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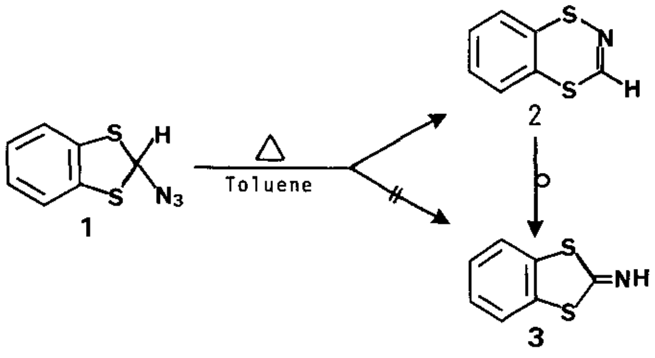
REARRANGEMENT OF 1,4,2-BENZODITHIAZINES TO 2-IMINO-1,3-BENZODITHIOLES. ITS UNPRECEDENTED CHARACTERISTIC FEATURES (AN EXTREME CASE OF SOLVENT EFFECT)

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

Abstract —— 3-Unsubstituted 1,4,2-benzodithiazines undergo a new thermal rearrangement to give 2-imino-1,3-benzodithioles. The most characteristic feature of this rearrangement is that it occurs smoothly only when benzodithiazines were heated without solvent, but it does not take place in non-polar solvents. A plausible mechanism of this rearrangement is proposed on the basis of available experimental data.

1,4,2-Dithiazines constitute an interesting 8 π-electron ring system, but little is known about their chemistry[1] compared to that of thier iso-π-electronic isomers, 1,4-dithiins and thiepins. We have previously shown that the thermolysis of 1,3-benzodithiol-2-yl azide (1) in refluxing toluene gives an excellent yield of 1,4,2-benzodithiazine (2) arising from insertion of the azide α-nitrogen into the C-S bonds with loss of nitrogen. No 2-imino-1,3-benzodithiole (3), product of insertion into the C-H bond, is formed.[1d] We now observed that the yellow oily compound (2) gradually rearranges to crystalline (3), mp 128 °C (lit.,[1b] mp 128 °C), when it was kept at room temperature without solvent in the dark.[2] This finding prompted us to examine this rearrangement in solutions, which disclosed that no rearrange occurs in non-polar solvents, even when its solution was heated for a prolonged period.



The following is illustrative of this phenomenon. A small sealed glass tube in which compound (2) was placed without solvent was immersed in a solution of (2) in carbon tetrachloride (0.02 M) which was placed in a round-bottomed flask equipped with a reflux condenser. The solution was then heated at reflux, thus allowing the both (2) in the glass tube and the solution to be heated at the same temperature and for the same period. After 22 h, (2) in the glass tube was completely consumed to give (3) in 79% yield,[3] while unchanged (2) was recovered from the solution in 97% yield.

At the beginning of mechanistic work of this rearrangement, (2) was heated in a variety of solvents and concentrations. Typical results are summarized in Table. This uncovered the following characteristic features. (a) Much to our surprise, dilution of (2) with its equal weight of less polar solvents (CCl_4, C_6H_6, and dioxane) retards the rearrangement completely. (b) In very polar solvents (pyridine, CH_3CN, and DMSO), the rearrangement takes place only in a concentrated solution, and the lowest limit of concentration that can bring about the rearrangement lies at about 5 wt %. (c) In a hydroxylic solvent ethanol, the rearrangement occurs even in a dilute solution, although the rate of rearrangement seems to depend slightly on concentration.[4]

Table Typical Results of Rearrangement of (2) to (3) in a Variety of Solvents and Concentrations[a]

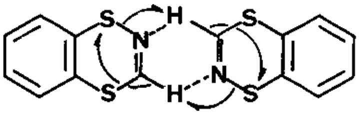
Solvent	Concentration (% by wt)	Yield of (3)[b] (%)	Yield of Recovered (2)[b] (%)
None	100	79	0
CCl_4	50	0	85
CCl_4	33	0	92
CCl_4	20	0	90
Pyridine	50	81	0
Pyridine	33	86	0
Pyridine	20	91	0
Pyridine	11	81	10
Pyridine	5.9	17	75
Pyridine	1.1	0	96
EtOH	50	86	0
EtOH	20	87	0
EtOH	1.4	81	10

[a] In all of runs, samples (2 mmol) in a sealed tube were heated for 22 h by immersing them in refluxing carbon tetrachloride placed in a large round-bottomed flask equipped with a reflux condenser.

[b] Yield based on purified material by column chromatography.

At this stage the followings were postulated as a working hypothesis. In a neat liquid, compound (2) exists in an associated form, probably in a cyclic dimeric form due to weak hydrogen bonding,[5] and therefore, the rearrangement proceeds by an acid-base catalysis mechanism (4)[6] probably in a concerted manner in which the substrate itself acts as a catalyst. This association is, however, so weak that (2) exists in a monomeric form in a solution where the rearrangement does not occur. In ethanol the rearrangement proceeds in a manner like (5). If this is the case, the rearrangement should meet the following requirements. (a) Catalysis (6) should be observed with substances such as 2-hydroxypyridine that have an acidic and a basic site in the same molecule and in which the sites have a tautomeric relationship to each other.[7] (b) The rearrangement should not be observed with (2) having a substituent on the 3-position. In this connection, substitution of deuterium on the 3-position should alter the rate of rearrangement.

Indeed 2-hydroxypyridine accelerated the rearrangement remarkably, and moreover, its effect was strongly dependent on the concentration of (2) in a solution. Heating a mixture of (2) and 0.1 equiv. of 2-hydroxypyridine (2 h, 79 °C, without solvent) gave (3) in 91% yield. On the other hand, an 11 wt % solution of (2) in benzene containing 1 equiv. of 2-hydroxypyridine, on being heated at 79 °C for 22 h, gave only 31% of (3) with 61% recovery of (2), while a 20 wt % benzene solution afforded 77% of (3) with 6% recovery of (2) under the same conditions.[8] A similar trend of catalytic effect was also observed with pyrazole though less prominent, Aniline is a weaker base than *N*,*N*-dimethylaniline, but it might act like (7) on (2) in analogy with ethanol, whereas *N*,*N*-dimethylaniline might not. In fact, heating (2) with 0.1 equiv. of aniline (2 h, 79 °C, without solvent), afforded (3) in 88% yield, while treatment of (2) with 0.1 equiv. of *N*,*N*-dimethyl-



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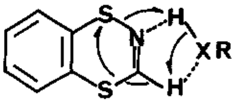
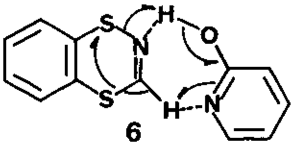


5; $RX = C_2H_5O$
7; $RX = PhNH$



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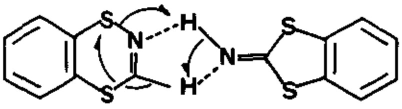

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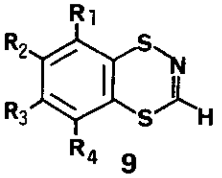
aniline under the same conditions resulted in the quantitative recovery of (2). Here the more important finding is that the rearranged product (3) itself catalyzes the rearrangement of (2), indicating that (3) might behave like (8) toward (2). Heating (2) with 0.1 equiv. of (3) (5 h, 79 °C, without solvent) produced (3) in 90% yield (exclusive of the added 3).[9]

The second requirement was easily satisfied by the findings that 3-phenyl-1,4,2-benzodithiazine[1d] was, on being heated at 79 °C for 1 month without solvent, recovered quantitatively, and some other 3-substituted 1,4,2-benzodithiazines[1d] could be kept without any change for ca. 3 years at ambient temperature. 3-Deuterio-1,4,2-benzodithiazine was prepared,[10] and its admixture with (2) was heated at 79 °C without solvent. The reaction was quenched when the total conversion was less than 50%. ^{1}H-NMR analysis showed that the rearrangement of (2) was the faster by a factor of ca. 1.2.[11]

Generality of the rearrangement was next examined. Heating a mixture of (9a) and (9a')[12] at 79 °C for 50 h without solvent afforded (10a) in 50% yield with 100% consumption of the starting mixture, while the mixture, on being heated with 0.1 equiv. of 2-hydroxypyridine at 79 °C for 5 h, gave (10a) in 81% yield. By contrast, heating a 20 wt % solution of the mixture in benzene at 79 °C for 200 h resulted in the quantitative recovery of the starting mixture. A similar trend of reactivity was also observed mixtures of (9b) and (9b') and of (9c) and (9c'),[12] which gave (10b) and (10c), respectively, on rearrangement.



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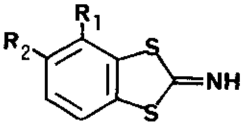
	R^1	R^2	R^3	R^4
a	Me	H	H	H
a'	H	H	H	Me
b	H	Me	H	H
b'	H	H	Me	H
c	H	Cl	H	H
c'	H	H	Cl	H



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	R^1	R^3
a	Me	H
b	H	Me
c	H	Cl

Finally it was found that rearrangement of (2) is also induced by strong bases (EtONa, t-BuOK, and BuLi).[13] For example treatment of (2) with sodium ethoxide (ca. 3 equiv.) in ethanol at ambient temperature for 10 min yielded (3) (63%) and 1,2-benzenedithiol (19%).[14] The mechanism operating here seems to differ from that of thermal rearrangement.[15]

In summary we found a new thermal rearrangement of unprecedented characteristic features, to whom we tentatively propose a mechanism (4) for initiating step and a mechanism (8) for propagating step. It is known that a variety of 1,4,2-dithiazines having no condensed benzene ring eliminate sulfur of the 4-position selectively, when heated, to give the corresponding isothiazoles.[1b,f] Thus, the observed thermal properties of 1,4,2-benzodithiazines are in remarkable contrast those of 1,4,2-dithiazines having no fused benzene ring.

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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, A. Tokiyama, and M. Hoshino, Tetrahedron Lett., 24, 3792 (1983).
2. Crystals of (3) begin to precipitate after several weeks. Workup of the mixture after 3 months gives (3) (69%) and (2) (20%).
3. In some cases the rearrangement is not complete within this period, and also, in a rare case, an induction period is observed. Although analytically pure (2) was employed throughout this work, the rate of rearrangement seems to depend slightly on the purity of (2) (method used for purification of 2).
4. The reaction in dioxane containing 11% of ethanol or water gave the starting material in over 80% yield. In acetic acid, (2) was considerably consumed to give an intractable mixture.
5. Direct evidence for this association is not available at present. ^{1}H-NMR and IR spectra were determined in carbon tetrachloride as solvent in a variety of concentrations. The chemical shift of C(3)-H and infrared absorption due to C(3)-H bond (easily identified by comparison of the spectrum with that of 3-deuterated compound; see ref 10) vary very small by changes in concentration.
6. T. M. Lowry and I. J. Faulkner, J. Chem. Soc., 127, 2883 (1925).
7. An analogy is found in the mutarotation of glucose; C. G. Swain and J. F. Brown, Jr., J. Am. Chem. Soc., 74, 2534, 2538 (1952).
8. Under the same conditions, the use of 1 equiv. of pyridine or phenol alone cannot bring about the rearrangement, but the use of a combination of pyridine and phenol gives (3) (21%) and resinous materials with 33% of recovery of (2).

9. This might be consistent with the observation of induction period.[3]

10. The compound was prepared in an isotopic purity of ca. 80% starting from 2-deuterio-1,3-benzodithiolium tetrafluoroborate; J. Nakayama, Bull. Chem. Soc. Jpn., 55, 2289 (1982).

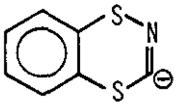
11. Two factors, viz., difference of ability of two compounds in forming hydrogen bonding and kinetic isotope effect may be both concerned with this result.

12. Thermal decomposition of 4-methyl-1,3-benzodithiol-2-yl azide gives a mixture of (9a) and (9a') in a ratio of about 1:1; see ref. 1e. For the same reason, mixtures of (9b) and (9b') and of (9c) and (9c') were employed for this study.

13. Acid such as p-toluenesulfonic acid (catalytic amount) cannot induce the rearrangement.

14. A separate experiment showed that (3) is converted to 1,2-benzenedithiol under the conditions.

15. The reaction probably procceds via the carbanion (11), although trapping of (11) with D_2O or MeI failed. For example treatment of (2) with BuLi in THF at -78 °C followed by addition of an exess of D_2O gave (3) (65%) and 1,2-benzenedithiol (30%).



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