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Unexpected formation of 5,5-diethoxy-5*H*-1,2,3-dithiazoles from 5*H*-1,2,3-dithiazole-5-thiones

Oleg I. Bol'shakov,[a] Lidia S. Konstantinova,[a] Rinat R. Aysin,[b] Natalia V. Obruchnikova,[a] Elena D. Lubuzh[a] and Oleg A. Rakitin*[a]

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

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5*H*-1,2,3-Dithiazole-5-thiones undergo an unexpected transformation into 5,5-diethoxy-5*H*-1,2,3-dithiazoles upon treatment with sodium ethoxide; the structure of the products was confirmed by Raman and IR spectra.

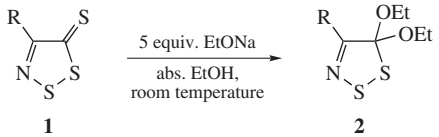
1,2,3-Dithiazoles are important compounds among the five-membered heterocycles containing nitrogen and sulfur atoms due to their biological activity and interesting chemical transformations.[1] Much attention in their chemistry is given to reactions of 5-arylimino-4-chloro-5*H*-1,2,3-dithiazoles with nucleophiles.[2] Recently, we have found that 4-substituted 5*H*-1,2,3-dithiazole-5-thiones **1** under treatment with primary amines underwent a new transformation into 1,2,5-thiadiazole-3(2*H*)-thiones.[3] To explore the synthetic utility of thiones **1** we studied their reactivity towards another strong nucleophile – ethoxide anion.

Interaction of 4-phenyl-5*H*-1,2,3-dithiazole-5-thione **1a** with sodium ethoxide in absolute ethanol at room temperature for 1.5 h afforded new product **2a**. Compound **2a**, a yellow oil with composition $C_{12}H_{15}N_2O_2S_2$, according to its mass spectrum, elemental analysis and ^{1}H and ^{13}C NMR spectra is a product of formal replacement of thione moiety by two ethoxy groups (Scheme 1). ^{1}H and ^{13}C NMR spectra showed the presence of two ethoxy groups, and absence of C=S bond in **2a** (no carbon signals in the region 160–220 ppm).

Careful investigation of this reaction showed that the best yield was achieved when 5-fold excess of sodium ethoxide was used (55% yield). Note that this amount significantly exceeded the required quantity of the reagent (one or two equivalents). However, when less amount of the reagent was used, some of the starting thione **1a** remained unchanged (TLC data). The use of greater excess of EtONa (6, 7 or more equivalents) also dropped the yield of **2a**.

Extention of this reaction to other 1,2,3-dithiazole-5-thiones **1** gave the corresponding 5,5-diethoxy derivatives **2** in moderate yields† (Scheme 1).

Treatment of 4-chloro-5*H*-1,2,3-dithiazole-5-thione with sodium ethoxide in EtOH at room temperature led to its full decomposition and none of the individual products was isolated from the reaction mixture. Apparently, the chlorine atom is readily



1 **2**

a R = Ph, 55%
b R = 4-$O_2NC_6H_4$, 61%
c R = 4-FC_6H_4, 23%
d R = 4-$MeOC_6H_4$, 33%
e R = 2-thienyl, 25%
f R = 2-benzofuryl, 32%

Scheme 1

† *General procedure for the preparation of 5,5-diethoxy-5*H*-1,2,3-dithiazoles* **2**. A solution of sodium ethoxide prepared from sodium metal (115 mg, 5 mmol) and absolute ethanol (5 ml) was added to a solution of **1** (1 mmol) in absolute ethanol (15 ml) at 0 °C. The reaction mixture was stirred at room temperature for 1.5 h, poured into 1% HCl (100 ml) and extracted with CH_2Cl_2 (3×10 ml). The combined extracts were washed with H_2O, dried with $MgSO_4$ and evaporated. The residue was separated by column chromatography (Silica gel Merck 60, light petroleum–CH_2Cl_2).

The IR spectra of the studied compounds prepared as KBr pellets and thin films (for liquid sample) were recorded in the region 300–3500 cm^{-1}, using a Carl Zeiss Specord M82 spectrophotometer. Raman spectra of all samples were obtained in the region 100–3500 cm^{-1}, using a laser Raman spectrometer Jobin-Yvon LabRAM 300. Excitation line was red line at 632.8 nm of a He–Ne laser with 6 mW output power. Theoretical calculations of the geometry and NCA were performed in Gaussian 03 C.01[8] program at the DFT level with PBE functional[9] and 6-311G(d,p)[10] basis sets. Potential energy distributions were calculated using NCA99 program.[11]

New compounds were characterised by elemental analysis, ^{1}H and ^{13}C NMR and mass spectra.

For **2a**: yield 55%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (t, 6H, 2Me, *J* 7.3 Hz), 3.37 (m, 2H, CH_2), 3.93 (m, 2H, CH_2), 7.40 (m, 3H, Ar), 8.07 (d, 2H, Ar, *J* 5.9 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8 (2Me), 62.8 (2CH_2), 127.5, 128.6 and 130.3 (5CH, Ar), 131.3, 143.1 and 155.5 (3C_{sp^2}). MS (EI, 70 eV), *m*/*z* (%): 269 (M^+, 32), 241 (15), 135 (20), 104 (100). IR (KBr, ν/cm^{-1}): 2976, 2928 (C–H), 2888, 1540, 1392, 1268, 1136, 1112, 1088, 1072, 1044, 1032, 984, 792, 768, 688, 620. Raman (ν/cm^{-1}): 1538 (C=N), 1266, 622, 569, 492 (S–S). Found (%): C, 53.68; H, 5.79; N, 5.17. Calc. for $C_{12}H_{15}NO_2S_2$ (%): C, 53.50; H, 5.61; N, 5.20.

For **2b**: yield 61%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.24 (t, 6H, 2Me, *J* 6.8 Hz), 3.36 (m, 2H, CH_2), 3.94 (m, 2H, CH_2), 8.24 (s, 4H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8 (2Me), 63.2 (2CH_2), 123.8 (2CH, Ar), 128.3 (2CH, Ar), 137.0, 142.2, 148.4 and 153.5 (4C_{sp^2}). MS (EI, 70 eV), *m*/*z* (%): 314 (M^+, 12), 206 (42), 177 (27), 149 (93). IR (KBr, ν/cm^{-1}): 2976, 2928 (C–H), 1596, 1536, 1528, 1516, 1348, 1168, 1136, 1112, 1088, 1072, 1028, 984, 856, 796. Found (%): C, 45.98; H, 4.53; N, 9.03. Calc. for $C_{12}H_{14}N_2O_4S_2$ (%): C, 45.85; H, 4.49; N, 8.91.

For **2c**: yield 23%, colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (t, 6H, 2Me, *J* 7.3 Hz), 3.34 (m, 2H, CH_2), 3.91 (m, 2H, CH_2), 7.05 (m, 2H, Ar), 8.06 (m, 2H, Ar). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8 (2Me), 62.9 (2CH_2), 115.7 (d, 2CH, Ar, *J* 21 Hz), 129.8 (2CH, Ar), 116.0, 127.6, 154.6 and 164.0 (d, 4C_{sp^2}, *J* 250 Hz). MS (EI, 70 eV), *m*/*z* (%): 287 (M^+, 3), 259 (2), 242 (1), 153 (12), 122 (100). IR (KBr, ν/cm^{-1}): 2976, 2952, 2928 (C–H), 2888, 1672, 1600, 1504, 1472, 1440, 1392, 1272, 1252, 1236, 1160, 1136, 1112, 1040, 1028, 984, 844, 776. Found (%): C, 49.98; H, 5.03; N, 4.90. Calc. for $C_{12}H_{14}FNO_2S_2$ (%): C, 50.15; H, 4.91; N, 4.87.

Table 1 Raman and IR (in parentheses) salient analytical bands of compounds **2a–7** and their assignment.[a]

Compound	ν_{S-S}	$\nu_{C-S} + \nu_{N-S}$	$\nu_{C-C} + \nu_{C-C'}$	$\nu_{C=N}$	$\nu_{C=X,\,(X = O,\,S)}$
2a	490 m (490 m)	566 vw (564 w), 622 m (618 s)	1269 m (1266 m)	1539 s (1537 w)	
3	467 s (468 m)	512 s (508 m), 634 m (634 s)	1262 vw (1260 s)	1576 vw (1574 m)	1640 m, 1655 m (1640 s, 1656 s)
4	488 s (490 m)	541 s (540 s), 661 s (665 s)	1227 m (1230 m)	1551 s (1555 s)	1644 m, 1676 m (1645 vs, 1680 vs)
5	499 m (500 m)	569 m (565 m), 604 m (611 w)	1270 s (1268 s)		1140/1132 s (1136 s)
6	486 s (486 w)	522 m (522 m), 599 s (600 m)	1248 s (1250 s)	1501 w (1498 w)	1085 s (1098 vs)
7	488 w (482 w)	528 w (528 m), 633 m (632 s)	1280 m (1276 m)	1500 s,1598 s (1588 s, 1604 s)	

[a]vw – very weak, w – weak, m – medium, s – strong, vs – very strong.

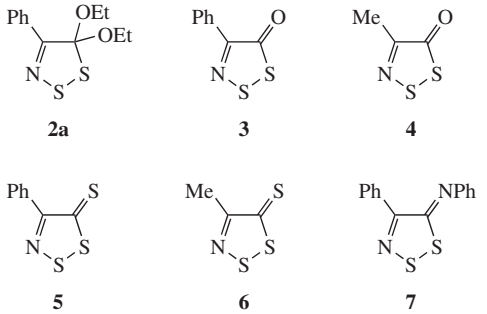


Figure 1

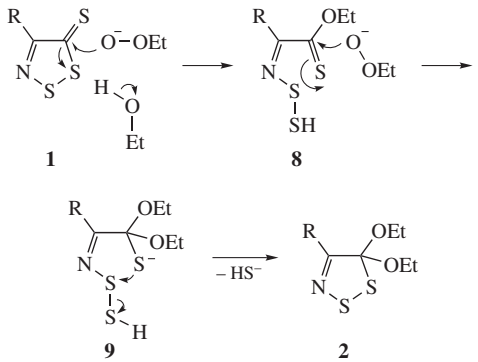
expelled as a chloride anion on the action of NaOEt as it was reported for 5-arylimino-4-chloro-5*H*-1,2,3-dithiazoles.[4]

Unfortunately, we could not prove the structure of diethoxy derivatives **2** by X-ray analysis because all 1,2,3-dithiazoles **2** were oils which would vitrify but not crystallize upon deep cooling.

To elucidate the structure of diethoxy derivatives **2**, IR and Raman spectra of the compound **2a**, along with those for relatives **3–7** (Figure 1) were studied. Quantum-chemical calculations of normal-mode frequencies and eigenvectors (NCA) in a harmonic approximation and as well as IR intensities for the free molecules **2a**, **4–7** were carried out at the DFT level. According to the NCA results, the frequency of the stretching vibration of the S–S bond (ν_{S-S}) is situated in the 460–500 cm^{-1} region. This mode is of mixed origin, ν_{S-S} stretching contribution to potential energy distribution ranging within 60–75%. Taking into account large polarizability of sulfur atoms, the Raman intensity of this mode is expected to be high. The low frequency region of the experimental Raman spectra of **2a–7** reveals several lines of strong and middle intensity (Table 1). The line at 482–500 cm^{-1} is assigned to ν_{S-S} stretch, its intensity is high in the case of **3**, **4**, **6** and middle in the case of **2a**, **5**, **7**. Thus, the heterocyclic structure, ascribed to **2a**, can be confirmed, the NCA results for structure **2a** agree well with the experimental spectrum in particular.

To the best of our knowledge, 5,5-dialkoxy-5*H*-1,2,3-dithiazoles are unknown compounds. Similar to 5,5-diethoxy derivatives, 5-substituted 5-alkoxy-5*H*-1,2,3-dithiazoles were synthesized by treatment of β-ketoenamines with sulfur monochloride in the presence of methanol.[5] Other *spiro* azetidin-1,2,3-dithiazoles are also known.[6] The formation of *gem*-dialkoxy heterocyclic derivatives was proposed only for 1-methyl-2-(substituted phenyl)-quinazoline-4(1*H*)-thiones.[7]

The plausible mechanism for the formation of 5,5-diethoxy-5*H*-1,2,3-dithiazoles **2** from thiones **1** is given in Scheme 2. The reaction could start with nucleophilic attack of ethoxide anion at the 5-position of the dithiazole ring followed by its opening into S–S bond and the formation of thioester **8**. The attack of the second ethoxide anion afforded diethoxy derivative **9** which can suffer intramolecular cyclization to the 1,2,3-dithiazole by nucleophilic attack of sulfide ion with extrusion of hydrosulfide anion.



Scheme 2

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For **2d**: yield 33%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (t, 6H, 2Me, *J* 7.3 Hz), 3.36 (m, 2H, CH_2), 3.85 (s, 3H, OMe), 3.93 (m, 2H, CH_2), 6.89 (d, 2H, Ar, *J* 8.8 Hz), 8.03 (d, 2H, Ar, *J* 8.8 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8 (2Me), 55.4 (OMe), 62.7 (2CH_2), 113.9 (2CH, Ar), 129.2 (2CH, Ar), 124.0, 143.1, 155.2 and 161.2 (4C_{sp^2}). MS (EI, 70 eV), *m*/*z* (%): 299 (M^+, 56), 254 (35), 234 (37), 192 (35), 134 (100). IR (KBr, ν/cm^{-1}): 2976, 2928 (C–H), 1604, 1512, 1464, 1440, 1300, 1256, 1180, 1136, 1096, 1088, 1072, 1052, 1032, 984, 836, 812. Found (%): C, 52.34; H, 5.83; N, 4.63. Calc. for $C_{12}H_{14}N_2O_4S_2$ (%): C, 52.15; H, 5.72; N, 4.68.

For **2e**: yield 25%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.27 (t, 6H, 2Me, *J* 7.3 Hz), 3.43 (m, 2H, CH_2), 3.96 (m, 2H, CH_2), 7.06 (m, 1H, Ar), 7.41 (d, 1H, Ar, *J* 5.1 Hz), 7.76 (d, 1H, Ar, *J* 2.9 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.8 (2Me), 62.9 (2CH_2), 126.8, 127.7, 129.1 (3CH, Ar), 135.0, 142.3, 151.8 (3C_{sp^2}). MS (EI, 70 eV), *m*/*z* (%): 275 (M^+, 14), 201 (15), 110 (100). IR (KBr, ν/cm^{-1}): 2976, 2936 (C–H), 1456, 1424, 1260, 1232, 1164, 1136, 1112, 1088, 1076, 1040, 1028, 952, 856, 756, 708, 664, 624, 616. Found (%): C, 43.54; H, 4.83; N, 5.03. Calc. for $C_{12}H_{14}N_2O_4S_2$ (%): C, 43.61; H, 4.76; N, 5.09.

For **2f**: yield 32%, yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.29 (t, 6H, 2Me, *J* 7.3 Hz), 3.48 (m, 2H, CH_2), 3.98 (m, 2H, CH_2), 7.28 (m, 1H, Ar), 7.39 (m, 1H, Ar), 7.43 (s, 1H, Ar), 7.58 (d, 1H, Ar, *J* 8.1 Hz), 7.67 (d, 1H, Ar, *J* 8.1 Hz). ^{13}C NMR (75.5 MHz, $CDCl_3$) δ: 14.9 (2Me), 63.2 (2CH_2), 107.2, 111.7, 122.5, 123.6 and 126.5 (5CH, Ar), 127.8, 142.4, 147.9, 148.4 and 155.6 (5C_{sp^2}). MS (EI, 70 eV), *m*/*z* (%): 309 (M^+, 17), 217 (19), 181 (19), 172 (20), 144 (100). IR (KBr, ν/cm^{-1}): 2976, 2956, 2924 (C–H), 1448, 1300, 1260, 1176, 1164, 1144, 1112, 1076, 1048, 1028, 1008, 816, 752, 744, 652. Found (%): C, 54.34; H, 4.83; N, 4.63. Calc. for $C_{14}H_{15}NO_3S_2$ (%): C, 54.35; H, 4.89; N, 4.53.

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