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Chemistry of *β*-Functionalized α-Nitroso Ethylenes. Methyl *β*-Nitroso Acrylate as Heterodienophile in [4 + 2]-Cycloaddition to Cyclic Dienes

Alexander A. Tishkov, Il'ya M. Lyapkalo, Sema L. Ioffe,* Yuri A. Strelenko, and Vladimir A. Tartakovsky

*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47 Leninsky prosp., 117913 Moscow, Russian Federation*

iof@cacr.ioc.ac.ru

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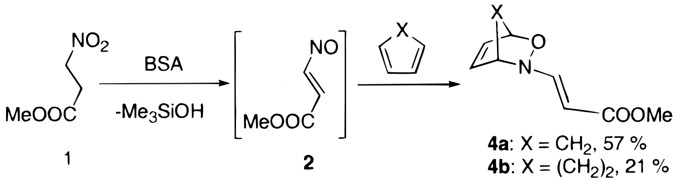
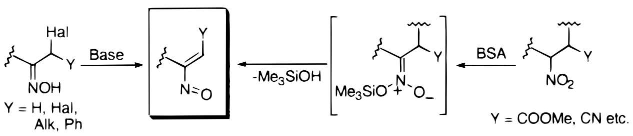
ABSTRACT



β-Functionalized nitroso alkene 2, obtained from methyl β-nitropropionate 1 and *N,O*-bis(trimethylsilyl)acetamide, can function as a good heterodienophile in Diels–Alder reactions. Therefore, 2 was trapped by cyclic dienes to give adducts 4 with the corresponding stereoselectivity. Cycloadduct 4a undergoes *retro*-[4 + 2]-cycloaddition at 33 °C in solution; thus 4a can be used to generate nitroso alkene 2 in neutral medium. Cyclopentadiene reacts with adduct 4a according to an *endo*-[4 + 2]-cycloaddition scheme to give cycloadduct 5 in low yield.

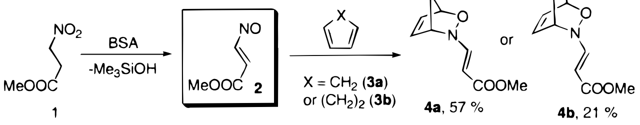
For nearly 20 years, conjugated nitroso alkenes have been employed as potent intermediates in organic synthesis due to their ability to react as 1,3-heterodienes in Diels−Alder cycloadditions.[1] Nitroso alkenes are normally generated in situ because of their instability and high reactivity. Most examples of their application are reactions of nitroso alkenes which are smoothly generated from available α-halogen-substituted keto-oximes and various bases[2] (Scheme 1).

Scheme 1



Recently, an alternative approach to the novel type of nitroso alkenes bearing an electron-withdrawing substituent in a *β*-position was found which implies silylation of *β*-functionalized aliphatic nitro compounds. For example, the reaction of methyl *β*-nitropropionate **1** proceeds through the initial formation of trimethylsilyl nitronate followed by Me$_3$SiOH elimination (Schemes 1 and 2).[3]

Scheme 2



β-Functionalized nitroso alkenes were shown to act as *N*-electrophiles in reactions with silyl nitronates. They can also act as 1,3-heterodienes in [4 + 2]-cycloadditions with electron-enriched alkenes.[3]

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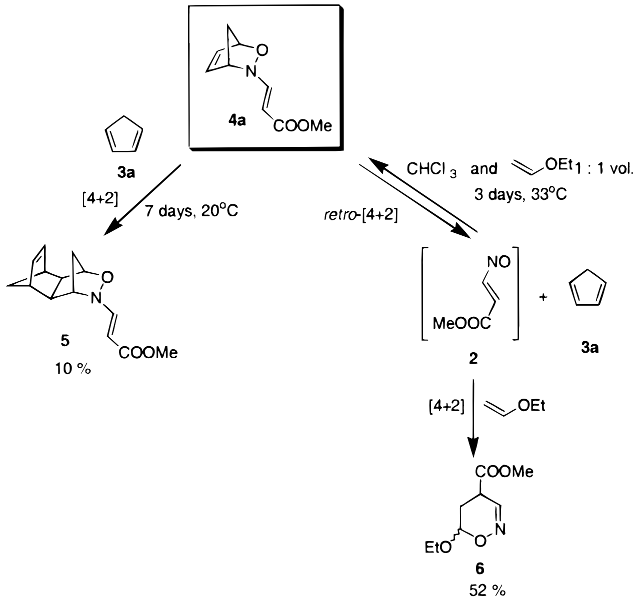
Now we report that nitroso alkene **2** behaves as a heterodienophile toward cyclic dienes. Intermediate **2** can be efficiently trapped by cyclopentadiene **3a** or cyclohexadiene **3b** during the silylation of compound **1** with *N*,*O*-bis(trimethylsilyl)acetamide (BSA) (Scheme 2).[4]

It is noteworthy that most nitroso alkenes react with either dienes or alkenes as 1,3-heterodienes to give the corresponding oxazines in moderate yields.[1,5]

Both reactions presented in Scheme 2 are chemo- and stereoselective; cycloadducts **4a** and **4b** were isolated as individual *endo*-(*E*)-isomers (according to NMR data).

The reaction of methyl β-nitropropionate **1** with BSA in a solution in pure diene **3a** resulted (after 7 days) in partial transformation of cycloadduct **4a** into bisadduct **5**; a 4:1 mixture of **4a** and **5** was obtained.[6] Individual cycloadduct **5** can be isolated in lower yield after exposure of the 4:1 mixture of **4a** and **5** in cyclopentadiene (Scheme 3).[7] The configuration of bisadduct **5** is presented in Scheme 3 and confirmed by NMR data.

Scheme 3



Cycloadduct **4a** proved to be unstable in contrast to **4b**. **4a** can undergo facile *retro*-[4 + 2]-cycloaddition in solution to give nitroso intermediate **2** which can be trapped by an external dienophile.

For example, exposure of the solution of **4a** in a 1:1 v/v mixture of CHCl$_3$ and ethyl vinyl ether for 3 days at 33 °C gave a moderate yield of oxazine **6** (Scheme 3).[8]

Crystalline cycloadduct **4a** can thus be considered to be a "source" of intermediate **2** in neutral medium. This can obviously be significant for synthetic applications of β-fuctionalized nitroso alkenes.[9]

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Supporting Information Available: Characterization data for compounds **4a**,**b**, **5**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(4) **Typical procedure:** To a stirred solution of **1** (1 g, 7.5 mmol) in CH$_2$Cl$_2$ (30 mL) and diene **3a** (6.16 mL, 75.0 mmol) or **3b** (4.65 mL, 75.0 mmol) was added distilled BSA (9.3 mL, 37.6 mmol) at 0 °C in an inert atmosphere, and the mixture was kept at 20 °C for 48 h. Then it was concentrated at 0.1 Torr. For **4a**: the residue was diluted with hexane and the white precipitate was filtered off to give 0.78 g of **4a** (57%). For **4b**: the residue was diluted with MeOH (3 mL), stirred for 10 min, poured into water (20 mL), and extracted with hexane (3 × 20 mL). The extract was dried (Na$_2$SO$_4$) and evaporated to give 0.31 g of white crystalline **4b** (21%).

(5) Clorinated nitroso alkenes are the exception; they react with conjugated cyclic dienes as heterodienophiles. The adducts formed, however, are unstable and rearrange to give epoxyaziridines (see Francotte, E.; Merenyi, R.; Vandenbulcke-Coyette, B.; Viehe, H. G. *Helv. Chim. Acta* **1981**, *64*, 1208. Francotte, E.; Merenyi, R.; Viehe, H. G. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 936. Viehe, H. G.; Merenyi, R.; Francotte, E.; Van Merssche, M.; Germain, G.; Declarcq, J. P.; Bodart-Gilmont, J. *J. Am. Chem. Soc.* **1977**, *99*, 2340).

(6) To a stirred solution of **1** (1 g, 7.5 mmol) in cyclopentadiene **3a** (12.4 mL, 151.5 mmol) was added distilled BSA (9.3 mL, 37.6 mmol) at 0 °C in an inert atmosphere, and the mixture was kept at 20 °C for 7 days. For the workup, see typical procedure[4] for **4a**. The yield is 0.58 g (4:1 of **4a** and **5**, respectively).

(7) The 4:1 mixture of **4a** and **5** (0.2 g) was dissolved in freshly distilled cyclopentadiene **3a** (1.5 mL) and kept for 7 days at 20 °C. Then it was evaporated at 0.1 Torr; the residue was dissolved in MeCN (5 mL) and extracted with hexane (4 × 7 mL). The combined hexane layers were evaporated to ca. 2 mL, and the precipitate was filtered off to give 30 mg (10%) of white crystalline **5**.

(8) Cycloadduct **4a** (90 mg, 0.5 mmol) was dissolved in CHCl$_3$ (3 mL) and ethyl vinyl ether (3 mL), and the solution was kept at 33 °C for 3 days. Then the mixture was evaporated, the residue was extracted with hexane (5 × 5 mL), and the combined hexane layers were filtered through Cellite and evaporated to give 50 mg (52%) of **6** as yellowish oil. The ^{1}H NMR for **6** was in good agreement with literature data.[3]

(9) White crystalline cycloadduct **4a** is easy to handle and it could be stored at −5 °C for several months.