645. *Nucleotides. Part XLII.* The Preparation of the 2′ : 5′- and 3′ : 5′-Diphosphates of Adenosine.*

By F. Cramer, G. W. Kenner, N. A. Hughes, and Sir Alexander Todd.

Adenosine-2′ : 5′ diphosphate has been obtained by treating triphosphopyridine nucleotide with a pyrophosphatase,[1] and similar enzymic degradation of coenzyme A [2] has yielded adenosine-3′ : 5′ diphosphate which is also a constituent part of "active sulphate." [3] The preparation of these two diphosphates was therefore of importance to us as part of our researches on nucleotide coenzyme synthesis. Unambiguous synthesis of each by using suitably protected intermediates, although doubtless capable of realisation, would be laborious and the known ease of phosphoryl migration in ribonucleotides would be a complicating factor. We therefore decided to phosphorylate adenosine directly, using an excess of phosphorylating agent; attack on the primary 5′-hydroxyl group was likely to occur first, followed by reaction at position 2′ and/or 3′. Phosphorylation at all three positions seemed unlikely to occur to any large extent and in the event no trisubstituted material was formed.

Adenosine was treated with excess of dibenzyl phosphorochloridate in cold pyridine, and the product washed with water and then heated with lithium chloride in 2-ethoxyethanol [4] to remove one benzyl group from each phosphate residue. This partial debenzylation was considered a desirable preliminary to complete debenzylation by hydrogenolysis, since we have observed that fully benzylated nucleotides are often more resistant to hydrogenolysis than the monobenzyl esters. In our first experiments further hydrogenolysis proceeded satisfactorily although less than the expected amount of hydrogen was absorbed, and a product with the expected properties was obtained in modest and rather variable yield. It seemed likely that this might be due to loss of nucleotidic material during the initial aqueous washing of the phosphorylation product, and this step was therefore omitted in the preparation described in detail in the Experimental portion. A much better yield (33%) was then obtained but it was necessary to add a final alkaline treatment, since the product obtained even after prolonged hydrogenolysis still contained some ester groups. This whole series of unexpected difficulties can, however, be satisfactorily explained. In the first experiments the exceptional reactivity of triesters of phosphoric acid containing a vicinal hydroxyl group [5] doubtless resulted in substantial hydrolysis during the washing with water so that only a comparatively small amount of neutral material passed on to the later stages in the preparation. Loss of this nature was avoided by omitting the aqueous washing but good opportunity for alcoholysis was provided during the replacement of pyridine by ethoxyethanol prior to lithium chloride treatment. Any ethoxyethyl groups introduced in this way would survive both anionic debenzylation and hydrogenolysis, but would be removed by alkali. All the electrophoretic data on the intermediate products accord with these explanations.

The mixture of adenosine diphosphates was separated from adenosine-5′ phosphate and other impurities by ion-exchange chromatography, but the diphosphate mixture could not be resolved into its components by this means. Experiments by Drs. R. F. Webb and R. J. W. Cremlyn have suggested that counter-current distribution might provide a feasible if laborious separation, but we have not proceeded further on these lines. For such purposes as the synthesis of triphosphopyridine nucleotide by the carbodi-imide method [6] separation is in any case hardly worthwhile, since migration of the phosphoryl

* Part XLI, preceding paper.

[1] Kornberg and Pricer, *J. Biol. Chem.*, 1950, **186**, 557.
[2] Wang, Shuster, and Kaplan, *ibid.*, 1954, **206**, 299.
[3] Robbins and Lipmann, *J. Amer. Chem. Soc.*, 1956, **78**, 2652.
[4] Clark and Todd, *J.*, 1950, 2031.
[5] Brown, Magrath, and Todd, *J.*, 1955, 4396.
[6] Hughes, Kenner, and Todd, *J.*, 1957, in the press.

group between $C_{2'}$ and $C_{3'}$ would almost certainly occur during the synthesis. For this reason we feel it desirable to publish at this stage our method for preparing a mixture of adenosine-2′ : 5′ and -3′ : 5′ diphosphate. The mixture has been used successfully in this laboratory to prepare both triphosphopyridine nucleotide [6] and " active sulphate." [7]

Experimental.—Adenosine (5·0 g.; dried at 110°/1 mm.) was dissolved in boiling anhydrous pyridine (330 c.c.). The solution was cooled quickly to −50°, solidifying without crystallisation of the adenosine. Dibenzyl phosphorochloridate (from 26 g. of dibenzyl phosphite) was added and the mixture was allowed to warm slowly until a clear solution was obtained; this was kept at −30° for 5 hr. and at 0° for a further 18 hr. before addition of 2-ethoxyethanol (13 c.c.). The pyridine hydrochloride which separated within 30 min. was collected and the filtrate was evaporated. After addition of 2-ethoxyethanol (50 c.c.) and re-evaporation, the syrup was taken up in ethoxyethanol (100 c.c.) containing anhydrous lithium chloride (12 g.) and kept at 100° for 3 hr. with exclusion of moisture. Addition of ether (500 c.c.) to the cooled solution precipitated a gum, which was converted into a solid by shaking it with acetone (300 c.c.) and ethanol (100 c.c.). The product was centrifuged off and washed twice more with ethanolic acetone, a cream-coloured powder (11·0 g.) being obtained. This was hydrogenated in 50% aqueous ethanol (250 c.c.) containing acetic acid (2 c.c.) during 4 days at atmospheric pressure and temperature with 10% palladised charcoal (1 g.) and palladium oxide (0·2 g.); most of the hydrogen was absorbed during the first 24 hr. Catalyst was filtered off and 3N-sodium hydroxide (80 c.c.) was added to the filtrate. After 40 hr. the solution was neutralised with dilute hydrochloric acid, extracted with ether (2 × 50 c.c.), and concentrated to 150 c.c. The changes brought about by these treatments are indicated by the following distances of migration of the major component in paper electrophoresis; after treatment with lithium chloride, 5·3 cm.; after hydrogenation, 7·9 cm.; after treatment with alkali, 10·5 cm. (during 6 hr. on Whatman no. 54 paper in 0·05M-disodium hydrogen phosphate at 5 v/cm.; migration of adenosine-5′ phosphate, 6·2 cm.; P^1P^2-diadenosine-5′ pyrophosphate, 4·6 cm.). The solution was passed through a column (20 × 20 cm.²) of Dowex-50 cation-exchange resin (lithium form), which was washed with water. When no more light-absorbing (260 mμ) material was eluted, the solution was evaporated. A mixture of acetone (400 c.c.) and ethanol (100 c.c.) was added gradually with shaking to the residual syrup, and the solid was centrifuged down. It was washed with a second portion of ethanolic acetone before being dried. This solid (8·0 g.) was dissolved in water (500 c.c.) and neutralised (pH 7) with sodium hydroxide before being adsorbed on a column (10 × 12 cm.²) of Dowex-2 anion-exchange resin (chloride form). The column was washed with water (500 c.c.), which was transparent at 260 mμ, and then with 0·003N-hydrochloric acid (2 l.), which removed adenosine-5′ phosphate (0·06 g.). The product was subsequently eluted with 0·03N-hydrochloric acid (3 l.), and the eluate was concentrated to 200 c.c. and neutralised (pH 8) with 2N-lithium hydroxide. The syrup obtained by evaporating the neutralised solution was treated with acetone (400 c.c.) and ethanol (100 c.c.), and the solid product was washed with ethanolic acetone until the washings were free from chloride ions. The solid was taken up in water (300 c.c.), and the filtered solution concentrated to 200 c.c. before being passed through a column (7 × 20 cm.²) of Dowex-50 cation-exchange resin (hydrogen form). The column was washed with water (800 c.c.) until no more light-absorbing (260 mμ) material was eluted. The eluate was concentrated to 20 c.c. and diluted with acetone (250 c.c.). The flocculent colourless precipitate was allowed to stand for several hours before being centrifuged down and dried (2·75 g.) (Found, in material dried at 60°/1 mm.: C, 30·3; H, 4·0; N, 15·7; P, 14·2. $C_{10}H_{15}O_{10}N_5P_2,\frac{1}{2}C_3H_6O$ requires C, 30·3; H, 4·0; N, 15·4; P, 13·6%). On Whatman no. 1 paper in 5% disodium hydrogen phosphate it had R_F 0·85 (cf. ref. 2), in propan-2-ol–1% ammonium sulphate (3 : 2) R_F 0·48, in butan-1-ol–acetic acid–water (5 : 2 : 3) R_F 0·10. On careful elution with 0·008N-hydrochloric acid from Dowex-2 resin, it showed no sign of resolution into two components.

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[7] Pennington, Todd, and Webb, unpublished work.

646. cyclo*Hexane Derivatives. Part III.* The Mechanism of Catalytic Hydrogenation of Cyclic Compounds and the Skita Rule.*

By R. J. Wicker.

The work described in Part II * has been extended to include the reduction of phenols with Adams platinum catalyst at 20° in acetic acid. Examination of the results (Table 1) with regard to their conformity with the Skita rule leads to the following observations.

Table 1. *Proportions of isomers produced by catalytic hydrogenation of substituted phenols.*

	Stable isomer produced (%)						
	Pt in AcOH			Ni			
Phenol reduced	%	Temp.	Ref.	%	Temp.	Time	Ref
o-Cresol	75	20°	†	73	160°	—	*
	all unstable *cis*	25	†	68	180	—	*a*
m-Cresol	51	20	†	55	160	9 hr.	*
				83	160	14 hr.	*
				85	200	—	*b*
p-Cresol	61	20	†	63	160	—	*
				82	180	—	*a*
*p-cyclo*Hexylphenol	—	—	—	54	160	—	*

* Details of these reductions with nickel catalyst are given in Part II. † Present work.
[a] Jackman, Macbeth, and Mills, *J.*, 1949, 1717. [b] Macbeth and Mills, *J.*, 1945, 709.

o-Cresol, contrary to the rule, gives substantially more of the stable *trans*-isomer under acid or alkaline conditions, with the exception of the result reported by Baker and Schuetz [1] whose analysis by fractional distillation is probably unreliable.

With *m*-cresol the product obtained at 160° in 9 hr. with nickel does not differ significantly from that obtained with platinum and acetic acid, which is not in agreement with the rule. The higher percentages of stable isomer obtained at 160° in 14 hr. and at 200° are due to isomerisation, which is favoured by the increased contact time with the catalyst in one case, and the higher temperature in the other. Similarly *p*-cresol gives almost identical products with platinum and acetic acid and with nickel at 160°, which does not conform with the rule. A higher proportion of the stable *trans*-isomer is formed at 180°, owing to isomerisation.

Many years ago Vavon and Bertin [2] showed that the cresols hydrogenate *via* the corresponding *cyclo*hexanones. They considered that each molecule is hydrogenated to the ketone, which is then desorbed back into the solution where it competes with the remaining phenol for hydrogen. In this event it would be expected that identical products would be obtained from reduction of cresols and the corresponding methyl*cyclo*hexanones. The results shown in Table 2 are not in accordance with this prediction. If one assumes,

Table 2. *Proportions of isomers produced by catalytic hydrogenation of substituted* cyclo*hexanones * and phenols with platinum in acetic acid at* 20°.

Compound reduced	Stable isomer (%)	Compound reduced	Stable isomer (%)
2-Methyl*cyclo*hexanone	30	*o*-Cresol	75
3-Methyl*cyclo*hexanone	75	*m*-Cresol	51
4-Methyl*cyclo*hexanone	53	*p*-Cresol	61

* Details of the ketone reductions are given in Part II.

however, that the transition occurs, not only as Vavon and Bertin suggest, but also *via* the enolic form of the ketone, the reduction of the enol may occur whilst the compound is still

* Part II, *J.*, 1956, 2165.

[1] Baker and Schuetz, *J. Amer. Chem. Soc.*, 1947, **69**, 1250.
[2] Vavon and Bertin, *Bull. Soc. chim. France*, 1925, (4), **37**, 296.

absorbed on the active centres of the catalyst. If it is assumed that this reaction occurs to some extent, it will be seen from Table 4 in Part II (in which the expected preponderance of isomer from the reductions of enolic and ketonic forms of ketones is shown) that the proportions of stereoisomers produced will differ from those obtained when the corresponding methyl*cyclo*hexanones are reduced, since these exist essentially in the ketonic form.

The results obtained in this and the earlier papers of this series have been more fully discussed, and possible mechanisms for hydrogenations of simple carbocyclic compounds outlined elsewhere.[3]

From a practical point of view the major factor controlling the proportion of isomers from hydrogenation of a phenol or *cyclo*hexanone appears to be the encouragement or otherwise of isomerisation, and the following practical rules are suggested: (*a*) To obtain a preponderance of the more stable isomer, hydrogenation should be with an alkaline catalyst (preferably nickel) or with Adams platinum catalyst which has not been acid-treated, and acid solvents must not be used. The temperature should be as high as is permissible without causing undesirable side reactions. The experiment should be prolonged beyond the point at which hydrogen absorption is complete in order to permit isomerisation to take place. (*b*) To obtain a preponderance of the less stable isomer the reaction should be at room temperature, and should be stopped as soon as hydrogen absorption ceases. Prolongation of the experiment in order to reduce the last traces of unsaturated compound is undesirable since isomerisation may then occur. Reduction of the ketone with nickel is preferable to reduction of either the ketone or the corresponding phenol with Adams catalyst in acetic acid.

Experimental.—Diazo-coupling was used for detecting phenols in reduction products.

Platinum catalyst was removed by decantation, nickel by filtration through a bed of kiesulguhr supported on asbestos wool.

Commercial cresols (from Monsanto Chemical Co.) were distilled and an 80% middle fraction was collected. This gave *o*-cresol, f. p. 30·5°, *m*-cresol, f. p. 11·0°, *p*-cresol, f. p. 34·0°. The authentic f. p.s are 30·60°, 11·10°, and 34·55° respectively.[4]

Hydrogenations with Adams platinum catalyst. These were carried out as described in Part II, but whereas in the case of ketones conversions were almost quantitative, the cresols yielded simultaneously methyl*cyclo*hexane (20—25%), as has been found by previous workers.[2]

(1) *o*-Cresol (25 g.) in glacial acetic acid (20 ml.) and Adams catalyst (2·5 g.) was hydrogenated at 20°/1 atm. The 2-methyl*cyclo*hexanol produced had d_4^{20} 0·9199 and therefore contained 75% of *trans*-2-methyl*cyclo*hexanol (ketone and phenol absent).

(2) *m*-Cresol treated similarly gave 3-methyl*cyclo*hexanol, d_4^{20} 0·9104, containing 51% of *cis*-isomer (ketone and phenol absent).

(3) *p*-Cresol gave 4-methyl*cyclo*hexanol, d_4^{20} 0·9092, containing 61% of *trans*-isomer (ketone and phenol absent).

(4) 4-*cyclo*Hexylphenol. Three attempts to hydrogenate this compound in glacial acetic acid gave incompletely reduced products.

I thank the Directors of Messrs. Howards of Ilford for permission to publish this paper.

RESEARCH DEPARTMENT, HOWARDS OF ILFORD LTD.,
ILFORD, ESSEX. [*Received, October 8th,* 1956.]

[3] R. J. Wicker, Ph.D. Thesis, London University, 1956.
[4] " Physical Properties of Organic Compounds," Amer. Chem. Soc., New York, 1955.

647. *Kinetics of the Bromination of Iodo-ethers by Hypobromous Acid.*

By S. J. Branch and Brynmor Jones.

In a recent extensive study [1] of the kinetics of the bromination of aromatic ethers by hypobromous acid in 75% acetic acid it was hoped to include data for a number of iodo-ethers. It was found however that a deep colour appeared when solutions of 4-bromo-2-iodoanisole (0·00250 mole l.$^{-1}$) and hypobromous acid (0·00746 mole l.$^{-1}$) in 75% acetic acid were mixed at 20°, and that this almost instantaneous reaction was accompanied by no immediate fall in titre when portions of the solution were added to aqueous potassium iodide and titrated against thiosulphate. Instead, a slow fall with time was observed. Results typical of many obtained are given below.

Bromination of 4-bromo-2-iodoanisole by HOBr *at* 19·8°.

[Ether] = a; [HOBr] = b.

Estimated titre for HOBr before mixing = 14·90 ml. of thiosulphate.

Time (sec.)	Titre (ml.) of 0·00505N-thiosulphate	$(a - x)$	$(b - 2a - x)$	k_{bi}
0	14·88	0·00250	0·00246	—
1760	14·36	0·00223	0·00219	0·0294
4800	13·65	0·00188	0·00184	0·0288
8200	12·98	0·00155	0·00151	0·0296

The values of k_{bi} in the last column were derived by assuming that the initial rapid reaction led to the formation of an iodoso-compound,

$$MeO{\cdot}C_6H_3BrI + 2HOBr \xrightarrow{Rapid} MeO{\cdot}C_6H_3Br{\cdot}IO + Br_2 + H_2O \quad . \quad . \quad . \quad . \quad . \quad (1)$$

and that this reaction was followed by a slow nuclear bromination of the iodoso-ether:

$$MeO{\cdot}C_6H_3Br{\cdot}IO + HOBr \xrightarrow{slow} MeO{\cdot}C_6H_2Br_2{\cdot}IO + H_2O \quad . \quad . \quad . \quad . \quad . \quad (2)$$

Such behaviour would account for the red coloration, and also for the initial absence of fall in the titre. Both products of reaction (1) can be titrated against thiosulphate after the addition of potassium iodide since

$$Br_2 + 2HI \longrightarrow 2HBr + I_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

$$R{\cdot}IO + 2HI \longrightarrow RI + H_2O + I_2 \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (4)$$

Reaction (4) is practically irreversible, and has been used for the quantitative estimation of iodoso-compounds.[2] If equations (1) and (3) are combined with (4), then:

$$2HOBr + 4HI = 2I_2 + 2H_2O + 2HBr$$

and, since $2HOBr \equiv 2I_2$, no fall in titre would be expected unless hypobromous acid is also removed slowly in accord with reaction (2). It therefore seems probable that the bimolecular constant refers to the rate of bromination of 4-bromo-2-iodosoanisole. Recent studies [3] have shown that the iodoxy-group is strongly electron-attracting, and if the iodoso-group is similarly electron-attracting, a value of 0·029 seems reasonable for the bromination of a compound such as the bromoiodoanisole. Some support for the view

[1] Branch and Brynmor Jones, *J.*, 1954, 2317; 1955, 2921.
[2] Sandin, *Chem. Rev.*, 1943, **32**, 249.
[3] Masson, Race, and Pounder, *J.*, 1935, 1669; Bothner-By and Medalia, *J. Amer. Chem. Soc.*, 1952, **74**, 4402.

that the red colour does not arise from the displacement of iodine is provided by the fact that the observed coefficient does not correspond with the rate for the bromination of either 2 : 4-dibromoanisole (0·373 l. mole^{-1} sec.$^{-1}$) or *p*-bromoanisole (approx. 68·0 l. mole^{-1} sec.$^{-1}$).

Experimental.—4-Bromo-2-iodoanisole was prepared by direct iodination. A solution of *p*-bromoanisole (10 g.) in chloroform (25 c.c.) containing iodine (13·6 g.) was stirred at room temperature with mercuric oxide (13 g.) and sulphuric acid (5 c.c.) for 12 hr. After the sediment had been filtered and washed with ether, the filtrate was shaken with thiosulphate, and the ether layer was dried (Na_2SO_4). Evaporation of the solvent yielded a solid which, after several crystallisations from ligroin, separated in almost colourless plates, m. p. 64°.

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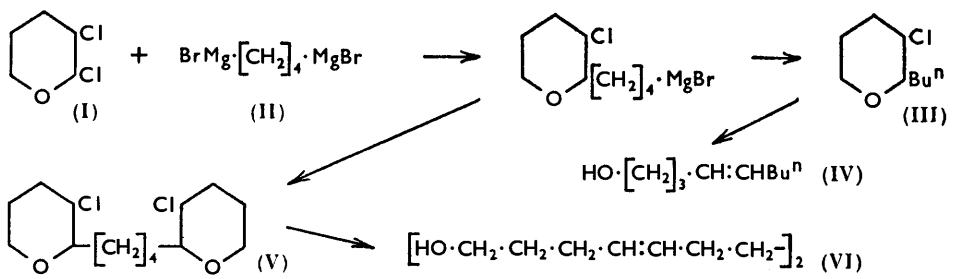
648. *The Reaction of the Double Grignard Reagent of 1 : 4-Dibromobutane with 2 : 3-Dichlorotetrahydropyran.*

By M. F. ANSELL and D. A. THOMAS.

THE method of chain extension by four or five carbon atoms by treatment of an alkyl- or aralkyl-magnesium halide with 2 : 3-dichlorotetrahydro-furan or -pyran and ring scission of the 2-alkyl- or aralkyl-3-chloro-intermediate is well established,[1] and has been applied to two successive extensions by four [2] or five [3] carbon atoms. The availability of double Grignard reagents [4] suggested the simultaneous extension of a carbon chain by ten carbon atoms. We therefore treated 2 : 3-dichlorotetrahydropyran (I) with an excess of the double reagent from 1 : 4-dibromobutane (II), obtaining 2-butyl-3-chlorotetrahydropyran



(III), identified by conversion into *trans*-non-4-en-1-ol (IV) together with a mixture of stereoisomeric 1 : 4-di-(3-chlorotetrahydropyran-2-yl)butanes (V). The latter gave, on ring scission with sodium, tetradeca-4 : 10-diene-1 : 14-diol (VI) which is probably *trans-trans* as both double bonds arise by the fission of pyran rings.[1b] Its structure was confirmed by hydrogenation to the known tetradecane-1 : 14-diol.

Similar chain extension by ten carbon atoms has been effected by Riobé and Gouin [5]

[1] Crombie and Harper, (*a*) *J.*, 1950, 1707, (*b*) *J.*, 1950, 1714.
[2] Ansell and Selleck, *J.*, 1956, 1238.
[3] Crombie, Harper, Gold, and Stokes, *J.*, 1956, 136.
[4] Nenitzescu and Necsoiu, *J. Amer. Chem. Soc.*, 1950, **72**, 3483.
[5] Riobé and Gouin, *Compt. rend.*, 1956, **243**, 1424.

using dimagnesioacetylene dibromide and 2 : 3-dichlorotetrahydropyran, and analogously by eight carbon atoms from 2 : 3-dichlorotetrahydrofuran.

Experimental.—1 : 4-*Di*-(3-*chlorotetrahydropyran*-2-*yl*)*butane*. The double Grignard reagent [4] (0·51 mole by estimation [6]) from 1 : 4-dibromobutane [7] (130 g., 0·6 mole) and magnesium (44 g., 1·8 g.-atoms) in ether (600 ml.) was left overnight and the organic material (two layers) then decanted from the residual magnesium and treated (Hershberg stirrer) with 2 : 3-dichloropyran [1a] [from 2 : 3-dihydropyran (67·2 g., 0·8 mole)] in ether (160 ml.) at such a rate that steady refluxing was maintained. After being boiled and stirred for a further 3 hr. the mixture was cooled and decomposed by pouring it on ice–ammonium chloride. The ether layer was separated and the aqueous layer extracted with ether. Distillation of the dried ($MgSO_4$), combined, concentrated extracts gave a fraction (26 g.), b. p. 40—80°/1 × 10^{-2} mm., followed, after an intermediate fraction (6 g.), by a mixture of the stereoisomeric 1 : 4-di-(3-chlorotetrahydropyran-2-yl)butanes (64 g., 59%), b. p. 110—170°/1 × 10^{-2} mm., n_D^{20} 1·4910 (Found : C, 57·4; H, 8·35; Cl, 23·65. Calc. for $C_{14}H_{24}O_2Cl_2$: C, 57·15; H, 8·15; Cl, 24·15%).

Redistillation of the first fraction gave a mixture of *cis*- and *trans*-2-butyl-3-chlorotetrahydropyran (19·5 g., 15%), b. p. 80—102°/11 mm., n_D^{20} 1·4592—1·4664. Crombie and Harper [1a] record b. p. 83—108°/11 mm., n_D^{20} 1·4532—1·4670. With sodium [1a] this gave *trans*-non-4-en-1-ol (11 g.), b. p. 103—104°/14 mm., n_D^{20} 1·4494—1·4496; 3 : 5-dinitrobenzoate [from ice-cold light petroleum (b. p. 40—60°)], m. p. and mixed m. p. 32° (authentic specimen, prepared from a sample of alcohol having n_D^{20} 1·4482, had m. p. 31·5—32°). Crombie and Harper [1a] record b. p. 101—105°/13 mm., n_D^{20} 1·4476; Paul and Riobé [8] record b. p. 108·5°/17 mm., n_D^{18} 1·4494; 3 : 5-dinitrobenzoate, m. p. 33°.

Tetradeca-4 : 10-*diene*-1 : 14-*diol*. Sodium (20·5 g., 0·9 g.-atom) was powdered under xylene, then thoroughly rinsed with ether and covered with the same solvent (50 ml.). A little 1 : 4-di-(3-chlorotetrahydropyran-2-yl)butane was added and the suspension stirred until reaction commenced. The remaining 1 : 4-di-(3-chlorotetrahydropyran-2-yl)butane (60 g. in all, 0·2 mole) in ether (200 ml.) was then added at such a rate that steady refluxing was maintained. The thick blue suspension was stirred and heated under reflux for a further 5 hr., then cooled, and ice and water were cautiously added. The ether layer was separated and the aqueous layer extracted with ether. After being washed, dried ($MgSO_4$), and concentrated the product was distilled to give *tetradeca*-4 : 10-*diene*-1 : 14-*diol* (38 g., 82%), b. p. 155—165°/0·1—0·15 mm., which solidified. The analytical sample had b.p. 158—164°/0·1—0·15 mm., m. p. 40° [from ice-cold ether–light petroleum (b. p. 40—60°)] (Found : C, 74·55; H, 11·7. $C_{14}H_{26}O_2$ requires C, 74·3; H, 11·6%). Hydrogenation at atmospheric pressure in the presence of Adams catalyst gave tetradecane-1 : 14-diol, m. p. 84—85° (from ethanol) (Found : C, 72·8; H, 12·9. Calc. for $C_{14}H_{30}O_2$: C, 73·0; H, 13·1%). Wojcik and Adkins [9] record m. p. 85° and Carothers and McEwen,[10] m. p. 83—85°.

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MILE END ROAD, LONDON, E.1. [*Received, February 4th*, 1957.]

[6] Gilman, Wilkinson, Fishel, and Meyers, *J. Amer. Chem. Soc.*, 1923, **45**, 150.
[7] Wilson, *J.*, 1945, 48.
[8] Paul and Riobé, *Compt. rend.*, 1947, **224**, 474.
[9] Wojcik and Adkins, *J. Amer. Chem. Soc.*, 1933, **55**, 4939.
[10] Carothers and McEwen, *Org. Synth.*, Coll. Vol. II, 154.

649. *The Synthesis of a 1 : 5-Dienoic Acid and its Behaviour with Hot Alkali.*

By B. M. A. de Surville, D. E. A. Rivett, and D. A. Sutton.

In 1942, Farmer [1] stated that isoprenic hydrocarbons containing 1 : 5-diene groups, such as squalene, dihydromyrcene, and rubber failed to give conjugated isomers when treated with alkali under conditions which succeeded with linoleic and linolenic acids. This statement was based on unpublished experiments by Farmer and Sutton who used refractive-index and density measurements to show that the hydrocarbons were unchanged. Later, the observation that squalene does not give a conjugated isomer when treated with alkali at 180° in ethylene glycol was confirmed in this laboratory,[2] by ultraviolet spectroscopy. From the behaviour of squalene it has been assumed that acids containing the di-*cis*-system ·CH:CH·CH_2·CH_2·CH:CH· would not become conjugated when treated in the same way.

It was important to check this assumption, since the hexadecatetraenoic acid,[3] eicosapentaenoic acid,[4] and docosahexaenoic acid [5] of pilchard oil do not contain penta-1 : 5-dienyl groups, whereas other workers have reported their presence in similar natural acids.[6]

Squalene is a poor model substance in relation to natural fatty acids since it has a methyl branch attached to each diene system and no carboxyl group. For this reason, we have synthesised trideca-*cis*-5 : *cis*-9-dienoic acid, using Strong's unambiguous acetylenic route.[7] (Since the natural acids are usually all-*cis* and as the isomerisation of methylene-interrupted systems containing *trans* double bonds is slower,[8] we have confined ourselves to an all-*cis* model.) Its structure was confirmed by ozonolytic degradation to glutaric and succinic acids and by hydrogenation to *n*-tridecanoic acid. The acid was shown to be substantially pure by reverse-phase chromatography on non-wetting kieselguhr.[9] The predominantly *cis*-configuration of the double bond was demonstrated by the absence of any large infrared band near 10·3 μ.

After treatment with 21% potassium hydroxide in ethylene glycol at 180° for 30 min.[10] less than 2% of conjugated diene was formed. As the result of oxidative degradations Toyama and his co-workers proposed penta-1 : 5-dienyl structures for some of the highly unsaturated acids from fish oils and certain other natural materials.[11] They reported [12] that these acids undergo isomerisation with alkali. Our result makes these structures unlikely.

Experimental.—*1-Chlorododeca-4 : 8-diyne.* Nona-1 : 5-diyne [13] (25 g.) in dry ether (25 ml.) was slowly added to a stirred suspension of sodamide in liquid ammonia (650 ml.), prepared from sodium (4·7 g.) in the presence of ferric nitrate (0·06 g.), and insulated with cotton waste. After 2 hours' stirring 1-chloro-3-iodopropane (29 g.) in dry ether (25 ml.) was added dropwise and the solution then stirred for 44 hr., ammonia being added periodically to keep the volume constant. The mixture was set aside overnight without insulation, most of the ammonia

[1] Farmer, *Trans. Faraday Soc.*, 1942, **38**, 356.
[2] Silk, Hahn, and Whitcutt, unpublished work.
[3] Silk and Hahn, *Biochem. J.*, 1954, **57**, 582.
[4] Whitcutt and Sutton, *Biochem. J.*, 1956, **63**, 469.
[5] Whitcutt, unpublished work.
[6] Herb, *J. Amer. Oil Chemists' Soc.*, 1955, **32**, 153.
[7] Strong *et al.*, *J. Amer. Chem. Soc.*, 1950, **72**, 4263, and previous papers.
[8] Wheeler, *J. Amer. Oil Chemists' Soc.*, 1952, **29**, 229.
[9] Silk and Hahn, *Biochem. J.*, 1954, **56**, 406; Crombie, *J.*, 1955, 3510.
[10] "Official and Tentative Methods of the American Oil Chemists' Society," Chicago, 2nd edn., 1946, revised 1951, C—d, 7—48.
[11] Hilditch, "The Chemical Constitution of Natural Fats," Chapman and Hall, London, 1956, p. 539.
[12] Toyama and Shimo-Oka, *Mem. Fac. Eng., Nagoya Univ.*, 1954, **5**, 323.
[13] Raphael and Sondheimer, *J.*, 1950, 120.

evaporating. Pentane and water were added, the aqueous phase was extracted with pentane, and the combined organic extracts were washed with dilute sulphuric acid, sodium hydrogen carbonate solution, and water, and dried. Removal of the solvent and distillation of the residue gave unchanged nona-1 : 5-diyne, b. p. 67°/20 mm. (12·5 g.), and 1-chlorododeca-4 : 8-diyne, b. p. 107—108°/20 mm. (7·5 g.). The yield is poor because chloroiodopropane is the limiting case in this type of reaction.[7]

Trideca-5 : 9-*diynoic acid.* A solution of 1-chlorododeca-4 : 8-diyne (7·5 g.) in ethanol (100 ml.) containing sodium cyanide (4·8 g.) was refluxed for 98 hr. under nitrogen, sodium hydroxide (3 g.) in water (20 ml.) then added, and the mixture refluxed for a further 90 hr. The acid fraction (7 g.) was extracted with ether and crystallised from hexane, to give the *acid* (5·2 g.), m. p. 41·2—41·6° (Found : C, 75·9; H, 9·1%; equiv., 207. $C_{13}H_{18}O_2$ requires C, 75·7; H, 8·8%; equiv., 206).

Trideca-cis-5 : cis-9-*dienoic acid.* The diacetylenic acid on hydrogenation in ethyl acetate over Lindlar catalyst absorbed 2·08 mols. of hydrogen and was converted into the diethylenic *acid*, m. p. −46·5° to −45·5° (Found : C, 74·0; H, 10·7%; equiv., 210; I no., 241. $C_{13}H_{22}O_2$ requires C, 74·25; H, 10·5%; equiv., 210; I no., 243).

Hydrogenation of the diacetylenic acid in ethanol with Adams catalyst followed by crystallisation of the product from hexane afforded tridecanoic acid, m. p. 41·4—41·6° (Found : C, 73·0; H, 12·1%; equiv., 215. Calc. for $C_{13}H_{26}O_2$: C, 72·9; H, 12·2%; equiv., 215). The recorded m. p.[14] for tridecanoic acid is 41·76°.

Excess of bromine was added to a hexane solution of the diethylenic acid; the precipitated *tetrabromo-acid*, recrystallised twice from dichloroethane, had m. p. 119—120° (Found : C, 29·4; H, 4·4; Br, 60·4. $C_{13}H_{22}O_2Br_4$ requires C, 29·45; H, 4·2; Br, 60·3%).

We thank Miss P. M. Hughes for the microanalyses, Miss W. Albrecht for the infrared spectrum, Dr. S. C. Mossop for the m. p. of the diethylenic acid, and the South African Council for Scientific and Industrial Research for permission to publish the paper.

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PRETORIA, S. AFRICA. [*Received, February 4th,* 1957.]

[14] Ralston, " Fatty Acids and their Derivatives," John Wiley and Sons, New York, 1948, p. 323.

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650. *Some Derivatives of 2-2′-Aminoethylglyoxaline.*

By P. C. JOCELYN.

2-2′-AMINOETHYL-1-METHYLGLYOXALINE, required for a study of histamine-like compounds, was synthesised from 2-hydroxymethyl-1-methylglyoxaline [1] by conversion *via* the corresponding 2-chloromethyl- into the cyanomethyl-derivative, followed by hydrogenation with lithium aluminium hydride.

With the object of preparing related dihydroglyoxalines, the di-β-phthalimidopropionates of ethylenediamine, *N*-methylethylenediamine, and 1-amino-2-methylaminopropane (prepared from 1-amino-2-chloropropane hydrochloride [2] by treatment with methylamine) were heated with their corresponding dihydrochlorides at 200°. The reaction did not proceed as expected (see, *e.g.*, ref. 3), In the case of ethylenediamine, diphthalimidoethane resulted, but the other two diamines gave their *N*-phthaloyl derivative hydrochlorides.

Ethyl β-phthalimidopropionimidate hydrochloride (prepared from β-phthalimidopropionitrile [4]) also gave no dihydroglyoxaline on treatment at low temperatures with the

[1] Grindley and Pyman, *J.*, 1927, 3128.
[2] Jones, Langsjoen, Neumann, and Zomlefer, *J. Org. Chem.*, 1944, **9**, 125.
[3] Waldmann and Chwala, *Ber.*, 1941, **74**, 1763.
[4] Galat, *J. Amer. Chem. Soc.*, 1945, **67**, 1414.

free diamines although in other respects this substance behaved as a typical imidate hydrochloride, yielding ethyl β-phthalimidopropionate with water and the corresponding amide above its melting point.

Experimental.—1-*Methylglyoxaline.* Rung and Behrend's method [5] gives yields below 30%. Much improved yields were obtained as follows. Glyoxaline (10 g.) was dissolved in a solution from sodium (3·7 g.) in ethanol (70 ml.), and methyl iodide (23 g.) was added during 1 hr. with stirring at 0°. After 12 hr. at 15° the solvent was evaporated and the residue extracted with chloroform. Drying, evaporation, and distillation gave 1-methylglyoxaline (7·7 g., 75%), b. p. 93°/13 mm.

2-*Hydroxymethyl*-1-*methylglyoxaline.* Pyman's method [1] was modified as follows: Formaldehyde was bubbled through 1-methylglyoxaline (23·5 g.) at 160—170° until 8·5 g. had been absorbed (about 2 hr.). The liquid remaining was distilled; after a forerun, the product (10 g., 36%) was collected at 145°/1 mm. and slowly solidified (m. p. 114°; Pyman gives m. p. 116°).

2-*Chloromethyl*-1-*methylglyoxaline hydrochloride.* 2-Hydroxymethyl-1-methylglyoxaline (2·0 g.) was added during 15 min. to thionyl chloride (4·0 g.) with shaking and cooling. The solution was refluxed for 15 min., the excess of thionyl chloride evaporated, and the residue dissolved in hot ethanol (5 ml.). The *product* (2·5 g.) crystallised and had m. p. 168° (Found: Cl, 42·0. $C_5H_8N_2Cl_2$ requires Cl, 42·5%).

2-*Cyanomethyl*-1-*methylglyoxaline.* 2-Chloromethyl-1-methylglyoxaline (2·8 g.) in ethanol (12 ml.) was added in 30 min. to a solution of potassium cyanide (9·0 g.) in water (10 ml.) with stirring at −10°. After 15 hr. at 15°, anhydrous sodium carbonate (2 g.) in water (10 ml.) was added to the filtered solution. The water and ethanol were evaporated and the crude product was isolated from the residue as a dark oil by extraction with ethyl acetate and evaporation after drying. The precipitate obtained by adding picric acid solution to the oil was dissolved in hot water, treated with charcoal, and filtered.

2-*Cyanomethyl*-1-*methylglyoxaline picrate* (2·3 g.) crystallised and had m. p. 165—166° (Found: C, 41·6; H, 2·8; N, 23·4. $C_{12}H_{10}O_7N_6$ requires C, 41·2; H, 2·85; N, 24·0%).

2-2′-*Aminoethyl*-1-*methylglyoxaline.* The base (0·5 g.) prepared from 2-cyanomethyl-1-methyl glyoxaline picrate, in ether (70 ml.), was added in 15 min. to lithium aluminium hydride (0·5 g.) in ether (100 ml.), and the solution refluxed for 1 hr. Ethanol (40 ml.) was slowly added and the solvents were evaporated from the filtered solution. The residue was dissolved in water and neutralised with acetic acid, and the product isolated as the *dipicrate* (0·5 g., 20%), m. p. 196° (Found: N, 22·2. $C_{18}H_{17}O_{14}N_9$ requires N, 21·6%). This was converted into the *dihydrochloride*, m. p. 262—263° (Found: N, 20·9; Cl, 35·3. $C_6H_{13}N_3Cl_2$ requires N, 21·3; Cl, 35·8%).

1-*Amino*-2-*methylaminopropane.* 1-Amino-2-chloropropane hydrochloride (11 g.) and 25% aqueous methylamine solution (40 ml.) were kept at 15° for 12 hr., then refluxed for 12 hr. The liquid was distilled, 30 ml. of distillate being collected and saturated with potassium hydroxide. The separated upper layer was dried and distilled, the *product* (2·7 g.) being collected at 110—113° (Found: N, 31·5. $C_4H_{12}N_2$ requires N, 31·8%). It was converted into the *dihydrochloride*, m. p. 163—164° (Found: N, 17·2; Cl, 43·9. $C_4H_{14}N_2Cl_2$ requires N, 17·4; Cl, 44·2%).

Preparation of the diamine di-β-phthalimidopropionates. To a solution of the diamine in ethanol was added β-phthalimidopropionic acid (2 mols.) in ethanol. After 2 hr. at 0° the product was collected and recrystallised from ethanol. Thus were prepared the *di-β-phthalimidopropionates* of ethylenediamine, m. p. 164° (Found: N, 11·0. $C_{24}H_{26}O_8N_4$ requires N, 11·3%), *N*-methylethylenediamine, m. p. 142° (Found: C, 58·5; H, 5·5; N, 10·8. $C_{25}H_{28}O_8N_4$ requires C, 58·5; H, 5·5; N, 10·9%), and 1-amino-2-methylaminopropane, m. p. 141° (Found: C, 59·3; H, 5·8; N, 10·2. $C_{26}H_{30}O_8N_4$ requires C, 59·5; H, 5·7; N, 10·65%).

These salts were mixed with an equal weight of dihydrochloride of the same base and heated at 200° for 30 min. After cooling, the viscous mixture was dissolved in hot ethanol; the product crystallised from the filtered solution. Thus were obtained: from ethylenediamine, diphthalimidoethane, m. p. and mixed m. p. with an authentic specimen,[6] 243°; from *N*-methylethylenediamine, 1-*methylamino*-2-*phthalimidoethane hydrochloride*, m. p. 240° (Found: C, 55·1;

[5] Rung and Behrend, *Annalen*, 1892, **271**, 28.
[6] Gabriel, *Ber.*, 1887, **20**, 2224.

H, 5·5; N, 11·8. $C_{11}H_{13}O_2N_2Cl$ requires C, 55·0; H, 5·4; N, 11·65%); and from 1-amino-2-methylaminopropane, *2-methylamino-1-phthalimidopropane hydrochloride*, m. p. 242° (Found: C, 56·6; H, 5·7; N, 10·8. $C_{12}H_{15}O_2N_2Cl$ requires C, 56·6; H, 5·9; N, 11·0%).

Ethyl β-phthalimidopropionimidate hydrochloride. β-Phthalimidopropiononitrile (70 g.) was stirred in chloroform (300 ml.) and ethanol (15 ml.) at −10° while hydrogen chloride was passed through the solution, the temperature being kept below 0° until saturation. After 24 hr. at 0° the chloroform was evaporated. The *product*, recrystallised from anhydrous ethanol, had m. p. 110—111° (Found: N, 9·6; Cl, 12·0. $C_{13}H_{15}O_3N_2Cl$ requires N, 9·9; Cl 12·6%). When the compound was dissolved in water, ethyl β-phthalimidopropionate, m. p. 73°, rapidly crystallised (m. p. undepressed by admixture with an authentic specimen,[7] m. p. 73°).

β-Phthalimidopropionamide. (i) β-Phthalimidopropionyl chloride was dissolved in benzene and poured into aqueous ammonia (*d* 0·88) with stirring. The precipitate was collected and recrystallised from ethanol, to yield the *product*, m. p. 201° (Found: N, 13·2. $C_{11}H_{10}O_3N_2$ requires N, 12·9%). (ii) Ethyl β-phthalimidopropionimidate hydrochloride was heated at 120° until the liquid resolidified. The product, recrystallised from ethanol, had m. p. 201°, undepressed by a specimen prepared as above.

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[*Received, February 25th*, 1957.]

[7] Gabriel, *Ber.*, 1905, **38**, 633.

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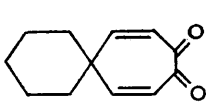
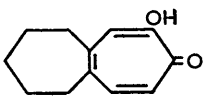
651. *Ring Expansion. Part II.*[1] *The Attempted Preparation of a Bicyclic Tropolone from* spiro[5 : 6]*Dodecane*-3 : 4-*dione.*

By R. H. BURNELL and W. I. TAYLOR.

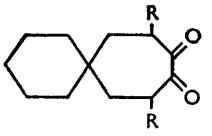
IN Part I [1] it was shown that *spiro*[5 : 5]undeca-1 : 4-diene-3-one underwent the dienone–phenol rearrangement to form benzo*cyclo*hepten-2′-ol. This led us to attempt a formally similar reaction the conversion of *spiro*[5 : 6]dodeca-1 : 5-diene-3 : 4-dione (I) into the bicyclic tropolone (II). If such a transformation could be realised then a feasible synthesis for colchicine could be envisaged.[2] For this purpose *spiro*[5 : 6]dodecane-3 : 4-dione was required as starting material. Ring closure of diethyl *cyclo*hexane-1 : 1-bis-β-propionate, by the high-dilution technique developed for the preparation of cyclic acyloins, afforded traces of the dione of questionable purity. That 3 : 3-disubstitution of a pimelate is at least partially responsible for the low yield of *cyclo*heptanedione by the acyloin procedure was confirmed when it was found that the 3-ethyl-3-methyl derivative gave a 7% yield of dione which should be compared with 57% for the unsubstituted pimelate,[3] which we have



(I)



(II)



(III): R = CO_2Et

(IV): R = H

duplicated. Ring expansion with diazomethane, of 4-benzyl-4-methyl*cyclo*hexanone as an example, followed by oxidation with selenium dioxide to furnish the dione, was also unpromising. Naumov and Perminova [4] have shown, and this has been confirmed,[5] that condensation of diethyl pimelate and diethyl oxalate under the correct conditions gave

[1] Part I, *J.*, 1954, 3486.
[2] Burnell, Ph.D. Thesis, New Brunswick, Canada, 1955.
[3] Cram and Knight, *J. Amer. Chem. Soc.*, 1951, **73**, 4136.
[4] Naumov and Perminova, *Acta Univ. Asiae Mediae*, 1937, VI, Fasc. 28, 1.
[5] Cook, Loudon, and Steel, *J.*, 1954, 530.

diethyl 2 : 3-dioxo*cyclo*heptane-1 : 4-dicarboxylate which was then converted by acid-catalysed hydrolysis and decarboxylation into *cyclo*heptane-1 : 2-dione. In our hands diethyl pimelate, its 3-ethyl-3-methyl derivative, and diethyl *cyclo*hexane-1 : 1-bis-β-propionate gave the corresponding dioxo*cyclo*heptanedicarboxylates in 83, 19, and 7% yield respectively. Refluxing these esters in dilute sulphuric acid gave the diones in fairly good yield.

Bromination and subsequent dehydrobromination of both the compounds (III) and (IV) failed to give the desired dienedione (I). The products were oily and acid treatment gave neither ultraviolet absorption spectra nor colour reactions consistent with the presence of a tropolone. These and studies on related compounds are covered in detail by Burnell.[2] Catalytic dehydrogenation was also tried without success.

Experimental.—Ultraviolet spectra were measured for EtOH solutions.

3-*Acetyl*-3-*methylpimelic acid*. Hydrolysis of 3-acetyl-3-methylpimelonitrile with 15% aqueous potassium hydroxide under reflux gave the diacid (79%), m. p. 129° (from ethylene dichloride) (Found : C, 55·6; H, 7·5. Calc. for $C_{10}H_{16}O_5$: C, 55·5; H, 7·5%).

3-*Ethyl*-3-*methylpimelic acid*. The above acid (88 g.), potassium hydroxide (68·2 g.), and 64% hydrazine hydrate (61 ml.) were refluxed together for 8 hr. The excess of hydrazine and water were distilled off until the temperature reached 207°, after which the residue was refluxed for a further 3 hr. The cooled solution was poured into water (2 l.), acidified, and extracted with ether which yielded the *acid* (55 g.), m. p. 112·5° (from ethylene dichloride) (Found : C, 59·3; H, 8·9. $C_{10}H_{18}O_4$ requires C, 59·4; H, 8·9%). The *diethyl ester* had b. p. 164—169°/15 mm. (Found : C, 64·5; H, 9·9. $C_{14}H_{26}O_4$ requires C, 65·1; H, 10·1%).

Ethyl 5-*ethyl*-5-*methyl*-2-*oxo*cyclo*hexanecarboxylate*. To sodium (7·3 g.) in dry ethanol (250 ml.) was added slowly the above diester (41 g.), then the whole was refluxed for 3 hr., ethanol removed *in vacuo*, and the residue heated *in vacuo* at 130—140° for 4 hr. Addition of water to the cooled product gave an insoluble sodium salt (50 g.) from which the *carboxylate* (28 g.), $\lambda_{max.}$ 257 mμ (ε 10,000), was liberated by dilute hydrochloric acid (Found : C, 68·0; H, 9·6; OEt, 20·5. $C_{12}H_{20}O_3$ requires C, 67·9; H, 9·5; 2OEt, 21·2%).

4-*Ethyl*-4-*methyl*cyclo*hexanone*. Refluxing the keto-ester (9·0 g.) in ethanolic hydrochloric acid for 4 hr. afforded the ketone (3·3 g.), b. p. 95—98°/16 mm., characterised as its 2 : 4-*dinitrophenylhydrazone*, m. p. 141° (Found : C, 56·5; H, 6·3. $C_{15}H_{20}O_4N_4$ requires C, 56·3; H, 6·3%), *semicarbazone*, m. p. 195° (Found : C, 61·0; H, 9·8; N, 21·2. $C_{10}H_{19}ON_3$ requires C, 60·9; H, 9·7; N, 21·3%), and *dinitroso-derivative*, m. p. 215° (decomp.), $\lambda_{max.}$ 270 mμ (ε 12,500) (Found : N, 14·1. $C_9H_{14}O_3N_2$ requires N, 14·1%).

Diethyl 6-*ethyl*-6-*methyl*-2 : 3-*dioxo*cyclo*heptane*-1 : 4-*dicarboxylate*. Sodium ethoxide (prepared from sodium, 4·2 g.) was dissolved in ether (150 ml.) and diethyl oxalate (13·3 g.), then diethyl 3-ethyl-3-methylpimelate (23·5 g.) was added. After 12 hr. at room temperature the whole was evaporated to dryness, then heated *in vacuo* several times with xylene until thoroughly dry. Dry xylene (150 ml.) was added and slowly distilled off during 2 hr. (bath-temp. 145—175°). The cooled product was triturated with water and ether, and the insoluble sodium salt (10·7 g.) was filtered off and washed with water, acetone, and ether. This salt, on being shaken with dilute hydrochloric acid and ether, gave from the latter solvent the cyclo*heptanedicarboxylate* (5·4 g.), a low-melting solid, $\lambda_{max.}$ 305 mμ (ε 15,000) (Found, on a sublimed sample : C, 61·9; H, 9·0. $C_{16}H_{24}O_6$ requires C, 61·5; H, 7·8%), whose *quinoxaline derivative* had m. p. 165° (Found : N, 7·1. $C_{22}H_{28}O_4N_2$ requires N, 7·3%). From the original ether washings, ethyl 5-ethyl-5-methyl-2-oxo*cyclo*hexanecarboxylate (9·2 g.) was isolated.

5-*Ethyl*-5-*methyl*cyclo*heptane*-1 : 2-*dione*. The above dioxo*cyclo*heptanedicarboxylate (4·3 g.) was refluxed with 15% sulphuric acid for 10 hr., to yield the oily dione (2·4 g.), which was purified by vacuum-sublimation and characterised as its *quinoxaline derivative*, m. p. 148° (Found : N, 11·5. $C_{16}H_{20}N_2$ requires N, 11·7%). The same dione was obtained in 7% yield by the acyloin ring closure of diethyl 3-ethyl-3-methylpimelate by Cram's general procedure.[3]

4-*Benzyl*-4-*methyl*cyclo*hexanone*. By methods analogous to those described for the preparation of the corresponding ethyl-methyl compounds, there were obtained from 3-benzoyl- and 3-benzyl-3-methylpimelic acid, the diethyl ester of the latter, ethyl 5-benzyl-5-methyl-2-oxo-*cyclo*hexanecarboxylate, and finally 4-benzyl-4-methyl*cyclo*hexanone, b. p. 120°/1 mm., characterised as its *semicarbazone*, m. p. 164° (Found : C, 69·3; H, 8·2. $C_{15}H_{21}ON_3$ requires

C, 69·5; H, 8·2%), and 2 : 4-*dinitrophenylhydrazone*, m. p. 167—168° (Found : C, 63·1; H, 5·8. $C_{20}H_{22}O_4N_4$ requires C, 62·8; H, 5·8%).

Diethyl spiro[5 : 6]*dodecane*-3 : 4-*dione*-2 : 5-*dicarboxylate*. This compound was prepared from diethyl *cyclo*hexane-1 : 1-bis-β-propionate (3·96 g.) and diethyl oxalate as described above for *cyclo*heptanediones. The yield of the spiro-*ester* (III), m. p. 72—74° (300 mg.), $\lambda_{max.}$ 305 mμ (ε 13,500) (Found : C, 63·8; H, 7·8. $C_{18}H_{26}O_6$ requires C, 63·9; H, 7·7%), was 7%. From the mother-liquors the Dieckmann product was isolated in 81% yield.

spiro[5 : 6]*Dodecane*-3 : 4-*dione* (IV). The above compound (300 mg.) was refluxed for 10 hr. in 20% sulphuric acid to afford, after purification by vacuum-sublimation, the *dione* (85 mg.) (Found : C, 73·4; H, 9·6. $C_{12}H_{18}O_2$ requires C, 74·1; H, 9·3%), characterised as its bis-2 : 4-dinitrophenylhydrazone, m. p. 144—145°.

Diethyl 2 : 3-*dioxo*cyclo*heptane*-1 : 4-*dicarboxylate*. Diethyl pimelate (16 g.) was slowly added to a solution of diethyl oxalate (10·8 g.) and sodium ethoxide (from 3·4 g. of sodium), then refluxed for 12 hr. and worked up as described for the ethyl-methyl derivative, giving 14·5 g. of diethyl *cyclo*heptanedicarboxylate, m. p. 68° (from light petroleum), $\lambda_{max.}$ 303 mμ (ε 15,000) (Found : C, 57·7; H, 6·8; OEt, 34·5. Calc. for $C_{13}H_{18}O_6$: C, 57·8; H, 6·7; 2OEt, 33·4%) [*quinoxaline derivative*, m. p. 142° (from methanol) (Found : C, 66·4; H, 6·3; N, 8·2. $C_{19}H_{22}O_4N_2$ requires C, 66·6; H, 6·5; N, 8·2%)].

cyclo*Heptanedione*. Hydrolysis of the above diester (2·9 g.) with 10% sulphuric acid gave the dione (0·8 g.), b. p. 105°/15 mm. (Found : C, 66·3; H, 8·5. Calc. for $C_7H_{10}O_2$: C, 66·6; H, 8·0%) [*dioxime*, m. p. 177—179° (Found : C, 53·9; H, 7·9. $C_7H_{12}O_2N_2$ requires C, 53·8; H, 7·7%)].

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652. *The Alkylation of (±)-1-Phenylpropane-2-thiol by Di- and Tri-arylmethanols.*

By C. L. ARCUS and P. A. HALLGARTEN.

BALFE, KENYON, and SEARLE [1] recorded examples of the alkylation of thio-*p*-cresol by arylmethanols which undergo alkyl–oxygen fission in acid. If an asymmetric thiol is alkylated by a carbonium ion derived from a dissymmetric arylmethanol, two diastereoisomeric sulphides may be formed. Reaction of (±)-1-phenylpropane-2-thiol with several arylmethanols in the presence of formic acid has been investigated, the course of reaction being considered to be :

$$\text{(i)} \quad CRR'R''\cdot OH + H\cdot CO_2H \longrightarrow CRR'R''\cdot OH_2^+ + H\cdot CO_2^-$$

$$\text{(ii)} \quad CRR'R''\cdot OH_2^+ \longrightarrow {}^+CRR'R'' + H_2O$$

$$\text{(iii)} \quad {}^+CRR'R'' + CH_2Ph\cdot CHMe\cdot SH \longrightarrow CH_2Ph\cdot CHMe\cdot S\cdot CRR'R'' + H^+$$

Although the carbonium ion of stages (ii) and (iii) is planar, the transition states are diastereoisomeric, and the rates of formation of the diastereoisomeric sulphides will, in principle, differ.

Alkylation with the symmetrical alcohols tri- and di-phenylmethanol gave respectively

[1] Balfe, Kenyon, and Searle, *J.*, 1950, 3309.

crystalline (±)-α-methylphenethyl triphenylmethyl sulphide and a low-melting diphenylmethyl sulphide which on oxidation yielded (±)-diphenylmethyl α-methylphenethyl sulphone.

(±)-*p*-Dimethylaminodiphenylmethanol yielded two crystalline sulphides in ratio 52 : 48, so the rates of formation of the diastereoisomers differ little.

(±)-*p*-Methoxy- and (±)-*p*-ethoxy-diphenylmethanol gave oily sulphides and oxidation oily sulphones. Reaction of (±)-4-α-chlorobenzyldiphenyl, which would be expected to react *via* the carbonium ion,[1] with the thiol in formic acid, gave a single crystalline (±)-sulphide, but the amount isolated was not sufficient necessarily to render this diastereoisomer the major product.

On the basis of the present results, therefore, reaction (iii) does not proceed with marked dissymmetry.

Experimental.—M. p.s are corrected. Heating, throughout, was on a steam-bath.

Triphenylmethanol (3·2 g.) and (±)-1-phenylpropane-2-thiol [2] (1·75 g.) in 90% formic acid (10 ml.) were heated for 45 min. and poured into ice-water. The product (2·5 g.), on fractional crystallisation from ethanol, yielded (±)-α-*methylphenethyl triphenylmethyl sulphide* (1·1 g.), rhombs, m. p. 118—118·5° (Found : C, 85·15; H, 6·7; S, 7·8. $C_{28}H_{27}S$ requires C, 85·25; H, 6·65; S, 8·15%), and material (0·7 g.), m. p. 78—89°, considered to be triphenylmethane (the latter is known to be formed by the reaction of triphenylmethanol with formic acid [3]).

Similar reaction of the thiol (1·75 g.) and diphenylmethanol (1·22 g.) in 90% formic acid (25 ml.), under nitrogen, yielded a sulphide (1·10 g.), m. p. 33—35°, which could not be recrystallised satisfactorily. It (0·57 g.) was heated in acetic acid (5 ml.) for 10 min. with 34% hydrogen peroxide (3 ml.), acetic acid (8 ml.) being added to maintain homogeneity. The solution was chilled to −80° and then allowed to attain room temperature; it gave a product (0·42 g.), m. p. 119—120°, which on crystallisation from ethanol yielded (±)-*diphenylmethyl α-methylphenethyl sulphone* (0·30 g.), plates, m. p. 138·5° (Found : O, 9·7; S, 9·45. $C_{22}H_{22}O_2S$ requires O, 9·15; S, 9·15%).

(±)-*p*-Dimethylaminodiphenylmethanol (4·62 g.) and the thiol (3·08 g.) were heated under reflux in chloroform (14 ml.) for 3 hr.; the solution was then chilled at −80° for 15 min.; no crystallisation occurred; 99% formic acid (3 drops) was added and heating under reflux continued for 3 hr. The solvent was evaporated at room temperature, finally *in vacuo*. By fractional crystallisation of the product, from methanol, two diastereoisomers were separated : (±)-p-*dimethylaminodiphenylmethyl α-methylphenethyl sulphide-A* (2·10 g.), needles, m. p. 103—103·5° (Found : N, 3·95; S, 8·75. $C_{24}H_{27}NS$ requires N, 3·9; S, 8·9%), and (±)-*sulphide-B* (2·25 g.), more soluble rods, m. p. 65·5° (Found : N, 3·8; S, 9·0%).

(±)-4-α-Chlorobenzyldiphenyl (0·85 g.) and the thiol (0·50 g.), in 99% formic acid (10 ml.), were heated for 5 min. then poured into ice-water. The product, after being crystallised from methanol and twice from ethanol, yielded (±)-α-4-*diphenylylbenzyl α-methylphenethyl sulphide* (0·16 g.), needles, m. p. 105—105·5° (Found : S, 7·85. $C_{28}H_{26}S$ requires S, 8·1%).

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BATTERSEA POLYTECHNIC, LONDON, S.W.11. [*Received, March 6th*, 1957.]

[2] Arcus and Hallgarten, *J.*, 1956, 2987.
[3] Kauffmann and Pannwitz, *Ber.*, 1912, **45**, 769.

653. 2-*Amino*-1-*ethylthioethanol Hydrochloride.*

By L. Hough and Mahmoud I. Taha.

Reaction of 2-aminoacetaldehyde diethyl acetal with ethanethiol and cold hydrochloric acid (*d* 1·18) yielded 2-amino-1-ethylthioethanol hydrochloride; none of the diethyl dithioacetal was isolated. This behaviour is related to that of 2-amino-2-deoxy-D-glucose hydrochloride which is unusually resistant to thioacetal formation [1] owing to the field effect of the cationoid nitrogen atom.[2] On the other hand, 2-acetamido-2-deoxy-D-glucose readily forms a mixture of mono- and di-ethylthio-derivatives.[3] Acetylation of 2-amino-1-ethylthioethanol hydrochloride afforded a crystalline diacetyl derivative. On oxidation with periodate the latter rapidly consumed 1 mol. of the oxidant, no formic acid or formaldehyde being liberated, in agreement with similar oxidations [3] of 2-acetamido-2-deoxy-D-glucopyranosylthioethanes and 2-acetamido-3 : 4 : 5 : 6-tetra-*O*-acetyl-2-deoxy-D-glucose diethyl dithioacetal. Reductive desulphurisation of 2-acetamido-1-acetoxy-1-ethylthioethane yielded 1-acetamido-2-acetoxyethane which was resistant to periodate oxidation.

Experimental.—2-*Amino*-1-*ethylthioethanol hydrochloride.* 2-Aminoacetaldehyde diethyl acetal (20 g.) was cooled to −10° (acetone–carbon dioxide), and ice-cold concentrated hydrochloric acid (25 ml.) was added dropwise with shaking. To the cold solution was added ethanethiol (25 g.) with shaking and the mixture stored at 0°. The crystalline *hydrochloride* (*ca.* 15 g., was filtered off and washed several times with acetone; it had m. p. 103° (Found : C, 30·8; H) 8·1; N, 8·9; S, 19·8; Cl, 23·9. $C_4H_{12}ONSCl$ requires C, 30·5; H, 7·6; N, 8·9; S, 20·3; Cl, 22·6%), and was unstable in the presence of water or alcohols.

2-*Acetamido*-1-*acetoxy*-1-*ethylthioethane.* A mixture of 2-amino-1-ethylthioethanol hydrochloride (10 g.), dry pyridine (20 ml.), and acetic anhydride (20 ml.) was set aside at room temperature for 24 hr., then poured into ice-water (*ca.* 200 ml.). The solution was extracted with chloroform (3 × 50 ml.), and the combined extracts were washed successively with 2N-hydrochloric acid (2 × 50 ml.), 2N-sodium hydrogen carbonate solution (2 × 50 ml.) and water and dried ($MgSO_4$). Subsequent concentration gave a colourless syrup (12 g.) which crystallised at 0°. Recrystallisation from ether–light petroleum (b. p. 40—60°) gave the *acetate* as needles, m. p. 45° [Found : C, 46·9; H, 7·2; N, 6·9; S, 15·8; Ac, 39·6%; *M* (Menzies and Wright's method [4]), 201·5. $C_8H_{15}O_3NS$ requires C, 46·8; H, 7·3; N, 6·8; S, 15·6; Ac, 42·0%; *M*, 205].

1-*Acetamido*-2-*acetoxyethane.* A mixture of 2-acetamido-1-acetoxy-1-ethylthioethane (2·0 g.) and fresh Raney nickel (2 g.), suspended in absolute ethanol (25 ml.), was heated under reflux for 24 hr. After filtration and concentration a syrup (0·6 g.) was obtained which crystallised at 0°. Recrystallisation from ether–light petroleum (b. p. 40—60°) gave 1-*acetamido*-2-*acetoxyethane* as needles, m. p. 36° [Found : C, 49·6; H, 7·9; N, 10·2%; *M* (as above), 140·5. $C_6H_{11}O_3N$ requires C, 49·4; H, 7·6; N, 9·7%; *M*, 145].

The University, Bristol. [*Received, March 11th*, 1957.]

[1] Wolfrom and Anno, *J. Amer. Chem. Soc.*, 1952, **74**, 6150; Kent and Posternak, *J.*, 1954, 2315.
[2] Moggridge and Neuberger, *J.*, 1938, 745.
[3] Hough and Taha, *J.*, 1956, 2042; *J.*, 1957, in the press.
[4] Menzies and Wright, *J. Amer. Chem. Soc.*, 1921, **23**, 2309, 2314.

654. *The Denitration of* N-*Methyl*-N′-*nitroguanidine : Correction.*

By Muriel L. Hardy-Klein.

In a recent paper [1] it was suggested, erroneously owing to an algebraical mistake in the derivation of equation (13), that denitration of *N*-methyl-*N*′-nitroguanidine in 71·7—81·3% sulphuric acid depends on the bimolecular reaction $MePH^+ + HA \longrightarrow$ Products, where $MePH^+$ represents the methylnitroguanidine cation and HA the acid species H_2SO_4 and H_3O^+.

The experimental result obtained, *viz.*,

$$\log k_1 - \log (H_2SO_4) + H_0 - \log (H_2O) = \text{constant}$$

still stands. Now, since $H_0 = -\log \{(H^+)f_B/f_{BH^+}\}$ (cf. Hammett [2]), it can be expressed as

$$k_1 = \text{const.}(H_2SO_4)(H^+)(H_2O)f_B/f_{BH^+}$$

Thus, with $H_2O + H^+ \rightleftharpoons H_3O^+$, the rate, $k_1[MePH^+]$, becomes

$$\text{Rate} = \text{const.}[MePH^+](H_2SO_4)(H_3O^+)f_B/f_{BH^+}$$

This equation allows the following interpretations: (*a*) the reaction is termolecular, $MePH^+ + H_2SO_4 + H_3O^+ \longrightarrow$ Products, or (*b*) the reaction is bimolecular, with initial solvation of the methylnitroguanidine cation, *e.g.*:

$$MePH^+ + H_2SO_4 \rightleftharpoons \{MePHH_2SO_4\}^+ \quad \ldots \text{ Fast}$$

$$\{MePH,H_2SO_4\}^+ + H_3O^+ \longrightarrow \text{Products} \quad \ldots \text{ Slow}$$

It is assumed for both these mechanisms that the function $(f_{BH^+} \cdot f_{MePH^+})/(f_B \cdot f_{tr^{2+}})$ of the activity coefficients is constant, as has been shown experimentally for 75—95% sulphuric acid by Bonner and Lockhart.[3] The author is obliged to Dr. T. G. Bonner for pointing out the algebraical mistake.

Royal College of Science and Technology, Glasgow. [*Received, March 12th,* 1957.]

[1] Hardy-Klein, *J.*, 1957, 70.
[2] Hammett, "Physical Organic Chemistry," McGraw Hill Book Co., New York, 1st edn., 1940, p. 267.
[3] Bonner and Lockhart, *J.*, 1957, 364.

655. 2-*Methyleneaminomethylbenziminazole.*

By E. S. Lane.

In view of a recent recorded preparation of 2-formylbenziminazole,[1] we record the failure to prepare this compound by the Sommelet reaction. When 2-chloromethylbenziminazole was refluxed with sodium iodide and hexamine in acetone, a quaternary iodide was formed which rapidly hydrolysed in hot water to give 2-methyleneaminomethylbenziminazole. The insolubility of this compound in organic solvents and the fact that in acid solution it displays aldehyde reactions (owing to hydrolysis to formaldehyde) may lead to its false identification as 2-formylbenziminazole. 2-Methyleneaminomethylbenziminazole was also obtained when hexamine and 2-aminomethylbenziminazole were refluxed together in acid under a variety of conditions and when hexamine and 2-chloromethylbenziminazole were refluxed in alcohol or acetone. 2-Aminomethylbenziminazole, which cannot be prepared by more conventional methods from glycine and *o*-phenylenediamine,[2] is readily made by fusing together equimolecular quantities of *o*-phenylenediamine and ethyl aminoacetate hydrochloride.

Experimental.—2-Benziminazolylmethylhexamine iodide. 2-Chloromethylbenziminazole (8·3 g.), sodium iodide (7·5 g.), hexamine (7·0 g.), and acetone (200 ml.) were refluxed together for 2 hr., and the insoluble residue filtered off. The above *salt* was recrystallised with difficulty from ethanol in which it was only sparingly soluble. It had no definite m. p. but was completely decomposed at 160° (Found: C, 42·8; H, 4·9; N, 20·7; I, 31·6. $C_{14}H_{19}N_6I$ requires C, 42·2; H, 4·8; N, 21·1; I, 31·9%).

2-*Methyleneaminomethylbenziminazole.* (*a*) The above salt (5·0 g.) was refluxed in water (50 ml.) (in which it was initially soluble) for 15 min., and the insoluble residue filtered off and dried (2·3 g.). The *base* was substantially insoluble in common organic solvents but was finally recrystallised with difficulty from ethylene glycol. It had m. p. 277° (decomp.) (Found: C, 67·9; H, 5·5; N, 26·0. $C_9H_9N_3$ requires C, 67·9; H, 5·6; N, 26·4%). With 2 : 4-dinitrophenylhydrazine in 2N-hydrochloric acid a crystalline precipitate was formed, m. p. 160°, which was identified by its mixed m. p. with formaldehyde 2 : 4-dinitrophenylhydrazone.

(*b*) 2-Aminomethylbenziminazole dihydrochloride (12·7 g.), hexamine (10 g.), and water (100 ml.) were refluxed together for 30 min. The insoluble material, when filtered off and washed (7·3 g.), had m. p. 270° (decomp.) (from ethylene glycol) (Found: N, 26·2%).

(*c*) 2-Aminomethylbenziminazole dihydrochloride (11·0 g.), hexamine (8·5 g.), 35% formaldehyde (6 ml.), and 50% acetic acid (45 ml.) were refluxed together for 1 hr., then cooled and basified with sodium carbonate. The resulting white precipitate was filtered off, washed, and dried (5·7 g.). It had m. p. 265° (decomp.) (Found: N, 26·0%).

(*d*) 2-Chloromethylbenziminazole (8·3 g.) and hexamine (7·0 g.) were refluxed together in acetone for 2 hr. The insoluble material (10·1 g.) had m. p. 265—270° (decomp.) (Found: N, 26·2%).

2-*Aminomethylbenziminazole.* Ethyl aminoacetate hydrochloride (14·0 g.) and *o*-phenylenediamine (11·0 g.) were finely ground, intimately mixed, and heated in nitrogen for 2 hr. at 180—200°. When cold, the glassy melt was dissolved in dilute hydrochloric acid, boiled with charcoal, and filtered. The filtrate was evaporated to dryness (steam-bath), triturated with ethanol, and filtered. The residue of the *dihydrochloride* (12·7 g.) was washed with ethanol until colourless and had m. p. 263—265° (from ethanol). Hughes and Lions [2] give m. p. 263°.

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Harwell, nr. Didcot, Berks.

[*Received, March 18th*, 1957.]

[1] Baganz, *Angew. Chem.*, 1956, **68**, 151.
[2] Hughes and Lions, *J. Proc. Roy. Soc. New South Wales*, 1938, **71**, 209.

656. *The Formylation of the Pyrazole Nucleus.*

By I. L. Finar and G. H. Lord.

4-Formyl-1-phenylpyrazole, prepared by Finar and Godfrey [1] by the Sommelet reaction from 4-chloromethyl-1-phenylpyrazole, has now been prepared by the direct formylation of 1-phenylpyrazole. The last compound, prepared from phenylhydrazine hydrochloride and 1 : 1 : 3 : 3-tetraethoxypropane,[2] was treated with dimethylformamide and phosphoryl chloride.[3] Hydrolysis then gave 4-formyl-1-phenylpyrazole. *N*-Methylformanilide [4] could be used instead of dimethylformamide, but the yield was lower.

1-Methylpyrazole [5] has been prepared from methylhydrazine sulphate and 1 : 1 : 3 : 3-tetraethoxypropane, and by the treatment of pyrazole with methyl iodide and potassium hydroxide. Formylation as above gave 4-formyl-1-methylpyrazole, which was oxidised to 1-methylpyrazole-4-carboxylic acid.

Attempts to formylate pyrazole failed, and attempts with 1-benzoyl- and 1-benzenesulphonyl-pyrazole merely resulted in hydrolysis of the protecting group.

The isomeric aldoximes of 4-formyl-1-phenylpyrazole have been prepared and characterised by the action of *n*-butylamine on their acetyl derivatives.[6] The lower-melting α-isomer is converted into the β-isomer by hot ethanol or at its melting point. The α-*O*-acetylaldoxime, on treatment with *n*-butylamine, regenerated the α-aldoxime alone. The β-*O*-acetylaldoxime, similarly treated, gave 4-cyano-1-phenylpyrazole and the β-aldoxime. On this evidence, the α-isomer is the *syn*- and the β-isomer is the *anti*-aldoxime. Both aldoximes when refluxed with acetic anhydride gave 4-cyano-1-phenylpyrazole which was hydrolysed to 1-phenylpyrazole-4-carboxylic acid by boiling sulphuric acid.

Experimental.—*4-Formyl-1-phenylpyrazole.* To 1-phenylpyrazole [2] (50 g., 1 mol.) and dimethylformamide (25·3 g., 1 mol.), stirred at 95—100°, phosphoryl chloride (53·2 g., 1 mol.) was added during 1·5 hr. Heating and stirring were maintained for a further 2·5 hr., then the reactants were cooled in ice, and water was cautiously added. Sodium hydroxide solution was added to pH 4. After 2 hr. the solution was filtered, giving 4-formyl-1-phenylpyrazole (30·2 g., 51%). The filtrate was made alkaline with excess of sodium hydroxide and extracted with ether. The extracts were dried, evaporated, and distilled, giving 1-phenylpyrazole (17 g., 76% based on recovered 1-phenylpyrazole).

1-Methylpyrazole. (*a*) 1 : 1 : 3 : 3-Tetraethoxypropane (22·0 g., 1 mol.) and methylhydrazine sulphate (14·4 g., 1 mol.) were refluxed in ethanol (9 c.c.) and water (3 c.c.) for 2 hr. Sodium carbonate (11·1 g.) and water (10 c c.) were then added. The sodium sulphate was filtered off and washed with ether. The aqueous layer was extracted with the ether washings and then with chloroform (2 × 25 c.c.). The ether and chloroform extracts were dried and evaporated. The residual red oils were combined and distilled, to give 1-methylpyrazole (5·65 g., 69%), b. p. 126—127°, identified as the picrate, m. p. 148°.

(*b*) Pyrazole (7·52 g.) was warmed with potassium hydroxide (6·2 g.) in ethanol (5 c.c.) and water (1 c.c.) until homogeneous. Methyl iodide (25 g.) in ether (10 c.c.) was added during 30 min., then the mixture refluxed for 0·5 hr., then extracted with ether and chloroform, and the extracts were combined and dried. Evaporation, followed by distillation, gave 1-methylpyrazole (7·0 g., 77%), b. p. 126—127°.

4-Formyl-1-methylpyrazole. 1-Methylpyrazole (4·75 g.) and dimethylformamide (11·0 g.) were warmed to 95—100°, and phosphoryl chloride (9·0 g., 5·5 c.c.) was added dropwise. After the initial evolution of hydrogen chloride the reactants were warmed on the steam-bath for 1·5 hr., cooled to 10°, and hydrolysed by water. Extraction with ether, and then chloroform,

[1] Finar and Godfrey, *J.*, 1954, 2293.
[2] Finar and Hurlock, 3024.
[3] Campaigne and Archer, *J. Amer. Chem. Soc.*, 1953, **75**, 989.
[4] Vilsmeir and Haak, *Ber.*, 1927, **60**, 119.
[5] Huttel, Wagner, and Jochum, *Annalen*, 1955, **593**, 179.
[6] Hauser and Jordan, *J. Amer. Chem. Soc.*, 1935, **57**, 2450; 1936, **58**, 1772.

followed by drying, evaporation, and distillation, gave 4-*formyl*-1-*methylpyrazole* (2·1 g., 33%), b. p. 106—108°/20 mm. (Found: C, 54·2; H, 5·95; N, 25·2. $C_5H_6ON_2$ requires C, 54·5; H, 5·45; N, 25·45%). The 2 : 4-*dinitrophenylhydrazone* formed red needles (from glacial acetic acid), m. p. 264—265° (Found: C, 45·3; H, 3·40; N, 28·8. $C_{11}H_{10}O_4N_6$ requires C, 45·5; H, 3·45; N, 29·0%).

1-*Methylpyrazole*-4-*carboxylic acid*. 4-Formyl-1-methylpyrazole (1·8 g.) was refluxed with alkaline potassium permanganate for 0·5 hr. Filtration, followed by acidification of the filtrate, gave colourless needles of 1-*methylpyrazole*-4-*carboxylic acid* (1·25 g., 60·5%), m. p. 205—206° (Found: C, 47·3; H, 4·77; N, 21·5. $C_5H_6O_2N_2$ requires C, 47·6; H, 4·76; N, 22·2%). Bromination under standard conditions for 4-substitution gave unchanged acid, indicating formylation in the 4-position of 1-methylpyrazole.

1-*Benzenesulphonylpyrazole*. To pyrazole (10 g.) in pyridine (20 c.c.) benzenesulphonyl chloride (27 g.) was added slowly. After being warmed on the steam-bath for 15 min., the reactants were poured into water (600 c.c.). Crystallisation from acetone gave 1-*benzenesulphonylpyrazole* (30·5 g., 99%), m. p. 103·5—104° (Found: C, 51·3; H, 3·6; N, 13·2; S, 15·2. $C_9H_8O_2N_2S$ requires C, 51·9; H, 3·8; N, 13·4; S, 15·4%).

4-*Formyl*-1-*phenylpyrazole oximes*. (*a*) 4-Formyl-1-phenylpyrazole (10 g.) and hydroxylamine hydrochloride (10 g.) were refluxed for 2 hr. in pyridine (50 c.c.) and ethanol (50 c.c.), then poured into water (1 l.), and the resultant precipitate was filtered off, washed with cold water, and dried at 80°. Recrystallisation from 50% aqueous ethanol gave the anti-*oxime* (10·2 g., 94%), m. p. 173° (Found: C, 64·4; H, 4·8; N, 22·2. $C_{10}H_9ON_3$ requires C, 64·2; H, 4·8; N, 22·4%).

(*b*) Sodium ethoxide solution (from 2·19 g. of sodium in 50 c.c. of ethanol) was added to hydroxylamine hydrochloride (6·65 g.) in water (10 c.c.), and sodium chloride removed. 4-Formyl-1-phenylpyrazole (5·55 g.) in ethanol (50 c.c.) was added and the mixture kept at room temperature for 60 hr. The syn-*oxime* (2·0 g., 33%) was obtained as colourless needles m. p. 135° (Found: C, 64·0; H, 4·9; N, 22·4%). Addition of water to the mother-liquor gave a further 4·0 g., m. p. 128—129°.

(*c*) The *anti*-oxime (3·65 g.) was kept in cold acetic anhydride (9 c.c.) for 0·5 hr. Colourless needles of the O-*acetyloxime* (1·2 g., 27%), m. p. 98—99°, were obtained, and a further quantity (1·0 g.) was obtained by treatment of the filtrate with excess of water, followed by recrystallisation of the precipitate from aqueous acetone (Found: C, 63·1; H, 4·7; N, 17·9. $C_{12}H_{11}O_2N_3$ requires C, 62·9; H, 4·8; N, 18·3%).

This acetate (1·15 g.) dissolved rapidly in *n*-butylamine (3 c.c.). Addition of crushed ice after 10 min. gave a precipitate of 4-cyano-1-phenylpyrazole, which was filtered off, washed with 3N-sodium hydroxide, then with water, and recrystallised from aqueous ethanol as needles (0·45 g.), m. p. 95—96° (undepressed on admixture with authentic 4-cyano-1-phenylpyrazole). Acidification of the alkaline washings gave regenerated *anti*-oxime (0·2 g.), m. p. 171—173°.

The *syn*-oxime (1·9 g.) was kept in acetic anhydride (3 c.c.) for 0·5 hr., then poured into water (50 c.c.). The precipitate was filtered off and crystallised from ethanol and then aqueous acetone, to give needles of the syn-*acetate* (0·9 g., 38%), m. p. 102·5—103° (Found: C, 62·7; H, 4·5; N, 18·4%).

This acetyloxime (0·25 g.), treated with *n*-butylamine (1 c.c.), as above, regenerated *syn*-oxime (0·2 g.), m. p. 135°.

4-*Cyano*-1-*phenylpyrazole*. The *anti*-oxime (1·1 g.) was refluxed with acetic anhydride (10 c.c.) for 0·5 hr. Addition of water gave a white precipitate, which crystallised from ethanol to give 4-*cyano*-1-*phenylpyrazole* (0·85 g., 85%), m. p. 95° (Found: C, 70·7; H, 4·2; N, 24·7. $C_{10}H_7N_3$ requires C, 71·1; H, 4·1; N, 24·8%). Hydrolysis of this with 75% sulphuric acid gave 1-phenylpyrazole-4-carboxylic acid.

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657. *Ethylidene Derivatives of Methyl Aldopyranosides.*

By JOHN HONEYMAN and THEO. C. STENING.

O'MEARA and SHEPHERD [1] have described the preparation of methyl 4 : 6-*O*-ethylidene-β-D-glucoside by treatment of methyl β-D-glucopyranoside with 1 : 1-dimethoxyethane in the presence of sulphuric acid. That this reagent differs from paraldehyde in not giving oxydiethylidene derivatives with vicinal *trans*-hydroxyl groups has now been confirmed by the preparation of methyl 4 : 6-*O*-ethylidene-α-D-glucoside in consistently higher yield than results by Honeyman and Morgan's method : [2] no oxydiethylidene derivative was detected even after reaction for 48 hours. The known aldehyde derivatives of aldopyranosides are obtained in the 2-, 3-, and 4-positions from adjacent *cis*-hydroxyl groups only, with the hydroxyl groups equatorial-axial, except that when an aliphatic aldehyde or one of its polymers is used an oxydialkylidene derivative may be formed from adjacent *trans*-hydroxyl groups. This is in agreement with the suggestion [3] that vicinal *cis*-glycol groups in six-membered rings afford cyclic acetals, whereas the *trans*-isomers normally do not, although a few cyclic *iso*propylidene derivatives of *trans*-glycols have been prepared.[4] In the aldohexopyranoside series *n*-alkylidene, benzylidene, and *iso*propylidene derivatives are formed in the 4 : 6-position but usually only under vigorous conditions or on prolonged reaction.[5]

Methyl α-L-rhamnopyranoside with 1 : 1-dimethoxyethane gives methyl 2 : 3-*O*-ethylidene-α-L-rhamnopyranoside, characterized as its toluene-*p*-sulphonate identical with the compound prepared by condensation of methyl α-L-rhamnoside 4-toluene-*p*-sulphonate [6] with 1 : 1-dimethoxyethane. Thus reaction involved the 2 : 3-hydroxyl groups which are equatorial-axial in the preferred conformation,[7] but not the axial-axial 3 : 4-pair. Methyl α-D-fucopyranoside also gave a monoethylidene derivative. The predicted conformation [7] of methyl α-D-fucoside indicates that the 3 : 4-hydroxyl groups (equatorial-axial) are favourably placed for acetal formation, so that the compound isolated is probably methyl 3 : 4-*O*-ethylidene-α-D-fucoside. The corresponding ketal, methyl 3 : 4-*O*-*iso*propylidene-α-D-fucoside, had been prepared and characterized previously.[8] The 2 : 3-hydroxyl groups of methyl α-D-fucopyranoside are equatorial-equatorial if the glycoside reacts in this predicted conformation, so by analogy with the D-glucoside the formation of an oxydiethylidene derivative may be expected when paraldehyde is the source of acetaldehyde. That such a compound was not isolated suggests that an ethylidene compound is formed preferentially whenever three hydroxyl groups are placed suitably for either kind of acetal formation.

Methyl α-D-mannopyranoside gave methyl 2 : 3-4 : 6-di-*O*-ethylidene- and methyl 4 : 6-*O*-ethylidene-α-D-mannoside on treatment with 1 : 1-dimethoxyethane containing sulphuric acid, further evidence that the reagent will react with adjacent *cis*- but not *trans*-hydroxyl groups.

Experimental.—Preparation of methyl α-D-fucopyranoside. Methanol (500 ml.) containing hydrogen chloride (4%) and 1 : 2-3 : 4-di-*O*-*iso*propylidene-D-fucose [9] (22 g.) was boiled under

[1] O'Meara and Shepherd, *J.*, 1955, 4232.
[2] Honeyman and Morgan, *J.*, 1955, 3660.
[3] Mills, *Adv. Carbohydrate Chem.*, 1955, **10**, 1.
[4] Angyal and McDonald, *J.*, 1952, 686; Christian, Gogek, and Purves, *Canad. J. Chem.*, 1951, **29**, 911; Fenton, Salcedo, and Franz, Abs. Papers, Amer. Chem. Soc., Sept. 1956, p. O 7.
[5] Jones, *Canad. J. Chem.*, 1956, **34**, 840; Ault, Haworth, and Hirst, *J.*, 1935, 1012; Labaton and Newth, *J.*, 1953, 992.
[6] Percival and Percival, *J.*, 1950, 690.
[7] Reeves, *J. Amer. Chem. Soc.*, 1950, **72**, 1499.
[8] MacPhillamy and Elderfield, *J. Org. Chem.*, 1939, **4**, 150.
[9] Schmid and Karrer, *Helv. Chim. Acta*, 1949, **32**, 1371.

reflux for 14 hr.; acid was neutralized with silver (or lead) carbonate, and the solution was decolorized with charcoal. Evaporation of the filtered solution gave a syrup which, crystallized from ethanol, gave methyl α-D-fucopyranoside (6·5 g.), m. p. 155°. The evaporated mother-liquor was again treated with methanolic hydrogen chloride, yielding a further quantity of methyl α-D-fucopyranoside (total, 65%), m. p. 155°, $[\alpha]_D^{21}$ +189° (*c* 2·0 in H_2O). MacPhillamy and Elderfield [8] record m. p. 155—156°.

Preparation of acetals. The sugar (30 g.), 1 : 1-dimethoxyethane (125 ml.), and concentrated sulphuric acid (1·3 ml.) were shaken together for 2—3 hr., then acid was neutralized with solid potassium carbonate. The filtered mixture was evaporated under reduced pressure and the syrupy product was recrystallized from ether–light petroleum. Yields are not increased if the reaction time is prolonged.

The compounds prepared by this method include: methyl 4 : 6-*O*-ethylidene-α-D-glucoside (57%); *methyl* 3(?) : 4(?)-O-*ethylidene*-α-D-*fucopyranoside* (39%), b. p. 69°/0·05 mm., m. p. 84°, $[\alpha]_D^{22}$ +153° (*c* 1·0 in $CHCl_3$) (Found: C, 52·8; H, 8·0; CH_3·CHO, 21·1. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9; CH_3·CHO, 21·6%); and *methyl* 2 : 3-O-*ethylidene*-α-L-*rhamnopyranoside* (37%), b. p. 76°/0·2 mm., m. p. 53°, $[\alpha]_D^{21}$ −44·9° (*c* 0·4 in $CHCl_3$) (Found: C, 52·9; H, 7·9; CH_3·CHO, 22·0. $C_9H_{16}O_5$ requires C, 52·9; H, 7·9; CH_3·CHO, 21·6%).

Methyl 4 : 6-O-*ethylidene*-α-D-*mannoside and* 2 : 3-4 : 6-*di*-O-*ethylidene*-α-D-*mannoside.* Finely ground methyl α-D-mannopyranoside (5·0 g.) was shaken in 1 : 1-dimethoxyethane (25 ml.) containing concentrated sulphuric acid (0·25 ml.) for 1·5 hr. Starting compound (1 g.) was filtered off, and the solution was neutralized with anhydrous potassium carbonate. Evaporation of the filtered solution gave a syrup which solidified on being shaken with water. This, recrystallized from aqueous ethanol, was methyl 2 : 3-4 : 6-di-*O*-ethylidene-α-D-mannoside (3·4 g., 66% of mannoside consumed). The aqueous filtrate was evaporated to a white solid which was recrystallized from carbon tetrachloride, to give methyl 4 : 6-*O*-ethylidene-α-D-mannoside (0·6 g., 13%), m. p. 116—117°.

Characterization of methyl 2 : 3-O-*ethylidene*-α-L-*rhamnopyranoside.* Solutions of methyl 2 : 3-*O*-ethylidene-α-L-rhamnoside (1·3 g.) in pyridine (5 ml.) and toluene-*p*-sulphonyl chloride (1·3 g.) in pyridine (2 ml.) were mixed at 0° and kept at 0° for 4 days. The solid 4-*toluene*-*p*-*sulphonate*, precipitated when the mixture was poured into ice-water and recrystallized from methanol, had m. p. 81° (0·5 g.), $[\alpha]_D^{20}$ +14·8° (*c* 0·8 in $CHCl_3$) (Found: C, 53·6; H, 6·2. $C_{16}H_{22}O_7S$ requires C, 53·3; H, 6·1%).

A solution of methyl α-L-rhamnopyranoside 4-toluene-*p*-sulphonate [6] (0·33 g.) in 1 : 1-dimethoxyethane (10 ml.) containing concentrated sulphuric acid (4 drops) was shaken at room temperature for 6 hr. After neutralization with anhydrous potassium carbonate, the filtered solution was evaporated to dryness, and the residue was dissolved in the minimum quantity of warm methanol. The cooled solution was poured into ice-water, and the resultant solid, recrystallized from methanol, was the above 4-toluene-*p*-sulphonate (0·14 g., 36%), m. p. and mixed m. p. 80—81°, $[\alpha]_D^{20}$ +15·0° (*c* 1·0 in $CHCl_3$).

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658. *Plutonium Alkoxides.*

By D. C. Bradley, B. Harder, and F. Hudswell.

Since plutonium appears not to form a stable anhydrous tetrachloride, preparation of plutonium(IV) tetra-alkoxides started from the stable pyridinium chloride complex $(C_5H_6N)_2PuCl_6$. The complex chloride, when treated in suspension in benzene–propan-2-ol with excess of ammonia, gave a soluble product corresponding in analysis to a mixture of $Pu(OPr^i)_4$ and $Pu(OPr^i)_4,C_5H_5N$, thus resembling the zirconium [1] and cerium [2] analogues (which gave partly solvated tetra*iso*propoxides) and contrasting with the thorium analogue [3] (which gave a chloride *iso*propoxide). We explained the behaviour of the thorium compound in terms of the basic nature of thorium alkoxides; by this token quadrivalent plutonium is less basic than thorium and nearer in basicity to quadrivalent cerium, and this is supported by the fact that the Th^{4+} ion is larger than the Pu^{4+} ion.

The plutonium product, on crystallisation from propan-2-ol, gave an emerald-green solvate $Pu(OPr^i)_4,Pr^iOH$, analogous to the zirconium, hafnium, and cerium compounds (thorium *iso*propoxide does not form solvates). Plutonium *iso*propoxide sublimed at *ca.* 220°/0·05 mm.; by alcohol interchange with *tert.*-butyl alcohol it gave a pale green product which sublimed at *ca.* 112°/0·05 mm., which although not analysed was doubtless the tetra-*tert.*-butoxide. Similarly, 3-ethylpentan-3-ol gave a product which was volatile above 150°/0·05 mm. The plutonium alkoxides were extremely easily hydrolysed but appear to be unaffected by dry air (cf. uranium tetra-alkoxides [4] which are oxidised by air).

Experimental.—The experimental procedure was essentially that employed earlier [1–3] with precautions against radiation. Plutonium was analysed by dissolving a weighed sample in dilute nitric acid and then " counting " on a suitable aliquot part by means of a Simpson counter with 2π geometry. The ^{239}Pu isotope was used. The chloride content was determined by Volhard's method.

Dipyridinium plutonium hexachloride. This was prepared by Katz and Rabinowitz's method [5] and dried at 120°/0·05 mm. for 2 hr. A small quantity of pyridine hydrochloride was sublimed off by this treatment but this did not materially affect the product [Found: Pu, 39·1; Cl, 33·7. Calc. for $(C_5H_6N)_2PuCl_6$: Pu, 39·0; Cl, 34·8%].

Plutonium iso*propoxide.* The vigorously shaken suspension of the complex chloride (9·7 g.) in benzene (60 c.c.) and propan-2-ol (90 c.c.) was treated with ammonia until the reaction appeared complete. The ammonium chloride and a small quantity of unchanged complex were removed and the filtrate evaporated to dryness under reduced pressure, giving a grass-green product (5·56 g.) (Found: Pu, 45·8%; Cl, 0). This product (5·3 g.) was dissolved in hot propan-2-ol (20 c.c.); on cooling, the *solvate* (2·3 g.) was deposited [Found: Pu, 45·1. $Pu(OPr^i)_4,Pr^iOH$ requires Pu 44·7%]. In a small-scale experiment, the *iso*propoxide was interchanged with a large excess of benzene–*tert.*-butyl alcohol azeotrope; evaporation to dryness gave the tetrabutoxide. Reaction with an excess of 3-ethylpentan-3-ol proceeded as stated.

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Atomic Energy Research Establishment,
Harwell, near Didcot, Berks. [*Received, March 20th,* 1957.]

[1] Bradley, Halim, Sadek, and Wardlaw, *J.*, 1952, 2032.
[2] Bradley, Chatterjee, and Wardlaw, *J.*, 1956, 2260.
[3] Bradley, Saad, and Wardlaw, *J.*, 1954, 1091.
[4] Jones, Karmas, Martin, and Gilman, *J. Amer. Chem. Soc.*, 1956, **78**, 4285.
[5] Katz and Rabinowitz, N.N.E.S., Vol. VIII-5, McGraw-Hill, London, p. 793.

659. *Exchange of Radiochlorine between Pyridinium Chloride and Acid Chlorides in Chloroform Solution.*

By M. J. Frazer.

Recent reports of the rapid exchange of radiochlorine between chloride ion and nitrosyl chloride,[1] phosphorus oxychloride,[2,3] arsenic trichloride,[3] thionyl chloride,[2,3] and selenium oxychloride,[2,3] and the slow heterogeneous exchange with carbonyl chloride [4] prompt publication of an investigation of ^{36}Cl exchange, in chloroform solution, between pyridinium chloride and boron trichloride, phosphorus trichloride, thionyl chloride, sulphuryl chloride, and acetyl chloride. In each case complete exchange occurred at 20°, under strictly anhydrous conditions, within the time of separation (three minutes).

The results are shown in the Table. The exchange may be explained either in terms of ionisation of the acid chloride, or by the intermediate formation of an addition complex between the chloride ion and acid chloride.

Acid halide (MX)	Concn. (moles/l.) MX	Concn. (moles/l.) Cl^-	Exchange (%) MX	Exchange (%) Cl^-	Acid halide (MX)	Concn. (moles/l.) MX	Concn. (moles/l.) Cl^-	Exchange (%) MX	Exchange (%) Cl^-
BCl_3	0·040	0·010 *	98	99	$SOCl_2$	0·026	0·017 *	97	102
PCl_3	0·007	0·006 *	99	97	,, ...	0·052 *	0·040	103	100
,, ...	0·013 *	0·001	100	98	,, ...	0·011	0·003 *	99	100
CH_3·COCl ...	0·057	0·056 *	100	98	SO_2Cl_2	0·015	0·224 *	97	97
					,, ...	0·044 *	0·043	98	102

* Initially active.

Experimental.—Radiochlorine was obtained in the form of 1·6N-hydrochloric acid; this was converted into hydrogen chloride which, by reaction with pyridine in anhydrous ether, gave anhydrous pyridinium chloride. Active acid chlorides were formed by the exchange reaction. The chloroform was dried ($CaCl_2$) and distilled twice. The acid chlorides were purified by fractionation.

Separation was achieved by rapid vacuum-distillation, at 20°, of the acid chloride and chloroform into a trap at −80°. Activities were measured on aqueous extracts of the pyridinium chloride residue and the acid chloride distillate, standard counting apparatus being used. Correction was made for background count. Control experiments showed no exchange with the chloroform.

In the boron trichloride experiment a white precipitate (probably $C_5H_5NH^+BCl_4^-$; see ref. 5) was obtained. Measurements in the separated excess of boron trichloride indicated exchange.

The % exchange, $100F$, was calculated from the expression, $F = \frac{S_t - S_0}{S_\infty - S_0}$, where S_0, S_t, S_∞ are the specific activities (counts/min./g.-ion of Cl^-) initially, after 3 min., and after 24 hr. respectively.

Chemistry Department, Royal Military College of Science,
Shrivenham, Swindon, Wilts. [*Received, March 21st*, 1957.]

[1] Lewis and Wilkins, *J.*, 1955, 56; 1956, 150.
[2] Masters, Potter, Ash, and Norris, *J. Amer. Chem. Soc.*, 1956, **78**, 4252.
[3] Lewis and Sowerby, *J.*, 1957, 336.
[4] Huston, *J. Inorg. Nuclear Chem.*, 1956, **2**, 128.
[5] Lappert, *Proc. Chem. Soc.*, 1957, 121.

660. *The Conversion of Fatty Acids into Aldehydes.*

By S. S. Nigam and B. C. L. Weedon.

In connection with other studies a convenient method was required for the conversion of both saturated and unsaturated fatty acids into the corresponding aldehydes. Weygand *et al.*[1-3] have shown that lithium aluminium hydride reduction of the *N*-methylanilides of a wide variety of acids gives aldehydes in good yield :

$$R\cdot CO_2H \longrightarrow R\cdot CO\cdot NMePh \longrightarrow R\cdot CHO$$

Hitherto this method has been applied only to one long chain fatty acid, *viz.* palmitic.[2] We now summarise the results obtained with five saturated acids ranging from octanoic to stearic, the ethylenic acids undec-10-enoic and oleic, and the acetylenic acids dec-9-ynoic and undec-10-ynoic. The products were characterised as their 2 : 4-dinitrophenylhydrazones. The yields were uniformly good.

Weygand *et al.*[2] state that side reactions leading to alcohols are not favoured under the experimental conditions used. Although infrared examination of our reduction products showed that alcoholic impurities were present, these could be eliminated by fractional distillation or crystallisation. The product from oleic acid possessed no absorption band at 10·3 μ, showing that no stereomutation of the (*cis*)-double bond had occurred.

Weygand's method for preparing aldehydes therefore compares favourably with those previously used in the fatty acid field (see a review by Mosettig [4]).

Experimental.—M. p.s were determined on a Kofler block and are corrected.

The general procedures used are outlined below. The properties and amounts of starting materials and products are given in the Tables.

Table 1. *Preparation of* N-*methylanilides.*

Acid	M. p.	Wt. (g.)	Acid chloride: B. p./mm.	Acid chloride: n_D/temp.	Acid chloride: Yield, %
Saturated					
Octanoic	16°	5·0	22—26°/0·1	1·4375/18°	90
Decanoic	31·5	4·5	48—52/0·2	1·4420/20	96
Tetradecanoic	54	5·7	84—90/0·1	1·4500/18	90
Octadecanoic	69—70	6·0	165—170*/10^{-5}	1·4540/23	94
Unsaturated					
Undec-10-enoic	24	18·4	74—78/0·1	1·4530/23	82
Octadec-*cis*-9-enoic	13	5·0	100—110*/10^{-5}	1·4625/21	80
Dec-9-ynoic [b]	22	23·7	58—64/0·1	1·4610/21	86
Undec-10-ynoic	43	10·0	68—70/0·1	1·4605/21	80

Acid	*N*-Methylanilide: B. p.*/10^{-5} mm.	n_D/temp.	Yield, %	Analysis †
Saturated				
Octanoic	125—135°	1·5060/20°	81	N, 6·05 (6·0)
Decanoic	125—135	1·5010/20	84	N, 5·35 (5·35)
Tetradecanoic	155—165	1·4950/20	76	N, 4·5 (4·4)
Octadecanoic	155—165 (m. p. 28) (m. p. 48) [a]	—	84	C, 80·45 (80·35); H, 11·6 (11·6); N, 3·9 (3·75)
Unsaturated				
Undec-10-enoic	185—195	1·5070/22	85	C, 79·05 (79·05); H, 9·85 (9·95)
Octadec-*cis*-9-enoic	155—165	1·4980/22	77	N, 3·8 (3·75)
Dec-9-ynoic [b]	145—155	1·5190/22	85	C, 78·8 (79·35); H, 8·85 (9·0); N, 5·55 (5·45)
Undec-10-ynoic	165—175	1·5155/18	79	C, 79·8 (79·65); H, 9·2 (9·3); N, 5·4 (5·15)

[1] Weygand and Eberhardt, *Angew. Chem.*, 1952, **64**, 458.
[2] Weygand, Eberhardt, Linden, Schäfer, and Eigen, *ibid.*, 1953, **65**, 525.
[3] Weygand and Mitgau, *Chem. Ber.*, 1955, **88**, 301.
[4] Mosettig, *Org. Reactions*, 1954, **8**, 218.

TABLE 2. *Preparation of aldehydes.*

N-Methylanilide		Aldehydic product		2 : 4-Dinitrophenylhydrazone		
	Wt. (g.)	M. p.	Yield, %	M. p.	Yield, %	Analysis †
Saturated						
Octanoic	4·0	17°	77	107° [e]	58	N, 17·6 (18·15)
Decanoic	4·0	18 [d]	90	108 [e]	74	C, 56·65 (57·15); H, 7·3 (7·2); N, 16·85 (16·65)
Dodecanoic [f] ...	2·5	44	58	—	—	
Tetradecanoic ...	1·0	23 [g]	73	108	59	N, 14·1 (14·3)
Hexadecanoic [h] ...	—	—	—	108	98	
Octadecanoic ...	1·0	63	70	110	56	N, 12·75 (12·5)
Unsaturated						
Undec-10-enoic...	4·0	—	69	92 [j]	57	
Oleic	2·4	(b. p. 125—130*/10^{-5} mm.)	69	68 [k]	55	
Dec-9-ynoic [b] ...	21·0	—	85	73·5 [l]	56	
Undec-10-ynoic	2·6	—	83	86	60	N, 16·45 (16·2)

* Bath temp. † Calculated figures shown in parentheses.

[a] Crystallised from methanol. [b] See Nigam and Weedon, *J.*, 1956, 4049. [c] "Organic Reagents for Organic Analysis," Hopkin and Williams Ltd., Essex, 1950, gives m. p. 106°. [d] Semicarbazone, m. p. 102°. *Op. cit.*[c] gives m. p. 102°. [e] *Op. cit.*[c] gives m. p. 104°. [f] Quoted from Shah, Ph.D. Thesis, London, 1955. [g] Stephen, *J.*, 1925, **127**, 1874, gives m. p. 23°. [h] Quoted from Weygand *et al.*[2]. [i] Polymer. Feulgen and Behrens, *Z. physiol. Chem.*, 1928, **177**, 221, give m. p. 63·5°. [j] Grundmann, *Annalen*, 1936, **524**, 31, gives m. p. 91°. [k] *Idem, ibid.*, gives m. p. 68°. [l] Walborsky, Davis, and Howton, *J. Amer. Chem. Soc.*, 1951, **73**, 2590, give m. p. 73—74°.

Acid chlorides. The acid and thionyl chloride (2·2 mol.) were boiled gently under reflux until evolution of hydrogen chloride ceased. The excess of thionyl chloride was distilled off, and the residual acid chloride was then distilled under reduced pressure.

N-*Methylanilides.* Methylaniline (1·2 mol.) in an equal volume of pyridine was added slowly to a cooled (ice-bath) solution of the acid chloride in benzene (3 vol.). The mixture was shaken occasionally and kept at 20° for 30 min. Water was added and the product extracted with benzene. The extract was washed thoroughly with 2N-hydrochloric acid, then with water, and dried (Na_2SO_4) and evaporated. The *N*-methylanilide was distilled under reduced pressure in a short-path still.

Aldehydes. Lithium aluminium hydride (0·33 mol.) in ether was added slowly to a cooled (0°) and well-stirred solution of the *N*-methylanilide in ether. Stirring was continued at 0° for a further 3 hr., and the excess of lithium aluminium hydride was then destroyed by the addition of ethyl acetate. 2N-Hydrochloric acid was added and the product was extracted with ether. The extract was washed thoroughly with 2N-hydrochloric acid, then with water and dried (Na_2SO_4) and evaporated.

The crude products were characterised directly; some were purified by distillation or crystallisation.

Microanalyses and spectral measurements were carried out in the microanalytical (Mr. F. H. Oliver) and spectrographic laboratories (Mr. R. L. Erskine) of this Department. One of the authors (S. S. N.) thanks the University of Saugar, India, for study leave.

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661. *The Reactions of Methyl Radicals with Thiols.*

By J. A. KERR and A. F. TROTMAN-DICKENSON.

THE high reactivity of thiols with free radicals is well known; for this reason thiols are extensively used as chain-transfer agents in polymerisations. Little quantitative work on the kinetics of their reactions in solutions has been reported and still less appears to have been done on the gas phase. This Note records an attempt to investigate the kinetics of the attack of methyl radicals on thiols:

$$CH_3\cdot + RSH = CH_4 + RS\cdot \quad \ldots\ldots\ldots\ldots (1)$$

The photolysis of acetone was used to provide methyl radicals. In general the procedure of Trotman-Dickenson and Steacie [1] was followed. Photolysis was carried out in a Pyrex vessel so that no light was absorbed by the thiols. The gases produced were analysed with a standard low-temperature distillation apparatus; carbon monoxide was oxidised over copper oxide.

During the photolysis methane, ethane, and carbon monoxide were produced by the following reactions:

$$CH_3\cdot CO\cdot CH_3 + h\nu = CH_3\cdot CO\cdot + CH_3\cdot \quad \ldots\ldots\ldots\ldots (2)$$

$$CH_3\cdot CO\cdot = CH_3\cdot + CO \quad \ldots\ldots\ldots\ldots (3)$$

$$CH_3\cdot + RSH = CH_4 + RS\cdot \quad \ldots\ldots\ldots\ldots (1)$$

$$CH_3\cdot + CH_3\cdot CO\cdot CH_3 = CH_4 + \cdot CH_2\cdot CO\cdot CH_3 \quad \ldots\ldots\ldots\ldots (4)$$

$$2CH_3\cdot = C_2H_6 \quad \ldots\ldots\ldots\ldots (5)$$

It can be shown that:

$$\frac{k_1}{k_5^{\frac{1}{2}}} = \frac{R_{CH_4} - (k_4/k_5^{\frac{1}{2}})[CH_3\cdot CO\cdot CH_3]R^{\frac{1}{2}}_{C_2H_6}}{R^{\frac{1}{2}}_{C_2H_6}[RSH]}$$

where the k's are the rate constants of the reactions and R_{CH_4} and $R_{C_2H_6}$ are the rates of formation of the products. Application of this equation involves a knowledge of k_4. The value of this rate constant is uncertain at less than 100° because methane is also formed by additional reactions, probably including the reactions of the acetyl radical.[2] The present experiments could not be carried out at temperatures as high 100° because the rate of reaction (1) was so great that it was impossible to obtain reproducible results. Accordingly all the rate constants were determined at 30°. The uncertainties in k_4 were unimportant because it is about one-thousand times less than k_1. The results obtained with the higher thiols were not very reproducible. The mean values of 10^{-7} (mole^{-1} cm.^{3} sec.$^{-1}$), based on the value of k_5 advocated by Shepp,[3] are:

MeSH 1·8; EtSH 3·5; Pr^{i}SH 4·1; Bu^{t}SH 5·9

This order of reactivity is the same as that deduced from the photodecomposition of acetaldehyde catalysed by thiols.[4] If $\log_{10} A$ (mole^{-1} cm.^{3} sec.$^{-1}$) for these reactions is of the order of 11·3, as it is for many reactions of methyl, then the activation energies of these reactions lie between 5·6 and 4·9 kcal./mole.

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THE UNIVERSITY, EDINBURGH. [*Received, April 1st*, 1957.]

[1] Trotman-Dickenson and Steacie, *J. Chem. Phys.*, 1951, **19**, 329.
[2] Ausloos and Steacie, *Canad. J. Chem.*, 1955, **33**, 47.
[3] Shepp, *J. Chem. Phys.*, 1956, **24**, 939.
[4] Birrell, Smith, Trotman-Dickenson, and Wilkie, *J.*, 1957, 2807.

662. *The Action of Hydrogen Chloride on the Nickel and Palladium Derivatives of Dimethylglyoxime—A Correction.*

By A. G. Sharpe and D. B. Wakefield.

The addition of hydrogen chloride to bisdimethylglyoximepalladium(II) was previously reported [1] to give the pale yellow compound $[Pd(DH_2)_2Cl_2]$,* which yielded a diacetyl derivative $[Pd(DHAc)_2Cl_2]$; both substances were non-conductors in acetone solution, neither could be purified by recrystallisation, and the formulæ were based on a mistaken analogy with the more closely investigated nickel compounds.

Further investigations have shown that when bisdimethylglyoximepalladium(II) is treated with cold concentrated hydrochloric acid, the previously unknown pale yellow compound $[Pd(DH_2)Cl_2]$, which is a non-conductor in acetone and does not react with acetyl chloride, is produced. Comparison of *X*-ray powder photographs indicates that the product formulated as $[Pd(DH_2)_2Cl_2]$, although apparently homogeneous, is a mixture of $[Pd(DH_2)Cl_2]$ and dimethylglyoxime, and that the supposed acetyl derivative is a mixture of $[Pd(DH_2)Cl_2]$ and diacetyldimethylglyoxime. The analogous compound $[Pd(RH_2)Cl_2]$ * has been prepared (i) by the action of hydrochloric acid on bisethylmethylglyoximepalladium(II), and (ii) from excess of potassium chloropalladite and an acidic solution of ethylmethylgloxime. In this instance the solubilities of the complexes $[Pd(RH_2)Cl_2]$ and $Pd(RH)_2$ appear to be such that even in dilute hydrochloric acid the former is precipitated.

The structures assigned to the nickel complexes are not affected by this re-interpretation: the compound $[Ni(DH_2)Cl_2]$ has previously been reported [2] (as a brown solid); and *X*-ray powder photography shows that $[Ni(DH_2)_2Cl_2]$, which is pale blue, is structurally different from the material obtained by interaction of hydrogen chloride and bisdimethylglyoxine palladium.

Experimental.—Bisdimethylglyoximepalladium(II) was shaken with cold concentrated hydrochloric acid; the pale yellow *product* was washed with the acid and dried *in vacuo* at room temperature (Found: Pd, 35·9; C, 16·5; H, 2·7. $C_4H_8O_2N_2Cl_2Pd$ requires Pd, 36·4; C, 16·3; H, 2·7%).

Bischloroethylmethylglyoximepalladium(II) was prepared similarly from bisethylmethylglyoximepalladium(II) (Found: C, 19·7; H, 3·4. $C_5H_{10}N_2O_2Cl_2Pd$ requires C, 19·5; H, 3·2%)

University Chemical Laboratory, Cambridge. [*Received, April 3rd*, 1957.]

* In this communication DH_2 = dimethylglyoxime, RH_2 = ethylmethylglyoxime.

[1] Sharpe and Wakefield, *J.*, 1957, 496.
[2] Paneth and Thilo, *Z. anorg. Chem.*, 1925, **147**, 196.

663. *Bis-2 : 3-dichloropropyl Disulphide.*

By W. Davies and A. V. Robertson.

3-Chloro-1-mercaptopropan-2-ol [1,2] with thionyl chloride gives about a 10% yield of crystals, m. p. 70—71°. This substance is also formed in 97% yield by bromine oxidation of 2 : 3-dichloropropane-1-thiol,[2,3] proving that the product must be bis-2 : 3-dichloropropyl disulphide. On the other hand, this structure was assigned without proof, by

[1] Sjöberg, *Ber.*, 1941, **74**, 64.
[2] Davies and Savige, *J.*, 1951, 774.
[3] Culvenor, Davies, and Heath, *J.*, 1949, 282.

Pope and Smith,[4] to an oil, b. p. 190°/11 mm., made by addition of sulphur monochloride to allyl chloride. On repetition of this preparation a small yield of the above crystals was obtained from the oily product. The oil is undoubtedly a mixture, containing both *meso* and racemic forms of the bisdichloropropyl disulphide rather than much of the isomeric *iso*propyl disulphide derivative. Hence the sulphonates obtained by oxidation of the oil probably have the *n*-propyl structure Pope and Smith assigned to them. The stereochemistry of the crystals, m. p. 70—71°, has not been examined.

Syntheses of Bis-2 : 3-dichloropropyl Disulphide.—(1) *From 3-chloro-1-mercaptopropan-2-ol.* 3-Chloro-1-mercaptopropan-2-ol (10 g.) reacted violently with thionyl chloride (20 g.; 100% excess), and after the mixture had been refluxed on a water-bath until evolution of hydrogen chloride ceased (2 hr.), the excess of thionyl chloride was removed at 30 mm. The part of the residue which solidified in the refrigerator overnight crystallised (charcoal) from light petroleum in needles (1·3 g., 10%), m. p. 70—71° after recrystallisations from ligroin or ethanol (Found : C, 25·1; H, 3·4. $C_6H_{10}Cl_4S_2$ requires C, 25·0; H, 3·5%).

(2) *From 2 : 3-dichloropropane-1-thiol.* Bromine (3·0 g.) was added dropwise to a stirred solution of 2 : 3-dichloropropane-1-thiol (5·0 g.) in light petroleum (25 ml.), and the solid was washed with water and recrystallised from light petroleum. The product (4·8 g., 97%), had m. p. and mixed m. p. 69—70° with specimens of *bis-2 : 3-dichloropropyl disulphide*, from methods (1) and (3) (Found: C, 25·1; H, 3·6%).

(3) *Pope and Smith's method.*—A mixture of freshly distilled allyl chloride (30·6 g., 0·4 mole) and freshly distilled sulphur monochloride (27 g., 0·2 mole) gradually developed a deep shade of orange (contrast Pope and Smith, *loc. cit.*) during 13 days at room temperature (17°). Attempted distillation caused extensive charring with evolution of hydrogen chloride, and only 33 g. of a dark oil (b. p. 190—196°/20 mm.) were obtained. At 0·3 mm., a low-boiling fraction (8 g.; b. p. 40—60°) was removed from this material, followed by a yellow oil (14·8 g.; b. p. 100—160°), leaving an undistillable residual dark viscous oil (9·6 g.). After 12 hr. at about 0°, both the high-boiling fraction and the residue deposited solid material (1·3 g. and 1·1 g. respectively) which crystallised from light petroleum in needles, m. p. 69—70° (Found: S, 22·1. Calc. for $C_6H_{10}Cl_4S_2$: S, 22·2%), identical (mixed m. p.) with the products obtained in methods (1) and (2).

This very low yield (4%) was not increased by performing the first distillation at 0·1 mm. pressure. However, crystallisation was initiated by seeding another batch of mixed allyl and sulphur chlorides which had been kept in the dark for two weeks, and after a further 4 weeks an 8% yield of the almost pure crystals (m. p. 65—68°) was obtained.

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[4] Pope and Smith, *J.*, 1922, 1166.