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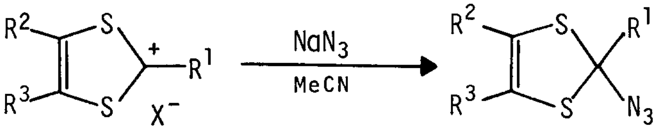
THERMOLYSIS OF 1,3-DITHIOL-2-YL AZIDES AND THERMAL PROPERTIES OF THE RESULTING 1,4,2-DITHIAZINES

Juzo Nakayama,* Atsuhiro Sakai, Akira Tokiyama, and Masamatsu Hoshino
Department of Chemistry, Faculty of Science, Saitama University,
Urawa, Saitama 338, Japan

Summary: 2-Substituted 1,3-dithiol-2-yl azides, on thermolysis in refluxing toluene, give 3-substituted 1,4,2-dithiazines which thermally extrude sulfur atom of the 4-position selectively to yield 3-substituted isothiazoles, while 2-unsubstituted 1,3-dithiol-2-yl azides undergo both ring expansion yielding 1,4,2-dithiazines and peculiar thermal dissociation into 1,3-dithiol-2-ylidene carbenes and hydrogen azide.

1,4,2-Dithiazines constitute an interesting 8 π-electron (π-excess) ring system, but little attention has been focused on their chemistry,[1] although the chemistry of their iso-π-electronic isomers, 1,4-dithiins and thiepins, has been extensively studied. The first successful synthesis of this ring system was reported by Fanghänel who had obtained comparable yields of 3-(methylthio)-1,4,2-dithiazines and 2-(*N*-methylthio)imino-1,3-dithioles by thermal decomposition of 2-(methylthio)-1,3-dithiol-2-yl azides at room temperature.[1a,b,2] We also recently reported the synthesis of 1,4,2-benzodithiazines.[1d] We now report the results of thermolysis of 2-substituted and 2-unsubstituted 1,3-dithiol-2-yl azides and thermal properties of the resulting 1,4,2-dithiazines.

1,3-Dithiol-2-yl azides (**2a-e**)[3] were prepared from the corresponding 1,3-dithiolium salts (**1a-e**)[4] by treatment with sodium azide in acetonitrile at room temperature. The azides **2** are thermally labile, and solid azides **2a-d** decompose with an evolution of gas, when heated at their melting points or slightly higher than these temperatures.



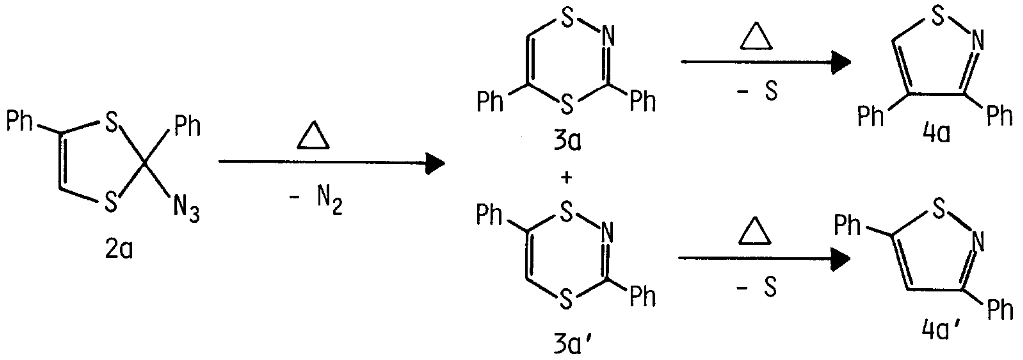
1   2

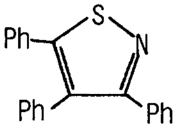
a : $R^1 = R^2 = Ph$, $R^3 = H$
b : $R^1 = R^2 = R^3 = Ph$
c : $R^1 = H$, $R^2 = R^3 = Ph$
d : $R^1 = R^3 = H$, $R^2 = Ph$
e : $R^1 = R^2 = R^3 = H$

A solution of **2a** in toluene was refluxed for 15 min. Workup of the mixture by column chromatography gave 3,5-diphenyl- and 3,6-diphenyl-1,4,2-dithiazines (**3a**, 36%, mp 49-52 °C and **3a'**, 15%, mp 69-71 °C),[5] 3,4-diphenyl- and

3,5-diphenylisothiazoles [4a, 2%, mp 84-84.5 °C (lit.,[6] mp 82-83.5 °C) and 4a', 33%, mp 82-82.5 °C (lit.,[7] mp 79.5-80.5 °C)], and sulfur.[8] These results may best be explained as follows. On thermolysis, insertion of the azide α-nitrogen into two C-S bonds occurs almost equally with simultaneous loss of N_2 to yield 3a and 3a'. 3a and 3a' then extrude the sulfur atom of 4-position to give 4a and 4a', respectively. The formation of 4 from 3 was ascertained by separate experiments; refluxing a solution of 3a in toluene for 2 h gave 4a (46%) and sulfur with recovery of 50% of 3a, while 3a' gave 4a' (80%) and sulfur with recovery of 10% of 3a' under the same conditions. The results agree with the findings by Fanghänel who obtained 3-(methylthio)isothiazoles by thermolysis of 3-(methylthio)-1,4,2-dithiazines at 180-200 °C.[1b]

Thermolysis of 2b (reflux in toluene for 30 min) gave only 3,4,5-triphenylisothiazole (4b), mp 211.5-212.5 °C,[5] in 80% yield.[8] No 3,5,6-triphenyl-1,4,2-dithiazine was detected in this case, thus indicating that it extrudes the sulfur atom of 4-position completely under the conditions.





4b

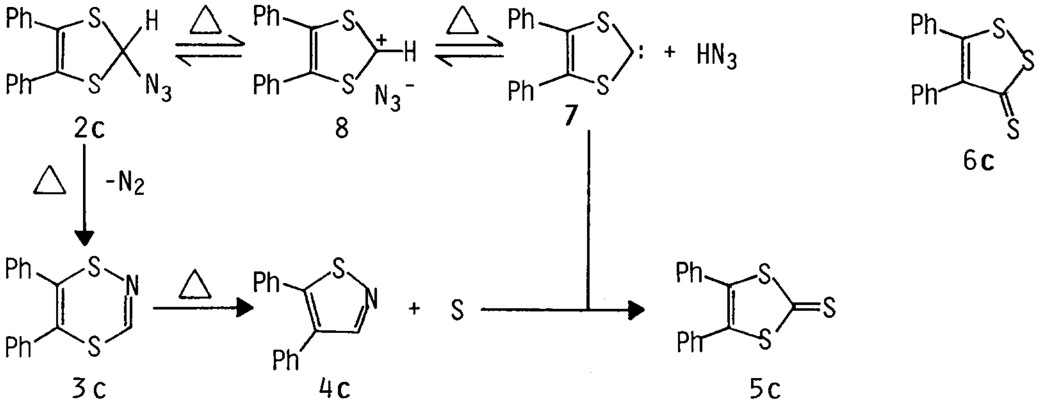
Refluxing a solution of 2c in toluene for 30 min gives isothiazole 4c (58%), mp 102-103.5 °C (lit.,[9] mp 101-103.5 °C), 1,3-dithiole-2-thione 5c (31%), mp 119-120 °C (lit.,[10] mp 119-120 °C), 1,2-dithiole-3-thione 6c (5%), mp 157 °C (lit.,[11] mp 159.5 °C), and sulfur. The results are well expalained assuming two competitive decomposition pathways. One involves the ring expansion yielding diphenyldithiazine 3c, and the other involves the thermal dissociation into diphenyl-1,3-dithiol-2-ylidene carbene 7 and hydrogen azide, which proceeds via the dithiolium azide 8.[12,13] 3c thus formed expels sulfur to give 4c, while the carbene 7 captures the sulfur to give 5c.[14] Evidence for the intermediacy of 8 is provided by conducting the thermolysis in the presence of N,N-dimethylaniline (1.1 equiv.), which afforded a 21% yield of 2-[p-(N,N-dimethylamino)-phenyl]-4,5-diphenyl-1,3-dithiole 9, a product of electrophilic substitution of 8 with N,N-dimethylaniline.[15] The formation of 5c by reaction of 7 with sulfur was established by a separate experiment. Treatment of 1c by base generates

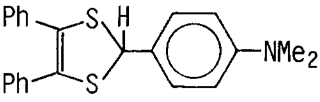
7.[16] Thus, 7 generated from 1c in boiling pyridine was allowed to react with sulfur to give 5c as the main product. However, mechanism of the formation of 6c still remains uncertain.[17]

Similarly, thermolysis of 2d in refluxing toluene for 30 min gave an isomeric mixture of phenylisothiazoles, 4d and 4d',[7] in a comparable ratio and in a 32% combined yield and 1,3-dithiole-2-thione 5d (3%).[4a] In this case, no 1,2-dithiole-3-thione 6d was formed. Thermolysis of the parent azide 2e gave a complex mixture containing considerable amounts of tarry materials.

We showed that 2-substituted 1,3-dithiol-2-yl azides, on thermolysis, give 1,4,2-dithiazines, while 2-unsubstituted 1,3-dithiol-2-yl azides undergo both ring expansion yielding dithiazines and thermal dissociation into 1,3-dithiol-2-ylidene carbenes and hydrogen azide, and, moreover, dithiazines thus produced readily extrude the sulfur atom of 4-position selectively in a quite general manner to give isothiazoles. These thermal properties are in remarkable contrast with those of 1,4,2-benzodithiazines (10) which rearrange to 2-imino-1,3-benzodithioles (11) on heating.[1f]

1,4-Dithiins[18] and thiepins,[19] on being heated, extrude sulfur to give thiophenes and benzenes, respectively. The driving force of this process consists in the formation of aromatic 6 π-electron ring systems with release from unstable 8 π-electron ring systems. The present study established that the same holds for the present system in a quite general manner.





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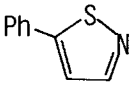
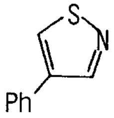
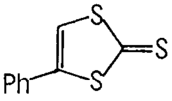


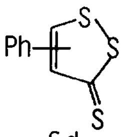
4d



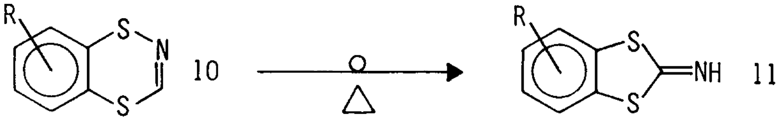
4d'



5d



6d



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1. a) E. Fanghänel, *Z. Chem.*, **5**, 386, (1965); b) E. Fanghänel, *J. prakt. Chem.*, **318**, 127 (1976); c) E. Fanghänel, R. Ebisch, and B. Alder, *Z. Chem.*, **13**, 431 (1973); d) J. Nakayama, M. Ochiai, K. Kawada, and M. Hoshino, *J. Chem. Soc., Perkin Trans. 1*, 618 (1981); e) J. Nakayama, H. Fukushima, R. Hashimoto, and M. Hoshino, *J. Chem. Soc., Chem. Commun.*, 612 (1982); f) J. Nakayama, A. Sakai, and M. Hoshino, Abstracts of Papers, The 10th Symposium on Organic Sulfur and Phosphorus Chemistry (Chemical Society of Japan), p. 72, January, 1982, Gifu, Japan.

2. Fanghänel also reported that thermolysis of 4,5-tetramethylene-1,3-dithiol-2-yl azide proceeds in a less distinct way to give 5,6-tetramethylene-1,4,2-dithiazine in a low yield.[1b]

3. **2a**: mp 61-63 °C dec; ν (N_3) 2100 cm^{-1}; δ (CCl_4) 6.33 (1H, s), 7.2-7.6 (8H, m), and 7.7-8.1 (2H, m). **2b**: mp 100-101 °C dec; ν (N_3) 2105 and 2145 (sh) cm^{-1}; δ ($CDCl_3$) 7.2-7.6 (13H, m) and 7.9-8.1 (2H, m). **2c**: mp 90 °C dec; ν (N_3) 2110 cm^{-1}; δ ($CDCl_3$) 5.65 (1H, s) and 7.20 (10H, s). **2d**: mp 35-37.5 °C; ν (N_3) 2100 cm^{-1}; δ (CCl_4) 5.83 (1H, s), 6.30 (1H, s), and 7.1-7.5 (5H, m). **2e** is a known compound; J. Nakayama, K. Fujiwara, and M. Hoshino, *J. Org. Chem.*, **45**, 2024 (1980).

4. a) D. Leaver, W. A. H. Robertson, and D. M. McKinnon, *J. Chem. Soc.*, 5104 (1962); b) A. Takamizawa and K. Hirai, *Chem. Pharm. Bull.*, **17**, 1924 (1969).

5. Satisfactory elemental analyses and supporting spectral data were obtained for these compounds.

6. M. Kojima and M. Maeda, *J. Chem. Soc., Chem. Commun.*, 386 (1970).

7. R. A. Olofson, J. M. Landesberg, R. O. Berry, D. Leaver, W. A. H. Robertson, and D. M. McKinnon, *Tetrahedron*, **22**, 2119 (1966).

8. Benzonitrile was formed in a trace amount in these reactions. This indicates that dithiazines may decompose to α-dithiones and benzonitrile as a minor path. However, an attempt to trap α-dithiones by Diels-Alder reaction with dimethyl acetylenedicarboxylate (DMAD) failed; heating a mixture of **3a** and **3a'** with a slight excess of DMAD in boiling toluene gave only **4a** and **4a'** along with a trace amount of benzonitrile, no adduct with DMAD being isolated.

9. H. Gotthart, *Tetrahedron Lett.*, 1281 (1971).

10. K. M. Pazdro, *Rcozniki Chem.*, **43**, 1089 (1969).

11. A. Lüttringhaus, H. B. König, and B. Böttcher, *Liebigs Ann. Chem.*, **560**, 201 (1947).

12. An analogy is found in the thermal dissociation of 2-alkoxy-1,3-benzodithioles into 1,3-benzodithiol-2-ylidene carbene and alcohols: J. Nakayama, *Synthesis*, 168 (1975); see also, J. Nakayama, *J. Chem. Soc., Perkin Trans. 1*, 525 (1975).

13. The formation of hydrogen azide was established by two ways. a) When the gaseous product evolved during the thermolysis was conducted into an aqueous solution of silver nitrate, the precipitation of silver azide was observed. b) The gaseous product was conducted into an aqueous dilute solution of sodium hydroxide. The resulting solution was mixed with a solution of benzyl chloride in benzene. The two-phase mixture was stirred in the presence of a catalytic amount of trioctylmethylammonium chloride (phase transfer catalyst) and then refluxed for a short period. Workup of the mixture gave benzyl azide.

14. Very recently we have shown that 1,3-benzodithiol-2-ylidene reacts with sulfur and selenium to give 2-thioxo- and 2-selenoxo-1,3-benzodithioles, respectively, in good yields; J. Nakayama, H. Sugiura, and M. Hoshino, *Tetrahedron Lett.*, in press.

15. Compound **9**, mp 150-151 °C, was alternatively obtained from **1c** and N,N-dimethylaniline quantitatively in acetonitrile at room temperature.

16. M. Narita and C. U. Pittman, Jr., *Synthesis*, 489 (1976).

17. Compound **5c** does not isomerize to **6c** under the conditions.

18. W. E. Parham and V. J. Traynelis, *J. Am. Chem. Soc.*, **76**, 4960 (1954) and K. Kobayashi, *Yuki Gosei Kyokai Shi*, **40**, 642 (1982).

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