Addition of primary *N*-nitroamides to activated olefins

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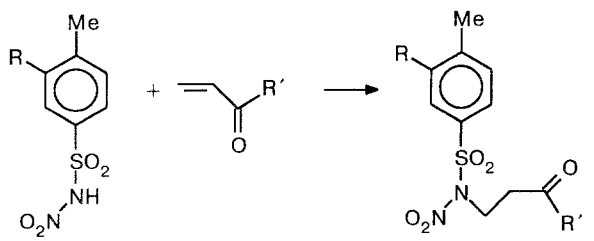
Primary *N*-nitrosulfamides readily undergo addition to acrolein and vinyl ketones to yield *N*-γ-oxoalkyl-*N*-nitrosulfamides. The presence of a second substituent at the double bond hinders the reaction. *N*-Nitrourethane reacts with activated carbonyl compounds and α-nitroolefins.

Key words: *N*-nitrosulfamides; *N*-nitrourethane; *N*-γ-oxoalkyl-*N*-nitroamides; *N*-β-nitroalkyl-*N*-nitrourethanes; *N*-γ-oxoalkyl-*N*-nitroamines; Michael-type reaction; activated olefins.

The most general synthesis of secondary *N*-nitroamides (NA) is based on the nitration of secondary amides.[1] This approach is also suitable in the synthesis of functional derivatives of secondary NA when the corresponding starting compounds are both easily accessible and can withstand the conditions of nitration. To prepare some β-derivatives of NA the addition of primary NA to activated olefins may alternatively be chosen. Reactions of this type are not described in the literature, but it is known that in the presence of basic catalysts primary *N*-nitroamines, which are both chemically and structurally similar to NA, readily add to esters, amides, and nitriles of α,β-unsaturated acids, activated unsaturated ketones, and α-nitroolefins.[1] Taking into account these data we have studied the addition of *N*-nitrosulfamides (NSA) and *N*-nitrourethane (NU) to activated olefins.

It was found that *N*-nitro-*m*-nitro-*p*-toluenesulfamide (**2**) readily reacts with methylvinylketone (**4**) upon mere mixing of the reagents. The reaction occurs in solution (water, ether) or without solvents, and basic catalysts are not necessary. The yield of the product **6c** is 96—98 % (Scheme 1).

Scheme 1



1,2 **3—5** **6a—d**

1: R = H
2: R = NO_2

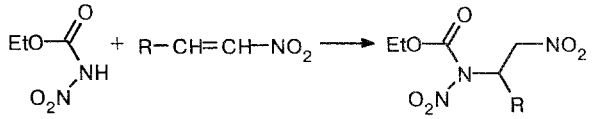
3: R′ = H
4: R′ = Me
5: R′ = Ph

a: R = H, R′ = Me
b: R = NO_2, R′ = H
c: R = NO_2, R′ = Me
d: R = NO_2, R′ = Ph

Similarly, but less readily, nitroamide **2** reacts with phenylvinylketone (**5**) to give compound **6d**. *N*-Nitro-*p*-toluenesulfamide (**1**) also reacts with α,β-unsaturated carbonyl compounds and, although the reaction with vinylmethylketone **4** (compound **6a**) is less effective, the yield of the addition product is more than 80 %.

Therefore, the reaction does not significantly depend on the nature of the substituents R' at the carbonyl group of compounds **3—5** and appears to be general. On the other hand, the introduction of even a single methyl group to the double bond strongly prevents the addition of NSA. Thus, **2** does not react visibly with crotonaldehyde at room temperature or at higher temperatures (60—70 °C). According to IR-spectroscopy data, the addition does occur, but it is accompanied by strong resinification, which does not permit one to isolate the desirable product in an individual state.

The ease of the addition of **1** and **2** to conjugated carbonyl compounds allowed one to expect that NSA would react analogously with other activated olefins. However, the addition of **2** to methyl acrylate, acrylonitrile, or nitroethylene even at elevated temperatures or in the presence of basic catalysts did not be occur. Obviously, this result is due to the poor nucleophilicity of NSA anions. In fact, using more nucleophilic NA permits the addition to the activated olefins to occur. Thus, *N*-nitrourethane (**7**) reacts with nitroethylene and 1-nitro-1-propene in the presence of bases to give a high yield of adducts (**8a,b**).



7 **8a,b**

a: R = H; **b**: R = Me

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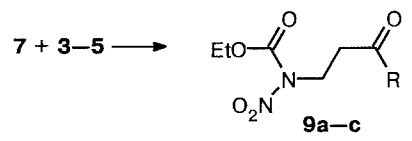
It also should be noted that the addition of urethane **7** to nitroolefines is rather sensitive to steric effects of the substituent. For example, the transition to 3-nitro-ω-nitrostyrene does not occur to any large degree at room temperature.

The addition of **7** to conjugated unsaturated aldehydes and ketones **3—5** occurs without any difficulties to give the corresponding adducts (**9a—c**).



9a—c

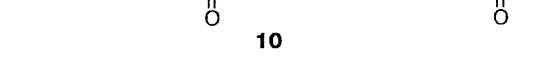
a: R = H; **b**: R = Me; **c**: R = Ph

The addition of **7** to nitroolefins and unsaturated carbonyl compounds was carried out in the presence of a catalytic amount of NaOH. As was shown with **7** and **4**, the reaction also occurs in the absence of bases, although at a lower rate. For example, in two runs that were identical except for the absence of the base in the second run, yields of adducts were 67 and 31 %, respectively.

Like in the case with NSA, the attempts to add nitrourethane **7** to acrylonitrile and methyl acrylate were unsuccessful.

Thus, the addition of primary NA to activated olefins depends on the nature of both the NA and the olefins.

A common method of the synthesis of primary *N*-nitroamines is the treatment of secondary NA with bases, which results in their deacylation and the formation of nitroamine salts. Earlier we showed[2] that the action of bases on *N*-γ-oxoalkyl-*N*-nitrosulfamides results mainly or exclusively in the formation of NSA salts, rather than primary *N*-γ-oxoalkyl-*N*-nitroamines, *i.e.*, a retro-Michael reaction takes place. Taking into account the difference between the nucleophilicities of sulfo groups and ester groups one could expect that treating the products of the addition of nitrourethane to unsaturated carbonyl compounds with bases would result in the formation of formerly inaccessible primary *N*-γ-oxoalkyl-*N*-nitroamines. This fact was confirmed with compound **9b,** which reacted with ammonia to give a high yield of salt **10** and urethane.



10

The ^{1}H NMR spectrum of the salt obtained has no signals of EtO group protons which indicates that the reaction involves the amido groups of compound **9b.** When salt **10** was acidified free *N*-nitro-*N*-(3-oxobutyl)amine (**11**) formed.

Experimental

^{1}H NMR spectra were recorded using a Perkin Elmer R-12 spectrometer (60 MHz). IR spectra were recorded using a UR-10 spectrometer. The spectra of liquids were obtained without a solvent, spectra of solids, as pellets with KBr.

***N*-Nitro-*N*-(3-oxobutyl)-*p*-toluenesulfamide (6a).** Ketone **4** (0.45 g) was added to a solution of sulfamide **1** (0.69 g) in a minimum amount of ether, and the mixture was kept for 3 days. Then sulfamide **6a** was filtered. Yield 0.73 g (83 %), m.p. 118—120 °C (from benzene : hexane, 1 : 1). Found (%): C, 45.92; H, 5.18; N, 9.78; S, 10.83. $C_{11}H_{14}N_2O_5S$. Calculated (%): C, 46.15; H, 4.90; N, 9.80; S, 11.20.

***N*-Nitro-*N*-(3-oxopropyl)-*m*-nitro-*p*-toluenesulfamide (6b).** Acrolein **3** (0.52 mL) was added to a solution of amide **2** (1 g) in a minimum amount of ether, and the reaction mixture was kept for 5 days. Then the volatile compounds were removed *in vacuo* using a water-jet pump at 50 °C and the residue was washed with water. The yield of **6b** is 0.97 g (81 %), m.p. 108—109 °C (from benzene). Found (%): C, 37.99; H, 3.66; N, 13.69; S, 9.93. $C_{10}H_{11}N_3O_7S$. Calculated (%): C, 37.90; H, 3.47; N, 13.25; S, 10.10.

***N*-Nitro-*N*-(3-oxobutyl)-*m*-nitro-*p*-toluenesulfamide (6c).** The reaction of nitroamide **2** (1.6 g) with ketone **4** (1 mL) was carried out as described above. After 4 h, the yield of **6c** was 2.0 g (98 %), m.p. 118—122 °C (from CCl_4). Found (%): C, 39.35; H, 3.91; N, 12.70; S, 9.75. $C_{11}H_{13}N_3O_7S$. Calculated (%): C, 39.75; H, 3.93; N, 12.70; S, 9.66. IR spectrum (ν/cm^{-1}): 1580, 1530, 1280 (NO_2); 1700 (C=O); 1170 (SO_2). ^{1}H NMR (δ): 2.1 (s, 3 H, CH_3CO); 2.63 (s, 3 H, $CH_3C_6H_3$); 3.05 (t, 2 H, CH_2CO); 4.45 (t, 2 H, CH_2N); 7.75—8.5 (m, 3 H, C_6H_3).

***N*-Nitro-*N*-(3-oxo-3-phenylpropyl)-*m*-nitro-*p*-toluenesulfamide (6d).** Ketone **5** (1.12 g) was added to a solution of sulfamide **2** (1.1 g) in a minimum amount of ether. After 3 days, the adduct **6d** was filtered off. Yield 1.58 g (96 %), m.p. 143—145 °C (decomp., from benzene). Found (%): C, 49.28; H, 4.24; N, 10.67; S, 7.56. $C_{16}H_{15}N_3O_7S$. Calculated (%): C, 48.92; H, 3.82; N, 10.68; S, 8.11.

Ethyl *N*-(2-nitroethyl)-*N*-nitrocarbamoate (8a). A catalytic amount of NaOH was added to a solution of nitroethylene (0.96 g) and urethane **7** (1.66 g) in a minimum amount of ether. After 6 days, the ether was distilled off, the residue was washed with a dilute acid and dried with Na_2SO_4, and ester **8a** was isolated by distillation. Yield 2.26 g (87 %), b.p. 122—124 °C (0.4 Torr), n^{23}_D 1.4746. Found (%): C, 29.24; H, 4.54; N, 20.13. $C_5H_9N_3O_6$. Calculated (%): C, 29.00; H, 4.35; N, 20.29.

Ethyl *N*-(2-nitroisopropyl)-*N*-nitrocarbamoate (8b) was prepared similarly to **8a** from 1-nitro-1-propene (2.34 g) and urethane **7** (3 g). The reaction was carried out for 2 weeks. The yield of **8b** was 58 %, b.p. 110—112 °C (0.4 Torr), $n^{23.5}_D$ 1.4658. Found (%): C, 32.91; H, 5.14; N, 19.52. $C_6H_{11}N_3O_6$. Calculated (%): C, 32.58; H, 4.98; N, 19.03.

Ethyl *N*-(3-oxopropyl)-*N*-nitrocarbamoate (9a). A catalytic amount of NaOH was added to a mixture of urethane **7** (3 g) and **3** (2.64 mL). The reaction was carried out for 5 days at 20 C and 7 h at 60 C. Acrolein was removed *in vacuo*. The residue was dissolved in benzene and the solution was washed with 5 % hydrochloric acid and water, dried with Na_2SO_4, then **9a** was distilled off. Yield 2.68 g (63 %), b.p. 109 °C

(0.4 Torr), $n^{18.5}_D$ 1.4683. Found (%): C, 37.35; H, 5.48; N, 15.06. $C_6H_{10}N_2O_5$. Calculated (%): C, 37.89; H, 5.26; N, 14.74.

Ethyl *N*-(3-oxobutyl)-*N*-nitrocarbamoate (9b). A mixture of urethane **7** (3 g), ketone **4** (3.12 mL), and a catalytic amount of NaOH was kept for 4 days. The excess **4** was removed *in vacuo* and the mixture was treated as described for **9a**. The yield of **9b** was 3.98 g (87 %), b.p. 98 °C (0.4 Torr), n^{22}_D 1.4630. Found (%): C, 41.18; H, 6.02; N, 14.15. $C_7H_{12}N_2O_5$. Calculated (%): C, 41.18; H, 5.88; N, 13.73.

Ethyl *N*-(3-oxo-3-phenylpropyl)-*N*-nitrocarbamoate (9c). A solution of ketone **5** (1.71 g), **7** (2.06 g), and a catalytic amount of NaOH in a minimum amount of ether was kept for 2 weeks. The ether was distilled off, the residue was dissolved in benzene, the solution was washed with a dilute acid and water and dried with Na_2SO_4, and the benzene was distilled off to give oily crystals. Crystals were pressed out on a plate and recrystallized from hexane to yield **9c** (1.19 g, 34.5 %), b.p. 54—56 °C. Found (%): C, 53.84; H, 5.24; N, 10.56. $C_{12}H_{14}N_2O_5$. Calculated (%): C, 54.13; H, 5.26; N, 10.53.

***N*-Nitro-*N*-(3-oxobutyl)amine (11).** NH_3 was bubbled through a solution of ester **9b** (6.89 g) in absolute ether (50 mL) at 0 °C until the formation of the precipitation ceased. The precipitate was filtered off and washed with ether to yield 4.52 g (90.8 %) of ammonium salt **10**, m.p. 100—103 °C (decomp.). The ^1H NMR spectrum of the salt (in D_2O) showed CH_2 two triplets and a singlet related to the CH_3 groups (the ratio 2 : 2 : 3). Then **10** was dissolved in a minimum amount of water, acidified with 5 % hydrochloric acid, then the aqueous solution was saturated with NaCl and extracted with ether. The extract was dried with Na_2SO_4 and distilled to yield 2.75 g of nitroamine **11** (68.5 % relative to the salt), b.p. 110—112 °C (0.4 Torr), n^{20}_D 1.4830. Found (%): N, 21.23. $C_4H_8N_2O_3$. Calculated (%): N, 21.21. IR spectrum (ν/cm^{-1}): 3300 (NH); 1710 (C=O); 1580, 1330 (NO_2).

References

1. S. S. Novikov, G. A. Shvekhgeimer, V. V. Sevost'yanova, and V. A. Shlyapochnikov, *Khimia alifaticheskikh i alitsiklicheskich nitrosoedinenii* [*Chemistry of Aliphatic and Alicyclic Nitrocompounds*], Khimia, Moscow, 1974, 415 (in Russian).
2. O. A. Luk'yanov, V. P. Gorelik, V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim.*, 1994, 94 [*Russ. Chem. Bull.*, 1994, **43**, 89 (Engl. Transl.)].

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