ELSEVIER
Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 2020, **30**, 674–675
Mendeleev Communications

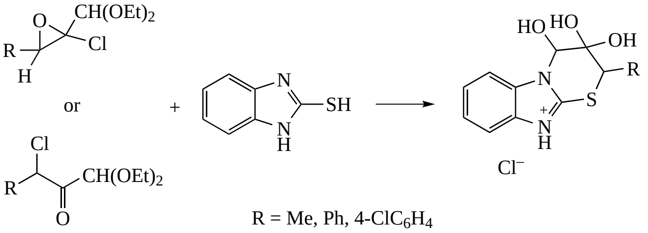
Recyclization of diethoxymethyl substituted benzimidazo-fused thiazolium salts

Firudin I. Guseinov,*[a,b] Mikhail F. Pistsov,[c] Vladislav M. Malinnikov,[b] Oksana M. Lavrova,[c] Eldar M. Movsumzade[a] and Leonid M. Kustov[a,b]

[a] *N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 119991 Moscow, Russian Federation. E-mail: guseinoveltos@mail.ru*
[b] *National University of Science and Technology 'MISIS', 119049 Moscow, Russian Federation*
[c] *Kazan National Research Technological University, 420015 Kazan, Russian Federation*

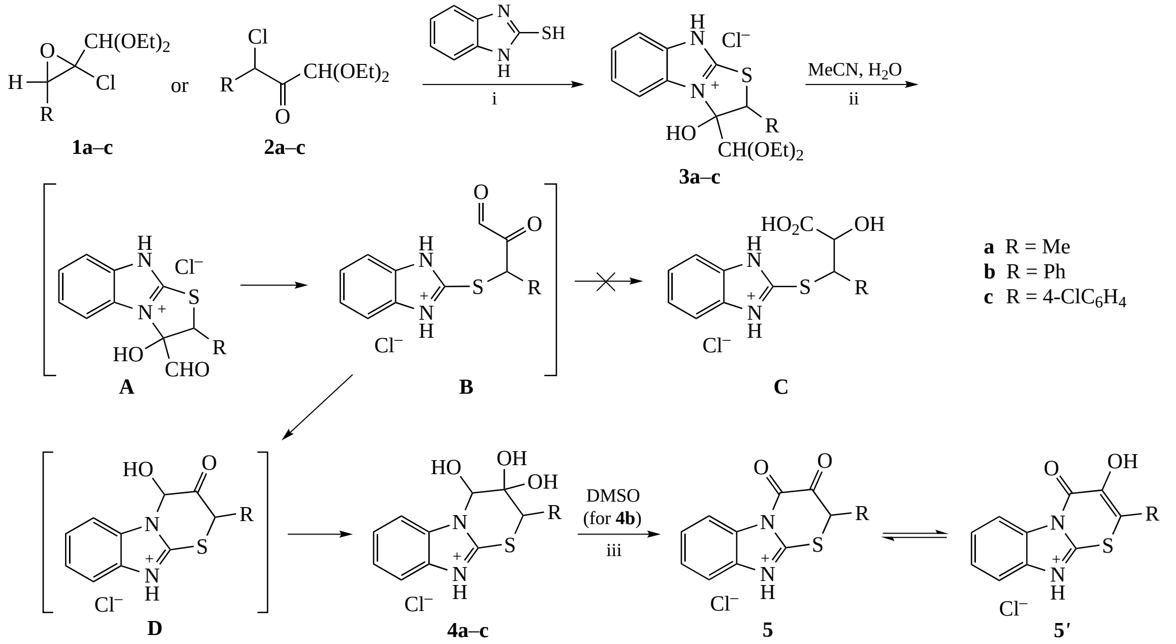
DOI: 10.1016/j.mencom.2020.09.041

3-Diethoxymethyl-3-hydroxy-3,9-dihydro-2*H*-benz[4,5]imidazo[2,1-*b*]thiazol-4-ium salts were synthesized by reaction of chloro oxiranes or isomeric α-chloro ketones with 2-mercaptobenzimidazole. The acetal group of the aforementioned salts undergoes hydrolysis in acidic medium to liberate aldehyde which would react with the NH-moiety of mercaptobenzimidazole, thus leading to cycle expansion with the formation of 3,3,4-trihydroxy-3,4-dihydro-2*H*-benz[4,5]imidazo[2,1-*b*][1,3]thiazinium salts. In DMSO solution, the 3,3,4-trihydroxythiazine moiety of the latter compounds is oxidized into 3,4-dioxothiazine one existing in enol form.



Keywords: benz[4,5]imidazo[2,1-*b*]thiazoles, α-chloro oxiranes, α-chloro ketones, X-ray crystallography, 2-mercaptobenzimidazole, benz[4,5]imidazo[2,1-*b*][1,3]thiazines.

Substituted benzo[4,5]imidazo[2,1-*b*][1,3]thiazines are important intermediates in organic synthesis[1–3] and possess pronounced antiviral,[4] antitumor,[5] antimicrobial activity against tuberculosis pathogens,[6] and also have the ability to lower cholesterol level[7] and demonstrate antioxidant properties.[8] Acetal-containing α-chloro oxiranes in reactions with bi- and polyfunctional nucleophiles turned out to be convenient in molecular design of various heterocyclic systems, in particular, heterocyclic carbaldehydes and their derivatives.[9–14]



Scheme 1 *Reagents and conditions*: i, EtOH (abs.), room temperature, 4 h; ii, MeCN/H_2O (10 : 1), reflux, 4 h; iii, air, room temperature, 7 days.

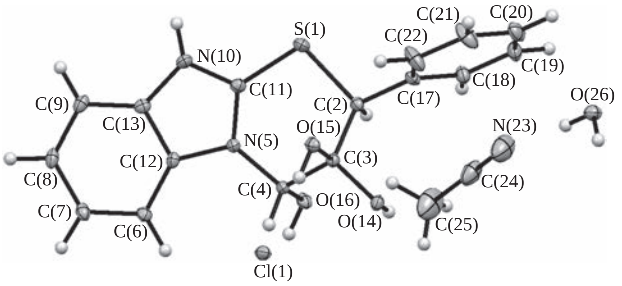


Figure 1 Molecular structure of compound **4b**.

Previously, we showed that thiazolo[2,3-*a*]pyridinium chlorides containing 4-positioned hydroxy and acetal groups would undergo an unusual intramolecular redox reaction when heated in acidic medium yielding α-hydroxy acids.[11] To determine the scope of similar reactions, we studied herein the behavior of 3-diethoxymethyl-3-hydroxy-3,9-dihydro-2*H*-benz[4,5]imidazo[2,1-*b*]thiazolium salts **3a–c**, representing similar heterocyclic systems (Scheme 1). Compounds **3a–c** were synthesized by the reaction of α-chloro oxiranes **1a–c** or α-chloro ketones **2a–c** with 2-mercaptobenzimidazole at room temperature in ethanol in 90–92% yields. Unexpectedly, boiling these benzimidazole salts **3a–c** in acetic medium for several hours afforded benzo[4,5]imidazo[2,1-*b*][1,3]thiazine derivatives **4a–c** instead of expected hydroxy acids **C**.

The proposed mechanism for formation of compounds **4a–c** comprises the initial hydrolysis of the acetal group in reactants **3a–c** to give aldehydes **A**. Intermediates **A** undergo ring opening to generate α-keto aldehydes **B**. Their expected intramolecular redox transformation into hydroxy acids **C** did not occur. Instead, cyclic ketones **D** were formed upon the reaction of aldehyde group of intermediates **B** with the NH-moiety. Hemiaminals **D** easily add water molecule giving trihydroxy compounds **4a–c**. In DMSO solution at room temperature on contact with air, product **4b** underwent oxidation to dioxo derivative **5** that would exist in enol form **5′**.

Compounds **3a–c**, **4a–c** and **5′** are white crystalline substances soluble in DMF, DMSO and in less polar organic solvents when heated. Their structure was confirmed by ^{1}H and ^{13}C NMR spectroscopy, elemental analysis, as well as X-ray diffraction analysis for compound **4b** (Figure 1).[†]

In conclusion, the recyclization of 3-diethoxymethyl-3-hydroxy-3,9-dihydro-2*H*-benz[4,5]imidazo[2,1-*b*]thiazolium salts in an acidic medium proceeds with an expansion of the cycle and can serve as a convenient synthesis of dioxo-substituted benz[4,5]imidazo[2,1-*b*][1,3]thiazines.

This work was carried out with financial support from the Ministry of Education and Science of the Russian Federation in the framework of Increase Competitiveness Program of NUST ‘MISiS’ (grant no. K2A-2019-026).

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2020.09.041.

References

1 X. Guo, L. Wang, J. Hu and M. Zhang, *RSC Adv.*, 2018, **8**, 22259.
2 M. Godumala, J. Yoon, S. Y. Park, C. Lee, Y. Kim, J.-E. Jeong, S. Park, H. Y. Woo, M. J. Cho and D. H. Choi, *Front. Chem.*, 2020, **8**, 61.
3 J. Matysiak, M. M. Karpińska, A. Skrzypek, J. Wietrzyk, D. Kłopotowska, A. Niewiadomy, B. Paw, M. Juszczak and W. Rzeski, *Arab. J. Chem.*, 2019, **12**, 2655.
4 I. Nikolova, I. Slavchev, M. Ravutsov, M. Dangalov, Y. Nikolova, I. Zagranyarska, A. Stoyanova, N. Nikolova, L. Mukova, P. Grozdanov, R. Nikolova, B. Shivachev, V. E. Kuz’min, L. N. Ognichenko, A. S. Galabov and G. M. Dobrikov, *Bioorg. Chem.*, 2019, **85**, 487.
5 W. S. Hamama, M. A. Waly, I. I. El-Hawary and H. H. Zoorob, *J. Heterocycl. Chem.*, 2016, **53**, 953.
6 J.-X. Gong, Y. He, Z.-L. Cui and Y.-W. Guo, *Phosphorus, Sulfur Silicon Relat. Elem.*, 2016, **191**, 1036.
7 E. Abele, R. Abele, P. Arsenyan, S. Belyakov, M. Veveris and E. Lukevics, *Chem. Heterocycl. Compd.*, 2007, **43**, 220 (*Khim. Geterotsikl. Soedin.*, 2007, 274).
8 O. A. R. Rodriguez, N. E. M. Vergara, J. P. M. Sanchez, M. T. S. Martinez, Z. G. Sandoval, A. Cruz and A. R. Organillo, *J. Mol. Struct.*, 2020, **1199**, 127036.
9 F. I. Guseinov, S. Sh. Tagiev and V. V. Moskva, *Russ. J. Org. Chem.*, 1995, **31**, 86 (*Zh. Org. Khim.*, 1995, **31**, 96).
10 F. I. Guseinov and N. A. Yudina, *Chem. Heterocycl. Compd.*, 1998, **34**, 115 (*Khim. Geterotsikl. Soedin.*, 1998, 124).
11 F. I. Guseinov, R. N. Burangulova, E. F. Mukhamedzyanova, B. P. Strunin, O. G. Sinyashin, I. A. Litvinov and A. T. Gubaidullin, *Chem. Heterocycl. Compd.*, 2006, **42**, 943 (*Khim. Geterotsikl. Soedin.*, 2006, 1089).
12 M. F. Pistsov, O. M. Lavrova, A. M. Saifutdinov, R. N. Burangulova, L. M. Kustov, F. I. Guseinov and R. Z. Musin, *Russ. J. Gen. Chem.*, 2017, **87**, 2887 (*Zh. Obshch. Khim.*, 2017, **87**, 2076).
13 F. I. Guseinov, M. F. Pistsov, E. M. Movsumzade, L. M. Kustov, V. A. Tafeenko, V. V. Chernyshev, A. V. Gurbanov, K. T. Mahmudov and A. J. L. Pombeiro, *Crystals*, 2017, **11**, 327.
14 F. I. Guseinov and V. V. Moskva, *Zh. Org. Khim.*, 1994, **30**, 360 (in Russian).
15 G. M. Sheldrick, *SADABS*, Bruker AXS, Madison, WI, 1997.
16 A. Altomare, G. Cascarano, C. Giacovazzo and D. Viterbo, *Acta Crystallogr.*, 1991, **A47**, 744.
17 G. M. Sheldrick, *SHELX-97, Programs for Crystal Structure Analysis* (Release 97-2), Version 1.2, University of Göttingen, 1997.
18 L. J. Farrugia, *J. Appl. Crystallogr.*, 1999, **32**, 837.
19 *APEX2* (Version 2.1), *SAINTPlus, Data Reduction and Correction Program* (Version 7.31A), Bruker AXS, Madison, WI, 2006.

Received: 13th March 2020; Com. 20/6160

[†] *Crystal data for* **4b**. $C_{16}H_{15}N_2O_3S^+\cdot C_2H_3N\cdot H_2O\cdot Cl^-$ (M = 409.89), triclinic, space group $P\bar{1}$ at 150 K: a = 8.0155(9), b = 9.52025(11) and c = 14.0284(17) Å, α = 71.499(2)°, β = 76.161(2)°, γ = 75.480(2)°, V = 967.8(2) Å^3, Z = 2, d_{calc} = 1.407 g cm^{-3}, μ = 0.334 mm^{-1}, F(000) = 428. The data was obtained at T = 150 K on a Smart APX II CCD Bruker automatic diffractometer [λ(MoKα) = 0.71073 Å, ω-scan], $2\theta < 54°$, R_{int} = 0.044. 10931 reflections were measured out of which 4155 were independent, the number of observed reflections with $I > 2\sigma(I)$ was 3569. Final value of factors of deviation R = 0.0415, wR_2 = 0.1333, GOOF = 0.94, the number of determined parameters was 265. Considering that absorption was carried out using the program SADABS.[15] The structure was found using a straightforward method with program SIR[16] and confirmed using SHELXL-97.[17] All calculations were carried out using WINGX[18] and APEX2.[19]

CCDC 970273 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.