chemistry proceedings

MDPI

Proceedings

Stable Anionic σ-Complexes of Highly Electrophilic Aromatics and C-Nucleophiles: Synthesis and Oxidation

Alexey Starosotnikov *, Maxim Bastrakov and Vladimir Kokorekin

N.D. Zelinsky Institute of Organic Chemistry RAS, Leninsky prosp. 47, Moscow 119991, Russia
* Correspondence: alexey41@list.ru

Abstract: Reactions of dinitrobenzoannulated heterocycles (furazan, thiadiazole, selenadiazole, pyridine) with anionic C-nucleophiles (mono- and diketones, nitroalkanes and related compounds) provided stable anionic adducts in high yields. Consecutive oxidation with ammonium cerium (IV) nitrate resulted in re-aromatization with formation of the corresponding substitution products, formally representing C-H-functionalized benzoheterocycles.

Keywords: CH-functionalization; nitroarenes; carbon nucleophiles; nucleophilic addition; anionic σ-complexes

1. Introduction

Functionalization of arenes provides their chemical diversity and opens a way to valuable substances that are widely used in medicine, pharmaceutics, agriculture, energetic and other areas. In recent years, the functionalization of the CH bond has become an important tool for the implementation of such processes. Nucleophilic substitution of hydrogen (S_NH) in arenes has acquired an intensive development as more prospective way of functionalization than classical SNAr processes occurring through ipso-substitution of a nucleofuge. Two general S_NH processes are oxidative (ONSH) and vicarious (VNSH) nucleophilic substitution of hydrogen proceeding through the generation of σ^H-adduct. In case of highly electrophilic substrates, the intermediate sigma-adducts can be isolated, identified and their chemical behavior can be studied.

It is well-known that highly electrophilic arenes and heteroarenes (superelectrophiles) readily form adducts with nucleophiles of various nature, including weak neutral nucleophiles such as π-excessive (het)arenes, enamines, etc. [1–3]. In case of C-nucleophiles these adducts can be isolated. Earlier we reported on reactions of some azolo[b]pyridines with 1,3-dicarbonyl compounds [4–6]. In this work we studied the reactions of dinitrobenzoannulated heterocycles (thiadiazole, selenadiazole, pyridine) with anionic C-nucleophiles (mono- and diketones, nitroalkanes and related compounds).

2. Results and Discussion

Among numerous highly electrophilic nitro (het)arenes the following were selected for this study: 4,6-dinitrobenzothiadiazole **1a** [7], 4,6-dinitrobenzoselenadiazole **1b** [8], 5,7-dinitroquinoline **1c** [9] and 5,7-dinitroquinoline-*N*-oxide **1d** [9]. It was found that their reactions with mono- and diketones as well as 2-nitropropane in the presence of a base provided the previously unknown stable anionic adducts **2** in high yields (Figure 1, Table 1). These adducts were isolated in pure form and characterized by NMR and HRMS. Oxidation of compounds **2** with ammonium cerium (IV) nitrate was studied. In some cases (Table 1, entries 1, 2, 6, 8) the corresponding substitution products **3** were isolated formally representing C-H-functionalized benzoheterocycles. In case of adduct **2c** decomposition was observed while in case of dinitroquinoline complex **2i** the starting compound **1c** appeared to be the sole isolable product. In all other cases ^{1}NMR spectra showed 1:1 mixture of target substitution product and the corresponding starting material (Table 1, entries 4, 5, 7, 10, 11).

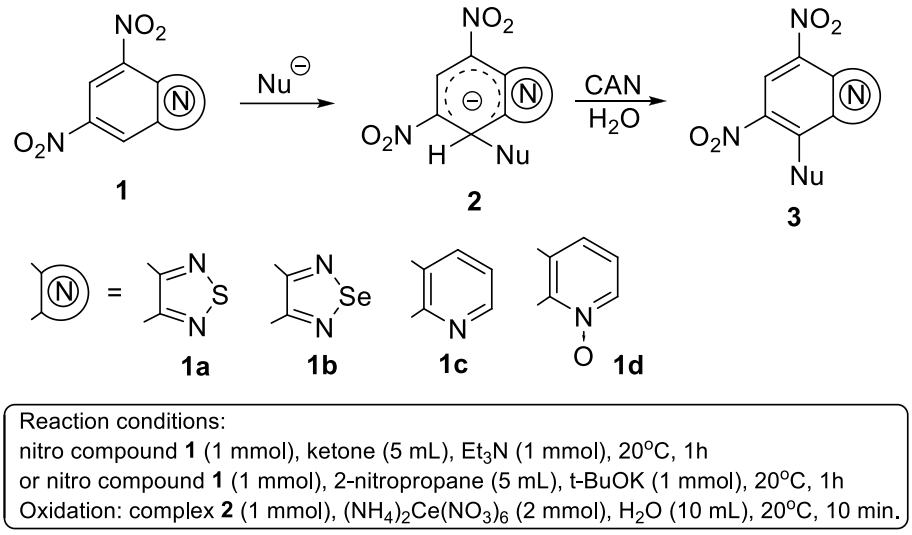

Figure 1. Formation of anionic complexes with C-nucleophiles and their oxidation.

Table 1. Yields of anionic σ-adducts **2** and oxidation products **3**.

Entry	Compound 1	NuH	Compound 2, Yield (%)	Compound 3, Yield (%)
1	**1a**	PhCOMe	**2a**, 88	**3a**, 47
2	**1a**	4-Cl-C_6H_4COMe	**2b**, 84	**3b**, 36
3	**1a**	Me_2CHNO_2	**2c**, 64	-[2]
4	**1a**	Cyclohexanone	**2d**, 67	-[3]
5	**1a**	MeCOCH_2COMe	**2e**, 87	-[3]
6	**1a**	Acetone	**2f**, 82	**3f**, 46
7	**1b**	Me_2CHNO_2	**2g**, 92	-[3]
8	**1c**	PhCOMe	**2h**, -[1]	**3h**, 28
9	**1c**	Me_2CHNO_2	**2i**, 98	-[4]
10	**1d**	PhCOMe	**2j**, 77	-[3]
11	**1d**	Me_2CHNO_2	**2k**, 24	-[3]

[1] Compound **2h** was not isolated in pure form and was oxidized without further purification. [2] Decomposition. No identified product was isolated. [3] A 1:1 mixture of oxidation product **3** and starting compound **1** formed [4] Compound **1c** was recovered (20%) along with unidentified decomposition products.

As it follows from the data presented in Table 1, the oxidation of adducts **2** generally proceed in two directions: formation of target substitution products **3** and decomposition to give starting compounds **1**. Such behavior of anionic σ-complexes is not surprising since it was reported earlier for 1,3,5-trinitrobenzene (TNB) adducts with CH-acidic compounds [10]. Kinetic study of decomposition of TNB-acetophenone complex revealed strong dependence on the pH of the reaction media. However, in number of cases we were able to isolate polyfunctional derivatives of highly electrophilic benzoannulated heterocycles (Figure 2).

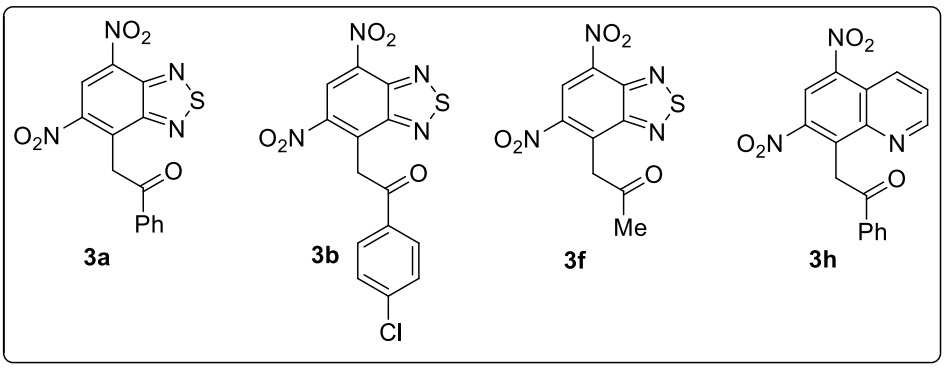

Figure 2. Compounds synthesized by oxidation of anionic σ-complexes of dinitrobenzohetarenes and C-nucleophiles.

3. Experimental Procedures

Anionic σ-adducts 2a,b,d-f,h,j (general procedure). To a solution of dinitro compound **1** in appropriate ketone (5 mL) was added Et_3N (0.14 mL, 1 mmol). The mixture was stirred for 1 hour at 20 °C, poured in ether (50 mL) and the resulting precipitate was filtered off, washed with ether and dried to give target adduct (see Table 1 for yields).

Anionic σ-adducts 2c,g,I,k (general procedure). To a solution of dinitro compound **1** in 2-nitropropane (5 mL) was added t-BuOK (0.112 g, 1 mmol). The mixture was stirred for 1 hour at 20 °C, poured in ether (50 mL) and the resulting precipitate was filtered off, washed with ether and dried to give target adduct (see Table 1 for yields).

Oxidation of adducts 2 (general procedure). To a solution of the corresponding adduct **2** (1 mmol) in 5 mL of H_2O was added a solution of $(NH_4)_2Ce(NO_3)_4$ (1.1 g, 2 mmol) in H_2O (5 mL). The mixture was stirred for 10 min at 20 °C and extracted with $CHCl_3$ (3 × 10 mL). Organic layers were washed with brine, dried over Na_2SO_4 and evaporated to give target compound **3** which was then purified by column chromatography (SiO_2, $CHCl_3$) (see Table 1 for yields).

4. Conclusions

Thus, a series of the previously unknown dinitrobenzoazoles and azines functionalized at benzene ring were synthesized using stable anionic σ-adducts as key intermediates of C-H functionalization of π-deficient nitroarenes.

Author Contributions: Conceptualization, A.S. and M.B.; methodology, A.S., M.B. and V.K.; investigation, A.S. and V.K.; writing—original draft preparation, A.S.; writing—review and editing, M.B.; project administration, V.K. All authors have read and agreed to the published version of the manuscript.

Funding: This research was funded by the Russian Science Foundation, grant number 19-73-20259.

Conflicts of Interest: The authors declare no conflict of interest.

References

1. Terrier, F.; Kizilian, E.; Halle, J.C.; Buncel, E. 4,6-Dinitrobenzofuroxan: A stronger electrophile than the p-nitrobenzenediazonium cation and proton. *J. Am. Chem. Soc.* **1992**, *114*, 1740–1742.
2. Remennikov, G.Y.; Kempf, B.; Ofial, A.R.; Polborn, K.; Mayr, H. 5-Methoxyfuroxano[3,4-d]pyrimidine: A highly reactive neutral electrophile. *J. Phys. Org. Chem.* **2003**, *16*, 431–437.
3. Remennikov, G.Y.; Pirozhenko, V.V.; Vdovenko, S.I.; Kravchenko, S.A. -Complexes in the pyrimidine series. 13. Reaction of 7- and 5-methoxyfuroxano[3,4-d]pyrimidines with some C-nucleophiles. *Chem. Heterocycl. Compd.* **1998**, *34*, 104–110.
4. Starosotnikov, A.M.; Shkaev, D.V.; Bastrakov, M.A.; Fedyanin, I.V.; Shevelev, S.A.; Dalinger, I.L. Nucleophilic dearomatization of 4-aza-6-nitrobenzofuroxan by CH-acids in the synthesis of pharmacology-oriented compounds. *Beilstein J. Org. Chem.* **2017**, *13*, 2854–2861.

5. Starosotnikov, A.M.; Shkaev, D.V.; Bastrakov, M.A.; Fedyanin, I.V.; Shevelev, S.A.; Dalinger, I.L. Dearomatization of oxa- or selenadiazolopyridines with neutral nucleophiles as an efficient approach to pharmacologically relevant nitrogen compounds. *Mendeleev Commun.* **2018**, *28*, 638–640.
6. Starosotnikov, A.M.; Ilkov, K.V.; Bastrakov, M.A.; Fedyanin, I.V.; Kokorekin, V.A. Mild and efficient addition of carbon nucleophiles to condensed pyridines: Influence of structure and limits of applicability. *Chem. Heterocycl. Compd.* **2020**, *56*, 92–100.
7. Pesin, V.G.; Khaletskii, A.M.; Sergeev, V.A. *J. Gen. Chem. USSR* **1963**, *33*, 1714–1719.
8. Elvidge, J.A.; Newbold, G.T.; Percival, A.; Senciall, I.R. 3-Nitro-*o*-phenylenediamines: A new route. *J. Chem. Soc.* **1965**, 5119-5120.
9. Starosotnikov, A.M.; Nikol'skiy, V.V.; Borodulya, A.N.; Kachala, V.V.; Bastrakov, M.A.; Solkan, V.N.; Shevelev, S.A. Synthesis and functionalization of 5,7-dinitroquinoline and its N-oxide. *Asian J. Org. Chem.* **2016**, *5*, 685–690.
10. Renfrow, R.A.; Strauss, M.J.; Terrier, F. Stability of carbon-bonded anionic sigma-complexes. 3. Decomposition in aqueous acidic media. *J. Org. Chem.* **1980**, *45*, 471–475.