

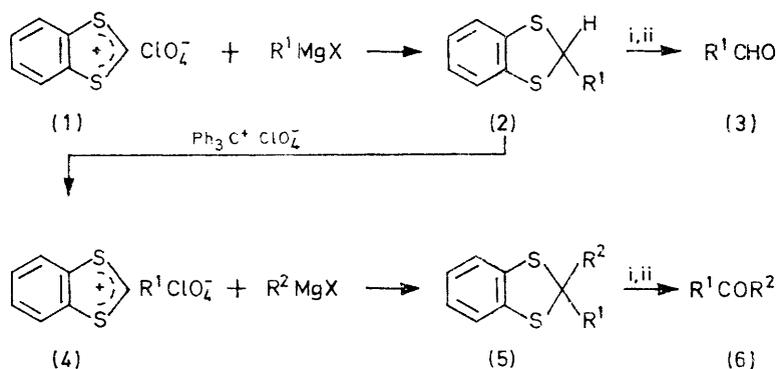
Pentatomic Heteroaromatic Cations. Part VI.¹ New Syntheses of Aldehydes and Ketones by Reaction of 1,3-Benzodithiolylium Salts with Grignard Reagents

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2-Substituted and 2,2-disubstituted 1,3-benzodithiols are formed when 1,3-benzodithiolylium and 2-phenyl-1,3-benzodithiolylium perchlorates, respectively, react with Grignard reagents. The products can be hydrolysed to aldehydes and ketones by treatment with chloramine T followed by mercury(II) chloride. This procedure offers a sound alternative method for the synthesis of aldehydes by formylation of Grignard reagents, and it suggests a new route for the total synthesis of symmetric and asymmetric ketones from alkyl and aryl halides *via* such reagents.

We have previously shown that 1,3-benzodithiolylium salts are useful intermediates in the synthesis of aldehydes^{1,2} and ketones.^{1,3} 1,3-Benzodithiolylium salts have not been exploited hitherto for this purpose because

good method for the synthesis of 2-alkoxy-1,3-benzodithiols has been developed;⁶ these can be regarded as immediate precursors of unsubstituted 1,3-benzodithiolylium salts.



SCHEME 1, Chloramine T-EtOH; ii, HgCl₂-Me₂SO

its precursors (benzene-1,2-dithiol^{4a-c} or its derivatives^{5a-c}) were hard to obtain. Recently, however, a

Treatment of 2-(3-methylbutoxy)-1,3-benzodithiols⁶ with perchloric acid, in fact, readily produced 1,3-

¹ Part V, I. Degani and R. Fochi, *J.C.S. Perkin I*, 1976, 323.
² L. Costa, I. Degani, R. Fochi, and P. Tundo, *J. Heterocyclic Chem.*, 1974, **11**, 943.

³ I. Degani, R. Fochi, and P. Tundo, *Gazzetta*, 1975, **105**, 907.

⁴ (a) W. R. H. Hurlley and S. Smiles, *J. Chem. Soc.*, 1926, 1821; (b) S. Hünig and E. Fleckenstein, *Annalen*, 1970, **738**, 192; (c) A. Ferretti, *Org. Synth.*, Coll. Vol. V, 1973, 419.

⁵ (a) D. S. Breslow and H. Skolnik, in 'Multi-sulfur and Sulfur and Oxygen Five- and Six-membered Heterocycles,' ed. A. Weissberger, Interscience, New York, 1966, ch. 5, and references therein; (b) H. Prinzbach and E. Futterer, *Adv. Heterocyclic Chem.*, 1966, **7**, 39, and references therein; (c) E. Campaigne and R. D. Hamilton, *Quart. Reports Sulfur Chem.*, 1970, **5**, 275, and references therein.

⁶ J. Nakayama, *Synthesis*, 1975, 38.

benzodithioliylum perchlorate (1). This salt can be handled and stored without significant decomposition, and aldehydes and ketones were obtained from it as shown in the Scheme.

Reaction between the perchlorate (1) and Grignard

reduction. Subsequent hydrolysis of the adducts (2) gave aldehydes in high yields (Table 2). This procedure appears a sound alternative to previously reported methods for the formylation of Grignard reagents.^{7a-e}

Ketone synthesis in this way was investigated by

TABLE 1

Compd.	R ¹	R ²	Yield ^a (%)	Chromatography solvent ^b	M.p. ^c (°C)	Lit. m.p. (°C)	δ (CDCl ₃)
(2a)	Ph		87	LP	72—73	72 ^d	6.21 (1 H, s, CH), 6.98—7.72 (9 H, m, ArH)
(2b)	4-MeO-C ₆ H ₄		87	LP—B (1 : 1)	71—72	72 ^e	3.76 (3 H, s, Me), 6.25 (1 H, s, CH), 6.88 and 7.56 (2 d, 2 : 2, AB system, Ph, J _{AB} 9.5 Hz), 6.82—7.60 (4 H, m, ArH)
(2c)	Pr ⁿ		88	LP—B (9.5 : 1)	42—43		0.89 (3 H, t, Me, J 6.4 Hz), 1.15—2.10 (4 H, m, CH ₂ -CH ₂), 4.88 (1 H, t, CH, J 7.5 Hz), 6.95—7.35 (4 H, m, ArH)
(2d) ^f	cyclo-C ₆ H ₁₁		53	LP—B (9.5 : 1)	70—71		0.95—2.25 (11 H, m, cyclo-C ₆ H ₁₁), 4.79 (1 H, d, CH, J 6.8 Hz), 6.90—7.35 (4 H, m, ArH)
(5a)	Ph	Me	66	LP	82—83	83 ^d	2.35 (3 H, s, Me), 6.98—7.52 and 7.76—8.02 (2 m, 7 : 2, ArH)
(5b) ^h	Ph	Ph	30	LP—B (9.5 : 1)	122—123 ⁱ		6.92—7.42 and 7.65—7.85 (2 m, 10 : 4, ArH)

^a Based on 1,3-benzodithioliylum perchlorate for (2a—d) and on 2-phenyl-1,3-benzodithioliylum perchlorate for (5a and b).
^b LP = light petroleum (b.p. 60—80 °C); B = benzene. ^c From 95% ethanol. ^d Ref. 4a. ^e W. R. H. Hurtley and B. Smiles, *J. Chem. Soc.*, 1927, 534. ^f Found: C, 61.2; H, 6.1; S, 32.65. C₁₀H₁₂S₂ requires C, 61.2; H, 6.12; S, 32.65%. ^g Found: C, 66.05; H, 6.85; S, 27.1. C₁₃H₁₆S₂ requires C, 66.1; H, 6.8; S, 27.1%. ^h Found: C, 74.45; H, 4.6; S, 20.95. C₁₅H₁₄S₂ requires C, 74.5; H, 4.6; S, 20.9%. ⁱ From benzene-ethanol.

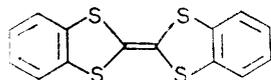
TABLE 2

Hydrolysis of compounds (2) and (5) to aldehydes (3) and ketones (6)

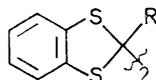
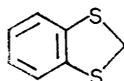
Compd.	R ¹	R ²	Procedure	Yield (%)	Chloramine T (mol. equiv.)	Reaction medium ^a (ml EtOH : MeOH)
(3a)	Ph		{ A	99	2	100 : 20
(3b)	4-MeO-C ₆ H ₄		{ B	90	2	100 : 20
(3c)	Pr ⁿ		{ C	94	2.5	200 ^b : 30
(3d)	cyclo-C ₆ H ₁₁		{ B	90 ^e	2	100 : 20
(6a)	Ph	Me	A	92	3	100 : 30
(6b)	Ph	Ph	A	Quant.	3	300 : 60

^a For 10 mmol of 1,3-benzodithiole. ^b 95% EtOH. ^c Isolated as 2,4-dinitrophenylhydrazone.

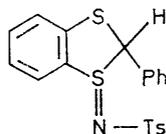
reagents led to high yields of 2-substituted 1,3-benzodithioles (2) (Table 1).^{*} Small amounts of bi-(1,3-benzodithiol-2-ylidene) (7) and bi-(1,3-benzodithioly) (8a) were always present in the reaction mixtures.



(7)

(8) a; R = H
b; R = Ph

(9)



(10)

Where the reagents underwent elimination, 1,3-benzodithiole (9) was also isolated as the result of a competitive

^{*} 1,3-Benzoxathioliylum perchlorate is unstable and cannot be used in the same way with Grignard reagents (unpublished data).

treating 2-phenyl-1,3-benzodithioliylum perchlorate (4; R¹ = Ph) (readily obtained from 2-phenyl-1,3-benzodithiole and trityl perchlorate) with Grignard reagents. Introduction of the second radical at C-2 proceeded in smaller yields than offered by 2-phenyl-1,3-benzoxathioliylum perchlorate in the analogous reactions,³ while the yield of the dimer (8b) increased (see Table 1 and Experimental section). Nevertheless, 1,3-benzodithioliylum salts can be used for total synthesis of symmetric and asymmetric ketones from alkyl and aryl halides *via* Grignard reagents.

This pathway is the opposite of that followed in Corey and Seebach's method,⁸ in that the reagent polarities are reversed. In the latter method the protected acyl agent is a carbanion stabilised by two adjacent sulphur

⁷ (a) I. Carnduff, *Quart. Rev.*, 1966, **20**, 169; (b) I. T. Harrison and S. Harrison, in 'Compendium of Organic Synthetic Methods,' vol. 1, Wiley-Interscience, New York, 1971, section 55, and references therein; (c) *ibid.*, vol. 2, 1974, section 55, and references therein; (d) J. Mathieu and J. Weill-Raynal, in 'Formation of C—C Bonds,' vol. 1, Thieme, Stuttgart, 1973, ch. 1F, and references therein; (e) A. I. Meyers, in 'Heterocycles in Organic Synthesis,' eds. E. C. Taylor and A. Weissberger, Wiley, New York, 1974, ch. 9, and references therein.

⁸ D. Seebach and E. J. Corey, *J. Org. Chem.*, 1975, **40**, 231, and references therein.

atoms, whereas in our method it is a carbocation, and the two adjacent stabilising S atoms belong to an aromatic system.

For hydrolysis of the adducts (2) and (5) we employed *N*-chlorotoluene-*p*-sulphonamide sodium salt (chloramine τ) followed by mercury(II) chloride. In recent years, chloramine τ has been used for the hydrolysis of 1,3-oxathiolans,⁹ 1,3-dithiolans,¹⁰ and 1,3-dithians.¹¹ It has only recently been shown that the reaction involves intermediate mono-*N*-tosylsulphimides; these are normally unstable and hence susceptible to further, immediate hydrolysis.¹¹ In the case of the adducts (2) and (5) the corresponding mono-*N*-tosylsulphimides are more stable. In the reaction between 2-phenyl-1,3-benzodithiole and chloramine τ , for example, compound (10) precipitated spontaneously from the reaction mixture. Although protracted heating of the mixture may occasionally lead to complete hydrolysis, in most cases mercury(II) chloride facilitated the reaction and its use resulted in purer products and higher yields.*

EXPERIMENTAL

1,3-Benzodithiolylium Perchlorate (1).—A solution of anthranilic acid (20.55 g, 0.15 mol) in dioxan (50 ml) was added dropwise over 45 min to a stirred, gently refluxing solution of 3-methylbutyl nitrite (21.05 g, 0.18 mol), 3-methylbutan-1-ol (26.4 g, 0.30 mol), and carbon disulphide (75 ml) in 1,2-dichloroethane (400 ml).⁶ The mixture was then refluxed for 30 min, and slowly distilled under reduced pressure (water-bath at 50 °C), to remove part of the solvent and the excess of reagents. A portion (10 g) of the residue (total 50–60 g) was dissolved in dry ether (150 ml); the solution was treated with charcoal and filtered, and then perchloric acid (5 ml) was added dropwise with stirring and cooling. 1,3-Benzodithiolylium perchlorate (1) was precipitated immediately. It was filtered off and washed several times with dry ether; yield (based on anthranilic acid) 55–60%; m.p. 182° (explosive) (from acetonitrile-ether) [lit.,¹² 182° (explosive)]. The n.m.r. spectrum was identical with that reported.¹² The product must be protected from moisture and light if not required for immediate use.

Reaction of 1,3-Benzodithiolylium Perchlorate (1) with Grignard Reagents; Typical Procedure.—2-Phenyl-1,3-benzodithiole (2a). To the Grignard reagent from bromobenzene (2.36 g, 15 mmol) and magnesium turnings (0.36 g, 15 g atom) in dry ether (70–80 ml), freshly prepared or freshly recrystallised 1,3-benzodithiolylium perchlorate (2.53 g, 10 mmol) was slowly added at room temperature with vigorous stirring. The reaction was immediate. Stirring was continued for 10 min and the mixture was then decomposed with saturated aqueous ammonium chloride. The usual work-up produced a crude residue which was chromatographed through silica gel with petroleum as eluant to afford 2-phenyl-1,3-benzodithiole (1.96 g, 87% based on

1,3-benzodithiolylium perchlorate), m.p. 72–73° (from 95% ethanol) (lit.,^{4a} 72°), a small amount of bi-(1,3-benzodithiol-2-ylidene) (7), m.p. 237–238° (from benzene) (lit.,¹³ 234–236°), and traces of bi-(1,3-benzodithiol-2-yl) (8a), m.p. 253–254° (from benzene) (Found: C, 54.95; H, 3.3; S, 41.9. C₁₄H₁₀S₄ requires C, 54.9; H, 3.25; S, 41.85%), *M*⁺ 306, δ 4.65 (1 H, s) and 7.05–7.50 (4 H, m), identified by comparison with a sample produced by reduction of 1,3-benzodithiolylium perchlorate with zinc dust in acetonitrile [m.p. 253–254° (from benzene); quantitative yield].

In a similar way, compounds (2b–d) were prepared. In the cases of (2c and d), 1,3-benzodithiole (9) was also isolated (7 and 32%, respectively), m.p. 23–24° (from 95% ethanol). This was identified by comparison with a sample produced by reduction of 1,3-benzodithiolylium perchlorate with lithium aluminium hydride in dry ether (yield 95%), and purified by distillation; b.p. 109–110° at 0.9 Torr, m.p. 23–24° (from ethanol) (lit.,¹⁴ 21.5°), n.m.r. spectrum identical with that reported.¹⁵

Details for these reactions are given in Table 1.

2-Phenyl-1,3-benzodithiolylium Perchlorate (4).—A solution of 2-phenyl-1,3-benzodithiole (2a) (1.15 g, 5 mmol) in acetonitrile (5 ml) was added to a suspension of trityl perchlorate¹⁶ (1.71 g, 5 mmol) in acetonitrile (5 ml). The mixture was heated at 50 °C for 2–3 min until dissolution was complete. After cooling, compound (4) began to precipitate out; then dry ether was added to complete the precipitation; yield 1.55 g (94%), m.p. 232–233° (decomp.) (from acetonitrile-ether), m.p. and spectroscopic data identical with those reported.¹⁷

Reaction of 2-Phenyl-1,3-benzodithiolylium Perchlorate (4) with Grignard Reagents; Typical Procedure.—2-Methyl-2-phenyl-1,3-benzodithiole (5a).—Compound (5a) was prepared exactly as described for (2a), by reaction between methylmagnesium iodide [from methyl iodide (2.13 g, 15 mmol) and magnesium (0.36 g, 15 g atom)] and 2-phenyl-1,3-benzodithiolylium perchlorate (3.29 g, 10 mmol) in dry ether (70–80 ml). The reaction was immediate and a white precipitate was formed. After decomposition of the mixture with saturated aqueous ammonium chloride, the solid was filtered off. The ethereal solution was dried and evaporated and the residue was chromatographed (silica gel column; eluted with petroleum) to afford 2-methyl-2-phenyl-1,3-benzodithiole (1.61 g, 66% based on 2-phenyl-1,3-benzodithiolylium perchlorate), m.p. 82–83° (from ethanol) (lit.,^{4a} 83°).

The solid was washed several times with water, with ethanol, and then with ether to give 2,2'-diphenylbi-(1,3-benzodithiol-2-yl) (8b) (15%), m.p. 271–273°; the product was not recrystallised because it is insoluble and decomposes on heating (Found: C, 68.2; H, 3.9; S, 27.85. C₂₆H₁₈S₄ requires C, 68.1; H, 3.95; S, 27.95%). It was identical with a sample produced by reduction of 2-phenyl-1,3-benzodithiolylium perchlorate with zinc dust in acetonitrile. The mass spectrum showed a very intense peak at *m/e* 229, corresponding to 2-phenyl-1,3-benzodithiolylium cation.

* The direct use of mercury(II) chloride for the hydrolysis of (2) and (5) was not satisfactory.

⁹ D. W. Emerson and H. Wynberg, *Tetrahedron Letters*, 1971, 3445.

¹⁰ W. F. J. Hurdeman, H. Wynberg, and D. W. Emerson, *Tetrahedron Letters*, 1971, 3449.

¹¹ R. B. Greenwald, D. H. Evans, and J. R. DeMember, *Tetrahedron Letters*, 1975, 3885.

¹² G. Scherowsky and J. Weiland, *Annalen*, 1974, **743**, 403.

¹³ J. Nakayama, *J.C.S. Perkin I*, 1975, 525.

¹⁴ D. Seebach, K. H. Geib, A. K. Beck, B. Graf, and H. Daum, *Chem. Ber.*, 1972, **105**, 3280.

¹⁵ G. Scherowsky and J. Weiland, *Chem. Ber.*, 1974, **107**, 3155.

¹⁶ H. J. Dauben, jun., L. R. Honnen, and K. M. Harmon, *J. Org. Chem.*, 1960, **25**, 1442.

¹⁷ I. Degani, R. Fochi, and P. Tundo, *J. Heterocyclic Chem.*, 1974, **11**, 507.

The compound gave 2-phenyl-1,3-benzodithiolylium tetrafluoroborate on heating with boron trifluoride-ether complex.

In the preparation of compound (5b), the yield of (8b) was 50%. Details for these reactions are given in Table 1.

Hydrolysis of 2-Substituted and 2,2-Disubstituted 1,3-Benzodithioles (2) and (5) to Aldehydes and Ketones; Typical Procedure.—Hydrolysis of compound (2a). A solution of chloramine T (5.63 g, 20 mmol) in methanol (20 ml) was added at 25 °C, in one portion, to a solution of 2-phenyl-1,3-benzodithiole (2.30 g, 10 mmol) in absolute ethanol (100 ml). The temperature of the mixture increased spontaneously to 29–30 °C. A white precipitate of sodium chloride and the intermediate (10) began to form almost immediately.* When (2a) had disappeared [*ca.* 5 min; t.l.c. on SiO₂ in benzene-petroleum (1 : 1)], the solvent was removed under reduced pressure by heating at 50 °C. The residue was dissolved in dimethyl sulphoxide-water (48 ml; 5 : 1 v/v) and mercury(II) chloride (10.86 g, 40 mmol) was added.

Procedure A. The mixture was heated under reflux for 5 min and then diluted with water and extracted several times with petroleum. The organic layers were washed successively with 10% potassium iodide, 5% sodium hydroxide, and water, dried and evaporated to afford benzaldehyde (1.05 g, 99%).

Procedure B. The mixture was heated in a Claisen flask fitted with thermometer and dropping funnel. Steam

* The mixture of 2-phenyl-1-*p*-tolylsulphonylimino-1,3-benzodithiole (10) and sodium chloride was filtered off and treated with chloroform to dissolve the former (10). The extract was evaporated and (10) was recrystallised from benzene; m.p. 160–161° (Found: C, 60.2; H, 4.3; N, 3.5; S, 24.0. C₂₀H₁₇NO₂S₃ requires C, 60.15; H, 4.25; N, 3.5; S, 24.05%), δ (CDCl₃) 2.48 (3 H, s, CH₃), 6.06 (1 H, s, CH), 7.21 and 7.80 (2d, 2 : 2, AB system, Ts, J_{AB} 9.0 Hz), and 7.15–7.88 (9 H, m, ArH).

distillation was initiated, and water (40 ml) was added dropwise through the dropping funnel over 30–40 min. While a yellow precipitate was formed, distillate (*ca.* 40–50 ml) was collected at 100–120 °C. This was extracted with ether, and the extract was washed with water, dried, and evaporated to yield pure benzaldehyde (0.95 g, 90%).

All isolated aldehydes and ketones were identified by comparison of their i.r. and n.m.r. spectral data and g.l.c. retention times with those of authentic samples. Details are given in Table 2.

Procedure C. Hydrolysis of compound (2b). As described above, a solution of chloramine T (7.04 g, 25 mmol) in methanol (30 ml) was added at 25 °C to a solution of 2-(*p*-methoxyphenyl)-1,3-benzodithiole (2.60 g, 10 mmol) in 95% ethanol (100 ml). A mildly exothermic reaction occurred and a white precipitate of sodium chloride began to separate after a few min. T.l.c. [SiO₂; benzene-petroleum (1 : 1)] showed that *p*-methoxybenzaldehyde was beginning to form. After heating at 50 °C for 15–30 min, the hydrolysis was complete. The mixture was diluted with water and extracted several times with petroleum. The extracts were washed with 5% sodium hydroxide and then with water. Work-up was facilitated by leaving the mixture at room temperature for 12 h. The solvent was removed to give *p*-methoxybenzaldehyde (1.28 g, 94%). Its i.r. and n.m.r. spectra were identical with those of an authentic sample and demonstrated its purity.

Compound (2a) was also hydrolysed by this procedure. G.l.c., however, indicated that the benzaldehyde produced was not sufficiently pure.

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