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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 5203–5205

Novel synthesis of α-nitroalkenes from nitroalkanes via halogenation of intermediate *N*,*N*-bis(silyloxy)enamines

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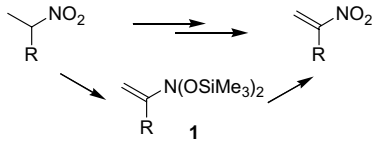
Received 20 April 2005; revised 19 May 2005; accepted 25 May 2005
Available online 14 June 2005

Abstract—An approach to conjugated nitroalkenes via oxidation of *N*,*N*-bis(silyloxy)enamines with bromine or iodine in the presence of tetra-*n*-butylammonium acetate is described. The acetate ion plays a key role by acting as a mild desilylating reagent. This new strategy allows the synthesis of α-nitroalkenes from the corresponding nitroalkanes.

Conjugated nitroalkenes have found widespread use in organic synthesis as Michael acceptors,[1] dienophiles,[1a,2] and heterodienes.[3] Therefore, the development of new convenient procedures for their synthesis constitutes an important goal.

Several strategies for the synthesis of nitroalkenes are known. The most straightforward methodology involves condensation of nitroalkanes with carbonyl compounds (Henry reaction[4]), proceeding through the intermediacy of β-nitroalcohols. Other approaches utilize starting materials with a 'preformed' carbon skeleton. Examples include nitromercuration[5] and nitroselenation[6] of alkenes, with subsequent transformation of the Hg- and Se-containing intermediates, and *ipso*-nitration of vinyl stannanes.[7]

Selective oxidation of the carbon skeleton of nitroalkanes would be a particularly attractive method for the synthesis of nitroalkenes (Scheme 1). However, there is only one publication along these lines, which described elimination from intermediate α-seleno-substituted nitro compounds.[8] Obviously, the high cost of selenium reagents and the moderate yields of products narrow the applicability of this procedure.



Scheme 1.

Herein, we present a mild and convenient protocol for the synthesis of nitroalkenes using an oxidative strategy, through bis-*O*-silyl derivatives of nitro compounds—*N*,*N*-bis(silyloxy)enamines (BENAs). The intermediate BENAs **1** can be easily obtained by double *O*-silylation of nitro compounds and detailed procedures for this step were reported previously.[9] In this letter, the major emphasis is placed on transformation of enamines **1** into α-nitroalkenes.

The oxidation of BENAs was performed by reaction with halogens (Br_2 or I_2) in the presence of tetra-*n*-butylammonium acetate (Scheme 2, Table 1). As reported previously,[10] BENAs can behave as mild nucleophilic reagents with a reactivity comparable to that of silyl enol ethers. It is thus quite likely that on interaction of BENAs **1** with halogens the iminium cations **2** are initially formed, which lose a trimethylsilyl group leading to the previously unknown β-halo silyl nitronates **3**. The latter species readily eliminate a molecule of halosilane (Me_3SiX) affording nitroalkenes **4**.[11]

The thermodynamically driven halosilane elimination seems to be the key step of the present protocol.

Keywords: Nitroalkenes; *N*,*N*-bis(silyloxy)enamines; Halogenation; Silyl nitronates.
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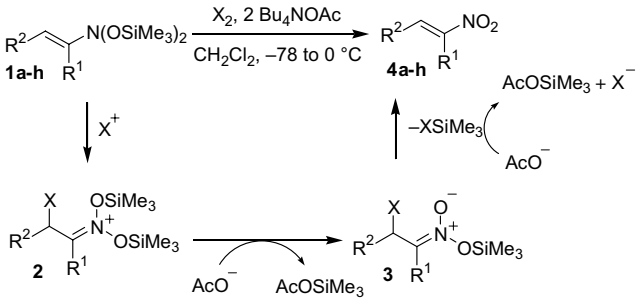
doi:10.1016/j.tetlet.2005.05.113



Scheme 2.

Table 1. Synthesis of nitroalkenes **4**

Entry	R^1	R^2	Procedure[a]	**4**	Yield of **4** (%)[b]
1	$(CH_2)_2CO_2Me$	H	A	**4a**	82
2			B	**4a**	92
3	Bn	H	A	**4b**	62
4			B	**4b**	82
5	CH_2OTBS	H	A	**4c**	76
6			B	**4c**	78
7	Me	H	A	**4d**	95[c]
8			B	**4d**	71[c]
9	H	H	A	**4e**	82[d]
10	Ph	H	A	**4f**	75[e]
11	H	*n*-C_5H_{11}	A	**4g**	76
12	H	Me	A	**4h**	90[c]
13			B	**4h**	23[c]

[a] Procedure A: **1**:Br_2:*n*-Bu_4NOAc = 1:1.1:2.2. Procedure B: **1**:I_2:*n*-Bu_4NOAc = 1:1:2.2.
[b] Isolated yield, unless otherwise stated.
[c] Determined by NMR spectroscopy with an internal standard.
[d] Yield of the cycloadduct of **4e** with cyclopentadiene.
[e] Compound **4f** is highly prone to polymerization on concentration of its solutions.

According to the literature data,[12] as a rule, in equilibrium mixtures of silyl nitronates, trans-isomers dominate, which cannot undergo concerted halosilane elimination. However, this process can take place from minor concentrations of cis-isomers resulting from rapid 1,3-*O*,*O*-migration of the silyl group.[13]

It should be pointed out that the use of standard halogenating agents (Cl_2, Br_2, ICl, SO_2Cl_2, NCS, NBS) in the absence of tetra-*n*-butylammonium acetate resulted in complete conversion of starting BENA, but gave only traces or low yields of target nitroalkenes **4**. This may be associated with a high reactivity of iminium ion **2**, which is capable of decomposition and rearrangement of the starting BENA.[14] Furthermore, the halosilanes Me_3SiX (X = Br or I) formed in the course of the reaction can also consume BENA.[9a] We believe that acetate ions serve to minimize these side processes by desilylating the cation **2** and scavenging Me_3SiX. Attempts to use quaternary ammonium chloride and fluoride salts for these purposes were unsuccessful.[15]

The optimal procedure for the synthesis of nitroalkenes **4a–h** includes mixing of the reagents at −78 °C in dichloromethane followed by warming to room temperature.[16] To achieve good yields of internal nitroalkenes, the use of bromine is preferable (cf. entries 12 and 13).

The isolation of the simplest nitroalkenes can be accompanied by losses of the material due to their volatility and propensity to polymerization. Nevertheless, such compounds can be used in further transformations without isolation from the reaction mixtures, as exemplified by trapping of nitroethylene with cyclopentadiene (entry 9). Nitroalkenes **4g**,**h** with internal double bonds were formed as *E*-isomers exclusively.

In conclusion, a new mild protocol for the synthesis of conjugated nitroalkenes by selective oxidation of the carbon skeleton of the corresponding nitro compounds by means of halogenation of an intermediate BENA is described. Taking into account that generation of BENAs from secondary nitroalkanes is a highly regioselective process,[9a] this approach allows one to control the position of the C=C-double bond in the target nitroalkene.

Acknowledgments

This work was supported by the Russian Foundation for Basic Research (project 05–03–32733).

Supplementary data

Supplementary data associated with this article can be found, in the online version at doi:10.1016/j.tetlet.2005.05.113.

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16. (a) Bromination of BENAs (general procedure A, Table 1). A solution of Br_2 (57 μL, 1.1 mmol) in CH_2Cl_2 (1 mL) was added to a solution of *n*-Bu_4NOAc (665 mg, 2.2 mmol) in CH_2Cl_2 (2.5 mL) at −78 °C. Then, a solution of BENA **1** (1 mmol) in CH_2Cl_2 (1.5 mL) was slowly added with vigorous stirring, the mixture was kept for 15 min at −78 °C, and the cooling bath was removed. The mixture was allowed to warm to room temperature, concentrated, the residue treated with ether (10 mL), stirred for an additional 15 min and the precipitate was filtered off. The filtrate was concentrated and the residue was purified by chromatography on silica gel eluting with hexane/ethyl acetate (see supplementary data for details). (b) Iodination of BENAs (general procedure B, Table 1). *n*-Bu_4NOAc (665 mg, 2.2 mmol) and I_2 (254 mg, 1.1 mmol) were dissolved in CH_2Cl_2 (3.5 mL). After stirring for 15 min at room temperature, the mixture was cooled to −78 °C and a solution of BENA (1 mmol) in CH_2Cl_2 (1.5 mL) was added slowly with vigorous stirring. After 15 min at −78 °C, the cooling bath was removed, the mixture was allowed to warm to room temperature and worked up as described in the previous procedure (see supplementary data for details).