Synthesis of 3,4-Bischloromethyl-1,2,5-thiadiazole: an Unexpected Chloromethylation; Contrasting Selectivity in Dihalogenations by *N*-Chlorosuccinimide and *N*-Bromosuccinimide

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Summary 1,2,5-Thiadiazole, previously thought to be resistant to electrophilic substitution, has been shown to undergo chloromethylation; *N*-chlorosuccinimide is more selective than *N*-bromosuccinimide in the dihalogenation of 3,4-dimethyl-1,2,5-thiadiazole.

Hitherto, 1,2,5-thiadiazole (**1**) has been thought to be resistant to electrophilic substitution.[1] Microwave[2] and electron diffraction[3] studies, however, indicate that the ring system is as aromatic as thiophen which readily undergoes chloromethylation. We report that treatment of 1,2,5-

thiadiazole with HCl in refluxing acetic acid–formaldehyde forms the bischloromethylated compound (**3b**) [b.p. 68—75° at 0·2 mmHg; τ ($CDCl_3$) 5·10]. This compound was also the principal product from the chlorination of 3,4-dimethyl-1,2,5-thiadiazole (**2**) with *N*-chlorosuccinimide (NCS).

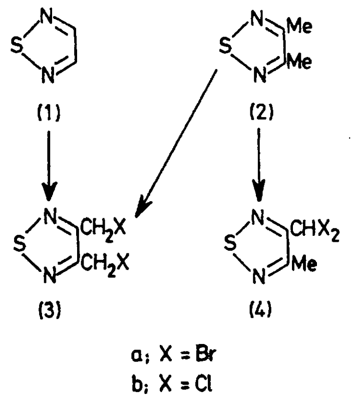
TABLE

Composition (%) of reaction mixture[a]

Compound	NBS, 3 h[b]	NCS, 15 days[b]
(**2**)	0	0
Monohalogeno-compound	23	16
(**3**)	22	50
(**4**)	38	10
Trihalogeno-compounds	17	23

[a] Determined by ^1H n.m.r. analysis.
[b] In refluxing CCl_4, with benzoyl peroxide and tungsten light.

We have found that there are significant differences in the distribution of products from 'benzylic' dihalogenation of the dimethyl compound (**2**) when *N*-bromosuccinimide (NBS) is used in place of NCS (see Table). This contrasts with the generally accepted belief that these two reagents act in a parallel manner in various halogenations.[4] Although treatment of compound (**2**) with an excess of NBS gave a mixture in which the major component was the dibromomethyl compound (**4a**), the use of NCS resulted in the formation of 50% of the bischloromethyl compound (**3b**) together with only 10% of the isomer (**4b**). The different selectivity of NCS allows the ready separation of the bishalogenomethyl compound (**3b**) in preparatively useful quantities.



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[1] L. M. Weinstock, Ph.D. Dissertation, Indiana University, 1958; F.-H.Marquardt, Ph.D. Dissertation, Indiana University, 1960; Reviewed by L. M. Weinstock and P. I. Pollack, *Adv. Heterocyclic Chem.*, 1968, **9**, 107.

[2] S. V. Dobyns and L. Pierce, *J. Amer. Chem. Soc.*, 1961, **83**, 3553.

[3] F. A. Momany and R. A. Bonham, *J. Amer. Chem. Soc.*, 1961, **83**, 4475.

[4] M. F. Hennelynck and R. H. Martin, *Bull. Soc. chim. belges*, 1950, **59**, 193; *Chem. Abs.*, 1951, **45**, 2411h; N. P. Buu-Hoi and P. Demerseman, *J. Org. Chem.*, 1953, **18**, 649; A. G. Anderson, Jr., J. A. Nelson, and J. J. Tazuma, *J. Amer. Chem. Soc.*, 1953, **75**, 4980; F. L. Lambert, W. D. Ellis, and R. J. Parry, *J. Org. Chem.*, 1965, **30**, 304.