Hypervalent iodine-induced oxidative nucleophilic additions to alkenes: a novel acetoxy thiocyanation reaction in 1,1,1,3,3,3-hexafluoropropan-2-ol

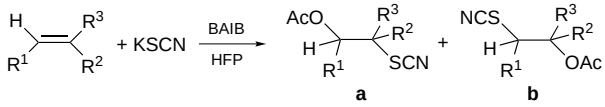
Antonella De Mico,[a] Roberto Margarita,[a] Andrea Mariani[a] and Giovanni Piancatelli*[b]

[a] *Centro CNR di Studio per la Chimica delle Sostanze Organiche Naturali (Associated to Istituto Nazionale di Coordinamento 'Chimica die Sistemi Biologici'), Università 'La Sapienza', P.le A. Moro 5, 00185 Roma, Italy*
[b] *Dipartimento di Chimica, Università 'La Sapienza', P.le A. Moro 5, 00185 Roma, Italy*

The combination of [bis(acetoxy)iodo]benzene and thiocyanate anion in a polar, protic non nucleophilic solvent such as 1,1,1,3,3,3-hexafluoropropan-2-ol is able to perform an oxidative nucleophilic addition to alkenes, leading to acetoxy thiocyanate derivatives, stereoselectively and with good regioselectivity.

1,1,1,3,3,3-Hexafluoropropan-2-ol (HFP) is described as a non-nucleophilic, strongly ionising solvent,[1] and seems to be the only solvent which is more polar than water on the Reichard E_T scale.[2] The strongly stabilising influence of HFP upon electrophilic intermediates has been utilised to study chemical reactions which proceed *via* the formation of both cations and radical cations.[3,4] Additionally, the weak acidic character of HFP (pK_a = 9.3) has been reported to affect the reactivity of charged nucleophiles.[5]

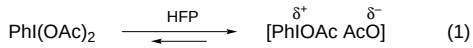
Our interest in the chemistry of hypervalent iodine(III) reagents[6] prompted us to exploit the reactivity of [bis(acetoxy)-iodo]benzene (BAIB) in HFP. We report herein the use of BAIB, HFP and thiocyanate anion, as nucleophile, to perform a novel stereospecific and regioselective acetoxy thiocyanation reaction with alkenes. The overall transformation is a fast, one-pot formal addition of AcOSCN to a double bond, which must be considered an interesting outcome. (Scheme 1).



Scheme 1

The BAIB–KSCN ratio plays a pivotal role on the outcome of the reaction. Since the reactivity of hard nucleophiles exhibits strong deactivation in HFP,[5] an excess of BAIB has to be added to suppress the formation of dithiocyanate derivatives. Parallel experiments in other non-nucleophilic aprotic solvents provided exclusively dithiocyanate derivatives.[6]

Our results clearly show that the reactions proceed *via* a reactive intermediate which is electrophilic in nature, and can be explained by referring to the mechanism described for the hypervalent iodine(III) reagent by Moriarty *et al.*[7] In HFP (ε_r = 22.3), BAIB may undergo an ionisation process (eqn. 1) and



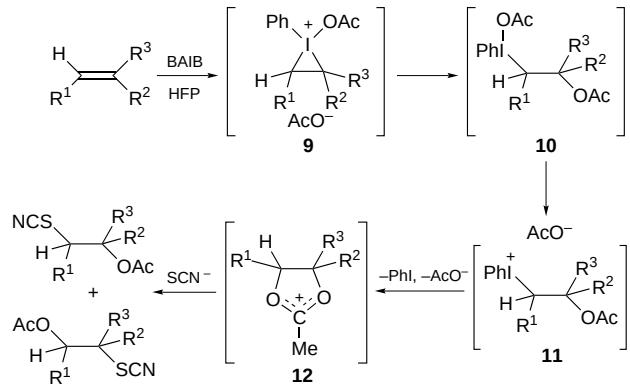
(1)

then an electrophilic addition to the alkene may follow yielding the intermediate **9**, subsequent addition of the acetoxy anion giving **10** (Scheme 2). An intramolecular S_N2 displacement of iodobenzene by the neighbouring acetoxy substituent leads to the cyclic intermediate **12**. Regioselective opening by thiocyanate anion furnishes the acetoxy thiocyanate derivatives.† Competing addition on **9** by thiocyanate leading to dithiocyanates may occur (Table 1, entries 6 and 7). The stereochemical outcome can be explained through the intermediate **12** since other reported mechanisms would yield the *cis* rather than *trans* products.[7,8]

The stereospecificity of the reaction seems to exclude competing radical processes. The formation of 1-(2-thiocyanoethyl)cyclohexene in entry 4, although in low yields (2–5%), reveals the occurrence of an ionic addition pathway since the above product clearly rises from an 1,2 proton shift of the initial formed secondary carbocation to the more stable tertiary one and subsequent elimination.

The acetoxy thiocyanation reaction has proven to be particularly successful with terminal alkenes (R = H), where a high regioselectivity is achieved, meanwhile it is only fair with non symmetrically substituted ones (compare Table 1 entries 2 and 5). Synthetic utility is very important with symmetrical and cyclic systems, where the addition is regio- and stereo-specific. This is also a valid method for the dissymmetrisation of olefinic compounds.

The reaction with methylcyclohexene, a more substituted system, furnishes transposition and elimination products as well as the expected acetoxy thiocyanate. Electron poor systems were recovered unreacted from the reaction medium, while



Scheme 2

Table 1 Acetoxy thiocyanation of alkenes with BAIB–KSCN in HFP

Entry	R^1	R^2	R^3	Yield[a] (%)	Regio-selectivity (**a**/**b**)	Stereo-specificity
1	Butyl	H	H	90	83/17	—
2	Hexyl	H	H	90	83/17	—
3	Octyl	H	H	90	83/17	—
4	Cyclohexyl	H	H	80	63/37	—
5	Pentyl	H	Me	80	63/37	*anti*
6	–$(CH_2)_4$–		H	80[b]	> 99	*anti*
7	–$(CH_2)_5$–		H	55[c]	> 99	*anti*

[a] The reported yields refer to isolated, chromatographically pure compounds. All the structures have been confirmed by IR, ^{1}H NMR and ^{13}C NMR analysis. [b] Additional 10% of *anti* dithiocyanate derivative was isolated. [c] Additional 30% of *anti* dithiocyanate derivative was isolated.

electron rich ones, such as dihydropyran, provided diacetoxy and dithiocyanate derivatives as the main products; this latter reactivity may be ascribed to the high stability of the cationic intermediate. Styrene derivatives immediately underwent a polymerisation process when they were dissolved in HFP; this phenomenon is probably catalysed by the acidity of the reaction medium. All the collected data are in agreement with the suggested reaction mechanism.

In conclusion, our studies on the reactivity in HFP show it to be very promising, and the results broaden the utility of BAIB, opening a route to new synthetic applications in organic chemistry. Research in this field is currently in progress, since acetoxy thiocyanate and dithiocyanate derivatives have been shown to possess good fungicidal activity.

Footnotes

* E-mail: piancatelli@axrma.uniroma1.it

† Typical experimental procedure: a solution of the alkene (1 mmol) in 4 ml of HFP was treated with 1.2 mmol of KSCN and 4 mmol of BAIB and the resulting reaction mixture is stirred at room temperature for 20 min. The reaction was quenched with saturated aqueous $Na_2S_2O_3$ (5 ml) and extracted with EtOAc (4 × 5 ml). The combined organic extracts were washed with aqueous $NaHCO_3$ and brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. Column chromatography on SiO_2 (light petroleum–EtOAc) afforded pure products.

^{1}H NMR spectra ($CDCl_3$) for **2a**: 5.1 (1 H, m), 3.2 (1 H, dd, *J* 3.9 and 14.0 Hz), 3.0 (1 H, dd, *J* 6.5 and 14.0 Hz), 2.1 (3 H, s), 1.9–1.1 (10 H, m), 0.85 (3 H, t). For **2b**: 4.3 (1 H, dd, *J* 5.1 and 12.0 Hz), 4.2 (1 H, dd, *J* 7.2 and 12.0 Hz), 3.3 (1 H, m), 2.1 (3 H, s), 1.9–1.1 (10 H, m), 0.85 (3 H, t). For **6a**: 4.7 (1 H, dt, *J* 10.3 and 4.6 Hz), 3.1 (1 H, dt, *J* 10.3 and 4.3 Hz), 2.3–2.0 (2 H, m), 2.06 (3 H, s), 1.9–1.1 (6 H, m). For **7a**: 4.9 (1 H, ddd, *J* 9.0, 3.7 and 7.4 Hz), 3.4 (1 H, dt, *J* 9.0 and 3.4 Hz), 2.3–2.0 (2 H, m), 2.08 (3 H, s), 2.0 1.4 (8 H, m).

^{13}C NMR spectra ($CDCl_3$) for **2a**: 171.0 (C=O), 112.5 (SCN), 72.2, 37.8, 33.2, 31.4, 28.4, 29.6, 22.4, 21.0, 13.9. For **2b**: 171.0 (C=O), 110.4 (SCN), 66.1, 48.9, 33.2, 31.4, 28.4, 29.6, 22.4, 21.0, 13.9. For **6a**: 170.5 (C=O), 111.1 (SCN), 74.9, 51.5, 32.6, 32.3, 25.7, 23.8, 21.1. For **7a**: 170.5 (C=O), 111.8 (SCN), 77.8, 54.6, 32.5, 32.0, 27.8, 25.7, 22.3, 21.2.

IR spectra ($CHCl_3$, cm^{-1}) for **2a**: 2140 (SCN, sharp peak), 1733 (C=O, broad peak). For **2b**: 2140 (SCN, sharp peak), 1735 (C=O, broad peak). For **6a**: 2175 (SCN, sharp peak), 1730 (C=O, broad peak). For **7a**: 2145 (SCN, sharp peak), 1730 (C=O, broad peak).

References

1 B. Allard, A. Casadevall, E. Casadevall and C. Largeau, *Nouv. J. Chem.*, 1979, **3**, 995; F. L. Schadt, T. W. Bentley and P. V. R. Schleyer, *J. Am. Chem. Soc.*, 1976, **98**, 7667.
2 C. Reichardt, *Solvent and Solvent Effect in Organic Chemistry*, Verlag Chemie, Veinhein, 1988.
3 L. Eberson, M. P. Hartshorm and O. Persson, *J. Chem. Soc., Perkin Trans 2*, 1995, 1735; 1995, 1331; L. Eberson, M. P. Hartshorm, F. Radner and O. Persson, *Chem. Commun.*, 1996, 215.
4 Y. Kita, H. Tohma, K. Hatanaka, T. Takada, S. Fujuta, S. Mitoh, H. Sakurai and S. Oka, *J. Am. Chem. Soc.*, 1994, **116**, 861.
5 L. Eberson, M. P. Hartshorm and O. Persson, *J. Chem. Soc., Perkin Trans 2*. 1996, 141; 1996, 151.
6 A. De Mico, R. Margarita, A. Mariani and G. Piancatelli, *Tetrahedron Lett.*, 1996, **37**, 1899.
7 R. A. Moriarty, R. K. Vaid and G. F. Koser, *Synlett*, 1990, **2**, 365.
8 C. A. Ramsden, *Chem Soc. Rev.*, 1994, **23**, 111.

Received in Cambridge, UK, 24th March 1997; Com. 7/01998J