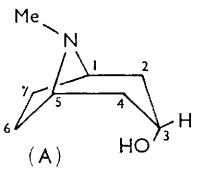
NOTES

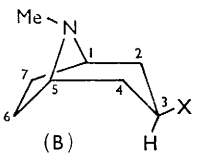
628. *The Conformations of Tropine and 3-Halogenotropanes and their Hydrohalides as Solutes*

By C.-Y. CHEN and R. J. W. LE FÈVRE

ECKERT AND LE FÈVRE [1] recently concluded from polarisation and polarisability measurements that tropine (I), 3-bromotropane (II), and 3-chlorotropane (III) are appropriately represented by (A) and (B), respectively. However, these authors pointed out that their assignments depended crucially on the stereochemistry of the ROH ⟶ RX reactions,

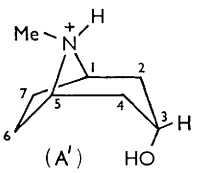


(A)

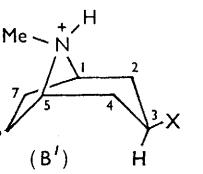


(B)

X = Br for (II)
= Cl for (III)



(A′)



(B′)

X = Br for (V)
= Cl for (VI)

i.e., on the relationship of bromo- and chloro-tropane to pseudotropine, and that the tropine ⟶ halogenotropane substitutions should occur with inversion.[2,3] We now report further physical evidence which supports the above conformations, gives information on the hydrohalides of these molecules, and confirms the occurrence of inversion in the tropine ⟶ halogenotropane transformations.

The proton magnetic resonance (p.m.r.) spectrum of tropine (I) at 60 Mc. is shown in Figure 1. Its most interesting feature is the pseudo-triplet arising from the C-3 proton at τ 6·23 p.p.m. An enlargement of the triplet is given in Figure 2.

From the symmetry of the molecule, the C-3 proton of (I) is expected to give rise to the X-part of two ABX systems with spacing between the terminal lines equal to $2(J_{AX} + J_{BX})$. (Long-range and virtual couplings are neglected; however, such simplification will not affect our conformational assignments.) When $\delta_{AB} \geqslant 20$ c./sec. and $J_{AX} \gg J_{BX}$, the X-part of two ABX systems should exhibit a 9-line spectrum [4,5] from which the exact coupling constants can be extracted; when $J_{AX} = J_{BX}$, the X-part should degenerate into a 5-line spectrum, with the spacing between neighbouring lines equal to J_{AX} or J_{BX}. On the other hand, when J_{AX} is nearly but not exactly equal to J_{BX}, the situation is much more complicated, especially if δ_{AB} is less than 20 c./sec.; nevertheless, it is certain that the C-3 proton of (I) cannot involve a " trans-" coupling, $J_{180°}$, which is of

[1] J. M. Eckert and R. J. W. Le Fèvre, *J.*, 1962, 784.
[2] Sir C. K. Ingold, " Structure and Mechanism in Organic Chemistry," Cornell Univ. Press, Ithaca, 1953, p. 393.
[3] C. W. Shoppee, *J.*, 1946, 1138, 1147.
[4] F. A. L. Anet, *J. Amer. Chem. Soc.*, 1962, **84**, 1054.
[5] D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.*, 1964, **86**, 2742.

the order of 10 c./sec.; therefore, the C-3 proton must be equatorially attached to a six-membered ring.[5,6] Furthermore, the half-width and the base-width of the pseudo-triplet are 9·8 and 16·8 c./sec., respectively, *i.e.*, almost exactly the same as the partial spectrum of the C-4 proton of the β-isomer of 1-methyl-2,6-diphenylpiperidin-4-ol. Since the last named compound has already been proven [7] to have the C-4 proton equatorial, there should be little doubt that the C-3 proton in tropine (I) is also equatorial. The spectral

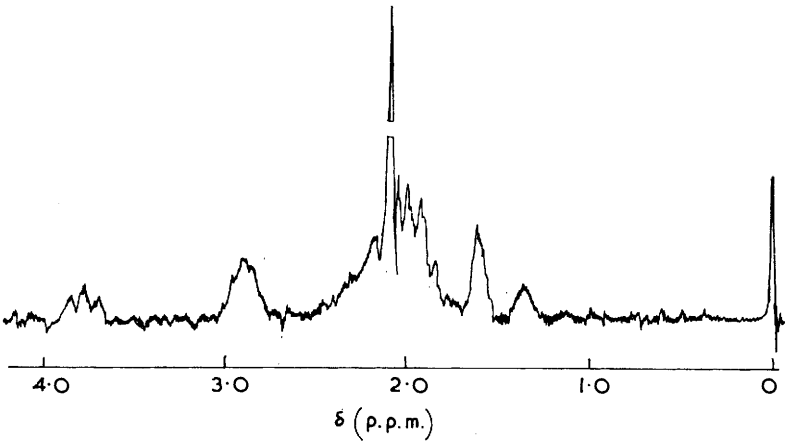


FIGURE 1. The p.m.r. spectrum of tropine (I) in deuteriochloroform

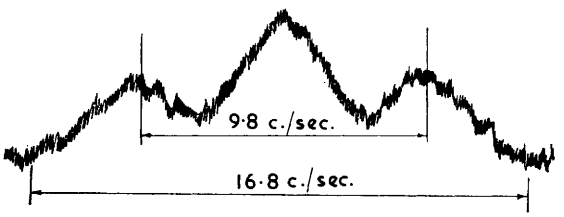


FIGURE 2. The pseudo-triplet arising from the C-5 proton of tropine (I)

similarity between these two compounds indicates that long-range and/or virtual couplings are unimportant when the proton concerned has an equatorial disposition. In addition, the C-1 and C-5 protons of (I) give a broad and poorly resolved signal at τ 7·11 p.p.m. The half-width and the base-width (9·5 and 18·0 c./sec.) of this signal require that no "eclipsed" coupling [8] is included; hence the piperidine ring must be present as a chair form. Thus, tropine (I) is shown by its p.m.r. spectrum to be represented by (A).

Such a molecular skeleton is evidently retained by the cation of tropine hydrochloride (IV), in deuterium oxide solutions, since the p.m.r. spectrum of (IV) in D_2O shows two bands, one at τ 6·11 p.p.m. and the other at τ 5·87 p.plm. corresponding to the C-1 and C-5 protons and the C-3 proton, the half-widths and the base-widths of these two bands (9·9, 17·5, 10·4, 16·3 c./sec.) being essentially the same as those from the free base, although the protonation of the lone-pair on the nitrogen atom makes the spectrum more complicated causing an envelope for the C-1 and C-5 protons and an apparent 7-line splitting for the C-3 proton. It has been shown [9] that the more stable isomer of the 3-substituted tropane deuteriohalides is the one which has the *N*-methyl group in an equatorial position; the conformation of the cation of (IV) should, then, be (A'), as illustrated.

As for the p.m.r. spectra of 3-bromotropane (II), 3-bromotropane hydrobromide (V), 3-chlorotropane (III), and 3-chlorotropane hydrochloride (VI), the pertinent information is summarised in the Table. The marked broadening of the C-3 proton signals listed in

[6] A. C. Huitric, J. B. Carr, W. F. Trager, and B. J. Nist, *Tetrahedron*, 1963, **19**, 2145.
[7] C.-Y. Chen and R. J. W. Le Fèvre, preceding Paper.
[8] R. U. Lemieux and J. W. Lown, *Canad. J. Chem.*, 1964, **42**, 893, and references therein; see also K. L. Williamson, *J. Amer. Chem. Soc.*, 1963, **85**, 516.
[9] G. L. Closs, *J. Amer. Chem. Soc.*, 1959, **81**, 5456.

Proton magnetic resonance data for compounds (II), (V), (III), and (VI)

Compound	Chemical shifts [a] (τ, in p.p.m.) C-3 proton [b]	C-1 and C-5 protons [c]
(II)	5·82 { half-width 28 c./sec. / base-width 34 c./sec.	6·85 { half-width 9·6 c./sec. / base-width 21 c./sec.
(V)	5·47 { half-width 27 c./sec. [d] / base-width 34 c./sec.	6·10 { half-width 10·2 c./sec. / base-width 20 c./sec.
(III)	5·85 { half-width 26 c./sec. / base-width 35 c./sec.	6·79 { half-width 9·8 c./sec. / base-width 20 c./sec.
(VI)	5·55 { half-width 26 c./sec. [d] / base-width 34 c./sec.	6·05 { half-width 9·7 c/sec. / base-width 21 c./sec.

[a] Chemical shifts quoted are believed to be accurate to within 0·02 p.p.m. [b] Half-widths and base-widths are subjected to errors of ±1 c./sec. due to extensive splitting. [c] The widths quoted are accurate to ±0·3 c./sec. for half-widths, and ±0·5 c./sec. for base-widths. [d] Signal partially obscured.

the Table reveals that the C-3 protons in the compounds (II), (V), (III), and (VI) must be in axial dispositions.[10] The half-widths of the C-1 and C-5 signals once more demands that the piperidine ring be in a chair form. Owing to the presence of an axial C-3 proton, long-range and virtual coupling would be echanced [11,12] and, therefore, the base-line widths of the C-1 and C-5 signals (centred around 20 c./sec.) from the compounds (II), (V), (III), and (VI) are somewhat larger than those in the spectra of tropine (I) and its hydrochloride (IV). All this evidence points unambiguously to the conformations of 3-bromotropane (II), 3-chlorotropane (III), and the corresponding hydrohalides, being represented properly by (B) and (B'), and to the tropine ⟶ halogenotropane reactions occurring with inversion, as previously established from chemical considerations.[2,3]

Experimental.—The samples used were those of ref. 1. The spectra were recorded with a Varian A-60 spectrometer operating at 40°. The free bases were dissolved in deuteriochloroform ($CDCl_3$) with tetramethylsilane added as internal reference. The hydrohalides were dissolved in deuterium oxide with 3-trimethylsilylpropane-1-sulphonic acid sodium salt as internal reference. The concentration of the solutions used was *ca.* 5—7% (w/v).

The authors thank Mr. C. D. Dehlsen for running the p.m.r. spectra, and one of them (C-Y. C.) is grateful to the University of Sydney for a Research Studentship.

UNIVERSITY OF SYDNEY, N.S.W., AUSTRALIA. [*Received, December 7th*, 1964.]

[10] H. M. van Dort and Th. J. Sekuur, *Tetrahedron Letters*, 1963, 1301.
[11] J. I. Musher and E. J. Corey, *Tetrahedron*, 1962, **18**, 791.
[12] B. Waegell and C. W. Jefford, *Bull. Soc. chim. France*, **1964**, 844.

629. *Macrocyclic Musk Compounds. Part VII.* New Syntheses of Civetonedicarboxylic Acid and its Conversion into* trans-*Civetone*

By K. K. CHAKRAVARTI, U. G. NAYAK, S. C. BHATTACHARYYA, and (in part) V. K. BALAKRISHNAN and R. K. RAZDAN

CIVETONEDICARBOXYLIC ACID (III), is a key intermediate in the synthesis of civetone,[1,2] and is normally obtained from methyl (or ethyl) hydrogen azelate. We now report a convenient preparation of the ethyl half-ester from oleic acid and a number of new routes to (III).

$R{\cdot}[CH_2]_7{\cdot}CO_2H$ (I) $\quad R{\cdot}[CH_2]_7{\cdot}CO{\cdot}[CH_2]_7{\cdot}R$ (II) $\quad HO_2C{\cdot}[CH_2]_7{\cdot}CO{\cdot}[CH_2]_7{\cdot}CO_2H$ (III)

a: R = $CH_3{\cdot}C{\vdots}C-$ c: R = $CH_3{\cdot}[CH_2]_7{\cdot}CH{:}CH-$
b: R = $CH_3{\cdot}CH{:}CH-$ d: R = $CH_3{\cdot}[CH_2]_7{\cdot}CH(OH){\cdot}CH(OH)-$

* Part VI, M. S. R. Nair, H. H. Mathur, and S. C. Bhattacharyya, *J.*, 1964, 4154.

[1] Hunsdiecker, *Ber.*, 1943, **76**, 142; Blomquist, Holley, and Spencer, *J. Amer. Chem. Soc.*, 1948, **70**, 34; Stoll, Hulstkamp, and Rouve, *Helv. Chim. Acta*, 1948, **31**, 543; Mathur and Bhattacharyya, *J.*, 1963, 114.
[2] Stoll, *Helv. Chim. Acta*, 1948, **31**, 143.

Undec-9-ynoic acid (Ia), undec-*cis*-9-enoic acid (Ib), oleic acid (Ic), and the diacetate of *threo*-9,10-dihydroxy stearic acid (Id), were converted, *via* the acid chlorides, into the ketones (IIa—d) by Blomquist's method.[3] Ketones (IIa—c) were also prepared by Claisen condensation [4] of the ethyl esters of (Ia—c). Partial reduction of (IIa) gave (IIb) and hydroxylation of (IIc) gave (IId). Oxidation of the ketones (II) under appropriate conditions gave (III), which was converted into *trans*-civetone by a slight modification of Stoll's procedure.[2]

Experimental.—Ethyl hydrogen azelate. Hydroxylation [5] of oleic acid (282 g.) with peracetic acid gave *threo*-9,10-dihydroxystearic acid (205 g.), m. p. 89—90°. The ethyl ester (86 g.; m. p. 60°) of the latter was oxidised in aqueous ethanol with sodium metaperiodate (54 g.) giving nonal (34 g.) and ethyl ω-formyloctanoate (46 g.), b. p. 93—102°/0·4 mm. Oxidation of the aldehyde (70 g.) in acetone (500 ml.) and acetic acid (25 ml.) with potassium permanganate (40 g.) in water (500 ml.) led to the required half-ester (62 g.), b. p. 130—135°/0·3 mm., n_D^{25} 1·4420.

Pentatriconta-9,26-*dien*-18-*one* (IIc).[6] A mixture of ethyl oleate (100 g.), anhydrous xylene (100 ml.), and sodium ethoxide [from sodium (10 g.)] was heated at 120—140° and then slowly distilled in vacuum during 6 hr. to remove xylene along with the alcohol formed. The resultant β-keto-ester was refluxed (without isolation) with ethanolic potassium hydroxide (150 ml.; 5%) for 2 hr. The neutral product on extraction with ether and processing yielded (IIc; 70 g.) as a thick pale yellow liquid which solidified on cooling at 0°.

Alternatively, oleoyl chloride, prepared from oleic acid (10 g.) with thionyl chloride (5 ml.), was treated (30°, 48 hr., nitrogen atmosphere) with anhydrous benzene (100 ml.) containing triethylamine (5 g.). After separation of the precipitated triethylamine hydrochloride, benzene was distilled off; the residual keten dimer was hydrolysed by refluxing with ethanolic potassium hydroxide (100 ml.; 20%) for 2 hr. and processed as usual to yield the *ketone* (IIc; 10 g.) (Found: C, 83·7; H, 12·7. $C_{35}H_{22}O$ requires C, 83·6; H, 13·2%).

9,10,25,26-*Tetrahydroxypentatricontan*-18-*one* (IId). The chloride of 9,10-diacetoxystearic acid (10 g.) on treatment with triethylamine (5 g.) in anhydrous benzene (200 ml.) and further processing as for (IIc) gave in the neutral portion 9,10,25,26-*tetrahydroxypentatricontan*-18-*one*, m. p. 104—105° (from alcohol). The tetraol (18 g.) was also obtained by hydroxylation of (IIc; 15 g.) in chloroform (50 ml.) with peracetic acid in chloroform (20 ml.; 60%) at 20—25° under stirring for 24 hr., followed by refluxing with alcoholic potassium hydroxide (100 ml.; 10%) for 2 hr. and crystallisation from alcohol (Found: C, 73·5; H, 12·02. $C_{35}H_{70}O_5$ requires C, 73·6; H, 12·4%).

Heneicosa-2,18-*dien*-11-*one* (IIb). Undec-9-ynoic acid (Ia) and undec-9-enoic acid (Ib) were prepared according to the method of Ames and Bowman.[7] The acid chloride of the acid (Ib, 2 g.) with triethylamine (1·5 g.) in anhydrous benzene (100 ml.) after the usual processing yielded *heneicosa*-2,18-*dien*-11-*one* (1·2 g.), m. p. 60° (from alcohol).

Claisen condensation followed by hydrolysis converted ethyl undec-9-enoate (50 g.), with sodium ethoxide (8 g.) and xylene (200 ml.), into the same ketone (30 g.) (Found: C, 82·1; H, 12·2. $C_{21}H_{38}O$ requires C, 82·3; H, 12·5%).

Heneicosa-2,18-*diyn*-11-*one* (IIa). The chloride from the acid (Ia), on subjection to the keten-dimerisation procedure, yielded *heneicosan*-2,18-*diyn*-11-*one*, m. p. 61° (from alcohol) (Found: C, 83·4; H, 11·3. $C_{21}H_{34}O$ requires C, 83·4; H, 11·3%). On hydrogenation in the presence of palladised calcium carbonate it gave (IIb), m. p. 60°.

9-*Oxoheptadecanedioic acid* (III). (i) The acid chloride (58 g.; b. p. 108—110°/0·3 mm.) obtained from ethyl hydrogen azelate (54 g.) and thionyl chloride (32 g.), on subjection (30°; 48 hr.) to the keten dimerisation reaction in nitrogen, using triethylamine (39 ml.) in anhydrous benzene (700 ml.), followed by separation of triethylamine hydrochloride by filtration, removal of benzene by distillation, hydrolysis of the residue with ethanolic potassium hydroxide (250 ml.; 20%) for 3 hr., removal of alcohol by distillation, and subsequent acidification, gave the dicarboxylic acid (III; 33 g.) m. p. 114° (from benzene).

[3] Blomquist *J. Amer. Chem. Soc.*, 1952, **74**, 4203; Sauer, *ibid.*, 1947, **69**, 2444.
[4] Briese and McElvin, *J. Amer. Chem. Soc.*, 1933, **55**, 1697.
[5] King, *J.*, 1938, 1826.
[6] Hatt and Lamberton, *Austral. J. Chem.*, 1955, **8**, 506.
[7] Ames and Bowman, *J.*, 1952, 677; Krafft, *Ber.*, 1896, **29**, 2234; Colland, *Helv. Chim. Acta*, 1943, **26**, 1064.

(ii) Ozonisation (2 hr.) of the dienone (IIc, 5 g.; or IIb, 2 g.) in carbon tetrachloride (50 ml.), removal of solvent, decomposition of the ozonide with water on a steam-bath, removal of nonal (in the case of IIc) by steam-distillation, and oxidation of the residual keto-dialdehyde in acetone (50 ml.) with potassium permanganate also gave the dicarboxylic acid (III) (60%).

(iii) The dicarboxylic acid was also obtained by oxidising the tetraol (IId; 5 g.) in ethanol (100 ml.) with an aqueous solution of sodium metaperiodate (5 g.), extracting with ether, removing nonal by steam-distillation, and oxidising the residue with permanganate in acetone solution. The product had m. p. 114° (from alcohol) (Found: C, 64·9; H, 9·65. Calc. for $C_{17}H_{30}O_5$: C, 64·9; H, 9·6%).

trans-*Civetone*. Diethyl 9-oxoheptadecanedioate (370 g.), m. p. 54°, in benzene (3·75 l.) was ketalised with ethylene glycol (200 g.) and toluene-*p*-sulphonic acid (2 g.). Acyloin condensation of the ethylene ketal (275 g.) in xylene (7 l.) with sodium (70 g.) gave the ethylene ketal of 17-hydroxyheptadecane-1,9-dione (170 g.). The product (244 g.) was directly reduced with lithium aluminium hydride (17 g.) in ethereal solution to the ethylene ketal of 9-oxo-1,17-heptadecanediol (240 g.), m. p. 93—94° [from ether–light petroleum (b. p. 40—60°)]. The ketal diol (328 g.), without crystallisation, was treated with hydrogen bromide in acetic acid and acetic anhydride, and then with zinc and methanol, giving *trans*-civetone, b. p. 128—132°/0·0001 mm.; semicarbazone, m. p. 182—183°; $\nu_{max.}$ 1706, 1410, and 963 cm.$^{-1}$.

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630. *The Viscosities of Solutions of Acids in Tri-n-butyl Phosphate*

By A. S. Kertes and P. J. Lloyd

In a recent Article, Tuck[1] has correlated the viscosities of extract solutions of mineral acids in tri-n-butylphosphate (TBP) with the structure of the acid complexes in the organic phase. It was shown that there is a continuous increase in viscosity with increasing concentration of the stronger mineral acids, hydrochloric, hydrobromic, and perchloric, but that variations in viscosity at similar organic loadings were slight when the weaker nitric and trichloroacetic acids were extracted. With the strong acids, it seemed probable that the acid complex was of the form solvated-$(H_9O_4)^+X^-$, where X^- is Cl^-, Br^-, or ClO_4^-. The increase in viscosity was therefore ascribed to " an increasing number of strong interactions between these ion-paired species with increasing acid concentration " and to the bulky nature of the cation. The weaker nitric and acetic acids apparently form TBP,HX, which may be slightly hydrated at low concentrations.[2,3] As these species are apparently not ion-paired [1,3] and of relatively small size, the viscosity remains low.

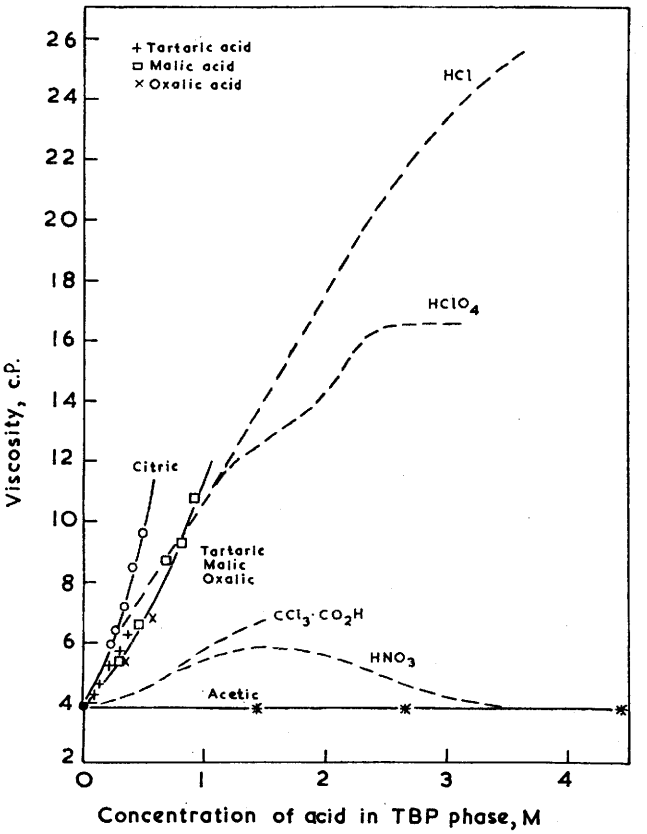
Work on the extraction of the organic acids, citric,[4] malic,[5] tartaric,[5] trihydroxyglutaric,[6] oxalic,[7] and acetic,[7] into undiluted tributyl phosphate has indicated that the acids are probably extracted as $3TBP,2H_2O,C_3H_4(OH)(CO_2H)_3$; $2TBP,H_2O,C_2H_2(OH)_2(CO_2H)_2$; $2TBP,1{\cdot}5H_2O,C_2H_3(OH)(CO_2H)_2$; $2TBP,C_3H_3(OH)_3(CO_2H)_2$; $2TBP,H_2O,(COOH)_2$; and $TBP,H_2O,CH_3{\cdot}COOH$, respectively. In each case, each replaceable hydrogen is apparently solvated by a single tributyl phosphate molecule. Some water is evidently present in one or more of these $CO_2H \longrightarrow TBP$ bonds.

The species formed in the extraction of the polybasic acids must be quite large, and so would be expected to have a marked influence upon the viscosity of the tributyl phosphate extract phases. It was therefore of interest to study the viscosity behaviour of extract solutions of these compounds in an attempt to substantiate further the hypotheses advanced by Tuck.

[1] D. G. Tuck, *J.*, 1963, 3905.
[2] E. Hesford and H. A. C. McKay, *J. Inorg. Nuc. Chem.*, 1960, **13**, 156.
[3] D. G. Tuck, *Trans. Faraday Soc.*, 1961, **57**, 1297.
[4] Z. N. Tsvetkova and N. S. Povitskii, *Russ. J. Inorg. Chem.*, 1960, **5**, 1364.
[5] V. B. Shevchenko and E. V. Renard, *Russ. J. Inorg. Chem.*, 1963, **8**, 268.
[6] V. B. Shevchenko, E. V. Renard, and A. S. Solovkin, *Russ. J. Inorg. Chem.*, 1960, **5**, 1138.
[7] K. Naito and T. Suzuki, *J. Phys. Chem.*, 1962, **66**, 983.

The variation in the viscosity of the extract solutions with concentration of the solute is shown in the Figure, molar concentrations are used in this, since it is upon the molecular structure of the solute complex that the viscosity behaviour evidently depends. The most striking feature of the Figure is the similar viscosities of the extract solutions of the weak polybasic acids and the strong mineral acids.

Study of the Figure makes it apparent that the size of the complex formed markedly influences the viscosity. The trisolvated citric acid complex causes the greatest increase



Variation of viscosity of acid solutions in tributyl phosphate, with acid concentration [results for HCl from ref. 11, $HClO_4$ ref. 13, and HNO_3 and $CCl_3 \cdot CO_2H$ ref. 1]

in viscosity with acid concentration; the dibasic tartaric, malic, and oxalic acids all show a similar rate of increase of viscosity; and the monobasic acids cause only relatively slight variations in viscosity.

The complexes of the strong mineral acids, hydrochloric and perchloric, in the organic phase are also bulky, since they involve the ($H_9O_4^+$) cation [1] solvated by 3 or 4 tributyl phosphate molecules [8] at comparable acid loadings. Thus, it is not unexpected that their viscosities should be similar to those of the polybasic acids. It is puzzling, however, that the viscosity should continue to increase at higher concentrations of the strong mineral acids in tributyl phosphate since, in this region, the ester : acid ratio decreases [2,9–12] to roughly 1 : 1, whilst water is displaced [2,7,10–13] towards a water acid ratio of 2 : 1. This seems to indicate a smaller complex.

[8] Y. Marcus, *Chem. Revs.*, 1963, **63**, 139.
[9] D. C. Whitney and R. M. Diamond, *J. Phys. Chem.*, 1963, **67**, 209.
[10] A. S. Kertes, *J. Inorg. Nuc. Chem.*, 1960, **14**, 104.
[11] A. S. Kertes and V. Kertes, *Canad. J. Chem.*, 1960, **38**, 612.
[12] A. S. Kertes and V. Kertes, *J. Appl. Chem.*, 1960, **10**, 287.
[13] W. H. Baldwin, C. E. Higgins, and B. A. Soldano, *J. Phys. Chem.*, 1959, **63**, 118.

We feel that size is the factor that determines viscosity in the lower region of acid concentrations in tributyl phosphate. There is some evidence [7,14] that the organic acids are monomeric in the phosphate phase, which would strengthen this view. Strong interactions along lines suggested by Tuck [1] may only become important at high acid concentrations, though there is at present no experimental evidence known to the authors to support such a view.

Experimental.—The experimental technique was identical to that employed by Tuck,[1] except that the measurements were made at 26·9° ± 0·01°.

This research was supported in part by U.S. Atomic Energy Commission.

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(P. J. L.) South African Atomic Energy Board, Pretoria, South Africa.

[*Received, March 31st*, 1964.]

[14] H. A. Pagel and F. W. McLafferty, *Analyt. Chem.*, 1948, **20**, 272.

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631. *The Cyclo-dimerisation of Glycyl-L-prolylglycine*

By J. A. Reader and P. W. G. Smith

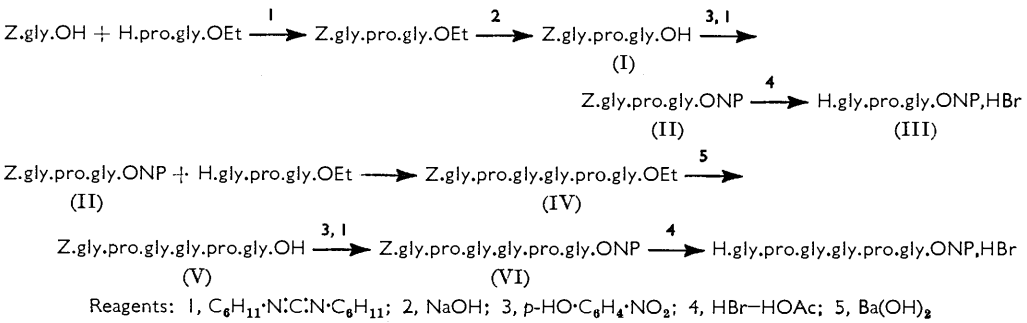
A recent Paper by Schwyzer and his co-workers [1] on the cyclisation of certain activated esters of glycyl-L-prolylglycine, and of the related hexapeptide, provides conclusive evidence that the product is cyclo(glycylprolyldiglycylprolylglycyl), thereby correcting previous assignments of a cyclotripeptide structure [2,3] to the product obtained by cyclising the tripeptide derivatives. Similar results have also been presented briefly by Rothe, Steffen, and Rothe.[4]

Our work on the cyclisation of the tripeptide and the hexapeptide *p*-nitrophenyl esters further supports the cyclohexapeptide structure, and those of our experimental results which extend the observations of Schwyzer *et al.* are recorded here. In particular, we find that the cyclic hexapeptide can readily be isolated in the form of a well-defined crystalline 1 : 1 complex with *p*-nitrophenol. Continuous ether extraction of the aqueous solution of the complex was necessary to free it from *p*-nitrophenol, enabling the cyclic peptide to be obtained as the crystalline monohydrate. The infrared spectrum showed minor differences from that of the previously obtained DL-compound, as had been noted by Schwyzer *et al.*[1] The paper-chromatographic behaviour of the L- and the DL-compounds (in butan-1-ol–acetic acid–water) was identical.

The structure was confirmed by partial hydrolysis experiments. It was first shown that paper chromatography using the butanol–acetic acid solvent system would not separate the linear tripeptide from the linear hexapeptide. Clear separation was however achieved by thin-layer chromatography on silica gel (see Experimental section). Chromatographic investigation of the product obtained by treatment of the cyclic peptide with barium hydroxide solution under the mildest conditions that would effect ring-fission showed the main product to be the linear hexapeptide. Our efforts at the determination of the molecular weight of the cyclic peptide were concentrated on an ebullioscopic method using trifluoroacetic acid,[5] but low values were obtained.

The synthesis of the required peptide *p*-nitrophenyl esters was accomplished according to the schemes shown. In contrast to the results of Schwyzer *et al.*,[1] we obtained both benzyloxycarbonylglycyl-L-prolylglycine *p*-nitrophenyl ester (II) and the corresponding peptide ester hydrobromide (III) as analytically pure solids. Although our initial coupling

[1] R. Schwyzer, J. P. Carrion, B. Gorup, H. Nolting, and Aung Tun-Kyi, *Helv. Chim. Acta*, 1964, **47**, 441.
[2] P. W. G. Smith, *J.*, 1957, 3985.
[3] B. Gorup and R. Schwyzer, *Angew. Chem.*, 1960, **72**, 270.
[4] M. Rothe, K. D. Steffen, and I. Rothe, *Angew. Chem.*, 1963, **75**, 1206.
[5] G. W. Kenner, P. J. Thompson, and J. M. Turner, *J.*, 1958, 4148.



Reagents: 1, $C_6H_{11}\cdot N{:}C{:}N\cdot C_6H_{11}$; 2, NaOH; 3, p-$HO\cdot C_6H_4\cdot NO_2$; 4, HBr–HOAc; 5, $Ba(OH)_2$

components were different from those used by Schwyzer, we also obtained poor yields of the protected tripeptide (I) by saponification of the corresponding ethyl ester obtained when coupling was carried out in chloroform solution using ethyl chloroformate. It appears from our results that both the coupling and the hydrolysis stages proceed abnormally; the former was improved by Schwyzer by using tetrahydrofuran as solvent; we found coupling using dicyclohexylcarbodi-imide effective. The low yields on hydrolysis of the ethyl ester are unexpected as this ester is not one which might undergo a Wessely type degradation,[6] although Debabov and Shibnev [7] record similar low yields on saponification of the methyl ester. Esterification of (I) with *p*-nitrophenol was effected in good yield in acetonitrile solution [8] using dicyclohexylcarbodi-imide, and removal of the protecting group to give (III) proceeded normally.

Coupling of the protected *p*-nitrophenyl ester (II) with glycylprolylglycine ethyl ester [9] readily yielded the protected hexapeptide ethyl ester (IV), but saponification of this proved troublesome (cf. ref. 7). Hydrolysis with sodium hydroxide in dioxan–methanol [10] was fairly effective, but the use of barium hydroxide greatly facilitated the isolation of the water-soluble benzyloxycarbonyl-hexapeptide (V) in the pure state.

Esterification with *p*-nitrophenol was again accomplished by the di-imide method, the protected ester (VI) being isolated as the monohydrate. Final removal of the benzyloxycarbonyl group gave a product which appeared to be contaminated with the hexapeptide.

*Experimental.—Derivatives of glycyl-*L*-prolylglycine.* (a) *The benzyloxycarbonyl-peptide.* Benzyloxycarbonylglycine (4·18 g.) in tetrahydrofuran (20 ml.) was treated with the suspension obtained by adding triethylamine (2·8 ml.) to a solution of L-prolylglycine ethyl ester hydrochloride [9] (4·73 g.) in dichloromethane (40 ml.). Dicyclohexylcarbodi-imide (4·32 g.) in dichloromethane (20 ml.) was added, and the mixture was set aside overnight after stirring for 15 min. Dicyclohexylurea (4·05 g.) was filtered off, washed with dichloromethane, and the filtrate and washings were evaporated. The residue was extracted with ethyl acetate and the filtered solution washed with N-hydrochloric acid (5 ml.), water (10 ml.), saturated aqueous sodium hydrogen carbonate (5 ml.), and water (10 ml.). Evaporation of the dried solution yielded a very pale yellow oil (7·5 g., 96%), $[\alpha]_D^{24}$ −67° (*c* 2 in EtOH). This oil (3·75 g.) was shaken at room temperature with N-sodium hydroxide (9·8 ml.) for 6 hr. Ethyl acetate (10 ml.) was added, and the mixture was acidified (Congo Red) with 5N-hydrochloric acid. The aqueous phase was separated and extracted with ethyl acetate (3 × 10 ml.) and the combined, dried, ethyl acetate solution was concentrated to *ca.* 10 ml. When crystallisation began, ether (10 ml.) was added gradually. Next day, the benzyloxycarbonyl-tripeptide (2·5 g., 69% overall), m. p. 141° (lit.,[9] 143—144°), $[\alpha]_D^{29}$ −79° (*c* 1·60 in MeCN), was filtered off.

When the above components were coupled in chloroform solution using ethyl chloroformate, the yield of neutral oil was nearly quantitative, but saponification under a variety of conditions invariably led to low yields (*ca.* 30%) of the protected tripeptide, m. p. 143—144°, $[\alpha]_D^{29}$ −80° (*c* 0·78 in MeCN). On the other hand, coupling using the dimethylformamide–sulphur trioxide

[6] J. A. MacLaren, *Austral. J. Chem.*, 1958, **11**, 360.
[7] V. G. Debabov and V. A. Shibnev, *Izvest. Akad. Nauk S.S.S.R., Otdel. khim. Nauk*, 1962, 1031.
[8] J. C. Sheehan and G. P. Hess, *J. Amer. Chem. Soc.*, 1955, **77**, 1067.
[9] H. N. Rydon and P. W. G. Smith, *J.*, 1956, 3642.
[10] R. Schwyzer and P. Sieber, *Helv. Chim. Acta*, 1958, **41**, 2190.

complex [11] gave a lower yield (53%) of oil which gave, after saponification, somewhat improved yields of product (68%, 35% overall), m. p. 140—141°, $[\alpha]_D^{29}$ −80° (*c* 1·55 in MeCN).

The benzyloxycarbonyl-tripeptide (1·81 g.) was re-esterified by azeotropic distillation with benzene–ethanol in the presence of toluene-*p*-sulphonic acid. The isolated ester (1·30 g.) was saponified as above, when recovery of the tripeptide derivative was 0·8 g. (66%).

(b) *The benzyloxycarbonyl-peptide* p-*nitrophenyl ester*. A solution of the above benzyloxycarbonyl-peptide (3·19 g.) in hot acetonitrile (50 ml.) was cooled to 0°, and treated with *p*-nitrophenol (1·47 g.) in acetonitrile (10 ml.), followed by dicyclohexylcarbodi-imide (1·82 g.) in acetonitrile (10 ml.). After 45 min., the mixture was allowed to warm to room temperature. Next day, dicyclohexylurea (1·9 g.) was filtered off and washed with a little acetonitrile. The filtrate and washings were concentrated under reduced pressure (crystallisation began), treated with ether (20 ml.), cooled, and filtered. *Benzyloxycarbonylglycyl-*L*-prolylglycine* p-*nitrophenyl ester* (3·0 g., 70%) had m. p. 151—153°, $[\alpha]_D^{29}$ −82° (*c* 0·56 in EtOH) (Found: C, 56·6; H, 4·9; N, 11·7. $C_{23}H_{24}N_4O_8$ requires C, 57·0; H, 5·0; N, 11·6%). Subsequently, material of m. p. 155° (95%) was obtained.

(c) *The peptide* p-*nitrophenyl ester hydrobromide*. The above ester (1·21 g.) was dissolved in hydrogen bromide–acetic acid (25% solution; 3·5 ml.) and set aside for 1 hr. Anhydrous ether (50 ml.) was added, and after 90 min. the pale yellow solid was filtered off and washed with boiling ether (20 ml.), warm acetonitrile (10 ml.), cold acetonitrile (10 ml.), and cold ether (20 ml.). The colourless, amorphous *hydrobromide* (0·92 g., 85%) had m. p. 175—176° (decomp.), $[\alpha]_D^{29}$ −65° (*c* 0·77 in dimethylformamide) (Found: C, 41·4; H, 4·7; Br, 18·7; N, 12·9. $C_{15}H_{19}BrN_4O_6$ requires C, 41·8; H, 4·4; Br, 18·5; N, 13·0%).

*Derivatives of glycyl-*L*-prolyldiglycyl-*L*-prolylglycine*. (a) *The benzyloxycarbonyl-peptide ethyl ester*. Benzyloxycarbonylglycyl-L-prolylglycine *p*-nitrophenyl ester (4·40 g.) was added to a suspension of glycyl-L-prolylglycine ethyl ester hydrochloride [9] (2·68 g.) in dry chloroform (36 ml.) containing triethylamine (1·28 ml.), and the resulting pale yellow solution was set aside overnight, washed in the usual way, dried, and evaporated. Crystallisation of the residue from ethanol–ether afforded the *benzyloxycarbonyl-peptide ethyl ester* (4·60 g., 84%), m. p. 163—164°, $[\alpha]_D^{29}$ −88° (*c* 0·62 in EtOH) (Found: C, 55·8; H, 6·3; N, 14·1. $C_{28}H_{38}N_6O_9$ requires C, 55·8; H, 6·4; N, 14·0%).

(b) *The benzyloxycarbonyl-peptide*. (i) The above ester (1·00 g.) was dissolved in a mixture of dioxan (46 ml.) and methanol (6 ml.), and treated with 0·5N-sodium hydroxide (7 ml.). After 1 hr. at room temperature the reaction product was worked up [10] to yield a product (0·6 g., 63%), m. p. 212—213°, which contained a trace of chloride ions; a specimen, crystallised from methanol–water (3 : 1), yielded the *benzyloxycarbonyl-peptide monohydrate*, m. p. 218—219°, $[\alpha]_D^{29}$ −80° (*c* 0·42 in EtOH) (Found: C, 52·9; H, 5·7; N, 14·4. $C_{26}H_{34}N_6O_9,H_2O$ requires C, 52·7; H, 6·1; N, 14·2%). (ii) The above ester (1·00 g.) was dissolved in a warm mixture of dioxan (40 ml.) and methanol (10 ml.) and the solution was cooled to 18°. 0·259N-Barium hydroxide (13·7 ml.) was added and the mixture was set aside at room temperature for 1 hr. 0·510N-Sulphuric acid (6·95 ml.) was added, and the mixture was evaporated under reduced pressure at 40—50° to give a residue which was warmed with water (10 ml.) and again evaporated. The residue was then extracted with water (20 ml.), filtered through a bed of kieselguhr, and evaporated; this residue was dissolved in ethanol, evaporated, and finally redissolved in ethanol (5 ml.). Ether was added to precipitate the product as a gummy solid, which was allowed to crystallise overnight. Filtration and washing with ether yielded product (0·90 g., 94%) of m. p. 215—216°.

(c) *The benzyloxycarbonyl-peptide* p-*nitrophenyl ester*. A solution of the above benzyloxycarbonyl-peptide (0·60 g.) in a hot mixture of acetonitrile (4·6 ml.) and water (0·8 ml.) was cooled to 0° and treated with *p*-nitrophenol (0·175 g.) in acetonitrile (3 ml.). The mixture was set aside at 0° for ½ hr. and at room temperature for 2 hr., after which dicyclohexylurea (0·21 g.) was filtered off and washed with a little acetonitrile. The filtrate and washings were concentrated under reduced pressure, treated with ether (10 ml.), and the product (0·58 g., 80%), m. p. 178—180°, was filtered off. The *benzyloxycarbonyl-peptide* p-*nitrophenyl ester* crystallised from acetonitrile as the monohydrate, m. p. 187—188° (Found: C, 53·6; H, 5·5; N, 13·6. $C_{32}H_{37}N_7O_{11},H_2O$ requires C, 53·8; H, 5·5; N, 13·7%).

(d) *The peptide* p-*nitrophenyl ester hydrobromide*. The above ester was cleaved with hydrogen bromide–acetic acid as for the tripeptide derivative. The amorphous product of indefinite

[11] D. W. Clayton, J. A. Farrington, G. W. Kenner, and J. M. Turner, *J.*, 1957, 1398.

melting point was not obtained analytically pure and was used directly in the cyclisation experiments.

The p-*nitrophenol complex of* cyclo(*glycyl-*L-*prolyldiglycyl-*L-*prolylglycyl*). (*a*) The tripeptide *p*-nitrophenyl ester hydrobromide (0·538 g.) in dry dimethylformamide (10 ml.) was added during 3 hr. to a stirred solution of triethylamine (0·95 ml.) in dimethylformamide (100 ml.) at room temperature. After stirring for a further 2 hr., the resulting yellow solution was worked up as two equal portions. (i) Solvent was removed by distillation under reduced pressure at 50°, the residue was extracted with water (7 ml.), and the filtered extract was concentrated to 2 ml. On standing, off-white needles (decomp. >250°) of the *cyclic hexapeptide* p-*nitrophenol complex* (62 mg., 35%) separated and were filtered off, washed with boiling ether, and recrystallised from water (Found: C, 51·3; H, 5·6; N, 17·5. $C_{18}H_{26}N_6O_6,C_6H_5NO_3$ requires C, 51·3; H, 5·6; N, 17·5%); $\nu_{max.}$ (KCl disc) 3400, 3080, 2940, 1665, 1645, 1600, 1525, 1510, 1460, 1420 (infl.), 1345, 1295, 1240, 1165, 1110, 1035, 865, 860 cm.$^{-1}$. (ii) After concentration in the above manner to remove most of the solvent, ether (70 ml.) was added and the precipitated product was filtered off and washed with ether. It was then extracted with water and concentrated as before. No product separated on cooling; the solution was then warmed with *p*-nitrophenol (30 mg.) and cooled, to yield needles (34 mg.) of the above complex. When the cyclisation was repeated, working up entirely as in (i) above, the yield of complex was 240 mg. (68%). However, only one of several attempts to crystallise directly the crude product obtained as in (ii), above, was successful, the cyclic peptide usually being obtained in an amorphous form.

(*b*) The hexapeptide *p*-nitrophenyl ester (0·490 g.) was cyclised and worked up as in (*a*) (i), above. The resulting *p*-nitrophenol complex (198 mg., 46%) had an infrared spectrum identical with that previously obtained.

Cyclo(*glycyl-*L-*prolyldiglycyl-*L-*prolylglycyl*). The above complex (240 mg.) was dissolved in water (20 ml.), and the resulting yellow solution was continuously extracted with ether overnight. The colourless aqueous phase was evaporated and the residue was crystallised from water to yield the *cyclic peptide monohydrate* (103 mg.), $[\alpha]_D^{27}$ +45° (*c* 0·2 in H_2O) [Found: (i) after drying *in vacuo* over phosphoric oxide at room temperature for 12 hr., C, 49·5; H, 5·5; N, 19·5. $C_{18}H_{26}N_6O_6,H_2O$ requires C, 49·1; H, 6·4; N, 19·1%; (ii) after similar drying at 100°, C, 51·4; H, 6·2; N, 19·7%; *M*, *ca.* 340. Calc. for $C_{18}H_{26}N_6O_6$: C, 51·2; H, 6·2; N, 19·9%; *M*, 422], $\nu_{max.}$ (KCl disc) 3320, 3080, 2950, 1665, 1645, 1540, 1460 (infl.), 1445, 1420 (infl.), 1340, 1280, 1240, 1210, 1035 cm.$^{-1}$.

Partial hydrolysis. Chromatography was on 60-cm. plates layered with silica gel, using the system butan-1-ol–ethanol–acetic acid–water (9 : 3 : 2 : 4), with a running time of 18 hr. The R_F values of some linear peptides were: glycylprolyldiglycylprolylglycine, 0·07; glycylprolylglycine, 0·12; prolylglycine, 0·14; glycylproline, 0·14. The ninhydrin-positive spots obtained after hydrolysis of the cyclic peptide with 0·13N-barium hydroxide under the following conditions were: (a) at 100° for 20 min., R_F 0·07 (hexapeptide), R_F 0·10 (possibly a tetrapeptide), R_F 0·14 (a dipeptide), R_F 0·21 (glycine); (b) at 18° for 24 hr., nil; (c) at 18° for 24 hr. and then at 100° for 5 min., R_F 0·07 (hexapeptide) only.

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632. *Comment on the "Through-space" Contribution to Fluorine–Fluorine Coupling Constants*

By N. BODEN, J. FEENEY, and L. H. SUTCLIFFE

CONVINCING evidence has recently been brought forward for the existence of "through-space" coupling between fluorine nuclei.[1] However, there are several shortcomings in the relationship that Petrakis and Sederholm [2] suggest exists between the fluorine–fluorine spatial separation and the coupling constant; these preclude its current use [1] as a method for predicting F–F coupling constants. While it appears that spatially close fluorine nuclei interact strongly, we consider that there is no evidence for the existence of a smooth

[1] S. Ng and C. H. Sederholm, *J. Chem. Phys.*, 1964, **40**, 2090.
[2] L. Petrakis and C. H. Sederholm, *J. Chem. Phys.*, 1961, **35**, 1243.

relationship between conformationally corrected [1] values of J_{FF} and the spatial separation of the fluorine atoms concerned. The main criticisms may be summarised as follows:

(1) It is seen from the geminal fluorine coupling constants contained in Table 1 that the observed values extend over a much wider range than that quoted by Ng and Sederholm [1] (150—400 c./sec.). However, the calculated internuclear separations between

TABLE 1

Geminal F–F coupling constants

Compound	J_{FF}(c./sec.)	F–F distance (Å)	Ref.
Cyclo-C_6F_{12}	285	2·17	5
Fluorocyclobutanes	211	2·17	6
1,1-Difluoro-2-methylcyclopropane	157	*ca.* 2·17	6
Fluoroethylenes	7—87	2·12	7
PF_5, base (octahedral)	55	2·45	8
Disubstituted phosphorus pentafluorides (pentagonal bipyramid)	26—27	2·32	9
ClF_3	435	2·30	10
BrF_5	77	2·26	11
IF_5	81	*ca.* 2·3	10
SF_4	78	2·26	12
$(CF_3)_2CFSF_3$	4·8 (SF_2–SF)	2·26	13
Aliphatic sulphur pentafluorides	150	2·22	14, 15

the interacting fluorine nuclei are not very different, indicating that a large fraction of the coupling is achieved by means of a through-bond coupling mechanism. A corollary of this conclusion is that if a through-space contribution is present it could be as large as 400 c./sec. Since the two contributions cannot be resolved, one must eliminate the point referring to geminal coupling constants from Figure 2 of reference 2.

(2) An earlier criticism [3] of the relationship was based on the fact that in fluoroalkanes J_{FF} vic and J_{FF} [1,3] are of opposite sign, whereas the original postulate of Petrakis and Sederholm considered only the magnitudes of the coupling constants. Also, the occurrence of large J_{FF} vic values in some fluoroethanes [4] appears to be inconsistent with the proposed curve. Ng and Sederholm have answered both criticisms by assuming that vicinal F–F coupling constants have unknown contributions from through-space and through-bond interactions. They assume that the through-space coupling is zero for an internuclear distance of 2·73 Å, and have gone on to conclude that a zero vicinal coupling results when the sum of the substituent electronegativities is very high. However, a zero coupling constant might equally well arise from cancellation of appreciable through-space and through-bond contributions owing to their being of opposite sign. Because of this uncertainty, values from vicinal coupling constants are of little use at present in establishing a distance/coupling constant relationship.

(3) The fluoroalkane coupling constants that appear to be most suitable for consideration are those of the long-range type, that is when more than three bonds separate the interacting nuclei. We differ from Ng and Sederholm in considering that it is also preferable to exclude unsaturated compounds, because fluorine nuclei that are spatially well separated can have appreciable coupling, as may be seen from the last two examples listed in Table 2. Obviously, values from particular molecules can only be included in a distance relationship when their conformational behaviour is fully understood.

[3] D. F. Evans, *Discuss. Faraday Soc.*, 1962, **34**, 139.
[4] R. K. Harris and N. Sheppard, *Trans. Faraday Soc.*, 1963, **59**, 606.
[5] J. Feeney and L. H. Sutcliffe, *Trans. Faraday Soc.*, 1960, **56**, 1559.
[6] W. D. Phillips, *J. Chem. Phys.*, 1956, **25**, 949.
[7] T. D. Coyle, S. L. Stafford, and F. G. A. Stone, *Spectrochim. Acta*, 1961, **17**, 968.
[8] E. L. Muetterties, T. A. Bither, M. W. Farlow, and D. D. Coffman, *J. Inorg. Nuclear Chem.*, 1960, **16**, 52.
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[11] H. S. Gutowsky, D. W. McCall, and C. P. Slichter, *J. Chem. Phys.*, 1953, **21**, 279.
[12] E. L. Muetterties and W. D. Phillips, *J. Amer. Chem. Soc.*, 1959, **81**, 1084.
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[14] N. Boden, J. W. Emsley, J. Feeney, and L. H. Sutcliffe, *Trans. Faraday Soc.*, 1963, **59**, 620.
[15] C. I. Merrill, S. M. Williamson, G. H. Cady, and D. F. Eggers, *Inorg. Chem.*, 1962, **1**, 215.

TABLE 2
Non-geminal F–F coupling constants

Compound	$J_{CF_3 \cdot CF_3}$ (c./sec.)	Conformationally-corrected coupling constants (c./sec.)	F–F distance (Å)	Ref.
$CF_3 \cdot SF_4 \cdot CF_2 \cdot SF_5$	~11 ($SF_4 \cdot SF_4$)	~88 (=11 × 16/2)	1·8	16
cis-1,2-Bis(trifluoromethyl)cyclobutanes	10—12	45—54 (= 10—12 × 9·2)	2·0	1
$(CF_3)_2O$	8·0	36 (= 8·0 × 9/2)	2·1	17
$CF_3 \cdot CF_2 \cdot CF_3$	7·3	32·8 (= 7·3 × 9/2)	2·5	18
$CF_3 \cdot CFI \cdot CF_3$	9·5	42·7 (= 9·5 × 9/2)	2·5	19
trans-1,2-Bis(trifluoromethyl)cyclobutanes	0	0	3·0	1
cis-$CF_3 \cdot CCl{=}CCl \cdot CF_3$	13·4	60 (= 13·4 × 9/2)	2·0—2·4 *	20
2,3-Bis(trifluoromethyl)pyridine	12·8	58 (= 12·8 × 9/2)	2·2—2·5 *	1
trans-$CF_3 \cdot CCl{=}CCl \cdot CF_3$	1·44	6·5 (= 1·44 × 9/2)	4·7	20
$CF_3 \cdot C{\equiv}C \cdot CF_3$	2·2	2·2	4·9	19

* A range is given because it is not possible to predict the most stable configuration.

Table 2 contains a selection of compiled data which we believe comply (apart from the last four examples) with the conditions laid down above. It is clear that there is not a smooth relationship between conformationally-corrected [1] values of J_{FF} and the spatial separations of the fluorine atoms concerned. However, the general correlation of long-range F–F coupling constants with short non-bonded F–F distances may indicate the presence of a through-space contribution for internuclear separations of 2—2·5 Å. Of the acceptable data given in Table 2, there are only two instances of internuclear separations lying outside this range, hence many more results are required in order to discern a general trend of the type envisaged by Petrakis and Sederholm.

The 1,3 F–F coupling constants listed in Table 2 probably have positive signs,[21] but should any of these prove to be of opposite signs then our conclusions are strengthened.

DONNAN CHEMICAL LABORATORIES,
THE UNIVERSITY, LIVERPOOL. [*Received, December 24th*, 1964.]

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[20] G. V. D. Tiers, *J. Chem. Phys.*, 1961, **35**, 2263.
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633. *Reactions at Position* 1 *of Carbohydrates. Part VII.*[1] *The Action of Potassium Hydroxide on Aryl* 2-*Deoxy*-α-D-*glucopyranosides*

By R. J. FERRIER, W. G. OVEREND, and MISS A. E. RYAN

THE only well-characterised products of the action of alkali on aryl hexosides are the corresponding 1,6-anhydrohexoses.[2] The ease with which these 1,6-anhydrides are formed depends on the nature of the hexose and the aglycone and on the anomeric configuration of the glycoside. In particular in a β-glycoside a hydroxyl group at C-2 *trans* to the aglycone facilitates production of the hexosan which is formed *via* a 1,2-epoxide.[2] However, the factors influencing the reactivity of aryl glycosides towards alkali are complex. Competing reactions must be considered and no single mechanism operates generally. The investigation now reported stems from an attempt to assess the influence at C-1 of the C-2-OH group. (Cf. A study of the stability to acids of hexopyranosides relative to the corresponding 2-deoxyhexopyranosides.[3])

Aryl 2-deoxy-β-D-glucopyranosides have not been described and our attempts to prepare them were unsuccessful. Application of the Koenigs-Knorr reaction to crystalline

[1] Part VI, I. R. L. Barker, W. G. Overend, and C. W. Rees, *J.*, 1964, 3254.
[2] See C. E. Ballou, *Adv. Carbohydrate Chem.*, 1954, **9**, 59.
[3] W. G. Overend, C. W. Rees, and J. S. Sequeira, *J.*, 1962, 3429.

3,4,6-tri-*O*-benzoyl-2-deoxy-α-D-glucosyl bromide (prepared according to Bergmann *et al.*[4]) and phenol in quinoline in the presence of silver oxide did not afford any crystalline β-glycoside. Treatment of pure α- or β-tetra-*O*-acetyl-2-deoxy-D-glucose and a phenol with either zinc chloride or toluene-*p*-sulphonic acid [5] resulted only in the isolation of crystalline aryl 2-deoxy-α-D-glucopyranoside 3,4,6-triacetate which could be readily deacetylated by the Zemplén method. (See Table for glycosides so prepared.) Consequently our studies have been confined to these α-glycosides.

The products of the action of alkali on the glycosides are dependent on the strength of the alkali used. Treatment of phenyl, *p*-chlorophenyl, *p*-tolyl or *p*-nitrophenyl 2-deoxy-α-D-glucopyranoside with hot 0·05N-aqueous potassium hydroxide gave the same chromatographically homogeneous product, the properties of which are consistent with its structure being 1,6-anhydro-2-deoxy-β-D-glucose. A sample of the chromatographically pure syrup ($[\alpha]_D$ −33·1°; in EtOH) did not reduce akaline iodine solution [6] but gave 2-deoxy-D-glucose on acidic hydrolysis. It consumed 1·05 mol. (calculated for an anhydrodeoxyhexose) of sodium metaperiodate but much more slowly than do 2-deoxyglycopyranosides.[7] This relative stability to oxidation by periodate was expected since in the 1,6-anhydrodeoxyhexose the diol which is attacked is held close to the *trans* diaxial arrangement by the 1,6-anhydro-bridge. It was found that if *p*-nitrophenyl 2-deoxy-α-D-glucoside is hydrolysed with hot 0·001N-aqueous potassium hydroxide no 1,6-anhydride is detectable amongst the products. Instead 2-deoxy-D-glucose and its 3,6-anhydride (a product of alkaline treatment of the deoxy-sugar [8]) are formed. It appears therefore that in the stronger alkali nucleophilic attack at C-1 occurs intramolecularly by the ionised hydroxymethyl group at C-5 whereas with more dilute reagent solvolysis predominates. In this respect the aryl 2-deoxyglucosides resemble the glycosyl fluorides.[9]

When the rates of the reactions between the aryl glycosides and excess of 0·05N-aqueous potassium hydroxide were followed good first-order rate coefficients were obtained in all cases. Measurements over suitable temperature ranges (see Table) were made and activation energies and first-order velocity constants at 100° (k_{100}) were calculated. Between log k_{100} and the Hammett constant (σ) for the aromatic ring substituent there was a linear relationship showing that electronic factors alone govern the differences in the rates of reactions of the four glycosides. A similar relationship has been found with the substituted phenyl glucosides,[2] and in this series too electron-withdrawing groups on the aromatic ring increase the susceptibility to alkali.

Comparison of the rates of reaction of *p*-nitrophenyl α-D-glucopyranoside and its 2-deoxy-derivative (see Table) makes it clear that a hydroxyl substituent at C-2 of the

Summary of kinetic experiments

α-D-Glucoside	Temp. of reaction (*t*°c)	k_t (min.$^{-1}$)	log k_{100}	σ	*E* (kcal. mole^{-1})
p-Tolyl 2-deoxy-	147·4	$8{\cdot}25 \times 10^{-4}$	−4·82	−0·17	26·6
	167·0	$3{\cdot}42 \times 10^{-3}$			
Phenyl 2-deoxy-	130·5	$3{\cdot}68 \times 10^{-4}$	−4·77	0·00	30·3
	148·8	$1{\cdot}88 \times 10^{-3}$			
	170·0	$1{\cdot}015 \times 10^{-2}$			
p-Chlorophenyl 2-deoxy-	127·1	$1{\cdot}88 \times 10^{-3}$	−3·92	+0·23	27·9
	145·5	$6{\cdot}79 \times 10^{-3}$			
	173·3	$5{\cdot}41 \times 10^{-2}$			
p-Nitrophenyl 2-deoxy-	64·0	$6{\cdot}7 \times 10^{-4}$	−1·61	+1·27	25·2
	73·6	$1{\cdot}74 \times 10^{-3}$			
	96·0	$1{\cdot}84 \times 10^{-2}$			
p-Nitrophenyl	35·3	$2{\cdot}75 \times 10^{-3}$	+0·075	—	22·4
	51·9	$1{\cdot}51 \times 10^{-2}$			
	76·1	$1{\cdot}81 \times 10^{-1}$			

[4] M. Bergmann, H. Schotte, and W. Leschinsky, *Ber.*, 1923, **56**, 1052.
[5] B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, 1933, **66**, 378.
[6] S. K. Chanda, E. L. Hirst, J. K. N. Jones, and E. G. V. Percival, *J.*, 1950, 1289.
[7] R. J. Ferrier and W. G. Overend, *J.*, 1959, 3638.
[8] R. J. Ferrier, W. G. Overend, and A. E. Ryan, *J.*, 1962, 1488.
[9] F. Micheel and A. Klemer, *Adv. Carbohydrate Chem.*, 1961, **16**, 85.

pyranoid ring also increases the ease of liberation of the phenol. In the reaction of aryl α-glucosides with alkali this hydroxyl group is unlikely to play any direct part and so this observation further illustrates the important influence which polar groupings at C-2 have on reactions involving ionic attack at the anomeric centre.

Experimental.—The aryl 2-deoxyglucosides were prepared by the method of Shafizadeh and Stacey [10] and had melting points in good agreement with those reported by these workers. Whereas the *p*-nitrophenyl and *p*-tolyl derivatives are stated [10] to have $[\alpha]_D$ +210° and +166° respectively in methanol, we find the values to be +224° and +177° in this solvent. Several values have been reported for the m. p. and $[\alpha]_D$ of the 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucose which is an intermediate in these syntheses. By acetylation of 2-deoxy-D-glucose with pyridine and acetic anhydride, Overend, Stacey, and Staněk [11] obtained a product with m. p. 91°, $[\alpha]_D^{20}$ +12·3° (EtOH), but another crystalline acetate {m. p. 75—78°, $[\alpha]_D^{20}$ +30° (EtOH)} was obtained with acetic anhydride and sodium acetate as the reagents. Shafizadeh and Stacey [10] obtained a product of m. p. 108—109°, $[\alpha]_D^{19}$ +105° (MeOH) from treatment of the deoxy-sugar with acetic anhydride and pyridine. Bonner [12] has prepared subsequently the α- and β-tetra-acetates, m. p. 109·7—110·7°, $[\alpha]_D^{25}$ +107·7° ($CHCl_3$) and m. p. 92·2—93·2°, $[\alpha]_D^{25}$ −2·82° ($CHCl_3$), respectively. We had obtained the same results (see Ryan [13]) since from the acetylation of 2-deoxy-D-glucose with acetic anhydride–pyridine we separated by fractional crystallisation from ethanol two products, m. p. 93°, $[\alpha]_D^{20}$ −4·4° (MeOH) and m. p. 108—109°, $[\alpha]_D^{20}$ +106° (MeOH). We demonstrated that the material of m. p. 75—78° obtained previously was a mixture of the two anomers. Fusion of either form of the tetra-acetate with phenol in the presence of zinc chloride or toluene-*p*-sulphonic acid afforded only a single crystalline product—phenyl 2-deoxy-α-D-glucoside triacetate.

Chromatography was carried out with n-butanol-ethanol-water (4 : 1 : 5, upper phase) with the descending technique, and Whatman No. 1 or No. 3 paper. The R_F values so determined of 2-deoxyglucose and its 1,6- and 3,6-anhydro-derivatives were 0·25, 0·48, and 0·55 respectively (Whatman No. 1 paper).

Rate measurements. The glycoside solutions (*ca.* 10^{-3}M in oxygen-free 0·05N-aqueous potassium hydroxide) were heated in individual sealed tubes under nitrogen in a thermostatically-controlled oil-bath. (Initial experiments indicated that it was essential to exclude oxygen to avoid partial oxidation of the liberated phenol which was shown to occur and to lead to erroneous results.) At suitable intervals tubes were removed and cooled, and the phenol concentration determined. Liberated *p*-nitrophenol was determined spectrophotometrically as the anion; phenol, cresol, and *p*-chlorophenol were determined by Folin and Ciocalteu's [14] method. A minimum of six determinations were made on each glycoside at each temperature.

1,6-*Anhydro*-2-*deoxy*-D-*glucose*. A solution of *p*-nitrophenyl 2-deoxy-α-D-glucoside (10^{-3}M) in 0·05N-potassium hydroxide was heated at 95° until reaction was complete as determined by liberation of *p*-nitrophenol. The cooled solution was neutralised (CO_2), evaporated to dryness under diminished pressure and the residue extracted with dry ethanol. The extract was separated chromatographically on paper (Whatman No. 3) and the carbohydrate product was isolated as a colourless non-reducing syrup ($[\alpha]_D^{20}$ −33·1° (*c* 0·7 in EtOH)), which was chromatographically homogeneous. Oxidation with periodate (0·004M) was complete only after 11 days; methyl 2-deoxy-α-D-glucopyranoside was oxidised in 2 hr. with the reagent.

We thank the D.S.I.R. for a studentship (held by A. E. R.).

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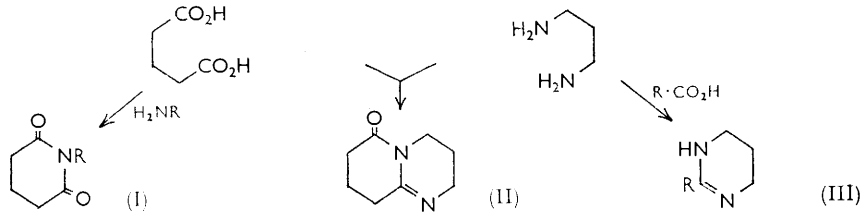
[10] F. Shafizadeh and M. Stacey, *J.*, 1957, 4612.
[11] W. G. Overend, M. Stacey, and J. Staněk, *J.*, 1949, 2841.
[12] W. A. Bonner, *J. Org. Chem.*, 1961, **26**, 908.
[13] A. E. Ryan, Ph.D. Thesis, University of London, 1960.
[14] O. Folin and V. Ciocalteu, *J. Biol. Chem.*, 1927, **73**, 627.

634. *A One-step Synthesis of* 10-*Oxo*-1,5-*diazabicyclo*[4,4,0]-*dec*-5-*ene*

By Johannes Dale and Raymond Coulon

Recently a simple pyrolytic depolymerisation method was described for the synthesis of cyclic diamides through the corresponding polyamides.[1] When we tried to prepare the 10-membered ring, trimethylene glutaramide, in this way, the corresponding polymer could not be obtained from glutaric acid and 1,3-diaminopropane. Instead, they gave on heating a new compound, m. p. 58°, which distilled off in 73% yield, leaving no residue. This was not the desired monocyclic diamide, later synthesised by a different method,[1] but proved to have a bicyclic structure (II). This novel substance, 10-oxo-1,5-diazabicyclo[4,4,0]dec-5-ene, belongs to a relatively difficultly accessible class of heterocyclic compounds.[2] Its formation can be considered as a combination of two well-known reactions: the formation of glutarimides [3] (I) and of tetrahydropyrimidines [4] (III). In spite of the surprising facility of the formation in this case, it depends very critically on ring size; thus, homologues with one or two 5- or 7-membered rings could not be obtained by a similar procedure.



The structure of (II) was established by analysis, molecular weight, and spectral data. The infrared spectrum showed the absence of NH and the presence of two bands in the 6 μ region (glutarimide [5] has only one band here). An ultraviolet band at 223 mμ had the same intensity as the glutarimide absorption [6] at 198 mμ. Attempts to reduce (II) with lithium aluminium hydride led to complete disruption; one volatile product is indistinguishable by gas chromatography from tetrahydropyran, and the other is 1,3-diaminopropane, known to arise from hydropyrimidines by sodium reduction.[7] The substance was perfectly stable to catalytic hydrogenation on platinum dioxide and Raney nickel.

Experimental.—Glutaric acid and 1,3-diaminopropane (1 : 1 molar ratio) were mixed whereby an exothermal reaction was observed. After heating at 200° for 1 hr. at atmospheric pressure, the pressure was reduced to 2—3 mm. and the heating increased, the intention being to remove water and effect polycondensation. However, a liquid started at once to distil off and solidified in the condenser. After sublimation the bicyclic compound melted at 58° (yield 73%) [Found: C, 63·0; H, 8·0; O, 11·15%; *M* (Rast), ~190. $C_8H_{12}N_2O$ requires C, 63·1; H, 7·95; O, 10·5%; *M*, 152]. The compound is slightly hygroscopic and soluble in water giving a basic reaction. The infrared spectrum, as liquid film, shows a band at 3·02 μ, which is too weak and sharp to be NH (probably overtone), and bands at 5·94 and 6·10 μ (C=N, C=O). The ultraviolet spectrum (in ethanol) has a maximum at 223 mμ (ε 14,100) which does not change when sodium hydroxide is added, but is displaced to 226 mμ (ε 16,700) when HCl is added. The n.m.r. spectrum in deuterochloroform showed lines at δ −1·87 (multiplet), −2·63 (triplet), −3·45 (triplet), and −3·70 (triplet) with the intensity ratio 4 : 4 : 2 : 2 attributable to CH_2 in positions 3 + 8, 7 + 9, 2(or 4), and 4(or 2), respectively. Reduction with lithium aluminium hydride in refluxing tetrahydrofuran overnight led to volatile products; after hydrolysis and

[1] Dale and Coulon, *J.*, 1964, 182.
[2] Mosby, " The Chemistry of Heterocyclic Compounds," ed. Weissberger, vol. XV, Interscience, New York, 1961, p. 1141.
[3] Hoey and Lester, *J. Amer. Chem. Soc.*, 1951, **73**, 4473.
[4] Haga and Majima, *Ber.*, 1903, **36**, 333.
[5] Kornfeld, Jones, and Parke, *J. Amer. Chem. Soc.*, 1949, **71**, 150.
[6] Turner, *J.*, 1957, 4555.
[7] Rodd, " Chemistry of Carbon Compounds," vol. IVB, Elsevier, Amsterdam, 1959, p. 1295.

evaporation no substance could be extracted with ether or chloroform. In another experiment most of the solvent was evaporated before hydrolysis, and the solution obtained by acid hydrolysis was examined by gas chromatography; it showed a peak whose retention time was undistinguishable from that of tetrahydropyran. Alkali liberated 1,3-diaminopropane.

Attempts were also made to hydrogenate the bicyclic compound on platinum oxide in benzene at 20 and 60° for 8 hr., and on Raney nickel (Fluka) at 100° and 50 atm. for 3 days. In both cases the starting material was recovered unchanged.

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635. *Heptacosan-1-ol from the Fruit of* Citrullus colocynthis

By H. EL KHADEM and M. M. ABDEL RAHMAN

THE higher alcohol which had been isolated [1] from the peel of *Citrullus colocynthis* has now been isolated from the pulp and identified as heptacosan-1-ol. Analysis agreed with the formula $C_{27}H_{56}O$, the compound formed a monoacetate, and no unsaturation was detected with tetranitromethane. The infrared spectrum showed OH bands at 3360 and 1050, and $[CH_2]_n$ bands at 1920, 1850, 1470, and a doublet at 730 and 710 cm.$^{-1}$.[2] The n.m.r. spectrum showed a triplet at τ 9·13 which was assigned to the terminal methyl group.[3] The protons of the $[CH_2]_n$ groups showed as a strong unresolved band at τ 8·70, and the two protons of the C-1 methylene group as a triplet at τ 6·3. The singlet at τ 8·22 was assigned to the hydrogen of the hydroxyl groups. These assignments are in good agreement with the integration curves; the intensities ascribed to the terminal CH_3, $[CH_2]_n$, C-1, CH_2, and OH bands were in the ratio 3 : 50·5 : 2·1 : 0·9, which is close to the theoretical ratio of 3 : 50 : 2 : 1 for heptacosan-1-ol. As expected for a higher primary alcohol the mass spectrum consisted of peak groups fourteen mass units apart which increase in intensity with decreasing molecular weight. This gradual increase in intensity is strongly indicative of a primary alcohol, in contrast to secondary or tertiary alcohols which usually show abnormally strong peaks of intermediate mass from fragmentation at the position of the hydroxyl group.[4] The highest molecular weight observed was 393, corresponding to M-3. Peaks corresponding to M-1 and M-2, detectable for lower alcohols, were absent. A M-18 peak caused by loss of water, and common to the mass spectra of all alcohols, could be detected. The M-46 peak, likewise commonly found in alcohols and caused by the loss of water and ethylene, fell in the middle of the C_{25} fragmentation group of peaks.

Experimental.—Infrared spectra were measured on a Perkin-Elmer Infracord spectrophotometer. N.m.r. and mass spectra were determined in the laboratories of Professor E. Hardegger, Eidgenossische Technische Hochschule, Zurich, and *X*-ray data by W. Rond, Ohio State University.

Heptacosan-1-ol. (a) *From the peel.* Powdered dried peel of *Citrullus colocynthis* (6·3 kg.), treated as described previously,[1] yielded heptacosan-1-ol (5 g.), m. p. 76°, $\nu_{max.}$ (KBr) 3360 and 1050 (OH), 1920, 1850, 1470, 730, and 710 cm.$^{-1}$ ($[CH_2]_n$), *X*-ray powder pattern interplanar spacing (Å); Cu K_α radiation; relative intensity estimated visually; the strongest lines are numbered (1 = strongest)]: 6·10w, 5·43vs(1), 3·69s(2), 301w, 2·51m(3), 2·38w, 1·78w (Found: C, 82·0, 81·7, 82·1; H, 14·0, 14·0, 14·1. Calc. for $C_{27}H_{56}O$: C, 81·7; H, 14·2%); acetate, m. p. and mixed m. p.[1] 62—64°.

(b) *From the pulp.* Powdered dried pulp of *Citrullus colocynthis* (3 kg.), extracted with light petroleum and treated as for the peel, yielded heptacosan-1-ol (1 g.), m. p. and mixed m. p.

[1] H. El Khadem and M. M. Abdel Rahman, *J.*, 1963, 4991.
[2] N. Nakanishi, "Infrared Absorption Spectroscopy," Holden-Day, San Francisco, 1962, p. 20.
[3] N. S. Bhacca, L. F. Johnson, and J. N. Shoolery, "Varian High Resolution Nuclear Magnetic Resonance Spectra Catalog," Varian Associates, Palo Alto, California, 1962, No. 282 for the n.m.r. spectrum of decan-1-ol.
[4] H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, San Francisco, 1964, p. 35.

76° (Found: C, 82·0; H, 14·0%), with the same mobility on paper chromatograms, the same infrared spectrum, and giving the same acetate as the product from (a).

The authors are indebted to Professor E. Hardegger for determining the n.m.r. and mass spectra.

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636. *A Method of Obtaining Crystalline Anhydrous αα-Trehalose*

By G. BIRCH

αα-TREHALOSE (mycose, or mushroom sugar) [1] is soluble in water and practically insoluble in absolute ethanol. From aqueous ethanol it invariably crystallises as the dihydrate. An anhydrous crystalline form has been obtained by dissolving the dihydrate in pyridine and distilling the solution at atmospheric pressure in order to achieve azeotropic removal of the water of crystallisation. The properties of the anhydrous material, which crystallises from the hot solution, are summarised in the following Table, and compared with the corresponding properties of the dihydrate.

	Trehalose,$2H_2O$	Trehalose (anhydrous)
M. p.	94—100°	214—216°
$[\alpha]_D^{20}$ (water)	+180°	+199°
Solubility in pyridine	Soluble	Practically insoluble
Sp. gr.	1·52 g./ml. (24°/24°)	1·58 g./ml. (24°/24°)
Carbohydrate content (% theory) [2, 3]	98·5	96·5

This is believed to be the first simple crystallisation of the anhydrous αα-sugar, and the melting point of the crystals is very close to that reported recently by Perlin [4] for an anhydrous trehalose prepared by heating the dihydrate in an open dish for 4 hours.

Preliminary investigations indicate that the method may be extended to other sugars that crystallise as hydrates (*e.g.*, lactose and glucose).

Experimental.—Preparation of anhydrous crystalline trehalose. A typical preparation was carried out as follows. Commercial αα-trehalose dihydrate (10 g.) was dissolved in hot pyridine (200 ml.; AnalaR), and the solution distilled at atmospheric pressure. When the temperature had risen to 115·3° all the water had been removed and 73 ml. of distillate had been collected; most of the anhydrous material had already crystallised at this stage. The mass of crystalline material (6·8 g.) was washed with ether to give 6·1 g. of product (Found: C, 42·65; H, 6·65. $C_{12}H_{22}O_{11}$ requires C, 42·1; H, 6·5). Better yields could be obtained by more prolonged distillation.

Preparation of anhydrous crystalline lactose. This was carried out in exactly the same way as for trehalose (Found: C, 42·3; H, 6·35%).

Preparation of anhydrous crystalline glucose. The preparation was carried out as for trehalose, but crystallisation had to be induced in the pyridine solution by addition of light petroleum.

Infrared analysis. A Unicam S.P. 200 spectrometer and Nujol mulls were used. The spectra show the following peaks due to water of crystallisation. Maltose, H_2O, 1680 (broad) $cm.^{-1}$; glucose, H_2O, 1660—1680 (broad) $cm.^{-1}$; lactose, H_2O, 1660 (sharp) $cm.^{-1}$; trehalose, $2H_2O$, 1690 (sharp) $cm.^{-1}$.

The figure quoted in the literature for water of crystallisation in carbohydrates [5] is 1645 $cm.^{-1}$. It is hoped that the results of *X*-ray diffraction (see below) will throw some light on the above figures. All the anhydrous crystalline materials prepared by the method reported here show complete absence of the peak due to water of crystallisation.

[1] G. G. Birch, *Adv. Carbohydrate Chem.*, 1964, **18**, 201.
[2] M. Dubois, K. A. Gilles, J. K. Hamilton, P. A. Rebers, and F. Smith, *Analyt. Chem.*, 1956, **28**, 350.
[3] G. G. Birch, *Proc. Assoc. Clinical Biochem.*, 1963, **2**, no. 8, 216.
[4] H. J. Reisener, H. R. Goldschmid, G. A. Ledingham, and A. S. Perlin, *Canad. J. Biochem. Physiol.*, 1962, **40**, 1248.
[5] S. A. Barker, E. J. Bourne, and D. H. Whiffen, *Methods Biochem. Analysis*, 1956, **3**, 213.

X-Ray analysis. *X*-Ray analysis of the trehalose crystals is being undertaken by Dr. Beevers at Edinburgh University, and it has already been shown that neither the anhydrous form, nor the dihydrate, belong to the cubic system.

The author is grateful to Professor W. J. Whelan and Dr. D. Steele for advice.

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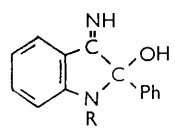
637. *The Autoxidation of 3-Aminoindoles*

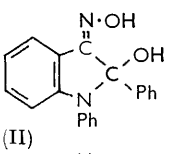
By C. W. BIRD

IN all examples so far investigated, autoxidation of indole derivatives has proceeded through formation of the 3-indoleninyl hydroperoxide.[1] Reinvestigation of some earlier observations on the autoxidation of 3-aminoindoles has shown that in this case, however, the hydroperoxide group is introduced at position 2. (An alternative explanation [2] is available for observations previously believed [3] to indicate hydroperoxide formation at position 2.)

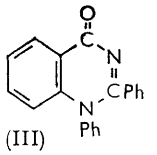
It was previously reported [4] that both the *N*-phenyl and *N*-ethyl derivatives of 3-amino-2-phenylindole were rapidly autoxidised in ethereal solution, giving yellow, basic products to which the structures (Ia) and (Ib) were assigned. In addition, 3-amino-1,2-diphenylindole gave a colourless product which was thought to have the structure (II); this lost water above its melting point yielding a basic compound, tentatively assigned the quinazolone structure (III). The same transformation was also brought about by either ethanolic hydrogen chloride or aqueous sodium hydroxide, although ethanolic potassium hydroxide converted it into *N*-phenylanthranilic acid.



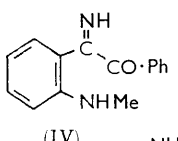
(I) a : R = Ph
b : R = Et
c : R = Me



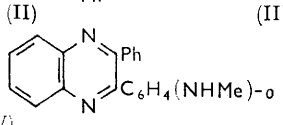
(II)



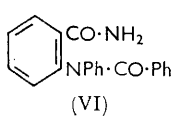
(III)



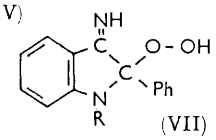
(IV)



(V)



(VI)



(VII)

3-Amino-1-methyl-2-phenylindole was obtained by hydrogenation of the corresponding 3-nitroso-compound [5] and characterised as its acetyl derivative. It was rapidly autoxidised in ethereal solution to a yellow compound, which was obviously the analogue of (Ib). The infrared spectrum did not permit differentiation between structures (Ic) and (IV) for this compound. The absorption between 2600 and 3300 cm.$^{-1}$ was characteristic of hydrogen bonded OH and/or NH together with a sharp peak at 3240 cm.$^{-1}$ (N–H?). The band at 1650 cm.$^{-1}$ could be assigned to either C=O or C=N. Similar spectra were observed for (Ia). Reaction of compound (Ic) with σ-phenylenediamine gave the expected quinoxaline (V) with a characteristic absorption at 3400 cm.$^{-1}$ (NH), absent from the spectrum of the monoacetyl derivative.

The infrared spectrum of the colourless product from the autoxidation of 3-amino-1,2-diphenylindole did not agree with the assigned structure (II). In particular, absorption

[1] E. G. E. Hawkins, " Organic Peroxides," Spon Ltd., London, 1961, pp. 127—132.
[2] F. Ying-Hsiueh Chen and E. Leete, *Tetrahedron Letters*, 1963, 2013; H. H. Wasserman and M. B. Floyd, *ibid.*, p. 2009.
[3] B. Witkop, J. B. Patrick, and M. Rosenblum, *J. Amer. Chem. Soc.*, 1951, **73**, 2641.
[4] Huang-Hsinmin and F. G. Mann, *J.*, 1949, 2903.
[5] N. Campbell and R. C. Cooper, *J.*, 1935, 1208.

bands indicative of NH_2 (3430 and 3490 cm.$^{-1}$) and carbonyl groups (1680 cm.$^{-1}$) were observed, suggesting that the correct structure was (VI). This was confirmed by synthesising (VI) from σ-anilinobenzamide and benzoyl chloride. The dehydration of (VI) to the quinazolone (III) ($\nu_{max.}$ 1650 cm.$^{-1}$) is unexceptional.

The formation of these autoxidation products is readily rationalised if the first stage is formation of the hydroperoxide (VII), which is then transformed by reduction into (I) or by rearrangement into (VI) in the usual way.

Experimental.—*3-Amino-1-methyl-2-phenylindole.* A suspension of 1-methyl-3-nitroso-2-phenylindole (18 g.) was hydrogenated in ethanol (100 ml.) using a 5% palladium–charcoal catalyst at room temperature and atmospheric pressure. Hydrogen (3750 ml., 1·02 moles) was slowly taken up. The catalyst was filtered off and the ethanol removed by distillation under nitrogen. Distillation of the residue gave the product (10·6 g.) as a golden yellow syrup, b. p. 196—200°/1·5 mm., which slowly crystallised, m. p. 81—84°. Consistent analyses could not be obtained owing to ready autoxidation. It was characterised as its *acetyl derivative*, m. p. 172—173° (from aqueous ethanol) (Found: C, 77·2; H, 6·1; N, 10·5. $C_{17}H_{16}N_2O$ requires C, 77·3; H, 6·1; N, 10·6%).

Autoxidation of 3-Amino-1-methyl-2-phenylindole. The amino-indole (2 g.) was dissolved in ether (20 ml.) and stirred with free access of air at room temperature for 14 hr. The yellow *3-imino-compound* (Ic) which was deposited (0·85 g.) had m. p. 140—141° (from chloroform–benzene) (Found: C, 75·6; H, 6·1; N, 11·7. $C_{15}H_{14}N_2O$ requires C, 75·6; H, 5·9; N, 11·8%). This compound (0·85 g.) and σ-phenylenediamine (0·34 g.) in ethanol (10 ml.) were heated under reflux for 30 min. Cautious addition of water gave a product which was recrystallised from aqueous methanol to give 2-[o-(*methylamino*)*phenyl*]-*3-phenylquinoxaline* (0·41 g.), m. p. 129—130° (Found: C, 80·9; H, 5·7; N, 13·5. $C_{21}H_{17}N_3$ requires C, 81·0; H, 5·5; N, 13·5%). This was converted, by refluxing in acetic anhydride, into its *acetyl derivative*, m. p. 182—183° (from aqueous methanol) (Found: C, 78·4; H, 5·6; N, 12·2. $C_{23}H_{19}N_3O$ requires C, 78·2; H, 5·4; N, 11·9%).

N-(σ-*Carboxyamidophenyl*)-N-*phenylbenzamide* (VI). σ-Anilinobenzamide [6] (1 g.) and benzoyl chloride (0·55 ml.) were warmed together on a steam-bath for 20 min. and the mixture was crystallised from ethanol to give the product (VI) (0·65 g.), m. p. and infrared spectrum identical with those of the product obtained by autoxidation of 3-amino-1,2-diphenylindole.

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[*Received, November 30th*, 1964.]

[6] M. Goodman, N. Arbiter, and G. Powell, *J. Amer. Chem. Soc.*, 1933, **55**, 4294.

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638. *Radical Selectivity: The Initial Stages of Alkane Oxidations*

By J. H. KNOX and J. M. C. TURNER

THE major initial products of the gas-phase oxidation of simple alkanes above 300° are olefins containing the same number of carbon atoms as the parent alkanes;[1–3] with alcohols, the initial oxidation products are often carbonyl compounds and hydrogen peroxide.[4–6] These observations have been explained by means of HO_2 radical chains:

$$R + O_2 = AB + HO_2 \quad (1)$$

$$RH + HO_2 = R + H_2O_2 \quad (2)$$

where RH is an alkane or alcohol and AB an olefin or carbonyl compound.

[1] J. H. Knox and C. H. J. Wells, *Trans. Faraday Soc.*, 1963, **59**, 2786, 2801.
[2] J. H. Knox, *Trans. Faraday Soc.*, 1960, **56**, 1225.
[3] A. P. Zeelenberg and A. F. Bickel, *J.*, 1961, 4014.
[4] C. F. Cullis and E. J. Newitt, *Proc. Roy. Soc.*, 1956, *A*, **237**, 530; 1957, *A*, **242**, 516.
[5] A. R. Burgess, C. F. Cullis, and E. J. Newitt, *J.*, 1961, 1884; A. R. Burgess and C. F. Cullis, *J.*, 1961, 3041.
[6] C. F. Cullis and E. J. Newitt, *Proc. Roy. Soc.*, 1960, *A*, **257**, 402.

The bond strength D[H–OOH] is now fairly well established [7] as 89 ± 2 kcal. mole^{-1}, and most hydrogen abstractions by HO_2 from alkanes will be endothermic. The selectivity of HO_2 in abstraction reactions should therefore be high and similar to that of the bromine atom, since D[H–Br] = 87 kcal. mole^{-1}. It is then difficult to explain the data of Falconer, Knox, and Trotman-Dickenson [8] on the basis of an HO_2 radical chain. They found that the radical, or mixture of radicals, removing alkanes in co-oxidations had a selectivity only slightly greater than that of the chlorine atom and much less than that of the bromine atom, and suggested that OH might indeed be the attacking radical, not HO_2. Recently, supporting evidence for the low reactivity of HO_2 has been provided from studies of the oxidations of hydrogen,[9] methane,[10] and ethane [11] at 500—650°. Nevertheless, one cannot avoid reactions (1) and (2) in the very early stages of reaction, where the concentrations of primary products and other free radicals will be very low. The low selectivity observed by Falconer, Knox, and Trotman-Dickenson may, in fact, be peculiar to the later stages of the reaction, since their experiments gave selectivities averaged over the first 10—20% of the reaction. If HO_2 propagation indeed gives way to OH propagation, it ought to be possible to observe a marked change in selectivity as the reaction proceeds.

In order to test this hypothesis, we have carried out competitive oxidations with propane and isobutane at 300°. Both hydrocarbons give 80 ± 2% conversion to the appropriate olefin if the overall alkane consumption is kept below 1%. Under these conditions, the ratio of rate constants for attack of the propagating radical on the two alkanes in the early stages [8] is given by

$$\frac{k(\text{isobutane})}{k(\text{propane})} = \frac{[i\text{-}C_4H_8][C_3H_8]}{[C_3H_6][i\text{-}C_4H_{10}]}.$$

The alkane concentrations can be taken as the initial pressures, and the olefin concentrations can be found by gas-chromatographic analysis of the reaction products, provided that suitable allowance is made for olefins produced by processes other than reaction (1).

Two sets of experiments were carried out, using mixtures of isobutane and propane. The isobutane contained 0·4% of propane and 0·04% of ethane. The propane contained 0·81% of isobutane and 0·33% of propene.

(A) Mixtures of propane, isobutane, and oxygen in the molar ratio 2 : 2 : 1 were allowed to react in a 600-ml. Pyrex reaction vessel at 300° and a total pressure of 200 mm. Samples (2 ml.) were taken from the reaction vessel from time to time by means of a multiple-sampling device and analysed later for the two olefins. The gas-chromatographic equipment was of conventional design and employed a flame-ionisation detector. The sensitivity of the detector to propene was assumed to be 0·75 times that to isobutene. This assumption is unlikely to be in error by more than 2%.[12]

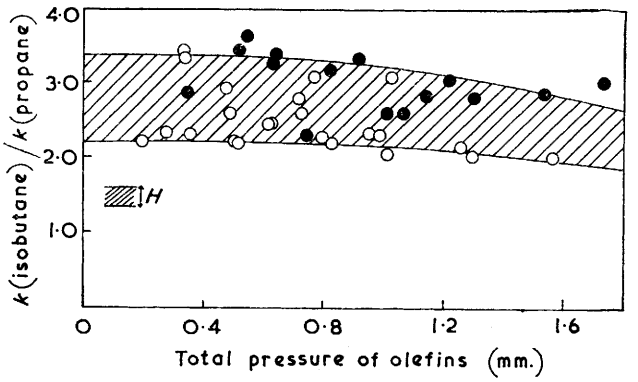
The measured propene yields included both propene originally present in the propane and that formed from the oxidation of isobutane. The amount formed from isobutane was assumed to be the same as would have been obtained by oxidising isobutane in the absence of propane. This assumption may be slightly in error, owing to the uncertain role of surface in the reaction.[13] The quantity of propene formed from the propane was then obtained by difference. The total correction was 75% of the total yield of propene at the lowest conversions, and about 30% at conversions of 1%, the highest used. The

[7] S. N. Foner and R. L. Hudson, *J. Chem. Phys.*, 1962, **36**, 2681.
[8] W. E. Falconer, J. H. Knox, and A. F. Trotman-Dickenson, *J.*, 1961, 782.
[9] R. R. Baldwin and L. Mayor, *Trans. Faraday Soc.*, 1960, **56**, 80, 93, 103.
[10] L. V. Karmilova, N. S. Enikolopyan, A. B. Nalbandyan, and N. N. Semenov, *Russ. J. Phys. Chem.*, 1960, **34**, 562.
[11] R. J. Sampson, *J.*, 1963, 5095.
[12] J. C. Sternberg, W. S. Gallaway, and D. T. L. Jones, "Gas Chromatography," ed. Brenner, Callen, and Weiss, Academic Press, New York, 1961, p. 231; L. S. Ettre, *ibid.*, p. 307.
[13] J. Hay, J. H. Knox, and J. M. C. Turner, 10th Internat. Symp. on Combustion, Butterworths, London, 1964, in the press.

mean of 26 measurements of k(isobutane)/k(propane) was 2·53, and the standard deviation was 0·33.

(B) The competitive oxidation of propane and isobutane could also be studied by using the sample of propane which contained 0·81% of isobutane. With this mixture, no correction was required for the propene formed from isobutane. The mean of 14 measurements was 3·01, with a standard deviation of 0·32.

In the Figure, the data are plotted against the extent of oxidation. Although there appears to be a slight fall in selectivity as the extent of oxidation increases, this is well within the limits of experimental error, and may not be significant. The mean selectivity at zero consumption of alkane is about 2·8, with a possible error of ±0·3. The mean selectivity obtained by Knox, Smith, and Trotman-Dickenson [14] and Falconer, Knox, and



k(isobutane)/k(propane) as a function of extent of reaction at 300°

○ Series (A): i-C_4H_{10} : C_3H_8 : O_2 = 2 : 2 : 1; total pressure = 200 mm. ● Series (B): C_3H_8 : O_2 = 2 : 1; total pressure = 225 mm.; C_3H_8 contained 0·81% of i-C_4H_{10}. H = range at high conversions, from ref. 8.

Trotman-Dickenson [8] for 10—20% consumption of alkane was 1·3, with a possible error of ±0·1.

There is evidently a marked decrease in selectivity between the earliest stages of the reaction and intermediate stages when 10—20% of the alkane has been consumed. The selectivities observed in these two oxidation systems are compared in the Table with those

Radical selectivities at 300°

			Oxidation			
Radical	F	Cl	(1%)	(20%)	CH_3	Br
k(isobutane)/k(propane)	1·1	1·1	2·8	1·3	2·4	3·7
Ref.	16	17	Present work	8	18	19

calculated for other free radicals. The initial selectivity is slightly less than that calculated for Br, but much greater than that for Cl, while the later selectivity is much closer to that for Cl. The data confirm the ideas already put forward that a selective radical, such as HO_2, removes the alkane in the earliest stages of oxidation, while a more reactive species, such as OH, is important later. Since reaction (1) must occur throughout the reaction, there must be some process which converts HO_2 to OH. This process does not occur in

[14] J. H. Knox, R. F. Smith, and A. F. Trotman-Dickenson, *Trans. Faraday Soc.*, 1958, **54**, 1509.
[15] G. Skirrow and A. Williams, *Proc. Roy. Soc.*, 1962, *A*, **268**, 537.
[16] G. C. Fettis, J. H. Knox, and A. F. Trotman-Dickenson, *J.*, 1960, 1064.
[17] J. H. Knox and R. L. Nelson, *Trans. Faraday Soc.*, 1959, **55**, 937.
[18] A. F. Trotman-Dickenson, " Gas Kinetics," Butterworths, London, 1955.
[19] P. C. Anson, P. S. Fredericks, and J. M. Tedder, *J.*, 1959, 918; G. C. Fettis, J. H. Knox, and A. F. Trotman-Dickenson, *J.*, 1960, 4177.

the early stages of the reaction, and so presumably depends upon the reaction of HO_2 with some major product. The only product formed in sufficient quantity is the olefin AB. A process which could bring about the endothermic conversion, $HO_2 = OH + \frac{1}{2}O_2$, is

$$A{=}B \xrightarrow{HO_2} \cdot ABO{\cdot}OH \xrightarrow{O_2} \cdot O{\cdot}OABO{\cdot}OH \xrightarrow{HO_2} HO{\cdot}OABO{\cdot}OH \longrightarrow HO + OA + BO + OH + O_2 \quad (3)$$

This olefin oxidation mechanism results in the conversion of two HO_2 radicals to two OH radicals for each olefin molecule oxidised to the carbonyl products AO and BO. Such products are known to be the major initial products of olefin oxidations in the gas phase.[13,15]

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639. *Seven-co-ordinate Halogenocarbonyl Anions of Molybdenum(II) and Tungsten(II)*

By M. C. GANORKAR and M. H. B. STIDDARD

HALOGEN oxidation of di(tertiary arsine)-substituted carbonyls constitutes a valuable method for the preparation of seven-co-ordinate complexes of chromium(II), molybdenum(II), tungsten(II), and rhenium(III).[1] As a further extension of this work, halogen oxidation of the halogenocarbonyl anions $[M(CO)_5X]^-$ (M = Mo and W; X = Br and I)[2] has been studied. Oxidation of the carbonyl anion $[Cr(CO)_5I]^-$ is known to lead to the six-co-ordinate chromium(I) complex $[Cr(CO)_5I]$.[3] During the present investigation, King[4] reported similar, but less extensive, experiments.

The zerovalent halogenocarbonyl anions are oxidised readily with two equivalents of the appropriate halogen to give both simple and mixed seven-co-ordinate anions, *e.g.*, $[Mo(CO)_4I_3]^-$ and $[Mo(CO)_4IBr_2]^-$. These compounds are yellow to orange, diamagnetic, and behave as typical 1 : 1 electrolytes in nitrobenzene. They are unstable in air and difficult to purify. The compound $Et_4N[W(CO)_4Br_3]$ is particularly unstable and its analysis unsatisfactory. The infrared spectra of these compounds in the C–O stretching region are given in Table 1. Nujol mulls were used, as solutions were too unstable for spectroscopic purposes.

TABLE 1

Infrared spectra (C–O stretching bands, $cm.^{-1}$) of complexes in Nujol

1. $[MeN(C_5H_5)][Mo(CO)_4I_2]$	2083m	2018vs	1961s	1942s
2. $[MeN(C_5H_5)][Mo(CO)_4IBr_2]$	2085m	2040vs	1968s	1925sh
3. $Et_4N[Mo(CO)_4Br_3]$	2083m	2040s	2000vs	1932vs
4. $Et_4N[Mo(CO)_4BrI_2]$	2083m	2020vs	1961s	1925sh
5. $Et_4N[W(CO)_4I_3]$	2083m	2016vs	1964s	1925s
6. $Et_4N[W(CO)_4IBr_2]$	2090m	2037s	2000vs	1932vs
7. $Et_4N[W(CO)_4Br_3]$	2080m	2041s	2000vs	1925vs
8. $Et_4N[W(CO)_4BrI_2]$	2078m	2025s	1965vs	1923vs

Experimental.—Infrared spectra were measured with a Grubb–Parsons GS 2A double-beam grating spectrometer.

Preparation of complexes. To a suspension of the zerovalent halogenocarbonyl salt (*ca.* 1·0 g.) in chloroform (50 ml.) was added 2 equiv. of the appropriate halogen in the same solvent (50 ml.) in a closed system. After filtration and concentration, excess of light petroleum was added, and crystals separated at room temperature. The *product* was filtered off, washed with

[1] W. J. Kirkham, A. G. Osborne, R. S. Nyholm, and M. H. B. Stiddard, *J.*, 1965, 550, and references quoted therein.
[2] E. W. Abel, I. S. Butler, and J. G. Reid, *J.*, 1963, 2068.
[3] H. Behrens and H. Zizlsperger, *Z. Naturforsch.*, 1961, **16**b, 349.
[4] R. B. King, *Inorg. Chem.*, 1964, **3**, 1039.

light petroleum, and dried *in vacuo*. Yields and analyses are given in Table 2. The compounds are soluble in acetone, chloroform, dichloromethane, and nitrobenzene, but insoluble in light petroleum. Solutions are unstable.

TABLE 2

Preparation and analysis of compounds

	Yield	Found (%)						Required (%)					
Complex	(%)	C	H	Br	I	N	Mo/W	C	H	Br	I	N	Mo/W
1.*	79	17·7	1·2	—	56·0	2·1	14·0	17·5	1·2	—	55·8	2·2	14·0
2.	70	19·9	1·2	26·7	21·2	2·5	16·6	20·4	1·3	27·1	21·4	2·3	16·3
3.	75	24·5	3·8	39·8	—	2·2	16·7	24·9	3·5	41·6	—	2·4	16·6
4.†	71	21·3	3·2	11·7	37·9	2·0	13·9	21·4	3·0	11·9	37·8	2·1	14·2
5.	70	17·7	2·6	—	46·1	1·6	22·7	18·2	2·5	—	48·1	1·8	23·5
6.	76	20·3	3·1	22·2	17·9	2·0	21·3	20·2	2·8	22·4	17·7	2·0	20·5
7.	68	24·3	3·2	29·8	—	2·6	—	21·6	3·0	36·0	—	2·1	27·6
8.	70	19·6	3·1	10·9	16·9	2·1	24·1	18·9	2·6	10·5	16·7	1·8	24·2

* Prepared also by King.[4] † Also: Found: O, 9·5. Calc. 9·5%.

One of us (M. C. G.) thanks the Vice-Chancellor, Osmania University, Hyderabad, for granting leave of absence.

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640. *Extractives from East African Timbers. Part I*

By D. A. H. TAYLOR

THERE has been considerable interest recently in oxidised triterpene derivatives of similar structure to limonin, which have been found to be widespread in the family Meliaceae. The present Paper records the examination of heartwood samples of a number of East African members of this family, and also of three *Podocarpus* species from South Africa.

Experimental.—Method. The timber samples were pulverised and then extracted in a hot percolator with light petroleum ("isohexane" fraction). Sometimes a solid separated from the extract, and this was filtered off. The extract was concentrated and the residue macerated with ether. The insoluble portion was mixed with the original precipitate, if any, and recrystallised from methanol. If no solid material was obtained in this way, the extract was chromatographed over neutral alumina. In most cases there was either a large amount of extract which crystallised readily, or a small amount which appeared to be mainly fatty esters or sterols, and from which no crystals were obtained.

Results. Entandrophragma angolense (*Welw.*) *C.DC.* Four Uganda samples of this were examined. All samples agreed, and differed from West African material in giving extracts from which neither gedunin, methyl angolensate, nor any other meliacin could be obtained. The absence of any but trace amounts of meliacins was confirmed by thin-layer chromatography. As the specimens also present some botanical differences from those obtained in West Africa, it seems possible that they may not be strictly the same species.

Entandrophragma bussei *Harms.* This gave a large amount of extract from which a solid separated. On crystallisation from methanol this gave *bussein* (*ca.* 0·1%) as colourless prisms, m. p. 300—304° (decomp.) (Found: C, 60·6, 60·8; H, 6·5, 6·6. N.m.r. proton count, 52. $C_{40}H_{52}O_{16}$ requires C, 60·9; H, 6·6%). This substance is being further investigated. Chromatography of the mother-liquors gave entandrophragmin (*ca.* 0·1%), m. p. 256°, identical in m. p. and infrared spectrum with a sample from *Entandrophragma cylindricum* [1] (in this reference the m. p. of entandrophragmin is wrongly given as 241°). Further elution furnished β-sitosterol (*ca.* 0·05%).

Entandrophragma caudatum *Sprague.* Extraction of a Southern Rhodesian sample of this timber gave results similar to those obtained with *Entandrophragma bussei* except that the

amount of bussein was much less (*ca.* 0·01%). As only one sample of each timber was investigated it is not possible to say if this represents a species distinction or only an individual variation.

Entandrophragma delevoyi *De Wild.* Extraction of this timber gave a semi-solid material which was not readily purified by crystallisation. Chromatography over alumina yielded gedunin (0·02%), identical with material from Nigerian *Entandrophragma angolense*,[1] and also β-sitosterol.

Entandrophragma excelsum (*Dawe and Sprague*) *Sprague.* Two Uganda samples of this were investigated; neither gave any crystalline product. A Tanganyika sample of *Entandrophragma stolzii* Harms, now considered to be the same species, gave similar results.

Trichilia splendida *A. Chev.* This gave an oily extract from which, on long standing, a very small amount of crystalline material, m. p. 278°, separated. The infrared spectrum was generally similar to that of khivorin,[2] but different in detail from that of any other meliacin we have seen. Insufficient of this material was obtained for further investigation.

Xylocarpus granatum *Koen.* (syn. X. benadirensis *Mattei*). The timber of this common mangrove gave gedunin (0·1%), identical in infrared spectrum and m. p. with an authentic sample.

In addition to the above, the following timbers were extracted, but no crystalline material was obtained from them: *Carapa grandiflora* Sprague, *Lovoa brownii* Sprague, and *Pseudobersama mossambicensis* Verdcourt.

Podocarpus *species.* Specimens of three species, *P. elongatus* L'Hérit. ex Pers., *P. henkelii* Stapf, and *P. latifolius* R. Br. were collected in the Kirstenbosch Botanical Garden, Cape Town, by kind permission of the Director. All three gave extracts very similar qualitatively to those previously recorded for *P. milanjuianus*,[3] containing principally totarol with a large amount of its 16-oxo- and some 16-hydroxy-derivative. The samples were not large enough to permit more detailed investigation.

Pseudobersama mossambicensis was collected by the Kenya Forestry Department. All the other specimens were collected by the author, and all are supported by herbarium material deposited in the Forest Herbarium at Oxford. This work was mostly carried out during a study leave spent at Kampala, and the author is grateful to Professor M. Crawford for the hospitality of his department. The author is also grateful to the Forest Departments of Kenya, Tanganyika, and Uganda and to the Warden of the Victoria Falls National Park for permission and assistance in collecting material, and to Mr. F. White and Dr. B. T. Styles of the Commonwealth Forestry Institute, Oxford, for advice and identification of specimens.

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[1] A. Akisanya, C. W. L. Bevan, J. Hirst, T. G. Halsall, and D. A. H. Taylor, *J.*, 1960, 3827.
[2] C. W. L. Bevan, T. G. Halsall, M. N. Nwaji, and D. A. H. Taylor, *J.*, 1962, 768.
[3] C. W. L. Bevan and D. A. H. Taylor, *J.*, 1963, 6050.

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641. *Displacement Reactions of Galactose 6-Sulphonate Derivatives*

By (Mrs.) S. Nadkarni and N. R. Williams

Some recently published studies [1,2] on the nucleophilic displacement of primary sulphonate groups in carbohydrates prompts us to record our observations on the displacement of 6-methanesulphonate and 6-toluene-*p*-sulphonate groups in galactopyranose ester derivatives. It is well known [3] that the displacement of these groups by sodium iodide in acetone occurs much less readily in derivatives of galactose than in similar derivatives of glucose

[1] M. Akagi, S. Tejima, and M. Haga, *Chem. and Pharm. Bull.* (*Japan*), 1963, **11**, 559.
[2] J. M. Sugihara and W. J. Teerlink, *J. Org. Chem.*, 1964, **29**, 550.
[3] R. S. Tipson, *Adv. Carbohydrate Chem.*, 1953, **8**, 181.

and other hexoses, the effect being most marked for the esters of 1,2:3,4-di-*O*-isopropylidene-α-D-galactopyranose. We were interested to see whether the effect could be attributed to the presence in these derivatives of the ketal rings, and particularly whether the methyl groups in the 3,4-*O*-isopropylidene residue exerted any steric effect. Accordingly, we studied the rate of the reaction when one or both of these methyl groups are replaced by hydrogen, using ethylidene and methylene acetals in place of isopropylidene, and we have compared these rates with that for methyl 2,3,4-tri-*O*-methyl-α-D-galactopyranoside 6-toluene-*p*-sulphonate, to observe the effect of the two acetal rings on the rate. In order to discover whether the reaction is also subject to solvent effects, we studied the same compounds under similar conditions with dimethylformamide or dimethyl sulphoxide as solvent. Our results are summarised in the Table.

The results show that replacement of isopropylidene by ethylidene makes no significant difference to the rate of the reaction, whereas the 3,4-*O*-methylene derivatives shows a rate increase of 50%. Replacement of the two acetal rings by *O*-methyl groups doubles the rate. However, the rates are still much slower than is generally found for analogous derivatives of other hexoses,[3] which exhibit more or less complete reaction after several hours at 80—100°, and the small increases in rate observed indicate that the size of the substituent attached to the C-4 oxygen can have only a minor influence in retarding the displacement.

The slower rate of displacement of the methanesulphonate compared with the toluene-*p*-sulphonate group has already been noted [4,5] for primary sulphonate esters, and renders

Percentage exchange of 6-sulphonate groups of galactose derivatives by iodide or thiocyanate in acetone, dimethylformamide (DMF), or dimethyl sulphoxide (DMSO) at 120—125° for 5·5 hours

Reagent:	Sodium iodide			Sodium iodide		Sodium thiocyanate
Ester:	Toluene-*p*-sulphonate			Methanesulphonate		Toluene-*p*-sulphonate
Solvent:	Acetone	DMF	DMSO	Acetone	DMF	Acetone
1,2:3,4-Di-*O*-isopropylidene-α-D-galactose	24·7	26·9	26·6	10·6	13·5	7·9
1,2-*O*-Ethylidene-3,4-*O*-isopropylidene-α-D-galactose	24·6	26·1	—	11·1	14·6	7·0
1,2:3,4-Di-*O*-methylene-α-D-galactose	35·7	38·6	—	16·3	17·8	13·5
Methyl 2,3,4-tri-*O*-methyl-α-D-galactopyranoside	52·2	52·1	—	—	—	—

unlikely any marked steric interaction between the 4-*O*-substituent and the sulphonate group. The small difference in rate observed on changing the solvent from acetone to the highly polar dimethylformamide or dimethyl sulphoxide is compatible with the S_N2 mechanism expected for the displacement, indicating that the change in rate is not associated with a change to an S_N1 mechanism; this is borne out by the slower rate observed with thiocyanate than with iodide, in agreement with its lower nucleophilicity in S_N2 displacements at a saturated carbon.[6]

The displacement of the toluene-*p*-sulphonate group in the di-isopropylidene derivative by electrically neutral nucleophiles apparently proceeds under much milder conditions, *i.e.*, with liquid ammonia at room temperature [7] or with anhydrous hydrazine at 60°,[8] which suggests that the rate is very sensitive to the presence or absence of charge on the nucleophile. For this reason, we conclude, with Sugihara and Teerlink,[2] that the lower reactivity of the galactose derivatives may best be explained by an electronic field effect of the lone pairs of electrons of the ring oxygen and the axial C-4 oxygen, which tend to repel

[4] A. B. Foster, W. G. Overend, M. Stacey, and L. F. Wiggins, *J.*, 1949, 2542.
[5] J. H. Chapman and L. N. Owen, *J.*, 1950, 579.
[6] J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, 1962, **84**, 16.
[7] K. Freudenberg and A. Doser, *Ber.*, 1925, **58**, 294.
[8] K. Freudenberg and R. M. Hixon, *Ber.*, 1923, **56**, 2119.

negatively charged nucleophiles approaching the rear side of the sulphonate ester group in its most stable conformation.

Experimental.—The following compounds were prepared by methods described in the literature: 1,2:3,4-di-*O*-isopropylidene-α-D-galactose 6-toluene-*p*-sulphonate [4,8] and 6-methanesulphonate; [9] 3,4-*O*-ethylidene-1,2-*O*-isopropylidene-α-D-galactose 6-toluene-*p*-sulphonate [10] and 6-methanesulphonate.[10] Zemplén degradation of 1,2:3,4-di-*O*-methylene-α-D-galactose 6-acetate [11] afforded 1,2:3,4-*di*-O-*methylene*-α-D-*galactose*, which after distillation and precipitation from ethyl acetate–light petroleum, was obtained crystalline; it had m. p. 80—81° (from toluene), $[\alpha]_D$ −60·8 (*c* 1·3 in chloroform) (Found: C, 46·9; H, 5·75. $C_8H_{12}O_6$ requires C, 47·05; H, 5·9%). The sulphonates were prepared in the usual way. The 6-*toluene*-p-*sulphonate* had m. p. 91—91·5, $[\alpha]_D$ −74·9 (*c* 1·3 in chloroform) (Found: C, 50·15; H, 5·05; S, 9·3. $C_{15}H_{18}O_8S$ requires C, 50·3; H, 5·05; S, 8·95%). The 6-*methanesulphonate* had m. p. 99·5—100° (Found: C, 38·05; H, 5·05; S, 11·9. $C_9H_{14}O_8S$ requires C, 38·3; H, 5·0; S, 11·35%). Methyl α-D-galactopyranoside 6-toluene-*p*-sulphonate [12] was subjected to the Kuhn methylation procedure,[13] to yield *methyl* 2,3,4-*tri*-O-*methyl*-α-D-*galactopyranoside* 6-*toluene*-p-*sulphonate*, obtained as a syrup, $[\alpha]_D$ +48·5 (*c* 1·3 in chloroform) (Found: C, 50·45; H, 6·5; OMe, 31·65. $C_{17}H_{26}O_8S$ requires C, 52·25; H, 6·65; OMe, 31·75%).

Comparative exchange reactions. (a) *In acetone.* The sulphonate (0·02 mole) and sodium iodide (0·02 mole) were dissolved in dry acetone (15 ml.), and heated in a sealed tube for 5·5 hr. in a heating block previously equilibrated at 120—125°. The tube was then removed, cooled, and opened, and the precipitated sodium sulphonate collected in a sintered glass crucible. The precipitate was washed with a little dry acetone, dried at 120° for 1 hr., and weighed. The results given in the Table include a correction to allow for the solubility of the sodium sulphonate in acetone.

(b) *In dimethylformamide or dimethyl sulphoxide.* The reactions were carried out as for acetone, except that at the end of the reaction the solvent was completely removed *in vacuo* and the residue was leached with dry acetone (15 ml.) heated under reflux for 1 hr. The solution was then cooled, and the precipitate collected and weighed as before.

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MALET STREET, LONDON W.C.1. [*Received, December 31st*, 1964.]

[9] B. Helferich, H. Dressler, and R. Griebel, *J. prakt. Chem.*, 1939, **153**, 285.
[10] A. B. Foster, W. G. Overend, and M. Stacey, *J.*, 1951, 980.
[11] L. Hough, J. K. N. Jones, and M. S. Magson, *J.*, 1952, 1525.
[12] W. N. Haworth, J. Jackson, and F. Smith, *J.*, 1940, 620.
[13] R. Kuhn, H. Trischmann, and I. Löw, *Angew. Chem.*, 1955, **67**, 32.

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642. *The Melting Point and Structure of Tryptamine*

By A. H. JACKSON and A. E. SMITH

TRYPTAMINE (I) has been accorded three different melting points in the literature: 145°;[1] 101°;[2] and by most authors a melting point in the range 114—118°.[3-8] We now present evidence that the correct melting point is 118°, that the product of m. p. 145° is probably *N*-isopropylidenetryptamine, and that the product of m. p. 101° is probably impure tryptamine.

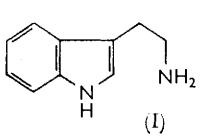
The product of m. p. 145° (hydrochloride m. p. 246°, picrate m. p. 242°) was obtained

[1] A. Ewins, *J.*, 1911, **99**, 270.
[2] G. R. Clemo, *J.*, 1936, 1695.
[3] R. H. F. Manske, *Canad. J. Res.*, 1931, **5**, 592.
[4] R. Majima and T. Hoshimo, *Ber.*, 1925, **58**, 2042.
[5] J. Thesing and F. Schülde, *Chem. Ber.*, 1952, **85**, 324.
[6] D. A. Lyttle and D. I. Weisblat, *J. Amer. Chem. Soc.*, 1955, **77**, 5747.
[7] E. H. P. Young, *J.*, 1958, 3493.
[8] M. E. Speeter and W. C. Anthony, *J. Amer. Chem. Soc.*, 1954, **76**, 6208.

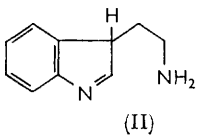
by Ewins [1] in the earliest recorded synthesis of tryptamine, although when Manske [3] later used the same method his product had m. p. 118° (hydrochloride m. p. 246°, picrate m. p. 242°).

In connection with other work,[9] we have prepared tryptamine by two different methods,[7,8] and our products had m. p. 118° after recrystallisation from light petroleum (b. p. 60—80°); however, if the products were recrystallised from acetone a substance of m. p. 146° was obtained. The infrared spectrum of this material was considerably different from that of the base with m. p. 118°, and in particular exhibited an intense peak at 6·02 μ (C=N) which suggested that it was *N*-isopropylidenetryptamine. This was confirmed by elemental analysis and by its proton magnetic resonance spectrum. The hydrochloride (m. p. 248°) and the picrate (m. p. 244°) obtained from the latter were identical with the hydrochloride and picrate obtained from tryptamine, thus showing that the isopropylidenetryptamine is readily hydrolysed as well as readily formed. In view of the closeness of the melting points we conclude that Ewin's product [1] was probably *N*-isopropylidenetryptamine, and may have arisen from impurity in his solvents, or from attempts to recrystallise it from acetone; he reported crystallising his product of m. p. 145° from benzene, and also from ethanol, both of which we found satisfactory for *N*-isopropylidenetryptamine but unsuitable for tryptamine, m. p. 118°, on account of its greater solubility.

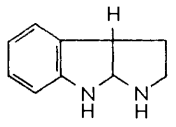
The product of m. p. 101° [2] was obtained as an alkaline degradation product from strychnine, and was isolated initially as its red picrate " m. p. 253—254° (decomp.), after darkening from 245°." The base " (C) " [2] was prepared by regeneration from this picrate, and on crystallisation from ether gave " faintly brown prisms, m. p. 100—101°," or, after sublimation in a high vacuum at 180°, " colourless prisms, m. p. 101—102°." Metcalfe (see ref. 2) repeated Majima and Hoshimo's preparation [4] of tryptamine and obtained, " after three recrystallisations from ether, a faintly brown poorly crystalline solid, m. p. 114°," mixed m. p. with the base (C) obtained from strychnine, 102—112°. The picrate of the base of m. p. 114° had the same crystalline form and decomposition point as the picrate of the base (C), and " furthermore, the base regenerated from the picrate formed prisms (from ether), m. p. 101°, unchanged by admixture with (C), and gives well-formed prisms, m. p. 101°, on sublimation."



(I)



(II)



(III)

Clemo suggested [2] that the base (C) might be the tautomeric indolenine form (II) of tryptamine. However, this now seems very unlikely as it would be expected to cyclise immediately to the tricyclic indoline (III) by analogy with similar cyclisations in the physostymine series.[10] In addition, spectroscopic studies [9,11] (u.v. and p.m.r.) have shown that tryptamine exists entirely in the indolic form (I) in neutral solution, and that there is no evidence of the existence of any tautomeric forms.

We therefore reinvestigated formation of the picrate of tryptamine, and regeneration of the free base with alkali as described by Clemo. However, our picrate had m. p. 242°, in accord with all other authors' results,[3-8] and on regeneration the free base had m. p. 110° (from ether). The infrared and ultraviolet spectra of this product were identical with those of the original tryptamine, m. p. 118°, and on recrystallisation from light petroleum the melting point was raised to 118°. We therefore conclude that Clemo's product, m. p.

[9] A. H. Jackson and A. E. Smith, *J.*, 1964, 5510.
[10] " Heterocyclic Compounds," Vol. III, ch. 1, ed. R. C. Elderfield, Wiley, New York.
[11] L. A. Cohen, J. W. Daly, H. King, and B. Witkop, *J. Amer. Chem. Soc.*, 1960, **82**, 2184.

101°, was probably impure tryptamine, the low melting point being due to the use of a solvent (ether) which we have found is not satisfactory for the recrystallisation of tryptamine.

Experimental.—Tryptamine was prepared by reduction of 3-(2-nitrovinyl)indole,[7] or 3-indolylglyoxylamide,[8] and crystallised from light petroleum (b. p. 60—80°) to give needles, m. p. 118°. (It crystallised from ether as buff coloured prisms, m. p. 114°.) $\lambda_{max.}$ (ethanol) 222, 282, 290 mμ; log ε 4·56, 3·78, 3·71. The hydrochloride formed minute needles, m. p. 248° (from ethanol–ethyl acetate), and the picrate crystallised from ethanol as red needles, m. p. 242° (unchanged even after prolonged heating in boiling ethanol). Treatment of this picrate with alkali as described by Clemo, gave a gum which was crystallised from ether and sublimed at 180°/0·01 mm., to give a product, m. p. 110°. The latter had ultraviolet and infrared spectra identical with those of the original tryptamine, and on recrystallisation from light petroleum (b. p. 60—80°) the m. p. was raised to 118°.

N-*Isopropylidenetryptamine.* Tryptamine (m. p. 118°) was recrystallised from acetone and gave N-*isopropylidenetryptamine* as rosettes of needles, m. p. 145—146° (Found: C, 77·9; H, 8·2; N, 13·2. $C_{13}H_{16}N_2$ requires C, 78·0; H, 8·1; N, 14·0%.) $\lambda_{max.}$ (mμ) (log ε) in ethanol: 222 (4·57), 282 (3·79), and 289 (3·71); $\nu_{max.}$ ($CHCl_3$): 6·02 μ. The hydrochloride, m. p. 248°, and the picrate, m. p. 242°, prepared in ethanol were shown by mixed m. p. comparisons to be identical with the hydrochloride and picrate of tryptamine.

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643. *Tetraphenyldiphosphine monoxide*

By J. MCKECHNIE, D. S. PAYNE, and W. SIM

IT was recently stated[1] that the reaction of chlorodiphenylphosphine with ethylamine carried out without the rigorous exclusion of moisture or oxygen led to a mixture of tetraphenyldiphosphine and its dioxide, together with diphenylphosphinic acid. Further investigation has shown this to be incorrect, the product obtained under these conditions being largely tetraphenyldiphosphine monoxide. The operative reagent is water, since its deliberate addition during the reaction leads to increased yields of the monoxide. Further, the monoxide can be obtained in 84% yield by the reaction of chlorodiphenylphosphine with water in the presence of triethylamine as hydrogen-chloride acceptor. The reaction may proceed by the initial formation of diphenylphosphinous acid, $Ph_2P{\cdot}OH$, which then rearranges to diphenylphosphine oxide, $Ph_2P(:O)H$,[2] and reacts with one further mole of chlorodiphenylphosphine thus:

$$Ph_2PCl + H_2O \xrightarrow{Base} Ph_2P{\cdot}OH + Base,HCl$$

$$Ph_2P{\cdot}OH + Ph_2PCl \xrightarrow{Base} Ph_2P(:O)H + Base,HCl$$

$$Ph_2P(:O)H + Ph_2PCl \xrightarrow{Base} Ph_2P{\cdot}P(:O)Ph_2 + Base,HCl$$

In the case of the reaction employing ethylamine as base, there is a competitive reaction involving the formation of $Ph_2P{\cdot}NHEt$, which can be isolated. However, the possibility that $Ph_2P{\cdot}NHEt$ undergoes a proton migration similar to $Ph_2P{\cdot}OH$, leading to $Ph_2P{\cdot}P(:NR)Ph_2$, cannot be excluded. This phosphazene, if formed, would then undergo hydrolysis to the monoxide.

The identity of tetraphenyldiphosphine monoxide was established by analysis and by

[1] G. Ewart, A. P. Lane, J. McKechnie, and D. S. Payne, *J.*, 1964, 1543.
[2] B. B. Hunt and B. C. Saunders, *J.*, 1957, 2413.

conversion into the dioxide and the mixed oxide sulphide, $Ph_2P(:S)\cdot P(:O)Ph_2$. Attempts to prepare quaternary salts were not successful. Reaction with elemental bromine in benzene

$$Ph_2P\cdot P(:O)Ph_2 \xrightarrow{Br_2} Ph_2PBr_3 + Ph_2P(:O)Br$$

solution gave almost quantitative precipitation of tribromodiphenylphosphorane. A comparison of the infrared spectrum of tetraphenyldiphosphine monoxide with that of the dioxide shows very few differences. The absorption at 1175 cm.$^{-1}$, usually attributed to the phosphoryl group, was the same in both, in marked contrast to the behaviour of the corresponding carbonyls and 1,2-dicarbonyls. Similarly, the 1175 cm.$^{-1}$ absorption appears in the spectrum of the oxide sulphide, which, however, also shows absorption at 648 and 612 cm.$^{-1}$ in accord with previously reported compounds containing P=S.[1] The published spectra of tetraphenyldiphosphine,[3] recently confirmed,[4] also show a strong absorption at 1175 cm.$^{-1}$, which is not to be expected by comparison with, for example, the spectrum of triphenylphosphine and is not present in tetraphenyldiphosphine disulphide. However, preparation of tetraphenyldiphosphine by reduction of the monoxide with lithium aluminium hydride led to material which similarly possessed the 1175 cm.$^{-1}$ absorption, and the origin of this peak is, therefore, still not clear.

Experimental.—Preparation of tetraphenyldiphosphine monoxide using ethylamine as base. Chlorodiphenylphosphine (34·2 g., 0·155 mole) was dissolved in sodium-dried benzene (300 ml.), and a suspension of water (2·8 g., 0·155 mole) in a solution of sodium-dried ethylamine (12·55 g., 0·279 mole) in benzene (200 ml.) was added during ½ hr. The reaction was carried out at 0° under nitrogen. The amine hydrochloride was filtered off and the benzene removed, to give a white solid and a yellow oil which were separated to yield ethylaminodiphenylphosphine (19·3 g., 54·4%) and *tetraphenyldiphosphine monoxide* (12·6 g., 36·4%), m. p. 155—158° [Found: C, 74·5; H, 5·4; P, 16·1%; *M* (cryoscopic in benzene), 390. $C_{24}H_{20}OP_2$ requires C, 74·6; H, 5·2; P, 16·1%; *M*, 386]. It is only slightly soluble in benzene, toluene, and ethanol in the cold, and is very sparingly soluble in diethyl ether and di-n-butyl ether. It is conveniently recrystallised from acetone–water, and is completely stable in air for short periods; on long standing in moist air it becomes sticky and diphenylphosphinic acid is formed.

Preparation of tetraphenyldiphosphine monoxide using triethylamine as base. Chlorodiphenylphosphine (11·2 g., 0·051 mole) was treated, as described above, with water (0·46 g., 0·026 mole) and triethylamine (6·0 g., 0·052 mole), to yield (I) (8·19 g., 83·5%), m. p. 155—158°.

Conversion into tetraphenyldiphosphine dioxide. Compound (I) (2·29 g., 6·7 mmoles) was suspended in toluene (30 ml.), cooled in ice, and a stream of dry air bubbled through for 3 hr. The temperature of the suspension was then raised to the boiling point of toluene to dissolve the solid, and, on cooling, a white *solid* (0·73 g., 27%) appeared, m. p. 169—173° (from toluene) (Found: C, 71·6; H, 5·0; P, 15·2. $C_{24}H_{20}O_2P_2$ requires C, 71·7; H, 5·0; P, 15·4%).

Conversion into tetraphenyldiphosphine oxide sulphide. Compound (I) (5·43 g., 14 mmoles) and sulphur (0·48 g., 15 mmoles), dissolved in carbon disulphide (150 ml.), were refluxed in a nitrogen stream for 6 hr. After evaporation to about 40 ml., the solution was filtered and cooled, to give *tetraphenyldiphosphine oxide sulphide* (2·2 g., 37%), which was purified by chromatography on silica gel in benzene–acetone of steadily increasing acetone concentration to give lustrous white needles, m. p. 166—170° (from aqueous acetone) (Found: C, 68·9; H, 4·9; P, 14·8; S, 7·6. $C_{24}H_{20}OP_2S$ requires C, 68·9; H, 4·8; P, 14·8; S, 7·7%).

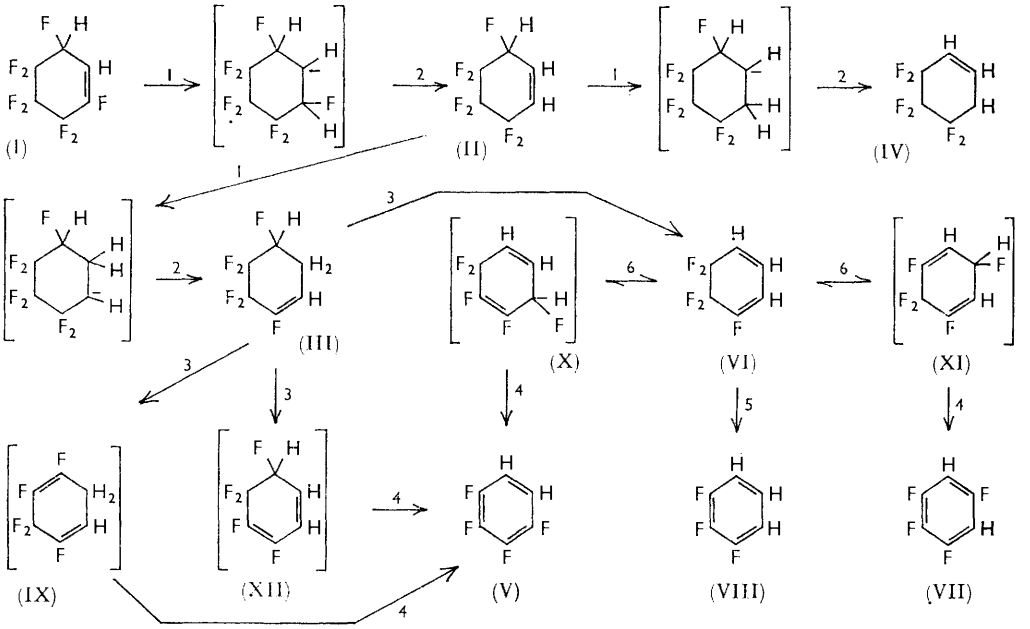
CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW W.2. [*Received, January 11th*, 1965.]

[3] W. Kuchen and H. Buchwald, *Chem. Ber.*, 1958, **91**, 2871.
[4] S. E. Frazier, R. P. Nielsen, and H. H. Sisler, *Inorg. Chem.*, 1964, **3**, 292.

644. *Fluorocyclohexanes. Part IX.*[1] *Lithium Aluminium Hydride Reduction of* 1H,2H,3H-*Heptafluorocyclohexene, a Route to* 1,2,3-*Trifluorobenzene*

By W. J. Feast and R. Stephens

1H,6H-Octafluorocyclohexene (I) with lithium aluminium hydride in ether gave[1] predominantly 1*H*,2*H*,3*H*-heptafluorocyclohexene (II), together with two other impure components which have now been isolated by preparative gas chromatography and characterised as 1*H*,5*H*,6*H*,6*H*- (III) 1*H*,2*H*,3*H*,3*H*-hexafluorocyclohexene (IV); these are the reduction products of 1*H*,2*H*,3*H*-heptafluorocyclohexene (II) expected by the depicted addition–elimination pathway, and they were in the proportions expected from the relative electron-attracting powers of the CF_2 and CFH groups. This reduction is an exception to the earlier[2] provisional claim that reaction can occur only if four or more fluorine atoms are present on the vinylic and α-carbon atoms; *e.g.*, 1*H*,6*H*,6*H*-heptafluorocyclohexene does not react with lithium aluminium hydride under these conditions.[1]



Reagents: 1, $LiAlH_4$; 2, loss of F^-; 3, KOH aq.; 4, facile loss of HF; 5, iron gauzes at 520°; 6, iron gauzes at 520° probably catalysed by traces of F^-

The characterisation of the olefins (III) and (IV) was largely based on infrared and nuclear magnetic resonance (n.m.r.) spectroscopy with reference to the spectra of a large number of related systems.[1,2] The predominating olefin (III) was also characterised by dehydrofluorination with aqueous alkali to give the known 1,2,3,4-tetrafluorobenzene (V) and the hitherto unknown 1*H*,2*H*,3*H*-pentafluorocyclohexa-1,3-diene (VI); the poor yield and black aqueous phase are analogous to occurrences in other dehydrofluorinations where a diene is formed.[3] The diene (VI) was characterised by ultraviolet and infrared

[1] Part VIII, D. E. M. Evans, W. J. Feast, R. Stephens, and J. C. Tatlow, *J.*, 1963, 4828.
[2] E. Nield, R. Stephens, and J. C. Tatlow, *J.*, 1960, 3800.
[3] R. Stephens and E. H. Wiseman, *J.*, 1963, 2083.

spectroscopy. The dehydrofluorination is of interest, when considered in conjunction with earlier work,[1] as an example of the interplay of C–F bond strength and hydrogen " acidity " in such processes. Thus, the diene (VI), the major product, arises by loss of fluorine from the CHF group which results from attack by base on what should be the less acidic hydrogen of the CH_2 group. The aromatic compound could arise either from a 1,4-elimination, involving attack by base on the CH_2 group followed by rapid dehydrofluorination of the resulting 1,3-diene (XII), or from a 1,2-elimination, involving attack by base on the CHF group followed by a rapid dehydrofluorination of the resulting 1,4-diene (IX).

1*H*,2*H*,3*H*-Pentafluorocyclohexa-1,3-diene (VI) was of further interest as a potential route to the hitherto undescribed 1,2,3-trifluorobenzene (VIII), the last of the twelve possible fluorobenzenes. Thus, pyrolysis of the diene over iron gauze at 520° gave 1,3,4,5-tetrafluorobenzene (VII) and 1,2,3-trifluorobenzene with an infrared spectrum distinct from those of any of the other eleven fluorobenzenes, and identical, except for several very weak absorptions, with that of 1,2,3-trifluorobenzene prepared by a different, unpublished route involving chloride–fluoride exchange processes.[4] The very weak absorption maxima corresponded to the strong absorptions in the spectrum of 1,2,3,4-tetrafluorobenzene which possesses the same gas-chromatographic retention volume on the stationary phase used. Mass spectrometry confirmed that 1,2,3-trifluorobenzene was the main component together with about 5% of a tetrafluorobenzene. Additional structural evidence was provided by ultraviolet spectroscopy, which showed the multiplet absorption maximum in the 2400—2700 Å region characteristic of fluoro-aromatic compounds, and by the ^{19}F n.m.r. spectrum which displayed two signals in the intensity ratio of 2 : 1. The 1,3,4,5- and 1,2,3,4-tetrafluorobenzenes presumably arise from the spontaneous dehydrofluorination of the 1,4-dienes (X) and (XI) formed by the pyrolytic isomerisation of the 1,3-diene (VI), a process catalysed by fluoride ion.[5]

Experimental.—Reaction of 1H,6H-*octafluorocyclohexene* (I) *with lithium aluminium hydride.* The olefin (I) (38·8 g.) was added to a stirred suspension of lithium aluminium hydride (8·6 g.) in ether (250 c.c.) at 0°. After the initial reaction had subsided the mixture was refluxed for 2 hr. and the excess lithium aluminium hydride destroyed by the addition of sulphuric acid (50% v/v). The dried ($MgSO_4$) ethereal solution was evaporated through a vacuum-jacketed column (1 ft. × 1 in.) packed with glass helices, and the residue (b. p. >34°) separated by gas chromatography [column A (4·8 m. × 75 mm.; dinonyl phthalate–kieselguhr, 1 : 2), 100°, N_2 60 l./hr.], to give: (i) ether; (ii) 1*H*,6*H*-octafluorocyclohexene (I) (1·5 g.) with a correct infrared spectrum; (iii) 1*H*,2*H*,3*H*-heptafluorocyclohexene (II) (3·5 g.) with a correct infrared spectrum; (iv) 1H,2H,3H,3H-*hexafluorocyclohexene* (IV) (3·1 g.) (Found: C, 37·5; H, 2·2. $C_6H_4F_6$ requires C, 37·9; H, 2·1%), $\nu_{max.}$ 3050 (=C–H), 2950 (>C–H), and 1695vw cm.$^{-1}$ (–CH=CH–); the ^{19}F n.m.r. spectrum [6] showed three bands of equal intensity at 35·2, 41·6, and 62·3 p.p.m. with respect to trifluoroacetic acid as external reference; the ^1H n.m.r. spectrum displayed a broad singlet and a triplet (J_{HF} ~13 c./sec.) of equal intensities centred at 5·8 and 2·7 p.p.m. with respect to tetramethylsilane as external reference; (v) 1H,5H,6H,6H-*hexafluorocyclohexene* (III) (10·0 g.), b. p. 138° (Found: C, 37·8; H, 2·1%); mass spectrometry [7] gave a top mass peaks of 190 ($C_6H_4F_6$); $\nu_{max.}$ 3050 (=C–H), 2950 (>C–H), and 1710m cm.$^{-1}$ (–CH=CF–); the ^{19}F n.m.r. spectrum [6] showed four bands at 44·8, 55·7, 59·3 (=C–F), and 128·5 (>CHF) p.p.m. with respect to trifluoroacetic acid as external reference in the intensity ratio of 2 : 2 : 1 : 1.

Dehydrofluorination of 1H,5H,6H,6H-*hexafluorocyclohexene* (III). This compound (10·3 g.), potassium hydroxide (10 g.), and water (18 c.c.) were shaken together in a sealed Pyrex tube (1 ft. × 1 in.) at 100° for 2½ hr. The organic product (4·5 g.) was removed from the black aqueous layer and separated by gas chromatography [column B (4·8 m. × 35 mm.; dinoyl phthalate–kieselguhr, 1 : 2), 100°, N_2 16 l./hr.], to give: (i) 1,2,3,4-tetrafluorobenzene (0·25 g.) with a correct infrared spectrum; (ii) 1H,2H,3H-*pentafluorocyclohexa*-1,3-*diene* (1·15 g.), b. p.

[4] G. C. Finger and C. W. Kruse, Abs. 130th Meeting Amer. Chem. Soc., Sept. 1956, p. 44N.
[5] W. T. Miller, J. H. Fried, and H. Goldwhite, *J. Amer. Chem. Soc.*, 1960, **82**, 3091; T. W. Rimmington, M.Sc. Thesis, Birmingham, 1962.
[6] L. F. Thomas, personal communication.
[7] J. R. Majer, personal communication.

112° (Found: C, 42·4; H, 1·7. $C_6H_3F_5$ requires C, 42·4; H, 1·8%), $\nu_{max.}$ 1690m and 1620m cm.$^{-1}$ (conjugated –CF=CH– and –CH=CH–), $\lambda_{max.}$ (in ethanol) 2625 Å (ε 4000); (iii) 1*H*,5*H*,6*H*,6*H*-hexafluorocyclohexene (1·80 g.) with a correct infrared spectrum.

Defluorination of 1H,2H,3H-*Pentafluorocyclohexa*-1,3-*diene*. The diene (1·0 g.) was passed in a stream of nitrogen (1 l./hr.) through a steel tube (5 × 30 cm.) containing rolled iron gauzes at 520°, the product (0·35 g.) was trapped at –180° and separated by gas chromatography (column B), to give: (i) 1,3,4,5-tetrafluorobenzene (0·08 g.) with a correct infrared spectrum; (ii) 1,2,3-*trifluorobenzene* (0·20 g.), $\nu_{max.}$ 3100 (=C–H) and 1525 and 1640 cm.$^{-1}$ (fluorinated aromatic nucleus), $\lambda_{max.}$ (in ethanol) 2540 Å (ε 220); the ^{19}F n.m.r. spectrum [6] consisted of two bands at 59·7 and 86·5 p.p.m. with respect to trifluoroacetic acid as external reference, in the intensity ratio of 2 : 1. Mass spectrometry [7] gave a total mass peak of 132 ($C_6H_3F_3$) and the expected fragments, and revealed the presence of a tetrafluorobenzene (*ca.* 5%).

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