



Pergamon

Tetrahedron Letters 41 (2000) 2903–2905

TETRAHEDRON
LETTERS

Direct α -iodination of ketones using iodine/ SeO_2

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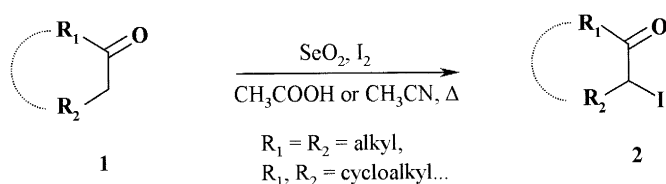
Received 27 December 1999; accepted 18 February 2000

Abstract

A satisfactory yield one-pot synthesis of various α -mono iodoketones **2** was achieved by iodination under oxidative conditions of ketones **1**. The monoiodination of different aliphatic or cyclic ketones (1-tetralones) showed the quite general applicability of the method. © 2000 Elsevier Science Ltd. All rights reserved.

During the last few years, methods were reported for the synthesis of α -iodoketones¹ from olefins,^{2a} epoxides,^{2b} or ketones and derivatives (enol esters and enol ethers). Although some of them permitted significant advances,^{3,4} the use of highly toxic reagents (thallium acetate) or difficulties in the synthesis and purification of enol silylethers represented serious disadvantages. Generally, enol acetates or enol silylethers were treated with silver acetate/iodine followed by triethylammonium fluoride,⁵ or copper(II) nitrate.⁵ Horiuchi et al. reported the direct α -iodination of ketones with iodine–copper(II) acetate or iodine–cerium(IV) ammonium nitrate in acetic acid.⁶

New efficient syntheses of α -iodoketones, in particular of 2-iodoindanones and 2-iodotetralones,⁷ are still desirable in view of the possible involvement of these cyclic compounds in inter(intra)molecular radical reactions.⁸ This paper reports a rapid (3 h) and convenient one-pot synthesis of α -iodoketones from the corresponding ketones with iodine and selenium dioxide under neutral or acidic conditions (Scheme 1).





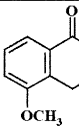
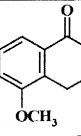




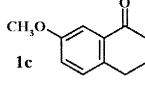
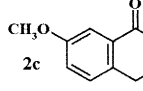


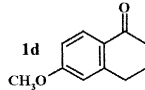
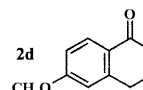



Scheme 1.

Treatment of ketones (**1a–f**) with 0.55 molar equivalent of iodine in acetic acid (or acetonitrile) and 0.55 molar equivalent of powdered SeO_2 afforded the corresponding α -monoiodoketones (**2a–f**)

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in satisfactory yields⁹ (Table 1). A catalytic amount of oxidant (0.1 mol) gave no significant results. The reaction was carried out successfully for 3-iodochroman-4-one (**2g**) in moderate yield. In the case of unsymmetrical aliphatic ketones (**1h**), two monoiodinated regioisomers (**2h–2h'**) were obtained and separated by chromatography. This method failed for 1-iodo-2-tetralones, leading to by-products.

Table 1
 α -Iodoketones

Ketones 1	α -Iodoketones 2	Solv. t °C, h	Yield (%) ¹¹	Ketones 1	α -Iodoketones 2	Solv. t °C, h	Yield (%)
		AcOH 70 °C 3 h	82 ²			CH ₃ CN 80 °C 48 h	79 ¹²
		AcOH 70 °C 3 h	78 ^{3a}			AcOH 80 °C 3 h	69 ¹
		AcOH 70 °C 3 h	82 ¹³			AcOH 90 °C 3 h	48 ¹⁴
		AcOH 75 °C 3 h	89 ¹⁵			AcOH 80 °C 3 h	78 ¹⁶
		CH ₃ CN 75 °C 4 h	85 ¹⁵				

Concerning the reaction mechanism, D'Auria et al. reported that iodonium ions could be the reacting species after oxidation of iodine.¹⁰ Direct treatment of ketones **1** with iodine without any oxidant did not afford any iodoketone. In contrast, in the conditions described above, anisole was iodinated into 4-iodoanisole (yield=39%). Thus, selenium dioxide was supposed to act as a Lewis acid catalyst (with possibly formation of selenious enol ester) and as oxidant of iodide into the iodonium ion.

In conclusion, the main interest of the process is that it allows us to dispense with the enol silylated ether intermediate, the purification of which was tedious according to the literature, especially for 6-methoxy-1-tetralone. Iodination of ketones with selenium dioxide and iodine represents a convenient procedure for α -monoiodination of 1-tetralones, due to the simple conditions and satisfactory yields.

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9. General procedure for the preparation of **2**: To a solution of **1** (0.1 mol) in 50 mL of solvent, finely powdered SeO₂ (6.10 g, 55 mmol) and iodine (13.97 g, 55 mmol) were added. The mixture was warmed (see Table 1). After filtration over a short SiO₂ column for removing the red precipitate (selenium), the dark solution was diluted with 200 mL of H₂O and extracted with CH₂Cl₂. The organic phase was extracted with 100 mL of 10% Na₂S₂O₃ solution and then with H₂O. After drying, the solvents were removed and the residue purified by column chromatography or crystallization to yield **2** (light sensitive).
10. D'Auria, M.; D'Onofrio, F.; Piancatelli, G.; Scettri, A. *Synth. Commun.* **1982**, *12*, 1127–1138.
11. Yield is expressed in analytically pure iodoketone (after purification by chromatography or crystallization).
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13. 2-Iodo-7-methoxytetralone: m.p.=44–45°C (CH₂Cl₂/petroleum ether); IR (KBr): 1679 cm⁻¹; ¹H NMR (200 MHz, δ ppm): 7.53 (d, J =2.7 Hz, 1H, H8); 7.18 (d, J =8.6 Hz, 1H, H5); 7.08 (dd, J =8.6 Hz and 2.7 Hz, 1H, H6); 4.99 (t, J =3.4 Hz, 1H, H2); 3.82 (s, 3H, OMe); 3.02 (m, 1H, H4); 2.78 (dt, J =16.5 Hz and 4.0 Hz, 1H, H4); 2.16 (m, 2H, H3).
14. 3-Iodochroman-4-one: m.p.=70°C (CH₂Cl₂/petroleum ether); IR (KBr): 1673 cm⁻¹; ¹H NMR (200 MHz, δ ppm): 7.94 (dd, J =7.8 Hz and 1.6 Hz, 1H, H5); 7.54 (td, J =7.6 Hz and 1.6 Hz, 1H, H7); 7.09 (t, J =7.8 Hz, 1H, H6); 7.05 (d, J =7.6 Hz, 1H, H8); 4.90 (dd, J =4.2 Hz, and 3.0 Hz, 1H, H3); 4.50 (dd, J =12.0 Hz and 4.2 Hz, 1H, H2); 4.45 (dd, J =12.0 Hz and 3.0 Hz, 1H, H2).
15. 2-Iodo-6-methoxytetralone: m.p.=90–91°C (CH₂Cl₂/petroleum ether); IR (KBr): 1661 cm⁻¹; ¹H NMR (200 MHz, δ ppm): 8.40 (d, J =8.7 Hz, 1H, H8); 6.85 (dd, J =8.7 Hz and 2.5 Hz, 1H, H7); 6.71 (d, J =2.5 Hz, 1H, H5); 4.96 (t, J =3.0 Hz, 1H, H2); 3.86 (s, 3H, OMe); 3.11 (m, 1H, H4); 2.82 (dt, J =17.0 and 3.8 Hz, 1H, H4); 2.15 (m, 2H, H3).
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