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Reactivity of the low-nucleophilic *N*-dinitromethyl carbanion center in polynitromethylazoles

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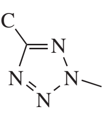
Reactivity of *N*-dinitromethylazoles possessing extremely high CH acidity (pK_a –1.75–0) was investigated in Michael, Henry and alkylation reactions. *N*-Dinitromethylazole K-salts and hexamethylenetetramine under acidic conditions yield bis-Mannich bases (86–100%) whose secondary amine moiety can be N-nitrated with HNO_3–H_2SO_4 system.

Polynitromethyl carbanions, such as those of trinitromethane and dinitroacetonitrile, possess low nucleophilicity, which makes them distinct from ordinary nitro carbanions.[1,2] We have recently developed a general approach to another family of such compounds, *N*-dinitromethylazoles **1**, whose CH acidity (pK_a –2.4 to 0.25)[3,4] in some cases is lower than that of trinitromethane (pK_a 0.06)[5] and comparable with inorganic acids. Reactions of polynitromethyl compounds leading to C–C bond formation such as alkylation, addition to the activated double bond, oxymethylation and aminomethylation were investigated mostly for trinitromethane and less acidic polynitroalkanes.[1,2] Polynitrated *N*-dinitromethylazoles are of practical interest in light of high-energy materials.[6,7] Here, we report on the investigations of above reactions extended to compounds **1a**–**f** of azole series. It is of note that structural changes on moving from trinitromethane to compounds **1** can cause unpredictable changes in their reactivity. We first studied the reactivity of 2-dinitromethyl-5-nitrotetrazole **1b**, which is readily available, low nucleophilic (pK_a –1.7) and the most interesting with respect to energy.[3]

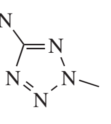
R–CH(NO_2)$_2$	R = CN	R = NO_2
1	pK_a –6.23[5]	pK_a 0.06[5]

1a R =



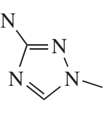
pK_a –1.7

1b R =



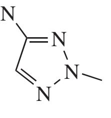
pK_a –1.7

1c R =



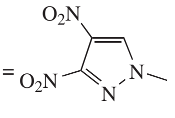
pK_a 0.1

1d R =



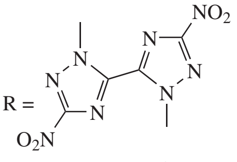
pK_a 0.2

1e R =



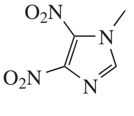
pK_a 0.25

1f R =



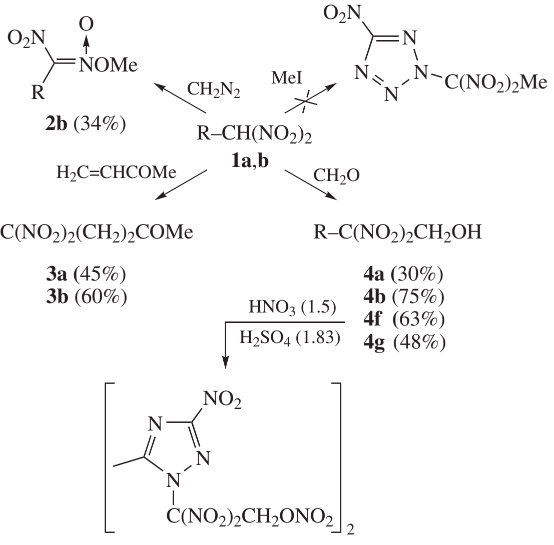
pK_a –1.75

1g R =



pK_a –1.7

In fact, potassium salt of **1b** did not react with MeI in acetone at 20 °C and even in 14 days was recovered from the reaction mixture, whereas trinitromethane under similar conditions is readily converted to 1,1,1-trinitroethane.[8] Diazomethane (3 equiv.) reacts with **1b** vigorously in diethyl ether at 0–5 °C to afford stable *O*-methyl ester **2b**.



Scheme 1

The structure of compound **2b** was established by microanalysis and spectroscopy. The IR and UV spectra of **2b** contain the bands typical of O_2N–C=N(O)–OMe fragment (see ref. 9). The ^{1}H NMR spectrum shows the singlet at 4.06 ppm that corresponds to the methoxy group at the N atom.[10]

The reaction of diazomethane with **1b** proceeds chemoselectively without any traces of the C-alkylation product, while with trinitromethane ~20% of 1,1,1-trinitroethane is formed.[11] More recent studies indicate that the treatment of trinitromethane with 4 equiv. diazomethane in benzene at 5 °C results in 2,2-dinitropropane (62%) and 3-nitro-4,5-dihydroisoxazole 2-oxide (23%), which could be assumed to be the products of further transformation of intermediate 1,1,1-trinitroethane and trinitromethane *O*-methyl ester.[12] However, the reaction between diazomethane and trinitromethane in equimolar amounts yields only trinitromethane *O*-methyl ester that affords *gem*-dinitroaziridines in the presence of acetylenes.[13]

N-Dinitromethyltetrazoles **1a**,**b** like trinitromethane[2] and dinitroacetonitlrile[14] can be easily add at the activated double bond of methyl vinyl ketone (water, room temperature, several minutes, no catalyst) to furnish the corresponding pentanones **3a**,**b**.

β-Polynitroalcohols similar to 2,2,2-trinitroethanol[2] are important semi-products for aliphatic high-energy materials.

N-Dinitromethylazoles and formaldehyde in stoichiometric ratios in water readily produce the corresponding β-nitro alcohols (the Henry reaction, *cf.* published data[2]), which can be separated from the reaction mixture as analytically pure crystals. The reaction can be run in a heterogeneous manner starting from *N*-dinitromethylazole salts and paraformaldehyde in dilute H_2SO_4. This procedure is convenient for poorly soluble nitro compounds. Unreacted *N*-dinitromethylazoles are easily regenerated as K-salts by quenching the mother liquor with AcOK.

It is known for the polynitro-Henry reaction, that the more acidic polynitro compounds are, the greater the equilibrium is shifted towards the starting reagents.[5]

A synthesis of β-polynitro alcohols from strong CH acids should usually be performed with high reagents concentrations and a high formaldehyde excess similarly to the synthesis of 2-cyano-2,2-dinitroethanol.[14] In spite of much stronger acidity of *N*-dinitromethylazoles as compared to trinitromethane, there is no need to follow standard procedures[5,14] as they react with formaldehyde even in dilute water solution. The resulting 2,2-dinitro-2-(*N*-azolyl)ethanols **4a**,**b**,**f**,**g** are luckily insoluble in water, which facilitates the equilibrium shifting towards the final products.

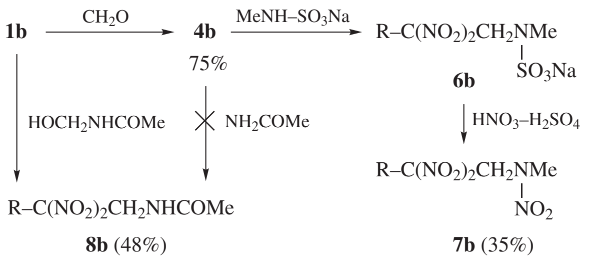
Compounds **4a**,**b**,**f**,**g** are readily soluble in absolute alcohols, diethyl ether and acetonitrile. In these solvents they do not dissociate to starting reagents, whereas addition of little water causes their transformation to *N*-dinitromethylazoles: the corresponding dinitrocarbanion fragments were quantitatively observed in the UV spectra (λ = 330–340 nm[4]).

The hydroxyl group of 2,2-dinitro-(2-*N*-azolyl)ethanol **4f** can be nitrated as was shown in the case of **5f**. However, the nitrate group in **5f** is sensitive to moisture: it is reversed to starting **4f** at ~20 °C in a few minutes in methanol and even in conc. HNO_3.

Aminomethylation of polynitroalkanes (the Mannich reaction) is usually performed in two variants:[1,2] (1) condensation of nitro compound with aldehyde and corresponding amine, and (2) interaction of β-polynitroalcohol with amine. Up to now the Mannich reactions with nitroalkanes more acidic than trinitromethane remained unknown. In fact, under the standard aminomethylation conditions and in a broad pH range, *N*-dinitromethylazole with formaldehyde and ammonia or methylamine does not produce corresponding Mannich bases yielding merely *N*-dinitromethylazole salts [*e.g.*, with hexamethylenetetramine (HMTA)] and β-polynitro alcohols.

However, we found that the reaction of *N*-methylsulfamic acid sodium salt and **4b** in the stoichiometric ratio in water solution afforded Mannich base **6b** (Scheme 2) that was further converted into *N*-nitramine **7b**. The reagents ratio and the cation (Na) are crucial: the use of K derivative resulted only in K-salt of **1b**.

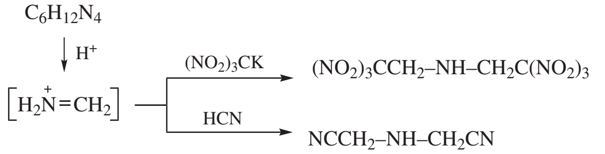
Amidomethylation of **1b** proceeds under mild conditions (20–60 °C) using pre-synthesized *N*-hydroxymethylacetamide to yield **8b**. This product, however, is not formed on condensation of **1b** with acetamide and formaldehyde, as well as corresponding alcohol **4b** with acetamide, since *N*-hydroxymethylacetamide can be generated only in alkaline media at high temperatures (100–150 °C), whereas the final steps of the transformation proceed in acidic media. Various *N*-hydroxymethylamines were used previously in the trinitromethane reaction,[15] although in some cases the condensation failed probably due to the absence of acid. The reagents ratio and solvent amount do not affect the **8b** yield. According to literature data on the acid catalysis for such processes,[16] the addition of H_2SO_4 (10% by volume) accelerates the reaction. So, the aminomethylation should be performed in optimal strong media, permitting, however, dissociation of *N*-nitromethylazoles to occur.



Scheme 2

In contrast to alcohol **4b**, amide **8b** does not undergo hydrolysis in solutions upon water dilution, however, upon the addition of alkali it quantitatively degrades to the starting *N*-dinitromethylazole **1b**.

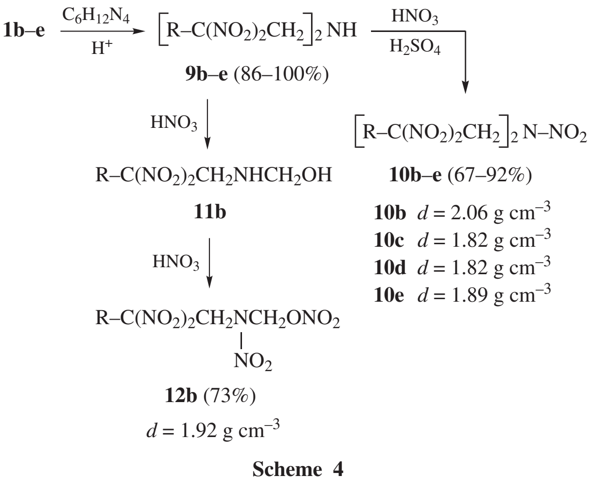
The aminomethylation rate in proton media is higher than that in aprotic solvents,[17] therefore water is the best solvent. The final covalent *N*-dinitromethylazoles are insoluble in water and precipitate from the reaction mixture shifting the equilibrium in the required direction.



Scheme 3

In some cases HMTA was used to generate the required *N*-hydroxymethylamine capable of aminomethylation. Its hydrolysis constant increases by 20-fold upon pH lowering from 6 to 2.[18] In particular, hydrolysis products of HMTA reacting with HCN produce the disubstituted Mannich base (Scheme 3) in concentrated acidic (HCl, H_2SO_4) water solutions.[19] The process is characterized by strong acidic catalysis. The equilibria between ammonia and formaldehyde in water containing HMTA and its hydrolysis products (such as protonated HMTA, methyleneimine, trimethyleneimine, and various *N*-hydroxymethylamines) were investigated in detail.[18] The US patent[20] describes trinitromethane aminomethylation with the proton concentration of 0.94 mol dm^{-3} (3.3% HCl) (Scheme 3). Meanwhile, in our reaction performed under the patent conditions HMTA reacts with *N*-dinitromethylazole **1b** yielding only corresponding HMTA salt in a small amount.

We found that the molar ratio **1b**:HMTA of 6:1 provided the optimal synthetic conditions for a good yield of **9b** (64%) (Scheme 4). The ratio was stoichiometric for formaldehyde, since the hydrolysis of HMTA resulted in formation of 6 mol of



Scheme 4

formaldehyde and 4 mol of ammonium ions. A double decrease of the **1b**:HMTA ratio caused the formation of merely HMTA salt of **1b**, despite the reaction pH was < 0. Small H_2SO_4 amounts (3% by volume in the reaction solution) accelerated the reaction by a factor of 2.5–3. The dilution of the reaction mixture with water resulted in formation of β-nitro alcohol **4b** only.

We developed a general and efficient synthetic procedure to prepare bis-Mannich bases directly from readily available *N*-dinitromethylazole K-salts by varying reagent concentrations and acidity of the media in H_2SO_4 solutions with the starting proton concentration [H^+] 2.3 times higher than that equivalent to 10% H_2SO_4, described in the patent.[20] Decrease of [H^+] to 1.2 mol dm^{-3} (equivalent to 6% H_2SO_4) sufficiently decelerated *N*-dinitroazole salt conversion.

Thus, Mannich bases **9b–e**, *N*-dinitromethylazoles with higher or the same acidity than that of trinitromethane, were synthesized from poorly soluble K-salts of **1b–e** in high yields (86–100%) in the heterogeneous media.

Using UV spectra the purity of compounds **9b–e** was confirmed by their susceptibility to a rapid and quantitative hydrolysis into alcohols: in nonabsolute methanol solution of **9b–e** we observed a maximum at 330–340 nm, corresponding to anion $N–C(NO_2)_2^-$,[3,4] which rapidly increased in time. The addition of 3–5% water to this solution increased the optical density, approving 100% hydrolysis of **9b–e** to **1b–e**. Molar weights of **9b–e** estimated from the optical density at the end of the hydrolysis and corresponding molar extinction coefficients of **1b–e**,[3,4] were in accordance with the **9b–e** structure, derived from molar ratio of *N*-dinitromethylazole:formaldehyde:ammonia equal to 2:2:1.

Mannich bases **9b–e** were nitrated at the N atom in the heterogeneous media using the $HNO_3–H_2SO_4$ (1:2, v/v) mixture. Usually the maximal nitration rate is observed in 89–90% H_2SO_4 solution as a result of considerable increase in [NO_2^+] concentration from 0 to 98% in 81–93% H_2SO_4, followed by subsequent reduction in 93–100% H_2SO_4.[21] In the case of N-nitration of nitrotriazoles **9c**,**d** and dinitropyrazole **9e** derivatives, the addition of 10 vol% water to the nitration mixture increased the yields of **10c**,**d**,**e** by 10–20%, finally enhancing the total yield up to 70–90%. In 100% HNO_3 in homogeneous solution the nitrotetrazole derivative **9b** dissociated to alcohol **11b**, followed by further nitration at N and O atoms that afforded **12b**.

The structures of **10b–e** were approved by microanalysis, IR, ^{1}H and ^{13}C NMR spectral data.

In conclusion, the chemistry here developed can be useful in the design of new high-energy materials.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mencom.2010.11.010.

References

1 *Chemistry of Nitro and Nitroso Groups*, ed. H. Foyer, John Wiley & Sons, New York–London–Sydney–Toronto, 1969.

2 S. S. Novikov, G. A. Shvekhgeimer, V. V. Sevost'yanova and V. A. Shlyapochnikov, *Khimiya alifaticheskikh i alitsiklicheskikh nitrosoedinenii* (*Chemistry of Aliphatic and Alicyclic Nitro Compounds*), Khimiya, Moscow, 1974 (in Russian).

3 V. V. Semenov, M. I. Kanischev, S. A. Shevelev and A. S. Kiselyov, *Tetrahedron*, 2009, **65**, 3441.

4 V. V. Semenov, S. A. Shevelev, A. B. Bruskin, M. I. Kanishchev and A. T. Baryshnikov, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 2014 (*Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 2077).

5 T. N. Hall, *J. Org. Chem.*, 1964, **29**, 3587.

6 M. A. Ilyushin and I. V. Tselinsky, *Ross. Khim. Zh. (Zh. Ross. Khim. Ob-va im. D.I. Mendeleeva)*, 1997, no. 4, 3 (in Russian).

7 V. V. Semenov and A. A. Gakh, *Symbiotic Chemistry of Aliphatic and Heterocyclic Nitro Compounds*, 218th ACS National Meeting, New Orleans, 1999.

8 V. I. Erashko, S. A. Shevelev and A. A. Fainzil'berg, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1977, 136 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1977, **26**, 117).

9 A. I. Ivanov, I. E. Chlenov, V. A. Tartakovskii, V. I. Slovetskii and S. S. Novikov, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1965, 1491 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1965, **14**, 1458).

10 V. A. Tartakovskii, I. E. Chlenov, G. V. Lagodzinskaya and S. S. Novikov, *Dokl. Akad. Nauk SSSR*, 1965, **161**, 136 (in Russian) (*Chem. Abstr.*, 1965, **62**, 14646).

11 A. A. Onishchenko and V. A. Tartakovskii, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1970, 948 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1970, **19**, 903).

12 E. M. Budynina, E. B. Averina, O. A. Ivanova, N. V. Yashin, T. S. Kuznetsova and N. S. Zefirov, *Synthesis*, 2004, **16**, 2609.

13 E. M. Budynina, E. B. Averina, O. A. Ivanova, T. S. Kuznetsova and N. S. Zefirov, *Tetrahedron Lett.*, 2005, **46**, 4657.

14 C. O. Parker, W. D. Emmons, A. S. Pagano, H. A. Rolewicz and K. S. McCallum, *Tetrahedron*, 1962, **17**, 89.

15 I. V. Ovchinnikov, A. S. Kulikov, M. A. Epishina, N. N. Makhova and V. A. Tartakovsky, *Izv. Akad. Nauk, Ser. Khim.*, 2005, 1306 (*Russ. Chem. Bull., Int. Ed.*, 2005, **54**, 1346).

16 H. E. Zaugg and W. B. Martin, in *Organic Reactions*, ed. A. C. Cope, John Wiley & Sons, New York–London–Sydney, 1965, vol. 14, p. 52.

17 F. F. Blicke, in *Organic Reactions*, ed. R. Adams, John Wiley & Sons, New York–London, 1942, vol. 1, p. 303.

18 J. F. Walker, *Formaldehyde*, Reinhold Publishing Corporation, New York, 1964.

19 J. V. Dubsky, *Chem. Ber.*, 1921, **54**, 2659.

20 W. Murray and Ch. Sauer, *US Patent* 3006957, 1957 (*Chem. Abstr.*, 1962, **56**, 2330c).

21 D. S. Ross, K. F. Kuhlmann and R. Malhotra, *J. Am. Chem. Soc.*, 1983, **105**, 4299.

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