Oxidative Synthesis of α,β-Unsaturated Ketone from α-Iodo Ketone Using Peracid

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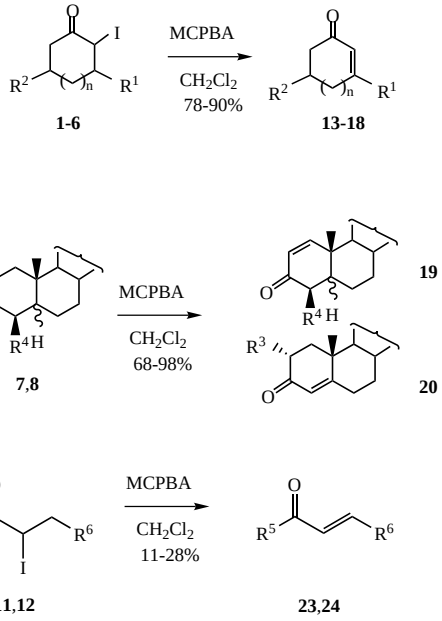
Abstract: Oxidation of α-iodo ketone in CH_2Cl_2 using *m*-chloroperbenzoic acid yields α,β-unsaturated ketone by β-H elimination in good yield. This reaction affords a new and convenient synthetic method for α,β-unsaturated ketone from α-iodo ketone.

Key words: α-iodo ketone, oxidation, elimination reaction, α,β-unsaturated ketone

Synthesis of α,β-unsaturated ketones is an important process for organic synthetic chemistry. They are usually prepared by one of the following methods: direct oxidation of ketones using the Collins reagent,[1] dehydrobromination of α-bromo ketones by treatment of nitrogenous bases and by lithium salts,[2] β-elimination of α-phenylseleno carbonoyl compounds,[3] dehydrogenation of steroidal ketone using DDQ (2,3-dichloro-5,6-dicyano-1,4-benzoquinone) in boiling benzene,[4] dehydrogenation of 3-oxo steroids using selenium dioxide in *tert*-butyl alcohol,[5] or allylic oxidation of Δ^5-steroids.[6] However, in the case of steroidal α,β-unsaturated ketones, it is known that these reactions tend to give abnormal products, i.e., α′,β′-unsaturated ketones. It is difficult to separate these isomers having similar properties.[7]

Reaction of alkyl iodides with peracetic acid has been investigated by Ogata and his co-workers.[8] More recently, Beeley and Sutherland have proposed an elimination of hypoiodous acid to account for olefin formation during the Baeyer–Villiger oxidation of an iodonorbornanone.[9] Reich et al., [10] reported that the oxidation of acyclic alkyl iodides bearing strong electron-attracting substituents such as carbomethoxy and sulfonyl gives the unsaturated compounds. However, the oxidation of α-iodocycloalkanone with peracid (MCPBA) has not been reported until now.

α-Iodocycloalkanones are important intermediates in organic synthesis, which have been investigated by our laboratory with a new method.[11] During the course of our investigations to prepare useful products from these iodo compounds, we found that irradiation of α-iodocycloalkanone with a high-pressure mercury lamp in hexane gave the corresponding α,β-unsaturated ketone,[12] and in aqueous alcohol, photocleavage of the carbon–carbon bond occurred to afford the corresponding ω,ω-dialkoxyalkanoic ester.[13] In this paper, we report that the oxidation of α-iodocycloalkanones **1**–**6** and steroidal α-iodo ketones **7**,**8** with MCPBA in CH_2Cl_2 yields the corresponding α,β-unsaturated ketone (Scheme 1). These results are summarized in Table 1.



Scheme 1

As can be seen from Table 1, it was found that this method is applicable to α-iodocycloalkanones and steroidal α-iodo ketones.

It is known that oxidative elimination of alkyl iodide and α-carbomethoxy iodide affords olefins by a *syn* elimination process.[10] The most reasonable explanation for the original observation is that the iodide is oxidized to an iodoso-intermediate which then eliminates 'HOI' to yield the unsaturated compounds.[8,9] In the present case, it seems that the oxidation of α-iodocycloalkanones with peracid (MCPBA) undergoes also the same process of elimination of 'HOI'. However, in the case of 3,4-dihydro-2-iodo-1(2*H*)-naphthalenone (**9**),[14] 1-naphthol (**21**) was obtained in 75% yield (Table 1, entry 18). Moreover, the reaction of α-iodo acyclic ketones **11** and **12** gave the corresponding (*E*)-α,β-unsaturated ketones in low yields. Apparent-

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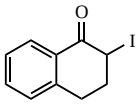
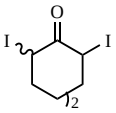
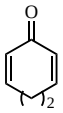
Table 1 Oxidative Elimination of α-Iodo Cyclic Ketone with MCPBA in CH_2Cl_2[a]

Entry		Substrate	Temp (°C)	Time (h)	Product (%)[b] GLC Yield (Isolated)	
1	**1**	(n = 1, R^1 = R^2 = H)	0	13	**13**	78 (61)[16a]
2	**2**	(n = 1, R^1 = Me, R^2 = H)	0	13	**14**	79 (66)[16b]
3	**3**	(n = 1, R^1 = H, R^2 = Me)	0	13	**15**	79 (69)[16b]
4	**4**	(n = 2, R^1 = R^2 = H)	0	15	**16**	78 (65)[16c]
5	**5**	(n = 3, R^1 = R^2 = H)	0	15	**17**	81 (70)[16d]
6	**6**	(n = 7, R^1 = R^2 = H)	0[c]	15	**18**	63 (50)[16e]
7	**6**	(n = 7, R^1 = R^2 = H)	0	15	**18**	90 (83)
8	**6**	(n = 7, R^1 = R^2 = H)	r.t.	12	**18**	79 (71)
9	**6**	(n = 7, R^1 = R^2 = H)	reflux	8	**18**	61 (49)
10	**6**	(n = 7, R^1 = R^2 = H)	0[d]	15	**18**	75 (62)
11	**6**	(n = 7, R^1 = R^2 = H)	r.t.[d]	15	**18**	67 (53)
12	**7**	(5α, R^3 = I, R^4 = H)	0	4	**19**	(98)[15]
13	**7**	(5α, R^3 = I, R^4 = H)	r.t.	4	**19**	(68)
14	**7**	(5α, R^3 = I, R^4 = H)	0[d]	10	**19**	(66)
15	**7**	(5α, R^3 = I, R^4 = H)	r.t.[d]	10	**19**	(60)
16	**8**	(5β, R^3 = H, R^4 = I)	0	6	**20**	(75)[16f]
17	**8**	(5β, R^3 = H, R^4 = I)	r.t.	6	**20**	(69)
18	**9**		0	20	**21**	75 (67)
19	**9**		r.t.	20	**21**	60 (55)
20	**10**		0[e]	20	**22** 	50 (46)
21	**10**		r.t.[e]	20	**22**	45 (40)
22	**11**	(R^5 = C_4H_9, R^6 = C_2H_5)	r.t.	4	**23**	(11)
23	**12**	(R^5 = C_4H_9, R^6 = C_3H_7)	r.t.	4	**24**	(28)

[a] All reactions were carried out in the dark.
[b] Determined by GLC analysis using *n*-dodecane as an internal hydrocarbon standard and isolated yields are given in parentheses. All products were characterized by IR, NMR, and HRMS and the superscript is the reference number.
[c] 0.5 molar equiv. MCPBA was employed.
[d] MeCN was employed.
[e] 2-Cyclohepten-1-one (**16**) and cycloheptanone were also obtained.

ly, α-iodo acyclic ketones are more unstable than α-iodocycloalkanones.

In order to discuss the reaction conditions, oxidation reaction of α-iodocyclododecanone (**6**) as a model compound was carried out. The oxidation of α-iodocyclododecanone with MCPBA gave cyclododecenone (**18**) in 90% yield at 0 °C. The results are summarized in Table 2. From these results, it was found that either the reaction temperature or the molar ratio of the oxidizing agent shows important effects. For example, low temperature is more favorable for the same content of the oxidizing agent (Table 2, entries 3–5). On the other hand, 2 molar equivalents of the oxidizing agent is required under these conditions (Table 2, entries 1–3).[10]

Table 2 Oxidation of α-Iodocyclododecanone (**6**) with MCPBA[a]

Entry	Solvent	MCPBA (molar equiv.)	Temp (°C)	Time (h)	Product (**18**)/% [b] GLC Yield (Isolated)
1	CH_2Cl_2	0.5	0	15	63 (50)
2	CH_2Cl_2	1.0	0	15	75 (65)
3	CH_2Cl_2	2.0	0	15	90 (83)
4	CH_2Cl_2	2.0	r.t.	12	79 (71)
5	CH_2Cl_2	2.0	reflux	8	61 (49)
6	CH_3CN	2.0	0	15	75 (62)
7	CH_3CN	2.0	r.t.	15	67 (53)

[a] Solvent (30 mL) was employed.
[b] GLC yield and isolated yield in parentheses.

In conclusion, this method is simple and convenient for the synthesis of α,β-unsaturated ketone. It is particularly noteworthy that this reaction affords a new synthetic method for α,β-unsaturated ketone.

Melting points are uncorrected and were measured by a Yanaco Mp-52777 (Yanaco Co. Ltd, Kyoto, Japan). IR spectra were recorded using a JASCO FT/IR-230 grating infrared spectrometer. ^1H and ^{13}C NMR spectra were measured using a JEOL GSX 400 Model spectrometer in $CDCl_3$ with TMS as an internal standard. HRMS were recorded at 75 eV on a JEOL JMS-01SG-2 instrument with a direct inlet.

Oxidative Elimination of 7 with *m*-Chloroperbenzoic Acid; Typical Procedure

MCPBA (0.135 g, 0.78 mmol) in CH_2Cl_2 solution (10 mL) was added dropwise into a CH_2Cl_2 solution (20 mL) of 2α-iodo-5α-cholestan-3-one (**7**) (0.20 g, 0.39 mmol) at 0 °C over a period of 1 h and the mixture was stirred for 4 h. The mixture was diluted with water (5 mL). The organic phase was washed with aq $Na_2S_2O_3$ to remove the iodine produced, and dried (Na_2SO_4) and then concentrated. The resulting solid was separated by column chromatography on silica gel, eluting with hexane–Et_2O (5:1, 150 mL) to give 5α-cholest-1-en-3-one (**19**) (0.148 g, 98%). Colorless needles were obtained from EtOH; mp 97–99 °C (lit.[15] 99 °C).

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(14) The starting material α-iodo cyclic ketones used in our experiments were prepared according to the literature procedures.[11] The physical data of typical compound 3,4-dihydro-2-iodo-1(2*H*)-naphthalenone (**9**) is listed.
Colorless needles; mp 78.5–79.6 °C.
IR (KBr): 1672, 1593 cm^{-1}.
^1H NMR ($CDCl_3$): δ = 5.02 (t, *J* = 3.7 Hz, 1 H, C2), 7.31 (m, 2 H), 7.51 (m, 1 H), 8.09 (d, *J* = 7.7 Hz, 1 H).
^{13}C NMR ($CDCl_3$): δ = 27.8, 30.7, 32.7, 127.0, 128.7, 128.8, 129.4, 134.0, 142.8, 191.8.
HRMS: *m*/*z* calcd for $C_{10}H_9OI$ [M]: 271.9699; found: 271.9734.
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