Transannular Brominolysis of 5,7,12,14-Tetrahydrodibenzo[*c,h*][1,6]dithiecins by Pyridinium Hydrobromide Perbromide

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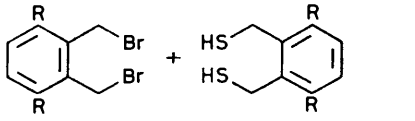
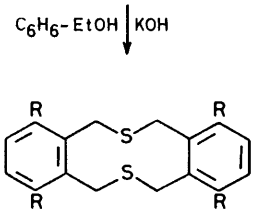
A facile ring-opening reaction has been observed for 5,7,12,14-tetrahydrodibenzo[*c,h*][1,6]dithiecin (5) and 1,4,8,11-tetramethyl-5,7,12,14-tetrahydrodibenzo[*c,h*][1,6]dithiecin (6) on treatment with pyridinium hydrobromide perbromide. Compound (5) gave mainly bis(*o*-bromomethylbenzyl) disulphide (9) together with trace amounts of 1,2-bis(bromomethyl)benzene and 1,4-dihydro-2,3-benzodithiin (8). Similar products were isolated for compound (6). A reaction pathway involving the participation of the two transannular sulphur atoms in these systems is proposed.

As part of our continuing interest in sulphur-containing medium-size ring compounds,[1] we undertook the synthesis of 5,7,12,14-tetrahydrodibenzo[*c,h*][1,6]dithiecin (5) and 1,4,8,11-tetramethyl-5,7,12,14-tetrahydrodibenzo[*c,h*][1,6]dithiecin (6), seemingly attractive precursors for the corresponding dibenzo[*a,e*]cyclo-octenes. For example, application of the Ramberg–Bäcklund reaction [2] on the α-halogenated bis-sulphones of (5) and (6), in principle, would simplify the construction of these dibenz-annelated cyclo-octatetraenes which have now become valuable starting materials for the intriguing 5,6,11,12-tetradehydrodibenzo[*a,e*]cyclo-octene and related systems.[3] In this context, we have examined the bromination of (5) and (6), and have observed the first example of ring-opening involving the participation of two transannular sulphur atoms.

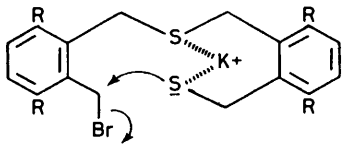


(1) R = H (2) R = H
(3) R = Me (4) R = Me



(5) R = H
(6) R = Me

In the presence of potassium hydroxide, reactions of 1,2-bis(bromomethyl)benzene (1) with 1,2-bis(mercaptomethyl)benzene (2), and of 2,3-bis(bromomethyl)-1,4-dimethylbenzene (3) with 2,3-bis(mercaptomethyl)-1,4-dimethylbenzene (4) proceeded smoothly to give compounds (5) and (6), respectively, in good yields. The structures of the products agreed with the spectral data and elemental analyses. Remarkably, these cyclisations needed not be carried out at high dilution. It is conceivable that, in a manner analogous to crown ether formation,[4] the two sulphur atoms in the intermediate sulphide ion (7) are held on the same side by the potassium cation so that the two reacting ends can



(7)

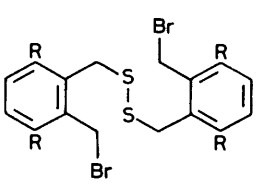
be brought into close proximity for subsequent cyclisation.

Bordwell and Williams [5] reported the conversion of benzyl sulphide into benzyl α-bromobenzyl sulphone by successive treatment with bromine and *m*-chloroperbenzoic acid. Our attempts to similarly treat compounds (5) and (6) were interrupted at the initial stages where addition of 2 molar equivalents of bromine at 50—60 °C resulted in ring-cleavage with loss of sulphur giving mainly the corresponding dibromides (1) and (3). In contrast, treatment of compounds (5) and (6) with an equimolar quantity of pyridinium hydrobromide perbromide in dry tetrahydrofuran at 0 °C yielded mainly products whose molecular weights corresponded to the incorporation of one molar equivalent of bromine into the starting material. In addition, compound (5) gave two minor products, the dibromide (1) and 1,4-dihydro-2,3-benzodithiin (8). In the case of compound (6), the dibromide (3) was also obtained in trace amounts but the expected 5,8-dimethyl-1,4-dihydro-2,3-benzodithiin eluded isolation.

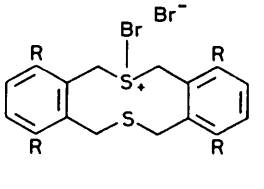
The i.r. spectra of the 1 : 1 adducts of (5) and (6) with bromine did not reveal conclusive information for structure assignment. The n.m.r. and mass spectral data were consistent with the ring-opened disulphide structures (9) and (10) but could not completely rule out halogenosulphonium salt formulations of the type depicted by (11) and (12) or equivalent structures.[6,7] Further characterisation was necessary to distinguish between these two possibilities. An *X*-ray crystallographic analysis [8] of the 1 : 1 (5)-bromine compound has established (9) as the correct structure.

The observed transannular brominolysis of the strain-free tetrahydrodibenzodithiecin system by pyridinium

hydrobromide perbromide is surprising since only small sulphur heterocycles such as thiirans [9] and thietans [10]

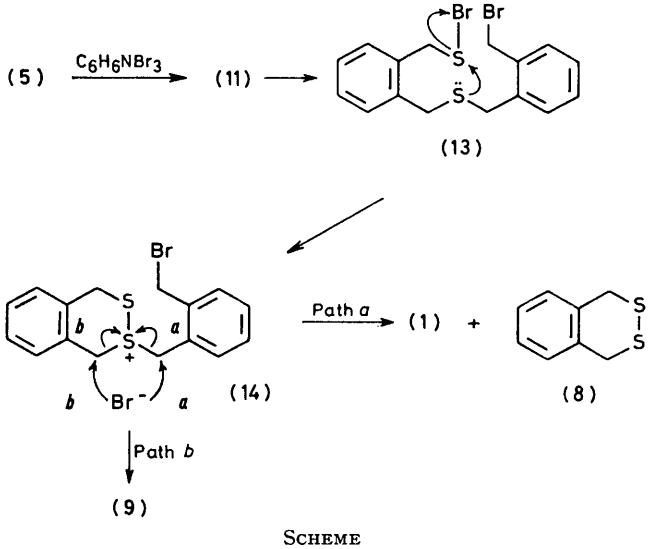


(9) R = H
(10) R = Me



(11) R = H
(12) R = Me

have been found previously to undergo similar reactions with halogens yielding disulphides. The formation of compounds (1), (8), and (9) may be readily accounted for by the mechanism depicted in the Scheme.



SCHEME

The C–S bond cleavage in (5) by pyridinium hydrobromide perbromide, possibly *via* complex (11) to give the sulphenyl bromide intermediate (13), is analogous to the mechanism previously proposed for the brominolysis of thiiran [9a] and thietan.[10] An internal displacement of (13) is invoked here for the generation of thiosulphonium bromide (14). The latter may well serve as a common intermediate undergoing two competing reactions, depicted by *a* and *b*, which lead to the formation of all the observed products.

EXPERIMENTAL

M.p.s were determined with a Koefler hot-stage apparatus. ^{1}H N.m.r. spectra were recorded with a JEOL 60HL spectrometer using tetramethylsilane as internal standard. Molecular weights were determined by mass spectrometry using a Varian M66 instrument. Elemental analyses were performed by the Australian Microanalytical Service, Parkville, Victoria. 1,2-Bis(mercaptomethyl)-benzene (2), m.p. 45—46° (from pentane) (lit.,[11] 46—47°), was prepared in 80% yield from 1,2-bis(bromomethyl)-benzene by a standard procedure.[1,12] 2,3-Bis(bromomethyl)-1,4-dimethylbenzene (4), prepared by the method of Ho,[13], had m.p. 97—99° (lit.,[13] 97—98°).

2,3-Bis(mercaptomethyl)-1,4-dimethylbenzene (4).—To a boiling solution of thiourea (4.5 g, excess) in ethanol (80 ml) was added the dibromide (2) (4.34 g) in portions over 10 min. Boiling was continued until half the solvent had evaporated off. Potassium hydroxide–water (40 ml; 25% w/v) was added and the resulting mixture was again boiled for 0.5 h. The clear solution was chilled in an ice-bath and acidified cautiously with concentrated HCl. After standing at 0 °C for 2 h, the precipitate was filtered off, washed thoroughly with water, and dried *in vacuo*. Crystallisation from light petroleum (b.p. 40—60 °C) gave the *dithiol* (4) (2.5 g, 84%) as needles, m.p. 63—65° (Found: C, 60.6; H, 7.2. $C_{10}H_{14}S_2$ requires C, 60.6; H, 7.1%), τ(CCl_4) 8.45 (1 H, t, *J* 7 Hz, SH), 7.67 (3 H, s, ArMe), 6.25 (2 H, d, *J* 7 Hz, $ArCH_2S$), and 3.18 (1 H, s, ArH).

5,7,12,14-Tetrahydrodibenzo[c,h][1,6]*dithiecin* (5).—A solution of the dibromide (1) (2.64 g, 10 mmol) in benzene (40 ml) and a separate solution of the dithiol (2) (1.70 g, 10 mmol) in 60% v/v ethanol–water (40 ml) containing potassium hydroxide (1.2 g) were added simultaneously to a solution of benzene (20 ml) and ethanol (40 ml) with vigorous stirring over a period of 1 h. The mixture was then stirred at room temperature for an additional 5 h. Evaporation of solvent under reduced pressure gave a white residue which was extracted with boiling dichloromethane (4 × 20 ml). The combined extracts were washed with 5% w/v sodium hydrogencarbonate–water (2 × 30 ml) and with water (2 × 30 ml) and dried ($MgSO_4$). Removal of solvent *in vacuo* followed by crystallisation of the residue from benzene gave the *tetrahydrodibenzodithiecin* (5) (1.05 g, 75%) as needles, m.p. 249—251° (Found: C, 70.3; H, 5.9; S, 23.8. $C_{16}H_{16}S_2$ requires C, 70.5; H, 5.9; S, 23.6%); M^+ 272; τ($CDCl_3$) 6.55 (1 H, s, $ArCH_2S$) and 2.20—2.75 (1 H, m, ArH).

Similarly, *1,4,8,11-Tetramethyl-5,7,12,14-tetrahydrodibenzo*[c,h][1,6]*dithiecin* (6) was prepared from the dibromide (3) and the dithiol (4) in 60% yield as needles, m.p. 218—220° (from acetone) (Found: C, 72.9; H, 7.2; S, 19.3. $C_{20}H_{24}S_2$ requires C, 73.1; H, 7.4; S, 19.5%); M^+ 328; τ($CDCl_3$) 7.65 (3 H, s, ArMe), 6.25 (2 H, s, $ArCH_2S$), and 3.10 (2 H, s, ArH).

Reaction of 5,7,12,14-Tetrahydro[c,h][1,6]*dibenzodithiecin* (5) *with Bromine*.—Bromine (320 mg, 2 mmol) in CCl_4 (10 ml) was added dropwise during 15 min at room temperature to a stirred suspension of the tetrahydrodibenzodithiecin (5) (272 mg, 1 mmol) in CCl_4 (10 ml). The mixture was gradually brought to 50 °C and stirred at this temperature for 6 h. After cooling to room temperature the resulting dark brown solution was washed with 10% w/v sodium thiosulphate–water (2 × 10 ml) and with water (2 × 10 ml), dried ($MgSO_4$), and evaporated. Crystallisation of the residue from pentane gave the dibromide (1) (320 mg, 61%), identical in all respects with an authentic sample.

Reaction of 1,4,8,11-Tetramethyl-5,7,12,14-tetrahydrodibenzo[c,h][1,6]*dithiecin* (6) *with Bromine*.—Reaction of the tetramethyltetrahydrodibenzodithiecin (6) with bromine (2 mol. equiv.) in CCl_4 at 50 °C as described above for the tetrahydrodibenzodithiecin (5) gave the dibromide (3) in 58% yield.

Ring-opening Reaction of 5,7,12,14-Tetrahydrodibenzo[c,h][1,6]*dithiecin* (5) *by Pyridinium Hydrobromide Perbromide*.—A mixture of the tetrahydrodibenzodithiecin (5) (544 mg, 2.0 mmol) and pyridinium hydrobromide per-

bromide (640 mg, 2.0 mmol) in tetrahydrofuran (20 ml) was stirred at room temperature for 4 h. The solvent was evaporated off, water (20 ml) was added, and the aqueous suspension was extracted with dichloromethane (3 × 20 ml). The combined extracts were washed with water (2 × 15 ml), dried ($MgSO_4$), and evaporated to yield an off-white solid. Two crystallisations of this material from CCl_4 gave *bis*(o-*bromomethylbenzyl*) *disulphide* (9) (298 mg, 35%) as cream-coloured prisms, m.p. 114—116° (Found: C, 44.7; H, 3.9; S, 14.6; Br, 36.6. $C_{16}H_{16}S_2Br_2$ requires C, 44.5; H, 3.7; S, 14.8; Br, 36.9%), *m/e*, 430, 432 (M^+), and 434; τ($CDCl_3$), 6.15 (1 H, s, $ArCH_2S$), 5.35 (1 H, s, $ArCH_2Br$), and 2.60—2.75 (2 H, m, ArH).

The mother liquors from above were combined and evaporated to dryness. The residue was taken up in dichloromethane (4 ml) and poured onto a column of silica gel. Elution with hexane gave the *dibromide* (1) (25 mg, 5%). Further elution with hexane–ethyl acetate (2 : 1) gave 1,4-dihydro-2,3-benzodithiin (8) (13 mg, 4%), m.p. 77—78°, undepressed on admixture with an authentic sample.[14]

The disulphide (9) was also obtained in slightly better yields (45—50%) when the tetrahydrodibenzodithiecin (5) was treated with an equimolar quantity of bromine in $CHCl_3$ containing a two-fold excess of triethylamine.

Ring-opening Reaction of 1,4,8,11-*Tetramethyl*-5,7,12,14-*tetrahydrodibenzo*[c,h][1,6]*dithiecin* (6) *by Pyridimiun Hydrobromide Perbromide*.—A mixture of the tetramethyltetrahydrodibenzodithiecin (6) (492 mg, 1.5 mmol) and pyridinium hydrobromide perbromide (480 mg, 1.5 mmol) in tetrahydrofuran (20 ml) was stirred at room temperature for 4 h. Work-up as described above for the reaction of the tetrahydrodibenzodithiecin (5) gave *bis*(2-*bromomethyl*-3,6-*dimethylbenzyl*) *disulphide* (10) (492 mg, 67%), m.p. 148—150° (from acetone) (Found: C, 49.5; H, 4.8; S, 13.0; Br, 32.9. $C_{20}H_{24}S_2Br_2$ requires C, 49.2; H, 4.9; S, 13.1; Br, 32.7%); *m/e* 486, 488 (M^+), and 490; τ($CDCl_3$) 7.16 (3 H, s, $ArCH_3$), 5.90 (1 H, s, $ArCH_2S$), 5.41 (1 H, s, $ArCH_2Br$), and 2.82 (1 H, s, ArH).

The acetone mother liquor was evaporated to dryness. The residue was dissolved in $CHCl_3$ (4 ml) and chromatographed on silica gel. Elution with light petroleum (b.p. 40—60 °C) gave the *dibromide* (3) (17 mg, 4%). Further elution with more polar solvents failed to give a well-defined product.

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