A CONVENIENT PROCEDURE FOR THE SYNTHESIS OF 2,3-DIHYDRO-1,4-DITHIAPHENANTHRENE DERIVATIVES

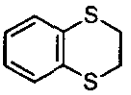
Gemma Esteban,[1] Berta López,[2] Joaquín Plumet,[1*] and Alberto del Valle[2]

[1] Departamento de Química Orgánica I, Facultad de Química, Universidad Complutense de Madrid, 28040 Madrid, Spain. [2] Universidad San Pablo (C.E.U.), 28668 Boadilla del Monte, Madrid, Spain

Abstract- A convenient method for the synthesis of 2,3-dihydro-1,4-dithiaphenanthrene derivatives starting from *S,S*-acetals of tetralones is described. A feasible mechanism for this transformation is also proposed.

In contrast with the chemistry of cyclic sulfides,[1] the chemistry of cyclic disulfides has received few attention with exception of the 1,3-dithiane ring system.[2] In the case of benzofused 1,4-dithiane derivatives (**1**) there are only small numbers of general methods for the synthesis of this heterocyclic ring system.[3-6] To the best of our knowlegde, cyclization of the disodium salt of *ortho*-dimercaptobenzene with 1,2-dibromomethane,[3] the reaction of 7-oxanorbornenone with ethanedithiol in presence of $BF_3{\cdot}OEt_2$,[4] and the ring aromatization of *S,S*-acetals of cyclohexanone using halogens in chlorinated solvents,[5] have been used for the preparation of the parent compound and some derivatives.[6]

On the other hand, fused 1,4-benzodithianes of general structure (**2**), carrying substituents on the benzenoides rings have, to the best of our knowledge, never been prepared, with exception of the unsubstituted compound (R_1=R_2=H).[5]



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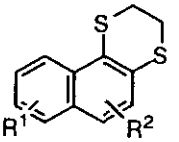

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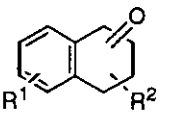

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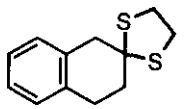
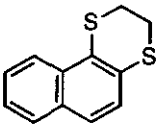
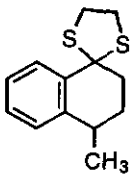
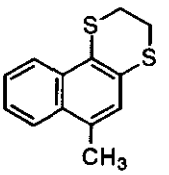
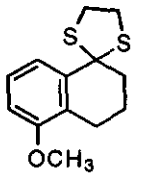
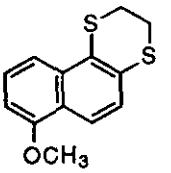
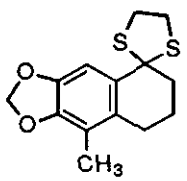
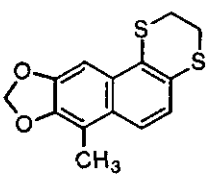
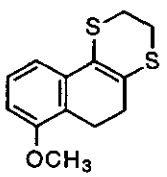
In this paper we wish to report a convenient, general method for the synthesis of these compounds starting from readily available *S,S*-acetals of the related ketones (**3**) by treatment with NBS in CCl_4.[7] This method constitutes a modification of the procedure indicated in reference 5, avoiding undesired side reactions such as the bromination in the benzenoid ring. Furthermore, a feasible mechanistic pathway for the transformation of **3** to **2** is reported.

The reactions of the appropiate ketones with 1,2-ethanedithiol in the presence of $BF_3{\cdot}OEt_2$ affords almost quantitatively the related *S,S*-acetals (**4-7**). Treatment of these compounds with NBS in CCl_4 at 25°C gave dithianes (**8-11**). Isolated yields are indicated in **Table 1**.

Table 1. Reactions of *S,S*-diacetals (**4-7**) with NBS in CCl_4 at 25°C.

Starting material	Product	Isolated yield(%)[a]
 **4**	 **8**	74
 **5**	 **9**	80
 **6**	 **10**	98
 **7**	 **11**	90

[a] Compound (**8**) was purified by destillation and some loss of material was observed during this process. The remaining products were purified by chromatography (compounds (**9**) and (**10**)) or recrystallization (compound (**11**)). For details, see **Experimental Section**.



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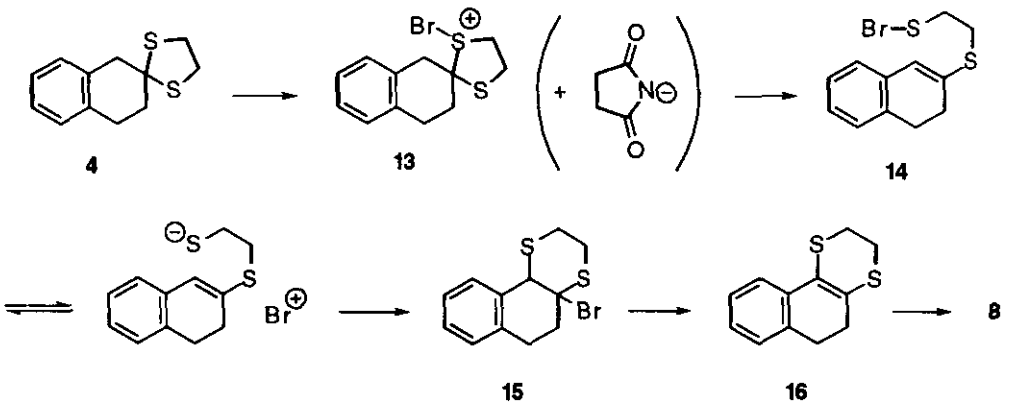
The reaction times in all cases were 20-25 h. Observation of TLC allowed us the presence of an intermediate which, in the case of the transformation of **6** to **10**, could be isolated and identified as dithiane (**12**) (75% isolated yield).

In the remaining cases, a mixture of dithiane intermediate and the final product was observed (NMR).

At longer reaction times, compounds (**4-7**) evolve to the final products (**8-11**).

A reasonable reaction pathway for this transformation can be formulated as follows (**Scheme 1**) using compound (**4**) as an example. In the first step, the reaction of **4** with NBS affords the sulfonium salt (**13**).[8] In the presence of succinimide ion a β-elimination occurs to give sulfinyl halide (**14**) which, by intramolecular deprotonation[9] followed by Pummerer like displacement affords (**15**).[10] Dehydrohalogenation gives dithiane (**16**), the observed intermediate. Final spontaneus aromatization of **16** affords **8**.



Scheme 1

In summary, we report here a convenient method for the transformation of substitued tetralones in 2,3-dihydro-1,4-dithiaphenanthrene derivatives in two steps with good overall yields.

EXPERIMENTAL SECTION

General. IR espectra were recorded on a Perkin-Elmer 297 spectrophotometer. ^{1}H NMR and ^{13}C NMR were obtained on Varian XL-300, Bruker AM-250 and Bruker AM-300 spectrometers. Chemical shifts (δ) are reported in ppm from internal $(CH_3)_4Si$. Silica gel Merck 60 (230-400 mesh) and Merck $60F_{254}$ plates were used for purification and analytical (TLC) chromatography, respectively. Melting points were determined on a Gallenkamp instrument and are uncorrected. Dichloromethane and $BF_3{\cdot}OEt_2$ were distilled over CaH_2 and NBS was recrystallized from water before use. 5-Methyl-6,7-methylenedioxy-1-tetralone was prepared in our laboratory using an intramolecular Friedel-Crafts cyclization from the appropiate 4-arylbutanoic acid. The remaining 1-tetralones were commercially available and were recrystallized before use.

General Procedure for the Synthesis of the 1,3-Dithianes (4-7). 1,2-Ethanedithiol (0.376 g, 4

mmol) and a few drops of $BF_3{\cdot}Et_2O$ were added dropwise to a solution of the appropiate tetralone (1 mmol) in CH_2Cl_2 (5 mL). The resulting mixture was refluxed until total consumption of the starting material (TLC) and then cooled at rt. The solution was washed with aqueous 5% NaOH, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The corresponding 1,3-dithianes were obtained after purification by recrystallization in the indicated solvents.

Spiro[2,5-dithiacyclopentane-1,2'-(1',2',3',4'-tetrahydronaphthalene)] (4). From 2-tetralone after 20 h of reaction and purification by recrystallization from ethanol a pale yellow solid (97%) was obtained. mp: 78-79°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.32 (t, CH_2, 2H, J = 6.5 Hz), 3.04 (t, CH_2, 2H, J = 6.5 Hz), 3.29-3.45 (m, SCH_2CH_2S, 4H), 3.37 (s, CH_2, 2H), 6.94-7.17 (m, ArH, 4H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 29.3, 39.0, 39.1 (2C), 46.4, 66.0, 126.0, 126.5, 129.0 (2C), 134.6, 135.4. IR (KBr): ν 3020, 2930, 2830, 1580, 780, 755 cm^{-1}. Anal. Calcd for $C_{12}H_{14}S_2$: C, 64.82; H, 6.35. Found: C, 64.89; H, 6.28.

Spiro[2,5-dithiacyclopentane-1,1'-(4'-methyl-1',2',3',4'-tetrahydronaphthalene)] (5). From 4-methyl-1-tetralone after 25 h of reaction a yellow oil which solidified at low temperature was obtained (98%). This compound was used without further purification. mp: 33-35°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.30 (d, CH_3, 3H, J = 7.0 Hz), 1.68-2.20 (m, CH_2, 2H), 2.88-3.00 (m, CH, 1H), 3.39-3.67 (m, SCH_2CH_2S, 4H), 7.08-7.21 (m, ArH, 3H), 7.94 (d, ArH, 1H, J = 7.0 Hz). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 22.8, 30.8, 32.4, 40.8, 40.9, 41.1, 69.2, 126.1, 127.5, 127.9, 130.9, 138.6, 142.3. IR (KBr): ν 3060, 3020, 2925, 2850, 1485, 1445, 760, 745 cm^{-1}. Anal. Calcd for $C_{13}H_{16}S_2$: C, 66.05; H, 6.82. Found: C, 66.00; H, 6.91.

Spiro[2,5-dithiacyclopentane-1,1'-(5'-methoxy-1',2',3',4'-tetrahydronaphthalene)] (6). From 5-methoxy-1-tetralone after 16 h of reaction and recrystallization from ethanol a yellow solid was obtained (87%). mp: 104-105°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.96-2.04 (m, CH_2, 2H), 2.35-2.39 (m, CH_2, 2H), 2.68 (t, CH_2, 2H, J = 6.4 Hz), 3.41-3.64 (m, SCH_2CH_2S, 4H), 3.79 (s, OCH_3, 3H), 6.67 (dd, ArH, 1H, J = 8.1, 0.7 Hz), 7.16 (t, ArH, 1H, J = 8.1 Hz), 7.58 (dd, ArH, 1H, J = 8.7, 0.7 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 22.0, 22.9, 40.8 (2C), 43.2, 55.3, 68.6, 107.8, 122.4, 125.9, 126.7, 140.2, 156.2. IR (KBr): ν 2940, 2840, 1435, 1255, 1240, 765, cm^{-1}. Anal. Calcd for $C_{13}H_{16}OS_2$: C, 61.87; H, 6.39. Found: C, 61.44; H, 6.30.

Spiro[2,5-dithiacyclopentane-1,1'-(5'-methyl-6',7'-methylenedioxy-1',2',3',4'-tetrahydronaphthalene)] (7). From 5-methyl-6,7-methylenedioxy-1-tetralone after 50 h of reaction and recrystallization from AcOEt a pale brown solid was obtained (88%). mp: 188-189°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.94-2.02 (m, CH_2, 2H), 2.04 (s, CH_3, 3H), 2.33 (m, CH_2, 2H), 2.53 (t, CH_2, 2H, J = 6.8 Hz), 3.36-3.59 (m, SCH_2CH_2S, 4H), 5.87 (s, OCH_2O, 2H), 7.32 (s, ArH, 1H). ^{13}C NMR ($CDCl_3$, 300 MHz): δ 11.5, 22.5, 26.2, 40.7 (2C), 43.3, 69.8, 100.4, 107.7, 115.8, 130.2, 131.6, 144.7, 145.3. IR (KBr): ν 3000, 2950, 2920, 1500, 950, 860, 840, 750, 580 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_2S_2$: C,

H, 5.75. Found: C, 59.79; H, 5.55.

General Procedure for the Synthesis of 2,4-Dithiaphenanthrene Derivatives (8-12). NBS (0.178 g (1 mmol) for **6** and **7**, 0.267 g (1.5 mmol) for **4** and **5**) was added to a solution of the 1,3-dithiane (1 mmol) in CCl_4 (10 mL). After stirring the resulting mixture at rt until complete desappearance of the starting material (TLC), water (5 mL) was added. The organic layer was washed with 5% aqueous $NaHSO_3$, water and brine and dried ($MgSO_4$). After concentrating under reduced pressure, the product was purified by chromatography and/or recrystallization.

2,3-Dihydro-1,4-dithiaphenanthrene (8). After 20 h of reaction and destillation under reduced pressure a yellow liquid was obtained (74%) from **4**. bp : 170-172°C/1 mm Hg. ^{1}H NMR: 3.26-3.37 (m, SCH_2CH_2S, 4H), 7.17 (d, ArH, 1H, J = 9.0 Hz), 7.38 (ddd, ArH, 1H, J = 8.1, 6.9, 1.2 Hz), 7.45 (d, ArH, 1H, J = 9.0 Hz), 7.48 (ddd, ArH, 1H, J = 8.4, 6.9, 1.2 Hz), 7.70 (dd, ArH, 1H, J = 8.4, 0.9 Hz), 8.11 (dd, ArH, 1H, J = 8.1, 0.9 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.8, 30.1, 122.6, 125.2, 125.5, 126.7, 127.0, 127.2, 128.6, 129.1, 131.6, 132.2. IR (neat): ν 3050, 2920, 1615, 1590, 815, 770 cm^{-1}. Anal. Calcd for $C_{12}H_{10}S_2$: C, 66.02; H, 4.62. Found: C, 66.11; H, 4.57.

2,3-Dihydro-1,4-dithia-6-methylphenanthrene (9). From **5** after 20 h of reaction and purification by column chromatography (Hexane/benzene 4:1) a yellow oil was obtained (80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.57 (s, CH_3, 3H), 3.27-3.40 (m, SCH_2CH_2S, 4H), 7.06 (s, ArH, 1H), 7.42-7.54 (m, ArH, 2H), 7.88 (dd, ArH, 1H, J = 7.2, 1.4 Hz), 8.16 (d, ArH, 1H, J = 8.1 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.2, 28.7, 30.2, 123.1, 124.8, 124.9, 125.3, 126.4, 127.4, 128.0, 131.1, 131.6, 132.3. IR (neat): ν 3060, 2920, 2860, 1555, 1445, 1360, 845 cm^{-1}. Anal. Calcd for $C_{13}H_{12}S_2$: C, 67.20; H, 5.21. Found: C, 66.97; H, 5.28.

2,3-Dihydro-1,4-dithia-7-methoxyphenanthrene (10). From **6** after 25 h of reaction and purification by column chromatography (Hexane/CH_2Cl_2 1:1) a pale brown oil was obtained (98%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.24-3.34 (m, SCH_2CH_2S, 4H), 3.91 (s, OCH_3, 3H), 6.73 (d, ArH, 1H, J = 7.5 Hz), 7.17 (d, ArH, 1H, J = 9.0 Hz), 7.37 (dd, ArH, 1H, J = 8.7, 7.5 Hz), 7.69 (d, ArH, 1H, J = 8.7 Hz), 7.91 (d, ArH, 1H, J = 9.0 Hz). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 28.6, 29.8, 55.5, 103.6, 114.7, 118.9, 123.3, 125.9, 126.6, 129.56, 132.7, 132.9, 155.6. IR (neat): ν 3070, 3010, 2965, 2925, 2860, 2840, 1590, 1455, 1260, 1020, 795 cm^{-1}. Anal. Calcd for $C_{13}H_{12}OS_2$: C, 62.87; H, 4.87. Found: C, 62.96; H, 4.59.

2,3-Dihydro-1,4-dithia-7-methyl-8,9-methylenedioxyphenanthrene (11). From **7** after 22 h of reaction and recrystallization from ethanol a yellow solid was obtained (90%). mp 145-146°C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.41 (s, CH_3, 3H), 3.22-3.36 (m, SCH_2CH_2S, 4H), 5.99 (s, OCH_2O, 2H), 7.13 (d, ArH, 1H, J = 8.9 Hz), 7.42 (d, ArH, 1H, J = 0.5 Hz), 7.44 (dd, ArH, 1H, J = 8.9, 0.5 Hz).^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.1, 29.4, 30.3, 97.9, 100.8, 112.0, 120.4, 125.0, 127.5, 127.8, 128.1,

129.6, 145.0, 147.4. IR (KBr): ν 2910, 1465, 925, 870, 840, 810, 775, 745 cm^{-1}. Anal. Calcd for $C_{14}H_{12}O_2S_2$: C, 60.84; H, 4.38. Found: C, 61.07; H, 4.11.

1,4-Dithia-7-methoxy-2,3,5,6-tetrahydrophenanthrene (12). From **6** after 2.5 h of reaction a brown oil was obtained (75%) without further purification. ^1H NMR ($CDCl_3$, 300 MHz): δ 2.34 (t, CH_2, 2H, J = 7.7 Hz), 2.81 (t, CH_2, 2H, J = 7.7 Hz), 3.24-3.35 (m, SCH_2CH_2S, 4H), 3.83 (s, OCH_3, 3H), 6.76 (dd, ArH, 1H, J = 8.1, 1.1 Hz), 7.10 (dd, ArH, 1H, J = 8.1, 1.1 Hz), 7.14 (t, ArH, 1H, J = 8.1 Hz).^{13}C NMR ($CDCl_3$, 75 MHz): δ 20.1, 27.7, 30.0, 31.1, 55.6, 109.2, 114.7, 119.0, 122.6, 126.2, 126.7, 135.3, 155.8. IR (neat): ν 3070, 2920, 2840, 1470, 1115, 785, 745, 710 cm^{-1}. Anal. Calcd for $C_{13}H_{14}OS_2$: C, 62.36; H, 5.64. Found: C, 62.53; H, 5.48.

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