Iodine Monoacetate for Efficient Oxyiodinations of Alkenes and Alkynes

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Abstract A novel and inexpensive, environmentally friendly method for the preparation of iodine monoacetate is presented using iodine and Oxone in acetic acid/acetic anhydride. The reagent is used in a highly efficient approach for the regio- and diastereoselective iodoacetoxylation of alkenes and alkynes in a simple one-pot process.

Key words alkenes, alkynes, iodine, iodine(I)acetate, oxyiodination

Iodine monoacetate is an important reagent for the functionalisation of alkenes, alkynes and ketones. It has been reported to be easily accessible from an equimolar mixture of silver acetate and iodine and higher homologues of the reagent have been made from silver carboxylates and iodine for the synthesis of aliphatic esters. However, iodine monoacetate has not yet been isolated and has only been characterised by $^1$H NMR and spectrophotometrically. As silver acetate is an expensive reagent, there are alternative ways of generating iodine monoacetate. It can be prepared from very toxic mercuric acetate, lead tetraacetate, or (diacetoxyiodo)benzene by reaction with iodine.

Herein, we report a novel method for the synthesis of iodine monoacetate using elemental iodine and Oxone in combination with acetic anhydride and acetic acid (Scheme 1).

Scheme 1 Formation of iodine monoacetate using iodine and Oxone.

Oxone is an inexpensive and environmentally safe oxidant which is known to oxidise iodine salts such as ammonium iodide to iodine(I). This has been explored in the synthesis of $\alpha$-iodinated ketones or to prepare iodoalkyl and iodoesters from alkenes and, in combination with sodium iodide, to make $\alpha$-aryl ketones from arylalkenes. We started our investigation to form iodine monoacetate using iodine and Oxone in acetic acid/acetic anhydride. The success of the reaction was indicated by a subsequent reaction with styrene as test substrate which reacts in an iodoacetoxylation to 2a. Best results for the iodoacetoxylation were achieved by treatment of iodine with 2 equivalents of Oxone in a mixture of acetic acid and acetic anhydride at 50 °C for 21 h. After addition of styrene (1a) and 2 h reaction time at room temperature, only the Markovnikov product 2a was obtained in 84% yield in this one-pot synthesis. Further optimisation experiments such as concentration of the reagents and reaction times are described in the supporting information (Table S1). An iodoacetoxylation in the absence of acetic anhydride did not provide 2a and with traces of acetic acid in acetic anhydride a much longer reaction time and a higher amount of oxone were necessary, indicating that both, acetic acid and acetic anhydride, are necessary for the success of this reaction. The reaction scope with iodine monoacetate was explored with different arylalkenes (Scheme 2). The phenyl-substituted aromatic ring in 1b did not affect the yield of 2b (79%) and also 2-vinylnaphthalene (1c) provided 2c with good yield (74%). A chlorine substituent in 3-position led to an almost quantitative yield of 2d (98%), whereas a methyl substituent in 3-position gave 83% of 2e together with the corresponding iodohydrin (4%). Furthermore, 2,6-dichlorostyrene (1f) gave similar yield (79%). Strong electron withdrawing groups such as fluoro- (2g) and nitro substituents (2h) reduced the yield to 70%, whereas a methyl substituent did not affect the outcome of the reaction (2i, 79%). Afterwards, the effect of substituents in $\alpha$-position was investigated. A high yield was achieved for the iodoacetoxylation of 1j with a phenyl substituent in $\alpha$-position (2j, 91%). A methyl substituent gave 71% yield of 2k. An inseparable mixture of ketones 2l and 2m (1.25:1) was obtained using $\alpha$-bromostyrene as starting material.
Next, the influence of substituents in the β-position was investigated. To our delight, reactions of ethyl cinnamate (1n) and cinnamonitrile (1o) demonstrated the tolerance of substituents in the β-position to give regio- and diastereoselective iodoacetoxylation providing the trans-product 2n in good yield (64%). However, the cyanide substituent slows down the reaction. After a reaction time of 4 days 2o was isolated in 34% yield and 59% of 1o recovered. Additionally, cyclic alkenes such as 1,2-dihydronaphthalene (1p), indene (1q) or 1-phenyl-1-cyclohexene (1r) can be used in this one-pot functionalisation to give reasonable yields of compounds 2p, 2q and 2r (53% to 72%). The heteroaromatic compound 2-vinylpyridine (1s) was converted in excellent yield (88%) to 2s and chalcone (1t) gave product 2t in good yield (70%).

The reactivity of non-conjugated alkenes with iodine monoacetate was explored (Scheme 3). As expected, allylbenzene (3a) provided a mixture of regioisomers and the Markovnikov product 4a and anti-Markovnikov product 5a were obtained in almost equal amounts (35% and 32%). A larger excess of Markovnikov product (1.5:1) was obtained with a methoxy substituent in 4-position (3b) to give 4b and 5b in 40% and 27% yield, respectively. 1-Hexene (3c) gave a better regioselectivity and 4c/5c in 42% combined yield (4c/5c = 2:1). Furthermore, 1,5-hexadiene (3d) provided diastereomers of product 4d (12%) and 5d in addition to a third regioisomer (27% combined yield). Surprisingly, 2-methyl-3-buten-2-ol (3e) led to the rearranged product 5e (40%).

Alkenes 3f and 3g were functionalised in moderate yields to exclusively 5f (46%) and 5g (38%).

Interestingly, alkynes also reacted smoothly under the same reaction conditions in good yields to the iodoacetoxylated products. A mixture of 7a and 8a was obtained by reaction of phenylacetylene (6a) in 60% combined yield. 8a is the result of a second iodoacetoxylation of 7a followed by ketal cleavage. On the contrary, 1-phenyl-1-propyne (6b) led exclusively to product 7b (71%) and 1-hexyne (6c) gave only the diiodoketone 7c in 73% yield. Compound 6d did not react in the expected way and the diiodinated product 7d was obtained (39%) as verified by literature spectra. Additionally, propiophenone (6e) could be iodinated in the α-position to give 7e in good yield (70%). Compound 8e was obtained as side product in 5% yield.
To further verify the existence of iodine monoacetate, acetic acid and acetic anhydride were removed and the remaining oil was examined, which was protected from moisture to prevent decomposition, via $^1$H NMR. A peak at δ_H = 2.19 ppm reveals the formation of iodine monoacetate. To get further insight into the role of acetic acid and acetic anhydride, acetic acid was replaced by deuterated acetic acid-d$_4$ followed by reaction with styrene (Scheme 4). In this case, partial deuteration of product 2a was observed (D/H = 2:1), which indicates again that both, acetic acid and acetic anhydride, play an important role in the formation of iodine monoacetate.

Scheme 4 Iododeuteroacetoxylation of 1a in acetic acid-d$_4$.

In conclusion, we have demonstrated a novel and inexpensive, environmentally friendly method for the formation of iodine monoacetate using iodine and Oxone in a mixture of acetic acid and acetic anhydride. The reagent was used in a highly efficient approach for the regio- and diastereoselective iodoacetoxylation of alkenes and alkynes in a simple one-pot process. Scope and limitation of the method was illustrated with a broad range of alkenes and alkynes. Styrenic derivatives gave highest yields, whereas allylic and aliphatic olefins produced regioisomeric mixtures in lower yields. Alkynes led to mono- and diiodinations in comparable yields. Compared to previous procedures, this inexpensive, metal-free and environmentally friendly method provides high yields and mild reaction conditions.

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Supporting Information

Yes.

Primary Data

No.

References and Notes