# NOTES.

## 89. *Electronic Correlation of Molar Refraction.*

By Santi R. Palit and G. R. Somayajulu.

The molar refraction of a given molecule is customarily treated as the sum of the refractions of atoms, groups, and bonds in it. However, the molar refraction $R$ can also be correlated with the number of electrons, $n$, in the molecule, and this gives additional information about the electronic structure of the groups present. We take the methylene group as standard, for which the average refraction, $R_e$, per electron is 0·581 c.c. at 20° in sodium D light. The refraction $R_x|X$ of any group, containing $n_x$ electrons, attached to the methylene group is given by

$$R_x = n_x R_e - \rho_x \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (1)$$

where $\rho_x$ is an empirical constant characteristic of the group. In general, for a molecule

$$R = nR_e - \sum \rho_x \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (2)$$

Using eqn. (2) and the data of Vogel and his co-workers,[1] we have calculated $\rho$ for various atoms and groups in organic compounds (see Table). The calculated average deviations are generally low, and the agreement between observed and calculated values of $R$ are usually good. Even so, the practical calculation of molar refractivities is usually more easily done in the ordinary way from those of the groups present, and we have recorded such values in the Table which we regard as better than those at present in the literature. The interest lies in the significance of $\rho$, which is brought out by rewriting

| Atom or group | Refraction (c.c.) | $\rho$ (eqn. 2) | Average deviation of $\rho$ | $\sigma$ (eqn. 3) | Atom or group | Refraction (c.c.) | $\rho$ (eqn. 2) | Average deviation of $\rho$ | $\sigma$ (eqn. 3) |
|---|---|---|---|---|---|---|---|---|---|
| $\diagdown CH_2$ | 4·648 | 0 | | 0 | $-NH_2$ | 4·449 | 0·78 | 0·04 | 0·087 |
| $-H$ | 0·991 | −0·41 | 0·02 | −0·410 | $\diagdown NH$ | 3·638 | 1·01 | 0·05 | 0·126 |
| $-F$ | 0·799 | 4·43 | 0·05 | 0·493 | $\geq N$ | 2·787 | 1·28 | 0·11 | 0·183 |
| $-Cl$ | 5·857 | 4·02 | 0·03 | 0·236 | $-NO_2$ | 6·723 | 6·64 | 0·01 | 0·289 |
| $-Br$ | 8·765 | 11·57 | 0·02 | 0·331 | $-NO_3$ | 9·941 | 8·07 | 0·04 | 0·260 |
| $-I$ | 13·953 | 16·84 | 0·04 | 0·318 | $-O{\cdot}NO$ | 7·233 | 6·13 | 0·03 | 0·266 |
| $-O-$ | 1·748 | 2·90 | 0·03 | 0·362 | $\diagdown N{\cdot}NO$ | 7·882 | 4·90 | 0·06 | 0·223 |
| $-S-$ | 7·936 | 1·36 | 0·05 | 0·085 | $-C{\equiv}N$ | 5·453 | 2·10 | 0·03 | 0·162 |
| $-S-S-$ | 16·072 | 2·52 | 0·04 | 0·079 | $-SCN$ | 13·519 | 3·43 | 0·06 | 0·118 |
| $-OH$ | 2·569 | 2·66 | 0·03 | 0·296 | $-C_6H_{11}$ | 26·717 | 0·59 | 0·08 | 0·012 |
| $-SH$ | 8·767 | 1·11 | 0·03 | 0·065 | $-C_5H_9$ | 22·119 | 0·54 | 0·03 | 0·014 |
| $-CHO$ | 5·965 | 2·85 | 0·05 | 0·190 | $-C_4H_7$ | 17·831 | 0·18 | 0·03 | 0·006 |
| $-CO_2H$ | 7·263 | 6·10 | 0·05 | 0·265 | $-C_3H_5$ | 13·473 | −0·11 | 0·03 | −0·005 |
| $\diagdown CO$ | 4·644 | 3·49 | 0·04 | 0·249 | $-C_6H_5$ | 25·471 | −1·65 | 0·03 | −0·040 |
| $-O{\cdot}OCH$ | 7·513 | 5·85 | 0·06 | 0·254 | $-CH{=}CH_2$ | 9·815 | −1·10 | 0·05 | −0·073 |

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[1] Vogel, *J.*, 1945, 133; 1948, 607, 610, 616, 624, 644, 654, 1804, 1809, 1820, 1825, 1833; Jeffery and Vogel, *J.*, 1948, 658, 674; Vogel, Cresswell, Jeffrey, and Leicester, *J.*, 1952, 514.

eqns. (1) and (2) as (3) and (4), where $\sigma$ is now a constant representing the average value of $\rho$ per electron for each group and may be taken as representing that part of the expected

$$R_x = n_x(R_e - \sigma_x) \quad . \quad . \quad (3); \qquad R = \sum n_x(R_e - \sigma_x) \quad . \quad (4)$$

refraction which each electron of the group fails to show. This failure may result from the following factors: (i) the inner-shell electrons of an atom are usually little polarised and contribute little to the total refraction; (ii) electrons forming bonds contribute more than valency-shell electrons not so engaged; (iii) electrons forming bonds show less refraction than expected when the bound atoms differ in electronegativity [an expression similar to Schomaker and Stevenson's [2] expression for bond length can be written for the refraction $R_{A\text{-}B}$ of a bond A–B

$$R_{A\text{-}B} = \tfrac{1}{2}(R_{A\text{-}A} + R_{B\text{-}B}) - \gamma|x_A - x_B|$$

where $\gamma$ is an empirical constant ($\simeq 0{\cdot}37$ for single bonds) and $x_A$, $x_B$ are the electronegativities of atoms A and B]; and (iv) delocalisation and hybridisation further affect the refraction of the bonding electrons. The effect of each of these factors alone on $\sigma$ cannot be determined yet, but in essence $\sigma$ represents the effect of nuclear charge on the optical polarisation of electrons, the effect being greater the more electronegative the atom (see values for F, O, and N in the Table). Among the halogens, however, chlorine is exceptional.

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[*Received, January 27th*, 1958.]

[2] Schomaker and Stevenson, *J. Amer. Chem. Soc.*, 1941, **63**, 37.

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## 90. *Ion-exchange Studies of Phosphates. Part IV.* Ion-exchange and* pH-*Titration Studies of Copper–Triphosphate Complexes in Solution.*

By C. HEITNER-WIRGUIN, J. E. SALMON, and E. MAYER.

HETEROMETRIC studies by Bobtelsky and Kertes [1] indicated the formation of two triphosphate complexes of copper, namely, $[Cu(P_3O_{10})]^{3-}$ and $[Cu_5(P_3O_{10})_3]^{5-}$. The stability constants for the formation of the mononuclear complexes with one and two triphosphate ligands in nitrate media, and also for mixed ammine–triphosphate complexes, have been quoted.[2] Evidence is now given which indicates that in the presence of chloride mixed chloro-triphosphato-complexes may be formed.

*Experimental.—Ion exchange.* The batch technique described by Salmon [3] was employed with 50 ml. of solution and 1·000 g. of anion-exchanger DeAcidite FF.

pH-*Titrations.* The method described previously [4] was used.

*Analyses.* Copper was determined by an EDTA method; [5] triphosphate, after conversion into orthophosphate, by weighing as phosphomolybdate; and nitrate volumetrically.[6]

*Reagents.* Sodium triphosphate was recrystallised four times from 1 : 4 alcohol–water.[7] Other reagents were of analytical grade. Sodium triphosphate–copper triphosphate solutions were prepared by passage of a sodium triphosphate solution through a column of Zeo-Karb 225 in the copper form.

*Results.*—Cation-exchange experiments failed to show the presence of cationic complexes,

* Part III, *J.*, 1959, 459.

[1] Bobtelsky and Kertes, *J. Appl. Chem.*, 1955, **5**, 675.

[2] Bjerrum, Schwarzenbach, and Sillen, " Stability Constants of Metal-Ion Complexes," Part II, *Chem. Soc. Special Publ.*, No. 7, 1958, p. 62.

[3] Salmon, *Rev. Pure Appl. Chem.* (*Australia*), 1956, **6**, 24.

[4] Holroyd and Salmon, *J.*, 1956, 269.

[5] Flaschka and Abdine, *Chemist-Analyst*, 1956, **2**, 45.

[6] Leithe, *Anal. Chem.*, 1948, **20**, 1082.

[7] Quimby, *J. Phys. Chem.*, 1954, **58**, 603.

and all remaining experiments were carried out with DeAcidite FF. Experiments with sodium triphosphate solution (0·02—0·20M; pH at equilibrium 9·1—9·4) and chloride-form resin showed that the mean charge on the triphosphate ions sorbed was between 4 and 5 units, in accord with the value of $pK_5 = 8{\cdot}73$ for triphosphoric acid.[8] The results obtained with solutions containing sodium, copper, triphosphate, and other ions and with the anion-exchanger in various forms are shown in the Table.

Slight inflections in the pH-titration curves were possibly indicative of the formation of 1 : 2, 1 : 1, and 2 : 1 ($P_3O_{10}$ : Cu) complexes.

*Discussion.*—The fact that in the ion-exchange experiments the ratio $N_{\text{triP}} : N_{\text{Cu}}$ (see Table) rarely rose above 2, even for the higher mole ratios $P_3O_{10}$ : Cu in solution, indicated that complexes containing more than two triphosphate ligands were not readily formed, particularly when allowance was made for the fact that $N_{\text{triP}}$ included both free and bound triphosphate. The pH-titration experiments likewise failed to provide evidence for complexes with more than two triphosphate groups.

*Sorption of copper and triphosphate from mixed solutions of copper salts* (M/10) *and sodium triphosphate* (M/10).

| Aqueous phase | | | Resin phase | |
|---|---|---|---|---|
| Initial | | | | |
| mole ratio $P_3O_{10}$ : Cu | other ions present | Final pH | $N_{\text{Cu}}$ * | $\frac{N_{\text{triP}}}{N_{\text{Cu}}}$ * |
| 4·4 (*a*) | — (*c*) | 8·56 | 0·135 | 2·07 |
| 4·4 (*b*) | — (*c*) | 8·76 | 0·125 | 1·93 |
| 2·0 | $NO_3^-$ (*d*) | 7·77 | 0·053 | 1·75 |
| 2·6 | $NO_3^-$ (*d*) | 7·98 | 0·055 | 2·09 |
| 3·0 | $NO_3^-$ (*d*) | 8·15 | 0·035 | 2·38 |
| 4·0 | $NO_3^-$ (*d*) | 8·50 | 0·037 | 2·42 |
| 1·3 | $NO_3^-$, $Cl^-$ (*e*) | 6·65 | 0·100 | 0·97 |
| 2·0 | $NO_3^-$, $Cl^-$ (*e*) | 7·18 | 0·116 | 1·04 |
| 2·0 | $NO_3^-$, $Cl^-$ (*e*) | 7·06 | 0·082 | 1·35 |
| 2·7 | $NO_3^-$, $Cl^-$ (*e*) | 7·94 | 0·082 | 1·61 |
| 3·0 | $NO_3^-$, $Cl^-$ (*e*) | 8·20 | 0·084 | 1·85 |
| 4·0 | $NO_3^-$, $Cl^-$ (*e*) | 8·62 | 0·076 | 1·77 |
| 6·0 | $NO_3^-$, $Cl^-$ (*e*) | 8·79 | 0·076 | 2·29 |
| 1·3 | $Cl^-$ (*f*) | 7·29 | 0·237 | 1·01 |
| 2·0 | $Cl^-$ (*f*) | 8·37 | 0·191 | 1·18 |
| 4·0 | $Cl^-$ (*f*) | 8·55 | 0·155 | 1·38 |

(*a*) & (*b*) Cu concentrations 0·02 and 0·004M respectively; (*c*) some $Cl^-$ present in triphosphate form resin; (*d*) as $Cu(NO_3)_2$ and nitrate form resin; (*e*) nitrate as $Cu(NO_3)_2$, chloride as chloride form resin; (*f*) as $CuCl_2$ and chloride form resin.

* $N_{\text{Cu}}$ and $N_{\text{triP}}$ indicate moles of Cu and triphosphate respectively sorbed per g.-equivalent of resin.

The ion-exchange results for the system containing neither nitrate nor chloride were consistent with the sorption of a complex with one triphosphate group, or a mixture of this and the one with two triphosphate groups, together with free triphosphate. Addition of nitrate (as copper nitrate and nitrate-form resin) resulted in a strong sorption of nitrate and reduced sorption of the copper triphosphate complex. However, the partial replacement of the nitrate by chloride (by use of chloride-form in place of nitrate-form resin) resulted in a marked increase in $N_{\text{Cu}}$ and lowering of the ratio $N_{\text{triP}} : N_{\text{Cu}}$ for any given mole ratio of $P_3O_{10}$ : Cu in the original solution. These effects were even more marked when the nitrate was entirely replaced by chloride, the values of $N_{\text{Cu}}$ being nearly four times as great as, and the values of $N_{\text{triP}} : N_{\text{Cu}}$ being nearly 40% less than, for the corresponding solutions containing nitrate only.

It appears that when chloride is present a 1 : 1 complex is formed which is more strongly sorbed by the resin in competition with other ions than are the complexes formed in the absence of chloride. A possible deduction is that, under these conditions, mixed chloro-triphosphato-complexes are formed.

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[*Received, May* 25*th*, 1959.]

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[8] Watters, Laughran, and Lambert, *J. Amer. Chem. Soc.*, 1954, **78**, 4855.

# 91. Organic Fluorine Compounds. Part XIII.* An Ester of "Phospho-enol-fluoropyruvic Acid" [1-Alkoxycarbonyl-2-fluorovinyl Dialkyl Phosphate] and Related Compounds.

By Ernst D. Bergmann and Israel Shahak.

THE biological properties of fluoropyruvic acid[1] and the central position of its enol phosphate ("phosphoenol-pyruvate") in carbohydrate metabolism made it interesting to prepare a "phosphoenol-fluoropyruvate" (1-alkoxycarbonyl-2-fluorovinyl dialkyl phosphate), $(RO)_2P(O)O{\cdot}C(CO_2R'){:}CHF$, for biological testing. A convenient method appeared to be provided by the recently discovered reaction between ethyl bromopyruvate and triethyl phosphite:[2]

$$P(OR)_3 + CH_2Br{\cdot}CO{\cdot}CO_2R' \longrightarrow (RO)_2P(O){\cdot}O{\cdot}C(CO_2R'){:}CH_2 + RBr$$

It was necessary to devise a practical synthesis of bromofluoropyruvic acid, $BrFCH{\cdot}CO{\cdot}CO_2H$; fluoropyruvic acid or its ester can only be brominated with great difficulty with *N*-bromosuccinimide. The sodium derivative of the enol of ethyl ethoxalylfluoroacetate)[3] was brominated, to give a 46% yield of ethyl bromoethoxalylfluoroacetate. This ester was hydrolysed by hydrochloric acid to bromofluoropyruvic acid in 35% yield. When the methyl ester of this acid was treated with triethyl phosphite, the desired com pound was obtained in 50% yield, as a colourless liquid which distils without decomposition *in vacuo*.

Analogously, the phospho-enol derivatives were prepared from ethyl bromoethoxalylfluoroacetate and from ethyl α-bromo-αγ-difluoroacetoacetate.

The bromofluoro-keto-esters used in this study reacted smoothly with *p*-nitro- and 2,4-dinitro-phenylhydrazine; the products have lost their halogen and contain two hydrazine residues per molecule. The group CFBr reacts like carbonyl; thus, ethyl bromoethoxalylfluoroacetate gave the bis-2,4-dinitrophenylhydrazone and the known[4] bis-*p*-nitrophenylhydrazone of diethyl dioxosuccinate; methyl bromofluoropyruvate and ethyl α-bromo-αγ-difluoroacetoacetate gave the bis-2,4-dinitrophenylhydrazones of ethyl mesoxalaldehydate and ethyl γ-fluoro-αβ-dioxobutyrate, respectively.

*Experimental.*—*Ethyl bromoethoxalylfluoroacetate.* To a suspension of sodium methoxide (14·4 g., 0·3 mole) in benzene (150 ml.), diethyl oxalate (44 g., 0·3 mole) was added during 10 min. with cooling, followed by ethyl fluoroacetate (31·8 g., 0·3 mole). After 36 hr. at room temperature, the azeotropes of benzene with methyl and ethyl alcohol were distilled off in a short column until the b. p. of benzene was reached. Then the product was cooled to room temperature and treated dropwise with bromine, at such a rate that the temperature did not exceed 50°. When the colour of bromine remained, the product was washed with water and sodium sulphite solution, dried, and distilled. The *ester* (38 g., 46%) boiled at 105—107°/2·5 mm.; it gave no reaction with ferric chloride solution (Found: C, 32·8; H, 3·8; F, 6·2; Br, 30·0. $C_8H_{10}O_5FBr$ requires C, 33·7; H, 3·5; F, 6·7; Br, 28·1%). It contained a trace of ethyl dibromoethoxalylacetate (b. p. 165—168°/20 mm.)[5] not removable by distillation.

When 2,4-dinitrophenylhydrazine reagent was added to the ester, *diethyl bis-2,4-dinitrophenylhydrazonosuccinate* was precipitated. It melted at 240—241° after recrystallization from butyl alcohol (Found: C, 43·1; H, 3·0; N, 20·5. $C_{20}H_{18}O_{12}N_8$ requires C, 42·7; H, 3·2; N, 20·0%). With *p*-nitrophenylhydrazine, the corresponding *bis*-p-*nitrophenylhydrazone* was obtained, which had the m. p. (189°) indicated by Chattaway and Adair.[4]

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* Part XII, Bergmann, Cohen, and Shahak, *J.*, 1959, 3286.

[1] Cf., *inter alia*, Blank and Mager, *Experientia*, 1954, **10**, 77; Avi-Dor and Lipkin, *J. Biol. Chem.*, 1958, **233**, 69.

[2] Cramer and Gaertner, *Chem. Ber.*, 1958, **91**, 704; Pudovik and Biktirnirova, *Zhur. obshchei Khim.*, 1958, **28**, 1496; Pudovik and Chebotareva, *ibid.*, p. 2492; Arbuzov, Vinogradova, and Polezhaeva, *Doklady Akad. Nauk S.S.S.R.*, 1958, **121**, 641.

[3] Blank, Mager, and Bergmann, *Bull. Res. Council Israel*, 1957, **3**, 101.

[4] Chattaway and Adair, *J.*, 1932, 1022; Chugreeva, *Zhur. obshchei Khim.*, 1958, **28**, 1365, described the derivatives of dioxosuccinic acid.

[5] Wislicenus, *Ber.*, 1889, **22**, 2912.

*Bromofluoropyruvic acid.* Ethyl bromoethoxalylfluoroacetate (57 g.) was stirred with concentrated hydrochloric acid (200 ml.) for 3 hr. at room temperature. The oil disappeared and a very small amount of a solid was precipitated, which melted at 116° after recrystallization from alcohol and was identified by analysis as dibromopyruvic acid (lit.,[6] m. p. 93°) (Found: C, 14·2; H, 0·9; Br, 65·2. Calc. for $C_3H_2O_3Br_2$: C, 14·6; H, 0·8; Br, 65·0%). (We have not been able to reproduce the low m. p. recorded in the literature.) The acidic solution was concentrated at 15 mm. and the residue distilled at 1·5 mm. The portion boiling at 70—100°, which contained some oxalic acid, was dissolved in a little benzene, filtered from the (insoluble) oxalic acid and redistilled. *Bromofluoropyruvic acid* (13 g., 35%) boiled at 90—92°/1·5 mm. (Found: C, 19·2; H, 1·0; F, 9·9; Br, 43·0. $C_3H_2O_3BrF$ requires C, 19·5; H, 1·1; F, 10·3; Br, 43·2%).

*Methyl bromofluoropyruvate.* The preceding acid (12 g.) was treated in ether (50 ml.) with a slight excess of diazomethane. The *ester* (12 g., 90%) boiled at 94—95°/20 mm. (Found: C, 23·8; H, 2·2; F, 9·9; Br, 40·5. $C_4H_4O_3BrF$ requires C, 24·1; H, 2·0; F, 9·5; Br, 40·2%).

The *bis-2,4-dinitrophenylhydrazone* of methyl mesoxaldehydate, prepared from methyl bromofluoropyruvate and 2,4-dinitrophenylhydrazine, had m. p. 254° (Found: C, 40·6; H, 2·9; N, 23·6. $C_{16}H_{12}O_{10}N_8$ requires C, 40·3; H, 2·5; N, 23·0%).

*Diethyl phospho-enol derivative of methyl fluoropyruvate.* To methyl bromofluoropyruvate (12 g.) in benzene (30 ml.), triethyl phosphite (10 g.) in benzene (20 ml.) was added slowly (exothermic reaction). After 1 hr. at room temperature, the solution was concentrated and the *product* (6·9 g., 50%) distilled *in vacuo* (b. p. 135°/1·3 mm.) (Found: C, 37·9; H, 5·8; F, 7·0; P, 11·5. $C_8H_{14}O_6FP$ requires C, 37·5; H, 5·5; F, 7·4; P, 12·1%).

*Diethyl phospho-enol derivative of ethyl ethoxalylfluoroacetate.* Triethyl phosphite (8·3 g.) and ethyl bromoethoxalylfluoroacetate (14·3 g.) in benzene (40 ml.) gave, in 1 hr., the *phosphate* (8·6 g., 50%), b. p. 155—157°/1·2 mm. (Found: C, 41·9; H, 6·2; F, 5·3; P, 9·4. $C_{12}H_{20}O_8FP$ requires C, 42·1; H, 5·8; F, 5·6; P, 9·1%).

*Ethyl α-bromo-αγ-difluoroacetoacetate.* The sodium derivative of the enol of ethyl αγ-difluoroacetoacetate was prepared from ethyl fluoroacetate (21 g.) and sodium hydride (4·8 g.) in ether (150 ml.)[7] and isolated after 20 hr. by addition of light petroleum (b. p. 60—90°; 300 ml.) and filtration. To its suspension in carbon tetrachloride (100 ml.) bromine was added slowly until the colour of the halogen no longer disappeared. The solution was washed with water and sodium sulphite solution, dried, and distilled. The *bromo-ester* (12 g., 25%) boiled at 100—102°/2 mm. (Found: C, 29·7; H, 2·6; F, 15·2. $C_6H_7O_3BrF_2$ requires C, 29·4; H, 2·9; F, 15·5%). With the hydrazine it gave *ethyl αβ-bis-2,4-dinitrophenylhydrazono-γ-fluorobutyrate*, m. p. 262° (decomp.) (Found: C, 41·0; H, 3·0; N, 20·9; F, 3·4. $C_{18}H_{15}O_{10}N_8F$ requires C, 41·4; H, 2·9; N, 21·4; F, 3·6%).

With triethyl phosphite (4 g.) in benzene (15 ml.), it (10 g.) gave, in 1 hr., the *phosphate* (5 g., 50%), b. p. 128—130°/1·1 mm. (Found: C, 39·6; H, 5·5. $C_{10}H_{17}O_6F_2P$ requires C, 39·7; H, 5·6%).

The phosphorus and fluorine in the phosphates were determined by the method of Eger and Lipke.[8]

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[*Received, June 1st,* 1959.]

[6] Beilstein's " Handbuch," Vol. III, p. 624; 2nd Suppl., p. 409.

[7] Blank, Mager, and Bergmann, *J.*, 1955, 2190; cf. ref. 3.

[8] Eger and Lipke, *Analyt. Chim. Acta*, 1959, **20**, 548.

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# **92.** *Organic Fluorine Compounds. Part XIV.*[1] *Some Pyrimidines Derived from Fluoroacetamidine.*

By ERNST D. BERGMANN and SASSON COHEN.

SOME 2-fluoromethylpyrimidines have been prepared starting from fluoroacetamidine hydrochloride.[2] With diethyl malonate and methylmalonate, 2-fluoromethyl-4,6-dihydroxypyrimidine (I; R = H) and 2-fluoromethyl-4,6-dihydroxy-5-methylpyrimidine

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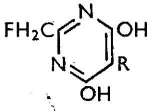
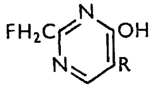
[1] Part XIII, Bergmann and Shahak, preceding paper.

[2] Buckle, Heap, and Saunders, *J.*, 1949, 912.

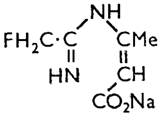
(I; R = Me), and with ethyl α-formylpropionate 2-fluoromethyl-4-hydroxy-5-methylpyrimidine (II; R = Me) were obtained. Ethyl β-ethoxy-α-formylpropionate gave 5-ethoxymethyl-2-fluoromethyl-4-hydroxypyrimidine (II; R = EtO·CH$_2$). Ethyl acetoacetate condensed under the usual operating conditions to give only sodium β-fluoroacetamidoylaminocrotonate (II), which was cyclized by sodium methoxide solution to the desired 2-fluoromethyl-4-hydroxy-6-methylpyrimidine (IV). The 4-hydroxy-group of the pyrimidine (II; R = Me) was replaced by the amino-group by successive treatment with phosphorus oxychloride and ammonia.



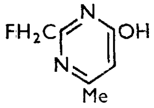
(I)



(II)



(III)



(IV)

*Experimental.*—2-*Fluoromethyl*-4,6-*dihydroxypyrimidine* (I; R = H). A mixture of fluoroacetamidine hydrochloride (12 g.), diethyl malonate (17 g.), and 2M-methanolic sodium methoxide (100 ml.) was kept for 48 hr. at room temperature. The solvent was removed under diminished pressure, the residue taken up in a little water, and the solution acidified with hydrochloric acid. The *pyrimidine* crystallised. It was purified by dissolving it in alkali and reprecipitating with acid. The product (3 g., 21%) decomposed without melting, above 250° (Found: C, 41·8; H, 3·7. $C_5H_5O_2N_2F$ requires C, 41·7; H, 3·5%).

2-*Fluoromethyl*-4,6-*dihydroxy*-5-*methylpyrimidine* (I; R = Me). Fluoroacetamidine hydrochloride (34 g.), diethyl methylmalonate (52 g.), and 2M-methanolic sodium methoxide (300 ml.) was kept at room temperature for 4 days and refluxed for 1 hr. The solvent was removed *in vacuo* and the residue dissolved in water and acidified with dilute hydrochloric acid. The microcrystalline *product* was refluxed with methanol, filtered, and dried. For the analysis it was recrystallised from water; it sublimed at about 300° without melting (yield, 20 g., 42%) (Found: C, 46·0; H, 5·0; F, 12·0. $C_6H_7O_2N_2F$ requires C, 45·6; H, 4·4; F, 12·0%).

2-*Fluoromethyl*-4-*hydroxy*-5-*methylpyrimidine* (II; R = Me). To a suspension of sodium hydride (4·8 g.) in absolute ether, a mixture of ethyl propionate (20·4 g.) and ethyl formate (15 g.) in ether (50 ml.) was added dropwise and with stirring. The mixture was kept fluid by the addition of more ether, stirred for 6 hr., and kept overnight. Filtration gave the sodium derivative of the enol of ethyl α-formylpropionate (20 g.).

This derivative (15·2 g.) was mixed with fluoroacetamidine hydrochloride (11·3 g.) and 2M-methanolic sodium methoxide (50 ml.) and left for 60 hr., with occasional shaking, then evaporated under reduced pressure. An aqueous solution of the residue was acidified with hydrochloric acid and evaporated. The *product* was extracted with hot ethyl acetate and the extract treated with charcoal, concentrated, and chilled to yield the desired *pyrimidine* (3 g., 21%) which was best purified by sublimation (Found: C, 50·2; H, 5·0. $C_6H_7ON_2F$ requires C, 50·6; H, 5·0%).

5-*Ethoxymethyl*-2-*fluoromethyl*-4-*hydroxypyrimidine* (II; R = CH$_2$·OEt). The sodium derivative from ethyl α-formyl-β-ethoxypropionate was prepared as follows: a mixture of ethyl β-ethoxypropionate (72 g.) and ethyl formate (40 g.) was added dropwise within 4 hr. to a stirred suspension of sodium hydride (12 g.) in ether (60 ml.). The mixture was stirred for a further 2 hr., kept overnight, and filtered. The product was washed with anhydrous ether and dried to constant weight at 70°. It formed an almost colourless, fluffy powder (44 g.).

To a solution of sodium methoxide (from 5·2 g. of sodium and 50 ml. of methanol), the above derivative (44 g.) and fluoroacetamidine hydrochloride (26 g.) were added and the mixture was stirred for 18 hr. at room temperature and for 6 hr. at the b.p. Solvent was removed *in vacuo* and an aqueous solution of the residue acidified with dilute hydrochloric acid and evaporated. The residue was extracted with boiling ethanol; the solution, on evaporation, left a viscous product which was purified by repeated sublimation. 5-*Ethoxymethyl*-2-*fluoromethyl*-4-*hydroxypyrimidine* (3·5 g., 8·4%) melted at 180° (sublimation) (Found: F, 10·6. $C_8H_{11}O_2N_2F$ requires F, 10·2%).

*Sodium* β-*fluoroacetoamidoylaminocrotonate* (III). To fluoroacetamidine hydrochloride (7·5 g.), ethyl acetoacetate (9 g.), and anhydrous ethanol (7 ml.), powdered sodium hydroxide (2·8 g.)

was added portionwise, with stirring, and the whole was kept over sulphuric acid in an evacuated desiccator for 4 days. The completely dry residue was powdered and extracted with anhydrous ethanol. Addition of ether to its alcoholic solution, gave the *salt* (3 g., 25%) (Found: C, 38·9; H, 4·0; F, 10·1. $C_6H_8O_2N_2FNa$ requires C, 39·5; H, 4·4; F, 10·4%).

*2-Fluoromethyl-4-hydroxy-6-methylpyrimidine* (IV). The above salt (2·5 g.) was kept in 2M-sodium methoxide (10 ml.) overnight. The solvent was removed under diminished pressure and the solid residue taken up in water and acidified with hydrochloric acid. The acid solution was brought to dryness under diminished pressure and the solid residue extracted with ethyl acetate. The extract was concentrated and chilled, whereupon *2-fluoromethyl-4-hydroxy-6-methylpyrimidine* (1 g., 52%), m. p. 166—168°, crystallised (Found: C, 50·8; H, 4·7; F, 12·7. $C_6H_7ON_2F$ requires: C, 50·6; H, 5·0; F, 13·4%).

*4-Amino-2-fluoromethyl-5-methylpyrimidine.* The compound (II; R = Me) (3 g.), phosphorus oxychloride (15 g.), and dimethylaniline (5 g.) were refluxed for 30 min., then poured on ice. The product was extracted with ether, washed with sodium carbonate solution, dried, and recovered as an oil. This was heated with 8% ethanolic ammonia (15 ml.) for 6 hr. at 100° in a sealed tube and the filtered solution evaporated. The residue was extracted with boiling chloroform, the extract evaporated, and an aqueous solution of this residue treated with charcoal, filtered, and brought to dryness again. The *product*, purified by sublimation under reduced pressure, had m. p. 158—160° (0·2 g., 6·5%) (Found: C, 50·9; H, 6·1. $C_6H_8N_3F$ requires C, 51·1; H, 5·7%).

This study was sponsored by the United States National Institute of Health.

THE SCIENTIFIC DEPARTMENT, MINISTRY OF DEFENCE,
TEL-AVIV, ISRAEL.

[*Received, June 19th,* 1959.]

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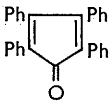
## 93. *Polarographic Reduction of Tetraphenylcyclopentadienone in Dimethylformamide.*

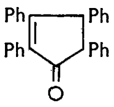
By P. H. GIVEN and M. E. PEOVER.

IN connection with work on the structure of coal, we have, with J. Schoen, surveyed the polarographic behaviour in dimethylformamide of some aromatic carbonyl compounds of known structure.[1] We have now extended this study to tetraphenylcyclopentadienone (I); the results present some unusual features.

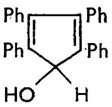
The ketone showed two waves of half-wave potential —0·33 and —0·89 v (against a mercury-pool anode) of height ($i_d/cm^{2/3}t^{1/6}$) 2·2 and 1·7, indicating two additions of one electron: the concentration range was 0·2—0·75 mM. In the presence of acetic anhydride (20 mM) only one wave was observed, of half-wave potential —0·32 v and height 3·8 (cf. behaviour of anthraquinone under similar conditions [1]).



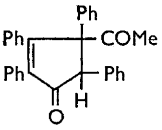
(I)



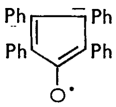
(II)



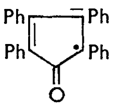
(III)



(IV)



(V)



(VI)

The ketone was also reduced electrolytically in dimethylformamide at a stirred mercury cathode controlled at —1·0 v against a separate mercury-pool reference electrode. The solution was intensely brown during reduction. When the current had fallen to a few milliampères (total consumption equivalent to 2·08 faradays per mole), dilute hydrochloric acid was added, and the mixture was extracted with chloroform. The extract gave a 90% yield of a product having the m. p. (163°) and ultraviolet spectrum recorded [2] for

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[1] Given, Peover, and Schoen, *J.*, 1958, 2674.

tetraphenylcyclopentenone (II); the expected cyclopentadienol (III) has a lower m. p. and a distinct spectrum.[2] The product showed an intense carbonyl band at 1695 cm.$^{-1}$ and a band at 2950 cm.$^{-1}$ indicating C–H vibrations on saturated carbon atoms, but no hydroxyl band near 3300 cm.$^{-1}$. The cyclopentenone obtained had half-wave potentials —1·10, —1·50, and —1·96 and heights 2·2, 1·2 (average, varying with concentration), 0·7.

A further sample (2 g.) of the cyclopentadienone (I) was reduced electrolytically as before but at —0·5 v and with the addition of 10 ml. of acetic anhydride. The product was an orange-yellow oil containing some solid (0·6 g.) which proved to be the cyclopentenone. The filtered oil solidified on long standing, but it could not be recrystallized satisfactorily from any of the common solvents. The crude material showed a strong carbonyl band at 1700 cm.$^{-1}$ with a shoulder at 1680 cm.$^{-1}$, a weak ester band at 1765 cm.$^{-1}$, and fairly strong methyl absorption at 1366 and 1455 cm.$^{-1}$. The region around 1200 cm.$^{-1}$, normally of diagnostic value for oxygen-containing groups, contained too many bands to be assigned with certainty. The methyl absorption establishes the presence of a substantial acetyl content, and the carbonyl absorptions strongly suggest that predominantly *C*-acetylation had occurred rather than reductive acetylation of C=O. The compound (IV) as a major constituent of the product would be consistent with the observations.

The reduction of tetraphenylcyclopentadienone has been studied by Sonntag, Linder, Becker, and Spoerri,[2] who report that it gives with lithium aluminium hydride good yields of either the cyclopentenone (II) or the alcohol (III) according to the conditions. This result suggests that the 3- and the 4-position do not differ greatly in nucleophilic reactivity from the 1-position; the same conclusion appears to follow from calculations by the molecular-orbital method.[3] Granted this unusual reactivity, it is not surprising that polarographic reduction yields the ketone (II). It is, however, unexpected that the half-wave potentials for the reduction of an aromatic system should be so low (close to the values for anthraquinone).

*C*-Acetylation during electrolysis in the presence of acetic anhydride could arise as follows. The reactivity of the 3-position suggests that in the cyclopentadienone (I) the extended system $\mathrm{C{=}C{-}C{=}O} \longleftrightarrow \overset{+}{\mathrm{C}}\mathrm{{-}C{=}C{-}}\overset{-}{\mathrm{O}}$ has a similar polarity to that normally expected of the carbonyl group ($>\mathrm{C}^{+} - \mathrm{O}^{-}$). In this case the mononegative ion, formed in the first polarographic wave by addition of one electron, would have a structure best represented as (V) or (VI). The carbanion might then react with acetic anhydride in the same way as a quinol ion,[1] yielding an acetyl derivative and an acetate ion. Addition of a second electron and abstraction of a proton from the solvent completes the process.

*Experimental.*—Tetraphenylcyclopentadienone, prepared by Dilthey and Quint's method,[4] had the m. p. and ultraviolet spectrum reported.[2,4] Polarography and electrolysis were carried out in dimethylformamide with 0·1N-tetraethylammonium iodide as supporting electrolyte; the procedures and apparatus were as described.[1,5] All potentials are referred to a mercury pool as standard electrode. The infrared and ultraviolet spectra were measured in Unicam SP.100 and SP.500 spectrometers respectively.

The authors are indebted to Dr. J. K. Brown for the infrared spectra.

BRITISH COAL UTILISATION RESEARCH ASSOCIATION,
LEATHERHEAD, SURREY.

[*Received, June* 8*th*, 1959.]

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[2] Sonntag, Linder, Becker, and Spoerri, *J. Amer. Chem. Soc.*, 1953, **75**, 2283.

[3] Bergmann, *Bull. Soc. chim. France*, 1951, **18**, 661; "Progress in Organic Chemistry," Vol. 3, Butterworths, London, 1955, pp. 118—119.

[4] Dilthey and Quint, *J. prakt. Chem.*, 1930, **128**, 139.

[5] Given and Peover, Proc. Inst. Fuel Conf. "Science in the Use of Coal," 1958, p. A–33.

## 94. *The Kinetics of Alkyl–Oxygen Fission in Ester Hydrolysis. Part VII.** p-*Methoxydiphenylmethyl Benzoate.*

By S. R. Johns and V. R. Stimson.

The *p*-methoxydiphenylmethyl group has considerable electron-releasing power. The chloride undergoes solvolysis[1] at a rate probably *ca.* $10^5$ times that of t-butyl chloride. Studies[2] of the behaviour of its optically active esters and ethers have shown that alkyl–oxygen fission occurs in a variety of acid-catalysed reactions, and isotopic tracer experiments have demonstrated that this type of fission occurs for the hydrogen phthalate[3] in neutral hydrolysis (mechanism $B_{AL}1$), and for the acetate[4] in acid-catalysed and neutral hydrolyses (mechanisms $A_{AL}1$ and $B_{AL}1$). As benzoates[5] generally hydrolyse by mechanism $A_{AC}2$ more slowly than acetates do by a factor of *ca.* 100, it is likely that *p*-methoxydiphenylmethyl benzoate is hydrolysed with alkyl–oxygen fission.

*First-order rate constants for the hydrolysis of* p-*methoxydiphenylmethyl benzoate.*

| Temp. | $10^2C_A$ (mole/l.) | $10^2C_E$ (mole/l.) | $10^3k_1$ (min.$^{-1}$) | $10k_A/C_A$ (min.$^{-1}$ l. mole$^{-1}$) | Temp. | $10^2C_A$ (mole/l.) | $10^2C_E$ (mole/l.) | $10^3k_1$ (min.$^{-1}$) | $10k_A/C_A$ (min.$^{-1}$ l. mole$^{-1}$) |
|---|---|---|---|---|---|---|---|---|---|
| | *In* 80% (*v*/*v*) *acetone* | | | | | *In* 60% (*v*/*v*) *acetone* | | | |
| 97·2° | — | 0·89 | 6·6 | | 97·2° | — | 0·58 | 53 | |
| | 0·33 | 0·88 | 17·2 | 32 | | 1·37 | 0·76 | 100 | 34 |
| 85·0 | — | 0·44 | 2·2 | | 85·0 | — | 1·20 | 19·5 | |
| | 1·30 | 0·67 | 11·9 | 7·5 | | 2·51 | 1·20 | 40 | 8·2 |
| | 2·18 | 1·45 | 18·5 | 7·5 | 75·0 | — | 0·58 | 7·2 | |
| 75·0 | — | 0·44 | 0·85 | | | — | 1·44 | 7·2 | |
| | — | 1·46 | 0·90 | | | 2·12 | 1·28 | 12·7 | 2·6 |
| | 0·65 | 0·65 | 2·6 | 2·6 | | 2·58 | 1·38 | 14·3 | 2·7 |
| | 1·28 | 0·71 | 3·9 | 2·3 | | 3·16 | 1·25 | 15·5 | 2·6 |
| | 1·30 | 0·67 | 4·1 | 2·5 | | 4·10 | 1·44 | 18·1 | 2·7 |
| | 2·18 | 1·45 | 6·2 | 2·4 | | 6·81 | 1·25 | 23·6 | 2·4 |
| | 3·75 | 1·53 | 8·9 | 2·1 | 70·0 | — | 0·75 | 4·3 | |
| | 3·86 | 1·33 | 9·6 | 2·3 | | — | 1·24 | 4·3 | |
| | 5·56 | 1·33 | 12·8 | 2·1 | 50·0 | — | 0·70 | 0·49 | |
| | 5·70 | 1·53 | 12·6 | 2·1 | | | | | |
| 70·0 | — | 1·11 | 0·51 | | | | | | |
| | 1·92 | 1·11 | 2·9 | 1·25 | | | | | |

$k_A$ is the first-order rate constant for the acid-catalysed reaction.
$C_A$ and $C_E$ are the concentrations of hydrochloric acid and ester, respectively.

In acidic aqueous acetone, acid-catalysed and neutral hydrolyses of *p*-methoxydiphenylmethyl benzoate occur simultaneously. The mechanisms are presumably $A_{AL}1$ and $B_{AL}1$ respectively, and the kinetics of each have been isolated (cf. Table). The rate by the former is *ca.* fifty times that of diphenylmethyl benzoate[6] (cf. Part V). The Arrhenius parameters are: for 60% acetone, $E$ (graphical, kcal./mole) = 28·8, 23·2, and $\log_{10} A$ ($A$ in sec.$^{-1}$ l. mole$^{-1}$; sec.$^{-1}$) = 15·8, 10·6; and for 80% acetone, $E$ = 29·7, 23·2, and $\log_{10} A$ ($A$ as above) = 16·3, 9·7 for $A_{AL}1$ and $B_{AL}1$ respectively, and are consistent with those found for similar hydrolyses.[6]

*Variation of Rate with Solvent Composition.*—The rate-controlling steps for the two reactions are:

$$\mathrm{Ph{\cdot}CO_2HR^+} \longrightarrow \mathrm{Ph{\cdot}CO_2H + R^+} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad A_{AL}1$$

$$\mathrm{Ph{\cdot}CO_2R} \longrightarrow \mathrm{Ph{\cdot}CO_2^- + R^+} \quad . \; . \; . \; . \; . \; . \; . \; . \; . \; . \; . \quad B_{AL}1$$

where R represents *p*-methoxydiphenylmethyl. In the terms of the Hughes–Ingold

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* Part VI, *J.*, 1956, 4676.

[1] Estimated from values given by Altscher, Baltzly, and Blackman, *J. Amer. Chem. Soc.*, 1952, **74**, 3649.

[2] Balfe, Doughty, Kenyon, and Poplett, *J.*, 1942, 605.

[3] Bourns, Bunton, and Llewellyn, *Proc. Chem. Soc.*, 1957, 120.

[4] Bunton and Hadwick, *J.*, 1957, 3043.

[5] Timm and Hinshelwood, *J.*, 1938, 862.

[6] Parts I—V, *J.*, 1954, 2848; 1955, 2010, 2673, 4020; 1956, 3629.

theory of solvent effects,[7] increase in polarity of the solvent should result in a small decrease in the rate of this step for $A_{AL}1$ and a large increase for $B_{AL}1$. For the former the ratio of the rate in 60% acetone to that in 80% acetone, $k_{60}/k_{80}$, is 0·7, when allowance is made for the protonating power of the medium; [8] this value is comparable with that found for other hydrolyses by this mechanism. By way of contrast, $k_{60}/k_{80}$ for the latter is 8·5, a value somewhat lower than that found for the $S_N1$ solvolyses of alkyl halides,[9] reactions of the same charge type, when a comparable change in solvent is made, but its difference from that for mechanism $A_{AL}1$ is significant.

*Experimental.*—*p*-Methoxydiphenylmethyl benzoate, prepared by the method of Kenyon *et al.*, had m. p. 58° when recrystallised from ethanol. The ester contained no free acid and complete hydrolysis yielded 100 ± 1 mol. % of acid. The experimental procedure was like that described in Part II. The hydrolyses followed the first-order rate law. Generally the uncatalysed reactions accompanied the acid-catalysed hydrolyses; when the correction for the former was applied, the first-order rate constants for the latter were proportional to the acid concentration (cf. Table). For the neutral solvolyses the integrated rate constants rose slowly as the reaction proceeded, presumably owing to autocatalysis, $k_1^{(0.5)}/k_1^{(0)}$ being *ca.* 1·05. $k_1^{(0)}$ was found by extrapolation to $t_0$.

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[*Received, June 16th, 1959.*]

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[7] Hughes and Ingold, *J.*, 1935, 252; Ingold, " Structure and Mechanism in Organic Chemistry," Bell, 1953, p. 347.

[8] Values for 0·1M-HCl by Braude and Stern (*J.*, 1948, 1976) are used.

[9] For refs. see Grunwald and Winstein, *J. Amer. Chem. Soc.*, 1948, **70**, 846.

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## 95. *Hydrogen Isotope Effect in the Bromination of 2-Ethoxycarbonylcyclopentanone at −19·98°.*

By J. R. HULETT.

RECENT work on the hydrogen isotope effect in the base-catalysed bromination of 2-ethoxycarbonylcyclopentanone in the temperature range 10—50° has indicated that the reaction may exhibit quantum-mechanical leakage of protons through the energy barrier opposing the reaction.[1] Of the various bases used, the fluoride ion showed this effect most markedly, although the curvature which is to be expected in the Arrhenius plot when tunnelling is considerable [2] was not observed.

The proton-transfer reaction for fluoride-ion catalysis in protium oxide has also been studied at temperatures between −20° and +15° in 5·2M-sodium bromide solutions.[3] Below −10° marked curvature in the direction required for tunnelling is observed. By using the figures obtained for the hydrogen isotope effect at higher temperatures, and Bell's equations,[4] it can be shown that the reaction catalysed by fluoride ion should exhibit a large isotope effect at −20° whereas that for catalysis by the solvent should be comparatively small. The calculated figures for $k_H/k_D$ at −20° are, for fluoride-ion catalysis, 16, and for catalysis by deuterium oxide, 4·8,[3] which may be contrasted with the smaller values of 2·67 and 3·3 observed in the region of +30°.[1] ($k$ is the first-order rate constant for the reaction, in sec.$^{-1}$, the subscripts H and D referring to proton- and deuteron-transfer respectively.)

The object of the present work is to investigate the isotope effect for the bromination of the protio- and deutero-esters in deuterium oxide solution at −19·98° catalysed by fluoride ion.

*Experimental.*—The method of following the reaction was essentially that used by Bell, Smith, and Woodward [5] and Hulett,[3] with the following modifications: In each experiment

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[1] Bell, Fendley, and Hulett, *Proc. Roy. Soc.*, 1956, *A*, **235**, 453.

[2] Bell, *Proc. Roy. Soc.*, 1935, *A*, **148**, 241.

[3] Hulett, *Proc. Roy. Soc.*, 1959, *A*, **251**, 274.

[4] Bell, *Trans. Faraday Soc.*, 1959, **55**, 1.

[5] Bell, Smith, and Woodward, *Proc. Roy. Soc.*, 1948, *A*, **192**, 479.

the total quantity of solution to be used (*ca.* 7 ml.) was placed in a tube which had a long narrow neck fitted with a ground-glass stopper and sealed with waterproof tape. The solution was made up from separate solutions of " specially pure " sodium fluoride and " AnalaR " hydrochloric acid, both in deuterium oxide 5·2M in sodium bromide. A small quantity of " AnalaR " bromine, in excess of that required for complete bromination of the ester, was added to each tube. For work with the protio-ester, a small quantity of ester was added to the solution after addition of bromine, whilst for work with the deutero-ester, the protio-ester was added to the solution and allowed to stand for 2 days at room temperature to ensure complete replacement of protium by deuterium at the 2-position before the bromine was added. At intervals samples were withdrawn and added to excess of aqueous allyl alcohol in stoppered vessels weighed before and after the introduction of the sample. The bromo-ester formed was estimated as described by previous workers.[3,5] To estimate the initial concentration of the ester (*ca.* $4 \times 10^{-2}$ mole $l.^{-1}$), a sample was withdrawn from each tube and kept at room temperature for two days to ensure complete bromination, and the bromo-ester was estimated as before.

The low-temperature thermostat was that described by Hulett.[3] Results are as tabulated.

| | Protio-ester | Deutero-ester |
|---|---|---|
| Buffer concn. (M) .................. | $[F^-] = 0{\cdot}0341$, $[HF] = 0{\cdot}0034$ | $[F^-] = 0{\cdot}0320$, $[HF] = 0{\cdot}0058$ |
| Overall vel. const. (sec.$^{-1}$) ...... | $k_H^{F^-,D_2O} = 3{\cdot}24 \times 10^{-6}$ | $k_D^{F^-,D_2O} = 4{\cdot}60 \times 10^{-7}$ |

(The superscripts $F^-$,$D_2O$ indicate the basic catalysts used.) These results give an overall isotope effect $k_H/k_D$ of approximately 7 at $[F^-] = 0{\cdot}033$M.

*Discussion.*—In order to obtain the value for the isotope effect in the portion of the reaction catalysed by fluoride ion, it is necessary to know $k_H$ and $k_D$ for catalysis by deuterium oxide under the same conditions but, since these reactions will be inconveniently slow, the experiments have not been performed. (Even the fluoride-catalysed reaction with the deutero-ester was only 50% complete after three weeks.) However, by making reasonable assumptions about the relative rates of the reactions involved on the basis of previous work,[1,3,4] it is possible to calculate an approximate figure for the ratio $(k_H/k_D)^{F^-}$ from this overall isotope effect of 7. Thus if $(k_H/k_D)^{D_2O}$ is taken at its maximum value of 4·8,[3] a figure of 10 is obtained for $k_H/k_D)^{F^-}$, whilst if $(k_H/k_D)^{D_2O}$ is smaller than 4·8, then $(k_H/k_D)^{F^-}$ is greater than 10. The magnitude of this effect clearly confirms the theoretical conclusion that where there are indications of considerable tunnelling a large isotope effect is to be expected at low temperatures.[2,4] In view of the approximations involved, it is satisfactory that the experimental ratio $(k_H/k_D)^{F^-}$ of greater than 10 approaches the maximum theoretical figure for this reaction of 16.

I acknowledge an Imperial Chemical Industries Fellowship and thank Mr. R. P. Bell, F.R.S., for discussions.

PHYSICAL CHEMISTRY LABORATORY, OXFORD. [*Received, July 1st,* 1959.]

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## 96. *Tricarbonylchromium Derivatives of Aromatic Compounds; some Discrepancies.*

By W. R. JACKSON, B. NICHOLLS, and M. C. WHITING.

IN general the three papers [1,2,3] describing these derivatives are in good agreement, but a few discrepancies require reconciliation. The most important is the arene-displacement reaction; we [1] reported the failure of dimethylaniline to react with tricarbonyltoluenechromium, but, in agreement with Natta *et al.*,[3] we have now obtained a 60% yield of the dimethylaniline complex under vigorous conditions.

Reported values for the m. p.s show some serious disagreement; our earlier data [1]

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[1] Nicholls and Whiting, *J.*, 1959, 551.

[2] Fischer, Öfele, Essler, Fröhlich, Mortensen, and Semmlinger, *Ber.*, 1958, **91**, 2763.

[3] Natta, Ercoli, Calderazzo, and Santambrogio, *Chimica e Industria*, 1958, **40**, 1003.

were uncorrected, and the corrected values given below are closer to those of the Milan and the Munich group. We still, however, find m. p. 133—134° for tricarbonyl(acetanilide)-chromium, as compared with m. p. 170° (decomp.);[3] our specimen had the correct carbon and hydrogen content and was characterised by infrared and ultraviolet spectra, as against only a carbon monoxide analysis reported by the Milan group.[3] Our value for the chlorobenzene complex (m. p. 102—103°, against 94—95° [3] and 96—98° [2]) has also been confirmed. Here, prolonged reaction or use of imperfectly dried reagents gives lower-melting specimens, from which after replacement of the chlorine by methanolysis the benzene complex can easily be isolated. Similarly, our value (now m. p. 172—174°) for the mesitylene complex is still distinctly higher than those (m. p. 168—169° [3] and 165° [2]) of the other workers. Here again we believe that the high temperature of the reaction under pressure may have given by-products not easily separated. Our value [1] for the aniline complex was a transcription error.

For the phenol and anisole complexes our results (m. p. 113—115° and 83—84°) compare with those of the Munich [m. p. 114 and 80—92° (*sic*)] and Milan [m. p. 105—106° and 82—83°] group.

*Experimental.*—After correction, the specimens of the complexes prepared [1] had the following m. p.s: benzene, 161·5—163°; toluene, 80—81°; *o*-xylene, 98·5—99°; mesitylene, 172—174° (Found: C, 56·2; H, 4·75. Calc. for $C_{12}H_{12}O_3Cr$: C, 56·25; H, 4·7%); tetralin, 114—115°; anisole, 83—84°; phenol, 113—115°; methyl benzoate, 95·5—96°; chlorobenzene, 102—103°; dimethylaniline, 145—146°; aniline, 161—162°; acetanilide, 133—134°.

The Dyson Perrins Laboratory, University of Oxford. [*Received, July 9th,* 1959.]

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## 97. *Urea and Related Compounds. Part VII.* Isomerisation of 1,O-Dimethyl-2-thioisobiuret to 1,S-Dimethyl-2-thioisobiuret.*

By Frederick Kurzer and Sheila A. Taylor.

In a paper dealing with the cyclisation of thiobiurets to 3-hydroxy-1,2,4-thiadiazoles, we recently described [1] the synthesis of 1,*O*-dimethyl-2-thioisobiuret (cf. I) and its dealkylation to 1-methyl-2-thiobiuret (II).

After storage, however, samples of 1,*O*-dimethyl-2-thioisobiuret hydrochloride failed to yield the expected 1-methyl-2-thiobiuret on acid hydrolysis. The cause of this has been traced to spontaneous isomerisation of 1,*O*-dimethyl- (I) to 1,*S*-dimethyl-2-thioisobiuret hydrochloride (V). The latter gave methanethiol on treatment with alkali, and therefore contained an *S*-methyl group. It was identified by two independent syntheses: 1-methyl-2-thiobiuret (II) was converted by methyl iodide into 1,*S*-dimethyl-2-thioisobiuret hydriodide (V; X = I), the picrate of which was identical with that obtained from the isomerisation product (V; X = Cl). The formulation of the synthesised specimen (as V) is supported by the general experience that the thioureido-system (*e.g.*, in thiourea,[2] amidinothiourea,[3] thiobiurets,[4] and dithiobiurets [5]) is invariably alkylated at the sulphur under these conditions. In the alternative synthesis, *N*-cyano-*N'S*-dimethylisothiourea [6] (III) was treated with ethanolic hydrogen chloride, giving fair yields of the desired product (V; X = Cl) in one step; this reaction involves the well-known expansion of the cyano-

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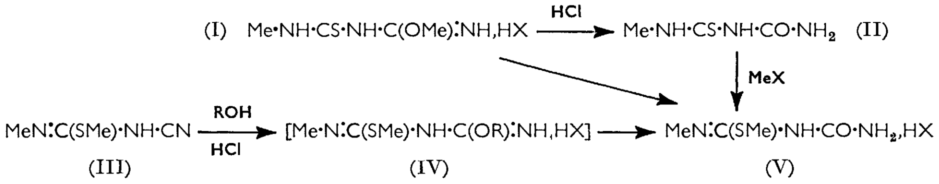
* Part VI, *J.*, 1959, 1058.

[1] Kurzer and Taylor, *J.*, 1958, 379.
[2] Lecher, *Annalen*, 1924, **438**, 169.
[3] Slotta and Tschesche, *Ber.*, 1929, **62**, 1398; Kurzer, *J.*, 1955, 1.
[4] Lakra and Dains, *J. Amer. Chem. Soc.*, 1929, **51**, 2220.
[5] American Cyanamid Co., " New Product Bulletin," Coll. Vol. I, p. 54 (1952); Tursini, *Ber.*, 1884, **17**, 585; Fromm and Schneider, *Annalen*, 1906, **348**, 161.
[6] Curd, Hendry, Kenny, Murray, and Rose, *J.*, 1948, 1630.

into the imidoyl ester grouping,[7] followed by its dealkylation under the conditions of isolation (cf. Experimental section) (III ⟶ IV ⟶ V). Because of the uncertain decomposition temperatures of salts of this type, the identity of the hydrochlorides from the two sources (I and III) was confirmed by a comparison of their ultraviolet absorption spectra. Attempts to convert *N*-cyano-*N′S*-dimethylisothiourea (III) directly into the amide (V) by the standard method, using alkaline hydrogen peroxide,[8] were unsuccessful, the reactant being decomposed in the alkaline media into intractable oils, with elimination of methanethiol.



$$\text{(I)}\ \text{Me}\cdot\text{NH}\cdot\text{CS}\cdot\text{NH}\cdot\text{C(OMe)}\text{:NH,HX} \xrightarrow{\text{HCl}} \text{Me}\cdot\text{NH}\cdot\text{CS}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}_2\ \text{(II)} \xrightarrow{\text{MeX}} \text{(V)}$$

$$\underset{\text{(III)}}{\text{MeN:C(SMe)}\cdot\text{NH}\cdot\text{CN}} \xrightarrow[\text{HCl}]{\text{ROH}} \underset{\text{(IV)}}{[\text{Me}\cdot\text{N:C(SMe)}\cdot\text{NH}\cdot\text{C(OR):NH,HX}]} \longrightarrow \underset{\text{(V)}}{\text{MeN:C(SMe)}\cdot\text{NH}\cdot\text{CO}\cdot\text{NH}_2\text{,HX}}$$

1,*S*-Dimethyl-2-thioisobiuret was unaffected by acid hydrolysis under conditions which demethylated the *O*-methyl isomer (I). With alkaline sodium plumbite it gave lead methanethiol, but the precursor (I) gave lead sulphide; this difference served as a rapid guide to the extent to which isomerisation had occurred; its progress was followed more accurately by observing the simultaneous changes in the ultraviolet absorption spectrum (cf. Experimental section). In the solid state at room temperature, isomerisation was substantially complete after 4—6 days' storage in closed vessels. In very dilute aqueous solution, however, ultraviolet measurements suggested that 1-methyl-2-thiobiuret was the final product.

The present isomerisation appears to be a general reaction of *O*-alkyl-1-methyl-2-thioisobiuret hydrochlorides, analogous observations being made with the *O*-ethyl homologue; but it is confined to suitable hydrohalides, since *O*-ethyl-1-methyl-2-thioisobiuret (and 1-aryl analogues [1]) remained unaffected on prolonged storage. The isomerisation is therefore likely to be initiated by elimination of alkyl halide, followed by its incorporation at the reactive thiol-centre (I ⟶ II ⟶ V). It is interesting that this change should occur so rapidly in the solid state.

*Experimental.*—1-Methyl-2-thiobiuret and 1,*O*-dimethyl-2-thioisobiuret hydrochloride were prepared as described previously.[1] In the preparation of picrates, aqueous picric acid saturated at 30° (containing 0·06 mole per l.) [9] was employed unless otherwise stated. In view of the dependence of the m. p.s (decomp.) of the salts on the rate of heating, it is essential to determine mixed m. p.s of pairs of picrates (or hydrochlorides) simultaneously with the m. p.s of their constituents.

Ultraviolet absorption measurements were made with a "Unicam SP.500" spectrophotometer and 0·0001M-aqueous solutions.

1-Methyl-2-thiobiuret had $\lambda_{\text{min.}}$ 232 mμ (log ε 3·32), $\lambda_{\text{max.}}$ 256 mμ (log ε 4·2).

1,*O*-Dimethyl-2-thioisobiuret hydrochloride had $\lambda_{\text{min.}}$ 228 mμ (log ε 3·86), $\lambda_{\text{max.}}$ 250 mμ (log ε 4·13).

*N*-Cyano-*N′S*-dimethylisothiourea, prepared in 60% yield by the method of Curd *et al.*[6] formed white platelets, m. p. 200—201° (decomp.) (from acetone–benzene) [Curd *et al.* give m. p. 196° (decomp.)] (Found: C, 37·2; H, 5·2; N, 33·1; S, 24·4. Calc. for $C_4H_7N_3S$: C, 37·2; H, 5·4; N, 32·6; S, 24·8%). It gave a yellow precipitate with hot alkaline sodium plumbite.

1,*S*-*Dimethyl-2-thioisobiuret.* (*a*) Spontaneous isomerisation of 1,*O*-dimethyl-2-thioisobiuret hydrochloride. Specimens of this salt,[1] after storage in closed vessels at room temperature for more than 1 week, had m. p. 165—167° (decomp.) and absorption at $\lambda_{\text{max.}}$ 223 mμ (log ε 4·1). Recrystallisation from methanol (25 ml. per g., recovery 75%; odour of methanethiol) gave

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[7] Pinner, "Die Iminoaether," Berlin, 1892; Stieglitz and McKee, *Ber.*, 1900, **33**, 1517; McKee, *Amer. Chem. J.*, 1901, **26**, 245.

[8] Radziszewski, *Ber.*, 1885, **18**, 355; McMaster and Noller, *J. Indian Chem. Soc.*, 1935, **12**, 652.

[9] Dolinski, *Ber.*, 1905, **38**, 1836.

prisms of 1,S-*dimethyl-2-thioisobiuret hydrochloride*, m. p. 171—173° (decomp., odour of methanethiol) (after sintering at 168°; subject to the rate of heating; inserted at 150°) (Found: C, 26·4; H, 5·4; S, 16·8; Cl, 18·8. $C_4H_9ON_3S,HCl$ requires C, 26·2; H, 5·45; S, 17·4; Cl, 19·3%), $\lambda_{max.}$ 225 mμ (log ε 4·1). With boiling alkaline sodium plumbite, it gave lead methanethiol (on subsequent cooling) (Found: C, 7·6; H, 2·2. Calc. for $C_2H_6S_2Pb$: C, 8·0; H, 2·0%).

The salt (0·01 mole) was recovered (90%) after being refluxed in methanol (20 ml.) containing concentrated hydrochloric acid (4 ml.) during 6 min. (*i.e.*, conditions under which 1,*O*-dimethyl-2-thioisobiuret hydrochloride yields 1-methyl-2-thiobiuret [1]).

A solution of the salt (0·92 g., 0·005 mole) in water (10 ml.), when added to aqueous picric acid (0·005 mole), gave the *picrate* (90%), m. p. 174—175° (decomp.; after sintering at 170°; subject to the rate of heating; inserted at 160°) (Found: C, 31·2; H, 3·0. $C_4H_9ON_3S,C_6H_3O_7N_3$ requires C, 31·9; H, 3·2%).

After storage during 1 week, 0·001M-aqueous solutions of 1,*O*-dimethyl-2-thioisobiuret hydrochloride gave the absorption spectrum of 1-methyl-2-thiobiuret (measured in 0·001M hydrochloric acid).

(*b*) Methylation of 1-methyl-2-thiobiuret. A solution of 1-methyl-2-thiobiuret (0·67 g., 0·005 mole) in methanol (10 ml.) and methyl iodide (35·5 g., 0·25 mole) was refluxed during 4 hr. The crystalline precipitate which began to separate after 10 min. gradually increased in quantity; it was collected at 0°, and rinsed with methanol–ether [m. p. 166—168° (decomp.); 1·17 g., 85%] (filtrate A). Crystallisation from hot water (5 ml. per g.; recovery 50%) gave prisms of 1,S-*dimethyl-2-thioisobiuret hydriodide*, m. p. 171—173° (decomp.; odour of methanethiol; after sintering at 168°; subject to the rate of heating; specimens inserted at 160°) (Found: C, 18·0; H, 3·7; N, 15·2; I, 44·4. $C_4H_9ON_3S,HI$ requires C, 17·5; H, 3·6; N, 15·3; I, 46·2%). The salt gave, with alkaline sodium plumbite, a pale yellow precipitate, and methanethiol. Evaporation of filtrate A to quarter-bulk gave further small quantities (5—8%) of crude hydriodide.

Treatment of an aqueous solution of the hydriodide (0·28 g., 0·001 mole) with aqueous picric acid (0·001 mole) gave the picrate (0·37 g., 97%), m. p. [and mixed m. p. with specimens obtained as in (*a*) and (*c*)] 174—175° (decomp.; subject to the rate of heating; inserted at 160°).

(*c*) Hydrolysis of *N*-cyano-*N'S*-dimethylisothiourea. A suspension of *N*-cyano-*N'S*-dimethylisothiourea (1·94 g., 0·015 mole) in ethanol (20 ml.) and 3M-ethanolic hydrogen chloride (10 ml., 0·03 mole) was warmed gently, and the resulting solution stored at room temperature during 4 days. The mixture was slowly distilled to one-third bulk at atmospheric pressure, and the crystalline product was collected at 0° and rinsed with ethanol–ether [m. p. 166—168° (decomp.); 1·70 g., 62%] (filtrate M). Crystallisation from methanol–ether (40 and 5 ml., respectively, per g., recovery 50—60%) gave prisms of 1,*S*-dimethyl-2-thioisobiuret hydrochloride, m. p. [and mixed m. p. with material obtained as in (*a*)] 172—173° (decomp., after sintering at 165°; subject to the rate of heating; inserted at 150°), $\lambda_{max.}$ 225 mμ (log ε 4·10) (Found: C, 26·7; H, 5·5; N, 22·8; Cl, 19·5. Calc. for $C_4H_9ON_3S,HCl$: C, 26·2; H, 5·45; N, 22·9; Cl, 19·3%]. Vacuum-evaporation of filtrate M to small volume, followed by dilution with ether, gave more (6—14%) crude hydrochloride, m. p. 170—172° (decomp.).

The hydrochloride was convertible, as described in (*a*), into the picrate (85%), m. p. and mixed m. p. 174—175° (decomp.; subject to the rate of heating; inserted at 160°) (Found: C, 32·4; H, 3·3. Calc. for $C_4H_9ON_3S,C_6H_3O_7N_3$: C, 31·9; H, 3·2%).

A solution of *N*-cyano-*N'S*-dimethylisothiourea (1·29 g., 0·01 mole) in water (20 ml.) and 10N-sodium hydroxide (3 ml.), when treated dropwise with 30% hydrogen peroxide (1·7 ml., 0·015 mole) during 10 min. at 40—50°, gave an oil (odour of methanethiol). Neither the hydrochloride nor the picrate of (V) could be isolated.

O-*Ethyl*-1-*methyl*-2-*thio*iso*biuret*.[1] In 0·0001M-ethanolic solution this had $\lambda_{min.}$ 226 mμ (log ε 3·97), $\lambda_{max.}$ 249 mμ (log ε 4·53), $\lambda_{infl.}$ 269—272 mμ (log ε 4·23). It was unchanged after 1 year at room temperature. It had m. p. 90—91° and gave lead sulphide with hot alkaline sodium plumbite. Its hydrochloride,[1] after storage, gave methanethiol or lead methyl sulphide with alkali or alkaline sodium plumbite, respectively, and had $\lambda_{max.}$ 221 mμ (log ε 4·12)], resembling (V) but differing from (I).

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