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A New Alkoxyiodination and Nitratoiodination of α,β-Unsaturated Ketone and Ester Using Iodine-Cerium(IV) Ammonium Nitrate

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Reaction of α,β-unsaturated ketones and electron-deficent unsaturated esters with iodine-cerium(IV) ammonium nitrate in alcohols (methanol, ethanol, or 1-propanol) under 0 °C-reflux gave the corresponding β-alkoxy-α-iodoketones and esters in good yields. In the case of acetonitrile and acetonitrile-water, β-nitrato- and β-hydroxy-α-iodo compounds were obtained, respectively.

β-Alkoxy-α-bromoketone and ester derivatives are important synthetic intermediates. They are usually prepared by one of the following method: β-alkoxy-α-bromination for α,β-unsaturated ketone using NBS in methanol,[1] alkyl hypohalite containing a small amount of boron trifluoride,[2] bromine with NBS in methanol,[3] and bromination of methoxy mercury complex.[4]

However, no study on the β-alkoxy-, β-nitrato-, and β-hydroxy-α-iodination of α,β-unsaturated ketones and esters have been described in the literature. Recently, Guidon *et al.* reported that *trans*-iodocyclization of carbamates involving α,β-unsaturated esters is greatly facilitated by the use of excess silver(I) triflate.[5]

We have been investigating a novel iodination method using iodine-copper(II) acetate.[6] These procedures suffer some deficiencies. They have problem that the produced iodide ions are consumed as copper(I) iodide. In previous papers, we reported a novel α-iodination of ketones in acetic acid or methanol;[7] a new alkoxyiodination and nitratoiodination of olefins;[8] and new oxidative aromatization of α,β-unsaturated cyclohexenones with iodine-cerium(IV) ammonium nitrate (CAN) in alcohol.[9] Now in this paper, we would like to report that the reactions of α,β-unsaturated ketones and esters in alcohol gave the corresponding β-alkoxyiodo compounds in good yields, while in the case of acetonitrile and acetonitrile-water, β-nitrato- and β-hydroxy-α-iodo derivatives were obtained in good yields, respectively. A mixture of ethyl crotonate(**4**), (582 mg, 5.10 mmol), iodine (647 mg, 2.55 mmol), CAN (2.796 g, 5.10 mmol), and acetonitrile (20 ml) was stirred at 50 °C for 15 h. The reaction mixture was poured into water and extracted with ether. The ethereal solution was washed with water, dried, and concentrated. The resulting oil was chromatographed on silica gel. Elution with hexane-acetone (9:1)(200 ml) gave β-nitrato-α-iodo derivative (**11d**), (1.322 g) as an oil. These results are summarized in Table 1.

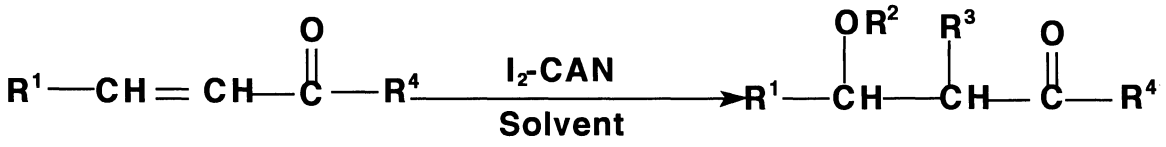
As can be seen in the Table 1, the reaction proved to have general applicability in the synthesis of the alkoxy iodo adducts of a variety of less reactive α, β-unsaturated ester. All of the products in the Table 1 have not been reported previously. The synthesis described in this paper is certainly the most convenient procedure (and probably unique in certain cases) for preparing alkoxy iodides from this type of olefin.

In the case of α, β-unsaturated ketone (**1**) with iodine-CAN in alcohol at 0 °C, the β-alkoxy-α-iodo keto-

Table 1. Reaction of α,β-Unsaturated Ketones and Esters with Iodine -Cerium (IV) Ammoium Nitrate in Alcohol, Acetonitrile, or Acetonitrile-Water

Run	Substrate	Solvent	Temp/ °C	Time/ h	Product (Yield/%)
1	**1**[a)]	MeOH	0	1	**5a** (34) + **6a** (58)
2	**1**[a)]	MeOH	50	1	**5a** (40) + **6a** (34) + **7a** (18)
3	**1**[a)]	MeOH	50	5	**5a** (37) + **6a** (10) + **7a** (29)
4	**1**[a)]	MeOH	reflux	6	**5a** (87)
5	**1**[a)]	EtOH	0	1	**6b** (54)
6	**1**[a)]	EtOH	RT	5	**5b** (22) + **6b** (53) + **7b** (<1)
7	**1**[a)]	EtOH	reflux	8	**5b** (83)
8	**2**[a)]	MeOH	0	1	**8a** (9) + **9a** (63)
9	**2**[a)]	MeOH	50	6	**8a** (35) + **9a** (41)
10	**2**[a)]	MeOH	reflux	6	**8a** (93)
11	**2**[a)]	EtOH	reflux	8	**8b** (90)
12	**3**	MeOH	50	15	**10a** (95)
13	**3**	EtOH	50	15	**10b** (83)
14	**3**[a)]	EtOH	50	15	**10b** (49)
15	**3**	*n*-PrOH	50	15	**10c** (89)
16	**3**	MeCN	50	15	**10d** (74)
17	**3**	MeCN-H_2O (10:1)	reflux	9	**10d** (54) + **10e** (39)
18	**4**	MeOH	50	15	**11a** (92)
19	**4**	EtOH	50	15	**11b** (81)
20	**4**[a)]	EtOH	50	15	**11b** (58)
21	**4**	*n*-PrOH	50	15	**11c** (89)
22	**4**	MeCN	50	15	**11d** (85)
23	**4**	MeCN-H_2O (10:1)	50	15	**11d** (66) + **11e** (28)
24	**4**	MeCN-H_2O (1:1)	reflux	8	**11e** (76)

a) Substrate (5.10 mmol), iodine (2.55 mmol), CAN (2.55 mmol), and solvent (20 ml) were employed.



1-4 5-11

1:R^1=H, R^4=Et
2:R^1=Me, R^4=Et
3:R^1=H, R^4=OEt
4:R^1=Me, R^4=OEt
5:R^1=R^3=H, R^4=Et
6:R^1=H, R^3=I, R^4=Et
7:R^1=R^3=H, R^4=$CHICH_3$
8:R^1=Me, R^3=H, R^4=Et
9:R^1=Me, R^3=I, R^4=Et
10:R^1=H, R^3=I, R^4=OEt
11:R^1=Me, R^3=I, R^4=OEt

a:R^2=Me
b:R^2=Et
c:R^2=Pr
d:R^2=NO_2
e:R^2=H

Table 2. The Composition of Reaction Mixtures of 1-Methoxy-3-pentanone (**5a**) with Iodine-Cerium(IV) Ammonium Nitrate in Methanol at 50 °C

Time/h	Products/%[a]		
	Me-CH_2-C(=O)-CH_2-CH_2-OMe (**5a**)	Me-CH_2-C(=O)-CH(I)-CH_2-OMe (**6a**)	Me-CH(I)-C(=O)-CH_2-CH_2-OMe (**7a**)
0.5	48	22	30
1.0	31	30	39
3.0	6	40	54
6.0	2	41	57
10.0	5	39	56
15.0	2	30	68

a) The composition of reaction mixture was determined from the peak area of ^{1}H-NMR spectrum.

ne (**6a**) and β-alkoxy ketone (**5a**) were obtained. At 50 °C, **5a**, **6a**, and the β-alkoxy-α'-iodo ketone (**7a**) were yielded. In order to clarify the progress of β-alkoxy-α'-iodo ketone, the reaction of ethyl vinyl ketone (**1**) with iodine-CAN in methanol at 50 °C was followed by the NMR spectra at certain intervals (Table 2). As can be seen from the results of examination by the NMR spectra, it was found that relative amounts of β-methoxy-α'-iodo ketone obtained from **1** as compared with β-methoxy-α-iodo ketone are considerably increased. From these results, it was assumed that iodine of α-iodo ketone rearranges from α- to α'-position. This assumption was, however, denied by the facts that the isomerization of the β-methoxy-α-iodo ketone (**6a**) under conditions of β-methoxy-α-iodination described above proceeds to give a mixture of **6a** and the reduced

product (**5a**). Therefore we presumed that the β-methoxy-α-iodo ketone was reducted to β-methoxy ketone and then reiodinated at α'-carbon. Moreover, the reaction of α, β-unsaturated ketone under reflux yielded β-alkoxy ketone in good yield.

It is interesting that the reaction of electron-deficient alkenes in α, β-unsaturated ester with iodine and CAN in alcohol gave the β-alkoxy-α-iodo ester in good yield. In the case of acetonitrile, β-nitrato-α-iodo compounds were obtained. On the other hand, the reaction with iodine-CAN in acetonitrile-water gave the β-hydroxy-α-iodo compound. From these results, it was found that the β-hydroxy-α-iodo ester was yielded through hydrolysis of β-nitrato-α-iodo compounds. Thus, it is assumed that in the reaction of the ester with iodine-CAN, cerium(IV) ion is coordinated to the oxygen of the carbonyl and ethoxy groups.

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