NOTES.

738. *Synthesis of Diethyl-2,2-dimethylhydrazinoaluminium.*

By Robert P. Nielsen and Harry H. Sisler.

We report the synthesis of diethyl-2,2-dimethylhydrazinoaluminium and its conversion into a compound $(Me_2N{\cdot}N{\cdot}AlEt)_x$. No evidence for the existence of the molecular addition complex $Et_3Al,NMe_2{\cdot}NH_2$ was observed.

Experimental.—Diethyl-2,2-dimethylhydrazinoaluminium. Triethylaluminium (8·0321 g., 0·0704 mole) was distilled *in vacuo* into a 100-ml. flask fitted with stirrer, thermometer, and a side-arm leading to a " Precision " wet-test meter. The triethylaluminium was frozen (solid carbon dioxide–acetone) and 1,1-dimethylhydrazine (4·44 g., 0·0739 mole) was added in very small portions, the system being warmed to 10° between additions. Ethane [identified by vapour-phase chromatography; evolved, 1·596 l; required, 1·577 l.] was the only gaseous product and no material condensed at −78°. Evolution was slow and controllable, and evident as low as −60°. The system was then kept overnight at 25°.

The excess of dimethylhydrazine was removed at 45°/0·15 mm. The white crystalline

product (10·11 g.; 99·6% yield) had m. p. 43—44° (sealed tube) [Found: C, 50·05; H, 11·6; N, 19·7; Al, 18·6; Et (by hydrolysis), 40·8%; *M* (in benzene), 281·4. $Et_2Al{\cdot}NH{\cdot}NMe_2$ requires C, 50·0; H, 11·9; N, 19·4; Al, 18·7; Et, 40·3%; *M*, 288·4]. The proton magnetic resonance spectrum indicated that only one molecular species was present and showed that Al–Et and N–Me are present, but because of the uncertainty associated with the N–H region, no structure could be assigned. Infrared spectral data favour a six-membered ring structure, however.

Action of heat. At 150° the diethyldimethylhydrazinoaluminium rapidly lost 1 mole of ethane to give a dark tar (Found: Et, 25·5. $Me_2NNAlEt$ requires Et, 25·45%). The material is polymeric [*M*, 646 (in benzene)].

The authors thank Dr. W. S. Brey for the nuclear magnetic resonance work and Mr. H. Latz for help in furnishing infrared spectral facilities. This work was supported by the Petroleum Research Fund, administered by the American Chemical Society.

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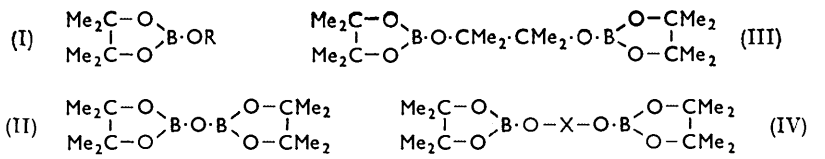
739. *Organic Derivatives of Boron. Part V.*[1] *Pinacol Derivatives.*

By R. C. Mehrotra and G. Srivastava.

In continuation of our syntheses of cyclic orthoborates by the azeotropic-distillation technique,[1-3] similar derivatives have been prepared from ethyl borate and pinacol. The reaction, in 1 : 1 molar ratio, gives an ester (I; R = Et) whereas the more complex derivative (III) is obtained by the reaction in 2 : 3 or 1 : 2 molar ratio. The latter product is converted into the former by refluxing it with a mol. of ethyl borate. Derivatives (I; R = Et or Pr^n) were also prepared, as thermally stable colourless liquids, by refluxing an equimolar mixture of boric acid and pinacol with the alcohol in benzene and removing water azeotropically. The ester (III) is crystalline and comparatively resistant to hydrolysis, and sublimes under reduced pressure. The higher thermal stability of the ester (I) and hydrolytic stability of ester (III) than of the corresponding derivatives from trimethylene and propylene glycol [3] and butane-2,3- and -1,3-diols [4] appear to be due to steric effects in the branched pinacol molecule.



Esters (I) with phenyl or higher alkyl groups (R) are obtained as monomeric liquids by alcoholysis of the ethyl derivative. The t-butyl and t-pentyl esters (I) are of interest as the first mixed cyclic t-alkoxides of boron. The 2-aminoethyl derivative, however, is a white solid which is immediately precipitated on admixture of the reactants in benzene.

Slow distillation of water from an equimolar mixture of boric acid and pinacol yielded the crystalline pyroborate (II), easily converted into the alkyl cyclic borates (I) and into the alkylene diborates (IV). These diborates have also been obtained by reaction of borates (I) with glycols in a 2 : 1 molar ratio.

Experimental.—Analytical procedures and methods for drying the reagents have been described before.[5] The back-titration method with chromic acid [6] has been extended to the

[1] Part IV, Mehrotra and Srivastava, *J.*, 1962, 1032.
[2] Mehrotra and Srivastava, *J.*, 1961, 4045.
[3] Mehrotra and Srivastava, *J. Indian Chem. Soc.*, 1962, **39**, 203.
[4] Mehrotra and Srivastava, unpublished work.
[5] Mehrotra and Srivastava, *J. Indian Chem. Soc.*, 1961, **38**, 1.
[6] Bradley and Wardlaw, *J.*, 1950, 3450.

estimation of pinacol. Pinacol (B.D.H., L.R.) was distilled before use. Molecular weights were determined ebullioscopically in a semimicro-ebulliometer (Gallenkamp) in benzene. M. p.s were determined in sealed capillary tubes.

Ethyl 1,1,2,2-tetramethylethylene borate. (*a*) Ethyl borate (8·54 g., 1 mol.) was refluxed with pinacol (6·91 g., 1 mol.) in benzene (40 g.) for 2 hr. Ethanol (5·21 g., 1·94 mol.) was removed azeotropically, and the *product* (8·9 g., 88%) was distilled at 64°/6 mm. (Found: C, 55·2; H, 9·8; B, 6·3; EtO, 25·6%; *M*, 171. $C_8H_{17}BO_3$ requires C, 55·8; H, 9·9; B, 6·3; EtO, 26·1%; *M*, 172).

(*b*) The diborate (IV; X = CMe_2·CMe_2) (4·18 g., 1 mol.) was refluxed with ethyl borate (1·65 g., 1 mol.) in benzene (10 g.) for 4 hr. After removal of the benzene, the ethyl monoborate (I; R = Et) (5 g., 86%) was obtained at 66°/7 mm. (Found: B, 6·3%).

1,1,2,2-*Tetramethylethylene bis*-(1,1,2,2-*tetramethylethylene borate*) (IV; X = CMe_2·CMe_2). Refluxing pinacol [(i) 5·95 g., 1·5 mol.; (ii) 12·52 g., 2 mol.] and ethyl borate [1 mol.; (i) 4·91 g., (ii) 7·75 g.] in benzene (40 g.) for 2 hr., followed by fractionation, yielded ethanol [(i) 4·53 g., 2·93 mol.; (ii) 7·2 g., 2·95 mol.] in the azeotrope. After removal of the excess of benzene and cooling, crystals of the *diborate* [(i) 6 g., 96%; (ii) 10·36 g., 80%], m. p. 215°, were obtained and were purified by sublimation at 240°/0·01 mm. (Found: C, 57·9; H, 9·7; B, 5·8; pinacol, 94·2%. *M*, 364. $C_{18}H_{36}B_2O_6$ requires C, 58·4; H, 9·7; B, 5·8; pinacol, 94·2%; *M*, 370).

For complete hydrolysis of the compound refluxing with an excess of dilute alkali is necessary.

Bis-1,1,2,2-*tetramethylethylene pyroborate* (II). Distillation of a mixture of pinacol (6·25 g., 1 mol.) and boric acid (3·28 g., 1 mol.), after 4 hours' refluxing at 160—170°, yielded water (2·3 g., 96%) and then the *pyroborate* (6·5 g., 91%), m. p. 55—60°, b. p. 115°/0·1 mm. (Found: C, 53·0; H, 8·7; B, 8·0%; *M*, 265. $C_{12}H_{24}B_2O_5$ requires C, 53·3; H, 8·9; B, 8·0%; *M*, 270).

Alkyl cyclic borates (I). Pinacol (10·0 g.), boric acid (5·25 g.), and ethanol (40 ml.) in benzene (75 ml.) were refluxed for 2 hr., then the water was removed azeotropically and the residue fractionated. The borate (I; R = Et) (13 g., 89%) was obtained at 66°/7 mm. (Found: B, 6·3; EtO, 25·8. Calc. for $C_8H_{17}BO_3$: B, 6·3; EtO, 26·2%).

Similarly *n-propyl* 1,1,2,2-*tetramethylethylene borate* (8·2 g., 91%), b. p. 71°/3 mm., was obtained by slow fractionation after refluxing of pinacol (5·73 g.) and boric acid (3·01 g.) in n-propanol (20 g.) (Found: B, 5·8%; *M*, 188. $C_9H_{19}BO_3$ requires B, 5·8%; *M*, 186).

Isopropyl 1,1,2,2-*tetramethylethylene borate* (91%), b. p. 80°/5 mm., was similarly prepared (Found: B, 5·75; Pr^iO, 31·2%; *M*, 180. $C_9H_{19}BO_3$ requires B, 5·8; Pr^iO, 31·7%; *M*, 186).

Other *borates* (I) were prepared from the ethyl ester (I) by alcohol interchange in benzene. For example, butan-1-ol (2·1 g.) was refluxed with ester (I; R = Et) (6·5 g.) in benzene (40 g.) for 2 hr. Then slow fractionation yielded 1·62 g. of ethanol in the azeotrope. After removal of the excess of benzene, the product was distilled under reduced pressure. For similar preparations details are given in the annexed Table.

Bisborates (IV). (*a*) The pyroborate (II) (5·39 g., 1 mol.) and butane-1,3-diol (1·8 g., 1 mol.) in benzene (40 g.) were refluxed for 2 hr., then fractionated, yielding the benzene–water azeotrope, excess of benzene, and finally 1-*methyltrimethylene bis*-(1,1,2,2-*tetramethylethylene borate*) (6·2 g., 91%) at 140°/0·01 mm. (Found: C, 55·8; H, 9·2; B, 6·3. $C_{16}H_{32}B_2O_6$ requires C, 56·1; H, 9·3; B, 6·3%).

Alkyl 1,1,2,2-tetramethylethylene borates (I).

	EtOH	Yield		Found (%)				Required (%)		
R	(%)	(%)	B. p./mm.	C	H	B	Formula	C	H	B
Bu^n	94	92	80°/0·7	59·8	10·4	5·4	$C_{10}H_{21}BO_3$	60·0	10·5	5·4
Bu^i	96	95	77°/1	59·6	10·5	5·4	,,	,,	,,	,,
Bu^s	94	90	85°/6	59·7	10·4	5·4	,,	,,	,,	,,
Bu^t	92	88	82°/2	59·8	10·4	5·4	,,	,,	,,	,,
n-C_5H_{11}	97	97	85°/1·5	61·4	10·6	5·1	$C_{11}H_{23}BO_3$	61·7	10·7	5·1
iso-C_5H_{11}	96	92	84°/2	61·5	10·5	5·1	,,	,,	,,	,,
CMe_2Et	93	90	88°/4	61·8	10·6	5·1	,,	,,	,,	,,
$CHMeBu^i$ ...	95	91	100°/3·5	—	—	4·7	$C_{12}H_{25}BO_3$ *	—	—	4·7
Cyclohexyl ...	95	95	113°/3	63·4	10·1	4·8	$C_{12}H_{23}BO_3$	63·7	10·2	4·8
Ph	96	94	104°/0·1	65·3	7·6	4·8	$C_{12}H_{17}BO_3$	65·5	7·7	4·9
CH_2Ph	96	95	120°/0·2	—	—	4·6	$C_{13}H_{19}BO_3$ †	—	—	4·6
NH_2·$[CH_2]_2$ ...	98	99	200°/0·1 ‡	—	—	5·7	$C_8H_{18}BNO_3$	—	—	5·8

* Found: *M*, 225. Reqd.: *M*, 228. † Found: *M*, 235. Reqd.: *M*, 234. ‡ M. p. 165°; sublimes. Found: N, 7·3. Reqd.: N, 7·5%.

Alkylene bis-(1,1,2,2-tetramethylethylene borates) (IV).

X	EtOH (%)	Yield (%)	B. p./mm.	M. p.	Found (%) C	H	B	Formula	Required (%) C	H	B
$[CH_2]_3$	96	90	135°/0·5	70°	54·6	9·0	6·6	$C_{15}H_{30}B_2O_6$	54·9	9·1	6·6
$CHMe{\cdot}CH_2{\cdot}CMe_2$ ...	95	88	180°/0·01	*170	58·2	9·6	5·8	$C_{18}H_{36}B_2O_6$	58·4	9·7	5·8
CHMe·CHMe	96	92	114°/0·01	100—103	55·9	9·2	6·3	$C_{16}H_{32}B_2O_6$	56·1	9·3	6·3
$NH(CH_2{\cdot}CH_2^-)_2$ ...	97	89	170—175°/0·01	80	—	—	5·9	$C_{16}H_{33}B_2NO_6$	—	—	6·05

* Sublimes.

(*b*) Ethylene glycol (0·75 g., 1 mol.) was refluxed with the isopropyl cyclic borate (I) (4·51 g., 2 mol.) in benzene (35 g.) for 2 hr., then fractionated. 1·35 g. of propan-2-ol (2 mol. require 1·45 g.) were obtained in the azeotrope. After removal of the excess of benzene, *ethylene bis-(1,1,2,2-tetramethylethylene borate)* was obtained at 121°/0·01 mm. (Found: C, 53·3; H, 8·8; B, 6·9%; *M*, 310. $C_{14}H_{28}B_2O_6$ requires C, 53·5; H, 8·9; B, 6·9%; *M*, 314).

(*c*) Other *bisborates* (IV) (see Table) were prepared from ethyl 1,1,2,2-tetramethylethylene borate by the above method.

One of the authors (G. S.) is grateful to the Council of Scientific and Industrial Research, New Delhi, for the award of a Junior Research Fellowship.

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740. *Preparation of Some Peroxy-acids derived from Optically Active Amino-acids.*

By K. BALENOVIĆ and I. BREGOVEC.

IN our studies concerning the asymmetric synthesis of sulphoxides [1] several optically active peroxy-acids of known configuration were required. The only known compound of this type was peroxycamphoric acid.[2] The preparation is now described of L-α-phthalimidoperoxypropionic acid, L-β-phthalimidoperoxybutyric acid,* and α-methyl hydrogen *N*-phthaloyl-L-peroxyglutamate.

N-Phthaloyl derivatives of the corresponding L-amino-acids were converted into peroxy-acids by using 50% hydrogen peroxide and 95% sulphuric acid, according to the procedure described by Parker *et al.*[3] From phthaloylalanine the mixture of phthalimidoperoxypropionic acid and starting material could not be separated by fractional crystallisation or chromatography on cellulose. However, the starting material reacted selectively at −50° with the equivalent amount of ethereal diazomethane. Crystallisation from ether–light petroleum then afforded the pure peroxy-acid and the more soluble methyl ester of the initial amino-acid. The relative stability of the peroxy-acid in ethereal diazomethane at −50° is in accord with the structures suggested for these compounds.[4]

Experimental.—*L-α-Phthalimidoperoxypropionic acid.* To a solution of *N*-phthaloyl-L-alanine [5] (2·3 g.; 10·5 mmoles; m. p. 142—144°; $[\alpha]_D^{24}$ −22·7°) in 95% sulphuric acid (2·5 c.c.; at 0°), 50% hydrogen peroxide (1·5 c.c.; at 0°) was added dropwise at such a rate as to maintain the temperature at 0° (30 min.). More sulphuric acid (1 c.c.) was then added, and stirring at 0° was continued for 2 hr. The mixture was poured on to ice (several volumes) and extracted with ether. The extracts were washed with water and with saturated aqueous ammonium sulphate, and dried (Na_2SO_4). The solvent was removed *in vacuo* at room temperature. The

* In this paper the symbol L is used in an extension to β-amino-acids of the convention for α-amino-acids.

[1] Balenović, Bregant, and Francetić, *Tetrahedron Letters*, 1960, No. 6, 20; Balenović, Bregovec, Francetić, Monković, and Tomašić, *Chem. and Ind.*, 1961, 469.
[2] Milas and McAlevy, *J. Amer. Chem. Soc.*, 1933, **55**, 349.
[3] Parker, Ricciutti, Ogg, and Swern, *J. Amer. Chem. Soc.*, 1955, **77**, 4037.
[4] Swern, Witnauer, Eddy, and Parker, *J. Amer. Chem. Soc.*, 1955, **77**, 5537.
[5] Fischer, *Ber.*, 1907, **40**, 489.

residue contained the peroxy-acid (1·427 g.; according to the determination of active oxygen [6]) and starting material (0·873 g.). Ethereal diazomethane (3·98 mmoles) was added to the mixture in ether, and left at −50° for 2 hr. The solvent was removed at room temperature and from the residue the pure *peroxy-acid* was obtained by repeated crystallisation from ether–light petroleum (0·56 g.; 39%); it had m. p. 88° (decomp.), $[\alpha]_D^{23}$ −23° ± 0·5° (*c* 1·00 in 96% ethanol) (Found: C, 56·5; H, 4·2. $C_{11}H_9NO_5$ requires C, 56·2; H, 3·9%).

L-β-*Phthalimidoperoxybutyric acid*. Similarly prepared from L-β-phthalimidobutyric acid [7] (2·3 g.; m. p. 80°; $[\alpha]_D^{20}$ +43°), L-β-*phthalimidoperoxybutyric acid* (2·3 g.; 89·6% pure), m. p. 55—60° slowly crystallised. The analytical sample was precipitated from ether–hexane; it had m. p. 65—67° (decomp.), $[\alpha]_D^{22}$ +41·3° ± 0·5° (*c* 0·920 in methanol) (Found: C, 58·1; H, 4·5. $C_{12}H_{11}NO_5$ requires C, 57·8; H, 4·4%).

α-*Methyl hydrogen* N-*phthaloyl-*L-*peroxyglutamate*. A solution of l-methyl hydrogen *N*-phthaloyl-L-glutamate [8] (2 g.; m. p. 134—137°; $[\alpha]_D^{20}$ −48·5°) in 95% sulphuric acid was treated with hydrogen peroxide as described above. l-Methyl hydrogen *N*-phthaloyl-L-peroxyglutamate was obtained as a yellow oil containing 92% of the peroxy-acid; this slowly crystallised (2·06 g., 95%). Crystallisation from ether–hexane afforded clusters of fine needles, m. p. 77—79° (decomp.), $[\alpha]_D^{23}$ −48·1° ± 0·3° (*c* 0·800 in methanol) (Found: C, 54·8; H, 4·15%; iodometric equiv., 305. $C_{14}H_{13}NO_7$ requires C, 54·7; H, 4·25%; equiv. 307).

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[*Received, January 15th*, 1962.]

[6] Roth and Schuster, *Mikrochim. Acta*, 1957, 840.
[7] Balenović, Bregant, and Cerar, *J.*, 1956, 3982.
[8] Tipson, *J. Org. Chem.*, 1956, **21**, 1353.

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741. *The* ortho : para-*Ratio in Aromatic Substitution. Part VI.*[1] *The Nitration of Benzeneboronic Acid.*

By D. R. HARVEY and R. O. C. NORMAN.

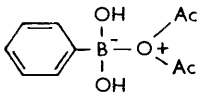
THE nitration of benzeneboronic acid by mixed acid at −20° has been reported to give the *m*-nitro-derivative in 70% yield,[2] whereas nitration with fuming nitric acid in acetic anhydride at −15° gave 60% of *o*-nitro- and 2% of *p*-nitro-benzeneboronic acid.[3] These unusual results prompted us to study the nitrations quantitatively.

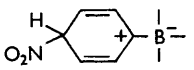
Benzeneboronic acid was recrystallised from water immediately before use to ensure that reaction took place on the acid and not on the readily formed anhydride.[4] Nitrations were carried out at −15° with (*a*) mixed acid, and (*b*) fuming nitric acid in acetic anhydride, and the nitro-products were converted into chloronitrobenzenes which were analysed by gas–liquid chromatography. The conversion was shown not to result in the preferential loss of any of the isomers, and the results were reproducible to ±2% and were confirmed by injection of synthetic mixtures. A small amount of nitrobenzene was detected in both experiments, indicating some nitrodeboronation[5] (cf. ref. 6). The isomer distributions (*o* : *m* : *p*, expressed as percentages) were: (*a*) 22 : 73 : 5; (*b*) 63 : 23 : 14.

The formation of mainly the *meta*- and *ortho*-nitro-derivatives, respectively, in (*a*) and (*b*) is in agreement with previous reports,[2,3] but we found each of three nitro-derivatives under both conditions of nitration. The difference is the greater in (*b*): we found that about twice as much of the *meta*- as the *para*-derivative was formed, whereas in preparative work the *meta*-derivative was not isolated.[3] An earlier discussion of these nitrations which presupposed the non-formation of one isomer in each case [7] has therefore to be modified.

[1] Part V, *J.*, 1961, 3888.
[2] Ainley and Challenger, *J.*, 1930, 2171.
[3] Seaman and Johnson, *J. Amer. Chem. Soc.*, 1931, **53**, 711.
[4] Wasburn, Levens, Allbright, Billig, and Cernak, "Advances in Chemistry Series," American Chemical Society, No. XXIII, 1959, p. 102.
[5] Torssell, *Arkiv Kemi*, 1956, **10**, 513.
[6] Kuivila and Easterbrook, *J. Amer. Chem. Soc.*, 1951, **73**, 4629.

In (*a*), *meta*-direction arises from the $-M$ effect of $B(OH)_2$,[5,7] and the high *ortho* : *para*-ratio (4 : 4) is consistent with that observed in analogous cases, such as the nitration of nitrobenzene (11·0) and benzonitrile (4·3), which we have discussed previously.[8]


(I)


(II)

Enhanced *ortho*-reactivity has been observed in the nitration of several monosubstituted benzenes in acetic anhydride, and has been ascribed to interaction between substituent and reagent that facilitates *ortho*-substitution.[9] That explanation is inadequate for the present results in acetic anhyride, since it should result in the same *meta* : *para*-ratio for both nitrating conditions (*a*) and (*b*). The results are, however, consistent with the hypothesis that the boron atom forms a complex with acetic anhydride, giving structure (I) which is activating and *ortho* : *para*-directing because of the $+I$ effect of the boron anion.[6] (The strong complex-forming ability of boron in benzeneboronic acid has been described previously.[4]) It has been pointed out that in aromatic substitutions in which the reagents are of high reactivity, the *ortho* : *para*-ratio is determined by the relative electron densities at these positions in the ground state.[8] The high value of the ratio in the present case is consistent with the greater effect of the inductively releasing boron anion at the *ortho*- than at the *para*-position. Similarly, the inductive effect of the boron anion might be expected to be transmitted more strongly to the *meta*- than to the *para*-position and to give rise to a *meta* : *para*-ratio greater than that observed, which is close to the statistical value. It is known, however, that the inductive effect of a similar saturated substituent of opposite charge, the NMe_3^+ group, is barely greater at the *meta*- than at the *para*-position, as measured by σ-values (0·88 and 0·82, respectively). It must also be emphasised that any deformation of the aromatic sextet in the transition state of the reaction should favour *para*(and *ortho*)- rather than *meta*-substitution because of the contribution of structure (II) in which opposite charges are juxtaposed when reaction occurs at the *para*-position.

Experimental.—Benzeneboronic acid and its *m*- and *p*-nitro-derivatives were prepared as reported in the literature.[2,3] *o*-Nitrobenzeneboronic acid [3] was found (by gas-chromatographic analysis of the *o*-chloronitrobenzene obtained by treating it with cupric chloride [2]) to contain the *meta*- and *para*-isomers and benzeneboronic acid, which could not be removed by recrystallisation. By using 2½ times the quantity of nitric acid used previously [3] a mixture (M) of nitrobenzeneboronic acids of high *ortho*-content and free from benzeneboronic acid was obtained.

Nitrations were carried out at −15° with (*a*) mixed acid and (*b*) fuming acid in acetic anhydride as previously reported,[2,3] but on a smaller scale. After reaction, the solutions were poured on ice, neutralised with sodium hydrogen carbonate, made slightly acid, and then extracted with ether. The extract was converted into a mixture of chloronitrobenzenes by heating it with cupric chloride in water,[2] and this mixture was analysed by gas–liquid chromatography. The column (400 cm. × 2·6 mm.) was packed with trinitrofluorenone (20%) [10] coated on aqua regia-treated firebrick [11] and was operated at 150°. The relative proportions of the components in the mixture were determined as previously described; [8] the isomer distributions reported are the mean values of four analyses from two reaction mixtures for each set of conditions.

The conversion procedure was shown not to cause preferential loss of any of the isomers by analysing known mixtures of M and pure *p*-nitrobenzeneboronic acid in the same way. It was also shown that nitrobenzene was not chlorinated under these conditions.

THE DYSON PERRINS LABORATORY, OXFORD. [*Received, February* 13*th*, 1962.]

[7] de la Mare and Ridd, " Aromatic Substitution," Butterworths Scientific Publ., 1959, p. 86.
[8] Norman and Radda, *J.*, 1961, 3610.
[9] Norman and Radda, *J.*, 1961, 3030.
[10] Norman, *Proc. Chem. Soc.*, 1958, 151.
[11] Zlatkis, Ling, and Kaufman, *Analyt. Chem.*, 1959, **31**, 945.

742. *Organo-phosphorus Compounds. Part IV.* The Preparation of OO-Dialkyl and O-Alkyl Hydrogen Methylphosphonothioates.*

By Z. Pelchowicz, H. Leader, S. Cohen, and D. Balderman.

The resolution [1] of *O*-ethyl hydrogen ethylphosphonothioate and the importance of compounds R·PS(OR′)$_2$ and R·PO(SH)·OR′ as starting materials for potential new insecticides made it desirable to develop more convenient syntheses for these compounds.

The preferred method for preparation of *OO*-dialkyl methyl- and ethyl-phosphonothioates (see review by Hoffmann *et al.*[2]) is the reaction of the alkylphosphonothioic dichloride R·PSCl$_2$ with a sodium alkoxide.[3]

It has been found that esters Me·PS(OR)$_2$ (R = Me, Et, Pr^n, Bu^n) are more easily prepared by refluxing the dichloride with an excess of the appropriate alcohol in the presence of a catalytic amount of boron trifluoride (Table 1), though the role of the

Table 1.

OO-Dialkyl methylphosphonothioates, Me·PS(OR)$_2$.

	Reflux	Yield			Found (%)					Calculated (%)			
R	(hr.)	(%)	B. p./mm.	n_D (temp.)	C	H	P	S	Formula	C	H	P	S
Me	0·5	71	40—42°/2—2·5	1·4738 (26°)	26·0	6·4	21·9	23·0	$C_3H_9O_2PS$	25·7	6·4	22·1	22·9
Et	1·5	80	89—92°/25	1·4610 (28°)	35·5	7·6	18·3	19·3	$C_5H_{13}O_2PS$	35·7	7·8	18·4	19·1
Pr^n	3	70	71—73°/0·45—0·5	1·4606 (24°)	42·7	8·3	15·8	16·4	$C_7H_{17}O_2PS$	42·8	8·7	15·8	16·3
Bu^n	4	81	93—94°/0·7	1·4605 (25°)	47·8	9·5	14·0	14·25	$C_9H_{21}O_2PS$	48·2	9·4	13·8	14·3

Table 2.

Neutral esters Me·PS(OR)$_2$ and acid esters Me·PO(SH)·OR obtained from a dichloride Me·PSCl$_2$ and secondary alcohol.

	Yield			Found (%)					Calculated (%)			
R	(%)	B. p./mm.	n_D (temp.)	C	H	P	S	Formula	C	H	P	S
Neutral esters												
Pr^i	39	42—44°/0·25	1·4513 (26°)	42·4	8·7	15·5	16·0	$C_7H_{17}O_2PS$	42·8	8·7	15·8	16·3
Bu^s *	35	58—60°/0·6	1·4600 (28°)	47·85	9·4	14·4	14·6	$C_9H_{21}O_2PS$	48·2	9·4	13·8	14·3
Acid esters												
Pr^i	40	73—74°/0·3	1·4810 (26°)	31·1	7·2	20·0	20·3	$C_4H_{11}O_2PS$	31·2	7·2	20·1	20·8
Bu^s *	31	99—100°/0·6—0·7	1·4770 (28°)	35·7	8·1	18·1	18·9	$C_5H_{13}O_2PS$	35·7	7·8	18·4	19·1

* New compound.

trifluoride is not understood. A likely intermediate is a labile complex between the dichloride and the trifluoride which would react more readily with the alcohol than would the chloride. Indeed, in the absence of the catalyst, the reaction of the chloride with alcohols is very slow and does not appear to be significantly accelerated by hydrochloric or sulphuric acid. In this connexion, the formation of a stable complex between phosphoryl chloride and aluminium chloride [4] is recalled.

With secondary alcohols, such as propan-2-ol and butan-2-ol, higher-boiling fractions were also obtained, but results were erratic and distillation of the crude products involved extensive decomposition; this was eliminated by removal of the catalyst before distillation (Table 2). These higher fractions have been identified as the corresponding *O*-alkyl hydrogen methylphosphonothioates Me·PO(SH)·OR (R = Pr^i, Bu^s). It appears that the reaction here proceeds to the stage Me·PS(Cl)·OR and that further reaction is sterically hindered.

* Part III, *J.*, 1961, 4348.

[1] Aaron, Shryne, and Miller, *J. Amer. Chem. Soc.*, 1958, **80**, 107.
[2] Hoffmann, Wadsworth, and Weiss, *J. Amer. Chem. Soc.*, 1958, **80**, 3945.
[3] Gryszkiewicz-Trochimowski, Bousquet, and Quinchon, *Bull. Soc. chim. France*, 1961, 1222.
[4] Dye, *J. Amer. Chem. Soc.*, 1948, **70**, 2595.

Known methods [5,6] leading to *O*-alkyl hydrogen methylphosphonothioates are based on partial alkaline hydrolysis of the diesters. This enabled us to prepare the acid esters in one step from the dichloride, by treating methylphosphonothioic dichloride with an excess of an alcohol and three mol. of potassium hydroxide:

$$Me{\cdot}PSCl_2 + ROH + 3KOH \longrightarrow Me{\cdot}PO(OR){\cdot}OK + 2KCl + 2H_2O$$

This fast reaction is superior to the known methods for preparation of these esters. The results are summarised in Table 3 for methanol, ethanol, propan-1-ol, propan-2-ol,

TABLE 3.

O-Alkyl hydrogen methylphosphonothioates Me·PO(SH)·OR.

	Yield *			Found (%)					Calculated (%)			
R	(%)	B. p./mm.	n_D (temp.)	C	H	P	S	Formula	C	H	P	S
Me	71	75—83°/0·3—0·5	1·5008 (27°)	18·8	5·3	24·5	25·3	$C_2H_7O_2PS$	19·0	5·5	24·6	25·4
Et	83	87—93°/0·55—0·6	1·4907 (28°)	25·6	6·3	22·4	22·8	$C_3H_9O_2PS$	25·7	6·4	22·1	22·9
Pr^n	65	92—93°/0·5	1·4855 (28°)	31·3	7·2	20·0	20·55	$C_4H_{11}O_2PS$	31·2	7·2	20·1	20·8
Pr^i	44	84—85°/0·6	1·4795 (23°)	31·5	7·2	20·0	20·7	,,	,,	,,	,,	,,
Bu^n	58	107—110°/0·6—0·7	1·4820 (28°)	35·6	8·0	18·65	19·1	$C_5H_{13}O_2PS$	35·7	7·8	18·4	19·1
Bu^s	30	109—110°/0·75	1·4780 (28°)	35·5	7·8	18·0	19·25	,,	,,	,,	,,	,,

* Yields of neutral ester formed concurrently were, in the same order, 0, 0, 12·5%, trace, 13·4%, trace.

butan-1-ol, and butan-2-ol; under these conditions the last four alcohols yield also a certain amount of the diesters; this side-reaction is especially pronounced with propan-1-ol and butan-1-ol. The first step is possibly the formation of the diester, which is hydrolysed by the alkali, an assumption supported by the observation that longer reaction times decrease the yield of the diester and increase that of the salt of the monoester.

The acid esters were identified by analysis and as their dicyclohexylamine salts (see Table 4).

TABLE 4.

Dicyclohexylamine salts, $Me{\cdot}PO(OR){\cdot}SNH_2(C_6H_{11})_2$.

		Found (%)						Calculated (%)				
R	M. p.	C	H	P	S	N	Formula	C	H	P	S	N
Me	179—180°	54·4	10·2	9·5	10·1	4·8	$C_{14}H_{30}NO_2PS$	54·7	9·8	10·1	10·4	4·6
Et	161—163	55·9	10·0	9·7	10·1	4·4	$C_{15}H_{32}NO_2PS$	56·0	10·0	9·6	10·0	4·4
Pr^n	144—145	57·1	9·7	9·2	9·7	4·1	$C_{16}H_{34}NO_2PS$	57·3	10·2	9·2	9·6	4·2
Pr^i	171—173	56·95	10·5	8·8	9·6	4·1	,,	,,	,,	,,	,,	,,
Bu^n	159—160	58·75	10·55	9·2	8·9	3·95	$C_{17}H_{36}NO_2PS$	58·4	10·4	8·9	9·2	4·0
Bu^s	149—151	58·15	10·55	8·7	8·8	4·0	,,	,,	,,	,,	,,	,,

Experimental.—OO-*Dialkyl methylphosphonothioates.* (*a*) Primary alcohols. Methylphosphonothioic dichloride [7] (1 mole) was added cautiously to the alcohol (5 moles) containing the boron trifluoride–ether complex (10 ml.). When the exothermic reaction subsided, the mixture was refluxed for the period specified in Table 1. The excess of alcohol was removed under reduced pressure and the product distilled directly from the reaction flask.

(*b*) Secondary alcohols. Methylphosphonothioic dichloride (0·5 mole) was added to the alcohol (2·5 moles) containing boron trifluoride–ether (2 ml.). The mixture was refluxed for ~6 hr. or to incipient turbidity, then cooled, and a solution of potassium hydroxide (3 g.) in the appropriate alcohol was added cautiously. The excess of alcohol was removed under reduced pressure, the residue taken up in dry ether, and the ethereal solution filtered and fractionated. The yields, physical constants, and analyses of the products are shown in Table 2.

O-*Alkyl hydrogen methylphosphonothioates.* To 85% potassium hydroxide (1·5 moles), dissolved in the appropriate alcohol (500 ml.), methylphosphonothioic dichloride (0·5 mole) was added dropwise at 0—4° with stirring which was continued at room temperature for

[5] Kabachnik, Kurochkin, Mastryukova, Ioffe, Popov, and Rodionova, *Doklady Akad. Nauk. S.S.S.R.*, 1955, **104**, 861.

[6] Hoffmann, Kagan, and Canfield, *J. Amer. Chem. Soc.*, 1959, **81**, 148.

[7] Kabachnik and Godovikov, *Doklady Akad. Nauk. S.S.S.R.*, 1956, **110**, 217.

30 min., and then the mixture was refluxed for 2 hr. After cooling, potassium chloride was filtered off and the excess of alcohol removed under reduced pressure. The residue was dissolved in water, extracted with ether (2 × 200 ml.), and acidified with concentrated hydrochloric acid. The acid ester was isolated by repeated extractions with ether (4 × 200 ml.). After drying (Na_2SO_4) and removal of the ether, the product was distilled at <1 mm. (Table 3).

The dicyclohexylamine salts (Table 4) were recrystallised from ethanol.

Physical properties recorded in the Tables agreed substantially with those recorded by Hoffmann *et al.*[6]

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743. *The Reaction of Methylene with Buta-1,3-diene.*

By MISS B. GRZYBOWSKA, J. H. KNOX, and A. F. TROTMAN-DICKENSON.

RECENTLY we reported [1] an investigation of the reaction of methylene with buta-1,3-diene in which we found vinylcyclopropane and the various pentadienes to be the major products. Franzen [2] later informed us that he had obtained cyclopentene as a product. We therefore reinvestigated the reaction and found that we had incorrectly identified cyclopentene as *cis*-penta-1,3-diene. After the reinvestigation was complete we learned that Frey had also studied the reaction and his work has since appeared.[3] We found it necessary to postulate a reaction:

$$CH_2 + CH_2{:}CH{\cdot}CH{:}CH_2 \longrightarrow \text{Cyclopentene} \quad \ldots (15)$$

in addition to those of Frey. Apart from this, as can be seen from the Table (Frey's symbolism is used), the two sets of results are in broad agreement. The values of k_6—k_{10} for keten are half those of Frey, presumably because we used the full light from a medium-pressure mercury arc, filtered only by the Pyrex glass of the reaction vessel; there was therefore more light of long wavelength.

Rate constants for the addition of methylene to buta-1,3-diene.

		Source of methylene			
		Keten		Diazomethane	
Rate constant [a]	Product	This work	Frey	This work	Frey
k_1/k_a [b]	Vinylcyclopropane [c]	0·86		0·78	
k_2/k_a	*cis*-Penta-1,3-diene	0·048 } 0·093		0·084 } 0·132	
k_3/k_a	*trans*-Penta-1,3-diene	0·045 }		0·048 }	
k_4/k_a	Isoprene	0·040		0·060	
k_{15}/k_a	Cyclopentene	0·010		0·030	
k_5	Vinylcyclopropane: assumed value 10^{10} sec.$^{-1}$ atm.$^{-1}$				
k_r	All products	2·6	5·3	12·3	12·4
k_6	Penta-1,4-diene	0·75	1·55	4·1	
k_7	*cis*-Penta-1,3-diene	0·35	0·71	1·7	
k_8	*trans*-Penta-1,3-diene	0·42	0·77	3·3	
k_9	Isoprene	0·00	0·00	0·00	
k_{10}	Cyclopentene [c]	1·20	2·40	3·5	
k_{11}	Cyclopentene: assumed value 10^{10} sec.$^{-1}$ atm.$^{-1}$				
k_{12}	Cyclopentadiene + H_2	0·66		1·0	
k_6/k_r	Penta-1,4-diene	0·29	0·28	0·33	
k_7/k_r	*cis*-Penta-1,3-diene	0·13 } 0·29	0·13 } 0·27	0·14 } 0·41	
k_8/k_r	*trans*-Penta-1,3-diene	0·16 }	0·14 }	0·27 }	
k_{10}/k_r	Cyclopentene	0·46	0·44	0·28	

[a] All unimolecular rate constants are in 10^8 sec.$^{-1}$.
[b] $k_a = k_1 + k_2 + k_3 + k_4 + k_{15}$ = Total rate constant for addition of CH_2 to C_4H_6.
[c] Represents an activated molecule.

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[*Received, February* 27*th*, 1962.]

[1] Grzybowska, Knox, and Trotman-Dickenson, *J.*, 1961, 4402.
[2] Franzen, Heidelberg, personal communication.
[3] Frey, *Trans. Faraday Soc.*, 1962, **58**, 516.

744. *Self-condensation of Quinoline-2-aldehyde.*

By H. Andrews, S. Skidmore, and H. Suschitzky.

Benzoin condensations of quinoline-2- and -4-aldehyde have been studied by Buehler and Harris [1] and by Phillips,[2] respectively. Results varied with reaction conditions but neither aldehyde gave the expected benzoin. In high dilution and with a small amount of potassium cyanide quinoline-2-aldehyde yielded the ethanediol (I; R = R′ = 2-quinolyl); in more concentrated solutions and with a larger quantity of catalyst the ethylenediol (II; R = R′ = 2-quinolyl) isomeric with the expected benzoin (III; R = R′ = 2-quinolyl) was obtained. Quinoline-4-aldehyde is reported to furnish a mixture of diol (I; R = R′ = 4-quinolyl) and cinchoninic acid presumably by the reaction:

$$2R{\cdot}CHO \longrightarrow R{\cdot}CO{\cdot}CH(OH){\cdot}R \xrightarrow[+R{\cdot}CHO]{} R{\cdot}CH(OH){\cdot}CH(OH){\cdot}R + R{\cdot}CO_2H$$

We obtained from quinoline-2-aldehyde in presence of cyanide ions, not only the reported diol (I; R = R′ = 2-quinolyl) but also quinaldic acid in a quantity commensurate with the above reaction scheme. Thus under " benzoin conditions " the self-condensation product of either aldehyde can undergo reduction at the expense of further quinolinealdehyde.

In experiments with quinoline-2-aldehyde certain heterocycles with " reactive " methyl groups brought about self-condensation as efficiently as cyanide ions. For instance, heating an ethanolic solution of the aldehyde in a sealed tube at 100° gave the same products [quinaldic acid; (I) and (II) (R = R′ = 2-quinolyl)] with lepidine as with potassium cyanide. Similar results were observed when a small quantity of quinaldine, 2-picoline, or 1-methylisoquinoline was added, while under the same reaction conditions the aldehyde alone remained unchanged. Several factors appear to influence the outcome of these reactions. A little freshly distilled diethylamine causes the aldehyde to undergo reaction with 1-methylisoquinoline to give the ethanol (IV; R = 2-quinolyl, R′ = 1-isoquinolyl) in preference to self-condensation. Ethanol formation (IV; R = 2-quinolyl, R′ = 4-quinolyl) also predominated over self-condensation when the reaction mixture with lepidine was heated at only 80°.

Quinoline-4-aldehyde, when treated with one equivalent of quinaldine in a sealed tube at 100°, gave, unlike its 2-isomer, only the ethanol (IV; R = 4-quinolyl, R′ = 2-quinolyl), and a small quantity of quinaldine had no effect on the aldehyde.

$R{\cdot}CH(OH){\cdot}CH(OH){\cdot}R'$ (I) $\quad R{\cdot}C(OH){=}C(OH){\cdot}R'$ (II) $\quad R{\cdot}CH(OH){\cdot}COR'$ (III)

(IV) $R{\cdot}CH(OH){\cdot}CH_2R'$ $\quad R{\cdot}CH{=}CH{\cdot}R'$ (V)

Since quinoline-2- and -4-aldehyde react in a similar manner in presence of cyanide, it is not clear why they behave differently towards quinaldine.

The union of two molecules of quinaldine-2-aldehyde by quinaldine is presumably effected by the quinaldyl anion $C_9H_6N{\cdot}CH_2^-$ formed by incipient ionisation, and other methyl-heterocycles behave correspondingly. This anion presumably plays a role in the self-condensation similar to that of the cyanide ion [3] in the benzoin reaction.

Attempts to use quinaldine in place of potassium cyanide for the preparation of benzoin from benzaldehyde failed. The ethanol (IV; R = Ph, R′ = 2-quinolyl) was the sole product when the aldehyde and quinaldine were refluxed in ethanol, and the ethylene (V; R = Ph, R′ = 2-quinolyl) was formed when this mixture was heated in a sealed tube. on a water-bath in presence of potassium cyanide (0·2 g.) for 30 min. A brown solid (1·3 g.)

Experimental.—Self-condensation of quinoline-2-aldehyde. (*a*) In presence of potassium cyanide. The aldehyde (2 g.), dissolved in pyridine (20 ml.) and water (400 ml.), was heated

[1] Buehler and Harris, *J. Amer. Chem. Soc.*, 1950, **72**, 5015.
[2] Phillips, *J. Amer. Chem. Soc.*, 1946, **68**, 2568.
[3] Ingold, " Structure and Mechanism in Organic Chemistry," Bell and Sons Ltd., London, 1953, p. 677.

separated which on recrystallisation from *NN*-dimethylformamide gave 1,2-di-2′-quinolylethane-1,2-diol, m. p. 218°. Slight acidification of the mother-liquor followed by addition of a 10% aqueous solution of copper sulphate (25 ml.) and heating on a water-bath for 1 hr. precipitated copper quinaldate (0·66 g.). Decomposition of the salt with hydrogen sulphide gave quinaldic acid (0·58 g.), m. p. 151—152°.

(*b*) In presence of methyl-heterocycles. The aldehyde (5 g.), methyl heterocycle (1 g. or 5 g.), and 80% ethanol (25 ml.) were heated in a sealed tube at 100° for 6 hr. A solid was filtered off, washed with ethanol, and extracted with hot carbon tetrachloride. The residue was 1,2-di-2′-quinolylethane-1,2-diol, m. p. 212°, and the material soluble in carbon tetrachloride was 1,2-di-2′-quinolylethylene-1,2-diol, m. p. 228—230°. The ethanolic mother-liquor from the reaction gave a red gum on evaporation; this was taken up in benzene and extracted with aqueous 2N-sodium hydroxide. From the extract copper quinaldate was obtained by neutralisation and addition of copper sulphate solution. Results of this reaction are tabulated.

Self-condensation of quinoline-2-aldehyde (5 g.) in presence of methyl-heterocycles (1 g.).

	Products (R = 2-quinolyl)		
Methyl-heterocycle	(II)	(I)	Cu quinaldate
Quinaldine	2·28 g.	1·50 g.	0·46 g.
2-Picoline	1·72	1·72	0·54
1-Methylisoquinoline	1·85	1·31	0·64
Lepidine	1·27	1·63	0·75

Reaction between quinoline-4-aldehyde and quinaldine. The aldehyde (2 g.), treated with quinaldine (2 g.) in ethanol (80%) as described for quinoline-2-aldehyde, gave only 1-4′-quinolyl-2-2′-quinolylethanol (71%), m. p. 180°.

Reaction between benzaldehyde and quinaldine. The aldehyde (5 g.) and quinaldine (5 g.) were refluxed in 80% ethanol for 30 hr. Steam-distillation of the mixture left 1-phenyl-2-2′-quinolylethanol [4] (10%), m. p. 128°. When the mixture was heated in a sealed tube at 100° for 30 hr., the residue after steam-distillation was 2-styrylquinoline [4] (17%), m. p. 99:.

We thank the Governors of the Royal College of Advanced Technology for a research demonstratorship (to H. A.).

Royal College of Advanced Technology, Salford, Lancs.
The Harris College, Preston, Lancs. [*Received, February 28th*, 1962.]

[4] Skidmore and Tidd, *J.*, 1959, 1641.

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745. *Proton Magnetic Resonance Investigation of the Difluoromethyl Group.*[1]

By B. H. Arison, T. Y. Shen, and N. R. Trenner.

In an examination of compounds of biological interest by proton magnetic resonance spectroscopy, the problem arose of confirming the presence and location of the difluoromethyl group. While its characteristic widely spaced triplet disposed of the former aspect, an unexpected variation of the proton–fluorine coupling constant allowed us to decide among *C*-, *O*-, and *N*-difluoromethylation. Two examples containing CHF_2·S-groups were indistinguishable from the carbon analogues by this method. The annexed Table lists the compounds examined and the observed chemical shifts and coupling constants.

The results show that for the system X·CHF_2 the proton–fluorine coupling constant increases with increasing electronegativity of X. The fact that the carbon and sulphur analogues are indistinguishable follows logically from the equivalent electronegativities of these atoms.[2] Further, trifluoromethane, which may be looked upon as the fluorinated

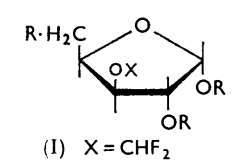
[1] First reported by L. H. Sarett and T. Y. Shen, 140th Amer. Chem. Soc. Meeting, Chicago, Illinois, September, 1961.

[2] Pauling, " Nature of the Chemical Bond," 2nd edn., Cornell Univ. Press, Ithaca, N.Y., 1948, p. 60.

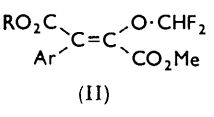
Proton magnetic resonance results.
(τ = centre of triplet; J in cycles.)

No.	Compound	τ	J	No.	Compound	τ	J
1	$CHF_2 \cdot CO_2Me$	4·10	53·4	13	(V)	3·60	73·2
2	$CHF_2 \cdot CAr(CO_2Me)_2$	3·17	54·9	14	(VI)	3·58	73·2
3	$R \cdot CH_2 \cdot C(CHF_2)(CO_2Et)_2$	3·52	55·2		Average for CHF_2–O		74·0
4	$1\text{-}C_{10}H_7 \cdot C(CHF_2)(CO_2Me)_2$	3·12	54·6	15	(VII; R = CO_2Et)	1·59	59·4
	Average for CHF_2–C		54·5	16	(VIII)	1·89	58·5
5	(I)	3·80	72·0	17	(IX)	2·45	59·1
6	(II; R = H)	3·39	75·6			2·23 *	57·3
7	(II; R = Me)	3·38	75·6	18	(VII; R = CH_2·OH)	2·53	60·3
8	(III)	2·93 *	73·8	19	$CHF_2 \cdot N(CH{:}R)_2$	2·64	60·6
9	(IV)	3·28	75·6		Average for CHF_2–N		59·2
10	$CHF_2 \cdot OPh$	3·55	73·8	20	$CHF_2 \cdot S \cdot CH_2R$	2·95 †	54·6
11	$p\text{-}CHF_2 \cdot O \cdot C_6H_4Me$	3·60	74·7	21	$p\text{-}CHF_2 \cdot S \cdot C_6H_4 \cdot CH_2R$	3·25	57·0
12	2-Difluoromethoxyquinoline	2·29	72·6		Average for CHF_2–S		55·8

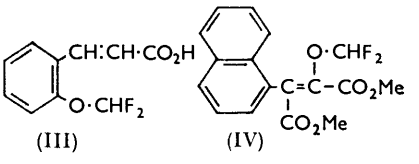
* In deuteroacetone. † In D_2O.



(I) X = CHF_2

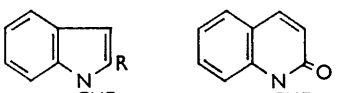


(II)

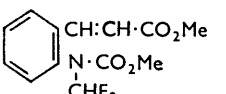


(III) (IV)

(V)* (VI)*



(VII) (VIII)



(IX)

* Steroid A ring.

analogue of $X \cdot CHF_2$, shows a larger splitting (81 cycles) than any compound in the present series.[3] It appears also that the magnitude of the coupling constant is determined primarily by the first atom to which the difluoromethyl group is attached, in agreement with recent work on fluorohydrocarbons.[4]

Although a correlation between coupling constants and the electronegativity of adjacent groups is unusual in most organic structural problems, it has been well established in ^{13}C–proton studies. In terms of the proposals developed in the relevant papers,[5-7] as well as those of Karplus,[8] it is reasonable to view the trends in the difluoromethyl series as arising from a varying H–F–F trihedral angle induced by C–F bond-order changes which are brought about by F–C–X interactions. Additional support for such a quasi-mesomeric system is inferred from the unusually large influence of distant groups on the proton chemical shift, as in particular for nos. 1 and 2, and 10 and 12. (While cases such as nos. 15 and 18 may also be cited, the anisotropic shielding effects of the spatially nearby carbonyl group may be largely responsible for this difference.) The observation, moreover, of a systematic increase in the proton–fluorine coupling constant with increasing fluorination of methane [3] would also be consistent with this hypothesis.

Because of the overriding influence of environmental factors, the possibility of using the proton chemical shift to decide the nature of X does not appear promising. Even in the nitrogen series, where the average shift position is lower than for the others, overlap from the oxygen group (no. 12) sometimes occurs. The role of solvents has not been fully explored, but our limited results do not suggest an appreciable influence.

Experimental.—The proton magnetic resonance data were obtained with a 60 megacycle Varian Associates model 4300B spectrometer. Unless otherwise stipulated, spectra were run

[3] Gutowsky, *J. Phys. Chem.*, 1953, **57**, 481.
[4] Elleman, Brown, and Williams, *J. Mol. Spectroscopy*, 1961, **7**, 307.
[5] Shoolery, *J. Chem. Phys.*, 1959, **31**, 1427.
[6] Muller and Pritchard, *J. Chem. Phys.*, 1959, **31**, 768, 1471.
[7] Malinowski, *J. Amer. Chem. Soc.*, 1961, **83**, 4479.
[8] Karplus, *J. Chem. Phys.*, 1959, **30**, 11.

on 5—10% solutions in deuterochloroform. The resonance positions were determined relative to an external benzene reference and scaled by the use of side bands [9] generated by a Hewlett–Packard audio-oscillator model 200 CD. The shielding numbers were calculated from the equation [10] $\tau = \Delta\nu/\nu_0 + 3{\cdot}60$ where $\Delta\nu$ is the observed resonance displacement from benzene in cycles per second, and ν_0 is the spectrometer frequency in megacycles. For acetone and D_2O solutions, values of 2·85 and 3·50, respectively, were used as the constant. The precision of the chemical shifts and coupling constants is approximately ± 1 cycle.

We acknowledge the technical contributions of G. Arth, D. Hoff, W. Holtz, S. Lucas, C. H. Stammer, A. H. Todd, J. D. Willett, and T. B. Windholz in the preparation of the difluoromethyl compounds.

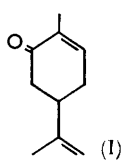
MERCK SHARP & DOHME RESEARCH LABORATORIES, DIVISION OF MERCK & CO., INC., RAHWAY, N.J., U.S.A. [*Received, February 13th*, 1962.]

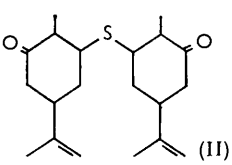
[9] Arnold and Packard, *J. Chem. Phys.*, 1951, **19**, 1608.
[10] Tiers, *J. Phys. Chem.*, 1958, **62**, 1151.

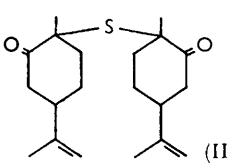
746. *The Constitution of "Carvone Hydrosulphide."*

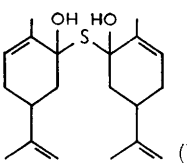
By J. D. LEE, C. J. TIMMONS, and S. C. WALLWORK.

IN the course of structural studies of molecular complexes, "carvone hydrosulphide," [1] $C_{20}H_{30}O_2S$, has been investigated since the discrepancies in the various structures, (II),[2,3] (III),[3,4] and (IV),[5] proposed for it and the readiness with which carvone (I) may be regenerated from the "hydrosulphide" suggested that it might be a molecular complex rather than a compound.


(I)


(II)


(III)



(IV)

Pale yellow needle-like crystals, m. p. 223—225°, were obtained by bubbling hydrogen sulphide into a solution of (+)-carvone in alcoholic ammonia.

The ultraviolet spectrum of the material in ethanol had bands at 227 and 285 mμ (ε 1370 and 63, respectively). The second of these indicates the presence of at least one and probably two non-conjugated carbonyl groups per unit of $C_{20}H_{30}O_2S$. The infrared spectrum showed bands at 3396 (C=O overtone) and 3080 (=C–H) in a hexachlorobutadiene mull, 1717 (six-membered ring ketone) and 1648 (C=C) in $CHCl_3$ and 895 cm.$^{-1}$ ($\rangle C{=}CH_2$) in a KBr disc. These results rule out structure (IV) which does not contain a keto-group and also make a molecular complex structure unlikely.

The proton resonance spectrum at 60 Mc./sec. in chloroform solution showed a doublet (J 5·2 c./sec.) and a singlet (τ = 9·00 and 8·45, respectively) in the methyl region, which are in agreement with the resonances to be expected for the methyl groups in structure (II), whereas both methyl resonances would be unsplit for structure (III).

Crystal data, from single-crystal Weissenberg photographs, are as follows: Monoclinic, $a = 10{\cdot}48$, $b = 10{\cdot}06$, $c = 9{\cdot}59$ (all $\pm 0{\cdot}02$) Å, $\beta = 95° \pm \frac{1}{2}°$, $U = 1007 \pm 6$ Å^3, $D_m = 1{\cdot}103 \pm 0{\cdot}005$ (by flotation), $Z = 2$ units of $C_{20}H_{30}O_2S$, $D_c = 1{\cdot}103 \pm 0{\cdot}006$. Space group $P2_1$ (C_2^2, No. 4) or $P2_1/m$ (C_{2h}^2, No. 11); observation of a pyroelectric effect indicates $P2_1$. Since the general position in $P2_1$ is two-fold no molecular symmetry is implied by these crystal data and no distinction between the various possible structures could be made

[1] Varrentrapp, in "Handwörterbuch der reinen und angewandten Chemie," ed. Liebig, Poggendorff, and Wöhler, Brunswick, 1849, Vol. IV, 686.
[2] Padmanabhan, *Current Sci.*, 1935, **4**, 95.
[3] Challenger, Paton, and Smith, *J.*, 1923, 1046.
[4] Wallach, "Terpene und Campher," 2nd edn., Verlag von Veit, Leipzig, 1914, p. 68; Hooper, Macbeth, and Price, *J.*, 1934, 1147.
[5] Harries and Stirm, *Ber.*, 1901, **34**, 1928; Dulou, *Bull. Inst. Pin.*, 1934, [2], 205; *Chem. Zentr.*, 1935, I, 2540.

on these grounds. Thus, in view of the spectroscopic and nuclear magnetic resonance results, structure (II) is correct.

CHEMISTRY DEPARTMENT, THE UNIVERSITY, NOTTINGHAM. [*Received, March 22nd,* 1962.]

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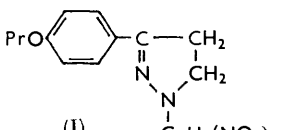
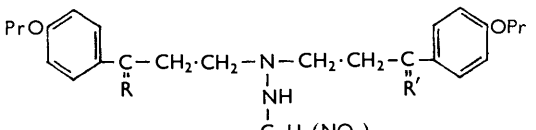
747. *The Formation of* 1-(2,4-*Dinitrophenyl*)-2-*pyrazolines from* αβ-*Unsaturated Ketones.*

By R. F. CURTIS, C. H. HASSALL, and J. WEATHERSTON.

HESSE and LETTENBAUER [1] have suggested that 1-hydroxypent-3-en-2-one reacts with 2,4-dinitrophenylhydrazine under mild conditions to give 1-(2,4-dinitrophenyl)-3-hydroxymethyl-5-methyl-2-pyrazoline. No evidence for this structure of the product was given, but two related cases were quoted as precedents for the formation of a pyrazoline derivative through a 2,4-dinitrophenylhydrazone. Although there is no doubt that hydrazones and phenylhydrazones of αβ-unsaturated ketones cyclise to give pyrazolines, it is commonly considered that the corresponding 2,4-dinitrophenylhydrazones do not undergo ring closure under the conditions used for the preparation of hydrazone derivatives.[2] As the reaction suggested by Hesse *et al.* had important implications in the argument [3] concerning the constitutions of the glycosides of *Calotropis procera* we have re-examined the two precedents.



(I)



[II ; R = R′ = O]

[III ; R = N·NH·C$_6$H$_3$(NO$_2$)$_2$, R′ = O]

[IV ; R = R′ = N·NH·C$_6$H$_3$(NO$_2$)$_2$]

In the first example, the reaction between 3-methylbut-3-en-2-one and 2,4-dinitrophenylhydrazine was interpreted by Nazarov *et al.*[4] as giving 1-(2,4-dinitrophenyl)-3,4-dimethyl-2-pyrazoline. This interpretation has been corrected. Whereas Nazarov *et al.* gave no evidence for the constitution of their product, recent studies [5] have shown clearly that it is the 2,4-dinitrophenylhydrazone of the αβ-unsaturated ketone.

In the second case it has been suggested by von Profft and his co-workers [6] that 1-(2,4-dinitrophenyl)-3-*p*-propoxyphenyl-2-pyrazoline (I) is the product, m. p. 176°, when 2,4-dinitrophenylhydrazine reacts with *p*-propoxyphenyl vinyl ketone. Apart from the m. p. and nitrogen analysis, no information was given concerning the properties of this compound. We have re-examined this reaction. Some of the 2,4-dinitrophenylhydrazone of *p*-propoxyphenyl vinyl ketone [7] was formed, but the major product, which was also obtained by von Profft,[8] had the formula $C_{30}H_{34}N_4O_8$. The infrared absorption spectrum of this compound has the following characteristics. There is an NH stretching frequency at 3300 and a strong band at 1680 cm.$^{-1}$ characteristic of the CO·Ph group. The bands in the ultraviolet region ($\lambda_{max.}$ 274, 348 mμ, log ε 4·62, 4·12) are consistent with the presence of an isolated 2,4-dinitrophenylhydrazine chromophore [9] ($\lambda_{max.}$ 352 mμ, log ε 4·17) and two isolated 4-propoxypropiophenone [10] residues (each with $\lambda_{max.}$ 274 mμ, log ε 4·22). This

[1] Hesse and Lettenbauer, *Annalen*, 1959, **623**, 142.
[2] Elderfield, "Heterocyclic Compounds," Wiley and Sons Inc., New York, 1950, Vol. V, p. 57.
[3] Curtis, Hassall, and Weatherston, unpublished work.
[4] Nazarov, Vartanyan, and Matsoyan, *J. Gen. Chem.* (*U.S.S.R.*), 1955, **25**, 1111.
[5] Blum and Gaudemaris, *Bull. Soc. chim. France*, 1954, 996; Timmons, *J.*, 1957, 2613; Yang, Yang, and Ross, *J. Amer. Chem. Soc.*, 1959, **81**, 133.
[6] von Profft, Runge, and Jumar, *J. prakt. Chem.*, 1954, **1**, 57.
[7] Bräuniger and Raudonat, *Arch. Pharm.*, 1954, **287**, 109.
[8] von Profft, personal communication.
[9] Roberts and Green, *J. Amer. Chem. Soc.*, 1946, **68**, 214.
[10] Hannig, *Arch. Pharm.*, 1955, **288**, 560.

leads to the structure (II) which is similar to that assigned to the products of condensation of αβ-unsaturated aryl ketones with hydroxylamine and substituted hydroxylamines.[11]

Treatment of the compound formulated as (II) with an equivalent amount of 2,4-dinitrophenylhydrazine gave a product, m. p. 179—181°. This was identical with the compound which had been assumed by von Profft *et al.* to be the pyrazoline (I) but is evidently the mono-2,4-dinitrophenylhydrazone (III) of the diketo-amine (II). An excess of 2,4-dinitrophenylhydrazine led to the formation of the bis-2,4-dinitrophenylhydrazone (IV).

These results indicate that there is no precedent for the formation of 1-(2,4-dinitrophenyl)-2-pyrazolines from αβ-unsaturated ketones under the conditions normally used for the preparation of 2,4-dinitrophenylhydrazones. This is the result, no doubt, of the reduction in base strength due to the nitro-substituents. However, it deserves mention that this cyclisation may occur when an αβ-unsaturated 2,4-dinitrophenylhydrazone is refluxed for long periods with a mixture of acetic and hydrobromic acids.[12]

Experimental.—Ultraviolet absorption spectra were determined for ethanol solutions with Unicam S.P. 500 and Optica CF 4 (recording) spectrophotometers. Infrared spectra for potassium bromide discs were measured on Grubb–Parsons GS2 and Perkin–Elmer " Infracord " spectrometers. R_F values refer to thin-film chromatography carried out with Desaga apparatus and Merck alumina G, with development by benzene–ethyl acetate (95 : 5). Distinctive colours were produced by spraying the chromatograms with 2N-sodium hydroxide.

2,4-*Dinitrophenyl*-NN′-*di*-(2-p-*propoxybenzoylethyl*)*hydrazine* (II). β-Chloro-4-propoxypropiophenone [6] (2·3 g.) was heated under reflux with fused potassium acetate (1·2 g.) in dry methanol (10 ml.) for 1 hr. Potassium chloride was removed and the filtrate treated with 2,4-dinitrophenylhydrazine (1 g.) in 3N-sulphuric acid (250 ml.), to yield a red gum (1·4 g.). Chromatography on activated alumina (20 × 4 cm.) and elution with benzene–dichloromethane (1 : 1) gave the 2,4-*dinitrophenylhydrazone* (25 mg.) of *p*-propoxyphenyl vinyl ketone as dark red plates (from ethyl acetate), m. p. 192° (lit.,[7] 177°) (Found: C, 57·9; H, 5·1; N, 14·8. Calc. for $C_{18}H_{18}N_4O_5$: C, 58·3; H, 4·9; N, 15·1%), $\lambda_{max.}$ 392 mμ (log ε 4·41), $\nu_{max.}$ 3290 cm.$^{-1}$, R_F 0·86. Elution with methanol and crystallisation from ethyl acetate gave the *hydrazine* (II) as yellow needles (1·02 g.), m. p. 125—126°, $\lambda_{max.}$ 274, 348 mμ (log ε 4·62, 4·12) (Found: C, 62·8; H, 6·0; N, 9·6; O, 22·3. $C_{30}H_{34}N_4O_8$ requires C, 62·3; H, 5·9; N, 9·7; O, 22·1%), $\nu_{max.}$ 3300 (NH), 1667 cm.$^{-1}$ (aromatic C=O), R_F 0·27.

This compound (II) (576 mg., 1 mol.) in hot methanol (200 ml.) was treated with 2,4-dinitrophenylhydrazine (198 mg., 1 mol.) in methanol (25 ml.) and concentrated sulphuric acid (5 ml.); it gave the *mono*-2,4-*dinitrophenylhydrazone* (III) as deep red lustrous plates (222 mg.), m. p. 179—181°, $\lambda_{max.}$ 255, 387 mμ (log ε 4·61, 4·30) (Found: C, 57·4; H, 4·8; N, 14·5; O, 23·6. $C_{36}H_{38}N_8O_{11}$ requires C, 57·0; H, 5·1; N, 14·8; O, 23·2%), $\nu_{max.}$ 3300 (NH), 1667 cm.$^{-1}$ (aromatic C=O), R_F 0·23.

" 1-(2,4-Dinitrophenyl)-3-(*p*-propoxyphenyl)-2-pyrazoline (I)," kindly supplied by Professor von Profft, was purified by chromatography on activated alumina, eluted with benzene–methanol (200 : 1), and crystallised from ethyl acetate, to give the same mono-2,4-dinitrophenylhydrazone (III), m. p. and mixed m. p. 179°, with identical infrared and ultraviolet absorption spectra.

The compound (II) (576 mg., 1 mol.) in boiling methanol (200 ml.) was treated with 2,4-dinitrophenylhydrazine (396 mg., 2 mol.) in methanol (25 ml.) and concentrated sulphuric acid (5 ml.). A deep red colour developed and next morning the solid was collected. Material which was insoluble in boiling ethyl acetate (70 ml.) was recrystallised from toluene, to give the *bis*-2,4-*dinitrophenylhydrazone* (IV) as bright red prisms (178 mg.), m. p. 208—210°, $\lambda_{max.}$ 257, 377 mμ (log ε 4·59, 4·65) (Found: C, 53·65; H, 4·5; N, 17·8. $C_{42}H_{42}N_{12}O_{14}$ requires C, 53·7; H, 4·5; N, 17·9%), $\nu_{max.}$ 3280 cm.$^{-1}$ (NH), no aromatic C=O absorption, R_F 0·17. The ethyl acetate-soluble material yielded the mono-2,4-dinitrophenylhydrazone (III) (243 mg.), m. p. 176°.

We are grateful to British Petroleum Ltd. for a studentship (to J. W.) and to Imperial Chemical Industries Limited for financial support.

Department of Chemistry, University College of Swansea,
Singleton Park, Swansea. [*Received, March 23rd*, 1962.]

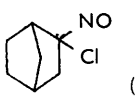
[11] Casey and Marvel, *J. Org. Chem.*, 1959, **24**, 1022.
[12] Chambers and Willard, *J. Amer. Chem. Soc.*, 1960, **82**, 3373.

748. *A Dimeric* gem-*Chloronitroso-compound.*

By JOHN S. DAVIDSON and G. EGLINTON.

ALTHOUGH simple *C*-nitroso-compounds are almost invariably associated as dimers in the solid state, no dimeric *gem*-chloronitroso-compounds, derived from ketoximes, have as yet been reported.[1] The two nitroso-groups present in *cis*-1,4-dichloro-1,4-dinitrosocyclohexane are, however, said to form intramolecular bonds.[2] *gem*-Chloronitroso-compounds studied in this Department have all proved to be monomeric, in the solid state, with the exception of the case described below.

The dimer of 2-chloro-2-nitrosonorbornane was obtained by direct chlorination of norcamphor oxime[3] as a colourless lachrymatory solid, melting at 44° to a deep blue liquid. Its solutions in the common organic solvents are also blue and appear to contain only the monomeric species [(I); stereochemistry undefined], as Beer's law held over the concentration range studied (up to 1·3% for alcohol and benzene), and the freezing-point depression of a 1·32% solution in benzene corresponds to a molecular weight of 156 (Calc. for $C_7H_{10}ClNO$: *M*, 159·7). A strong absorption band ascribed[4] to ν(N=O) was at 1574 cm.$^{-1}$ ($\Delta\nu_{\frac{1}{2}}$ 13 cm.$^{-1}$, ε^a_{molar} 160; with subsidiary, incompletely resolved peak at 1560 cm.$^{-1}$ ε^a_{molar} 100) in a 0·15M-carbon tetrachloride solution. This band was not present in the infrared spectrum of the solid (KCl disc), where the strongest bands were at 1319m, 1302s, and 1287s cm.$^{-1}$, as would be expected for a dimeric nitroso-compound.[2,4]



(I)

Experimental.—Into a solution of norcamphor oxime (1·5 g.) in dry ether (40 ml.) at 0° a slow stream of chlorine was passed until the blue colour changed to green. After evaporation, a solid remained which was first washed with pentane, then sublimed at 40°/1 mm. on to a cold finger (solid carbon dioxide–acetone). The *dimer* (0·6 g.) sublimed as a colourless solid, m. p. 44°, $\lambda_{max.}$ (in EtOH) 6500 Å (ε 26; 0·0176M-solution) (Found: C, 52·4; H, 6·5; Cl, 22·1; N, 8·9. $[C_7H_{10}ClNO]_2$ requires C, 52·7; H, 6·3; Cl, 22·2; N, 8·8%); like all chloronitroso-compounds, it slowly decomposed on exposure to daylight (in an alcoholic solution, $\gamma = 0·3$).

We thank Dr. S. T. R. S. Mitchell for his interest, the Gas Council for a research scholarship (to J. S. D.), and Mrs. F. Lawrie for the infrared measurements.

THE CHEMISTRY DEPARTMENT, THE UNIVERSITY, GLASGOW, W.2. [*Received, March 29th*, 1962.]

[1] Sidgwick, " The Organic Chemistry of Nitrogen," Oxford, 1942, p. 207.
[2] Gowenlock and Lüttke, *Quart. Rev.*, 1958, **12**, 337.
[3] Alder and Rickert, *Annalen*, 1940, **543**, 1; Alder and Stein, *Annalen*, 1936, **525**, 218.
[4] Tarte, *Bull. Soc. chim. belges*, 1954, **63**, 525.

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749. *Nitric Oxide and Oxygen as Inhibitors in Ketone Photolyses.*

By EILEEN L. METCALFE and A. F. TROTMAN-DICKENSON.

PHOTOLYSES of diethyl ketone with added nitric oxide, and of methyl propyl ketone with nitric oxide and oxygen, have been used to check the efficiency of the inhibitors, because the photolytic acts are well established.[1-3]

Diethyl ketone, at pressures between 30 and 40 mm., was photolysed at 145° and 210° with pressures of added nitric oxide between zero and 100 mm. The light source was an unfiltered Osram 125w medium-pressure mercury arc. The condensable products were analysed by gas-chromatography. When the nitric oxide pressure : ketone pressure exceeded 2 : 3, the products of radical combination, disproportionation, and abstraction were completely suppressed. However, even at high inhibitor pressure a small constant amount of ethylene was produced. This could be formed by the reaction: $C_2H_5 + NO \longrightarrow C_2H_4 + HNO$; alternatively it could result from a primary process: $C_2H_5{\cdot}CO{\cdot}C_2H_5 + h\nu \longrightarrow C_2H_4 + C_2H_5{\cdot}CHO$. If $\phi_{CO} = 1·0$,[1] then $\phi_{C_2H_4} = 0·03$, independently of inhibitor pressure.

[1] Davis, *J. Amer. Chem. Soc.*, 1948, **70**, 1868.
[2] Nicholson, *Trans. Faraday Soc.*, 1954, **50**, 1067.
[3] Borkowski and Ausloos, *J. Phys. Chem.*, 1961, **65**, 2257.

Methyl propyl ketone, at 30 mm., was photolysed at 145° alone and with added nitric oxide, and at 85° and 168° with added oxygen. Pressures of 20 mm. of either inhibitor were sufficient to suppress radical reactions. Intramolecular photolytic processes are:

$$CH_3{\cdot}CO{\cdot}C_3H_7 + h\nu \longrightarrow \begin{cases} \longrightarrow C_2H_4 + CH_3{\cdot}CO{\cdot}CH_3 \\ \longrightarrow C_3H_6 + CH_3{\cdot}CHO \end{cases}$$

The yield of ethylene was independent of temperature and presence or absence of either inhibitor. If all light absorbed by the ketone causes some decomposition, the quantum yields are $\phi_{CO} = 0{\cdot}50$, $\phi_{C_2H_4} = 0{\cdot}47$, and $\phi_{C_3H_6} = 0{\cdot}03$. Borkowski and Ausloos [3] also found ϕ_{CO} and $\phi_{C_2H_4}$ equal at short wavelengths, in the photolysis of methyl 2,3,3-trideuteropropyl ketone, although their value is 0·42. They found $\phi_{C_2H_4}$ to decrease with the pressure of added oxygen, but for the undeuterated ketone and at short wavelengths this effect was less pronounced. In the present work variations between zero and 64 mm. of nitric oxide, and between 20 and 77 mm. of oxygen, did not affect the yield of ethylene. The yield of propene was independent of nitric oxide pressure. It was not positively identified in runs with added oxygen, because of relatively large amounts of an oxygenated compound eluted at the same time. As before, propene may be formed by the reaction of propyl with nitric oxide.

Acknowledgment is made to the donors of the Petroleum Research Fund administered by the American Chemical Society for a grant.

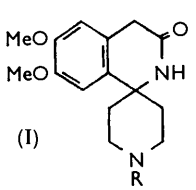
CHEMISTRY DEPARTMENT, EDINBURGH UNIVERSITY. [*Received, April 2nd,* 1962.]

750. 1,2,3,4-*Tetrahydroisoquinoline*-1-*spiro*-4′-*piperidines*.

By E. CRUNDWELL.

IN contrast with aldehydes, ketones do not normally react with phenethylamines to give tetrahydroisoquinolines. Little *et al.*[1] reported that the favourably substituted 3,4-dihydroxyphenethylamine did not condense with cyclohexanone in strongly acidic media. Gardent [2] claimed low yields of tetrahydroisoquinolines from the reaction of 3,4-diethoxyphenethylamine with cyclohexanone and cyclopentanone, catalysed by hydrogen chloride in 85% orthophosphoric acid. The latter conditions have been found ineffective in promoting reaction between 3,4-dimethoxyphenethylamine and cyclopentanone, and catalysis of this reaction was also not effected by use of polyphosphoric acid or methanolic boron trifluoride.

Belleau [3] suggested that phenylacetamides might be more reactive than phenethylamines and obtained a product from the reaction of phenylacetamide and cyclohexanone in polyphosphoric acid. This reagent was found to promote condensation of 3,4-dimethoxyphenylacetamide with cyclopentanone. The reaction of this amide with piperidin-4-ones was therefore investigated as these ketones are highly reactive.[4] 1-Ethylpiperidin-4-one gave a product with infrared absorption spectrum characteristic of a secondary amide (maxima at 1660 and 1527 cm.$^{-1}$). Its nuclear magnetic resonance spectrum showed only two aromatic protons, *para* to each other (τ 3·70 and 3·25), confirming cyclization as shown in (I). Compounds of structure (I; R = Ph·CH_2 and Ph·CH_2·CH_2) were similarly prepared, and the compound (I; R = H) was obtained by catalytic debenzylation.



(I)

The hydrochlorides of the spirans (I; R = Et and Ph·CH_2) lacked analgesic potency in the rat when tested by the method of Randall and Selitto.[5]

[1] Little, Smith, Taylor, and Thomas, *J.*, 1954, 2636.
[2] Gardent, *Ann. Chim. (France)*, 1955, **10**, 413.
[3] Belleau, *Canad. J. Chem.*, 1957, **35**, 651.
[4] Beckett, Casy, and Kirk, *J. Medicin. Pharmaceut. Chem.*, 1959, **1**, 37.
[5] Randall and Selitto, *Arch. int. Pharmacodyn.*, 1957, **111**, 409; **113**, 233.

Experimental.—Equivalents were determined by titration with perchloric acid in acetic acid. Infrared spectra were obtained for Nujol mulls. Nuclear magnetic resonance spectra (tetramethylsilane as internal standard, τ 100) were determined for carbon tetrachloride solutions.

1,2,3,4-*Tetrahydro*-6,7-*dimethoxy*-3-*oxoisoquinoline*-1-*spiro*-4′-*piperidines*. Phosphorus pentoxide (35 g.) was dissolved in 88% orthophosphoric acid (20 ml.). The polyphosphoric acid was heated on a steam-bath and 3,4-dimethoxyacetamide [6] (1·95 g., 0·01 mole) was added. The appropriate *N*-substituted piperidin-4-one (0·015 mole) was then added. The mixture was stirred at 100° for 8 hr., allowed to cool, diluted with water (100 ml.), and extracted with chloroform (from which 3,4-dimethoxyacetamide could be recovered). The aqueous layer was poured on ice and potassium hydroxide (125 g.) in water (125 ml.) and extracted with chloroform; this organic extract was dried (Na_2SO_4) and concentrated *in vacuo*. The residual oil was chromatographed on alumina (50 g.). Elution with benzene (100 ml.) gave oils. Elution with chloroform (300 ml.) then gave solids (~25%) which crystallized from ethyl acetate.

Hydrochlorides were prepared by dissolving the base in hot propan-2-ol (10 ml. per g.) and adding the calculated amount of 10N-hydrogen chloride in propan-2-ol. The product crystallized out on cooling. In this way were prepared:

1′-*Ethyl*-1,2,3,4-*tetrahydro*-6,7-*dimethoxy*-3-*oxoisoquinoline*-1-*spiro*-4′-*piperidine* (I; R = Et), rods, m. p. 151—153° (Found: C, 67·0; H, 7·9; N, 9·3%; equiv., 299. $C_{17}H_{24}N_2O_3$ requires C, 67·1; H, 7·9; N, 9·2%; equiv., 304) [*hydrochloride*, flakes, m. p. >300° (Found: equiv., 345. $C_{17}H_{25}ClN_2O_3$ requires equiv., 340·5)].

1′-*Benzyl*-1,2,3,4-*tetrahydro*-6,7-*dimethoxy*-3-*oxoisoquinoline*-1-*spiro*-4′-*piperidine*, needles, m.p. 186° (Found: C, 71·9; H, 7·3%; equiv., 372. $C_{22}H_{26}N_2O_3$ requires C, 72·1; H, 7·1%; equiv., 366) [*hydrochloride*, flakes, m. p. >300° (Found: Cl, 8·8; N, 7·3%; equiv., 406. $C_{22}H_{27}ClN_2O_3$ requires Cl, 8·8; N, 7·3%; equiv., 402·5)].

1,2,3,4-*Tetrahydro*-6,7-*dimethoxy*-3-*oxo*-1′-*phenethylisoquinoline*-1-*spiro*-4′-*piperidine*, rods, m. p. 171° (Found: C, 72·3; H, 5·7%; equiv., 377. $C_{23}H_{28}N_2O_3$ requires C, 72·6; H, 7·4%; equiv., 380).

The hydrochloride of the benzyl compound (1·1 g.) was hydrogenated in absolute ethanol (100 ml.) and water (30 ml.) over 10% palladium–charcoal (0·1 g.) (uptake ~1 mol.). The solution was filtered, concentrated somewhat by evaporation, made basic with potassium hydroxide (0·5 g.), and extracted with chloroform. The extract was dried (Na_2SO_4) and evaporated *in vacuo* on a steam-bath, to give 1,2,3,4-*tetrahydro*-6,7-*dimethoxy*-3-*oxoisoquinoline*-1-*spiro*-4′-*piperidine* which from benzene formed irregular crystals, m. p. ~260° (decomp.) (Found: C, 65·6; H, 7·3. $C_{15}H_{20}N_2O_3$ requires C, 65·2; H, 7·3%).

This work was carried out during the tenure of a Miles-Ames Research Fellowship at the School of Pharmacy, Chelsea College of Science and Technology. I am grateful to Dr. A. H. Beckett for many stimulating discussions, and to Dr. J. Harley-Mason, Cambridge University, for the nuclear magnetic resonance data.

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[*Received, April 9th*, 1962.]

[6] Wenner, *J. Org. Chem.*, 1959, **15**, 548.

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751. *Nucleophilic Displacements in Organic Sulphites. Part VIII.*[1] *The Heats of Hydrolysis of Some Organic Sulphites.*

By NORMA PAGDIN, ANGELA K. PINE, J. G. TILLETT, and H. F. VAN WOERDEN.

WESTHEIMER and his co-workers have found that the alkaline hydrolyses of five-membered cyclic phosphates are much more rapid than those of the corresponding six-membered and open-chain phosphates and have attributed the differences in rate to ring-strain in the five-membered cyclic phosphates.[2] This has been confirmed thermochemically,[3] the

[1] Part VII, Tillett, *J.*, 1960, 5138.

[2] Kumamoto, Cox, and Westheimer, *J. Amer. Chem. Soc.*, 1956, **78**, 4858; Westheimer, *Chem. Soc. Special Publ.*, No. 8, 1957, 1; Haake and Westheimer, *J. Amer. Chem. Soc.*, 1961, **83**, 1102.

[3] Cox, Wall, and Westheimer, *Chem. and Ind.*, 1959, 929.

heat of hydrolysis of ethylene methyl phosphate, for example, exceeding that for hydroxyethyl dimethyl phosphate by *ca.* 7—9 kcal. mole^{-1}.

In previous papers [4] we have noted that both aliphatic and aromatic cyclic sulphites show similar differences in the rates of alkaline hydrolysis, and we have drawn attention to the fact that it was not known whether the internal strain which makes the transition state easily accessible for the sulphites is reflected in the heats of reaction as it is in the case of ethylene phosphate.[3]

The present investigation was designed specifically to determine this fact and hence to establish whether the factors which determine that the five-membered ring compounds are highly reactive are concerned with initial-state strain or with some special feature of the relevant transition states.

Experimental.—A simple calorimeter consisting of a 900-ml. Dewar flask was provided with a tight-fitting stopper, Beckmann thermometer, glass stirrer, ampoule-breaker, and resistance for calibration purposes.[5] The ampoule-breaker was constructed of brass. The ampoule itself, made of thin glass, rested horizontally in a cylindrical frame and was held in place by gentle pressure from a plunger. It was broken against the frame by screwing down the plunger which completely shattered the ampoule, thus ensuring rapid mixing.

The calibration heater consisted of a 12-ft. length of constantin wire (resistance 7·270 Ω) wound on a glass former. The ends of the coil were soldered to two thick copper leads which were encased in glass and passed out through the stopper. The coil and the soldered joints were coated with " Araldite " which prevented electrolysis but still allowed rapid heat exchange with the surrounding liquid. For calibration of the calorimeter a 6-v accumulator was the source of current; thus a current of 0·728 amp. passed for 3·00 min. gave a rise in temperature of 0·380° c which corresponded to the liberation of 166 cal.

Procedure for a typical determination. The ampoule containing 5 ml. of a 0·500M-solution of the organic sulphite in dioxan was placed in 500 ml. of a 0·100M-solution of sodium hydroxide in 50% dioxan–water (v/v) and left overnight to reach thermal equilibrium. Stirring was commenced about 15 min. before the ampoule was broken and continued for about 20 min. thereafter. The adiabatic change in temperature was determined from a temperature–time curve by a standard procedure.[6] The " heat of breaking " was found to be negligible. Identical experiments in the absence of sulphite indicated that the heat of dilution of sodium hydroxide caused by the introduction of the dioxan in the ampoule was also negligible.

Experiments were carried out with portions (5 ml.) of 0·500M-catechol, of ethylene glycol, and of phenol (the products of hydrolysis of *o*-phenylene sulphite, ethylene sulphite, and diphenyl sulphite, respectively) to determine the heats of neutralisation of these compounds. The hydrolysis of one mole of diphenyl sulphite produces two moles of phenol and so to obtain the net heat of hydrolysis of diphenyl sulphite, the heat of neutralisation of two moles was subtracted from the total heat of reaction of one mole of sulphite with an excess of alkali. The results for 0·100M-sodium hydroxide at 20° are indicated in the Table.

The heats of reaction are independent of the concentration of hydroxide ion. Thus, for *o*-phenylene sulphite the heats of total reaction were 56·0, 55·0, and 54·6 kcal. mole^{-1} in solutions of 0·500, 0·100, and 0·050M-sodium hydroxide, respectively. Also, the total heat evolved in 0·010M-sodium hydroxide (40·3 kcal./mole) corresponds reasonably to the heat of hydrolysis alone since this solution contains equivalent amounts of the two reactants and there should be no contribution from the heat of neutralisation.

Sulphite	Total heat of reaction (kcal. mole^{-1})	Heat of neutraln. of products (kcal. mole^{-1})	Net heat of hydrolysis (kcal. mole^{-1})
o-Phenylene	55·0 ± 1·2	15·8 ± 0·8	39·2 ± 2·0
Diphenyl	50·4 ± 1·0	8·80 ± 0·5 †	41·6 ± 1·5
Ethylene	30·1 ± 0·5	1·70 ± 0·1	28·4 ± 0·6
Trimethylene *	29·5 ± 0·5	0·0 ± 0·2	29·5 ± 0·7

* In 0·500M-NaOH. † For two moles.

[4] Cf. Tillett, *J.*, 1960, 37; de la Mare, Tillett, and van Woerden, *Chem. and Ind.*, 1961, 1533.

[5] Cf. Pritchard and Skinner, *J.*, 1950, 272; O'Hara, Wu, and Hepler, *J. Chem. Educ.*, 1961, 512; Larsson and Berzner, *Arkiv Kemi*, 1959, 143.

[6] Sturtevant, in Weissberger's " Techniques of Organic Chemistry," Interscience Publ., Inc., New York, 1949, p. 744.

The value for ethylene sulphite agrees reasonably with that obtained by Davis [7] (*ca.* 33 kcal. mole^{-1}), in view of the different solvent and temperature. Our value for the heat of neutralisation of phenol is similar to that obtained by Fernandez and Hepler [8] (*ca.* 4·7 kcal. mole^{-1}).

Since the completion of this work, Davis [7] has published related work in which dimethyl sulphite and ethylene sulphite are compared. Being apparently unaware of our recent note,[4] he has mistakenly attributed to Bunton and to us the view that 1,3-non-bonded interactions between oxygen atoms give rise to strain in all cyclic esters. In fact, we have been concerned, as he has, to establish whether or not the experimental similarities between the sequence of reactivities of phosphates and sulphites were derived from the same cause.

We find in fact that, although *o*-phenylene sulphite reacts with alkali about 10^3 times faster than diphenyl sulphite, the thermochemical evidence suggests that the rate-difference is not determined by relative strain in the initial states, the two heats of hydrolysis being identical within experimental error.

Thus we confirm Davis's measurements on the aliphatic sulphites and have extended them to the aromatic analogues. We agree, in general, with his conclusion that five-membered sulphites are not strained relative to the six-membered or open-chain sulphites. The theoretical implications of these results are to be discussed in a forthcoming paper.

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[7] Davis, *J. Amer. Chem. Soc.*, 1962, **84**, 599.
[8] Fernandez and Hepler, *J. Amer. Chem. Soc.*, 1959, **81**, 1783.

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752. *The Synthesis and Nuclear Magnetic Resonance Spectrum of Methylphosphinic Acid.*

By D. FIAT, M. HALMANN, L. KUGEL, and J. REUBEN.

METHYLPHOSPHINIC ACID, MeHPO·OH, has been mentioned several times in the literature,[1] but its synthesis and properties have not explicitly been described. It was prepared by low-temperature methanolysis of dichloromethylphosphine: $MePCl_2 + 2MeOH \longrightarrow MeHPO{\cdot}OH + 2MeCl$. It is a strong monobasic acid (pK 2·3), which is oxidised by aqueous bromine to methylphosphonic acid, $Me{\cdot}PO_3H_2$. An aqueous solution of methylphosphinic acid or its sodium salt is stable when heated in an open tube at 100° for several minutes. The neat acid is stable at room temperature *in vacuo* for several months, since no smell of methylphosphine develops, and only a trace of methylphosphonic acid which is easily detected by paper chromatography. Thus, the oxidative disproportionation stated [2] to occur when alkylphosphinic acids are heated does not readily take place with methylphosphinic acid. In contrast to trifluoromethylphosphinic acid, which is volatile,[3] methylphosphinic acid has no appreciable vapour pressure, probably owing to stronger hydrogen bonding of the liquid acid.

The proton magnetic resonance spectrum in aqueous solution showed that methylphosphinic acid has a proton bound to phosphorus (since this proton line was split to a doublet by indirect spin-spin interaction with phosphorus) as well as a methyl group bound to phosphorus, the line of which was again split to a doublet by interaction with the phosphorus spin (see Figure). The spin coupling constants J (in cycles per second) measured as the distance between the lines of the doublets, and the chemical shifts δ of the centres of the doublets are given in the Table. The resonance line of the water protons (and of the rapidly exchanging PO·OH protons) is used as internal standard for measurements of chemical shift. Results in the Table are there compared with others published, and with those for dimethylphosphinic acid.

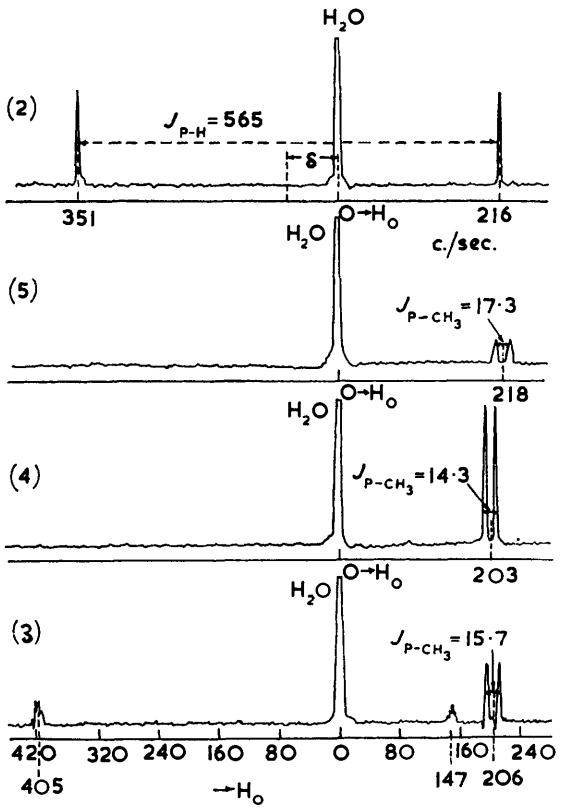
[1] Guichard, *Ber.*, 1899, **32**, 1572; Hofmann, *Ber.*, 1871, **4**, 605; Petrov, Bliznyuk, Studnev, and Kolomiets, *Zhur. obshchei Khim.*, 1961, **31**, 179.
[2] Kosolapoff, "Organophosphorus Compounds," J. Wiley and Sons, New York, 1950, p. 141; Crofts, *Quart. Rev.*, 1958, **12**, 344.
[3] Burg and Griffiths, *J. Amer. Chem. Soc.*, 1961, **83**, 4333.

Proton and ^{31}P chemical shifts δ (in p.p.m.) and spin coupling constants J (in c./sec.) for phosphorus compounds.

	^1H-resonance				^{31}P-resonance		
	H bound to P		CH_3–H				
Compound	δ(H)	J(P–H)	δ(H)	J(P–CH_3)	δ(P)	J(P–H)	J(P–CH_3)
1. Me_4P^+		515					
2. $H_2PO{\cdot}OH$ ...	−1·15	565					
3. $MeHPO{\cdot}OH$	−2·10 ± 0·05	561 ± 2	+3·50 ± 0·05	15·7	−35·0 ± 0·1	557 ± 2	15·5 ± 0·2
4. $Me_2PO{\cdot}OH$...			+3·38	14·3	−55·3 ± 0·1		14·2 ± 0·2
5. $MePO(OH)_2$			+3·6	17·3	−31·0 ± 0·1		17·3 ± 0·2
6. $PO(OMe)_3$ ...				11·2			
7. $MePCl_2$					−193·0 ± 0·5		16·9 ± 0·2

(1) Silver and Luz, *J. Amer. Chem. Soc.*, 1961, **83**, 786. (2) Gutowsky, McCall, and Slichter, *J. Chem. Phys.*, 1953, **21**, 2791; Quinn and Brown, *ibid.*, p. 1605; Roux, *Helv. Phys. Acta*, 1958, **31**, 511. (5) Martin and Mavel, *Compt. rend.*, 1961, **253**, 644. (6) Axtman, Shuler, and Eberly, *J. Chem. Phys.*, 1959, **31**, 850. Measurements recorded for (2—5) and (7) are present work: (3) 12% aq. soln.; (4) 57% aq. soln.; (5) 58·3% aq. soln.; (7) neat liquid.

At still higher resolution, the proton magnetic resonance spectrum of methylphosphinic acid showed further splitting of the methyl doublet, obviously owing to interaction with the proton bound to phosphorus, and $J(CH_3–H) = 2·15 \pm 0·15$ c./sec. Quadruplet splitting was observed on the proton doublet with the same coupling constant.



Proton magnetic resonance spectra. For key see Table.

In ^{31}P magnetic resonance spectra, chemical shifts were similarly measured relative to 85% orthophosphoric acid as an external standard. The chemical shifts observed for methylphosphonic and dimethylphosphinic acid and for dichloromethylphosphine compare

well with those published.[4] However, in the present work higher resolution also permitted measurements of the splitting due to spin-spin interaction with the methyl protons. Each ^{31}P line was split into four equally spaced lines (15—17 c./sec. intervals). The coupling constants $J(P–CH_3)$ thus obtained agree with those found from the proton magnetic resonance spectra (see Table, columns 5 and 8).

Experimental.—Methylphosphinic acid. To dichloromethylphosphine [5] (0·64 g.; b. p. 80°) at −180° methanol (2 ml.; reagent grade) was added. The whole was evacuated at 10^{-4} mm. for 3 hr. while immersed in a bath of brine, and for several hours at room temperature, until constant weight was attained. An aqueous solution of the product was analysed by potentiometric titration with sodium hydroxide, a Titrigraph Radiometer recording glass electrode pH-meter being used (Found: equiv., 82·3. Calc. for CH_5O_2P: equiv., 80·0). The product was a monobasic acid; the acid dissociation constant was calculated, by means of the equation $K = [H^+][B + (H^+)]/\{C - [B + (H^+)]\}$, where B is the concentration of added base and C the total concentration of methylphosphinic acid. It contained 5% of a dibasic acid impurity, probably methylphosphonic acid. Paper chromatography [6] (ascending from propan-1-ol–ammonia–water, 6 : 3 : 1) gave R_F 0·56 for methylphosphinic acid, and R_F 0·30 for traces of methylphosphonic acid. Elution of the methylphosphinic acid fraction gave a product whose titration curve was that of a pure monobasic acid. Paper electrophoresis [6] gave $R_P = 0·56$ for methylphosphinic acid and for methylphosphonic acid.

Oxidation with aqueous bromine at 100° converted methylphosphinic acid completely into methylphosphonic acid (identified by paper chromatography), but aqueous bromine or concentrated nitric acid caused only partial oxidation at room temperature.

Spectral measurements. Proton magnetic resonance measurements were made with a Varian HR-60 V-4300B spectrometer at a frequency of 56·4 Mc. sec.$^{-1}$. Phosphorus magnetic resonance was measured at a frequency of 8·13 Mc. sec.$^{-1}$. Calibrations were by the side-band technique, and the audio-oscillator frequency was monitored by a Hewlett–Packard model 524B electronic counter. For measurements of chemical shift, a tube of 1 mm. internal diameter, containing 85% orthophosphoric acid, was introduced into sample test-tubes of 13 mm. internal diameter.

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Rehovoth, Israel. [*Received, April 11th*, 1962.]

[4] Finegold, *Ann. New York Acad. Sci.*, 1958, **70**, 875; Moedritzer, *J. Amer. Chem. Soc.*, 1961, **83**, 4383.
[5] Parshall, *J. Inorg. Nuclear Chem.*, 1960, **12**, 372.
[6] Hanes and Isherwood, *Nature*, 1949, **164**, 1107; Halmann and Kugel, *Bull. Res. Council Israel*, 1961, **10***A*, 124.

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753. *The Enol Acetylation of* 3β-*Acetoxycholestan*-6-*one.*

By M. P. Hartshorn and A. F. A. Wallis.

Enol acetylation of the ketone (I) by acetic anhydride–sulphuric acid or carbon tetrachloride–acetic anhydride–perchloric acid gave the enol acetate (II), the structure of which was proved by reaction with bromine, yielding the known [1] 5α-bromo-ketone (IV).

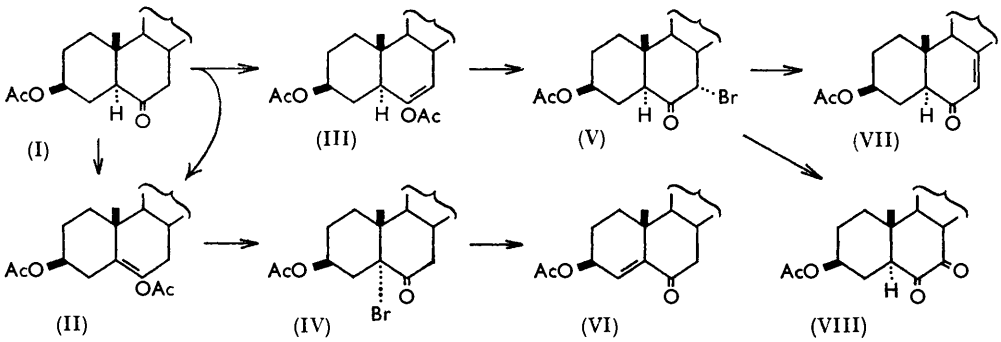
Enol acetylation of the ketone (I) by isopropenyl acetate–toluene-*p*-sulphonic acid gave, after chromatography, a low yield (22%) of an enol acetate sample (A). Crystallisation of this gave material, m. p. 70—71°, which on bromination gave a 1 : 1 mixture of 5α- and 7α-bromo-ketones (IV and V). Thus the crystalline material must be a mixture of Δ^5- and Δ^6-enol acetates (II and III; *ca.* 1 : 1). This enol acetate mixture could not be resolved into its components by chromatography on deactivated alumina (contrast the ready separation [2] of the Δ^6- and Δ^7-enol acetates of 3β-acetoxycholestan-7-one).

The ratio of isomers ($\Delta^5 : \Delta^6$) formed on enol acetylation by isopropenyl acetate–toluene-*p*-sulphonic acid was estimated by measurements of specific rotation and optical rotatory dispersion for the bromination products of enol acetate (A). The results obtained are consistent with a $\Delta^5 : \Delta^6$ ratio of 11 : 9.

[1] Heilbron, Jones, and Spring, *J.*, 1937, 801.
[2] Jones and Wluka, *J.*, 1959, 911.

Dehydrobromination of the 7α-bromo-ketone (V) with lithium carbonate in boiling dimethylformamide gave the Δ^7-conjugated ketone [3] (VII) in reasonable yield. Repetition of the reaction [1] of the bromide (V) with silver nitrate in boiling pyridine, followed by chromatography, allowed the isolation of the Δ^7-conjugated ketone (VII) (*ca.* 13%) in addition to the dione (VIII) (*ca.* 23%) reported earlier.

Finally, dehydrobromination of the 5α-bromo-ketone (IV) with lithium carbonate in boiling dimethylformamide gave the Δ^4-conjugated ketone (VI) in good yield.



Experimental.—M. p.s are corrected. Rotations were measured for chloroform solutions at room temperature. Infrared and ultraviolet spectra were recorded for carbon disulphide and methanol solutions, respectively. Alumina used for chromatography was Peter Spence's grade H, to which 5% of 10% acetic acid had been added. Silica gel was Crosfield Sorbsil grade 60—120. Light petroleum refers to the fraction of b. p. 50—70°.

Enol acetylation of 3β-*acetoxycholestan*-6-*one* (I). (*a*) A solution of the ketone (5 g.) in carbon tetrachloride (130 c.c.) was treated with acetic anhydride (7 c.c.) and 60% aqueous perchloric acid (0·5 c.c.) and kept at 20° for 18 hr. The material isolated by means of ether was adsorbed on alumina (500 g.). Elution with light petroleum–benzene (20 : 7) afforded solid 3β,6-diacetoxycholest-5-ene [4] (II) (3·74 g.), and crystallisation from methanol–ether gave needles, m. p. 108—109°, $[\alpha]_D$ −49° (*c* 0·98), $\nu_{max.}$ 1761 and 1205 (enol acetate), 1745 and 1241 (OAc), and 1701 cm.$^{-1}$ (C=C).

Elution with benzene afforded unchanged starting material (750 mg.), identified by m. p. 129°, $[\alpha]_D$ −24° (*c* 0·93), $\nu_{max.}$ 1739 and 1236 (OAc), and 1721 cm.$^{-1}$ (C=O).

(*b*) A solution of the ketone (451 mg.) in acetic anhydride (8 c.c.) and 36N-sulphuric acid (0·02 c.c.) was heated under reflux for 1 hr. Isolation by means of ether afforded an oil (519 mg.) which was adsorbed on alumina (50 g.). Elution with 10 : 3 light petroleum–benzene and crystallisation from ether–methanol gave the enol acetate (II) (339 mg.) as needles, m. p. 108—109°, $[\alpha]_D$ −49° (*c* 0·88), $\nu_{max.}$ 1761 and 1205 (OAc), and 1701 cm.$^{-1}$ (C=C).

(*c*) The solvent was fractionally distilled at 96° from a solution of the ketone (8·01 g.) and toluene-*p*-sulphonic acid (1·27 g.) in isopropenyl acetate (200 c.c.). After 8 hr. (50 c.c. of distillate) the remaining solvent was removed at 20 mm. The material isolated by means of ether was adsorbed on alumina (800 g.). Elution with light petroleum–benzene (10 : 3) gave an enol acetate sample (A) (1·90 g.). Crystallisation of part of this sample from methanol gave needles, m. p. 70—71°, $[\alpha]_D$ −47° (*c* 1·07) (Found: C, 76·1; H, 10·1. Calc. for $C_{31}H_{50}O_4$: C, 76·5; H, 10·3%), $\nu_{max.}$ 1761 and 1209 (enol acetate), 1742 and 1238 (OAc), and 1701 cm.$^{-1}$ (C=C).

Further elution with benzene gave unchanged starting material (5·28 g.), m. p. 128—129°, $[\alpha]_D$ −24° (*c* 0·85), $\nu_{max.}$ 1739 and 1236 (OAc), and 1721 cm.$^{-1}$ (C=O).

Bromination of 3β,6-*diacetoxycholest*-5-*ene* (II). Bromine (250 mg., 1·5 mol.) in acetic acid (1 c.c.) was added to a solution of the enol acetate (500 mg.) in 1 : 10 pyridine–acetic acid (4·5 c.c.) at 20°. The material recovered by means of chloroform in the usual manner was adsorbed on silica gel (50 g.). Elution with 1 : 1 light petroleum–benzene and crystallisation from ether–light petroleum gave the 5α-bromo-compound [1] (IV) (450 mg.) as needles, m. p. 167—168°, $[\alpha]_D$ −131° (*c* 0·96), $\nu_{max.}$ 1745 and 1236 (OAc), and 1724 cm.$^{-1}$ (*ax*-bromo-ketone).

Bromination of the enol acetate, m. p 70—71°. Bromine (182 mg., 1·1 mol.) in carbon tetrachloride (0·46 c.c.) was added to a solution of the enol acetate (502 mg.) in carbon tetrachloride

[3] Harvey and Bloch, *Chem. and Ind.*, 1961, 595.
[4] Hartshorn, *J.*, 1962, 3168.

(16 c.c.) containing propylene oxide (0·15 c.c.). Isolation by means of ether, followed by the filtration of a 2 : 1 light petroleum–benzene solution of the crude product through a short column of silica gel, gave a bromo-ketone sample (440 mg.), m. p. 125—135°, $[\alpha]_D$ −43° (*c* 0·88), $\nu_{max.}$ 1745 and 1236 (OAc) and 1721 cm.$^{-1}$ (*ax*-bromo-ketone). The specific rotation of the mixed bromo-ketones corresponds to a 5α : 7α ratio of 1 : 1.

Bromination of enol acetate (A). Bromine (250 mg., 1·5 mol.) in acetic acid (1·0 c.c.) was added to a solution of the enol acetate (500 mg.) in 1 : 10 pyridine–acetic acid (4·5 c.c.) at 20°. Isolation by means of ether gave a crude bromo-ketone mixture (511 mg.), m. p. 115—125°, $[\alpha]_D$ −50° (*c* 0·93), $\nu_{max.}$ 1745 and 1236 (OAc) and 1721 cm.$^{-1}$ (*ax*-bromo-ketone). R.D. in methanol: [*M*] (3275 Å), −3600°; (3250), −4050°; (2800), +5400°; (2760), +5000°.

Filtration of a solution of the crude product in 2 : 1 light petroleum–benzene through silica gel gave a bromo-ketone mixture (430 mg.), $[\alpha]_D$ −50° (*c* 0·99), $\nu_{max.}$ 1745 and 1236 (OAc) and 1721 cm.$^{-1}$ (*ax*-bromo-ketone). R.D. in methanol: [*M*] (3262 Å), −4200°; (3225), −4500°; (2850), +5970°; (2813), +5850°.

The specific rotations and the optical rotatory dispersion data for the bromo-ketone mixtures both before and after filtration through silica gel indicate a 5α : 7α ratio of 11 : 9.

3β-*Acetoxycholest-7-en-6-one* (VII). The 7α-bromo-ketone (V) (250 mg.) was added to a boiling suspension of lithium carbonate (900 mg.) in dimethylformamide (25 c.c.) and heated under reflux in nitrogen for 3 hr. Isolation by means of ether and filtration of a benzene–ether (50 : 1) solution of the crude product through silica gel gave on removal of solvents at 20 mm. a solid (136 mg.) which on crystallisation from methanol afforded the conjugated ketone as needles, m. p. 152—153°, $[\alpha]_D$ +1° (*c* 0·98) (Found: C, 78·6; H, 10·2. Calc. for $C_{29}H_{46}O_3$: C, 78·7; H, 10·5%), $\lambda_{max.}$ 2450 Å (ε 21,400). R.D. in methanol: [*M*] (5890 Å), +800°; (5000), +550°; (4000), +1300°; (3450), +6500°; (3100), −6000°.

Attempted dehydrobromination of 3β-*acetoxy-7α-bromocholestan-6-one* [1] (V). The bromo-ketone (719 mg.) was heated under reflux with pyridine (15 c.c.) and silver nitrate (1·5 g.) for 5 hr. Working up in the normal manner gave a dark tar (520 mg.), and this was adsorbed on silica gel (50 g.). Elution with 1 : 2 light petroleum–benzene and crystallisation from methanol gave the 6,7-dione (VIII) (147 mg.) as needles, m. p. 162—163°, $[\alpha]_D$ −115° (*c* 1·01), $\nu_{max.}$ 3424 (OH), 1742 and 1233 (OAc), and 1680 cm.$^{-1}$ (C=C–C=O), $\lambda_{max.}$ 2740 Å (ε 11,700). R.D. in methanol: [*M*] (5890 Å), −350°; (5000), −150°; (4000), −1150°; (3250), −5000°; (3000), −1500°; (2975) −500°. Further elution with benzene–ether (50 : 1) and crystallisation from methanol gave 3β-acetoxycholest-7-en-6-one (VII) (75 mg.) as needles, m. p. 152—153°, $[\alpha]_D$ +1° (*c* 1·01), $\lambda_{max.}$ 2450 Å (ε 21,000).

3β-*Acetoxycholest-4-en-6-one* [1] (VI.) The 5α-bromo-ketone (IV) (950 mg.) was added to a boiling suspension of lithium carbonate (3·5 g.) in dimethylformamide (100 c.c.), and the mixture heated under reflux for 4 hr. Isolation by means of ether, filtration of a solution of the crude product in 2 : 1 light petroleum–benzene through alumina, and removal of solvents at 20 mm. gave a solid (552 mg.) which on crystallisation from methanol afforded the conjugated ketone (VI) as needles, m. p. 111°, $[\alpha]_D$ −50° (*c* 1·06), $\lambda_{max.}$ 2360 Å (ε 5800).

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754. *The Preparation of Pure Solid Diazonium Sulphates.*

By M. R. Piercey and E. R. Ward.

An excellent general method of preparing solid diazonium hydrogen sulphates was described by Hodgson and Mahadevan,[1] the amines being diazotised in sulphuric–acetic acid by nitrosylsulphuric acid (generated by reaction of sodium nitrite with sulphuric acid), and the diazonium salts being subsequently precipitated by ether. The method was applicable to a wide variety of substituted anilines and naphthylamines, including the phenylenediamines, but failed with compounds containing several nitro-groups (*e.g.*, 2,4-dinitroaniline, 2,4-dinitro-1-naphthylamine, 1,6-dinitro-2-naphthylamine) where ether did not

[1] Hodgson and Mahadevan, *J.*, 1947, 325.

precipitate the diazonium salt. This method gave salts admixed with sodium hydrogen sulphate, but for preparative purposes this was of no consequence. However, for the detailed investigation of diazo-reactions it is often required to have available *pure* solid diazonium salts and modification of the Hodgson–Mahadevan technique provides a very convenient general method for obtaining pure solid diazonium hydrogen sulphates. The original method can be applied to this purpose by using solid nitrosylsulphuric acid as the diazotising agent,[2] but we have now found that a better general procedure is to diazotise the amines by adding a solution or suspension of the amine in acetic acid to a solution of *solid* nitrosylsulphuric acid in acetic acid, then to precipitate the diazonium salt with ether. The salt is purified by reprecipitation from acetic acid by ether. Although no solid diazonium salt could be subsequently precipitated, it was surprising to find that polynitroanilines, including 2,4,6-trinitroaniline could be diazotised in this way; indeed for some purposes this diazotisation technique provides an attractive method, especially where it is desired to avoid the presence of excessive amounts of strong mineral acid. Moreover, with the polynitroanilines diazotisation can be completed at 50—60° without apparent decomposition. The yields of pure solid diazonium hydrogen sulphates ($Ar{\cdot}N_2^+HSO_4^-$) were: aniline 94, *o*- 80, *m*- 80, and *p*-toluidine 87, *p*-chloroaniline 95, *p*-aminophenol 69, *o*- 78, *m*- 85, and *p*-nitroaniline 88, 2-naphthylamine 60%.

Although solid diazonium borofluorides have been used for a variety of preparative diazo-decompositions and in mechanistic investigations, it might be more convenient to use diazonium hydrogen sulphates prepared as above; further, their preparation and subsequent decomposition involve no toxic materials.

Experimental.—Solid nitrosylsulphuric acid. Nitric acid (*d* 1·5) was placed in a tall lipless beaker (400 ml.), fitted with a Polythene cap (1 cm. thick) through which passed two glass tubes (15 mm. in diameter), one of which passed below the surface of the acid and the other just touching it, the cap and tubes being sealed with paraffin wax. Sulphur dioxide (dried over H_2SO_4) was passed into the tube dipping below the acid and this was continued until the whole appeared to be completely solid (external cooling being applied by tap water). The solids were collected at the pump on a sintered-glass funnel and quickly washed free from nitric acid by acetic acid (minimum amount) and then by carbon tetrachloride (Na-dried). The acid was stored in a Polythene-capped bottle in a desiccator; if required it can again be washed by acetic acid and carbon tetrachloride before use. The yield was 70% calculated on nitric acid.

Diazotisation. The amine (2 g.) was dissolved or suspended in acetic acid (10 ml.) and added slowly, with stirring, to a solution of solid nitrosylsulphuric acid (10% excess) in acetic acid (10 ml.). Halogeno- and nitro-anilines were added rapidly (cooling in ice); aniline, unsubstituted naphthylamines, toluidines, and aminophenols required dropwise addition, with time for reaction to be completed between each addition of 0·5 ml. The mixture was then kept for 30 min., and pure sodium-dried ether (100 ml.) was added slowly with stirring and cooling in ice. Some diazonium salts were precipitated immediately in crystalline form (*e.g.*, *p*-hydroxy- and *p*-chloro-benzene- and toluene-*m*- and -*p*-diazonium hydrogen sulphate), but nitrobenzenediazonium salts first formed emulsions which crystallised on stirring at 0°. The solids were collected as soon as possible, redissolved in acetic acid (10 ml.), and reprecipitated by ether (100 ml.) at 0°, then collected and washed with ether (5 × 20 ml.). Quantities up to 30 g. were prepared by this technique.

Polynitroanilines, *e.g.*, 2,4-di- and 2,4,6-tri-nitroaniline, were diazotised by rapid addition to the nitrosylsulphuric acid, without cooling, and the mixture subsequently heated to 50—60° to complete the diazotisation, which even then was slow. 2,4,6-Trinitroaniline required 48 hr. for diazotisation at room temperature. Subsequent addition of ether gave oils which did not solidify on treatment with alcohol (cf. Hodgson and Mahadevan [1]). Similar oils were obtained from 1-naphthylamine and *m*-phenylenediamine.

Apart from those from aniline and *m*-toluidine, which decomposed within a few days to give coloured liquids, the diazonium salts were stable for several months in the absence of light.

p-Nitrobenzenediazonium hydrogen sulphate was analysed for sulphate ion (gravimetrically) and by coupling to an excess of 3-nitro-1-naphthylamine (the resulting azo-compound being weighed in each case 98·5% purity was indicated [as $Ar{\cdot}N_2^+HSO_4^-$]. The coupling was carried

out in 1 : 1 v/v acetic acid–water at room temperature, the dye was collected, and then the filtrate; heated to 50°, whereupon a further small amount of dye was precipitated. The combined solids were washed by hot dilute hydrochloric acid (to remove the excess of amine), then water, and dried to constant weight. Coupling to 1-naphthylamine was unsatisfactory since part of the dye was precipitated as sulphate, as confirmed by sulphate determinations on the filtrate from the coupling reaction, which then appeared to account for all the sulphate ion in the system.

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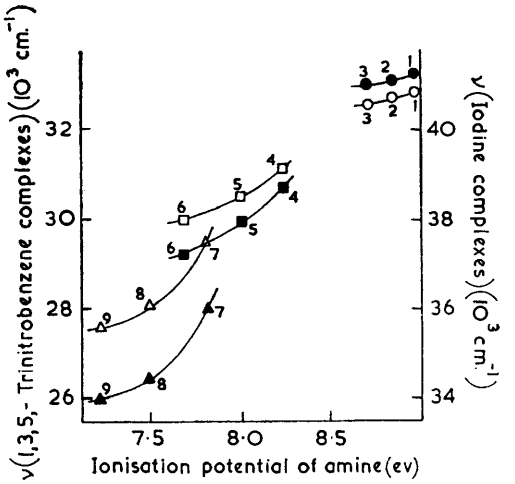
755. *Intermolecular Charge-transfer Complexes of* 1,3,5-*Trinitrobenzene with Aliphatic Amines.*

By R. FOSTER and R. K. MACKIE.

WHEREAS the interaction of 1,3,5-trinitrobenzene with aromatic amines yields normally only π–π intermolecular charge-transfer complexes,[1] with aliphatic amines a series of products is formed.[2,3] Various workers [3,4] have suggested that in the latter case, a n–π intermolecular charge-transfer complex may be formed initially. In most solvents subsequent reaction makes the direct verification of such a species difficult.



Plots of frequencies (ν) of absorption bands of 1,3,5-trinitrobenzene complexes of primary amines ●, secondary amines ■, and tertiary amines ▲ and of frequences (ν) of iodine complexes of primary amines ○, secondary amines □, and tertiary amines △, against ionisation potentials of the amines: 1 = methylamine, 2 = ethylamine, 3 = isopropylamine, 4 = dimethylamine, 5 = diethylamine, 6 = di-n-butylamine, 7 = trimethylamine, 8 = triethylamine, 9 = tri-n-propylamine.

Charge-transfer complex formation is most favoured in solvents of low ionising power.[5] The optical absorption spectra of 1,3,5-trinitrobenzene in cyclohexane in the presence of a series of aliphatic amines show greater absorption in the region ~280—420 mμ than do solutions of trinitrobenzene alone in cyclohexane. The difference in absorption corresponds to a new absorption band, not present in the spectrum of either component alone, and the position of the maximum depends on the particular amine. The frequencies of the maxima of these bands vary with ionisation potential of the respective amines in a way very similar to the variation in frequency of the absorption bands of the corresponding iodine–aliphatic amine complexes. Yada, Tanaka, and Nagakura [6] have adduced evidence that the latter are charge-transfer complexes. The close correlation of the frequencies of the bands with those for the complexes studied by us leads

[1] Bier, *Rec. Trav. chim.*, 1956, **75**, 866; Foster and Hammick, *J.*, 1954, 2685.
[2] Miller and Wynne-Jones, *J.*, 1959, 2375.
[3] Briegleb, Liptay, and Canter, *Z. phys. Chem.* (*Frankfurt*), 1960, **26**, 55; Foster and Mackie, *Tetrahedron*, 1961, **16**, 119.
[4] Allen, Brook, and Caldin, *J.*, 1961, 2171.
[5] Foster and Thomson, *Trans. Faraday Soc.*, 1962, **58**, 860.
[6] Yada, Tanaka, and Nagakura, *Bull. Chem. Soc. Japan*, 1960, **33**, 1660.

us to suggest that the bands observed for 1,3,5-trinitrobenzene–aliphatic amine systems are the result of intermolecular charge-transfer complexes.

Experimental.—Materials. 1,3,5-Trinitrobenzene, recrystallised four times from ethanol, then twice from carbon tetrachloride, had m. p. 123°. Solutions of the gaseous amines were prepared by dropping aqueous solutions of the corresponding recrystallised hydrochlorides on to solid sodium hydroxide; the resulting gases were dried through columns of sodium hydroxide pellets, and concentrated solutions obtained by direct absorption in cyclohexane. Other amines were fractionated after refluxing over sodium hydroxide. The tertiary amines were first treated with toluene-*p*-sulphonyl chloride to remove any primary or secondary amine. Cyclohexane was B.D.H. " Special for Spectroscopy " grade.

Method. Spectra were measured on an Optica CF4R grating spectrophotometer with, generally, 10-cm. cuvettes. For each determination the absorption of cyclohexane containing 1,3,5-trinitrobenzene (2×10^{-4}M) and amine (2×10^{-3} to 8×10^{-2}M) was measured against cyclohexane containing 1,3,5-trinitrobenzene alone at a concentration equal to that in the first solution. Some measurements were repeated with 1-cm. cuvettes. For each amine, spectra were measured for a series of solutions in which the concentration of amine was varied by a factor of 5—10. The bands are broad, having a band width at half-height of ~6000 cm.$^{-1}$. The observed constancy of the maximum of the absorption band (± 2 mμ) suggests that the maxima are real and are not the result of light scattering.[7] This constancy is also the justification for the assumption implicit in the technique described, namely, that the charge-transfer absorption band appears in the complex in addition to the absorptions characteristic of the components.[8]

The absorption maxima for the iodine complexes are those given by Yada, Tanaka, and Nagakura,[6] with the exception of that for the di-n-butylamine complex which has been measured in the present work. Ionisation potentials of the amines are photoionisation values determined by Watanabe and Mottl.[9]

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[7] Evans, *Chem. and Ind.*, 1953, 1061.
[8] Foster, *Tetrahedron*, 1960, **10**, 96.
[9] Watanabe and Mottl, *J. Chem. Phys.*, 1957, **26**, 1773.