RECYCLIZATION OF 4-OXO-1,3-BENZOTHIAZINIUM SALTS. SYNTHESIS OF o-MERCAPTOPHENYL-1,2,4-TRIAZOLES AND METAL CHELATES BASED ON THEM

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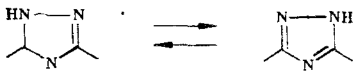
A method based on the reaction of 4-oxo-1,3-benzothiazinium perchlorates with hydrazines is developed for synthesizing 5-(o-mercaptophenyl)-1,2,4-triazoles. Their complexes with Ni(II), Co(II), and Zn(II) are prepared. The o-mercaptophenyltriazoles are capable of undergoing oxidative dimerization to give disulfides.

Salts of 4-oxo-1,3-benzoxazine are versatile synthons for preparing practically useful o-hydroxyphenyl-substituted 1,2,4-triazoles, 1,2,4-oxadiazoles, and 1,3,5-triazines [1-6]. In continuation of these studies and also investigations on the synthesis and recyclization of their sulfur analogs, salts of 4-oxo-1,3-benzothiazine [7, 8], we have developed a method for preparing the previously unknown o-mercaptophenyl-1,2,4-triazoles through reaction of benzothiazinonium perchlorates I [7] with twice the amount of hydrazine hydrate, phenyl-, and benzylhydrazine in glacial acetic acid. The yield of triazoles if 50-80%. It is noteworthy that the recyclization does not occur under these conditions for methyl- and ethylhydrazine. The corresponding benzothiazinones **II** are isolated in 65-70% yield even with boiling for 2 h [9]. However, **II** under these conditions are converted to the triazoles in 40-45% yield using phenylhydrazine. The phenylhydrazones do not form. The relative molecular mass and composition of the synthesized triazoles were confirmed by mass spectrometry and elemental analyses (C, H, N, S).

Formation of the triazole ring was confirmed by IR spectroscopy. Absorption bands of carbonyl characteristic of products from opening and cleavage of the benzothiazinone ring are not seen. In the region of multiple bonds, the highest frequency absorption is a group of bands at 1600-1495 cm^{-1}. These are due to combination vibrations of the triazole and aromatic rings. The SH group cannot always be identified in PMR spectra of solutions of triazoles and in IR spectra of their crystalline samples. However, the presence of the thiophenol substituent is indirectly confirmed by a qualitative reaction, the formation of yellow crystals on treatment of the synthesized compounds with an alcohol solution of Pb(II) acetate. Moreover, the S—H stretching band appearing at 2575-2495 cm^{-1} in spectra of their solutions in CCl_4 are consistent with a thiol group in the prepared compounds. A slight shift to low frequency of this band from that characteristic of free thiols [10] and the lack of dependence of its position and shape on the concentration indicates formation of an intramolecular H-bond between the SH group and the N atom of the triazole ring. The IR spectrum of the NH-triazole contains deformation (1654) and stretching (3160 and 3040 cm^{-1}) bands of the NH group. The doublet nature and the shift to low frequency of the stretching absorption from the region characteristic of free NH vibrations are consistent with the existence in these compounds, as in pyrazoles, of an intermolecular H-bond between the NH group of one molecule and $N_{(2)}$ of the heterocyclic ring of another molecule. A one-proton doublet for the NH group, which appears on deuteration by CF_3CO_2D (but not D_2O), is seen in PMR spectra of the NH-triazole in various solvents (pyridine-D_5, acetone, DMF-D_7) at 2.4-2.8 ppm. As the temperature is increased to 130°C, this signal coalesces. This is consistent with the tautomeric process A ⇄ B, which according to the literature [11] occurs intermolecularly:



A B

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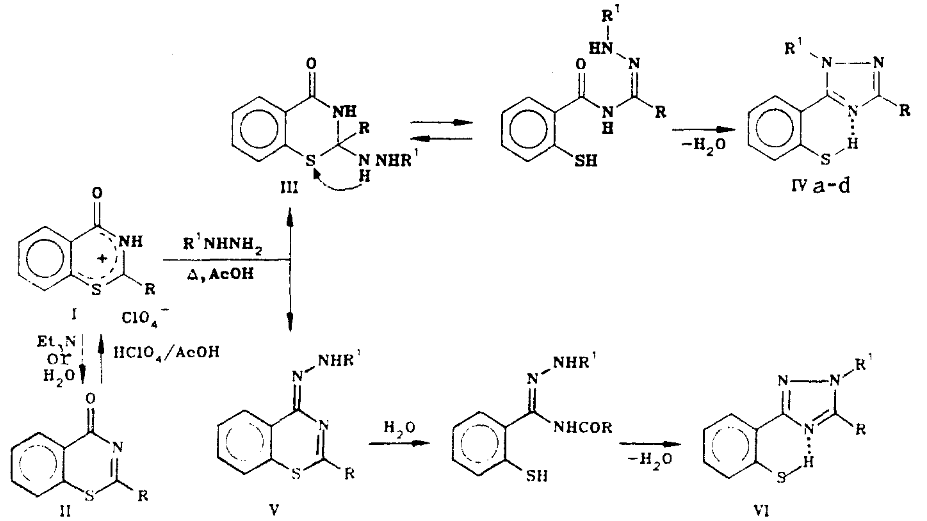
One of the isomeric triazoles **IV** or **VI** could be expected depending on the initial attack of the primary amine of the monosubstituted hydrazines at positions 2 or 4 of the thiazinone ring, the most electrophilic sites, and the subsequent alternate recyclizations.



IV a R=Ph, R¹=H; b R=R¹=Ph; c R=Ph, R¹=CH_2Ph; d R=CH_2Ph, R¹=Ph;
e R=p-$NO_2C_6H_4$, R¹=Ph

This supposition is based on the fact that a similar reaction in a series of 4-oxo-1,3-benzoxazinium salts, as was demonstrated by dipole moments, the Kerr effect [1, 3, 4], and x-ray structure analysis (XSA) [6], follows the path **III** → **IV**, whereas a report on the possible synthesis of the oxime of benzothiazinone [9], an analog of phenylhydrazone **V**, indicates that the recyclization can take the path **V** → **VI**.

Therefore, the reaction of the synthesized triazoles with acetates of divalent 3*d*-metals (Co, Ni, Cu, Zn) was studied since complexes based on both triazole **IV** and **VI** can be prepared. Since the majority of previous efforts [12] have been involved with investigating the chelating ability of o-hydroxyphenylazoles, it seemed interesting to determine whether the S atom would behave differently [13, 14] in the synthesis and structure of the complexes. The investigations showed that the o-mercaptphenyltriazoles **IVb** and **c** react differently with methanol solutions of the metal acetates depending on the nature of the metal. Coordination compounds are formed for Co, Ni, and Zn in yields of 53-84% whereas Cu(II) oxidizes the mercapto group, producing the disulfides in 80% yield.

The elemental analyses (C, H, N, S, M) of the prepared complexes are consistent with the formulas ML_2 (LH = triazole ligand). This and the inability of the disulfide to form coordination complexes on boiling with metal acetates in methanol suggest that complexes are formed. This is also supported by IR spectra, in which the bands of the triazole and phenol rings at 1595-1590 and 1570-1565 cm^{-1} are shifted to lower frequency by 5-15 and 15-25 cm^{-1}, respectively, compared with the starting ligands. This is caused by the increased quasiaromaticity of the chelate ring that arises on replacing the H by a metal owing to the coordination bond being stronger than the H-bond (Tables 1 and 2).

The magnetochemical measurements are consistent with a planar configuration for the Ni complexes ($\mu_{\text{eff}} = 0\mu_B$). This agrees with the reported square-planar structure of complexes with model aromatic azomethines [13, 14]. However, it contradicts previous results [13] in which tetrahedral geometry occurs in chelates of heterocyclic azomethines with the same coordinating atoms regardless of the nature of the metal. Judging from the effective magnetic moments, the Co complexes ($\mu_{\text{eff}} = 4.20\text{-}4.62\ \mu_B$), like those of o-hydroxyphenylazoles, may be both tetrahedral [12] or polymeric-octahedral [15, 16]. However, XSA of the Co complex revealed a tetrahedral coordination sphere.* The internal angles in the metallocycle S—Co—N, S—Co—S, and N—Co—N are 97, 125, and 115°, respectively.

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*The XSA data obtained by A. S. Antsyshkina in the N. S. Kurnakov Institute of General and Inorganic Chemistry of the Academy of Sciences of the USSR (directed by Corresponding Member M. A. Porai—Koshits) will be reported separately.

TABLE 1. Characteristics of 5-(o-Mercaptophenyl)-1,2,4-triazoles **IVa-d**

Compound	Empirical formula	mp, °C*	IR spectrum, cm^{-1}	m/z (I_{rel}, %)**	Yield, %***
IVa	$C_{14}H_{11}N_3S$	268...269	3160, 3040, 1654, 1580, 1535, 1500, 1255	253 (100), 251 (64), 150 (64), 149 (15), 119 (19), 118 (32), 101 (19), 103 (14), 91 (16)	55
IVb	$C_{20}H_{15}N_3S$	94...95	1595, 1570, 1515, 1495, 1265	329 (50), 328 (30), 296 (10), 252 (5), 225 (7), 198 (8), 194 (9), 104 (11), 103 (4), 91 (100)	80
IVc	$C_{21}H_{17}N_3S$	117	1590, 1565, 1515, 1495, 1280	343 (56), 342 (6), 252 (9), 240 (12), 239 (7), 193 (20), 136 (22), 135 (13), 106 (82), 104 (33), 91 (100)	80
IVd	$C_{21}H_{17}N_3S$	159	1600, 1560, 1500, 1265	343 (88), 342 (93), 310 (9), 266 (6), 264 (11), 232 (7), 225 (20), 207 (3), 118 (13), 91 (100)	50
IVe	$C_{20}H_{14}N_4O_2S$	144	1600, 1565, 1515, 1350		70

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*Triazoles **IVa** were recrystallized from a mixture of glacial acetic acid and DMF; **IVb-e** from isopropanol.

The peak $M^{+\cdot}$ and the 10 strongest peaks in the range m/z = 90—$M^{+\cdot}$ are given n the mass spectra. The relative molecular mass of triazole **IVb (332), determined cryoscopically in benzene, agrees satisfactorily with that calculated (329).

***The PMR spectra of triazoles **IVa** (pyridine-D_5): 2.45-2.55 (1H, d, J = 8 Hz, NH), 7.00-8.40 (9H, m, Ar); **IVa** (DMF-D_7): 2.68-2.80 (1H, d, J = 10 Hz, NH), 7.20-8.30 (9H m, Ar); **IVc** ($CDCl_3$): 5.12 (2H, s, CH_2), 6.90-8.30 (14H, m, Ar); **IVd** ($CDCl_3$): 4.15 (2H, s, CH_2), 6.90-8.10 ppm (14H, m, Ar).

TABLE 2. Characteristics of Complexes of o-Mercaptophenyl-1,2,4-triazoles

Compound	Empirical formula	R'*	M	mp, °C	Color	IR spectrum, cm^{-1}	Yield, %
VIIa	$C_{40}H_{28}CoN_6S_2$	Ph	Co	279...280 (dec.)	Bright green	1580, 1545, 1520, 1490	80
VIIb	$C_{40}H_{28}N_6NiS_2$	Ph	Ni	300	Dark green	1580, 1545, 1525, 1490	70
VIIc	$C_{40}H_{28}N_6S_2Zn$	Ph	Zn	284...285	Colorless	1585, 1547, 1525, 1490	81
VIId	$C_{40}H_{32}CoN_6S_2$	CH_2Ph	Co	253...255 (dec.)	Dark green	1585, 1550, 1515, 1485	55
VIIe	$C_{40}H_{32}N_6NiS_2$	CH_2Ph	Ni	264...265 (dec.)	Grayish-blue	1585, 1550, 1515, 1480	53

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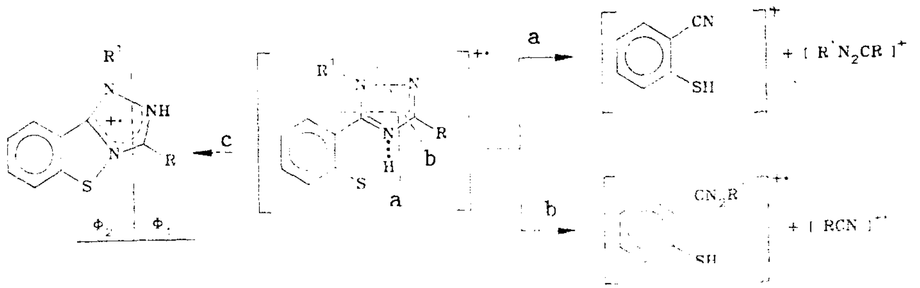
*R = Ph.

Therefore, the chelate structure of the complexes was confirmed using XSA. Moreover, it was demonstrated that the Co complex obtained is based on triazole **IVc**. This suggests that hydrazines react with benzothiazinonium salts, analogously to benzoxazinonium salts [1, 3, 4, 6] by path **III** → **IV** with initial attack of the primary amine at position 2 of the heterocycle.

It is noteworthy that the bifunctionality of the benzylhydrazine can lead to formation of **IVc** by another route. This is initial attack at position 2 of the thiazinone ring not by the primary N but by the alkylated N of the benzylhydrazine. However, the similarity of the mass spectra of this triazole and triazoles **IVb** and **d**, prepared by reaction of benzothiazinonium perchlorates **Ia** and **b** with phenylhydrazine, for which the primary N atom is more nucleophilic, repudiates this argument.

Therefore, the synthesized triazoles have structure **IV** (Table 1) and their complexes, structure **VII** (Table 2), corresponding to the molecular structure of the Co complex.

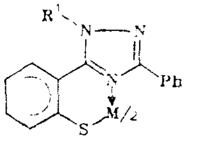
The mass spectrometric investigation of triazoles **IV** (cf. Table 1) revealed that they are highly stable to electron impact (I_{rel} = 50-100%). Fragmentation of the triazole ring occurs mainly by paths **a** and **b**. This is characteristic of substituted 1,2,4-triazoles [17, 18]:



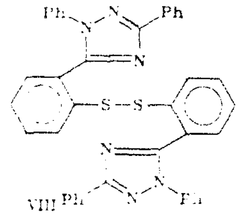
Moreover, loss from the molecular ion of H, SH, and the phenyl group is characteristic of the N-substituted triazoles **IVb-d**. For the NH-triazole **IVa**, a structural rearrangement (path **c**) accompanied by loss from the daughter ion of H_2 and N_2 with simultaneous appearance of the primary fragmentation products Φ_1 and Φ_2 is characteristic. The presence of cations Φ_1 and Φ_2 in **IVb-d** indicates the occurrence of an analogous rearrangement in N-substituted triazoles.

Such peculiar behavior for the o-mercaptophenyltriazoles apparently enables mass spectrometry to be used to establish their isomeric structure since the fragmentation products of isomeric triazoles **IV** and **VI** will be different after rearrangement in spite of the obvious similarity in the principal fragmentation.

The synthesized o-mercaptophenyltriazoles can be oxidized at the SH group to form disulfides **VIII** on prolonged storage in air or by Cu(II), as noted above. This can also happen during their synthesis by heating the reaction mixture for an hour.



VII



VIII

The oxidative dimerization can be avoided by carrying out the syntheses in an inert atmosphere or by strictly controlling the reaction temperature. The structure of disulfide **VIII** was confirmed by mass spectrometry and by retrograde synthesis to the starting triazole **IVb** in boiling glacial acetic acid with Zn. The molecular ion of the disulfide (m/z 656), in contrast with aliphatic disulfides, which are subject to asymmetric fragmentation to form AlkSS and AlkSSH [19], fragments symmetrically at the S—S bond to form an ion (m/z 328) for which the fragmentation is similar to that of the molecular ion of triazole **IVb**.

EXPERIMENTAL

IR spectra of all compounds were taken on Specord IR-71 and Specord IR-75 spectrophotometers in the range 3700-700 cm^{-1} as mineral oil mulls. The spectra of triazoles **IVb, c, e** were also recorded in CCl_4 at 10^{-2}-10^{-3} M with cd = const. The PMR spectra of solutions of triazoles were recorded on a Tesla BS-487 C (80 MHz) at 20°C with HMDS as an internal standard. The spectrum of the NH-triazole **IVa** in DMF-D_7 was also recorded at 130°C. Mass spectra of triazoles **IV** were recorded on Finnigan 4021 and Varian MAT-212 mass spectrometers at ionization energy 70 eV with direct sample insertion. The purity and identity of the triazoles were monitored using TLC (Al_2O_3, in $CHCl_3$).

Elemental analyses for C, H, N, S, and M corresponded with those calculated.

The effective magnetic moments of complexes were determined from the measured magnetic susceptibilities of crystalline samples using the Faraday method at 298 K and Pascal's diamagnetic constants for the ligands [20].

1,3-Diphenyl-5-(o-mercaptophenyl)-1,2,4-triazole (IVb). A. Phenylhydrazine (0.7 ml, 7 mmoles, distilled over Zn powder) was added to a suspension of benzothiazinonium perchlorate **Ia** (1.15 g, 3.5 mmoles) [7] in glacial acetic acid (5 ml). The reaction mixture was boiled for 15 min, cooled, and diluted with a tenfold excess of ice water. The oily product that separated was kept for 1 day in a refrigerator to induce crystallization and then filtered off. If it did not crystallize, the product was extracted with ether. The extract was dried over anhydrous Na_2SO_4 and evaporated. Yield of triazole 0.51 g (60%).

Triazoles IVa, c-e. These were prepared analogously to **IVb**. Triazoles **IVb, d** were also synthesized by a modified method from benzothiazinones **II** [9], obtained by deprotonation of the corresponding perchlorates **I** [7].

The synthesized triazoles **IV** are colorless (**IVe** is bright yellow) crystalline compounds, very soluble in polar organic solvents, and practically insoluble in water.

B. A suspension of disulfide **VIII** (6.56 g, 10 mmoles) and previously activated Zn dust (3.25 g, 50 mmoles) in glacial acetic acid (50 ml) was refluxed with vigorous stirring for 2 h. The reaction mixture was cooled and filtered. The filtrate was diluted with twice the volume of water. The oily product that separated was kept in a refrigerator until it crystallized (~4 h) and filtered off. The product was then dissolved in NaOH (1 N, 25 ml) and filtered to remove the Zn. The filtrate was acidified by dropwise addition of concentrated HCl until the pH was 5-6. The oily product that separated was kept in a refrigerator until it crystallized (~1 day), filtered off, and recrystallized from isopropanol. Yield of triazole **IVb** 3.25 g (50%).

Complexes of o-Mercaptophenyltriazoles IVb, c (VIIa-e). Triazole **IVb** or **IVc** (4 mmoles) and the divalent metal acetate (Co, Ni, Zn, 2 mmoles) were dissolved in the minimal volumes of methanol with heating. The precipitate that separated on mixing the hot solutions obtained was filtered off after the reaction mixture cooled, washed three times with hot methanol, and dried in a vacuum desiccator over P_2O_5. Yield 53-84%.

The complexes are high-melting finely crystalline compounds that are difficultly soluble in organic solvents and insoluble in water.

Bis{2-[5-(1,3-diphenyl-1,2,4-triazolyl)]phenyl}disulfide (VIII, $C_{40}H_{28}N_6S_2$). A suspension of benzothiazinonium perchlorate **Ia** (1.15 g, 3.5 mmoles) and phenylhydrazine (0.7 ml, 7 mmoles) in glacial acetic acid (10 ml) was boiled for 1 h, cooled, and diluted with ice water. The oily product that formed was extracted with ether. The extract was dried over anhydrous Na_2SO_4 and evaporated. The caramel-colored product obtained was ground and recrystallized from isopropanol. Yield 0.9 g (80%) of **VIII**. Colorless crystals, mp 259-260°C. IR spectrum: 1600, 1555, 1510, 1500, 1270 cm^{-1}. $M_{calc} = 656$, $M^{+\cdot}/2 = 328$.

Disulfide **VIII** was also prepared by oxidation of triazole **IVb** by oxygen in air on boiling in glacial acetic acid for 1 h.

The disulfide, in contrast with mercaptophenyltriazole **IVb**, is difficulty soluble in the majority of organic solvents.

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SYNTHESIS OF 1,2,4-TRIAZOLO[4,3-*a*]QUINOLINE-9-, 1,2,3,4-TETRAZOLO[4,3-*a*]QUINOLINE-9 AND 1,2,4-TRIAZINO[4,3-*a*]QUINOLINE-10-CARBOXYLIC ACIDS FROM 2-CHLORO- AND 2-HYDRAZINOCINCHONINIC ACIDS

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UDC 547.832

Treatment of 2-chlorocinchoninic acid with hydrazine gives 2-hydrazinocinchoninic acid and with aroylhydrazines to give 1,2,4-triazolo[4,3-a]quinoline-9-carboxylic acids. These are also prepared by the action of benzoyl chloride or the carboxylic acid on 2-hydrazinocinchoninic acid. With pyruvic acid the latter gives 3-methyl-4-oxo-1,2,4-triazino[4,3-a]quinoline-10-carboxylic acid and with nitrous acid gives 1,2,3,4-tetrazolo[4,3-a]quinoline-9-carboxylic acid.

In a previous report [1] we have described 2-hydrazino- and 2-(β-acylhydrazino)cinchoninic acid amides and shown that they can be converted to 1,2,4-triazolo[4,3-*a*]quinoline-9-carboxylic acid amides.

The aim of the present study was to synthesize analogs with a free carboxyl group. To do so we studied the reaction of 2-chlorocinchoninic acid with hydrazine and acylhydrazines and of 2-hydrazinocinchoninic acid with benzoyl chloride, carboxylic acids, and nitrous acid.

It has been shown that 2-chlorocinchoninic acid (I) reacts with hydrazine hydrate upon heating in ethanol for 3 h to form 2-hydrazinocinchoninic acid (II, Table 1) (see scheme below).

Carrying out the reaction in DMF gives the 1,2,4-triazolo[4,3-*a*]quinoline-9-carboxylic acid (IIIa). The same compound, and its $C_{(3)}$ (IIIb) derivative, are also formed by heating acid II with formic or acetic acids.

In contrast to the 2-chlorocinchoninic acid amides [1], heating acid I with aroylhydrazines leads not to 2-aroylhydrazinocinchoninic acids but to 3-aryl-1,2,4-triazolo[4,3-*a*]quinoline-9-carboxylic acids (IIIc, d). Compound IIIc is also formed by reaction of acid II with benzoyl chloride.

Heating acid II with diethyloxalate in DMF gives IV.

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