Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2015, **25**, 476–478
Mendeleev Communications

Unexpected formation of 6-[benzofuran-3(2*H*)-ylidene]-3,3a,9,9a-tetrahydroimidazo[4,5-*e*]thiazolo[3,2-*b*][1,2,4]triazine-2,7-dione derivative

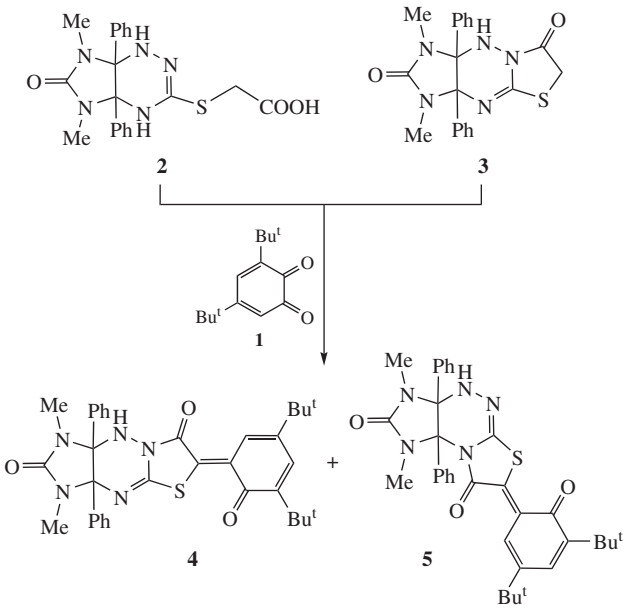
Angelina N. Kravchenko,*[a] Sergei V. Vasilevskii,[a] Galina A. Gazieva[a] and Yulia V. Nelyubina[b]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax:+7 499 135 5328; e-mail: kani@server.ioc.ac.ru*
[b] *A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, 119991 Moscow, Russian Federation. Fax:+7 499 135 5085; e-mail: unelya@xrlab.ineos.ac.ru*

DOI: 10.1016/j.mencom.2015.11.027

Condensation of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone with 1,3-dimethyl-3a,9a-diphenyl-3,3a,9,9a-tetrahydroimidazo[4,5-*e*]-thiazolo[3,2-*b*][1,2,4]triazine-2,7(1*H*,6*H*)-dione in AcOH gives a new 6-(benzofuranylidene)tetrahydroimidazo[4,5-*e*]thiazolo[3,2-*b*]-[1,2,4]triazine-2,7-dione derivative, whose structure was confirmed by X-ray diffraction analysis.

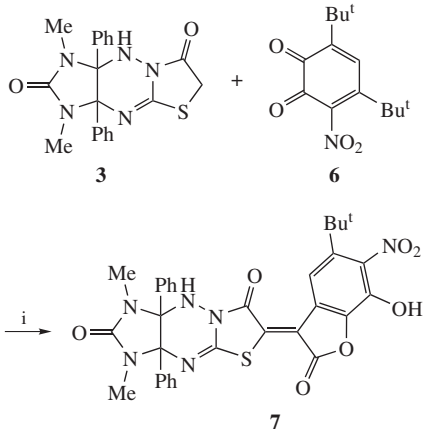
The reactivity of 1,2-benzoquinone derivatives is being studied incessantly.[1–4] Their reactions with active methylene heterocyclic compounds can proceed by various pathways depending on the reactant structure.[1] In many cases, multistage reactions involving 1,2-benzoquinones begin with aldol condensation, then its products undergo subsequent transformations, probably due to their instability. We have recently found that 3,5-di(*tert*-butyl)-1,2-benzoquinone **1** can undergo aldol condensation with [(imidazotriazin-3-yl)thio]acetic acid **2** and imidazothiazolotriazinedione **3** to give two isomers **4** and **5** (Scheme 1).[4] Compounds **2** and **3** undergo similar reactions with N-substituted isatins.[5,6]



Scheme 1

Here, we report on the reaction of tricycle **3** with 3,5-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** following the unusual pathway, which results in a new polyheterocyclic compound **7** as the main product (Scheme 2).

The reaction of nitroquinone **6** with tricyclic compound **3** was studied under various conditions: glacial acetic acid as the solvent, reaction time from 30 min to 7 days, reaction temperature from 22 to 70 °C. Reaction progress was followed by TLC (ethyl acetate–hexane, 1:2). The compound with $R_f = 0.25$ was isolated and its structure was determined based on X-ray diffraction (XRD) data. Unexpectedly, it turned out to be a hitherto unknown polyheterocyclic compound **7** which contained imidazolidine, triazine, thiazolidine and benzofuranylidene moieties (see Scheme 2).[†] The best conditions for the synthesis of compound **7** in an optimum yield of 47% were as follows: keeping the reaction mixture in glacial acetic acid for 7 days at 22 °C.

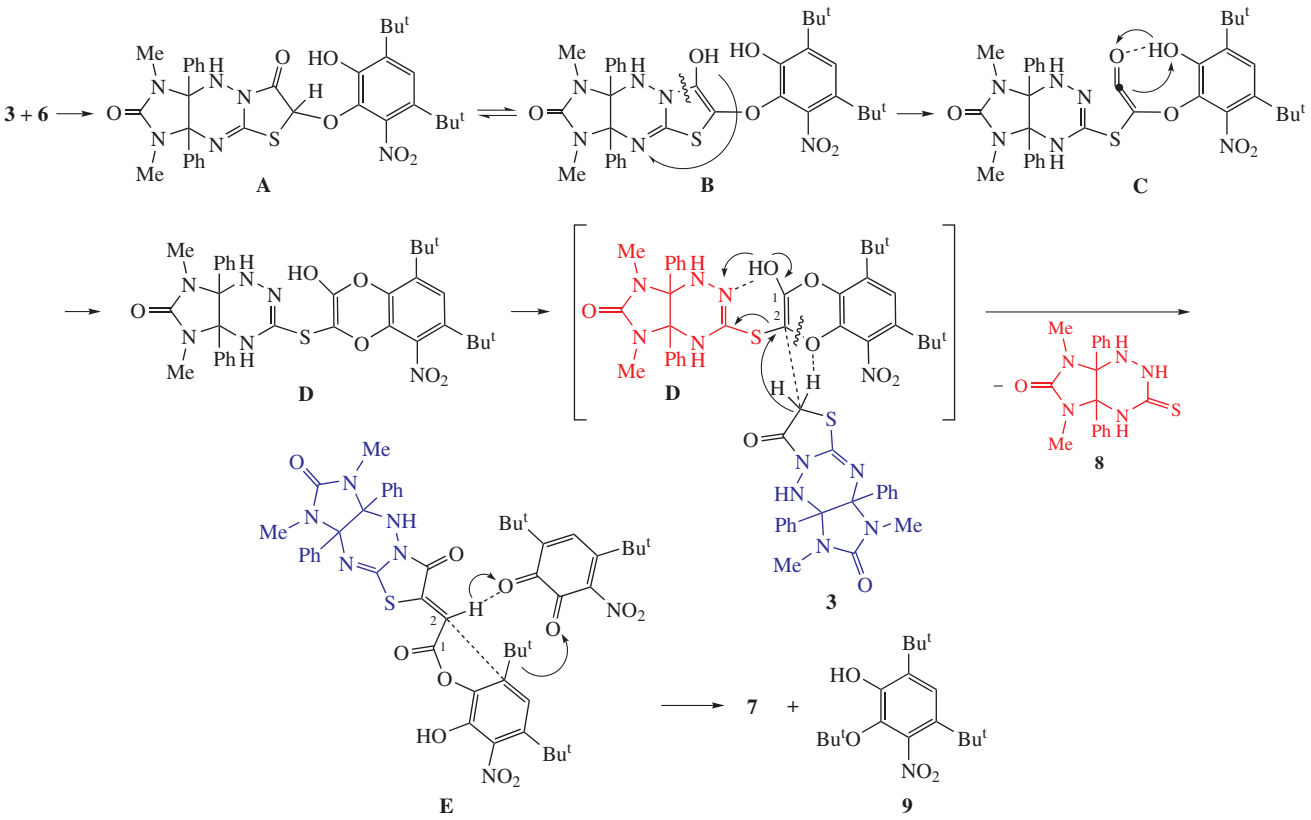


Scheme 2 *Reagents and conditions*: i, AcOH, 22 °C, 7 days.

The presence of a furanylidene moiety in the product molecule was particularly unusual. Apparently, nitroquinone **6** does not

[†] ^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer (300.13 MHz) in DMSO-d_6 (TMS as the internal standard). Melting points were determined in a Sanyo GALLENKAMP instrument. A 1100 LC/MSD (Agilent Technologies, USA) LC-mass spectrometer equipped with an ELSD PL-ELS-1000 mass detector and an Onyx monolithic C18 column (50×4.6 mm) was used. The flow rate of the eluent was 3.75 ml min^{-1} [eluent A: acetonitrile–water (2.5:97.5) containing 0.1% of trifluoroacetic acid; eluent B: acetonitrile–water (97.5:2.5) containing 0.1% of trifluoroacetic acid; elution mode gradient: 100% A (0 min) → 100% B (4.2–4.6 min) → 100% A (4.8 min)]. Compound **7**, $R_t = 4.37$ min.

Tricycle **3** was prepared by the reaction of bromoacetic acid with imidazotriazine **8** in glacial acetic acid.[8] Imidazotriazine **8** was obtained by α-ureidoalkylation of thiosemicarbazide with 1,3-dimethyl-4,5-dihydroxy-4,5-diphenylimidazolidin-2-one,[9] which in turn was synthesized by the reaction of 1,2-dioxo-1,2-diphenylethane (benzil) with 1,3-dimethylurea.[10] 4,6-Di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** was obtained by treatment of 2,4,6-tri(*tert*-butyl)phenol with 60% nitric acid.[11]



Scheme 3

react with tricyclic compound **3** to give products of aldol condensation, in contrast to the reaction with quinone **1**, due to steric factors (the nitro group is in the carbonyl plane). It seems likely that the nitroquinone is involved in cascade process initiated by nucleophilic 1,4-addition of active methylene compound **3** to benzoquinone system to afford intermediate **A** (Scheme 3). The mechanism of benzodioxin **D** formation involves opening of the thiazolidine ring (**A** → **C**). The further transformation of **D** is possible by the 'concerted' mechanism. The reaction of dioxin adduct **D** with the second tricyclic molecule **3** can result in the dioxin ring opening with elimination of imidazotriazine **8** to give ester **E**. An example of dioxin ring opening with C-nucleophiles was described in detail previously.[7] Intramolecular condensation **E** → **7** occurs with oxidation and de-*tert*-butylation, which involves a second molecule of nitro-1,2-benzoquinone **6**. The *tert*-butyl ether of pyrocatechol **9** was not detected in the reaction mixture. However, similar intramolecular condensations involving de-*tert*-butylation were discussed in literature.[1(*b*)]

Single crystals of compound **7** for XRD were grown from isopropyl alcohol resulting in a 1:1 crystallosolvate **7**. According to XRD data (Figure 1),‡ the imidazolidine and triazine cycles in **7** adopt an envelope conformation with the C(3) and N(2) atoms deviating by 0.39(1) and 0.50(1) Å, respectively; the other heterocycles are planar within 0.02(1) Å. The planarity of the central fragment is apparently also governed by a C(27)–H···O(2) [H···O 2.20(1) Å, ∠CHO 134(1)°] intramolecular bond and a O(3)···S(1) contact [O···S 2.728(3) Å]. The latter may be rationalized as a charge transfer from a lone electron pair of the oxygen atom O(3) to the σ*-orbital of the S(1)–C(4) bond, as judged by the O(3)S(1)C(4) [167.15(2)°] angle being close to linear.

In a crystal, the molecules of **7** form homochiral chains through an N(2)–H···O(1) hydrogen bond [N···O 2.846(3) Å, ∠NHO 137(1)°]; however, the resulting crystal structure is centro-

*6-[5-*tert*-Butyl-7-hydroxy-6-nitro-2-oxo-1-benzofuran-3(2*H*)-ylidene]-1,3-dimethyl-3a,9a-diphenyl-3,3a,9,9a-tetrahydroimidazo[4,5-*e*]thiazolo-[3,2-*b*][1,2,4]triazine-2,7(1*H*,6*H*)-dione* **7**. A mixture of 4,6-di(*tert*-butyl)-3-nitro-1,2-benzoquinone **6** (1.25 g, 5 mmol) and tricycle **3** (1.96 g, 5 mmol) in AcOH (25 ml) was stirred for seven days at 22 °C. The minor precipitate of the original compound **3** was filtered off and washed with glacial acetic acid. The filtrate was diluted with cold water (275 ml). The oily precipitate was successively extracted with equal volumes of dichloromethane (3×50 ml) and ethyl acetate (3×50 ml). The extracts were washed with a sodium carbonate solution (3×50 ml) and water (3×50 ml) in a separating funnel and kept for 3–4 h over anhydrous Na_2SO_4. The dry solutions were combined and concentrated to a minimum volume to give 1.5 g of compound **7**, yield 47%, yellow crystals, mp 293–295 °C (ethyl acetate–hexane, 1:2). ^{1}H NMR, δ: 1.32 (s, 9H, Bu^t), 2.62 (s, 3H, MeN), 2.69 (s, 3H, MeN), 6.71–7.24 (m, 10H, 2Ph), 8.07 (s, 1H, NH), 8.78 (s, 1H, C^{4}H), 11.67 (s, 1H, OH). ^{13}C NMR, δ: 25.52, 25.57 (NMe), 30.60 (*Me*$_3$*C*), 35.66 (Me$_3$*C*), 79.79, 82.28 (*C*Ph), 116.85, 120.69, 122.85, 126.36, 127.51, 127.66, 128.06, 128.12, 128.41, 133.72, 134.41, 136.32, 140.84, 143.15, 147.31, 158.92, 159.18, 167.17 (C=O). MS, *m*/*z*: 641.2 [M+H]$^+$, 642.1 [M+2H]$^+$ (Calc. for $C_{32}H_{28}N_6SO_7$, *m*/*z*: 641.1818 [M+H]$^+$).

‡ *Crystallographic data for* **7**. The crystals of **7** ($C_{38}H_{44}N_6O_9S$, M = 760.85) are monoclinic, space group $P2_1/n$, at 10 K: a = 11.3193(14), b = 14.0131(17) and c = 24.123(3) Å, β = 96.620(3)°, V = 3800.8(8) Å^3, Z = 1, d_{calc} = 1.330 g cm^{-3}, μ(MoKα) = 1.48 cm^{-1}, F(000) = 1608. The intensities of 28252 reflections were measured with a Bruker SMART 1000 CCD diffractometer [λ(MoKα) = 0.71072 Å, ω-scans, 2θ < 54°], and 8277 independent reflections (R_{int} = 0.1011) were used in further refinement. The structure was solved by the direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic-isotropic approximation. The hydrogen atoms of OH and NH groups were found in difference Fourier synthesis; the H(C) atom positions were calculated. All hydrogen atoms were refined in the isotropic approximation within the riding model. The refinement converged to wR_2 = 0.1064 and GOF = 1.008 for all the independent reflections [R_1 = 0.0533 was calculated against F for 4020 observed reflections with $I > 2\sigma(I)$]. All calculations were performed using SHELXTL PLUS.[12]

CCDC 1061751 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* http://www.ccdc.cam.ac.uk.

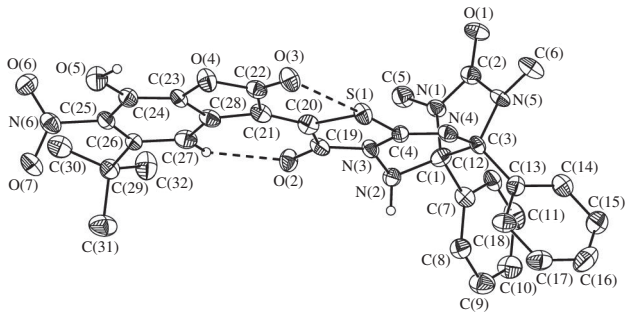


Figure 1 General view of heterocycle **7** in representation of atoms *via* thermal ellipsoids (p = 50%). Hydrogen atoms, except those of NH and OH groups and the H(C) atom involved in an intramolecular hydrogen bond, are omitted for clarity.

symmetric (space group $P2_1/n$) owing to hydrogen bonding with two isopropyl alcohol molecules [O···O 2.554(3) and 2.815(3) Å, ∠NHO 147(1) and 145(1)°] and between them [O···O 2.715(3) Å, ∠NHO 162(1)°]. It assembles neighboring molecules of **7** into centrosymmetric dimers in such a manner that their benzofuran moieties face each other (the shortest C···C distance is *ca*. 3.7 Å). These dimers, which link neighboring homochiral H-bonded chains, seem to be additionally stabilized by a short O(6)···S(1) contact [O···S 3.162(3) Å]; in this case, charge transfer occurs from a lone electron pair of the S(1) sulfur atom to the σ*-orbital of the O(6)–N(6) bond [∠SON 132.26(2)°].

In conclusion, we were the first to study the condensation of tricycle **3** with 3,5-di(*tert*-butyl)-3-nitro-1,2-benzoquinone to obtain a new polyheterocyclic compound, 6-[5-*tert*-butyl-7-hydroxy-6-nitro-2-oxo-1-benzofuran-3(2*H*)-ylidene]-1,3-dimethyl-3a,9a-diphenyl-3,3a,9,9a-tetrahydroimidazo[4,5-*e*]thiazolo[3,2-*b*]-[1,2,4]triazine-2,7(1*H*,6*H*)-dione. The mechanism of its cascade formation process initiated by nucleophile 1,4-addition has been suggested.

We are grateful to Dr. Yu. A. Sayapin (Research Institute of Physical and Organic Chemistry, Southern Federal University, Rostov-on-Don) for the fruitful discussions on the subject of this publication.

This study was supported by the Russian Foundation for Basic Research (project no. 14-03-31729).

References

1 (*a*) D. N. Bang, Yu. A. Sayapin, K. Lam, N. D. Dyk and V. N. Komissarov, *Chem. Heterocycl. Compd*., 2015, **51**, 291 (*Khim. Geterotsikl. Soedin.*, 2015, **51**, 291); (*b*) Yu. A. Sayapin, I. O. Tupaeva, E. A. Gusakov, G. V. Shilov, V. V. Tkachev, S. M. Aldoshin and V. I. Minkin, *Dokl. Chem*., 2015, **460**, 33 (*Dokl. Akad. Nauk*, 2015, **460**, 412); (*c*) I. O. Tupaeva, Yu. A. Sayapin, D. N. Bang, V. N. Komissarov, V. V. Tkachev, G. V. Shilov, S. M. Aldoshin and V. I. Minkin, *Russ. Chem. Bull., Int. Ed*., 2013, **62**, 492 (*Izv. Akad. Nauk, Ser. Khim*., 2013, 491); (*d*) Yu. A. Sayapin, E. A. Gusakov, D. N. Bang, I. O. Tupaeva, V. N. Komissarov, I. V. Dorogan, V. V. Tkachev, S. M. Aldoshin and V. I. Minkin, *Russ. Chem. Bull., Int. Ed.*, 2013, **62**, 480 (*Izv. Akad. Nauk, Ser. Khim.*, 2013, 480); (*e*) V. V. Tkachev, Yu. A. Sayapin, I. V. Dorogan, B. C. Gorkovez, A. A. Kolodina, V. N. Komissarov, G. V. Shilov, S. M. Aldoshin and V. I. Minkin, *Russ. J. Org. Chem.*, 2013, **49**, 439 (*Zh. Org. Khim.*, 2013, **43**, 451); (*f*) Yu. A. Sayapin, B. N. Duong, V. N. Komissarov, I. V. Dorogan, N. I. Makarova, I. O. Bondareva, V. V. Tkachev, G. V. Shilov, S. M. Aldoshin and V. I. Minkin, *Tetrahedron*, 2010, **66**, 8763; (*g*) S. M. Aldoshin, Yu. A. Sayapin, Z. N. Bang, I. O. Bondareva, V. N. Komissarov, I. V. Dorogan, V. V. Tkachev, G. V. Shilov and V. I. Minkin, *Russ. Chem. Bull., Int. Ed*., 2011, **60**, 1372 (*Izv. Akad. Nauk, Ser. Khim*., 2011, 1350).

2 J. Kaizer, G. Speier, E. Ösz, M. Giorgi and M. Réglier, *Tetrahedron Lett*., 2004, **45**, 8011.

3 J. M. Bolster and R. M. Kellogg, *J. Org. Chem*., 1982, **47**, 4429.

4 A. N. Kravchenko, G. A. Gazieva, S. V. Vasilevskii and Yu. V. Nelyubina, *Mendeleev Commun*., 2014, **24**, 119.

5 S. V. Vasilevskii, Yu. V. Nelyubina, N. G. Kolotyrkina, P. A. Belyakov, L. B. Kulikova and A. N. Kravchenko, *Mendeleev Commun*., 2010, **20**, 285.

6 G. A. Gazieva, E. A. Shishkova, L. B. Kulikova, N. G. Kolotyrkina, N. V. Sigay and A. N. Kravchenko, *J. Heterocycl. Chem.*, 2014, **51**, 921.

7 Yu. A. Sayapin, Z. N. Bang, V. N. Komissarov, I. V. Dorogan, V. V. Tkachev, G. V. Shilov, S. M. Aldoshin and V. I. Minkin, *Russ. J. Org. Chem*., 2009, **45**, 1663 (*Zh. Org. Khim.*, 2009, **45**, 1671).

8 S. V. Vasilevskii, P. A. Belyakov, G. A. Gazieva, Yu. V. Nelyubina, N. G. Kolotyrkina and A. N. Kravchenko, *Mendeleev Commun.*, 2010, **20**, 47.

9 A. S. Sigachev, A. N. Kravchenko, K. A. Lyssenko, P. A. Belyakov, O. V. Lebedev and N. N. Makhova, *Mendeleev Commun*., 2003, 190.

10 R. G. Neville, *J. Org. Chem*., 1958, **23**, 15.

11 K. Ley and E. Müller, *Chem. Ber.*, 1956, **86**, 1402.

12 G. M. Sheldrick, *Acta Crystallogr., Sect. A*, 2008, **64**, 112.

Received: 29th April 2015; Com. 15/4613