Reduction of Benzaldehyde by Methoxide Ion in Aqueous Methanol[1-4]

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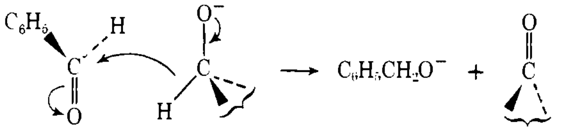
Abstract: In contrast to previous studies of the Cannizzaro reaction using isotopically labeled reactants, the benzyl alcohol from reaction of 0.60 M benzaldehyde-α-d and 0.25 M NaOH in 74% CH_3OH-26% H_2O solution at 100 °C includes a substantial percentage of benzyl-α-d_1 alcohol (21% after half consumption of hydroxide ion) rather than only benzyl-α-d_2 alcohol. Products from C_6H_5CHO in CH_3OH, CH_3OD, and CD_3OH solutions indicate that the side reactions responsible for hydrogen exchanges and adding to the yield of benzyl alcohol are (1) bimolecular hydride transfer to benzaldehyde from methoxide ion, (2) a nearly equal amount of crossed Cannizzaro reaction from the resulting formaldehyde, (3) a smaller amount of hydride transfer to benzaldehyde from the resulting sodium formate leading to sodium carbonate, and (4) a less frequent combination of two benzaldehydes plus methoxide ion leading to benzaldehyde dimethyl acetal. Decreasing the initial concentration of C_6H_5CHO to 5×10^{-4} M decreases the relative contributions of the three termolecular reactions and causes the bimolecular hydride transfer (1) to become the dominant reaction. Its $k_{CH_3O^-}/k_{CD_3O^-}$ isotope effect is 2.2 ± 0.2.

This report concerns five different hydride transfers to benzaldehyde (I) that occur to significant extents with 0.60 M I and 0.25 M NaOH in 74% methanol-26% water (v/v) at 100 °C, and produce benzyl alcohol (II) plus sodium benzoate (III), formaldehyde, sodium formate, sodium carbonate, and benzaldehyde dimethyl acetal (IV), respectively.


I

These conditions are typical and probably nearly optimal for the Cannizzaro reaction of I (to give II and III). Under these conditions, I is mostly free (not hydrate or hemiacetal), the UV absorption by its carbonyl group at 282 nm being diminished less than 11% relative to a solution of the same concentration in cyclohexane.

Neither loss of aldehydic hydrogen to the solvent nor incorporation of solvent hydrogen on carbon in the products has been observed in previous isotopic tracer studies[5] of Cannizzaro reactions of benzaldehyde (I), formaldehyde, or glyoxal, but those studies were limited to room temperature and to water solutions (no CH_3OH or C_2H_5OH) or heterogeneous conditions.

Such exchange *does* occur with 0.60 M C_6H_5CDO and 0.25 M NaOH in 74% CH_3OH-26% H_2O at 100 °C. After 6 h the products include 25 ± 1% benzyl alcohol, 24 ± 1% III, and 54 ± 2% recovered C_6H_5CDO, of the same isotopic purity (96% d_1) as the starting material. Of the total benzyl alcohol, only 79% is $C_6H_5CD_2OH$, 21% being C_6H_5CHDOH.[6]

$$2C_6H_5CDO + NaOH \xrightarrow[H_2O]{CH_3OH} [C_6H_5CD_2OH + C_6H_5CHDOH] + \underset{III}{C_6H_5CO_2Na}$$

To determine the source of the α protium of the C_6H_5CHDOH, we next labeled the solvent instead of the aldehyde. C_6H_5CHDOH amounting to 5% of the total benzyl alcohol was found after 6 h in CD_3OH-H_2O, but none in CH_3OD-D_2O. Evidently this 5% of α deuterium and the 21% of α protium above arise from oxidation of methoxide ion, with isotope effects accounting for the difference. The use of C_6H_5CDO favors this side reaction relative to the Cannizzaro, whereas use of CD_3O^- reverses the advantage. In an all-protium system, hydride transfer from CH_3O^- should produce about 15% of the total II after 6 h, via eq 2.[7]

$$CH_3OH + HO^- \rightleftharpoons CH_3O^- + H_2O \quad (1)$$

$$C_6H_5CHO + CH_3O^- \rightarrow C_6H_5CH_2O^- + H_2CO \quad (2)$$

$$C_6H_5CH_2O^- + H_2O \xrightarrow{fast} C_6H_5CH_2OH\ (II) + HO^- \quad (3)$$

The isotope effect ($k_{CH_3O^-}/k_{CD_3O^-}$) for hydride or deuteride transfer from methoxide ion was found to be 2.2 ± 0.2 by use of only 5×10^{-4} M C_6H_5CHO with 0.56 M NaOH in 74% CH_3OH or 74% CD_3OH to make this reaction strongly predominant over the Cannizzaro reaction (since the latter is second order in I and third order overall).

A crossed Cannizzaro reaction (eq 4) would be expected to consume quickly the formaldehyde formed.

$$C_6H_5CHO + H_2CO + HO^- \rightarrow C_6H_5CH_2O^- + HCO_2H \quad (4)$$

$$C_6H_5CH_2O^- + HCO_2H \xrightarrow{fast} C_6H_5CH_2OH + HCO_2^- \quad (5)$$

Equation 2 should therefore be the rate-determining step for formation of sodium formate. Molt[8] found 1.3% (6.0×10^{-4} M) sodium formate after 6 h and 39% reaction (hydroxide consumption) with 0.047 M I and 0.023 M NaOH in 50% CH_3OH at 100 °C. We found 1.8% (0.011 M) sodium formate after 6 h and 54% reaction with 0.60 M I and 0.25 M NaOH in 74% CH_3OH at 100 °C, but 0.062 M sodium formate after 6 h when 0.070 M formaldehyde was added initially. The combination of formaldehyde and hydroxide ion evidently constitutes a much more reactive hydride donor than methoxide. Of course, methoxide may also replace hydroxide, because methyl formate hydrolyzes rapidly under these conditions.

Formate ion appears to be less reactive than methoxide ion as a hydride donor (eq 6).

$$C_6H_5CHO + HCO_2^- \rightarrow C_6H_5CH_2O^- + CO_2 \quad (6)$$

$$CO_2 + HO^- \xrightarrow{fast} HCO_3^- \quad (7)$$

$$HCO_3^- + HO^- \xrightarrow{fast} CO_3^{2-} + H_2O \quad (8)$$

When sodium formate (0.060 M) was added initially to 0.60 M I and 0.25 M NaOH in 74% CH_3OH at 100 °C, 0.055 M was still present after 7 h, which corresponds, after correction

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for what is normally formed, to decarboxylation of only 24% of the added formate, in spite of the fact that, unlike CH_3O^-, it is entirely in its reactive (anionic) form.

Benzaldehyde dimethyl acetal ($C_6H_5CH(OCH_3)_2$, IV) is another product found (2% conversion based on initial C_6H_5CHO) after 48% reaction of 0.60 M C_6H_5CHO and 0.25 M NaOH in 74% CH_3OH at 100 °C, possibly the first example of the formation of an acetal in basic solution, This may result from hydride transfer to benzaldehyde (eq 10) from a reversibly formed methoxide adduct (eq 9), followed by solvolysis of the resulting α-methoxybenzyl benzoate (eq 11, 12)

$$2C_6H_5CHO + CH_3O^- \rightleftarrows CH_3OCH(C_6H_5)OCH(C_6H_5)O^- \tag{9}$$

$$\mathrm{I} + CH_3OCH(C_6H_5)OCH(C_6H_5)O^- \rightarrow \mathrm{II} + CH_3OCH(C_6H_5)OCOC_6H_5 \tag{10}$$

$$CH_3OCH(C_6H_5)OCOC_6H_5 \rightarrow CH_3O^+{=}CHC_6H_5 + \mathrm{III} \tag{11}$$

$$CH_3O^+{=}CHC_6H_5 + CH_3OH \xrightarrow{\text{fast}} \mathrm{IV} \tag{12}$$

or direct displacement by CH_3O^- on α-methoxybenzyl benzoate.

Hydride transfers from alkoxide ions to aldehydes or ketones under alkaline conditions or with metal alkoxides have often been reported,[9] but none has been demonstrated previously from methoxide ion or methanol. The Cannizzaro reaction has in fact usually been carried out in aqueous methanol rather than aqueous ethanol in order to eliminate condensation products formed from acetaldehyde. This eliminates subsequent aldol condensations (including mixed aldol condensations with the starting aldehyde) and products (some colored or tarry) derived from aldols. This change to aqueous methanol does not eliminate aldehyde formation, but the formaldehyde formed augments the yield of product alcohol by a crossed Cannizzaro reaction with the starting aldehyde (eq 4).

We studied the mechaniam of the Cannizzaro reaction of I in aqueous methanol, rather than with hydroxide ion in water, aqueous dioxane, or any other water-ether solvent, because homogeneous Cannizzaro reactions have usually in practice been conducted in aqueous methanol, and only rarely in water, aqueous dioxane, or other solvents. We were able to exclude rigorously five mechanisms for the main reaction (three from the literature and two other plausible ones) not eliminated by previous experimental work, and are left with yet another hydride transfer to I, this time from the combination of benzaldehyde (I) and hydroxide ion (eq 13).[4]

$$C_6H_5CHO + C_6H_5CHO + HO^- \rightarrow C_6H_5CH_2O^- + C_6H_5CO_2H \tag{13}$$

$$C_6H_5CH_2O^- + C_6H_5CO_2H \xrightarrow{\text{fast}} C_6H_5CH_2OH\ (\mathrm{II}) + C_6H_5CO_2^-\ (\mathrm{III}) \tag{14}$$

The other four hydride transfer reactions noted in this paper (eq 2, 4, 6, and 10) caused no difficulty in our mechanistic study of this Cannizzaro reaction.[4]

Experimental Section[2]

Reagents. Benzaldehyde (I) was Eastman white label grade, washed with 10% Na_2CO_3, dried over Na_2SO_4, and freshly distilled under prepurified N_2 before each use, bp 179–181 °C. All solutions containing purified I were prepared and transferred in a glovebag under N_2. All containers used with purified I or its solutions were dried in an oven at 110 °C and cooled in a vacuum desiccator under N_2.

Benzaldehyde-α-*d* (C_6H_5CDO) was purchased from the Volk Radiochemical Co. and treated similarly, bp 179.0–180.0 °C. Mass spectra showed it to be 96% deuterated.

Benzyl alcohol (II) was Eastman white label, redistilled under prepurified N_2. Inorganic chemicals were reagent grade.

Benzyl-α-*d* alcohol was synthesized by slow addition of an ether solution of 2.18 g of freshly distilled I to a stirred ether solution of 0.23 g of $LiAlD_4$. The solution was stirred for 30 min under N_2, hydrolyzed with 20 mL of 10% H_2SO_4, extracted with three 50-mL portions of ether, dried over Na_2SO_4, and concentrated on a rotary evaporator. The product was purified by GLC on an F & M gas chromatograph fitted with a 20 × 1.25 cm stainless steel column of 10% Dowex 710 silicone oil on Chromosorb P at 240 °C. The C_6H_5CHDOH was collected in a capillary tube which was immediately sealed. It contained 5.1% of $C_6H_5CH_2OH$ by NMR.

Benzyl-α-d_2 alcohol was synthesized by addition of 0.15 g of $LiAlD_4$ in 20 mL of ether to 0.98 g of methyl benzoate in 10 mL of ether with rapid stirring. After 30 min, 20 mL of 10% H_2SO_4 was added, and the solution was extracted with ether and worked up as before. The compound contained 3.7% C_6H_5CHDOH by NMR.

Benzaldehyde dimethyl acetal (IV) was prepared as follows. A solution of 12.0 g (0.375 mol) of CH_3OH, 15.5 g (0.146 mol) of I, 0.2 g (0.001 mol) of p-$CH_3C_6H_4SO_3H$, and 30 mL of petroleum ether was refluxed for 12 h in a Dean-Stark trap, basified with $NaOCH_3$ in CH_3OH, distilled, bp 65–69 °C (25 mm), then purified by GLC on a 0.95 × 180 cm Apiezon L column at 130 °C. The retention times were 7 min for I and 15 min for IV. The purified IV contained 2% I by GLC, NMR (neat) δ 3.1 (s, 6 H), 5.3 (s, 1 H), and 7.1–7.4 (m, 5 H).

Solvents. All water used for reaction solutions was prepared from laboratory distilled H_2O, redistilled from alkaline $KMnO_4$. D_2O was 99.5%. All CH_3OH was reagent grade. CH_3OD was prepared by refluxing CH_3OH with a ten-fold excess of D_2O and distilled on a spinning band column, bp 63–65 °C. The NMR of 250 μL of the CH_3OD was recorded and the OH peak integrated. Three 25-μL increments of CH_3OH were added and the OH peak was integrated after each addition. A graph of integration intensity vs. added CH_3OH showed that the 250-μL sample was initially 90% deuterated. CD_3OD (5.0 g) was refluxed with 19 g of H_2O, the CD_3OH was distilled on a spinning band column, bp 63–65 °C, and the exchange was repeated. Mass spectral analysis showed <1% CD_3OD since the M + 1 peak was 1.12 ± 0.27% of M (CD_3OH).

Degree of Solvation of I. The UV spectrum of I was recorded on a Zeiss PMQII spectrometer at 25 °C. The UV spectrum of I in cyclohexane shows a series of $n \rightarrow \pi^*$ peaks from 370 ($\epsilon \sim 30$) to 310 nm and a pattern between 270 and 290 nm ($\epsilon \sim 10^3$) corresponding to $\pi \rightarrow \pi^*$ transitions. *tert*-Butylbenzene, toluene, and II do not have $\pi \rightarrow \pi^*$ absorption in this region. When the spectrum of I is taken in 74% CH_3OH–26% H_2O, the $n \rightarrow \pi^*$ peaks are shifted and broadened to become continuous with the tailing of the $\pi \rightarrow \pi^*$ absorption. However, in the 270–290-nm region there is a smooth absorption peak with λ_{max} at 282 nm corresponding to the $\pi \rightarrow \pi^*$ absorption observed when cyclohexane is used as solvent. The value of ϵ at 282 nm in cyclohexane is 1220. The absorbance at 282 nm in 74% CH_3OH was 0.43 for 4.0×10^{-4} M I. Thus, only 11% of the C=O bonds are solvated in 74% CH_3OH at 25 °C. At 100 °C the extent of solvation should be even smaller. With I and 0.1 M NaOH in 74% CH_3OH at 25 °C, the absorbance was 0.44, which corresponds to only 10% solvation of the C=O bonds.

Formaldehyde, on the other hand, is heavily hydrated in aqueous solutions, the equilibrium constant for dissociation of the hydrate having a value[10] between 10^{-4} and 10^{-3}.

Products. A 12.5-mL portion of 1.0 M NaOH, 1.5 mL of H_2O, and 3.0 mL of 0.6 M I was diluted to 50 mL with CH_3OH. Aliquots (4 mL) were placed in Teflon tubes. IV (25 μL) was added to one of them. Teflon stoppers were clamped on and the tubes placed in a 100 ± 0.5 °C bath for 6 h, then cooled in an ice bath. Three aliquots were used to determine the yields of II and of III. Excess NaOH was neutralized with 0.1 M HCl to a thymolphthalein end point. III was analyzed by GLC on 0.64 × 60 cm of 20% diethylene glycol succinate on Chromosorb W. The response factor was 1.091 using $C_6H_5CH_2COC_6H_5$ as internal standard. II and I were analyzed on 0.32 × 180 cm of 10% Carbowax 4000 on Chromosorb W. The response factors were 1.432 and 1.150, respectively, using m-$CH_3C_6H_4COCH_3$ as internal standard. III (24 ± 1%), II (25 ± 1%), and I (54 ± 2%) were present. An aliquot was extracted with 0.5 mL of CCl_4, and NMR showed the following δ values (and integrated intensities): 1.5 (16), 3.1 (6), 3.3 (20), 4.5 (14), 5.3 (1), and 7.2–7.9. The peaks at δ 1.5 and 4.5 are consistent with RO*H* and

$C_6H_5CH_2OH$, respectively. The peak at δ 3.3 was shown to be CH_3OH by the addition of methanol. The δ 3.1 and 5.3 peaks were shown to be consistent with IV by addition of IV. Two aliquots were combined and extracted with 0.60 mL of CCl_4. The NMR spectrum of 0.40 mL of the extract was recorded between δ 3.0 and 3.4. IV (5 μL) was added and the spectrum recorded; this step was repeated twice. A graph of integration intensity vs. microliters of acetal showed a 2% yield of IV. The aliquot to which IV had been added was found to contain 90% of the IV expected; therefore, the 2% yield of IV represents at least 90% of the IV formed in the reaction.

Cannizzaro Reaction of C_6H_5CDO. A benzene solution of C_6H_5CDO (0.8 mL, 0.76 ± 0.04 mole fraction in the aldehyde by flame ionization GLC) was added to a 10-mL volumetric flask in a N_2-filled glovebag, then NaOH (1 M, 2.5 mL) was added, followed by 0.3 mL of H_2O. The flask was filled to the mark with CH_3OH. Final concentrations were 0.62 M aldehyde, 0.16 M benzene, and 0.25 M NaOH in 74% CH_3OH. Aliquots (4 mL) were placed in Teflon-lined Pyrex tubes, sealed, and placed in a constant temperature bath at 100 ± 0.5 °C for 6 h. Each aliquot was removed, added to 25 g of ice, and titrated to a brom thymol blue end point by 1.0 M HCl. Each solution was extracted with three 40-mL portions of ether, dried over $MgSO_4$, and analyzed on an F & M 720 gas chromatograph fitted with a 183 × 1.25 cm stainless steel column of 10% Dow-Corning 710 silicone oil on Chromosorb P. I and II were collected separately at the exit port in Pyrex capillary tubes and immediately sealed. The mass spectra of these compounds were recorded on a C. E. C. Model 21-130 mass spectrometer at 13.6 eV and 7×10^{-7} mm. Mass spectra were measured at the same time, on the same machine and at identical instrumental settings, for authentic synthesized samples of C_6H_5CHDOH and $C_6H_5CD_2OH$. The spectra indicated an incorporation of protons into the α position of benzyl alcohol of 21%. They also showed that there was no proton exchange with the solvent in the unreacted aldehyde.

Cannizzaro Reaction in $CH_3OH–D_2O$. A solution of NaOD (0.4 g) in 10 mL of D_2O was 1.052 M by titration of samples with 1.00 M HCl. A 2.4-mL sample of this solution, 0.4 mL of D_2O, and 0.6 mL of 0.6 M I were diluted to 10 mL with CH_3OD. Three 2-mL aliquots were placed in Teflon tubes. Teflon stoppers were clamped on, and the tubes were placed in a 100 °C bath for 6 h. Excess NaOH was acidified with 0.1 M HCl. H_2O (40 mL) was added and the solution was extracted with three 10-mL portions of ether. The combined extracts were washed with saturated NaCl solutions and dried with Na_2SO_4, and the solution was concentrated to 2 mL on a rotary evaporator. I and II were separated by GLC on 0.95 × 350 cm of Carbowax 4000 on Chromosorb W at 158 °C, collected in glass capillaries, immediately sealed, and analyzed by mass spectrum, giving 0.3% C_6H_5CDO and 0.6 ± 0.4% C_6H_5CHDOH, values not significantly different from zero.[2b]

Cannizzaro Reaction in $CD_3OH–H_2O$. A 2.5-mL portion of 1.00 M NaOH, 0.3 mL of H_2O, and 0.6 mL of 0.6 M I were diluted to 10 mL with CD_3OH. Three aliquots were reacted, and I and II separated and analyzed as above, giving 0.0% C_6H_5CDO and 4.1, 4.6, and 4.8% (average 4.5 ± 0.4%) of C_6H_5CHDOH.[2b]

The mass spectra of I were treated in the manner outlined by Biemann.[11] The observed intensities of the peaks at mass 105 for C_6H_5CO, 106 for C_6H_5CHO, and 107 for C_6H_5CDO were corrected for contributions due to the natural abundances of ^{13}C, ^{17}O, ^{18}O, and ^{2}H, and expressed relative to the most intense peak, 105, which is due to a single isotopically pure ion so that there are no corrections to be applied to its intensity.[2a]

The mass spectra of the benzyl alcohols were analyzed similarly. The two peaks of interest after correction for the natural abundance of isotopes were *m/e* 109 for C_6H_5CDHOH and *m/e* 110 for $C_6H_5CD_2OH$. However, the complexity of the fragmentation of the ions from benzyl alcohol required correction of the intensity at *m/e* 109 for contributions from fragmentation of the *m/e* 110 ion. This correction was based on the observed fragmentation pattern for the synthesized C_6H_5CHDOH and $C_6H_5CD_2OH$. As in the benzaldehyde case, there were no peaks below mass 105 in the fragmentation pattern. A correction was made for the original purity of the C_6H_5CDO.[2a]

Formate Ion Analysis. To determine the amount of formate ion, Cannizzaro reaction mixtures were acidified to 0.05 M with HCl and the formic acid equilibrated with methyl formate at 100 °C for 10 min. The solution was then compared with standard methyl formate solutions on an Aerograph Hi-Fy Model 600-D flame ionization gas chromatograph equipped with a 150 × 0.32 cm column of UCON (polyalkene glycol) on Fluoropak (Teflon) at 35 °C. An experimental determination of the amount of formic acid in a sample mixture of water, methanol, I, II, formic acid, and benzoic acid with this column showed good separation of the methyl formate from the methanol and no interference from I or II. The areas of the experimental and standard peaks were determined by a planimeter. This method is satisfactory for formic acid concentrations from 0.004 to 0.095 M. The equilibrium composition is 85 ± 3% conversion to methyl formate in 0.05 M HCl, by comparison with standard solutions of formic acid and methyl formate in aqueous methanol. Concentrations were corrected for the dilution factor due to acidification by HCl.[2a]

Table I. Kinetics of Reduction of C_6H_5CHO (I) by CH_3O^- and CD_3O^- [a]

CH_3O^-		CD_3O^-	
h[b]	A[c]	h[b]	A[c]
1.00	861	1.00	959
3.00	822	7.20	874
6.50	710	15.25	748
10.00	588	26.14	561
13.50	521	39.35	456
21.20	363	52.00	347
27.0	284	63.50	240
37.0	222	76.35	217
80.75	98	99.15	171
$t_{1/2}$ = 16.4 ± 0.9 h		$t_{1/2}$ = 35.7 ± 2.6 h	

[a] [PhCHO] = 5.0×10^{-4}, [NaOH] = 0.56 M, in 74 vol % CH_3OH at 103.5 °C. [b] Time in h. [c] A = (absorbance of the reaction − absorbance of solution without I) × 1000.

Kinetics. A 1.80-μL sample of I was added to 10 mL of 2.00 M NaOH and shaken. A 1.40-mL portion of this solution was added by a 2-mL syringe to a 5.0-mL volumetric flask, CH_3OH was added to the mark, and the flask was shaken thoroughly. By syringe 0.5-mL aliquots were placed in Teflon tubes, Teflon stoppers were clamped in place and the tubes were placed in a 99.5 °C bath. Tubes were placed in a 25 °C bath for 15–20 min, contents were transferred to a 0.2-cm UV cell with a total volume of 0.5 mL, and absorbance was determined on a Zeiss PMQ II spectrophotometer. Blanks were prepared in the same manner except that no I was added to the NaOH.

From the third-order rate equation

$$\frac{1}{2b-a}\left[\frac{2x}{a(a-2x)}-\frac{1}{2b-a}\ln\frac{(b-x)a}{(a-2x)b}\right]=k_3t \qquad (9)$$

where b = [initial base], a = [initial I], and x = [base] reacted at time t, the Cannizzaro part of this reaction of 5×10^{-4} M I and 0.56 M NaOH in 74% CH_3OH should require 590 h for 10% reaction. The half-life for the disappearance of I is actually 23.4 h. The absorbance (A) of the reaction mixture minus that of the blank at 222 nm (λ_{max} of III) is 0.080 at zero time and 0.073 at 142.5 h. If all the I formed III, the final A would be 0.33. This indicates that <4% of C_6H_5CHO is oxidized to III either by the Cannizzaro reaction or by O_2. To determine the rate constant for oxidation of CH_3O^-, the rate constant for decrease of I must be divided by 2 to account for the stoichiometric reaction of 2 mol of C_6H_5CHO/mol of base. The resulting k_2 is 0.7×10^{-5} ln 2/(23.4)(3600)(0.56)(2) = 0.74×10^{-5} M^{-1} s^{-1}, from which it has been calculated[2b] that only 16 ± 2% of II is formed from 0.60 M I and 0.25 M NaOH in 74% CH_3OH at 100 °C by this k_2 step.

The data in Table I for the isotope effect ($k_{CH_3O^-}/k_{CD_3O^-}$) were determined in the same way except that 5.0 g of CD_3OD and 5.0 g of CH_3OD were each refluxed with 20 mL of 5.0 M $NaOH/H_2O$ for 24 h before distillation by a spinning band column. The temperature was slightly higher (103.5 °C), but identical for these two experiments.

References and Notes

(1) Supported in part by the National Science Foundation and the National Institutes of Health.

(2) For further experimental details, cf. (a) S. R. Alpha, Ph.D. Thesis in Organic Chemistry, Massachusetts Institute of Technology, 1972; (b) R. P. Dunlap,

Ph.D. Thesis in Organic Chemistry, Massachusetts Institute of Technology, 1972.

(3) C. G. Swain, A. L. Powell, C. R. Morgan, T. J. Lynch, S. R. Alpha, and R. P. Dunlap, Abstracts, 166th National Meeting of the American Chemical Society, Chicago, Ill., 1973, No. ORGN-27.

(4) For related work on the mechanism of the Cannizzaro reaction, see C. G. Swain, A. L. Powell, W. A. Sheppard, and C. R. Morgan, *J. Am. Chem. Soc.*, preceding paper in this issue.

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(6) This deuterium exchange was first demonstrated by T.J.L. in our laboratory in Oct 1966.

(7) This hydride donation from methoxide ion to benzaldehyde should be first order in benzaldehyde rather than second. Least-squares fitting of four Cannizzaro runs in the literature for 50% aqueous methanol where benzaldehyde and hydroxide were varied independently (E. Tommila, *Ann. Acad. Sci. Fenn., Ser. A*, **59** (8), 19 (1942)) does show a deviation in this direction: $x \ln \log k_3 = x \log [C_6H_5CHO] + y \log [NaOH] + \log k_3^0$ is −0.16 ± 0.06, correlation coefficient 0.86. This is a minor side reaction under usual Cannizzaro conditions and therefore did not interfere with our previous mechanistic study of the Cannizzaro reaction.[4]

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Eliminations Forming Carbon–Heteroatom Multiple Bonds. Base-Promoted Dehydrochlorination of *N*-Chlorobenzylmethylamines[1]

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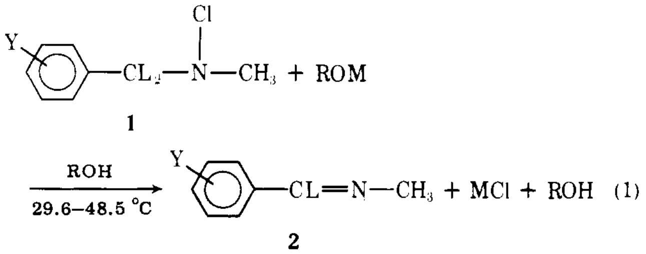
Abstract: Reactions of *N*-chlorobenzylmethylamines, **1**, with MeONa-MeOH and *t*-BuOK-*t*-BuOH have been studied kinetically. The eliminations are quantitative and regiospecific, producing only benzylidenemethylamines. The reactions are first order in base and first order in chloramine and an E2 mechanism is evident. Reactions of **1** with MeONa-MeOH and *t*-BuOK-*t*-BuOH give Hammett ρ values of +1.52 and +1.68, respectively. From eliminations of $PhCD_2N(Cl)CH_3$ and its undeuterated analogue induced by MeONa-MeOH and *t*-BuOK-*t*-BuOH, k_H/k_D values of 5.1–6.5 were calculated. For eliminations from *N*-halobenzylmethylamines, k_{Br}/k_{Cl} = 11.9 and 10.8 were observed with MeONa-MeOH and *t*-BuOK-*t*-BuOH, respectively. Comparison of these results with those for eliminations from 2-halo-1-phenylpropanes provides insight into closely related imine- and alkene-forming eliminations.

Olefin formation by base-promoted 1,2 elimination of HX from vicinal carbon atoms has been extensively investigated.[3a,4a] Similarly, base-induced HX eliminations from vinylic substrates have received considerable attention.[3b,4b,5,6] In sharp contrast, if the reverse of simple carbonyl and Schiff's base addition reactions are excluded, relatively little is known about the formation of multiple bonds between carbon and the heteroatoms N, O, and S by base-promoted 1,2 elimination of HX.[3c,4c]

Significant differences between carbon-heteroatom and carbon-carbon multiple bond forming eliminations are readily apparent. In general, the former are much more facile than the latter. For instance, eliminations from 1,1-difluoroalkanes require strong bases such as *t*-BuOK-*t*-BuOH.[7] However, even water is sufficiently basic to cause elimination from alkyldifluoramines.[8,9]

The greater facility of carbon-heteroatom multiple bond forming eliminations has been attributed to a lower stability of the heteratom-leaving group bond, greater strength of the resultant multiple bond, or increased acidity of the β hydrogen.[10] The relative importance of these three factors has not been assessed.

In order to compare closely related imine- and alkene-forming eliminations, we have investigated reactions of *N*-chlorobenzylmethylamines, **1**, with alkali metal alkoxides in the corresponding alcohols (eq 1). Corresponding alkene-forming eliminations from 1-aryl-2-halopropanes have been studied by other workers.[11,12]



	Y	L		Y	L
a	H	H	f	*m*-Me	H
b	H	D	g	*p*-Cl	H
c	*p*-MeO	H	h	*m*-Br	H
d	*m*-MeO	H	i	*p*-NO_2	H
e	*p*-Me	H	j	*m*-NO_2	H

Results

N-Chlorobenzylmethylamines, **1**, were prepared by quantitative N-chlorination of the corresponding benzylmethylamines with *N*-chlorosuccinimide in pentane. Following filtration to remove succinimide, the pentane was exchanged with the desired alcoholic solvent (see Experimental Section).

Eliminations from **1** were induced by mixing the alcoholic solution of **1** with MeONa-MeOH or *t*-BuOK-*t*-BuOH. Kinetics of the eliminations were followed by measuring the appearance of absorption at the λ_{max} for the *N*-benzylidenemethylamines, **2**, in the region 240–280 nm. Pseudo-first-order conditions (base in at least tenfold excess) were employed. Excellent pseudo-first-order kinetic plots which covered at least 2 half-lives were obtained. Pseudo-first-order rate constants were divided by the base concentration to provide the second-order rate coefficients recorded in Tables I and II.

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