Acetyl Exchange between Acetylmesitylene and Acetyl Chloride under Friedel–Crafts Conditions

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Summary The kinetics of acetyl exchange, catalysed by aluminium chloride, between acetylmesitylene and acetyl chloride have been determined for homogeneous solutions in nitromethane, and provide the first direct proof of reversibility in a classical Friedel–Crafts acylation.

It is generally accepted that most Friedel–Crafts acylations are irreversible.[1] However, for ketones with bulky neighbouring substituents (*ortho* or *peri*), whose acyl groups in consequence are tilted out-of-plane with respect to the aromatic nucleus to which they are attached, resonance stabilisation will be reduced, and reversible acylation becomes feasible. Attempts at illustrating such reversibility have concentrated on the related phenomena of deacylations, acyl-exchanges, or acyl rearrangements, always studied at best semi-quantitatively. Acyl rearrangements have been demonstrated recently in polyphosphoric acid.[2]

Reversible acylation in a classical Friedel–Crafts system has not previously been demonstrated directly and unequivocally. An attempt had been made to achieve reversible acylation when acetophenone, labelled with ^{14}C in the carbonyl group, was treated with an excess of inactive acetyl chloride and aluminium chloride,[3] but no radioactive acetyl chloride could be detected after 24 h at 50 °C.

We have now shown that acetylmesitylene undergoes acetyl-exchange in the presence of aluminium chloride in nitromethane solution. A nitro-solvent was used in order to minimise ($<1\%$) formation of diacetylmesitylene.[4] [α-^{14}C]Acetic anhydride was converted *in situ*, by an excess (4 mol. equiv.) of aluminium chloride, into the acetylating species (I), [equation (1)].[5] 0·92 mol. equiv. of

$$\begin{aligned}&(CH_3{}^*CO)_2O + 2AlCl_3 \longrightarrow \\ &\quad \underset{\text{(I)}}{CH_3{}^*COCl,AlCl_3} + CH_3{}^*CO_2AlCl_2\end{aligned} \qquad (1)$$

acetyl chloride could be aspirated from the solution, showing that the second acetyl species was chemically bound and not available for acetylation.[6] After addition of acetylmesitylene, aliquot portions were taken at intervals, and samples of chemically unaltered but labelled acetylmesitylene were isolated. A plot of log(1 − fraction exchange) *vs.* time gave $T_{\frac{1}{2}}$, and the rate R was then calculated, using a modified form[7] of the exchange-rate equation of McKay[8] [equation (2)], where a and b are total concentrations of (labelled

$$R\ \ (=k_2ab) = [ab/(a+b)] \times (\ln 2/T_{\frac{1}{2}}) \qquad (2)$$

+ unlabelled) acetyl chloride, and acetylmesitylene, respectively. The rate constant, k_2, remained unaltered, within experimental error ($\pm 3\%$), when concentration of either reactant was doubled. The kinetic and thermodynamic data obtained are as follows: for $a = b = 0{\cdot}204$ mol dm^{-3}, temp. range 293—309 K, corr. coeff. 0·987, k_2 (298·15 K, *calc.*) $8{\cdot}22 \times 10^{-6}$ dm^3 mol^{-1} s^{-1}; E_A 52·3 kJ mol^{-1}; log A 4·082, $\Delta H^{\ddagger}$ 49·8 kJ mol^{-1}, $\Delta S^{\ddagger}$ -175 J mol^{-1} K^{-1}, $\Delta G^{\ddagger}$ 102·0 kJ mol^{-1}. The exchange reaction is slow, and is characterised by a relatively low enthalpy of activation and a very low entropy of activation.

From an acylation at 40 °C in nitromethane solution, for reactant concentrations of *ca.* 2 mol dm^{-3},[4] a yield of 70% acetylmesitylene could be obtained after 0·5 h, corresponding to $T_{\frac{1}{2}}$ *ca.* 0·2 h. Comparison of this with $T_{\frac{1}{2}}$ (40 °C) = *ca.* 2·2 h for the acetyl-exchange reaction suggests that reversible acylation, though significant, is not of major importance in this system.

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[1] P. H. Gore, *Chem. and Ind.*, 1974, 727.

[2] I. Agranat and D. Avnir, *J.C.S. Chem. Comm.*, 1973, 323; I. Agranat. Y.-S. Shih, and Y. Bentor, *J. Amer. Chem. Soc.*, 1974, **96**, 1259; I. Agranat, Y. Bentor, and Y.-S. Shih, *ibid.*, in the press; I. Agranat and Y.-S. Shih, *Synth. Comm.*, 1974, **4**, 119; *Synthesis*, 1974, 865.

[3] M. Frangopol, A. Gerunche, N. Negoita, P. T. Frangopol, and A. T. Balaban, *Tetrahedron*, 1967, **23**, 841.

[4] P. H. Gore and J. A. Hoskins, *J. Chem. Soc.* (*C*), 1970, 517.

[5] R. E. Van Dyke, *J. Amer. Chem. Soc.*, 1951, **73**, 398; R. E. Van Dyke and H. E. Crawford, *ibid.*, p. 2018.

[6] P. H. Gore, in 'Friedel-Crafts and Related Reactions,' ed. G. A. Olah, Interscience, New York, 1964, vol. III, part 1, p. 16.

[7] O. E. Myers and R. J. Poestwood, in 'Radioactivity Applied to Chemistry,' eds. A. C. Wahl and N. A. Bonner, Wiley, New York, 1951, p. 6.

[8] H. A. C. McKay, *J. Amer. Chem. Soc.*, 1943, **65**, 702.