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Metallation Reactions. XXVI. α,α'-Dimetallation of 1,2-Bis(methylthiobenzene)

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Abstract: α,α'-Dimetallation of bis(methylthio)benzene (**1**) with butyllithium or with superbases gives **2** with good yield. This species allows the simultaneous introduction of two electrophiles in thiomethyl groups. Alternatively it was possible to functionalize these groups with two different electrophiles by two successive one-flask monometallations. Compound **2** rise to gives heterocyclic compounds.

Heteroatom-promoted metallations play an important role in the synthesis of polysubstituted aromatic compounds and heterocycles.[1-8] New methods to metallate the lateral chains bonded to aromatic substrates directly or through a heteroatom have been developed.[8] We have been involved in the study of sulphur chemistry for many years: we showed that (methylthio)arenes are useful synthons to introduce identical or different groups in the lateral chain or in the ring or in both, through "one-step" or "one-pot" metallations.[9,10]

In this work we report the one-step synthesis of *alpha*-derivatives of 1,2-*bis*(methylthio)benzene (**1**) and their use in the synthesis of heterocycles.

We prepared the α,α'-dimetallo intermediate **2** (Scheme 1) starting from **1** using butyllithium or the superbasic mixture LICKOR (butyllithium/potassium *tert*-butoxide). The quenching of **2** with iodomethane gave 1,2-*bis*(ethylthio)benzene (**3a**); thus confirming that both methylthio groups were deprotonated. We could therefore bifunctionalize compounds using various electrophiles. Thus, quenching with iodoethane, allyl bromide, carbon dioxide, [(chlorocarbonyl)oxy]methane, methyl benzoate, methyl 4-methylbenzoate and chloro(trimethyl)silane afforded compounds **3**-**8** with good yields (53-88%).

Starting from **1** we developed a new synthesis of seven membered heterocycles. Using dichlorodimethylsilane we obtained 1,5,3-benzodithiasilepin **8** through a one-step process. Product **5** was reacted (without previous isolation) with lithiumdiisopropylamide (LDA) to give in one-flask the 3,4-disubstituted 1,5-benzodithiepin (**9**), that can be converted into 2*H*-1,5-benzodithiepin-3(4*H*)-one (**10**).

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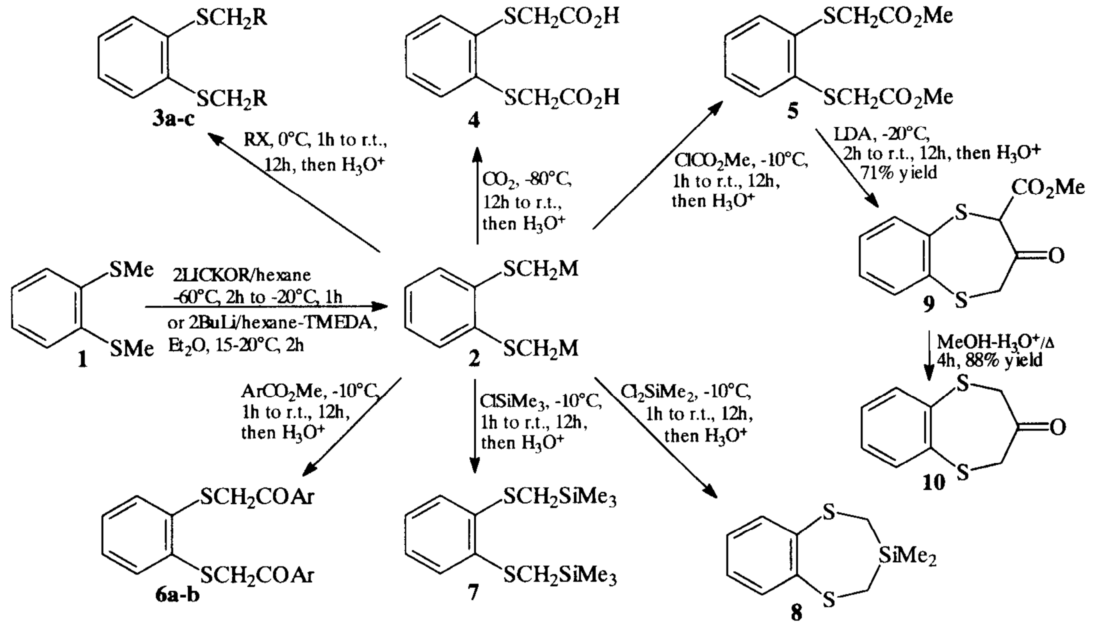
Scheme 1



2: M = Li or K

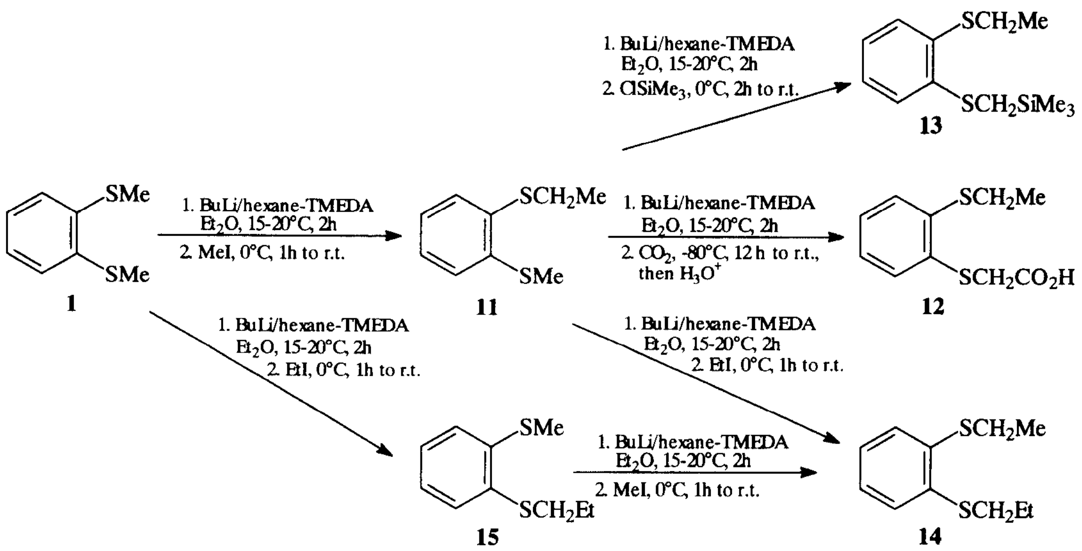
3a: R = Me; **3b**: R = Et; **3c**: R = $CH_2CH=CH_2$

6a: Ar = C_6H_5; **6b**: Ar = 4-Me-C_6H_4

Electrophile	Product	Yield (%)	Electrophile	Product	Yield (%)
MeI	**3a**	85	C_6H_5COCl	**6a**	75
EtI	**3b**	88	4-MeC_6H_4COCl	**6b**	71
$CH=CHCH_2Br$	**3c**	85	$ClSiMe_3$	**7**	83
CO_2	**4**	81	Cl_2SiMe_2	**8**	53
$ClCO_2Me$	**5**	75			

It is also possible to functionalize one or both thiomethylic moieties of **1** with the same or different groups in one flask using one molar equivalent of organometallic, followed by the quenching with the first electrophile; then a further treatment with the second molar equivalent of organometallic and treatment with the second electrophile. In this way (Scheme 2) we obtained **11** using iodomethane as first electrophile and **12**, **13**, **14** using carbon dioxide, chlorotrimethylsilane and iodoethane, respectively, as second electrophile. The same product **14** was obtained through intermediate **15**.

Scheme 2



1^{st} Electrophile	Product	Yield (%)	2^{nd} Electrophile	Product	Yield (%)
MeI	**11**	84	CO_2	**12**	70
MeI	**11**		$ClSiMe_3$	**13**	63
MeI	**11**		EtI	**14**	61
EtI	**15**	75	MeI	**14**	65

Experimental Section

Solutions of butyllithium in hexane were purchased from Aldrich Chemical Co. and were analyzed by the Gilman double titration method.[11] Analytical TLC plates and silica gel (230-400 mesh) were purchased from Merck. IR spectra were recorded on a Perkin-Elmer 1310 grating spectrophotometer using NaCl plates. ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-300 spectrometer with tetramethylsilane as internal reference; δ values are given in ppm and J values in Hz. Mass spectra were obtained at 70 eV with a Hewlett-Packard 5989A mass spectrometer, using the direct-inlet system. Microanalyses were carried out on a Carlo Erba 1106 Elemental Analyzer.

Reagent-grade commercially available reagents and solvents were used. 1,2-Bis(methylthio)benzene (**1**) was prepared according to the reported method.[12]

Metallation procedure with butyllithium

A vigorously stirred solution of **1** (4.25 g, 25 mmol), anhydrous diethyl ether (50 ml) and TMEDA (7 g, 60 mmol) was treated with a 1.4 M solution of *n*-butyllithium in hexane (43 ml, 60 mmol) at 15-20°C under argon. After 2 h, the mixture was cooled at 0°C and iodomethane (8.6 g, 60 mmol) was slowly added, the cooling bath removed and the reaction completed by stirring overnight at room temperature. The reaction mixture was poured into water and the pH adjusted to 4-5 by addition of 10% aqueous hydrochloric acid. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The crude product was flash-chromatographed using light petroleum as eluent, and identified as **1,2-bis(ethylthio)benzene (3a)**.[13] Yield 85%; viscous pale yellow oil; n_D^{20} = 1.583; IR (neat, cm^{-1}): 750 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 1.22 (t, 6H, CH_3, J = 7.4), 2.84 (q, 4H, CH_2, J = 7.4), 7.09 (m, 4H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 14.59 (CH_3), 24.18 (CH_2), 127.50, 129.19, 139.43; MS *m/z*: 198 (100%, M^+), 170 (75%, M^+-C_2H_4), 169 (75%, M^+-C_2H_5), 153 (15.5%, $C_6H_4S_2CH^+$), 142 (41%, $C_6H_4S_2H_2^+$), 141 (38%, $C_6H_4S_2H^+$), 135 (52%, $C_6H_4SC_2H_3^+$), 110 (14%, $C_6H_5SH^+$), 109 (17%, $C_6H_4SH^+$), 105 (15%, $C_6H_4C_2H_5^+$), 96 (18%, $C_5H_4S^+$), 91 (52%, $C_7H_7^+$), 45 (29%, CHS^+). Anal. Calcd for $C_{10}H_{14}S_2$: C, 60.56; H, 7.11; S, 32.33. Found C, 60.41; H, 7.05; S, 32.16.

Metallation procedure with superbases

A 1.4 M solution of *n*-butyllithium in hexane (43 ml, 60 mmol) was cooled to −60°C under argon and a solution of **1** (4.25 g, 25 mmol) in hexane (30 ml) was added. Finely powdered potassium *tert*-butoxide (6.7 g, 60 mmol) was added and the temperature allowed to rise to -20°C. The mixture was kept for 1 h at −20°C, after which the temperature was allowed to rise to −10°C. After 3 h, iodomethane (8.6 g, 60 mmol) was added, the cooling bath removed and the reaction completed by stirring overnight at room temperature. The reaction mixture was poured into water and worked up in the same manner above described. In this manner **3a** in 83% yield was obtained and identified by comparison with the same product above described.

The following compounds were obtained by the same procedures using iodoethane, allyl bromide, carbon dioxide, [(chlorocarbonyl)oxy]methane, ethyl benzoate, ethyl 4-methylbenzoate, chloro(trimethyl)silane and dichloro(dimethyl)silane, respectively, as electrophiles:

1,2-Bis(propylthio)benzene (*3b*). The crude product was flash-chromatographed using light petroleum as eluent. Yield 88%; viscous pale yellow oil,[14] n_D^{20} = 1.579; IR (neat, cm^{-1}): 745 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 0.97 (t, 6H, CH_3, J = 7.3), 1.62 (m, 4H, CH_3CH_2), 2.81 (t, 4H, $CH_3CH_2CH_2$, J = 7.0), 7.04 (m, 2H, Ar-*H*) 7.18 (m, 2H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 13.55 (CH_3), 22.18 (CH_2CH_3), 35.15 (SCH_2), 125.89, 128.52, 137.11; MS *m/z*: 226 (39%, M^+), 184 (50%, M^+-C_3H_6), 155 (11%, $C_7H_7S_2^+$), 153 (9%, $C_6H_4S_2CH^+$), 150 (8%, $C_6H_4SC_3H_6^+$), 142 (100%, $C_6H_6S_2^+$), 141 (31%, $C_6H_5S_2^+$), 109 (8%, $C_6H_5S^+$), 97

(10%, $C_5H_5S^+$), 91 (29%, $C_7H_7^+$), 78 (24.5%, $C_6H_6^+$), 77 (24%, $C_6H_5^+$), 65 (8%, $C_5H_5^+$), 45 (13%, CHS^+), 43 (18%, $CH_3CH_2CH_2^+$), 41 (37%, $CH_2{=}CHCH_2^+$). Anal. Calcd for $C_{12}H_{18}S_2$: C, 63.69; H, 8.02; S, 28.28. Found C, 63.60; H, 7.94; S, 28.17.

1,2-Bis-(3-butenylthio)benzene (*3c*). Yield 85%; flash-chromatography (9/1 diethyl ether/light petroleum); viscous pale yellow oil, n_D^{20} = 1.562; IR (neat, cm^{-1}): 1639 ($CH{=}CH_2$), 740 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 2.42 (m, 4H, SCH_2CH_2), 2.97 (t, 4H, SCH_2, J = 7.8), 5.10 (m, 4H, $CH{=}CH_2$), 5.85 (m, 2H, $CH{=}CH_2$), 7.29 (m, 4H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 31.05 (SCH_2), 33.36 (SCH_2CH_2), 117.45 ($CH{=}CH_2$), 127.79, 129.74, 133.65 ($CH{=}CH_2$), 139.02; MS *m/z*: 250 (23%, M^+), 196 (100%, M^+-$CH_2{=}CHCH{=}CH_2$), 167 (12%, $C_8H_7S_2^+$), 155 (42%, $C_7H_7S_2^+$), 154 (13%, $C_6H_4S_2CH_2^+$), 153 (47%, $C_6H_4S_2CH^+$), 142 (77%, $C_6H_6S_2^+$), 121 (5%, $C_6H_4SCH^+$), 109 (6%, $C_6H_5S^+$), 91 (53%, $C_7H_7^+$), 77 (17%, $C_6H_5^+$), 55 (93%, $CH_2{=}CHCH_2CH_2^+$), 45 (10%, CHS^+). Anal. Calcd for $C_{14}H_{18}S_2$: C, 67.15; H, 7.25; S, 25.61. Found C, 67.07; H, 7.20; S, 25.50.

2-({2-[(2-hydroxy-2-oxoethyl)thio]phenyl}thio)acetic Acid (*4*). The metallated mixture of **1** was poured onto *ca.* 100 g of crushed solid carbon dioxide. After 24 h the residue was treated with 10% aqueous sodium bicarbonate and then with diethyl ether. The alkali layer was separated, washed with diethyl ether, and then acidified with cold concentrated hydrochloric acid, extracted with diethyl ether, dried (Na_2SO_4), and concentrated. Yield 81%; the crude product was crystallised from aqueous ethanol as white plates, mp 208-210°C; IR (KBr, cm^{-1}): 3450-3080 (OH), 1700 (C=O), 748 (1,2-disubstituted benzene); ^1H NMR (DMSO-d_6) δ 3.80 (s, 4H, SCH_2), 7.20 (m, 2H, Ar-*H*), 7.30 (m, 2H, Ar-*H*), 10.20 (s, 1H, OH); ^{13}C NMR (DMSO-d_6) δ: 29.41 (SCH_2), 128.90, 129.34, 136.42, 173.01 (*C*O); MS *m/z*: 258 (98%, M^+), 240 (7%, M^+-H_2O), 214 (14%, (M^+-CO_2), 212 (12%, M^+-H_2O-CO), 200 (10%, M^+- H_2O-CO-H_2O), 199 (92%, M^+-CH_2CO_2H), 196 (13%, M^+-CO_2-H_2O), 184 (12%, M^+-H_2O-CO-CO), 181 (18%, M^+-CH_2CO_2H-H_2O), 170 (8%, M^+-2CO_2), 169 (11%, M^+-CO_2-CO_2H), 168 (23.5%, M^+-$(CO_2H)_2$), 167 (11%, M^+-$(CO_2H)_2$-H), 166 (13%, M^+-$(CO_2H)_2$-2H), 153 (100%, $C_6H_4S_2CH^+$), 140 (10%, $C_6H_4S_2^+$), 124 (10%, $C_6H_4SCH_3^+$), 123 (16%, $C_7H_7S^+$), 108 (8%, $C_6H_4S^+$), 91 (6%, $C_7H_7^+$), 77 (1%, $C_6H_5^+$). Anal. Calcd for $C_{10}H_{10}O_4S_2$: C, 46.50; H, 3.90; S, 24.82. Found: C, 46.43; H, 3.85; S, 24.71.

Methyl 2-({2-[(2-Methoxy-2-oxoethyl)thio]phenyl}thio]acetate (*5*). Yield 75%; flash-chromatography (3/10 diethyl ether/light petroleum); viscous pale yellow oil, n_D^{28} = 1.581; IR (neat, cm^{-1}): 1735 (C=O), 743 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 3.60 (s, 4H, CH_2), 3.71 (s, 6H, CH_3), 7.30 (m, 4H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 28.20 (SCH_2), 52.50 (OCH_3), 127.77, 129.95, 138.22, 170.40 (*C*O); MS *m/z*: 286 (8%, M^+), 254 (2%, M^+-CH_3OH), 277 (5%, M^+-CO_2CH_3), 167 (2%, $C_8H_7S_2^+$), 154 (26%, $C_6H_4S_2CH_2^+$), 153 (100%, $C_6H_4S_2CH^+$), 140 (5%, $C_6H_4S_2^+$), 121 (2%, $C_6H_4SCH^+$), 96 (6%, $C_5H_4S^+$), 77 (8%, $C_6H_5^+$), 45 (11%, CHS^+). Anal. Calcd for $C_{12}H_{14}O_4S_2$: C, 50.33; H, 4.93; S, 22.39. Found: C, 50.24; H, 4.86; S, 22.27.

2-({2-[(2-Oxo-2-phenylethyl)thio]phenyl}thio)-1-phenyl-1-ethanone (*6a*). Yield 75%; the crude product was crystallized from ethanol as pale yellow plates, mp 140-142°C; IR (nujol, cm^{-1}): 1680 (C=O); ^1H NMR ($CDCl_3$) δ: 4.35 (s, 4H, C*H*$_2$), 7.38 (m, 10H, Ar-*H*), 7.93 (m, 4H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 40.20 (S*C*H$_2$), 127.70, 128.59, 131.12, 133.42, 135.37, 136.16, 193.98 (*C*O); MS *m/z*: 378 (10%, M^+), 273 (7%, M^+-C_6H_5CO), 259 (4%, M^+-$C_6H_5COCH_2$), 258 (4%, M^+-$C_6H_5COCH_3$), 238 (9%, M^+-$C_6H_4S_2$), 237 (45%, M^+-$C_6H_4S_2H$), 154 (31%, $C_6H_4S_2CH_2^+$), 153 (100%, $C_6H_4S_2CH^+$), 140 (5%, $C_6H_4S_2^+$), 105 (87%, $C_6H_5CO^+$), 91 (15%, $C_7H_7^+$), 77 (69%, $C_6H_5^+$). Anal. Calcd for $C_{22}H_{18}O_2S_2$: C, 69.81; H, 4.79; S, 16.94. Found: C, 69.73; H, 4.85; S, 16.81.

1-(4-Methylphenyl)-2-[(2-{[2-(4-methylphenyl)-2-oxoethyl]thio}phenyl)thio]-1-ethanone (*6b*). Yield 71%; the crude product was crystallized from ethanol as pale yellow plates, mp 128-130°C; IR (nujol, cm^{-1}): 1640 (C=O); ^1H NMR ($CDCl_3$) δ: 2.42 (s, 6H, C*H*$_3$), 4.33 (s, 4H, C*H*$_2$), 7.15 (m, 8H, Ar-*H*), 7.82 (m, 4H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 21.53 (*C*H$_3$), 34.01 (S*C*H$_2$), 128.45, 128.81, 129.14, 132.01, 138.45, 142.94, 194.15 (*C*O); MS *m/z*: 406 (2%, M^+), 287 (26%, M^+-$CH_3C_6H_4CO$), 272 (33%, M^+-$CH_3C_6H_4COCH_3$), 266 (6%, M^+-$C_6H_4S_2$), 265 (29%, M^+-$C_6H_4S_2$-H), 154 (18%, $C_6H_4S_2CH_2^+$), 153 (69%, $C_6H_4S_2CH^+$), 134 (7%, $CH_3C_6H_4COCH_3^+$), 119 (100%, $CH_3C_6H_4CO^+$), 105 (12%, $C_6H_5CO^+$), 91 (49%, $C_7H_7^+$), 77 (14%, $C_6H_5^+$), 65 (19%, $C_5H_5^+$). Anal. Calcd for $C_{24}H_{22}O_2S_2$: C, 70.90; H, 5.45; S, 15.77. Found: C, 70.82; H, 5.41; S, 15.65.

(Trimethylsilyl)methyl 2-{[(Trimethylsilyl)methyl]thio}phenyl Sulfide (*7*). Yield 83%; flash-chromatography (15/1 hexane/ethyl acetate); viscous pale yellow oil, n_D^{20} = 1.576; IR (neat, cm^{-1}): 1251, 845 (C-Si), 748 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 0.21 (s, 18H, C*H*$_3$), 2.22 (s, 4H, C*H*$_2$), 7.20 (m, 4H, Ar-*H*); ^{13}C NMR δ: 3.82 (*C*H$_3$), 15.15 (S*C*H$_2$), 127.38, 128.05, 141.18); MS *m/z*: 314 (3%, M^+), 313 (6%, M^+-1), 241 (11%, M^+-$SiMe_3$), 228 (10%, $C_7H_7S_2SiMe_3^+$) 227 (13%, $C_7H_6S_2SiMe_3^+$) 213 (23%, $C_7H_7S_2SiMe_2^+$), 198 (10%, $C_7H_7S_2SiMe^+$), 183 (23%, $C_7H_7S_2Si^+$), 153 (29%, $C_6H_4S_2CH^+$), 140 (6%, $C_6H_4S_2^+$), 121 (6%, $C_6H_4SCH^+$), 109 (10%, $C_6H_5S^+$), 96 (10%, $C_5H_4S^+$), 91 (19%, $C_7H_7^+$), 77 (18%, $C_6H_5^+$), 73 (100%, Me_3Si^+), 59 (26%, Me_2SiH^+), 45 (48%, CHS^+). Anal. Calcd for $C_{14}H_{26}O_2S_2Si_2$: C, 53.44; H, 8.33; S, 20.38. Found C, 53.32; H, 8.37; S, 20.20.

3,3-Dimethyl-3,4-dihydro-2*H*-1,5,3-benzodithiasilepin (*8*). Yield 53%; flash-chromatography (first 9/1 hexane/ethyl acetate, then diethyl ether/light petroleum 4/6); viscous pale yellow oil, n_D^{20} = 1.568; IR (neat, cm^{-1}): 1245, 851 (C-Si), 746 (1,2-disubstituted benzene); ^1H NMR (CDCl3) δ: 0.20 (s, 6H, C*H*$_3$), 2.51 (s, 4H, C*H*$_2$), 7.22 (m, 4H, Ar-*H*); ^{13}C NMR δ: 3.30 (*C*H$_3$), 19.36 (S*C*H$_2$), 127.53, 128.45 141.50; MS *m/z*: 226 (45%, M^+), 211 (39%, M^+-CH_3), 183 (21%, M^+-$SiCH_3$), 165 (55%, $C_6H_4S_2CCH^+$), 154 (27%, $C_6H_4S_2CH_2^+$), 153 (100%, $C_6H_4S_2CH^+$), 137 (11%, $C_6H_4SCH_2CH^+$), 121 (6%, $C_6H_4SCH^+$), 91 (11%, $C_7H_7^+$), 77 (24%, $C_6H_5^+$), 73 (23%, $(CH_3)_3Si^+$), 72 (27%, $Si(CH_3)_2CH_2^+$), 59 (11%, $(CH_3)_2SiH^+$). Anal. Calcd for $C_{10}H_{14}O_2S_2Si$: C, 53.05; H, 6.23; S, 28.32. Found: C, 52.95; H, 6.28; S, 28.21.

Methyl 3-Oxo-3,4-dihydro-2*H*-1,5-benzodithiepin-2-carboxylate (*9*). The above reaction mixture of **7**, before the hydrolysis procedure, was added dropwise under argon at –20°C to a vigorously stirred mixture of LDA, obtained from diisopropylamine (1.8 g, 18 mmol) in dry tetrahydrofuran (20 ml) and butyllithium (12 ml, 18 mmol). After 2h the cooling bath was removed and the reaction completed by stirring overnight at room temperature. The reaction mixture was then poured into water, the organic layer separated and worked up in the same manner described above. The crude product was flash-chromatographed using diethyl ether/light petroleum (9:1) as eluent. Yield 71%; crystallized from ethanol as pink plates, mp 197-198°C; IR (nujol, cm^{-1}): 1740 (C=O), 1720 (C=O), 743 (1,2-disubstituted benzene); ^{1}H NMR ($CDCl_3$) δ: 3.68 (s, 3H, CH_3), 4.15 (s, 1H, SC*H*), 4.77 (q, 2H, SCH_2), 7.09 (m, 2H, Ar-*H*), 7.41, (2H, Ar-*H*); ^{13}C NMR δ: 42.03 (SCH_2), 52.37 (CH_3), 52.54 (SCH), 126.69, 127.12, 129.19, 130.25, 136.76, 138.65, 171.63 (CO_2Me), 191.75 (CH_2CO); MS *mz*: 254 (23%, M^+), 222 (18%, M^+-CH_3OH), 195 (18%, M^+-CO_2CH_3), 166 (19%, $C_8H_6S_2^+$), 154 (32%, $C_7H_6S_2^+$), 153 (100%, $C_7H_5S_2^+$), 134 (25%, $C_8H_6S^+$), 121 (8%, $C_7H_5S^+$), 96 (10%, $C_5H_4S^+$), 77 (32%, $C_6H_5^+$), 69 (20%, C_3HS^+), 51 (9%, $C_4H_3S^+$), 45 (23%, CHS^+). Anal. calcd for $C_{11}H_{10}O_3S_2$: C, 51.95; H, 3.96; S, 25.21. Found: C, 51.84; H, 3.90; S, 25.09.

2*H*-1,5-benzodithiepin-3(4*H*)-one (*10*). A solution of **9** (1 g, 4 mmol) in methanol (10 ml) was treated with a mixture of concentrated hydrochloric acid (5 ml) and water (5 ml) and heated under reflux. After 4h, the reaction mixture was poured onto ice and filtered. The product was crystallised from ethanol as pink plates. Yield 88%; mp 77-78°C; IR (nujol, cm^{-1}): 1710 (C=O), 743 (1,2-disubstituted benzene); ^{1}H NMR ($CDCl_3$) δ: 3.55 (s, 4H, SCH_2), 7.23 (m, 2H, Ar-*H*), 7.64 (m, 2H, Ar-*H*).;^{13}C NMR ($CDCl_3$) δ: 43.66 (SCH_2), 126.94, 129.01, 138.37, 187.83 (*C*O); MS *mz*: 196 (58.5%, M^+), 154 (31%, $C_7H_6S_2^+$), 153 (100%, $C_7H_5S_2^+$), 140 (11%, $C_6H_4S_2^+$), 121 (9%, $C_7H_5S^+$), 96 (9%, $C_5H_4S^+$), 91 (2%, C_7H_7), 78 (5%, $C_6H_6^+$), 77 (18%, $C_6H_5^+$), 45 (13%, CHS^+). Anal. Calcd for $C_9H_8OS_2$: C, 55.07; H, 4.11; S, 32.67. Found: C, 55.01; H, 4.07; S, 32.58.

2-{[2-(Ethylthio)phenyl]thio}acetic Acid (*12*). A vigorously stirred solution of **1** (4,25 g, 25 mmol), anhydrous diethyl ether (50 ml) and TMEDA (3.5 g, 30 mmol) was treated with a 1.4 M solution of butyllithium in hexane (21.5 ml, 30 mmol) at 15-20°C under argon. After 2 h, the mixture was cooled at 0°C and iodomethane (4,3 g, 30 mmol) was slowly added, the cooling bath removed and the reaction completed by stirring overnight at room temperature. To this mixture was then added TMEDA (3.5 g, 30 mmol) and then butyllithium in hexane (21.5 ml, 30 mmol). After the usual work-up, the resulting solution was poured onto ca 100 g of crushed solid carbon dioxide and worked-up in the same manner described for **6**. Yield 70%; the crude product was crystallised from aqueous ethanol as pale yellow plates, mp 208-210°C; IR (KBr, cm^{-1}): 3500 (OH), 1710 (C=O), 740 (1,2-disubstituted benzene); ^{1}H NMR (DMSO-d_6) δ: 1.44 (t, 3H, CH_3, J = 7.3), 2.57 (s, 2H, CH_2CO_2H) 3.05 (q, 2H, CH_2CH_3, J = 7.3), 6.80 (s, 1H, O*H*), 7.15 (m 2H, Ar-*H*), 7.55 (m 2H, Ar-*H*); ^{13}C NMR (DMSO-d_6) δ: 14.59 (CH_3), 24.18 (SCH_2CH_3), 29.41 (SCH_2CO_2H), 128.15, 128.25, 128.59, 129.94, 137.02, 138.83, 173.01(*C*O); MS *m/z*: 228 (57%, M^+), 184 (1%, M^+-CO_2), 183 (3%,

M^+-CO_2H) 169 (17%, M^+-CH_2CO_2H), 156 (10%, $C_7H_8S_2^+$), 155 (26%, $C_7H_7S_2^+$), 154 (42.5%, $C_7H_6S_2^+$), 153 (100%, $C_7H_5S_2^+$), 141 (16%, $C_6H_5S_2^+$), 140 (19%, $C_6H_4S_2^+$), 138 (18%, $C_8H_{10}S^+$), 124 (33%, $C_7H_8S^+$), 123 (8%, $C_7H_7S^+$), 121 (11%, $C_7H_5S^+$), 109 (12%, $C_6H_5S^+$), 108 (10%, $C_6H_4S^+$), 97 (8%, $C_5H_5S^+$), 96 (15%, $C_5H_4S^+$), 91 (48%, $C_7H_7^+$), 77 (22%, $C_6H_5^+$), 45 (26%, CHS^+). Anal. Calcd for $C_{10}H_{12}O_2S_2$: C, 52.61; H, 5.30; S, 28.08. Found C, 52.50; H, 5.24; S, 27.99.

If the reaction mixture was hydrolyzed before the second metallation **1-(ethylthio)-2-(methylthio)benzene** (*11*) was obtained. Yield 84%; pale yellow oil. This compound was identified by comparison with an authentic sample.[15]

({[2-(Ethylthio)phenyl]thio}methyl)(trimethyl)silane (*13*). A vigorously stirred solution of **1** (4,25 g, 25 mmol), anhydrous diethyl ether (50 ml) and TMEDA (3.5 g, 30 mmol) was treated with a 1.4 M solution of butyllithium in hexane (21.5 ml, 30 mmol) at 15-20°C under argon. After 2 h, the mixture was cooled at 0°C and iodomethane (4,3 g, 30 mmol) was slowly added, the cooling bath removed and the reaction completed by stirring overnight at room temperature. TMEDA (3.5 g, 30 mmol) was added to this mixture and then a 1.4 M solution of *n*-butyllithium in hexane (21.5 ml, 30 mmol). After the usual work-up, the resulting solution was cooled at 0°C and treated dropwise with chlorotrimethylsilane (3.2 g, 30 mmol), the cooling bath removed and the reaction completed by stirring overnight at room temperature. The reaction mixture was poured into water and the pH adjusted to 4-5 by addition of 10% aqueous hydrochloric acid. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. The crude product was flash-chromatographed using light petroleum as eluent. Yield 63%; pale yellow oil, n_D^{20} = 1.543; IR (neat, cm^{-1}): 1240, 845 (C-Si), 746 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 0.14 (s, 9H, $SiCH_3$), 1.17 (t, 3H, CH_2CH_3, J = 7.4), 2.41 (s, 2H, SCH_2Si), 2.84 (q, 2H, CH_2CH_3, J = 7.4 Hz), 6.94 (m, 1H, Ar-*H*)), 7.15 (m, 1H, Ar-*H*), 7.20 (d, 1H, Ar-*H*, J = 7.8), 7.38 (d, 1H, Ar-*H*, J = 7.9); ^{13}C NMR ($CDCl_3$) δ: 3.82 ($SiCH_3$), 14.59 (SCH_2CH_3), 16.15 (SCH_2Si), 24.18 (SCH_2CH_3), 127.41, 127.46, 128.08, 129.16, 138.31, 142.29; MS *m/z*: 256 (3%, M^+), 228 (6%, M^+-C_2H_4), 227 (3%, M^+-C_2H_5), 213 (26%, $C_7H_7S_2SiMe_2^+$), 198 (13%, $C_7H_7S_2SiMe^+$), 183 (17%, $C_9H_{11}S_2^+$), 153 (25%, $C_6H_4S_2CH^+$), 140 (9%, $C_6H_4S_2^+$), 121 (10%, $C_6H_4SCH^+$), 109 (13%, $C_6H_5S^+$), 96 (9%, $C_5H_4S^+$), 91 (23%, $C_7H_7^+$), 77 (16%, $C_6H_5^+$), 73 (100%, Me_3Si^+), 59 (31%, Me_2SiH^+), 45 (44%, CHS^+). Anal. Calcd for $C_{12}H_{20}S_2Si$: C, 56.19; H, 7.86; S, 25.00. Found: C, 56.08; H, 7.81; S, 24.89.

In the same manner using iodomethane as first electrophile and iodoethane as second the following compound was preparated:

1-(Ethylthio)-2-(propylthio)benzene (*14*). Yield 61%; pale yellow oil, n_D^{20} = 1.5745; IR (neat, cm^{-1}): 741 (1,2-disubstituted benzene); ^1H NMR ($CDCl_3$) δ: 0.97 (t, 3H, $SCH_2CH_2CH_3$, J = 7.4), 1.18 (t, 3H, SCH_2CH_3, J = 7.4), 1.60 (m, 2H, $SCH_2CH_2CH_3$), 2.85 (q, 2H, SCH_2CH_3, J = 7.4), 3.09 (q, 2H, $SCH_2CH_2CH_3$, J = 7.0), 6.9 (m, 2H, Ar-*H*), 7.18 (m, 2H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 13.75 ($\mathrm{SCH_2CH_2\mathit{C}H_3}$), 14.59 ($\mathrm{SCH_2\mathit{C}H_3}$), 22.79 ($\mathrm{SCH_2\mathit{C}H_2CH_3}$), 24.18 ($\mathrm{S\mathit{C}H_2CH_3}$), 34.48 ($\mathrm{S\mathit{C}H_2CH_2CH_3}$), 126.71, 127.31, 128.90, 129.00, 139.23, 140.40; MS *m/z*: 212 (51%, M^+), 184 (48%, M^+-C_2H_4), 183 (47%, M^+-C_2H_5), 170 (100%, M^+-C_3H_6), 153 (11.5%, $C_6H_4S_2CH^+$), 150 (7%, $C_6H_4SC_3H_6^+$), 142 (38%,$C_6H_4S_2H_2^+$), 141 (28%, $C_6H_5S_2^+$), 135 (44%, $C_6H_4SC_2H_3^+$), 110 (16%, $C_6H_5SH^+$), 109 (6%, $C_6H_5S^+$), 97 (10%, $C_5H_5S^+$), 96 (14%, $C_5H_4S^+$), 91 (36%, $C_7H_7^+$), 78 (22%, $C_6H_6^+$), 77 (19%, $C_6H_5^+$), 65 (7%, $C_5H_5^+$), 45 (20%, CHS^+), 43 (15%, $CH_3CH_2CH_2^+$), 41 (40%, $CH_2{=}CHCH_2^+$). Anal. Calcd for $C_{11}H_{16}S_2$: C, 62.21; H, 7.59; S, 30.19. Found: C, 62.30; H, 7.65; S, 30.07.

The same compound **14** was obtained in 65% yield using iodoethane as first electrophile and iodomethane as second. In this case, if the reaction mixture was hydrolyzed before the second metallation **1-(methylthio)-2-(propylthio)benzene (*15*)** was obtained. Yield 75%; pale yellow oil, n_D^{20} = 1.585; IR (neat, cm^{-1}): 743 (1,2-disubstituted benzene); ^{1}H NMR ($CDCl_3$) δ: 0.96 (t, 3H, $\mathrm{SCH_2CH_2C\mathit{H}_3}$, J = 7.3), 1.58 (m, 2H, $\mathrm{SCH_2C\mathit{H}_2CH_3}$), 2.47 (s, 3H, $\mathrm{SC\mathit{H}_3}$), 3.07 (t, 2H, $\mathrm{SC\mathit{H}_2CH_2CH_3}$, J = 7.0), 6.95 (m, 2H, Ar-*H*)), 7.20 (m, 2H, Ar-*H*); ^{13}C NMR ($CDCl_3$) δ: 13.75 ($\mathrm{SCH_2CH_2\mathit{C}H_3}$), 16.52 ($\mathrm{S\mathit{C}H_3}$), 22.79 ($\mathrm{SCH_2\mathit{C}H_2CH_3}$), 34.48 ($\mathrm{S\mathit{C}H_2CH_2CH_3}$), 127.49, 127.30, 18.96, 129.33, 139.57, 140.37; MS *m/z*: 198 (54%, M^+), 169 (4%, M^+-C_2H_5), 156 (100%, M^+-C_3H_6), 154 (20%, M^+-C_3H_8), 153 (12%, $C_6H_4S_2CH^+$), 141 (37%, $C_6H_5S_2^+$), 121 (5%, $C_7H_5S^+$), 109 (6.5%, $C_6H_5S^+$), 97 (4%, $C_5H_5S^+$), 91 (23%, $C_7H_7^+$), 78 (3%, $C_6H_6^+$), 77 (14.5%, $C_6H_5^+$), 65 (6%, $C_5H_5^+$), 45 (18%, CHS^+). Anal. Calcd for $C_{10}H_{14}S_2$: C, 60.56; H, 7.11; S, 32.33. Found C, 60.45; H, 7.03; S, 32.18.

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