

THIOPHENES AND THIAPYRANS*

Part VIII. A New Synthesis of Dibenzothiophene and Its Derivatives; Its Scope and Limitations

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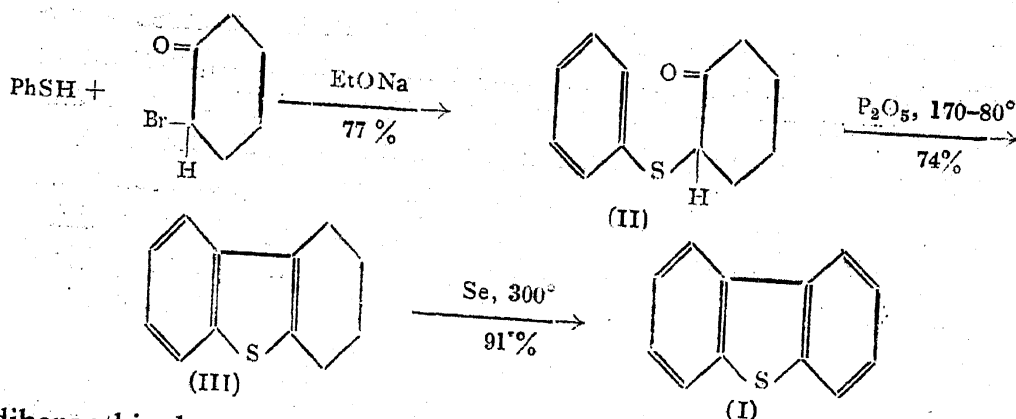
DIBENZOTHIOPHENE (I) accompanies phenanthrene in the distillation of coal tar.¹ Attempts to prepare dyes² and physiologically active substances³ from (I) have been reported. Several syntheses of (I) have been described in the literature,⁴⁻⁷ but these are not very satisfactory, especially for substituted derivatives. A few 4-substituted derivatives of (I) have been prepared through metalation⁶ and 2-substituted and 2:8-disubstituted derivatives are obtainable by direct substitution.⁷⁻¹⁰ With the exception of these compounds other derivatives of (I) are not easily accessible.

Recently 3-methylthionaphthene and a number of 2:3-dimethylthionaphthenes and naphthothiophenes have been prepared by Werner¹² by the cyclization of α -arylmercaptoketones by treatment with phosphorus pentoxide or fused zinc chloride. The mercaptoketones were obtained by the con-

densation of aryl thiols with α -haloketones of the type; $R_1-\overset{x}{\underset{|}{\text{CH}}}-\text{CO}-R_2$, where x = halogen and R_1 and R_2 are alkyl groups. By the condensation of aryl thiols with α -halo cyclic ketones such as 2-bromocyclohexanone and ring-closure of the intermediate 2-arylmercaptocyclohexanones, it should be possible to fuse a tetrahydrothionaphthene ring system to the aromatic nucleus of the thiol. Dehydrogenation of the tetrahydro derivative would then lead to polycyclic derivatives containing a thionaphthene ring. This was in fact realized and dibenzothiophene (I) was prepared starting from thiophenol and 2-bromocyclohexanone by the following steps, the overall yield of pure (I) being 52%:

Dibenzofuran¹³ and carbazole derivatives¹⁴ have been prepared in a similar manner starting from phenols and aryl amines and 2-chlorocyclohexanone. A brief account of the above new synthesis of dibenzothiophene has been reported¹⁵ upon recently by us, and the present paper gives the experimental details of the synthesis. The hitherto unreported 2-methyl-

* A general study of the synthesis of thiophenes and thiapyrans by different methods is projected and the title of the series has been modified accordingly.



dibenzothiophene (VI) and 3-methyldibenzothiophene (IX) have now been prepared by the above general method in addition to the known 4-methyldibenzothiophene⁶ (XII) and 4-methoxydibenzothiophene⁶ (XV). Synthesis of 2-methoxydibenzothiophene could not be completed on account of the low yields of 2-methoxy-6:7:8:9-tetrahydrodibenzothiophene (XVII) in the cyclization of 2-(4-methoxyphenylmercapto)cyclohexanone (XVI). Similar low yields have also been observed earlier in the cyclization of *p*-methoxyphenyl ω -dimethoxyethyl sulphide.¹⁶ Attempts to synthesize 2-nitrodibenzothiophene were likewise unsuccessful. The condensation of *o*-methoxythiophenol and 2-bromocyclohexanone in ethanolic solution of sodium ethoxide gave a poor yield of 2-(2'-methoxyphenylmercapto)cyclohexanone (XIII). When the condensation was carried out in the presence of 35% aqueous sodium hydroxide¹² the yield of (XIII) was 77%. The synthesis of the dibenzothiophenes from the relevant thiophenols and the yield of the pure intermediates and final compounds in the synthesis have been summarized in Chart I.

CHART I

	2-Arylmercapto-cyclohexanones		Tetrahydro-dibenzo-thiophenes		Dibenzothiophenes	
$R_1=Me; R_2=R_3=H$	—68%→	(IV)	—60%→	(V)	—46%→	(VI)
$R_2=Me; R_1=R_3=H$	—80%→	(VII)	—78%→	(VIII)	—79%→	(IX)
$R_3=Me; R_1=R_2=H$	—85%→	(X)	—62%→	(XI)	—57%→	(XII)
$R_3=OMe; R_1=R_2=H$	—77%→	(XIII)	—47%→	(XIV)	—33%→	(XV)
$R_1=OMe; R_2=R_3=H$	—75%→	(XVI)	→	(XVII)	Characterized as picrate	
$R_1=NO_2; R_2=R_3=H$	—93%→	(XVIII)				

The synthesis of dibenzothiophene and its derivatives described above demonstrates the general applicability of the new synthesis. The scope of the synthesis appears to be as wide as the synthesis of thiophenes and thiapyrans which have been described in previous communications.¹⁷ Whereas in the latter synthesis a thiophene or a thiapyran ring is fused to an aromatic ring system of the aryl thiol, in the present synthesis, a thionaphthene ring is fused to the aryl nucleus of the thiol. The only requisites appear to be aryl thiols with free *o*- or *peri*-positions (in the case of naphthalene) to enable cyclization to take place.

The scope of the synthesis in the preparation of monosubstituted derivatives of dibenzothiophene appears to be limited to 2-, 3- and 4-substituted derivatives. Ortho- and para-substituted thiophenols lead to 4- and 2-substituted derivatives respectively. In the case of a *m*-substituted thiophenol, 1- or 3-substituted dibenzothiophene may result, depending on the direction of ring-closure of the intermediate 2-(3'-substituted-phenylmercapto) cyclohexanone. The cyclization of the latter however probably leads to a 3-substituted derivative in preference to a 1-substituted derivative on account of steric considerations. It has been noted earlier that in the analogous cyclization of 3-methylphenyl ω -dimethoxyethyl sulphide only 6-methylthionaphthene was formed (unpublished work). The cyclization product of (VII) is therefore constituted as 3-methyl-6:7:8:9-tetrahydrodibenzothiophene (VIII).

Starting from naphthalene monothiols and dithiols polycyclic compounds containing naphthalene and thionaphthene or benzothiapyran ring systems can be synthesized. Some of these compounds have already been prepared and will be reported upon in subsequent communications. Similarly starting with aryl thiols and substituted 2-bromocyclohexanones new substituted derivatives of (I) may be synthesized by the above method. By using suitably oriented bromotetralones in place of 2-bromocyclohexanone, other sulphur-containing polycyclic ring systems could also be synthesized.

One of the limitations of the synthesis at present is the drastic treatment involved in the cyclization of 2-arylmercapto-cyclohexanone with phosphorus pentoxide and in the subsequent selenium dehydrogenation of the tetrahydrodibenzothiophenes which may preclude its application to compounds which are unstable under these conditions. Experiments to carry out these steps under milder conditions are in progress.

EXPERIMENTAL

2-Phenylmercaptocyclohexanone (II)

Thiophenol (8.6 g.), sodium (2 g.), 2-bromocyclohexanone (15 g.) and alcohol (50 c.c.) were refluxed for 3 hours. The crude condensation product (16.5 g.) on distillation gave a colourless oil (12.8 g., yield 77%), b.p. 152–53° (bath temp.)/10 mm. (Found: C, 69.7; H, 6.5; $C_{12}H_{14}OS$ requires C, 69.9; H, 6.8%). The 2:4-dinitrophenylhydrazone gave lustrous yellow needles from alcohol-ethyl acetate, m.p. 162–3° (Found: C, 56.6; H, 5.1; N, 14.1. $C_{18}H_{18}N_4O_4S$ requires C, 56.0; H, 4.7; N, 14.5%).

1:2:3:4-Tetrahydrodibenzothiophene (III)

A mixture of (II) (7.4 g.) and phosphorus pentoxide (20 g.) was heated at 170–80° for 45 minutes. The product (6 g.) on distillation gave a colourless oil (5.01 g., yield, 74%), b.p. 141° (bath temp.)/10 mm. (Found: C, 76.6; H, 6.5. Calc. for $C_{12}H_{12}S$: C, 76.6; H, 6.4%). The compound has been reported upon earlier being prepared by Clemmensen reduction of 1-keto-1:2:3:4-tetrahydrodibenzothiophene.¹⁸ The *picrate* gave orange needles from alcohol, m.p. 108–09° (Found: N, 9.6. $C_{18}H_{15}N_3O_7S$ requires N, 10.1%).

Dibenzothiophene (I)

Tetrahydrodibenzothiophene (III) (1.5 g.) and selenium (1.4 g.) were heated at 300° for 22 hours. Extraction of the mixture with alcohol gave a crystalline product (1.33 g., yield 91%) which on crystallization from alcohol gave long colourless needles, m.p. 98°, of dibenzothiophene (literature^{6, 18} m.p., 95–6° and 99°) (Found: C, 77.8; H, 4.5. Calc. for $C_{12}H_8S$: C, 78.3; H, 4.4%). The *picrate* gave yellow needles from alcohol, m.p. 123–4° (Gilman and Jacoby,⁶ 125°) (Found: N, 10.3. Calc. for $C_{18}H_{14}N_3O_3S$: N, 10.2%).

2-(4'-Methylphenylmercapto)cyclohexanone (IV)

p-Thiocresol (9 g.), sodium (1.8 g.), 2-bromocyclohexanone (13.5 g.) and alcohol (50 c.c.) were refluxed for 5 hours. The condensation product (12.5 g.) on distillation gave a straw coloured oil (10.8 g., yield 68%), b.p., 168–73° (bath temp.)/5 mm. (Found: C, 70.8; H, 7.2. $C_{13}H_{16}OS$ requires C, 70.9; H, 7.3%). The 2:4-dinitrophenylhydrazone gave orange needles from alcohol-ethyl acetate, m.p. 161–2° (Found: N, 14.6. $C_{19}H_{20}N_4O_4S$ requires N, 14.0%).

2-Methyl-6:7:8:9-tetrahydrodibenzothiophene (V)

A mixture of (IV) (6.1 g.) and phosphorus pentoxide (18 g.) was heated at 175–80° for 30 minutes. The cyclization product which was a brown oil (4.6 g.) on distillation gave a colourless liquid (3.38 g., yield 60%), b.p. 165–70° (bath temp.)/5 mm. (Found: C, 77.2; H, 7.5. $C_{13}H_{14}S$ requires C, 77.2; H, 6.9%). The *picrate* gave orange red needles from alcohol, m.p. 112–3° (Found: N, 9.5. $C_{19}H_{17}N_3O_7S$ requires N, 9.7%).

2-Methyldibenzothiophene (VI)

A mixture of (V) (2.07 g.) and selenium (1.9 g.) was heated at 300° for 16 hours. The mixture on extraction with alcohol gave cream coloured crystals (0.93 g., yield 46%), m.p. 80–3°. After two crystallizations from alcohol the thiophene (VI) gave colourless needles, m.p. 85.5° (Found: C, 78.6; H, 5.1. $C_{13}H_{10}S$ requires C, 78.8; H, 5.1%). The *picrate* gave curved orange needles from alcohol, m.p. 117–8° (Found: N, 9.7. $C_{19}H_{13}N_3O_7S$ requires N, 9.8%).

2-(3'-Methylphenylmercapto)cyclohexanone (VII)

m-Thiocresol (10.1 g.), sodium (2 g.), 2-bromocyclohexanone (15.4 g.) and alcohol (50 c.c.) were refluxed for 6 hours. The condensation product (16.5 g.) on distillation gave a colourless oil (14.4 g., yield 80%), b.p. 168–70° (bath temp.)/11 mm. (Found: C, 70.4; H, 7.5. $C_{13}H_{16}OS$ requires C, 70.9; H, 7.3%). The 2:4-dinitrophenylhydrazone gave yellow needles from alcohol-ethyl acetate, m.p. 146–7° (Found: N, 13.9. $C_{19}H_{20}N_4O_4S$ requires N, 14.0%).

3-Methyl-6:7:8:9-tetrahydrodibenzothiophene (VIII)

A mixture of (VII) (4.2 g.) and phosphorus pentoxide (12 g.) was heated at 170–80° for 45 minutes. The thiophene (VIII; 3.1 g.) on distillation gave a colourless liquid (3.02 g., yield 78%), b.p. 137–9° (bath temp.)/9 mm. (Found: C, 76.9; H, 7.0. $C_{13}H_{14}S$ requires C, 77.2; H, 6.9%). The *picrate* crystallized from alcohol in orange-red needles, m.p. 88–9° (Found: N, 9.4. $C_{19}H_{17}N_3O_7S$ requires N, 9.7%).

3-Methyldibenzothiophene (IX)

The above thiophene (VIII) (1.57 g.) and selenium (1.36 g.) were heated at 300° for 22 hours. The crude product (1.22 g.) isolated by extraction with alcohol on distillation gave a colourless oil (1.15 g., yield 79%), b.p. 175–80° (bath temp.)/10 mm. (Found: C, 78.5; H, 5.4. $C_{13}H_{10}S$ requires C, 77.8; H, 5.1%). The *picrate* gave yellow needles from alcohol, m.p. 97° (Found: N, 9.8. $C_{19}H_{13}N_3O_7S$ requires N, 9.8%).

2-(2'-Methylphenylmercapto)cyclohexanone

o-Thiocresol (10.7 g.), sodium (2.1 g.), 2-bromocyclohexanone (16 g.) and alcohol (50 c.c.) were refluxed for 7 hours. The condensation product (18.3 g.) on distillation gave a pale yellow oil (15.6 g., yield 85%), b.p. 165–70° (bath temp.)/8 mm. (Found: C, 71.3; H, 7.6. $C_{13}H_{16}OS$ requires C, 70.9; H, 7.3%). The 2:4-dinitrophenylhydrazone gave orange yellow needles from alcohol-ethyl acetate, m.p. 143–44° (Found: N, 13.9. $C_{19}H_{20}N_4O_4S$ requires N, 14.0%).

4-Methyl-6:7:8:9-tetrahydrodibenzothiophene (XI)

A mixture of (X) (7.8 g.) and phosphorus pentoxide (24 g.) was heated at 165–70° for 45 minutes. The cyclization product (5.7 g.) on distillation gave a pale yellow oil (4.39 g., yield 62%), b.p. 145–50° (bath temp.)/6 mm. (Found: C, 77.3; H, 7.2. $C_{13}H_{14}S$ requires C, 77.2; H, 6.9%). The picrate gave orange yellow needles from alcohol, m.p. 95–6° (Found: N, 9.9. $C_{19}H_{17}N_3O_7S$ requires N, 9.7%).

4-Methyldibenzothiophene (XII)

A mixture of (XI) (2.99 g.) and selenium (2.7 g.) was heated at 300° for 22 hours. The crude product isolated by means of alcohol was a brown liquid (2.56 g.) which solidified on cooling and showed green fluorescence. On distillation it gave a pale yellow liquid, b.p. 100–04° (bath temp.)/5 mm. which partly solidified. The product was therefore purified through the picrate which was decomposed with 1% aqueous ammonia. The colourless crystals of the purified thiophene (XII) (1.4 g., yield 51%), m.p. 59–61° after two crystallizations from alcohol gave lustrous, colourless plates, m.p. 66.5° (Found: C, 78.6; H, 5.1. Calc. for $C_{13}H_{10}S$: C, 78.8; H, 5.1%). The picrate gave lemon yellow needles from alcohol, m.p. 110° (Found: N, 9.7. $C_{19}H_{12}N_3O_7S$ requires N, 9.8%).

2-(2'-Methoxyphenylmercapto)cyclohexanone (XIII)

o-Methoxythiophenol (10.2 g.) was dissolved in 35% aqueous sodium hydroxide (8.35 c.c., 1 mol.). After cooling the solution to 20–25°, 2-bromocyclohexanone (13.5 g., 1 mol.) was added dropwise in 15 minutes under stirring and cooling. After stirring for one hour, the contents were diluted with water and extracted with ether. The product (17.7 g.) on distillation gave a colourless oil (13.2 g., yield 77%), b.p. 190–5° (bath temp.)/5 mm. (Found: C, 65.4; H, 6.5. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%). The 2:4-dinitrophenylhydrazone gave orange needles from alcohol, m.p. 130–1° (Found: N, 13.5. $C_{19}H_{20}N_4O_5S$ requires N, 13.5%).

4-Methoxy-6:7:8:9-tetrahydrodibenzothiophene (XIV)

A mixture of (XIII) (2.7 g.) and phosphorus pentoxide (9 g.) was heated at 170–80° for 30 minutes. The product, a thick dark oil (1.8 g.), gave on distillation a yellow oil (1.2 g., yield 47%), b.p. 180–200° (bath temp.)/5 mm., which soon solidified. On crystallization from alcohol, the thiophene (XIV) gave colourless needles, m.p. 83.5° (Found: C, 71.1; H, 6.4. $C_{13}H_{14}OS$ requires C, 71.5; H, 6.4%). The *picrate* gave orange-red needles from alcohol, m.p. 134.5° (Found: N, 9.5. $C_{19}H_{17}N_3O_8S$ requires N, 9.4%).

4-Methoxydibenzothiophene (XV)

A mixture of (XIV) and selenium (1.35 g.) was heated at 300° for 16 hours. The crystals (0.5 g.) isolated by extraction with alcohol gave on sublimation at 130–5°/5 mm. colourless needles (0.45 g., yield 30%), m.p. 122°; unaltered by crystallization from alcohol (Gilman and Jacoby⁶ quote m.p. 123°) (Found: C, 73.1; H, 4.8. Calc. for $C_{13}H_{10}OS$: C, 72.9; H, 4.7%). The *picrate* gave orange-red needles from alcohol, m.p. 118° (Found: N, 9.3. $C_{19}H_{13}N_3O_8S$ requires N, 9.5%).

2-(4'-Methoxyphenylmercapto)cyclohexanone (XVI)

p-Methoxythiophenol (9 g.), sodium (1.6 g.), 2-bromocyclohexanone (12.4 g.) and alcohol (50 c.c.) were refluxed for 6 hours. The product (15.2 g.) on distillation gave a straw-coloured oil (11.8 g., yield 75%), b.p. 175–80° (bath temp.)/5 mm. (Found: C, 65.3; H, 6.8. $C_{13}H_{16}O_2S$ requires C, 66.1; H, 6.8%). The 2:4-dinitrophenylhydrazone gave orange red needles from alcohol-ethyl acetate, m.p. 120–1° (Found: N, 14.1. $C_{19}H_{20}N_4O_5S$ requires N, 13.5%).

2-Methoxy-6:7:8:9-tetrahydrodibenzothiophene (XVII)

A mixture of (XVI) (3.64 g.) and phosphorus pentoxide (11 g.) was heated at 170–5° for 30 minutes. The cyclization product (1.65 g.) on distillation gave a fraction (0.14 g.), b.p. 175–80° (bath temp.)/5 mm. which gave a *picrate*. Lower boiling fraction mainly consisted of the parent thiol. The above fraction was converted into the *picrate* which on two crystallizations from alcohol gave orange red needles, m.p. 120–1° (Found: C, 52.6; H, 4.3; N, 8.8. $C_{19}H_{17}O_8N_3S$ requires C, 51.0; H, 3.8; N, 9.4%).

2-(4'-Nitrophenylmercapto)cyclohexanone (XVIII)

A solution of *p*-nitrothiophenol (8 g.) in 35% aqueous sodium hydroxide (5.9 c.c., 1 mol.) was cooled to 20–25° and 2-bromocyclohexanone (9.5 g.) was gradually added in 10 minutes under stirring and cooling. After stirring for 1½ hours the reaction mixture was diluted with water and the product

which separated was collected (12 g., yield 92%) and crystallized from benzene-petroleum ether. It gave minute needles, m.p. 93–4° (Found: C, 56.6; H, 4.8; N, 5.4. $C_{12}H_{13}O_3NS$ requires C, 57.4; H, 5.2; N, 5.6%). The 2:4-dinitrophenylhydrazone gave orange plates from alcohol, m.p. 167–8° (Found: N, 15.8. $C_{18}H_{17}N_5O_6S$ requires N, 16.2%).

SUMMARY

A new synthesis of dibenzothiophene (I) which has been extended to its substituted derivatives has been developed. It consists in the condensation of thiophenol with 2-bromocyclohexanone to give 2-phenylmercaptocyclohexanone (II), cyclization of (II) with phosphorus pentoxide to 1:2:3:4-tetrahydrodibenzothiophene and selenium dehydrogenation of the latter compound to give (I) (overall yield 52%).

Starting with suitably substituted thiophenols, 2-methyl-, 3-methyl and 4-methyldibenzothiophenes and 4-methoxydibenzothiophene have been synthesized. The synthesis of 2-methoxydibenzothiophene could not be completed due to the low yield of 2-methoxy-6:7:8:9-tetrahydrodibenzothiophene. Attempts to cyclize 2-(4'-nitrophenylmercapto)cyclohexanone by means of phosphorus pentoxide by the usual method were unsuccessful.

The scope and limitations of the new synthesis are discussed.

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