Pergamon

Tetrahedron Letters 41 (2000) 979–982

TETRAHEDRON LETTERS

One-pot selective synthesis of β-nitrostyrenes from styrenes, promoted by Cu(II)

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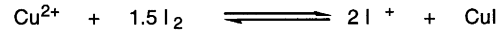
Received 3 November 1999; accepted 24 November 1999

Abstract

A convenient, inexpensive and efficient 'one-pot' process is described for the selective nitration of styrenes to the corresponding β-nitrostyrenes under mild conditions. The procedure tolerates such functional groups as alkyl, aryl, alkoxy, acyloxy and chlorine on the aromatic ring and can be applied to derivatives substituted on the vinyl group.

Despite the fact that β-nitrostyrenes have been described as useful and versatile building blocks in organic synthesis,[1] their preparation cannot be considered a simple task. This is particularly true for the direct nitration of styrenes, since the reaction can also cause nitration of the aromatic ring or polymerization through the vinyl group. Several methods have been reported to give β-nitrostyrenes via direct nitration of styrenes but some of the nitration agents used lead to ring nitration,[2] different products depending on the nature of the styrenes,[3] or are expensive.[4] Other methods require extreme caution.[5]

In an earlier study, we described how a mixture of iodine and $CuO{\cdot}HBF_4$ generates very low concentrations of I^+ at room temperature (Scheme 1) which react with unsaturated systems in the presence of different nucleophiles to give 1,2-iodofunctionalized compounds under mild conditions.[6] In particular, we carried out the reaction using cyclohexene as the unsaturated system and $NaNO_2$ as the nucleophile to obtain *trans*-1-iodo-2-nitrocyclohexane (Scheme 2). The reaction between the I^+ and NO_2^- probably leads to the formation of an NO_2I species which attacks the unsaturated system. Since reaction of NO_2I with styrene leads to the formation of 1-iodo-2-nitro-1-phenylethane,[7] we felt that it would be of interest to apply our methodology to the preparation of such nitro-iodate compounds, since they are precursors of β-nitrostyrenes. Herein, we wish to report our results in this field.



Scheme 1.

First, we treated styrene with a mixture of iodine, $CuO{\cdot}HBF_4$ and $NaNO_2$ in acetonitrile. We were pleased to find that after 7 h of stirring at room temperature, the reaction led to the direct formation of

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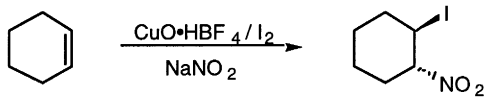
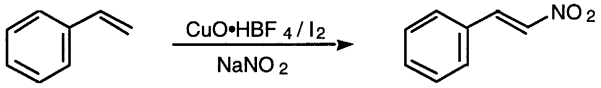


Scheme 2.

the *trans*-β-nitrostyrene instead of the expected 1-iodo-2-nitro-1-phenylethane (Scheme 3). The direct generation of the nitrostyrene could be explained as a dehydro-iodination of the iodonitro compound catalyzed by the copper(I) salts formed during the course of the reaction.[8] For the *trans*-1-iodo-2-nitrocyclohexane, the dehydro-iodination must occur through a non-favorable *cis* elimination and, consequently, was not observed previously.



Scheme 3.

We next investigated the nitration of a number of substituted styrenes. The results are given in Table 1. We found that the procedure tolerates such functional groups on the aromatic ring as alkyl (entries 2 and 3), aryl (entry 4), alkoxy (entry 5), acyloxy (entry 6) and chlorine (entry 7) and can also be applied to derivatives substituted on the vinyl group (entries 8 and 9). In all cases, acceptable to good yields (31–72%) of the corresponding nitrostyrenes (with a *trans* relationship between the phenyl and nitro groups) were obtained. The α-methylstyrene gave a mixture of *E*- and *Z*-isomers in a ratio of 6:1, as determined by ^{1}H NMR spectroscopy. We were able to isolate both isomers by column chromatography and we confirmed that the *Z*-product isomerizes to the *E*-isomer in the presence of PPh_3.[9] In all the cases tested, some polymeric material was obtained and the products needed to be purified by column chromatography on silica gel. No ring nitration products were detected.

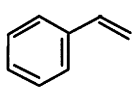
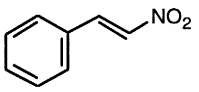
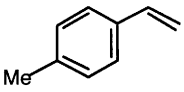
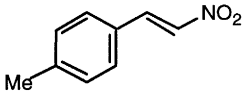
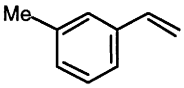
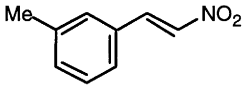
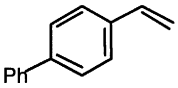
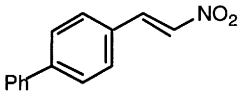
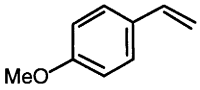
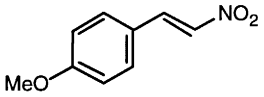
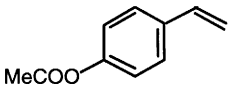
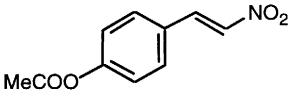
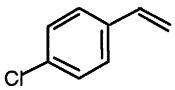
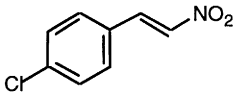
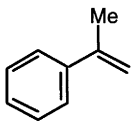
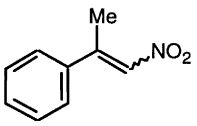
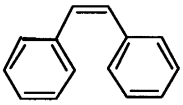
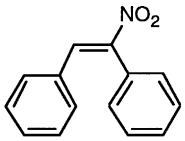
In summary, we have developed a convenient, inexpensive and efficient 'one-pot' operation for the selective nitration of styrenes to the corresponding β-nitrostyrenes under mild conditions. Further studies to extend the scope of this reaction are planned.

Typical procedure for conversion of styrenes into β-nitrostyrenes: Acetonitrile (20 ml) and $NaNO_2$ (1.66 g, 24 mmol) were added to a solution of copper(II) tetrafluoroborate, prepared from 35% aq. HBF_4 (1.62 ml, 8 mmol) and CuO (0.32 g, 4 mmol). After the mixture had been stirred for 2 min, iodine (1.52 g, 6 mmol) and the styrene (20 mmol) were introduced into the reaction flask and the mixture was stirred at room temperature for 7 h. The precipitated copper(I) iodide was filtered off after addition of water (25 ml) and the filtrate was extracted with CH_2Cl_2 (3×25 ml), washed with 5% aq. sodium thiosulphate (25 ml), dried over anhydrous Na_2SO_4, and evaporated under reduced pressure. The resulting crude materials were purified by column chromatography (silica gel; hexane:diethyl ether, 9:1).

Acknowledgements

This work was supported by the Spanish DGICYT (PB97-0589) and the Universidad de La Rioja (API-99/B05). One of us (B.G.) would like to thank the Comunidad Autónoma de La Rioja (Spain) for a fellowship.

Table 1

entry	substrate	product	yield (%)[a,b]
1			47
2			43
3			53
4			65
5			39
6			38
7			31
8			72[c]
9			65

[a] All compouds were purified by chromatography on silica gel. Yields are for pure isolated products, relative to I^+. [b] The configuration assignments were made on the basis of ^1H NMR coupling constants (entries **1-7**) or differenc NOESY experiments (entries **8** and **9**). [c] *E* : *Z* ratio = 6 : 1, determined by ^1H NMR of the crude reaction.

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