Mercury(II) Chloride-Iodine: A Useful Reagent for the Direct and Regiospecific Synthesis of α-Iodocarbonyl Compounds

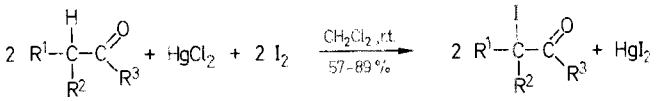
José Barluenga*, José M. Martinez-Gallo, Carmen Najera, Miguel Yus

Departamento de Química Orgánica, Facultad de Química, Universidad de Oviedo, Oviedo, Spain

α-Iodoaldehydes and α-iodoketones are obtained by direct iodination of the corresponding carbonyl compounds with mercury(II) chloride-iodine in a regiospecific manner.

Most of the methods to prepare α-iodocarbonyl compounds use enol derivatives[1-4] or α-bromoketones[5] as starting materials. The same α-iodo derivatives can also be obtained from olefins by direct oxidation-iodination[6]. Only one method for the direct iodination of ketones has been described[7] using the system copper(II) acetate/iodine and affording the corresponding mixture of regioisomers in the case of unsymmetric ketones.

In connection with our studies on the utilization of mercury(II) salts-halogen as reagents for the stereoselective bromo- and iodo-functionalization of olefins[8] we have found that mercury(II) chloride-iodine is an appropriate system for the direct and regiospecific preparation of α-iodocarbonyl compounds.



1 2a-j

1, 2	R^1	R^2	R^3
a	CH_3	H	CH_3
b	C_2H_5	H	H
c	CH_3	CH_3	H
d	n-C_3H_7	H	H
e	C_2H_5	CH_3	H
f	i-C_3H_7	H	H
g	H	H	t-C_4H_9
h	n-C_5H_{11}	H	CH_3
i	H	H	C_6H_5
j	C_2H_5	H	C_6H_5

The reaction of aldehydes and ketones **1** with mercury(II) chloride and iodine in dichloromethane at room temperature affords the corresponding α-iododerivatives **2** (Table).

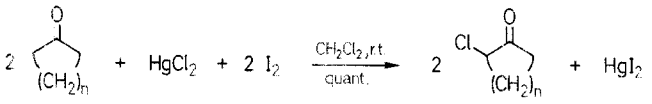
The reaction takes place under acidic conditions due to the *in situ* formation of hydrogen chloride. The initial iodination agent seems to be $(HgICl_2)^- I^+$, while $(HgI_2Cl)^- I^+$ may act in a further stage because the reaction is carried out using a 1:2 molar ratio of mercury(II) chloride:iodine. In both cases the electrophilic species is I^+.

Table. α-Iodination of Carbonyl Compounds

Product No.	Reaction Time (min)	Yield[a] [%]	b.p. [°C]/ torr	Molecular Formula[b] or Lit. b.p. [°C]/ torr or m.p. [°C]	IR (neat)[c] ν [cm^{-1}]	^{1}H-NMR (CCl_4, TMS)[d] δ [ppm]	^{13}C-NMR (CCl_4)[d,e] δ [ppm][f]
2a	75	85	62–64/15	148–150/667[10] (decomp.)	1700 (C=O)[10]	1.8 (d, 3H, J = 7.5 Hz, CH_3—CH); 2.3 (s, 3H, CH_3CO); 4.55 (q, 1H, J = 7.5 Hz, CH)[10]	22.7 (CH_3—CH); 26.7 (CH_3—CO); 27.1 (CH); 202.9 (CO)[11]
2b	45	76	50–52/15	68–9/35[5]	2700 (HCO) 1710 (C=O)	1.0 (t, 3H, J = 7.5 Hz, CH_3); 1.9 (quint., 2H, J = 7.5 Hz, CH_2); 4.3 (m, 1H, CHI); 9.2 (s, 1H, CHO)	15.3 (CH_3); 26.6 (CH_2); 40.8 (CHI); 192.5 (CO)
2c	20	76	44–46/15	C_4H_7IO[g]	2700 (HCO) 1710 (C=O)	1.9 (s, 6H, CH_3); 9.0 (s, 1H, CH)	30.6 (CH_3); 50.9 (CI); 193.3 (CO)
2d	60	75	72–74/15	C_5H_9IO[g]	2700 (HCO) 1710 (C=O)	0.9 (t, 3H, J = 7.5 Hz, CH_3); 1.4 (m, 2H, CH_2—CH_3); 1.9 (m, 2H, CH_2—CH); 4.4 (td, 1H, J = 9 and 4 Hz, CHI); 9.25 (d, 1H, J = 4 Hz, CHO)	15.2 (CH_3); 24.4 (CH_2—CH_3); 35.7 (CH_2—CH); 39.2 (CHI); 192.9 (CO)
2e	30	67	64–66/15	C_5H_9IO[g]	2700 (HCO) 1715 (C=O)	1.05 (t, 3H, J = 7.5 Hz, CH_3—CH_2); 1.7–2.15 (m, with s at 1.9, 5H, CH_2 and CH_3—C); 9.2 (s, 1H, CH)	13.7 (CH_3—CH_2); 27.0 (CH_3—C); 35.2 (CH_2); 59.65 (CI); 193.2 (CO)
2f	60	85	68–70/15	C_5H_9IO[g]	2700 (HCO) 1690 (C=O)	0.8, 0.9 (2d, 6H, J = 7.5 Hz, CH_3); 1.6 (quint., 1H, J = 7.5 Hz, CH—CH_3); 4.0 (dd, 1H, J = 7.5 and 4 Hz, CHI); 9.0 (d, 1H, J = 4 Hz, CHO)	23.1, 24.2 (2 × CH_3); 31.1 (CH—CH_3); 50.6 (CHI), 193.0 (CO)
2g	15	66	90–92/15	$C_6H_{11}IO$ (226.1)	1700 (C=O)	1.0, 1.03 (2s, 9H, CH_3); 3.7, 3.73 (2s, 2H, CH_2I)	6.9 (CH_2); 29.1 (CH_3); 45.9 (C—CO); 208.6 (CO)
2h	15	74	60–62/0.1	61–63/3[12]	1705 (C=O)	0.9 (deformed t, 3H, CH_3—CH_2); 1.3, 1.8 (2m, 8H, 4 × CH_2); 2.4 (s, 3H, CH_3—C); 4.4 (t, 1H, J = 8 Hz, CHI)	15.6 (CH_3—CH_2); 27.3 (CH_3—CO); 24.0, 30.5, 32.6, 35.8 (4 × CH_2); 36.0 (CHI); 202.4 (CO)
2i	20	57	74–76/0.1	34.4[13]	1680 (C=O)[14]	4.3 (s, 2H, CH_2); 7.3–7.7; 7.8–8.2 (2m, $5H_{arom}$)[14]	6.2 (CH_2); 130.5, 134.7, 135.4 (C_6H_5); 194.2 (CO)
2j	60	89	86–88/0.1	$C_{10}H_{11}IO$ (274.1)	1680 (C=O)	1.0 (t, 3H, J = 7.5 Hz, CH_3); 2.15 (quint., 2H, J = 7.5 Hz, CH_2); 5.2 (t, 1H, J = 7.5 Hz, CH); 7.3–7.6, 7.8–8.1 (2m, $5H_{arom}$)	15.8 (CH_3); 29.8 (CH_2); 30.85 (CHI); 130.1, 130.2, 134.9, 135.6 (C_6H_5); 195.4 (CO)

[a] Yield of crude pure product (as evidenced by ^{1}H- and ^{13}C-NMR) based on starting compounds **1**.
[b] Satisfactory microanalyses obtained: C ±0.3, H ±0.18.
[c] Recorded on a Perkin-Elmer 298 infrared spectrophotometer.
[d] Recorded on a Varian FT-80A spectrometer with a D_2O capillary.
[e] Assignment based on undecoupled NMR experiment.
[f] Referred to the solvent CCl_4.
[g] No analysis performed due to partial decomposition of the distilled product.

In the case of unsymmetrical ketones such as **1a**, **h** only the more substituted position is iodinated. When cyclic ketones such as cyclopentanone and cyclohexanone are treated in the same conditions as above only the corresponding α-chloroketones **3** are obtained[9]. We cannot find any reason to explain this result.



3a,b

n	3	Yield [%]	Reaction time
2	**a**	100	1 h
3	**b**	100	30 min

This process constitutes a new, easy synthetic method for the iodination of aldehydes and ketones under mild conditions. The reaction of unsymmetrical ketones is regiospecific and avoids the use of enol derivatives.

α-Iodination of Carbonyl Compounds; General Procedure:
To a solution of the carbonyl compound **1** (5 mmol) and mercury(II) chloride (0.68 g, 2.5 mmol) in dichloromethane (10 ml) is added iodine (1.27 g, 5 mmol). The mixture is stirred (see Table) till no more precipitation of mercury(II) iodide is observed, after which the precipitate is filtered off. The filtrate is washed with 0.1 normal aqueous sodium thiosulfate (10 ml) and saturated potassium iodide solutions (10 ml). The organic layer is dried with sodium sulfate, evaporated and distilled to give the corresponding α-iodocarbonyl compound **2**.

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