

EFFICIENT METHOD FOR α -IODINATION OF KETONES

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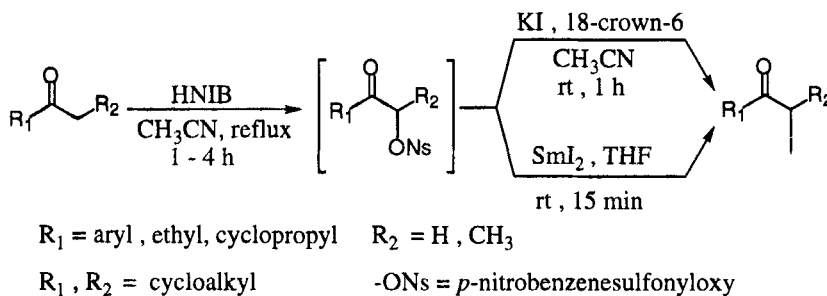
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ABSTRACT: α -Iodoketones are prepared in high yields from the initial reaction of various ketones with HNIB in CH_3CN and subsequent treatment of potassium iodide or samarium(II) iodide.

α -Iodoketones are important intermediates in organic transformation.¹ The direct preparation of α -iodoketones are generally performed by the treatment of ketones with iodine-copper(II) acetate,² iodine-cerium(IV) ammonium nitrate,³ iodine-mercury(II) chloride,⁴ and KI-KIO₃.⁵ However, these reactions were generally conducted under acidic conditions which limits their utilities. We have previously reported an efficient method for the direct α -[(*p*-nitrobenzene)sulfonyl]-oxylation of ketones and 1,3-dicarbonyl compounds in the presence of [hydroxy-(*p*-nitrobenzenesulfonyloxy)iodo]benzene (HNIB).⁶⁻⁷ Now we report on new and efficient methods for direct α -iodination of ketones under neutral conditions based on sulfonyloxylation of ketones and subsequent iodination of preformed α -[(*p*-nitrobenzene)sulfonyl]oxy ketones with potassium iodide or samarium(II) iodide in

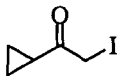


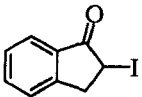
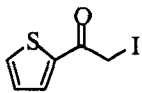
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one-pot fashion. Treatment of various ketones with HNIB in CH_3CN at reflux for 1 - 4 h afforded α -[(*p*-nitrobenzene)sulfonyl]oxy ketone intermediates as the sole product. Subsequent treatment of KI (2.0 equiv.) with a catalytic amount of 18-crown-6 at room temperature for 1 h afforded the corresponding α -iodoketones in high yields. Replacing HNIB by Koser's reagent, [hydroxy(tosyloxy)iodo]benzene (HTIB),⁸ in sulfonyloxylation step at same conditions provided reduced yields as indicated in Table (entries 1 and 5). Having established that this method gave satisfactory results in most of ketones except cyclic ketones (entries 11 and 12), we changed the iodinating agent from KI to SmI_2 . Samarium iodide(II) has been widely employed as a powerful reduction reagent.⁹⁻¹¹ However, only a few cases have been shown the iodinating ability of SmI_2 which include preparation of 3-iodo-2-cyclohexanol by the reaction of 2,3-epoxycycloalkanone hydrazone¹² and formation of iodohydrines via ring opening of cyclic ethers in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ ¹³. Therefore, we investigated the possibility of using SmI_2 to bring about the α -iodination of α -[(*p*-nitrobenzene)sulfonyl]oxy ketones at present reaction



conditions. Much to our satisfaction, the reaction between α -[(*p*-nitrobenzene)sulfonyl]oxy ketones with SmI_2 led to corresponding α -iodoketones. Thus, treatment of ketones with HNIB with reflux for 1- 4 h, followed by removal of

Table. Conversion of ketones into α -iodoketones.

Entry	Product	% Yield ^a using KI	% Yield ^a using SmI ₂
1	PhCOCH ₂ I	84 (67) ^b	82 (62) ^b
2	<i>p</i> -CH ₃ C ₆ H ₄ COCH ₂ I	86	84
3	<i>p</i> -CH ₃ OC ₆ H ₄ COCH ₂ I	84	81
4	<i>p</i> -ClC ₆ H ₄ COCH ₂ I	83	79
5	PhCOCHICH ₃	86 (71) ^b	83 (60) ^b
6	<i>p</i> -CH ₃ C ₆ H ₄ COCHICH ₃	85	83
7	<i>p</i> -CH ₃ OC ₆ H ₄ COCHICH ₃	84	81
8	<i>p</i> -PhCH ₂ OC ₆ H ₄ COCHICH ₃	82	82
9	CH ₃ CH ₂ COCHICH ₃	61	79
10		83	81
11		45	71
12		52	78
13		81	84
14		85	80

^a Isolated yield. ^b Yields obtained from replacing HNIB by HTIB in sulfonyloxylation step.

solvent and addition of SmI_2 (1.0 equiv.) in THF for 15 min gave desired α -iodoketones in high yields. At present reaction conditions samarium(II) iodide found to be more efficient iodinating agent than KI in terms of reaction rate and higher yields in cases of cyclic ketones (entries 11 and 12) as seen from the Table. However in this method, changing of solvent by THF instead of CH_3CN was necessary to obtain faster reaction rates with higher yields in the iodination step. It is presumed that the real iodinating agent in the present reaction appears to be SmI_3 which may be produced in the SmI_2 reduction of iodobenzene, one of the products of the α -[(*p*-nitrophenyl)sulfonyl]oxylation reaction.

In conclusion, we have shown that the treatment of α -[(*p*-nitrobenzene)-sulfonyl]oxy ketone intermediates with two different iodinating reagents, KI or SmI_2 , can serve as efficient iodination methods for the facile preparation of α -iodoketones under neutral reaction conditions.

Experimental Section

^1H NMR spectra were recorded on a Varian Gemini 2000 (300 MHz) spectrometer. GC-Mass spectra were acquired with a Hewlett-Packard HP 5988 spectrometer. Merck silica gel (230-400 mesh A.S.T.M.) was employed for flash column chromatography. All other reagents were commercially obtained in high purity.

General Iodination Procedure with KI: A mixture of ketone (1.0 mmol) and HNIB (0.55 g, 1.3 mmol) in acetonitrile (20 mL) was heated at reflux for 1-4 h. After reaction mixture was cooled to room temperature, potassium iodide (2.0 mmol) and 18-crown-6 (0.2 mmol) were added and stirring was continued for 1 h. Then the solvent was evaporated to dryness and the residue was purified by flash

column chromatography on silica gel eluting with EtOAc:Hexane (1:4) to afford pure α -iodoketone. All products showed spectral data consistent with the assigned structures.

General Iodination Procedure with SmI₂: A mixture of ketone (1.0 mmol) and HNIB (0.55 g, 1.3 mmol) in acetonitrile (20 mL) was heated at reflux. After a reaction time of 1 - 4 h the solution was evaporated to dryness and the resulting residue diluted with THF (10 mL). To this solution 1.0 mmol of 0.1 M SmI₂-THF was added and stirred at room temperature. After 15 min, complete conversion into the α -iodoketone was observed as assessed by TLC. Purification by flash column chromatography on silica gel eluting with EtOAc:Hexane (1:4) afforded pure α -iodoketone.

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