Halogenation Using Quaternary Ammonium Polyhalides XXVII.[1] Chloroiodination of Alkenes with Benzyltrimethylammonium Dichloroiodate

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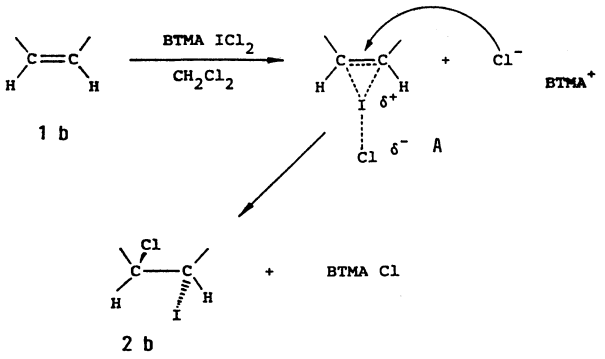
Synopsis. The reaction of alkenes with benzyltrimethylammonium dichloroiodate in dichloromethane gave the chloro iodo adducts in anti-stereospecific and regioselective manner; in methanol these adducts were obtained along with methanol-incorporated products.

We have recently shown that stable solid benzyltrimethylammonium dichloroiodate (BTMA ICl_2) is an excellent iodinating agent for electrophilic substitution.[2] In the present paper we wish to report on the chloroiodination of alkenes (**1**) with BTMA ICl_2 in aprotic and protic solvents.

The reaction of **1** with BTMA ICl_2 in dichloromethane at room temperature gave chloro iodo adducts (**2**). The results are summarized in Table 1. BTMA ICl_2 reacted with cyclohexene (**1b**) in a manner of stereospecific anti-chloro iodo addition. This completely anti-stereospecific addition can be explained by assuming an $AdEC_2$-type mechanism[8] involving an attack of a chloride ion on a three-center bound π complex-type intermediate (**A**), as shown in Scheme 1.

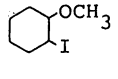


Scheme 1.

Recently, Negoro et al. have shown such an anti-stereospecific addition on the bromochlorination of **1** by the use of tetrabutylammonium chlorobromate (TBA $BrCl_2$).[9]

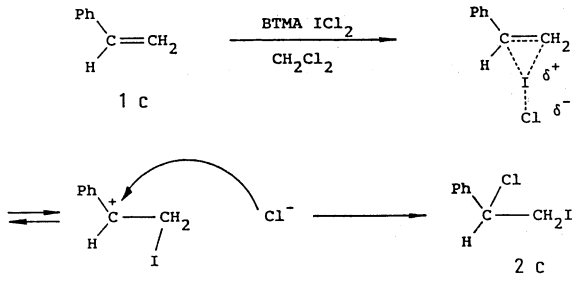
The reaction of styrene (**1c**) with BTMA ICl_2 in

Table 1. Reaction of **1** with BTMA ICl_2 in Aprotic and Protic Solvent

Substrate **1**	Reaction conditions temp/°C	time/h	Solvent	Product **2, 3**	Yield[a] %	Mp(°C) or Bp(°C)/mmHg
$CH_3(CH_2)_5$-CH=CH_2 (**1a**)	R.t.	2	CH_2Cl_2	$CH_3(CH_2)_5$-CHCl-CH_2I (**2a**)	82	—[b]
(**1b**)	R.t.	2	CH_2Cl_2	 (*trans*-)[3] (**2b**)	83	115/20
	R.t.	2—24	CH_3OH	**2b**	—(60)[c]	
				 (*trans*-)[4] (**3b**)	—(40)	
Ph-CH=CH_2 (**1c**)	R.t.	2	CH_2Cl_2	Ph-CHCl-CH_2I[5] (**2c**)	75	42—44
	R.t.	2	CH_3OH	**2c**	14(14)	42—44
				Ph-CH(OCH_3)-CH_2I[6] (**3c**)	75(86)	—[b]
Ph-CH=CH-COOH (*E*-) (**1d**)	R.t.	24	CH_3OH	Ph-CH(OCH_3)-CHI-COOH[7] (**3d**)	27	179—181
				1e	65	36
Ph-CH=CH-$COOCH_3$ (*E*-) (**1e**)	Reflux	24	CH_3OH	Ph-CH(OCH_3)-CHI-$COOCH_3$[7] (**3e**)	—(50)	

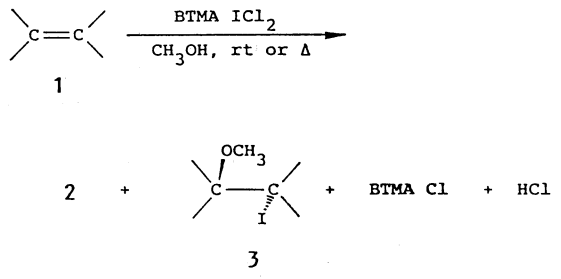
a) Yield of isolated product. b) Product was obtained as a high bp liquid. c) Yield, which was shown in parenthesis, was based on ^1H NMR.

dichloromethane gave 1-chloro-2-iodo-1-phenylethane (**2c**). It can be explained that the chloride ion exclusively attacked the phenyl-substituted carbon atom of the double bond, as illustrated in Scheme 2.



Scheme 2.

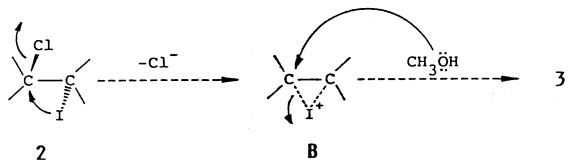
The reaction of **1** with BTMA ICl_2 in methanol at room temperature or under reflux gave a mixture of the corresponding **2** and 1-iodo-2-methoxy compounds (**3**) in a manner of anti-stereospecific and regioselective addition (Scheme 3). The results are shown in Table 1.



Scheme 3.

Incidentally, there is a possibility that neighboring group participations are present in some of these reaction processes. Thus, the neighboring iodo group in compound **2** may attack carbon at the reaction center as an internal neucleophile; the leaving chloro group is lost and a bridged iodonium ion intermediate **B** is formed. This undergoes an attack by an external neucleophile (methanol) to yield product **3** (Scheme 4). The overall stereochemistry is determined by the way in which the bridged ion **B** is formed and the way in which it reacts, and apparently differs from the stereochemistry which may be observed for a simple S_N2 attack on **2** by the external nucleophile.

Actually, as described above, the reaction of **1** with BTMA ICl_2 in methanol gave the anti-stereospecific and regioselective product **3**.



Scheme 4.

In order to make sure that the above-mentioned neighboring group participation actually occurs, the reaction of **2b** with methanol was tried both at room temperature and under reflux conditions. However, the reactions did not proceed at all. Furthermore, regarding the reaction of **1b** with BTMA ICl_2 in methanol at room temperature, a product ratio of **2b** and **3b** (60 : 40) did not change, no matter how long a reaction time was allowed. It may be concluded that the reaction of **1** with BTMA ICl_2 in methanol gave **2** and a solvent-incorporated product **3** by an anti-stereospecific manner in which a neucleophilic attack of a chloride ion and methanol to the bridged intermediate **A** may occur competitively.

Moreover, regarding the reaction of **1** with BTMA ICl_2 in methanol, methyl hypoiodite (CH_3OI) is conceivably the main active species, instead of iodine monochloride.[2a]

The reaction of (*E*)-cinnamic acid (**1d**) gave methyl (*E*)-cinnamate (**1e**) in substantial yield. In this case, **1e** should be obtained from the reaction of **1d** with methanol by a catalytic action of the generated proton.

The chloro iodo addition of **1** was previously achieved by the use of iodine monochloride.[10] However, this reagent is not easy to handle because of its viscous and toxic character. Therefore, the in situ generation of iodine monochloride by the reaction of iodine with mercury(II),[11] gold(I),[11] silver(I),[11] copper(I),[11] and copper(II) chlorides[3] has been carried out. Our stable reagent, BTMA ICl_2 (mp 126 °C), can be used instead of iodine monochloride; it has a large merit in that it can be treated easily, safely, and quantitatively under mild conditions.

Experimental

^1H NMR spectra were recorded on a JEOL-MH-100 spectrometer. The chemical shifts are expressed in ppm, with tetramethylsilane as an internal standard.

1-Chloro-2-iodo-1-phenylethane (2c); Typical Procedure in Aprotic Solvent: To a solution of styrene (**1c**) (0.25 g, 2.40 mmol) in dichloromethane (20 mL) was added BTMA ICl_2 (0.92 g, 2.64 mmol). After the mixture was stirred for 2 h at room temperature, sodium sulfite solution (5%, 20 mL) was added to the solution. The mixture was washed with water (20 mL), and then extracted with dichloromethane (20 mL). Organic layer was separated and dried on magnesium sulfate, filtered and evaporated in vacuo to give **2c** as colorless crystals; yield 0.47 g (75%); mp 42—44 °C (from hexane) (lit,[5] mp 40.5—41.0 °C).

2-Chloro-1-iodooctane (2a): Colorless oil; ^1H NMR ($CDCl_3$) δ=0.75—1.05 (3H, br. t, CH_3), 1.16—2.08 (10H, m, $-(CH_2)_5-$), and 3.18—4.35 (3H, m, -CHCl-CH_2I). Found: C, 34.67; H, 5.70%. Calcd for $C_8H_{16}ClI$: C, 35.00; H, 5.87%.

***trans*-1-Chloro-2-iodocyclohexane (2b):** Bp 115 °C/20 mmHg (lit,[3] bp 37 °C/0.2 mmHg); ^1H NMR ($CDCl_3$) δ=1.36—2.71 (8H, m, $-(CH_2)_4-$) and 4.30—4.68 (2H, m, -CHCl-CHI-).

Reaction of Cinnamic Acid (1d) in Methanol; Typical Procedure in Protic Solvent: To a solution of **1d** (0.50 g, 3.37 mmol) in methanol (20 mL) was added BTMA ICl_2 (1.17 g, 3.37 mmol); the mixture was stirred for 24 h at room temperature. Methanol was distilled off and the residue was extracted with ether (20 mL). The ether solution was treated with a sodium sulfite solution (5%, 20 mL), washed with water (20 mL) and dried on magnesium sulfate; it was

then filtered and evaporated in vacuo. The residue was separated by column chromatography on silica gel using benzene and ethyl acetate as eluents. From the first eluant 2-iodo-3-methoxy-3-phenyl propionic acid (**3d**) was obtained as colorless crystals; yield 0.27 g (27%). From the second eluant methyl cinnamate (**1e**) was obtained; yield 0.36 g (65%). **3d**; mp 179—181 °C (from hexane-chloroform (lit,[7] mp 167—168 °C); ^{1}H NMR ($CDCl_3$) δ=3.30 (3H, s, CH_3), 4.46 (1H, d, J=10.4 Hz, -C<u>H</u>I-COOH), 4.66 (1H, d, J=10.4 Hz, -C<u>H</u>(OCH_3)-), 7.45 (5H, s, C_6H_5), and 10.28—10.51 (1H, br. s, COOH). Found: C, 39.46; H, 3.79%. Calcd for $C_{10}H_{11}O_3I$: C, 39.24; H, 3.62%.

Reaction of Cyclohexene (1b) in Methanol: A mixture of compound **2b** and *trans*-1-iodo-2-methoxycyclohexane (**3b**) was obtained. **3b**: ^{1}H NMR ($CDCl_3$) δ=1.36—2.71 (8H, m, -$(CH_2)_4$-), 3.13—3.37 (1H, m, -C<u>H</u>(OCH_3)-), 3.45 (3H, s, OCH_3), and 3.95—4.19 (1H, m, -C<u>H</u>I-). This NMR spectrum was identical with that of isolated **3b** which was prepared according to a procedure described in the literature.[4]

Reaction of 1c in Methanol: Compound **2c** and 2-iodo-1-methoxy-1-phenylethane (**3c**) were isolated. **3c**: brown oil (lit,[6] bp 107—108 °C/5 mmHg); ^{1}H NMR ($CDCl_3$) δ=3.34 (3H, s, CH_3), 3.36 (2H, br. d, -C<u>H_2</u>I), 4.34 (1H, br. t, -C<u>H</u>(OCH_3)-), and 7.44 (5H, s, C_6H_5). Mass m/z: 262 (M^+).

Reaction of 1e in Methanol: Methyl 2-iodo-3-methoxy-3-phenylpropionate (**3e**) was obtained. **3e**: ^{1}H NMR ($CDCl_3$) δ=3.22 (3H, s, OCH_3), 3.82 (3H, s, $COOCH_3$), 4.45 (1H, d, J=11.3 Hz, -C<u>H</u>I-$COOCH_3$), 4.68 (1H, d J=11.3 Hz, -C<u>H</u>(OCH_3)-Ph), and 7.42 (5H, s, C_6H_5).

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