Available online at www.sciencedirect.com
ScienceDirect
*Mendeleev Commun.*, 2010, **20**, 348–349
Mendeleev Communications

# Nitraminofurazans in aza-Michael reactions

**Aleksei B. Sheremetev,* Natal'ya S. Aleksandrova, Andrei A. Bykov and Marina I. Struchkova**

*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax: +7 499 135 5328; e-mail: sab@ioc.ac.ru*

DOI: 10.1016/j.mencom.2010.11.016

**The aza-Michael addition of primary nitraminofurazans to α,β-unsaturated carbonyl acceptors proceeds without a catalyst; the adducts or their 2,4-dinitrophenylhydrazones undergo retro-Michael fragmentation under basic conditions.**

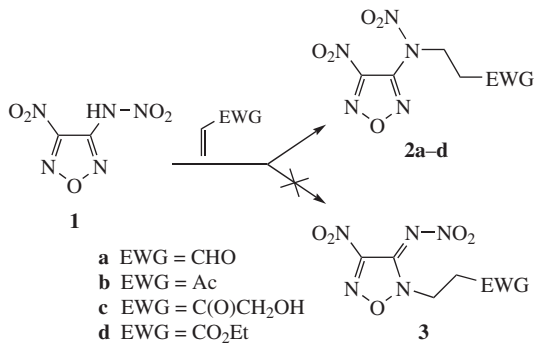
The conjugate addition of nucleophiles to activated C=C bond (the Michael reaction) is widely used in targeted organic synthesis.[1] In aza-Michael version[2] amines and some of their derivatives, as well as azoles containing the N–H fragment are typically employed as N-nucleophiles. Several cases involving weak N-nucleophiles such as primary nitramines are also known.[3] In fact, reactions of alkyl-,[4–13] aryl-,[5] hetaryl-,[14] carbalkoxy-[15] and sulfonylnitramines,[15] as well as dinitramide[16] with alkenes activated with acyl,[4,8,11,14–16] alkoxycarbonyl,[4,6,14] nitrile,[4,9] sulfonyl[10] and nitro groups,[5,7,15] as well as the diazenoxide fragment,[12] have been documented, with the reaction outcome being strongly substrate-dependent. Note that the only hetaryl-nitramine (nitraminotriazole) involved in this reaction behaves differently than the other nitramines;[14] the alkene is added to the ring nitrogen atom rather than to the nitramine fragment.

As part of our efforts to develop nitraminofurazan chemistry,[17] we became interested in employing the aza-Michael reaction to modify 3-nitramino-4-nitrofurazan (3-nitramino-4-nitro-1,2,5-oxadiazole) **1**.[17(e),18] Taking literature data into account, one could expect that two types of products can be formed (Scheme 1), namely, secondary nitramine **2** and ring-alkylated nitrimine **3**.

We have found that compound **1** reacted with acrolein (EWG = CHO) and methyl vinyl ketone (EWG = Ac) in the absence of a catalyst in diethyl ether at room temperature.† The reaction proceeded slowly (in ~3 days) and selectively afforded one product in a yield of about 80%. Attempts to accelerate the reaction by catalytic amounts of bases ($NEt_3$, $HNEt_2$, pyrrolidine, piperidine, $Na_2CO_3$) resulted in reduced yields.

The structure assignment for the products as tertiary amines **2** was confirmed by comparison of their NMR characteristics with data reported for nitraminofurazans[19] and N-substituted 1,2,5-oxadiazoles.[20]

When 4-hydroxybut-1-en-3-one [EWG = C(O)$CH_2$OH], readily prepared from butyne-1,4-diol by its isomerization in the presence of mercury salts in aqueous medium at 20 °C, was added to compound **1** within two days, product **2c** was formed in 72% yield.




**Scheme 1**

Unsaturated cyclic ketones, such as cyclopenten-2-one and cyclohexen-2-one, do not react with compound **1** in diethyl ether, whereas in pure DMF and in the presence of basic catalysts the reaction produced complex unseparable mixtures.

The reaction of ethyl acrylate (EWG = $CO_2$Et) with nitramine **1** in diethyl ether occurred very slowly; after a lapse of one week, chromatographic separation of the reaction mixture gave 4% of product **2d** and 90% of the recovered starting material **1**. Yield of product **2d** was slightly improved (12%) when the reaction was carried out in DMF in the presence of catalytic amounts of $NEt_3$. Attempted addition of acrylonitrile (EWG = CN) to compound **1** failed either in $Et_2O$ or in DMF, even in the presence of basic catalysts.

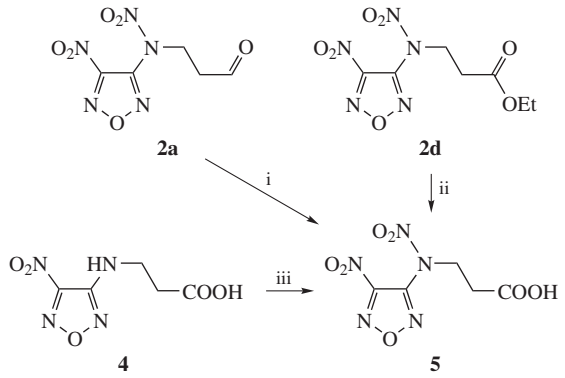
Oxidation of aldehyde **2a** with $CrO_3$ in dilute sulfuric acid, hydrolysis of ester **2d** with 15% hydrochloric acid, or nitration of amino acid **4** with nitric acid (*d* 1.5) all led to the same nitramino acid **5** in 59, 64 or 75% yields, respectively (Scheme 2). This result provides further support for the proposed structure.

We have shown that compounds **2a–d** readily undergo the retro-Michael fragmentation. For example, treatment of a 5–10% solution of compounds **2a–d** in an $Et_2O$–EtOH mixture (2:1) at 0 °C with a small excess of 10% NaOEt in ethanol quantitatively gives a precipitate of the sodium salt of compound **1**.

Dinitrophenylhydrazones **6a**,**b** were obtained from carbonyl compounds **2a** and **2b** in acid medium (Scheme 3). However, compounds **6a**,**b** turned out being unstable and would

† *Preparation of* N-*(4-nitrofurazan-3-yl)*-N-*(3-oxobutyl)nitramides* **2b** (*general procedure*). A mixture of nitramine **1** (0.75 g, 4.3 mmol) and methyl vinyl ketone (0.336 g, 4.8 mmol) in diethyl ether (6 ml) was stirred at room temperature. The progress of the reaction was monitored by TLC ($CH_2Cl_2$–$C_5H_{12}$, 3:1). After completion of the reaction (3 days), the mixture was diluted with $CH_2Cl_2$ (20 ml), washed with water (3×10 ml), dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was column chromatographed on silica gel using $CH_2Cl_2$–light petroleum (4:1) as eluent to get the pure product **2b** (80%), viscous oil, $R_f$ 0.4 ($CH_2Cl_2$–$C_5H_{12}$, 3:1). IR (NaCl, $\nu$/cm$^{-1}$): 2924, 1716, 1588, 1548, 1428, 1376, 1284, 1212, 1172, 1108, 1032, 828. $^1$H NMR ($CDCl_3$) $\delta$: 2.14 (s, 3H, Me), 3.10 (t, 2H, $CH_2CO$, $J$ 5.5 Hz), 4.43 (t, 2H, $CH_2N$, $J$ 5.5 Hz). $^{13}$C NMR ($CDCl_3$) $\delta$: 29.5 (Me), 40.2 ($CH_2Ac$), 48.7 ($CH_2N$), 147.4 ($CNNO_2$), 155.8 (t, C–$NO_2$, $^1J_{^{14}N,^{13}C}$ 19 Hz), 206.4 (C=O). $^{14}$N NMR ($CDCl_3$) $\delta$: –38.8 (C–$NO_2$, $\nu_{1/2}$ 17.5 Hz), –42.4 (N–$NO_2$, $\nu_{1/2}$ 35 Hz). Found (%): C, 29.52; H, 2.96; N, 28.51. Calc. for $C_6H_7N_5O_6$ (%): C, 29.40; H, 2.88; N, 28.57.

Analogously, compounds **2a** (73%), **2c** (64%) and **2d** (12%) were synthesized. For characteristics of compounds **2a**,**c**,**d**, **5** and **6a**,**b**, see Online Supplementary Materials.



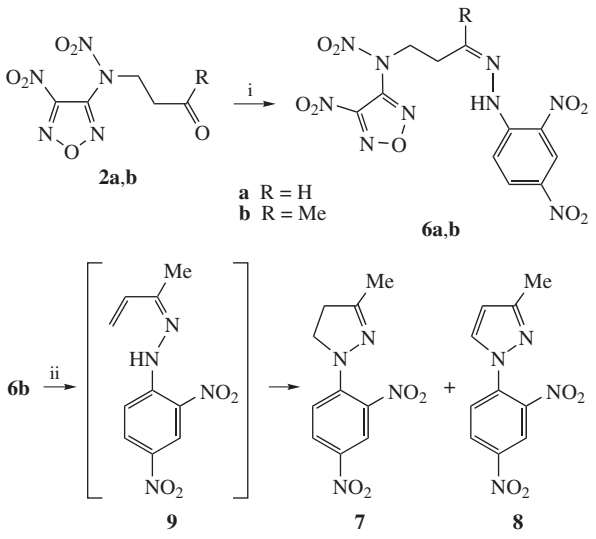
**Scheme 2** *Reagents and conditions*: i, $CrO_3$, 5% $H_2SO_4$, room temperature, 12 h; ii, 15% HCl/$H_2O$, 50 °C, 8 h; iii, 100% $HNO_3$, 0 °C, 1 h.

decompose in neutral or weakly alkaline media. In fact, even in 5 min after dissolution of compound **6b** in DMSO it was no longer detectable by TLC, whereas pyrazoline **7** (32%) and pyrazole **8** (46%) were isolated from the reaction mixture by chromatography.‡

Probably, a hydrazone undergoes a retro-Michael transformation, and the intermediate **9** would cyclize into pyrazoline **7**, which aromatizes to pyrazole **8** under the reaction conditions due to oxidation with atmospheric oxygen or with decomposition products of nitramine **1**. Note that a similar denitramination accompanied by formation of a pyrazole ring was previously observed during treatment of PhCOCH=CHN($NO_2$)Me with hydrazine.[23]

In conclusion, the aza-Michael reaction can be applied to modification of primary nitraminofurazans, in particular, on using acrolein and vinyl ketones providing the highest yields of adducts. The reversibility of this reaction allows Michael-adducts to be used for the temporary protection of the nitramine group.

This work was partially supported by the program of the Presidium of the Russian Academy of Sciences (OKhNM-04), Russian Foundation for Basic Research (grant no. 09-03-12230) and State contract no. 02.740.11.0258.



**Scheme 3** *Reagents and conditions*: i, 2,4-$(O_2N)_2C_6H_3NHNH_2$, EtOH, $H_2SO_4$, 50 °C, 1 h; ii, DMSO, 40 °C, 0.5 h.

‡ The identity of products **7**[21] and **8**[22] was confirmed by NMR spectra, elemental analysis, melting points, mass spectra and comparison with literature data.

*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2010.11.016.

## References


1 V. A. Smit and A. D. Dilman, *Osnovy sovremennogo organicheskogo sinteza* (*Fundamentals of Modern Organic Synthesis*), Binom, Moscow, 2009, p. 233 (in Russian).

2 P. R. Krishna, A. Sreeshailam and R. Srinivas, *Tetrahedron*, 2009, **65**, 9657.

3 (*a*) A. L. Fridman, V. P. Ivshin and S. S. Novikov, *Usp. Khim*., 1969, **38**, 1448 (*Russ. Chem. Rev*., 1969, **38**, 640); (*b*) S. S. Novikov, G. A. Shveikhgeimer, V. V. Sevost'yanova and V. A. Shlyapochnikov, *Khimiya alifaticheskikh i alitsiklicheskikh nitrosoedinenii* (*Chemistry of Aliphatic and Alicyclic Nitro Compounds*), Khimiya, Moscow, 1974, p. 266 (in Russian).

4 L. W. Kissinger and M. Schwartz, *J. Org. Chem*., 1958, **23**, 1342.

5 H. Feuer and R. Miller, *J. Org. Chem*., 1961, **26**, 1348.

6 L. W. Kissinger, M. Schwartz and W. E. McQuistion, *J. Org. Chem*., 1961, **26**, 5203.

7 I. S. Ivanova, Yu. V. Konnova and S. S. Novikov, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1962, 920 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1962, **11**, 858).

8 I. S. Ivanova, N. N. Bulatova and S. S. Novikov, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1962, 1858 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1962, **11**, 1765).

9 I. S. Ivanova, G. F. Bogdanova, T. A. Alekseeva and S. S. Novikov, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1962, 2236 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1962, **11**, 2136).

10 B. Unterhalt and D. Thamer, *Arch. Pharm*., 1974, 466.

11 I. L. Vereshchagin, L. P. Kirillova, G. M. Luzgina and G. A. Gareev, *Zh. Org. Khim*., 1984, **20**, 34 [*J. Org. Chem. USSR* (*Engl. Transl*.), 1984, **20**, 29].

12 G. A. Marchenko, A. S. Mukhametzyanov, I. V. Tselinskii and A. S. Ermoshkin, *Zh. Org. Khim*., 1985, **21**, 1429 [*J. Org. Chem. USSR* (*Engl. Transl*.), 1985, **21**, 1300].

13 A. A. Spiridonova, M. S. Fedoseev and A. I. Spiridonova, *Izv. Akad. Nauk, Ser. Khim*., 1999, 621 (*Russ. Chem. Bull*., 1999, **48**, 615).

14 O. P. Shitov, V. L. Korolev and V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim*., 2009, 2275 (*Russ. Chem. Bull., Int. Ed*., 2009, **58**, 2347).

15 O. A. Luk'yanov, V. P. Gorelik, O. S. Reshetova and V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim*., 1994, 1261 (*Russ. Chem. Bull*., 1994, **43**, 1197).

16 O. A. Luk'yanov, Yu. V. Konnova, T. A. Klimova and V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim*., 1994, 1264 (*Russ. Chem. Bull*., 1994, **43**, 1200).

17 (*a*) A. B. Sheremetev, *Ross. Khim. Zh. (Zh. Ross. Khim. Ob-va im. D. I. Mendeleeva)*, 1997, **41** (2), 43 [*Mendeleev. Chem. J*., 1997, **41** (2), 62]; (*b*) A. B. Sheremetev, V. O. Kulagina, I. A. Kryazhevskikh, T. M. Mel'nikova and N. S. Aleksandrova, *Izv. Akad. Nauk, Ser. Khim*., 2002, 1411 (*Russ. Chem. Bull., Int. Ed*., 2002, **51**, 1533); (*c*) A. B. Sheremetev and N. S. Aleksandrova, *Izv. Akad. Nauk, Ser. Khim*., 2005, 1665 (*Russ. Chem. Bull., Int. Ed*., 2005, **53**, 1715); (*d*) K. Yu. Suponitsky, K. A. Lyssenko, M. Yu. Antipin, N. S. Aleksandrova, A. B. Sheremetev and T. S. Novikova, *Izv. Akad. Nauk, Ser. Khim*., 2009, 2065 (*Russ. Chem. Bull., Int. Ed*., 2009, **58**, 2129); (*e*) A. B. Sheremetev, N. S. Aleksandrova, K. Yu. Suponitsky, M. Yu. Antipin and V. A. Tartakovsky, *Mendeleev Commun*., 2010, **20**, 249.

18 R. L. Willer, R. S. Day and D. J. Park, *US Patent 5460669*, 1995 (*Chem. Abstr*., 1996, **124**, 33168).

19 D. E. Dmitriev, Yu. A. Strelenko and A. B. Sheremetev, *Izv. Akad. Nauk, Ser. Khim*., 2002, 277 (*Russ. Chem. Bull., Int. Ed*., 2002, **51**, 290).

20 A. B. Sheremetev, Yu. A. Strelenko, T. S. Novikova and L. I. Khmel'nitskii, *Tetrahedron*, 1993, **49**, 5905.

21 (*a*) R. L. Forman, H. M. Mackinnon and P. D. Ritchie, *J. Chem. Soc., C*, 1968, 2016; (*b*) J. Elguero and A. Fruchier, *J. Chem. Res. (M)*, 1990, **7**, 1501.

22 (*a*) N. A. Keiko, L. G. Stepanova, I. D. Kalikhman and M. G. Voronkov, *Izv. Akad. Nauk SSSR, Ser. Khim*., 1983, 2651 (*Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1983, **32**, 2381); (*b*) M. A. Garcia, R. M. Claramunt and J. Elguero, *Magn. Reson. Chem*., 2008, **46**, 697.

23 L. I. Vereschagin, L. P. Kirillova, G. M. Luzgina and G. A. Gareev, *Zh. Org. Khim*., 1985, **21**, 886 [*J. Org. Chem. USSR* (*Engl. Transl*.), 1985, **21**, 806].


*Received: 22nd April 2010; Com. 10/3512*