etherification and esterification; m.p. after several recrystallizations from hexane 59.5° (lit. (11) m.p. 60°). A mixed melting point determination with compound **4** was not depressed, and all spectroscopic data are identical to those determined for compound **4**.

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Organic sulfur compounds. VI.[1] Reduction of three α-(*o*-nitrophenylthio)ketones with sodium borohydride

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Reduction of three α-(*o*-nitrophenylthio)ketones with sodium borohydride and palladium–charcoal gave mainly α-(*o*-nitrophenylthio)alcohols and, as minor products, α-(*o*-aminophenylthio)alcohols. Only two benzothiazines were formed. Bis[2-(3-phenyl-2*H*-1,4-benzothiazine)] was a minor product of the catalyzed reduction of ω-(*o*-nitrophenylthio)acetophenone whereas 1-(3,4-dihydro-4-hydroxy-3-oxo-2*H*-1,4-benzothiazin-2-yl)benzyl alcohol was the main product of the catalyzed reduction of α-benzoyl-α-(*o*-nitrophenylthio)acetate.

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Methyl α-(*o*-nitrophenylthio)acetate (**1***a*) and its simple derivatives are readily reduced by means of sodium borohydride and palladium–charcoal (1–3) to give 2*H*-1,4-benzothiazine hydroxamic acids (**2**). It was of interest to extend these studies to the reductive cyclization of α-(*o*-nitrophenylthio)ketones (**3**) to see if 2*H*-1,4-benzothiazine 4-oxides (**4**) could be obtained in this way. This proved not to be the case; however, some unexpected reactions were observed and they are now reported.

The ketones (**3***a–c*) were prepared in good yields by the interaction of *o*-nitrobenzenesulfenyl chloride with acetone, acetophenone, and ethyl benzoylacetate respectively, using acetonitrile as solvent (4, 5). Reduction of (*o*-nitrophenylthio)propan-2-one (**3***a*) with sodium borohydride in the presence of catalytic quantities of palladium-on-charcoal yielded mainly 1-(*o*-nitrophenylthio)propan-2-ol (**5***a*), characterized as its 3,5-dinitrobenzoate. The same nitroalcohol was also the product of the reduction of (**3***a*) using sodium borohydride without catalyst. An additional minor product of

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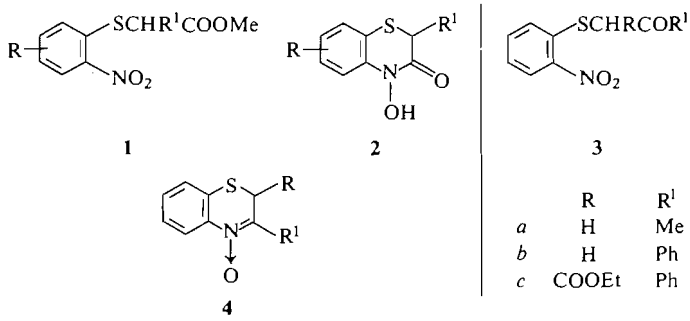
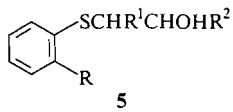


1 2 3

4

	R	R^1
a	H	Me
b	H	Ph
c	COOEt	Ph

the catalyzed reaction was deduced to be 1-(*o*-aminophenylthio)propan-2-ol (**5***b*) by comparing it with an authentic sample prepared from *o*-aminothiophenol and propylene glycol (6). Failure of the nitro-group in **5***a* to reduce readily in the catalyzed reaction was surprising in view of the ease with which this group was converted to the hydroxylamine when related esters were treated with the same reducing system (1, 3).



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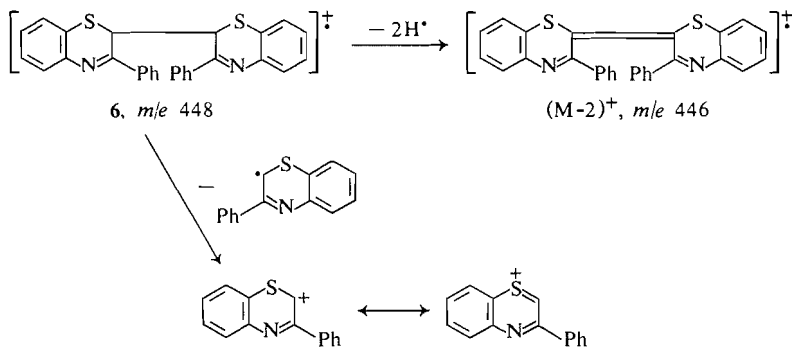
	R	R^1	R^2
a	NO_2	H	Me
b	NH_2	H	Me
c	NO_2	H	Ph
d	NH_2	H	Ph
e	NO_2	COOEt	Ph

In a similar manner, reduction of ω-(*o*-nitrophenylthio)acetophenone (**3***b*) with sodium borohydride in the presence or absence of palladium catalyst gave good yields 2-(*o*-nitrophenylthio)-1-phenylethanol (**5***c*), and 2-(*o*-aminophenylthio)-1-phenylethanol (**5***d*) was isolated from the catalyzed reduction only, in very low yield. Catalyst poisoning was apparently occurring and so the reduction of **3***b* was repeated using a much larger quantity of palladium–charcoal. Basic and neutral products were then formed. The neutral fraction was an oil from which one component was isolated, using column chromatography, as a bright orange solid, $C_{28}H_{20}N_2S_2$. Its mass spectrum showed a molecular ion of *m/e* 448, a strong $(M-2)^+$ ion at *m/e* 446 and a base peak of mass 224. The ions proposed in Scheme 1 are compatible with these observations and enable identification of this product as bis[2-(3-phenyl-2*H*-1,4-benzothiazine)] (**6**). The same compound was isolated by Fujii (7) when he attempted to prepare the picrate of 3-phenyl-4*H*-1,4-benzothiazine. The basic fraction again was 2-(*o*-aminophenylthio)-1-phenylethanol (**5***d*), the mass spectrum of which showed prominent ions of *m/e* 245, 139, 125 and 124. The formation of each fragment ion proposed in Scheme 2 was supported by the presence of a metastable ion of appropriate mass.

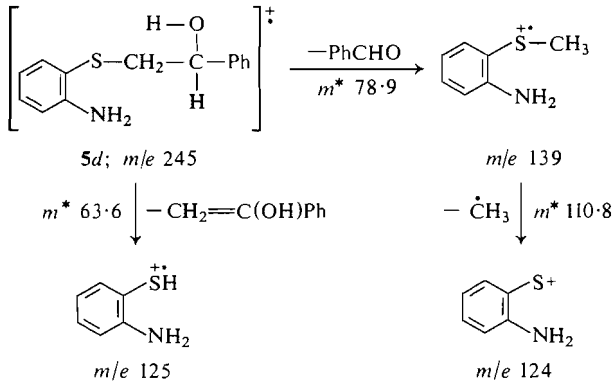
When ethyl α-benzoyl-α-(*o*-nitrophenylthio)-acetate (**3***c*) was reduced with sodium borohydride



6, *m/e* 448 $(M-2)^+$, *m/e* 446

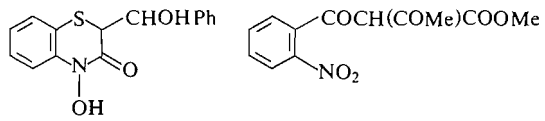
m/e 224

SCHEME 1



SCHEME 2

in the absence of catalyst, the product was not the expected nitro-alcohol (**5***e*). The ethoxycarbonyl group was lost during the reduction and 2-(*o*-nitrophenylthio)-1-phenylethanol (**5***c*) was obtained. When the reaction was repeated in the presence of catalyst, two identifiable products were isolated. The major one was an acidic viscous yellow oil which gave a violet color with ethanolic ferric chloride solution. Addition of water to this solution precipitated a purple ferric chelate. The infrared (i.r.) spectra of the oil and its ferric chelate were consistent (8) with the product being the cyclic hydroxamic acid 1-(3,4-dihydro-4-hydroxy-3-oxo-2*H*-1,4-benzothiazin-2-yl)benzyl alcohol (**7**). A purple ferrous chelate was also isolated which analyzed satisfactorily for $C_{30}H_{24}FeN_2O_6S_2$. It is of interest to contrast this result with the one obtained when another β-keto-ester, namely methyl *o*-nitrobenzoylacetoacetate (**8**), was reduced with sodium borohydride



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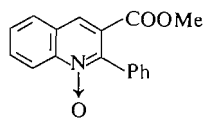
8



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and palladium–charcoal (9). The product then was the *N*-oxide (**9**). The other product of the catalyzed sodium borohydride reduction of (**3***c*) was 1-(*o*-aminophenylthio)propan-2-ol (**5***b*). Once again, the ethoxycarbonyl group in **3***c* did not survive the reduction.

Experimental

Melting points and boiling points are uncorrected. The i.r. spectra were measured on KBr discs or thin films with a Beckman IR 10 spectrophotometer. Mass spectra were measured with an A.E.I. MS9 or MS12 spectrometer, using the direct insertion technique.

Preparation of α-(o-Nitrophenylthio)ketones (3)

General method: *o*-Nitrobenzenesulfenyl chloride (10 g) and an excess of the appropriate ketone (15 g) were dissolved in acetonitrile (100 ml) and the solution was heated under reflux for 2.5 to 4.5 h. Acetonitrile (80 ml) was then removed by distillation and the reaction mixture cooled to yield the product which was purified by crystallizing from methanol or ethanol.

(*o*-Nitrophenylthio)propan-2-one (**3***a*) was prepared from acetone in 97% yield as yellow crystals, m.p. 77–79° (from methanol); lit. (4) m.p. 81°.

ω-(*o*-Nitrophenylthio)acetophenone (**3***b*) was the product obtained in 93% yield when acetophenone was the ketone used in the reaction. It was a yellow solid, m.p. 143–145° (from methanol); lit. (4) m.p. 147°.

Ethyl α-benzoyl-α-(*o*-nitrophenylthio)acetate (**3***c*) was isolated in 95% yield as a yellow solid, m.p. 121–124° (from ethanol) when ethyl α-benzoylacetate was the ketone used. The i.r. spectrum: 1590, 1630 (β-ketoester C=O); 1510, 1335, 845 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{17}H_{15}NO_5S$: C, 59.12; H, 4.38; N, 4.06; S, 9.28. Found: C, 59.25; H, 4.40; N, 4.00; S, 9.34.

Catalyzed Sodium Borohydride Reductions of α-(o-Nitrophenylthio)ketones (3)

General method: A solution of sodium borohydride (0.5 g) in water (5 ml) was added to a suspension of palladium (10%)-on-charcoal (0.1 g) in water (5 ml). Dioxane (10 ml) was added to the mixture and nitrogen gas was bubbled through it (1–2 min). The (*o*-nitrophenylthio)ketone (1.0 g), dissolved in a minimum of dioxane, was added to the reduction mixture over a period of 10 min. Nitrogen gas was bubbled through the reaction mixture during the addition of ketone and for an additional 30 min.

The reaction mixture was filtered and the filtrate extracted with ether (ether extract *i*). The aqueous layer

was acidified with concentrated hydrochloric acid, keeping the temperature below 30°, and then extracted with ether (ether extract *ii*). Ether extracts *i* and *ii* were then combined and extracted to completion with portions of 10% sodium hydroxide solution (extract A), washed with water, extracted to completion with portions of 10% hydrochloric acid solution (extract B), and washed with water. The ether layer was then dried (Na_2SO_4), and evaporated to yield the neutral product.

Basic extract A and its washings were acidified with concentrated hydrochloric acid and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4), and evaporated to yield the acidic product.

Acidic extract B and its washings were basified with 10% sodium hydroxide solution and extracted with ether. The ether layer was washed with water, dried (Na_2SO_4), and evaporated to yield the basic product.

(*a*) Reduction of (*o*-nitrophenylthio)propan-2-one (**3***a*) (0.98 g), using the general method, gave a neutral product (0.65 g) and a basic product (0.03 g). No acidic product was isolated. The neutral product, 1-(*o*-nitrophenylthio)-2-propanol (**5***a*) was a yellow oil; i.r. spectrum: 3350 (broad, OH); 1510, 1335, 860 (NO_2) cm^{-1}.

The 3,5-dinitrobenzoate of **5***a* had a m.p. 144.5–146° (from ethanol); i.r. spectrum: 1723 (C=O); 1515, 1340, 860 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{16}H_{13}N_3O_8S$: C, 47.17; H, 3.22; N, 10.36. Found: C, 47.53; H, 3.57; N, 10.36.

The basic fraction was a brown oil, mol. wt. (mass spectrum) 183 (calcd. for $C_9H_{13}NOS$: 183), which formed a hydrochloride, m.p. 166–167°; lit. (6) m.p. 159–160°. The i.r. spectra of the base and its hydrochloride were identical with authentic samples of **5***b* and **5***b*·HCl, prepared from propylene glycol and *o*-aminothiophenol using the reported (6) method.

(*b*) Reduction of ω-(*o*-nitrophenylthio)acetophenone (**3***b*) (0.94 g) using the general method gave a neutral fraction (0.86 g) and a basic fraction (0.01 g). No acidic fraction was isolated.

The neutral product, 2-(*o*-nitrophenylthio)-1-phenylethanol (**5***c*), was isolated as an orange oil which, on standing, slowly solidified to a yellow solid, m.p. 98–99°. The i.r. spectrum: 3300 (broad, OH); 1505, 1335, 840 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{14}H_{13}NO_2S$: C, 61.07; H, 4.76; N, 5.09; S, 11.65. Found: C, 61.03; H, 4.60; N, 4.92; S, 11.52.

The *p*-nitrobenzoate of **5***c* had a m.p. 139–141° (from ethanol). The i.r. spectrum: 1732 (C=O); 1525, 1340, 850 (NO_2) cm^{-1}.

Anal. Calcd. for $C_{21}H_{16}N_2O_6S$: C, 59.42; H, 3.80; N, 6.60. Found: C, 59.58; H, 4.21; N, 6.67.

The basic product was a brown oil which had an i.r. spectrum identical with that of 2-(*o*-aminophenylthio)-1-phenylethanol (**5***d*) obtained as described below.

(*c*) Reduction of ω-(*o*-nitrophenylthio)acetophenone (**3***b*) using excess catalyst.

The title compound (10.03 g) was reduced using the general method on a 10-fold scale, except that the quantity of catalyst was increased to 2.64 g. A neutral fraction (3.83 g), a basic fraction (4.08 g), and an acidic fraction (0.74 g, starting material) were isolated.

The neutral product was an orange–red oil which was chromatographed on a neutral alumina column (1.1 × 15 cm) with petroleum ether as solvent. One bright orange component moved ahead of the remainder of the mixture and was collected. Subsequent elution with benzene and benzene/ethanol mixtures achieved some separation. Evaporation of the solvent in each instance gave a viscous orange oil and none of these oils were homogeneous as shown by mass spectrometry. Removal of the solvent from the bright orange solution described above gave 2,2′-*bis*(3-phenyl-2*H*-1,4-benzothiazine) (**6**, 0.31 g) as orange needles (from acetone), m.p. 243–244°; lit. (7) m.p. 234–236°. An i.r. spectrum confirmed the absence of C=O and NO_2 groups in **6**. Mass spectrum: 450(0.7), 449(3), 448(11), 447(29), 446(80), 445(13), 413(11), 369(10), 342(13), 325(12), 235(11), 225(32), 224(100), 223(28), 211(13), 121(23), 77(14), 76(10), 52(15), 51(14), 39(16), *m/e* (% relative abundance).

Anal. Calcd. for $C_{28}H_{20}N_2S_2$: C, 74.96; H, 4.49; N, 6.24. Found: C, 74.80; H, 4.94; N, 6.35.

The basic fraction was 2-(*o*-aminophenylthio)-1-phenylethanol (**5***d*) which was isolated as a brown oil. Its hydrochloride was a colorless solid, m.p. 180–181° (from acetone/*n*-hexane); lit. (6) m.p. 172°.

Anal. Calcd. for $C_{14}H_{16}ClNOS$: C, 59.67; H, 5.72; N, 4.97. Found: C, 60.08; H, 6.03; N, 5.12.

(*d*) Reduction of ethyl α-benzoyl-α-(*o*-nitrophenylthio)acetate (**3***c*) (1.93 g) using the general method gave a neutral product (0.32 g), an acidic product (0.91 g), and a basic product (0.18 g).

The acidic product, 1-(3,4-dihydro-4-hydroxy-3-oxo-2*H*-1,4-benzothiazin-2-yl)benzyl alcohol (**7**), was a viscous yellow oil which gave a violet color with ethanolic ferric chloride solution. The i.r. spectrum: 1690 (hydroxamate C=O), 2700–3600 (hydrogen-bonded OH) cm^{-1}. The ferric chelate was prepared as a purple–brown solid by dissolving the oil (100 mg) in the minimum of ethanol, adding excess ethanolic ferric chloride solution and flooding the mixture with water. The i.r. spectrum: 3450 (OH), 1528 (chelated C=O) (8) cm^{-1}. The ferrous chelate was prepared by dissolving the hydroxamic acid (50 mg) in glacial acetic acid (1 ml) and adding a solution of ferrous chloride (15 mg) in glacial acetic acid (1 ml) and then water (6 ml). The chelate was washed with 10% sodium hydroxide solution, then water, and dried to give a purple solid (38 mg), m.p. 140–145°.

Anal. Calcd. for $C_{30}H_{24}FeN_2O_6S_2$: C, 57.33; H, 3.85; Fe, 8.89. Found: C, 57.42; H, 3.61; Fe, 8.94.

The neutral fraction was a viscous oil which was not identified. Its i.r. spectrum differed from that of **5***c*.

The basic product was a viscous yellow oil with an i.r. spectrum which was superimposable upon that of 2-(*o*-aminophenylthio)-1-phenylethanol (**5***d*).

Reduction of α-(o-Nitrophenylthio)ketones (3) with Sodium Borohydride in the Absence of Catalyst

(*o*-Nitrophenylthio)propan-2-one (**3***a*) (0.95 g) was dissolved in dioxane (15 ml) and a solution of sodium borohydride (0.5 g) in water (10 ml) was added. After 1 h, the solution was acidified with dilute hydrochloric acid and extracted with ether. The ether solution was washed with 10% sodium hydroxide solution, then water, dried (Na_2SO_4), and evaporated to yield 1-(*o*-nitrophenylthio)propan-2-ol (**5***a*) (0.95 g) as a yellow oil,

which was characterized by its i.r. spectrum (identical to that of product obtained in the catalyzed reduction of **3***a*). The 3,5-dinitrobenzoate had m.p. 144–146°.

In the same way reduction of ω-(*o*-nitrophenylthio)-acetophenone (**3***b*) (0.62 g) gave 2-(*o*-nitrophenylthio)-1-phenylethanol (**5***c*) (0.58 g), m.p. 97–98°, and reduction of ethyl α-benzoyl-α-(*o*-nitrophenylthio)acetate (**3***c*) (0.52 g) yielded the same product (**5***c*) (0.39 g), m.p. 96–98°.

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