[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Structure of Ketene Diphenyl Acetal

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The first member of the class of ketene acetals to be prepared was ketene diphenyl acetal, $CH_2{=}C(OC_6H_5)_2$, which Biginelli[1] obtained from the reaction of methylchloroform with phenol in alkaline solution. The reaction was later formulated[2] as proceeding in the following manner

$$CH_3CCl_3 + 3KOC_6H_5 \longrightarrow CH_3C(OC_6H_5)_3 \longrightarrow CH_2{=}C(OC_6H_5)_2 + C_6H_5OH$$

While subsequent investigators[2,3] in the field of ketene acetals have mentioned Biginelli's early work, apparently no one has attempted to confirm the structure of his product. This structure was based on rather meager experimental evidence. Thus the only fact other than analysis offered in support of the formula was the observation that the compound added bromine to form a dibromide. While it is stated that addition occurred without evolution of hydrogen bromide, the test was made by adding bromine water to an alcoholic solution of the compound. It is not evident how any hydrogen bromide formed would be detected under these conditions.

Apparently it has remained unnoticed in this connection that practically simultaneously with Biginelli's work, Heiber[4] studied the reaction of methylchloroform with phenol in alkaline solution and reported the formation of phenyl orthoacetate, $CH_3C(OC_6H_5)_3$, m. p. 98–98.5° (compare Biginelli's compound, m. p. 95–96°). This ester on bromination gave a tribromo derivative, m. p. 132–133° (compare Biginelli's dibromide, m. p. 125°). While both investigators analyzed their products it happens that the percentage compositions of the compounds are practically the same, so that the analyses obtained agree with both formulas. Since the two investigators used very similar conditions of reaction and the same reagents, and Biginelli furthermore states that his product was formed under almost any conditions through the reaction of methylchloroform, phenol and alkali, it is very probable that regardless of the structure of the compound, both investigators obtained the same product.

In this investigation the reaction of methylchloroform and phenol was carried out under the conditions used by Biginelli and by Heiber, with the intention of comparing the products and determining their structure. However, although the reaction was repeated many times, and the proportions of the reactants were varied in order to allow for an accidental excess of one of the reagents in the original preparations, no alkali insoluble product whatever was formed in any case. A large amount of phenol was always recovered from the alkaline solution, together with a small yield of *o*- and *p*-hydroxyacetophenone, formed through a normal Reimer–Tiemann reaction. Both Biginelli and Heiber expected to obtain these phenolic ketones, but instead both obtained the neutral product.

Since both investigators state that their product crystallized well and is easily isolated, it seems unlikely that the failure of many attempts to confirm their results is due to inability to duplicate their experimental conditions. The only questionable point in their procedures appeared to be in the quality of the methylchloroform which they employed; neither investigator gave either the source or any indication of the purity of this reagent. The only possible impurity which has a boiling point approaching that of methylchloroform (b. p. 75°) is ethylene chloride (b. p. 84°). Methylchloroform was prepared until recently by the chlorination of ethylidene chloride,[5] CH_3CHCl_2, which in turn was often prepared by the chlorination of ethyl chloride.[5,6] Since the latter reaction is known to give a mixture of ethylidene chloride and ethylene chloride,[6] their methylchloroform might have contained ethylene chloride, if it had been prepared in this manner. Ethylene chloride reacts readily with phenol in alkaline solution to give the diphenyl ether of ethylene glycol,[7] m. p. 97–98°. Both the melting point and analysis of this compound agree with those reported by Biginelli and Heiber for their product, so this structure is certainly to be considered in attempting to decide what they actually had obtained.

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(1) Biginelli, *Gazz. chim. ital.*, **21**, 261 (1891).

(2) Staudinger and Rathsam, *Helv. Chim. Acta*, **5**, 646 (1922).

(3) Scheibler, Marhenkel and Nikolic, *Ann.*, **458**, 21 (1927).

(4) Heiber, *Ber.*, **24**, 3678 (1891).

(5) Städel, *Ann.*, **195**, 184 (1879).

(6) D'Ans and Kautzsch, *J. prakt. Chem.*, [2] **80**, 310 (1909).

(7) Solonina, *J. Russ. Phys.-Chem. Soc.*, **30**, 607 (1898); *Chem. Centr.*, **70**, I, 25 (1899).

Fortunately Heiber carried out the reaction with the cresols and *o*-nitrophenol as well as with phenol, so that the melting point of a series of diaryl ethers of ethylene glycol could be compared with those of the corresponding aryl orthoacetates which he reported. The correspondence proved to be remarkably close, as is shown in Table I, and became exact within experimental error when pure samples of the diaryl ethers of ethylene glycol were prepared. Likewise the di-*p*-bromophenyl ether has the same melting point as that reported by Heiber for the tribromo derivative of phenyl orthoacetate, and the same is true of the *o*-bromo-*p*-cresyl ether and the corresponding ester. The two series of compounds, although by no means isomeric, have very similar percentages of composition, so that Heiber's analyses agree as well with the ether as with the ester formula. The only discrepancy in the series is in the *p*-bromo-*m*-cresyl ether, which was found to melt 13° lower than the bromo derivative of *m*-cresyl orthoacetate according to Heiber. However, it is believed that the perfect agreement of melting points in seven cases is sufficient to establish the identity of the two series of compounds. Since *m*-cresol is a liquid and apt to be less pure than the other phenols which Heiber used, the deviation in this one case is regarded as much less significant than the agreement in the other seven cases.

TABLE I

COMPARISON OF ETHYLENE GLYCOL DIARYL ETHERS WITH THE CORRESPONDING ARYL ORTHOACETATES

	Aryl of $ArOCH_2CH_2OAr$	M. p., °C. (uncorr.)	Formula	Calcd., % C	Calcd., % H	Calcd., % Br	Found, % C	Found, % H	M. p. of the corresponding $CH_3C(OAr)_3$,[a] °C.	Formula	Calcd., %[j] C	Calcd., %[j] H	Calcd., %[j] Br
1	C_6H_5[b]	98–98.5 (97–98)[d]	$C_{14}H_{14}O_2$	78.46	6.58				98–98.5	$C_{20}H_{18}O_3$	78.43	5.88	
2	*p*-BrC_6H_4[c]	134–135	$C_{14}H_{12}O_2Br_2$	45.16	3.25	42.97	45.30	3.35	132–133	$C_{20}H_{15}O_3Br_3$	44.20	2.78	44.11
3	*o*-$CH_3C_6H_4$	85–86 (79)[e]	$C_{16}H_{18}O_2$	79.29	7.49		79.32	7.62	87.5–89	$C_{23}H_{24}O_3$	79.31	6.90	
4	*m*-$CH_3C_6H_4$	98–99 (91)[f]	$C_{16}H_{18}O_2$	79.29	7.49		79.10	7.61	99–100	$C_{23}H_{24}O_3$	79.31	6.90	
5	*p*-Br, *m*-$CH_3C_6H_3$	137–138	$C_{16}H_{16}O_2Br_2$	48.00	4.03	39.96	48.22	4.21	151.5–153	$C_{23}H_{21}O_3Br_3$	47.18	3.59	41.02
6	*p*-$CH_3C_6H_4$	135–136 (134.5)[g]	$C_{16}H_{18}O_2$	79.29	7.49				135.5	$C_{23}H_{24}O_3$	79.31	6.90	
7	*o*-Br, *p*-$CH_3C_6H_3$	160–161 (156)[h]	$C_{16}H_{16}O_2Br_2$	48.00	4.03	39.96	47.92	3.87	160–161	$C_{23}H_{21}O_3Br_3$	47.18	3.59	41.02
8	*o*-$NO_2C_6H_4$	167–168 (163)[i]	$C_{14}H_{12}O_6N_2$	55.24	3.97				167–168	$C_{20}H_{15}O_9N_3$	54.42	3.40	

[a] *Cf.* Ref. 4. [b] Compare also $CH_2{=}C(OC_6H_5)_2$ (Ref. 1); m. p. 95–96°; $C_{14}H_{12}O_2$; calcd. C, 79.24; H, 5.66. [c] Compare also $CH_2{=}C(OC_6H_4Br)_2$ (Ref. 1); m. p. 125°; $C_{14}H_{10}O_2Br_2$; calcd. C, 45.16; H, 3.22; Br, 43.01. [d] *Cf.* Ref. 7. [e] Staedel, *Ann.*, **217**, 41 (1883). [f] Gattermann, *ibid.*, **357**, 378 (1907). [g] Fuchs, *Ber.*, **2**, 625 (1869). [h] Stoermer and Göhl, *ibid.*, **36**, 2875 (1903). [i] Wagner, *J. prakt. Chem.*, [2] **27**, 201 (1883). [j] Heiber's analytical results (Ref. 4) are not tabulated in order to conserve space; his hydrogen analyses agree better with the ether than with the ester formula, while the opposite is true in general with the carbon and bromine analyses. The difference is not sufficiently great to permit decision of the correct formula on the basis of analysis.

The probability that Heiber's compounds were really aryl ethers rather than ortho esters is substantiated by the properties which he reported. His products were practically unaffected by boiling with strong acids and alkalies, a behavior which is certainly more characteristic of ethers than ortho esters. While Heiber reported that his "phenyl orthoacetate" was partially hydrolyzed to phenol and acetic acid on long refluxing with concentrated alcoholic alkali, the acetic acid was characterized only "through the acetic ester reaction." The formation of a trace of acetic acid might have been due to partial oxidation of the alcohol used as a solvent in some stage of the procedure.

The reaction of phenol with a mixture of ethylene chloride and methylchloroform in alkaline solution was found to give the diphenyl ether of ethylene glycol, and from the yield obtained it was calculated that Heiber's methylchloroform need have contained only 22% of ethylene chloride in order to have formed the small yield which he reported of the alkali insoluble product. This therefore seems the most likely explanation of the origin and structure of the series of compounds prepared by Heiber. If the identity of the products obtained by Heiber and Biginelli is granted, then the "ketene diphenyl acetal" prepared by Biginelli was likewise in reality the diphenyl ether of ethylene glycol.

Experimental Part

Reaction of Methylchloroform[8] with Phenol and Alkali.—Since no alkali insoluble product was obtained in any case, only one set of experiments, modeled after Heiber's procedure, will be described in detail. Three solutions containing phenol and sodium hydroxide were prepared, one from 38.4 g. of phenol and 15.0 g. of sodium hydroxide in 23 cc. of water, and the other two containing a 10% excess of phenol in one case, and a 10% excess of sodium

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[8] The methylchloroform was obtained from the Eastman Kodak Co. It was prepared by the addition of hydrogen chloride to 1,1-dichloroethylene and consequently was free from ethylene chloride. It was refractionated before use.

hydroxide in the other. The solutions were heated at 85–90° under reflux for ninety hours and a total of 16.8 g. of methylchloroform added to each in four equal portions at twelve-hour intervals during the first thirty-six hours. The solutions were then diluted with two volumes of ice and water, made alkaline with additional dilute sodium hydroxide and extracted three times with ether. The ether extracts were washed with sodium hydroxide to remove phenol and then evaporated. The residue in each case was from 0.1 to 0.2 g. of a brown oil, which failed to crystallize on standing for several months. The three alkaline solutions were combined, acidified with concentrated hydrochloric acid, and extracted with ether. The extract was distilled at atmospheric pressure; 94 g. (82%) of phenol was recovered. The small high boiling residue was distilled in vacuum; 5 g. of distillate was obtained, approximately half of which solidified. The solid on recrystallization gave 2.0 g. of pure *p*-hydroxyacetophenone, m. p. 109–110° (110°),[9] which was identified as the semicarbazone, m. p. 198–199° (197–198°),[10] and the oxime, m. p. 145–146° (144–145°).[11] The liquid was identified as *o*-hydroxyacetophenone through the preparation of the semicarbazone, m. p. 209–210° (209–210°),[12] and the oxime, m. p. 116–117° (117°).[13] The relative proportion of *o*- and *p*-hydroxyacetophenone isolated is not significant, since the former is a liquid and lower boiling, so that probably much more of it was lost in the phenol fraction.

Preparation of Ethylene Glycol Diaryl Ethers.—The ethers were prepared from ethylene bromide and the potassium salts of the various phenols under conditions similar to those used by Lippmann.[14] The phenol (0.2 mole) and potassium hydroxide (0.2 mole) were dissolved in 60 cc. of alcohol and 25 g. of ethylene bromide added. The mixture was refluxed for two hours except with *o*-cresol (four hours) and *o*-nitrophenol (forty hours). The solutions were then cooled, filtered and the potassium bromide washed out with water. The ethers so obtained were practically pure and were further purified by recrystallization from alcohol. The yield was 30% except with *o*-nitrophenol, which gave a 5–10% yield. The yields were low due to a considerable side reaction producing vinyl bromide from the ethylene bromide. Better yields (70–85%) were obtained when ethylene chloride was substituted for the bromide and the reaction carried out in water solution, but long refluxing (forty-eight hours) was required and the products obtained were less pure, so that the first method is preferable.

Dibromo Derivatives.—The dibromo derivatives of the phenyl and *m*- and *p*-cresyl ethers were prepared according to the procedure used by Heiber[4] for the corresponding "ortho esters." A slight excess of bromine in acetic acid was added to a saturated solution of the ethers in acetic acid at room temperature. The crystalline dibromo derivatives separated at once, and were filtered and recrystallized from alcohol, benzene and acetic acid, respectively. The yields were 50–70%. The melting points and analyses of the new bromo derivatives and of the other aryl ethers found to have considerably higher melting points than those previously reported are included in Table I. The position of the bromine in the dibromo derivatives of the phenyl and *m*-cresyl ethers was established by preparing the *p*-bromophenyl and *p*-bromo-*m*-cresyl ethers from pure crystalline samples of *p*-bromophenol and *p*-bromo-*m*-cresol through reaction of the potassium salts with ethylene bromide according to the procedure used with the simple aryl ethers. The products thus obtained had the same melting points as those obtained through bromination and mixed melting points showed no depression. The *o*-bromo-*p*-cresyl ether had been synthesized previously by a similar method which established its structure (Ref. *h*, Table I).

The low melting point of the *p*-bromo *m*-cresyl ether (compared with the bromo derivative of the corresponding "ortho ester") is not due to impurity. This was established by purifying by crystallizing to constant melting point from several solvents; by sublimation in high vacuum, and by synthesis as described above from pure *p*-bromo-*m*-cresol, m. p. 61–62°. In order to remove all doubt as to the purity of the *m*-cresyl derivatives, a sample of *m*-cresol was prepared from pure *m*-nitrotoluene, m. p. 15–16°, through reduction, diazotization and hydrolysis. The *m*-cresyl ether and *p*-bromo-*m*-cresyl ether prepared from this pure *m*-cresol had the same melting points as those previously prepared.

Reaction of $NaOC_6H_5$ with a Mixture of Methylchloroform and Ethylene Chloride.—The first procedure described for the reaction of methylchloroform with phenol was repeated with a mixture of 3.36 g. of ethylene chloride and 13.44 g. of methylchloroform. A yield of 5.15 g. (71%) of the diphenyl ether of ethylene glycol, m. p. 98–98.5°, was obtained. On the basis of this yield Heiber's methylchloroform must have contained 22% of ethylene chloride in order to account for the yield which he reported of the neutral product. Such a mixture of ethylene chloride and methylchloroform would be formed by the chlorination of ethyl chloride, and would be very difficult to separate by fractionation.

Summary

The reaction of methylchloroform with phenol in the presence of sodium hydroxide gives a small yield of a mixture of *o*- and *p*-hydroxyacetophenone through the Reimer–Tiemann reaction. The neutral product obtained by previous investigators from this reaction and formulated in one case as ketene diphenyl acetal[1] and in another as phenyl orthoacetate[4] probably originated from ethylene chloride present as an impurity in the methylchloroform used, and was in reality the diphenyl ether of ethylene glycol. This conclusion is supported by an exact correspondence in melting points of seven diaryl ethers of ethylene glycol with the corresponding compounds previously formulated as aryl orthoacetates.

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[9] Pfeiffer, *Ann.*, **383**, 142 (1911).

[10] Perkin, *J. Chem. Soc.*, **71**, 810 (1897).

[11] Tutin, Caton and Hann, *ibid.*, **95**, 2123 (1909).

[12] Pauly and Lockemann, *Ber.*, **48**, 30 (1915).

[13] Anschütz and Scholl, *Ann.*, **379**, 337 (1911).

[14] Lippmann, *Compt. rend.*, **68**, 1269 (1869).