NOVEL RING CONTRACTIONS OF 2,7-DIHYDRO-3,6-DIPHENYL-1,4,5-THIADIAZEPINE VIA A HALOGENATION-DEHALOGENATION PROCESS

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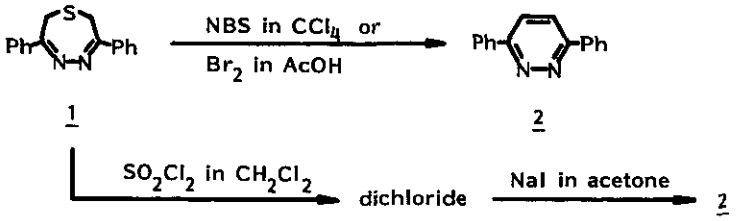
Abstract —— 2,7-Dihydro-3,6-diphenyl-1,4,5-thiadiazepine undergoes novel ring contractions via a halogenation-dehalogenation process in methanol, giving sulfur-containing five-membered cyclic compounds: this result is a great contrast to the ring contraction with extrusion of sulfur reported previously.

In 1963 Loudon and Young[1] demonstrated that a seven-membered cyclic 1,2-diaza compound, 2,7-dihydro-3,6-diphenyl-1,4,5-thiadiazepine 1, gave 3,6-diphenylpyridazine 2 via an intermediary episulfide on treatment with N-bromosuccinimide in carbon tetrachloride or bromine in acetic acid, while the chlorination of 1 with sulfuryl chloride in dichloromethane gave a dichloride which was subsequently transformed into 2 (Scheme 1).



Scheme 1.

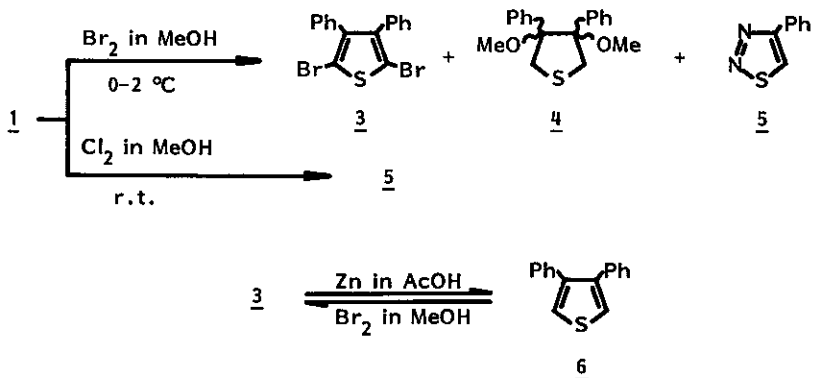
In the course of a survey of halogenations of seven-membered cyclic 1,2-diaza compounds[2-4], we have found that ring contraction reactions via a halogenation-dehalogenation process strongly depend upon the reaction conditions, particularly upon the solvents used, as well as upon the structures of cyclic 1,2-diaza compounds. Thus, we planned to reinvestigate halogenations of the dihydrothiadiazepine 1 under

various conditions. In this communication we wish to describe novel ring contractions of 1.

The reaction of 1[5] with bromine in carbon tetrachloride at room temperature gave a mixture of unstable azinium perbromides, which on heating under reflux was converted into 2 and/or 4-bromo-3,6-diphenylpyridazine[6]. On treatment with bromine in methanol, however, novel ring contractions of 1 took place to give sulfur-containing cyclic compounds.

A solution of bromine (120 mmol) in methanol (40 mL) was added, drop by drop, over a period of 1 h to a suspension of 1 (20 mmol) in methanol (40 mL) at 0-2 °C; during the addition, 1 gradually dissolved with the evolution of nitrogen and crystals separated out again. The reaction mixture was stirred at the same temperature for another 1 h, and then subjected to chromatography (SiO_2, $CHCl_3$) to give three sulfur-containing products, 2,5-dibromo-3,4-diphenylthiophene 3 (mp 148-149 °C), 3,4-dimethoxy-3,4-diphenyltetrahydrothiophene 4 (mp 116.5-117.5 °C) and 4-phenyl-1,2,3-thiadiazole 5 (mp 78-79 °C, lit.[7] mp 77-78 °C), in 44, 12 and 4% yields, respectively (Scheme 2), but no sulfur-free products such as 2 were obtained.

The spectral data and elementary analyses satisfied all the assigned structures 3-5[8]. When treated with zinc dust in acetic acid, 3 was changed to a known compound, 3,4-diphenylthiophene 6[9], which again readily reverted to 3 on bromination in methanol; both the interconversions occurred almost quantitatively.

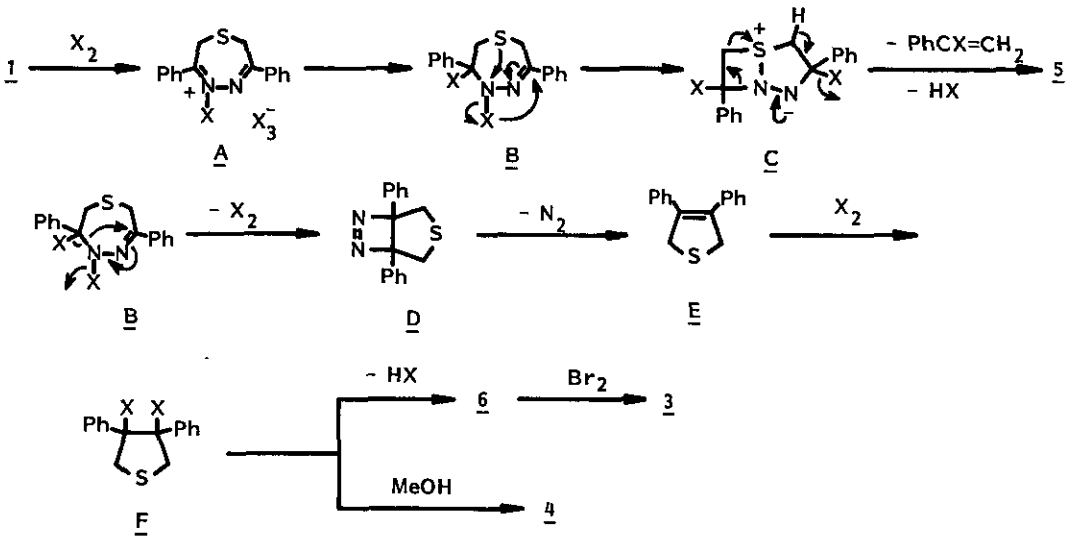


Scheme 2.

Next, we have investigated the chlorination of 1. In contrast to the chlorination in carbon tetrachloride or dichloromethane leading to the formation of dichloro- and tetrachlorodihydrothiadiazepines[10], the treatment of 1 with excess chlorine gas in methanol at room temperature afforded 5 in 22% yield, together with a mixture of

unidentified products.

The probable pathways for the above novel ring contractions are depicted in Scheme 3. The dihydrothiadiazepine 1 reacts with halogen in methanol to yield a dihalide B via a perhalide A[11]. The dihalide B undergoes ring contractions through two different routes; one is a necleophilic attack of the sulfur on 1-position with



Scheme 3.

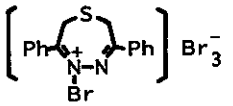
concurrent 1,3-migration of halide ion to yield a bicyclic betaine C, and the other is the formation of a bicyclic azo intermediate D via a dehalogenation, followed by extrusion of nitrogen to give a dihydrothiophene E. The formations of 5 from C, and of 3 and 4 from E can be easily understood as illustrated in Scheme 3.

REFERENCES AND NOTES

1. J. D. Loudon and L. B. Young, J. Chem. Soc., 1963, 5496.
2. O. Tsuge and K. Kamata, Heterocycles, 1975, 3, 15.
3. O. Tsuge and K. Kamata, ibid., 1975, 3, 547.
4. O. Tsuge, K. Kamata, and S. Yogi, Bull. Chem. Soc. Jpn., 1977, 50, 2153.
5. The dihydrothiadiazepine 1 was early prepared by the reaction of diphenacyl sulfide with hydrazine hydrate (E. Fromm and A. Erhardt, Ber., 1921, 54, 187). However, we have prepared by a new method: α-Bromoacetophenone azine (O. Tsuge, M. Tashiro, K. Kamata, and K. Hokama, Org. Prep. & Proced. Int., 1971, 3, 289) was allowed to react with sodium sulfide in ethanol to give 1 (mp 176-177 °C,

lit.[1] mp 175 °C) in 95% yield.

6. The dihydrothiadiazepine 1 reacted with bromine in carbon tetrachloride at room temperature to give a mixture of unstable three azinium perbromides, 7-9, whose ratios depended upon the amounts of bromine used. Details will be reported elsewhere.



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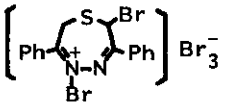

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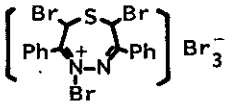

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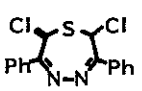
7. C. D. Hurd and R. I. Mori, J. Am. Chem. Soc., 1955, 77, 5359.

8. 3: colorless prisms; ^{13}C NMR ($CDCl_3$) δ 109.5, 134.3, 142.1 (each s); MS m/e 392, 394, 396 (M^+). 4: colorless plates; ^1H NMR ($CDCl_3$) δ 3.15 (6H, s, OCH_3), 3.37 (4H, s, CH_2), 7.16 (10H, ArH); ^{13}C NMR ($CDCl_3$) δ 33.8 (t, CH_2), 52.0 (q, OCH_3), 91.0 (s, 3- and 4-C), 137.4 (s); MS m/e 300 (M^+). Although the stereochemistry of 4 is not clear, trans configuration between two phenyl groups will be more probable than cis one. The compound 5 was identical with an authentic sample prepared by the reported method[7].

9. H. J. Backer and W. Stevens, Recl. Trav. Chim. Pays-Bas, 1940, 59, 423.

10. The dihydrothiadiazepine 1 reacted with N-chlorosuccinimide (4 equiv.) in carbon tetrachloride (reflux, 1 h) or with sulfuryl chloride (2.5 equiv.) in dichloromethane (room temp., 1.5 h) to give trans-2,7-dichloro derivative 10 (mp 157-158 °C (dec)) in 32 or 63% yield, respectively, while with large excess of chlorine gas in dichloromethane 1 gave 2,2,7,7-tetrachloride 11 (mp 181-182 °C) in 45% yield. Details will be reported elsewhere. 10: ^1H NMR (DMSO-d_6) δ 6.80 (2H, s, CH), 7.40-7.75 (6H, m, ArH), 7.75-8.20 (4H, m, ArH); ^{13}C NMR (DMSO-d_6) δ 55.1 (d, 2- and 7-C), 147.8 (s, 3- and 6-C); MS m/e 334, 336, 338 (M^+). Thus, the dimorphous crystals, mp 158 or 179 °C (dec), which were assumed as either 2,2- or 2,7-dichloride[1], can be assigned as 2,7-dichloride.



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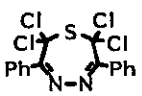

11

11. As cited in Ref. 6, we have confirmed the formation of A (X=Br, 7). The formation of such a perhalide as A has been reported in the reaction of benzaldehyde azine with bromine (F. L. Scott and P. A. Cashell, J. Chem. Soc. (C), 1970, 2674).

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