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Diacetoxyiodobenzene-mediated oxidative addition of 1,3-dicarbonyl compounds to olefins: an efficient one-pot synthesis of 2,3-dihydrofuran derivatives

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Abstract—A variety of olefins react with -dicarbonyl compounds at 0°C in the presence of diacetoxyiodobenzene to afford highly substituted 2,3-dihydrofuran derivatives in good to excellent yields.

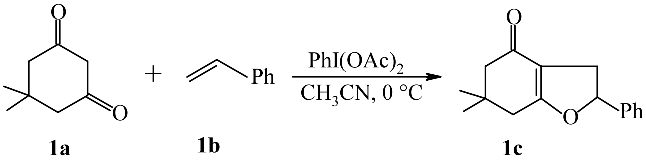
The dihydrofuran ring system is found prevalently at the central position of diverse classes of naturally occurring and biologically active heterocycles.[1] A number of syntheses of dihydrofurans are available which offer a variety of intermediates and reaction conditions.[2] The majority of synthetic approaches have been accomplished via ionic[3] or radical[4] pathways through oxidative addition of 1,3-dicarbonyl compounds to appropriate olefins. Although all of these methodologies afford the dihydrofuran moiety in a reasonable yield, simple and efficient synthetic approaches still remain scarce.[5]

Recently there has been considerable growth in the application of hypervalent iodine reagents for carrying out synthetic organic transformations.[6] Diacetoxyiodobenzene, (DIB) is a hypervalent iodine reagent which is readily available, frequently used in several oxidative transformations.[7] In this communication, we wish to report the use of DIB in the oxidative addition of 1,3-dicarbonyl compounds to olefins to afford functionalised dihydrofuran derivatives.

We initiated the study by investigating the reaction of dimedone **1a** with styrene **1b** in the presence of DIB. When the above reaction mixture in acetonitrile was stirred at 0°C for 1.5 h, the 2,3-dihydrofuran derivative **1c** was indeed formed in 71% yield (Scheme 1).[8]

Mechanistically, the formation of dihydrofuran derivatives may proceed through the initial reaction of the fairly electrophilic DIB with the nucleophilic enol form of the 1,3-dicarbonyl compound to give the intermediate **2**. The tendency of intermediate **2** to expel iodobenzene converts the initial electron rich active methylene carbon into an electron deficient centre.[6a] Carbon–carbon bond formation is then established by trapping of the alkene to form a relatively stable carbocation **3** which is attacked by the oxygen lone pair to form a cyclic product **4**. Finally, the acetate anion abstracts an acidic hydrogen from **4** to give the 2,3-dihydrofuran derivative **1c** (Scheme 2).

In order to assess the generality of the methodology, DIB-mediated oxidative addition was carried out with some representative alkenes and 1,3-dicarbonyl compounds. The results are summarised in Table 1. Aromatic olefins such as styrene (entry 1), cinnamyl acetate (entries 2, 9 and 12) and indene (entry 3) underwent oxidative addition to form the corresponding dihydrofuran derivatives in good to excellent yields. Simple alkenes such as allyl chloride (entry 5) and 1-methylcyclohexene (entries 6 and 10) were rather unreactive and



Scheme 1.

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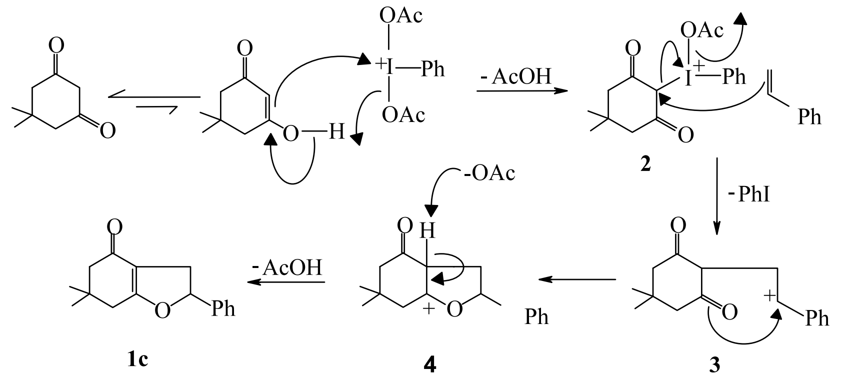
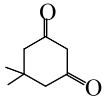
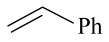
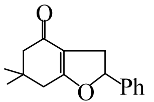
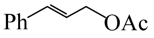
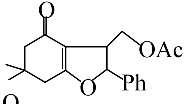
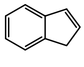
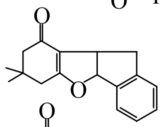
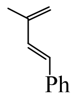
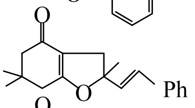
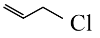
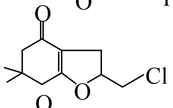
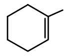
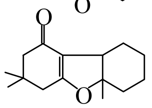
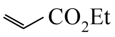
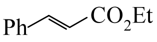
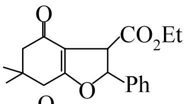
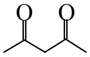
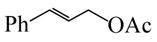
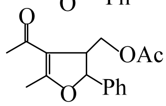
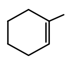
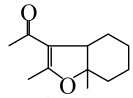
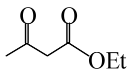
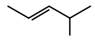
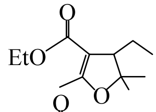
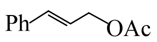
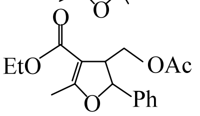


Scheme 2.

Table 1. Oxidative addition of β-dicarbonyl compounds to olefins using iodobenzenediacetate in CH_3CN at 0°C

Entry	β-Dicarbonyl compound **a**	Olefin **b**	Product **c**	Time (h)	Yield[a, b] (%)
1				1.5	71
2				1	77
3				1	76
4				1.5	69
5				2	58
6				2	62
7			No Reaction	4	-
8				3	52
9				2	59
10				2	46
11				1.5	43
12				1	51

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[a] Yields refer to isolated products.

[b] All the products gave satisfactory spectral data.[3,4]

[c] Relative stereochemistry of compounds **2c**, **3c**, **6c**, **8c**, **9c**, **10c** and **12c** was not determined.

gave the corresponding products in inferior yields. The reaction between electron deficient olefins such as ethyl acrylate (entry 7), ethyl cinnamate (entry 8) and dimedone was also studied. Since the success of dihydrofuran formation involves trapping of the relatively 'stable carbocation' intermediate, no product formation occurred in the case of ethyl acrylate. However, ethyl cinnamate underwent regioselective addition to dimedone to form the dihydrofuran in 52% yield.

In a separate report, the synthesis of dihydrofuran from iodonium ylides of β-diketones and alkenes in the presence of $Cu(acac)_2$ yields complex mixtures of inseparable products under thermal conditions.[9] The yields of dihydrofurans are very low in the case of the single electron oxidant [CAN and $Mn(OAc)_3$]-mediated oxidative addition of β-dicarbonyl compounds to styrene derived olefins.[4] This is due to the susceptibility of styrenic olefins to polymerisation and therefore, an excess of the olefin is needed. Thus it appears that the present methodology is quite advantageous in comparison to single electron oxidants and iodonium ylide procedures.

In conclusion, we have developed an efficient DIB-mediated oxidative addition of β-dicarbonyl compounds to olefins resulting in a one-pot synthesis of highly substituted dihydrofuran derivatives. We hope that the present methodology will be a useful synthetic entry in the use of DIB for carbon–carbon bond forming reactions.

General procedure: To a magnetically stirred solution of dimedone (3 mmol) and styrene (3 mmol) in acetonitrile (15 ml) was introduced diacetoxyiodobenzene (3 mmol). The reaction mixture was stirred at 0°C for 1.5 h and the progress of the reaction was monitored by TLC. After completion of reaction, the mixture was washed with water (10 ml), extracted with CH_2Cl_2 and dried over anhydrous sodium sulphate. Removal of the solvent and subsequent silica gel chromatography afforded the pure product **1c** in 71% yield.

Acknowledgements

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8. Spectral data of 6,6-dimethyl-2-phenyl-2,3,4,5,6,7-hexahydro-1-benzofuran-4-one **1c**: ^{1}H NMR (300 MHz; $CDCl_3$): δ_H 1.08 (6H, s), 2.05 (2H, s), 2.18 (2H, s), 3.61 (2H, d, $J=5.9$ Hz), 5.29 (1H, t, $J=5.9$ Hz), 7.12–7.38 (5H, m). ^{13}C NMR: δ_c 196.3, 160.4, 135.3, 132.0, 129.7, 128.2, 127.0, 75.7, 39.4, 31.8, 29.4, 21.7. IR (cm^{-1}, KBr): 3012, 2957, 2843, 1712, 1604, 1468, 1254, 1095, 793. Anal calcd for $C_{16}H_{18}O_2$: C, 79.33; H, 7.43. Found: C, 79.36; H, 7.41.
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