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# Nucleophilic substitution in azasydnone-modified dinitroanisoles

**Tatyana K. Shkineva, Alexandr V. Kormanov and Igor L. Dalinger***

*N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: dalinger@ioc.ac.ru*

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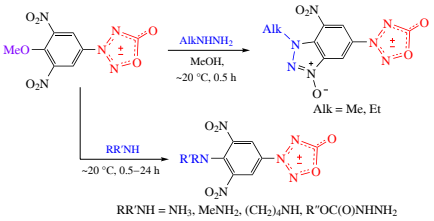
**Reactions of 3-(4-methoxy-3,5-dinitrophenyl)-1,2,3,4-oxatriazolium-5-olate with *N*-nucleophiles under mild conditions results in the displacement of the methoxy group leaving 1,2,3,4-oxatriazolium-5-olate (azasydnone) moiety intact. In the case of alkylhydrazines, further cyclization involving nitro group into benzo[*d*][1,2,3]triazole 3-oxides occurs.**



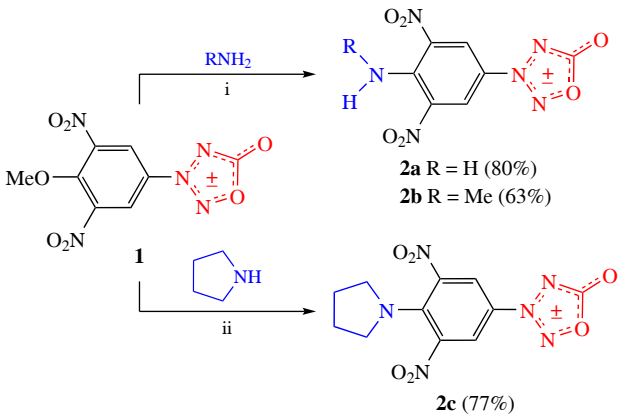

*Keywords*: azasydnones, dinitroanisoles, dinitroanilines, 1,2,3,4-oxatriazolium-5-olate, nucleophilic substitution, methoxy group, benzo[*d*][1,2,3]triazole 3-oxide, mesoionic compounds, nitrogen rich heterocycles.

Heterocycles play an important role in organic chemistry, and numerous studies concerning the development of new heterocyclic scaffolds have been published. Nearly 3/4 of all drug candidates have nitrogen heterocycles in their structures.[1] Mesoionic 1,2,3,4-oxatriazolium-5-olates (azasydnones),[2] relatively rare and poorly studied compounds, can be considered as bioisosters of 1,2,3-oxadiazolium-5-olates (sydnones), which are NO donors.[3] Azasydnones exhibit hypotensive,[4] antiplatelet,[5] thrombolytic,[3,6] or bronchiolytic activity,[7] are patented as promising substances for the treatment of sexual disorders,[8] and possess herbicidal properties.[9] Recently,[10–13] we have shown that the azasydnone cycle is of interest for the design of energetic compounds; this promoted the study of azasydnones both as high-energy density compounds[14–17] and as biologically active substances.[18,19] Therefore, the search for methods to synthesize new azasydnone derivatives is a current trend in the chemistry of heterocycles.

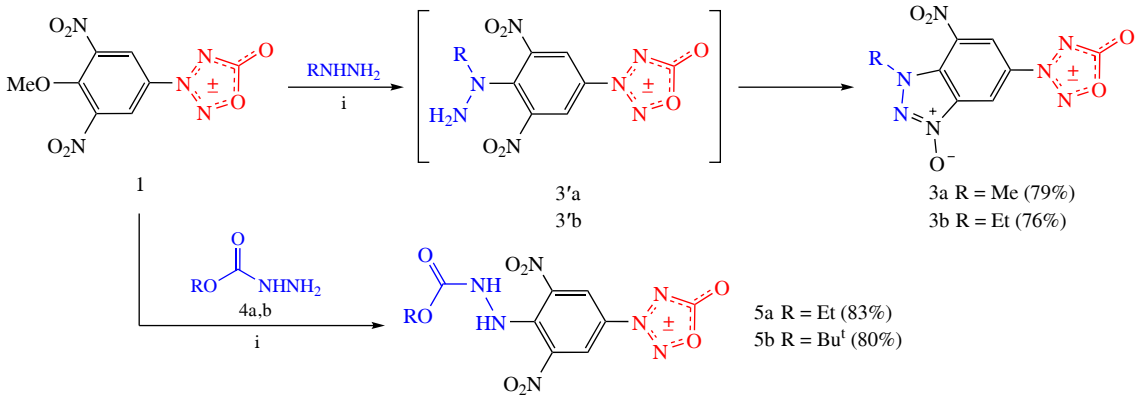
Previously, we have performed functionalization of arylazasydnones with preservation of the azasydnone cycle based on the nitration of phenylazasydnones[20] and on the $S_NAr$ reaction of nitroaryl-substituted azasydnones.[21,22] These studies demonstrated the diverse pattern of the reactivity of arylazasydnones in nucleophilic substitution reactions depending on both the nature of the nucleophile and the mutual arrangement of the substituents. At the same time, our work on the reactions of all azasydnones with ammonia showed that the ring-opening of the azasydnone moiety with the formation of azides and carboxamides did occur.[21] A similar result was often observed in reactions of arylazasydnones with primary or secondary amines.[21] In this work, we continued to study the behavior of nitroarylazasydnones in nucleophilic substitution reactions.

In fact, in 3-(4-methoxy-3,5-dinitrophenyl)azasydnone **1**[20] the methoxy group of the dinitroanisole part is activated by two *ortho*-nitro groups at once along with the azasydnone moiety at the *para*-position. As a result of their coordinated action, the azasydnone cycle is preserved under the action of ammonia at room temperature to give compound **2a**, the first example of aminodinitrophenyl-substituted azasydnone (Scheme 1). Thus, azasydnone **1** behaves similarly to trinitroanisole under these conditions.[23] The reaction of azasydnone **1** with methylamine and pyrrolidine also results in substituted dinitrophenylazasydnone amines **2b**,**c** (see Scheme 1). These reactions occur much faster than in the case of the corresponding azasydnones bearing a mononitroaryl moiety.[21] It should be noted that this synthesis performed for a longer time or with a large excess of the initial *N*-nucleophiles does not result in the azasydnone cycle opening and the products of its opening, *i.e.*, azides or carboxamides, were not detected in any of the cases.

Azasydnone-modified dinitroanisole **1** also undergoes nucleophilic substitution reactions with hydrazines (Scheme 2). In the case of alkylhydrazines, benzo[*d*][1,2,3]triazole 3-oxides **3a**,**b** are formed in just 30 min at room temperature. According to the literature data,[24] the reaction can involve either substituted or unsubstituted nitrogen atom in $RNHNH_2$, depending on the type of this substituent. Methyl- and ethylhydrazines would attack the dinitroanisole core by the substituted nitrogen atom due to its higher nucleophilicity. The presence of adjacent amino- and nitro-groups in the intermediates **3′a**,**b** formed leads to their further cyclization to give *N*-alkyl-substituted tricyclic compounds **3a**,**b**. The reactivity of compound **1** in the reaction with alkylhydrazines is much higher than that of picryl chloride




**Scheme 1** *Reagents and conditions*: i, MeOH, room temperature, 20 min; ii, MeCN, room temperature, 1 h.




**Scheme 2** *Reagents and conditions*: i, MeOH, room temperature, 0.5 h (for **3a**,**b**) or 24 h (for **5a**,**b**).

on treatment with hydrazine, a known method to synthesize benzo[*d*][1,2,3]triazole 3-oxides.[25]

On the other hand, electron acceptor groups in hydrazine, *e.g.*, the ethoxycarbonyl group, reduce the nucleophilicity of the nitrogen atom bound to them, and as a result, carbazates **4a**,**b** add to compound **1** through the unsubstituted nitrogen atom to form products **5a**,**b** (see Scheme 2). The substitution pattern in compounds **5a**,**b** cannot provide their further cyclization to benzo-[*d*][1,2,3]triazole oxides, in distinction to cases with AlkNHNH$_2$. Moreover, in contrast to all the above cases, the reaction with carbazates **4a**,**b** occurs much more slowly, namely, complete conversion of substrate **1** requires 24 h.

It should be noted that benzo[*d*][1,2,3]triazoles are promising compounds for a wide range of applications.[26] As isosteres of the purine nucleus, benzotriazole derivatives possess a wide range of biological activities.[27–29] They are used in materials chemistry,[30] including the applications as high-energy density compounds,[25,31] as metal corrosion inhibitors,[32] and as building blocks in organic chemistry.[33,34]

The compounds obtained were characterized by IR, $^1$H, $^{13}$C, $^{14}$N NMR spectroscopy and HRMS spectrometry. In all the cases, the IR spectra contained a peak at 1812 ± 26 cm$^{-1}$ corresponding to the carbonyl group in the azasydnone cycle. The $^{13}$C NMR spectra show characteristic signals in the region of δ 165–166 ppm corresponding to the carbon atom of the azasydnone cycle. The $^{14}$N NMR spectra, in addition to the signal of the nitro group, show a signal of the charged nitrogen atom of the cycle in the region from –78 to –80 ppm for compounds **2a**–**c** and **5a**,**b**, which shifts downfield in the case of fused products **3a**,**b** (~ –76 ppm).

In summary, we have found mild conditions that allow the directed functionalization of dinitroaryl-containing azasydnones with preservation of the azasydnone cycle to be performed using the S$_N$Ar reaction. As a result, novel 3-(4-amino-3,5-dinitrophenyl)-azasydnones were obtained. A one-step method for the synthesis of *N*-substituted benzo[*d*][1,2,3]triazole 3-oxides was developed, and the first representatives of such compounds containing the azasydnone substituent were obtained.

*Online Supplementary Materials*

Supplementary data associated with this article can be found in the online version at doi: 10.71267/mencom.7614.

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