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Regioselective 1,2-Alkoxy, Hydroxy, and Acetoxy Iodination of Alkenes with I_2 Catalyzed by $Ce(SO_3CF_3)_4$

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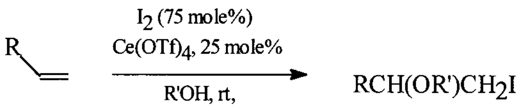
Abstract—The reaction of alkenes and iodine in water, alcohols and acetic acid is catalyzed with ceric triflate under mild conditions. The corresponding 1,2-alkoxy, acetoxy, and hydroxy iodides are obtained in good yields with easy procedure. © 2000 Elsevier Science Ltd. All rights reserved.

The functionalization of alkenes is an important process in organic synthesis.[1] Recently, 1,2-chloro- and 1,2-bromo-acetoxylation of alkenes with HCl gas in *N*,*N*-dimethylacetamide/*m*-chloroperbenzoic acid or oxone[1c] and $PhI(OAc)_2/Et_4NBr$[1d], respectively were reported. The reaction of halogen with alkenes in aqueous media is considered a general method for synthesis of halohydrins.[2,3] The reaction of alkenes with $I_2–H_2O$ is carried out effectively in the presence of $AgNO_3$,[4] HgO,[5] $CuO.HBF_4$,[6] $Cu(OAc)_2$,[3] and oxidizing agents.[7] Other routes for iodo-functionalization of alkenes is the use of alkyl hypoiodites[8] or iodine and a silver salt as reaction promoter followed by addition of a nucleophile.[9] However this latter method is limited only to strong nucleophiles which can make stable I–Nu compounds. This drawback was overcome by using $I(Py)_2BF_4$ in MeOH, AcOH and water together with HBF_4 or BF_3, but still the method suffers from complexity of the reagent and the acidic reaction conditions.[9] In the course of our studies[10] on the applicability of $Ce(SO_3CF_3)_4$[11] in synthesis, we observed its ability to act as catalyst for the reaction of olefins with iodine in nucleophilic solvents. In this work we report a very simple and efficient method for alkoxy, acetoxy and hydroxy iodination of alkenes.

We studied the reaction of indene (1 mmol) and iodine (0.75 mmol) in methanol/dioxane (1:1) in the presence of 0.25 molar equivalents of $Ce(OTf)_4$ at room temperature (Scheme 1). The reaction was found to be highly regioselective and only *trans*-1-methoxy-2 iodoindane was obtained in 80% yield after 1 h together with 10–15% unreacted indene. The same reaction in the absence of $Ce(OTf)_4$ produces only 10% of the product after 5 days. In order to study the effect of Lewis acids on this transformation, the reaction was performed in the presence of 0.25 molar equivalents of various metal salts. The results are summarized in Table 1.

The results in Table 1 show the efficiency of $Ce(OTf)_4$ among the studied Lewis acids for this transformation. This reaction was then studied for iodoalcoholysis of some other alkenes.

The results obtained for alkoxy iodination of some other alkenes are summarized in Table 2.



Scheme 1. Alkenes: R=Ph–, *n*-C_6H_{11}–, *n*-$C_{16}H_{33}$–, cyclohexene, 1-methylcyclohexene, indene R′=Me, Et, *i*-Pr, Ac, H.

Table 1. Reactions of indene (1 mmol) with I_2 (0.75 mmol) in MeOH/dioxane (1:1) in the presence of various Lewis acids (0.25 mmol) at room temperature

Lewis acid	Time (h)	*trans*-1-Methoxy-2-iodoindane (%)
$NiCl_2{\cdot}6H_2O$[a]	3	35
$CuSO_4$	4	50
$CeCl_3{\cdot}7H_2O$[a]	2	50
$Ce(NO_3)_6(NH_4)_2$[b]	3	55
$Zn(NO_3)_2{\cdot}6H_2O$[b]	4	50
$MgCl_2{\cdot}6H_2O$[a]	3	35
$Co(OAc)_2{\cdot}4H_2O$	2	60
$Ce(OTf)_4$	1	80
Without catalyst	5 days	10

[a] Unreacted starting material (25–30%) together with 20–25% of 1-chloro-2-iodoindane were obtained.
[b] In addition to the starting material (25–30%), a side product (10–15%) was also obtained.

Keywords: alkoxy iodination; hydroxy iodination; acetoxy iodination; alkene; ceric triflate.

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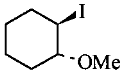
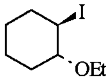
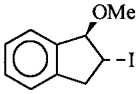
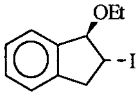
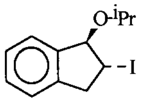
Table 2. 1,2-Iodofunctionalization of olefins (1 mmol) in the presence of I_2 (0.75 mmol) and $Ce(OTf)_4$ (0.25 mmol) at room temperature

Substrate	Solvent	Time (h)	Yield (%)	Product[a]	Reference to the product
Cyclohexene	MeOH/dioxane (3:1)	1	80		8,9b
Cyclohexene	EtOH/dioxane (3:1)	1.5	73		9b
Styrene	MeOH/dioxane (2:1)	1.5	80	$PhCH(OMe)CH_2I$	8, 9a
Styrene	EtOH/dioxane (2:1)	2	82	$PhCH(OEt)CH_2I$	8, 9a
Indene	MeOH/dioxane (1:1)	1	80		8
Indene	EtOH/dioxane (1:1)	1.5	70		–[b]
Indene	^{i}PrOH/dioxane (1:1)	2	73		–[b]
1-Octadecene	MeOH/dioxane (1:1)	4	78	$C_{16}H_{31}CH(OMe)CH_2I+C_{16}H_{31}CHICH_2OMe$ (76:24)[c]	8
1-Octene	MeOH/dioxane (1:1)	4	70	$C_6H_{11}CH(Ome)CH_2I+C_6H_{11}CHICH_2Ome$ (70:20)[d]	8

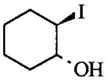
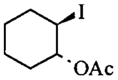
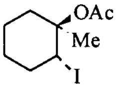
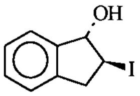
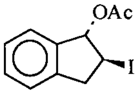
[a] Product was isolated and identified by spectroscopic techniques.

[b] The product was compared with a known sample prepared according to the Ref. 8; 2-Iodo-1-ethoxyindane (Found: C, 45.6; H, 4.4; I, 44, $C_{11}H_{13}IO$ requires C, 45.8, H, 4.5, I, 44.1; ^1H NMR δ (ppm) 7.35 (2H, m), 7.15 (2H, m), 5.1 (1H, d), 4.4 (1H, m), 3.7 (3H, m), 3.25 (1H, m), 1.2 (3H, t); ^{13}C NMR δ (ppm) 141.0, 139.9, 133.0, 132.1, 128.4, 124.8, 66.2, 43.9, 42.7, 27.0, 16.2.; 2-Iodo-1-isopropoxyindane C, 47.6; H, 4.8; I, 42.1, $C_{12}H_{15}IO$ requires C, 47.7, H, 4.96, I, 42.0; ^1H NMR δ (ppm) 7.35 (2H, m), 7.15 (2H, m), 5.1 (1H, d), 4.4 (1H, m), 4.0 (1H, m), 3.6 (1H, m), 3.2(1H, m), 1.1 (6H, d); ^{13}C NMR δ (ppm) 142.0, 141.5, 132.4, 129.1, 125.0, 124.8, 90.0, 72.6, 43.5, 28.2, 23.8, 23.0.

[c] Gc yield for distribution of the isomers, R=n-$C_{16}H_{31}$–.

[d] Gc yield for distribution of the isomers, R=n-C_6H_{11}–.

Table 3. 1,2- Iodofunctionalization of olefins (1 mmol) in the presence of I_2 (0.75 mmol) and $Ce(OTf)_4$ (0.25 mmol) at room temperature

Substrate	Solvent	Time (h)	Yield (%)	Product[a]	Reference to the product
Cyclohexene	H_2O/dioxane (2:1)	3	75		3, 9b, 12
Cyclohexene	HOAc/dioxane (2:1)	4	75		–[b]
1-Methylcyclohexene	HOAc/dioxane (2:1)	4	78		3, 9b
Styrene	H_2O/dioxane (2:1)	3	88	$PhCH(OH)CH_2I$	3, 9b
Styrene	HOAc/dioxane (2:1)	3	83	$PhCH(OAc)CH_2I$	9b
Indene	H_2O/dioxane (1:1)	2	75		12
Indene	HOAc/dioxane (1:1)	1	60		–[c]
1-Octene	H_2O/dioxane (1:1)	5	72	$RCH(OH)CH_2I+RCHICH_2OH$ (80:20)[d]	13
1-Octene	HOAc/dioxane (1:1)	5	70	$RCH(OAc)CH_2I+RCHICH_2OAc$ (70:30)[d]	–

[a] Product was isolated and identified by spectroscopic techniques.

[b] *trans*-2- Iodo-1-acetoxycyclohexane (Found: C, 35.5; H, 4.6; I, 47.2, $C_8H_{13}IO_2$ requires C, 35.8, H, 4.85, I, 47.4); ^1H NMR δ (ppm) 4.8 (1H, m), 4.0 (1H, m), 2.3 (3H, s), 1.2–2.3 (8H, m); ^{13}C NMR δ (ppm) 170.3, 71.3, 67.4, 38.3, 32.0, 27.4, 23.9, 21.6.

[c] *trans*-2-Iodo-1-acetoxyindane (Found: C, 43.6; H, 3.5; I, 42.2, $C_{11}H_{11}IO_2$ requires C, 43.7, H, 3.6, I, 42.0; ^1H NMR δ (ppm) 7.35 (1H, m), 7.15 (3H, m), 5.4 (1H, m), 4.2 (1H, m), 3.1 (2H, m), 2.2 (3H, s); ^{13}C NMR δ (ppm) 169.0, 133.9, 132.0, 127.3, 126.0, 123.5, 120.8, 62.0, 38.9, 21.1.

[d] Distribution of the isomers (R=n-C_6H_{11}–) was determined by gc and NMR analysis of the crude reaction mixture.

This reaction was also performed in water and acetic acid and the corresponding 2-hydroxy- and 2-acetoxy iodides were isolated in good yields. The results obtained are shown in Table 3. The reaction of *trans*-stilbene in methanol under similar reaction conditions was also studied, but no reaction occurred under these conditions. This could be due to steric effects for formation of the iodinium ion intermediate. The high regioselectivity (except in the case of 1-octene and 1-octadecane) observed in these reactions is controlled by electronic effects and attack of solvent molecule occurs on that carbon atom which can effectively stabilize the developing positive charge. In conclusion, 1,2-alkoxy, hydroxy and acetoxy iodides can be easily prepared from alkenes using ceric triflate as catalyst. The availability of the reagents and simplicity of the method, good yields and high regioselectivity are considered as advantage of this method.

Experimental

All yields refer to isolated products after column chromatography. All products were characterized by spectroscopic techniques. IR spectra were run on a Perkin–Elmer 781 spectrophotometer. NMR spectra were recorded on a Brucker Avance DPX-250. Mass spectra were recorded on a Shimadzu GCMS-QP 1000 EX. TLC on silica gel polygram SILG/UV_{254} plates and gas chromatography on a Shimadzu GC-10A instrument was used for monitoring of the reaction mixtures.

Typical procedure for the reaction of styrene and iodine in methanol with $Ce(OTf)_4$

Styrene (104 mg, 1 mmol) and $Ce(OTf)_4$ (184 mg, 0.25 mmol) were mixed together in methanol/dioxane (2:1, 4 ml). I_2 (190 mg, 0.75 mmol) was added in small portions to this mixture. The reaction mixture was stirred for 1.5 h at room temperature. Solvent was evaporated and chloroform (50 ml) was added. The excess of iodine was removed by addition of 10% aqueous solution of $Na_2S_2O_3$ (20 ml). The organic solution was further washed with water (2×10 ml) and dried with anhydrous Na_2SO_4. Evaporation of the organic solution was followed by column chromatography on a short column of silica gel using petroleum ether: chloroform (5:1) as eluent gave 1-methoxy-2-iodo-1-phenylethane[8,9a] as a colorless liquid in 80% yield.

Typical procedure for the reaction of cyclohexene and iodine in acetic acid with $Ce(OTf)_4$

To a magnetically stirred solution of cyclohexene (82 mg, 1 mmol), $Ce(OTf)_4$ (184 mg, 0.25 mmol) in acetic acid/dioxane (2:1, 4 ml) was added I_2 (190 mg, 0.75 mmol) in small portions. The reaction mixture was stirred for 4 h at room temperature. When the reaction was completed, solvent was evaporated and chloroform (40 ml) was added. The excess of iodine was removed by washing the organic solution with 10% aqueous solution of $Na_2S_2O_3$ (20 ml). The organic solution was further washed with 10% aqueous solution of $NaHCO_3$ followed by water (2×10 ml) and dried with anhydrous Na_2SO_4. The crude product was purified on a column of silica gel by using petroleum ether: chloroform (5:1) as eluent. 2-Iodo-1-acetoxycyclohexane was obtained as colorless liquid in 75% yield. Its elemental analysis and spectral data are given as footnote in Table 2.

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