Pergamon

Tetrahedron Letters 42 (2001) 7245–7247

TETRAHEDRON
LETTERS

Iodohydroxylation of alkenes promoted by molecular and hypervalent(III) iodine

Anna Rita De Corso, Barbara Panunzi and Marco Tingoli*

Dipartimento di Scienza degli Alimenti, Università di Napoli 'Federico II', I-80055 Portici (NA), Italy

Received 26 July 2001; revised 19 August 2001; accepted 20 August 2001

Abstract—Several iodohydrins are isolated in good yields starting from the corresponding alkenes and a mixture of molecular iodine and phenyliodine(III)bis(trifluoroacetate) (BTI), in $CH_3CN–H_2O$ as solvent, at −15°C. Hypoiodous acid is added to the terminal carbon–carbon double bond in a Markovnikov fashion. Moreover, the stereochemical features of the products show the *anti*-stereospecificity of the addition. © 2001 Elsevier Science Ltd. All rights reserved.

The reaction of hypoiodous acid with alkenes is usually difficult to achieve due to the ready reversibility of IOH addition to carbon–carbon double bonds. For this reason, in contrast with bromo- and chlorohydrins, iodohydrins are not obtained by the direct treatment of alkenes with iodine in water.[1] Several contributions to solve this problem appeared in the last few years in the literature. One of these is based on the in situ generation of IOH from the direct reduction of periodic acid ($HIO_4 \cdot 2H_2O$) with sodium bisulphate ($NaHSO_3$).[2] Alternatively, a stable neutral solution of hypoiodous acid, obtained from the dimethyldioxirane oxidation of iodomethane, is trapped by a series of alkenes that are readily transformed into the corresponding iodohydrins.[3] More recently, *N*-iodosuccinimide, employed in a mixture of H_2O–DME, was reported to act as a useful electrophilic iodinating agent, being able to transform in very mild conditions both electron-rich and electron-poor olefins into iodohydrins.[4]

The ability of iodine(III) species to oxidise a chalcogenate-type derivative as diphenyl diselenide was extensively studied and applied to the preparation of several oxy-selenenylated products.[5] More recently, we have observed in our laboratory that the commercially available phenyliodine(III)bis(trifluoroacetate) (BTI) is able to promote, at −15°C, the complete decolouration of a yellow–orange solution containing both the alkene and diphenyldiselenide in anhydrous CH_3CN. Using this treatment, several phenylethene derivatives were transformed into the hydroxyphenyl selenenylated compounds in a Markovnikov fashion.[6] In the light of these observations and with the aim to generate an efficient electrophilic iodinated agent in situ, we have tried to apply the same experimental conditions described above to an iodine-containing solution of CH_3CN. The first substrate allowed to react was styrene, treated with 0.6 molar equiv. of I_2 followed by 0.7–1.0 molar equiv. of BTI in 15 ml of anhydrous CH_3CN at −15°C. In a few minutes the complete disappearance of the dark red–brown colour was observed. The reaction mixture was allowed to warm up to room temperature and, after a simple work-up, the corresponding 2-phenyl-2-hydroxy-1-iodoethane, isolated and fully characterised as the acetate derivative, was recovered in 89% overall yield.

This result prompted us to apply our methodology to different alkenes but unfortunately only unstable iodinated products were isolated from any reaction mixtures, which spontaneously liberate I_2 after the evaporation of the extraction solvent.

In the case of styrene, the ligand transfer to the benzylic position is probably the fastest reaction process. In all the other cases, the halogen competes with the poor nucleophilic character of the trifluoroacetate anion.

The participation of water in electrophilic halogenation reaction of alkenes is one of the most thoroughly studied classes of cohalogenation.[1] So we found that also in our case the addition of water to CH_3CN forces the halonium ion intermediate to incorporate OH instead of the iodine anion.[7]

---

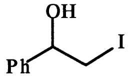
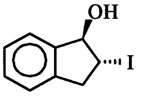
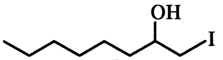
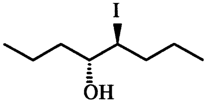
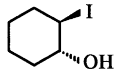
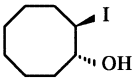
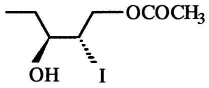
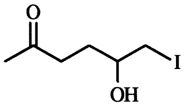
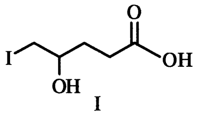
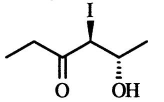
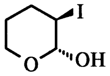
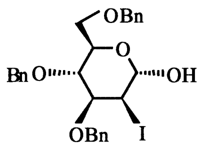
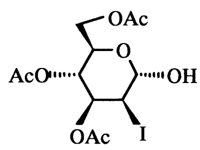
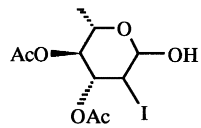
* Corresponding author. Tel.: +0039-817754903; fax: +0039-817754942; e-mail: tingoli@unina.it

0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(01)01509-X

Indeed, a 4:1 mixture of $CH_3CN–H_2O$ is an optimum choice to transform different classes of olefins into the corresponding iodohydrins in very good yields.[8] The results of these reactions are summarised in Table 1.

It is noteworthy that the amount of iodine used in all the reactions studied is very low (0.6 equiv.). Nevertheless, this quantity is sufficient to transform 1 equiv. of alkene to the parent iodohydrin derivative in good

Table 1. Conversion of alkenes and enolethers into iodohydrins promoted by I_2 and $PhI(OCOCF_3)_2$ inCH_3CN/H_2O at −15°C

Entry	Alkene	Reaction Products		Yield(%)[a]
1	Styrene		**1a**	95
2	Indene		**1b**	88[b]
3	1-Octene		**1c**	70
4	(*E*)-4-Octene		**1d**	62
5	Cyclohexene		**1e**	77
6	Cyclooctene		**1f**	70
7	(*Z*)-2-Pentenyl acetate		**1g**	65[c]
8	5-Hexen-2-one		**1h**	78
9	4-Pentenoic-acid		**1j**	80
10	(*E*)-4-Hexen-3-one		**1k**	63[b]
11	3,4-Dihydro-2*H*-pyran		**1l**	85
12	Tri-*O*-benzyl-D-glucal		**1m**	66
13	3,4,6-Tri-*O*-acetyl-D-glucal		**1n**	78
14	3,4-Di-*O*-acetyl-6-deoxy-L-glucal		**1o**	54[d]

[a]: Calculated on isolated products after acetylation af crude iodohydrin and purification; [b]: identified as iodohydrins; [c]: erytro-threo 1:3; [d]: mixture of C_2 epimers.

yield. The yields of the reactions are also unaffected by increasing the amount of BTI initially added.

The mechanism aspects of this reaction are not clear but the ratio of I_2/BTI/alkene chosen indicates that all the molecular halogen initially added is transformed by the hypervalent iodine species into the corresponding electrophilic-reactive iodine. For this reason it is not necessary to add iodine anion-trapping agent to avoid competition of this nucleophilic halogen anion.[9]

Furthermore, any reaction mixture quenched with H_2O shows an acidic pH (around 3), and all the attempts to perform the reaction under neutral conditions failed.

As depicted in Table 1 (entries 1, 3, 8 and 9), the addition of hypoiodous acid to terminal olefins produced vicinal iodoalcohols in a Markovnikov fashion. Moreover, in the case of stereodefined double bonds, an *anti* addition of IOH was observed (entries 5–7 and 10). In the case of (*Z*)-2-pentenol (entry 7), in order to avoid the competition of the free alcohol as nucleophile, the starting material has to be protected before use.

Also, an electron-poor olefin like (*E*)-4-hexen-3-one reacts smoothly but, in our case, the reaction was not stereoselective and a 1:3 *erythro*/*threo* mixture was recovered.

The last type of alkene allowed to react was a cyclic enol ether largely used as a protecting group for primary alcohols, dihydropyran (entry 11). This compound contains an electron-rich double bond very sensitive to acidic medium; under our reaction conditions, this did not decompose, but furnished the desired iodohydrin as a single regio- and *trans*-isomer in excellent yield. In the light of this result, we have tried to apply our mild reaction conditions to glycals that represent important precursors of 2-deoxysugars.[8] As reported in Table 1 (entries 12–14), the hypoiodous acid formed adds to protected glycals providing the 2-deoxy-2-iodo sugar derivatives in acceptable yields. Moreover, in the cases of glycals obtained from D-glucose, 2-deoxy-2-iodo-α-D-mannopyranose derivatives **1m** and **1n** were separated as the sole products.[9,10]

Finally, our results demonstrate that the use of both elemental and hypervalent iodine species in CH_3CN–H_2O solution represents a good alternative to the more expensive NIS (*N*-iodosuccinimide) in the preparation of iodohydrins.[4]

An extension of our method to the electrophilic iodination of aromatic and etheroaromatic molecules is currently under way.

Acknowledgements

Financial support from MURST (PRIN 1998 'Radicali Liberi e Radicali Ioni nei Processi Chimici e Biologici') and Università di Napoli 'Federico II' is gratefully acknowledged.

References

1. Rodriguez, J.; Dulcere, J.-P. *Synthesis* **1993**, 1177.
2. Masuda, H.; Takase, K.; Nishio, M.; Hasegawa, A.; Nishiyama, Y.; Ishii, Y. *J. Org. Chem.* **1994**, *59*, 5550.
3. Asensio, G.; Andreu, C.; Boix-Bernardini, C.; Mello, R.; González-Nuñez, M. E. *Org. Lett.* **1999**, *1*, 2125.
4. Smietana, M.; Gouverneur, V.; Mioskowski, C. *Tetrahedron Lett.* **2000**, *41*, 193.
5. Tingoli, M.; Tiecco, M.; Testaferri, L.; Temperini, A. *Synth. Commun.* **1998**, *28*, 1769.
6. Unpublished results from this laboratory.
7. *Typical procedure*: BTI (1.0 equiv.) was added at −15°C to a solution of alkene and I_2 (0.6 equiv.) in a 4:1 mixture of CH_3CN and H_2O and the vessel was allowed to reach room temperature. The red–brown colour of the solution disappears in a few minutes, and all the reactions described were completed in less than 2 h. After addition of brine, the reaction mixture was extracted with CH_2Cl_2 and dried under Na_2SO_4. Evaporation of the solvent gave the crude iodohydrin that was, in most cases, characterised as the acetate derivative after purification on a silica gel column, using light petroleum as eluant until iodobenzene deriving from the reduction of BTI, eluted out of the column. A mixture of light petroleum and diethyl ether as eluant are necessary to recover the iodohydrins. All products were fully characterised by ^{1}H and ^{13}C spectroscopy and MS spectrometry.
8. Costantino, V.; Imperatore, C.; Fattorusso, E.; Mangoni, A. *Tetrahedron Lett.* **2000**, *41*, 9177.
9. Miljković, D.; Djurendić, E.; Vukojević, N.; Gaši, K.; Csanádi, J. *Carbohydr. Res.* **1992**, *233*, 251.
10. *Selected experimental data*: Compound **1b**: solid, mp 112°C (uncorrected); δ_H ($CDCl_3$, 200 MHz): 7.45–7.35 (m, 1H), 7.35–7.20 (m, 3H), 5.40 (t, $J=6.5$ Hz, 1H), 4.20 (bq, 1H), 3.58 (dd, $J=16.1$, 7.1 Hz, 1H), 3.30 (dd, $J=16.1$, 8.1 Hz, 1H), 2.40 (d, $J=6.5$ Hz, OH); δ_C ($CDCl_3$, 50 MHz): 127.1, 125.8, 122.6, 122.2, 83.4, 40.6, 28.4; GC–EIMS: m/z 260 (M^+) (14), 242 (5), 133 (100), 127 (9), 115 (48), 105 (21). Compound **1k** δ_H ($CDCl_3$, 300 MHz): 4.38 (d, $J=8.2$ Hz, 1H), 4.3–4.1 (m, 1H), 3.08 (bs, OH), 3.0–2.7 (m, 1H), 2.7–2.4 (m, 1H), 1.4 (d, $J=6.2$ Hz, 3H), 1.0 (t, $J=7.3$ Hz, 3H); δ_C ($CDCl_3$, 50 MHz): 67.1, 34.3, 31.6, 19.6, 6.7; GC–EIMS: m/z 242 (M^+) (0.5), 198 (15), 168 (100), 127 (40), 57 (65). Compound **1m** (after acetylation of the anomeric OH) δ_H ($CDCl_3$, 200 MHz): 7.6–7.2 (m, 15H), 6.4 (bs, 1H), 4.9–4.4 (m, 8H), 4.1–3.6 (m, 3H), 3.3–3.15 (m, 1H), 2.0 (s, 3H); δ_C ($CDCl_3$, 50 MHz): 129.9, 129.6, 129.3, 97.0, 77.7, 76.4, 75.0, 72.6, 70.1, 32.6, 22.4.