

New ring-transformation reaction: the conversion of a tetrazole ring into a 1-oxa-3,4-diazine ring

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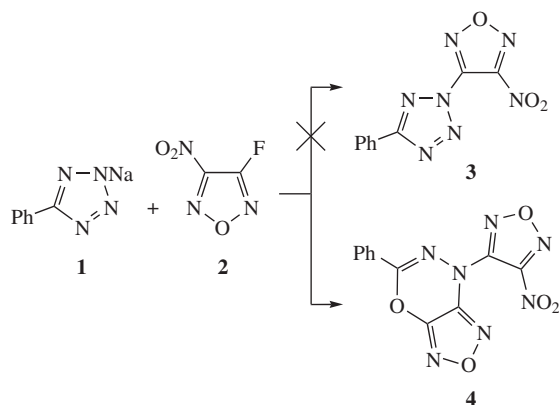
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New ring cleavage/ring closure reactions of tetrazole derivatives provide a route to a new heterocyclic system such as furazano[3,4-*e*]-1-oxa-3,4-diazine, which was characterized by ¹H, ¹³C and ¹⁴N NMR spectroscopy and X-ray crystallography.

Tetrazoles are useful reagents in heterocyclic synthesis and are widely used in ring cleavage/ring closure reactions with electrophilic reagents to form new C–N and N–N bonds. These reactions usually proceed *via* a dipolar nitrilimine intermediate; the resulting dipole frequently being designed to react further in a tandem electrocyclic cyclization process to generate a new heterocyclic ring.¹ Despite a relatively large number of known tri-, five-, and six-membered nitrogen heterocycles prepared in this way, there are very few incorporating oxygen or sulfur in new ring.^{1,2}

We recently discovered a reaction of tetrazole ring recyclization (Scheme 1) during an unsuccessful attempt to synthesize 3-(3-nitrofurazan-4-yl)-1-phenyltetrazole **3** from 3-fluoro-4-nitrofurazan **2**³ and the sodium salt of 1-phenyltetrazole **1**. We have investigated the reactivity of **2** with salt **1** anticipating a resulting typical nucleophilic displacement product.⁴



Scheme 1

On stirring these reactants in glym at room temperature, the rapid consumption of nitrofurazan was detected by TLC.[†] From this complex reaction we could not isolate **3**, but only a rather

low yield of a new product (34%). On isolation the product was found to have a molecular formula of C₁₁H₅N₇O₅, suggesting that two molecules of the starting nitrofurazan participated in the reaction and the new product resulted from destruction of the tetrazole ring. The structure of furazano[3,4-*e*]-1-oxa-3,4-diazine **4** was suggested by its ¹H, ¹³C and ¹⁴N NMR and mass spectra.[‡] Thus, the electron impact mass spectrum of **4** showed a strong molecular ion peak (*m/z* 315, 60%) and significant peaks due to loss of a nitro group (*m/z* 269, 5%), a nitrofurazanyl moiety (*m/z* 201, 23%) and of PhCN (*m/z* 212, 16%) from the molecular ion as might be expected from the structure.

In order to characterize the bicyclic compound unambiguously, a single crystal X-ray determination was carried out.[§] The structure of product **4** is based on a heterocyclic system in which the 1-oxa-3,4-diazine nucleus has been originated and annulated with the furazan ring. The asymmetric unit cell of **4** contains two molecules A and A' with similar structures (in Figure 1, only molecule A is shown).

The main difference in the molecular structures of A and A' is that the nitro group in A' is disordered over two positions while A molecule is totally ordered. In both molecules, Ph and furazan fragments are nearly coplanar to the central fused ring. The nitro group is almost perpendicular to the furazan ring that is due to steric repulsion between nitro oxygen and N1(1')

[‡] For compound **4**: mp 168–170 °C (CCl₄). ¹H NMR (CDCl₃) δ: 7.35–7.85. ¹³C NMR (CDCl₃) δ: 125.5, 127.0, 129.2, 133.5, 138.0, 144.8, 145.2, 151.6, 155.7. ¹⁴N NMR (CDCl₃) δ: –35.8 (NO₂). EI-MS, *m/z*: 315 [M]⁺, 269 [M – NO₂]⁺, 212, 211, 201, 171, 143, 129, 103, 77. Found (%): C, 41.94; H, 1.59; N, 31.08. Calc. for C₁₁H₅N₇O₅ (315.20) (%): C, 41.92; H, 1.60; N, 31.11.

[§] X-Ray quality single crystals of compound **4** were grown by slow evaporation of a CHCl₃ solution at room temperature. The single crystal (C₁₁H₅N₇O₅) is monoclinic, space group *P*2₁/*c*: *a* = 13.820(3), *b* = 16.074(3) and *c* = 11.388(2) Å, β = 107.273(4)°, *V* = 2415.8(8) Å³, *Z* = 8, *M* = 315.2, *d*_{calc} = 1.733 g cm^{–3}, μ = 0.124 mm^{–1}. 16515 reflections were collected on a SMART 1000 CCD diffractometer [λ(MoKα) = 0.71073 Å, graphite monochromator, ω-scans, 2θ < 56°] at 120 K. The structure was solved by the direct methods and refined by the full-matrix least-squares procedure in anisotropic approximation. 5759 independent reflections [*R*_{int} = 0.0287] were used in the refinement procedure that was converged to *wR*₂ = 0.0956 calculated on *F*_{hkl}² [GOF = 1.040, *R*₁ = 0.0518 calculated on *F*_{hkl} using 3557 reflections with *I* > 2σ(*I*)].

CCDC 714466 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2009.

[†] To a solution of salt **1** (0.34 g, 2 mmol) in dry glym (5 ml) was added a solution of **2** (0.27 g, 2 mmol) in dry glym (1 ml) all at once with efficient stirring. The mixture was allowed to stir at room temperature for 1 h. An examination of the reaction mixture by TLC showed the disappearance of almost all of the starting material. Then, 50 ml of CH₂Cl₂ and 40 ml of water were added. The organic solvent was collected, washed with cold water and dried. After removal of CH₂Cl₂ under reduced pressure, the residue was purified by chromatography on silica (pentane–CH₂Cl₂ 5:2 as an eluent) to provide compound **4** (0.11 g, 34%) as a colourless solid.

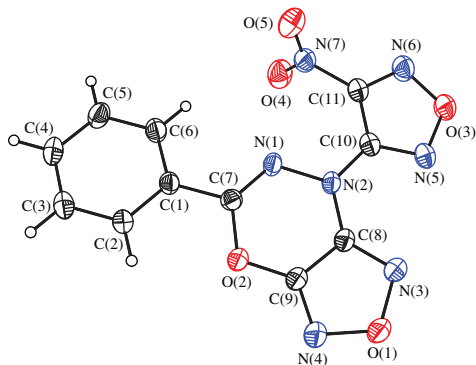


Figure 1 ORTEP view (thermal ellipsoids are shown with 50% probability) of 2-(3-nitrofuran-4-yl)-4-phenyl-4*H*-1,3,4-furazano[3,4-*e*]oxadiazine **4**. Selected bond lengths (Å): C(1)–C(7) 1.464(3) [1.464(3)], C(7)–N(1) 1.271(2) [1.274(2)], C(7)–O(2) 1.396(2) [1.393(2)], C(9)–O(2) 1.357(2) [1.357(2)], N(1)–N(2) 1.399(2) [1.395(2)], C(8)–N(2) 1.368(2) [1.369(2)], C(10)–N(2) 1.371(2) [1.369(2)]. Bonds lengths in square brackets correspond to A' molecule.

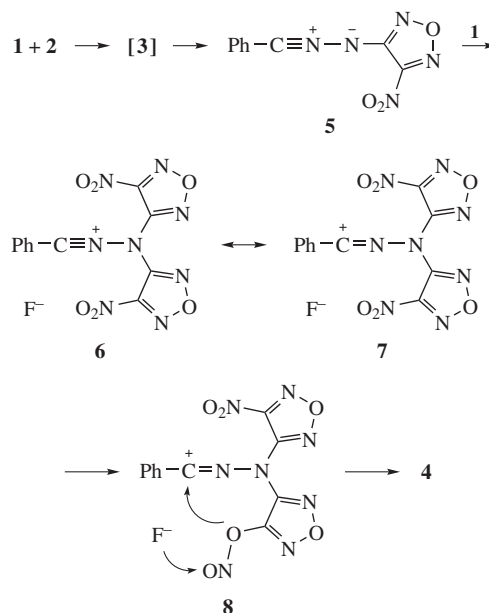
atoms. The planar structure of **4** implies the presence of π -conjugation. The bond lengths at N2(2') atom are in agreement with its planar geometry and C1(1')–C7(7') and C9(9')–O2(2') bonds are shorter than single C(ar)–C(O) bonds.⁵ This structure can be compared to an example of fused 1-oxa-3,4-diazine studied by X-ray method⁶ in which the six-membered ring adopts a boat conformation and π -conjugation is broken, which results in shortening of C=N bond and elongation of bonds at N2(2') atom and O2(2')–C9(9') bond.

In the crystal of **4**, molecules form a layered structure by means of O...O, O...N and stacking interactions. Each layer consists of the molecules of the same type. As in many cases of relatively dense molecules involving a nitro group and a furazan ring,⁷ the crystal structure of **4** is also stabilized by numerous slightly shortened O...O, O...N and N...N intermolecular contacts with distances at the boundary between normal and shortened ones.

The formation of this bicyclic system was particularly surprising, suggesting that a new type of reaction had occurred. The mechanism of this unusual reaction has not been unequivocally established, but one reasonable possibility is outlined in Scheme 2. Here, it is proposed that the nucleophilic displacement of fluoride at the furazan produces disubstituted tetrazole **3** in the normal manner. This labile intermediate is not isolated but is converted into nitrilimine **5** by opening of the tetrazole ring with extrusion of N₂. The second molecule of the highly electrophilic furazan **1** attacks nitrilimine **5** leading to salt **6**. This ionic species then undergoes a charge shift to produce **7**, which subsequently undergoes intramolecular nitro-nitrite rearrangement⁸ to give **8**. The final step involves oxadiazine ring closure, which is driven by the lone pair of electrons on oxygen, resulting in the elimination of FNO to generate final product **4**.

It is especially significant considering that the reaction is carried out at room temperature *i.e.* against the prevailing feeling that high temperatures are required to ring transformations of N-substituted tetrazole intermediates.

Note that ring cleavage/ring closure reactions of tetrazoles bearing at the N atom a (het)aryl moiety involving an *ortho* nitro group provide a route to five-membered heterocycles. These transformations require a tetrazole nitrogen loss and retaining the nitro group for nitroaryl moieties,⁹ or the participation in cyclization of the hetaryl moieties' carbon atom with the nitro group retained.^{9(a),10} However, in the foregoing researches deliberately prepared stable disubstituted tetrazoles were subjected to ring cleavage/ring closure reactions, *i.e.*, the reaction was lacking an electrophile (*o*-halonitro compound) able to react



Scheme 2

with nitrilimine intermediates yielding a compound of type **6**. The nitro-nitrite rearrangement is also achievable for the structure types used before, though it is facilitated by electron-acceptor substituents or can be induced by external impact.¹¹ It means that the discussed case may not be unique, and a similar reaction is likely to be encountered outside of the furazan family.

A strong driving force for described herein reaction would be derived from the high electrophilicity of fluorofurazans and susceptibility of nitrofurazans to intramolecular nitro-nitrite rearrangement in the presence of different nucleophiles. This reaction provides a facile route to potentially very interesting heterocyclic systems.

References

- (a) H. C. van der Plas, *Ring Transformations of Heterocycles*, Academic Press, London, New York, 1973, vols. 1, 2; (b) R. N. Butler, in *Advanced Heterocyclic Chemistry*, Academic Press, New York, 1977, vol. 21, pp. 323–435; (c) R. N. Butler, in *Comprehensive Heterocyclic Chemistry II*, ed. R. C. Storr, Pergamon, Oxford, 1996, vol. 4, p. 621; (d) D. Moderhack, *J. Prakt. Chem.*, 1998, **340**, 687; (e) G. I. Koldobskii and V. A. Ostrovskii, *Usp. Khim.*, 1994, **63**, 847 (*Russ. Chem. Rev.*, 1994, **63**, 797).
- G. I. Koldobskii and S. E. Ivanova, *Zh. Obshch. Khim.*, 1994, **64**, 1698 (*Russ. J. Gen. Chem.*, 1994, **64**, 1512).
- A. B. Sheremetev, N. S. Aleksandrova and D. E. Dmitriev, *Mendeleev Commun.*, 2006, 163.
- (a) A. B. Sheremetev, V. O. Kulagina, I. L. Yudin and N. E. Kuzmina, *Mendeleev Commun.*, 2001, 112; (b) A. B. Sheremetev, V. O. Kulagina, I. A. Kryazhevskikh, T. M. Melnikova and N. S. Aleksandrova, *Izv. Akad. Nauk, Ser. Khim.*, 2002, 1411 (*Russ. Chem. Bull., Int. Ed.*, 2002, **51**, 1533); (c) V. O. Kulagina, N. S. Aleksandrova, A. B. Sheremetev and Yu. A. Strelenko, *Izv. Akad. Nauk, Ser. Khim.*, 2003, 1369 (*Russ. Chem. Bull., Int. Ed.*, 2003, **52**, 1447); (d) A. B. Sheremetev, V. A. Andrianov, E. V. Mantseva, E. V. Shatunova, N. S. Aleksandrova, V. O. Kulagina, T. M. Melnikova, I. L. Yudin, D. E. Dmitriev, B. B. Averkiev and M. Yu. Antipin, *Izv. Akad. Nauk, Ser. Khim.*, 2004, 569 (*Russ. Chem. Bull., Int. Ed.*, 2004, **53**, 596).
- (a) F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen and R. Taylor, *J. Chem. Soc., Perkin Trans. 2*, 1987, S1; (b) *Cambridge Structural Database, version 5.29*, November, 2007.
- V. N. Knyazev, O. V. Shishkin and V. N. Drozd, *Zh. Org. Khim.*, 1999, **35**, 957 (*Russ. J. Org. Chem.*, 1999, **35**, 933).
- (a) R. L. Willer, R. S. Day, R. D. Gilardi and C. J. George, *J. Heterocycl. Chem.*, 1992, **29**, 1835; (b) A. B. Sheremetev, E. V. Mantseva, N. S. Aleksandrova, V. S. Kuz'min and L. I. Khmel'nitskii, *Mendeleev Commun.*, 1995, 25; (c) A. K. Zelenin, M. L. Trudell and R. D. Gilardi, *J. Heterocycl. Chem.*, 1998, **35**, 151; (d) R. W. Beal, C. D. Incarvito, B. J. Rhatigan, A. L. Rheingold and T. B. Brill, *Propellants, Explosives, Pyrotechnics*,

- 2000, **25**, 277; (e) B. B. Averkiev, M. Yu. Antipin, A. B. Sheremetev and T. V. Timofeeva, *Acta Crystallogr., Sect. C.*, 2003, **C59**, 383; (f) A. B. Sheremetev, E. A. Ivanova, N. P. Spiridonova, S. F. Melnikova, I. V. Tselinsky, K. Yu. Suponitsky and M. Yu. Antipin, *J. Heterocycl. Chem.*, 2005, **42**, 1237; (g) A. B. Sheremetev, I. L. Yudin and K. Yu. Suponitsky, *Mendeleev Commun.*, 2006, 264.
- 8 (a) A. B. Sheremetev, O. V. Kharitonova, T. M. Mel'nikova, T. S. Novikova, V. S. Kuz'min and L. I. Khmel'nitskii, *Mendeleev Commun.*, 1996, 141; (b) A. B. Sheremetev, V. O. Kulagina, N. S. Aleksandrova, D. E. Dmitriev, Yu. A. Strelenko, V. P. Lebedev and Yu. N. Matyushin, *Propellants, Explosives, Pyrotechnics*, 1998, **23**, 142; (c) A. B. Sheremetev, S. E. Semenov, V. S. Kuzmin, Yu. A. Strelenko and S. L. Ioffe, *Chem. Eur. J.*, 1998, **4**, 1023; (d) A. B. Sheremetev and N. S. Aleksandrova, *Mendeleev Commun.*, 1998, 238; (e) A. B. Sheremetev, O. V. Kharitonova, E. V. Mantseva, V. O. Kulagina, E. V. Shatunova, N. S. Aleksandrova, T. M. Melnikova, E. A. Ivanova, D. E. Dmitriev, V. A. Eman, I. L. Yudin, V. S. Kuzmin, Yu. A. Strelenko, T. S. Novikova, O. V. Lebedev and L. I. Khmel'nitskii, *Zh. Org. Khim.*, 1999, **35**, 1555 (*Russ. J. Org. Chem.*, 1999, **35**, 1525); (f) A. B. Sheremetev, N. S. Aleksandrova, T. M. Melnikova, T. S. Novikova, Y. A. Strelenko and D. E. Dmitriev, *Heteroatom Chem.*, 2000, **11**, 48; (g) A. B. Sheremetev, N. S. Aleksandrova, E. V. Mantseva and D. E. Dmitriev, *Khim. Geterotsikl. Soedin.*, 2003, 1541 [*Chem. Heterocycl. Compd. (Engl. Transl.)*, 2003, **39**, 1357].
- 9 (a) A. Konnecke, R. Dorre and E. Lippmann, *Tetrahedron Lett.*, 1978, 2071; (b) A. Konnecke, P. Lepom and E. Lippmann, *Z. Chem.*, 1978, **18**, 214; (c) N. A. Evans, *Aust. J. Chem.*, 1981, **34**, 691; (d) P. G. Houghton, D. F. Pipe and C. W. Rees, *J. Chem. Soc., Perkin Trans. 1*, 1985, 1471.
- 10 (a) H. Reimlinger, J. J. M. Vandewalle, G. S. D. King, W. R. F. Lingier and R. Merenyi, *Chem. Ber.*, 1970, **103**, 1918; (b) G. W. Adelstein, *J. Med. Chem.*, 1973, **16**, 309; (c) A. Konnecke and E. Lippmann, *Z. Chem.*, 1978, **18**, 175; (d) A. Konnecke, C. Richter and E. Lippmann, *Z. Chem.*, 1979, **19**, 101.
- 11 (a) J. H. Beynon, M. Bertrand and R. G. Cooks, *J. Am. Chem. Soc.*, 1973, **95**, 1739; (b) C. W. Hand, C. Merritt and C. DiPietro, *J. Org. Chem.*, 1977, **42**, 841; (c) V. V. Plakhtinskii, V. A. Ustinov and G. S. Mironov, *Izv. Vyssh. Uchebn. Zaved., Khim. Khim. Tekhnol.*, 1985, **28**, 3 (in Russian); (d) H. Sugimoto and Y. Kurokawa, *J. Org. Chem.*, 1989, **54**, 5945.

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