NOTES.

656. α-*Methyl-lœvulic Acid.*

By E. A. Braude and C. J. Timmons.

α-Methyl-lævulic acid (III) has been synthesised by a number of methods (see, *e.g.*, Bischoff, *Annalen*, 1881, **206**, 320; Fittig and Gottstein, *ibid.*, 1883, **216**, 31; Béhal, *Bull. Soc. chim.*, 1901, **25**, 245; Agello and Casmano, *Gazzetta*, 1940, **70**, 755; Nazarov and Elizarova, *Izvest. Akad. Nauk U.S.S.R.*; *Otdel. Khim. Nauk*, 1951, 295), none of which is very satisfactory. A more convenient route, readily adaptable to large-scale preparations, consists in the addition of hydrogen cyanide to pent-3-en-2-one (I) to give α-methyl-lævulonitrile (II), followed by alkaline hydrolysis. The nitrile was characterised by the semicarbazone, 2 : 4-dinitrophenylhydrazone, and an unstable phenylhydrazone. The

$$\underset{\text{(I)}}{\text{Me·CO·CH:CHMe}} \longrightarrow \underset{\text{(II)}}{\text{Me·CO·CH}_2\text{·CHMe·CN}} \longrightarrow \underset{\text{(III)}}{\text{Me·CO·CH}_2\text{·CHMe·CO}_2\text{H}}$$

formation of γ-keto-nitriles from αβ-ethylenic ketones, presumably by 1 : 4-addition, has been observed in other cases (cf. Lapworth, *J.*, 1904, **85**, 1218; Maire, *Bull. Soc. chim.*, 1908, **3**, 284; Huan, *ibid.*, 1938, **5**, 1341), though cyanohydrins are obtainable at low temperatures (Marvel and Brace, *J. Amer. Chem. Soc.*, 1948, **70**, 1775; Leupold and Vollmann, U.S.P. 2,166,600; Dykstra, U.S.P. 2,188,340; Hansley and Bristol, U.S.P. 2,456,188). The ultra-violet light absorption of the α-methyl-lævulic acid and its derivatives confirms the accepted open-chain structures (III).

Experimental.—M. p.s marked (K) were determined on a Kofler micro-melting point block and are corrected. Other m. p.s are uncorrected.

α-*Methyl-lævulonitrile.* A mixture of pent-3-en-2-one (84 g.), anhydrous hydrogen cyanide (42 g.), and potassium cyanide (1 g.) was kept for 15 hr. at room temperature, then neutralised with phosphoric acid and distilled, giving the *nitrile* (40 g.) as a colourless liquid, b. p. 68°/1 mm., n_D^{16} 1·4288, λ_{infl} 2600 Å (ε 90) in hexane (Found: C, 64·6; H, 8·2; N, 12·5. C_6H_9ON requires C, 64·8; H, 8·2; N, 12·6%). The *semicarbazone* separated from ethanol as colourless plates, m. p. 156° (K), $\lambda_{max.}$ 2260° Å (ε 11,000) in EtOH (Found: C, 50·6; H, 7·4; N, 33·5. $C_7H_{12}ON_4$ requires C, 50·0; H, 7·2; N, 33·3%). The phenylhydrazone crystallised from aqueous methanol and had m. p. 76—78°, but was unstable and liquefied on being kept. The 2 : 4-*dinitrophenylhydrazone* crystallised from ethanol–ethyl acetate in yellow needles, m. p. 130—131°, $\lambda_{max.}$ 3560 Å (ε 23,000) in $CHCl_3$ (Found: C, 49·8; H, 4·7; N, 24·7. $C_{12}H_{13}O_4N_5$ requires C, 49·5; H, 4·5; N, 24·1%).

α-*Methyl-lævulic acid.* (*a*) The above nitrile (40 g.) was heated under reflux with aqueous sodium hydroxide (20%, 200 ml.) for 20 min. After cooling, the solution was acidified with hydrochloric acid and then extracted with ether. Distillation of the ethereal extract gave α-methyl-lævulic acid as a colourless oil (20 g.), b. p. 103°/1 mm., n_D^{19} 1·4388, $\lambda_{infl.}$ 2790 Å (ε 22) in EtOH (Found: C, 55·4; H, 7·6. Calc. for $C_6H_{10}O_3$: C, 55·4; H, 7·7%) (Nazarov and Elizarova, *loc. cit.*, give b. p. 120—122°/4 mm., n_D^{22} 1·4400). The overall yield from the pentenone was 16%, but this is undoubtedly capable of improvement. The semicarbazone

separated from ethanol in needles, m. p. 182—183° undepressed on admixture with the sample described below, $\lambda_{max.}$ 2250 Å (ε 12,000) in EtOH (Found : C, 45·2; H, 7·2; N, 23·0. Calc. for $C_7H_{13}O_3N_3$: C, 44·9; H, 7·0; N, 22·5%) (Béhal, *loc. cit.*, gives m. p. 191—192°; Michael and Ross, *J. Amer. Chem. Soc.*, 1931, **53**, 2394, give m. p. 191°; Nazarov and Elizarova give m. p. 177—178°). The phenylhydrazone crystallised from water and had m. p. 130—132°; it rapidly decomposed on being kept (Pieroni and Veremscenco, *Gazzetta*, 1926, **56**, 469, give m. p. 134—135°; Ajello and Casmano, *loc. cit.*, give m. p. 130°).

(*b*) An authentic sample of the acid was prepared in the following manner (cf. Conrad, *Annalen*, 1877, **188**, 226; Bischoff, *loc. cit.*). Ethyl α-bromopropionate (56 g.) was added to a solution of ethyl acetoacetate (37 g.) and sodium (8 g.) in ethanol and the mixture was heated under reflux for 12 hr. after which it was neutral to litmus paper. Distillation gave the diethyl 1-acetyl-2-methylsuccinate (16 g.), b. p. 86—87°/0·4 mm., n_D^{24} 1·4398, $\lambda_{max.}$ 2250 Å (ε 2400) in EtOH (Found : C, 57·8; H, 7·7. Calc. for $C_{11}H_{18}O_5$: C, 57·4; H, 7·9%), which did not form a 2 : 4-dinitrophenylhydrazone under the usual conditions and appears to exist predominantly in the enol form under these conditions. The ester was hydrolysed with aqueous sodium hydroxide (5%; 70 ml.) and then heated with 50% (v/v) sulphuric acid (30 ml.), and the products were isolated with ether. Fractionation gave α-methyl-lævulic acid (4 g.; overall yield from ethyl bromopropionate, 10%), b. p. 98°/0·3 mm. [semicarbazone, m. p. 180—182° (K) from ethanol], and 3-carboxy-2 : 4-dimethylbut-3-enolide (4-hydroxypent-3-ene-2 : 3-dicarboxylic acid 2 → 4-lactone) (1·2 g.) which crystallised from chloroform in prisms, m. p. 179—180° (K), $\lambda_{max.}$ 2270 Å (ε 27,000) in EtOH (Found : C, 53·7; H, 5·3%; equiv., 155. Calc. for $C_7H_8O_4$: C, 53·8; H, 5·2%; equiv., 156). Sprankling (*J.*, 1897, 1159) gives m. p. 176°; Küster, Maurer and Palm (*Ber.*, 1926, **59**, 1020) give m. p. 175°. The lactone gives a positive Légal test and reduces Tollens's reagent, but not ammoniacal silver nitrate.

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657. *The Preparation and Properties of* cis- *and* trans-*Pent-2-en-4-yne.*

By J. L. H. ALLAN and M. C. WHITING.

THE simple hydrocarbon, pent-2-en-4-yne, is of interest in that its employment in mixed-coupling reactions with other acetylenic compounds has proved, in the hands of Sörensen and his collaborators, to be useful in the synthesis of naturally occurring compounds containing the terminal grouping $CH_3{\cdot}CH{:}CH{\cdot}[C{:}C]_2{\cdot}$. It was first prepared in 1948 by the action of potassium hydroxide on 1-methylbut-3-ynyl toluene-*p*-sulphonate as an apparently homogeneous liquid, b. p. 46—48°; this method was communicated to Prof. Sörensen before publication (Eglinton and Whiting, *J.*, 1950, 3650), who found evidence (Sörensen *et al.*, *Acta Chem. Scand.*, 1951, **5**, 1244) that the hydrocarbon was a mixture of isomers, though the separation achieved was by no means complete.

We now describe the separation of this hydrocarbon into two pure steroisomers. The boiling points and refractive indices of the fractions obtained (see p. 3316) constitute good evidence of separation into two entities, though one of these might in principle be an azeotrope. For this reason infra-red spectra (see Table) were examined. The strongest band of the lower-boiling fraction, at 723 cm.$^{-1}$, is absent from that of the fraction, b. p. 52·2°; it is, moreover, in a region (675—729 cm.$^{-1}$) characteristic for simple *cis*-1 : 2-disubstituted ethylenes (Sheppard and Simpson, *Quart. Reviews*, 1952, **6**, 1; McMurry and Thornton, *Analyt. Chem.*, 1952, **24**, 318). Accordingly the higher-boiling fraction is the pure *trans*-form, a conclusion in agreement with its strong band at 956 cm.$^{-1}$ (cf. the similar strong bands in simple *trans*-1 : 2-disubstituted ethylenes at 964—979 cm.$^{-1}$; *idem*, *locc. cit.*). The lower-boiling fraction also had a strong band at about the same frequency, however, in addition to that at 723 cm.$^{-1}$, and it was considered just possible that this was an azeotrope of the two forms; against this view was the fact that fairly strong bands at 1742, 1381, 1287, and, especially, 1027 cm.$^{-1}$, present in the spectrum of the higher-boiling fraction, were absent from that of the substance, b. p. 44·6°. The latter was therefore converted

into the mercury derivative (method of Johnson and McEwen, *J. Amer. Chem. Soc.*, 1926, **48**, 469), m. p. 48°, which after repeated crystallisation was decomposed, giving a hydrocarbon the infra-red spectrum of which was virtually unaltered. It therefore seems certain that the strong band at 958 cm.$^{-1}$ is properly attributed to *cis*-pent-2-en-4-yne and that the lower-boiling fraction was in fact this hydrocarbon in a state of high purity.

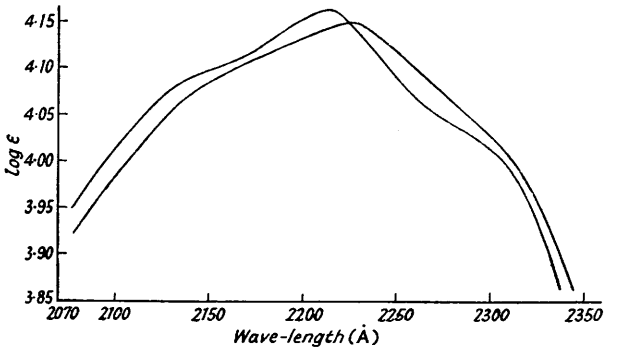
While no attempt has been made to analyse quantitatively the intermediate fractions

Infra-red absorption maxima for cis- *and* trans-*pent-2-en-4-yne.*

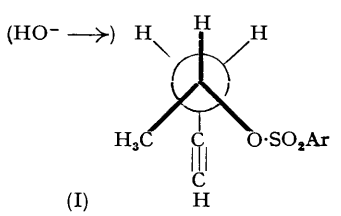
cis				*trans*			
ν (cm.$^{-1}$)	ε †	ν (cm.$^{-1}$)	ε †	ν (cm.$^{-1}$)	ε †	ν (cm.$^{-1}$)	ε †
3390	67 *	1623	7	3390	64 *	1634	8
3025	13	1444	24	3015	13	1447	26
2955	9	1425	13	2950	14	1381	8
2930	13	1366	21	2935	14	1287	8
2912	13	1227	13	2912	16	1221	11
2850	7	1035	0·2	2850	8	1027	24
2108	5	958	49 *	2112	8	956	138 *
1995	1·8	891	6	1998	0·6	900	14
1764	1·3	787	3·5	1823	1·6		
1679	4·5	723	114 *	1742	3·5		

* 0·05-cm. cell, 1% solution in CS_2.

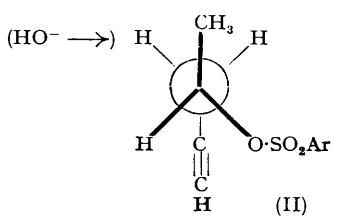
† These values are only approximate. They refer to the neat liquid in a 0·0025-cm. cell, except for those marked *.



obtained in the distillation, it is clear that the crude pent-2-en-4-yne contains about 60—65% of the *cis*-form, a fact for which only one explanation suggests itself. Apparently the conformation (I) is *either* (*a*) more probable, or (*b*) better able to react with OH^-, than (II) (the molecules are viewed along the line of the C–C bond which becomes ethylenic). There seems to be no foundation for hypothesis (*b*), but hypothesis (*a*) is supported by the probability of weak electrostatic interaction between alkyl groups and unsaturated systems in their vicinity, suggested by Braude and Coles (*J.*, 1951, 2085) in a less favourable case involving methyl and vinyl groups.



(I)



(II)

The ultra-violet absorption spectra of the two isomeric hydrocarbons are illustrated; the sharper fine structure in that of the *cis*-form is noteworthy, and may be tentatively ascribed to the increased rigidity resulting from the quasi-cyclic structure implied by attraction between the methyl and ethynyl groups.

Experimental.—Pent-2-en-4-yne. The hydrocarbon was prepared by Eglinton and Whiting's method (*loc. cit.*) from 1-methylbut-3-ynyl toluene-*p*-sulphonate (654 g.), and the crude dried product (170 g.) was used directly for fractionation. " Teepol," used in this experiment, is an alkali-stable proprietary detergent. In several runs yields of 93—97% were obtained.

Separation of cis- *and* trans-*isomers.* The apparatus, supplied by Griffin and Tatlock, Ltd., consists of a vacuum-jacketed glass column (45·7 × 1·7 cm.), packed with gauze rings (Dixon, *J. Soc. Chem. Ind.*, 1949, **68**, 88; 1949, **68**, 119) and fitted with a total-condensation still-head and automatic control of take-off. The electrically heated boiler incorporates a device for measuring the boil-up rate. From published data the efficiency should be at least 60 theoretical plates at a reflux ratio of 60 : 1.

Fraction no.	B. p.	Wt. (g.)	$n_D^{16\cdot5}$ *	Fraction no.	B. p.	Wt. (g.)	$n_D^{16\cdot5}$ *
1	43·8—44·5	7·7	1·4361	13	49·3—51·3	5·80	1·4406
2—10	44·5—44·6	61·8	1·4377 ± 0·0001	14	51·3—52·0	6·70	1·4408
11	44·6—45·0	7·05	1·4381	15—20	52·0—52·2	48·65	1·4407—1·4408
12	45·0—49·3	9·65	1·4399				

* Determined after *ca.* 24 hr. at 0°. The liquid had therefore undergone slight oxidation and/or polymerisation. For accurate values, see text.

The boiler charge was pent-2-en-4-yne isomers (160 g.), with benzene (25 c.c.) as chaser. After pre-flooding, the column was left on total reflux for 4½ hr. before the collection of fractions at a rate of 5·8 c.c./hr.; the boil-up rate remained at 360 c.c./hr. The atmospheric pressure remained almost constant throughout the distillation (766·7 ± 0·2 mm.). The Table lists detailed results. Fractions 6 and 18 were used for light-absorption determinations and the preparation of mercury derivatives.

Di-(cis-*pent-2-en-4-ynyl*)*mercury. cis*-Pent-2-en-4-yne (5·75 g.) in ethanol (20 vol.) was added during 30 min., at <0° with cooling and stirring, to a solution (124 c.c.) made by dissolving mercuric chloride (66 g.) and potassium iodide (163 g.) in water (163 c.c.) and adding 10% aqueous sodium hydroxide (125 c.c.). After further 5 minutes' stirring the crystalline precipitate was filtered off and washed with 50% aqueous ethanol. Recrystallisation from ethanol gave *di-*(cis-*pent-2-en-4-ynyl*)*mercury* (13·5 g., 94%) as plates, m. p. 48°, unaltered after several further recrystallisations from pentane (Found: Hg, 61·0. $C_{10}H_{10}Hg$ requires Hg, 60·6%). Light absorption: Max. 2035 and 2480 Å; ε = 25,000 and 27,000.

Di-(trans-*pent-2-en-4-ynyl*)*mercury. trans*-Pent-2-en-4-yne (2·0 g.) and the reagent solution (35 c.c.) similarly gave, after recrystallisation from benzene, *di-*(trans-*pent-2-en-4-ynyl*)*mercury* (4·6 g., 92%) as fine needles, m. p. 141—148° (decomp.) (Found: Hg, 60·5%). Light absorption: Max. 2030 and 2490 Å; ε = 31,000 and 30,000.

cis-*Pent-2-en-4-yne.* Di-(*cis*-pent-2-en-4-ynyl)mercury (13·0 g.) was heated under reflux with water (50 c.c.) and potassium cyanide (20·0 g.) for 2½ hr. After cooling, the regenerated hydrocarbon was distilled into a trap cooled in carbon dioxide–acetone, and, after drying ($CaCl_2$), redistillation gave *cis*-pent-2-en-4-yne (1·7 g.), b. p. 44·5—45°, $n_D^{22\cdot5}$ 1·4321, the infra-red and ultra-violet spectra of which were virtually the same as those of fraction 6.

Stability of cis- *and* trans-*pent-2-en-4-yne.* The two hydrocarbons, particularly the *cis*-form, were unstable in air even at −5° in the absence of light. The refractive index rose rapidly at first, the liquids becoming yellow. The *cis*-form, distilled after storage in the dark at −5° for 7 days, gave a residue (peroxide?) which detonated violently at 100°; quinol appeared to improve the stability. Measurements of absorption-spectra and *n* were made on freshly redistilled samples. The *cis*-isomer had n_D^{20} 1·4330, the *trans*-form n_D^{20} 1·4368; the temperature coefficients were 0·00064 and 0·00067 per degree respectively (a range of 15° was investigated and a linear graph obtained in each case).

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THE UNIVERSITY, MANCHESTER. [*Received, April 30th*, 1953.]

658. *The Properties of Penta-1 : 3-diyne.*

By E. R. H. Jones and M. C. Whiting.

Penta-1 : 3-diyne was first reported by Prévost (*Ann. Chim.*, 1928, **10**, 356), who obtained a hydrocarbon, b. p. 54—56°, by the action of potassium hydroxide on 1 : 2 : 3 : 4-tetrabromopentane. A substance, b. p. 55°, to which this structure was assigned was isolated from the residues obtained in the Hüls acetylene process (see Copenhaver and Bigelow, "Acetylene and Carbon Monoxide Chemistry," New York, 1949, p. 302). The next reference to it was made by Schlubach and Wolf (*Annalen*, 1950, **568**, 141) who found b. p. (*a*) 75—78·5° and (*b*) 76—77° for hydrocarbons obtained by the action of sodium acetylide on (*a*) methylene dichloride and (*b*) propargyl bromide, and considered both to be penta-1 : 3-diyne, formed by prototropic rearrangement of penta-1 : 4-diyne. Independently, Armitage, Jones, and Whiting had already prepared penta-1 : 3-diyne by the action of methyl iodide on monosodiodiacetylene and observed a boiling point of 76·5° (*J.*, 1952, 1993), and later Cook, Jones, and Whiting (*J.*, 1952, 2883) prepared this compound, b. p. 76°, by the action of sodamide on 1 : 4-dichloropent-2-yne. Recently Herbertz (*Ber.*, 1952, **85**, 475) has described "penta-1 : 3-diyne," b. p. 54—56°, obtained by the action of *sodium*, followed by methyl sulphate, on diacetylene, and, without referring to the two syntheses already published by Schlubach and Wolf, quoted Prévost's early work in support of his conclusions.

It is the purpose of the present communication to draw attention to the confused state of the literature on this compound. Our belief that the substance obtained in the laboratories at Manchester and those of Professor Schlubach, b. p. about 76°, is actually penta-1 : 3-diyne depends mainly on the proof from the former (*J.*, 1952, 1998) that its ultra-violet spectrum resembles that of hexa-2 : 4-diyne, and from the latter (*loc. cit.*) that this crystalline hydrocarbon can be obtained from it by methylation; much additional evidence is however cited in the publications referred to and later papers from these schools. On the other hand, neither Prévost nor Herbertz gave any evidence which would exclude the empirical formula C_5H_6 for their products. The physical constants tabulated suggest that these were probably mixtures of pent-1-en-3-yne and *trans*-pent-2-en-4-yne, which might not unreasonably be expected from the reactions employed, since (*a*) debromination

Physical constants of "penta-1 : 3-diyne."

	B. p.	d_4^t *	n_D (temp.)
Prevost	54—56°	0·7375 (21°)	1·4431 (21°)
Herbertz	54—56	0·7375 (?)	1·44305 (20°)
Schlubach and Wolf (*a*)	75—78·5	0·7926 (20°)	1·4717 (20°)
(*b*)	76—77	0·7909 (20°)	1·4817 (20°)
Armitage *et al.*	76·5	—	1·4790 (15°)
Cook *et al.*	76	—	1·4750 (18°)
$H_2C{:}CH{\cdot}C{:}C{\cdot}CH_3$ [1]	59·2°/760 mm.	0·7401 (20°)	1·4496 (20°)
trans-$CH_3{\cdot}CH{:}CH{\cdot}C{:}CH$ [2]	52·1°/766 mm.	—	1·4368 (20°)

* Temp. (*t*) in parentheses.

[1] Jacobson and Carothers, *J. Amer. Chem. Soc.*, 1933, **55**, 1750. [2] Allan and Whiting, preceding note.

to an olefin, rather than dehydrobromination to an acetylene, has already been observed when a 1 : 2-dibromide was treated with a strong base (Vaughn, Vogt, and Nieuwland, *J. Amer. Chem. Soc.*, 1934, **56**, 2120), and (*b*) sodium would be expected to *reduce* diacetylene to vinylacetylene, and methylation would then give pent-1-en-3-yne which might perhaps rearrange partly to the more acidic Δ^1-acetylene in the presence of excess of sodamide.

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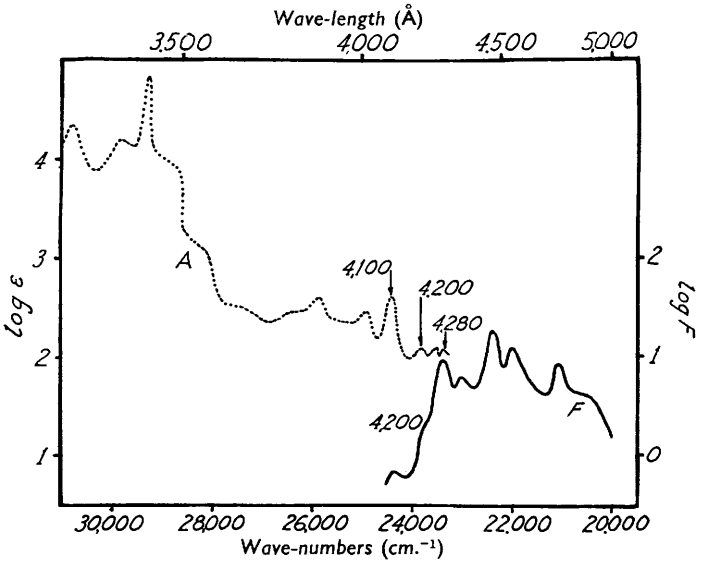
659. *The Fluorescence Spectrum of Coronene.*

By B. Brocklehurst.

Coronene has exceptional interest on account of its high degree of symmetry. Its absorption spectrum in benzene solution has been recorded by Clar (Clar, " Aromatische Kohlenwasserstoffe," Springer, Berlin, 1941), but there is no report of its fluorescence spectrum. The absorption spectrum consists of a very strong set of bands below 3600 Å, and a much weaker absorption between 3600 and 4100 Å, with some very weak bands beyond 4100 Å. In order to throw light on the relations between these sets of bands, the fluorescence spectrum of coronene in benzene has been measured.

The apparatus consisted of a Hilger double monochromator with a photo-electron multiplier attached to the exit slit. The response of the multiplier was further amplified to give readings on a micro-ammeter. The solution was placed in a silica cell in front of the monochromator slit, and was illuminated by light of wave-length 3135 Å from a mercury

Absorption and fluorescence spectra of coronene plotted against wave-numbers, to show the mirror-image relation. A, Absorption. F, Fluorescence.



lamp equipped with a suitable filter. The instrument was calibrated with a mercury lamp and thermopile, and the results are expressed in relative quanta.

The fluorescence spectrum (Figure, curve F) covers the range 4100—4800 Å, and shows much sharper fine structure than usual for hydrocarbons. The Figure shows that the fluorescence spectrum is the mirror image of the absorption (curve *A*) between 3600 and 4100 Å. This absorption must therefore correspond to a distinct, though but weakly allowed, transition to the lowest excited singlet state.

This conclusion is confirmed by measurements on the quenching of coronene fluorescence in chloroform by dissolved oxygen. Measurements were made at a fixed wave-length, the solution being saturated first with air then with purified coal-gas. The quenching constant (in the Stern–Volmer equation) is 4800 approximately. The " reaction rate " between coronene and oxygen is then given by 4800/(fluorescence efficiency) × (life-time of excited state). The fluorescence efficiency was calculated by measuring the area under the fluorescence spectrum and comparing it with that of anthracene. Taking the efficiency of anthracene as 0·24 (Bowen and Williams, *Trans. Faraday Soc.*, 1939, **35**, 765), and correcting for oxygen and concentration quenching, give a value 0·3 for coronene. The life-time of the excited state was calculated from the area of the absorption spectrum between 3600 and 4300 Å, by the equation of Lewis and Kasha (*J. Amer. Chem. Soc.*, 1945,

67, 994), and the value of about 2×10^{-7} sec. was obtained. This gives 8×10^{10} l.-mol.$^{-1}$ sec.$^{-1}$ for the " reaction rate " which may be compared with 6×10^{10} for anthracene (Bowen and Cook, unpublished work). If the coronene absorption band below 3600 Å represented the transition involved, this rate would be 100 times greater.

The weak absorption bands at 4280 and 4200 Å (23,360 and 23,800 cm.$^{-1}$) and the fluorescence bands at 4200 and 4100 Å (23,800 and 24,400 cm.$^{-1}$) are unusual and lead to the suggestion that transitions between the ground state and the lowest excited state are forbidden by symmetry, but become allowed when coupled with changes in the vibrational energy. This is to be expected from the analogy with benzene which has the same high degree of symmetry.

The first strong bands in the two spectra are, therefore, 0—1 transitions (4100 Å in absorption, 4280 Å in fluorescence) while the absorption at 4280 Å and the fluorescence at 4100 Å represent 1—0 transitions and should therefore be temperature-dependent. If this assignment is not correct, the gap between the main parts of the spectra could be explained by solvent interaction, but the presence of the weak bands would offer difficulty. In both spectra there is a weak band at 4200 Å, presumably corresponding to a 0—0 transition, *i.e.*, the transition is not completely forbidden in the absence of vibrational coupling.

Clar also reports an absorption band at 4260 Å, but no corresponding band occurs in chloroform solution (Patterson, *J. Amer. Chem. Soc.*, 1942, **64**, 1485), so that the observation may be incorrect. It is difficult to check this because of the low solubility of coronene in benzene.

I thank Dr. E. J. Bowen, F.R.S., under whose supervision this work was carried out, and Professor Wilson Baker, F.R.S., who provided a sample of pure coronene.

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660. *Dambonitol: Its Isolation from* Dyera lowii *and* Dyera costulata *and Its Constitution.*

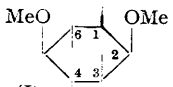
By A. J. COMOLLO and A. K. KIANG.

THE Dyera tree (or " jelutong "), indigenous to western Malasia, belongs to the family Apocyanaceae. It is of some economic importance as its latex is a source of the plastic " gum " (gutta jelutong), which is used in the manufacture of chewing gum. The latex is coagulated by the addition of phosphoric acid which gives a product with enhanced storage qualities (Georgi, *Malayan Forester*, 1934, **3**, 181; 1935, **4**, 8), and the serum, after the gutta is separated off, is run to waste.

From the serum of the latex of the Borneo tree, *Dyera lowii*, and of the Malayan tree, *D. costulata*, we obtained dambonitol which has previously been isolated from the latex of Gabbon rubber (Girard, *Compt. rend.*, 1868, **67**, 820), the juice of *Castilloa elastica* (Weber, *Ber.*, 1903, **36**, 3108), and Sumatran rubber latex (De Jong, *Rec. Trav. chim.*, 1908, **27**, 257). The serum from each source forms approximately 70% of the latex and contains 2—2·5% of dambonitol. Dambonitol gives a weak Scherer's reaction, does not reduce Fehling's solution, and forms a tetra-acetate. It contains two methoxy-groups, and both it and its tetra-acetate, when evaporated with excess of hydriodic acid, give *meso*inositol.

As far as we are aware, the constitution of dambonitol has not previously been established. Dambonitol is optically inactive, so the methoxy-groups must be in the 1 : 3-, 2 : 5-, or 4 : 6-positions. It does not form a cyclic acetal with acetone under the conditions employed by Posternak (*Helv. Chim. Acta*, 1950, **33**, 350) and Angyal and Macdonald (*J.*, 1952, 686). Although the latter authors have shown that *trans*-hydroxyl groups can lead to an *iso*propylidene derivative in special cases (*e.g.*, *epi*inositol), failure of the reaction in this case proves the absence of *cis*-α-hydroxyl groups; dambonitol is therefore not O^4O^6-dimethylinositol.

It is well known that, on oxidation with sodium metaperiodate, *meso*inositol (Fleury, Poiret, and Fivet, *Compt. rend.*, 1945, **220**, 664; Stephen, *J.*, 1952, 738) and its monomethyl ether, sequoyitol (Riggs, *J.*, 1949, 3199), consume much more than the amounts required for glycol fission and give rise to comparatively large amounts of strong acids. In contrast with these results, we have found that, dependent on the concentration of the periodate, the oxidation of dambonitol is practically ended in 4—5 hours with the consumption of two mols. of periodate. The resulting solution strongly reduces ammoniacal silver nitrate and Fehling's solution; a small but finite amount of " strong acid " is produced. Thus dambonitol is the 2 : 5-dimethyl ether of *meso*inositol, as the 1 : 3-isomer would certainly



(I)

$$OCH{\cdot}CH(OMe){\cdot}CHO \rightleftharpoons CHO{\cdot}C(OMe){:}CH{\cdot}OH$$
(II)

have produced at least one equivalent of formic acid per two mols. of periodate consumed. It is probable that in the oxidation dambonitol gives rise to two mols. of *O*-methyltartronaldehyde (II). The production of the " strong acid " up to a limiting amount of only 0·2—0·3 equivalent, on rapid consumption of up to 2 mols. of periodate, suggests that the acid is not produced by oxidation of the dialdehyde : the acidity may be due to the enol form of the dialdehyde. *O*-Methyltartronaldehyde may be less easily oxidised than tartronaldehyde by sodium metaperiodate, and it is worthy of note that malondialdehyde is less stable than its α-bromo- or its α-nitro-derivative (Hüttel, *Ber.*, 1941, **74**, 1825).

Experimental.—Isolation of dambonitol. The serum containing phosphoric acid was neutralised with ammonia and concentrated on a steam-bath to one-fifth of its volume. The light brown solution was filtered from the proteinaceous precipitate and treated with a hot solution of strontium hydroxide until no more precipitate was formed. The filtered solution was evaporated to dryness on a steam-bath. The slightly coloured residue was finely powdered and extracted (Soxhlet) with ethanol (6 c.c. per g.) until only a small amount of brown material remained. The crystals which appeared from the cooled extract were filtered off and, after being washed with ethanol, were practically colourless and had m. p. 200—208°. The mother-liquor and washings were evaporated to dryness and the residue heated with acetic anhydride (4 c.c./g.) and pyridine (0·5 c.c./g.) for 1—1½ hr. In this way dambonitol tetra-acetate was obtained. On the average, 1 l. of serum gave 20 g. of dambonitol and 12 g. of its tetra-acetate.

Two crystallisations of dambonitol from 95% ethanol (12 c.c./g.) gave colourless slender prisms, m. p. 210° (lit., m. p. 190°, 195·5°, and 206°) (Found : C, 46·1; H, 7·9; OMe, 30·4, 29·35. Calc. for $C_8H_{16}O_6$: C, 46·15; H, 7·75; OMe, 29·8%). The compound had a sweet taste, and was hygroscopic.

Time (hr.) :	½	1	2	3	4	6	8	10	24
				Periodate uptake.					
Solution a	1·10	1·43	1·79	1·91	1·98	2·02	2·00	2·01	2·08
,, b	1·36	1·86	1·93	1·97	1·98	2·00	2·02	2·00	2·00
,, c	1·76	1·98	2·12	2·16	2·14	2·18	2·20	2·20	2·20
,, d	1·77	2·00	2·12	2·14	—	—	—	—	2·14
				Strong acid liberated.					
Solution b	—	—	0·18	0·21	0·21	0·22	0·22	0·23	0·24
,, c	—	0·19	0·22	0·22	0·24	0·22	0·22	0·24	0·26
,, d	0·11	0·15	—	0·17	—	—	0·17	—	0·20

Solution a : $x = 0{\cdot}05967$; $y = 0{\cdot}2865$; $z = 0{\cdot}2470$.
,, b : $x = 0{\cdot}07600$; $y = 0{\cdot}365$; $z = 0{\cdot}4855$.
,, c : $x = 0{\cdot}07001$; $y = 0{\cdot}3363$; $z = 0{\cdot}665$.
,, d : dambonitol (0·07496 g., 0·36 millimole) was dissolved in 0·2495M-sodium metaperiodate (100 c.c.).

Dambonitol tetra-acetate. Dambonitol (0·5 g.) was heated under reflux with acetic anhydride (2·5 c.c.) for 1 hr. The product was poured into excess of water. The precipitate, recrystallised from methanol, had m. p. 195° (Maquenne, *Compt. rend.*, 1887, **104**, 1853, and De Jong, *loc. cit.*, give m. p. 193° and 195° respectively) (Found : C, 50·9; 51·1; H, 6·5, 6·65. Calc. for $C_{16}H_{24}O_{10}$: C, 51·1; H, 6·4%).

Demethylation. Dambonitol (0·5 g.) was evporated to dryness with constant-boiling hydriodic acid (2 c.c.) on a steam-bath. Water (2 c.c.) was added and the mixture again evaporated to dryness. The residue was rubbed, and the resulting crystals washed with ethanol (yield, 0·25 g.; m. p. 218—224°). Recrystallised by dissolution in the minimum amount of hot water and careful addition of ethanol, the product melted at 224—225°, undepressed by *meso*inositol.

Dambonitol tetra-acetate, treated in the same way, also gave *meso*inositol.

Periodate oxidation. Dambonitol (*x* g., *y* millimole) was dissolved in *z*M-metaperiodate (50 c.c.) and the solution made up to 100 c.c. with water. The mixture was kept in the dark at 27—28°. At intervals portions (5 c.c.) were treated with M-sodium hydrogen carbonate (2 c.c.), potassium iodide (0·1 g.), and 0·025N-sodium arsenite solution (15 c.c.), and after 5 min. the excess of arsenite was titrated against 0·025N-iodine. Further portions (5 c.c.) were rapidly titrated against 0·01N-sodium hydroxide (methyl-red). Consumption of periodate (moles/mole) and " strong acid " liberated (equiv./mole) are shown in the Table.

The authors thank Messrs. Malayan Guttas Ltd., and Lee Sawmills Ltd., Singapore, for the supply of the latex of *D. lowii* and *D. costulata* respectively, and Professor R. A. Robinson for his interest.

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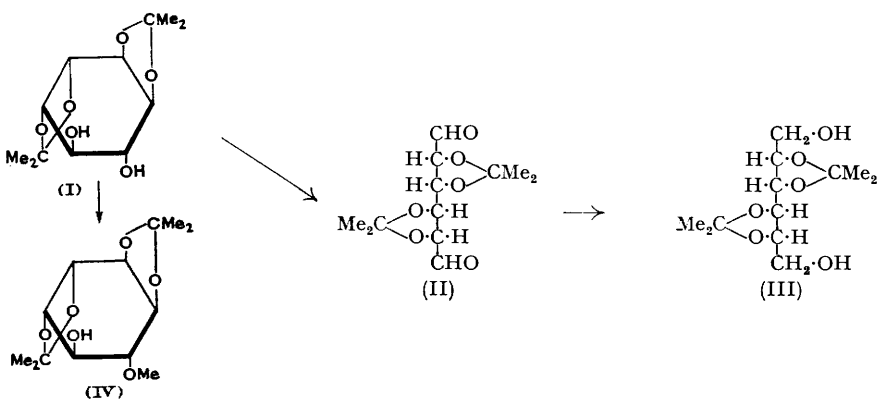
661. *The Structure of the Di-*O*-isopropylidene Derivatives of (−)-Inositol and Pinitol.*

By S. J. ANGYAL, C. G. MACDONALD, and N. K. MATHESON.

THE structures of the compounds named in the title were established as 1 : 2-5 : 6-di-*O-iso*propylidene-(−)-inositol (I) and 3-*O*-methyl-1 : 2-5 : 6-di-*O-iso*propylidene-(+)-inositol, respectively, on the assumption that acetal formation occurred between hydroxyl groups in *cis*-positions only (Angyal and Macdonald, *J.*, 1952, 686). While this assumption is, by past experience, reasonable, the recent discovery of derivatives in which *trans*-hydroxyl groups had combined with acetone (*idem, loc. cit.*) made an independent determination of these structures desirable. Anderson, Fischer, and MacDonald (*J. Amer. Chem. Soc.*, 1952, **74**, 1479) degraded di-*O-iso*propylidenepinitol to di-*O*-methyl-(−)-tartaric acid but this, again, needs the assumption of *cis*-acetal formation in order to serve as a proof of structure.

The correctness of structure (I) has now been proved by the following reactions: (I) was oxidised by lead tetra-acetate to a dialdehyde (II) which by the Meerwein–Ponndorf



reaction yielded a 2 : 3-4 : 5-di-*O-iso*propylidenehexitol (III), shown to be a derivative of L-mannitol by hydrolysis to the latter. Isolation of L-mannitol indicates that positions 1, 2, 5, and 6 of (−)-inositol are involved in acetal formation and thereby proves the 1 : 2-5 : 6-di-*O-iso*propylidene structure since the alternative 1 : 6-2 : 5- and 1 : 5-2 : 6-structures are sterically impossible.

These reactions, incidentally, confirm the configuration of (−)-inositol established by Posternak (*Helv. Chim. Acta*, 1936, **19**, 1007).

After this work had been completed, Ballou and Fischer reported (Amer. Chem. Soc. Meeting, Los Angeles, March, 1953) a similar degradation with (+)-inositol (*J. Amer. Chem. Soc.*, in the press). Their data agree well with ours.

1 : 2-3 : 4-Di-*O-iso*propylidene*epi*inositol was similarly oxidised to a dialdehyde which has not yet been further investigated.

The structure of 1 : 2-5 : 6-di-*O-iso*propylidenepinitol was confirmed by preparation of its enantiomorph (IV) from (I) by methylation. This proves that the acetal rings have the same position in the two compounds.

Experimental.—L-manno-2 : 3-4 : 5-*Di*(iso*propylidenedioxy*)*adipic dialdehyde* (II). To a solution of di-*O-iso*propylidene-(−)-inositol (4·07 g., 1 mol.) in dry chloroform (80 ml.) lead tetra-acetate (6·93 g., 1 mol.) was added and the mixture was vigorously shaken for 15 min. The separated lead acetate was filtered off and washed with chloroform, and the filtrate was evaporated under reduced pressure. The semicrystalline residue was extracted with boiling light petroleum (b. p. 60—90°; 100 ml.) which left some lead acetate undissolved; on cooling, the solution deposited crystals of the *dialdehyde* (3·29 g., 82%), m. p. 133—134°, $[\alpha]_D^{18}$ +12° (*c*, 2·5 in abs. EtOH) (Found: C, 55·9; H, 7·25. $C_{12}H_{18}O_6$ requires C, 55·8; H, 7·05%).

When a solution of *p*-nitrophenylhydrazine in acetic acid was added to an aqueous solution of the dialdehyde, the *bis*-p-*nitrophenylhydrazone* was precipitated. After several crystallisations from acetone–light petroleum it formed pale yellow blades, m. p. >250°, strongly dependent on the rate of heating (Found: N, 16·3. $C_{24}H_{28}O_8N_6$ requires N, 15·9%).

The dialdehyde was not reduced by hydrogen and palladised charcoal or Adams's catalyst, or by sodium amalgam in dilute acetic acid.

2 : 3-4 : 5-*Di*-O-iso*propylidene*-L-*mannitol* (III). After being shaken for 20 min., a mixture of di-*O-iso*propylidene-(−)-inositol (1·82 g.), lead tetra-acetate (3·10 g.), and dry chloroform (30 ml.) was filtered and evaporated under reduced pressure at 35°. A solution of aluminium *iso*propoxide (2·9 g.) in *iso*propanol (50 ml.) was added and the milky suspension slowly distilled until a test for acetone in the distillate was negative. The volume was kept constant by occasional additions of *iso*propanol. The solvent was removed under reduced pressure at 45°, and ice-cold sodium hydroxide solution (14 ml., 20%) was added. An oil separated which was extracted by ether (3 × 14 ml.); the ether was dried and evaporated, and the residual viscous oil dissolved in chloroform and washed with water. The chloroform was boiled off and the residue crystallised from benzene, to give a crop (0·28 g.), m. p. 87—89°; a second crop (0·17 g.) was obtained by the addition of light petroleum to the mother-liquor. Recrystallisation from light petroleum and sublimation at 120°/1 mm. gave pure *di*-O-iso*propylidene*-L-*mannitol*, m. p. 91·5°, $[\alpha]_D^{26}$ +1° (*c*, 1·1 in abs. EtOH) (Found: C, 54·5; H, 8·5. $C_{12}H_{22}O_6$ requires C, 54·95; H, 8·45%).

Hydrolysis of this compound with 0·1N-hydrochloric acid on the steam-bath for 10 min. gave a quantitative yield of L-mannitol, m. p. 165—166° (corr.) (Found: C, 39·75; H, 7·75. Calc. for $C_6H_{14}O_6$: C, 39·55; H, 7·75%) {hexabenzoate, m. p. 151—152° (corr.), $[\alpha]_D^{21}$ −50° (*c*, 1·8 in $CHCl_3$)} (Found: C, 71·35; H, 4·6. Calc. for $C_{48}H_{38}O_{12}$: C, 71·45; H, 4·75%). For L-mannitol Baer and Fischer (*J. Amer. Chem. Soc.*, 1939, **61**, 761) reported m. p. 163—164° (uncorr.); for the hexabenzoate of D-mannitol Power and Rogerson (*J.*, 1910, **97**, 1944) reported m. p. 149° (uncorr.), $[\alpha]_D$ +50·7° (*c*, 2·1 in $CHCl_3$).

allo-2 : 3-4 : 5-*Di*(iso*propylidenedioxy*)*adipic dialdehyde*. To a solution of 1 : 2-3 : 4-di-*O-iso*propylidene*epi*inositol (0·130 g.) (Angyal and Macdonald, *loc. cit.*) in dry chloroform (5 ml.) lead tetra-acetate (0·222 g.) was added and the mixture was vigorously shaken for 15 min. The separated lead acetate was filtered off and the filtrate evaporated under reduced pressure. The residue was extracted with light petroleum (3 × 4 ml.), which was evaporated; the residual solid, twice sublimed at 100°/0·5 mm., gave the *dialdehyde* (0·06 g., 45%), m. p. 102° (Found: C, 55·5; H, 7·2%).

3-O-*Methyl*-1 : 2-5 : 6-*di*-O-iso*propylidene*-(−)-*inositol* (IV). Di-*O-iso*propylidene-(−)-inositol (0·5 g.) was heated under reflux with methyl iodide (12 ml.) and silver oxide (0·6 g.) for 25 hr. The solution was filtered and the precipitate washed with acetone. The solvent was evaporated and the residue sublimed at 105—115° (bath-temp.)/1 mm. The sublimate, recrystallised several times from light petroleum, yielded the inositol derivative (0·1 g., 19%), m. p. 102—104°, $[\alpha]_D^{16}$ +45° (*c*, 1·3 in $CHCl_3$). For di-*O-iso*propylidenepinitol Anderson *et al.* (*loc. cit.*) reported m. p. 104·5—106°, $[\alpha]_D^{23}$ −45·4°.

When methylation was continued for 60 hr., an 85% yield of 3 : 4-*di*-O-*methyl*-1 : 2-5 : 6-*di*-O-iso*propylidene*-(−)-*inositol*, m. p. 88—89°, was obtained (Found : C, 58·6; H, 8·3. $C_{14}H_{24}O_6$ requires C, 58·3; H, 8·4%). For the enantiomorph Anderson *et al.* found m. p. 88—90°.

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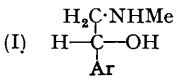
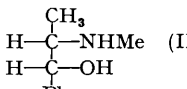
662. *The Configuration of Noradrenaline and Adrenaline.*

By C. E. DALGLIESH.

THE configuration of natural (−)-adrenaline and (−)-noradrenaline appears never to have been determined. Freudenberg ("Stereochemie," Deuticke, Leipzig, 1932, p. 697) assigned to (−)-adrenaline the configuration (I) [here and elsewhere, Ar = 3 : 4-$(HO)_2C_6H_3$]. No chemical evidence was produced to support this conclusion, which was based on the lævorotation of both (−)-adrenaline and (−)-ephedrine (II). The configuration of (−)-ephedrine is unambiguous (cf. Leithe, *Ber.*, 1932, **65**, 660; Freudenberg, Schoeffel, and Braun, *J. Amer. Chem. Soc.*, 1932, **54**, 234; Freudenberg and Nikolai, *Annalen*, 1934, **510**, 223) but rotational analogy for assignment of configuration is well known from Freudenberg's own work to be of uncertain reliability. Evidence now exists in the literature clearly establishing the configuration of adrenaline, which is in fact the opposite of that proposed by Freudenberg. The difference between the configurations at the β-carbon atoms of (−)-adrenaline and (−)-ephedrine raises interesting pharmacological questions.

(I) 

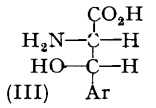
 (II)

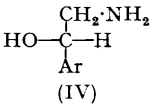
Dalgliesh and Mann (*J.*, 1947, 658) prepared β-3 : 4-dihydroxyphenylserine, by condensation of glycine ester and an aromatic aldehyde, and obtained only one of the two possible racemates. The stereochemistry of the product was not determined, but on enzymic decarboxylation one optical isomer of the racemate was decarboxylated to give (−)-noradrenaline (Blaschko, Holton, and Sloane-Stanley, *Brit. J. Pharmacol.*, 1948, **3**, 315; Blaschko, Burn, and Langemann, *ibid.*, 1950, **5**, 431). Dalgliesh later (*J.*, 1949, 90) prepared β-*p*-nitrophenylserine by the same method, and here again only one of the possible racemates was obtained. Interest in β-*p*-nitrophenylserine was stimulated by its relation to chloromycetin and many workers examined its stereochemistry. This work clearly showed that the method used by Dalgliesh for preparation of β-*p*-nitrophenylserine gave the *erythro*-racemate (Holland, Jenkins, and Nayler, *J.*, 1953, 273, and collected references therein). In particular β-*p*-hydroxyphenylserine prepared by this route also has the *erythro*-configuration (Holland *et al.*, *loc. cit.*). It is thus reasonable to assume that it is one optical isomer of the *erythro*-β-3 : 4-dihydroxyphenylserine which is decarboxylated to (−)-noradrenaline. Further confirmation has been provided by Fodor and Kiss (*Acta Univ. Szeged, Chem. et Phys.*, 1950, **3**, 26) who prepared β-3 : 4-dihydroxyphenylserine by a quite different route (involving nitrosation of an ω-carboxyacetophenone derivative), and obtained only one racemate which they found to be *erythro*, and which was enzymically decarboxylated to (−)-noradrenaline. Other β-phenylserine derivatives prepared by this second route also have the *erythro*-configuration (Hartung, Dittrich, and Chang, *J. Amer. chem. Soc.*, 1953, **75**, 238).

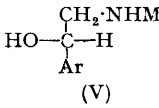
The decarboxylases which convert *erythro*-β-3 : 4-dihydroxyphenylserine into (−)-noradrenaline are specific for L-amino-acids (see Blaschko, *J. Physiol.*, 1942, **101**, 337; Blaschko, Holton, and Sloane-Stanley, *ibid.*, 1949, **108**, 427; and review by Schales, Chap. 50, in "The Enzymes," ed. Sumner and Myrbäck, Academic Press, New York, 1951, Vol. II, Part I, p. 216). The isomer undergoing decarboxylation must therefore be (III), and (−)-noradrenaline must therefore be (IV). This is confirmed by the work of Fones (*Arch. Biochem. Biophys.*, 1952, **36**, 486) who, using snake venom preparations, showed that

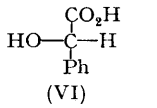
enzymic deamination and oxidation of *threo*-β-phenyl-DL-serine gave D(−)-mandelic acid, and of *erythro*-phenyl-DL-serine gave L(+)-mandelic acid. As again only the L-isomers of amino-acids are deaminated by such preparations the isomer of β-phenylserine analogous to (III) gave L(+)-mandelic acid (VI). It should be mentioned that enzymic attack at the α-carbon atom does not cause inversion at the β-carbon atom (Meister, *Nature*, 1951, **168**, 1119). Moreover *threo*-β-phenyl-D_S-serine has been correlated chemically with L-mandelic acid, and *threo*-β-phenyl-L_S-serine with phenyl-L-alanine (Vogler, *Helv. Chim. Acta*, 1950, **33**, 2111) in agreement with the above configurational assignments.

It is only recently that the physiological importance of (−)-noradrenaline has been realised and its properties determined (Tainter, Tullar, and Luduena, *Science*, 1948, **107**, 39; Tullar, *J. Amer. Chem. Soc.*, 1948, **70**, 2067), and the configurations of (−)-noradrenaline


(III)


(IV)


(V)


(VI)

and (−)-adrenaline have never been chemically correlated. However, there is much indirect evidence that these configurations are identical. Their structures are so similar that the analogous lævorotation itself carries much more weight than Freudenberg's analogy of adenaline with ephedrine (which contains an additional asymmetric carbon atom). Natural adrenaline and noradrenaline very frequently occur together (cf., *e.g.*, Goldenberg *et al.*, *Science*, 1949, **109**, 534; Tullar, *ibid.*, p. 536) and both are in all probability derived from β-phenylalanine (cf., *e.g.*, Gurin and Delluva, *J. Biol. Chem.*, 1947, **170**, 545) or the biogenetically equivalent tyrosine, *via* a common precursor. Noradrenaline is readily converted into adrenaline by suprarenal tissue both *in vitro* and *in vivo* (Bülbring, *Brit. J. Pharmacol.*, 1949, **4**, 234; Bülbring and Burn, *ibid.*, p. 245), the *N*-methyl groups in adrenaline being derived by transmethylation from methionine (Keller, Boissonnas, and du Vigneaud, *J. Biol. Chem.*, 1950, **183**, 627). There is no reason to suspect inversion of the CH·OH group in these reactions, and it is unlikely that a change from a $CH_2{\cdot}NH_2$ group to a $CH_2{\cdot}NHMe$ group would cause a reversal of the sign of rotation. There is therefore a very high degree of probability that (−)-adrenaline has the configuration (V).

There is no universally accepted rule for representing the correlation of configuration of a substance such as adrenaline with that of glyceraldehyde. If it were accepted that correlation should be as indicated by the projection formulæ (IV) and (V), then (−)-noradrenaline and (−)-adrenaline would become L-noradrenaline and L-adrenaline. As the prefix L is often (unjustifiably) used for these substances (*e.g.*, by Goldenberg *et al.* and by Tullar, *locc. cit.*), orientation as in (IV) and (V) would have the dual advantages of avoiding confusion and of making the naturally occurring isomer L, as for the amino-acids.*

I thank Dr. H. Blaschko, Dr. A. Neuberger, F.R.S., and Dr. W. Klyne for valuable discussions.

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* The assignment of L to (IV) and (V) proposed by the author is the opposite to that which follows from the Cahn–Ingold sequence rule (*J.*, 1951, 612). It is the same as that which follows from the proposals by Klyne (*Chem. and Ind.*, 1951, 1022) and others provided that noradrenaline (IV) is considered to be systematically named as 3 : 4 : β-trihydroxyphenethylamine, but the same proposals lead to the opposite (D) assignment for this stereoisomer on the basis of 2-amino-1-(3 : 4-trihydroxyphenyl)-ethanol. In such cases it may well be preferable, owing to lack of agreement, to use the italic capital letter together with such special conventions as an author wishes [in this case, *L* for (IV) and (V)], as was done by Linstead and his collaborators for a series of acids (*J.*, 1951, 1131 and later papers). However, the Editor, having been concerned in the published arguments, considers it inappropriate to do more than point out the present position. ED.

663. *The Degradation of Digoxigenin.*

By D. A. H. Taylor.

Steiger and Reichstein (*Helv. Chim. Acta*, 1938, **21**, 828) degraded digoxigenin diacetate by permanganate oxidation, etc., eventually obtaining a dihydroxy-acid and the corresponding diketo-acid, which was identified as 3 : 12-diketoetianic acid (Mason and Hoehn, *J. Amer. Chem. Soc.*, 1938, **60**, 2824), thus providing convincing evidence for the formulation of digoxigenin as a 3 : 12 : 14-trihydroxycard-20 : 22-enolide. The dihydroxy-acid was shortly afterwards identified with 3α : 12β-dihydroxyetianic acid (*idem, ibid.*, 1939, **61**, 1614); however the details of the comparison were perhaps not entirely satisfactory as derivatives were not prepared; and as all other cardiac aglycones and steroidal sapogenins whose constitution has since been proved have the 3β-configuration, it appeared of interest to repeat the degradation of digoxigenin. When this had been done, the author was informed by Professor T. Reichstein and by Dr. H. M. E. Cardwell that they had each independently shown that digoxigenin had the 3β-configuration. The present paper therefore reports only the details of the degradation which had already been carried out.

Experimental.—Rotations were measured in a 4-dm. tube, and m. p.s on the Kofler block.

3β : 12β-*Diacetoxy*-14β-*hydroxyetianic acid.* Digoxigenin diacetate (2·0 g.), in ethyl acetate (200 c.c.), was ozonised at −80°. When the solution had become deep blue it was allowed to warm to 0° and treated with zinc powder (2 g.) and acetic acid (10 c.c.). After being kept for 1 hr. the solution was washed with water, dried, and evaporated. The residue was taken up in methanol (130 c.c.), treated with potassium hydrogen carbonate (2 g.) in water (60 c.c.), and set aside overnight. The solution was then diluted with water and ethyl acetate and the organic layer evaporated, the residue being oxidised overnight with periodic acid (1·8 g.) in water (10 c.c.) and dioxan (100 c.c.). The acidic fraction of the product, crystallised from methanol, yielded the etianic acid (1·26 g.), m. p. 231—234°, $[\alpha]_D^{20}$ +38·4° ± 2° (*c*, 0·3 in $CHCl_3$). Steiger and Reichstein give m. p. 229—230°. The *methyl* ester, prepared with diazomethane, crystallised from methanol in plates, m. p. 183—184°, $[\alpha]_D^{21}$ +55·5° ± 0·5°, $[\alpha]_{5461}^{21}$ +64·3° ± 0·5° (*c*, 1 in $CHCl_3$) (Found : C, 66·4; H, 8·35. $C_{25}H_{38}O_7$ requires C, 66·6; H, 8·5%).

Methyl 3β : 12β-*diacetoxyeti*-14-*enate.* Methyl 3β : 12β-diacetoxy-14β-hydroxyetianate (1·0 g.) in pyridine (12 c.c.) was treated with freshly distilled phosphorus oxychloride (3 c.c.) and one drop of water. Next morning the mixture was poured on ice and ether, and the organic layer washed with dilute hydrochloric acid, sodium carbonate, and water, dried, and evaporated. The residue, which crystallised, had m. p. at 130—140°, and was chromatographed in benzene on alumina (30 g.). Benzene eluted *methyl* 3β : 12β-*diacetoxyeti*-14-*enate* (770 mg.), crystallising from methanol in fine matted needles, m. p. 144—145°, $[\alpha]_D^{23}$ +66·0° ± 2°, $[\alpha]_{5461}^{22}$ +77° ± 2° (*c*, 0·3 in $CHCl_3$) (Found : C, 69·2; H, 8·5. $C_{25}H_{36}O_6$ requires C, 69·35; H, 8·3%).

Methyl 3β : 12β-*diacetoxyetianate.* The foregoing ester (750 mg.) in acetic acid (25 c.c.) was hydrogenated over Adams's catalyst (50 mg.) (uptake complete in 15 min.), filtered from catalyst, and evaporated. The residue gave crystals, m. p. 130—164° (630 mg.), from methanol. Fractional crystallisation from methanol gave *methyl* 3β : 12β-*diacetoxyetianate* (500 mg.) as prisms, m. p. 143—144°, $[\alpha]_D^{22}$ +50·2° ± 2°, $[\alpha]_{5461}^{22}$ +62·8° ± 2° (*c*, 0·6 in $CHCl_3$) (Found : C, 68·8, 69·2; H, 8·6, 8·7. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%). This substance gave no depression of m. p. mixed with a specimen provided by Professor Reichstein which has recently been synthesised in his laboratory (personal communication). From the mother-liquors there was obtained after chromatography on alumina a substance which was probably *methyl* 3β : 12β-*diacetoxy*-14β-*etianate* (45 mg.), crystallising from methanol in pointed prisms, m. p. 206—208°, $[\alpha]_D^{21}$ +63·5° ± 4°, $[\alpha]_{5461}^{21}$ +80·0° ±4° (*c*, 0·2 in $CHCl_3$) (Found : C, 68·9; H, 8·9. $C_{25}H_{38}O_6$ requires C, 69·1; H, 8·8%).

Methyl 3β : 12β-*dihydroxyetianate.* 3β : 12β-Diacetoxyetianic acid was prepared by hydrolysis of the diacetate methyl ester with hot aqueous methanolic potassium hydroxide and crystallised from methanol in needles, m. p. 286—288°, $[\alpha]_D^{23}$ +30·2° ± 1°, $[\alpha]_{5461}^{23}$ +38·6° ± 1° (*c*, 0·6 in MeOH). Steiger and Reichstein give m. p. 282—286° (Found : C, 70·1; H, 9·9. Calc. for $C_{20}H_{32}O_4,\frac{1}{2}CH_3{\cdot}OH$: C, 69·9; H, 9·7%). The methyl ester, prepared with diazomethane, crystallised from methanol in laths, m. p. 187—188° (sublimes in needles above 160° on the Kofler block), $[\alpha]_D^{23}$ +38·2° ± 2°, $[\alpha]_{5461}^{22}$ +45·2° ± 2° (*c*, 0·4 in MeOH) (Found : C, 69·3; H,

10·1. Calc. for $C_{21}H_{34}O_4,CH_3{\cdot}OH$: C, 69·1; H, 9·95%). Steiger and Reichstein give m. p. 180—183°.

The author is grateful to Professor A. Stoll for a generous gift of digoxigenin, and to Dr. R. K. Callow for his interest.

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664. *Fluorine-substituted Phenylhydrazines.*

By H. SUSCHITZKY.

THE preparation of fluorophenylhydrazines was of interest in connection with the synthesis of *N*-heteroaromatic fluorine compounds (unpublished work). Reduction of the corresponding fluorobenzenediazonium chlorides with sodium hydrogen sulphite which has been found unsatisfactory for the preparation of halogenophenylhydrazines (Barclay and Campbell, *J.*, 1945, 530) proved unsuccessful also in this case. Stannous chloride in excess of hydrochloric acid was eventually used as a reducing agent under the conditions described by Bülow (*Ber.*, 1918, **51**, 404).

Experimental.—Nitrogen determinations were carried out by Kjeldahl's method, those of diazonium-nitrogen by Schiemann and Pillarsky's method (*Ber.*, 1929, **62**, 3035). Diazonium borofluorides were decomposed in a current of dry nitrogen.

o-*Fluorophenylhydrazine*. A fine suspension of *o*-fluoroaniline hydrochloride (from 12·6 g. of *o*-fluoroaniline) in concentrated hydrochloric acid (140 c.c.) was diazotised at −10° with 40% sodium nitrite solution and reduced with stannous chloride (76·8 g.). The resulting creamy precipitate was collected after 1 hr. Excess of acid was removed by washing with cold saturated sodium chloride solution and the pink solid was then transferred to a separator half immersed in a freezing mixture. Addition of a saturated solution of ammonium or sodium acetate (30—50 c.c.) liberated the base which was extracted with ether (2 × 30 c.c.). After drying (K_2CO_3) of the extract in the dark, the solvent was evaporated off and the residual oil twice distilled under reduced pressure. o-*Fluorophenylhydrazine* separated as nearly colourless needles from light petroleum (b. p. 60—80°)–ethanol (10 : 1 by vol.) and as plates from benzene; it had m. p. 47°, b. p. 95—96°/9 mm. (7·8 g., 55%), and was unstable to light and air (Found: N, 21·9. $C_6H_7N_2F$ requires N, 22·2%). It gave a *hydrochloride* (precipitated in ether), needles, m. p. 186° (decomp.) (Found: N, 16·8; Cl, 21·4. $C_6H_8N_2ClF$ requires N, 17·2; Cl, 21·8%), glucosazone, m. p. 199° (decomp.), *benzylidene*, m. p. 99° (Found: N, 12·8. $C_{13}H_{11}N_2F$ requires N, 13·0), *salicylidene*, m. p. 126° (Found: N, 12·0. $C_{13}H_{11}ON_2F$ requires N, 12·2), and α-*methylbenzylidene* derivative, m. p. 74° (Found: N, 12·0. $C_{14}H_{13}N_2F$ requires N, 12·3%).

A mixture of *o*-fluorophenylhydrazine (1 mol.) and *cyclo*hexanone (1 mol.) became warm and cloudy. A small quantity of ethanol was added and the mixture heated on a steam-bath (15 min.), then cooled, and ethanol and water were removed under diminished pressure. The residue solidified on trituration with light petroleum (b. p. 60—80°). cyclo*Hexanone* o-*fluorophenylhydrazone* was obtained from light petroleum (b. p. 60—80°)–ether (3 : 1 by vol.) as nearly colourless flakes, m. p. 38° (80%), which decomposed to a brown liquid within 1 hr. (Found: N, 13·2. $C_{12}H_{15}N_2F$ requires N, 13·6%).

m-*Fluorophenylhydrazine*, similarly prepared, crystallised from 1 : 1 ether–light petroleum (b. p. 60—80°) as fawn-coloured needles, m. p. 28°, b. p. 88°/2 mm. (64·0%) (Found: N, 21·8. $C_6H_7N_2F$ requires N, 22·2%), and gave a *hydrochloride*, m. p. 247° (decomp.) (Found: N, 17·2; Cl, 21·7%), glucosazone, m. p. 184° (decomp.), *benzylidene*, m. p. 118° (Found: N, 13·2%), *salicylidene*, m. p. 155° (Found: N, 12·1%), α-*methylbenzylidene*, m. p. 86° (Found: N, 12·2%), and cyclo*hexylidene* derivative, m. p. 41° (Found: N, 13·5%).

p-Fluorophenylhydrazine formed nearly colourless needles, m. p. 37·5°, b. p. 95—96°/3 mm. (67·5%), from 1 : 1 ether–light petroleum (b. p. 60—80°) (Found: N, 21·8%). Schiemann and Winkelmüller (*Ber.*, 1933, **66**, 727) give m. p. 39°. It gave a *hydrochloride*, m. p. 200° (decomp.) (Found: N, 17·2; Cl, 21·7%), glucosazone, m. p. 186—187° (decomp.) (*idem, loc. cit.*, give m. p. 187—188°), *benzylidene*, m. p. 140° (Found: N, 13·1%), salicylidene, m. p. 166° (Found: N, 12·0%) (*idem, loc. cit.*, give m. p. 166·5°), α-*methylbenzylidene*, m. p. 107° (Found: N, 12·0%), and cyclo*hexylidene* derivative, m. p. 80—82° (Found: N, 13·3%).

3-*Fluoro*-6-*methylphenylhydrazine*. A Balz–Schiemann reaction with 4-methyl-3-nitro-

aniline yielded 4-*methyl*-3-*nitrobenzenediazonium borofluoride*, m. p. 150—152° (decomp.) (85%) (Found: diazonium N, 10·7. $C_7H_6O_2N_3BF_4$ requires diazonium N, 11·1%). On thermal decomposition it gave 4-fluoro-2-nitrotoluene, b. p. 78°/5 mm. (55%), which was reduced with stannous chloride to 3-fluoro-6-methylaniline, m. p. 37·5°, b. p. 73°/5 mm. (84%) (Found: C, 67·3; H, 6·2; N, 11·2. Calc. for C_7H_8NF: C, 67·2; H, 6·4; N, 11·2%). Steck and Fletcher (*J. Amer. Chem. Soc.*, 1948, **70**, 439) give b. p. 100—101°/16 mm. It gave a *formyl*, colourless needles (from aqueous alcohol), m. p. 84·5° (Found: N, 9·2. C_8H_8ONF requires N, 9·1%), and *benzoyl* derivative, flakes (from ethanol), m. p. 130° (Found: N, 6·0. $C_{14}H_{12}ONF$ requires N, 6·1%). 3-Fluoro-6-methylaniline (12 g.), as described above, gave 3-*fluoro*-6-*methylphenylhydrazine* (9·2 g., 68·4%), prisms, m. p. 67°, b. p. 112°/3 mm., unchanged when kept for several weeks in the dark (Found: C, 60·3; H, 6·2; N, 19·8. $C_7H_9N_2F$ requires C, 60·0; H, 6·4; N, 20·0%). This formed a hydrochloride, m. p. 190° (decomp.), glucosazone, m. p. 210° (decomp.), *benzylidene*, m. p. 77° (Found: N, 11·9. $C_{14}H_{13}N_2F$ requires N, 12·2%), *salicylidene*, m. p. 118° (Found: N, 11·2. $C_{14}H_{13}ON_2F$ requires N, 11·4%), *α-methylbenzylidene*, m. p. 58° (Found: N, 11·3. $C_{15}H_{15}N_2F$ requires N, 11·5%), and cyclo*hexylidene* derivative, m. p. 65° (Found: N, 12·6. $C_{13}H_{17}N_2F$ requires N, 12·7%).

The author thanks Dr. F. L. Allen for his interest and support.

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665. *The Preparation of* n-*Octadecylamine Hydrochloride.*

By GEOFFREY W. WOOD.

n-OCTADECYLAMINE HYDROCHLORIDE has been prepared in excellent overall yield from *n*-octadecyl alcohol, *via* the iodide, by application of the Gabriel synthesis. The method avoids the use of catalytic reduction techniques, and all the reactions may be carried out under ordinary laboratory conditions with simple apparatus.

Experimental.—n-*Octadecyl iodide*. To a cooled mixture of "AnalaR" phosphoric acid (45 c.c.) and phosphoric oxide (22 g.), finely powdered potassium iodide (111 g.) and *n*-octadecyl alcohol (90 g.) were added. The mixture was heated in an oil-bath at 110—120°, with stirring, for 5 hr., then cooled, diluted with water, and extracted with ether. The ether extract was washed with aqueous sodium thiosulphate and water and dried ($MgSO_4$), the solvent removed, and the dark brown oily residue dissolved in light petroleum (b. p. 40—50°; 100 c.c.), which solution was chromatographed on activated alumina (370 g.; B.D.H.). Elution with light petroleum (b. p. 40—50°; 750 c.c.) gave *n*-octadecyl iodide (104 g., 85%), m. p. 29—32°; elution with ether–methanol (2 : 1; 1000 c.c.) gave unchanged *n*-octadecyl alcohol (7·3 g.).

N-n-*Octadecylphthalimide*. The iodide (10·2 g.), potassium phthalimide (5 g.), and dimethylformamide (40 c.c.) were heated, with vigorous stirring, in an oil-bath (bath temp. 65—70°) for 1·5 hr. After cooling, the mixture was diluted with water and extracted with chloroform. Removal of the solvent *in vacuo* and crystallisation from ethanol (charcoal) gave N-n-*octadecylphthalimide* (10·2 g.), white microcrystals, m. p. 75—76·5°. A small amount repeatedly crystallised from ethanol, for analysis, had m. p. 80—81° (Found: C, 78·35; H, 10·55; N, 3·6. $C_{26}H_{41}O_2N$ requires C, 78·15; H, 10·35; N, 3·5%).

n-*Octadecylamine hydrochloride*. A mixture of *N*-*n*-octadecylphthalimide (10·0 g.), 85% hydrazine hydrate (5·0 c.c.), and methanol (125 c.c.) was heated under gentle reflux on a water-bath for 2 hr. (after 1 hr. a copious precipitate began to form). The methanol was then removed *in vacuo*, and the residue heated under gentle reflux with a mixture of hydrochloric acid (*d* 1·14; 75 c.c.) and water (75 c.c.) for 1 hr. After cooling in ice, the mixture was filtered, the residue digested with hot 95% ethanol (100 c.c.), and undissolved phthalhydrazide (3·0 g.) removed by filtration. The filtrate, on cooling, gave *n*-octadecylamine hydrochloride as large lustrous plates (7·2 g.), m. p. 162—163°. Treatment of an alcoholic solution of the hydrochloride with aqueous calcium picrate afforded the picrate, m. p. 116—117° (Adkins and Billica, *J. Amer. Chem. Soc.*, 1948, **70**, 695, give m. p. 116°).

The author expresses his sincere thanks to Mr. A. H. Ford-Moore for his interest in this work and to Mr. F. E. Charlton and Miss B. A. Jones for the microanalyses.

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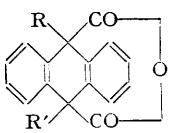
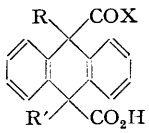
666. *Some* 9 : 10-*Dihydroanthracene*-9 : 10-cis-*dicarboxylic Anhydrides.*

By A. H. Beckett, R. G. Lingard, and B. A. Mulley.

During synthesis of anthracene derivatives of possible pharmacological interest, anhydrides (I; R and R′ = H or Me) were required. Only one such has been reported, namely (I; R = R′ = H) (Mathieu, *Ann. Chim.*, 1945, **20**, 215; Rigaudy, *ibid.*, 1950, **5**, 398), and its preparation involved addition of sodium to anthracene, carboxylation and subsequent tedious separation of the mono- and the *trans*- and the *cis*-di-carboxylic acids, followed by the conversion of the latter into the anhydride.

(I) 

 (II)

We have prepared the above anhydrides readily by treatment, with acetic anhydride, of the crude mixed acids resulting from the carbonation of the addition products of the appropriate anthracene derivative and sodium. The separation depended on the stability of the anhydrides at room temperature to dilute sodium hydroxide solution which extracted the unchanged acids from a chloroform solution of the mixture. The m. p. (195—196°) of our anhydride (I; R = R′ = H), even after repeated recrystallisation, was much lower than that reported by Mathieu and Rigaudy (*locc. cit.*); we therefore investigated it in some detail, because the possibility of intermolecular anhydrides exists. (A molecular model shows that the *trans*-dicarboxylic acid cannot form a monomeric anhydride.) Molecular-weight determinations, in conjunction with other evidence, showed that our product is an intramolecular anhydride. Furthermore, opening of the anhydride ring with methyl alcohol gave the monomethyl ester of 9 : 10-dihydroanthracene-9 : 10-*cis*-dicarboxylic acid (II; R = R′ = H; X = OMe) in 70% yield and with a melting point in agreement with that reported by Mathieu for the compound produced from his anhydride. Equivalent-weight determinations of the anhydride, the above monomethyl ester, and the monomorpholide are further proofs of the purity of our anhydride.

The ultra-violet absorption spectrum for 9 : 10-dihydroanthracene-9 : 10-*cis*-dicarboxylic anhydride is typical of that of dihydroanthracene derivatives: there are small maxima at 2640 and 2720 Å (Badger, Jones, and Pearce, *J.*, 1950, 1700; Phillips and Cason, *J. Amer. Chem. Soc.*, 1952, **74**, 2934), and generally feeble absorption (Clar and Wright, *Nature*, 1949, **163**, 921), with virtually none above 2900 Å (Phillips and Cason, *loc. cit.*). A number of authors (Martin, *Ann. combustibles liquides*, 1937, **12**, 97; Badger *et al.*, *loc. cit.*: Takaoka, *J. Faculty Sci., Hokkaido Imp. Univ.*, Ser. III, **3**, 1; *Chem. Abs.*, 1940, **34**, 7888) have reported three small maxima for dihydroanthracene derivatives in the region between 2500 and 2800 Å. However, the third peak, usually around 2550 Å, is probably due to the presence of traces of anthracene derivatives (Phillips and Cason, *loc. cit.*) which absorb much more strongly than dihydroanthracene derivatives. Solutions of 9 : 10-dihydroanthracene-9 : 10-*cis*-dicarboxylic anhydride developed this extra peak on storage for several days.

Experimental.—Microanalyses and molecular-weight determinations (ebullioscopic in acetone unless otherwise stated) were by Mr. Crouch, School of Pharmacy, London University. Ultra-violet absorption spectra were measured in ethanol with a Unicam S.P. 500 spectrophotometer.

9 : 10-*Dihydro*-9 : 10-*dimethylanthracene*-9 : 10-cis-*dicarboxylic Anhydride*.—9 : 10-Dimethylanthracene (3·1 g.) (Buu-Hoï, *J. Org. Chem.*, 1951, **16**, 874) in dry benzene (100 ml.) was shaken with finely divided sodium (5 g.) and dry ether (100 ml.) for 48 hr., the yellow solution changing to dark green. The product was slowly added to a large excess of a slurry of solid carbon dioxide in dry ether, excess of sodium destroyed with ethanol, water added, and the organic

layer extracted with dilute sodium hydroxide solution. Acidification of the cold alkaline extract and extraction with ethyl acetate gave crude acids (4·2 g.) on removal of the solvent. These were refluxed with acetic anhydride (10 ml.) for 30 min., chloroform (50 ml.) was added, and the unchanged acids were extracted with dilute sodium hydroxide solution. Evaporation of the chloroform solution after drying (Na_2SO_4) gave a solid which was recrystallised from dioxan to give 9 : 10-*dihydro*-9 : 10-*dimethylanthracene*-9 : 10-cis-*dicarboxylic anhydride* (0·5 g., 12%) as colourless, diamond-shaped crystals, m. p. 215—216° (material for analysis was recrystallised from acetic anhydride because the material from dioxan contained solvent of crystallisation : the m. p. was unchanged) [Found : C, 78·0; H, 5·2%; equiv. (refluxing with excess of alkali for 30 min. and back-titration), 138; *M*, 240. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·1%; equiv., 138; *M*, 278]. Light absorption : Max. at 261 (ε 1320) and 268 mμ (ε 1100).

The *monomorpholide* separated from butanol as plates, m. p. 291—292° (Found : C, 72·0; H, 6·3; N, 3·9%; equiv., 369. $C_{22}H_{23}O_4N$ requires C, 72·3; H, 6·3; N, 3·8%; equiv., 365).

9 : 10-*Dihydroanthracene*-9 : 10-cis-*dicarboxylic Anhydride*.—Anthracene (50 g.; commercial blue fluorescent) was shaken with finely divided sodium (13·5 g.) and glass beads in dry ether (750 ml.) for 4 hr. The resultant blue mixture, treated as above, yielded acids (55 g.) which, after 30 minutes' refluxing with acetic anhydride and subsequent recrystallisation from dioxan, gave 9 : 10-dihydroanthracene-9 : 10-*cis*-dicarboxylic anhydride (14·5 g., 28%) as fine colourless needles, m. p. 194—195° [Found : C, 77·3; H, 4·0%; equiv., 122; *M*, 250, (Rast) 275. Calc. for $C_{16}H_{10}O_3$: C, 76·8; H, 4·0%; equiv., 125; *M*, 250] (Rigaudy *et al.* give m. p. 233—234°). Light absorption : Max. at 264 (ε 560) and 272 mμ (ε 500).

The *monomorpholide*, prepared in theoretical yield, separated from butanol as colourless crystals, m. p. 222—223° (Found : C, 71·4; H, 5·9; N, 4·3%; equiv., 333. $C_{20}H_{19}O_4N$ requires C, 71·2; H, 5·6; N, 4·2%; equiv., 337). The monomethyl ester had m. p. 181—182° (from butyl ether) (Found : equiv., 143. Calc. for $C_{17}H_{14}O_4$: equiv., 141) (Mathieu, *loc. cit.*, reports m. p. 178—179°).

9 : 10-*Dihydro*-9-*methylanthracene*-9 : 10-cis-*dicarboxylic Anhydride*.—This *anhydride*, prepared from 9-methylanthracene (Seiglitz and Marx, *Ber.*, 1923, **56**, 1619) by the above method in 25% yield, formed plates, m. p. 222—223° (Found : C, 77·5; H, 4·5%; equiv., 137; *M*, 260. $C_{17}H_{12}O_3$ requires C, 77·2; H, 4·5%; equiv., 132; *M*, 264). Light absorption : Max. at 261 (ε 1140) and 268 mμ (ε 850).

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667. *Dimerisation of* 1-*Methyl*cyclo*hexene by Formic or Acetic Acid containing Perchloric Acid.*

By George F. Bloomfield.

The addition of formic or acetic acid to many olefins at above 150° has long been known, but the marked catalysis of this reaction by small amounts of perchloric acid is a very recent discovery (Knight, Koos, and Severn, *Chem. Eng. News*, 1952, **30**, 4615). Thus, the hydroxylated derivatives of oleic, elaidic, and linoleic acids, and of methyl oleate, oleyl alcohol, and hex-1-ene are easily and conveniently prepared, via the corresponding formates, in a few minutes at 100°.

*cyclo*Hexene has now been shown to react similarly to produce *cyclo*hexyl formate. With 1-methyl*cyclo*hexene, however, the major product is a hydrocarbon, $C_{14}H_{24}$, which is believed to be 2-methyl-1-1'-methyl*cyclo*hexyl*cyclo*hexene on the basis of the following observations and the assumption of ionic intermediates : (i) molecular weight and empirical formula; (ii) hydrogenation to the saturated hydrocarbon $C_{14}H_{26}$; and (iii) absence of olefinic units detectable by infra-red spectroscopic examination—implying the presence of tetra-substituted ethylenic units. The last feature is consistent with the slow rate of hydrogenation over the particular catalyst used.

The corresponding reactions with acetic acid proceed less efficiently.

Experimental.—Reactions with cyclo*hexene*. The two layers initially obtained on adding *cyclo*hexene (10 ml.) to formic acid (90%; 20 ml.) containing perchloric acid (60%; 0·25 ml.) formed a homogeneous brown solution within 20 min. at 100°; this yielded *cyclo*hexyl formate

(11·6 g., 90%), b. p. 48—50°/13 mm. (Found: C, 65·6; H, 9·45%; sap. no., 435. Calc. for $C_7H_{12}O_2$: C, 65·8; H, 9·4%; sap. no., 437), free from higher-boiling contaminants. Reduction of the catalyst concentration by 60% did not diminish the yield of the ester. Replacement of the formic acid by acetic acid gave *cyclo*hexyl acetate (8·6 g., 60%) (Found: C, 67·6; H, 9·95%; sap. no., 394. Calc. for $C_8H_{14}O_2$: C, 67·55; H, 9·9%; sap. no., 400), again free from higher-boiling by-products.

Reactions with 1-*methyl*cyclo*hexene*. When 1-methyl*cyclo*hexene (20 ml.) was treated with formic acid (90%; 40 ml.) containing perchloric acid (60%; 0·4 ml.) at 100° the lower acidic layer assumed a deep olive-green colour. After 1 hr. the mixture was poured into water and extracted with ether; the neutralised extract yielded on distillation a little unchanged hydrocarbon together with the following fractions: (i) b. p. 50—65°/13 mm. (4·0 g.); (ii) b. p. 110—125°/13 mm. (8·1 g.); (iii) b. p. 90—110°/0·03 mm. (2·0 g.); (iv) resinous residue (1·0 g.). Fraction (i) was mainly methyl*cyclo*hexyl formate, b. p. 62—64°/15 mm. (Found: C, 68·2; H, 10·0. Calc. for $C_8H_{14}O_2$: C, 67·5; H, 9·85%). Fraction (ii) was oxygen-free and is presumably 2-*methyl*-1-1′-*methyl*cyclo*hexyl*cyclo*hexene*, b. p. 90—92°/2 mm., 58—60°/0·03 mm., n_D^{20} 1·5000 (Found: C, 87·4; H, 12·4%; *M*, 185. $C_{14}H_{24}$ requires C, 87·5; H, 12·5%; *M*, 192). It absorbed 2 atoms of hydrogen per mole during 16 hr. over a palladium–Norit catalyst to give a *dimethyldi*cyclo*hexyl*, b. p. 55°/0·03 mm., n_D^{20} 1·4890 (Found: C, 86·5; H, 13·3%; *M*, 195. $C_{14}H_{26}$ requires C, 86·5; H, 13·5%; *M*, 194). The yellow fraction (iii) was heterogeneous and was divided into (*a*) b. p. 95—106/0·03 mm., n_D^{20} 1·5005 (Found: C, 82·15; H, 11·45%), and (*b*) b. p. 106—110/0·03 mm., n_D^{20} 1·5138 (Found: C, 84·6; H, 11·45%). These products accounted for 80—85% of the original 1-methyl*cyclo*hexene. Use of acetic acid in place of formic acid gave a much more favourable ratio of ester to dimer (2·4 g. and 0·5 g., respectively, from 10 ml. of 1-methyl*cyclo*hexene) but the overall yield of reaction products was low (35% based on olefin used).

This work forms part of the programme of research undertaken by the Board of the British Rubber Producers' Research Association. The author expresses his thanks to Mr. E. S. Waight for spectrographic data and to Dr. W. T. Chambers for microanalyses.

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668. *Isolation of a Sulphate of Ruthenium.*

By M. A. Hepworth and P. L. Robinson.

There is no certain evidence that a sulphate of ruthenium has been previously isolated. It is now shown that ruthenium tetroxide and sulphur trioxide react under ultra-violet radiation to give a dark brown solid of the empirical composition represented by ruthenium(VI) oxydisulphate, but which we believe should be formulated as the pyro-salt $Ru(VI)O_2S_2O_7$. The properties of the new sulphate are described.

It appears doubtful whether, in spite of their repetition in most compendia including Sidgwick's "Chemical Elements and their Compounds," Oxford University Press, 1950, p. 1477, any of the alleged isolations of sulphates of ruthenium are well founded. Early work on this theme resulted in the formation of solutions which, somewhat wishfully perhaps, were assumed to contain quadrivalent ruthenium presumably as sulphate. Thus Claus (*J. pr. Chem.*, 1847, **42**, 364), who added a more or less impure ruthenium disulphide [made by precipitating a ruthenium(IV) solution with hydrogen sulphide] to nitric acid, obtained an orange-red solution which he believed to contain the quadrivalent sulphate $Ru(SO_4)_2$. We have found, however, that on evaporation such a solution yields a sticky red mass which we believe to be a complex nitrosyl sulphate. Antony and Lucchesi (*Gazzetta*, 1898, **28**, ii, 139; 1899, **29**, ii, 314) later tried the successive actions of hydrochloric and sulphuric acids on barium ruthenate and obtained a bright red solution which, when treated with sulphur dioxide, became blue, but failed to yield a crystalline sulphate.

Recently, the problem has been approached quantitatively by Martin (*J.*, 1952, 3055),

who showed that the reduction of ruthenium tetroxide in sulphuric acid solution is brought about by a number of reducing agents ranging from NO_2^- to Fe^{++} with the formation, when the ruthenium is below a certain critical concentration, of intensely brown solutions in which the metal had been reduced to the quadrivalent condition. Above this critical concentration the tetroxide gave green solutions in which ruthenium(VI) was shown to be present, most probably, as the ion $RuO_2(SO_4)_2^{--}$, though the instability of this ion at high dilution prevented its being detected in an electrical transference cell. The intermediate 6-valency state was also produced by mixing ruthenium tetroxide with the freshly prepared brown solution, Ru(IV) + Ru(VIII) $\longrightarrow$ 2Ru(VI). Within an hour or two of its preparation, this green solution became brown, probably owing to a disproportionation to quadri- and octa-valent ruthenium.

These interesting reactions appeared to afford little possibility of isolating salts from the necessarily dilute solutions formed in the first instance. The earlier experiments, on the other hand, gave little promise of the successful removal of sulphuric acid from salts which are unstable at temperatures far below those required for this purpose. Wohler, Balz, and Metz (*Z. anorg. Chem.*, 1924, **139**, 213), however, have shown that in aqueous solution ruthenium tetroxide is reduced to the quadrivalent hydrated dioxide by ultraviolet radiation with the simultaneous liberation of oxygen. It therefore seemed worthwhile to study the behaviour of the ruthenium tetroxide–sulphur trioxide system under these conditions. Most interestingly in the light of Martin's work, we find that here again the reduction is to the intermediate sexavalent condition : Ru(VIII) $\longrightarrow$ Ru(VI). Furthermore, after the removal of the excess of sulphur trioxide the residue is a dark brown powder with a composition corresponding to the empirical formula $RuO(SO_4)_2$.

This compound is stable in dry air below about 150°, above which sulphur trioxide is liberated. In moist air it obviously suffers slow hydrolysis, since it then has the characteristic odour of the tetroxide. With water there is instant hydrolysis followed by precipitation of the hydrated dioxide, RuO_2,xH_2O. When added, however, to dilute sulphuric acid at room temperature it dissolves, giving the brown colour characteristic of the metal in the quadrivalent state, probably a solution of an oxysulphate of the type $Ru(IV)OSO_4$. Still more interesting is its behaviour on treatment with dilute sulphuric acid at 0°, for then a green solution, evidently the same as observed by Martin (*loc. cit.*), is formed which, as his does, gradually changes colour presumably by disproportionation. The distinctly different behaviour shown towards water and ordinary and cooled dilute sulphuric acid is not unaccountable if it be allowed that the material is pyrosulphate. The vigour of its reaction with a very little water and the liberation of sulphur trioxide in these circumstances make the formulation $Ru(VI)O_2S_2O_7$ probable. The three reactions may then be represented thus: (*a*) With dilute sulphuric acid at 0°, the ion is fixed by an electron transfer from the hydrogen atoms in the reacting water molecule: $Ru(VI)O_2S_2O_7 + H_2O \longrightarrow 2H^+ + Ru(VI)O_2(SO_4)_2^{--}$. (*b*) With dilute sulphuric acid at room temperature, instability is great enough to lead to loss of oxygen: $2Ru(VI)O_2S_2O_7 + H_2O \longrightarrow 2Ru(IV)OSO_4 + 2H_2SO_4 + O_2$. (*c*) With water in large excess the hydrolysis is carried a stage further: $2Ru(VI)O_2S_2O_7 + 4H_2O \longrightarrow 2RuO_2 + 4H_2SO_4 + O_2$.

When fused with potassium hydrogen sulphate part of the ruthenium volatilises as tetroxide and the residual melt is homogeneous, clear, and green. It dissolves in water with formation of a stable bright green solution.

Experimental

Sulphur trioxide was prepared from fuming sulphuric acid containing 65% of additional SO_3 by keeping it over phosphoric oxide for 24 hr. and distilling it. The vacuum apparatus employed was especially dried by flaming it under reduced pressure with a hand torch. When the mixture was warmed, α-sulphur trioxide distilled over as a colourless liquid. It was subsequently subjected to a trap-to-trap distillation with rejection of head and tail fractions before use.

A large excess of the α-sulphur trioxide was distilled in a vacuum on to the dry ruthenium tetroxide contained in a Pyrex bulb cooled with liquid oxygen. The bulb was sealed under

vacuum and the contents were allowed to come to room temperature. As the sulphur trioxide melted, the tetroxide dissolved to an intensely red solution. The bulb and contents were then exposed to ultra-violet light from a lamp kept at such a distance as to hold their temperature at about 40°. After one week the completion of the reaction was made evident by the settling of a dark brown precipitate, leaving the supernatant sulphur trioxide almost colourless. The excess of trioxide was removed at 100° in a vacuum (24 hr.), leaving the *oxysulphate* as a dark brown crystalline solid [Found: Ru, 32·8; SO_4, 61·4. $RuO(SO_4)_2$ requires Ru, 32·7; SO_4, 62·1%].

The methods of analysis used were: (*a*) Ruthenium by reduction of the compound in dry hydrogen to the metal. Reaction begins about 30° with slight inflammation but thereafter proceeds smoothly. When it was complete, the sulphuric acid and sulphur trioxide liberated were removed by heating in the hydrogen stream preparatory to weighing of the metal. (*b*) Sulphate by adding the compound to excess of 10% aqueous sodium hydrogen carbonate, coagulating the precipitated ruthenium dioxide by boiling for 3 min., and filtering it off, and determining sulphate in the filtrate as barium sulphate.

(*c*) The valency of the ruthenium in the compound was fixed by using Crowell and Yost's method (*J. Amer. Chem. Soc.*, 1928, **50**, 374). A known weight was treated with approx. 50 ml. of 2N-sulphuric acid containing 1 g. of potassium iodide, and the liberated iodine was titrated with 0·1N-thiosulphate in the presence of some carbon tetrachloride to assist in locating the end-point. Three equivs. of iodine were liberated per atom of ruthenium present, and the valency of the ruthenium in the compound is therefore $3 + 3 = 6$: $Ru(VI) + 3I^- \longrightarrow Ru(III) + 3I$.

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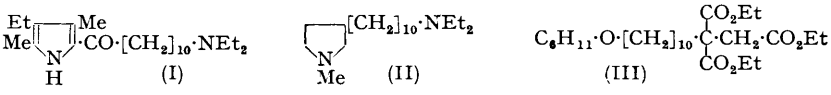
669. *Two Basically Substituted Pyrrolidines.*

By JEAN MCCONNEL, VLADIMIR PETROW, and BENNETT STURGEON.

Two open-chain analogues of conessine (Favre, Haworth, McKenna, Powell, and Whitfield, *J.*, 1953, 1115) were prepared in order to determine whether the amoebicidal activity of the latter was a function of the steroid nucleus, *per se*, or an expression of a specific biological property often associated with molecules containing two basic centres separated by a polymethylene chain (see, *e.g.*, Hall, Mahboob, and Turner, *J.*, 1950, 1842; 1952, 149, 1956).

2-11′-Diethylaminoundecyl-4-ethyl-3 : 5-dimethylpyrrolidine was synthesised as follows: condensation of 10-diethylaminodecyl cyanide with kryptopyrrolylmagnesium bromide in ethereal solution yielded the ketone (I), which was reduced to 2-11″-diethylaminoundecyl-4-ethyl-3 : 5-dimethylpyrrole by the Huang-Minlon modification of the Wolff–Kishner process (*J. Amer. Chem. Soc.*, 1949, **71**, 3301). The pyrrole ring was then saturated by hydrogenation over Raney nickel. Attempts to extend the synthesis to the use of pyrrolylmagnesium bromide proved unsuccessful.

3-10′-Diethylaminodecyl-1-methylpyrrolidine (II) was prepared by reduction of the corresponding succinimide. The latter was not obtained from 10-diethylaminodecyl chloride as reaction with ethyl sodiomalonate gave too low a yield for the route to be of



(I) (II) (III)

value. Condensation of 10-chlorodecanol with ethyl sodiomalonate proved equally unsuccessful, the alkylating agent undergoing resinification. Attention was therefore directed to building up the succinimide ring by employing a terminally-protected decyl halide, followed by replacement of the protecting group by the diethylamino-group.

The readily accessible 10-*cyclo*hexyloxydecyl bromide was condensed with ethyl sodio-

malonate, and the sodio-derivative of the resulting malonic ester alkylated with ethyl chloroacetate to give the tricarboxylic ester (III). Hydrolysis with potassium hydroxide in diethylene glycol at 200°, followed by decarboxylation and dehydration with acetic anhydride, yielded 10-*cyclo*hexyloxydecylsuccinic anhydride. Reaction with methylamine gave the corresponding methylimide, which was reduced to 3-10′-*cyclo*hexyloxydecyl-1-methylpyrrolidine by lithium aluminium hydride. Replacement of the 10-*cyclo*hexyloxy-group was accomplished by successive treatment with concentrated hydrobromic acid and diethylamine; the product (II) was an oil, which formed a characteristic dipicrate.

Only one of the ethoxycarbonyl groups of (III) was hydrolysed by potassium hydroxide at 150°, leading to the substituted ethyl hydrogen malonate. Decarboxylation of this product, followed by reduction with lithium aluminium hydride, yielded 2-10′-*cyclo*hexyloxydecylbutane-1 : 4-diol.

Experimental

2-11′-*Diethylaminodecyl*-4-*ethyl*-3 : 5-*dimethylpyrrole*.—Kryptopyrrole (25·8 g.) in dry ether (50 ml.) was slowly run into a mechanically stirred solution of ethylmagnesium bromide (from 6·5 g. of magnesium and 23·7 g. of ethyl bromide) in ether (80 ml.) under an atmosphere of nitrogen, and the mixture was heated under reflux for 2 hr. 10-Diethylaminodecyl cyanide (Linnell and Vora, *J. Pharm. Pharmacol.*, 1952, **4**, 55; 25 g.) was added and heating continued for 3 hr. Next morning, the mixture was decomposed by hot 10% ammonium chloride solution during 1 hr. Dilute hydrochloric acid was added, and the unchanged kryptopyrrole extracted with ether. The ketonic product (I) was liberated with sodium hydroxide, isolated with ether, and distilled as a viscous yellow oil (25 g.), b. p. 198°/0·05 mm.

The ketone, 100% hydrazine hydrate (30 ml.), sodium hydroxide (25 g.), and ethyleneglycol (350 ml.) were heated under reflux for 1 hr., and the condenser was then removed. The temperature was raised and maintained at 195°, for 3 hr. The mixture was diluted with water and the product extracted with ether. 2-11′-*Diethylaminodecyl*-4-*ethyl*-3 : 5-*dimethylpyrrole* (18·1 g.) was obtained as a pale yellow oil, b. p. 164°/0·05 mm. (Found: C, 79·1; H, 12·7; N, 8·3. $C_{23}H_{44}N_2$ requires C, 79·3; H, 12·6; N, 8·1%).

2-11′-*Diethylaminoundecyl*-4-*ethyl*-3 : 5-*dimethylpyrrolidine*, prepared by heating the pyrrole in ethanolic solution with hydrogen at 125°/160 atm. for 1 hr. in the presence of Raney nickel W 7, was obtained as an oil (98%), b. p. 145°/0·2 mm. (Found: C, 77·8; H, 13·3; N, 7·7. $C_{23}H_{48}N_2$ requires C, 78·4; H, 13·6; N, 8·0%).

Ethyl 10-cyclo*Hexyloxydecylmalonate*.—Sodium (1·47 g.) was dissolved in dry ethanol (62 ml.) and when the solution had cooled to 40°, sodium iodide (0·2 g.) and ethyl malonate (9·35 g.) were added, followed by 10-*cyclo*hexyloxydecyl bromide (Drake *et al.*, *J. Amer. Chem. Soc.*, 1946, **68**, 1536; 18 g.) in small portions. The mixture was heated on the steam-bath for 5 hr. The ethanol was evaporated off and the residue treated with water. *Ethyl* 10-cyclo*hexyloxydecylmalonate* (70%) was extracted with ether, and distilled as an oil, b. p. 172·5°/0·2 mm. (Found: C, 69·1; H, 10·4. $C_{23}H_{42}O_5$ requires C, 69·3; H, 10·6%).

Ethyl 12-cyclo*Hexyloxydodecane*-1 : 3 : 3-*tricarboxylate*.—A cold solution of sodium ethoxide [from sodium (1·95 g.) in dry ethanol (87 ml.)] was treated with ethyl 10-*cyclo*hexyloxydecylmalonate (33 g.) and sodium iodide (0·1 g.). After the solution had been shaken for 30 min. ethyl chloroacetate (13 g.) was added, and the mixture refluxed for 15 hr. Isolation of the product gave *ethyl* 12-cyclo*hexyloxydodecane*-1 : 3 : 3-*tricarboxylate* as an oil (Found: C, 66·7; H, 10·4. $C_{27}H_{48}O_7$ requires C, 67·0; H, 10·0%).

10-cyclo*Hexyloxydecylsuccinic Anhydride*.—The foregoing ester (28 g.), diethylene glycol (100 ml.), and 10N-potassium hydroxide solution (60 ml.) were heated without a condenser until the internal temperature reached 200°. The mixture was refluxed for 2 hr. and then poured into 20% sulphuric acid (400 ml.). The resulting acid was extracted with ethyl acetate and decarboxylated at 240° in a metal-bath for 30 min. The residue was heated under reflux with acetic anhydride (100 ml.) for 4 hr. and the product isolated by distillation at 214°/0·3 mm. 10-cyclo*Hexyloxydecylsuccinic anhydride* (31%) solidified on cooling and formed silky needles, m. p. 51°, from chloroform–light petroleum (b. p. 60—80°) (Found: C, 71·1; H, 10·3. $C_{20}H_{34}O_4$ requires C, 71·0; H, 10·3%).

3-10′-cyclo*Hexyloxydecyl*-1-*methylpyrrolidine*.—10-*cyclo*Hexyloxydecylsuccinic anhydride (9·4 g.) and 33% aqueous methylamine (50 ml.) were heated in a metal-bath to 260° (excess of amine evaporating), and then for 30 min. at that temperature. The resulting succinimide was

dissolved in ether and slowly added to a stirred solution of lithium aluminium hydride (5 g.) in ether (400 ml.). The mixture was refluxed for 8 hr. and then decomposed with water, and the product extracted with ether. 3-10′-cyclo*Hexyloxydecyl*-1-*methylpyrrolidine* distilled at 158—162°/0·3 mm. (Found: C, 77·1; H, 12·0; N, 5·2. $C_{21}H_{41}ON$ requires C, 78·0; H, 12·7; N, 4·3%).

3-10′-*Diethylaminodecyl*-1-*methylpyrrolidine*.—The corresponding 10-*cyclo*hexyloxy-compound (4·5 g.) and hydrobromic acid (*d* 1·48; 50 ml.) were boiled for 5 hr., the *cyclo*hexyl bromide being allowed to distil away occasionally. The acid was evaporated and the residue heated at 100° for 20 hr. with diethylamine (10 ml.) and ethanol (20 ml.) in a sealed tube. Dilute alkali was then added and the product extracted with ether and distilled. 3-10′-*Diethylaminodecyl*-1-*methylpyrrolidine* formed an oil, b. p. 140°/0·3 mm. (Found: C, 77·0; H, 13·5; N, 9·4. $C_{19}H_{40}N_2$ requires C, 77·0; H, 13·5; N, 9·5%). The *dipicrate* crystallised in spear-shaped plates (from ethanol), m. p. 140° (Found: C, 49·4; H, 6·2; N, 15·1. $C_{19}H_{40}N_2,2C_6H_3O_7N_3$ requires C, 49·5; H, 5·9; N, 14·9%).

2-10′-cyclo*Hexyloxydecylbutane*-1 : 4-*diol*.—Hydrolysis of ethyl 12-*cyclo*hexyloxydodecane-1 : 3 : 3-tricarboxylate at 150°, followed by decarboxylation of the acid and reduction with lithium aluminium hydride, gave this *glycol* as the main product, b. p. 136—137°/0·2—0·3 mm. (Found: C, 74·9; H, 12·9. $C_{19}H_{38}O_3$ requires C, 75·1; H, 12·6%).

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