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Dibenzothiepins, phthalans and phthalides from 4-heterosubstituted dibenzothiins

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Abstract—The lithiation of 4-heterosubstituted dibenzothiins **1** (phenoxathiin, phenothiazine and thianthrene) with lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB, 7.5% molar) in THF at temperatures ranging from −90 to −78°C gives the corresponding functionalised organolithium intermediate **I**, which by reaction with different electrophiles [H_2O, D_2O, Bu^tCHO, PhCHO, $Ph(CH_2)_2CHO$, Me_2CO, Et_2CO, $(CH_2)_5CO$, $(CH_2)_7CO$] at the same temperature, followed by hydrolysis, gives the expected functionalised thiols **2**. Cyclisation of some thiols **2** under acidic conditions leads to the corresponding seven-membered dibenzo heterocycles **5**. In the case of thianthrene **1c**, after addition of a carbonyl compound as the first electrophile [MeCHO, Bu^tCHO, Me_2CO, Et_2CO, $(CH_2)_5CO$], the corresponding intermediate **II** can be lithiated again and react with a second electrophile. Diols **3** are obtained after hydrolysis when a carbonyl compound [Bu^tCHO, PhCHO, $Ph(CH_2)_2CHO$, Me_2CO, Et_2CO, $(CH_2)_5CO$] is used as the second electrophile. Acidic cyclisation of diols **3** gives substituted phthalans **6** in almost quantitative yields. Finally, in the case of using carbon dioxide as the second electrophile, phthalides **4** are obtained after acidic hydrolysis.

1. Introduction

Probably the most elegant and direct strategy for the preparation of functionalised organolithium compounds[1] consists in the reductive opening of different appropriate oxygen, nitrogen and sulfur-containing heterocycles.[2] In addition, these highly reactive intermediates have also been prepared by halogen–lithium exchange, metal–lithium exchange, direct deprotonation, as well as by addition of organolithium compounds to unsaturated systems.[1,3] The interest of these systems lies in their utility in synthetic organic chemistry because polyfunctionalised molecules are obtained in only one step by their reaction with electrophilic reagents.[4] Polyfunctionalised molecules are also obtained by reaction of polylithium organic compounds[5] with electrophiles, however more interestingly in this case would be to introduce different electrophilic fragments in the polyanionic unit, the iterative sequential lithiation-reaction with the electrophile being the only way to achieve this goal, acting always functionalised organolithium compounds as intermediates. Since most functionalised organolithium compounds are very unstable molecules, they have to be prepared at low temperature in order to avoid their decomposition.[6] In the last few years a methodology was developed using, as lithiating agent, an excess of lithium in the presence of a catalytic amount of an arene (mainly naphthalene or DTBB).[7,8] More recently, polymer supported naphthalene, biphenyl[9] and also polyphenylene[10] have been used as electron transfer reagents in these processes.[11] Heterocycles can be reductively opened due to a release of strain energy[2] (three and four membered-rings), or due to the presence of activated bonds that can be reductively broken, as in the case of allylic[12] and benzylic[13] carbon-heteroatom bonds, as well as aryl ethers[14] and thioethers.[15] The application of the arene-catalysed version to some sulfur-containing heterocycles with benzylic carbon–sulfur bonds such as thietanes,[16] tetrahydrothiophenes,[16,17] tetrahydrothiopyrans,[16] and 2,7-dihydrodibenzoazepine[18] allows the direct preparation of functionalised organolithium compounds. On the other hand, the stoichiometric arene-mediated lithiation has been used in the reductive opening of different cyclic arylthioethers such as dihydrobenzothiophene,[19] 3,4-dihydro-2*H*-benzothiane,[19] and trimethylbenzo-1,3-thiazolidine.[19b,20] In this paper we report on the application of the mentioned arene-catalysed lithiation methodology to the reductive ring opening of 4-hetero-substituted dibenzothiins and the study of the synthetic utility of the resulting functionalised organolithium compounds.

2. Results and discussion

The reaction of 4-heterosubstituted dibenzothiins **1** with lithium and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB, 7.5 mol%) in THF at −78°C in the case of

Keywords: lithiation; heterocycle reductive opening; cyclisation; dianionic synthon.

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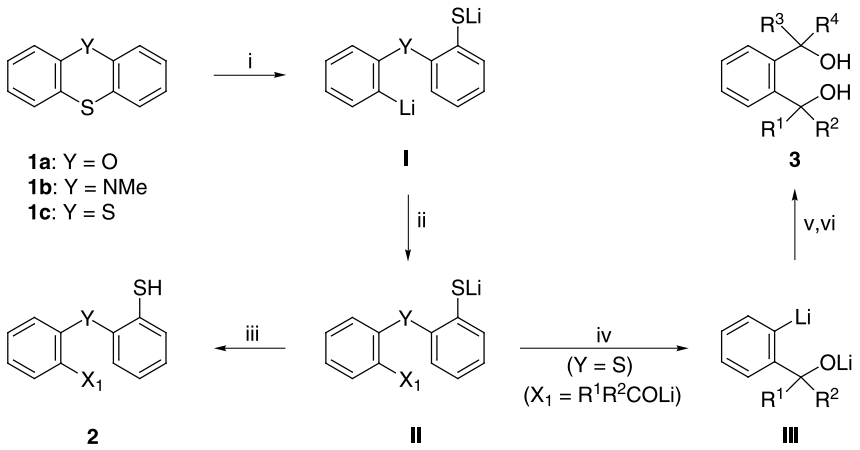


Scheme 1. *Reagents and conditions*: (i) Li, DTBB cat. (7.5%), THF, −78 (for **1a**) or −90°C (for **1b**,**c**), 45 min; (ii) E_1=H_2O, D_2O, Bu^{t}CHO, PhCHO, $Ph(CH_2)_2CHO$, Me_2CO, Et_2CO, $(CH_2)_5CO$, $(CH_2)_7CO$, −78 (for **1a**) or −90°C (for **1b**,**c**); (iii) H_2O, −78 (for **1a**) or −90°C (for **1b**,**c**) to 20°C, then 3 M HCl; (iv) −90°C, 45 min; (v) E_2=Bu^{t}CHO, PhCHO, $Ph(CH_2)_2CHO$, Me_2CO, Et_2CO, $(CH_2)_5CO$, −90 to −78°C, 30 min; (vi) H_2O, −78 to 20°C.

Table 1. Preparation of compounds **2**

Entry	Starting material **1**	Electrophile E_1	Product **2**[a]			
			X_1	No.	Yield (%)[b]	R_f[c]
1	**1a**	H_2O	H	**2aa**	50	0.54
2	**1a**	D_2O	D	**2ab**[d]	53	0.54
3	**1a**	Bu^{t}CHO	Bu^{t}CHOH	**2ac**	63	0.29
4	**1a**	PhCHO	PhCHOH	**2ad**	49	0.15
5	**1a**	$Ph(CH_2)_2CHO$	$Ph(CH_2)_2CHOH$	**2ae**	36	0.14
6	**1a**	Me_2CO	Me_2COH	**2af**	82	0.16
7	**1a**	Et_2CO	Et_2COH	**2ag**	44	0.11
8	**1a**	$(CH_2)_5CO$	$(CH_2)_5COH$	**2ah**	41	0.22
9	**1a**	$(CH_2)_7CO$	$(CH_2)_7COH$	**2ai**	31	0.13
10	**1b**	H_2O	H	**2ba**	95	0.59
11	**1b**	Bu^{t}CHO	Bu^{t}CHOH	**2bb**	25	0.24
12	**1b**	PhCHO	PhCHOH	**2bc**	64	0.31
13	**1b**	$Ph(CH_2)_2CHO$	$Ph(CH_2)_2CHOH$	**2bd**	48	0.16
14	**1c**	H_2O	H	**2ca**	98	0.57
15	**1c**	Bu^{t}CHO	Bu^{t}CHOH	**2cb**	39	0.20
16	**1c**	PhCHO	PhCHOH	**2cc**	52	0.18

[a] All products **2** were >95% pure (300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1**.
[c] Silica gel, hexane/ethyl acetate: 10:1.
[d] >90% Deuterium incorporation (MS).

phenoxathiin (**1a**) or −90°C for phenothiazine (**1b**) and thianthrene (**1c**) for 45 min gave the corresponding intermediate **I**, which after reacting with different electrophiles [H_2O, D_2O, Bu^{t}CHO, PhCHO, $Ph(CH_2)_2CHO$, Me_2CO, Et_2CO, $(CH_2)_5CO$, $(CH_2)_7CO$], followed by hydrolysis with hydrochloric acid, led to the expected functionalised thiols **2** (Scheme 1 and Table 1).[21] In the case of phenothiazine (**1b**) and thianthrene (**1c**), the process should be performed at −90°C because at higher temperature (−78°C) complex mixtures of reaction products were obtained. Also for thianthrene (**1c**) the final acidic hydrolysis has to be carried out immediately after the addition of the electrophile in order to avoid further lithiation.

Due to this latest reason, we found especially interesting thianthrene (**1c**), because it is possible to develop a sequential double lithiation-reaction with electrophiles to prepare polyfunctionalised molecules. Thus, when after reductive opening of **1c** and reaction with a carbonyl compound [Bu^{t}CHO, Me_2CO, Et_2CO, $(CH_2)_5CO$] at −90°C, the resulting intermediate **II** (Scheme 1, Y=S, X_1=R^1R^2COLi) was stirred for 45 min at the same temperature, a second lithiation occurred by reductive cleavage of one of the aryl–sulfur bonds of intermediate **II** to give intermediate **III** and dithiolate **IV** (Chart 1), because of the excess of lithium still present in the reaction medium. When this second lithiation was carried out at higher temperature (−78°C), the other possible aryl–sulfur bond reductive cleavage also took place leading to intermediates **V** and **VI** (Chart 1), so a complex mixture of products was obtained. The reaction of intermediate **III** with a second carbonyl compound [Bu^{t}CHO, PhCHO, $Ph(CH_2)_2CHO$,

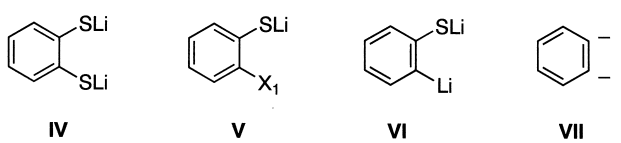


Chart 1. Intermediates IV–VII.

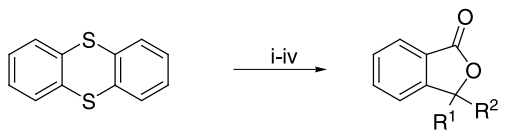
Table 2. Preparation of diols **3** from thianthrene **1c**

Entry	Electrophile E_1	Electrophile E_2	Product **3**[a]						
			R^1	R^2	R^3	R^4	No.	Yield (%)[b]	R_f[c]
1	Bu^tCHO	Bu^tCHO	H	Bu^t	H	Bu^t	**3a**	68[d]	0.47+0.46[e]
2	Me_2CO	Bu^tCHO	Me	Me	H	Bu^t	**3b**	81	0.36
3	Me_2CO	PhCHO	Me	Me	H	Ph	**3c**	76	0.31
4	Me_2CO	$Ph(CH_2)_2CHO$	Me	Me	H	$Ph(CH_2)_2$	**3d**	58	0.27
5	Me_2CO	Me_2CO	Me	Me	Me	Me	**3e**	64	0.28
6	Me_2CO	Et_2CO	Me	Me	Et	Et	**3f**	55	0.43
7	Me_2CO	$(CH_2)_5CO$	Me	Me	$(CH_2)_5$		**3g**	71	0.51
8	Et_2CO	Et_2CO	Et	Et	Et	Et	**3h**	47	0.51
9	$(CH_2)_5CO$	$(CH_2)_5CO$	$(CH_2)_5$		$(CH_2)_5$		**3i**	60	0.72

[a] All products **3** were >95% pure (300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1c**.
[c] Silica gel, hexane/ethyl acetate: 3:1.
[d] A *ca*. 1:1 mixture of diastereomers was obtained (GLC), which was separated by column chromatography (silica gel, hexane/ethyl acetate) giving 35+33% of both diastereomers.
[e] R_f value for each diastereomer.

Me_2CO, Et_2CO, $(CH_2)_5CO$] at temperatures ranging between −90 and −78°C for 10 min followed by final hydrolysis with water at −78 to 20°C led to the formation of diols **3** (Scheme 1, Table 2).[22] A 1:1 mixture of diastereomers was obtained when a prochiral carbonyl compound such as pivaldehyde was used in both steps, which could be separated by column chromatography (Table 2, entry 1). Through this methodology, thianthrene **1c** acts as a 1,2-dianionic synthon of benzene of type **VII** (Chart 1), allowing the introduction of two different electrophiles in a sequential manner at both carbanionic centres.

From a synthetic point of view, the use of carbonyl compounds as the first electrophile and carbon dioxide as the second electrophile, allowed the preparation of 3-substituted phthalides **4** in a one-pot process.[23] Thus, the DTBB-catalysed reductive opening lithiation of **1c** and reaction with a carbonyl compound [MeCHO, Bu^nCHO, $Me(CH_2)_7CHO$, PhCHO, Me_2CO, MeCOEt, $(CH_2)_5CO$] at −90°C gave intermediates **II**, which after a new lithiation at the same temperature afforded intermediates of type **III**. Treatment of these dianions by bubbling carbon dioxide at −70°C for 15 min and final acidic hydrolysis, led to the formation of 3-substituted phthalides **4** (Scheme 2 and Table 3). Many of these phthalides are natural occurring products with important biological activities. For instance, 3-methylphthalide (**4a**, Table 3, entry 1) shows anti-aggregatory and anti-inflammatory activity by inhibition of prostaglandin synthesis in platelets.[24] Meanwhile 3-*n*-butylphthalide (**4b**, Table 3, entry 2), which is a constituent of celery oil,[25] increases the duration of anaesthesia,[26] and exhibits cerebral antiischemic action.[27]



1c **4**

Scheme 2. *Reagents and conditions*: (i) Li, DTBB cat. (7.5%), THF, −90°C, 45 min; (ii) E_1=MeCHO, Bu^nCHO, $Me(CH_2)_7CHO$, PhCHO, Me_2CO, MeCOEt, $(CH_2)_5CO$, −90°C, 45 min; (iii) CO_2, −70°C, 15 min; (iv) H_2O, −70 to 20°C, then 3 M HCl.

Table 3. Preparation of phthalides **4** from thianthrene **1c**

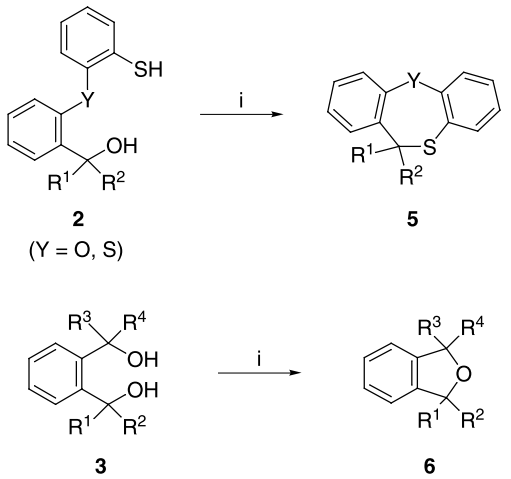
Entry	Electrophile E_1	Product **4**[a]				
		R^1	R^2	No.	Yield (%)[b]	R_f[c]
1	MeCHO	H	Me	**4a**	58	0.54
2	Bu^nCHO	H	Bu^n	**4b**	78	0.54
3	$Me(CH_2)_7CHO$	H	$Me(CH_2)_7$	**4c**	38	0.29
4	PhCHO	H	Ph	**4d**	58	0.15
5	Me_2CO	Me	Me	**4e**	59	0.14
6	MeCOEt	Me	Et	**4f**	78	0.16
7	$(CH_2)_5CO$	$(CH_2)_5$		**4g**	39	0.18

[a] All products **4** were >95% pure (300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **1c**.
[c] Silica gel, hexane/ethyl acetate: 10:1.

Finally, some functionalised hydroxythiols **2**, and diols **3** were cyclised under acidic conditions (85% phosphoric acid under toluene at reflux)[18] to give the corresponding seven-membered dibenzo compounds **5**[28,29] (Scheme 3 and Table 4) and substituted phthalans **6**[30] in almost quantitative yield (Scheme 3 and Table 5), respectively. The whole process **1→5** could be considered a homologation of the starting 4-heterosubstituted dibenzothiins **1**. A benzylic carbenium ion is probably involved in these reactions, which after intramolecular nucleophilic attack by the sulfur atom or the oxygen atom gives the final heterocycles **5** and **6**, respectively.

3. Conclusions

We report here that the reductive opening lithiation of 4-heterosubstituted dibenzothiins **1** at low temperature led to functionalised organolithium compounds **I**, which by reaction with electrophiles and final hydrolysis gave thiols **2**. In the case of thianthrene **1c** it is possible to perform a sequential double lithiation-reaction with electrophiles, **1c** behaving as a dianionic synthon of benzene of type **VII**.



Scheme 3. *Reagents and conditions*: (i) H_3PO_4 (85%), $PhCH_3$, 110°C.

Table 4. Preparation of compounds **5**

Entry	Starting material **2**	Product **5**[a]					
		Y	R^1	R^2	No.	Yield (%)[b]	R_f[c]
1	**2ad**	O	H	Ph	**5a**	78	0.57
2	**2ag**	O	Et	Et	**5b**	85	0.61
3	**2cb**	S	H	Bu^t	**5c**	74	0.64
4	**2cc**	S	H	Ph	**5d**	97	0.54

[a] All products **5** were >95% pure (300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/ethyl acetate) based on the starting material **2**.
[c] Silica gel, hexane/ethyl acetate: 10:1.

Table 5. Preparation of compounds **6**

Entry	Starting material **3**	Product **6**[a]						
		R^1	R^2	R^3	R^4	No.	Yield (%)[b]	R_f[c]
1	**3d**	Me	Me	H	$Ph(CH_2)_2$	**6a**	>95	0.11
2	**3e**	Me	Me	Me	Me	**6b**	>95	0.20
3	**3g**	Me	Me	$(CH_2)_5$		**6c**	>95	0.24
4	**3h**	Et	Et	Et	Et	**6d**	>95	0.16
5	**3i**	$(CH_2)_5$		$(CH_2)_5$		**6e**	>95	0.54

[a] All products **6** were >95% pure (300 MHz ^{1}H NMR and/or GLC).
[b] Isolated yield based on the starting material **3**.
[c] Silica gel, hexane.

4. Experimental

4.1. General

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware. All reagents were commercially available and were used as received. THF was distilled from sodium benzophenone ketyl. Melting points were recorded in a Reichert Thermovar and are uncorrected. IR spectra were measured (neat) with a Nicolet Impact 400 D-FT Spectrometer. NMR spectra were recorded with a Bruker AC-300 using $CDCl_3$ as the solvent. LRMS and HRMS were measured with Shimadzu GC/HS QP-5000 and Finingan MAT95 S spectrometers, respectively. The purity of volatile products and the chromatographic analyses (GLC) were determined with a Hewlett–Packard HP-5890 instrument equipped with a flame ionisation detector and a 12 m capillary column (0.2 mm diam, 0.33 μm film thickness), using nitrogen (2 mL/min) as carrier gas, $T_{injector}$=275°C, $T_{detector}$=300°C, T_{column}=80°C (3 min) and 80–270°C (15°C/min), P=40 kPa. Elemental analyses were performed by the Mycroanalyses Service at the University of Alicante.

4.2. Reductive lithiation of 4-hetero-substituted dibenzothiins 1 and reaction with electrophiles

Isolation of compounds ***2***. *General procedure*. To a blue suspension of lithium powder (100 mg, 14 mmol) and a catalytic amount of DTBB (40 mg, 0.15 mmol; 7.5 mol%) in THF (4 mL) was added the corresponding 4-hetero-substituted dibenzothiin **1** (2.0 mmol) at −78°C for **1a** and −90°C for **1b**,**c**, and the resulting mixture was stirred for 45 min at the same temperature. Then, the corresponding electrophile (2.4 mmol; 0.5 ml in the case of H_2O and D_2O) was added dropwise and stirring was continued for 5 min. After that the reaction mixture was hydrolysed with water, extracted with ether (3×20 mL) and the aqueous layer was acidified with 3 M HCl and extracted with ethyl acetate (3×20 mL), dried over anhydrous Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products. Yields and R_f values are given in Table 1, physical, analytical and spectroscopic data follow.

4.2.1. 2-Phenoxythiophenol (2aa).[31] Colorless liquid; ν (film) 3063, 3052, 3037, 3011 (ArH), 2576 cm^{-1} (SH); δ_H 3.79 (1H, s, SH), 6.86 (1H, d, J=7.9 Hz, ArH), 6.95–7.11 (4H, m, ArH), 7.29–7.36 (4H, m, ArH); δ_C 118.1, 119.3, 123.3, 124.1, 126.4, 129.75, 129.8, 152.5, 156.7 (ArC); *m/z* 202 (M^+, 100%), 201 (22), 169 (13), 141 (13), 97 (15), 96 (80), 77 (17), 69 (17), 65 (14), 63 (12), 51 (41), 50 (15), 45 (31); HMRS: M^+, found 202.0457. $C_{12}H_{10}OS$ requires 202.0452.

4.2.2. 2-(2-Deuteriophenoxy)thiophenol (2ab). Colorless liquid; ν (film) 3063, 3052, 3037, 3011 (ArH), 2576 cm^{-1} (SH); δ_H 3.80 (1H, s, SH), 6.87 (1H, dd, J=7.9, 1.8 Hz, ArH), 6.96–7.13 (4H, m, ArH), 7.30–7.35 (3H, m, ArH); δ_C 117.9 (t, J=24.4 Hz, CD), 118.1, 119.3, 123.4, 124.1, 126.5, 129.7, 129.8, 129.9, 152.5, 156.6 (ArC); *m/z* 203 (M^+, 100%), 202 (23), 170 (12), 97 (12), 96 (77), 78 (14), 69 (15), 52 (22), 51 (23), 45 (32), 40 (13); HMRS: M^+, found 203.0507. $C_{12}H_9DOS$ requires 203.0515.

4.2.3. 2,2-Dimethyl-1-[2-(2-sulfanylphenoxy)phenyl]-1-propanol (2ac). Colorless liquid; ν (film) 3460–3320 (OH), 3064, 3033 (ArH), 2587 cm^{-1} (SH); δ_H 1.02 [9H, s, $C(CH_3)_3$], 1.95 (1H, br s, OH), 3.77 (1H, s, SH), 4.89 (1H, s, C*H*OH), 6.72–6.79 (2H, m, ArH), 6.97–7.22 (4H, m, ArH), 7.32–7.36 (1H, m, ArH), 7.52–7.55 (1H, m, ArH); δ_C 26.0 [$C(CH_3)_3$], 36.6 [$C(CH_3)_3$], 75.6 (CHOH), 117.6, 118.3, 123.3, 123.7, 123.9, 126.5, 128.3, 129.4, 129.9, 132.8, 152.6, 153.6 (ArC); *m/z* 270 [M^+–(H_2O), 8%], 231 (13), 214 (18), 213 (100), 181 (22), 77 (16), 65 (15), 57 (17), 51 (13), 45 (13), 41 (32); HMRS: M^+–(H_2O), found 270.1072. $C_{17}H_{18}OS$ requires 270.1078.

4.2.4. Phenyl-[2-(2-sulfanylphenoxy)phenyl]methanol (2ad). Colorless oil; ν (film) 3520–3370 (OH), 3062, 3030 (ArH), 2569 cm^{-1} (SH); δ_H 3.05 (1H, br s, OH), 3.48 (1H, s, SH), 6.14 (1H, s, C*H*OH), 6.67 (2H, d, *J*=7.3 Hz, ArH), 6.97–7.00 (2H, m, ArH), 7.13–7.30 (6H, m, ArH), 7.39–7.41 (2H, m, ArH), 7.60 (1H, d, *J*=7.3 Hz, ArH); δ_C 71.6 (CHOH), 117.0, 119.1, 123.6, 124.0, 124.3, 126.5, 126.7, 127.5, 127.8, 128.4, 128.7, 129.9, 133.8, 143.1, 151.8, 153.4 (ArC); *m/z* 290 [M^+–(H_2O), 100%], 289 (26), 273 (11), 261 (14), 247 (10), 234 (11), 213 (25), 211 (14), 210 (87), 197 (28), 185 (31), 184 (22), 181 (14), 165 (30), 164 (11), 163 (10), 152 (20), 139 (11), 77 (13), 69 (12), 63 (17), 51 (20); HMRS: M^+–(H_2O), found 290.0762. $C_{19}H_{14}OS$ requires 290.0765.

4.2.5. 3-Phenyl-1-[2-(2-sulfanylphenoxy)phenyl]-1-propanol (2ae). Colorless oil; ν (film) 3520–3370 (OH), 3045, 3023 (ArH), 2563 cm^{-1} (SH); δ_H 2.26–2.46 (2H, m, $PhCH_2$), 2.59–2.65 (2H, m, $PhCH_2CH_2$), 3.13 (1H, br s, OH), 3.61 (1H, s, SH), 4.30 (1H, dd, *J*=8.8, 6.4 Hz, C*H*OH), 6.72–6.89 (5H, m, ArH), 6.92–7.28 (8H, m, ArH); δ_C 33.7, 35.5 (CH_2), 77.2 (CHOH), 114.7, 116.2, 120.3, 121.1, 126.0, 128.2, 128.3, 128.4, 128.7, 131.5, 133.3, 136.2, 136.9, 141.0, 153.4, 157.5 (ArC); *m/z* 336 (M^+, 1%), 318 (46), 229 (20), 228 (16), 227 (93), 224 (12), 223 (32), 213 (46), 197 (12), 194 (11), 193 (12), 181 (27), 165 (14), 147 (12), 137 (10), 134 (11), 115 (19), 92 (12), 91 (100), 77 (22), 65 (27), 51 (17), 45 (15), 44 (16), 40 (11); HMRS: M^+, found 336.1149. $C_{21}H_{20}O_2S$ requires 336.1184.

4.2.6. 2-[2-(2-Sulfanylphenoxy)phenyl]-2-propanol (2af). Colorless oil; ν (film) 3550–3415 (OH), 3065 (ArH), 2569 cm^{-1} (SH); δ_H 1.72 [6H, s, $C(CH_3)_2$], 3.25 (1H, br s, OH), 3.67 (1H, s, SH), 6.69 (1H, dd, *J*=7.9, 1.2 Hz, ArH), 6.91 (1H, dd, *J*=7.9, 1.2 Hz, ArH), 7.03–7.20 (4H, m, ArH), 7.38 (1H, dd, *J*=7.3, 1.8 Hz, ArH), 7.55 (1H, dd, *J*=7.3, 1.8 Hz, ArH); δ_C 30.1 (CH_3), 72.3 (COH), 117.5, 119.5, 123.4, 124.3, 124.6, 126.5, 126.8, 128.2, 130.3, 137.8, 152.0, 153.9 (ArC); *m/z* 242 [M^+–(H_2O), 48%], 228 (16), 227 (100), 194 (18), 165 (13), 149 (52), 148 (12), 147 (11), 135 (19), 134 (20), 115 (16), 107 (10), 91 (21), 77 (14), 65 (17), 59 (22), 51 (15), 43 (71); HMRS: M^+, found 260.0866. $C_{15}H_{16}O_2S$ requires 260.0871.

4.2.7. 3-[2-(2-Sulfanylphenoxy)phenyl]-3-pentanol (2ag). Colorless oil; ν (film) 3540–3320 (OH), 3058 (ArH), 2579 cm^{-1} (SH); δ_H 0.83 (6H, t, *J*=7.3 Hz, $2\times CH_2CH_3$), 1.82–1.94 (2H, m, CH_2CH_3), 2.14–2.26 (2H, m, CH_2CH_3), 2.58 (1H, br s, OH), 3.68 (1H, s, SH), 6.69 (1H, d, *J*=7.9 Hz, ArH), 6.81–7.30 (4H, m, ArH), 7.33–7.42 (2H, m, ArH), 7.56 (1H, dd, *J*=7.3, 1.8 Hz, ArH); δ_C 8.2 (CH_3), 33.2 (CH_2), 77.9 (COH), 117.8, 118.9, 123.2, 124.2, 126.7, 127.9, 128.8, 129.8, 130.1, 134.7, 152.2, 153.4 (ArC); *m/z* 270 [M^+–(H_2O), 15%], 242 (17), 241 (100), 209 (13), 208 (39), 207 (22), 177 (10), 115 (12), 107 (11), 91 (11), 77 (14), 65 (13), 57 (49), 45 (24), 43 (13), 41 (14); HMRS: M^+–(H_2O), found 270.1866. $C_{17}H_{18}OS$ requires 270.1878.

4.2.8. 1-[2-(2-Sulfanylphenoxy)phenyl]cyclohexanol (2ah). White solid, mp 166–167°C (dichloromethane/hexane); [Found: C, 71.58; H, 6.59; S, 9.93. $C_{18}H_{20}O_2S$ requires C, 71.97; H, 6.71; S, 10.67]; ν (KBr) 3565, 3435 (OH), 3064 (ArH), 2583 cm^{-1} (SH); δ_H 1.22–1.31 (2H, m, CH_2), 1.59–1.88 (4H, m, $2\times CH_2$), 2.03 (4H, t, *J*=4.3 Hz, $2\times CH_2$), 2.67 (1H, br s, OH), 3.68 (1H, s, SH), 6.68 (1H, d, *J*=7.9 Hz, ArH), 6.89 (1H, d, *J*=7.9 Hz, ArH), 7.03–7.17 (4H, m, ArH), 7.36 (1H, dd, *J*=7.3, 1.8 Hz, ArH), 7.53 (1H, dd, *J*=7.3, 1.8 Hz, ArH); δ_C 21.8, 25.5, 36.7 (CH_2), 73.2 (COH), 117.7, 119.6, 123.4, 124.6, 126.6, 126.8, 128.0, 129.7, 130.3, 138.2, 152.0, 154.4 (ArC); *m/z* 282 [M^+–(H_2O), 79%], 240 (26), 239 (100), 227 (11), 213 (16), 189 (22), 181 (24), 161 (10), 160 (15), 152 (11), 148 (16), 147 (39), 141 (12), 134 (11), 129 (20), 128 (24), 127 (11), 115 (32), 107 (15), 91 (30), 79 (13), 77 (24), 65 (17), 63 (11), 53 (16), 51 (16), 45 (16), 41 (22); HMRS: M^+, found 300.1175. $C_{18}H_{20}O_2S$ requires 300.1184.

4.2.9. 1-[2-(2-Sulfanylphenoxy)phenyl]cyclooctanol (2ai). Colorless oil; ν (film) 3520–3325 (OH), 3054, 3028 (ArH), 2555 cm^{-1} (SH); δ_H 1.26–1.87 (14H, m, CH_2), 2.55 (1H, br s, OH), 3.09 (1H, s, SH), 6.80–7.54 (8H, m, ArH); δ_C 27.3, 31.3, 34.5, 41.9 (CH_2), 72.4 (COH), 115.0, 118.1, 119.3, 120.8, 123.3, 124.2, 126.4, 129.75, 129.8, 129.9, 134.7, 155.6 (ArC); *m/z* 310 [M^+–(H_2O), 81%], 241 (14), 240 (27), 239 (92), 228 (19), 227 (100), 226 (24), 217 (14), 213 (34), 203 (13), 187 (10), 182 (16), 181 (45), 165 (13), 161 (23), 149 (17), 148 (33), 147 (58), 141 (16), 135 (20), 134 (18), 131 (11), 129 (22), 128 (25), 127 (12), 115 (30), 107 (23), 97 (11), 91 (28), 81 (13), 79 (12), 77 (21), 67 (36), 65 (21), 55 (38), 53 (21), 51 (17), 45 (20), 43 (13), 41 (70); HMRS: M^+–(H_2O), found 310.1405. $C_{20}H_{22}OS$ requires 310.1391.

4.2.10. 2-(*N*-Methylanilino)thiophenol (2ba). Colorless oil; ν (film) 3055 (ArH), 2550 cm^{-1} (SH); δ_H 3.19 (3H, s, NCH_3), 3.88 (1H, s, SH), 6.62 (2H, d, *J*=7.9 Hz, ArH), 6.78 (1H, t, *J*=7.0 Hz, ArH), 7.12–7.22 (5H, m, ArH), 7.37–7.40 (1H, m, ArH); δ_C 38.6 (CH_3), 113.9, 118.2, 126.7, 127.0, 128.6, 129.0, 129.2, 133.4, 145.2, 148.6 (ArC); *m/z* 215 (M^+, 100%), 214 (18), 199 (13), 182 (16), 181 (16), 180 (24), 167 (35), 136 (21), 109 (14), 104 (16), 91 (65), 84 (11), 78 (15), 77 (51), 69 (11), 65 (19), 51 (23), 45 (13); HMRS: M^+, found 215.0761. $C_{13}H_{13}NS$ requires 215.0769.

4.2.11. 2,2-Dimethyl-1-[2-(*N*-methyl-2-sulfanylanilino)-phenyl]-1-propanol (2bb). Colorless oil; ν (film) 3470–3290 (OH), 3055 (ArH), 2539 cm^{-1} (SH); δ_H 0.93 [9H, s, $C(CH_3)_3$], 2.89 (1H, br s, OH), 3.11 (3H, s, NCH_3), 3.93 (1H, s, SH), 4.55 (1H, s, C*H*OH), 6.60 (1H, dd, *J*=6.1, 3.7 Hz, ArH), 6.92–6.96 (2H, m, ArH), 7.17 (1H, t, *J*=7.3 Hz, ArH), 7.29–7.39 (3H, m, ArH), 7.48 (1H, d, *J*=7.9 Hz, ArH); δ_C 26.0 [$C(CH_3)_3$], 26.7 [$C(CH_3)_3$], 40.1 (NCH_3), 74.9 (COH), 121.5, 123.8, 124.7, 124.9, 126.3, 127.1, 127.7, 129.2, 130.1, 137.2, 148.3, 149.6 (ArC); *m/z* 283 [M^+–(H_2O), 15%], 227 (13), 226 (100), 194 (86), 179 (17), 77 (14), 44 (34), 41 (19); HMRS: M^+, found 301.1477. $C_{18}H_{23}NOS$ requires 301.1500.

4.2.12. Phenyl-[2-(*N*-methyl-2-sulfanylanilino)phenyl]-methanol (2bc). Colorless oil; ν (film) 3440–3310 (OH), 3055 (ArH), 2526 cm^{-1} (SH); δ_H 2.65 (1H, br s, OH), 3.15 (3H, s, NCH_3), 3.81 (1H, s, SH), 6.02 (1H, s, C*H*OH), 6.82 (1H, dd, *J*=7.6, 1.5 Hz, ArH), 6.89–7.01 (2H, m, ArH), 7.10 (1H, t, *J*=7.3 Hz, ArH), 7.18–7.33 (9H, m, ArH); δ_C 41.5 (NCH_3), 70.6 (COH), 121.7, 124.2, 124.4, 124.8,

126.5, 126.7, 127.0, 128.0, 128.5, 129.8, 130.5, 138.2, 142.8, 148.3, 148.8 (ArC); *m/z* 303 [M^+–(H_2O), 62%], 302 (20), 288 (33), 273 (28), 271 (27), 270 (100), 255 (14), 254 (21), 227 (13), 226 (75), 224 (19), 207 (14), 197 (19), 194 (51), 193 (11), 165 (30), 152 (26), 151 (10), 143 (10), 139 (15), 136 (13), 135 (33), 134 (11), 133 (12), 128 (24), 127 (36), 126 (12), 121 (14), 115 (17), 109 (15), 91 (20), 77 (24), 69 (11), 65 (20), 63 (17), 51 (19), 45 (15), 44 (12); HMRS: M^+–(H_2O), found 303.1089. $C_{20}H_{17}NS$ requires 303.1082.

4.2.13. 3-Phenyl-1-[2-(*N*-methyl-2-sulfanylanilino)phenyl]-1-propanol (2bd). Colorless oil; ν (film) 3470–3360 (OH), 3055 (ArH), 2533 cm^{-1} (SH); δ_H 1.35–1.46 (1H, m, CH*H*CHOH), 1.69–1.84 (1H, m, C*H*HCHOH), 2.32–2.42 (1H, m, CH*H*Ph), 2.58–2.68 (1H, m, C*H*HPh), 2.98 (1H, br s, OH), 3.01 (3H, s, NCH_3), 3.79 (1H, s, SH), 4.76 (1H, dd, *J*=9.2, 3.7 Hz, C*H*OH), 6.65–6.68 (1H, m, ArH), 6.89–6.98 (4H, m, ArH), 7.05–7.24 (7H, m, ArH), 7.41 (1H, d, *J*=7.9 Hz, ArH); δ_C 33.0, 39.3 (CH_2), 41.0 (NCH_3), 68.3 (COH), 121.0, 124.3, 124.9, 125.0, 125.6, 126.3, 127.6, 128.1, 128.2, 128.4, 129.1, 130.1, 139.0, 142.2, 147.5, 149.1 (ArC); *m/z* 331 [M^+–(H_2O), 57%], 298 (11), 241 (10), 240 (59), 227 (18), 226 (79), 225 (18), 224 (30), 223 (21), 208 (13), 207 (38), 206 (11), 195 (15), 194 (100), 193 (19), 192 (11), 180 (18), 179 (16), 166 (10), 147 (11), 115 (17), 109 (12), 107 (41), 91 (63), 78 (10), 77 (33), 65 (38), 63 (11), 51 (25), 45 (18); HMRS: M^+–(H_2O), found 331.1405. $C_{22}H_{21}NS$ requires 331.1395.

4.2.14. 2-Phenylsulfanylthiophenyl (2ca).[32] Colorless oil; ν (film) 3055 (ArH), 2555 cm^{-1} (SH); δ_H 4.23 (1H, s, SH), 7.06–7.11 (1H, m, ArH), 7.15–7.30 (6H, m, ArH), 7.37 (2H, d, *J*=7.9 Hz, ArH); δ_C 126.1, 126.7, 128.8, 129.2, 129.4, 131.7, 134.6, 135.2, 137.2 (ArC); *m/z* 218 (M^+, 70%), 185 (28), 184 (39), 141 (11), 140 (100), 109 (16), 108 (11), 96 (15), 92 (19), 77 (22), 69 (24), 65 (16), 51 (20), 45 (11); HMRS: M^+, found 218.0228. $C_{12}H_{10}S_2$ requires 218.0224.

4.2.15. 2,2-Dimethyl-1-[2-(2-sulfanylphenylsulfanyl)phenyl]-1-propanol (2cb). Colorless oil; ν (film) 3480–3310 (OH), 3055 (ArH), 2539 cm^{-1} (SH); δ_H 1.01 [9H, s, $C(CH_3)_3$], 2.86 (1H, br s, OH), 4.05 (1H, s, SH), 5.13 (1H, s, C*H*OH), 6.98–7.27 (6H, m, ArH), 7.34 (1H, d, *J*=7.9 Hz, ArH), 7.57 (1H, d, *J*=7.3 Hz, ArH); δ_C 26.0 [$C(CH_3)_3$], 36.8 [$C(CH_3)_3$], 77.1 (CHOH), 126.2, 126.7, 128.0, 128.3, 128.6, 129.6, 130.3, 133.0, 133.7, 133.9, 136.1, 142.5 (ArC); *m/z* 304 (M^+, 1.3%), 231 (11), 230 (21), 229 (100), 197 (24), 184 (11), 137 (21), 109 (16), 77 (15), 57 (15), 41 (30); HMRS: M^+, found 304.0944. $C_{17}H_{20}OS_2$ requires 304.0956.

4.2.16. Phenyl-[2-(2-sulfanylphenylsulfanyl)phenyl]-methanol (2cc). Colorless oil; ν (film) 3420–3290 (OH), 3052 (ArH), 2531 cm^{-1} (SH); δ_H 2.39 (1H, br s, OH), 3.89 (1H, s, SH), 6.25 (1H, s, C*H*OH), 6.91–7.32 (12H, m, ArH), 7.52 (1H, d, *J*=7.3 Hz, ArH); δ_C 73.2 (CHOH), 126.3, 127.0, 127.6, 127.7, 128.3, 128.4, 128.5, 129.8, 131.3, 132.5, 132.7, 133.4, 135.5, 142.5, 143.7 (ArC); *m/z* 306 [M^+–(H_2O), 59%], 274 (20), 273 (100), 272 (13), 271 (33), 229 (40), 198 (15), 197 (85), 184 (11), 165 (50), 164 (14), 163 (12), 153 (14), 152 (23), 139 (12), 137 (15), 136 (36), 91 (16), 77 (13), 69 (16), 63 (17), 51 (17), 45 (18); HMRS: M^+–(H_2O), found 306.0533. $C_{19}H_{14}S_2$ requires 306.0537.

4.3. Sequential double lithiation of thianthrene (1c) and reaction with carbonyl compounds

Isolation of compounds **3**. *General procedure*. To a blue suspension of lithium powder (100 mg, 14 mmol) and a catalytic amount of DTBB (40 mg, 0.15 mmol; 7.5 mol%) in THF (4 mL) thianthrene (**1c**, 430 mg, 2.0 mmol) was added at −90°C, and the resulting mixture was stirred for 45 min at the same temperature. Then, the corresponding carbonyl compound (2.1 mmol) was added dropwise and stirring was continued for 45 min at −90°C. After that, a second carbonyl compound was added (2.4 mmol) allowing the reaction temperature to rise to −78°C for 30 min and the resulting mixture was hydrolysed with water (10 mL), extracted with ethyl acetate (3×20 mL), dried over anhydrous Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products. Yields and R_f values are given in Table 2, physical, analytical and spectroscopic data follow.

4.3.1. 1-[2-(1-Hydroxy-2,2-dimethylpropyl)phenyl]-2,2-dimethyl-1-propanol (3a). First isomer: colorless liquid; ν (film) 3485–3360 (OH), 3065 (ArH), 1246 cm^{-1} (CO); δ_H 0.99 [18H, s, $C(CH_3)_3$], 2.07 (2H, br s, OH), 4.93 (2H, s, C*H*OH), 7.22 (2H, dd, *J*=5.9, 3.4 Hz, ArH), 7.42 (2H, dd, *J*=5.9, 3.4 Hz, ArH); δ_C 27.1 [$C(CH_3)_3$], 36.3 [$C(CH_3)_3$], 78.6 (CHOH), 126.6, 128.8, 140.6 (ArC); *m/z* 232 [M^+–(H_2O), 0.1%], 193 (11), 176 (12), 175 (84), 158 (14), 157 (100), 142 (31), 129 (16), 118 (12), 91 (13), 57 (19); HMRS: M^+, found 250.1933. $C_{16}H_{26}O_2$ requires 250.1933. Second isomer: colorless liquid; ν (film) 3455–3340 (OH), 3063 (ArH), 1242 cm^{-1} (CO); δ_H 0.88 [18H, s, $C(CH_3)_3$], 1.57 (2H, br s, OH), 4.87 (2H, s, C*H*OH), 7.25 (2H, dd, *J*=5.8, 3.4 Hz, ArH), 7.42 (2H, dd, *J*=5.8, 3.4 Hz, ArH); δ_C 26.0 [$C(CH_3)_3$], 35.1 [$C(CH_3)_3$], 76.5 (CHOH), 126.6, 126.7, 139.8 (ArC); *m/z* 232 [M^+–(H_2O), 0.4%], 193 (21), 175 (64), 158 (21), 157 (100), 142 (26), 129 (15), 91 (22), 57 (18); HMRS: M^+, found 250.1910. $C_{16}H_{26}O_2$ requires 250.1933.

4.3.2. 1-[2-(1-Hydroxy-1-methylethyl)phenyl]-2,2-dimethyl-1-propanol (3b). Colorless liquid; ν (film) 3453–3335 (OH), 3055 (ArH), 1265 cm^{-1} (CO); δ_H 0.96 [9H, s, $C(CH_3)_3$], 1.57 (3H, s, CH_3), 1.65 (3H, s, CH_3), 2.12 (2H, br s, OH), 5.54 (1H, s, C*H*OH), 7.10–7.19 (2H, m, ArH), 7.26 (1H, dd, *J*=7.3, 1.8 Hz, ArH), 7.57 (1H, dd, *J*=7.3, 1.8 Hz, ArH); δ_C 27.5 [$C(CH_3)_3$], 32.9, 33.4 (CH_3), 36.3 [$C(CH_3)_3$], 74.1 (COH), 75.9 (CHOH), 125.6, 126.6, 126.9, 129.3, 141.6, 145.5 (ArC); *m/z* 204 [M^+–(H_2O), 0.5%], 148 (11), 147 (100), 129 (59), 91 (14), 77 (12), 57 (15), 43 (38), 41 (32); HMRS: M^+–(H), found 221.1525. $C_{14}H_{21}O_2$ requires 221.15442.

4.3.3. 2-[2-(Hydroxyphenylmethyl)phenyl]-2-propanol (3c). Colorless liquid; ν (film) 3410–3295 (OH), 3062, 3030 (ArH), 1247 cm^{-1} (CO); δ_H 1.65 (3H, s, CH_3), 1.66 (3H, s, CH_3), 3.43 (2H, br s, OH), 6.56 (1H, s, CH), 7.13–7.32 (9H, m, ArH); δ_C 32.7, 32.8 (CH_3), 73.1 (CHOH), 74.6 (COH), 126.2, 126.5, 126.7, 127.2, 127.5, 128.1, 131.0,

141.6, 144.4, 145.5 (ArC); *m/z* 224 [M^+–(H_2O), 62%], 223 (32), 210 (16), 209 (100), 208 (17), 195 (13), 194 (46), 191 (12), 166 (10), 165 (31), 105 (17), 91 (11), 77 (26); HMRS: M^+–(H_2O), found 224.1202. $C_{16}H_{16}O$ requires 224.1201.

4.3.4. 1-[2-(1-Hydroxy-1-methylethyl)phenyl]-3-phenyl-1-propanol (3d). Colorless oil; ν (film) 3390–3255 (OH), 3062, 3026 (ArH), 1247 cm^{-1} (CO); δ_H 1.49 (3H, s, CH_3), 1.60 (3H, s, CH_3), 1.96–2.10 (1H, m, CHCH*H*), 2.16–2.29 (1H, m, CHC*H*H), 2.62–2.72 (1H, m, PhCH*H*), 2.83–2.93 (1H, m, PhC*H*H), 3.09 (2H, br s, OH), 5.46 (1H, dd, *J*=9.0, 4.3 Hz, C*H*OH), 7.12–7.28 (8H, m, ArH), 7.48–7.51 (1H, m, ArH); δ_C 32.45, 32.5 (CH_3), 33.0 (CH_2), 39.2 ($PhCH_2$), 69.9 (CHOH), 73.9 (COH), 125.6, 125.7, 127.1, 127.4, 127.9, 128.3, 128.4, 142.1, 142.6, 144.7 (ArC); *m/z* 252 [M^+–(H_2O), 5%], 148 (14), 147 (100), 129 (44), 105 (10), 103 (11), 91 (51), 77 (21), 65 (16), 51 (10), 43 (40), 41 (15); HMRS: M^+–(H_2O), found 252.1510. $C_{18}H_{20}O$ requires 252.1514.

4.3.5. 2-[2-(1-Hydroxy-1-methylethyl)phenyl]-2-propanol (3e).[32] White solid, mp 169–170°C (dichloromethane/hexane); [Found: C, 74.34; H, 9.14. $C_{12}H_{18}O_2$ requires C, 74.19; H, 9.34]; ν (KBr) 3340–3260 (OH), 3055 (Ar-H), 1264 cm^{-1} (CO); δ_H 1.64 (12H, s, CH_3), 7.09 (2H, dd, *J*=6.1, 3.7 Hz, ArH), 7.25 (2H, dd, *J*=6.1, 3.7 Hz, ArH); δ_C 33.5 (CH_3), 74.9 (COH), 126.3, 128.1, 145.6 (ArC); *m/z* 179 [M^+–(CH_3), 11%], 162 (12), 161 (95), 143 (46), 128 (25), 118 (12), 117 (19), 115 (12), 91 (16), 77 (13), 59 (13), 51 (14), 43 (100).

4.3.6. 3-[2-(1-Hydroxy-1-methylethyl)phenyl]-3-pentanol (3f). White solid, mp 131–132°C (dichloromethane/hexane); [Found: C, 75.62; H, 10.09. $C_{14}H_{22}O_2$ requires C, 75.63; H, 9.97]; ν (KBr) 3310–3190 (OH), 3058 (ArH), 1266 cm^{-1} (CO); δ_H 0.81 (6H, t, *J*=7.3 Hz, 2×CH_2CH_3), 1.75 (6H, s, 2×CH_3), 1.80–1.91 (2H, m, CH_2), 1.96–2.08 (2H, m, CH_2), 5.08 (2H, br s, OH), 7.11–7.19 (3H, m, ArH), 7.36 (1H, d, *J*=7.3 Hz, ArH); δ_C 8.4, 33.1 (CH_3), 37.5 (CH_2), 74.7, 80.4 (COH), 125.6, 126.4, 127.2, 129.4, 143.5, 146.5 (ArC); *m/z* 204 [M^+–(H_2O), 0.5%], 189 (8), 176 (13), 175 (100), 157 (26), 145 (11), 142 (22), 131 (11), 129 (14), 117 (14), 115 (13), 91 (11).

4.3.7. 1-[2-(1-Hydroxy-1-methylethyl)phenyl]cyclohexanol (3g).[33] White solid, mp 156–157°C (dichloromethane/hexane); [Found: C, 75.98; H, 9.44. $C_{15}H_{22}O_2$ requires C, 76.88; H, 9.46]; ν (KBr) 3305–3210 (OH), 3055 (ArH), 1266 cm^{-1} (CO); δ_H 1.58–1.88 (14H, m, 4×CH_2, 2×CH_3), 2.13–2.16 (2H, m, CH_2), 5.17 (2H, br s, OH), 7.14–7.17 (2H, m, ArH), 7.30–7.33 (1H, m, ArH), 7.37–7.40 (1H, m, ArH); δ_C 22.1, 25.6 (CH_2), 34.1 (CH_3), 39.8 (CH_2), 74.9, 75.3 (COH), 126.1, 126.2, 127.4, 128.5, 146.2, 146.4 (ArC); *m/z* 234 (M^+, 0.5%), 216 (12), 201 (25), 183 (11), 174 (13), 173 (100), 145 (38), 115 (14), 91 (13), 55 (15), 43 (60), 41 (21).

4.3.8. 3-[2-(1-Ethyl-1-hydroxypropyl)phenyl]-3-pentanol (3h). Colorless liquid; ν (film) 3330–3225 (OH), 3056 (ArH), 1265 cm^{-1} (CO); δ_H 0.80 (12H, t, *J*=7.0 Hz, 4×CH_2CH_3), 1.91–2.11 (8H, m, 4×CH_2CH_3), 5.77 (2H, br s, OH), 7.11–7.26 (4H, m, ArH); δ_C 8.4 (CH_3), 36.0 (CH_2), 80.0 (COH), 125.4, 129.4, 143.9 (ArC); *m/z* 221 [M^+–(CH_2CH_3), 3%], 204 (15), 203 (100), 157 (23), 145 (18), 143 (27), 131 (12), 129 (19), 117 (24), 115 (15), 91 (21), 59 (10), 57 (38), 45 (10), 43 (44), 41 (21); HMRS: M^+–(CH_2CH_3), found 221.1525. $C_{14}H_{21}O_2$ requires 221.1542.

4.3.9. 1-[2-(1-Hydroxycyclohexyl)phenyl]cyclohexanol (3i). White solid, mp 170–171°C (dichloromethane/hexane); [Found: C, 78.57; H, 9.27. $C_{18}H_{26}O_2$ requires C, 78.79; H, 9.55]; ν (KBr) 3415 (OH), 3055 (ArH), 1264 cm^{-1} (CO); δ_H 1.28–1.35 (2H, m, CH_2), 1.64–1.87 (14H, m, 7×CH_2), 2.05–2.24 (4H, m, 2×CH_2), 4.58 (2H, br s, OH), 7.08–7.25 (2H, m, ArH), 7.36–7.44 (2H, m, ArH); δ_C 22.2, 25.6, 40.3 (CH_2), 75.6 (COH), 126.1, 127.9, 147.0 (ArC); *m/z* 256 [M^+–(H_2O), 14%], 214 (17), 213 (100), 195 (11), 157 (32), 145 (14), 129 (22), 128 (11), 115 (14), 91 (13), 55 (29), 43 (23), 41 (37).

4.4. Sequential double lithiation of thianthrene (1c) and reaction with carbonyl compounds and carbon dioxide, respectively

Isolation of compounds **4**. *General procedure*. To a blue suspension of lithium powder (100 mg, 14 mmol) and a catalytic amount of DTBB (40 mg, 0.15 mmol; 7.5 mol%) in THF (4 mL) thianthrene (**1c**, 430 mg, 2.0 mmol) was added at −90°C, and the resulting mixture was stirred for 45 min at the same temperature. Then, the corresponding carbonyl compound (2.1 mmol) was added dropwise and stirring was continued for 45 min at −90°C. After that carbon dioxide was bubbled for 15 min at −70°C, and the reaction mixture was hydrolysed with water, extracted with ether (3×20 mL) and the aqueous layer was acidified with 3 M HCl and extracted with ethyl acetate (3×20 mL), dried over anhydrous Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products. Yields and R_f values are given in Table 3, physical, analytical and spectroscopic data follow.

4.4.1. 3-Methyl-1,3-dihydro-1-isobenzofuranone (4a).[34] Colorless liquid; ν (film) 3057 (ArH), 1758 (C=O), 1267 cm^{-1} (CO); δ_H 1.57 (3H, d, *J*=6.7 Hz, $CHCH_3$), 5.50 (1H, q, *J*=6.7 Hz, $CHCH_3$), 7.37 (1H, d, *J*=7.6 Hz, ArH), 7.46 (1H, t, *J*=7.6 Hz, ArH), 7.61 (1H, td, *J*=7.6, 1.0 Hz, ArH), 7.83 (1H, d, *J*=7.6 Hz, ArH); δ_C 20.4 (CH_3), 77.7 (CHO), 121.5, 125.7, 126.5, 129.0, 134.0, 151.2 (ArC), 170.4 (C=O); *m/z* 148 (M^+, 19%), 133 (66), 105 (100), 77 (30), 51 (16); HMRS: M^+, found 148.0502. $C_9H_8O_2$ requires 148.0524.

4.4.2. 3-Butyl-1,3-dihydro-1-isobenzofuranone (4b).[35] Colorless liquid; ν (film) 3056 (ArH), 1760 (C=O), 1267 cm^{-1} (CO); δ_H 0.84 (3H, t, *J*=7.1 Hz, CH_3), 1.24–1.44 (3H, m, CH_2, C*H*H), 1.63–1.75 (2H, m, CH_2), 1.92–2.03 (1H, m, CH*H*), 5.40 (1H, q, *J*=4.1 Hz, CH), 7.36 (1H, d, *J*=7.6 Hz, ArH), 7.45 (1H, t, *J*=7.6 Hz, ArH), 7.60 (1H, t, *J*=7.6 Hz, ArH), 7.82 (1H, d, *J*=7.6 Hz, ArH); δ_C 13.8 (CH_3), 22.4, 26.8, 34.4 (CH_2), 81.4 (CHO), 121.7, 125.7, 126.2, 129.0, 133.9, 150.1 (ArC), 170.6 (C=O); *m/z* 190 (M^+, 2%), 134 (11), 133 (100), 105 (29), 77 (12); HMRS: M^+, found 190.0983. $C_{12}H_{14}O_2$ requires 190.0994.

4.4.3. 3-Octyl-1,3-dihydro-1-isobenzofuranone (4c).[36] Colorless oil; ν (film) 3055 (ArH), 1763 (C═O), 1285 cm^{-1} (CO); δ_H 0.80 (3H, t, J=6.5 Hz, CH_3), 1.12–1.24 (11H, m, 5×CH_2, C*H*H), 1.36–1.41 (1H, m, C*H*H), 1.62–1.74 (1H, m, CH*H*), 1.91–2.00 (1H, m, C*H*H), 5.40 (1H, dd, J=7.8, 4.1 Hz, CH*H*), 7.36 (1H, d, J=7.7 Hz, ArH), 7.44 (1H, t, J=7.4 Hz, ArH), 7.59 (1H, t, J=7.4 Hz, ArH), 7.82 (1H, d, J=7.7 Hz, ArH); δ_C 14.0 (CH_3), 22.6, 24.8, 29.1, 29.3, 31.7, 34.7 (CH_2), 81.5 (CHO), 121.7, 125.6, 126.1, 129.0, 133.9, 150.1 (ArC), 170.7 (C═O); *m/z* 246 (M^+, 6%), 176 (12), 134 (15), 133 (100), 105 (21), 77 (11); HMRS: M^+, found 246.1609. $C_{16}H_{22}O_2$ requires 246.1620.

4.4.4. 3-Phenyl-1,3-dihydro-1-isobenzofuranone (4d).[37] White solid, mp 113–114°C (dichloromethane/hexane); [Found: C, 79.68; H, 4.68. $C_{14}H_{10}O_2$ requires C, 79.98; H, 4.79]; ν (KBr) 3056 (ArH), 1765 (C═O), 1281 cm^{-1} (CO); δ_H 6.33 (1H, s, CHO), 7.18–7.31 (6H, m, ArH), 7.48 (1H, t, J=7.3 Hz, ArH), 7.55–7.60 (1H, m, ArH), 7.89 (1H, t, J=7.3 Hz, ArH); δ_C 82.7 (CHO), 122.8, 125.6, 126.9, 128.4, 128.9, 129.3, 129.35, 134.3, 136.4, 149.7 (ArC), 170.5 (C═O); *m/z* 210 (M^+, 42%), 209 (10), 165 (18), 133 (10), 105 (100), 104 (30), 77 (36), 76 (19), 51 (31), 50 (19).

4.4.5. 3,3-Dimethyl-1,3-dihydro-1-isobenzofuranone (4e).[38] Colorless liquid; ν (film) 3056 (ArH), 1759 (C═O), 1266 cm^{-1} (CO); δ_H 1.65 (6H, s, 2×CH_3), 7.40 (1H, d, J=7.3 Hz, ArH), 7.49 (1H, t, J=7.3 Hz, ArH), 7.65 (1H, t, J=7.3 Hz, ArH), 7.85 (1H, d, J=7.3 Hz, ArH); δ_C 27.3 (CH_3), 85.4 (CO), 120.6, 125.2, 125.7, 128.9, 134.1, 154.9 (ArC), 169.8 (C═O); *m/z* 162 (M^+, 5%), 148 (12), 147 (100), 91 (27), 51 (14), 50 (18), 43 (30); HMRS: M^+, found 162.0675. $C_{10}H_{10}O_2$ requires 162.0681.

4.4.6. 3-Ethyl-3-methyl-1,3-dihydro-1-isobenzofuranone (4f).[39] Colorless liquid; ν (film) 3056 (ArH), 1758 (C═O), 1267 cm^{-1} (CO); δ_H 0.67 (3H, t, J=7.4 Hz, CH_2CH_3), 1.56 (3H, s, $COCH_3$), 1.75–1.90 (1H, m, C*H*HCH_3), 1.93–2.09 (1H, m, CH*H*CH_3), 7.29 (1H, d, J=7.7 Hz, ArH), 7.42 (1H, t, J=7.6 Hz, ArH), 7.59 (1H, t, J=7.6 Hz, ArH), 7.79 (1H, d, J=7.7 Hz, ArH); δ_C 7.7, 25.6 (CH_3), 32.8 (CH_2), 87.9 (CO), 120.8, 125.6, 128.0, 128.8, 134.0, 153.6 (ArC), 170.1 (C═O); *m/z* 176 (M^+, 2%), 148 (10), 147 (100), 91 (16); HMRS: M^+, found 176.0818. $C_{11}H_{12}O_2$ requires 176.0837.

4.4.7. Spirocyclohexane-3-[1,3-dihydro-1-isobenzofuranone] (4g).[40] Colorless oil; ν (film) 3055 (ArH), 1756 (C═O), 1266 cm^{-1} (CO); δ_H 1.72–1.85 (10H, m, 5×CH_2), 7.38 (1H, d, J=7.3 Hz, ArH), 7.48 (1H, t, J=7.3 Hz, ArH), 7.63 (1H, t, J=7.3 Hz, ArH), 7.85 (1H, d, J=7.3 Hz, ArH); δ_C 22.3, 24.7, 36.3 (CH_2), 86.9 (CO), 120.9, 125.4, 125.7, 128.9, 133.9, 154.9 (ArC), 170.1 (C═O); *m/z* 202 (M^+, 41%), 160 (15), 159 (94), 147 (15), 146 (100), 131 (24), 105 (13), 104 (24), 103 (11), 77 (15), 76 (27), 55 (11), 51 (17), 50 (20), 41 (19); HMRS: M^+, found 202.0999. $C_{13}H_{14}O_2$ requires 202.0994.

4.5. Cyclisation of hydroxythiols 2 and diols 3

Isolation of compounds **5** *and* **6**. *General procedure*. To a solution of the corresponding hydroxythiol **2** or diol **3** (0.5 mmol) in toluene (3 mL) 85% phosphoric acid (0.2 mL) was added. The reaction mixture was heated at 110°C for 12 h in the case of hydroxythiols **2** and for 2 h in the case of diols **3**, then toluene was removed by distillation and the resulting residue was hydrolysed with water and extracted with ethyl acetate (3×20 mL), the organic layer dried over anhydrous Na_2SO_4 and evaporated (15 Torr). The residue was purified by column chromatography (silica gel, hexane/ethyl acetate) to yield pure products **5** and **6**. Yields and R_f values are given in Tables 4 and 5, analytical and spectroscopic data follow.

4.5.1. 11-Phenyl-11*H*-dibenzo[*b*,*f*][1,4]oxathiepin (5a). Colorless oil; ν (film) 3048, 3017 (ArH) 1233 cm^{-1} (CO); δ_H 6.20 (1H, s, ArCH), 6.95 (2H, t, J=7.6 Hz, ArH), 7.04–7.09 (3H, m, ArH), 7.22–7.44 (8H, m, ArH); δ_C 47.9 (ArCH), 122.0, 122.4, 124.8, 125.3, 126.7, 127.75, 127.8, 127.9, 128.55, 128.6, 129.1, 129.2, 135.0, 138.5, 153.6, 156.2 (ArC); *m/z* 290 (M^+, 100%), 289 (26), 273 (13), 261 (14), 213 (23), 211 (14), 210 (83), 197 (30), 185 (32), 184 (20), 181 (15), 165 (29), 152 (18), 139 (11), 77 (11), 69 (11), 63 (15), 51 (16); HMRS: M^+, found 290.0756. $C_{19}H_{14}OS$ requires 290.0765.

4.5.2. 11,11-Diethyl-11*H*-dibenzo[*b*,*f*][1,4]oxathiepin (5b). Colorless oil; ν (film) 3060, 3026 (ArH) 1245 cm^{-1} (CO); δ_H 0.96 (6H, t, J=7.3 Hz, 2×CH_2CH_3), 2.03–2.15 (2H, m, CH_2CH_3), 2.26–2.38 (2H, m, CH_2CH_3), 6.98–7.26 (8H, m, ArH); δ_C 9.1 (CH_3), 32.3 (CH_2), 55.6 (CS), 121.6, 123.2, 124.7, 124.9, 127.1, 127.4, 128.3, 130.9, 136.3, 139.4, 151.7, 155.8 (ArC); *m/z* 270 (M^+, 23%), 255 (13), 243 (12), 242 (19), 241 (100), 209 (23), 208 (11), 207 (15), 181 (14), 177 (18), 163 (11), 149 (13), 115 (17), 107 (16), 91 (11), 77 (11), 51 (11), 45 (13), 44 (29), 41 (15), 40 (36); HMRS: M^+, found 270.1048. $C_{17}H_{18}OS$ requires 270.1078.

4.5.3. 11-(*tert*-Butyl)-11*H*-dibenzo[*b*,*e*][1,4]dithiepin (5c). Pale yellow oil; ν (film) 3055 (ArH), 739 cm^{-1} (CS); δ_H 1.21 [9H, s, $C(CH_3)_3$], 5.68 (1H, s, SCH), 6.88–6.98 (2H, m, ArH), 7.07–7.25 (3H, m, ArH), 7.31 (1H, d, J=7.3 Hz, ArH), 7.41 (1H, d, J=7.3 Hz, ArH), 7.56 (1H, d, J=7.9 Hz, ArH); δ_C 28.8 [C(*C*H_3)$_3$], 29.7 [*C*(CH_3)$_3$], 56.1 (SCH), 125.9, 126.0, 126.9, 127.4, 127.7, 127.9, 129.1, 130.7, 132.5, 134.7, 136.3, 137.3 (ArC); *m/z* 286 (M^+, 13%), 231 (12), 230 (27), 229 (100), 197 (48), 41 (18); HMRS: M^+, found 286.0835. $C_{17}H_{18}S_2$ requires 286.0850.

4.5.4. 11-Phenyl-11*H*-dibenzo[*b*,*e*][1,4]dithiepin (5d). Pale yellow oil; ν (film) 3056 (ArH), 745 cm^{-1} (CS); δ_H 6.66 (1H, s, SCH), 6.87–6.99 (4H, m, ArH), 7.08–7.22 (7H, m, ArH), 7.40–7.43 (1H, m, ArH), 7.51–7.54 (1H, m, ArH); δ_C 51.8 (SCH), 126.6, 127.5, 127.9, 128.2, 128.4, 128.8, 128.9, 129.1, 131.3, 132.8, 133.1, 134.4, 134.8, 138.4, 139.6, 142.1 (ArC); *m/z* 306 (M^+, 64%), 274 (22), 273 (100), 272 (12), 271 (33), 229 (44), 198 (12), 197 (84), 184 (12), 165 (48), 164 (14), 163 (12), 153 (15), 152 (25), 139 (14), 137 (16), 136 (43), 91 (18), 77 (14), 69 (17), 63 (18), 51 (18), 45 (19); HMRS: M^+, found 306.0561. $C_{19}H_{14}S_2$ requires 306.0537.

4.5.5. 3-(2-Phenylethyl)-1,1-dimethyl-1,3-dihydroisobenzofuran (6a). Colorless oil; ν (film) 3061, 3026

(ArH), 1257 cm^{-1} (CO); δ_H 1.48 (3H, s, CH_3), 1.58 (3H, s, CH_3), 1.94–2.06 (1H, m, CHCH*H*), 2.15–2.27 (1H, m, CHC*H*H), 2.67–2.85 (2H, m, $PhCH_2$), 5.27 (1H, dd, *J*=5.3, 3.8 Hz, CHO), 7.10–7.30 (9H, m, ArH); δ_C 29.0 (CH_3), 29.7 (CH_2), 31.4 (CH_3), 38.5 (CH_2), 80.7 (CHO), 84.8 (CO), 120.6, 121.0, 125.7, 127.3, 127.6, 128.3, 128.4, 141.2, 142.4, 147.4 (ArC); *m/z* 252 (M^+, 10%), 237 (11), 174 (13), 148 (11), 147 (100), 131 (11), 129 (30), 91 (43); HMRS: M^+, found 252.1490. $C_{18}H_{20}O$ requires 252.1514.

4.5.6. 1,1,3,3-Tetramethyl-1,3-dihydroisobenzofuran (6b).[41] Colorless oil; ν (film) 3055 (ArH), 1261 cm^{-1} (CO); δ_H 1.52 (12H, s, 4×CH_3), 7.09 (2H, dd, *J*=5.5, 3.1 Hz, ArH), 7.27 (2H, dd, *J*=5.5, 3.1 Hz, ArH); δ_C 30.8 (CH_3), 84.1 (CO), 120.7, 127.4, 146.1 (ArC); *m/z* 161 [M^+–(CH_3), 100%], 143 (29), 128 (16), 115 (10), 51 (11), 43 (58); HMRS: M^+, found 176.1196. $C_{12}H_{16}O$ requires 176.1201.

4.5.7. Spirocyclohexane-1-[3,3-dimethyl-1,3-dihydroisobenzofuran] (6c).[42] Colorless oil; ν (film) 3070, 3024 (ArH), 1263 cm^{-1} (CO); δ_H 1.50 (6H, s, 2×CH_3), 1.61–1.85 (10H, m, 5×CH_2), 7.07–7.11 (2H, m, ArH), 7.24–7.27 (2H, m, ArH); δ_C 22.4, 25.3 (CH_2), 31.1 (CH_3), 39.5 (CH_2), 83.8, 85.2 (CO), 120.8, 121.0, 127.2, 127.5, 146.3, 146.7 (ArC); *m/z* 216 (M^+, 25%), 201 (19), 174 (13), 173 (100), 145 (37), 115 (14); HMRS: M^+, found 216.1505. $C_{15}H_{20}O$ requires 216.1514.

4.5.8. 1,1,3,3-Tetraethyl-1,3-dihydroisobenzofuran (6d). Colorless oil; ν (film) 3070, 3027 (ArH), 1242 cm^{-1} (CO); δ_H 0.92 (12H, t, *J*=7.6 Hz, 4×CH_2CH_3), 1.69–1.89 (8H, m, 4×CH_2CH_3), 7.06 (2H, dd, *J*=5.5, 3.1 Hz, ArH), 7.24 (2H, dd, *J*=5.5, 3.1 Hz, ArH); δ_C 8.6 (CH_3), 32.6 (CH_2), 88.9 (CO), 121.5, 127.0, 145.5 (ArC); *m/z* 203 [M^+–(CH_2CH_3), 100%], 159 (14), 157 (18), 145 (11), 143 (22), 129 (15), 115 (13), 91 (15), 57 (21), 43 (29), 41 (16); HMRS: M^+–(CH_2CH_3), found 203.1428. $C_{14}H_{19}O$ requires 203.1436.

4.5.9. Spirocyclohexane-1-{spirocyclohexane-3-[-1,3-dihydroisobenzofuran]} (6e). Colorless oil; ν (film) 3047, 3029 (ArH), 1266 cm^{-1} (CO); δ_H 1.26–1.36 (2H, m, CH_2), 1.62–1.89 (18H, m, 9×CH_2), 7.08 (2H, dd, *J*=5.5, 3.1 Hz, ArH), 7.24 (2H, dd, *J*=5.5, 3.1 Hz, ArH); δ_C 22.6, 25.5, 39.7 (CH_2), 84.5 (CO), 121.0, 127.2, 146.9 (ArC); *m/z* 256 (M^+, 21%), 214 (18), 213 (100), 157 (28), 145 (12), 129 (15), 128 (12), 115 (14), 55 (20), 43 (12), 41 (29); HMRS: M^+, found 256.1926. $C_{18}H_{24}O$ requires 256.1827.

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