# Reaction Orders in the Addition of Methanol to Chloral in 1,4-Dioxan

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Reaction velocities are reported for the addition of methanol to chloral in dioxan at 25 °C. The reaction is first order with respect to chloral. In the absence of added catalysts the order with respect to methanol is three, indicating a cyclic transition state containing three methanol molecules, resembling that previously established for the addition of water to various carbonyl compounds. In the presence of carboxylic acids the catalysed reaction is first order with respect to catalyst, while the order with respect to methanol is between unity and 1·6. This indicates that the catalyst partially replaces methanol in the transition state, but a quantitative interpretation is complicated by association between methanol and carboxylic acids. Cryoscopic measurements show that methanol is only slightly associated in dioxan at the concentrations used in the kinetic experiments.

THERE is now an accumulation of evidence that in the reversible addition of water to carbonyl compounds the transition state contains several water molecules (probably two) in addition to the one that reacts, and that when these reactions are catalysed by acids or bases, one or more of the water molecules is replaced by a molecule of catalyst. This general idea was first put forward by Eigen,[1] and has received support from studies of the dependence of the reaction rate upon water concentration or activity in a number of solvents [2-5] and also by an analysis of hydrogen isotope effects.[5] Since one of the hydrogen atoms of each water molecule plays no part in the cyclic structures proposed for the transition states [see *e.g.* equation (3) of ref. 5], similar behaviour might be expected in the addition of alcohols to carbonyl groups to give hemiacetals. The present paper describes a kinetic study of the addition of methanol to chloral in dioxan.

## EXPERIMENTAL

Chloral oxidises readily to trichloroacetic acid, which is a very effective catalyst for the reaction studied, and precautions are necessary to ensure reproducible kinetic results. Reagent grade anhydrous chloral was distilled under a reduced pressure of dried nitrogen, after flushing the distillation apparatus with nitrogen for 2 h beforehand. The distillate was diluted with dioxan to give an approximately 0·03M solution, bubbled with nitrogen, and kept in a sealed vessel at −10 °C. This mixture was used within a week of preparation. AnalaR methanol, containing $<0{\cdot}05\%$ of water, was used without further purification. Spectroscopic grade 1,4-dioxan was refluxed over sodium for 4 h and distilled through a 20-plate column (b.p. 101 °C). It was stored in sealed vessels in the dark and used within a week of distillation.

Benzoic acid (reagent grade) was recrystallized from light petroleum (b.p. 60—80 °C) and dried in an oven. AnalaR chloroacetic acid was recrystallized from benzene and dried *in vacuo* over silica gel. AnalaR trichloroacetic acid was sublimed at 48 °C and 0·5 Torr. Stock solutions (50 ml) in dioxan were prepared from weighed quantities of catalyst and their concentrations were checked by titration.

For kinetic experiments, mixtures were made up by volume, and the reaction was initiated by adding a solution of methanol to one containing chloral and catalyst (if any). The disappearance of chloral was followed by monitoring the carbonyl absorption at 292 nm with a Unicam SP 500 or 700 spectrophotometer, with the cell compartment at 25·0 ± 0·1 °C. The molar absorbance of chloral at 292 nm in dioxan was found to be $36{\cdot}9 \pm 0{\cdot}2$ l mol$^{-1}$ cm$^{-1}$, which may be compared with 38·3 found by Bell and McDougall [6] at 290 nm in cyclohexane. The velocity constants were determined from plots of $\lg(D_t - D_\infty)$ against time, where $D_\infty$ is the optical density measured after at least 8 half-lives. These plots were strictly linear, except for solutions in which an appreciable fraction of the methanol was consumed during the reaction, when the velocity constants were derived from the initial slopes.

The final optical density was never quite zero, indicating a small equilibrium degree of dissociation of the hemiacetal: the observed optical densities, in the range 0·001—0·009, suggest a value of $2{\cdot}6\ (\pm 0{\cdot}3) \times 10^{-3}$ mol l$^{-1}$ for the dissociation constant $[\mathrm{CCl_3{\cdot}CHO}][\mathrm{MeOH}]/[\mathrm{CCl_3{\cdot}CH(OH){\cdot}OMe}]$. This low value implies that our observed first-order velocity constants refer essentially to the rate of hemiacetal formation, though a small correction for the reverse reaction (not exceeding 5%) was applied to the observed rates at the lowest methanol concentrations. It was shown by Meadows and Darwent [7] that even in pure methanol the further conversion of hemiacetal into acetal is detectable only in the presence of strong acids.

The f.p. measurements for solutions of methanol in dioxan were carried out by the Beckmann technique, successive portions of methanol being added from a microsyringe to dioxan (30 ml). The results shown in the Figure represent four separate series.

## RESULTS AND DISCUSSION

The kinetic results with no added catalyst are collected in Table 1. The kinetic order with respect to methanol, $n_{\mathrm{MeOH}}$, is very close to three. (A slightly higher value, 3·24, is obtained if concentrations are expressed as mole fractions rather than as molarities.) This behaviour is closely similar to that observed for the addition of water to 1,3-dichloroacetone in dioxan and acetonitrile,[2,5] and is consistent with a cyclic transition state containing three methanol molecules. The finding of a near-integral reaction order for the addition of water over a considerable concentration range seemed difficult to reconcile with the thermodynamic non-ideality of solutions of water in dioxan,[8] and it was suggested [2] that there must be a considerable cancellation of activity coefficients between the transition state and the initial state of water in solution. The same problem might arise in interpreting our results, but in fact solutions of methanol in dioxan are much closer to ideality than those of water. The Figure shows our f.p. measurements compared with those of Bell and Wolfenden for solutions of water and of a non-associating solute (chlorobenzene). The results for methanol are closer to the latter than to the former, and even at the highest concentration used in the kinetic measurements the osmotic coefficient has only fallen to 0·80. Thus the cancellation of activity coefficients between the initial and transition states is even more plausible than for the reaction with water.

TABLE 1

Velocity constants at 25 °C with no added catalyst

| [MeOH]/mol l$^{-1}$ | 0·673 | 0·895 | 1·12 | 1·35 | 1·79 | 2·01 | 2·24 |
|---|---|---|---|---|---|---|---|
| $10^5k^0$/s$^{-1}$ | 6·00 | 14·1 | 26·9 | 48·0 | 116 | 167 | 226 |

$n_{\mathrm{MeOH}} = 3{\cdot}04$.

The results for catalysis by carboxylic acids are less clear-cut. For each acid a series of measurements was made at one or more fixed concentrations of methanol and a series of acid concentrations. In each series the ob-

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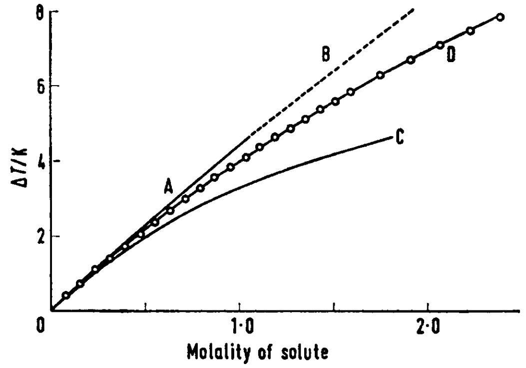
[6] R. P. Bell and A. O. McDougall, *Trans. Faraday Soc.*, 1960, **56**, 1281.

[7] G. W. Meadows and B. de B. Darwent, *Canad. J. Chem.*, 1952, **30**, 501; *Trans. Faraday Soc.*, 1952, **48**, 1015.

[8] R. P. Bell and J. H. Wolfenden, *J. Chem. Soc.*, 1935, 822.

served velocity constant could be expressed as $k(\text{obs.}) = k^0 + k^c[\text{acid}]$, where $k^0$ is the velocity constant for the uncatalysed reaction at the appropriate methanol concentration, and $k^c$ is the catalytic constant of the acid. Measurements were then made over a wider range of methanol concentrations, each with a single acid concentration chosen to give a convenient velocity. From the above equation $k^c$ was calculated, and its variation with [MeOH] examined. The results are given in Table 2.



Freezing point depressions in dioxan; A, results from ref. 8 for chlorobenzene; B, extrapolation of A, assuming ideal behaviour; C, results from ref. 8 for water; and D, present results for methanol

TABLE 2

Catalytic constants for carboxylic acids at 25 °C

| Benzoic acid | | Chloroacetic acid | | Trichloroacetic acid | |
|---|---|---|---|---|---|
| [acid]/mol l$^{-1}$ 0·015—0·13 | | [acid]/mol l$^{-1}$ 0·017—0·16 | | [acid]/mol l$^{-1}$ 0·003—0·16 | |
| [MeOH]/ mol l$^{-1}$ | $10^3k^c$/ l mol$^{-1}$ s$^{-1}$ | [MeOH]/ mol l$^{-1}$ | $10^3k^c$/ l mol$^{-1}$ s$^{-1}$ | [MeOH]/ mol l$^{-1}$ | $10^2k^c$/ l mol$^{-1}$ s$^{-1}$ |
| 0·066 | 8·65 | 0·062 | 4·49 | 0·062 | 0·98 |
| 0·192 | 25·7 | 0·076 | 5·46 | 0·190 | 5·75 |
| 0·411 | 55·9 | 0·190 | 13·7 | 0·353 | 16·4 |
| 0·411 | 57·3 | 0·411 | 31·6 | 0·353 | 16·4 |
| 0·617 | 83·6 | 0·617 | 50·1 | 0·353 | 16·5 |
| 0·948 | 127 | 0·822 | 72·4 | 0·617 | 38·4 |
| 1·03 | 135 | 1·03 | 97·3 | 0·705 | 48·8 |
| 1·44 | 185 | 1·44 | 148 | 1·03 | 86·7 |
| | | 1·44 | 152 | 1·03 | 87·1 |
| $n_{\text{MeOH}} = 0·99$ | | 1·44 | 150 | 1·06 | 92·0 |
| | | | | 1·41 | 140 |
| | | $n_{\text{MeOH}} = 0·96—1·39$ | | 1·44 | 146 |
| | | | | $n_{\text{MeOH}} = 1·58$ | |

The kinetic order $n_{\text{MeOH}}$ for catalysis by benzoic acid is close to unity, as was found for catalysis by carboxylic acids in the addition of water to 1,3-dichloroacetone.[2,5] For catalysis by chloroacetic and trichloroacetic acid $n_{\text{MeOH}}$ is somewhat greater than unity, and for the former acid varies with concentration, but is considerably less than the value found for the uncatalysed reaction.

Thus although these results support the idea that the acid catalyst replaces some of the methanol molecules in the transition state, it is difficult to give a consistent quantitative interpretation. This is probably due to association between methanol and acid, the extent of which varies with concentration and with the nature of the acid. The quantities $n_{\text{H}_2\text{O}}$ and $n_{\text{MeOH}}$ are interpreted as the differences between the numbers of water or methanol molecules in the transition state and the corresponding numbers in the initial state of the substrate and catalyst. In the addition of water to 1,3-dichloroacetone, $n_{\text{H}_2\text{O}}$ is reduced from three to unity on passing from the uncatalysed reaction to the reaction catalysed by carboxylic acids, and this was first interpreted as the replacement of two water molecules in the uncatalysed transition state by one molecule of carboxylic acid,[2] implying that the carboxylic acids are not hydrated in the initial state. However, it was concluded subsequently[5] that the carboxylic acids exist mainly as monohydrates in aqueous dioxan, so that the reaction order of unity with respect to water arises from the reaction scheme $\text{S} + \text{C},\text{H}_2\text{O} + \text{H}_2\text{O} \longrightarrow \text{SC},2\text{H}_2\text{O}^\ddagger$, where S is the substrate and C the catalyst, *i.e.* the carboxylic acids occupy only one position in the cyclic transition state. Strong association between water and carboxylic acids in dioxan has been recently confirmed by cryoscopic measurements,[9] which also showed less complete association between carboxylic acids and methanol. However, a simple interpretation of the observed reaction orders is only possible if the concentration of free water or methanol can be approximated by the stoicheiometric concentration. This is the case for the experiments on the hydration of 1,3-dichloroacetone,[2,5] in which the concentration of water always greatly exceeded that of catalyst, but the same is not true of the present work on the addition of methanol to chloral. A quantitative interpretation is therefore at present impossible.

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[9] Measurements in this laboratory by Dr. P. E. Sörensen, to be published.