# Hypervalent Iodine Induced Cyclisation of α-(Aryl)alkyl β-Dicarbonyl Derivatives

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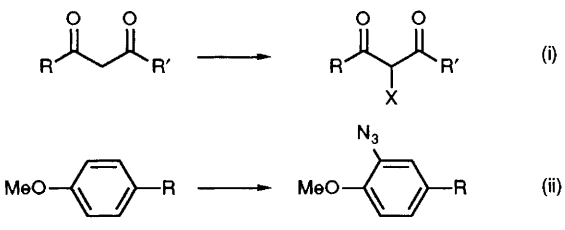
A novel and efficient intramolecular aromatic alkylation of α-(aryl)alkyl β-dicarbonyl derivatives using the hypervalent iodine reagent, phenyliodine(III) bis(trifluoroacetate) (PIFA), is described.

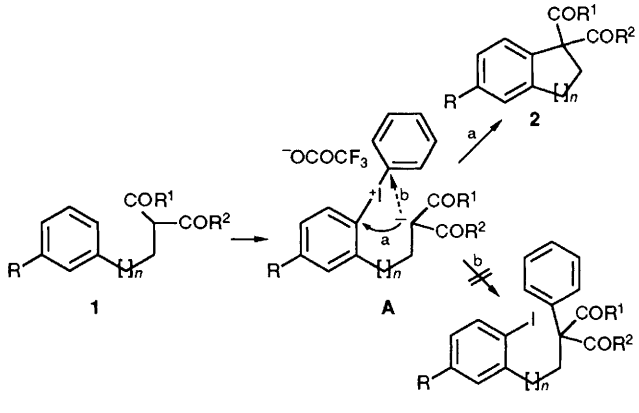
Hypervalent iodine oxidation[1,2] of organic compounds is of synthetic interest because it is simpler and safer than transition metal-based oxidation. It has been used for the oxidation of β-dicarbonyl compounds to α-functionalised β-dicarbonyl compounds [Scheme 1, reaction (i)].[3] Our recent results[4] on the novel oxidative azidation of electron-rich aromatic compounds by phenyliodine(III) bistrifluoroacetate (PIFA) and trimethylsilyl azide [Scheme 1, reaction (ii)] prompted us to investigate the hypervalent iodine oxidation of electron-rich aromatic compounds bearing a β-dicarbonyl group in the side chain. We have now found that reaction of α-(aryl)alkyl β-dicarbonyl derivatives **1** with PIFA followed by treatment with base gave the *para*-cyclised compounds **2** in high yields.

Typically, to a stirred solution of **1** in $(CF_3)_2CHOH$ was added 1.2 equiv. of PIFA. The mixture was stirred at room temperature for 30 min and concentrated under reduced pressure. The residue was dissolved in tetrahydrofuran (THF) and the solution was added dropwise to a suspension of 1.2 equiv. of Bu$^t$OK in THF. The mixture was stirred for 1 h under the same conditions and concentrated to give an oil, which was purified by column chromatography on silica gel to give **2**. The results are listed in Table 1.




**Scheme 1** *Reagents and conditions*: $PhI(OAc)_2$, $Me_3SiX$, X = $N_3$ or OAc; ii, $PhI(OCOCF_3)_2$ (PIFA), then $Me_3SiN_3$

A detailed study was performed under various conditions; several aspects are noteworthy. First, the present hypervalent iodine induced cyclisation of **1** gave the *para*-cyclised product **2** selectively in high yields (entries 1–11), although the free-radical cyclisation of **1h** induced by manganese(III) acetate afforded two possible substitution isomers (*para*-isomer **2h** and *ortho*-isomer **2h′**) in comparable amounts (**2h**:**2h′** = 44:47).[5] Secondly, the cyclisation proceeds smoothly in polar, low nucleophilic solvents such as $(CF_3)_2CHOH$ or $CF_3CH_2OH$, whereas the cyclised product could not be obtained in other solvents such as $CHCl_3$, MeCN and THF. Thirdly, an electron-rich aromatic ring is required to initiate the reaction. Other aromatic derivatives (**1k–l**) did not give satisfactory results (entries 12–14).




**Scheme 2** *Reagents and conditions*: PIFA in $(CF_3)_2CHOH$ or $CF_3CH_2OH$, then Bu$^t$OK in THF

**Table 1** Hypervalent iodine induced cyclisation of α-(aryl)alkyl β-dicarbonyl derivatives **1a–j** in $(CF_3)_2CHOH$ unless otherwise noted

| Entry | *n* | R | $R^1$ | $R^2$ | Starting compound | Product | Yield (%)[a] |
|---|---|---|---|---|---|---|---|
| 1[b] | 1 | OMe | Me | Et | **1a** | **2a** | 47 |
| 2 | 1 | OMe | Me | Et | **1a** | **2a** | 57 |
| 3 | 2 | OMe | Me | Et | **1b** | **2b** | 76 |
| 4 | 1 | $OCH_2OMe$ | Me | Et | **1c** | **2c** | 75 |
| 5 | 2 | $OCH_2OMe$ | Me | Et | **1d** | **2d** | 75 |
| 6 | 1 | $OSiMe_2Bu^t$ | Me | Et | **1e** | **2e** | 42 |
| 7 | 2 | $OSiMe_2Bu^t$ | Me | Et | **1f** | **2f** | 64 |
| 8 | 1 | OMe | Me | Me | **1g** | **2g** | 85 |
| 9 | 1 | OMe | Et | Et | **1h** | **2h** | 77 |
| 10 | 1 | $OCH_2OMe$ | Me | Me | **1i** | **2i** | 78 |
| 11 | 1 | OMOM | $-o$-$C_6H_4-$ | | **1j** | **2j** | 60 |
| 12 | 1 | H | Me | Et | **1k** | —[c] | |
| 13 | 1 | OH | Me | Et | **1l** | —[c] | |
| 14 | 1 | OAc | Me | Et | **1m** | —[c] | |

[a] Isolated yields by column chromatography (silica gel) are given. [b] In $CF_3CH_2OH$. [c] Complex mixture was obtained.

The reaction mechanism may be explained as follows. PIFA reacts initially with the electron-rich aromatic ring of **1** to give the diaryliodonium salt **A**† and intramolecular nucleophilic attack of the active methine anion occurs on the electron-rich phenyl ring (route *a*)‡[6] to give **2** (Scheme 2). To our knowledge, this is the first example of intramolecular nucleophilic attack on an aryliodonium salt. The application of the present cyclisation using PIFA to other aromatic systems is being studied.

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† The iodonium salt generated from the reaction of **1h** and PIFA was characterised by spectral evidence: IR, ν/cm$^{-1}$ ($CHCl_3$): 3400, 2990, 1740, 1720, 1660, 1585, 1565 and 1470 cm$^{-1}$; $^1$H NMR (200 MHz, $CDCl_3$): δ 1.27 (t, 6H, *J* 7 Hz, $CO_2CH_2Me$), 2.06–2.19 [m, 2H, $CH_2CH(CO_2Et)_2$], 2.85–2.95 [m, 2H, $CH_2CH_2CH(CO_2Et)_2$], 3.39 [t, 1H, *J* 7 Hz, $CH(CO_2Et)_2$], 3.84 (s, 3H, O*Me*), 4.21 (q, 4H, *J* 7 Hz, $CO_2CH_2Me$), 6.78 (dd, 1H, *J* 9, 3 Hz, ArH), 6.94 (d, 1H, *J* 3 Hz, ArH), 7.38 (t, 2H, *J* 8 Hz, ArH), 7.50 (t, 1H, *J* 8 Hz, ArH), 7.87 (d, 2H, *J* 8 Hz, ArH) and 7.98 (d, 1H, *J* 9 Hz, ArH).

‡ The present intramolecular nucleophilic attack occurs selectively on the electron-rich phenyl ring because of steric requirements although intermolecular nucleophilic attack generally occurs on the phenyl ring containing the electron-withdrawing group.[6]

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