Kinetics of the Acid-Catalyzed Condensation of Formaldehyde with *N,N*-Dimethyl-*m*-toluidine

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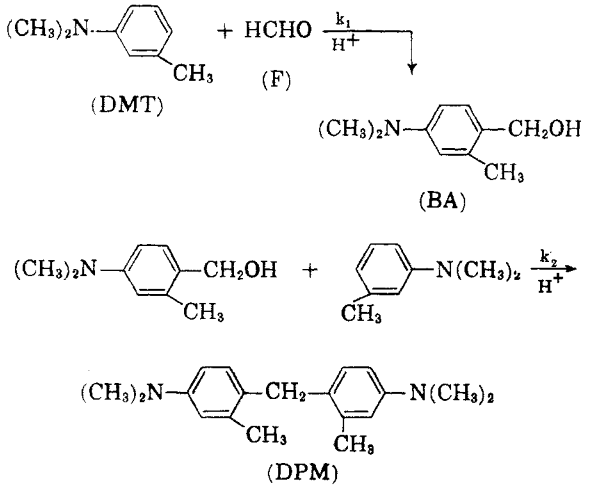
The acid-catalyzed reaction of an aldehyde with an aromatic tertiary amine to form a di- or triphenylmethane derivative is a familiar preparative process which has indeed been a mainstay of the commercial production of triphenylmethane dyes. In a preliminary kinetic investigation of this reaction which we are not now able to continue, we employed the reaction of dimethyl-*m*-toluidine with formaldehyde in a dioxane-water medium. From previous work, we expected the reaction to occur in two steps, of which the first would be rate-determining under conditions of moderate acidity.[1-4] The possibility of isolating the substituted benzyl alcohol (BA) under conditions of high acidity[5] suggested, however, that there is an inversion of relative specific rates k_1/k_2 as the acidity of the medium is increased. The earlier work indicated that in the absence of excessive concentrations of formaldehyde the reaction is uncomplicated by further additions, condensation, or polymerization, or by ortho addition. Our experiments have, however, led to the entirely unexpected conclusion that the rate of the reaction is markedly accelerated by oxygen, the major product remaining the diphenylmethane derivative (DPM). The evidence follows.



The extent of reaction at equal time (16 min.) of a series of reaction mixtures at 55° in solutions approximately $0.14M$ in formaldehyde, $0.20M$ in DMT, and $1.2M$ in pyridine, in a solvent approximately 65% dioxane by volume, revealed a dependence upon standing time before initiation of the reaction by addition of the formaldehyde. Pyridine was present as a buffer to prevent changes in acidity as the reaction progressed. The acidity was varied among the runs by addition of varying amounts of perchloric acid. Table I summarizes some typical results. The acidity is given as the ratio of the concentration of added perchloric acid to the sum of the initial concentration of DMT and the concentration of pyridine. No attempts were made in any but the last set of data to exclude atmospheric oxygen from the reaction mixtures, both before and during the reaction. Each of the groups in the table consists of runs made with the same solution. Reproducibility under identical conditions was reasonably good, as illustrated by the data of one of these groups.

TABLE I

Dependence of Conversion of Formaldehyde upon Standing Time of DMT-Pyridine-Dioxane-Water Solution Before Reaction

$\frac{(HClO_4)}{(DMT)_0 + [P]}$	Oxygen Excluded	Standing Time Before Reaction	% Conversion of F
0.00	No	20 Min.	0.0
0.14	No	20 Min.	5.7
0.43	No	20 Min.	11.3
0.43	No	20 Hr.	20.5
0.45	No	20 Min.	21.0
0.45	No	4 Hr.	26.8
0.46	No	20 Min.	27.4
0.46	No	6 Hr.	38.0
0.50	No	20 Min.	13.2
0.50	No	16 Hr.	24.4
0.51	No	20 Min.	14.0
0.51	No	20 Min.	14.2
0.44	Yes	15 Min.	3.4
0.44	Yes	5 Hr.	3.8
0.44	Yes	22 Hr.	3.6

Qualitatively similar results were obtained by a comparison of runs made in unbuffered reaction mixtures. This fact seems to eliminate the possibility of a role of pyridine in the reaction. Further work was undertaken to prepare the diphenylmethane base end product[2] under atmospheres of both nitrogen and oxygen. Results in both cases were quantitative yields, thus precluding the possibility of different reaction products when carried out in an atmosphere of oxygen. The reaction was considerably faster, however, in the oxygen environment.

The above results indicate an accelerative role of oxygen in the condensation reaction and suggest that the maximum reactivity occurs when there are appreciable amounts of both basic DMT and

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its conjugate acid in solution. The latter conclusion is of only qualitative value, however, in view of the marked oxygen effect.

EXPERIMENTAL

N,N-Dimethyl-*m*-toluidine was obtained from Eastman Kodak Co. and was purified by drying with magnesium sulfate and distillation through a 25-cm. vacuum-jacketed Vigreux column under an atmosphere of nitrogen. The boiling point was 211–212° at 760-mm. pressure, and the refractive index, n_D^{20}, was 1.5490. The amine was stored in sealed ampoules after distillation.

Pyridine was of reagent grade and was used without further purification. Commercial dioxane was purified and stored in the method given by Fieser.[6] Perchloric acid was of reagent grade.

Aqueous formaldehyde solutions were prepared by hydrolysis of paraformaldehyde in dilute phosphoric acid with subsequent distillation.

Analytical. The analysis of formaldehyde was carried out according to the method of de Jong[7] by addition to the reaction mixture of an excess of KCN followed by back titration of excess cyanide with mercuric nitrate using diphenyl carbazone as indicator. Mercuric nitrate solutions were prepared using triply distilled mercury as a primary standard,[8] and KCN solutions were checked against these. The reaction mixtures were quenched prior to analysis by addition of an excess of base. Reaction vessels were simple volumetric flasks.

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Reactions of (1-Nitrocyclohexyl)methanol

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Although (1-nitrocyclohexyl)methanol has been known for some time,[1] it appears to have been subjected to only one reaction, namely, catalytic reduction to the corresponding amino alcohol.[2–4] This paucity of published information regarding its chemical properties prompted the present investigation.

Attempts to prepare (1-nitrocyclohexyl)methyl bromide from (1-nitrocyclohexyl)methanol by treatment in the usual manner with phosphorus tribromide were unsuccessful as were attempts to prepare (1-nitrocyclohexyl)methyl iodide from the *p*-toluenesulfonate derivative of the alcohol by treatment with iodide ions. Failure of these nucleophilic displacement reactions to take place can be accounted for on the basis of the neopentyl-type structure of this primary alcohol.[5] However, (1-nitrocyclohexyl)methyl bromide was prepared by reaction of the alcohol with phosphorus tribromide in the presence of quinoline according to the method of Sommer *et al*,[6] for the successful conversion of neopentyl alcohol to the corresponding bromide.

Oxidation of (1-nitrocyclohexyl)methanol with nitrogen dioxide in chloroform under reaction conditions similar to those reported for converting primary alcohols to aldehydes[7,8] gave, instead, 1-nitrocyclohexanecarboxylic acid. The structure of this acid was established by the elemental and infrared analyses. The infrared spectrum has typical carboxyl absorption at 3.87 to 5.80μ as well as nitro absorption at 6.45 and 7.42μ.[9] The crystalline nitro acid was stable when stored at 0° but was unstable at room temperature, slowly decomposing with the evolution of gas. Attempts to obtain the nitro aldehyde by an Oppenhauer oxidation of the nitro alcohol in the presence of either acetone or cyclohexanone were unsuccessful as were attempts to prepare the nitro aldehyde by the reaction of the nitro alcohol with *N*-bromosuccinimide in carbon tetrachloride.[10]

Attempts to prepare the symmetrical ether, bis[(1-nitrocyclohexyl)methyl] ether, from (1-nitrocyclohexyl)methanol by dehydration under acidic conditions (sulfuric acid or *p*-toluenesulfonyl chloride[11]) and by the classical Williamson synthesis utilizing the potassium alcoholate and the nitro bromide were unsuccessful.

EXPERIMENTAL

(1-Nitrocyclohexyl)methanol. This compound, prepared according to Newman and Edwards[2] by the base-catalyzed condensation of nitrocyclohexane with paraformaldehyde, was purified by distillation; b.p. 100–102° (1 mm.), n_D^{25} 1.4846. This nitro alcohol is reported[3] to boil at 136–137° (5.5 mm.) with n_D^{25} 1.4853.

(1-Nitrocyclohexyl)methyl p-toluenesulfonate. A solution of 120 g. (0.75 mole) of (1-nitrocyclohexyl)methanol, and 150 g. (0.79 mole) of *p*-toluenesulfonyl chloride in 600 ml. of pyridine was kept at 10° for 3 days. The mixture was poured into water, and the white solid which formed was washed with dilute hydrochloric acid followed by water and then recrystallized from ethanol to give 220 g. (94% yield) of (1-nitrocyclohexyl)methyl *p*-toluenesulfonate, m.p. 57–58°,

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