

## General Acid Catalysed Hydrolysis of Benzaldehyde Aryl Methyl Acetals

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The kinetics of hydrolysis of substituted-benzaldehyde methyl phenyl acetals,  $\text{XC}_6\text{H}_4\cdot\text{CH}(\text{OMe})(\text{OPh})$  ( $\text{X} = m\text{-NO}_2, m\text{-MeO}, \text{H}, p\text{-Me}, \text{or } p\text{-MeO}$ ), and of benzaldehyde methyl substituted-phenyl acetals,  $\text{Ph}\cdot\text{CH}(\text{OMe})(\text{OC}_6\text{H}_4\text{Y})$  ( $\text{Y} = m\text{-NO}_2, m\text{-Br}, m\text{-F}, m\text{-MeO}, p\text{-Me}, \text{or } p\text{-MeO}$ ), catalysed by pivalic, acetic, 3-chloropropionic, formic, and chloroacetic acid, and by hydronium ions have been studied. The reactions of the benzaldehyde methyl substituted-phenyl acetals have non-linear Hammett plots which were thought to arise from a shift in the structure of the transition state from one bearing a negative charge on the phenolic oxygen to one bearing a positive charge as the substituent changes from being electron withdrawing to electron releasing. The  $\alpha$  values for these reactions become larger the more strongly electron releasing the substituent. The  $\alpha$  values for the reactions of the substituted-benzaldehyde methyl phenyl acetals increase as the electron withdrawing power of the substituent increases. The mechanisms of these reactions are discussed with reference to the relevant More O'Ferrall-Jencks diagram.

THE hydrolysis of benzaldehyde aryl methyl acetals was shown by Anderson and Capon to be general acid catalysed.<sup>1</sup> We now report a more extensive investigation of these reactions.

### RESULTS AND DISCUSSION

*Position of Bond Fission.*—The hydrolysis of benzaldehyde aryl methyl acetals could involve a rate-limiting aryloxy-carbon or methoxy-carbon bond fission. As discussed<sup>2</sup> for the hydrolysis of formaldehyde aryl methyl acetals (methoxymethoxybenzenes) a rate-limiting aryloxy-carbon bond fission would be expected *a priori* and the following experimental evidence supports this.

The rate of the hydrochloric acid catalysed hydrolysis of benzaldehyde methyl phenyl acetal ( $k$  41.0 l mol<sup>-1</sup> s<sup>-1</sup> at 25°) is faster than that of benzaldehyde dimethyl acetal ( $k$  29.6 l mol<sup>-1</sup> s<sup>-1</sup> at 25°). If the rate-limiting step involved methoxy-carbon bond cleavage the opposite would be expected. The kinetic n.m.r. experiment described in the Experimental section shows that the initial bond fission in the acetic acid catalysed methanolysis of benzaldehyde methyl phenyl acetal occurs between carbon and the phenoxy-oxygen atom and it would seem reasonable that the same process occurs in the acetic acid catalysed hydrolysis.

In addition to this evidence it is a reasonable assumption that all the rate constants for general acid catalysis arise from carbon-aryloxy bond fission as it is unlikely that carbon-methoxy bond fission would be general acid catalysed. However, there is a possibility that the rate constants for the hydronium-ion catalysed reactions (Table 6) contain a contribution from a process which involves carbon-methoxy bond fission, especially when the slower reacting compounds, although we consider this unlikely.

*The Kinetics of Hydrolysis.*—The experimental first-order rate constants,  $k_{\text{obs}}$ , were determined in a series of buffers of the same ionic strength and pH but with varying concentrations of weak acid. When the values of  $k_{\text{obs}}$  were plotted against the concentration of acetic acid

in buffers of ionic strength 0.1M a curve was obtained. This is seen from the results given in Table 1. When a linear least squares-analysis was applied to the results for the five lowest concentrations the value of  $k(\text{HCO}_2\text{H})$  was

TABLE 1

The acetic acid catalysed hydrolysis of benzaldehyde methyl phenyl acetal at 25°,  $I = 0.100\text{M}$

| $[\text{CH}_3\text{CO}_2\text{H}]^a/\text{M}$ | $10^3 k_{\text{obs}}/\text{s}^{-1}$ |
|---|-------------------------------------|
| 0.100   | 2.43, 2.47, 2.41                    |
| 0.090   | 2.28, 2.33, 2.34                    |
| 0.080   | 2.26, 2.24                          |
| 0.070   | 2.15, 2.15                          |
| 0.060   | 1.88, 1.88                          |
| 0.040   | 1.75, 1.72                          |
| 0.030   | 1.63, 1.64                          |
| 0.020   | 1.46, 1.48                          |
| 0.010   | 1.33, 1.35                          |

<sup>a</sup>  $[\text{CH}_3\text{CO}_2\text{Na}] = [\text{CH}_3\text{CO}_2\text{H}]$ , pH = 4.64.

Calculated from results for four highest concentrations,  $k(\text{CH}_3\text{CO}_2\text{H}) = 0.948 \times 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$  (s.d. 3.5%),  $k_{\text{int}} = 1.47 \times 10^{-3} \text{ s}^{-1}$  (s.d. 1.9%). Calculated from results for five lowest concentrations,  $k(\text{CH}_3\text{CO}_2\text{H}) = 1.35 \times 10^{-2}$  (s.d. 1.23%),  $k_{\text{int}} = 1.21 \times 10^{-3} \text{ s}^{-1}$  (s.d. 0.4%). Calculated from all the results,  $k(\text{CH}_3\text{CO}_2\text{H}) = 1.24 \times 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$  (s.d. 0.5%),  $k_{\text{int}} = 1.23 \times 10^{-3} \text{ s}^{-1}$  (s.d. 0.27%).

TABLE 2

The formic acid catalysed hydrolyses of benzaldehyde methyl phenyl acetal and benzaldehyde dimethyl acetal at 25°,  $I = 0.05\text{M}$

| $[\text{HCO}_2\text{H}]^a/\text{M}$ | $10^3 k_{\text{obs}}^b, c/\text{s}^{-1}$ | $10^3 k_{\text{obs}}^d/\text{s}^{-1}$ |
|-------------------------------------|--|---------------------------------------|
| 0.045                               | 1.32, 1.32                               | 7.38, 7.43                            |
| 0.036                               | 1.27, 1.26                               | 7.35, 7.44                            |
| 0.027                               | 1.22, 1.21, 1.22                         | 7.45, 7.36                            |
| 0.018                               | 1.16, 1.16, 1.15                         | 7.24, 7.28                            |
| 0.009                               | 1.09, 1.08, 1.09                         | 7.36, 7.12                            |

<sup>a</sup>  $[\text{HCO}_2\text{Na}] = [\text{HCO}_2\text{H}]$ , pH 3.565. <sup>b</sup> For hydrolysis of benzaldehyde methyl phenyl acetal. <sup>c</sup> Calculated from results for three highest concentrations,  $k(\text{HCO}_2\text{H}) 5.53 \times 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$  (s.d. 4.0%),  $k_{\text{int}} 1.07 \times 10^{-2} \text{ s}^{-1}$  (s.d. 0.7%). Calculated from results for three lowest concentrations  $k(\text{HCO}_2\text{H}) 7.45 \times 10^{-2} \text{ l mol}^{-1} \text{ s}^{-1}$  (s.d. 2.3%),  $k_{\text{int}} 1.02 \times 10^{-2} \text{ s}^{-1}$  (s.d. 0.3%). <sup>d</sup> For hydrolysis of benzaldehyde dimethyl acetal.

ca. 30% greater than that obtained from the four highest concentrations. Similar behaviour was found with

<sup>1</sup> E. Anderson and B. Capon, *Chem. Comm.*, 1969, 390; *J. Chem. Soc. (B)*, 1969, 1033.

<sup>2</sup> B. Capon, M. C. Smith, E. Anderson, R. H. Dahm, and G. H. Sankey, *J. Chem. Soc. (B)*, 1969, 1038.

formic acid buffers with concentration in the range 0.009–0.045M (see Table 2). Such behaviour has been reported previously<sup>3,4</sup> and ascribed to association of the

TABLE 3

The effect of electrolyte on the hydrolysis of *m*-methoxybenzaldehyde methyl phenyl acetal in formate buffers at 25°, *I* = 0.05M

| [HCO <sub>2</sub> H] <sup>a</sup> | 10 <sup>3</sup> <i>k</i> <sub>obs</sub> /s <sup>-1</sup> <sup>b</sup> | 10 <sup>3</sup> <i>k</i> <sub>obs</sub> /s <sup>-1</sup> <sup>c</sup> | 10 <sup>3</sup> <i>k</i> <sub>obs</sub> /s <sup>-1</sup> <sup>d</sup> |
|-----------------------------------|---|---|---|
| 0.025                             | 10.01, 10.02  | 10.02, 10.08  | 10.11, 10.2   |
| 0.020                             | 9.47, 9.88  | 10.01, 9.95   | 10.02, 9.91   |
| 0.015                             | 9.30, 9.10  | 9.58, 9.31  | 9.37, 9.59  |
| 0.010                             | 8.91, 8.71  | 9.21  | 9.29, 9.41  |
| 0.005                             | 8.27, 8.40  | 8.17  | 8.27, 8.29  |

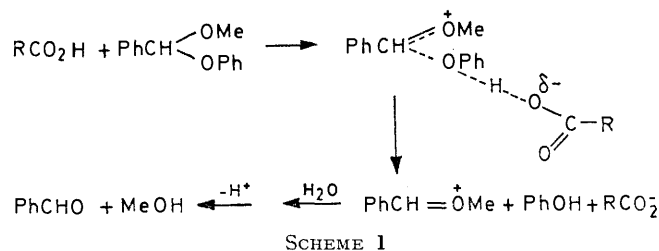
<sup>a</sup> [HCO<sub>2</sub>Na] = [HCO<sub>2</sub>H], pH 3.565. <sup>b</sup> Ionic strength maintained constant with KCl; *k*(HCO<sub>2</sub>H) = 8.68 × 10<sup>-2</sup> l mol<sup>-1</sup> s<sup>-1</sup> (s.d. 1.9%), *k*<sub>int</sub> = 7.89 × 10<sup>-3</sup> s<sup>-1</sup> (s.d. 0.33%). <sup>c</sup> Ionic strength maintained constant with NaNO<sub>2</sub>; *k*(HCO<sub>2</sub>H) = 8.29 × 10<sup>-2</sup> l mol<sup>-1</sup> s<sup>-1</sup> (s.d. 3.0%), *k*<sub>int</sub> = 8.19 × 10<sup>-3</sup> s<sup>-1</sup> (s.d. 0.52%). <sup>d</sup> Ionic strength maintained constant with NaClO<sub>4</sub>; *k*(HCO<sub>2</sub>H) = 8.93 × 10<sup>-2</sup> l mol<sup>-1</sup> s<sup>-1</sup> (s.d. 1.9%). *k*<sub>inc</sub> = 8.14 × 10<sup>-3</sup> s<sup>-1</sup> (s.d. 0.36%).

buffer. To avoid these complications all the catalytic constants were determined in buffers of ionic strength 0.05M with the concentration of acid varied from 0.005 to 0.025M. Five concentrations were used and each value of *k*<sub>obs</sub> determined at least twice. Under these conditions no curvature in the plots of *k*<sub>obs</sub> against [HA] was detected. In contrast to the behaviour of benzaldehyde methyl phenyl acetal the values of *k*<sub>obs</sub> for the hydrolysis of benzaldehyde dimethyl acetal were independent of the concentration of formic acid (Table 2).

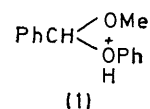
The importance of checking whether or not any apparent general acid catalysis arises from a salt effect has been emphasised.<sup>5</sup> This was done for several reactions by using three different salts, KCl, NaNO<sub>3</sub>, and NaClO<sub>4</sub>, to maintain the ionic strength constant. The results for the hydrolysis of *m*-methoxybenzaldehyde methyl phenyl acetal are shown in Table 3. The catalytic constants are within experimental error identical, as are the values of *k*<sub>obs</sub> for any given acid concentration. Therefore the observed general acid catalysis is genuine and not an artifact which arises from salt effects. Similar behaviour was found for the hydrolysis of benzaldehyde *m*-methoxyphenyl methyl acetal catalysed by formic acid and of benzaldehyde *p*-methoxyphenyl methyl acetal catalysed by acetic acid.

**Hammitt ρ Values, Brønsted α Coefficients, and Solvent Isotope Effects.**—As discussed previously<sup>1</sup> the most likely mechanism for the hydrolysis of benzaldehyde methyl phenyl acetal is that shown in Scheme I involving a concerted displacement of the PhCH::<sup>+</sup>OMe group by the acid. One way of regarding the change in mechanism of going from benzaldehyde dimethyl acetal to the

phenyl methyl acetal is to say that with the dimethyl acetal complete protonation of the methoxy-group is necessary for bond fission to occur and hence the reaction is specific acid catalysed whereas with the methyl phenyl acetal partial protonation leads to the commencement of fission of the carbon-phenoxy bond and



so this reaction is general acid catalysed. Alternatively one might argue<sup>6</sup> that the concerted process avoids the high-energy conjugate acid (1).



The effect of substituents in the pro-acyl<sup>7</sup> phenyl group is shown in Table 4. Hammett plots which included the points for the *p*-methyl and *p*-methoxy-substituents were concave upwards when σ- constants were used and concave downwards when σ+ constants were used. This behaviour is similar to that reported by Fife and Jao<sup>8a</sup> for the specific acid catalysed hydrolysis of benzaldehyde diethyl acetals in 50% aqueous dioxan and by Loudon and Berke in the general acid catalysed hydration of α-methoxystyrenes and the specific acid catalysed hydrolysis of acetophenone dimethyl acetals.<sup>8b</sup> It presumably arises because the carbonium ion being formed has both oxonium and carbonium ion character. Because of this curvature ρ values were calculated from the points for *m*-NO<sub>2</sub>, *m*-F, *m*-MeO, and H. There is a trend in the ρ values just outside the experimental error in the sense that the ρ value becomes more negative as the acid catalyst becomes weaker. This result can be rationalised by saying that there is less proton transfer in the transition state the weaker the acid catalyst, the leaving group is therefore poorer, and that there is therefore more C-O bond breaking and more carbonium ion character in the transition state. There is also a trend in the α values, again only slightly greater than experimental error, in the sense that α decreases as the electron-releasing power of the substituent increases. This may be rationalised by saying that the more easily the C-O bond is broken the less proton transfer there is in the transition state.

<sup>3</sup> V. Gold and D. C. A. Waterman, *J. Chem. Soc. (B)*, 1968, 839, 849.

<sup>4</sup> B. Capon and M. I. Page, *J. Chem. Soc. (B)*, 1972, 522.

<sup>5</sup> P. Salomaa, A. Kankaanpera, and M. Lahti, *J. Amer. Chem. Soc.*, 1971, **93**, 2084.

<sup>6</sup> Cf. J. E. Reimann and W. P. Jencks, *J. Amer. Chem. Soc.*, 1966, **88**, 3973; J. Hine, *ibid.*, 1972, **94**, 5766.

<sup>7</sup> Y. Chiang, A. J. Kresge, P. Salomaa, and C. I. Young, *J. Amer. Chem. Soc.*, 1974, **96**, 4494.

<sup>8</sup> (a) T. H. Fife and L. K. Jao, *J. Org. Chem.*, 1965, **30**, 1492; see however R. B. Dunlap, G. A. Ghanim, and E. H. Cordes, *J. Phys. Chem.*, 1969, **73**, 1898; (b) G. M. Loudon and C. Berke, *J. Amer. Chem. Soc.*, 1974, **96**, 4508.

There is also a trend in the  $\alpha$  values for the hydrolysis of benzaldehyde methyl substituted-phenyl acetals (Table 5) in the sense that the poorer leaving group the substituted phenoxy is, the greater the  $\alpha$  value. Thus it

hydrolysis curves with all the acid catalysts except  $\text{H}_3\text{O}^+$ . The rate constants decrease as the electron-withdrawing power of the substituent is decreased from *m*-nitro to hydrogen and then

TABLE 4

Catalytic constants for the general acid catalysed hydrolysis of substituted benzaldehyde methyl phenyl acetals at 25.0°,  $I = 0.05\text{M}$

| Acid                                | $pK_a$ | $\sigma(\sigma^+)$ | Substituent                       |                     |                       |                |                                  |                                   | $\rho(\text{s.d.})$ |
|-------------------------------------|--------|--------------------|-----------------------------------|---------------------|-----------------------|----------------|----------------------------------|-----------------------------------|---------------------|
|                                     |        |                    | <i>m</i> -NO <sub>2</sub><br>0.71 | <i>m</i> -F<br>0.34 | <i>m</i> -MeO<br>0.12 | H<br>0         | <i>p</i> -Me<br>-0.17<br>(-0.31) | <i>p</i> -MeO<br>-0.27<br>(-0.78) |                     |
| $10^3 k_{\text{cat}}/\text{s}^{-1}$ |        |                    |                                   |                     |                       |                |                                  |                                   |                     |
| Chloroacetic                        | 2.870  |                    | 19.7                              | 146                 | 300                   | 377            | 2 130                            | 5 850                             | -1.84<br>(0.22)     |
| Formic                              | 3.752  |                    | 1.48                              | 19.9                | 86.8                  | 74.5           | 364                              | 2 110                             | -2.57<br>(0.39)     |
| $\beta$ -Chloropropionic            | 4.100  |                    | 1.10                              | 9.82                | 36.7                  | 48.6           | 235                              | 1 230                             | -2.39<br>(0.16)     |
| Acetic                              | 4.756  |                    | 0.266                             | 2.18                | 9.64                  | 12.9           | 109                              | 281                               | -2.46<br>(0.16)     |
| Pivalic                             | 5.050  |                    | 0.0740                            | 1.56                | 7.26                  | 7.57           | 44.7                             | 234                               | -2.98<br>(0.38)     |
| $\alpha(\text{s.d.})$               |        |                    | 1.05<br>(0.09)                    | 0.92<br>(0.03)      | 0.78<br>(0.05)        | 0.77<br>(0.02) | 0.72<br>(0.05)                   | 0.68<br>(0.06)                    |                     |

TABLE 5

Catalytic constants for the general acid catalysed hydrolysis of benzaldehyde methyl substituted phenyl acetals at 25.0°,  $I = 0.05\text{M}$

| Acid                                | $pK_a$ | $\sigma$ | Substituent                       |                      |                     |                       |                |                       |                        |
|-------------------------------------|--------|----------|-----------------------------------|----------------------|---------------------|-----------------------|----------------|-----------------------|------------------------|
|                                     |        |          | <i>m</i> -NO <sub>2</sub><br>0.71 | <i>m</i> -Br<br>0.39 | <i>m</i> -F<br>0.34 | <i>m</i> -MeO<br>0.12 | H<br>0         | <i>p</i> -Me<br>-0.17 | <i>p</i> -MeO<br>-0.27 |
| $10^3 k_{\text{cat}}/\text{s}^{-1}$ |        |          |                                   |                      |                     |                       |                |                       |                        |
| Chloroacetic                        | 2.870  |          | 847                               | 770                  | 575                 | 606                   | 377            | 475                   | 1 291                  |
| Formic                              | 3.752  |          | 237                               | 217                  | 94.4                | 114                   | 74.5           | 120.8                 | 199                    |
| $\beta$ -Chloropropionic            | 4.100  |          | 231                               | 175                  | 79.7                | 58.2                  | 48.7           | 75.2                  | 142                    |
| Acetic                              | 4.756  |          | 88.5                              | 47.2                 | 24.5                | 25.5                  | 12.9           | 13.2                  | 16.5                   |
| Pivalic                             | 5.050  |          | 70.0                              | 28.9                 | 20.2                | 16.9                  | 7.57           | 5.49                  | 12.3                   |
| $\alpha(\text{s.d.})$               |        |          | 0.49<br>(0.04)                    | 0.65<br>(0.04)       | 0.67<br>(0.06)      | 0.71<br>(0.04)        | 0.78<br>(0.02) | 0.88<br>(0.08)        | 0.96<br>(0.07)         |

seems that the poorer the leaving group, the greater the amount of proton transfer in the transition state, a trend which may be extrapolated to benzaldehyde dimethyl acetal whose hydrolysis is specific acid catalysed. Similar behaviour has been reported by Gravitz and Jencks for the breakdown of the addition compounds of alcohols with *NO*-trimethylenephthalimidium ion.<sup>9</sup> The solvent-isotope effects (Table 6) for the hydrochloric acid catalysed hydrolysis show a similar trend to the  $\alpha$  values again indicating a greater degree of proton transfer in the transition state as the leaving group becomes poorer. Although this trend is towards the value shown by the specific acid catalysed hydrolysis of benzaldehyde dimethyl acetal, the lowest value obtained with the *p*-methoxy-compound ( $k_{\text{H}}/k_{\text{D}}$  0.62) is substantially different from that shown by benzaldehyde dimethyl acetal ( $k_{\text{H}}/k_{\text{D}}$  0.33).

The Hammett plots for the hydrolyses of the benzalde-

<sup>9</sup> N. Gravitz and W. P. Jencks, *J. Amer. Chem. Soc.*, 1974, **96**, 507.

increase again when the substituent is changed to *p*-methyl and *p*-methoxy (Table 5). It is unlikely that

TABLE 6

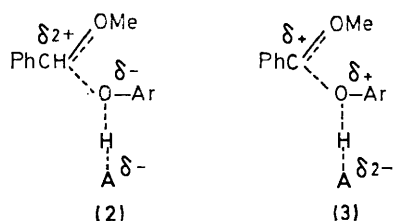
Rate constants ( $10^3 k_{\text{obs}}/\text{s}^{-1}$ ), Hammett  $\rho$  values, and solvent isotope effects ( $k_{\text{H}}/k_{\text{D}}$ ) for hydrolysis of benzaldehyde methyl substituted-phenyl acetals in hydrochloric acid (0.001M) at 25°

| Substituent               | In H <sub>2</sub> O | In D <sub>2</sub> O | $k_{\text{H}}/k_{\text{D}}$ |
|---------------------------|---------------------|---------------------|-----------------------------|
| <i>m</i> -NO <sub>2</sub> | 20.4 <sup>a</sup>   | 18.8 <sup>b</sup>   | 1.09                        |
| <i>m</i> -F               | 24.8                | 28.5                | 0.87                        |
| H                         | 41.0                | 59.4                | 0.69                        |
| <i>p</i> -Me              | 56.2                | 86.6                | 0.65                        |
| <i>p</i> -MeO             | 84.3                | 135                 | 0.62                        |
| $\rho(\text{s.d.})$       | -0.60<br>(0.11)     | -0.85<br>(0.10)     |                             |
| Dimethyl acetal           | 29.7                | 90.3                | 0.33                        |

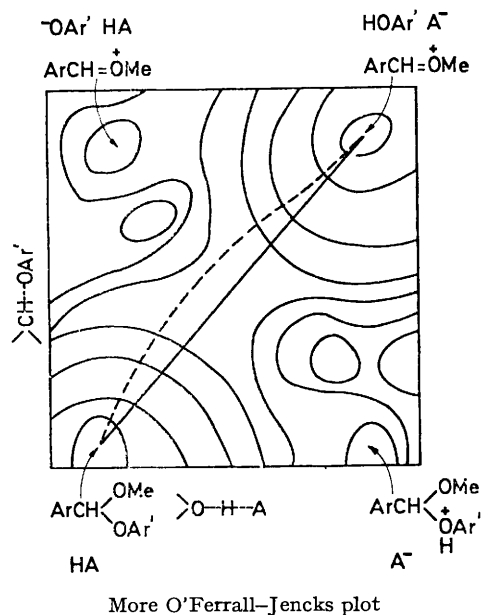
<sup>a</sup> Corrected for spontaneous hydrolysis,  $10^3 k_{\text{obs}} = 21.7 \text{ s}^{-1}$ ,  $10^3 k_{\text{spont}} = 1.3 \text{ s}^{-1}$ . <sup>b</sup> Corrected for spontaneous hydrolysis,  $10^3 k_{\text{obs}} = 19.7 \text{ s}^{-1}$ ,  $10^3 k_{\text{spont}} = 0.9 \text{ s}^{-1}$ .

this is the result of a change from rate limiting carbon-phenoxy bond fission to rate-limiting carbon-methoxy

bond fission as the latter process would not be expected to be general acid catalysed, since the hydrolysis of benzaldehyde dimethyl acetal is not general acid catalysed. Similar behaviour has been described by Gravitz and Jencks for the breakdown of the addition compounds of alcohols with *NO*-trimethylenephthalimidium ion.<sup>9</sup> In these reactions the rate constants decrease on going from the adduct of 2,2,2-trifluoroethanol to that of 2-chloroethanol and then increase on going to methanol. Our results would be most readily explained if there were varying amounts of proton transfer and C-O bond



breaking in the transition states such that with electron-withdrawing substituents C-O bond breaking runs ahead of O-H bond forming (2) whereas with electron-releasing substituents O-H bond forming runs ahead of C-O bond



breaking (3). Another way of viewing this is to consider the More O'Ferrall-Jencks<sup>10,11</sup> diagram (Figure). Here proton transfer is plotted on the *x*-axis and C-O bond breaking on the *y*-axis. If the transition state saddle point lies above the positively sloping diagonal there is more C-O bond breaking than O-H bond forming and increasing the electron-withdrawing power of the substituent causes the transition state to move towards the left and top of the diagram and its energy to decrease.

Conversely increasing the electron-releasing power of the substituent will cause the transition state to move towards the right and bottom of the diagram and increase in energy until the diagonal is passed. The saddle point then lies below the diagonal with more O-H bond breaking than C-O bond breaking and while increasing the electron-releasing ability of the substituent still causes the saddle point to move to the right and bottom of the diagram it now causes a decrease in energy of the transition state because the oxygen now carries a net positive charge.

The behaviour is not found in the hydronium ion catalysed reaction for which electron-releasing substituents are rate enhancing and electron-withdrawing substituents rate decreasing. This suggests that the transition state saddle point always lies below the positively sloping diagonal when the hydronium ion is the catalyst and that O-H bond forming always runs ahead of C-O bond breaking. The effect of substituents in the pro-acyl phenyl group is small (Table 7),  $\rho$  2.26,

TABLE 7

Rate constants ( $10^3 k_{\text{obs}}/s^{-1}$ ), Hammett  $\rho$  values, and solvent isotope effects ( $k_{\text{H}}/k_{\text{D}}$ ) for hydrolysis of substituted benzaldehyde methyl phenyl acetals in hydrochloric acid (0.001M) at 25°

| Substituent               | In H <sub>2</sub> O | In D <sub>2</sub> O | $k_{\text{H}}/k_{\text{D}}$ |
|---------------------------|---------------------|---------------------|-----------------------------|
| <i>m</i> -NO <sub>2</sub> | 1.45                |                     |                             |
| <i>m</i> -F               | 8.92                | 13.5                | 0.66                        |
| H                         | 41.0                | 59.4                | 0.69                        |
| <i>p</i> -Me              | 108                 | 114                 | 0.95                        |
| <i>p</i> -MeO             | 305                 | 370                 | 0.82                        |
| $\rho$ (s.d)              | -2.26<br>(0.15)     | -2.19<br>(0.33)     |                             |

which indicates that there is relatively little C-O bond breaking, consistent with this transition-state structure.

The dependence of the  $\alpha$  values for the reactions on structure follow closely what would be predicted from the discussion of More O'Ferrall.<sup>10</sup> If a perturbation is made along the reaction co-ordinate by putting a substituent in the pro-acyl phenyl group which stabilises the intermediate carbonium-oxonium ion the resulting 'downward "pull" at the top right hand corner' of the Figure causes a change in transition state structure towards that of the reactant (smaller  $\alpha$  value). On the other hand if a perturbation is made which is perpendicular to the reaction co-ordinate by placing a substituent in the phenoxy-group which stabilises the conjugate acid the resulting 'downward "pull" at the lower right hand corner' of Figure 1 causes a move in the transition-state structure towards that of the conjugate acid ( $\alpha$  increases).

The rate constants for the hydronium-ion catalysed reaction are  $10^2$ – $10^4$  times less than those predicted from the Brønsted plots for catalysis by carboxylic acids using 55.5M for the dissociation constant and  $p = 3$ ,  $q = 2$ . This type of behaviour has frequently been reported before.<sup>3,4,12</sup>

<sup>10</sup> R. A. More O'Ferrall, *J. Chem. Soc. (B)*, 1970, 274.

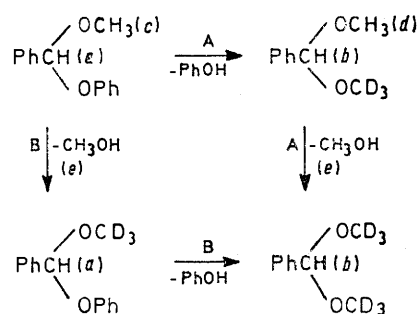
<sup>11</sup> W. P. Jencks, *Chem. Rev.*, 1972, **72**, 705.

<sup>12</sup> A. J. Kresge, H. L. Chen, Y. Chiang, E. Murrill, M. A. Payne, and D. S. Sagatys, *J. Amer. Chem. Soc.*, 1971, **93**, 413; A. J. Kresge, *Chem. Soc. Rev.*, 1973, **2**, 475.

## EXPERIMENTAL

*Preparation of Mixed Aryl Methyl Acetals.*—The method used was that described by Anderson and Capon<sup>1</sup> with a few modifications. The  $\alpha$ -chlorobenzyl methyl ethers were made by treating the benzaldehyde dimethyl acetal (0.5 mol) with freshly distilled acetyl chloride (0.8 mol) and thionyl chloride (0.1 mol) under nitrogen. After the initial reaction had subsided the mixture was left in a water-bath at 65° for up to an hour depending on the acetal. The excess of acetyl chloride and thionyl chloride was removed *in vacuo* at room temperature and the residue was used directly in the next stage. The extent of conversion of the acetal into chloride was checked by n.m.r. spectroscopy; the signal of the  $\alpha$ -proton of the acetal is at  $\delta$  ca. 5.35 and that for the chloride at  $\delta$  ca. 6.3. The chloride was converted into the mixed aryl methyl acetal as described by Anderson and Capon.<sup>1</sup> It was important to remove any adhering hydrocarbon from the sodium hydride by washing with sodium-dried light petroleum (b.p. 40–60°) as it

acetal methoxy-protons (*d*) would occur concurrently with an upfield shift of the signal methine-acetal proton (*a*) to that



SCHEME 2

of (*b*). Subsequently the signal of methanol (*e*) would be observed. Fission *via* pathway B would lead to loss of the

TABLE 8

Physical properties of substituted-benzaldehyde phenyl methyl acetals

| Substituent                    | B.p. [°C (mmHg)]                            | Analyses (%) |      |       |      | N.m.r. (CDCl <sub>3</sub> solution) |                    |
|--------------------------------|---|--------------|------|-------|------|-------------------------------------|--------------------|
|                                |   | Found        |      | Calc. |      | $\delta(\text{CH}_3)$               | $\delta(\text{H})$ |
|                                |   | C            | H    | C     | H    |                                     |                    |
| <i>m</i> -Nitro <sup>a,b</sup> | 95–100 ( $1 \times 10^{-2}$ )               | 64.7         | 5.0  | 64.9  | 5.25 | 3.40                                | 6.20               |
| <i>m</i> -Bromo                | 135–140 <sup>c</sup> ( $1 \times 10^{-3}$ ) | 57.5         | 4.6  | 57.35 | 4.5  | 3.36                                | 6.06               |
| <i>m</i> -Fluoro               | 160–165 <sup>c</sup> ( $5 \times 10^{-2}$ ) | 72.0         | 5.9  | 72.4  | 5.4  | 3.38                                | 6.08               |
| <i>m</i> -Methoxy              | 140–145 <sup>c</sup> ( $1 \times 10^{-4}$ ) | 72.75        | 6.61 | 73.75 | 6.6  | 3.38, 3.76                          | 6.05               |
| <i>p</i> -Methyl               | 90–95 <sup>c</sup> ( $5 \times 10^{-5}$ )   | 78.6         | 7.1  | 78.9  | 7.1  | 3.36, 2.35                          | 6.08               |
| <i>p</i> -Methoxy              | 125–130 <sup>c</sup> ( $8 \times 10^{-5}$ ) | 73.5         | 6.6  | 73.7  | 6.6  | 3.36, 3.80                          | 6.03               |

<sup>a</sup> Purified by t.l.c. and redistilled. <sup>b</sup> Found: N, 5.55. Calc. for C<sub>14</sub>H<sub>13</sub>NO<sub>4</sub>: N, 5.4%. <sup>c</sup> Bath temperature.

TABLE 9

Physical properties of benzaldehyde substituted-phenyl methyl acetals

| Substituent                   | B.p. [°C (mmHg)]                            | Analyses (%) |      |       |      | (CDCl <sub>3</sub> solution) |                       |
|-------------------------------|---|--------------|------|-------|------|------------------------------|-----------------------|
|                               |   | Found        |      | Calc. |      | $\delta(\text{CH}_3)$        | $\delta(\text{CH}_1)$ |
|                               |   | C            | H    | C     | H    |                              |                       |
| None                          | 118–120 (0.1)                               | 78.5         | 6.6  | 78.5  | 6.7  | 3.35                         | 6.10                  |
| <i>m</i> -Nitro               | 170–174 ( $4 \times 10^{-2}$ )              | 65.1         | 5.0  | 64.9  | 5.25 | 3.35                         | 6.10                  |
| <i>m</i> -Bromo               | 114–118 <sup>a</sup> ( $9 \times 10^{-2}$ ) | 57.7         | 4.65 | 57.3  | 4.4  | 3.35                         | 6.02                  |
| <i>m</i> -Fluoro              | 82–83 (0.1)                                 | 72.2         | 5.4  | 72.4  | 5.4  | 3.38                         | 6.10                  |
| <i>m</i> -Methoxy             | 140–145 <sup>a</sup> ( $10^{-4}$ )          | 73.9         | 6.7  | 73.75 | 6.6  | 3.38, 3.60                   | 6.08                  |
| <i>p</i> -Methyl <sup>c</sup> | 100–106 ( $1.5 \times 10^{-2}$ )            | 78.7         | 7.1  | 78.9  | 7.1  | 3.38, 2.28                   | 6.06                  |
| <i>p</i> -Methoxy             | 160 <sup>b</sup> ( $10^{-4}$ )              | 73.5         | 6.6  | 73.7  | 6.6  | 3.40, 3.73                   | 6.00                  |

<sup>a</sup> Bath temperature. <sup>b</sup> Found: F, 8.2. Calc. for C<sub>14</sub>H<sub>13</sub>FO<sub>2</sub>: F, 8.2%. <sup>c</sup> Purified further by t.l.c. and redistillation.

proved difficult to remove this contaminant at a later stage. The mixed aryl methyl acetals were purified by molecular distillation and identified by n.m.r. spectroscopy, the signal of the acetal proton occurring at  $\delta$  ca. 6.1 p.p.m. Their analyses are given in Tables 8 and 9.

*Acetic Acid Catalysed Methanolysis of Benzaldehyde Methyl Phenyl Acetal.*—The site of initial bond fission in acetic [<sup>2</sup>H]acid catalysed [<sup>2</sup>H<sub>a</sub>]methanolysis of benzaldehyde methyl phenyl acetal was investigated by following the change in the 100 MHz n.m.r. spectrum. The two possible modes of bond fission are shown in Scheme 2. If the reaction proceeded *via* pathway A an initial shift of signal of the mixed acetal methoxy-protons (*c*) to that of the dimethyl

signal of the methoxy-proton (*c*) concurrently with the appearance of the signal of free methanol (*e*) without any change in the signal of the methine proton (*a*).

If pathway A were followed, the equality (1) would be applicable since  $[\text{H}_c] = 3[\text{H}_a]$  and  $[\text{H}_d] + [\text{H}_e] = 3[\text{H}_b]$ ,

$$[\text{H}_a]/[\text{H}_b] = [\text{H}_c]/([\text{H}_d] + [\text{H}_e]) \quad (1)$$

whereas if pathway B were followed, the inequality (2) would be applicable since  $[\text{H}_c] < 3[\text{H}_a]$ ,  $[\text{H}_e] > 3[\text{H}_b]$ , and  $[\text{H}_d] = 0$ . The methine signals were clearly distinguishable

$$[\text{H}_a]/[\text{H}_b] > [\text{H}_c]/([\text{H}_d] + [\text{H}_e]) \quad (2)$$

on the 1 000 Hz sweep,  $\delta H_a$  611 and  $\delta H_b$  534 Hz downfield from internal tetramethylsilane, but the 50 Hz sweep was necessary to resolve the different methoxy-protons,  $\delta H_c$  335,  $\delta H_d$  328, and  $\delta H_e$  334 Hz. These signals were identified by the addition of 12  $\mu$ l of methanol to standard 10% solutions of the appropriate acetal in  $[^2H_4]$ methanol.

A solution of benzaldehyde methyl phenyl acetal (0.47M) in  $[^2H_4]$ methanol which contained acetic acid (2M) was injected into an n.m.r. tube and the spectrum measured. It was then placed in a thermostat at 65° and the spectrum remeasured after 60, 100, 140, and 180 min. A signal of increasing strength at 534 Hz was observed indicating the immediate formation of the dimethyl acetal as expected for pathway A. The spectra also showed a substantial signal corresponding to the methoxy of the dimethyl acetal ( $\delta H_d$  328 Hz) and a smaller signal corresponding to free methanol ( $\delta H_e$  334 Hz). It was shown that when benzaldehyde dimethyl acetal was heated under the same conditions it also underwent methanolysis slowly with formation of free methanol so the latter could have arisen *via* pathway A. The ratio of the signals given in equation (1) are listed in Table 10. Within experimental error the ratios are equal which indicates that Path A is followed.

TABLE 10

Ratio of signals in the n.m.r. spectrum of benzaldehyde methyl phenyl acetal after methanolysis in  $[^2H_4]$ -methanol containing acetic  $[^2H]$ acid (2M) at 65°

| <i>t</i> /min | $[H_c]/[H_b]$ | $[H_e]/([H_c] + [H_d])$ |
|---------------|---------------|-------------------------|
| 0             | 1/0           | 1/0                     |
| 60            | 1.60          | 1.52                    |
| 100           | 0.93          | 1.00                    |
| 120           | 0.50          | 0.52                    |
| 140           | 0.31          | 0.29                    |
| 180           | 0.26          | 0.28                    |

*Solutions and Buffers.*—The buffers were made from AnalaR grade acetic and formic acids, redistilled pivalic acid, and recrystallised (from light petroleum) chloroacetic and 3-chloropropionic acids. The formic acid was titrated with 0.1N-sodium hydroxide and shown to be 89.95% pure. Buffer solutions were prepared in distilled water with carbonate free sodium hydroxide solution and degassed and diluted with the appropriate volume of potassium chloride solution of the same ionic strength. All solutions contained 10<sup>-4</sup>M-EDTA to reduce any metal-ion catalysed autoxidation

of the products. Stock solutions of the acetals were prepared with Merck 'spectrograde' dioxan. The pH values of the buffers were measured with a Radiometer model 26 pH meter with an external temperature compensator. A Radiometer type G202C glass electrode and a type K401 calomel electrode were used. The pH meter was standardised against commercial standard buffers complying to BS. 1647, 1961.

*Kinetic Measurements.*—Reactions with half-lives of < 15 min were studied on a Zeiss PMQII spectrophotometer and slower reactions on a Cary 14 spectrophotometer. The cell blocks were thermostatted at 25 ± 0.03° by circulating water from a bath. 10 mm Cells were used except for the hydrolysis of benzaldehyde *m*-bromophenyl methyl acetal when 40 mm cells were used since owing to its low solubility a lower concentration of this compound had to be used. When 10 mm cells were used 25  $\mu$ l of a stock solution of the acetal in dioxan were added to 2.5 ml of the thermostatted buffer solution. The formation of aldehyde was followed at 250 nm (benzaldehyde), 245 nm (*m*-nitrobenzaldehyde), 248 nm (*m*-fluorobenzaldehyde), 255 nm (*m*-methoxybenzaldehyde), 261.5 nm (*p*-methylbenzaldehyde), and 278 nm (*p*-methoxybenzaldehyde). A voltage proportional to absorbance or transmittance was punched on paper tape using a Solatron compact data logger and the first-order rate constants determined by fitting the results to the equation  $A_\infty - A_t - (A_\infty - A_0)e^{-kt} = 0$  where the absorbances at zero and infinite time,  $A_0$  and  $A_\infty$ , and the rate constant  $k$  are adjustable parameters and the absorbances at time  $t$ ,  $A_t$ , and the times,  $t$ , are variables. The generalised least squares method described by Deming<sup>13</sup> and by Wentworth<sup>14</sup> was used and the calculations were performed on Glasgow University's KDF9 computer. The slopes and intercepts of the plots of  $k_{obs}$  against buffer concentration were also determined by a generalised least squares procedure and the slopes of the Hammett and Brønsted plots by a linear least squares procedure.

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<sup>13</sup> W. Deming, 'Statistical Adjustment of Data,' Dover, New York, 1964.

<sup>14</sup> W. E. Wentworth, *J. Chem. Educ.*, 1965, **42**, 96, 162.