Synthesis of α-iodoacetates from alkenes by cadmium acetate catalysed Woodward's reaction

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Alkenes on treatment with iodine and cadmium acetate in acetic acid give α-iodoacetates in high yields. The reaction is facile and α-iodoacetates are obtained from both acyclic and cyclic alkenes within 5–30 min.

Keywords: cadmium acetate, iodine, alkenes, acetic acid

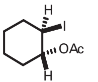
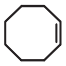
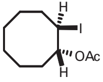
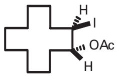
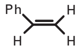
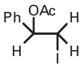
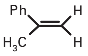
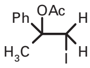
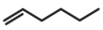
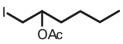
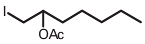
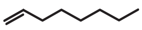
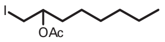
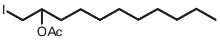
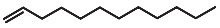
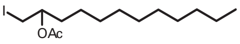
Synthesis of α-iodoacetates is an important reaction in organic synthesis. An alkene reacts readily with silver acetate or silver benzoate[1-3] and iodine in the presence of water to give a product corresponding to *cis*- or *trans*- hydroxylation *via* α-iodoacetate intermediates and the reaction is called the Woodward–Prevost reaction. Apart from this reaction, methods available in the literature include use of metal acetates such as thallium(I) acetate,[4-6] mercury(II) acetate,[7] bismuth(III) acetate,[8] copper(II) acetate,[9,10] or other reagents such as mercury(II)oxide–acetic anhydride,[11] per acetic acid/acetic acid/ethyl ether,[12] CuO–HBF_4 in CH_2Cl_2–AcOH,[13] KOAc/Al_2O_3,[14] N-iodosuccinimide/$CHCl_3$/AcOH[15] with iodine and an olefin.

Acetates of the highly expensive silver, thallium and mercury have been used earlier to give α-iodoacetates from olefins. Most of the reported methods generally require about 2–48 h for completion of the reaction, depending on the nature of the metal acetate and the substrates used for the reaction under the normal conditions. Sharpless and Herranz have reported the use of $Cd(OAc)_2$, $Zn(OAc)_2$, $Hg(OAc)_2$ and $Cu(OAc)_2$ for hydroxyamination of olefins by N-chloro-N-metallocarbamates earlier.[16] The relative rates of addition of hydroxyamination reagents across the double bond depend on the nature of the metal acetate used. While $Hg(OAc)_2$ takes 2 h, $Cd(OAc)_2$ and $Cu(OAc)_2$ require 5–10 h (for styrene), and in the case of (*E*)-5-decene the reaction takes 24 h with $Hg(OAc)_2$ and with $Zn(OAc)_2$ the reaction proceeds very slowly.

We now report a novel addition reaction of alkenes with iodine and $Cd(OAc)_2$ in acetic acid to give the corresponding α-iodoacetates within 5–30 min. We expect that preparation of α-iodoacetates from alkenes may be promoted by the use of $Cd(OAc)_2$.

$Cd(OAc)_2$ is readily available and from the point of view of the cost it is economical. We carried out the reaction of 1-hexene with iodine and $Cd(OAc)_2$ in acetic acid by stirring at 25 °C, and got 1-acetoxy-2-iodohexane in a 91% yield within 15 min. In order to extend this reaction to other alkenes, the reaction of I_2, $Cd(OAc)_2$ in HOAc with different substituted alkenes was investigated and the results are presented in Table 1.

Table 1 α-Iodoacetoxylation of olefins with $Cd(OAc)_2$[a] and iodine in acetic acid

Entry	Alkene	Product	Time/min	Yield[b]/%
1		 1	5	95
2		 2	10	88
3		 3	15	90
4		 4	10	83
5		 5	10	79
6		 6	10	78
7		 7	15	91
8		 8	20	93
9		 9	15	85
10		 10	30	86
11		 11	25	81

[a]Note: Cadmium is a toxic metal and its salts including cadmium acetate are cancer suspect agents. Handle carefully.
[b]Isolated by column chromatography.

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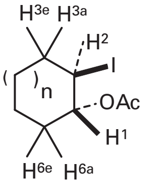
Table 2 α-Iodoacetoxylation of some representative olefins with various reagents and iodine

Entry	Reagent(s)	Cyclohexene time/yield/%	Styrene time/yield/%	α-Methylstyrene time/yield/%
1	Cadmium acetate[a]	5 min/88	10 min/78	10 min/75
2	Thallium(I) acetate[6]	48 h/85	48 h/98	48 h/98
3	Bismuth(III) acetate[8]	17.5 h/84	–	17.5h/91
4	Silver acetate[17]	5–6 h/70	–	–
5	KOAc-Al_2O_3/CH_2Cl_2[14]	42 h/70	48 h/75	–
6	NIS[b]/AcOH/$CHCl_3$[15]	1 h/95	–	–

[a] Present method.
[b] N-Iodosuccinimide.

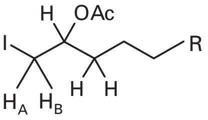
Table 3 Spectral data of the products prepared

Cyclic alkenes,



1–3

Acyclic alkenes



4, 5, 7–11

Product	IR (cm^{-1})	^1H NMR (δ, ppm)
1	1740, 1243, 1036, 420	2.06 (*s*, -COC$\underline{H}_3$), 4.01-4.07 (*ddd*, $J_{1,2} = J_{2,3a}$ = 10 Hz, $J_{2,3e}$ = 4 Hz,-C$\underline{H}$I-), 4.84-4.90 (*ddd*, $J_{1,2} = J_{1,6a}$ = 10 Hz, $J_{1,6e}$ = 5 Hz, -C$\underline{H}$COCH_3)[6]
2	1734, 1243, 1047, 410	2.07 (*s*, -COC$\underline{H}_3$), 4.38-4.43 (*ddd*, $J_{1,2} = J_{2,3a}$ = 6 Hz, $J_{2,3e}$ = 3 Hz, -C$\underline{H}$I-), 5.19-5.23 (*ddd*, $J_{1,2} = J_{1,6a}$ = 8 Hz, $J_{1,6e}$ = 4 Hz, -C$\underline{H}$COCH_3)
3	1745, 1238, 721, 416	2.09 (*s*, -COC$\underline{H}_3$), 4.33-4.40 (*ddd*, $J_{1,2} = J_{2,3a}$ = 6 Hz, $J_{2,3e}$ = 12 Hz,-C$\underline{H}$I-), 4.83-4.87 (*dd*, $J_{1,2} = J_{1,6a}$ = 6 Hz, $J_{1,6e}$ = 11 Hz, -C$\underline{H}$COCH_3)
4	1755, 1233, 1062, 545	2.14 (*s*, -COC$\underline{H}_3$), 3.46-3.49 (*dd*, *J* = 4 Hz, *J* = 8 Hz, -C$\underline{H}_2$I-), 5.86-5.90 (*dd*, *J* = 5 Hz, *J* = 8 Hz, -C$\underline{H}$COCH_3), 7.36-7.37 (*m*, 5H, Ph)[6]
5	1734, 1243, 1031, 545	2.08 (*s*, C$\underline{H}_3$), 2.09 (*s*, -COC$\underline{H}_3$), 3.25-3.28 (*dd*, *J* = 2.5 Hz, *J* = 5 Hz, -C$\underline{H}_2$I-), 7.26 (*s*, 5H, Ph)[6]
6	1719, 1279, 1166, 410	1.29 [*s*, (C$\underline{H}_3$)$_2$C(COCH_3)-], 1.54[*s*, (C$\underline{H}_3$)$_2$CI-], 2.20 (*s*, -COC$\underline{H}_3$)
7	1719, 1259, 1031, 415	2.08 (*s*, -COC$\underline{H}_3$), 3.22-3.37 (*dd* H_A, *dd* $\underline{H}_B$, *J* = 5 Hz, *J* = 10 Hz,-C$\underline{H}_A\underline{H}_B$I-), 4.66-4.72 (*quin*, *J* = 6 Hz, -C$\underline{H}$COCH_3)
8	1745, 1243, 1036, 498	2.09 (*s*, -COC$\underline{H}_3$), 3.22-3.38 (*dd* H_A, *dd* $\underline{H}_B$, *J* = 5 Hz, *J* = 10 Hz -C$\underline{H}_A\underline{H}_B$I-), 4.67-4.74 (*quin*, *J* = 7 Hz, -C$\underline{H}$COCH_3)
9	1740, 1243, 1036, 493	2.07 (*s*, -COC$\underline{H}_3$), 3.20-3.39 (*dd* H_A, *dd* $\underline{H}_B$, *J* = 5 Hz, *J* = 10 Hz -C$\underline{H}_A\underline{H}_B$I-), 4.66-4.72 (*quin*, *J* = 6 Hz, -C$\underline{H}$COCH_3)
10	1745, 1243, 1000, 420	2.08 (*s*, -COC$\underline{H}_3$), 3.23-3.37 (*dd* H_A, *dd* $\underline{H}_B$, *J* = 5 Hz, *J* = 10 Hz -C$\underline{H}_A\underline{H}_B$I-), 4.66-4.72 (*quin*, *J* = 6 Hz, -C$\underline{H}$COCH_3)
11	1750, 1238, 1031, 416	2.11 (*s*, -COC$\underline{H}_3$), 3.23-3.38 (*dd* H_A, *dd* $\underline{H}_B$, *J* = 5 Hz, *J*=10 Hz -C$\underline{H}_A\underline{H}_B$I-), 4.66-4.74 (*quin*, *J* = 5 Hz, -C$\underline{H}$COCH_3)

From Table 1, it is clear that different iodoacetates can be prepared under the above reaction conditions from both acyclic and cyclic alkenes in high yields. And cyclic alkenes exclusively furnish the *trans*-iodoacetates (entries 1–3). TLC of the crude products showed the formation of a single product in the case of **1** and **8**; in other cases the major product was isolated by column chromatography. Hence, the reaction is regioselective, in the sense that, the less substituted iodo product is formed selectively from terminal olefins (entries 4, 5, 7–11). All the compounds prepared by this procedure are characterised by IR and ^1H NMR spectral analysis after purification.

In conclusion, a mild, convenient and selective method for the preparation of α-iodoacetates in excellent yields from alkenes within 5–30 min has been developed by us using readily available cadmium acetate and iodine by stirring at 25 °C. We believe that this procedure is better and a more practical alternative to the existing methodologies. Comparison of the results of the reaction of some representative alkenes by our procedure with that of the other reagents/metal acetates has been provided in Table 2.

Experimental

All alkenes, cadmium acetate, iodine and glacial acetic acid were obtained from Spectrochem and Rankem. IR spectra were recorded on Nicolet 400D FT-IR spectrometer and ^1H NMR spectra were recorded on 400 MHz Bruker instrument and the chemical shift values (δ ppm) are reported relative to TMS in $CDCl_3$ as solvent.

General procedure for the preparation of 1-iodo-2-acetoxy hexane: Cadmium acetate (1.152 g, 5 mmol), glacial acetic acid (5 ml) and 1-hexene (0.84 g, 10 mmol) were taken in a two neck 50 ml round bottom flask. Iodine (2.54 g, 10 mmol) in glacial acetic acid (5 ml) was added slowly to the above mixture and stirred at 25 °C. The reaction was monitored by TLC (5% EtOAc: pentane) and after the completion of the reaction (15 min), the product was extracted into ether (3 × 10 ml) and the combined ethereal extract was washed with saturated $NaHCO_3$ solution, 5% $Na_2S_2O_3$ solution and water, and dried over anhydrous sodium sulphate and ether was removed on a rotary evaporator. The crude was then subjected to silica gel chromatography (eluent: 5% EtOAc: pentane) and 1-iodo-2-acetoxyhexane was obtained (2.46 g, 91%). Similar procedure was followed for the syntheses of different substituted α-iodoacetates. Yields (based on 10 mmol of starting alkene), IR and ^1H NMR spectral data of the products are given in Table 3.

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