

N-Quaternary Compounds. Part LVII.* Formation of *N*-vinyl Dipyridyl Sulfides *via* Ring Opening Reactions

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Symmetrical and unsymmetrical thiobis(2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olates) have been prepared from 8-hydroxy-2,3-dihydrothiazolo[3,2-*a*]pyridine-5(4*H*)- or -7(4*H*)-thiones and 5- or 7-halo-2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olates. The dihydrothiazolo rings are opened under alkaline conditions whereby the corresponding thiobis(*N*-vinylpyridines) are formed.

Our continued interest in the exploration of chemical and biological properties of novel dihydrothiazolo-azinium systems and their conversion to *N*-vinyl isomers² has lead us to investigate the preparation and isomerization reactions of thiobis(2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olates, whereby molecules containing two *N*-vinyl units are formed.

In an earlier work it was noticed that on thiation of 7-bromo-2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olate *1* to form the 7-thione *2* using potassium hydrogen sulfide, the symmetrical sulfide *3* could be an intermediate depending on the reaction conditions.³ In the same way the 5-chloro-2,3-dihydrothiazolo[3,2-*a*]pyridinium derivative *5* has been found to react with potassium hydrogen sulfide to yield the 5-thione *6*, which may react with another molecule of *5* to yield the symmetrical sulfide *7*; the reaction conditions are decisive for the isolation of *6* or *7* from the reaction. The unsymmetrical thioether *9* can be formed from the 7-bromide *1* and the 5-thione *6* in methanol solution. On heating these reagents in DMF, a mixture of three products is

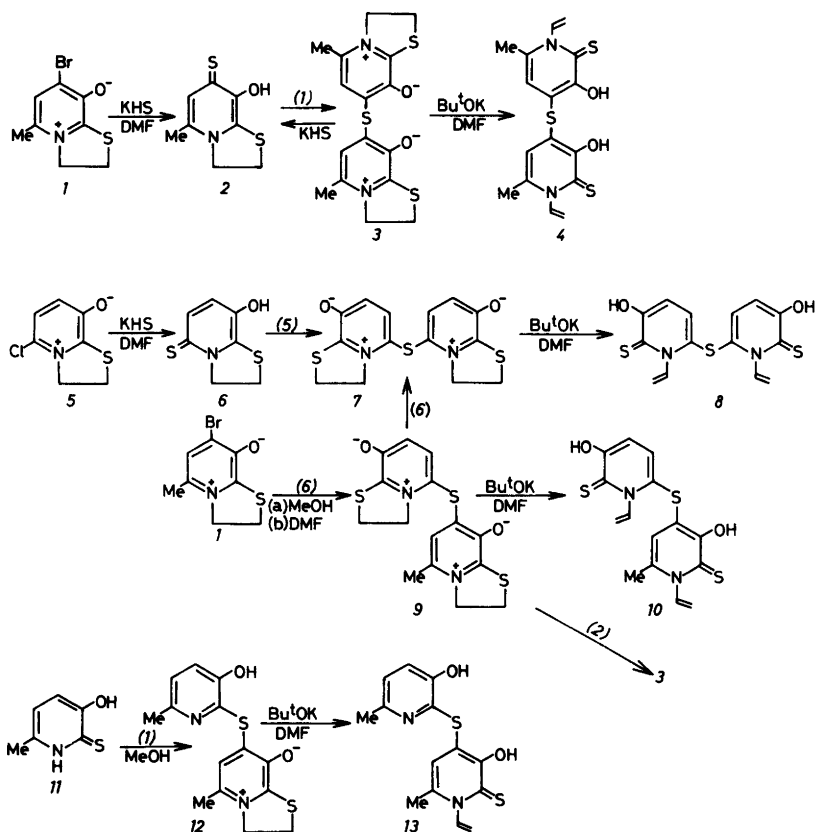
formed, *viz.* the unsymmetrical sulfide *9* and the two symmetrical sulfides *3* and *7*. The same product mixture in DMF was obtained from the reaction between the 7-thione *2* and the 5-chloride *5*. In the reaction of the 7-bromide *1* with the pyridine-2(1*H*)-thione *11* in methanol, formation of the unsymmetrical sulfide *12* results.

Both the halogen in *1* and *5* and the sulfur in the sulfide bridges are attached to active azine positions and therefore readily undergo the nucleophilic displacements observed; *e.g.* in the reaction of the 5-thione *6* with the 7-bromide *1* unreacted thione *6* may react with the unsymmetrical sulfide *9* to form the symmetrical sulfide *7*. The 7-thione *2*, which is the leaving group in the substitution, can attack another molecule of *9* in which case the symmetrical sulfide *3* is formed. In the same way the symmetrical sulfides can be attacked to yield the unsymmetrical sulfide; an equilibrium will finally be reached.

Treatment of the sulfide salts with potassium *tert*-butoxide in DMF gives the corresponding *N*-vinyl sulfides (4,8,10,13). *S*-Vinyl derivatives were not seen which is not unexpected since under the same conditions ring opening of the parent compounds, *viz.* 2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olate and its 5-methyl homologue, give the *N*-vinyl isomers in 98 and 95 % yields, respectively.⁴

The assignment of *N*-vinyl structures to the products is supported by their UV data. Simple 3-hydroxy-*N*-vinylpyridine-2-(1*H*)-thiones in ethanol have maxima in the regions 370–375, 275–280 and at *ca.* 260 nm whereas their *S*-vinyl isomers have maxima at *ca.* 310 and *ca.* 250 nm.⁵ The UV maxima at 382 and 270 nm for the ring

* Part LVI, see Ref. 1.



Scheme 1.

opened product from 12 are thus consistent with the *N*-vinyl formulation 13. Similarly the maxima for the symmetrical sulfide from 3 and 7 after the vinylation reaction, which occur at 393, 294 and 267 nm and at 415 and 268 nm, respectively, are consistent with structures 4 and 8. The product from the unsymmetrical sulfide 9 has its absorption maxima at intermediate wavelengths (388 and 294 nm) consistent with structure 10. The ^1H NMR spectra of the products formed from the symmetrical pyridinium sulfides 3 and 7 are only consistent with symmetrical divinyl derivatives, viz. the *N,N*-derivatives 4 and 8.

EXPERIMENTAL

The mass spectra are presented as MS [70 eV; m/z (% rel. int.)]

4,4'-Thiobis(3-hydroxy-6-methyl-1-vinylpyri-

dine-2(1H)-thione) 4. 7,7'-Thiobis(2,3-dihydro-5-methylthiazolo[3,2-*a*]pyridinium-8-olate) hydrobromide³ (2.6 g, 5 mmol) was stirred in dry DMF (250 ml) at room temperature while a solution of potassium *tert*-butoxide in *tert*-butanol (25 ml, 25 mmol) was added dropwise over 30 min. The mixture was stirred for another 20 min before most of the solvent was distilled off at reduced pressure. Water was added to the residue, the solution acidified with acetic acid and extracted with chloroform. Evaporation of the chloroform left the title compound; yield 0.75 g (40%), m.p. 212 °C (CHCl₃-MeOH). Anal. C₁₆H₁₆N₂O₂S₃; C, H. ^1H NMR (DMSO-*d*₆): δ 2.32(Me), 5.43 (H- β , *J* 16 Hz), 5.69 (H- β , *J* 8 Hz), 6.37 (H-5), 6.80 (H- α , dd.). UV (EtOH): 4.15 (log ϵ 4.20), 268 nm (3.65). MS: 364 (75, M), 331(40), 199(75), 198(80), 197(50), 196(50), 192(30), 167(70), 166(100).

8-Hydroxy-2,3-dihydrothiazolo[3,2-*a*]pyridine-5(4H)-thione 6. 5-Chloro-8-hydroxy-2,3-dihydro-

thiazolo[3,2-*a*]pyridinium chloride⁶ (4.5 g, 0.02 mol) and KHS (7.2 g, 0.1 mol) were heated together in refluxing DMF (100 ml) for 6 h. The insoluble material was removed by filtration of the hot reaction mixture and the filtrate concentrated to ca 10 ml at reduced pressure. The thione crystallized out on standing in the cold; yield 3.3 g (89%), m.p. 222 °C (EtOAc). Anal. C₇H₇NOS₂: C, H. ¹H NMR (TFA): 3.83 (2H-2), 5.10 (2H-3), 7.40 (H-6, H-7). MS: 185 (100, M), 184(80), 151(3), 142(4), 123(4), 112(3), 98(16).

5,5'-Thiobis(2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olate) 7 hydrochloride. A mixture of 5-chloro-8-hydroxy-2,3-dihydrothiazolo[3,2-*a*]pyridinium chloride⁶ (6.0 g, 27 mmol) and KHS (2.0 g, 28 mmol) in DMF (200 ml) was stirred and heated at 120 °C for 24 h. The mixture was filtered and the filtrate concentrated to ca 50 ml. The product which separated on cooling was recrystallized from dilute ethanol; yield 3.1 g (57%) m.p. 260 °C (decomp.). Anal. C₁₄H₁₄Cl₂N₂O₂S₃: C, H. ¹H NMR (TFA): δ 3.88 (2H-2), 5.32 (2H-3), 7.40 (H-6, J_{6,7} 8.5 Hz), 7.67 (H-7).

6,6'-Thiobis(3-hydroxy-1-vinylpyridine-2(1H)-thione) 8. Compound 8 was prepared from 5,5'-thiobis(2,3-dihydrothiazolo[3,2-*a*]pyridinium 8-olate and potassium *tert*-butoxide as described for 4; yield 45%, m.p. 192 °C (EtOAc). Anal. C₁₄H₁₂N₂O₂S₃: C, H. ¹H NMR (DMSO-*d*₆): δ 5.31 (H-β, J 15 Hz), 5.66 (H-β, J 7.5 Hz), 6.8 (H-α, H-4, H-5, m). UV (EtOH): 393 (log ε 3.84), 294 (3.72), 267 nm (4.03). MS: 336 (48, M), 303(21), 251(15), 250(14), 185(17), 184(20), 179(62), 178(100), 176(61).

7-(2,3-Dihydrothiazolo[3,2-*a*]pyridinium-8-olate-5-thio)-5-methyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium-8-olate 9·2HBr. 7-Bromo-8-hydroxy-5-methyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium bromide² (3.27 g, 0.01 mol) and 8-hydroxy-2,3-dihydrothiazolo[3,2-*a*]pyridine-5(4H)-thione (2.00 g, 0.011 mol) in methanol (50 ml) was stirred at room temperature for 24 h. The solution was then concentrated to a small volume and the precipitate collected from the cold mixture; yield 3.14 g (62%), m.p. 217 °C (decomp; MeOH). Anal. C₁₅H₁₆Br₂N₂O₂S₃: C, H. ¹H NMR (TFA): δ 2.58 (5-Me), 3.85 (2H-2, 2H-2'), 5.00 (2H-2), 5.33 (2H-3'), 7.00 (H-6), 7.62 (H-6', H-7'). MS: 350 (3, M), 258(6), 256(18), 199(28), 192(26), 185(100), 184(77), 160(26).

4-(3-Hydroxy-2(1H)-thioxo-1-vinylpyridine-6-thio)-3-hydroxy-6-methyl-1-vinylpyridine-2(1H)-thione 10. Compound 10 was prepared from 9 and potassium *tert*-butoxide as described for 4; yield 45%, m.p. 193 °C (decomp.; CHCl₃) Anal. C₁₅H₁₄N₂O₂S₃: C, H. ¹H NMR (DMSO-*d*₆): δ

2.32 (6-Me), 5.36 (H-β, H-β', J 16 Hz), 5.63 (H-β, H-β', J 8 Hz), 6.37 (H-5), 6.5–7.0 (H-α, H-α'), 7.1 (H-4', H-5'). UV (EtOH): 388 (log ε 3.94), 294 cm⁻¹ (3.83). MS: 350 (3, M), 317(2), 211(10), 193(19), 192(59), 151(50), 190(100), 185(9), 153(21), 152(34).

7-(3-Hydroxy-6-methylpyridine-2-thio)-8-hydroxy-5-methyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium bromide 12. A solution of 7-bromo-8-hydroxy-5-methyl-2,3-dihydrothiazolo[3,2-*a*]pyridinium bromide (3.27 g, 0.01 mol) and 3-hydroxy-6-methylpyridine-2(1H)-thione (1.55 g, 0.011 mol) in methanol (100 ml) was heated under reflux for 12 h and then concentrated to a small volume. The product, which crystallized from the cold solution, was obtained in 71% (2.73 g) yield, m.p. 230 °C (decomp.; H₂O). Anal. C₁₄H₁₅BrN₂O₂S₃: C, H. ¹H NMR (TFA): δ 2.45 (6'-Me), 2.70 (6-Me), 3.72 (2H-2), 4.87 (2H-3), 6.93 (H-6), 7.57 (H-5', J 8.5 Hz), 8.00 (H-4', J 8.5 Hz). MS: 306 (2, M), 294(1), 199(44), 155(18), 141(100), 128(7), 122(11).

4-(3-Hydroxy-6-methylpyridine-2-thio)-3-hydroxy-6-methyl-1-vinylpyridine-2(1H)-thione 13. Compound 13 was prepared from 12 as described for 4; yield 66% m.p. 174 °C (MeOH). Anal. C₁₄H₁₄N₂O₂S₂: C, H. ¹H NMR (DMSO-*d*₆): 2.26 and 2.37 (2 Me), 5.43 (H-β) J 16 Hz), 5.67 (H-β, J 8 Hz), 6.38 (H-5), 6.68 (H-α, dd.), 7.16 and 7.20 (H-4', H-5', J 8 Hz). UV (EtOH): 382 (log ε 4.14), 270 nm (4.02). MS: 306 (100, M), 273(73), 271(19), 247(10), 199(24), 198(24), 197(42), 168(16), 167(17), 166(61), 165(41), 141(47).

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Received July 4, 1983.