Selective Deuteriation of Chelated and Unchelated Acetyls in Strong Acid Media

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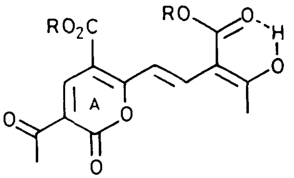
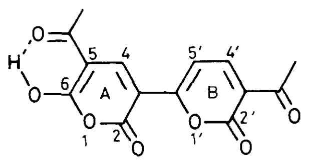
Unchelated C-acetyls are deuteriated in strong acids (D_2SO_4, F_3CCO_2D) leaving chelated C-acetyls essentially unaffected, thereby providing a method for selective isotopic labelling among acetyls.

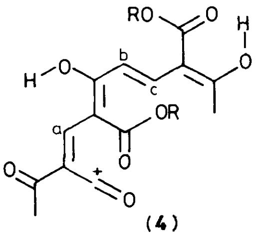
When treated with concentrated sulphuric acid, dimethyl- or diethyl-xanthophanic enol (**1**) or (**2**) gave a golden insoluble compound [m.p. 282—283 °C (M^+ 290)] formulated as (**3**).[1] In studying the reaction, the involvement of an acylium intermediate (**4**), formed by protonation of the pyrone oxygen of ring A, was postulated. Such an intermediate might be expected to permit deuterium exchange in D_2SO_4 or F_3CCO_2D at position b, but not at a or c, in (**4**) leading to deuteriation at C-5′ in the product (**3**). This was shown experimentally to be the case, the AB resonances of ring B in



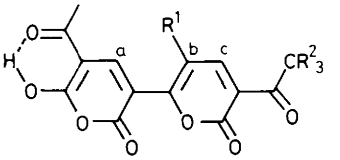
(1); R = Me
(2); R = Et



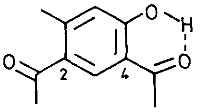
(3)



(4)



(5); $R^1 = R^2 = D$
(6); $R^1 = H, R^2 = D$



(7)

(3) at δ 7.99 (1H, d, *J* 8.6 Hz, 5′-H) and 8.70 (1H, d, *J* 8.6 Hz, 4′-H) being replaced by a single line at δ 8.63 (1H, s, 4′-H).† System (3) also has two acetyl groups (δ 2.86 and 2.93), both at first sight eligible for acid-catalysed deuteriation. In fact, whilst one had become almost completely deuteriated after 24 h, the other (δ 2.93) was unaffected, giving the tetradeuterio-compound (5) as the product, M^+ 294. Dissolution of pre-formed (3) in F_3CCO_2D caused no deuteriation at C-5′ in ring B but removed the proton signals at δ 2.86, known from other evidence to be associated with the unchelated acetyl, giving a trideuterio-product (6), M^+ 293. It was therefore postulated that under strong acid conditions deuteriation of an acetyl occurs by the usual mechanism, but that such enolisation of a chelated acetyl is extremely slow. This was tested further.

Whereas the acetyl methyls of acetophenone and *p*-hydroxyacetophenone were largely deuteriated after 24 h in F_3CCO_2D, that of *o*-hydroxyacetophenone was unaffected (n.m.r. integrals). The methyl of the latter could however be readily deuteriated under basic conditions using NaOMe–MeOD or $Mg(OMe)_2$–MeOD. 2,4-Diacetyl-5-hydroxytoluene (7)[2] was then employed as an aromatic test case containing both a chelated and an unchelated acetyl. After 24 h the unchelated acetyl signal at δ 2.48 had essentially disappeared leaving the chelated acetyl at 2.54 unaffected after 6 days in F_3CCO_2D.‡§ Such a selective deuteriation presents opportunities for practical exploitation in the specific deuteriation and tritiation of methyl groups.

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References

1 L. Crombie, D. E. Games, and M. H. Knight, *J. Chem. Soc. (C)*, 1967, 763.
2 L. Crombie, D. E. Games, and A. W. G. James, *J. Chem. Soc. Perkin Trans. 1*, 1979, 464.

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† N.m.r. data for F_3CCO_2H or F_3CO_2D as appropriate.

‡ A small peak at δ 2.48 still remains after 6 days because of equilibrium with protium removed by exchange.

§ The ^{13}C n.m.r. situation involving (7) is interesting. The region δ 20—30 contains three signals, 23.4 (ArMe) and 28.4 and 26.1 assigned to the two acetyl methyls (solvent: F_3CCO_2H containing 10% hexadeuteriobenzene for lock purposes). Kept in F_3CO_2D the carbon signal at δ 28.4 diappeared entirely from the spectrum. This is apparently a consequence of the greatly increased relaxation time of the trideuterio-methyl combined with septet splitting: the methyl signal has disappeared into the noise of the baseline.