Dithiols. Part 29.[1] Syntheses of *cis*- and *trans*-2-Phenyliminoperhydro-1,3-benzodithiole

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Reaction of *trans*-2-(phenylthiocarbamoylthio)cyclohexyl acetate and of *trans*-2-[(acetylthio)(phenylimino)-methylthio]cyclohexyl acetate with potassium hydroxide in ethanol gives *trans*-2-phenyliminoperhydro-1,3-benzodithiole. Overall retention of configuration is explained by the formation of an intermediate thiiranium ion. The same product, and the *cis*-isomer, are obtained when *trans*-perhydro-1,3-benzodithiole-2-thione and its *cis*-isomer, respectively, are successively treated with methyl iodide, aniline, and aqueous sodium hydroxide.

In a previous Part,[2] the selective reaction of phenyl isothiocyanate with the thiol function in *trans*-2-mercaptocyclohexanol was described. Treatment of the product, *trans*-2-(phenylthiocarbamoylthio)cyclohexanol (3), with thionyl chloride was expected to give *cis*-2-phenyliminoperhydro-1,3-benzodithiole (7) by analogy with the conversion of the mono(phenylthiourethane) (1) of *trans*-cyclopentane-1,2-diol into *cis*-2-phenyliminoperhydrocyclopenta-1,3-oxathiole (2),[3] but instead only the monothio-compound (6) was obtained; this was also the product when an attempt was made to prepare the

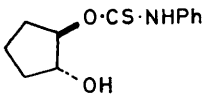
[1] Part 28, R. C. Forster and L. N. Owen, *J.C.S. Perkin I*, 1978, 822.

[2] M. E. Ali, N. G. Kardouche, and L. N. Owen, *J.C.S. Perkin I*, 1975, 748.

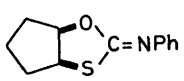
[3] L. Goodman, A. Benitez, C. D. Anderson, and B. R. Baker, *J. Amer. Chem. Soc.*, 1958, **80**, 6582.

O-toluene-*p*-sulphonate of the dithiourethane (3). The projected stereospecific synthesis of a *cis*-dithiol was thus thwarted.

A modified approach to this objective has now been made by use of the acetate (4), since an acetoxy function



(1)



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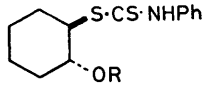
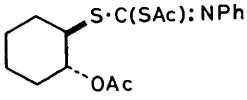


(3) R=H
(4) R=Ac



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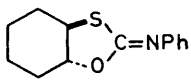

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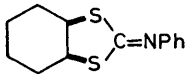

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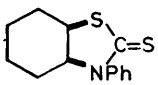

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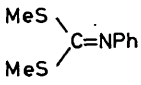

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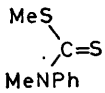

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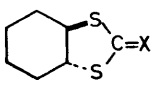
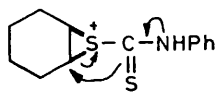


(11) X=O
(12) X=S
(13) X=NPh



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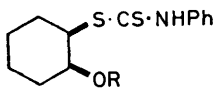
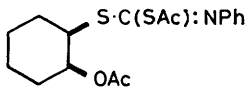


(15) R=H
(16) R=Ac



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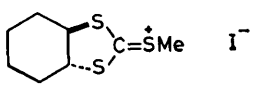

(18)

is known to be susceptible to intramolecular attack by thiolate anion.[4] It seemed possible that the desired cyclised product (7) could be formed by treatment of the acetate with base under mild conditions, though it was recognised that attack by the nitrogen atom, rather than the thione sulphur, might occur,[3,5] to give the isomeric thiazolidinethione (8). In the event, reaction of the acetate (4) or the diacetyl compound (5) with ethanolic potassium hydroxide yielded a crystalline product which had the required molecular formula $C_{13}H_{15}NS_2$, and it was encouraging to find that the u.v. spectrum was similar to that illustrated [6] for *N*-bismethylthiomethyleneaniline (9) and quite different from that of methyl *N*-methyl-*N*-phenyldithiocarbamate (10).[6] Furthermore, the i.r. spectrum contained a strong band at 1 580 cm^{-1} (*cf.* 1 570 cm^{-1} reported [7] for 2-phenylimino-1,3-dithiolan). The product was therefore hydrolysed, under acidic conditions, to the corresponding dithiolcarbonate. Surprisingly, this was identical to the known [8] *trans*-perhydro-1,3-benzodithiol-2-one (11), indicating that the cyclisation had proceeded with retention of configuration to give the *trans*-product (13), a disappointing stereochemical result. This can be explained by displacement of the acetoxy group in the acetate (4) by the vicinal sulphide group, rather than by the thione function, to give the episulphonium intermediate (14), from which the *trans*-compound (13) would be derived by the depicted rearrangement.

The yellow colour of the diacetyl compound (5) was immediately discharged on treatment with the basic reagent, indicating very rapid loss of the *S*-acetyl function to give the monoacetate (4), thus accounting for the similar yields of cyclised product obtained from both starting materials.

Cyclisation of the acetate (4) was further investigated under a variety of conditions, but when it occurred, for example by heating in dimethyl sulphoxide, the product was still the *trans*-compound (13).

It was now of obvious interest to study the reactions of the *cis*-analogues of the acetates (4) and (5). Base-catalysed reaction of *cis*-2-mercaptocyclohexanol with phenyl isothiocyanate (1 mol) gave the dithiourethane (15) which with an excess of acetic anhydride gave the diacetyl derivative (17); the use of less anhydride gave the monoacetate (16) which was also obtained by selective deacetylation of the diacetyl compound. No cyclic dithiolan derivative could be obtained by treatment of either the mono- or the di-acetyl compound with ethanolic potassium hydroxide; the main products isolated in each case were the parent alcohol (15) and *O*-ethyl *N*-phenylthiocarbamate, formed by simple solvolysis. This result supports the mechanism proposed for the formation of the cyclised product from the *trans*-acetate (4), since the *cis*-isomer cannot undergo a neighbouring group reaction to give an intermediate thiiranium ion.

To provide further evidence for the constitution and stereochemistry of the phenylimino compound (13), both this and the *cis*-isomer (7) were synthesised by an adaptation of the method used [9] for the conversion of 1,3-dithiolan-2-thione into 2-phenylimino-1,3-dithiolan. Reaction of *trans*-perhydro-1,3-benzodithiole-2-thione (12) with methyl iodide gave a crystalline salt (18) which contained almost four extra moles of methyl iodide not readily removed under high vacuum; subsequent treatment with aniline, followed by aqueous sodium hydroxide,

[4] L. W. C. Miles and L. N. Owen, *J. Chem. Soc.*, 1952, 817; J. S. Harding and L. N. Owen, *ibid.*, 1954, 1528, 1536; M. Kyaw and L. N. Owen, *ibid.*, 1964, 6252.

[5] *Cf.* B. R. Baker, K. Hewson, L. Goodman, and A. Benitez, *J. Amer. Chem. Soc.*, 1958, **80**, 6577; F. L. Scott, R. E. Glick, and S. Winstein, *Experientia*, 1957, **13**, 183.

[6] A. D. Ainley, W. H. Davies, H. Gudgeon, J. C. Harland, and W. A. Sexton, *J. Chem. Soc.*, 1944, 150.

[7] Y. Ueno, T. Nakai, and M. Okawara, *Bull. Chem. Soc. Japan*, 1970, **43**, 162.

[8] T. J. Adley, A. K. M. Anisuzzaman, and L. N. Owen, *J. Chem. Soc.* (*C*), 1967, 807.

[9] R. Mayer and K. Schäfer, *J. prakt. Chem.*, 1964, **26**, 279.

gave the *trans*-phenylimino-compound (13), identical with that obtained by the cyclisation process. The *cis*-isomer (7) was prepared by a similar series of reactions on *cis*-perhydro-1,3-benzodithiole-2-thione (the intermediate salt again contained an excess of methyl iodide), and also by reaction of *cis*-cyclohexane-1,2-dithiol with phenyl isothiocyanate under the conditions described [10] for conversion of ethane-1,2-dithiol into 2-phenylimino-1,3-dithiolan.

The mass spectra of the phenylimino compounds were generally similar to one another, but the *cis*-compound (7) showed a strong peak at *m/e* 146 ($C_6H_{10}S_2$) which was insignificant in that of the *trans*-isomer (13), whilst the latter showed a strong peak at *m/e* 114 ($C_6H_{10}S$) which was very weak in that of the *cis*-isomer. There were also characteristic differences in the i.r. spectra in the region 900—1 000 cm^{-1}.

EXPERIMENTAL

I.r. spectra were recorded for solutions in chloroform, u.v. spectra for solutions in ethanol, and ^1H n.m.r. spectra for solutions in deuteriochloroform (Varian T60 instrument). Mass spectra were recorded with a Perkin-Elmer 270 instrument. The adsorbent for t.l.c. was Kieselgel GF_{254} (Merck), the developing solvent being dichloromethane unless otherwise specified. Extracts were dried over magnesium sulphate. Petroleum refers to the solvent of b.p. 40—60 °C.

trans-2-*Phenyliminoperhydro*-1,3-*benzodithiole* (13).—(i) M-Potassium hydroxide in ethanol (2.2 ml) was added to a warm solution of *trans*-2-(phenylthiocarbamoylthio)cyclohexyl acetate [2] (0.63 g) in ethanol (9 ml), and the mixture was left at ambient temperature overnight. Water (7 ml) was then added, and the precipitated solid was collected and recrystallised from aqueous methanol to give the *phenylimino compound* (13) (0.27 g), m.p. 110°, $\nu_{max.}$ 1 580, 1 485, 1 445, 960, and 940 cm^{-1}, $\lambda_{max.}$ 238 (11 000) and 280 nm (ε 6 000), τ 2.4—3.2 (5 H, m), 6.4 (2 H, m), and 7.4—8.8 (8 H, m), *m/e* 249 (M^+, 70%), 167 ($PhNCS_2$, 10), 135 (PhNCS, 94), 114 ($C_6H_{10}S$, 31), 81 (C_6H_9, 100), 80 (C_6H_8, 66), and 77 (Ph, 34) (Found: C, 62.7; H, 6.1; N, 5.35; S 25.35. $C_{13}H_{15}NS_2$ requires C, 62.6; H, 6.1; N, 5.6; S, 25.7%). An additional quantity (57 mg) was isolated from the mother liquors by t.l.c.

(ii) Similar treatment of *trans*-2-[(acetylthio)(phenylimino)methylthio]cyclohexyl acetate [2] (0.36 g) in ethanol (6 ml) with M-potassium hydroxide (1.5 ml) gave the same product (13) (0.165 g), m.p. 105—107°.

(iii) A solution of *trans*-2-(phenylthiocarbamoylthio)-cyclohexyl acetate (68 mg) in dry dimethyl sulphoxide (0.5 ml) was kept at *ca.* 95 °C for 80 h. T.l.c. then gave some starting material and the phenylimino compound (19 mg), m.p. 110° (purified by sublimation).

Hydrolysis.—A solution of the phenylimino compound (13) (100 mg) in a mixture of acetic acid (12 ml) and concentrated hydrochloric acid (2.7 ml) was heated on a steam-bath for 70 h, then cooled, diluted with water (20 ml), and extracted with dichloromethane. Evaporation of the dried extract gave *trans*-perhydro-1,3-benzodithiol-2-one (11) (58 mg), m.p. 109—110° not depressed on admixture with an authentic sample,[8] m.p. 109—110°.

cis-2-(*Phenylthiocarbamoylthio*)*cyclohexanol* (15).—A solution of phenyl isothiocyanate (1.05 g) in dry benzene (3 ml) was slowly added (10 min) to a stirred mixture of *cis*-2-mercaptocyclohexanol [1] (1.0 g), triethylamine (0.1 g), and dry benzene (6 ml). After 12 h at ambient temperature the solution was concentrated to an oil which solidified on storage under benzene–petroleum at 0 °C. The product was washed with petroleum and recrystallised from carbon tetrachloride to give the *dithiourethane* (15) (1.2 g), m.p. 135—137°, $\nu_{max.}$ (paraffin mull) 3 370 (OH), 3 200 (NH), 1 600, 1 330, and 1 046 cm^{-1}, τ 0.42br (1 H, NH, exchanged), 2.4 (5 H, m, aryl), 5.6 (2 H, m), 7.6br (1 H, OH, exchanged), and 7.7—8.8 (8 H, m) (Found: C, 58.6; H, 6.7; N, 5.2; S 24.2. $C_{13}H_{17}NOS_2$ requires C, 58.4; H, 6.4; N, 5.2; S, 24.0%).

cis-2-[(*Acetylthio*)(*phenylimino*)*methylthio*]*cyclohexyl Acetate* (17).—A mixture of *cis*-2-(phenylthiocarbamoylthio)-cyclohexanol (1.0 g), pyridine (1.1 g), and acetic anhydride (2.0 g) was heated on a steam-bath for 10 min and then left overnight at ambient temperature. Addition of petroleum precipitated the *diacetyl compound* (17) (0.75 g), which after t.l.c. and recrystallisation from ether–petroleum had m.p. 115—117°, $\nu_{max.}$ 1 726 (OAc), 1 702 (SAc), 1 600, 1 495, 1 233, 1 163, and 1 081 cm^{-1}, τ 2.3—2.9 (5 H, m, aryl), 4.6 (1 H, m), 5.8 (1 H, m), 7.88 (3 H, s, SAc), 7.93 (3 H, s, OAc), and 7.7—8.7 (8 H, m) (Found: C, 57.8; H, 5.9; N, 4.0; S, 18.6. $C_{17}H_{21}NO_3S_2$ requires C, 58.1; H, 6.0; N, 4.0; S, 18.25%).

cis-2-(*Phenylthiocarbamoylthio*)*cyclohexyl Acetate* (16).—(i) A mixture of acetic anhydride (45 mg) and pyridine (1.0 ml) was gradually added (4 h) to a stirred solution of *cis*-2-(phenylthiocarbamoylthio)cyclohexanol (0.23 g) in pyridine (0.8 ml). After storage overnight the solution was diluted with water (20 ml) and extracted with dichloromethane to give an oil, which by t.l.c. was separated into starting material (90 mg) and the *acetate* (16) (61 mg), m.p. 108—111° (from carbon tetrachloride), $\nu_{max.}$ 3 355 (NH), 1 730 (OAc), 1 600, 1 505, 1 245, and 1 040 cm^{-1}, τ 1.05br (1 H, NH), 2.55 (5 H, m, aryl), 4.7 (1 H, m), 5.7 (1 H, m), 7.95 (3 H, s, OAc), and 7.7—8.7 (8 H, m) (Found: C, 58.3; H, 6.1; N, 4.4; S, 20.5. $C_{15}H_{19}NO_2S_2$ requires C, 58.2; H, 6.2; N, 4.5; S, 20.7%).

(ii) A solution of *cis*-2-[(acetylthio)(phenylimino)methylthio]cyclohexyl acetate (0.51 g) in chloroform (5 ml) was shaken with 3M-hydrochloric acid (8 ml) until the deep yellow colour had faded to pale yellow (30 min). The chloroform layer was washed with aqueous sodium hydrogencarbonate, then dried, and evaporated to give the acetate (16) (0.30 g), identical to that described in the preceding paragraph.

Reaction of cis-2-(*Phenylthiocarbamoylthio*)*cyclohexyl Acetate with Base*.—M-Potassium hydroxide in ethanol (0.5 ml) was added to a warm solution of the acetate (115 mg) in ethanol (2 ml) and the mixture was set aside overnight, then diluted with water and extracted with dichloromethane. Concentration of the extract gave a residue which by t.l.c. was separated into *O*-ethyl *N*-phenylthiocarbamate (25 mg), m.p. 67—69° (lit.,[11] 68—69°), and *cis*-2-(phenylthiocarbamoylthio)cyclohexanol (46 mg), m.p. 130—132°, both identified by their i.r. and ^1H n.m.r. spectra.

Reaction of cis-2-[(*Acetylthio*)(*phenylimino*)*methylthio*]-*cyclohexyl Acetate with Base*.—The diacetyl compound (214 mg) in warm ethanol (4 ml), treated with M-potassium hydroxide in ethanol (1.5 ml) by the procedure described for the monoacetate, gave *O*-ethyl *N*-phenylthiocarbamate (76

[10] A. Donche and C. Thibault, F. P. 1516855/1968; (*Chem. Abs.*, 1969, **70**, 115148).

[11] E. Fromm, *Ber.*, 1909, **42**, 1945.

mg), m.p. 68—69°, and *cis*-2-(phenylthiocarbamoylthio)-cyclohexanol (16 mg), identified spectroscopically.

trans-*Perhydro*-1,3-*benzodithiole*-2-*thione Methiodide* (18).—A mixture of *trans*-perhydro-1,3-benzodithiole-2-thione [1] (0.5 g), methyl iodide (0.75 g), and dichloromethane (6 ml) was set aside for 7 days. The dark red crystals which had been formed were collected, washed with benzene, and dried under high vacuum to give the *methiodide* (18) (0.30 g), m.p. 123—125°, which contained trapped methyl iodide (Found: C, 16.3; H, 2.2; I, 66.6. Calc. for $C_8H_{13}IS_3,4CH_3I$: C, 16.0; H, 2.8; I, 70.5%).

Reaction with Aniline.—A mixture of the methiodide (62 mg), aniline (40 mg), and methanol (1.5 ml) was left for 3 days and then diluted with ether (3 ml). The solution was shaken with 2M-sodium hydroxide (8 ml), and the ether layer was isolated, dried, and concentrated to a residue which was purified by t.l.c. to give *trans*-2-phenyliminoperhydro-1,3-benzodithiole (8.5 mg), m.p. 110—111°, (i.r. and mass spectra identical with those recorded earlier), and *trans*-perhydro-1,3-benzodithiol-2-one (6.2 mg), identified from the i.r. spectrum.

cis-*Perhydro*-1,3-*benzodithiole*-2-*thione Methiodide*.—Prepared from *cis*-perhydro-1,3-benzodithiole-2-thione [1] (0.24 g) as described for the *trans*-compound, the *methiodide* (0.10 g) formed dark red crystals, m.p. 86—88°, containing trapped methyl iodide (Found: C, 21.3; H, 2.9; S, 21.9. Calc. for $C_8H_{13}IS_3$, $1.5CH_3I$: C, 20.9; H, 3.2; S, 17.6%).

cis-2-*Phenyliminoperhydro*-1,3-*benzodithiole* (7).—(i) Treatment of the *cis*-methiodide (43 mg) with aniline (50 mg) and methanol (1.0 ml) as described for the *trans*-methiodide gave, after t.l.c., the *phenylimino compound* (7) (19 mg), m.p. 102—103° (depressed to 70—74° on admixture with the *trans*-isomer), $\nu_{max.}$ 1 585, 1 490, 1 450, and 955 cm^{-1}, τ 2.4—3.3 (5 H, m, aryl), 6.0 (2 H, m), and 7.7—8.7 (8 H, m), *m/e* 249 (M^+, 35%), 194 (11), 146 ($C_6H_{10}S_2$, 27), 135 (PhNCS, 24), 81 (C_6H_9, 100), 80 (C_6H_8, 11), and 77 (Ph, 38) (Found: C, 62.9; H, 6.0; N, 5.6; S, 25.4. $C_{13}H_{15}NS_2$ requires C, 62.6; H, 6.1; N, 5.6; S, 25.7%).

(ii) *cis*-Cyclohexane-1,2-dithiol [1] (240 mg) and phenyl isothiocyanate (400 mg) were heated together at 150 °C for 30 min and then allowed to cool. The product was purified by t.l.c. to give the phenylimino compound (7) (30 mg), recrystallised from aqueous methanol, m.p. and mixed m.p. 100—102°, and *cis*-perhydro-1,3-benzodithiole-2-thione (16 mg), recrystallised from ether–petroleum, m.p. and mixed m.p. 99—100°.

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