collected and recrystallized from water; m.p. 118–120°, mixed m.p. 119.5–120°; yield 0.19 g. (34.4%). An exactly similar oxidation of 1 g. of 3-benzylindole gave 0.20 g. (33.9%) of benzoic acid.

Attempted Reaction of 1-Methylgramine with Methylmagnesium Iodide.—To the Grignard reagent from 3.1 g. of methyl iodide in 10 ml. of ether was added a solution of 3.8 g. of 1-methylgramine in 25 ml. of dry xylene. The reflux condenser attached to the flask was drained to allow the ether to escape, and the resulting xylene suspension was refluxed for 24 hours. Hydrolysis of the mixture, finally with 1:1 hydrochloric acid, caused complete solution of the solids. Addition of ammonia to the acid solution caused the separation of an oil, presumably 1-methylgramine, which was not investigated. The organic solution was concentrated to a very small residue which could not be converted to a picrate.

When the reaction was carried out in ethyl ether no neutral product was obtained and 1-methylgramine, identified as the picrate, was recovered. No pure substance could be isolated when the reaction was carried out in pyridine.

Reaction of Gramine with Phenylmagnesium Bromide.—The reaction was carried out with 10.0 g. (0.0575 mole) of gramine and the Grignard reagent from 0.144 mole of bromobenzene in *n*-butyl ether. The mixture was refluxed for 39 hours, during which time an amine was evolved. After hydrolysis, as described above, the acid layer was treated with ammonium chloride and ammonia to permit the recovery of 2.5 g. (25%) of the gramine, identified by mixed melting point. The organic material obtained by concentration of the *n*-butyl ether solution after the hydrolysis was steam distilled to volatilize about 0.1 g. of crystalline material, presumably biphenyl. The non-volatile portion was collected in benzene, recovered, and sublimed at 0.5 mm., bath temperature 140°. The benzylindole so obtained melted at 107.8–108.3° and weighed 0.39 g. (3.3%).

Attempted Reaction of *o*-Dimethylaminomethylphenol with Phenylmagnesium Bromide.—The reagent was prepared by distillation of the commercial product (Rohm and Haas DMP-10) with collection of the fraction boiling at 62–65° (1 mm.), $n^{20}\text{D}$ 1.5303. Treatment of 22.7 (0.15 mole) of this material with an excess (0.4 mole) of phenylmagnesium bromide in *n*-butyl ether was accompanied by an immediate reaction, presumably that of the phenolic hydroxyl group with the Grignard reagent. Subsequent heating of the reaction mixture, finally under reflux for 24 hours, did not cause the liberation of any volatile amine. The cooled reaction mixture was hydrolyzed with hydrochloric acid and the organic layer was extracted with a second portion of the acid. From the organic layer 0.44 g. (1.4%) of biphenyl and 1.83 g. of phenol, identified as the tribromo derivative, were obtained. Treatment of the acid solutions with ammonia, extraction with ether, concentration, and distillation led to the recovery of 3.24 g. (14.3%) of the *o*-dimethylaminomethylphenol, b.p. 57–58° (0.8 mm.), $n^{20}\text{D}$ 1.5247. When a sample of the redistilled aminophenol used in this experiment was subjected to the extractions employed in this isolation, 14% of it was recovered with b.p. 53–54° (0.8 mm.) and $n^{20}\text{D}$ 1.5252, and phenol was also isolated. Thus it appears that phenol was not produced by reaction with the Grignard reagent, but was originally present as an impurity.

Reactions of Benzyltrimethylammonium Iodide and Benzylpyridinium Chloride with Phenylmagnesium Bromide.—The reaction was carried out with 0.1 mole of the benzyltrimethylammonium salt and 0.25 mole of the Grignard reagent in refluxing *n*-butyl ether over a period of 118 hours. There was no appreciable amine evolution. The organic layer after hydrolysis was dried and distilled to give 4.49 g. of biphenyl, b.p. 139–148° (25 mm.), m.p. and mixed m.p., 67–68.5°. A higher boiling fraction, collected at 100–200° (1 mm.), was oxidized by refluxing for 2 hours with a solution of 3 g. of potassium permanganate and 5 ml. of 10% sodium hydroxide in 75 ml. of water. No benzophenone, as such or as the dinitrophenylhydrazone, could be isolated from the neutral material remaining after the oxidation.

In a similar reaction with benzylpyridinium chloride, carried out in refluxing *n*-butyl ether for about 70 hours, biphenyl was isolated in a yield of only 4.3%. A few milligrams of a crystalline solid, perhaps a dihydropyridine derivative, was isolated by sublimation of the acid-soluble products. No diphenylmethane was found.

Reaction of 2-Dimethylaminomethylpyrrole Methiodide with Methylmagnesium Iodide.—When the reaction was carried out in refluxing *n*-butyl ether trimethylamine was formed; it was collected in a Dry Ice trap and identified as the picrate by mixed melting point. However, no 2-ethylpyrrole was found.

Reactions of 1-Methylgramine Methiodide with Phenyllithium and *p*-Tolylmercuric Chloride.—Modifications of the procedures used in the corresponding reaction with phenylmagnesium bromide were employed, and *n*-butyl ether was used as the solvent. Amine evolution was feeble in the phenyllithium reaction. The amine formed was condensed in a Dry Ice trap and proved as trimethylamine by conversion to the picrate. Evolution of amine from the *p*-tolylmercuric chloride reaction mixture was more copious. Neither reaction mixture gave any 1-methyl-3-benzylindole when subjected to the general procedure used above for the isolation of this product.

URBANA, ILLINOIS RECEIVED SEPTEMBER 11, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, OREGON STATE COLLEGE]

The Preparation of α-Bromoacetals[1]

BY ELLIOT N. MARVELL AND MICHEAL J. JONCICH

This paper describes a study carried out to find a more suitable brominating agent for acetals than free bromine. It has been shown that acetals can be brominated readily by N-bromosuccinimide (NBS). The predominant products of the treatment of the diethyl acetals of acetaldehyde, propionaldehyde, butyraldehyde and isobutyraldehyde were the α-bromoacetals. A by-product containing a more reactive bromine was noted in each case. An attempt was made to determine whether bromination can occur on the carbon containing the two ether linkages by treating benzaldehyde diethyl acetal with NBS. The sole isolable product was ethyl benzoate. The yields of pure α-bromoacetals suggest that this method is preferable to the use of elementary bromine for the preparation of low molecular weight α-bromoacetals.

Discussion

Although aldehydes can be brominated directly to give α-bromoaldehydes,[2] their preparation is generally carried out by bromination of the acetal followed by hydrolysis to the free aldehyde. Pinner[3] brominated acetals without providing for the removal of the hydrogen bromide generated in the reaction, but later workers have used either suspended calcium carbonate[4] or pyridine[5] to destroy the acid as rapidly as it is formed. It has

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(2) (a) A. Franke, *Ann.*, **351**, 421 (1907); (b) Dworzak and Prodinger, *Monatsh.*, **53/54**, 588 (1929).

(3) Pinner, *Ber.*, **5**, 147 (1872).

(4) E. Fischer and K. Landsteiner, *ibid.*, **25**, 2549 (1892).

(5) S. M. McElvain and P. M. Walters, THIS JOURNAL, **64**, 1963 (1942).

recently been shown[6] that this method does not give a pure product. For example, the product from the bromination of propionaldehyde diethyl acetal when distilled through a 10″ column packed with glass helices gave four fractions, b.p. 69.0 to 70.5° (15 mm.) having refractive indices varying from 1.4518 to 1.4700. The contaminant has been found to possess a more reactive bromine than does the α-bromoacetal and can be removed by preferential hydrolysis.

In view of these difficulties it seemed desirable to attempt to find a more effective brominating agent for acetals. Since N-bromosuccinimide has been found to be an excellent brominating agent and does not produce hydrogen bromide as a by-product, it seemed especially well suited for this purpose. The diethyl acetals of a series of aliphatic aldehydes have been brominated with NBS[7] and the results indicate that the method has some advantages over the earlier procedures. The reaction proceeds smoothly at room temperature and generally affords considerably better yields of pure α-bromoacetals than do other methods. The results of the bromination of four low molecular weight aldehydes are shown in Table I. Heptaldehyde diethyl acetal was also allowed to react with NBS but no pure product was isolated from that treatment.

TABLE I

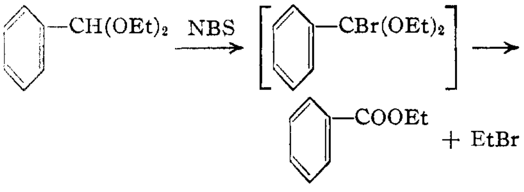
Diethyl acetal of[a]	Yield, %	B.p. °C.	B.p. Mm.	n^{20}_D	d^{20}_{20}	M_D Found	M_D Calcd.
α-Bromoacetaldehyde[8]	57	67	15	1.4401	1.286	40.4	40.9
α-Bromopropionaldehyde[13, b]	68	82–85	30	1.4371	1.207	45.9	45.6
α-Bromobutyraldehyde[10]	24	74–77	15	1.4418	1.170	50.9	50.2
α-Bromoisobutyraldehyde[9,11]	59	87.5	30	1.4345	1.141	50.6	50.2

[a] References below are to earlier work on the preparation of these same bromoacetals. [b] Reaction carried out with small amount of carbon tetrachloride added to provide fluidity.

The earliest brominations were carried out by adding the acetal dropwise to a solution of NBS in boiling carbon tetrachloride. After a short induction period the reaction commenced as indicated by the development of a red color in the solution. This reaction proved to be highly exothermic and often became violent. No pure products were isolated from these experiments, although trials were made with and without solvents, at room temperature and with external cooling. Apparently the presence of excess brominating agent is detrimental to the reaction. Consequently the brominations were carried out by adding successive small portions of dry NBS to the well-stirred acetal. The course of the reaction was followed easily by means of the red color which develops during the bromination process but disappears upon its completion. This color does not appear to be due to the presence of free bromine since no hydrogen bromide was ever detected during the reaction.

The use of solvents such as carbon tetrachloride or ethyl ether did not improve the yields. Since the bromination is exothermic, careful regulation was used to prevent overheating which had been found to decrease the yield markedly. Although external cooling seemed to help, the best yields were obtained when the rate of addition of NBS was regulated so as to maintain the temperature between 25 and 40°. The reaction is photo-catalyzed and all runs were carried out either in direct sunlight or with illumination from a 60-watt lamp.

The unidentified bromination product containing the more reactive bromine was present in the material from the NBS brominations. Since this compound appeared in the treatment of acetaldehyde diethyl acetal as well as in all other cases, it seemed likely that the reactive bromine was present on the carbon containing the two ether linkages. In order to test this theory benzaldehyde diethyl acetal was permitted to react with NBS. The reaction proceeded smoothly and apparently in the same manner as the other brominations. However, no pure bromine containing substance was isolated from the reaction product. The only pure material obtained was ethyl benzoate. This substance could have been formed by the reaction series illustrated by equation I.



(I)

The decomposition of the intermediate follows the scheme postulated by McElvain and Kundiger[12] to explain a similar decomposition. However, no ethyl bromide was isolated from the bromination of benzaldehyde acetal although an attempt was made to do so. A further investigation of this reaction is in progress.

In view of the fact that more than one bromination product was obtained and since few accurate data useful for the identification of α-bromoacetals are available, more readily identifiable materials were prepared from all the products. In general this consisted in the hydrolysis of the acetal and oxidation of the aldehyde. Thus it was shown that the major product of the bromination of acetals with NBS was always the α-bromoacetal.

Experimental[13]

Bromination of Acetals.—With the exception of acetaldehyde diethyl acetal which was obtained from Eastman Kodak Co. all acetals were prepared by modification of the method of Claisen,[14] and their physical properties agreed with those described in the literature. The freshly distilled acetals were brominated with equimolar quantities of dry NBS. The NBS was added in small portions at such a rate that the temperature did not rise above 40°. The

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[6] (a) S. M. McElvain, R. L. Clark and G. D. Jones, THIS JOURNAL, **64**, 1966 (1942); (b) E. R. Alexander and E. N. Marvell, unpublished results, University of Illinois, 1948.

[7] NBS will be used as an abbreviation for N-bromosuccinimide throughout the remainder of this paper.

[8] P. Z. Bedoukian, THIS JOURNAL, **66**, 651 (1944).

[9] J. R. Johnson, A. A. Larsen, A. D. Holly and K. Gerzon, *ibid.*, **69**, 2364 (1947).

[10] S. M. McElvain, R. L. Clark and G. D. Jones, *ibid.*, **64**, 1966 (1942).

[11] E. R. Alexander, *ibid.*, **70**, 2592 (1948).

[12] S. M. McElvain and D. Kundiger, *ibid.*, **64**, 254 (1942).

[13] All melting points are uncorrected.

[14] L. Claisen, *Ber.*, **29**, 1005 (1896).

reaction mixture was exposed to direct sunlight and stirred continuously throughout the course of the reaction. A deep red color appeared during the process but faded when the reaction was complete. After the mixture had cooled, crude succinimide was isolated by suction filtration and washed with carbon tetrachloride. The filtrate and washings were combined and shaken for 30 minutes with saturated sodium bicarbonate. The organic layer was separated, dried over anhydrous magnesium sulfate and the product distilled through a 10" packed column. The products were identified by the preparation of derivatives as follows.

The **semicarbazone** of **α-bromoacetaldehyde** was prepared from the acetal. Seven grams of the acetal was shaken with 20 ml. of hydrochloric acid for 48 hours and the product taken up in ether. The ether was allowed to evaporate, the residue dissolved in 20 ml. of ethanol and the semicarbazone prepared according to the directions of Shriner and Fuson.[15] The product melted at 129.5–130°. A melting point of 128° has been reported.[16]

α-Bromopropionanilide was prepared from the product of bromination of propionaldehyde diethyl acetal. Six grams of the product was shaken with 20 ml. of hydrochloric acid for several days, the mixture extracted with ether and the ether extracts washed with saturated sodium bisulfite solution. Enough 10% sodium hydroxide was added to the bisulfite solution to make it alkaline and the aldehyde oxidized to the acid with potassium permanganate. The mixture was acidified, treated with sodium bisulfite and the acid extracted with ether. α-Bromopropionanilide, m.p. 97°, was prepared according to the directions of Shriner and Fuson.[17] This corresponds to the melting point given in the literature[18] for α-bromopropionanilide.

α-Bromobutyraldehyde.—The acetal was hydrolyzed to the free aldehyde with hydrochloric acid as described earlier and isolated by means of its bisulfite addition complex. The aldehyde had n^{20}_{D} 1.4693 whereas 1.4683 had been reported[19] for that compound.

α-Bromoisobutyric acid was prepared from the product of bromination of isobutyraldehyde diethyl acetal. Five and one-half grams of the acetal was converted to α-bromoisobutyric acid according to the directions given for the preparation of α-bromopropionic acid. The solid acid was isolated in a Buchner funnel and then recrystallized from hot water, m.p. 48–49°. A melting point of 49° is recorded for this acid.[20]

Reaction of Benzaldehyde Diethyl Acetal with NBS.—Freshly distilled benzaldehyde diethyl acetal, 32.0 g. (0.195 mole), was caused to react with NBS under conditions identical with those described for the preparation of α-bromoacetaldehyde diethyl acetal. The product of this reaction, which gave an immediate and copious precipitate with alcoholic silver nitrate, was purified by distillation through a 10" electrically heated column packed with $^3/_{16}''$ glass helices, b.p. 40° (1.0 mm.); n^{20}_{D} 1.5058; d^{22}_{20} 1.07. The constants correspond to those of ethyl benzoate. Five ml. of this material was boiled under reflux with 40 ml. of 25% sodium hydroxide for 1 hour. This solution was subjected to distillation until 10 ml. of distillate had been collected and this distillate was saturated with potassium carbonate. The organic layer was separated and a 3,5-dinitrobenzoate prepared according to the directions of Shriner and Fuson.[21] The ethyl 3,5-dinitrobenzoate melted at 92–93°. The residue in the still pot was made acid to litmus with dilute phosphoric acid, the precipitate isolated by filtration and recrystallized from hot water, m.p. 120–121°.

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[15] R. L. Shriner and R. C. Fuson, "Identification of Organic Compounds," Second edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 142.

[16] H. Hibbert and H. S. Hill, THIS JOURNAL, **45**, 734 (1923).

[17] R. L. Shriner and R. C. Fuson, *loc. cit.*, p. 132.

[18] C. A. Bischoff and P. Walden, *Ber.*, **27**, 2939 (1894).

[19] A. Kirrmann, *Compt. rend.*, **184**, 525 (1927).

[20] W. Markownikoff, *Ann.*, **153**, 228 (1870).

[21] R. L. Shriner and R. C. Fuson, ref. 16, p. 138.

CORVALLIS, OREGON

RECEIVED AUGUST 14, 1950

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

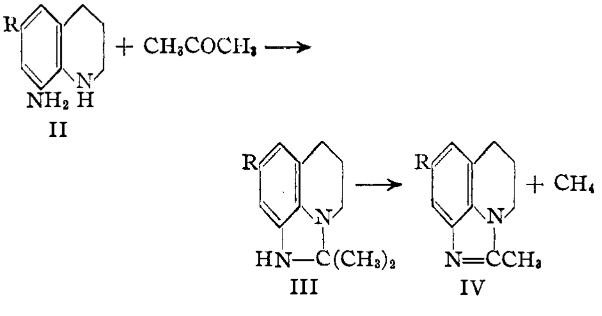
The Reaction of *o*-Phenylenediamines with Carbonyl Compounds. II. Aliphatic Ketones[1]

BY ROBERT C. ELDERFIELD AND JOHN R. MCCARTHY

Reaction of *o*-phenylenediamine and its monoalkyl derivatives with ketones has been shown previously to yield benzimidazoles. This reaction, which involves cleavage of a carbon–carbon bond under relatively mild conditions has been studied further. Factors which apparently govern the elimination of alkyl groups from benzimidazolines with the production of benzimidazoles are discussed. The bearing of these observations on previously reported reactions of *o*-phenylenediamine with ketones is also discussed.

In a preceding paper[2] it was shown that direct heating of *o*-phenylenediamine (I), or a mono-N-alkyl derivative of *o*-phenylenediamine with aldehydes or ketones results in the formation of derivatives of benzimidazole which arise from degradation of an intermediate imidazoline as illustrated by II-IV.

Although the elimination of a fragment of a carbonyl compound by cleavage of a carbon–carbon bond to form an azomethine linkage is a fairly common reaction, factors which govern such degradations have, in general, been subordinated to over-all synthetic considerations. An example may be found in Riehm's synthesis of 2,4-dimethylquinoline[3] from the reaction of aniline with acetone or mesityl oxide. Methane is evolved during the course of the reaction. Knoevenagel and Bahr,[4] Reddelien and Thurm,[5] and Craig[6] have advanced evidence that the reaction proceeds through 2,2,4-trimethyl-1,2-dihydroquinoline.



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[1] This paper comprises a dissertation submitted by John R. McCarthy in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

[2] Elderfield and Kreysa, THIS JOURNAL, **70**, 44 (1948).

[3] Engler and Riehm, *Ber.*, **18**, 2245 (1885).

[4] Knoevenagel and Bahr, *ibid.*, **55**, 1916 (1922).

[5] Reddelien and Thurm, *ibid.*, **65**, 1511 (1932).

[6] Craig, THIS JOURNAL, **60**, 1458 (1938).