Novel Iodination of the α-Methylene Group in 1,3-Diphenylpropane-1,3-dione and Related β-Diketones with Periodic Acid[1]

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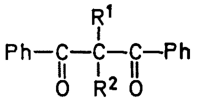
Summary On treatment with periodic acid, 1,3-diphenylpropane-1,3-dione is converted into α-iodo-derivatives.

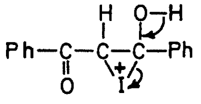
THE study of new applications of periodic acid in organic chemistry[2] has now been extended to specific iodination of the α-methylene group of certain β-diketones.

A solution of 1,3-diphenylpropane-1,3-dione [(**Ia**), enol content in $CDCl_3$, *ca.* 92%, by ^1H n.m.r.) (2·25 g, 10 mmoles) in glacial acetic acid (60 ml) was stirred with an aqueous solution (10 ml), of H_5IO_6 (1·82 g, 8 mmoles) (95°, 15 min.); then at room temp. (60 min.). The mixture was then treated with water (25—30 ml) at room temperature to yield snow-white needles of the 2-iodo-derivative (**Ib**), (43—46%), m.p. 108—109° (95% EtOH).† The filtrate contained unreacted starting material (*ca.* 40%) that could be recovered by extraction with $CHCl_3$. The monoiodo-derivative (**Ib**) was also obtained (50%) on treatment of (**Ia**) (10 mmoles) in AcOH (60 ml) with an aqueous solution (10 ml) of iodic acid (8 mmoles) (95° for 20 min., room temp. for 24 hr.).

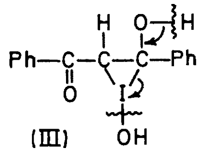


$$Ph-\underset{O}{\overset{\|}{C}}-\overset{R^1}{\underset{R^2}{C}}-\underset{O}{\overset{\|}{C}}-Ph$$

(Ia)R¹ = R² = H
(Ib)R¹ = H;R² = I
(Ic) R¹ = R² = I
(Id)R¹ = R² = Br



(II)



(III)

Treatment of an acetic acid solution (60 ml) of (**Ia**) (10 mmoles) with an aqueous solution (20 ml) of H_5IO_6 (2·28 g, 10 mmoles) at 95° for 30 min. and at room temperature for 30 min. gave yellow crystals of the 2,2-di-iodo-derivative (**Ic**), (19—21%), m.p. 152—153° (95% EtOH).†§

When iodic acid was used instead of periodic acid, little or no formation of the diiodo derivative (**Ic**) was observed. The use of a larger proportion of the reagents (iodic or periodic acid) did not improve the yields of the products (**Ib**) or (**Ic**).

Compounds (**Ib**) and (**Ic**) were readily converted into the known[3] dibromo-derivative (**Id**), m.p. 94—96°, on treatment of their solution in carbon tetrachloride with bromine at room temperature. Compounds (**Ib**) and (**Ic**) were converted into starting material (**Ia**) on extraction of their $CHCl_3$ solutions with an aqueous solution (5%) of $NaHSO_3$.

On treatment of solutions of the foregoing compounds in methanol with a solution of cupric acetate in methanol, the bis-copper chelate complex was precipitated, immediately for (**Ia**), after 3 min. for (**Ib**), and not at all after 24 hr. (a deep-green solution) for compounds (**Ic**) and (**Id**); this test serves to distinguish between these and related compounds. The progress of formation of the product was monitored by ^1H n.m.r. ($CDCl_3$) as follows: for disappearance of the enolic hydroxyl groups at δ 17·16 for (**Ia**), a shift of the peak at δ 6·82 ($-CH{=}C\langle$) for (**Ia**) to δ 6·97 ($-CH{=}C\langle$) for (**Ib**), and disappearance of the latter for (**Ic**).

Formation of the mono-iodo-derivative from other acyclic (enolic) β-diketones has been observed, *e.g.* from 1,3-diphenylbutane-1,3-dione, pentane-2,4-dione (which gives a vigorous reaction), hexane-2,4-dione, hexafluoropentane-2,4-dione, and others.

Application of *N*-iodosuccinimide, used in iodination of the methine group of certain enol acetates,[4] or of other iodinating reagents,[5] failed to iodinate the methylene group in (**Ia**). When $NaIO_4$ was used instead of periodic acid, or the acetic acid was replaced by *NN*-dimethylformamide or *p*-dioxan, none of the reactions mentioned was observed.

E.s.r. monitoring of the reaction of periodic acid with (**Ia**) showed no radical participation, indicating the ionic character of the iodination process. The behaviour of periodic (or iodic) acids towards (**Ia**) indicates structural lability of the I–O bond in the reagents. This high lability of the I–O bond may be associated with a relatively weak double-bond character.[6] Iodination of (**Ia**) can be envisaged as involving addition of the iodonium ion to the double bond, to give the intermediate (**II**), although addition of a molecule of hypoiodous acid, or its anion (an iodoso-ion IO^-), with subsequent elimination of a molecule of water to give (**Ib**), as shown in intermediate (**III**), is not excluded. The relatively modest yield of the iodo-compounds may be due to an association of the enolic diketone with the reagent[2] that could impede formation of intermediates (**II**) and (**III**).

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† Elemental and spectral analyses (mass and n.m.r.) were in agreement with the structures for the mono-iodo-(**Ib**) and di-iodo-(**Ic**) derivatives.

§ Compound (**Ic**) exhibits moderate stability [loss of iodine occurs, to give (**Ib**)] on storage as the solid, or in solution; it shows moderate loss of iodine on recrystallization from EtOH.

[1] Part of the series, Periodic Acid, a Novel Oxidant. For previous part, see *J. Org. Chem.*, in the press.

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[5] L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis," John Wiley, New York, 1967, pp. 500—511.

[6] L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, New York, 1948, ch. 7.