Long-chain Acyloins and Vicinal Diketones

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Several methods for the preparation of long-chain vicinal diketones are examined. The acyloin condensation, followed by oxidation, provides an excellent route to symmetrical compounds but is not satisfactory for unsymmetrical diketones. The latter are prepared (i) from dialkylacetylenes by semihydrogenation, hydroxylation, and oxidation with aqueous *N*-bromosuccinimide; and (ii) from an α-acetoxy-acid chloride and the sodio-derivative of a bistetrahydropyranyl or dibenzyl alkylmalonate, followed by removal of the protecting groups and decarboxylation to give the α-acetoxy-ketone, which is then hydrolysed and oxidised.

THE synthesis of long-chain α-diketones, especially unsymmetrical compounds, has received little attention. The acyloin condensation,[1] followed by oxidation of the acyloin (I) provides a convenient route to symmetrical diketones (II). Thus undecanoin gave docosane-11,12-dione in good yields when oxidised with bismuth oxide [2]

$$RCO_2Et \longrightarrow \underset{(I)}{RCH(OH)\cdot COR} \longrightarrow \underset{(II)}{RCO\cdot COR}$$

or aqueous *N*-bromosuccinimide;[3] other oxidising agents [4] gave less satisfactory results. Mixed acyloin condensations between two aliphatic esters have apparently not been reported, although a few examples involving substituted esters have been described.[5,6] Acyloin condensation of ethyl butyrate with ethyl undecanoate gave, on fractional distillation, a mixture of the two isomeric acyloins, 4(5)-hydroxypentadecan-5(4)-one (41%). Oxidation with bismuth oxide gave pentadecane-4,5-dione (63%). When ethyl hexanoate was condensed with ethyl undecanoate, however, the mixed acyloin could not be isolated by fractional distillation. [The difficulty involved in purifying simple acyloin condensation products has been commented on by earlier workers.[6-8] The difficulties are apparently due to formation of diol and diketone as well as of other by-products (*e.g.* from Claisen condensations [9]]. The crude product was oxidised but again separation of the diketones by fractional distillation was unsatisfactory.

The action of dialkylcadmium reagents with oxalyl chloride has been shown to give symmetrical vicinal diketones.[10] The use of oxalyl chloride in the ketone synthesis developed by Bowman and Fordham [11] has now been examined. Treatment of an alkylmalonic acid with dihydropyran gave the bistetrahydropyranyl ester (III); the sodium derivative, obtained by action of

$$\underset{(III)}{R^1CH(CO_2R^2)_2} \qquad \underset{(IV)}{R^1C(CO_2R^2)_2\cdot CO\cdot CO\cdot CR^1(CO_2R^2)_2}$$

$$\underset{(V)}{R^1CH_2\cdot CO\cdot CO\cdot CH_2R^1}$$

R^2 = tetrahydropyranyl

sodium hydride, condensed with oxalyl chloride to give the acylmalonate ester (IV). When this was heated with acetic acid, elimination of dihydropyran and carbon dioxide took place to give the symmetrical diketone (V) in poor yield (21—28%).

The acylmalonate approach can also be applied to the synthesis of unsymmetrical α-diketones. Bowman [12] prepared 1-phenylpentadecane-1,2-dione by condensation of *O*-acetylmandelyl chloride (VI; R^1 = Ph) with the sodio-derivative of dibenzyl dodecylmalonate to give the acylmalonate (VII; R^1 = Ph, R^2 = n-$C_{12}H_{25}$, R^3 =

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[2] W. Rigby, *J. Chem. Soc.*, 1951, 793.
[3] W. A. Cramp, F. J. Julietti, J. F. McGhie, and B. L. Rao, *J. Chem. Soc.*, 1960, 4257.
[4] M. Weiss and M. Appel, *J. Amer. Chem. Soc.*, 1949, **71**, 2269; E. P. Papadopoulous, A. Jerrar, and C. H. Issidorides, *J. Org. Chem.*, 1966, **31**, 615.
[5] P. Baudart, *Compt. rend.*, 1945, **220**, 404; 1945, **221**, 201; *Bull. Soc. chim. France*, 1946, **13** [5], 87.
[6] J. W. Lynn and J. E. English, *J. Amer. Chem. Soc.*, 1951, **73**, 4284.
[7] B. B. Corson, W. L. Benson, and T. T. Goodwin, *J. Amer. Chem. Soc.*, 1930, **52**, 3988.
[8] J. M. Snell and S. M. McElvain, *J. Amer. Chem. Soc.*, 1931, **53**, 750.
[9] Cf. J. J. Bloomfield, *Tetrahedron Letters*, 1968, 587, 591.
[10] M. Renson and J. Bonhomme, *Bull. Soc. chim. belges*, 1959, **68**, 437; J. Kolloritsch, U.S.P. 3,065,259/1962.
[11] R. E. Bowman and W. D. Fordham, *J. Chem. Soc.*, 1952, 3945.
[12] R. E. Bowman, *J. Chem. Soc.*, 1950, 325; D. E. Ames and R. E. Bowman, *ibid.*, 1951, 1079.

CH_2Ph), which on debenzylation and decarboxylation gave the acetoxy-ketone (VIII) and thence, by hydrolysis and oxidation with chromic acid, the diketone (IX).

$R^1CH(OAc)\cdot COCl$ (VI) $\quad R^1CH(OAc)\cdot CO\cdot CR^2(CO_2R^3)_2$ (VII)

$R^1CH(OAc)\cdot CO\cdot CH_2R^2$ (VIII) $\quad R^1CO\cdot CO\cdot CH_2R^2$ (IX)

This route gave satisfactory results when aliphatic α-acetoxy-acid chlorides were used. The intermediate acetoxy-ketone (VIII) could easily be isolated, and ester interchange with an alcohol in the presence of boron trifluoride as catalyst [13] yielded the unsymmetrical acyloin. This, or the mixture of isomeric acyloins obtained by alkaline hydrolysis, gave the α-diketone on oxidation.

When the bistetrahydropyranyl ester of an alkylmalonate was used in this synthesis, low yields were obtained, and the products were not easily isolated. These difficulties are presumably due to ester interchange between the acetoxy- and tetrahydropyranyloxycarbonyl-groups during removal of the protecting group (by heating with acetic acid).

The readily available dialkylacetylenes may also be conveniently converted into symmetrical and unsymmetrical aliphatic diketones by semihydrogenation to the *cis*-olefin, hydroxylation, and oxidation of the diol with *N*-bromosuccinimide (following the procedure used by McGhie and his collaborators [3] for the preparation of diketo-acids).

δ-Keto-nitriles were prepared by Bowman and Fordham [14] by condensation of acid chlorides with the sodio-derivative of dibenzyl 2-cyanoethylmalonate, and subsequent catalytic hydrogenation and decarboxylation. When 2-acetoxyundecanoyl chloride was used in this synthesis, 6-acetoxy-5-oxopentadecanonitrile (X) was obtained in good yield. Treatment with methanolic boron trifluoride, followed by oxidation with bismuth oxide, gave 5,6-dioxopentadecanonitrile (XI). The reduction of δ-keto-nitriles provides an efficient route to 2-alkylpiperidines.[14] When the nitrile (X) was hydrogenated with Raney nickel catalyst, however, 2-decylpiperidine was isolated; the acetoxy-group was presumably eliminated by hydrogenolysis of the acetoxy-ketone or of an intermediate acetoxyimine. 2-Decylpiperidine was similarly obtained by reduction of 5,6-dioxopentadecanonitrile but in one experiment a small amount of keto-amine (XII) was also isolated as the hydrochloride.

$CH_3\cdot[CH_2]_8\cdot CH(OAc)\cdot CO\cdot[CH_2]_3\cdot CN$ (X)

$CH_3\cdot[CH_2]_8\cdot CO\cdot CO\cdot[CH_2]_3\cdot CN$ (XI)

$CH_3\cdot[CH_2]_8\cdot COR$ (XII) $\quad R =$ 2-piperidyl

A number of long-chain 2,3-dialkylquinoxalines were prepared by condensation of 1,2-diketones with *o*-phenylene diamine. An alternative method of preparation, alkylation of 2,3-dimethylquinoxaline, was also examined. Bergstrom and Moffatt [15] obtained a dipotassio-derivative by action of potassamide on 2,3-dimethylquinoxaline in liquid ammonia. The derivative condensed with ethyl iodide to give 2,3-dipropylquinoxaline, the structure of which was shown by an independent synthesis.[15] Similarly the alkylation of 2,3-dimethylquinoxaline with dodecyl bromide in presence of sodamide (2 mol.) gave 2,3-bistridecylquinoxaline, more conveniently prepared from octacosane-14,15-dione. 2,3-Dimethylquinoxaline was also monoalkylated by using sodamide (1 mol.) and dodecyl bromide; the product, 2-methyl-3-tridecylquinoxaline, was also obtained from hexadecane-2,3-dione. 2-Methoxy-3-methylquinoxaline was similarly alkylated with dodecyl bromide to give 2-methoxy-3-tridecylquinoxaline.

EXPERIMENTAL

Evaporations were carried out under reduced pressure.

Acyloin Condensations.—Undecanoin. Treatment of ethyl undecanoate with sodium in xylene by Hansley's procedure [16] gave *undecanoin* (89%), m.p. 58—60° (from ethanol) (Found: C, 77·8; H, 12·9. $C_{22}H_{44}O_2$ requires C, 77·7; H, 12·9%).

Ethyl butyrate with ethyl undecanoate. Sodium (9·2 g.) and xylene (400 c.c.; sulphur-free) were stirred vigorously at 100° under nitrogen (oxygen-free), and a mixture of ethyl butyrate (11·6 g.) and ethyl undecanoate (21·4 g.) (0·1 mol. each) was added during 20 min. (temp. below 110°). The mixture was stirred at 95—105° for 2 hr., cooled to to 80°, and treated with methanol (15 c.c.). After addition of water (25 c.c.) and 6N-hydrochloric acid (80 c.c.), the mixture was stirred for 2 hr. and separated; the organic layer was washed with sodium hydrogen carbonate solution and water and evaporated. Butyroin (1·5 g.), b.p. 90—95°/18 mm., was removed and then repeated fractional distillation [Vigreux column (3 in.)] gave 4(5)-hydroxypentadecan-5(4)-one (2 isomers present) (5·45 g.), b.p. 106—112°/0·2 mm. (Found: C, 74·1; H, 12·1. Calc. for $C_{15}H_{30}O_2$: C, 74·3; H, 12·5%). Recrystallisation of the distillation residue from ethanol gave undecanoin, m.p. and mixed m.p. 56—58°.

Docosane-11,12-dione.—(*a*) Undecanoin (10 g.), bismuth oxide (7 g.), and acetic acid (40 c.c.) were stirred under reflux (bath 110°) for 30 min. (ref. 2). The hot mixture was filtered and the solid was washed with boiling benzene; the combined filtrates were washed with water, sodium hydrogen carbonate solution, and water, and evaporated to give *docosane-11,12-dione* (6·2 g.), m.p. 68—69° [from ethanol and then light petroleum (b.p. 60—80°)] (Found: C, 78·1; H, 12·4. $C_{22}H_{42}O_2$ requires C, 78·1; H, 12·7%), $\nu_{max.}$ 1710 cm.$^{-1}$.

(*b*) Undecanoin (3·8 g.) was added to *N*-bromosuccinimide (3·6 g.) in ethyl acetate (125 c.c.) and water (100 c.c.) under carbon dioxide.[3] The mixture was heated under reflux for 30 min., cooled, and separated, and the organic layer was washed with water. Evaporation left the dione (2·5 g.), m.p. 68·5—70°.

[13] J. F. McGhie, personal communication.
[14] R. E. Bowman and W. D. Fordham, *J. Chem. Soc.*, 1951, 2753.
[15] R. A. Ogg and F. W. Bergstrom, *J. Amer. Chem. Soc.*, 1931, **53**, 1846.
[16] V. L. Hansley, *J. Amer. Chem. Soc.*, 1935, **57**, 2303.

Pentadecane-4,5-dione.—Oxidation of 4(5)-hydroxypentadecan-5(4)-one with bismuth oxide as above gave *pentadecane-4,5-dione* (63%), b.p. 96—102°/0·3 mm., as yellow plates, m.p. 35—36°, after recrystallisations from methanol at −10° (Found: C, 74·5; H, 11·8. $C_{15}H_{28}O_2$ requires C, 75·0; H, 11·7%), $\nu_{max.}$ 1715 cm.$^{-1}$.

Condensations with Oxalyl Chloride.—*Octacosane-14,15-dione*. A solution of dodecylmalonic acid (13·6 g.) in dimethoxyethane (30 c.c.) and benzene (60 c.c.) was dried by azeotropic distillation. Concentrated sulphuric acid (2 drops) and dry dihydropyran (16·8 g.) were added successively (exothermic reaction).[11] The solution was left for 1 hr. at room temperature and then added to a suspension of sodium hydride (2·4 g.; 50%) in benzene (300 c.c.). The clear solution obtained was stirred while oxalyl chloride (2 c.c.) in benzene (50 c.c.) was added. After 1 hr., acetic acid (10 c.c.) was added and the mixture was heated under reflux for 1 hr. (bath 100—110°), cooled, and washed with sodium hydrogen carbonate solution and water. Evaporation left the dione (2·49 g.) as yellow plates, m.p. 81—82° (from methanol) (lit.,[17] 74°) (Found: C, 79·0; H, 12·7. Calc. for $C_{28}H_{54}O_2$: C, 79·6; H, 12·9%).

Similarly prepared were *hexadecane-8,9-dione* (28%), m.p. 43—45° (from methanol) (Found: C, 75·6; H, 12·2. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%); and eicosane-10,11-dione (21%), m.p. 63—64° (from methanol) (lit.,[18] 63—64°).

Condensations With α-Acetoxy-acid Chlorides.—(a) *Use of benzyl malonates*. Sodium (1·15 g.) was dissolved in dry ethanol (50 c.c.) and the solvent was removed (bath to 180°); then the pressure was reduced suddenly. Benzyl alcohol (10·8 g.), benzene (250 c.c.), and diethyl octylmalonate (13·6 g.) were added and the mixture was distilled through a Fenske column (30 cm.) for 3 hr. to remove the ethanol azeotrope. α-Acetoxypropionyl chloride (7·5 g.) was added and the mixture was left at room temperature for 60 hr. After addition of 0·1N-sulphuric acid and ice, the solution was rapidly extracted thrice with ethyl acetate, and the extracts were washed with water and evaporated (bath <30°). The residual gum in ethyl acetate (100 c.c.) was hydrogenated over palladised charcoal (6 g.; 10%); absorption was complete in 2 hr. The filtered solution was heated under reflux for 20 min. and distilled to give *2-acetoxydodecane-3-one* (6·35 g., 52%), b.p. 122—124°/1·5 mm. (Found: C, 69·3; H, 10·8. $C_{14}H_{26}O_3$ requires C, 69·4; H, 10·8%). Similarly prepared was *10-acetoxyeicosane-11-one* (49%), b.p. 188—192°/0·9 mm. (Found: C, 74·1; H, 11·5. $C_{22}H_{42}O_2$ requires C, 74·5; H, 11·9%).

When 2-acetoxyundecanoyl chloride (10·5 g.) and diethyl dodecylmalonate (13 g.) were used as starting materials, the very high-boiling acetoxy-ketone was not isolated; the crude product in methanol (100 c.c.) was treated with boron trifluoride–diethyl ether (5 c.c.) and the solution was heated to the b.p. and then left overnight. Filtration and recrystallisation from methanol gave *10-hydroxytetracosan-11-one* (4·9 g.; 33%), m.p. 58—60° (Found: C, 78·3; H, 12·7. $C_{24}H_{48}O_2$ requires C, 78·2; H, 13·1%). Oxidation of this acyloin with *N*-bromosuccinimide yielded tetracosane-10,11-dione (63%), m.p. 64—65°, as shining yellow plates from methanol (Found: C, 78·7; H, 12·6. $C_{24}H_{46}O_2$ requires C, 78·6; H, 12·7%).

Hydrolysis and oxidation (bismuth oxide) of 2-acetoxydodecan-3-one (4 g.) as described furnished *dodecane-2,3-dione* (1·9 g.), b.p. 74—77°/0·5 mm., f.p. 23° (Found: C, 72·5; H, 11·0. $C_{12}H_{22}O_2$ requires C, 72·7; H, 11·2%). Similarly hydrolysis and oxidation (*N*-bromosuccinimide) of 10-acetoxyeicosan-11-one gave eicosane-10,11-dione (51%), m.p. 62—63° (lit.,[18] 63—64°).

(b) *Use of tetrahydropyranyl malonates*. Dodecylmalonic acid (13·6 g.) was converted into the sodio-derivative of the bistetrahydropyranyl ester as described above. The solution was stirred while α-acetoxypropionyl chloride (7·5 g.) in benzene (50 c.c.) was added. After 1 hr., the mixture was treated with acetic acid (10 c.c.) and heated under reflux for 1·5 hr. Isolation and distillation gave crude *2-acetoxyhexadecan-3-one* (5·7 g.), b.p. 150—152°/0·5 mm., m.p. 20—22° (Found: C, 71·7; H, 11·4. $C_{18}H_{34}O_3$ requires C, 72·4; H, 11·5%). This (5·7 g.) in ethanol (50 c.c.) was heated under reflux under nitrogen for 2 hr. with potassium hydroxide (3 g.) in water (10 c.c.). Acidification and isolation with ethyl acetate gave the crude acyloin (2 isomers) which was oxidised with bismuth oxide (5 g.) in acetic acid (30 c.c.) as described. *Hexadecane-2,3-dione* (1·8 g.) had b.p. 133—135°/0·5 mm., m.p. 47—48° (from methanol) (Found: C, 75·3; H, 11·9. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%).

Similarly, hexylmalonic acid (9·4 g.) was esterified and condensed with 2-acetoxyundecanoyl chloride (13·2 g.) and the crude product was hydrolysed with alkali. The crude acyloin in ethyl acetate (250 c.c.) and water (200 c.c.) was heated under reflux with *N*-bromosuccinimide (17·8 g.) under carbon dioxide for 30 min. Isolation with ethyl acetate and recrystallisation from ethanol gave *octadecane-8,9-dione* (1·2 g.), m.p. 53—55° (Found: C, 76·2; H, 12·1. $C_{18}H_{34}O_2$ requires C, 76·5; H, 12·1%). Condensation of the sodio-derivative from undecylmalonic acid (12·3 g.) with 2-acetoxyundecanoyl chloride (13·2 g.), followed by similar hydrolysis and oxidation with *N*-bromosuccinimide, gave *tricosane-10,11-dione* (1·3 g.), m.p. 59—60° (from ethanol) (Found: C, 78·5; H, 12·9. $C_{23}H_{44}O_2$ requires C, 78·3; H, 12·6%).

The sodio-derivative from butylmalonic acid (8 g.) was similarly condensed with *O*-acetylmandelyl chloride (10·7 g.) to give *1-acetoxy-1-phenylheptan-2-one* (6·9 g.), b.p. 140—146°/1·2 mm. (Found: C, 72·4; H, 8·5. $C_{15}H_{20}O_3$ requires C, 72·6; H, 8·7%). Alkaline hydrolysis and oxidation (bismuth oxide) gave *1-phenylheptane-1,2-dione* (pentylphenylglyoxal) (2·75 g.), b.p. 94—104°/0·8 mm. (Found: C, 75·8; H, 8·0. $C_{13}H_{16}O_2$ requires C, 76·4; H, 7·9%), $\nu_{max.}$ 1675 and 1710 cm.$^{-1}$. Similarly prepared were 1-phenylpropane-1,2-dione (31%), b.p. 58—62°/0·7 mm. (lit.,[19] 126—128°/20 mm.) $\nu_{max.}$ 1680 and 1710 cm.$^{-1}$, and *1-phenylundecane-1,2-dione* (30%), b.p. 141—145°/0·6 mm. (Found: C, 78·1; H, 9·5. $C_{17}H_{24}O_2$ requires C, 78·4; H, 9·3%).

Long-chain Diketones From Dialkylacetylenes.—Pentyne (34·8 g.) was added to lithamide [from lithium (3·55 g.)] in liquid ammonia (800 c.c.) and tetrahydrofuran (400 c.c.). After addition of undecyl bromide (60 g.), the solution was stirred for 8 hr. and left to evaporate. Addition of dilute hydrochloric acid and isolation with ether gave *hexadec-4-yne* (53 g.), b.p. 110—118°/0·5 mm. (Found: C, 86·0;

[17] F. Bouquet and C. Paquot, *Bull. Soc. chim. France*, 1948, 1165.

[18] H. Bloch, H. Lehr, H. Erlenmeyer, and K. Vogler, *Helv. Chim. Acta*, 1945, **28**, 1410.

[19] H. W. Coles, R. H. F. Manske, and T. B. Johnson, *J. Amer. Chem. Soc.*, 1929, **51**, 2270.

H, 13·5. $C_{16}H_{30}$ requires C, 86·4; H, 13·6%). *Pentadec-7-yne*, similarly prepared, had b.p. 94—95°/0·1 mm. (Found: C, 86·1; H, 13·0. $C_{15}H_{28}$ requires C, 86·5; H, 13·5%).

Pentadec-7-yne (9·4 g.) in ethanol (50 c.c.) was hydrogenated with palladised barium sulphate (0·5 g.; 5%) until 1·0 mol. had been taken up. Filtration and distillation gave the crude olefin (b.p. 93—95°/0·1 mm.), which was dissolved in formic acid (35 c.c.) and chloroform (35 c.c.) and stirred while hydrogen peroxide (4·6 c.c.; 30%) was added.[20] The mixture was maintained at 40° for 2 hr. Addition of water and isolation with chloroform gave an oil which was heated under reflux for 1 hr. under nitrogen with 3N-sodium hydroxide (35 c.c.) and ethanol (35 c.c.). Acidification and extraction with ethyl acetate yielded threo-*pentadecane-7,8-diol* (8·1 g.), m.p. 49—50° (from ethyl acetate) (Found: C, 73·7; H, 12·9. $C_{15}H_{32}O_2$ requires C, 73·7; H, 13·2%). threo-*Hexadecane-4,5-diol*, similarly prepared, had m.p. 60—61° (from ethyl acetate) (Found: C, 74·6; H, 13·3. $C_{16}H_{34}O_2$ requires C, 74·4; H, 13·3%).

Oxidation of *threo*-pentadecane-7,8-diol with *N*-bromosuccinimide as described gave *pentadecane-7,8-dione* (35%), m.p. 41—42° (from ethanol at −20°) (Found: C, 74·5; H, 11·0. $C_{15}H_{28}O_2$ requires C, 75·0; H, 11·6%). *Hexadecane-4,5-dione* (35%), obtained similarly, had b.p. 116—128°/0·5 mm., m.p. 39—41° (from ethanol at −20°) (Found: C, 75·8; H, 11·7. $C_{16}H_{30}O_2$ requires C, 75·5; H, 11·9%). *erythro*-octadecane-9,10-diol [21] similarly gave octadecane-9,10 dione (70%), m.p. 56—57° (Found: C, 76·4; H, 12·2. $C_{18}H_{34}O_2$ requires C, 76·6; H, 12·1%).

6-Acetoxy-5-oxopentadecanonitrile.—The sodio-derivative of diethyl 2-cyanoethylmalonate [22] (21·3 g.) was subjected to ester interchange with benzyl alcohol (21·6 g.) and the product was condensed with 2-acetoxyundecanoyl chloride (23·0 g.) according to the general procedure.[14] Hydrogenation and decarboxylation gave *6-acetoxy-5-oxo-pentadecanonitrile* (14·5 g.), b.p. 155—160°/0·3 mm. (Found C, 69·7; H, 9·7; N, 5·1. $C_{17}H_{29}NO_3$ requires C, 69·1; H, 9·9; N, 4·7%). Similarly undecanoyl chloride gave *5-oxopentadecanonitrile* (37%), b.p. 140—143°/0·5 mm., f.p. 24—26° (Found: C, 76·0; H, 11·5; N, 5·6. $C_{15}H_{27}NO$ requires C, 75·9; H, 11·5; N, 5·9%). Alkaline hydrolysis gave 5-oxopentadecanoic acid, m.p. 80—81° (lit.,[23] 81—82°).

5,6-Dioxopentadecanonitrile.—The acetoxy-nitrile (4·3 g.) in methanol (40 c.c.) was treated with boron trifluoride–diethyl ether (2 c.c.) at room temperature for 2 days. Addition of water and isolation with ethyl acetate gave an oil which was dissolved in acetic acid (50 c.c.) and heated under reflux for 1 hr. with bismuth oxide (10 g.). Isolation as before yielded *5,6-dioxopentadecanonitrile* (1·65 g.), b.p. 155—160°/0·4 mm., forming yellow plates, m.p. 56—57° (from methanol at −10°) (Found: C, 72·0; H, 10·0; N, 5·4. $C_{15}H_{25}NO_2$ requires C, 71·7; H, 10·0; N, 5·6%).

Reduction of Keto-nitriles.—5-Oxopentadecanonitrile (5 g.) in ethanol (150 c.c.) was hydrogenated over Raney nickel (W7; freshly prepared [24]). Filtration and distillation gave *2-decylpiperidine* (3·8 g.), b.p. 102—105°/0·5 mm. (Found: N, 6·7. $C_{15}H_{31}N$ requires N, 6·2%); the *hydrochloride* had m.p. 153—154° (from ethanol–6N-hydrochloric acid) (Found: C, 68·3; H, 11·9; Cl, 13·3. $C_{15}H_{32}ClN$ requires C, 68·8; H, 12·3; Cl, 13·5%). 6-Acetoxy-5-oxo-pentadecanonitrile and 5,6-dioxopentadecanonitrile also gave this same product; hydrochloride, m.p. and mixed m.p. 153—154°. In one experiment a small amount of another product, m.p. 158—160° (from ethanol–6N-hydrochloric acid), was obtained from the dioxo-nitrile. This appeared to be *2-(1-oxodecyl)piperidine hydrochloride* (Found C, 65·4; H, 10·8; Cl, 13·0. $C_{15}H_{30}ClNO$ requires C, 65·3; H, 11·0; Cl, 12·8%), $\nu_{max.}$ 1720s cm.$^{-1}$ (C=O). The m.p. was depressed by admixture with 2-decylpiperidine hydrochloride.

Quinoxalines.—Docosane-11,12-dione (1·75 g.) and *o*-phenylenediamine (0·65 g.) in ethanol (10 c.c.) were heated under reflux for 3 hr. and cooled to 0°. Filtration and recrystallisations from methanol at 0° gave *2,3-didecylquinoxaline*, m.p. 25—26° (Found: C, 82·5; H, 11·2; N, 6·5. $C_{28}H_{46}N_2$ requires C, 81·9; H, 11·3; N, 6·8%). Similarly prepared were *2,3-bistridecylquinoxaline*, m.p. 36—37·5° (from methanol) (Found: C, 82·3; H, 11·7; N, 5·7. $C_{34}H_{58}N_2$ requires C, 82·5; H, 11·8; N, 5·7%) and *2-methyl-3-tridecylquinoxaline*, m.p. 59—60° [from light petroleum (b.p. 40—60°)] (Found: C, 80·4; H, 10·4; N, 8·5. $C_{22}H_{34}N_2$ requires C, 80·9; H, 10·5; N, 8·6%).

Alkylation of 2,3-Dimethylquinoxaline.—(a) *Monoalkylation*. 2,3-Dimethylquinoxaline (5·3 g.) was added to sodamide [from sodium (0·8 g.)] in liquid ammona (150 c.c.). After 1 hr., dodecyl bromide (10 g.) in ether (10 c.c.) was added and the mixture was left overnight to evaporate. Addition of water, isolation with ethyl acetate, and chromatography on alumina in light petroleum (b.p. 40—60°) gave 2-methyl-3-tridecylquinoxaline (5·5 g.), m.p. 59—60° (from methanol) (Found: C, 80·4; H, 10·4; N, 8·5. Calc. for $C_{22}H_{34}N_2$: C, 80·9; H, 10·5; N, 8·6%), identical with the material described above.

(b) *Dialkylation*. Sodium (1·6 g.) was converted into sodamide in liquid ammonia (200 c.c.), and 2,3-dimethylquinoxaline (4·6 g.) was added. After 1 hr., dodecyl bromide (20 g.) was added and the solvent was allowed to evaporate slowly. Addition of water, isolation with ethyl acetate, and trituration with methanol–ethyl acetate gave product (1·5 g.), m.p. 27—30°. Repeated recrystallisations from light petroleum (b.p. 40—60°) at −10° gave 2,3-bistridecylquinoxaline, m.p. and mixed m.p. 33—35°.

Quinoxaline N-Oxides.—2,3-Didecylquinoxaline (1·5 g.), acetic acid (15 c.c.), and hydrogen peroxide (4 c.c.; 30%) were warmed at 50—60° for 18 hr. Neutralisation with 5N-sodium hydroxide, repeated extractions with chloroform, and evaporation, gave a gum. Trituration with ethanol and recrystallisations from ethanol gave *2,3-didecylquinoxaline 1,4-dioxide* as yellow needles, m.p. 45—46° (Found: C, 76·0; H, 10·0. $C_{28}H_{46}N_2O_2$ requires C, 76·0; H, 10·5%). Similarly *2,3-bistridecylquinoxaline 1,4-dioxide* had m.p. 59—61° (from ethanol) (Found: C, 77·3; H, 11·1; N, 5·3. $C_{34}H_{58}N_2O_2$ requires C, 77·5; H, 11·1; N, 5·3%).

2-Methyl-3-tridecylquinoxaline (10 g.) in chloroform (300 c.c.) at 0° was treated with 0·35M-perbenzoic acid in chloroform (300 c.c.) and the mixture was kept at 0° overnight. The solution was washed with potassium carbonate solution and water, dried (Na_2SO_4), and evaporated. Fractional crystallisation of the residue from light petroleum (b.p. 60—80°) gave *2-methyl-3-tridecylquinoxal-*

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ine 1,4-*dioxide* (5·9 g.), m.p. 104—107° (from methanol) (Found: C, 74·5; H, 9·7; N, 7·9. $C_{22}H_{34}N_2O_2$ requires C, 73·7; H, 9·6; N, 7·8%). The more soluble component, presumably 2-*methyl*-3-*tridecylquinoxaline* 1-*oxide* (1·5 g.), formed needles from light petroleum and had m.p. 83—85° (Found: C, 77·0; H, 10·1; N, 8·2. $C_{22}H_{34}N_2O$ requires C, 77·1; H, 10·0; N, 8·2%).

Alkylation of 2-Methoxy-3-methylquinoxaline.—The quinoxaline [25] (5·5 g.) was added to sodamide [from sodium (0·8 g.)] in liquid ammonia (200 c.c.). The deep red-green solution was stirred for 1 hr., treated with dodecyl bromide (10 g.), and allowed to evaporate slowly. Addition of water and isolation with ethyl acetate gave 2-*methoxy*-3-*tridecylquinoxaline* (5·1 g.), m.p. 58—59° (from methanol–ethyl acetate) (Found: C, 76·6; H, 9·8; N, 8·4. $C_{22}H_{34}N_2O$ requires C, 77·1; H, 10·0; N, 8·2%). This (1 g.), acetic acid (25 c.c.) and hydrobromic acid (25 c.c.; 48% were heated under reflux for 3 hr. Evaporation left a gum which was heated at 70° with sodium carbonate solution; the cooled solution was filtered and the solid was recrystallised from methanol–ethyl acetate to give 2-*hydroxy*-3-*tridecylquinoxaline* (0·65 g.), m.p. 117—118° (lit.,[26] 123°) (Found: C, 76·6; H, 9·5; N, 8·6. Calc. for $C_{21}H_{32}N_2O$: C, 76·8; H, 9·8; N, 8·6%).

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