Benzyl(triphenyl)phosphonium Dichloroiodate: A New Reagent for Coiodination of Alkenes

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A mild, efficient, and regio- and stereoselective method for iodoalkoxylation and iodohydroxylation of olefins has been developed using benzyl(triphenyl)phosphonium dichloroiodate as iodine source. This procedure led to the corresponding iodoalkoxylated and iodohydroxylated products in moderate to excellent yields.

Introduction. – Iodoorganic compounds are valuable and versatile synthetic intermediates that have found diverse applications in polymer chemistry, pharmacology, medicine, *etc.* [1]. The vicinal functionalization of olefins is an important process in synthetic organic chemistry, especially when the reaction is carried out in a regio- and stereoselective fashion. Among the several methods found in the literature [2–5], halofunctionalization [6–10] of alkenes towards synthetically useful substrates attract much more attention. For example, iodoalkoxylation and iodohydroxylation of olefins is an important transformation in organic chemistry and the resulting alkoxyiodides and hydroxyiodides are important building blocks in organic, medicinal, as well as industrial chemistry [11–17].

Iodination of alkenes is a considerably slower reaction than chlorination and bromination, due to the low electrophilicity of I_2. Activation of I_2 for addition to alkenes by modifying its electrophilicity has been achieved using transition-metal salts [18–23] or oxidizing agents [24–27].

Other electrophilic iodinating agents commonly employed for the iodination of organic molecules include alkyl hypoiodides [28], *N*-iodosaccharin, and *N*-iodosuccinimide [29–31], bis(pyridine)iodonium tetrafluoroborate [32][33], I_2-clays [34–37], hypoiodous acid [38], triiodoisocyanuric acid [39], dichloroiodoisocyanuric acid [40], and *in situ* generated acyl hypoidoite using a combination of elemental I_2 and hypervalent iodine reagents [41–43], to name a few.

However, most of these methods suffer from one or more disadvantages, such as use of expensive and hazardous/toxic reagents, high reaction temperatures, long reaction times, low yields, and tedious workup procedures, which limit their use under the aspect of environmental benign process. Therefore, replacement of such reagents by nontoxic, mild, selective, and easy-to-handle reagents is very desirable and represents an important goal in the context of clean synthesis.

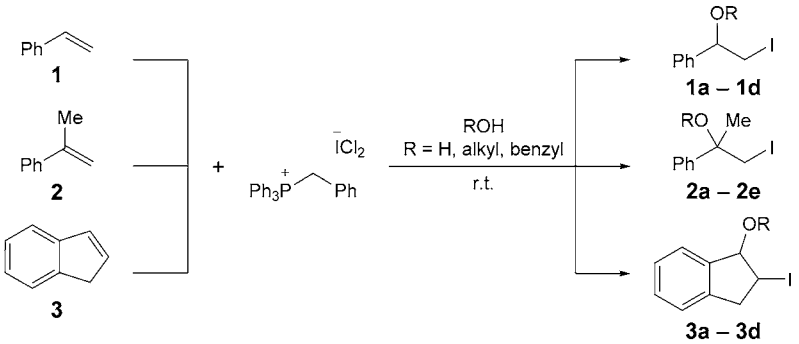
In our efforts towards the development of efficient procedures for coiodination of alkenes, we report a very simple and efficient method for 1,2-iodoalkoxylation and 1,2-

iodohydroxylation of alkenes in the presence of dichloroiodate salt, such as benzyl-(triphenyl)phosphonium dichloroiodate ($BTPPICl_2$), as an iodinated reagent under catalyst-free conditions at room temperature.

$BTPPICl_2$ and other dichloroiodate compounds are used as mild, efficient, and environmentally friendly iodination reagents for iodination of aromatic compounds [44–50].

Results and Discussions. – In the first stage of this study, we focused on the coiodination of α-methylstyrene (**2**; 1 mmol) by $BTPPICl_2$ (1.5 mmol) in MeOH and MeOH/solvent (MeCN, CH_2Cl_2, THF, hexane, and $CHCl_3$) as model reaction. The yield of (2-iodo-1-methoxy-1-methylethyl)benzene (**2a**) in MeOH after 40 min was 95% while in MeOH/solvent after 40 min it was 40, 65, 20, 50, and 70%, respectively. The best result in terms of solvent and yield of the desired product was obtained, when the reaction was conducted in MeOH as solvent and with O-bearing nucleophiles. To test the generality of this procedure, we examined the coiodination of different alkenes, and in most cases, β-iodo ethers were achieved in good to excellent yields (*Table*).

Table. *Coiodination of Alkenes in the Presence of $BTPPICl_2$ and O-Bearing Nucleophiles*



Entry	Alkene	R	Product	Time [min]	Yield [%][a])
1	**1**	Me	**1a**	40	92
2	**1**	Et	**1b**	45	90
3	**1**	^{i}Pr	**1c**	40	88
4[b])	**1**	H	**1d**	32	95
5	**2**	Me	**2a**	40	95
6	**2**	Et	**2b**	45	90
7	**2**	^{i}Pr	**2c**	45	90
8	**2**	Bn	**2d**	40	80
9[b])	**2**	H	**2e**	30	90
10	**3**	Me	**3a**	40	94
11	**3**	Et	**3b**	40	90
12	**3**	^{i}Pr	**3c**	45	80
13[b])	**3**	H	**3d**	35	85

[a]) Yield of isolated product. [b]) Reaction was performed in H_2O/MeCN 1:1.

As can be seen in the *Table*, when acyclic olefins such as styrene (**1**) and α-methylstyrene (**2**) were reacted with $BTPPICl_2$ in MeOH, EtOH, and ^{i}PrOH under optimum conditions, the corresponding 1,2-iodoalkoxy compounds, **1a** – **1c** and **2a** – **2c**, were obtained in good to excellent yields (*Entries 1 – 3* and *5 – 7*). Cyclic olefins, such as indene, which were reacted with the iodinating reagent in MeOH, EtOH, or ^{i}PrOH gave satisfactory yields of the corresponding β-iodoether compounds, **3a** – **3c** (*Entries 10 – 12*). Interestingly, the reaction between α-methylstyrene and $BTPPICl_2$ in benzylalcohol led to [(2-iodo-1-methyl-1-phenylethoxy)methyl]benzene (**2d**) in good yield (*Entry 8*). Furthermore, this reaction was also performed in H_2O and H_2O/solvent for iodohydroxylation of alkenes. The highest yields were obtained when the reaction was carried out in H_2O/MeCN. To test the generality of this procedure, we examined the coiodination of cyclic and acyclic alkenes. The corresponding halohydrin compounds (**1d**, **2e**, and **3d**) were achieved in good to excellent yields (*Entries 4*, *9*, and *13*).

Most importantly, the reaction was regioselective. Only *Markovnikov*'s addition product was obtained.

Conclusions. – In summary, we have developed a convenient route to vicinal halohydrines and β-halo ethers from alkenes. The reaction conditions are mild, the workup process is very simple, the reagents employed are stable, cheap, and readily available, and, furthermore, there is no need of special techniques and conditions.

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Experimental Part

General. Starting materials used in the reactions were supplied commercially from *Aldrich* or *Merck Chemical Co.* All yields refer to isolated products. Anal. thin layer chromatography (TLC): precoated *60 F_{254}* silica gel plates (SiO_2; *Merck*). Column chromatography (CC): SiO_2 (100 – 200 mesh). ^{1}H-NMR Spectra: *Bruker DRX-500* MHz *Avance*, *Bruker 400* MHz *Avance*, and *Bruker DRX-300* MHz spectrometer; in $CDCl_3$ or (D_6)DMSO; δ in ppm rel. to Me_4Si as internal standard, *J* in Hz.

Preparation of $BTPPICl_2$. A soln. of benzyl(triphenyl)phosphonium chloride (10 mmol) in 10 ml of H_2O was added to an orange soln. of $NaICl_2$ (11 mmol; prepared from 5.25% NaClO (15.6 ml), NaI (11 mmol, 1.65 g)), and 37% HCl (22 mmol, 2.2 ml) at 0° and stirred for 30 min at r.t. The resulting yellow precipitate was collected and washed with cooled H_2O and Et_2O, and dried in a desiccator to afford a yellow solid (90%). M.p. 162 – 164° [50].

General Procedure for Coiodination of Alkenes with $BTPPICl_2$. To a 50-ml flask equipped with a magnetic stirrer, $BTPPICl_2$ (0.5 mmol) was added to a soln. of alkene (1 mmol) in ROH (2 ml) or H_2O/MeCN 1:1. The mixture was stirred at r.t. for the specified time. The progress of the reaction was monitored by TLC. After completion, AcOEt was added, the mixture was filtered, and the org. layer was washed with 5% aq. $Na_2S_2O_3$ and dried ($MgSO_4$). The solvent was removed *in vacuo* and the crude mixture was purified by CC (AcOEt/hexane) and analyzed by ^{1}H-NMR spectroscopy.

(2-Iodo-1-methoxyethyl)benzene (**1a**). Yellowish liquid [27]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.43 – 7.32 (*m*, 5 arom. H); 4.31 (*dd*, *J* = 8.0, 4.8, CH–O); 3.36 (*d*, *J* = 5.2, 1 H of CH_2); 3.35 (*d*, *J* = 2.4, 1 H of CH_2); 3.32 (*s*, MeO).

(1-Ethoxy-2-iodoethyl)benzene (**1b**). Yellowish liquid [51]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.32 – 7.40 (*m*, 5 arom. H); 4.42 (*dd*, *J* = 8.0, 5.2, CH–O); 3.50 – 3.42 (*m*, CH_2O); 3.40 – 3.33 (*m*, CH_2I); 1.24 (*t*, *J* = 7.2, Me).

[2-Iodo-1-(1-methylethoxy)ethyl]benzene (**1c**). Yellowish liquid [36]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.39–7.33 (*m*, 5 arom. H); 4.53 (*t*, *J* = 6.4, Me_2CH–O); 3.58 (*m*, PhC*H*–O); 3.32 (*d*, *J* = 7.2, CH_2); 1.24 (*d*, *J* = 6.0, Me); 1.11 (*d*, *J* = 6.0, Me).

2-Iodo-1-phenylethanol (**1d**). Yellowish liquid [40]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.40–7.35 (*m*, 5 arom. H); 4.86 (*d*, *J* = 8.8, CH–O); 3.50 (*d*, *J* = 3.6, 1 H of CH_2); 3.44 (*d*, *J* = 8.8, 1 H of CH_2); 2.50 (*d*, *J* = 2.4, OH).

(2-Iodo-1-methoxy-1-methylethyl)benzene (**2a**). Yellowish liquid [52]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.45–7.29 (*m*, 5 arom. H); 3.53 (*d*, *J* = 10.4, 1 H of CH_2); 3.45 (*d*, *J* = 10.4, 1 H of CH_2); 3.15 (*s*, MeO); 1.72 (*s*, Me).

(1-Ethoxy-2-iodo-1-methylethyl)benzene (**2b**). Yellowish liquid [51]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.45–7.29 (*m*, 5 arom. H); 3.54 (*d*, *J* = 10.4, 1 H of CH_2I); 3.48 (*d*, *J* = 10.4, 1 H of CH_2I); 3.40–3.32 (*m*, 1 H of CH_2O); 3.25–3.18 (*m*, 1 H of CH_2O); 1.72 (*s*, Me); 1.23 (*t*, *J* = 6.8, Me).

[2-Iodo-1-methyl-1-(1-methylethoxy)ethyl]benzene (**2c**). Yellowish liquid. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.50–7.48 (*m*, 2 arom. H); 7.39–7.31 (*m*, 3 arom. H); 3.60 (*m*, CH–O); 3.53 (*d*, *J* = 10.0, 1 H of CH_2); 3.39 (*d*, *J* = 10.0, 1 H of CH_2); 1.80 (*s*, Me); 1.19 (*d*, *J* = 6.0, Me); 1.02 (*d*, *J* = 6.4, Me).

[(2-Iodo-1-methyl-1-phenylethoxy)methyl]benzene (**2d**). Yellowish liquid. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.53–7.29 (*m*, 10 arom. H); 4.41 (*d*, *J* = 11.2, 1 H of CH_2O); 4.30 (*d*, *J* = 11.2, 1 H of CH_2O); 3.67 (*d*, *J* = 10.4, 1 H of CH_2I); 3.57 (*d*, *J* = 10.4, 1 H of CH_2I); 1.87 (*s*, Me).

1-Iodo-2-phenylpropan-2-ol (**2e**). Yellowish liquid [40]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.49–7.45 (*m*, 2 arom. H); 7.41–7.37 (*m*, 2 arom. H); 7.34–7.28 (*m*, 1 arom. H); 3.68 (*d*, *J* = 10.0, 1 H of CH_2); 3.64 (*d*, *J* = 10.0, 1 H of CH_2); 2.39 (*s*, OH); 1.75 (*s*, Me).

*2,3-Dihydro-2-iodo-1-methoxy-1*H-*indene* (**3a**). Yellowish liquid [23]. ^{1}H-NMR (500 MHz, $CDCl_3$): 7.48–7.28 (*m*, 4 arom. H); 5.15 (*d*, *J* = 3.5, CH–O); 4.55–4.52 (*m*, CH–I); 3.78 (*dd*, *J* = 17.0, 6.8, 1 H of CH_2); 3.63 (*s*, MeO); 3.33 (*dd*, *J* = 17.0, 4.6, 1 H of CH_2).

*1-Ethoxy-2,3-dihydro-2-iodo-1*H-*indene* (**3b**). Yellowish liquid [23]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.50–7.31 (*m*, 4 arom. H); 5.19 (*d*, *J* = 3.6, CH–O); 4.49–4.45 (*m*, CH–I); 3.93–3.86 (*m*, 1 H of CH_2O); 3.81–3.77 (*m*, 1 H of CH_2); 3.76–3.72 (*m*, 1 H of CH_2O); 3.30 (*dd*, *J* = 17.0, 4.8, 1 H of CH_2); 1.28 (*t*, *J* = 2.4, Me).

*2,3-Dihydro-2-iodo-1-(1-methylethoxy)-1*H-*indene* (**3c**). Yellowish liquid [23]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.40–7.21 (*m*, 4 arom. H); 5.22 (*d*, *J* = 4.4, ArC*H*–O); 4.37–4.33 (*m*, CH–I); 4.14–4.08 (*m*, Me_2CH–O); 3.69 (*dd*, *J* = 16.8, 7.2, 1 H of CH_2); 3.29 (*dd*, *J* = 16.4, 6.4, 1 H of CH_2); 1.31 (*d*, *J* = 3.2, Me); 1.30 (*d*, *J* = 3.6, Me).

*2,3-Dihydro-2-iodo-1*H-*inden-1-ol* (**3d**). Solid. M.p. 112° [53]. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.46–7.24 (*m*, 4 arom. H); 5.42 (*t*, *J* = 6.0, CH–O); 4.23 (*m*, CH–I); 3.62 (*dd*, *J* = 16.2, 7.4, 1 H of CH_2); 3.33 (*dd*, *J* = 16.4, 8.0, 1 H of CH_2); 2.36 (*d*, *J* = 6.0, OH).

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