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A new useful entry of IBX: the synthesis and structure of α-(2-iodobenzoyloxy)ketones ☆

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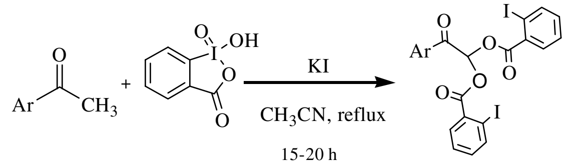
Abstract—α-Functionalized ketones can be conveniently prepared in one step by the reaction of ketones possessing α-methene with *o*-iodoxybenzoic acid (IBX) in the presence of potassium iodide. Methyl aryl ketones produced bi-substituted products, whereas the others gave mono-substituted ones.

IBX, *o*-iodoxybenzoic acid, has attracted increasing interest and research activity in the last 20 years.[1] It can be used as a reagent for the selective oxidation of alcohols to carbonyl compounds[1,2] and for other synthetically useful oxidative transformations.[1,3] Recently, Nicolaou and his co-workers have revealed that IBX is a powerful single-electron-transfer (SET) agent that readily accepts new heteroatom-based ligands[4] while it has also been explored in ionic liquid.[5]

α-Functionalized ketones are versatile intermediates for the synthesis of a variety of heterocyclic compounds, as well as natural products and related compounds. Other α-functionalized ketones such as tosyloxyketones,[6] acetoxyketones,[7] phosphoryketones,[6a,8] hydroxyketones,[9] alkoxyketones,[7b,10] iodoketones,[11] azidoketones,[12] and thiocyanatoketones[13] have been prepared by using appropriate hypervalent iodine(III) reagents but few are bi-substituted products.[10b] However, the synthesis of α-functionalized ketone compounds by using hypervalent iodine(V) reagents has been scarcely described in the literature.[14]

In this paper, we report the synthesis and structure of bi- and mono-substituted (Scheme 1 and Table 1) α-(2-iodobenzoyloxy)ketones by the reaction of ketones possessing α-methene with IBX in presence of potassium iodide, which is the first α-oxygenation of ketones by IBX. Two issues were approached: (a) the products atom economically remained the main skeleton of IBX, (b) a vivid iodine atom attached to the benzene ring had other synthetic applicability.[15]



2a-f **1** **3a-f** (53-78%)

a : Ar =Ph
b : Ar = *p*-Cl-Ph
c : Ar = *p*-Br-Ph
d : Ar = *p*-CH_3O-Ph
e : Ar = 2,4-dimethylphenyl
f : Ar = styryl

Scheme 1. The preparation of bi-substituted ketones.

Products were identified by ^1H and ^{13}C NMR, MS, IR, and X-ray crystallography diffraction. A representative crystallographic structure[16] (**3e**, Scheme 1) was shown in Figure 1. In particular, the α-protons and α-carbons of products were characterized by NMR peaks at $\delta = 4.8$–6.2 ppm and $\delta = 65$–90 ppm, respectively. The iodine-substituted phenylcarbons were indicated by NMR peaks near 94 ppm.[17]

When aliphatic ketones were explored, it was found that the ketones possessing at least two α-hydrogen atoms at

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Keywords: α-Functionalized ketones; Hypervalent iodine IBX; Structure; Synthesis.

☆ Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2004.03.158

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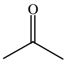
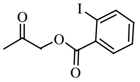
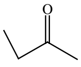
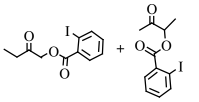
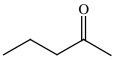
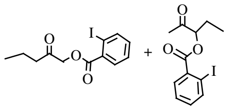
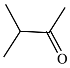
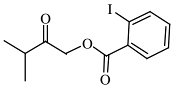
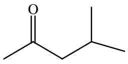
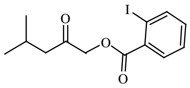
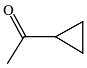
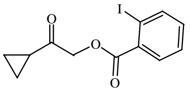
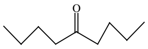
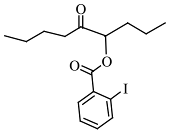
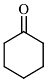
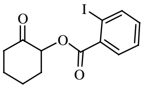
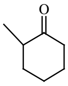
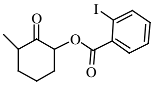
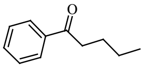
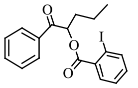
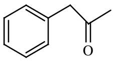
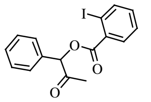
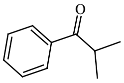
Table 1. The synthesis of mono-substituted ketones[a]

Entry	Substrate	Products	Yield[b] (%)	Time (h)
1			56	17
2			51[c]	17
3			52[d]	17
4			56	18
5			68	18
6			52	20
7			49	20
8			60	20
9			57	20
10			51	20
11			68	15
12		No reaction		20

[a] All reactions were carried out in boiling CH_3CN.

[b] Isolated yield of spectroscopically pure compounds.

[c] Regioselectivity analyzed by ^1H NMR was 1:1.

[d] Regioselectivity analyzed by ^1H NMR was 3:1.

one carbon atom could undergo this reaction and produce only mono-substituted products, even in an increasing amount of IBX, as demonstrated in Table 1. The effects of some solvent such as toluene, DMSO, CH_2Cl_2, CH_3CN, and THF on the reaction were tested and CH_3CN was found to be greatly favorable for the reaction. The temperature had somewhat influences on the reaction and the satisfied result was obtained at 80 °C. It was worth pointing out that these reactions would occur only under the condition that the amount of IBX or KI was not more than 1 or 0.7 equiv, respectively. The optimum ratio of IBX/ketone/KI was 1:1:1.[18] Another feature of this reaction was that various structure of ketones gave different regioselectivity products. The results were mainly dependent on the activity of α-hydrogen atoms and steric hindrance of α-carbon atoms. The activity of α-hydrogen atoms was much prior to the steric hindrance (entry 11). As to the activity of α-substituted ketones, it seemed to be that the more branches the substrates had, the more difficultly the reactions produced (entries 2, 3, 5, 10, 12). In the case of 2-butanone and 2-pentanone (entries 2, 3), the reaction gave a ratio of two isomers of 1:1 and 3:1, respectively. Under the same condition, the reactions of ketones with trivalent iodinanes such as 1-hydroxy-1,2-benziodoxol-3-(1H)-one(IBA) and iodobenzene diace-

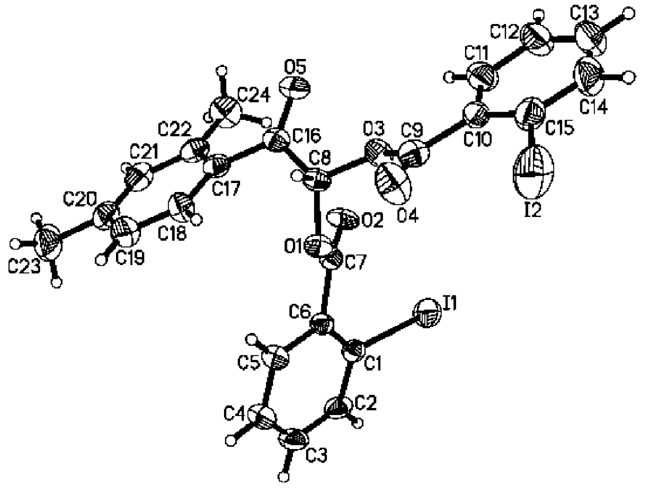


Figure 1. X-ray crystal structure of **3e**.

tate[PhI(OAc)$_2$] were also explored, but no expected products were obtained. Specifically, it was quite interesting that the substrates (entries 8–10) did not afford α,β-unsaturated ketones based on the early work of Nicolaou et al.[3a]

In conclusion, we have firstly found the α-oxygenation of ketones by IBX, in which 2-iodobenzoyloxy group, derived from IBX, was installed at α-position of ketones. It provides a new approach for the synthetic application of hypervalent iodine compounds. Further research on this topic and the exploration of the reaction mechanism are in progress now.

Acknowledgements

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16. Spectra and some physical data for **3e**. Solid. mp = 102–105 °C. IR (film): 1726, 1684, 1608, 1582, 1563, 1460, 743, 686 cm^{-1}. ^{1}H NMR (CDCl$_3$): δ 8.1–7.0 (m, 11H), 5.44 (s, 1H), 2.57 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (CDCl$_3$): δ 194.2, 165.8, 164.3, 143.1, 141.7 (2C), 139.7, 133.2 (2C), 133.0 (2C), 131.6 (2C), 128.6 (2C), 128.0 (2C), 126.5 (2C), 94.4 (2C), 67.8, 29.7, 29.3. FAB-MS: 641.1 (M+H$^+$). X-ray diffraction data were collected on a Bruker Siemens P4 diffractometer with graphite monochromated MoKα radiation (0.71073 Å). Crystal data for **3e** $C_{24}H_{18}I_2O_5$: $M_F = 640.18$, colorless, $0.36 \times 0.32 \times 0.22$ mm^3, triclinic, P^{-1}, $a = 7.903(1)$, $b = 12.706(2)$, $c = 12.743(2)$ Å, $\alpha = 67.11(1)°$ $\beta = 83.91(1)°$ $\gamma = 78.861(9)°$, $V = 1155.95(34)$ Å^3, $Z = 2$, $\rho_{\text{calculated}} = 1.839$ g cm^{-3}, $\mu = 2.753$ mm^{-1}. Data collection and refinement: ω scans $1.74° < 2\theta < 25°$, $T = 296(2)$ K, total data collected = 4751, independent refinement = 4012 ($R_{\text{int}} = 0.0119$). The data were corrected for absorption by empirical method (transmission factor: 0.9101–0.6601).

The structure was solved and refined by direct methods using SHELXS-97 and full-matrix least-squares refinement on F^2. $R_1 = 0.36$, $\omega R_2 = 0.089$ $[I > 2\sigma(I)]$ and $R_1 = 0.0574$, $\omega R_2 = 0.0845$ (all data). Hydrogen atoms were added theoretically. Crystallographic data (excluding structure factors) for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC-223844. Copies of the data can be obtained, free of change, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ. UK (Fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk).

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18. The typical procedure is as follows: Potassium iodide (2 mmol) and ketones (1 mmol for entries of bi-substituted products, 2 mmol for entries of mono-substituted products) were sequentially added to a suspension of IBX (2 mmol) in acetonitrile (15 mL). The red color appeared soon and the resulting mixture was heated to reflux under stirring for 15–20 h. The reaction was monitored by TLC (thin layer chromatography) until it complete. The mixture was allowed to cool and then quenched with sodium thiosulfate (5% aqueous solution, 20 mL). The mixture was transferred to a separating funnel and extracted with dichloromethane (3×20 mL). The organic phase was combined and sequentially washed with NaOH (5% aqueous solution, 2×30 mL), brine (2×30 mL) and dried over anhydrous sodium sulfate. The solvent was removed at reduced pressure. The resulting product was purified by column chromatography (hexane/ethyl acetate 30/1) to give oil liquid or solid.