product	Diynolide	Exaltolide
Retention time (min)	6·2	12	6·2

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[*] The author wishes to thank Dr. J. Carnduff for his assistance with this and the two subsequent experiments.

[21] G. Eglinton and A. R. Galbraith, *J. Chem. Soc.* 889 (1959).

The product, therefore, did not contain starting material but it was not possible to distinguish between the olefin and saturated compound. Adjustment of the temp to 185° and flow rate to 30 ml/min afforded no separation.

A sample of the reduction product (17·66 g) was further hydrogenated over PtO_2 (1 mg). A total volume of 1·25 ml H_2 was absorbed equiv to 68% double bond material.

von Rudloff oxidation of the reduction product. To a solution of the above reduction mixture (V, 13·8 mg) in t-butanol (100 ml), was added a solution of K_2CO_3 (250 mg) in water (10 ml) followed by $NaIO_4$ (1·02 g) and $KMnO_4$ (30 mg) dissolved in water (100 ml). The mixture was shaken for 30 hr at room temp then $Na_2S_2O_5$ added to reduce all free I_2 to iodide. Excess KOH was then added and the lactone hydrolyzed simultaneous with the removal of the t-butanol by heating at 60° on a rotary evaporator for 3 hr. On working up as before, a mixture of dicarboxylic and hydroxy acids was obtained and the latter were further oxidized by dissolving the mixture in acetone (100 ml) and treating with excess 9·7N chromic acid aq solution. The mixture was allowed to stand for 2 hr at room temp. The acetone removed under red. press. and the residue ether extracted for 8 hr to give a colourless gum (100 mg). This was treated with excess ethereal diazomethane and the product examined by GLC as described below.

GLC *of the Rudloff oxidation products.* Using exactly the same conditions as those already described for the four standards, the above esterified oxidation products were examined by GLC. The mixed esters gave a major peak with a retention volume corresponding to that of dimethyl undecamethylenedioate as obtained from the standard curve. This result suggested an apparent large scale migration of the double bond. Since the IR spectrum still showed the presence of some hydroxyl material, however, it seemed more likely that a hydroxy-acid ester was present which had the same retention time as the dimethyl undecamethylenedioate. The mixture was consequently retreated with excess chromic acid, methylated and examined by GLC as before. This time the peak ascribed to the undecamethylene diester had almost disappeared and the dimethyl tridecamethylenedioate peak had proportionately increased. Thus, under the experimental conditions used, the methyl ester of 15-hydroxypentadecanoic acid has the same retention time as dimethyl undecamethylenedioate. Results of the GLC are summarized in Table 1.

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