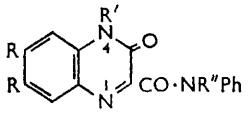
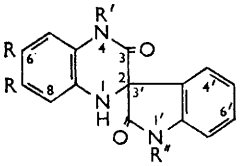
769. *Quinoxaline Derivatives. Part I. Intramolecular Rearrangement of Certain Quinoxalinecarboxyanilides to Spiroindoles.*

By Yusuf Ahmad, M. S. Habib, M. Iqbal, and M. Ikram Qureshi.

The rapid isomerisation of anilides (Ia—c) in concentrated sulphuric acid at 0° to the corresponding spiroindoles (IIa—c) has been attributed [1] to the presence of a strong electrophilic centre at position 2. However, the derivatives (Id—j) of 3,4-dihydro-6,7-dimethoxy-(or 6,7-dimethyl-)-2-(*N*-phenylcarbamoyl)-3-oxoquinoxaline, when treated with cold concentrated sulphuric acid at room temperature, were recovered unchanged. This was expected as the presence of the electron-releasing substituents would make position 2 less electrophilic. The intramolecular rearrangement of the anilides (Ie—i and III; R = Me) to the corresponding spiroindoles (IIe—i and IV; R = Me) was achieved by boiling with ethanolic hydrogen chloride. The use of sulphuric acid at a higher temperature was avoided as it would have resulted in the formation of sulphonated spiroindoles.[1] The mechanism of the formation of spiroindoles and the proof of their structure have been described.[1]

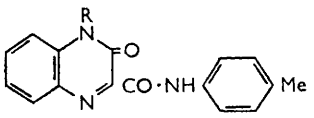


(I)

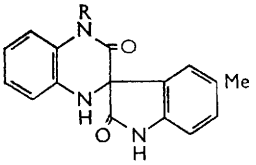


(II)

(a) R = R″ = H; R′ = Me
(b) R = R′ = H; R″ = Me
(c) R = H; R′ = R″ = Me
(d) R = MeO; R′ = Me; R″ = H
(e) R = MeO; R′ = R″ = H
(f) R = MeO; R′ = H; R″ = Me
(g) R = MeO; R′ = R″ = Me
(h) R = R′ = R″ = Me
(i) R = R″ = Me; R′ = H
(j) R = Me; R′ = R″ = H



(III)



(IV)

Weinberger and Day's method [2] for the preparation of 1,2-dimethoxy-4,5-dinitrobenzene gave a mixture of dinitro- and trinitro-compounds. An almost quantitative yield of the dinitro-compound was obtained by a modification of their method. Ethyl 3,4-dihydro-6,7-dimethoxy-3-oxoquinoxaline-2-carboxylate and ethyl 3,4-dihydro-6,7-dimethyl-3-oxoquinoxaline-2-carboxylate, obtained by the condensation of ethyl mesoxalate with 4,5-dimethoxy- and 4,5-dimethyl-*o*-phenylenediamine, respectively, were converted to the anilides (Id-j) by standard methods.[3] The rearrangement of the *N*-oxides of these anilides is under investigation.

Experimental.—Infrared spectra were measured on mulls in Nujol. Microanalyses were carried out by the Microanalytical Section at these laboratories.

1,2-*Dimethoxy*-4,5-*dinitrobenzene*. (Cf. Weinberger and Day.[2]) To 1,2-dimethoxy-4-nitrobenzene (18·3 g., 0·1 mole) in concentrated sulphuric acid (120 ml.) was added slowly with stirring sodium nitrate (9·4 g., 0·11 mole) in concentrated sulphuric acid below 0°. The mixture was stirred for 15 min. and allowed to attain room temperature. After another 15 min. the mixture was poured on ice. The precipitate thus obtained crystallised from ethyl acetate as

[1] Habib and Rees, *J.*, 1962, 123.
[2] Weinberger and Day, *J. Org. Chem.*, 1959, **24**, 1451.
[3] Habib and Rees, *J.*, 1960, 3371.

yellow needles, m. p. 131—132°. Ehrlich and Bogert [4] record m. p. 130—131°. 1,2-Dimethoxy-4,5-dinitrobenzene on hydrogenation over palladised charcoal in ethanol gave 4,5-dimethoxy-*o*-phenylenediamine,[2] m. p. 131°.

3,4-*Dihydro*-6,7-*dimethoxy*-3-*oxoquinoxaline*-2-*carboxylic acid*. 1,2-Dimethoxy-4,5-diaminobenzene (15 g.) in ethanol (200 ml.) and ethyl mesoxalate [5] (17 g.) were heated under reflux for 1 hr. On cooling, the solid which separated was crystallised from ethanol (charcoal) giving yellow needles of *ethyl* 3,4-*dihydro*-6,7-*dimethoxy*-3-*oxoquinoxaline*-2-*carboxylate* (9 g., 36%), m. p. 251—252° (Found: N, 9·9. $C_{13}H_{14}N_2O_5$ requires N, 10·1%). This ester (2 g.) was hydrolysed by hot 3N-sodium hydroxide (20 ml.) for 2 hr. The *acid* was obtained in good yield as yellow micro-needles, m. p. 291—293° (decomp.) (Found: N, 10·4. $C_{11}H_{10}N_2O_5,H_2O$ requires N, 10·45%).

3,4-*Dihydro*-6,7-*dimethoxy*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxylic acid*. Ethyl 3,4-dihydro-6,7-dimethoxy-3-oxoquinoxaline-2-carboxylate (0·3 g.) was methylated with dimethyl sulphate (0·1 ml.) and potassium carbonate (0·5 g.) in hot acetone (25 ml.) for 3 hr. The product crystallised from ethanol–water as yellow needles of *ethyl* 3,4-*dihydro*-6,7-*dimethoxy*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxylate* (0·1 g., 31%), m. p. 141—143° (Found: N, 9·4. $C_{14}H_{16}N_2O_5$ requires N, 9·6%). Hydrolysis in the usual way gave, in quantitative yield, the *acid*, m. p. 233—235° (decomp.) (Found: N, 10·5. $C_{12}H_{12}N_2O_5$ requires N, 10·6%).

3,4-*Dihydro*-6,7-*dimethoxy*-3-*oxoquinoxaline*-2-*carboxyamide*. Ethyl 3,4-dihydro-6,7-dimethoxy-3-oxoquinoxaline-2-carboxylate (3 g.) and concentrated ammonium hydroxide (30 ml.) were heated on the water-bath for 1 hr. The *carboxyamide* (quantitative yield) crystallised from dimethylformamide as yellow microcrystals, m. p. 283° (decomp.) (Found: N, 16·5. $C_{11}H_{11}N_3O_4$ requires N, 16·8%).

3,4-*Dihydro*-6,7-*dimethoxy*-4-*methyl*-3-*oxoquinoxaline*-2-*carboxyamide*. Ethyl 3,4-dihydro-6,7-dimethoxy-4-methyl-3-oxoquinoxaline-2-carboxylate, by the above method, gave the *carboxyamide* in good yield, as yellow needles (from dimethylformamide–ethanol) m. p. 304—305° (decomp.) (Found: N, 15·45. $C_{12}H_{13}N_3O_4$ requires N, 15·9%).

3,4-*Dihydro*-6,7-*dimethoxy*-2-N-*phenylcarbamoyl*-3-*oxoquinoxaline* (Ie). 3,4-Dihydro-6,7-dimethoxy-3-oxoquinoxaline-2-carboxyamide (0·9 g.) and aniline (10 ml.) were heated under reflux for 7 hr., and then cooled. The *anilide* crystallised from dimethylformamide as yellow microcrystals (0·6 g., 52%), m. p. 288—289° (decomp.) (Found: N, 12·7. $C_{17}H_{15}N_3O_4$ requires N, 12·9%); $\nu_{max.}$ 1710 cm.$^{-1}$ (amide C=O).

3,4-*Dihydro*-6,7-*dimethoxy*-4-*methyl*-2-N-*phenylcarbamoyl*-3-*oxoquinoxaline* (Id). 3,4-Dihydro-6,7-dimethoxy-2-*N*-phenylcarbamoyl-3-oxoquinoxaline (0·2 g.) was methylated with dimethyl sulphate (0·1 ml.) and potassium carbonate (0·5 g.) in hot acetone (20 ml.) for 3 hr. The yellow *anilide* crystallised from dimethylformamide as needles (0·1 g., 48%), m. p. 326° (decomp.) (Found: N, 12·2. $C_{18}H_{17}N_3O_4$ requires N, 12·4%); $\nu_{max.}$ 1700 cm.$^{-1}$ (amide C=O).

3,4-*Dihydro*-6,7-*dimethoxy*-2-(N-*methyl*-N-*phenylcarbamoyl*)-3-*oxoquinoxaline* (If). A mixture of phosphorus tri-(*N*-methylanilide) [6] [from phosphorus trichloride (1 ml.) and methylaniline (6·6 ml.)] and 3,4-dihydro-6,7-dimethoxy-3-oxoquinoxaline-2-carboxylic acid (3·8 g.) in dry toluene (30 ml.) was heated under reflux for 1 hr. The toluene layer was evaporated to dryness under reduced pressure; the solid crystallised from ethanol–benzene as light yellow cubes of the N-*methylanilide* (1·3 g., 26%), m. p. 238—239° (Found: N, 12·1. $C_{18}H_{17}N_3O_4$ requires N, 12·4%); $\nu_{max.}$ 1710 cm.$^{-1}$ (amide C=O).

3,4-*Dihydro*-6,7-*dimethoxy*-4-*methyl*-2-(N-*methyl*-N-*phenylcarbamoyl*)-3-*oxoquinoxaline* (Ig). The methylation of 3,4-dihydro-6,7-dimethoxy-2-(*N*-methyl-*N*-phenylcarbamoyl)-3-oxoquinoxaline (0·4 g.) with dimethyl sulphate (0·1 ml.) and potassium carbonate (0·5 g.) in hot acetone (30 ml.) for 3 hr. yielded the N-*methylanilide* (from ethanol–water) as white needles (0·33 g., 78%), m. p. 181—182° (Found: N, 11·55. $C_{19}H_{19}N_3O_4$ requires N, 11·9%); $\nu_{max.}$ 1675 cm.$^{-1}$ (amide C=O).

3,4-*Dihydro*-6,7-*dimethyl*-3-*oxoquinoxaline*-2-*carboxylic acid*. 4,5-Dimethyl-*o*-phenylenediamine [7] (3 g.), ethyl mesoxalate [5] (5 g.) and ethanol (50 ml.) were heated under reflux for 1 hr. The solution (charcoal) was filtered and reduced to a volume of 10 ml. Dilution with water gave an orange-coloured solid which crystallised from ethanol–water as micro-needles of

[4] Ehrlich and Bogert, *J. Org. Chem.*, 1945, **12**, 522.
[5] Astin, Newman, and Riley, *J.*, 1933, 393.
[6] Abramovitch, Hey, and Long, *J.*, 1957, 1787.
[7] Tishler, Wellman, and Ladenburg, *J. Amer. Chem. Soc.*, 1945, **67**, 2165.

ethyl 3,4-*dihydro*-6,7-*dimethyl*-3-*oxoquinoxaline*-2-*carboxylate* (2 g., 37%), m. p. 198—199° (Found: N, 11·3. $C_{13}H_{14}N_2O_3$ requires N, 11·4%). This ester was hydrolysed by hot 3N-sodium hydroxide for 1 hr. The *acid* (nearly quantitative yield) formed yellow needles, m. p. 309—310° (decomp.) (Found: N, 12·8. $C_{11}H_{10}N_2O_3$ requires N, 12·85%).

3,4-*Dihydro*-4,6,7-*trimethyl*-3-*oxoquinoxaline*-2-*carboxylic acid*. Ethyl 3,4-dihydro-6,7-dimethyl-3-oxoquinoxaline-2-carboxylate (0·15 g.) dimethyl sulphate (0·5 ml.), potassium carbonate (0·5 g.), and acetone (15 ml.) were heated on the water-bath for 5 hr. From the filtered solution, acetone was removed; the residue crystallised from benzene–light petroleum (b. p. 60—80°) as yellow needles of *ethyl* 3,4-*dihydro*-4,6,7-*trimethyl*-3-*oxoquinoxaline*-2-*carboxylate* (0·1 g., 60%), m. p. 124—126° (Found: N, 10·9. $C_{14}H_{16}N_2O_3$ requires N, 10·8%). The above ester on hydrolysis with hot 3N-sodium hydroxide for 1 hr. gave a good yield of the *acid* [purified by dissolution in aqueous sodium hydroxide (charcoal), and precipitation with dilute hydrochloric acid], m. p. 204—205° (decomp.) (Found: N, 11·8. $C_{12}H_{12}N_2O_3$ requires N, 12·1%).

3,4-*Dihydro*-6,7-*dimethyl*-2-N-*phenylcarbamoyl*-3-*oxoquinoxaline* (Ij). 3,4-Dihydro-6,7-dimethyl-3-oxoquinoxaline-2-carboxylic acid (2 g.), thionyl chloride (20 ml.), and benzene (20 ml.) were heated under reflux for 1 hr. The solid obtained after the removal of thionyl chloride and benzene under reduced pressure, was suspended in benzene and a solution of aniline (6 ml.) in benzene (15 ml.) was added dropwise. The mixture was shaken for 10 min. and washed with 2N-hydrochloric acid. The *anilide* crystallised from ethanol–water as yellow flakes (2·7 g., 100%), m. p. 330—331°, $\nu_{max.}$ 1700 cm.$^{-1}$ (amide C=O) (Found: N, 14·1. $C_{17}H_{15}N_3O_2$ requires N, 14·3%). Attempts to methylate this anilide were unsuccessful.

3,4-*Dihydro*-6,7-*dimethyl*-2-(N-*methyl*-N-*phenylcarbamoyl*)-3-*oxoquinoxaline* (Ii). 3,4-Dihydro-6,7-dimethyl-3-oxoquinoxaline-2-carboxylic acid (2 g.) was converted into the acid chloride and a solution of *N*-methylaniline (6 ml.) in benzene (15 ml.) was added. The mixture, treated as above, gave a buff-coloured solid which crystallised from ethanol–water as microcrystals of the N-*methylanilide* (1·8 g., 70%), m. p. 293—294° (decomp.), $\nu_{max.}$ 1690 cm.$^{-1}$ (Found: N, 13·4. $C_{18}H_{17}N_3O_2$ requires N, 13·7%).

3,4-*Dihydro*-4,6,7-*trimethyl*-2-(N-*methyl*-N-*phenylcarbamoyl*)-3-*oxoquinoxaline* (Ih). 3,4-Dihydro-6,7-dimethyl-2-(*N*-methyl-*N*-phenylcarbamoyl)-3-oxoquinoxaline (0·4 g.) was methylated with dimethyl sulphate (0·1 ml.) and potassium carbonate (0·5 g.) in boiling acetone (30 ml.) for 3 hr. The *tetramethylanilide* (0·2 g., 48%) crystallised from ethanol–water as light yellow needles, m. p. 243—244°, $\nu_{max.}$ 1675 cm.$^{-1}$ (Found: N, 13·4. $C_{19}H_{19}N_3O_2$ requires N, 13·1%).

3,4-*Dihydro*-2-(N-p-*tolylcarbamoyl*)-3-*oxoquinoxaline* (III; R = H). To the acid chloride,[3] from 3-hydroxyquinoxaline-2-carboxylic acid (4·5 g.), thionyl chloride (15 ml.), and benzene (20 ml.), was added dropwise a solution of *p*-toluidine (6·5 g.) in benzene (20 ml.). The mixture was shaken for 10 min. and washed with 2N-hydrochloric acid. The solid which separated crystallised from dimethylformamide as yellow leaflets of the *toluidide* (3 g., 48%), m. p. 337—339°, $\nu_{max.}$ 1700 cm.$^{-1}$ (Found: N, 14·55. $C_{16}H_{13}N_3O_2,0{\cdot}5H_2O$ requires N, 14·6%).

3,4-*Dihydro*-4-*methyl*-2-(N-p-*tolylcarbamoyl*)-3-*oxoquinoxaline* (III; R = Me). 3,4-Dihydro-2-(*N*-*p*-tolylcarbamoyl)-3-oxoquinoxaline (2 g.) was methylated with dimethyl sulphate (0·5 ml.) and potassium carbonate (2 g.) in boiling acetone (50 ml.) for 3 hr. The 4-*methyl* derivative (0·8 g., 38%) crystallised from ethanol–water as yellow needles, m. p. 184—185°, $\nu_{max.}$ 1710 cm.$^{-1}$ (amide C=O) (Found: N, 14·4. $C_{17}H_{15}N_3O_2$ requires N, 14·3%).

Spiroindoles. These were prepared in 40—60% yield by boiling the anilides (Ie—i and III; R = Me in ethanolic hydrogen chloride for 2—3 hr., and are described in the Table.

1,2,2′,3,3′,4-Hexahydro-2′,3-dioxoquinoxaline-2-spiro-3′-indoles.

Spiroindole	M. p.	Formula	N (%) Found	N (%) Required
6,7-*Dimethoxy*- (IIe)	260° (decomp.)	$C_{17}H_{15}N_3O_4,1{\cdot}5H_2O$	11·4 (C, 58·2; H, 5·25)	11·9 (C, 57·95; H, 5·1)
6,7-*Dimethoxy*-1′-*methyl*- (IIf)	228	$C_{18}H_{17}N_3O_4$	12·7	12·4
6,7-*Dimethoxy*-4,1′-*dimethyl*- (IIg)	301—302 (decomp.)	$C_{19}H_{19}N_3O_4$	11·6	11·9
6,7,1′-*Trimethyl*- (IIi)	216—218	$C_{18}H_{17}N_3O_2$	13·6	13·7
4,6,7,1′-*Tetramethyl*- (IIh)	244—245	$C_{19}H_{19}N_3O_2$	13·2	13·1
4,5′-*Dimethyl*- (IV; R = Me)	170 (decomp.)	$C_{17}H_{15}N_3O_2$	14·1	14·3

The amide C = O absorption shifts to a higher frequency (1750 cm.$^{-1}$) and in the case of (IIh) to 1725 cm.$^{-1}$. An N–H absorption band was shown by (IIg and h) at 3400 and 3425 cm.$^{-1}$, respectively. Compounds (IIe—g) were crystallised from ethanol; (IIh and i) from ethanol–water and (IV; R = Me) from benzene–light petroleum. All the compounds were pale yellow except (IIg and IV; R = Me) which were colourless and orange, respectively.

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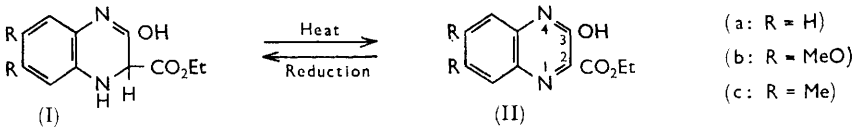
770. *Quinoxaline Derivatives. Part II.*[1] *A Direct Synthesis of 1,2-Dihydroquinoxalines.*

By YUSUF AHMAD, M. S. HABIB, M. IQBAL, and M. IKRAM QURESHI.

No direct proof has previously [2] been put forward that reduction of derivatives of 3-hydroxyquinoxaline-2-carboxylic acid causes saturation of the 1,2-double bond. An unambiguous synthesis of 1,2-dihydro-derivatives of a number of 3-hydroxyquinoxaline-2-carboxylic acids and their esters, is now reported. Condensation of *o*-phenylenediamine and its 4,5-



(I) (II)

dimethoxy- and 4,5-dimethyl-derivatives with ethyl bromomalonate gave 1,2-dihydroquinoxalines (Ia—c). Hydrolysis of these esters with hot aqueous alkali gave the corresponding acids (Ia—c; H for Et). These 1,2-dihydro-compounds were also obtained by reduction of the parent quinoxaline esters (IIa—c) and acids (IIa—c; H for Et) with sodium dithionite in 50% aqueous ethanol. Reversal of this reduction occurred readily when the compounds were heated at temperatures near their melting points.

Experimental.—Melting points varied with the rate of heating; they were therefore determined by inserting the tube near the melting point. Microanalyses were done by our Microanalytical Section.

General procedure for condensation. The diamine (0·5 g.) and ethyl bromomalonate (1 ml.) in ethanol (25 ml.) was heated under reflux for 1 hr. The volume of the mixture was reduced to 10 ml. and water was added. The solid which separated on cooling was crystallised from ethanol. The yields were 50—80%.

General procedure for reduction. (Cf. Habib and Rees.[2]) The compound (0·1 g.) and sodium dithionite (0·2 g.) in 50% aqueous ethanol were heated under reflux for 1 hr. The ethanol was removed whereupon the solid separated on cooling. With the dihydro-acids, the pH of the solution was adjusted to 2·5—3. The yields were 70—90%.

Ethyl 1,2-dihydro-3-hydroxyquinoxaline-2-carboxylate (Ia). *o*-Phenylenediamine gave the *1,2-dihydro-ester*, m. p. 145—146° (Found: N, 12·75. $C_{11}H_{12}N_2O_3$ requires N, 12·7%); the mixed m. p. with a sample (m. p. 145°) obtained by the reduction of ethyl 3-hydroxyquinoxaline-2-carboxylate [3] was the same.

1,2-Dihydro-3-hydroxyquinoxaline-2-carboxylic acid (Ia; H for Et). The hydrolysis of the 1,2-dihydro-ester (Ia) with hot 3N-sodium hydroxide for 0·5 hr. gave the 1,2-dihydro-acid, m. p. 151° (decomp.), undepressed by admixture with a sample [2] obtained by the reduction of 3-hydroxyquinoxaline-2-carboxylic acid. The dihydro-acid when heated at 150° gave 3-hydroxyquinoxaline-2-carboxylic acid, m. p. 260—264° (decomp.) (identical with an authentic sample [3]) and when heated at 250—260° gave 2-hydroxyquinoxaline, m. p. 276°, for which Gowenlock *et al.*[3] record m. p. 271°.

[1] Part I, Ahmad, Habib, Iqbal, and Qureshi, preceding Paper.
[2] Habib and Rees, *J.*, 1960, 3386.
[3] Gowenlock, Newbold, and Spring, *J.*, 1945, 622.

Ethyl 1,2-*dihydro*-3-*hydroxy*-6,7-*dimethoxyquinoxaline*-2-*carboxylate* (Ib). 4,5-Dimethoxy-*o*-phenylenediamine [4] gave the 1,2-*dihydro*-6,7-*dimethoxy*-*ester*, m. p. 245—246° (Found: N, 9·9. $C_{13}H_{16}N_2O_5$ requires N, 10·0%); the m. p. of a mixture with a sample (m. p. 245°) obtained by the reduction of ethyl 3-hydroxy-6,7-dimethoxyquinoxaline-2-carboxylate [1] was the same.

1,2-*Dihydro*-3-*hydroxy*-6,7-*dimethoxyquinoxaline*-2-*carboxylic acid* (Ib; H for Et). Hydrolysis of the ester (Ib) with 3N-sodium hydroxide gave the corresponding *acid*, m. p. 255—256° (decomp.) (Found: N, 11·4. $C_{11}H_{12}N_2O_5$ requires N, 11·1%); the m. p. was not depressed by admixture with a sample (m. p. 256°) obtained by the reduction of 3-hydroxy-6,7-dimethoxyquinoxaline-2-carboxylic acid.[1]

Ethyl 1,2-*dihydro*-3-*hydroxy*-6,7-*dimethylquinoxaline*-2-*carboxylate* (Ic). 4,5-Dimethyl-*o*-phenylenediamine [5] gave the 1,2-*dihydro*-6,7-*dimethyl*-*ester*, m. p. 199—200° (Found: N, 10·8. $C_{13}H_{16}N_2O_3$, $0{\cdot}5H_2O$ requires N, 10·8%); the mixed m. p. with a sample (m. p. 198—199°) obtained by the reduction of ethyl 3-hydroxy-6,7-dimethylquinoxaline-2-carboxylate [1] was undepressed, but was depressed below 172° by admixture with the unreduced ester [1] (IIc; m. p. 198—200°).

1,2-*Dihydro*-3-*hydroxy*-6,7-*dimethylquinoxaline*-2-*carboxylic acid* (Ic; H for Et). Hydrolysis of the ester (Ic) with 3N-sodium hydroxide gave the corresponding *acid*, m. p. 238—240° (decomp.) (Found: N, 12·7. $C_{11}H_{12}N_2O_3$ requires N, 12·7%); the m. p. was undepressed by admixture with a sample (m. p. 238°) obtained by the reduction of 3-hydroxy-6,7-dimethyl quinoxaline-2-carboxylic acid.[1] This dihydro-acid was reconverted into the unreduced compound (IIc; H for Et) in air at 240° for 5 min.

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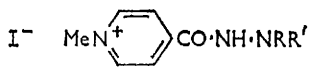
[4] Weinberger and Day, *J. Org. Chem.*, 1959, **24**, 1451.
[5] Tishler, Wellman, and Ladenburg, *J. Amer. Chem. Soc.*, 1945, **67**, 2165.

771. *Methylation and Protonation of Isonicotinoylhydrazine.*

By J. CYMERMAN CRAIG, J. L. GARNETT, and (MRS.) DIANA M. TEMPLE.

ISONICOTINOYLHYDRAZINE METHIODIDE has been prepared from hydrazine and an alkyl *iso*nicotinate methiodide.[1] Reaction of methyl iodide with *iso*nicotinoylhydrazine itself [2] afforded a substance, m. p. 248°, claimed to be the methiodide, but no analytical data was given. Repetition of the latter reaction yielded a product, m. p. 248—253° (undoubtedly identical with the material of reported [2] m. p. 248°), identified as isonicotinoylhydrazine monohydriodide by comparison with an authentic sample. About 8—10% of the methiodide was also obtained. The same monohydriodide was produced by reaction of isonicotinoylhydrazine with ethyl iodide (50% yield), with benzyl iodide (38% yield), while benzyl bromide afforded the corresponding hydrobromide salt.

The alkyl iodide was not the source of the proton, since use of a five-fold excess of dry methyl iodide did not increase the yield of the hydriodide above 50%; nor could the presence of ethylene or stilbene (from the dimerization of methylene or benzylidene radicals, respectively) be demonstrated when methyl or benzyl iodide were used. The reaction must therefore be one of *N*-methylation followed by proton-exchange with unreacted isonicotinoylhydrazine. This was confirmed by the use of tritiated methyl iodide, which made possible the identification of several methylated derivatives. In addition to isonicotinoylhydrazine hydriodide, showing insignificant activity, the reaction yielded *N*-isonicotinoyl-*N'*-methylhydrazine methiodide (I; R = H, R' = Me) and *N'*-isonicotinoyl-*NN*-dimethylhydrazine methiodide (I; R = R' = Me). Methiodides could be readily distinguished from the



(I)

[1] McMillan, Leonard, Meltzer, and King, *J. Amer. Pharmaceut. Assoc.* (*Sci. Edn.*), 1953, **42**, 457; Yale, Losee, Martins, Holsing, Perry, and Bernstein, *J. Amer. Chem. Soc.*, 1953, **75**, 1933; Beyerman, Bontekoe, van der Burg, and Veer, *Rec. Trav. chim.*, 1954, **73**, 109.
[2] Charronat and Boeme, *Compt. rend.*, 1953, **236**, 2251.

isomeric hydriodides since only the latter liberated carbon dioxide from aqueous bicarbonate. *N*-Methylation of *N*-isonicotinoyl-*N'*-methylhydrazine with methyl iodide has been reported [3] to give *N'*-isonicotinoyl-*NN*-dimethylhydrazine, but no analogous proton-exchange was observed since the reaction [3] was carried out in the presence of base.

The ionization constants of isonicotinoylhydrazine have been measured both potentiometrically [4,5] and spectroscopically [6] and the results show that $pK_{a1} = 1{\cdot}8 \pm 0{\cdot}3$, $pK_{a2} = 3{\cdot}65 \pm 0{\cdot}15$, and $pK_{a3} = 11{\cdot}0 \pm 0{\cdot}3$. One interpretation [4,5] of these figures is that the more weakly basic nitrogen is that of the primary amino-group in the hydrazine moiety, *cf.* glycine hydrazide (pK_a 2·4) and benzhydrazide [5] (pK_a 3·03), and attributes the higher value to the pyridine nitrogen, *cf.* isonicotinamide [7] (pK_a 3·61). Another interpretation [6,8] of the pK_a data points out that the ultraviolet absorption intensity of both isonicotinoylhydrazine and benzhydrazide reaches a maximum at pH 2·3 (corresponding to substantial ionization of the more basic nitrogen in the former) and claims that in both cases the terminal amino group is protonated.

The Table shows that in isonicotinoylhydrazine monohydriodide the proton is indeed attached to the hydrazine amino group in agreement with the assignment [6] of the higher pK_a to this nitrogen atom. The shift of $\lambda_{max.}$ from 263 mμ (pyridine nitrogen unprotonated) to 268—271 mμ (positive charge on ring nitrogen) supports this interpretation. Similar

Ultraviolet spectra.

Compound	Solvent	$\lambda_{max.}$ (mμ)	log $\varepsilon_{max.}$
Isonicotinoylhydrazine	H_2O	263	3·69
	95% alcohol	263	3·68
Isonicotinoylhydrazine methiodide	H_2O	271	3·81
Isonicotinoylhydrazine monohydriodide	H_2O	263	3·68
	95% alcohol	263	3·76
Isonicotinoylhydrazine sulphate [6]	36-*N*-H_2SO_4	269	3·68
Isonicotinoylhydrazine dihydrochloride	N-HCl	268	3·71
N'-isonicotinoyl-*NN*-dimethylhydrazine methiodide	H_2O	270	3·77

bathochromic shifts are shown from the unprotonated (266·5 mμ) to the protonated (272·5 mμ) forms of ethyl isonicotinate and of isonicotinic acid,[6] and between 2-aminoacridine (268 mμ) and its methochloride (276 mμ).[9] The position of the absorption maximum of 2-aminoacridine hydrochloride (276 mμ) was used to show [9] that monoprotonation of this base occurs at the ring nitrogen.

After the above work was completed, additional evidence for the position of the proton in isonicotinoylhydrazine monohydriodide was afforded by the nuclear magnetic resonance spectrum. Measured as a 6% (w/v) solution in dimethyl sulphoxide, the hydrogens of the pyridine nucleus appeared as two doublets with chemical shifts τ 1·03 (α-protons) and τ 2·07 (β-protons) ($J = 6$ c./sec.). The corresponding values for the chemical shifts in the parent base were τ 1·21 and 2·20, respectively ($J = 6$ c./sec.). This is in good agreement with expected values from the figures [10] for pyridine (τ 1·40 and 3·00) and 4-vinylpyridine (τ 1·48 and 2·78). If protonation of the ring nitrogen had occurred, the chemical shifts for the α and β positions would have been at approximately τ 0·21 and 1·20, respectively, and a third peak due to aromatic NH^+ would have appeared.

Treatment of benzhydrazide with methyl iodide gave, apart from *NNN*-trimethylbenzhydrazinium iodide, some *NN'*-dibenzoylhydrazine probably formed by nucleophilic attack of benzhydrazide on benzhydrazide hydriodide, with displacement of a hydrazine salt.

[3] Fox, Gibas, and Motchane, *J. Org. Chem.*, 1956, **21**, 349.
[4] Nagano, Tsukahara, Kinoshita, and Tamura, *Chem. Pharm. Bull.*, 1963, **11**, 797.
[5] Albert, *Experientia*, 1953, **9**, 370; *Nature*, 1956, **177**, 525.
[6] Cingolani and Gaudiano, *Rend. Ist. Super. Sanita*, 1954, **17**, 601.
[7] Jaffe and Doak, *J. Amer. Chem. Soc.*, 1955, **77**, 4441.
[8] Kruger-Thiemer, *Jahresber. Tuberkulose-Forschungsinstitut. Borstel*, 1954—1955, p. 191.
[9] Craig and Short, *J.*, 1945, 419; Turnbull, *J.*, 1945, 441.
[10] Bhacca, Johnson, and Shoolery, "NMR Spectra Catalog," Varian Associates, Palo Alto, 1962.

Experimental.—Melting points were determined using a Kofler hot-stage apparatus and are corrected. Ultraviolet and infrared spectra were measured on a Hilger "Uvispek" model 6 and on Perkin-Elmer "Infracord" model 137 or model 21-B spectrophotometers, respectively. Nuclear magnetic resonance spectra were obtained on a Varian 40 mc. instrument. Tritium analyses were performed according to the method of Garnett, Hannan, and Law [11] using the vibrating reed ion chamber technique.

Reaction of Isonicotinoylhydrazine with Methyl Iodide.—(*A*) A solution of isonicotinoylhydrazine (2·7 g., 0·02 mole) and methyl iodide (1·5 ml., 0·024 mole) in methanol (50 ml.) was refluxed on the steam-bath for 1 hr. A yellow solid was deposited during this period. The mixture was cooled and filtered, and the solid extracted three times with boiling methanol. The methanol-soluble portion on evaporation gave isonicotinoylhydrazine methiodide (0·47 g., 8·5%), m. p. and mixed m. p. 211—213°. With lithium picrate it gave the *methopicrate*, crystallizing from water as yellow prisms of a monohydrate, unchanged by drying at 60°/0·5 mm., m. p. 164—165° (Found: C, 36·8; H, 2·7; N, 20·1. $C_{19}H_{15}N_9O_{15},H_2O$ requires C, 36·4; H, 2·7; N, 20·1%).

The methanol-insoluble solid (m. p. 248—253°) was crystallized from water to give *isonicotinoylhydrazine hydriodide* (1·65 g., 31%), m. p. 256—260°, which on further heating resolidified and then melted at 281—287° (Found: C, 27·4; H, 3·15; I, 47·5%; N, 15·7; O, 6·7; Equiv. 263·4. $C_6H_8IN_3O$ requires C, 27·2; H, 3·0; I, 47·9; N, 15·85; O, 6·0%; Equiv. 265·1). A mixed m. p. with an authentic sample prepared from hydriodic acid and isonicotinoylhydrazine was undepressed.

(*B*) Repetition of the above experiment with methyl iodide alone (8 mols.) without methanol gave the hydriodide, m. p. 248—253°, in 47% yield. Addition of ether to the methanol extract of the hydriodide gave *N-isonicotinoyl-N′-methylhydrazine hydriodide* (16 mg.), crystallizing from ethanol–ether as prisms, m. p. 188—192° (Found: C, 30·0; H, 3·7. $C_8H_{10}IN_3O$ requires C, 30·1; H, 3·6%). Its infrared spectrum was identical with that of *N*-isonicotinoyl-*N′*-methylhydrazine hydrochloride.[12]

Reaction of Isonicotinoylhydrazine with Benzyl Bromide.—Repetition of expt. (*A*) with benzyl bromide in place of methyl iodide gave *isonicotinoylhydrazine hydrobromide* (26%), m. p. 295—297°, as needles from water, identical (mixed m. p.) with an authentic sample prepared from the base and hydrobromic acid (Found: C, 33·1; H, 3·5; N, 18·9. $C_6H_8BrN_3O$ requires: C, 33·05; H, 3·7; N, 19·3%).

Reaction of Isonicotinoylhydrazine with Tritiated Methyl Iodide.—Methyl iodide tritiated to constant specific activity by Wilzbachs [13] method was diluted with inactive methyl iodide and distilled twice (Activity,[11] 7×10^{-2} μc/mg.). A mixture of isonicotinoylhydrazine (1·37 g., 0·01 mole) and tritiated methyl iodide (3 ml., 0·05 mole) was sealed in a tube and heated at 100° for 1·5 hr. Working up as described above gave isonicotinoylhydrazine hydriodide (1·22 g., 47%), m. p. 248—252° [Found: Specific activity, $1·16 \times 10^{-3}$ μc/mg. almost equal to the background]. Partial evaporation of the mother-liquors and addition of ether precipitated a solid (0·22 g., 8%) which was crystallized to radiochemical purity from methanol–ether to give N-*isonicotinoyl*-N′-*methylhydrazine methiodide* (36 mg.) as needles, m. p. 189—191° (Found: N, 13·9%. Activity, $6·95 \times 10^{-2}$ μc/mg. $C_8H_{12}IN_3O$ requires N, 14·3%. For 2 CT_3 groups: activity, $6·8 \times 10^{-2}$ μc/mg.). The methanolic mother-liquors from the above methiodide on treatment with excess of ether deposited N′-*isonicotinoyl*-NN-*dimethylhydrazine methiodide* (98 mg.), crystallized to radiochemical purity as needles, m. p. 199—201° (Found: C, 34·8; H, 4·6%. Activity, $9·15 \times 10^{-2}$ μc/mg. $C_9H_{14}IN_3O$ requires C, 35·2; H, 4·6%. For 3 CT_3 groups: activity, $9·5 \times 10^{-2}$ μc/mg.).

N-*Isonicotinoyl*-N′-*methylhydrazine Methiodide.*—A solution of methyl isonicotinate methiodide [14] in methanol was treated with methylhydrazine (30% excess) and the mixture heated for 3 hr. on the steam-bath. The methiodide crystallized from ethanol as yellow needles, m. p. 190—191° (Found: C, 32·6; H, 4·2. Calc. for $C_8H_{12}IN_3O$: C, 32·8; H, 4·1%).

N-*Benzyl*-4-*methoxycarbonylpyridinium Bromide.*—Obtained from methyl isonicotinate and benzyl bromide in boiling methanol, the *quaternary bromide* (89%), m. p. 138—139°, crystallized from ethanol–ether as a hemihydrate even after being dried at 100°/2 mm. (Found:

[11] Garnett, Hannan, and Law, *Analyt. Chim. Acta*, 1961, **25**, 170.
[12] Cymerman Craig, and Willis, *J.*, 1955, 4135.
[13] Wilzbach, *J. Amer. Chem. Soc.*, 1957, **79**, 1013.
[14] Grob and Renk, *Helv. Chim. Acta*, 1954, **37**, 1672.

C, 53·5; H, 4·5; Br, 24·7; N, 4·1. $C_{14}H_{14}BrNO_2$, $0·5H_2O$ requires C, 53·0; H, 4·8; Br, 25·2; N, 4·4%).

N-*Benzyl*-4-*methoxycarbonylpyridinium Iodide*.—The *quaternary iodide* was obtained (79%) as needles, m. p. 159—161° (Found: C, 47·3; H, 4·0; N, 3·4. $C_{14}H_{14}INO_2$ requires C, 47·3; H, 4·0; N, 3·9%).

Reaction of N-*Benzyl*-4-*methoxycarbonylpyridinium Bromide with Hydrazine*.—Obtained from *N*-benzyl-4-methoxycarbonylpyridinium bromide and hydrazine hydrate in methanol, crystallization from methanol–ether gave the *quaternary hydrazide* (58%) as yellow needles, m. p. 171—172° (Found: C, 50·1; H, 4·6; N, 13·2. $C_{13}H_{14}BrN_3O$ requires C, 50·7; H, 4·6; N, 13·6%).

Reaction of N-*Benzyl*-4-*methoxycarbonylpyridinium Iodide with Hydrazine*.—The *quaternary hydrazide* was obtained (64%) as yellow needles, m. p. 141—142·5° (Found: C, 43·75; H, 4·0; N, 11·7. $C_{13}H_{14}IN_3O$ requires C, 44·0; H, 4·0; N, 11·8%).

Reaction of Benzhydrazide with Methyl Iodide.—A solution of benzhydrazide in methanol was treated with excess of methyl iodide and the mixture was refluxed for 2·5 hr. Evaporation *in vacuo* left *trimethylbenzhydrazinium iodide* (31%) as white needles, m. p. 156—157° (from methanol–ether), of a hemihydrate even when dried at 90°/0·5 mm. (Found: C, 38·0; H, 5·3; I, 40·8. $C_{10}H_{15}IN_2O,\frac{1}{2}H_2O$ requires C, 38·0; H, 5·1; I, 40·5%). It was identical (mixed m. p.) with a sample prepared from *NN*-dimethylbenzhydrazide and methyl iodide. Recrystallization from isopropyl alcohol–ether gave the compound as a hydrate (stable to drying at 75°/0·5 mm.) m. p. 188—189° (Found: C, 36·6; H, 5·3; N, 8·2; O, 10·4. $C_{10}H_{15}IN_2O,H_2O$ requires C, 37·0; H, 5·3; N, 8·6; O, 9·9%).

The ethereal mother-liquors slowly gave *NN'*-dibenzoylhydrazine (5%), crystallizing from ethanol–ether as needles, m. p. 239—242° (lit.,[15] m. p. 241°) (Found: C, 68·9; H, 5·2; N, 10·8. Calc. for $C_{14}H_{12}N_2O_2,\frac{1}{4}H_2O$: C, 68·7; H, 5·1; N, 11·4%).

NN-*Dimethylbenzhydrazide Hydrochloride*.—*NN*-Dimethylhydrazine and benzoyl chloride in pyridine gave the *hydrochloride* (85%), m. p. 165—168°, from ethanol (Found: C, 53·8; H, 6·3. $C_9H_{13}ClN_2O$ requires C, 53·9; H, 6·5%).

NN'-*Dibenzoyl*-NN'-*dimethylhydrazine*.—*NN'*-Dimethylhydrazine and benzoyl chloride, either in pyridine or aqueous sodium hydroxide solution, gave NN'-*dibenzoyl*-NN'-*dimethylhydrazine* as needles, m. p. 88—89°, from ethanol–ether (Found: C, 71·4; H, 5·8; N, 10·6. $C_{16}H_{16}N_2O_2$ requires C, 71·6; H, 6·0; N, 10·4%).

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[15] Curtiss, Koch, and Bartells, *Amer. Chem. J.*, 1909, **41**, 416.

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772. *Dissociation Constants of Substituted Phenylhydrazines.*

By A. Fischer, D. A. R. Happer, and J. Vaughan.

Inductive substituent constants for aryl groups have been obtained by Taft [1] from reactivities of benzene derivatives in which the functional centre is separated from the aromatic ring by at least one methylene group. The essential assumption in this approach is that there is no contribution, from resonance interaction between the substituent aryl group and the side-chain, to the free energy of the generalised reaction:

$$R{-}Y + R'{-}Y' \rightleftharpoons R{-}Y' + R'{-}Y$$

where R is Ph, R' is $X{\cdot}C_6H_4$, Y is the reactant side-chain, and Y' is the transition state (or product) side-chain. The assumption that the interposed methylene group inhibits resonance interaction between aryl and carboxyl (and carbethoxyl) groups was made by

[1] Taft, *J. Phys. Chem.*, 1960, **64**, 1805.

Taft [1] in evaluating σ° values from phenylacetic acid (and related) reactivities. Additional support for this assumption has been provided by a study of the dissociation constants of benzylamines.[2] It was considered to be of interest to study the effectiveness of an imino-group, rather than a methylene group, in isolating the reaction site from the aromatic ring. A convenient reaction series was the dissociation of arylhydrazinium ions, and the thermodynamic dissociation constants of the phenylhydrazinium ion and nine of its *meta*- and *para*-substituted derivatives were measured spectrophotometrically, in water, at 25°.

Experimental.—Reagents. Phenylhydrazine hydrochloride, *p*-chlorophenylhydrazine hydrochloride, and β-naphthylhydrazine hydrochloride were the commercial products. *p*-Nitrophenylhydrazine hydrochloride was prepared from *p*-nitrophenylhydrazine by heating with dilute hydrochloric acid. *m*-Nitrophenylhydrazine hydrochloride,[3] *m*-chlorophenylhydrazine hydrochloride,[4] *m*-tolylhydrazine hydrochloride,[5] and *p*-tolylhydrazine hydrochloride [4] were prepared by standard methods from the appropriately substituted anilines. m- and p-*Cyanophenylhydrazine hydrochlorides* were prepared by reduction of the corresponding diazonium salts, with stannous chloride [6] and sodium sulphite,[7] respectively.

m-Cyanophenylhydrazine hydrochloride was obtained in 59% yield and had m. p. 180° (Found: C, 49·4; H, 5·0; N, 24·25%). *p*-Cyanophenylhydrazine hydrochloride, obtained in 29% yield, had m. p. 240° (Found: C, 49·3; H, 4·8; N, 23·8. $C_7H_8ClN_3$ requires C, 49·6; H, 4·7; N, 24·8%).

Bromocresol Green (Hopkin and Williams Ltd.) was recrystallised twice from glacial acetic acid, and dried at 120° for 6 hr. All aqueous solutions were prepared with oxygen-free deionised water.

Apparatus and Procedure. Spectrophotometric measurements were made on a Beckman model DK-2A ultraviolet spectrophotometer, with 1 cm. fused-silica optical cells, maintained at 25 ± 0·1° during measurements. Aqueous solutions of arylhydrazines proved unstable at $[H^+] < 10^{-5}$ M. Hence the "indicator method" was used when possible, *i.e.*, the hydrogen-ion concentration of the arylhydrazine–arylhydrazine hydrochloride buffer was measured colorimetrically (Bromocresol Green as indicator). However, this method was frequently impracticable owing to the low solubility of the free base in water. The hydrazine was then dissolved in a buffer solution of known $[H^+]$, and the proportions of protonated and unprotonated forms determined spectrophotometrically. Determination of the extinction coefficients of the base forms, which proved difficult through rapid decomposition, even at minimum $[OH^-]$ (*ca.* 10^{-7} M), was normally done by measuring the changes over short time intervals and extrapolating to the time of preparation of the solution. In pK determinations, including that of Bromocresol Green, by the latter method, acetic acid–sodium acetate buffers were used for fixing the solutions at a known pH. The pK value of the phenylhydrazinium ion was determined by both methods, and satisfactory agreement was obtained. The method used for the calculation of the dissociation constants has been described previously.[8] The estimated accuracy of the measured dissociation constants is ±0·03 pK units.

Results and Discussion.—The results obtained are shown in the Table. When this work was carried out, the only dissociation constant measured was that of the phenylhydrazinium ion itself.[9,10] Since then, Stroh and Westphal [11] have reported values for a number of *ortho*-, *meta*-, and *para*-substituted phenylhydrazines, including the methyl, chloro, and nitro compounds. These dissociation constants were, however, determined by a potentiometric method, and appear mostly to lie about 0·15 pK-units above our values.

[2] Blackwell, Fischer, Miller, Topsom, and Vaughan, *J.*, 1964, 3588.
[3] Atkinson, Simpson, and Taylor, *J.*, 1954, 167.
[4] Bullock and Hand, *J. Amer. Chem. Soc.*, 1956, **78**, 5854.
[5] Snyder, Beilfuss, and Williams, *J. Amer. Chem. Soc.*, 1953, **75**, 1873.
[6] Hunsberger, Shaw, Fugger, Ketcham, and Lednicer, *J. Org. Chem.*, 1956, **21**, 394.
[7] Coleman, "Organic Syntheses," Coll. Vol. I, J. Wiley & Sons, New York, 1944, p. 442.
[8] Fickling, Fischer, Mann, Packer, and Vaughan, *J. Amer. Chem. Soc.*, 1959, **81**, 4226.
[9] Allen, *J. Amer. Chem. Soc.*, 1903, **25**, 421.
[10] Veley, *J.*, 1908, 2122.
[11] Stroh and Westphal, *Chem. Ber.*, 1963, **96**, 184.

pK Data for substituted phenylhydrazines.

Substituent	Method	pK	$\bar{\sigma}$	σ^-	$\bar{\sigma}$ (anilines)
p-Me	Indicator	5·32	−0·11	−0·15	−0·17
m-Me	Indicator	5·26	−0·06	−0·07	−0·05
H	Indicator	5·20	0·01	0·00	0·00
H	Direct	5·20	0·01	0·00	0·00
3,4-Benzo	Direct	5·06	0·11	0·04	0·12
p-Cl	Indicator	4·96	0·20	0·27	0·22
m-Cl	Indicator	4·78	0·35	0·37	0·37
m-CN	Direct	4·47	0·62	0·62	0·65
m-NO_2	Direct	4·36	0·71	0·70	0·74
p-CN	Direct	4·25	0·81	0·69	1·02
p-NO_2	Direct	3·70	1·26	0·82	1·25

The measured pK values were plotted against Taft's σ° values and a good correlation was obtained for all *meta*-substituents. A regression line fitted to the pK against σ° data for *meta*-substituents gave $\rho = 1{\cdot}170$ and $\log K_0 = -5{\cdot}193$. The agreement with Taft's σ° values is very poor for *para*-(−M)-substituents; more satisfactory correlation is obtained by plotting the pK of the arylhydrazinium ion against the pK of the corresponding anilinium ion. This is clearly shown (Table) by comparison of σ values [obtained from the relation $\bar{\sigma} = (5{\cdot}193 - pK)/1{\cdot}170$] with σ° values and $\bar{\sigma}$ values for anilinium ion dissociation (evaluated from the pK data cited in refs. 8 and 12). It appears, therefore, that although the value obtained for ρ is consistent with protonation occurring at the terminal amino-group, which is incapable of direct mesomeric interaction with the aromatic ring (cf. ρ for anilinium-ion dissociation [12] = 2·89, ρ for benzylammonium-ion dissociation [2] = 1·06), the $\bar{\sigma}$ values for *para*-(−M)-substituents are consistent with a considerable degree of conjugative electron-transfer to the reaction site.* We consider that these two facts are not irreconcilable; protonation does occur at the terminal amino group but the electron density at this position is affected markedly by the strong resonance interaction between a *para*-(−M)-substituent and the amino-group attached directly to the ring, and this is in turn relayed to the terminal group by an inductive mechanism.

We know of no previous report of such a mesomerically induced inductive effect. The apparent magnitude of the effect, as reflected by the exaltation of σ values, is surprisingly large. The exaltation is, in fact, only slightly smaller than that observed for the aniline series. However, Van Bekkum and his co-workers [14] have pointed out that the extent of resonance interaction is not proportional to the exaltation ($\Delta\sigma$), but to the product of the exaltation and ρ for the reaction. On this scale, the effect of resonance interaction between aryl group and side-chain is approximately one third of that in the aniline series.

Comparison of the ρ values for dissociation of aniline (2·89), benzylamine (1·06), and phenylhydrazine (1·17) shows that the fall-off factor for an imino-group is closely similar to that for methylene.

Phenylhydrazine (pK = 5·20) is a considerably weaker base than either hydrazine (pK = 8·07) [15] or ammonia (pK = 9·25).[16] Of the three, hydrazine appears to be anomalous. Replacement of one of the hydrogens in ammonia by the amino-group should decrease the basicity of the molecule considerably as the latter group has very strong electron-withdrawing (−I) properties. That such substitution results in a decrease in the pK value by only one unit suggests that there is a compensating base-strengthening effect. Since the latter apparently does not operate if there is a phenyl group attached to the amino-group, it is likely that it involves in some way the filled *p*-orbitals of the nitrogen atoms. This is borne out by observations that the alkylhydrazines resemble hydrazine in

* Evans and Kynaston [13] have shown by infrared spectroscopy that in phenylhydrazine hydrochloride the proton is attached to the terminal nitrogen atom.

[12] Biggs and Robinson, *J.*, 1961, 388.
[13] Evans and Kynaston, *J.*, 1963, 3151.
[14] Van Bekkum, Verkade, and Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.
[15] Hinman, *J. Org. Chem.*, 1958, **23**, 1587.
[16] Bates and Pinching, *J. Amer. Chem. Soc.*, 1950, **72**, 1393.

base strength, while hydrazines bearing substituents capable of withdrawing electrons by a conjugative mechanism (*e.g.*, semicarbazide) are very much less basic.

We consider that in the hydrazine molecule there is very strong repulsion between the filled *p*-orbitals of the linked amino-groups. This has a base-strengthening effect, as such repulsion is absent in the conjugate acid. In phenylhydrazine (and semicarbazide) the orbital repulsion can be relieved by interaction of the *p*-orbital of the imino-group with the π-electron system of the attached substituent. As a result of the reduction of the repulsion forces between the two filled *p*-orbitals of the free base the p*K* value reflects the much less completely compensated operation of the $-I$ effect of the imino-group. This is reflected in a much greater decrease in the basicity of the compound than would be expected from the simple electronic interactions arising from the introduction of a remote phenyl substituent.

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773. *Diazaindenes ("Azaindoles"). Part II.*[1] *Methyl Derivatives of 1,7-Diazaindene.*

By ADRIEN ALBERT and ROBERT E. WILLETTE.

THE ionization constants and ultraviolet spectra for the diazaindenes ("azaindoles") have been reported[1] and their pharmacological properties studied.[2] The 1,7-isomer lacks the profound convulsive effect on mice shown by the 1,4-, 1,5-, and 1,6-isomers. Instead, it produces paralysis. The methyl derivatives of 1,7-diazaindene, reported here, were prepared in an effort to elucidate the unusual physiological behaviour of the parent compound.

The three methyl-1,7-diazaindenes were prepared by a modified Madelung ring-closure of the corresponding 2-formamidolutidines[3] which were prepared by amination followed by formylation of the corresponding lutidines. The yields were lower than that for the parent compound.

Ionization constants for these compounds are (as expected) higher than that of 1,7-diazaindene, and show the same order of basic strength as 4-Me > 2-Me > 3-Me > pyridine and 4-Me > 6-Me > 5-Me > 2-aminopyridine.[4] The ultraviolet spectra closely resemble that of 1,7-diazaindene.

Preliminary pharmacological results for 6-methyl-1,7-diazaindene have been reported elsewhere.[2] Dr. T. K. Adler, University of California Medical Center, San Francisco, now reports that 5-methyl-1,7-diazaindene produces a marked, non-convulsive hyperexcitability in mice lasting about 90 minutes after an intraperitoneal dose of 100 mg./kg., but a larger dose (180 mg./kg.) produced a partial paralysis (non-analgetic). 4-Methyl-1,7-diazaindene has purely depressant properties; partial paralysis and loss of righting ability are seen in mice after 200 mg./kg., but there is no analgesia; smaller doses were without action.

Experimental.—Microanalyses were by Dr. J. E. Fildes and her staff. Ionization constants were determined by the methods used in this Department,[5] and the ultraviolet spectra were measured with a Perkin-Elmer spectracord, model 4000A, and the maxima checked with a Hilger Uvispek mark V manual instrument.

[1] Part I, Adler and Albert, *J.*, 1960, 1794.
[2] Adler and Albert, *J. Medicin. Chem.*, 1963, **6**, 480.
[3] Robison and Robison, *J. Amer. Chem. Soc.*, 1955, **77**, 6554.
[4] Albert in "Physical Methods in Heterocyclic Chemistry," ed. Katritzky, Vol. 1, Academic Press, London, 1963, pp. 67 and 73.
[5] Albert and Serjeant, "Ionization Constants of Acids and Bases," Methuen, London, 1962; see also Perrin, *Austral. J. Chem.*, 1963, **16**, 572.

Compound	M. p.	Ionization in H_2O (20°) * pK_a (basic)	Spread (±)	Concn. (10^{-4}M)	λ † (mμ)	Ultraviolet spectra in H_2O (20°) λ_{max} (mμ)	log ε	pH
1,7-Diazaindene ‡	105°					290 §	3·91	7·0
Cation		4·59	0·01	50	—	293	3·94	2·1
4-Methyl-	133					285	3·92	7·7
Cation		5·23	0·03	1	320	286	3·95	2·5
5-Methyl-	141					293, 295	3·89	7·7
Cation		4·91	0·04	1·25	315	295	3·93	2·5
6-Methyl-	136					293	3·99	8·0
Cation		5·18	0·01	0·40	310	301	4·06	2·0

* Ionic strength of buffers = 0·01. † Analytical wavelength. ‡ Physical properties from ref. 1. § All these compounds also have peaks near 220 mμ.

2-*Amino*-3,6-*dimethylpyridine*. 2,5-Lutidine (46·8 g.), sodamide (from 11·5 g. of sodium), and *NN*-dimethylaniline (60 ml., freshly distilled after refluxing with acetic anhydride) were heated at 165—170° with rapid stirring under nitrogen for 10 hr. The cooled mixture was decomposed with water (200 ml.) and extracted with ether (4 × 150 ml.). The dried (Na_2SO_4) extract was evaporated, and the residue distilled. The fraction collected at 92—104°/12—15 mm. solidified to give 2-*amino*-3,6-*dimethylpyridine* (16·7 g., 32%), m. p. 50—52°. The *hydrochloride* had m. p. 243—244° (from ethanol) (Found: C, 53·1; H, 7·0; N, 17·6. $C_7H_{11}ClN_2$ requires C, 53·0; H, 7·0; N, 17·7%). An attempted amination in xylene at 140° gave 75% recovery of starting material and no product.

2-*Formamido*-3,6-*dimethylpyridine*. The preceding amine (6·6 g.) was formylated [6] with 98—100% formic acid (2·5 ml.) and acetic anhydride (6·3 ml.) in ether (125 ml.). Long, silky needles were deposited overnight. After being kept at room temperature for 2 days, 5·7 g. (76%) of *the formamide*, m. p. 175—176°, were obtained. After sublimation at 100°/0·1 mm., and recrystallization from acetone–light petroleum (b. p. 40—60°), it had m. p. 180—181° (Found: C, 63·75; H, 6·75; N, 18·6. $C_8H_{10}N_2O$ requires C, 64·0; H, 6·7; N, 18·65%).

6-*Methyl*-1,7-*diazaindene*. The preceding formamide (2·25 g.) was cyclized in the presence of sodium anilide and potassium formate according to the improved procedure used by Robison and Robison,[3] except that the reaction flask was heated by complete immersion in a metal-bath. The mixture was decomposed with water (50 ml.), neutralized with glacial acetic acid (6 ml.), and extracted with ether (5 × 40 ml.). The dried (Na_2SO_4) extract was evaporated, and the red, oily residue chromatographed over silica gel (40 g.), eluting with 1 : 10 acetone–light petroleum (b. p. 60—80°). Evaporation of the eluates gave 6-*methyl*-1,7-*diazaindene* (260 mg., 13%) as plates. Sublimation at 80—100°/0·1 mm., and recrystallization from light petroleum (b. p. 80—100°), gave m. p. 136—137° (Found: C, 72·9; H, 6·1; N, 21·3. $C_8H_8N_2$ requires C, 72·7; H, 6·1; N, 21·2%).

2-*Amino*-3,5-*dimethylpyridine*. The crude reaction mixture, prepared as above from 3,5-lutidine (9·4 g.), was formylated directly. The *amine hydrochloride* was prepared by refluxing the following formamide in N-hydrochloric acid for 90 min. and evaporation of the solution to dryness *in vacuo*. Recrystallization from ethanol–ether gave light brown needles, m. p. 203—205° (Found: C, 52·9; H, 6·9; N, 17·4%).

2-*Formamido*-3,5-*dimethylpyridine*. Prepared as above from the preceding crude reaction mixture, this gave 2·3 g. (20% calc. on 3,5-lutidine) of *the formamide*, m. p. 157—158° (from acetone). Sublimation at 80—100°/0·6 mm. gave m. p. 159—161° (Found: C, 64·2; H, 7·0; N, 18·7%).

5-*Methyl*-1,7-*diazaindene*. This was prepared as above, but using a fluidized sand-bath for heating. Worked up as for the 6-methyl isomer, it gave 5-*methyl*-1,7-*diazaindene* (0·5 g., 38%) as light brown crystals. Sublimation at 80—100°/0·4 mm. and recrystallization from acetone gave colourless prisms, m. p. 141—143° (Found: C, 72·4; H, 6·1; N, 20·9%).

2-*Amino*-3,4-*dimethylpyridine*. Prepared as above from 3,4-lutidine (18·8 g.), the *product* (30 g., 15%) had b. p. 124°/10 mm., and was a low-melting solid. The *amine hydrochloride* had m. p. 239—240° (from ethanol) (Found: C, 52·6; H, 6·8; N, 17·9%).

2-*Formamido*-3,4-*dimethylpyridine*. This was prepared (93%) as above from the preceding amine (2·6 g.). Sublimation at 80—100°/0·5 mm. and recrystallization from ethanol gave *the formamide* as fine needles, m. p. 129—131° (Found: C, 64·1; H, 6·6; N, 18·6%).

[6] Clemo and Swan, *J.*, 1945, 603.

4-Methyl-1,7-diazaindene. Prepared as above from the preceding formamide (2·25 g.), the crude extract deposited *4-methyl-1,7-diazaindene* (0·46 g., 24%) as light brown needles. Sublimation at 100°/0·6 mm., and recrystallization from methanol, gave fine needles, m. p. 133—134° (Found: C, 72·8; H, 6·1; N, 21·1%).

We thank Dr. T. K. Adler for the above pharmacological report, Mr. D. Light for help in determining the ionization constants, and Mr. C. Arandjelovic for the spectra. One of us (R. E. W.) is indebted to the U.S. Public Health Service for a Postdoctoral Fellowship (National Institute of Mental Health).

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Canberra, Australia. [*Received, November 4th,* 1963.]

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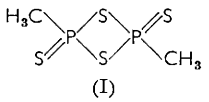
774. *A Least-squares Refinement of the Structure of "Methyl Metadithiophosphonate,"* $[CH_3 \cdot PS_2]_2$.

By J. J. Daly.

Wheatley [1] used *X*-ray diffraction methods to determine the structure of (I). The calculations, using three-dimensional intensity data, were all done by hand. A least-squares refinement has now been carried out using an Elliott 803B electronic computer, and with allowance for anisotropic thermal motion. The intensity data were the same for both sets of calculations. The quantity minimised was



(I)

$$R' = \Sigma w(|F_o| - |F_c|)^2,$$

with $w = 1/8{\cdot}4 + |F_o| + 0{\cdot}17|F_o|^2$. The anisotropic temperature factors, U_{ij}, were used in the form $\exp -2\pi^2(\sum_{i,j=1}^{3} U_{ij}h_ib_ih_jb_j)$. The h_i's are the indices of a reflection and the b_i's are the reciprocal lattice vectors. The value of R fell from 0·112 to 0·081 during the refinement, mainly as a result of the introduction of anisotropic thermal parameters. The final value of R' was 0·012; 252 values of F_o were used. The maximum value of Δ/σ in

Table 1.

Atomic co-ordinates and their standard deviations in Å.

	X	*Y*	*Z*
S(1)	0·0000(0)	1·5739(57)	0·0000(0)
S(2)	2·5598(33)	0·0000(0)	1·8556(35)
P	0·6697(32)	0·0000(0)	1·3160(30)
C	−0·4421(159)	0·0000(0)	2·7254(143)

Table 2.

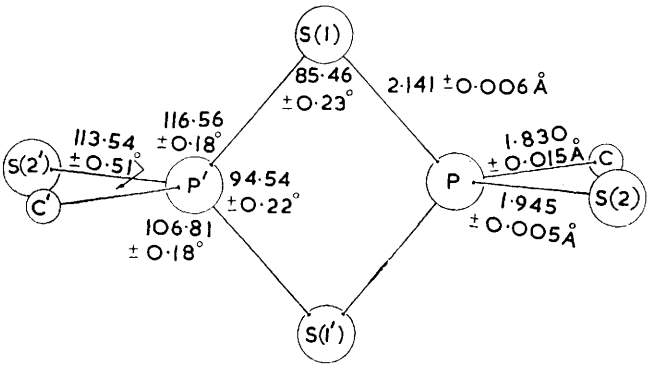
Anisotropic thermal parameters and their standard deviations in Å².

	U_{11}	U_{22}	U_{33}	$2U_{12}$	$2U_{23}$	$2U_{13}$
S(1)	0·0395(15)	0·0210(73)	0·0259(14)	0·0000(0)	0·0000(0)	−0·0080(24)
S(2)	0·0270(15)	0·0375(70)	0·0366(17)	0·0000(0)	0·0000(0)	−0·0057(26)
P	0·0257(14)	0·0278(60)	0·0191(13)	0·0000(0)	0·0000(0)	0·0052(22)
C	0·0449(76)	0·0377(229)	0·0300(62)	0·0000(0)	0·0000(0)	0·0352(110)

the final cycle was 0·25. The bond lengths have not been corrected for thermal motion. The atomic co-ordinates and their standard deviations (in parentheses) are given in Table 1; the anisotropic thermal parameters and their standard deviations (in parentheses) are given in Table 2. The space group is $I2/m$ with $a = 6{\cdot}79_3$, $b = 7{\cdot}04_6$, $c = 9{\cdot}20_7$ Å, $\beta = 92°\ 18'$. $Z = 2$ and the required molecular symmetry is $2/m$.

[1] Wheatley, *J.*, 1962, 300.

The bond lengths and angles, their standard deviations,[2] and the numbering of the atoms are shown in the Figure. The bond lengths and angles reported here do not differ significantly from those found previously,[1] though the accuracy has been improved. There are six van der Waals contacts which are less than 4·0 Å, the shortest being a S · · · S contact of 3·44 Å. The computer programmes were written by members of this laboratory.[3]



The bond lengths and angles, their standard deviations, and the labelling of the atoms.

There are some printing errors in the F_o and F_c list in Wheatley's Paper. The indices of the first three planes following each k change should be: 2.0.0, 4.0.0, 8.0.0 (for $k = 0$); 1.1.0, 3.1.0., 7.1.0 (for $k = 1$); 2.2.0, 4.2.0, 6.2.0 (for $k = 2$); 1.3.0, 5.3.0., 7.3.0 (for $k = 3$).

MONSANTO RESEARCH S.A., BINZSTRASSE 39,
ZURICH 3/45, SWITZERLAND.

[*Received, December 4th*, 1963.]

[2] Cruickshank and Robertson, *Acta Cryst.*, 1953, **6**, 698.
[3] Daly, Stephens, and Wheatley, Monsanto Research S.A., Final Report No. 52 (1963).

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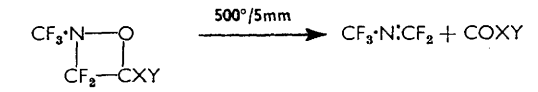
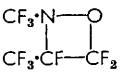
775. *Polyfluoroalkyl Derivatives of Nitrogen. Part XI.*[1] *The Photolytic Decomposition of Some Perfluoro-1,2-oxazetidines.*

By R. E. BANKS, R. N. HASZELDINE, and H. SUTCLIFFE.

PYROLYSIS of the oxazetidines (Ia)—(Id) yields,[2,3] essentially quantitatively, an equimolar mixture of perfluoro(methylenemethylamine) and a carbonyl halide, thus providing a good method of structure determination:



(Ia; X = Y = F)
(Ib; X = F, Y = Cl)
(Ic; X = Y = Cl)
(Id; X = F, Y = CF_3)



(II)

Photolysis of perfluoro-(2-methyl-1,2-oxazetidine) (Ia) and of a mixture of the isomeric oxazetidines (Id) and (II) has now been shown to occur similarly, but may be followed by extensive decomposition of the initial products. Since the latter reaction is relatively slow, however, useful information regarding the structures of the oxazetidines can be obtained if short irradiation periods are employed.

Photolysis of Perfluoro-(2-methyl-1,2-oxazetidine) (Ia).—The oxazetidine was unaffected on exposure to daylight for 2 months, but on irradiation, in silica, with ultraviolet light for 11 days it decomposed completely into carbonyl fluoride (92·5 moles %, calculated on the

[1] Part X, Birchall, Bloom, Haszeldine, and Willis, *J.*, 1962, 3021.
[2] Barr and Haszeldine, *J.*, 1955, 1881.
[3] Barr, Haszeldine, and Willis, *J.*, 1961, 1351.

basis of the scheme below), perfluoro(methylenemethylamine) (77%), tristrifluoromethylamine (12%), and traces of perfluoroethane, trifluoromethyl isocyanate, silicon tetrafluoride, nitrogen, and unidentified material. This result can be explained by cleavage of the N–O and C–C bonds of the oxazetidine ring, as in pyrolysis, followed by a reaction in which two molecules of perfluoro(methylenemethylamine) are converted into one molecule of tristrifluoromethylamine. A possible scheme is:

$$\text{(Ia)} \xrightarrow{h\nu} CF_3{\cdot}N{:}CF_2 + COF_2 \quad (1)$$

$$CF_3{\cdot}N{:}CF_2 \xrightarrow{h\nu} CF_3{\cdot} + CF_2{:}N{\cdot} \quad (2)$$

$$CF_3{\cdot}N{:}CF_2 + CF_3{\cdot} \longrightarrow (CF_3)_2N{\cdot}CF_2{\cdot} \quad (3)$$

$$(CF_3)_2N{\cdot}CF_2{\cdot} + CF_2{:}N{\cdot} \longrightarrow (CF_3)_3N + FCN \quad (4)$$

$$(CF_3)_2N{\cdot}CF_2{\cdot} + COF_2 \longrightarrow (CF_3)_3N + {\cdot}COF \quad (5)$$

$$2CF_3{\cdot} \longrightarrow C_2F_6 \quad (6)$$

Neither cyanogen fluoride nor its cyclic trimer, cyanuric fluoride, was isolated, and the fate of these compounds and of the free radicals $CF_2{:}N{\cdot}$ [formed in (2), but not all accounted for by (4)] and ·COF may lie in the unidentified products, which were shown by infrared analysis to contain COF and C:N groups. No carbon monoxide was detected, thus eliminating the possibility of the reaction:

$$(CF_3)_2N{\cdot}CF_2{\cdot} + {\cdot}COF \longrightarrow (CF_3)_3N + CO$$

Silicon tetrafluoride arose by attack on the reaction vessel; trifluoromethyl isocyanate nearly always accompanies perfluoro(methylenemethylamine), from which it is derived by hydrolysis or by reaction with silica;[4] the nitrogen must have been formed by total degradation of one or more of the intermediates.

No side-reactions occurred when the oxazetidine was irradiated for only 2 days, and a quantitative yield of an equimolar mixture of carbonyl fluoride and perfluoro(methylenemethylamine) was obtained (reaction 1).

Photolysis of a Mixture of Oxazetidines (Id) *and* (II).—Trifluoronitrosomethane combines with hexafluoropropene to give a mixture of the oxazetidines (Id) and (II);[3] these cannot be separated by either distillation or gas chromatography. Pyrolysis of the mixture, however, gives perfluoro(ethylidenemethylamine) and carbonyl fluoride [from isomer (II)], and perfluoro(methylenemethylamine) and trifluoroacetyl fluoride [from isomer (Id)]; the ratio of (II) to (Id) is thus determined[3] as 1 : 9.

A mixture of the oxazetidines, prepared as described previously but in four times the yield (31%), was 61% decomposed after irradiation in a silica tube for 8 hours. The product was a mixture of the compounds (moles % composition in parentheses): perfluoro(ethylidenemethylamine) (6·5), carbonyl fluoride (6), perfluoro(methylenemethylamine) (42), trifluoroacetyl fluoride (35), perfluoroethane (1·5), carbon monoxide (7), tristrifluoromethylamine, silicon tetrafluoride, and unidentified material (total 1·5). The yields of the first two products are consistent with their formation in equimolar amounts from isomer (II). The difference of 7% between the yields of the primary photolysis products from isomer (Id), perfluoro(methylenemethylamine) and trifluoroacetyl fluoride, is accounted for by the slow photolysis of the latter, as observed for chlorodifluoroacetyl fluoride:[5]

$$CF_3{\cdot}COF \xrightarrow{h\nu} {\cdot}CF_3 (\longrightarrow C_2F_6) + {\cdot}COF \xrightarrow{\text{silica}} (CO + SiF_4)$$

with some of the trifluoromethyl radicals used in the formation of tristrifluoromethylamine.

The ratios of the products did not vary greatly during photolysis of up to 65—70% of the oxazetidine mixture, thus suggesting that isomers (Id) and (II) photolyse at approximately equal rates. The products show that isomers (Id) and (II) are present in a ratio

[4] Barr and Haszeldine, *J.*, 1956, 3428.
[5] Haszeldine and Nyman, *J.*, 1959, 1084.

of 7 : 1, which is in reasonable agreement with the ratio 9 : 1 obtained by pyrolytic breakdown.

The initial products perfluoro(ethylidenemethylamine), perfluoro(methylenemethylamine), and trifluoroacetyl fluoride, were completely destroyed when the mixture was irradiated for 14 days, and a mixture containing carbon monoxide, carbonyl fluoride, perfluoroethane, tristrifluoromethylamine, a material which contained both NCO and COF groups, and an unidentified oil was obtained.

Experimental.—Analytically pure perfluoro-(2-methyl-1,2-oxazetidine) [2] and a mixture containing perfluoro-2,3- and -2,4-dimethyl-1,2-oxazetidine [3] were purified by distillation *in vacuo*.

Products were identified by spectroscopy, gas chromatography, and determination of molecular weight (Regnault's method). The compositions of mixtures were determined by molecular-weight measurements for binary mixtures, and by gas chromatography [8 m. × 4 mm. i.d. column packed with acid-washed 50—80 mesh Celite (Johns-Manville 545) coated with 30% w/w of Kel-F No. 1 oil; room temperature; nitrogen flow-rate 26 ml./min.; calibrated with mixtures of known composition].

Irradiations were carried out in the vapour phase in sealed silica tubes 15 cm. from a Hanovia 500w lamp.

Irradiation of perfluoro-(2-methyl-1,2-oxazetidine) (Ia). The oxazetidine (0·169 g., 0·85 mmole), irradiated in a 10-ml. silica tube for 2 days, gave carbonyl fluoride (51 moles %), perfluoro(methylenemethylamine) (48 moles %), and unchanged oxazetidine (1 mole %). Irradiation of the oxazetidine (2·860 g., 14·37 mmoles) in a 25-ml. silica tube for 11 days gave nitrogen (0·003 g., 0·1 mmole), carbonyl fluoride (0·88 g., 13·29 mmoles), perfluoro(methylenemethylamine) (1·45 g., 11·07 mmoles), tristrifluoromethylamine (0·19 g., 0·85 mmole), perfluoroethane, trifluoromethyl isocyanate, silicon tetrafluoride, and unidentified material (total 0·58 mmole). The unidentified material gave five peaks on a gas chromatogram, and showed absorption in the infrared at 2·86 and 6·68 (NH), 5·30 (COF), and 4·35 μ (C⋮N).

A mixture of perfluoro(methylenemethylamine) (1·15 g., 8·78 mmoles) and tristrifluoromethylamine (0·10 g., 0·46 mmole), obtained from a reaction of the above type, was shaken with water to remove the first component, dried (P_2O_5), and passed over powdered potassium hydroxide (to remove carbon dioxide formed during the hydrolysis), to yield pure tristrifluoromethylamine (0·089 g., 0·41 mmole) (Found: C, 16·6; N, 6·0%; *M*, 217. Calc. for C_3F_9N: C, 16·3; N, 6·3%; *M*, 221), spectroscopically identical with an authentic specimen prepared by the electrochemical fluorination of trimethylamine.

Irradiation of a mixture of the isomeric oxazetidines (Id) *and* (II). Three 10-ml. silica tubes were each filled with an equal amount of oxazetidine mixture (0·140 g., 0·550 mmole), and irradiated for 1, 2, and 3 hr., respectively. The compositions of the products (determined by gas chromatography) are given in the Table.

	Product composition (moles %)				
Time (hr.)	COF_2	$CF_3{\cdot}N{:}CF{\cdot}CF_3$	$CF_3{\cdot}COF$	$CF_3{\cdot}N{:}CF_2$	Oxazetidine
1	3	4	25	29	39
2	5	5	33	33	24
3	6	6	39	41	8

On a larger scale, the oxazetidine mixture (2·985 g., 11·99 mmoles) was irradiated in a 250 ml. silica tube for 8 hr., to yield, after fractionation, carbon monoxide (0·026 g., 0·94 mmole), carbonyl fluoride (0·057 g., 0·87 mmole), perfluoro(ethylidenemethylamine) (0·16 g., 0·89 mmole), trifluoroacetyl fluoride (0·54 g., 4·65 mmoles), perfluoro(methylenemethylamine) (0·74 g., 5·64 mmoles), perfluoroethane (0·03 g., 0·20 mmole), unchanged oxazetidine (1·17 g., 4·68 mmoles), tristrifluoromethylamine, silicon tetrafluoride, and unidentified material (0·21 mmole).

Irradiation of the oxazetidine mixture (2·561 g., 10·29 mmoles) in a 250-ml. silica tube for 14 days gave carbon monoxide (0·075 g., 2·68 mmoles), carbonyl fluoride (0·22 g., 3·36 mmoles), perfluoroethane (0·73 g., 5·26 mmoles), tristrifluoromethylamine (0·551 g., 2·25 mmoles), a material (0·625 g., 1·85 mmoles) which showed absorption in the infrared at 4·34 (NCO) and 5·30 μ (COF), and an unidentified yellow oil (0·461 g.).

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776. 1,2-*Dithiole*-3-*thione*.

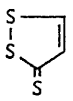
By R. J. S. Beer and R. A. Slater.

Satisfactory procedures are available for the synthesis of many alkyl- and aryl-1,2-dithiole-3-thiones but attempts [1-4] to prepare the parent compound, 1,2-dithiole-3-thione (I), have had disappointing results. The best method yet described appears to be that of Mayer and Kubasch,[4] who obtained the " trithione " in 10% yield by heating propane-1,3-dithiol with sulphur.

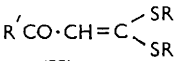
Reaction of β-ketoesters with sulphur and phosphorus pentasulphide gives adequate yields of the substituted trithiones, but ethyl formylacetate (in the form of its sodium derivative) afforded less than 1% of 1,2-dithiole-3-thione.[3] We have found that the acetal of ethyl formylacetate, ethyl ββ-diethoxypropionate, reacts smoothly with sulphur and phosphorus pentasulphide in carbon disulphide, giving the desired 3-thione in 45% yield, after purification by chromatography.

A second method, also involving an acetal, is based on Thuiller and Vialle's synthesis of trithiones,[5] the final step of which is the reaction of a keten mercaptal, *e.g.*, (II; R = alkyl) or the related *gem*-dithiol (II; R = H) with phosphorus pentasulphide. Treatment of 1,1-diethoxy-3,3,3-trisethylthiopropane (III) (prepared from the potassium derivative [6] of triethyl orthothioformate and bromoacetal) with phosphorus pentasulphide gave 1,2-dithiole-3-thione in 47% yield.

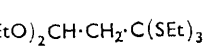
Extensions of these reactions are being investigated.



(I)



(II)



(III)

Experimental.—1,1-*Diethoxy*-3,3,3-*trisethylthiopropane* (III). Bromoacetal (10·2 g.) was added dropwise to a stirred solution of the potassium derivative [6] of triethyl orthothioformate (10 g.) in liquid ammonia (200 ml.). After the ammonia had been allowed to evaporate, water (100 ml.) was added and the product extracted with ether. Fractionation gave the *product* (III) as a straw-coloured liquid (8·9 g., 55%), b. p. 116—118°/0·2 mm., n_D^{15} 1·5128 (Found: C, 49·9; H, 9·0; S, 30·9. $C_{13}H_{28}O_2S_3$ requires C, 50·0; H, 9·0; S, 30·75%). On heating under reflux with methanolic 2,4-dinitrophenylhydrazine hydrochloride for 10 min., the acetal gave ββ-*bis*(*ethylthio*)*acraldehyde* 2,4-*dinitrophenylhydrazone*, which formed bright red needles, m. p. 109°, from methanol (Found: C, 43·8; H, 4·5; N, 15·4. $C_{13}H_{16}N_4O_4S_2$ requires C, 43·8; H, 4·5; N, 15·7%).

3H-1,2-*Dithiole*-3-*thione* (I). From ethyl ββ-diethoxypropionate. A mixture of ethyl ββ-diethoxypropionate [7] (6·1 g.), phosphorus pentasulphide (10 g.), sulphur (2 g.), sand (10 g.), and carbon disulphide (160 ml.) was sealed in an autoclave (capacity 200 ml.) equipped with a stirrer; the temperature was raised to 135° during 1 hr. and kept there for 10 min. The trithione was extracted with acetone from the crude product obtained by evaporation of the carbon disulphide solution, and a solution in benzene was then chromatographed on alumina. The crystalline product (2·0 g., 45%), m. p. 81°, was identical with the analytical sample described below.

From 1,1-diethoxy-3,3,3-trisethylthiopropane. A solution of 1,1-diethoxy-3,3,3-trisethylthiopropane (5·0 g.) in xylene (50 ml.) was added to a vigorously stirred suspension of phosphorus pentasulphide (7·5 g.) in boiling xylene (100 ml.). After heating for a further 10 min., the mixture was cooled, and the xylene decanted. The residue was extracted with hot benzene

[1] Lüttringhaus, König, and Böttcher, *Annalen*, 1948, **560**, 201.
[2] Challenger, Mason, Holdsworth, and Emmott, *J.*, 1953, 292.
[3] Schmidt, Lüttringhaus, and Trefzger, *Annalen*, 1960, **631**, 129.
[4] Mayer and Kubasch, *Angew. Chem.*, 1961, **73**, 220.
[5] Thuillier and Vialle, *Bull. Soc. chim. France*, 1959, 1398.
[6] Fröling and Arens, *Rec. Trav. chim.*, 1962, **81**, 1009.
[7] Dyer and Johnson, *J. Amer. Chem. Soc.*, 1934, **56**, 222; see also Šorm and Smrt, *Chem. listy*, 1953, **47**, 413 (*Chem. Abs.*, 1955, **49**, 175).

(50 ml.), and the product which was obtained by evaporation of the combined benzene and xylene solutions was dissolved in benzene and chromatographed on alumina, giving crystalline 3*H*-1,2-dithiole-3-thione (1·0 g., 47%). Recrystallisation from methanol yielded orange prisms, m. p. 81—82° (lit.,[2] m. p. 82°) (Found: C, 27·2; H, 1·6; S, 71·1. Calc. for $C_3H_2S_3$: C, 26·9; H, 1·5; S, 71·6%). The methiodide had m. p. 175° (lit.,[2] m. p. 175°). The n.m.r. spectrum of the 3-thione dissolved in deuterochloroform, measured on the Varian A-60 spectrometer, showed two matched doublets at τ 1·62 and 2·83, J 6 c.p.s.

One of us (R. A. S.) thanks the D.S.I.R. for the award of a maintenance grant.

THE ROBERT ROBINSON LABORATORIES,
THE UNIVERSITY OF LIVERPOOL. [*Received, December 12th,* 1963.]

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777. *Mercury and Cadmium Tricyano-complexes.*

By W. P. GRIFFITH.

MERCURIC tricyano-complexes were first reported by Grossmann and von der Forst [1] to be formed by the mixture in aqueous solution of 1 : 3 mercuric : cyanide ions; conductimetric and cryoscopic measurements on such solutions were interpreted as indicating the presence of a binuclear species, $[Hg_2(CN)_6]^{2-}$. A potassium salt $K[Hg(CN)_3]$ was isolated by Grüttner [2] but this was later shown by infrared spectra to be a mixture of $Hg(CN)_2$ and $K_2[Hg(CN)_4]$.[3] Poulet and Mathieu [4] concluded from their Raman studies on the aqueous solution in the 2000—2500 cm.$^{-1}$ region that the mercuric complex was $[Hg_2(CN)_6]^{2-}$ and had D_{3h} symmetry with a metal–metal bond, but Chantry and Plane [5] interpreted their Raman measurements over the same frequency range as indicating the presence of a mixture of $[Hg(CN)_2]$, $[Hg(CN)_3]^-$, and $[Hg(CN)_4]^{2-}$, and this was also the conclusion drawn by Penneman and Jones [3] from their infrared spectral studies in the same region. These latter authors also postulated the presence of a $[Cd(CN)_3]^-$ ion in 2 : 7 cadmium ion : cyanide mixtures in aqueous solution,[3] but this could not be confirmed by the Raman studies.[5] Recently, evidence has been obtained for the existence of $[Cd(CN)_3]^-$ ion from cryoscopic studies.[6]

Aqueous solutions containing potassium cyanide and mercuric cyanide in a 1 : 1 ratio were studied by the eutectic cryoscopic method of Jahr *et al.*,[7] a potassium nitrate–ice–water eutectic being used so that the molecular weight of the anion only was measured. The results in Table 4 indicate that the presence of a substantial amount of $[Hg_2(CN)_6]^{2-}$

TABLE 1.

Molecularity measurements on 1 : 1 mercuric cyanide : potassium cyanide solutions in a potassium nitrate–ice–water eutectic mixture.

Concn. mercury (g. atom/l.)	Depression of eutectic point (°C)	n *	Concn. mercury (g. atom/l.)	Depression of eutectic point (°C)	n *
0·073	0·13	0·94	0·036	0·07	0·88
0·064	0·11	0·98	0·033	0·07	0·79
0·043	0·08	0·90	0·032	0·06	0·90

K_o = 1·68 (Wiede, *Ber.*, 1897, **30**, 2178).

$$* n = \frac{\text{apparent molecular weight of complex anion}}{\text{molecular weight of } [Hg(CN)_3]^-}$$

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[1] Grossmann and von der Forst, *Ber.*, 1904, **37**, 4141; Corbet, *J.*, 1926, **129**, 3190.
[2] Jander and Grüttner, *Ber.*, 1948, **81**, 114.
[3] Penneman and Jones, *J. Inorg. Nuclear Chem.*, 1961, **20**, 19.
[4] Poulet and Mathieu, *Compt. rend.*, 1959, **248**, 2079.
[5] Chantry and Plane, *J. Chem. Phys.*, 1960, **33**, 736.
[6] Franzosini, *Ric. Sci. Rend.*, 1962, **2**, 200.
[7] Jahr, Brechlin, Blanke, and Rubens, *Z. anorg. Chem.*, 1952, **270**, 240.

ion is highly unlikely in the solution; the value of n in such a case should lie between 1 and 2 if any dimer were present, and would be unity if the only species present were $[Hg(CN)_2]$, $[Hg(CN)_3]^-$, and $[Hg(CN)_4]^{2-}$.

The Raman spectra of aqueous solutions of 1 : 1 potassium cyanide–mercuric cyanide solutions (2·5M) and of 3·5 : 1 potassium cyanide–cadmium bromide solutions (1·5M) in the 200—2500 cm.$^{-1}$ range are recorded in Table 2. For the cyanide stretching region of 2000—2500 cm.$^{-1}$, the frequency and polarisation data are in agreement with those of other workers.[5] In the 300—500 cm.$^{-1}$ region, three polarised bands of weak to moderate intensity were observed at 413, 358, and 344 cm.$^{-1}$. The first is likely to be the symmetric metal–carbon stretching mode (ν_2) of $[Hg(CN)_2]$ [8,9] and the last the corresponding mode in $[Hg(CN)_4]^{2-}$; the band at 358 cm.$^{-1}$ does not appear in the Raman spectra of either of these complexes alone and it seems reasonable to assign it to the symmetric metal–carbon stretch (ν_2) of $[Hg(CN)_3]^-$. The lower frequency bands at 234 and 273 cm.$^{-1}$ are depolarised and are likely to be deformation modes (the former is probably ν_5 of $[Hg(CN)_2]$. For the cadmium solutions, two bands, both polarised, were found between 300 and 500 cm.$^{-1}$ at 321 and 339 cm.$^{-1}$; the former is probably ν_2 of $[Cd(CN)_4]^{2-}$ and the weaker absorption at 339 cm.$^{-1}$ may arise from the ν_2 of $[Cd(CN)_3]^-$; the broad band at 254 cm.$^{-1}$ is depolarised and is likely to be a deformation mode.

TABLE 2.

Raman spectra (cm.$^{-1}$) of aqueous solutions of mercuric and cadmium tricyano complexes.

Mercury tricyanides	Assignments	Mercury tricyanides	Assignments
2190m, pol.	ν_1 of $[Hg(CN)_2]$ [a]	413w, pol.	ν_2 of $[Hg(CN)_2]$ [a]
2160s, pol.	ν_1 of $[Hg(CN)_3]^-$ [b]	358m, pol.	ν_2 of $[Hg(CN)_3]^-$
2146s, pol.	ν_1 of $[Hg(CN)_4]^{2-}$ [a]	344m, pol.	ν_2 of $[Hg(CN)_4]^{2-}$ [a]
2105w, depol.	? (see ref. b)	273w, depol.	ν_5 of $[Hg(CN)_2]$ [a]
		234m, depol.	Deformation
Cadmium tricyanides	**Assignments**	**Cadmium tricyanides**	**Assignments**
2140s, pol.	ν_1 of $[Cd(CN)_4]^{2-}$ + ν_1 of $[Cd(CN)_3]^-$ [b] *	321m, pol.	ν_2 of $[Cd(CN)_4]^{2-}$ [c]
339w, pol.	ν_2 of $[Cd(CN)_3]^-$	254b, depol.	Deformation

[a] Woodward and Owen, *J.*, 1959, 1055; Jones, *J. Chem. Phys.*, 1957, **27**, 665. [b] Chantry and Plane, *J. Chem. Phys.*, 1960, **33**, 736. [c] Poulet and Mathieu, *Compt. rend.*, 1959, **248**, 2079; Couture and Mathieu, *Ann. Phys.*, 1949, **3**, 521.

* This coincidence of frequencies is observed also in the infrared spectrum.[3] It is possible that by using much higher resolution in the Raman splitting of this band might be found.

These tricyano-ions may be planar (D_{3h}) or pyramidal (C_{3v}), in the latter case with or without a molecule of co-ordinated water. Both models would be expected from group-theoretical considerations to give rise to two Raman-active carbon-nitrogen stretches [$A_1' + E'$ for D_{3h}, $A_1 + E$ for C_{3v}, one polarised (A_1' or A_1) and one depolarised (E' or E)], the same rules also aplying to the metal–carbon stretches; for the D_{3h} model only the E' modes should also be infrared-active while for C_{3v} this should be so for both the A_1 and E vibrations. In view of the known tendency of mercuric ion to attain tetrahedral co-ordination in solution the C_{3v} model would seem to be the more likely, but these Raman results do not permit a decision to be made between the two models, since the asymmetric carbon–nitrogen and metal–carbon stretches (species E) for the pyramidal structure either may be very close to the corresponding symmetric modes [5] or, in the case of the metal–carbon vibration, may be too weak to observe in the Raman effect. There is no evidence for the presence of planar three-co-ordinate mercuric or cadmium ions in aqueous solutions, although such structures are found for crystalline salts of $(HgI_3)^-$ and $(HgBr_3)^-$ [10] and also in ionic melts.[11]

[8] Woodward and Owen, *J.*, 1959, 1055.
[9] Jones, *Spectrochim. Acta*, 1961, **17**, 188.
[10] White, *Acta Cryst.*, 1963, **16**, 397; Fenn, Oldham, and Phillips, *Nature*, 1963, **198**, 381.
[11] Janz and Jones, *J. Chem. Phys.*, 1963, **38**, 905; Wait and Janz, *Quart. Rev.*, 1963, **17**, 225.

If the assignments given above for ν_2 of $[Hg(CN)_3]^-$ and $[Cd(CN)_3]^-$ are correct, it will be observed that both ν_1 (symmetric carbon-nitrogen stretch) and ν_2 (symmetric metal–carbon stretch) increase in frequency along the series $[Hg(CN)_4]^{2-}$; $[Hg(CN)_3]^-$; $[Hg(CN)_2]$ and $[Cd(CN)_4]^{2-}$; $[Cd(CN)_3]^-$. If, in these systems, π-bonding effects are not of major importance [12] (as has recently been demonstrated for $[Hg(CN)_2]$) [13] then the greater the number of metal–carbon σ-bonds per metal atom the weaker is each σ-bond likely to be and the lower the frequency of the metal–carbon stretch (a similar effect has been observed for the series $(HgCl_4)^{2-}$; $(HgCl_3)^-$; $HgCl_2$).[11] Consequently, the weaker the σ-bond the lower will be the carbon–nitrogen stretching frequency—*i.e.*, the closer it will approach to that of the cyanide ion itself (*ca.* 2080 cm.$^{-1}$). If π-bonding between the metal and carbon atoms were important, the frequency seqence of ν_1 and ν_2 would be difficult to predict but might well be the reverse of that observed.

Experimental.—AnalaR reagents were used throughout, and all solutions for the Raman studies were passed through micro-filters before use. Standard 5-ml. cells and polarisation equipment were used with a Cary Raman model 81 spectrophotometer.

The author thanks Dr. R. D. Tunnicliff and the Shell Research and Development Corporation of Emeryville, California, for the use of a Cary Raman instrument on which the preliminary measurements were made, and Dr. W. A. Senior for the use of the Cary instrument at the Unilever Research Division, Port Sunlight, Cheshire.

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[*Received, December 20th,* 1963.]

[12] Nyholm, *Proc. Chem. Soc.*, 1961, 273.
[13] Jones, *Inorg. Chem.*, 1962, **2**, 777.

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778. *The Synthesis of Gluconasturiin.*

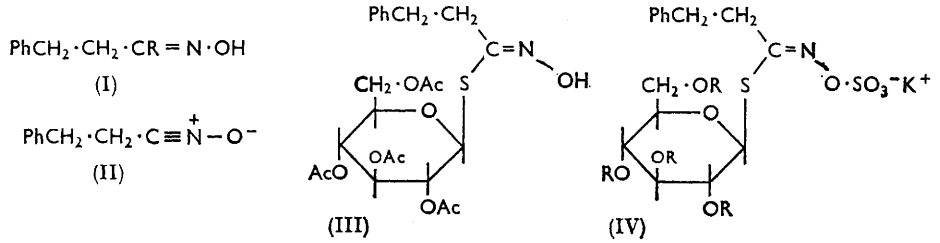
By M. H. Benn.

The flavour of *Nasturtium officinale* R. Br. (watercress) is due to a mustard oil, 2-phenylethyl isothiocyanate.[1] It is known that the mustard oils are derived from glucosidic precursors,[2] and the progenitor of this oil has been named gluconasturiin (IV; R = H).[1,2] Gluconasturiin has been detected and characterised, by its paper-chromatographic behaviour, in *N. officinale* and in many other plants of the families *Cruciferae* and *Resedaceae*.[2] However, there is only one reference [3] to the isolation of crystalline gluconasturiin, of unstated purity.

We report here the first synthesis of gluconasturiin, achieved by the same general route which we used for the synthesis of glucotropæolin [4] and glucocapparin.[5]

1-Chloro-3-phenylpropanal oxime (I; R = Cl) was obtained by chlorination of 3-phenylpropanal oxime (dihydrocinnamaldehyde oxime) (I; R = H). Treatment of an ethereal solution of the chloro-oxime with triethylamine generated 3-phenylpropionitrile oxide (II) which was condensed, *in situ*, with 2,3,4,6-tetra-*O*-acetyl-1-mercapto-β-D-glucopyranose to yield tetra-acetylprogluconasturiin (III). Sulphonation of tetra-acetylprogluconasturiin with pyridine–sulphur trioxide, and subsequent isolation of the product as the potassium salt, yielded pure crystalline tetra-acetylgluconasturiin (IV; R = Ac). Deacetylation of this tetra-acetate with methanolic ammonia yielded pure gluconasturiin, isolated as a stable, non-hygroscopic, quasi-crystalline solid, apparently the dihydrate. The physical constants were in reasonable accord with those reported by

[1] Gadamer, *Arch. Pharm.*, 1899, **237**, 507; *Ber.*, 1899, **32**, 2335.
[2] Kjaer, *Fortschr. Chem. org. Naturstoffe*, 1960, **18**, 169.
[3] Das, Kurup, and Rao, *Indian J. Med. Res.*, 1957, **45**, 191.
[4] Benn, *Canad. J. Chem.*, 1963, **41**, 2836.
[5] Benn, *Canad. J. Chem.*, 1964, **42**, 163.



the Indian workers [3] for the natural product, and the synthetic mustard oil glucoside (IV; R = H) underwent ready cleavage by an enzyme, isolated from *Brassica nigra* Koch, liberating the mustard oil, 2-phenylethyl isothiocyanate, further demonstrating its authenticity.

Experimental.—*1-Chloro-3-phenylpropanal oxime* (I; R = Cl). 3-Phenylpropanal oxime (1·60 g.) was dissolved in chloroform (20 ml.), the solution cooled to 0° in an ice–salt bath, and a slow stream of dry chlorine was bubbled through the solution for 20 min. Removal of the solvent under reduced pressure (bath >40°, otherwise a vigorous exothermic decomposition takes place) left a residual pale blue oil which crystallised from dry ether to yield small colourless platelets of the *oxime* (1·25 g., 68%), m. p. 65—66° (Found: C, 58·9; H, 5·5; N, 7·7; Cl, 19·25. $C_9H_{10}ClNO$ requires C, 58·85; H, 5·55; N, 7·65; Cl, 19·3%).

Tetra-acetylprogluconasturiin (III). 2,3,4,6-Tetra-*O*-acetyl-1-mercapto-β-D-glucopyranose (1·80 g.) and 1-chloro-3-phenylpropanal oxime (0·95 g.) were dissolved in dry ether (250 ml.). Triethylamine (1·2 g.) in dry ether (10 ml.) was added in one portion to the gently stirred blue solution. The blue colour was immediately discharged and a copious white precipitate separated. After 30 min. at room temperature, the mixture was shaken with dilute, ice cold *ca.* N-sulphuric acid (150 ml.). About 100 ml. of the ether was decanted, replaced by ethyl acetate (200 ml.), and the mixture shaken vigorously until all suspended solids had dissolved. The ethyl acetate–ether extract was combined with the decanted ether extract, and, after being dried ($MgSO_4$), the solvents were removed under reduced pressure, leaving a colourless, crystalline residue which crystallised from ethanol to give *tetra-acetylprogluconasturiin* (2·18 g., 86%), m. p. 198° (Found: C, 54·0; H, 5·8; N, 2·8. $C_{23}H_{29}NO_{10}S$ requires C, 54·0; H, 5·7; N, 2·75%), $[\alpha]_D^{24}$ −11° (*c* 2 in chloroform).

Tetra-acetylgluconasturiin (IV; R = Ac). Tetra-acetylprogluconasturiin (450 mg.) was dissolved in dry pyridine (4 ml.), pyridine–sulphur trioxide complex (250 mg.) added, and the mixture stirred for 24 hr. at room temperature and poured into a solution of potassium hydrogen carbonate (350 mg.) in water (20 ml.). The homogeneous solution was freeze-dried and the residual salts extracted with boiling 95% (v/v) aqueous ethanol (3 × 20 ml.). The extracts were filtered hot, combined, and stored at 0°. Fine felted needles of *tetra-acetylgluconasturiin* separated and were recrystallised from 95% ethanol (315 mg., 57%), m. p. 198—200° (decomp.) (Found: C, 44·2; H, 4·8; N, 2·1; S, 10·4; K, 6·6. $C_{23}H_{28}KNO_{13}S_2$ requires C, 43·9; H, 4·45; N, 2·2; S, 10·1; K, 6·2%), $[\alpha]_D^{24}$ −11 (*c* 1 in 50% v/v aqueous ethanol), $\nu_{max.}$ (in KBr) 3000 m, 1765vs, 1642w, 1590m. 1498m, 1440m, 1432m, 1380s, 1295s, 1235vs,br, 1127w, 1050vs,br, 1012w, 982w, 944w, 914s, 878s, 835w, 795vs, 768m, 754m, 726w, 702s cm.$^{-1}$.

Gluconasturiin (IV; R = H). Tetra-acetylgluconasturiin (240 mg.) was dissolved in anhydrous methanol (10 ml.) previously saturated with ammonia. The solution was kept at room temperature overnight and evaporated under reduced pressure (bath >40°) to a residual oil. This oil was taken up in a little hot methanol and absolute ethanol added until the solution became turbid. The solution was filtered, and the filtrate diluted with absolute ethanol (5 vol.), and stored at 0°. A flocculent white precipitate separated, which proved to be hygroscopic, setting to a hard, frangible mass in air. " Recrystallisation " by the same procedure finally yielded *gluconasturiin* (122 mg., 76%) as an off-white, non-hygroscopic powder, m. p. 170—172° (decomp.) (quite sharp, after preliminary coloration from 120° and sintering from 140°) (Found: C, 36·05; H, 4·75. $C_{15}H_{20}KNO_9S_2,2H_2O$ requires C, 36·2; H, 4·85%), $[\alpha]_D^{24}$ −23° (*c* 1 in H_2O) (lit.,[3] m. p. 163°, $[\alpha]_D$ −21°), $\nu_{max.}$ (in KBr) 3550vs, 3000w, 1640w, 1660w, 1505w, 1443m, 1267s, br, 1080s, 885m, 835m, 797m,b, 755w, 728w, 703m cm.$^{-1}$. The glucoside

was homogeneous when examined by paper chromatography [6] on Whatman No. 1 paper, in butanol–acetic acid–water (4 : 1 : 4), ascending, giving a single spot, R_F 0·32.

Enzyme-induced fission of the glucoside. The solution from the optical rotation measurement, containing 19·8 mg. of the glucoside, was diluted to 5 ml., phsophate buffer of pH 6·9 added (2 ml.), together with a myrosinase (20 mg.) isolated [7] from *Brassica nigra* Koch. After 1 hr. at room temperature, the strong characteristic watercress odour of 2-phenylethyl isothiocyanate could be detected. The mixture was then steam-distilled, 30 ml. of distillate being collected. Ammonia (0·5 ml.; *d* 0·88) was added to the distillate, and after 30 min. at room temperature the solution was evaporated under reduced pressure and the residue examined by paper chromatography.[8] A single spot, chromatographically identical with that for 2-phenyl ethylthiourea was obtained, turquoise blue to Grote's reagent.[9]

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CALGARY, ALBERTA, CANADA. [*Received, December 23rd,* 1963.]

[6] Schultz and Gmelin, *Z. Naturforsch.*, 1953, **8b**, 151.
[7] Benn, unpublished work.
[8] Kjaer and Rubinstein, *Acta Chem. Scand.*, 1953, **7**, 528.
[9] Grote, *J. Biol. Chem.*, 1931, **93**, 25.

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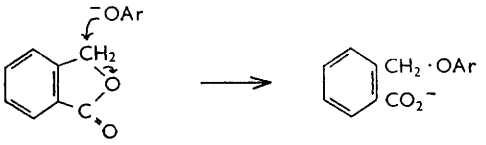
779. *Synthesis of 2-Carboxybenzyl Aryl Ethers.*

By ELLIS K. FIELDS.

ALTHOUGH benzyl phenyl ethers are readily made by nucleophilic attack of phenoxide ions on benzyl halides, 2-carboxybenzyl aryl ethers cannot be synthesized in this way. Indeed, the only such ether known is 2-carboxybenzyl phenyl ether, made by a five-step synthesis from phthalimidine.[1]

A simple new synthesis of these ethers has been discovered. It consists in heating sodium 2-hydroxymethylbenzoate (from sodium hydroxide and phthalide) with phenols. The reaction probably proceeds by formation of a small amount of phenoxide ion, with attack on phthalide to give the ether, an unusual reaction for the system phenoxide plus ester:



This was shown by treating anhydrous sodium phenoxide with phthalide at 180°, to give, after acidification, 2-carboxybenzyl phenyl ether in 67% yield.

When refluxed in *p*-cymene with a little activated alumina, sodium 2-hydroxymethylbenzoate gave di-2-carboxybenzyl ether. In an attempt to alkylate by way of the hydroxymethyl group, sodium 2-hydroxymethylbenzoate was heated with t-butylbenzene, 2-methylnaphthalene, and anisole. Below 170° there was no reaction; above 170°, 2,2′-dicarboxybenzyl ether was formed. With acetylacetone and diethyl phosphite the sodium salt gave phthalide.

Experimental.—Sodium 2-hydroxymethylbenzoate. A solution of phthalide (1 mole) in warm aqueous sodium hydroxide (1 mole) was evaporated, and the residue, dried at 80°, was dissolved in alcohol; addition of ether precipitated the *salt*, m. p. 220° (clear red melt) (Found: Na, 13·6. $C_8H_7NaO_3$ requires Na, 13·2%).

2-Carboxybenzyl ethers. Sodium 2-hydroxymethylbenzoate (34 g., 0·2 mole), stirred and refluxed with phenol (18·8 g., 0·2 mole) and *p*-cymene (100 ml.) under a Dean–Stark water trap, gave, after 18 hr., 2-carboxybenzyl phenyl ether (39·3 g., 86%), m. p. 126° (from heptane) (lit.,[1] 126°), $\varepsilon_{max.}$ 1675, 1275—1200, and 1075—1020 cm.$^{-1}$. The same compound was prepared (30%) by heating equimolar amounts of phenol and sodium 2-hydroxymethylbenzoate at 180° for

[1] Oppe, *Ber.*, 1913, **46**, 1098.

30 min., and also (67%) from equimolar amounts of phthalide and sodium phenoxide at 180° for 2 hr.

By the first method, the 2-carboxybenzyl *ethers* of the following phenols were prepared (80—90%): of *p*-bromophenol, m. p. 186° (from heptane) (Found: C, 54·7; H, 3·6; Br, 26·0. $C_{14}H_{11}BrO_3$ requires C, 54·8; H, 3·6; Br, 26·1%); of *p*-cresol, m. p. 122° (from heptane) (Found: C, 73·9; H, 6·7. $C_{15}H_{14}O_3$ requires C, 73·8; H, 6·6%); of 1-naphthol, m. p. 142° (from heptane) (Found: C, 77·5; H, 4·8. $C_{18}H_{14}O_3$ requires C, 77·7; H, 5·0%); of 2,2-bis-(*p*-hydroxyphenyl)-propane, m. p. 212° (from heptane) (Found: C, 75·2; H, 5·6. $C_{31}H_{28}O_6$ requires C, 75·0; H, 5·6%). *Di-2-carboxybenzyl ether* had m. p. 194—196° (from ethanol) (Found: C, 66·9; H, 4·6. $C_{16}H_{14}O_5$ requires C, 67·1; H, 4·9%).

2-Carboxybenzyl N-phenylcarbamate. This *ester*, obtained (88%) from sodium 2-hydroxymethylbenzoate and phenyl isocyanate in dimethylformamide, had m. p. 205° (decomp.) (from ethanol) (Found: C, 66·1; H, 4·9; N, 5·1. $C_{25}H_{13}NO_4$ requires C, 66·4; H, 4·8; N, 5·2%).

The author thanks Professor D. H. Hey, of King's College, London, for his interest and helpful discussions.

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780. *Conductance minima in the system Triethylmethylammonium iodide–methylene dichloride between 35 and −71°.*

By J. H. BEARD and P. H. PLESCH.

IN the course of work on the kinetics of the reaction between methyl iodide and triethylamine [1] we required the specific conductivities, κ, of solutions of triethylmethylammonium iodide in methylene dichloride at temperatures between 35 and −71° up to concentrations of the order of 10^{-1} mole/l. The preparation of materials and the techniques used have been described.[1,2]

The results of the conductivity measurements are shown in Table 1. The values of the

TABLE 1.

The specific conductivity (in mho cm.$^{-1}$) as a function of concentration (mole l.$^{-1}$).

35°	10^2c	7·065	5·293	4·231	3·244	2·591	2·080	1·672	1·391	1·162	0·9422
	$10^4\kappa$	4·650	3·332	2·588	1·959	1·555	1·255	1·026	0·8699	0·7490	0·6034
25°	10^2c	7·128	5·349	4·279	3·283	2·624	2·106	1·694	1·410	1·178	0·9551
	$10^4\kappa$	4·533	3·244	2·538	1·915	1·530	1·235	1·012	0·8610	0·7400	0·6261
0°	10^2c	7·320	5·485	4·397	3·379	2·703	2·172	1·762	1·456	1·216	0·9865
	$10^4\kappa$	4·010	2·923	2·300	1·740	1·403	1·148	0·944	0·7997	0·6948	0·5879
−20°	10^2c	7·494	5·637	4·517	3·470	2·776	2·231	1·795	1·495	1·249	1·013
	$10^4\kappa$	3·515	2·568	2·031	1·545	1·246	1·026	0·8453	0·7229	0·6136	0·5301
−40°	10^2c	7·668	5·771	4·626	3·555	2·845	2·286	1·839	1·532	1·280	1·038
	$10^4\kappa$	2·898	2·132	1·684	1·292	1·042	0·8535	0·7053	0·5996	0·5220	0·4428
				−55°					−71°		
	10^2c	1·667	1·297	0·8338	0·6144	0·4025	1·875	1·221	0·8063	0·5487	0·3734	0·2733
	$10^5\kappa$	5·426	4·415	3·147	2·533	1·908	4·400	3·123	2·270	1·733	1·338	1·117

equivalent conductance Λ pass through a minimum with increasing concentration, c, of salt, except at −55 and −71°, at which temperatures the range of concentrations was not sufficiently great to show up this effect.

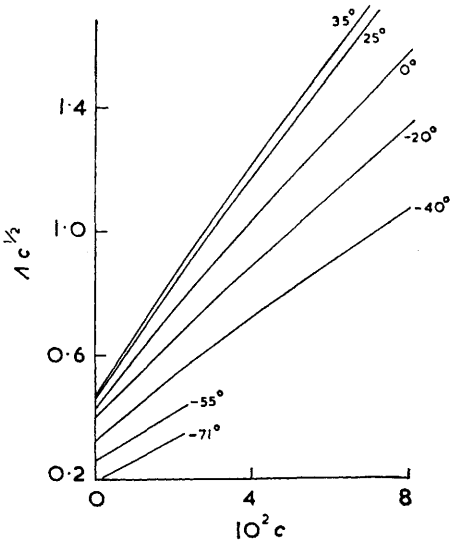
If the conductance minimum is interpreted by Fuoss and Kraus's theory [3] of triple-ion formation, plots of $\Lambda c^{\frac{1}{2}}$ against c (Figure) should have a slope $S = \Lambda_3^\circ K^{\frac{1}{2}}/K_3$ and an intercept I on the $\Lambda c^{\frac{1}{2}}$-axis of $I = \Lambda^\circ K^{\frac{1}{2}}$, where Λ_3° is the equivalent conductance of the triple ions,

[1] Beard, Thesis, Birmingham, 1963; Beard and Plesch, *J.*, 1964, 3682.
[2] Beard and Plesch, *J.*, 1964, in the press.
[3] Fuoss and Kraus, *J. Amer. Chem Soc.*, 1933, **55**, 21, 2387.

K_3 their dissociation constant, and K the dissociation constant of the ion pairs. The concentration at minimum Λ is given by

$$c_{\text{min.}} = K_3\Lambda^\circ/\Lambda_3^\circ = I/S$$

The results in Table 2 show that there is reasonable agreement between the values of I/S and the observed $c_{\text{min.}}$. The values of I/S (which are more accurate than $c_{\text{min.}}$), together with the assumption [3] that $\Lambda_3^\circ = \Lambda^\circ/3$, yield the values of K_3 shown in Table 2.



Fuoss–Kraus plots for triple-ion formation.

Because of the neglect of activity coefficients and other approximations in the above argument the values of K_3 cannot be considered as anything more than an indication of its order of magnitude; and whilst the fact that K_3 increases with decreasing temperature agrees with expectation,[4] values of ΔH° and ΔS° which could be derived from the variation of K_3 with temperature, cannot have any great significance.

TABLE 2.

Temp.	Slope	Intercept	$10^2\frac{\text{Intercept}}{\text{Slope}}$	$10^2c_{\text{min.}}$ (mole/l.)	$\Lambda_{\text{min.}}$ (mho cm.^{2} mole^{-1})	10^2K_3 (mole/l.)
+35°	17·74	0·508	2·86	2·7	5·97	0·953
+25	16·90	0·502	2·97	3·1	5·79	0·990
0	13·94	0·479	3·44	3·3	5·12	1·15
−20	11·26	0·436	3·87	3·5	4·43	1·29
−40	8·95	0·412	4·12	4·1	3·60	1·37

Despite the uncertainties of interpretation we have thought it useful to put our observations on record, because there are only very few similar results in the literature (and none covering so wide a temperature range), and because the whole question of triple-ion formation has recently been re-opened by Davies's work.[5]

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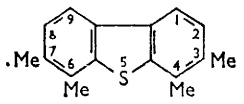
[*Received, December 31st*, 1963.]

[4] Harned and Owen, "The Physical Chemistry of Electrolyte Solutions," Reinhold, New York, 1950, p. 193.
[5] Davies, "Ion Association," Butterworth, London, 1962.

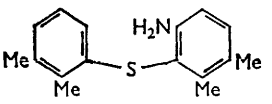
781. *Constituents of High-boiling Petroleum Distillates. Part IX.*[1] 3,4,6,7-*Tetramethyldibenzothiophen in a Kuwait Oil.*

By W. Carruthers and A. G. Douglas.

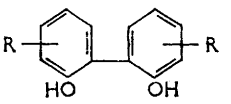
A tetramethyldibenzothiophen isolated previously [2] from distillates of a Kuwait oil has been identified as the 3,4,6,7-isomer (I) by synthesis of this compound by Pschorr cyclisation of the sulphide (II). The 2,6,7- and 2,4,8-trimethyl- and 2,4,6,7-tetramethyl-compounds, required for comparison, were prepared similarly from the appropriate amino-diaryl sulphides.



(I)



(II)



(III)

The Kuwait distillates used in this series of investigations have an unusually high sulphur content [3] and contain considerable amounts of alkyl dibenzothiophens; a number of tetramethyldibenzothiophens have been isolated and identified. Possible precursors of dibenzothiophens in the oil may be dihydroxydiphenyl derivatives of the type (III) formed by *ortho* coupling of phenols,[4] which are known to occur in some crude oils.[5] Reaction of such precursors with suitable constituents of the source rocks to form dibenzothiophens is conceivable, notwithstanding the poor conversions obtained in the laboratory (cf. ref. 2). A similar process may account also for the formation of derivatives of 11-thiabenz[a]fluorene in the Kuwait oil.

Experimental.—M. p.s were determined on a Kofler hot-stage apparatus. Ultraviolet spectra refer to solutions in 95% ethanol. Light petroleum had b. p. 60—80°.

2,2′,3,3′-*Tetramethyl*-6-*nitrodiphenyl Sulphide.*—A solution of 2,3-dimethyl(thiophenol) (4·2 g.), 3-chloro-4-nitro-*o*-xylene (5·6 g.), and sodium hydroxide (1·25 g.) in ethylene glycol (130 c.c.) was boiled for 15 min. The recovered product was chromatographed on alumina and the *sulphide* (6·7 g.) obtained as yellow plates, m. p. 88° (from cyclohexane) (Found: C, 67·1; H, 6·0. $C_{16}H_{17}O_2NS$ requires C, 66·9; H, 6·0%).

3,4,6,7-*Tetramethyldibenzothiophen.*—A solution of the nitro-compound (4·9 g.) in ethanol (90 c.c.) was added to a warm solution of stannous chloride (20 g.) and hydrochloric acid (30 c.c.) in ethanol (20 c.c.), and the solution was boiled for 1½ hr. Most of the ethanol was distilled off, the solution was made alkaline and the product extracted with ether.

The amine (3·6 g.), which was obtained as a pink solid, without further purification was dissolved in 25% sulphuric acid (250 c.c.) and diazotised at 0° with an aqueous solution of sodium nitrite (3 g.). Copper powder (6·5 g.) was added portionwise to the stirred solution, and the mixture was kept at room temperature for 12 hr. and then boiled for 2 hr. The product was extracted with hot benzene and the gum (3 g.) was chromatographed on alumina. Elution with light petroleum–benzene (19 : 1) gave 2,2′,3,3′-*tetramethyldiphenyl sulphide* (0·37 g.), m. p. 77° (from cyclohexane) (Found: C, 78·85; H, 7·3. $C_{16}H_{18}S$ requires C, 79·3; H, 7·5%); $\lambda_{max.}$ 252 and 276 mμ (log ε 4·18 and 3·73). Further elution with light petroleum–benzene (1 : 1) then gave 3,4,6,7-*tetramethyldibenzothiophen* (0·45 g.) as plates (from ethanol–benzene), m. p. 193° not depressed when mixed with the dibenzothiophen derivative, m. p. 196°, isolated from Kuwait oil (Found: C, 80·0; H, 6·7. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%); $\lambda_{max.}$ (236), 243, 269·5, 280·5, 290, 310, and 323 mμ [log ε (4·66), 4·75, 4·10, 3·90, 4·07, 3·36, and 3·42]. The *sulphone* formed blades (from benzene), m. p. 235—237° (decomp.) (Found: C, 71·1; H,

[1] Part VIII, *J.*, 1964, 724.
[2] Carruthers and Douglas, *J.*, 1959, 2813.
[3] Personal communication from Professor F. Morton, Manchester College of Science and Technology.
[4] Pummerer, Melamed, and Puttfarcken, *Ber.*, 1922, **55**, 3116.
[5] Lochte and Littmann, "The Petroleum Acids and Bases," Constable and Co., Ltd., London, 1955, ch. 12.

5·9. $C_{16}H_{16}O_2S$ requires C, 70·7; H, 5·8%). The s-*trinitrobenzene complex* gave yellow needles (from benzene–ethanol), m. p. 203—205° not depressed when mixed with the complex of the compound isolated from Kuwait oil (Found: C, 58·2; H, 4·0. $C_{22}H_{19}N_3O_8S$ requires C, 58·3; H, 4·2%), and the 2,4,7-*trinitrofluorenone complex* was obtained as red needles, m. p. 222—224° (from ethanol–benzene) (Found: C, 62·2; H, 3·9. $C_{29}H_{21}N_3O_7S$ requires C, 62·7; H, 3·8%).

2,4,6,7-*Tetramethyldibenzothiophen.*—2,2′,3,4′-*Tetramethyl-6-nitrodiphenyl sulphide*, prepared as described above from 2,4-dimethyl(thiophenol) (2 g.), 3-chloro-4-nitro-*o*-xylene (2·7 g.), and sodium hydroxide (0·6 g.) in boiling n-butanol (70 c.c.) for 30 min., formed orange cubes (1·9 g.), m. p. 89—91° (from light petroleum–benzene) (Found: C, 66·6; H, 6·3. $C_{16}H_{17}NO_2S$ requires C, 66·9; H, 6·0%).

The nitro-sulphide (1·85 g.) was reduced with stannous chloride as described above, and the crude amine was diazotised in 25% sulphuric acid and cyclised with copper powder (3 g.) on the water-bath. Chromatography of the crude product on alumina afforded 2,4,6,7-*tetramethyldibenzothiophen* (0·15 g.) as needles, m. p. 142—143° (from benzene–ethanol) (Found: C, 79·9; H, 6·4. $C_{16}H_{16}S$ requires C, 80·0; H, 6·7%); $\lambda_{max.}$ 244, (260), 270, 278, 286·5, 311·5, and 324·5 mμ [log ε 4·86, (4·24), 4·14, 4·10, 4·17, 3·32, and 3·45]. The *s*-trinitrobenzene complex formed yellow needles (from benzene–ethanol), m. p. 179—182°.

2,6,7- *and* 2,4,8-*Trimethyldibenzothiophen.*—2,3,4′-*Trimethyl-6-nitrodiphenyl sulphide* was obtained from 3-chloro-4-nitro-*o*-xylene (5 g.) and *p*-thiocresol (4·5 g.) as yellow prisms, m. p. 57—58° (Found: C, 65·8; H, 5·4. $C_{15}H_{15}NO_2S$ requires C, 65·9; H, 5·5%). Reduction by stannous chloride, and Pschorr cyclisation of the resulting amine (0·4 g.) as above, gave 2,6,7-*trimethyldibenzothiophen* (100 mg.) as blades, m. p. 125—126° (from benzene–ethanol) (Found: C, 79·5, H, 6·0. $C_{15}H_{14}S$ requires C, 79·6; H, 6·2%); $\lambda_{max.}$ 234, (240), 258, 268, 280, 290, 314, and 327 mμ [log ε 4·59, (4·57), 4·22, 4·15, 3·90, 4·14, 3·38, and 3·45]. The *sulphone* formed needles, m. p. 288—290° (from benzene) (Found: C, 70·1; H, 5·4. $C_{15}H_{14}O_2S$ requires C, 69·7; H, 5·5%); $\lambda_{max.}$ (in chloroform) (275), 285, 298, (320), and 328—330 mμ [log ε (3·83), 3·91, 3·89, (3·30), and 3·35]. Desulphurisation of the dibenzothiophen with Raney nickel in boiling ethanol [6] afforded 3,3′,4-*trimethylbiphenyl*, b. p. 100—105°/1·5 mm. (air bath) (Found: C, 91·8; H, 8·5. $C_{15}H_{16}$ requires C, 91·8; H, 8·2%); $\lambda_{max.}$ 256 mμ (log ε 4·16); $\nu_{max.}$ 878, 820, 781, and 700 cm.$^{-1}$.

Similarly, 2,4,4′-*trimethyl-6-nitrodiphenyl sulphide* was obtained from *p*-thiocresol and 4-chloro-5-nitro-*m*-xylene as yellow rhombs, m. p. 81—82° (Found: C, 66·1; H, 5·9. $C_{15}H_{15}NO_2S$ requires C, 65·9; H, 5·5%). Reduction and cyclisation as above then gave 2,4,8-*trimethyldibenzothiophen* as needles, m. p. 72—73° (from ethanol) (Found: C, 79·3; H, 6·15. $C_{15}H_{14}S$ requires C, 79·6; H, 6·2%); $\lambda_{max.}$ 233, 240, 258, 266, 281, 291, (305), 321, and 333 mμ [log ε 4·68, 4·60, 4·18, 4·08, 3·84, 4·12, (3·16), 3·44, and 3·54]. The s-*trinitrobenzene complex* formed yellow needles, m. p. 166—168° (Found: C, 58·0; H, 4·1. $C_{21}H_{17}N_3O_6S$ requires C, 57·4; H, 3·9%).

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THE UNIVERSITY, EXETER. [*Received, January 4th*, 1964.]

[6] Blicke and Sheets, *J. Amer. Chem. Soc.*, 1948, **70**, 3768; 1949, **71**, 4010.

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782. *Alkaloid Biosynthesis. Part V.*[1a] *Experiments on Opium Alkaloids using* 3,4-*Dihydroxyphenethylamine.*

By A. R. BATTERSBY and R. J. FRANCIS.

WHEN [2-^{14}C]tyrosine (I) is administered to *Papaver somniferum* plants, radioactive morphine (III; R = H) is formed which is labelled specifically, and about equally, at positions 9 and 16.[1b-3] It follows that morphine is biosynthesised from two aromatic C_6–C_2 units * (Ar–C–C). The oxygenation pattern of the 1-benzylisoquinolines, which

* See footnote to Part IV, p. 3600.

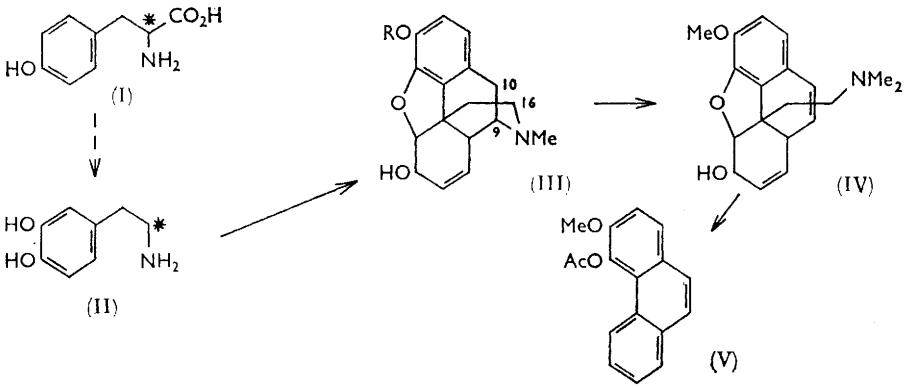
[1] (*a*) Part IV, *J.*, 1964, 3600 (*b*) Battersby and Harper, *Chem. and Ind.*, 1958, 364; Battersby, Binks, and Le Count, *Proc. Chem. Soc.*, 1960, 287.

[2] Battersby, Binks, and Harper, *J.*, 1962, 3534.

[3] Leete, *Chem. and Ind.*, 1958, 977; *J. Amer. Chem. Soc.*, 1959, **81**, 3948.

are intermediates on the pathway to morphine,[1b,4,5] leads to the conclusion [6] that the two aromatic units are further oxidised in the plant to yield the 3,4-dihydroxy-system [cf. (II)]. Moreover, it seems probable on simple structural grounds that the two units are different and that one could possibly be 3,4-dihydroxyphenethylamine, " dopamine " (II); this had been postulated as part of the early biogenetic schemes.[7] The incorporation of one unit of labelled dopamine into the phthalideisoquinoline hydrastine was demonstrated by Gear and Spenser [8] during the course of our work described below.

3,4-Dimethoxyphen[1-^{14}C]ethylamine [1a] was demethylated with hot concentrated hydrochloric acid to yield 3,4-dihydroxyphen[1-^{14}C]ethylamine hydrochloride which was injected as an aqueous solution into the capsules [2] of *P. somniferum* plants. The isolated morphine (III; R = H), codeine (III; R = Me), and thebaine were all radioactive,



though the last was very weakly so, no doubt as a result of the relatively long period (3 weeks) between feeding and harvesting the plants.[1a] The incorporation of activity into morphine was 0·26% of that fed.

Degradation of radioactive alkaloids.

	Rel. activity		Rel. activity
Morphine monohydrate (III; R = H)	1·00	Codeine (III; R = Me)	1·00
α-Codeimethine (IV)	1·02	α-Codeimethine (IV)	1·04
O-Acetylmethylmorphol (V)	0·00	*O*-Acetylmethylmorphol (V) ...	0·01

Degradation of the morphine by the route used previously [2] gave the results shown in the Table. The complete loss of activity when the ethanamine side-chain is eliminated to yield *O*-acetylmethylmorphol (V) is in keeping with the expected specific labelling at position 16 of morphine and proves the important point that position 9 carries no significant activity. Similar results were obtained for codeine (Table).

These results support the view that two different units are used by the plant to build the hydrophenanthrene alkaloids of opium and indicate that one unit is dopamine or some closely related substance; a brief report has already been made.[6b] The recent preliminary account by Leete and Murrill [9] of the incorporation of dopamine into morphine is in agreement with the foregoing work.

[4] Battersby and Binks, *Proc. Chem. Soc.*, 1960, 360; Battersby, *Quart. Rev.*, 1961, **15**, 259.
[5] Barton, Kirby, Steglich, and Thomas, *Proc. Chem. Soc.*, 1963, 203; Barton, *Proc. Chem. Soc.*, 1963, 293, and refs. therein; Barton, Battersby, Dobson, Kirby, Steglich, and Thomas, to be published.
[6] (*a*) Robinson, " The Structural Relations of Natural Products," Clarendon Press, Oxford, 1955; (*b*) Battersby, *Proc. Chem. Soc.*, 1963, 189, and refs. therein.
[7] Winterstein and Trier, " Die Alkaloide," Borntraeger, Berlin, 1910.
[8] Gear and Spenser, *Canad. J. Chem.*, 1963, **41**, 783, and refs. therein.
[9] Leete and Murrill, *Tetrahedron Letters*, 1964, 147.

Experimental.—**3,4-***Dihydroxyphen*[1-^{14}C]*ethylamine* (II). A solution of 3,4-dimethoxyphen-[1-^{14}C]ethylamine hydrochloride [1a] (156 mg.; 1·1 mc) in AnalaR concentrated hydrochloric acid (2 ml.) was heated in an evacuated sealed tube at 165° for 2 hr. The contents of the tube were evaporated to dryness and the crystalline residue was recrystallised from methanol–di-isopropyl ether to afford 3,4-dihydroxyphen[1-^{14}C]ethylamine hydrochloride (117 mg.; 0·98 mc) which was identified by comparison with authentic material.

Administration of the labelled precursor. A solution of the foregoing hydrochloride (24·4 mg.; 0·2 mc) in water (20 ml.) was injected [2] into the capsules of twenty *P. somniferum* plants (variety Noordster) in the 1962 season. The plants were harvested 3 weeks later and the alkaloids extracted by the improved method described in Part IV.[1a] The morphine (1·02 g.) had a specific activity of $5{\cdot}8 \times 10^5$ dis./100 sec./mmol. (0·26% incorporation). Inactive codeine and thebaine (240 mg. of each) were added to the non-phenolic alkaloids and these two bases were then isolated by the previously described method.[1a] The diluted codeine (302 mg.) had a specific activity of $1{\cdot}5 \times 10^5$ dis./100 sec./mmol.

The alkaloids were degraded as previously described [1a,2] and the products were identified by comparison with the earlier specimens.

Grateful acknowledgment is made to Edinburgh Pharmaceutical Industries Ltd. for gifts of alkaloids, to Dr. O. Isler and J. Würsch (F. Hoffmann–La Roche, Basle) for provision of radioactive material, to Mr. S. M. King for gifts of seed, and to the Government Grants Committee of the Royal Society and the D.S.I.R. for financial support. We also thank Dr. R. Binks and Dr. D. J. McCaldin for their generous help.

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THE UNIVERSITY OF LIVERPOOL. [*Received, January 10th,* 1964.]

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783. *The Photolysis of 2′,3′-Isopropylidene-5′-deoxyuridinylcobalamin.*

By A. W. JOHNSON, DIANE OLDFIELD, R. RODRIGO, and N. SHAW.

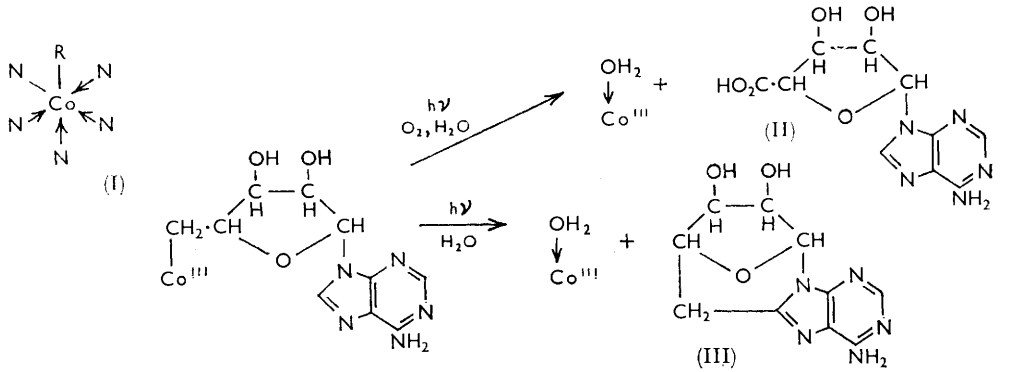
THE cobalt–carbon bond in the alkylcobalamins (partial structure I; the cobalamin chromophore is abbreviated to the five nitrogen atoms surrounding the cobalt atom) is readily split by photolysis of aqueous solutions and the subsequent fate of the fragments is consistent with the fission being homolytic in character. In presence of excess of oxygen, the cobalt-containing portion is obtained as hydroxocobalamin, containing trivalent cobalt, and the alkyl portion as an aldehyde or acid.[1] In the presence of a small amount of oxygen, photolysis of aqueous solutions of the alkylcobalamins yields vitamin B_{12r} containing divalent cobalt [2] and alkyl radicals which can be trapped by a radical acceptor such as a thiol [3] or allowed to produce stable products, *e.g.*, ethylene from ethylcobalamin or a mixture of methane and ethane from methylcobalamin.[1]

Similar reactions are observed during photolyses of the vitamin B_{12} coenzyme (I; R = 5′-deoxyadenosine). Photolysis of an aqueous solution of the coenzyme in presence of oxygen gives hydroxocobalamin and either the 5′-carboxylic acid [4] (II) or the 5′-aldehyde [5] of adenosine, whereas anaerobic photolysis yields vitamin B_{12r} and the cyclonucleoside (III), the so-called nucleoside A.[6]

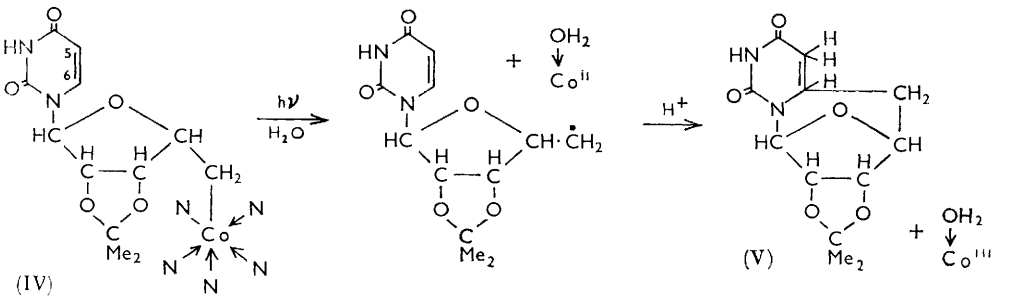
Anaerobic photolysis of 5′-deoxyinosylcobalamin [7] gave the cyclic nucleoside of hypoxanthine which was identical with the product obtained by the action of nitrous acid on

[1] Dolphin, Johnson, and Rodrigo, to be published.
[2] Hogenkamp, Barker, and Mason, *Arch. Biochem. Biophys.*, 1963, **100**, 353.
[3] Johnson, Shaw, and Wagner, *Biochem. Biophys. Acta*, 1963, **72**, 107.
[4] Johnson and Shaw, *J.*, 1962, 4608.
[5] Hogenkamp, Ladd, and Barker, *J. Biol. Chem.*, 1962, **237**, 1950.
[6] Hogenkamp, *J. Biol. Chem.*, 1963, **238**, 477.
[7] Johnson, Mervyn, Shaw, and Smith, *J.*, 1963, 4146.

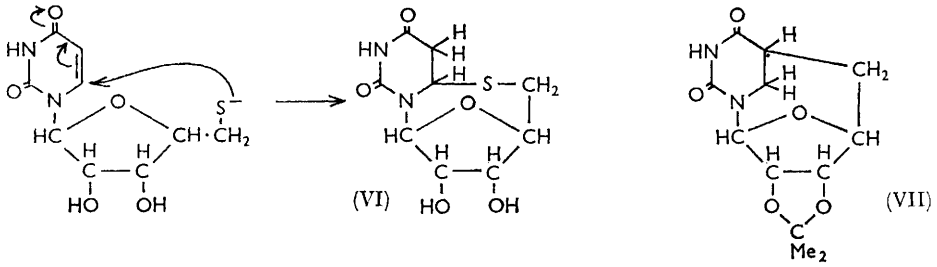
nucleoside A. In contrast to these results, the anaerobic photolysis of 5′-deoxy-2′,3′-isopropylideneuridinylcobalamin [7] (IV) has now been shown to give hydroxocobalamin (not vitamin B_{12r}) and a crystalline nucleoside which, on the basis of lack of the characteristic absorption maximum at 262 mμ, no longer contains the uracil chromophore. It appears



that the 5′-deoxyuridinyl free radical produced as the initial photolysis product, undergoes an intramolecular cyclisation by addition to the 5,6-double bond of the uracil ring. The resultant free radical is then reduced by vitamin B_{12r} to give 2′,3′-isopropylidenecyclodihydrouridine (V) and hydroxocobalamin. The structure of (V) is supported by its infrared and nuclear magnetic resonance spectra which indicate that the 5,6-double bond of uridine is no longer present in the product. The nuclear magnetic resonance spectrum of 2′,3′-isopropylideneuridine in deuterated dimethyl sulphoxide solution was measured and a doublet centred at τ 1·85 (J, 8·5 c./sec.) was associated with the olefinic proton at the pyrimidine C-6 position adjacent to the nitrogen atom. The pyrimidine C-5 proton appears as a quartet centred at τ 4·03. This consisted of a doublet (J, 8·2 c./sec.), caused by coupling with the C-6 proton, each component of the doublet being further split (J, 2·2 c./sec.) possibly by *m*-coupling with the diacylimino-group, the proton of which appeared as a broad singlet at τ −1·64. Other features of the spectrum included a doublet at 3·83 (1 proton; C-1′ of ribose group), a multiplet centred at 4·94 (2; C-2′ and C-3′ of ribose), a quartet centred at 5·7 (C-4′ of ribose) and a multiplet centred at 6·3 (2; C-5′ protons of ribose). The *gem*-dimethyl group was associated with 2 singlets at τ 8·42 and 8·64. In the cyclonucleoside (V), the spectrum, determined under similar conditions, contained a singlet at τ 4·12, which is associated with the C-1′ proton of the ribose chain. The lack of splitting of this band by the C-2′ proton (itself associated, together with the C-3′ proton, with a singlet, intensity 2, at τ 5·14) is ascribed to the modified shape of the cyclised nucleoside. Other features in this spectrum were multiplets at 5·39, 7·36, and 8·18 corresponding to the remaining pyrimidine and sugar protons and singlets at τ 8·53 and 8·65 (*gem*-dimethyl group) and −0·52 (imino-proton).



A related cyclisation has been reported [8] in the case of 5′-deoxy-5′-iodo-2′,3′-isopropylideneuridine, which with sodium hydrogen sulphide gave the cyclised product (VI). This, however, is an ionic reaction and the cyclisation would be expected to involve C-6 of the uracil ring both on steric and electronic grounds. Attack at C-6 has been assumed to occur also in the photolytic cyclisation but the alternative structure (VII) cannot be excluded entirely on the present evidence.



(VI) (VII)

The formation of cyclouridines of the anhydro-type [9] does not involve the 5,6-double bond of the uracil ring.

Experimental.—5′-Deoxy-2′,3′-isopropylideneuridinylcobalamin [7] (500 mg.) was dissolved in water (100 ml.) in the absence of light and the solution frozen. The pressure above the solid was reduced to 10^{-4} mm. and the solid melted. This process was repeated several times and then the solution was photolysed by irradiation for 12 hr. with a 40-watt bulb at a distance of 40 cm. The resulting solution was extracted with methylene dichloride (4 × 250 ml.) and the combined extract washed and dried. After removal of the solvent, the residue was crystallised from methanol; it formed plates (34 mg.; 40%) which could be sublimed at 210°/0·5 mm. (Found: C, 53·3; H, 5·95; N, 10·2. $C_{12}H_{16}N_2O_5$ requires C, 53·7; H, 6·0; N, 10·45%); $\lambda_{max.}$ ($CHCl_3$) 265 mμ (ε 119) (cf. uridine [10]: $\lambda_{max.}$ 262 mμ; ε, 9820); $\nu_{max.}$ (KBr disc) 1378, 1386, 1491, 1507, 1656, 1736, 1740, 2916, 2936, 2985, 3066, and 3187 $cm.^{-1}$. No absorption at 1617 $cm.^{-1}$, associated with the 5,6-double bond of the uracil ring,[8] was observed.

In another experiment, a solution of 5′-deoxy-2′,3′-isopropylideneuridinylcobalamin (1·42 mg.) in distilled water (10 c.c.) was degassed to 10^{-6} mm. and photolysed as before. The spectrum of the photolysis product (max. at 354 and 532 mμ) corresponded to that of hydroxocobalamin, and on treatment of the solution with alkaline cyanide, dicyanocobalamin was obtained, identified by its characteristic absorption max. at 367, 540, and 580 mμ.

We thank the D.S.I.R. for the award of maintenance grants (to D. O. and N. S.) and the University of Ceylon for granting study leave to one of us (R. R.).

Department of Chemistry, The University, Nottingham. [*Received, January 14th,* 1964.]

[8] Bannister and Kagan, *J. Amer. Chem. Soc.*, 1960, **82**, 3363.
[9] Fox and Wempen, *Adv. Carbohydrate Chem.*, 1959, **14**, 283; Codington, Fecher, and Fox, *J. Org. Chem.*, 1962, **27**, 163; Letters and Michelson, *J.*, 1961, 1410, and earlier refs.
[10] Ploeser and Loring, *J. Biol. Chem.*, 1949, **178**, 431.

784. *Fungicidal Activity and Chemical Constitution. Part XII.* Synthesis of 1-Fluoro-2,4-dinitronaphthalene.*

By D. R. Clifford and D. Woodcock.

The reported fungicidal activity of 1-chloro-2,4-dinitronaphthalene [1] and 1-fluoro-2,4-dinitrobenzene [2] against apple mildew, caused by *Podosphaera leucotricha* (Ell. & Everh.) Salm., made it desirable to prepare 1-fluoro-2,4-dinitronaphthalene for testing also against this plant pathogen.

Elias and Parker [3] first prepared this compound by nitration of 5-fluoro-1,2,3,4-tetrahydronaphthalene, followed by bromination at 100° with excess of liquid bromine, and subsequent dehydrobromination by heating at 180°. In our hands, 5-fluoro-1,2,3,4-tetrahydro-8-nitronaphthalene was also a major product of the nitration, and separation of the dinitro-derivative was extremely tedious. The last stage gave rise to much charring and the overall yield was so low that an improved method was sought. Attempts to prepare 1-fluoro-2,4-dinitronaphthalene from the corresponding 1-chloro-compound by halogen exchange in an aprotic solvent, using the method of Finger and Kruse [4] were unsuccessful despite the use of a variety of rigorously dried solvents and anhydrous potassium fluoride. The continual production of 2,4-dinitro-1-naphthol, despite all precautions, curiously resembles anomalous alcohol formation in the aprotic decomposition of a tosylhydrazine reported by Wilt and Schneider.[5] 1-Chloro-2,4-dinitronaphthalene can be prepared from 2,4-dinitro-1-naphthol by the action of toluene-*p*-sulphonyl chloride in diethylaniline,[6] but use of toluene-*p*-sulphonyl fluoride did not give 1-fluoro-2,4-dinitronaphthalene. Attempts to prepare this compound by the orthodox Schiemann reaction with 2,4-dinitro-1-naphthylamine, were prevented by diazo-oxide formation.

Nitration of 5-fluoro-1,2,3,4-tetrahydronaphthalene using nitronium fluoroborate in concentrated sulphuric acid, after the method of Kuhn and Olah,[7] gave the pure 6,8-dinitro-compound in reasonable yield. This is surprising since these authors imply that mononitration is usual even with excess of this reagent. Refluxing 5-fluoro-1,2,3,4-tetrahydro-6,8-dinitronaphthalene with *N*-bromosuccinimide in carbon tetrachloride solution, gave a dibromo-derivative which could be smoothly dehydrobrominated at 170° in sulpholane to give 1-fluoro-2,4-dinitronaphthalene.

Experimental.—5-Fluoro-1,2,3,4-tetrahydro-6,8-dinitronaphthalene. (*a*) Nitration of 5-fluoro-1,2,3,4-tetrahydronaphthalene (7·5 g.) [3] gave a viscous oil which was distilled. The first fraction, b. p. 130—140°/1 mm., crystallised frim ethyl alcohol to give pale yellow plates (2·25 g.), m. p. 64—65° (Found: C, 61·5; H, 5·15; N, 7·5. Calc. for $C_{10}H_{10}FNO_2$: C, 61·5; H, 5·1; N, 7·2%). This product did not depress the m. p. of, and had an identical infrared absorption curve to, 5-fluoro-1,2,3,4-tetrahydro-8-nitronaphthalene. The second fraction distilled with difficulty at 150—160°/0·005 mm. and crystallised from ethyl alcohol in needles (2·0 g.), m. p. 57—58° (Found: C, 50·0; H, 3·9; N, 11·6. Calc. for $C_{10}H_9FN_2O_4$: C, 50·0; H, 3·75; N, 11·7%). This product did not depress the m. p. of, and had an identical infrared absorption spectrum to, 5-fluoro-1,2,3,4-tetrahydro-6,8-dinitronaphthalene.

(*b*) 5-Fluoro-1,2,3,4-tetrahydronaphthalene (3 g. ≡ 2·1 ml.) was added dropwise during 10 min. to a stirred solution of nitronium fluoroborate (8 g.) in sulphuric acid (100%; 20 ml.) maintained at 20—30°. After 90 min. at 40°, the solution was poured on to crushed ice and the

* Part XI, Byrde, Clifford, and Woodcock, *Ann. Appl. Biol.*, 1962, **50**, 291.

[1] Soenen and Werotte, *Agricultura*, 1956, **4**, 421.
[2] Kirby and Frick, *Proc. 12th, Internat. Symp. on Crop Protection, Ghent*, 1960, 1215.
[3] Elias and Parker, *J.* 1962, 2616.
[4] Finger and Kruse, *J. Amer. Chem. Soc.*, 1956, **78**, 6034.
[5] Wilt and Schneider, *Chem. and Ind.*, 1963, 865.
[6] Ullmann and Bruck, *Ber.*, 1908, **41**, 3932.
[7] Kuhn and Olah, *J. Amer. Chem. Soc.*, 1961, **83**, 4570.

resulting yellow solid was crystallised from methyl alcohol (charcoal). It formed prisms (1·3 g.), m. p. 57—58° undepressed by an authentic specimen.

x-*Dibromo*-5-*fluoro*-1,2,3,4-*tetrahydro*-6,8-*dinitronaphthalene*. A solution of the above tetrahydro-compound (2·4 g.) in carbon tetrachloride (40 ml.) was refluxed with *N*-bromosuccinimide (4 g.; 2·2 equivs.) and benzoyl peroxide (0·3 g.) for 2 hr. The mixture was cooled and filtered, and the residual succinimide washed with carbon tetrachloride. The solvent was removed from the combined filtrate and washings under reduced pressure, and the residual gum triturated with and crystallised from methyl alcohol. The *dibromo-compound* formed stout prisms (3·8 g., 100%), m. p. 104–105° (Found: C, 30·3; H, 1·6; N, 7·2. $C_{10}H_7Br_2FN_2O_4$ requires C, 30·15; H, 1·8; N, 7·0%).

1-*Fluoro*-2,4-*dinitronaphthalene*.—A solution of the dibromo-compound (1 g.) in sulpholane (15 ml.) was heated at 170° for 6 hr. during which time a steady evolution of hydrogen bromide took place. The cooled mixture was poured into water, the product extracted with ether, and the extract washed with water and dried (Na_2SO_4). After removal of the solvent, the residual solid crystallised from benzene–light petroleum (b. p. 60—80°) (charcoal) in orange-yellow needles (0·5 g., 84%), m. p. 142—143° (Found: C, 51·1; H, 2·3; N, 11·7. Calc. for $C_{10}H_{15}FN_2O_4$: C, 50·9; H, 2·1; N, 11·9%). This compound did not depress the m. p. of an authentic specimen, and the infrared absorption spectra were identical.

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785. *The Synthesis of Aurantiacin.*

By R. L. Edwards and N. Kale.

Aurantiacin, isolated from the fungus *Hydnum aurantiacum* Batsch, has been identified as 2,5-dibenzoyloxy-3,6-di-*p*-hydroxyphenyl-1,4-benzoquinone through synthesis of its dimethyl ether.[1] Since this dimethyl ether cannot be demethylated without hydrolysis of the ester groups, and since no method for the selective esterification of the quinone hydroxyl groups has been reported we have synthesised aurantiacin through the corresponding acid labile di(methoxymethyl) ether.

Sodium *p*-nitrophenoxide with chlorodimethyl ether in toluene gave *p*-methoxymethoxynitrobenzene in good yield. Reduction of this nitro-compound to the amine proved troublesome. Considerable cleavage of the ether group occurred with platinum and hydrogen, and with palladised charcoal and hydrazine,[2] but a 75% yield of the required amine was obtained by using palladised charcoal and sodium borohydride.[3] The diazotised amine was condensed with 2,5-dichloro-1,4-benzoquinone in the presence of sodium acetate and the resultant arylated 2,5-dichloro-quinone was converted in turn into the 2,5-dihydroxy- and 2,5-dibenzoyloxy-compound. In all these reactions the methoxymethyl group remained intact. Aurantiacin was obtained quantitatively from the benzoate by warming it with dilute acid. Alternatively the dihydroxyquinone methoxymethyl ether gave a quantitative yield of atromentin with dilute acid.

Experimental.—p-*Methoxymethoxynitrobenzene*. Sodium ethoxide solution (23 g. sodium in 250 ml. alcohol) was added slowly with stirring to a solution of *p*-nitrophenol (139 g.) in hot toluene. The mixture was distilled to remove the alcohol; toluene was added during the distillation to keep the volume at 1 litre. The mixture was cooled to 10° and chlorodimethyl

[1] J. Gripenberg, *Acta Chem. Scand.*, 1956, **10**, 1111.
[2] Dewar and Mole, *J.*, 1956, 2556.
[3] Neilson, Wood, and Wylie, *J.*, 1962, 371.

ether (81 g.), added dropwise with stirring over 1·5 hr. After 12 hr. the solution was shaken with sodium hydroxide solution (250 ml.), the toluene layer washed twice with water, dried, and evaporated to remove the toluene. The residue was distilled *in vacuo* to yield p-*methoxymethoxynitrobenzene* (97 g.), b. p. 112°/0·6 mm. (Found: C, 52·3; H, 4·8; N, 7·5. $C_8H_9NO_4$ requires C, 52·5; H, 4·9; N, 7·6%).

p-*Methoxymethoxyaniline*. 10% Palladised charcoal (1 g.) was suspended in water (200 ml.), and sodium borohydride (15·6 g.) in water (300 ml.) was added. A slow stream of nitrogen was bubbled through the mixture and a solution of *p*-methoxymethoxynitrobenzene (36·6 g.) in alcohol (200 ml.) added dropwise during 15 min. with stirring and cooling to 5°. Stirring was continued for 15 min. and after filtration the mixture was evaporated under reduced pressure and then acidified with acetic acid. The mixture was extracted with ether and the ether layer washed with cold dilute hydrochloric acid. The base was liberated with alkali, and the solution was re-extracted with ether. Evaporation of the ether and distillation *in vacuo* yielded p-*methoxymethoxyaniline* (25 g.), b. p. 106°/0·8 mm. (Found: C, 62·6; H, 7·0; N, 9·2. $C_8H_{11}NO_2$ requires C, 62·75; H, 7·2; N, 9·1%).

2,5-*Dichloro*-3,6-*di*-p-*methoxymethoxyphenyl*-1,4-*benzoquinone*. *p*-Methoxymethoxyaniline (6·1 g.) in hydrochloric acid (11 ml. of acid plus 5 ml. of water) was diazotised below 5° with sodium nitrite (3 g. in 7 ml. of water). Sodium acetate was added until the solution was alkaline (Congo Red) and then the mixture was added to a solution of 2,5-dichloro-1,4-benzoquinone (7·1 g. in 800 ml. of alcohol) at 5°. The dark red solution was set aside overnight and the precipitate of 2,5-*dichloro*-3,6-*di*-p-*methoxymethoxyphenyl*-1,4-*benzoquinone* crystallised from acetic acid as red needles (4·6 g.), m. p. 212° (Found: C, 58·8; H, 3·7; Cl, 15·6. $C_{22}H_{18}Cl_2O_6$ requires C, 58·8; H, 4·0; Cl, 15·8%).

2,5-*Dihydroxy*-3,6-*di*-p-*methoxymethoxyphenyl*-1,4-*benzoquinone*. 2,5-Dichloro-3,6-di-*p*-methoxymethoxyphenyl-1,4-benzoquinone (0·5 g.) was suspended in a mixture of methanol (25 ml.) and sodium hydroxide solution (25 ml.; 2N). Heating on the water-bath for 1·5 hr., filtration, and acidification with acetic acid yielded 2,5-*dihydroxy*-3,6-*di*-p-*methoxymethoxyphenyl*-1,4-*benzoquinone*. This compound could be crystallised from pyridine as orange needles which turn brown in air with loss of pyridine or as brown rods from acetic acid (0·29 g.), m. p. 230° (from acetic acid) (Found: C, 63·8; H, 5·1. $C_{22}H_{20}O_8$ requires C, 64·1; H, 4·85%). This quinone (70 mg.), in hot acetic acid (10 ml.) was treated with sulphuric acid (2 drops; 2N), and the mixture was cooled slowly. Red-brown plates of *atromentin* (54 mg.) were deposited. The infrared spectrum was identical with that of a sample prepared from the methyl ether.[4]

2,5-*Dibenzoyloxy*-3,6-*di*-p-*hydroxyphenyl*-1,4-*benzoquinone* (*Aurantiacin*). Benzoyl chloride (5 drops) was added to 2,5-dihydroxy-3,6-di-*p*-methoxymethoxyphenyl-1,4-benzoquinone (0·2 g.) in warm pyridine (2·5 ml.). The purple solution turned red after 2—3 min. and crystals of benzoic acid were deposited; these were filtered off and the filtrate was poured into water. The yellow precipitate of 2,5-*dibenzoyloxy*-3,6-*di*-p-*methoxymethoxyphenyl*-1,4-*benzoquinone* crystallised from acetic acid as golden yellow needles (0·19 g.), m. p. 239° (Found: C, 69·85; H, 4·6. $C_{36}H_{28}O_{10}$ requires C, 69·7; H, 4·5%).

Sulphuric acid (3 drops; 2N) was added to a solution of the benzoate (0·1 g.) in hot acetic acid (8 ml.). After being boiled for 2—3 min. the solution turned red-brown, and brown needles (46 mg.) of *aurantiacin*, m. p. 305—308°, were deposited (lit.,[1] 285—295°) (Found: C, 72·4; H, 3·7. $C_{32}H_{20}O_8$ requires C, 72·2; H, 3·8%). In both samples the infrared frequencies were identical, but considerable variation in band intensities occurred throughout the spectrum. The intensity of the ester C=O (1736 cm.$^{-1}$) and quinone C=O (1670 cm.$^{-1}$) were almost identical in the synthetic sample but in the authentic material the intensity of the quinone carbonyl absorption was only about one third that of the ester.

We thank Dr. Jahl Gripenberg for providing a sample of authentic aurantiacin for comparative purposes and the Governors of Bradford Institute of Technology for a research scholarship (to N. K.).

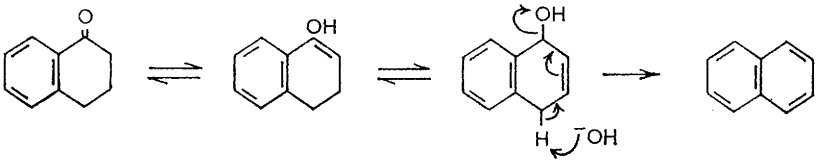
Department of Chemical Technology,
Bradford Institute of Technology, Bradford 7. [*Received, February 6th*, 1964.]

[4] Edwards, Keighley, and Lewis, *J. Appl. Chem.*, 1960, **10**, 246.

786. *A Direct Conversion of α-Tetralone into Naphthalene.*

By A. J. Birch and D. A. White.

The well-known base-catalysed dehydration of 1,2,3,4-tetrahydro-2-naphthol [1] to 1,2-dihydronaphthalene is one example of reactions which are initiated by removal of a benzylic or allylic proton. Examination of the action of base on the isomeric 1,2,3,4-tetrahydro-1-naphthol showed the formation of considerable amounts of naphthalene and it was thought that this might arise from α-tetralone. Indeed, the alkali-fusion of the latter gave



naphthalene in 58% yield; the mechanism is considered to be that shown. This is supported by the fact that 1-ethoxy-3,4-dihydronaphthalene on reaction with potassamide in liquid ammonia also gives naphthalene.

Since tetralone derivatives are frequent intermediates in the synthesis of aromatic compounds, this process may have some practical utility.

Experimental.—α-Tetralone (146 mg.) was heated at 220° for 5 hr. with a 1 : 1 mixture (47 mg.) of sodium and potassium hydroxide. Naphthalene sublimed on to the cooler part of the tube and was collected and recrystallised; it (75 mg.) had m. p. 80·5—81° undepressed by an authentic specimen.

α-Tetralone (3·7 g.) in ethanol (3·5 c.c.) and ethyl orthoformate (5 c.c.) containing toluene-*p*-sulphonic acid was left for 12 hr. The mixture was made alkaline with sodium ethoxide and distilled, the fraction, b. p. 120—130°/10 mm. being collected. The infrared spectrum showed that this was a mixture of starting material and 1-ethoxy-3,4-dihydronaphthalene, which was separated by chromatography on alumina (Spence H), the latter being eluted first with pentane; as an oil (1·47 g.). The structure was confirmed by the proton magnetic resonance spectrum τ 8·61 (3H, triplet, Me of ethyl group), τ 7·3—7·7 (4H, complex, H in 3- and 4-positions), τ 6·16 (2H, quartet, CH_2 of ethyl group), τ 5·16 (1H, triplet, H on aliphatic double-bond), and τ 2·5—3·0 (4H, complex, H on aromatic ring). It was very unstable, even in the refrigerator. The enol-ether gave no naphthalene with sodium methoxide in methanol, but when the oil (962 mg.) was treated with potassamide [from the metal (1·0 g.)] in liquid ammonia (100 c.c.) for 1 hr. the sole product was naphthalene. Similar reaction of α-tetralone itself gave no naphthalene.

We are indebted to the D.S.I.R. for a scholarship (to D. A. W.).

Department of Chemistry, University of Manchester. [*Received, March 13th*, 1964.]

[1] Straus and Lemmel, *Ber.*, 1921, **54**, 34.

787. *The Fluorotellurates*(IV).

By A. J. Edwards, M. A. Mouty, R. D. Peacock, and A. J. Suddens.

Although pentafluoroselenates(IV) have been prepared,[1] no reports of fluorotellurates(IV) appear in the recent literature. Early workers tried to show that complex tellurium fluorides are formed when tellurium dioxide is dissolved in concentrated hydrofluoric acid and alkali fluoride added,[2] but the evidence is conflicting and there is little doubt that some of the products contained water and that others were complex oxide fluorides. The present work developed from an observation of Campbell and Robinson,[3] who showed that tellurium dioxide reacts with liquid selenium tetrafluoride to give tellurium tetrafluoride and selenium oxide difluoride.

Experimental.—Selenium tetrafluoride was prepared from the elements according to the method of Aynsley, Peacock, and Robinson.[1]

Pentafluorotellurates(IV). A mixture of tellurium dioxide and alkali fluoride (about 1 g.), with the former in slight excess, was dissolved in warm selenium tetrafluoride (10 ml.). When the solution was allowed to cool colourless crystals of the complex fluoride appeared. The

$$TeO_2 + MF + 2SeF_4 \longrightarrow MTeF_5 + 2SeOF_2 \ (M = K, Rb, Cs)$$

excess of solvent was pumped off under a vacuum at 25°. When the residue was nearly dry, the temperature was raised gradually to 150° to remove both the remaining traces of solvent and the surplus tellurium tetrafluoride. The crystalline *products* were stored under a dry atmosphere (Found: Te, 48·2; F, 36·2. $KTeF_5$ requires Te, 48·8; F, 36·3%. Found: Te, 40·8; F, 30·6. $RbTeF_5$ requires Te, 41·4; F, 30·8%. Found: Te, 35·6; F, 27·4. $CsTeF_5$ requires Te, 35·9; F, 26·7%). A sodium salt was formed but was not obtained pure.

Attempted preparation of hexafluorotellurates(IV). (1) Potassium pentafluorotellurate(IV) was heated to 450° under a vacuum in a nickel tube. No weight-loss occurred, and a Debye *X*-ray photograph indicated that the material was unchanged. (2) Potassium pentafluorotellurate(IV) was fused at just below red heat with the stoicheiometric amount of potassium fluoride required to form the hexafluorotellurate(IV). A Debye *X*-ray photograph showed that the residue was a mixture of potassium fluoride and potassium pentafluorotellurate(IV). (3) A mixture of potassium fluoride and tellurium dioxide in the molar proportions 2 : 1 was treated as before with warm selenium tetrafluoride. A Debye *X*-ray powder photograph showed the residue to contain potassium pentafluorotellurate(IV) and potassium pentafluoroselenate(IV), and chemical analysis showed tellurium and selenium to be present.

Debye X-ray powder photographs. Samples were mounted in evacuated Pyrex capillaries by methods described previously, and photographs were taken with Cu-K_α radiation using a 19-cm. Hilger and Watts powder camera.

Infrared spectra. A thin layer of the dry, powdered sample was mounted between potassium bromide discs in a dry-box. Measurements were made using a Perkin-Elmer Infracord spectrometer (potassium bromide region) and a Perkin-Elmer model 21 spectrometer (sodium chloride region).

Analysis. Tellurium was determined gravimetrically as the dioxide or as the element. Fluorine was estimated volumetrically as the chloride equivalent by the Volhard procedure after distillation from aqueous sulphuric acid and precipitation as lead chlorofluoride.

Discussion.—The only series of fluorotellurates(IV) isolated is the quinqueco-ordinated series containing the TeF_5^- anion, and it does not seem that the sexico-ordinated ion TeF_6^{2-}, expected by analogy with the other complex halides of tellurium, is stable. The pentafluorotellurates(IV) are less reactive than the pentafluoroselenates(IV), but they decompose in moist air and are immediately hydrolysed in water Although the salts are crystalline

[1] Aynsley, Peacock, and Robinson, *J.*, 1952, 1231.
[2] Matzner, *Ann. Chim. Phys.*, 1898, **15**, 203.
[3] Campbell and Robinson, *J.*, 1956, 785.

and give, with the exception of the sodium salt, well resolved *X*-ray powder patterns, it has not proved possible to determine the unit-cell symmetry.

It is to be expected on general grounds that the pentafluorotellurate(IV) ion will prove to have a square-pyramidal configuration like the isoelectronic iodine pentafluoride molecule [4,5] and the pentafluoroantimonate(III) ion.[6] Information about symmetry, in the absence of resolvable *X*-ray data, may usefully be obtained from infrared measurements, and these are recorded in the Table. The probable symmetry (C_{4v}) calls for the appearance

Infrared absorption frequencies ($cm.^{-1}$).

IF_5	721 (A_1), 712m (A_1), 703 (A_1), 645s (E), 372m (E), 318m (A_1) (ref. 5)
$Cs(Rb)TeF_5$	1030m, 642ms sh (E), 627s (E), 475vs br (E) (Present work)
K_2SbF_5	740w (A_1), 558s (E) (Present work)

of six infrared frequencies, and in addition there should be some correspondence between the frequencies observed for isoelectronic molecules and ions. Fewer frequencies are actually obtained, but taking account of the lower limit of the instruments available (400 $cm.^{-1}$), and the fact that measurements were made using solids, this is to be expected. There is not an obvious relationship between the recorded spectrum of iodine pentafluoride and the fluorotellurate(IV) or fluoroantimonate(III) ions, but we have made a tentative assignment of frequencies, mainly on the basis of relative intensities

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Department of Chemistry, University of Birmingham,
Birmingham 15. [*Received, April 20th,* 1964.]

[4] Gutowsky and Hoffmann, *J. Chem. Phys.*, 1951, **19**, 1259.
[5] Lord, Lynch, Schumb, and Slowinski, *J. Amer. Chem. Soc.*, 1950, **72**, 522.
[6] Bystrom and Wilhelm, *Arkiv Kemi*, 1951, **3**, 461.