

A New Route to 3,4-Disubstituted Tetrahydrothiophenes

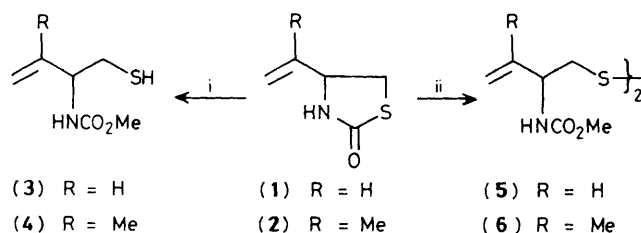
Eatedal H. M. Abd Elall, Mohamed I. Al Ashmawy, and John M. Mellor*

Department of Chemistry, The University, Southampton SO9 5NH, U.K.

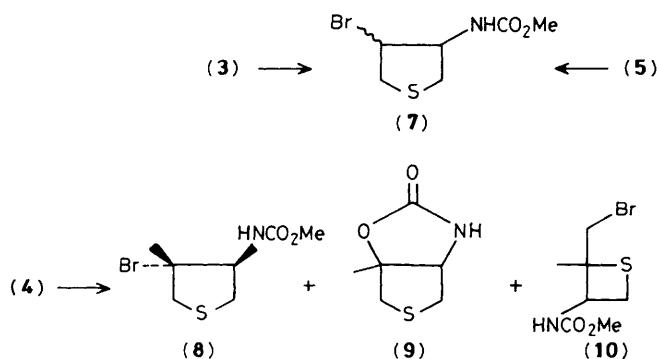
Reaction of readily available thiazolidinones with *N*-bromosuccinimide affords 3,4-disubstituted tetrahydrothiophenes.

A route to 3,4-disubstituted tetrahydrothiophenes can be envisaged by the attack of electrophiles on derivatives of 2-aminobut-3-ene-1-thiols. Such a cyclisation of acyclic derivatives is of interest because of recent reports¹ of the synthesis of such thiophenes stimulated by the need² to establish new routes to biotin. We have recently described³ the preparation of derivatives of 2-aminobut-3-ene-1-thiols from the unsaturated thiazolidinones (1) and (2) which are available in high yield from the appropriate 1,4-dihalogenobut-2-enes. We now describe not only the multistep conversion of the thiazolidinones (1) and (2) into 3,4-disubstituted tetrahydrothiophenes *via* derivatives of 2-aminobut-3-enes-1-thiols, but also the remarkably simple direct conversion of the thiazolidinones (1) and (2) with *N*-bromosuccinimide into 3-bromo-4-isocyanato-tetrahydrothiophenes.

The thiols (3) and (4) and the disulphides (5) and (6) have been obtained³ in good yield from the respective thiazolidinones (Scheme 1). Bromination of the thiol (3) or the disulphide (5) in dichloromethane gives the carbamates (7) in 63 and 61% yield, respectively (Scheme 2). In contrast, bromination of the thiol (4) gives three major products: the tetrahydrothiophene (8) (20%), the bicyclic compound (9) (28%), and the thietane (10) (35%) (Scheme 2). Bromination of the disulphide (6) gives the thietane (10) in 75% yield. The structures of the products were established by a combination



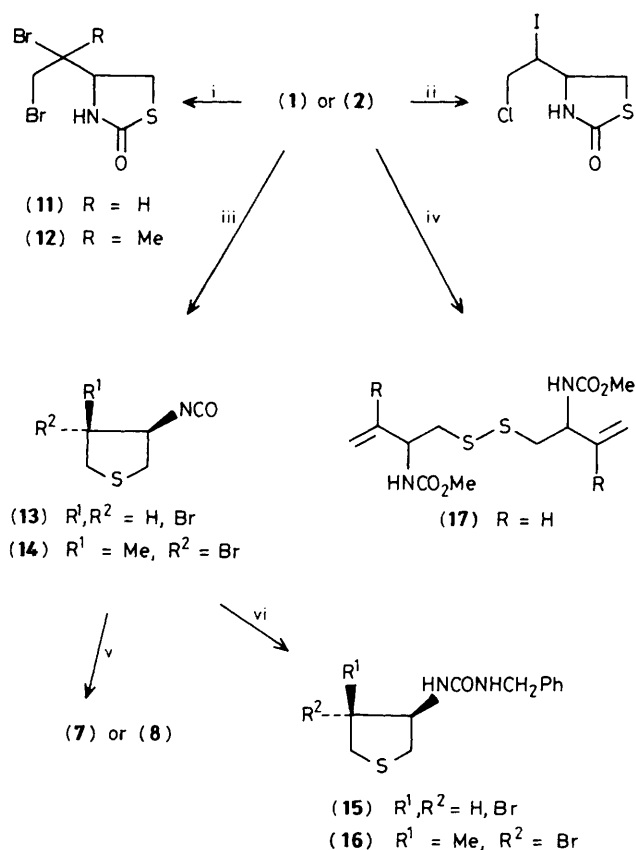
Scheme 1. Reagents: i, KOH, MeOH, N_2 ; ii, KOH, MeOH, O_2 .



Scheme 2

of spectroscopy (^1H and ^{13}C n.m.r.), microanalysis, and reactions to establish the skeleton (debromination with $\text{Zn}/\text{MeCO}_2\text{H}$ or Bu^n_3SnH) and the stereochemistry (with sodium hydride *trans*-derivatives afford aziridines,[†] in accord with literature precedent⁴).

Direct bromination of the thiazolidinones (1) and (2) in dichloromethane gives mixtures of the diastereoisomeric dibromides (11) and (12), respectively, although we note that addition of iodine monochloride to the thiazolidinone (1) proceeds in an anti-Markovnikov sense (Scheme 3). However reaction of the thiazolidinones (1) and (2) with *N*-bromosuccinimide in dichloromethane gives the bromo isocyanates (13) and (14), respectively, in 87 and 96% yields. From the thiazolidinone (1) a mixture of *cis*- and *trans*-isomers is obtained but from the thiazolidinone (2) the single isomer (14) is isolated (Scheme 3). The isocyanates (13) and (14) are sufficiently stable to permit distillation, but react readily with



Scheme 3. Reagents: i, Br_2 , CH_2Cl_2 ; ii, ICl , CH_2Cl_2 ; iii, *N*-bromosuccinimide, CH_2Cl_2 ; iv, *N*-iodosuccinimide, CH_2Cl_2 ; MeOH; v, MeOH; vi, PhCH_2NH_2 .

[†] Whereas *cis*-derivatives afford unsaturated monocyclic products.

alcohols and amines, *e.g.* with methanol the carbamates (7) and (8) are obtained, and with benzylamine the ureas (15) and (16) are formed in high yield.

Although the nature of the variety of products isolated from the foregoing reactions implies mechanistic complexities, which will be discussed in a full paper, it is likely that reaction of the thiazolidinones (1) and (2) with *N*-bromosuccinimide proceeds *via* initial electrophilic attack at sulphur with formation of an acyclic isocyanate. In support of this view we find that the thiazolidinone (1) on treatment with *N*-iodosuccinimide in dichloromethane gives the disulphide (17). In the reaction with *N*-bromosuccinimide the ready cyclisation of an intermediate sulphenyl bromide is expected, by analogy with results obtained in the penicillin⁵ and prostacyclin⁶ areas. Reaction of unsaturated thiols with iodine gives sulphenyl iodides, and their ready conversion, even in the absence of oxygen, into disulphides has been described.⁷ Our results not only suggest the use of unsaturated thiazolidinones as precursors of unsaturated sulphenyl halides; they also establish a route *via* the bromo isocyanates (13) and (14) to 3,4-disubstituted tetrahydrothiophenes in high yield.

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References

- 1 H. A. Bates, L. Smilowitz, and J. Lin, *J. Org. Chem.*, 1985, **50**, 899; H. A. Bates, L. Smilowitz, and S. B. Rosenblum, *J. Chem. Soc., Chem. Commun.*, 1985, 353, and references therein.
- 2 J. P. Bonjour, *Ann. N.Y. Acad. Sci.*, 1985, **447**, 97; E. T. Kornegay, *ibid.*, p. 112.
- 3 E. H. M. Abd Elall and J. M. Mellor, *J. Chem. Soc., Chem. Commun.*, 1986, 576; E. H. M. Abd Elall, M. I. Ashmawy, and J. M. Mellor, *J. Chem. Soc., Perkin Trans. I*, accepted for publication.
- 4 K. D. Kampe, *Liebigs Ann. Chem.*, 1971, **752**, 142.
- 5 T. Kamiya, T. Teraji, Y. Saito, M. Hashimoto, O. Nakaguchi, and T. Oku, *Tetrahedron Lett.*, 1973, 3001.
- 6 M. Shibasaki and S. Ikegami, *Tetrahedron Lett.*, 1978, 559.
- 7 K. C. Nicolaou, W. E. Barnette, and R. L. Magolda, *J. Am. Chem. Soc.*, 1981, **103**, 3472.