[Contribution No. 72 from the Chemistry Department of the University of Tennessee]

The Sommelet Reaction in the Synthesis of Aromatic Dialdehydes[1]

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While the Sommelet reaction[5] has been known for some time, a study of the general applicability of the method to the formation of aldehydes has not been made, and, in particular, no attempt has been made to determine its suitability for the synthesis of aromatic dialdehydes. This paper describes the formation and hydrolysis of ten hexamethylenetetramine - bis - (chloromethyl)-benzene salts from which five new aromatic dialdehydes resulted (Table I). In all cases, one mole of the bis-chloromethyl compound reacted with two moles of hexamethylenetetramine to give a quantitative yield of the salt. However, whether aldehydes formed or not upon hydrolysis of the salt depended upon the location of substituents with respect to the chloromethyl groups as well as the location of the chloromethyl groups with respect to each other. For example, the salts of *o*-bis-(chloromethyl)-benzenes gave no detectable quantity of *o*-dialdehydes upon hydrolysis even though the adjacent carbon atoms in the benzene ring were unsubstituted. Instead, basic nitrogen compounds resulted. On the other hand, salts of *p*- or *m*-bis-(chloromethyl)-benzenes gave satisfactory yields of dialdehydes provided that at least one position *ortho* to each chloromethyl group was unsubstituted. Where both *ortho* positions were substituted, basic nitrogen compounds again resulted. This finding is in keeping with a case previously reported.[6] The new aldehydes were characterized by conversion to the known dicarboxylic acids. The characterization of the basic nitrogen compounds is being attempted in the hope that the work will shed some light on the mechanism of the Sommelet reaction.

Experimental

Formation of the Hexamethylenetetramine Salt.—Equivalent quantities of the halide and hexamethylenetetramine were dissolved separately in a small excess of dry chloroform. After bringing the two chloroform solutions together, the mixture was maintained under reflux until precipitation was complete, usually two to three hours. The salt was removed by suction filtration and dried. The yields, based on the weight of the dry salt, were essentially quantitative.

In one case (2,5-bis-chloromethyl-*p*-xylene) the salt was a sticky, hygroscopic substance when obtained by the above procedure and it was found more convenient to use an aqueous alcohol solution for its preparation and to carry out the hydrolysis without isolating it.

4-Methoxyisophthalaldehyde.—A solution of the salt of 2,4-bis-(chloromethyl)-anisole[7] (59 g., 0.12 mole) in 500 ml. of water was refluxed for four hours. After filtering while hot and then cooling in an ice-bath, white needles separated. These were removed and washed with cold water; yield 14 g. (70%), m. p. 117–118°. One recrystallization from 60% alcohol gave 12.6 g. (63.1%), m. p. 119–120°. *Anal.* Calcd. for $C_9H_8O_3$: C, 65.85; H, 4.88. Found: C, 65.87; H, 4.86.

Alkaline oxidation of the dialdehyde by 5% potassium permanganate gave the known 4-methoxyisophthalic acid.

4-Thiomethylisophthalaldehyde.—A solution of the salt of methyl 2,4-bis-(chloromethyl)-phenyl thioether[8] (23 g., 0.05 mole) in 200 ml. of water was heated under reflux for four hours. The solution was filtered while hot. Upon cooling the filtrate in an ice-bath, light yellow needles separated. The solid was removed and washed with cold water; yield, 2.1 g. (24.4%), m. p. 116°. Recrystallization from 60% alcohol gave 1.8 g. (21%), m. p. 118°. *Anal.* Calcd. for $C_9H_8O_2S$: S, 17.77. Found: S, 17.30.

The **2,4-dinitrophenylhydrazone** was prepared in the usual way, m. p. 295°. *Anal.* Calcd. for $C_{21}H_{16}O_8N_8$: N, 20.86. Found: N, 20.56.

4,6-Dimethoxyisophthalaldehyde.—All attempts to isolate the necessary bis-chloromethyl compound by the chloromethylation of resorcinol dimethyl ether led to polymers. The following represents a method of obtaining a small portion of the desired chloromethylation product as the salt. To 5 g. (0.036 mole) of resorcinol dimethyl ether was added 10 g. (0.124 mole) of chloromethyl

Table I

Bis-chloromethyl compound	Hexamethylene-tetramine salt	Aqueous hydrolysis product	Yield,[a] %
2,4-Bis-(chloromethyl)-anisole	White, cryst.	4-Methoxyisophthalaldehyde	70
Methyl 2,4-bis-(chloromethyl)-phenyl thioether	White, cryst.	4-Thiomethylisophthalaldehyde	24
4,6-Bis-(chloromethyl)-resorcinol dimethyl ether	[b]	4,6-Dimethoxyisophthalaldehyde	[b]
Bis-(chloromethyl)-mesitylene	White, cryst.	Basic nitrogen compounds	..
2,5-Bis-(chloromethyl)-hydroquinone dimethyl ether	White, cryst.	2,5-Dimethoxyterephthalaldehyde	63
2,5-Bis-(chloromethyl)-*p*-xylene	Gummy, hygroscopic	2,5-Dimethylterephthalaldehyde	57
o-Xylylene bromide	White, cryst.	Basic nitrogen compounds	..
4,5-Bis-(chloromethyl)-*o*-xylene	White, cryst.	Basic nitrogen compounds	..
4,5-Bis-(chloromethyl)-veratrole	White, cryst.	Basic nitrogen compounds	..
3,4-Bis-(chloromethyl)-veratrole	Gummy, hygroscopic	Basic nitrogen compounds	..

[a] Yields are calculated on the basis of the hexamethylenetetramine salt (with the exception of 2,5-dimethylterephthalaldehyde). [b] Since the salt was derived from a mixture of chloromethyl compounds, the yield was not calculated.

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[4] University of Tennessee Fellow, 1947–1948.

[5] Sommelet, *Compt. rend.*, **157**, 852 (1913).

[6] Fuson and Denton, This Journal, **63**, 654 (1941).

[7] The chloromethyl compound was prepared by the method of Quelet and Anglade, *Bull. soc. chim.*, [5] **3**, 2200 (1936).

[8] The chloromethyl compound was prepared by the method of Wood, Perry and Tung, This Journal, **72**, 2989 (1950).

ether. After the reaction mixture had been stirred for three minutes at room temperature, 40 ml. of dry chloroform containing 17.4 g. (0.124 mole) of hexamethylenetetramine was added with stirring. Thus all chloromethyl compounds including unchanged chloromethyl ether were precipitated as the salt. The mixture was stirred for three hours before removing the salts. The mixture of salts was dissolved in 100 ml. of water and heated under reflux for four hours. After filtering while hot and then cooling, light yellow needles separated. These were recrystallized from hot water; yield one-half gram, m. p. 204°. *Anal.* Calcd. for $C_{10}H_{10}O_4$: C, 61.84; H, 5.19. Found: C, 61.98; H, 5.28.

Alkaline oxidation of the dialdehyde by 5% potassium permanganate gave the known 4,6-dimethoxyisophthalic acid.

2,5-Dimethoxyterephthalaldehyde.—A solution of 257.5 g. (0.5 mole) of the salt of 2,5-bis-(chloromethyl)-hydroquinone dimethyl ether[9] in 2 l. of water containing 100 ml. of 40% formalin was refluxed for four hours with stirring. A yellow precipitate formed and was filtered off after the mixture had cooled to room temperature. This yellow solid, 2,5-dimethoxyterephthalaldehyde, was converted into the bisulfite salt by heating with an excess of sodium metabisulfite dissolved in about 2 l. of water. As soon as solution of the aldehyde was complete, the hot solution was filtered to remove a small amount of insoluble material. After heating the filtrate for about an hour, concentrated hydrochloric acid was added slowly and with stirring. Care had to be taken while adding the acid in order that the sulfur dioxide evolved did not cause the mixture to foam over the sides of the beaker; vigorous stirring helped prevent excessive foaming. After adding enough hydrochloric acid to give about a 25% excess, the mixture was left standing three hours on the steam plate. The bright yellow solid that had settled out was filtered off and pressed as dry as possible on the funnel. It was washed by transferring to a 1500-ml. beaker and stirring with 1 liter of distilled water. The water was removed by filtration. The washing process was repeated twice. Finally, the material was filtered, washed with methanol, and dried in a vacuum desiccator over calcium chloride. The bright-yellow 2,5-dimethoxyterephthalaldehyde obtained weighed 61 g. (63%) and melted at 206°. A small sample recrystallized from 95% ethanol melted at 207°. *Anal.* Calcd. for $C_{10}H_{10}O_4$: C, 61.84; H, 5.19. Found: C, 61.43; H, 5.41.

2,5-Dimethylterephthalaldehyde.—To a solution of 5 g. (0.025 mole) of 2,5-bis-(chloromethyl)-*p*-xylene in 100 ml. of 60% alcohol was added 7 g. (0.05 mole) of hexamethylenetetramine. This mixture was then refluxed for eighteen hours. On cooling, 1.84 g. of crude dialdehyde precipitated. One recrystallization from 60% alcohol gave 1.5 g. (38%) of pure 2,5-dimethylterephthalaldehyde, m. p. 102–103°. *Anal.* Calcd. for $C_{10}H_{10}O_2$: C, 74.07; H, 6.17. Found: C, 74.45; H, 6.15. .

The **phenylhydrazone** was prepared in usual way, m. p. 232°. *Anal.* Calcd. for $C_{22}H_{22}N_4$: N, 16.37. Found: N, 16.29.

Abnormal Sommelet Reactions.—Bis-(chloromethyl)-mesitylene, *o*-xylylene bromide, 4,5-bis-(chloromethyl)-xylene,[8] 4,5-bis-(chloromethyl)-veratrole[8] and 3,4-bis-(chloromethyl)-veratrole[8] readily formed the hexamethylenetetramine salts in quantitative yields. Neutral hydrolysis of the salts gave only basic nitrogen compounds. These basic nitrogen compounds are being further investigated.

Summary

1. The reaction of ten bis-(halogenomethyl)-benzenes with hexamethylenetetramine in chloroform solutions is described.

2. Hydrolysis of the salts of *m*- and *p*-bis-(chloromethyl)-benzenes according to Sommelet's procedure gave satisfactory yields of *m*- and *p*-dialdehydes except in the cases where the two nuclear carbons *ortho* to each chloromethyl group were substituted. These formed basic nitrogen compounds instead.

3. Hydrolysis of the salts of *o*-bis-(chloromethyl)-benzenes gave basic nitrogen compounds rather than *o*-dialdehydes.

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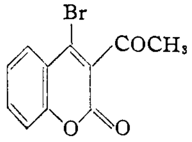
[9] The chloromethyl compound was made by the method of Wood and Gibson, THIS JOURNAL, **71**, 393 (1949).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

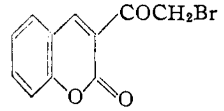
Bromination of 3-Acetocoumarin

BY C. F. KOELSCH

When 3-acetocoumarin is treated with bromine, there is obtained a monobromo derivative to which structure I has been assigned.[1] Such a derivative would be a useful intermediate in syntheses of compounds related to morphine. But the evidence for structure I, formation of an unstable addition compound during the bromination, and formation of salicylic acid when the bromo-compound is fused with alkali, does not exclude structure II. A study of the behavior of the substance toward thiourea now indicates that structure II is correct.



I



II

Of the compounds corresponding to structures I and II, only the latter could yield a thiazole with thiourea, and degradation shows that a thiazole, III, is formed with this reagent. When the thiourea product is diazotized in strong hydrochloric acid, it yields a chloro compound, IV. With alkali and methyl sulfate, the chloro compound yields an acid, V, and when this acid is oxidized with permanganate, it furnishes *o*-methoxybenzaldehyde and a new acid, VI. The composition of the latter indicates that it must contain a thiazole nucleus.

Because the bromination product from 3-acetocoumarin is not the nuclear derivative, I, it cannot be used as originally planned. But a preliminary investigation has shown that its

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[1] Rap, *Gazz. chim. ital.*, **27**, II, 500 (1897).