dure 1 failed. The bulk (85%) of the starting bromide Ia was recovered.

Mixture of IIIb *and* IVb. Substituting β-diethylaminoethanethiol and the bromide Ib in procedure 2 gave a 52% yield of a viscous liquid base, b.p. 221–223° (1.6 mm.), n_D^{25} 1.5756 $\lambda_{max}^{CHCl_3}$ 5.98 μ (m), 5.56 μ (m).

Anal. Calcd. for $C_{22}H_{27}NO_2S$: C, 71.51; H, 7.37; N, 3.79. Found: C, 71.32; H, 7.50; N, 3.86.

The relative intensities of the two carbonyl absorptions indicated that this product was a mixture of approximately equal quantities of IIIb and IVb. Attempts to prepare IIIb by procedure 1 gave 40–50% yields of triethylamine hydrobromide, but the basic fraction consisted mainly of unchanged aminomercaptan. Not a trace of thiol ester was formed (no absorption at 5.95–6.0 μ).

β-Diethylaminoethyl 5-phenyl-2,3,4,5-tetrahydro-1-benzoxepin-5-carbothiolate IIIc. Substituting β-diethylaminoethanethiol for the β-diethylaminoethanol in procedure 3a gave a 75% yield of IIIc, isolated as the hydrochloride salt, m.p. 165–166°, $\lambda_{max}^{CHCl_3}$ 5.94 μ.

Anal. Calcd. for $C_{23}H_{30}ClNO_2S$: C, 65.77; H, 7.20; N, 3.33. Found: C, 65.85; H, 7.09; N, 3.33.

3-(β-Diethylaminoethylmercaptopropyl)-3-phenyl-2-benzofuranone IVc. The reaction of 6.6 g. (0.02 mole) of Ic, 3.3 g. (0.025 mole) of β-diethylaminoethanethiol, and 1.2 g. (0.025 mole) of a 50% mineral oil dispersion of sodium hydride was carried out in 30 ml. of 1,2-dimethoxyethane according to procedure 2. The crude basic product (5.9 g.) obtained as a thick green oil showed in its infrared spectrum only a single carbonyl peak at 5.55 μ indicating that IVc was the sole product containing no detectable amounts of thiolester IIIc. Treatment with ethereal hydrogen chloride gave 5.7 g. of IVc hydrochloride, m.p. 110–112°. Several recrystallizations from dry ethanol-ether raised the m.p. to 117–118°.

Anal. Calcd. for $C_{23}H_{30}ClNO_2S$: C, 65.77; H, 7.20; N, 3.33. Found: C, 65.55; H, 7.59; N, 3.39.

Treatment of 3-(β-bromoethyl)-3-phenyl-2-benzofuranone (Ib) *with sodium acetate in methanol.* A solution of 5.0 g. (0.0158 mole) of Ib and 1.3 g. (0.0158 mole) of freshly fused sodium acetate in 50 ml. of dry methanol was refluxed for 24 hr. The methanol was removed under reduced pressure using a rotating evaporator, and 50 ml. of water was added to the semisolid residue. Insoluble oil was taken up in ether, and dried over anhydrous magnesium sulfate. Filtration and removal of the ether by distillation gave 4.2 g. (100%) of pale yellow oil having an infrared spectrum qualitatively identical to that of methyl 4-phenyl-4-chromancarboxylate (V).[1] When Ib was refluxed in neutral methanol, no reaction occurred. When mineral acid was present, the methanolysis took an entirely different course.[4]

Methanolysis of the mixed anhydride VII. A solution of 4.0 g. of 4-phenyl-4-chromancarboxylic acid (VI)[1] in 60 ml. of dry benzene was gassed for 0.5 hr. with ketene (excess).[15] After standing for 1 hr. at room temperature, the benzene and excess ketene were removed under reduced pressure using a rotating evaporator. The infrared spectrum of the residual light yellow oil indicated (λ_{max}^{liq} 5.52 μ, 5.75 μ) complete conversion to the mixed anhydride VII. There was no evidence for the presence of any starting material VI ($\lambda_{max}^{CHCl_3}$ 5.85 μ and 7.35 μ both absent). This oil was taken up in 50 ml. of dry methanol, 1.3 g. of fused sodium acetate was added and the mixture was refluxed for 24 hr. Removal of the methanol in the usual way followed by appropriate work-up gave 0.3 g. of a neutral oil (not further investigated) and 3.4 g. (85%) of starting acid VI, m.p. 150–151°, identified by mixed melting point.

Acknowledgment. Portions of the experimental work were carried out by N. F. Ryan. E. F. Shelberg was responsible for the microanalyses and W. H. Washburn for the infrared spectra.

NORTH CHICAGO, ILL.

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[15] W. E. Hanford and J. C. Sauer, *Org. Reactions*, 132 (1946).

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, NORTHWESTERN UNIVERSITY]

A New Type of Assistance at a Distance

R. K. SUMMERBELL AND SHERRI R. FORRESTER[1]

Received May 26, 1961

Mercuric chloride in refluxing chloroform replaces one of the two iodine atoms of *meso-* or of racemic-1,4-diiodo-2,3-butanediol, (I) or (III), rapidly to yield the corresponding 1-chloro-4-iodo-2,3-butanediols (II or IX), but the second iodine atom is relatively inert even to an excess of mercuric chloride. A cyclic intermediate (XIII) is proposed to explain the activating influence of one iodine atom on another at a distance of four carbon atoms. Similar enhanced activity of the first iodine over the second is shown by 1,4-diiodo-2,3-diethoxybutane (VII) and *cis*-2,3-bis(iodomethyl)-*p*-dioxane (VIII) in contrast to *trans*-2,3-bis(iodomethyl)-*p*-dioxane (XI) and *cis*-2,6-bis(iodomethyl)-*p*-dioxane (XII) in which both iodine atoms are unreactive. Preliminary experiments indicate that 1,4-diiodobutane reacts to form the chloroiodo derivative more rapidly than does 1,5-diiodopentane, and much more rapidly than does 1,3-diiodopropane. Butyl iodide is also relatively inert. The supposed diiodobutanediol in the literature has been shown to be *erythro* II.

There are a large number of displacement reactions in which a properly placed nucleophile within the molecule aids in the removal of the leaving group, a phenomenon known as neighboring group participation. Halogens are among the nucleophiles commonly listed as neighboring group participants, and of the halogens, iodine is particularly effective. Whereas many of these neighboring groups are at varying distances from the reaction site, the examples employing halogen that we have found in the literature are those in which the halogen atom is on the carbon adjacent to that of the leaving group. In the present work are several examples in which an iodine atom assists in the replacement of a second iodine atom four carbons removed.

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[1] This research was supported by N.S.F. Grant 7335.

In an attempted synthesis of a seven-membered oxygen heterocyclic compound by a method analogous to that developed in our laboratory[2a,b] for the preparation of a substituted 1,4-dioxane, a new compound, I, m.p. 131°, later proved to be a 1,4-diiodo-2,3-butanediol, was the only product isolated. The procedure involved treating a glycol with butadiene and aqueous mercuric nitrate, followed by precipitation with iodide and treatment with iodine. Evidently the water rather than the glycol had reacted with the mercurinium ion intermediates. The glycol was omitted in subsequent experiments (Chart I). As both *dl* and *meso* isomers are possible, this product was tentatively assigned the *meso* configuration because it melted higher than another material II, m.p. 109°, that had previously been described[3] and assigned the 1,4-diiodo-2,3-butanediol structure.

In a modified reaction in which mercuric acetate replaced the nitrate, another diiodobutanediol (III), m.p. 103–104°, was isolated in addition to I. An investigation of the structures of the three compounds was undertaken as three "isomers" seemed to exist whereas only two 1,4-diiodo-2,3-butanediols are possible. Therefore, the synthesis of II was repeated[3] exactly as described, and analysis soon showed that even the empirical formula assigned to this substance by Nesmeyanov and Lutsenko[3] was in error. Their assignment of structure was based on oxidation to iodoacetic acid, and no analysis was reported; our analysis indicated a chloroiodobutanediol, and a qualitative test confirmed the presence of both chlorine and iodine.

To test our assignment of structure, the *dl*- and *meso*-1,4-diiodo-2,3-butanediols were prepared by an independent method. The oxidation of *trans*-1,4-dichloro-2-butene was reported to give the two corresponding dichlorobutanediols.[4a,b] The *dl* isomer was obtained by *cis* oxidation of the *trans*-olefin with potassium permanganate, while the *meso* isomer was formed by *trans* oxidation of the same *trans*-olefin with performic acid. Because of the ease of obtaining pure starting material, our oxidations were carried out on *trans*-1,4-dibromo-2-butene. The two dibromobutanediols obtained were converted to the corresponding iodides with sodium iodide in acetone. *meso*-1,4-Dibromo-2,3-butanediol (IV)[5] yielded I, and *dl*-1,4-dibromo-2,3-butanediol (V)[6] was converted to III. The samples of I and III prepared from IV and V were identical with the respective isomers obtained from the reaction of butadiene with aqueous mercuric salts in both melting points and infrared spectra. Finally, the structure II was proved by treating it with sodium iodide which converted it to I, indicating that II was the *erythro*-1-chloro-4-iodo-2,3-butanediol.

The preparation of II differed from that of I or III in one step only; the organomercurial had been precipitated as the chloride rather than as the iodide (Chart I). The precipitated chloride (VI) was treated with iodine in the former case to give the 1-chloro-4-iodo-2,3-butanediol (II), while I and III were obtained from bis(iodomercuri) precursors. In the formation of II, RHgCl seemed to have reacted with iodine to yield RCl. There are numerous examples in the literature of RHgCl yielding RI on treatment with iodine, but none that we are aware of where the organic product is RCl. Plausible mechanisms for such a replacement may be written. If the bis(chloromercuri) compound VI upon treatment with iodine were to give an appreciable amount of the monochloromonoiodo derivative II, one would expect it to be accompanied by some dichloride and some diiodide I. Although I would be readily isolated if it were present, only II was found. To investigate further this type of reaction, looking particularly for chlorine in the product, we prepared other chloromercuri compounds as precursors and treated them with iodine. However, the conversion of 2,5-dimethyl-2,5-bis(chloromercurimethyl)-*p*-dioxane and 1,4-bis(chloromercuri)-2,3-diethoxybutane to 2,5-dimethyl-2,5-bis(iodomethyl)-*p*-dioxane and *meso*-1,4-diiodo-2,3-diethoxybutane (VII),[7] respectively, indicates that the formation of II was an unusual reaction.

The fact that the iodination reaction which produced II, mercuric chloride, and mercuric iodide had required a much longer period of time for completion than was usually necessary suggested the possibility that I was formed first and was then converted to II upon extended contact with mercuric chloride. To test this possibility, I was treated with one equivalent of mercuric chloride under similar conditions, and II was indeed isolated as the only product. Additional examples of the replacement of only one iodine atom in molecules which contain two apparently equivalent iodine atoms were found. Diiodide III, *meso*-1,4-diiodo-2,3-diethoxybutane (VII), and *cis*-2,3-bis(iodomethyl)-*p*-dioxane (VIII)[1] were converted to *threo*-1-chloro-4-iodo-2,3-butanediol (IX), *erythro*-1-chloro-4-iodo-2,3-diethoxybutane, and 2-chloromethyl-3-iodomethyl-*p*-dioxane (X), respectively. Two closely related compounds, *trans*-2,3-bis(iodomethyl)-*p*-dioxane (XI)[1] and *cis*-2,6-bis(iodo-

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[2] (a) R. K. Summerbell and G. J. Lestina, *J. Am. Chem. Soc.*, **79**, 3878 (1957); (b) The mechanism for the addition of aqueous mercuric salts to diolefins is discussed in more detail by R. K. Summerbell, G. Lestina, and H. Waite, *J. Am. Chem. Soc.*, **79**, 234 (1957).

[3] A. N. Nesmeyanov and I. F. Lutsenko, *Bull. acad. sci. U.R.S.S., Classe sci. chim.*, 366 (1942); *Chem. Abstr.* **39**, 1637[1] (1945).

[4] (a) L. N. Owen, *J. Chem. Soc.*, 241 (1949); (b) J. B. Miller, *J. Org. Chem.*, **25**, 1279 (1960).

[5] P. Champion, *Z. fur Chem.*, 348 (1871).

[6] G. Griner, *Compt. rend.*, **117**, 555 (1893).

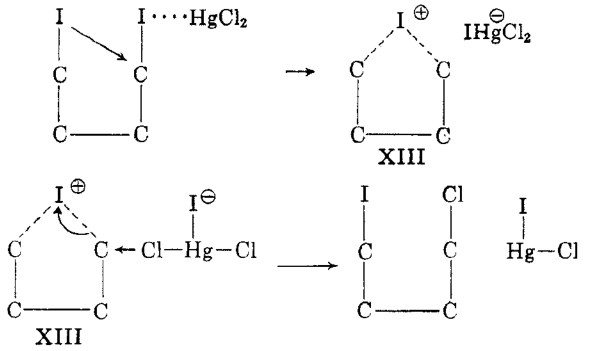
[7] J. R. Johnson, W. H. Jobling, and G. W. Bodamer, *J. Am. Chem. Soc.*, **63**, 131 (1941).

methyl)-*p*-dioxane (XII)[8] were unchanged under similar conditions, and compounds II and IX were inert to a second equivalent of mercuric chloride. A variation of the latter experiment, treatment of III with two equivalents of mercuric chloride, again formed only IX and no dichlorobutanediol. Evidently for the reaction to occur, two iodine atoms must be at the right distance in molecules of the correct shape.

Although all of the above compounds that showed the enhanced activity had oxygen on the carbon vicinal to that on which replacement took place, experiments with α,ω-alkyl diiodides show that the presence of the oxygen is not necessary. Using vapor phase chromatography to follow the action of mercuric chloride on C_3, C_4, and C_5 terminal diiodides in chloroform, preliminary studies show that 1,4-diiodobutane is rapidly converted to 1-chloro-4-iodobutane to the extent of more than 50%, while replacement of the second iodide is almost negligible in the time period considered. The five-carbon diiodide shows somewhat slower conversion to 1-chloro-5-iodopentane, but it is still accelerated in comparison with 1,3-diiodopropane, which showed no noticeable replacement. Butyl iodide also exhibited little tendency to react. More detailed studies are planned.

These results indicate that the two possible reaction sites in each molecule, although at a reasonable distance from one another, are not behaving independently of each other, particularly where they are four carbon atoms apart. Independent behavior would predict random attack by the chloride nucleophile to replace any iodide with equal facility, resulting in a statistical distribution of 25% dichloride, 25% unchanged diiodide, and at the most, 50% chloroiodide. However, more than 50% chloroiodide has been found. This suggests that some type of cyclic intermediate is formed during the course of the reaction, bringing the two ends of the molecule into close proximity.

One such intermediate would be a five-membered iodonium ring (XIII), formed simultaneously by backside attack of one iodide as the electron-deficient mercuric salt pulls off the other iodide. A mercury complex ion could then donate a chloride ion to open the ring and form the chloroiodide.[9]



Analogy for this mechanism can be found in those neighboring group reactions in which hydroxyl participates in the solvolysis of 1-chloro-4-hydroxybutane[10] and the methoxide group in the acetolysis of 4-methoxy-*n*-butyl-*p*-bromobenzenesulfonate.[11] In each case, the removal of the leaving group was accelerated by the nucleophile placed four carbon atoms away which could form a similar five-membered cyclic intermediate.

The fact that *cis*-2,3-bis(iodomethyl)-*p*-dioxane (VIII) is readily converted to X whereas the *trans* isomer XI can be recovered unchanged is another point in favor of the five-membered cyclic iodonium intermediate. Models of the two diiodides show that VIII can easily assume the required configuration while XI cannot. A little surprising is the fact that the *cis*-2,6-bis(iodomethyl)-*p*-dioxane (XII) does not appear to undergo the replacement at all. This may be due to the fact that in the more stable diequatorial position the two iodomethyl groups are too far apart to form the required intermediate.

The failure of II and IX to be converted to the dichlorobutanediols would likewise be expected with a mechanism involving the proposed iodonium intermediate because of the large difference in nucleophilicity between chloride and iodide. Despite the favorable geometry, chloride cannot readily form the corresponding chloronium ion necessary to aid in the removal of the iodide. This difference in ability to form the halonium ion is demonstrated in the reactivities of substituted cyclohexanols with fuming hydrobromic acid[12] where *trans*-2-iodocyclohexanol is 700 times more reactive and *trans*-2-chlorocyclohexanol 6250 times *less* reactive than the unsubstituted cyclohexanol. Similarly, *trans*-2-iodocyclohexyl-*p*-toluenesulfonate undergoes acetolysis 1170 times faster than the unsubstituted *p*-toluenesulfonate,[13] while *trans*-2-chlorocyclohexyl-*p*-bromobenzenesulfonate is 2174

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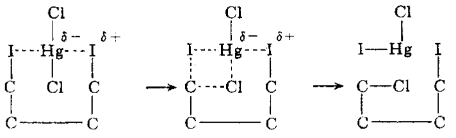
[8] R. K. Summerbell and J. R. Stephens, *J. Am. Chem. Soc.*, **76**, 731 (1954).

[9] An alternate cyclic intermediate might be a seven-membered ring in which the electron-seeking mercuric ion bridges the space between the two nucleophilic iodides. In a four-centered reaction, the mercury might exchange one of its chlorides for an iodide to form the observed product.



[10] H. W. Heine, A. D. Miller, W. H. Barton, and R. W. Greiner, *J. Am. Chem. Soc.*, **75**, 4778 (1953).

[11] S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, **3**, 1 (1958).

[12] S. Winstein, E. Grunwald, R. E. Buckles, and C. Hanson, *J. Am. Chem. Soc.*, **70**, 816 (1948).

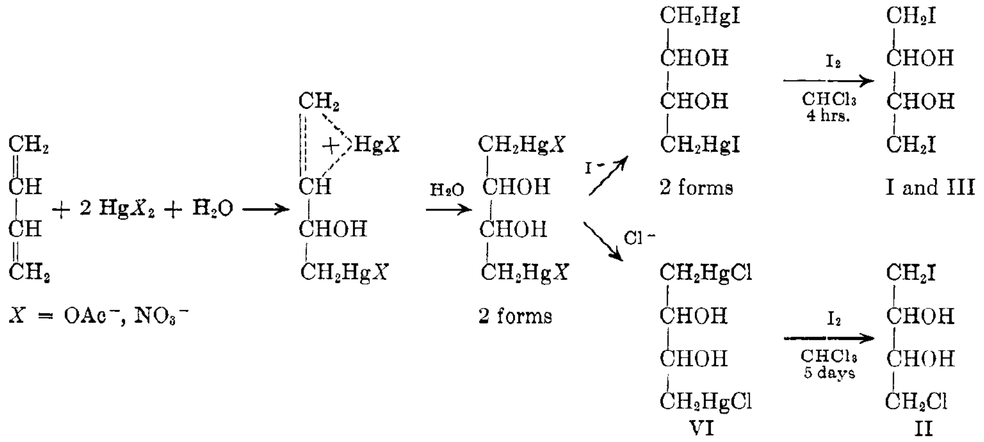
[13] S. Winstein, E. Grunwald, and L. L. Ingraham, *J. Am. Chem. Soc.*, **70**, 821 (1948).

TABLE I

REACTION OF DIIODIDES WITH MERCURIC CHLORIDE

Product	M.P.	Recryst. Solv.	Formula	Carbon, %		Hydrogen, %	
				Calcd.	Found	Calcd.	Found
threo-1-Chloro-4-iodo-2,3-butanediol (IX)	65	Petroleum ether	$C_4H_8O_2ClI$	19.26	19.55	3.23	3.15
erythro-1-Chloro-4-iodo-2,3-diethoxybutane	22–24	Petroleum ether	$C_8H_{16}O_2ClI$	31.34	32.03	5.26	5.41
1-Chloromethyl-4-iodomethyl-*p*-dioxane	43.5–44.5	Benzene	$C_6H_{10}O_2ClI$	26.06	25.79	3.65	3.54

CHART I



times less reactive than its corresponding unsubstituted *p*-bromobenzenesulfonate.

EXPERIMENTAL

1,4-Diiodo-2,3-butanediols (I) *and* (III). Butadiene (0.1 mole previously collected in a Dry Ice trap) was bubbled slowly into a solution of 64 g. (0.2 mole) of mercuric acetate in 200 cc. of water. When a negative test for mercuric ion was obtained, the reaction mixture was made basic with 10% sodium hydroxide and treated with aqueous potassium iodide to precipitate a white solid (A). After drying, solid A was refluxed for 4 hr. with 45 g. of iodine in chloroform until the color of the solution remained constant. Excess iodine was removed with 10% sodium thiosulfate and the mercuric iodide dissolved with aqueous potassium iodide. The chloroform layer was dried over anhydrous magnesium sulfate and the solvent was removed to leave 7.5 g. of crude product. In addition, 9.1 g. of unchanged A was recovered. On recrystallization of the crude product from chloroform, 2.7 g. of I, m.p. 129–131° was separated from III. After repeated recrystallizations from chloroform, a pure sample of III, m.p. 103–104°,[14] was obtained. The same products are obtained when mercuric nitrate replaces mercuric acetate.

Anal. Calcd. for $C_4H_8O_2I_2$: C, 14.05; H, 2.36. Found: (I) C, 14.12; H, 2.39. (III) C, 14.04; H, 2.30.

erythro-1-Chloro-4-iodo-2,3-butanediol (II). The procedure of Nesmeyanov and Lutsenko[3] was followed. Iodination of the 1,4-bis(chloromercuri)-2,3-butanediol was slow and, consequently, was continued for 5 days before the reaction mixture was worked up.

Anal. Calcd. for $C_4H_8O_2Cl$ I: C, 19.26; H, 3.23. Found: C, 19.33; H, 3.06.

Detection of chlorine and iodine. A sample of II was refluxed in absolute ethanol with powdered sodium hydroxide for 2.5 hr. The solution was acidified, heated in a casserole, and treated with potassium peroxydisulfate until iodine was no longer liberated.[15] Addition of aqueous silver nitrate to the remaining solution formed a curdy white precipitate which was soluble in ammonium hydroxide.

I *and* III *from trans-1,4-dibromo-2-butene.* a. *dl-1,4-Dibromo-2,3-butanediol* (V). A solution of 9 g. of *trans*-1,4-dibromo-2-butene in ethanol was treated with an aqueous solution of potassium permanganate by the method of Owen.[4a] Six grams of V was obtained, m.p. 83–85.°[6]

b. *Conversion of* V *to* III. To 2.5 g. (0.017 mole) of sodium iodide in 50 cc. of refluxing dry acetone was added 2 g. (0.008 mole) of V in 15 cc. of acetone. After 24 hr., sodium bromide was filtered off, the solvent evaporated, and the residue recrystallized from chloroform as white needles, m.p. 102–103°, having the same infrared spectrum in potassium bromide as III.

c. *meso-1,4-Dibromo-2,3-butanediol* (IV). *trans*-1,4-Dibromo-2-butene was treated with formic acid and 30% hydrogen peroxide, using the method of Owen[4a] for the oxidation of the corresponding *trans*-1,4-dichloro-2-butene. Two-tenths gram of IV, m.p. 136–137.5°,[5] was obtained.

d. *Conversion of* IV *to* I. A mixture of 0.2 g. (0.0008 mole) of IV and 0.25 g. of sodium iodide in 10 cc. of dry acetone was refluxed for 24 hr. On removal of sodium bromide, the filtrate was evaporated, and the residue recrystallized from chloroform to yield white crystals, m.p. 128–130.5°, whose infrared spectrum in potassium bromide was identical with that of I.

Conversion of II *to* I. A solution of 0.9 g. (0.0035 mole) of II in 25 cc. of dry acetone was refluxed for 48 hr. with 0.53 g. (0.0035 mole) of sodium iodide. The filtrate was evaporated, and the resulting residue recrystallized from chloroform to yield a solid whose melting point and infrared spectrum were identical with those of I.

2,5-Dimethyl-2,5-bis(iodomethyl)-p-dioxane. A mixture of 40 cc. of methallyl alcohol and 32 g. (0.1 mole) of mercuric acetate was stirred for 16 hr. The resulting paste was diluted, treated with 6 g. of sodium chloride in water, dissolved in

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[14] All melting points were taken on a Fisher-Johns block and are uncorrected.

[15] C. H. Sorum, *Introduction to Semimicro Qualitative Analysis,* 2nd ed., Prentice-Hall, Inc., New York, 1953, p. 164.

10% sodium hydroxide, and the filtrate reprecipitated with 50% acetic acid. The chloromercuri compound was refluxed with iodine in chloroform and worked up as described in the preparation of I to yield 9 g. of product, m.p. 88°, and 5 g., m.p. 173°. These solids are identical in melting points and infrared spectra with those obtained in a similar synthesis using potassium iodide in place of sodium chloride. The proof of their structure will be reported elsewhere.

meso-1,4-Diiodo-2,3-diethoxybutane (VII). Butadiene was bubbled through a mixture of 32 g. (0.1 mole) of mercuric acetate in 150 cc. of absolute ethanol to form a precipitate. Aqueous sodium chloride was added to the suspension, and the resulting water-insoluble precipitate was filtered, dissolved in 10% sodium hydroxide, and reprecipitated with 50% acetic acid. The solid was treated as described in the preparation of I and 6 g. of material, m.p. 45–47°, was obtained. This was identical with VII prepared by the method of Johnson and co-workers.[7]

Treatment of diiodides with mercuric chloride. a. Conversion of I *to* II. A 0.7-g. sample of I (0.002 mole) was refluxed with 0.3 g. of mercuric chloride in 35 cc. of chloroform for 119 hr. The yellow mercuric salt formed was filtered, and the filtrate evaporated to leave a solid, m.p. 108°, whose infrared spectrum matched that of II.

b. Preparations of other chloroiodides are compiled in Table I.

c. When *trans*-2,3-bis(iodomethyl)-*p*-dioxane and *cis*-2,6-bis(iodomethyl)-*p*-dioxane were treated with 1 equivalent of mercuric chloride as above, they were recovered unchanged almost quantitatively after 5 days. When II and IX were treated with 1 equivalent of mercuric chloride as above, they were recovered unchanged. When III was treated with 2 equivalents of mercuric chloride, the only material found was IX.

Preliminary vapor phase chromatography studies an α,ω-alkyldiiodides. The treatment of 1,4-diiodobutane with mercuric chloride is representative of the experiments performed on all the alkyldiiodides. A mixture of 5 g. (0.016 mole) of 1,4-diiodobutane and 4.4 g. (0.016 mole) mercuric chloride was refluxed in 21 cc. of chloroform for 4 days, and 0.5-cc. samples were withdrawn at intervals. Excess solvent was allowed to evaporate. At the end of the 4 days, the samples were injected into an Aerograph vapor phase chromatograph containing a 10-ft. column of 8% 550 Silicon Oil on firebrick and maintained at 200°. The percentages of components present in each sample were calculated from the ratio of the areas of the peaks recorded. Peak areas were obtained as the product of peak height times width at half-height. A graph of time *vs.* per cent composition was plotted to indicate the relative rates of formation of monochloro- and dichloro- derivatives.

EVANSTON, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF ORGANIC CHEMISTRY, PHARMACEUTICAL FACULTY, UNIVERSITY OF ZAGREB AND RESEARCH INSTITUTE "PLIVA," PHARMACEUTICAL AND CHEMICAL WORKS]

Fragmentation of α-Phthalimido-β-methylmercaptopropiophenone with Aluminum Chloride[1]

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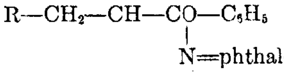
Received June 26, 1961

Under the normal conditions of Friedel-Crafts reaction with benzene, the title compound yielded various products depending on the amount of aluminum chloride. With one mole of aluminum chloride the unchanged acid chloride was isolated, while with two moles of catalyst, α-phthalimido-β-methylmercaptopropiophenone was obtained. With three moles of aluminum chloride, *S*-methyl-*N*-phthaloylcysteinyl chloride or α-phthalimido-β-methylmercaptopropiophenone underwent a fragmentation reaction, yielding phthalimidoacetophenone and diphenylmethane.

As shown by experiments in these laboratories α-phthalimidopropionyl chloride and its β-methoxy and β-ethoxy derivatives react with benzene in the presence of aluminum chloride to yield the normal products of Friedel-Crafts reaction.[4] The yield of propiophenone derivatives, however, largely depended on the character of the β-substituents (Table I).

When *S*-benzyl-*N*-phthaloyl-L-cysteinyl chloride was subjected to the same reaction, L-α-phthalimido-β-propiothiolactone (I) was obtained with two moles of aluminum chloride, while a polythio ester (II) was isolated when the reaction had been performed with one mole of catalyst.[5]

TABLE I



$$\underset{\displaystyle\text{N}{=}\text{phthaloyl}}{\text{R—CH}_2\text{—CH—CO—C}_6\text{H}_5}$$

R	Yield, %
OCH_3	63
OC_2H_5	25
H	90
SCH_3	51

Continuing the studies of the course of Friedel-Crafts reaction with substituted propionyl chlorides, the reaction of *S*-methyl-*N*-phthaloylcysteinyl chloride with aluminum chloride in benzene was

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[1] Presented before 1st Yugoslav Congress of Pure and Applied Chemistry, Zagreb, June 1960.

[2] Present address: Organsko Kemijska Industrija, Boškovićeva 33, Zagreb.

[3] Taken from the thesis submitted by M.D. in partial fulfillment of the requirement for the degree of Doctor of Chemistry at the University of Zagreb.

[4] D. Fleš, B. Balenović, R. Marušić, and N. Manger, *Arhiv. kem.*, **27**, 1 (1955); D. Fleš and B. Balenović, *Arhiv. kem.*, **27**, 149 (1955); D. Fleš and A. Markovac-Prpić, *Croat. Chem. Acta*, **29**, 183 (1957).

[5] D. Fleš. A. Markovac-Prpić, and V. Tomašić, *J. Am. Chem. Soc.*, **80**, 4654 (1958).