Fe$_2$(SO$_4$)$_3$-mediated coiodination of alkenes with acetic acid: a convenient and regioselective eco-friendly preparation of β-iodoacetates

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The reaction of alkenes with I$_2$ and Fe$_2$(SO$_4$)$_3$ in acetic acid at room temperature produced the corresponding β-iodoacetates in 79–92% isolated yields and high regioselectivity.

Keywords: green chemistry, cohalogenation, β-iodoacetates, iodoacetoxylation, alkenes

The regioselective functionalisation of alkenes is an important process in organic chemistry. Among the several methodologies, the so-called "cohalogenation" (halogenation of an alkene in the presence of a nucleophilic solvent) provides vicinal halo-functionalised products regioselectively, which are useful intermediates for diverse synthetic applications.[1]

β-Iodoacetates are important intermediates for the preparation of epoxides,[2] iodohydrins,[2] and cis-[3] and trans-diols.[4] Traditional methodologies for the 1,2-iodoacetoxylation of alkenes include the reaction of I$_2$ with an alkene in the presence of acetic acid mediated by diverse heavy metal salts such as Tl(I),[2] Ag(I),[3,4] Pb(II),[5] Bi(III),[6] Hg(II),[7] Ce(IV),[8] Cu(II),[9] Co(II)[10] or oxidising reagents.[11] Alternate methodologies are the reactions of alkenes with excess iodine and KOAc supported on Al$_2$O$_3$,[12] diacetoxyiodine(I) complexes[13] or in situ generated acyl hypoiodite,[14] and also the reactions with NIS[15] or Ipy$_2$BF$_4$[16] in the presence of acetic acid. Recently, Chavan and Sharma published the intramolecular coiodination of unsaturated carboxylic acids to produce iodo-lactones mediated by catalytic FeCl$_3$.[17]

In previous work,[18] we reported an easy and efficient synthesis of iodohydrins from the coiodination of alkenes with water mediated by diverse metal salts, one of the most effective being the ready available, less toxic and inexpensive Fe$_2$(SO$_4$)$_3$. Continuing our interest in cohalogenation of alkenes with oxygenated nucleophiles,[19] we present here our results on the coiodination with acetic acid mediated by Fe$_2$(SO$_4$)$_3$.

The results of the Fe$_2$(SO$_4$)$_3$-mediated coiodination of alkenes with acetic acid to produce the corresponding β-iodoacetates are summarised in Scheme 1. The reactions were carried out stirring together 10 mmol of the alkene with 1.5 mol equiv. of I$_2$ and 1.2 mol equiv. of the Fe(III) salt in acetic acid at room temperature within 4.5–7.0 h. In all the reactions the purity of the isolated product (> 95%) was confirmed by ^{1}H and ^{13}C NMR and high-resolution gas chromatography (HRGC). The yields of the β-iodoacetates were good to excellent and the products were characterised by comparison of their spectral data with those previously reported.[2,8] No significant amounts of vicinal diiodoalkanes, diols, iodohydrins or diacetates were detected in the crude products and although we have used acetic acid without further purification in an open flask, no loss of stereoselectivity in the reaction of cyclohexene arising from small amounts of water was detected either.[20] On the other hand, coiodination of styrene with acetic acid in the absence of the Fe(III) salt was disappointing, as several products were obtained along with unreacted substrate. However, the reaction in the absence of any metal salt was successfully achieved with 2 mol equiv. of iodine when water or alcohols were used as nucleophiles with various alkenes.[21]

The coiodination reactions were highly regio- and stereoselective and only one product was detected by the

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i: I$_2$ / Fe$_2$(SO$_4$)$_3$ / HOAc / r.t.
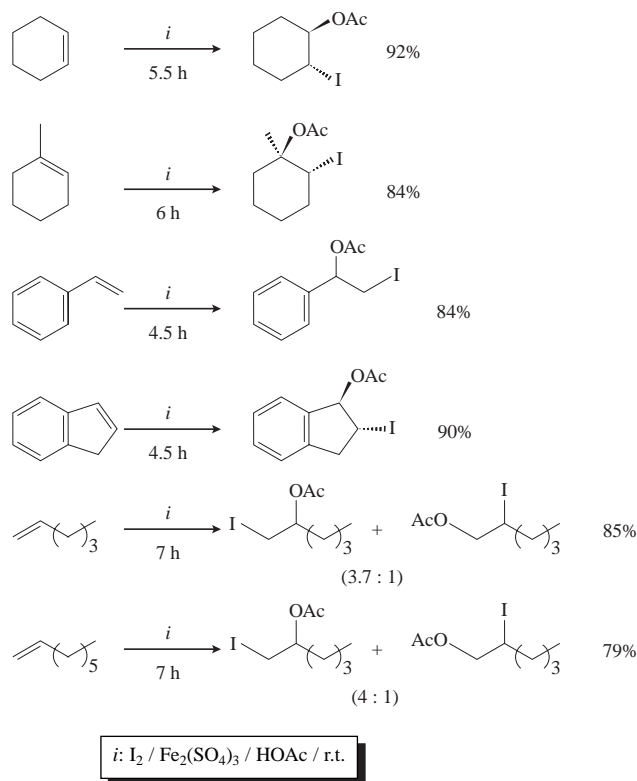
Scheme 1

analytical techniques employed. As expected,[22] only in the cases of the aliphatic monosubstituted 1-hexene and 1-octene did the reaction give predominantly the secondary acetate mixed with ca 20% (by HRGC) of its regioisomer.

In summary, we have developed a simple and efficient route to β-iodoacetates from alkenes. Due to environmental problems involved with the heavy metal salts traditionally used in such transformation, our methodology becomes very attractive and consistent with green chemistry challenges,[23] as iron salts are eco-friendly.[24]

Experimental

The alkenes were purified by distillation, solvents and inorganic reagents were used without further purification. Analyses by HRGC were performed on a HP-5890-II gas chromatograph with FID by using a 30 m (length), 0.25 mm (ID) and 25 μm (phase thickness) RTX-5 silica capillary column and H$_2$ (flow rate 50 cm/s) as carrier gas (split 1:20). Mass spectra were obtained on a Hewlett-Packard HP5896-A HRGC-MS using electron impact (70 eV). ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker AC-200 (200 MHz and 50 MHz, respectively) spectrometer for CDCl$_3$ solutions with tetramethylsilane as internal standard. In all the reactions, the purity of the isolated product (> 95%) was confirmed by ^{1}H NMR, ^{13}C NMR, and HRGC analyses.

Typical procedure for the preparation of β-*iodoacetates:* To a stirred solution of the appropriate alkene (10 mmol) and $Fe_2(SO_4)_3$ (4.80 g, 12 mmol) in acetic acid (20 ml) was added iodine (3.81 g, 15 mmol) in small portions at room temperature. After the specified time (see Scheme 1), FeI_3 was filtered off and CH_2Cl_2 (25 ml) was added. The solution was washed with 5% Na_2SO_3 to remove the excess iodine. After further wash with water (4×50 ml), the organic extract was dried (anhydrous Na_2SO_4) and filtered through a small column of SiO_2. The solvent was evaporated on a rotatory evaporator and then concentrated under reduced pressure to give the pure β-iodoacetate as a colourless or light orange oil.

trans-1-Acetoxy-2-iodocyclohexane: δ_H 1.20–1.64 (m, 5H), 2.04–2.20 (m, 2H), 2.10 (s, 3H), 2.57 (m, 1H), 4.06 (m, 1H), 4.80 (m, 1H). δ_C 21.2, 23.6, 27.1, 31.7, 37.9, 53.4, 76.7, 169.9. *m/z* 268, 208, 141, 81, 43 (100%).

trans-1r-Acetoxy-1-methyl-2-iodocyclohexane: δ_H 1.37–1.40 (m, 4H), 1.62 (s, 3H), 1.90–2.03 (m, 2H), 2.08 (s, 3H), 2.25–2.35 (m, 2H), 4.86 (dd, J = 5.52 and 7.20 Hz, 1H). δ_C 19.7, 20.1, 24.0, 24.8, 27.6, 37.2, 42.9, 75.5, 170.1. *m/z* 282, 155 (100%), 113, 95, 71, 69, 43.

1-Acetoxy-2-iodo-1-phenylethane: δ_H 2.09 (s, 3H), 3.41–3.50 (m, 2H), 5.85–5.89 (m, 1H), 7.12–7.39 (m, 5H). δ_C 7.8, 21.0, 75.1, 125.7, 127.6, 128.7, 138.4, 169.8. *m/z* 163 (M+-I), 163, 149, 121, 103, 43 (100%).

trans-1-Acetoxy-2-iodoindane: δ_H 2.09 (s, 3H), 3.14–3.40 (m, 2H), 4.35 (m, 1H), 5.43 (d, J = 4.00 Hz, 1H), 7.10–7.35 (m, 4H). δ_C 21.4, 28.6, 39.1, 85.0, 120.5, 124.3, 127.9, 129.8, 132.6, 138.5, 170.0. *m/z* 302, 175, 113, 91, 77, 43 (100%).

2-Acetoxy-1-iodohexane: δ_H 0.94 (s, 3H), 1.26–1.64 (m, 6H), 2.08 (s, 3H), 3.37–3.63 (m, 2H), 3.74 (m, 1H). δ_C 8.2, 13.8, 21.7, 22.3, 30.9, 38.7, 69.3, 170.3. *m/z* 270, 210, 143, 55 (100%), 43.

2-Acetoxy-1-iodooctane: δ_H 0.90 (s, 3H), 1.20–1.60 (m, 10H), 2.12 (s, 3H), 3.40–3.45 (m, 2H), 4.60 (m, 1H). δ_C 13.9, 16.8, 21.2, 21.9, 22.5, 30.0, 35.9, 36.3, 72.4, 169.9. *m/z* 298, 213, 171, 111, 83, 69, 43 (100%).

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