Hypervalent Iodine Oxidation of α,β-Unsaturated Ketones: Chromone, Flavone, Chalcone, and Flavanone

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Reaction of the title compounds with $PhI(OAc)_2$ and MeOH–KOH leads to α-hydroxydimethylacetal β-methoxy products regiospecifically and stereospecifically, as demonstrated by *X*-ray diffraction.

Recently we described the use of iodosobenzene and *o*-iodosobenzoic acid for the conversion of enolizable ketones into α-hydroxydimethylacetals.[1] The reaction involves enolate anion formation by base abstraction of an α-hydrogen and nucleophilic addition of the enolate to the iodine(III) followed by C–I bond cleavage.

We now report on the $PhI(OAc)_2$, MeOH–KOH reaction applied to systems which cannot form an anion by α-hydrogen abstraction, namely, α,β-unsaturated ketones.† Chromone (**1**) yields (**2**) in 53% yield and flavone (**3**) yields (**4**) in 67% yield.

The structure of (**2**) (an oil) is based upon the following: *m/z*

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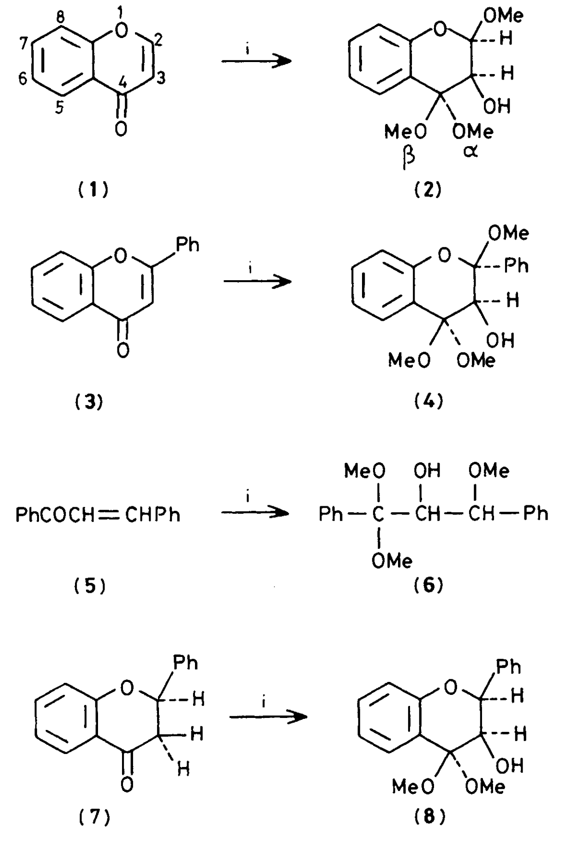
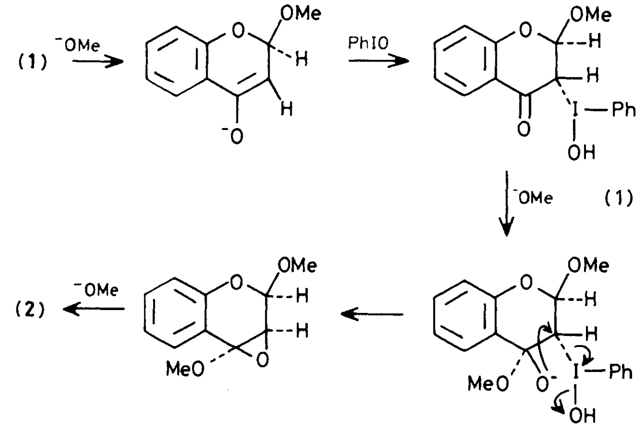
† α,β-Unsaturated systems which do possess α- and δ-CH_2 units have been studied *e.g.* isophorone, which yields products derived from three possible enolates.



Reagents: i, PhI(OAc)$_2$, KOH-MeOH.



240 (M^+, 4%), 209 (16), 166 (100); ^{1}H n.m.r. (CDCl$_3$) δ 3.1 (2-OMe), 3.65 (s, 4-OMe-β), 3.4 (s, 4-OMe-α),[‡] 5.18 (d, 2-H), 4.06 (dd, *J* 3.0 Hz, d in D$_2$O, 3-H),[2] 2.5 (d, 3-OH). Similarly, the structure of (**4**): m.p. 129—30 °C; *m/z* 285 (*M*−31, 2%), 136 (60), 167 (100); n.m.r. (CDCl$_3$) δ 2.95 (2-OMe), 3.42 (s, 4-OMe-β), 3.25 (s, 4-OMe-α),[‡] 4.32 (d, s in D$_2$O, 3-H), was assigned on the basis of spectroscopic data. The stereochemistry in each case results from initial Michael addition of MeO$^-$, followed by electrophilic *anti* addition of PhIO to the thus formed enolate anion, with sequential addition of MeO$^-$ to the carbonyl group and intramolecular reductive elimination of iodine as PhI with inversion of configuration. The reaction is completed by a second addition of MeO$^-$ to the oxirane, equation (1).

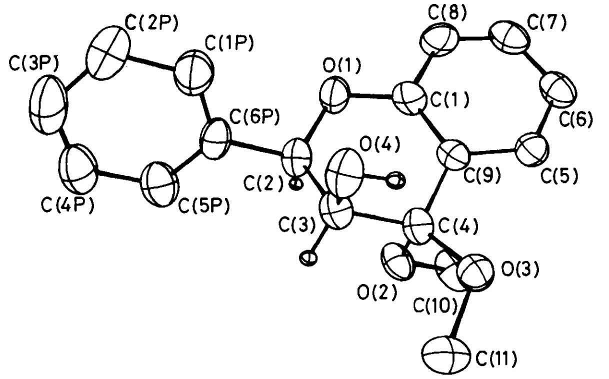


Figure 1. Molecular structure of (**8**). Hydrogen atoms other than those on C(2), C(3), and O(4) have been omitted. C(6P) and O(4) are *cis*. The oxo ring is puckered with C(2) and C(4) below the (approximate) ring plane and C(3) above it.

Chalcone (**5**) represents an acyclic example of the above reactions, and, analogously yields (**6**) in 60% yield: m.p. 118—20 °C; *m/z* 271 (*M*−31, 0.2%), 151 (100); ^{1}H n.m.r. (CDCl$_3$) δ 2.76 (s, CH-O*Me*), 3.92 (d, *J* 4 Hz, C*H*-OMe),[2] 4.08 (dd, d in D$_2$O, C*H*OH), 3.23 (s, C-O*Me*), 3.13 (s, C-O*Me*).

Finally flavanone (**7**) yielded (**8**) in 68% yield: m.p. 126—27 °C; *m/z* (M^+, 3%), 286, 255 (*M*−31, 3), 166 (90), 121 (100); ^{1}H n.m.r. (CDCl$_3$) δ 3.38 (s, 4-OMe-β), 3.2 (s, 4-OMe-α), 5.35 (d, 2-H), 4.05 (dd, *J ca.* 3 Hz, d in D$_2$O, 3-H),[2] 1.8 (d, 3-OH).

The *cis* relationship of the C(2)-phenyl and C(3)-hydroxy groups is based upon the assumed double inversion mechanism at C(3) as described above. Reversible ring-opening to *o*-hydroxychalcone does not alter this stereochemical conclusion because *o*-hydroxychalcone yields (**8**) under the reaction conditions. The 2-H–3-H coupling constant of $J_{\text{ax.-e}}$ 3.0 Hz is consistent with this stereochemical assignment.

Final confirmation of the stereochemistry of (**8**) [and, by extension, of (**2**) and (**4**)] was obtained by an *X*-ray crystal structure determination (Figure 1).[§] Bond distances and angles in this structure were within normal ranges. Some dihedral angles about C(2)–C(3) are: H–C(2)–C(3)–H −59.8(3), H–C(2)–C(3)–O(4) −180.1(3), O(1)–C(2)–C(3)–O(4) −61.0(3), C(6P)–C(2)–C(3)–C(4) 179.0(3)°.

The above reactions represent a striking way of functionalizing three centres in a regiospecifically and stereospecifically pure fashion. These novel 1-benzopyran derivatives are obvious precursors for synthesis of a wide range of com-

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[‡] We tentatively assign the 4-OMe-α as the more highly shielded because of its position below the plane of the adjacent benzene ring.

[§] *Crystal data* for (**8**) C$_{17}$H$_{18}$O$_4$: monoclinic, space group $P2_1/a$, a = 9.999(4), b = 13.394(3), c = 11.712(2) Å, β = 112.35(2)°, Z = 4, U = 1450.8(7) Å^3, D_c = 1.311 g cm^{-3}. Data were collected on a Picker FACS-1 diffractometer modified by a Krisel control update package. A total of 2063 reflections were measured in the range $2.0 < 2\theta < 45.0°$ and 1781 unique reflections with $F > 3.0\sigma(F)$ were used in the structure analysis. The structure was solved by direct methods (ACSHEL-X, G. Shedrick, Programs for Crystal Structure Determination, Cambridge, 1975) and refined to R = 0.0714, R_w = 0.0443. All non-hydrogen atoms were refined anisotropically and the hydrogen atoms were placed at calculated positions.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

pounds. We thank the USAMRDC and the Petroleum Research Fund for support of this work.

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2 For related examples of coupling constants in the flavanone series, see D. M. X. Donnelly, A. K. Keenan, T. Leahy, and E. M. Philbin, *Tetrahedron Lett.*, 1970, **16**, 1333.