Reductive Elimination of Phenylsulfonyl Groups in the 3-Position of Benzo[*a*]heptalene-2,4-diols

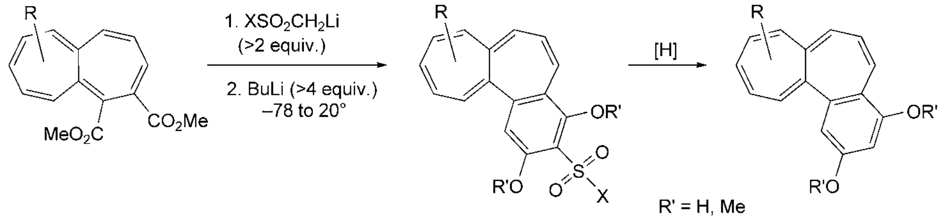
by **Mohy eldin Abdel Fattah**[a]), **Samir El Rayes**[a])[1]), **El Sayed Ahmed Soliman**[b]), **Anthony Linden**[c]), **Khaled Abou-Hadeed***[c]), and **Hans-Jürgen Hansen***[c])

[a]) Faculty of Science, University of Suez Canal, Ismailia, Egypt
[b]) Faculty of Science, University of Ain Shams, Cairo, Egypt
[c]) Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

3-(Phenylsulfonyl)benzo[*a*]heptalene-2,4-diols **1** can be desulfonylated with an excess of $LiAlH_4$/MeLi · LiBr in boiling THF in good yields (*Scheme 6*). When the reaction is run with $LiAlH_4$/MeLi, mainly the 3,3′-disulfides **6** of the corresponding 2,4-dihydroxybenzo[*a*]heptalene-3-thiols are formed after workup (*Scheme 7*). However, the best yields of desulfonylated products are obtained when the 2,4-dimethoxy-substituted benzo[*a*]heptalenes **2** are reduced with an excess of $LiAlH_4/TiCl_4$ at −78 → 20° in THF (*Scheme 10*). Attempts to substitute the $PhSO_2$ group of **2** with freshly prepared MeONa in boiling THF led to a highly selective ether cleavage of the 4-MeO group, rather than to desulfonylation (*Scheme 13*).

Introduction. – Dimethyl heptalene-4,5-dicarboxylates, when reacted at −78 to 20° with an excess of lithiomethyl sulfones in the presence of alkyl lithium (BuLi, MeLi · LiBr), yield in a one-pot procedure 3-(X-sulfonyl)benzo[*a*]heptalene-2,4-diols (X = Ph, NR_2) [1–3] (see also [4]), thus opening a new access to colchicinoids. However, for the synthesis of colchicinoids, it is necessary to exchange the target X-sulfonyl group by a MeO or other ether group. Since all attempts to replace the sulfonyl group in a nucleophilic substitution reaction by MeO^- failed (see below), we decided to remove the X-sulfonyl group reductively and to add an O-functionality in a second step (*Scheme 1*)[2]). We now report a new, highly selective cleavage reaction of diaryl sulfones (X = Ph) and aryl sulfonamides (X = NR_2), as present in the envisaged 3-(X-sulfonyl)benzo[*a*]heptalene-2,4-diols.

Scheme 1



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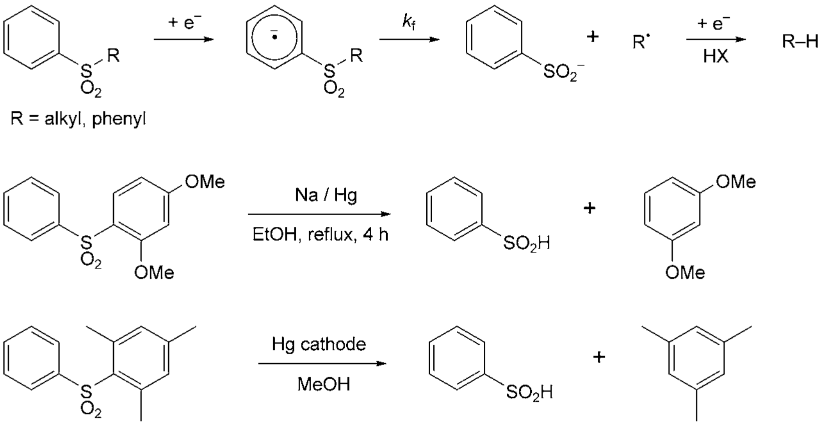
[1]) Part of the Ph.D. thesis of *S. E. R.*, Suez Canal University, 2003; scholar at the University of Zurich 2000–2002, with a scholarship of the Egyptian Channel Programme.

[2]) We reported on this procedure already during the autumn meeting of the *Swiss Chemical Society*, Zurich, October 12, 2001 [5].

Results and Discussion. – The reductive cleavage of aryl alkyl and diaryl sulfones by alkali amalgams in the presence of protic solvents [6–8], or under *Birch* conditions by Na/NH_3 or $Li/MeNH_2$ [9], or electrochemically at different cathodes [10–13] is a well-established reaction known for more than 50 years[3]). It has been characterized as a two-electron process, whereby, after the uptake of the first electron, C–S fission takes place to yield the corresponding arenesulfinate and a C-radical, which is reduced by the second electron to the carbanion (*Scheme 2*). The carbanion is then protonated or captured by other electrophiles. It is of interest to note that sulfones unsymmetrically substituted by σ- and π-donor groups are cleaved highly selectively at the sterically more-congested C–S bond, which rationalizes why the fission rate (k_f) is rate-determining. Two examples of this fission selectivity of diaryl ethers are shown in *Scheme 2*. Despite these favorable aspects, we were not interested to do electrochemistry or to work with alkali amalgams in a preparative way.

Scheme 2



A first hint that under favorable circumstances complex hydrides may also induce C–S bond cleavage of diaryl sulfones came from an investigation of *Brown et al.* who found that the reaction of $LiEt_3BH$ (and other 'super-hydrides' of this type) and diphenyl sulfone in boiling THF gave ethylbenzene (or the corresponding alkylbenzenes) and lithium phenylsulfinate as cleavage products (*Scheme 3*) [15].

Scheme 3

$$\mathrm{Ph_2SO_2} + 2\ \mathrm{LiEt_3BH} \xrightarrow[\text{reflux, 2 h}]{\text{THF}} \mathrm{Ph{-}Et} + \mathrm{PhSO_2Li}$$

Since an Et group is biochemically isosteric with a MeO group, we tried to react 3-(phenylsulfonyl)benzo[*a*]heptalene-2,4-diol (**1a**), without further protection, with $LiEt_3BH$ (10 equiv.; to account for the free OH groups), as shown in *Scheme 4*. However, **1a** was recovered almost quantitatively. When we performed the reaction

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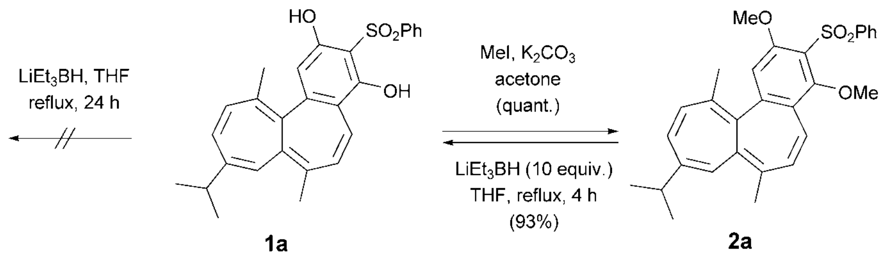
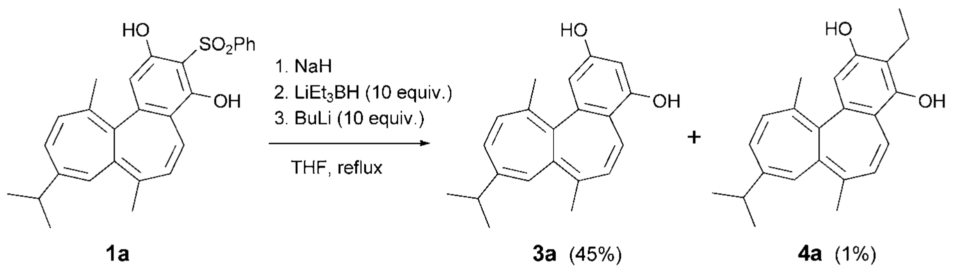
[3]) The reductive cleavage of Ph_2SO_2 was first realized with *Raney*-Ni in boiling EtOH more than 60 years ago [14]. However, it can be assumed that the reduction starts, in this case, at the S-atom (see below).

with the dimethoxy derivative **2a**, we were surprised to observe an excellent demethylation reaction of the ether functions, but no desulfonylation at all. The situation did not change when **1a** was first deprotonated with NaH in THF, and then treated with $LiEt_3BH$. When we used the same procedure as before, but added at the end BuLi (10 mol-equiv.) in two portions, this being a strong base and promoter for alkanide or hydride transfer, the desulfonylated product **3a** was formed in acceptable yield (45%), together with a small quantity of the envisaged 3-ethylated benzo[*a*]heptalene-2,4-diol **4a** (*Scheme 5*).

Scheme 4



Scheme 5



Since the presence of $LiEt_3BH$ did not lead to a significant yield of **4a**, we substituted the reagent by a large excess of $LiAlH_4$[4]) and used the MeLi · LiBr complex as the promoting agent for reduction, and to keep the Li^+ concentration, a weak *Lewis* acid, as high as possible. These conditions, indeed, led to good yields of the corresponding desulfonylated products. In the case of the substrate **1a**, these products were accompanied by a small amount of deoxygenated **5a** (*Scheme 6*). Neither $LiAlH_4$ nor MeLi · LiBr alone in refluxing THF gave the results of their combined action. In the first case, **1a** was recovered unchanged, and in the second one, it was destroyed. However, when we used a mixture of $LiAlH_4$ and MeLi alone, the product pattern changed substantially (*Scheme 7*). After workup, we found mainly the disulfides **6** of the corresponding 3-(sulfanyl)benzo[*a*]heptalene-2,4-diols, accompanied, in the case of **1a**, by small amounts of **3a** and **5a**.

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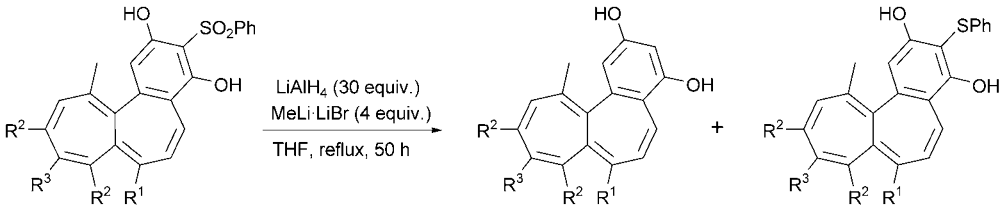
[4]) It is known that $LiAlH_4$ does not react with diphenyl sulfone [16]. However, it has been demonstrated that cyclic four- and five-membered sulfones can be reduced with $LiAlH_4$ in Et_2O to the corresponding thia cycles [17].

Scheme 6



1a R^1 = Me, R^2 = H, R^3 = i-Pr
1b R^1 = R^3 = H, R^2 = Me

3a (71%)
3b (68%)

5a (5%)
5b (not observed)

The reduction of *N*,*N*-dialkylsulfonamides by $LiAlH_4$ to the corresponding thiols is well-established [18]. The formation of **6a** from **1d**, therefore, offers no new aspects. It has also been reported that complex hydrides such as DIBAL (diisobutylaluminum hydride) are able to reduce alkyl aryl sulfones or diaryl sulfones at temperatures $> 100°$ in toluene/hexane to the corresponding sulfides [19]. It seems reasonable, therefore, to assume that under our conditions the phenyl sulfones **6a** and **6b** are first deoxygenated to the phenyl thioethers, as witnessed by the presence of **5a** in the reaction mixtures of **1a** (*Scheme 6* and *7*). In the next step, the Ph–S bond is cleaved reductively to yield the corresponding benzo[*a*]heptalene-3-thiolates, which are present, after workup, as the corresponding disulfides **6**, because oxygen has not been excluded during workup. Finally, the C(3)–S bond of the 2,4-dioxidobenzo[*a*]heptalene-3-thiolates must be cleaved reductively. We suppose that the alkyl lithium reagents (BuLi, MeLi) are necessary for the formation of alkyl aluminum hydrides, which reduce the phenyl sulfones to the corresponding sulfides (see above). The formed 3-(phenylsulfanyl)-benzo[*a*]heptalene-2,4-diolates should be suitable bidentate ligands for the formation of cyclic five-membered aluminum hydrido complexes. Since the phenyl ring should be oriented parallel to the Al–H bonds in such complexes according to an AM1 calculation of a model structure (*Fig. 1,a*), an intramolecular hydride transfer to C_{ip} of the phenyl ring can occur, following the 'principle of least motion', thus leading at the end to the thiolates and benzene. The 2,4-oxidobenzo[*a*]heptalene-3-thiolates should again be excellent ligands for the formation of cyclic five-membered aluminum hydrido complexes (*Fig. 1,b*). However, an intramolecular hydride transfer to C(3) is now much more difficult due to the high electron density on the benzene ring. The reaction stops, therefore, in the presence of a $LiAlH_4$/MeLi mixture, and, after air oxidation, the corresponding disulfides **6a** and **6b**, respectively, are isolated.

The situation changes in the presence of Br^- ions, which are imported by the use of MeLi·LiBr. It seems that Br^- is necessary to induce, by nucleophilic attack on the tetrahedral Al-atom, the intramolecular hydride transfer under formation of the desulfonylated products **3** and sulfide ions (*Scheme 6*)⁵). The discussed mechanism of the reduction process of 3-(phenylsulfonyl)benzo[*a*]heptalene-2,4-diols is summarized in *Scheme 8*.

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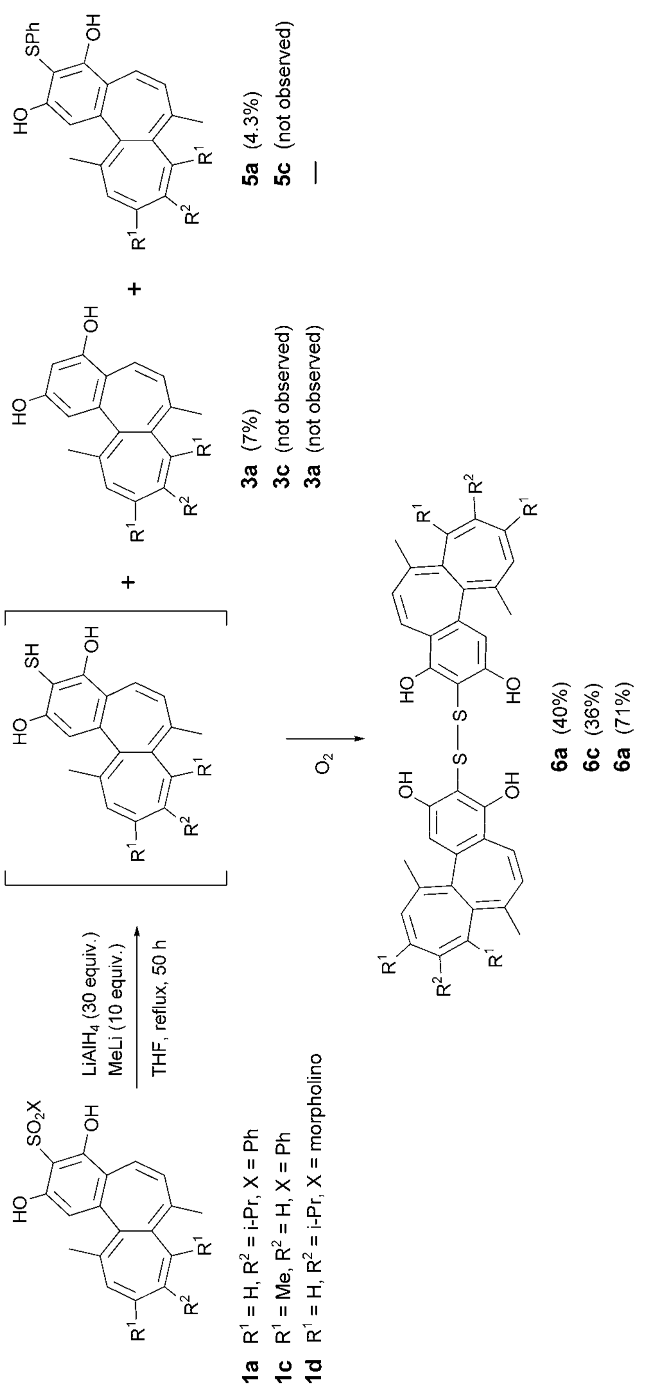
5) The smell of H_2S was recognized after acidification of the reaction mixtures.

Scheme 7


SO$_2$X
HO
OH
R^1
R^2
1a R^1 = H, R^2 = i-Pr, X = Ph
1c R^1 = Me, R^2 = H, X = Ph
1d R^1 = H, R^2 = i-Pr, X = morpholino
LiAlH$_4$ (30 equiv.)
MeLi (10 equiv.)
THF, reflux, 50 h
SH
+
3a (7%)
3c (not observed)
3a (not observed)
+
SPh
5a (4.3%)
5c (not observed)
—
O$_2$
S
S
6a (40%)
6c (36%)
6a (71%)

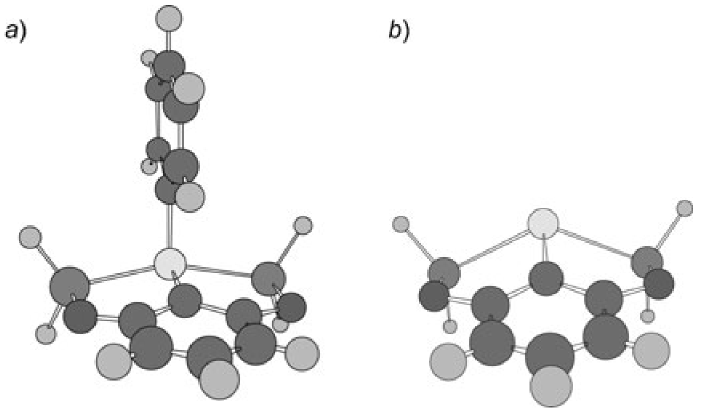
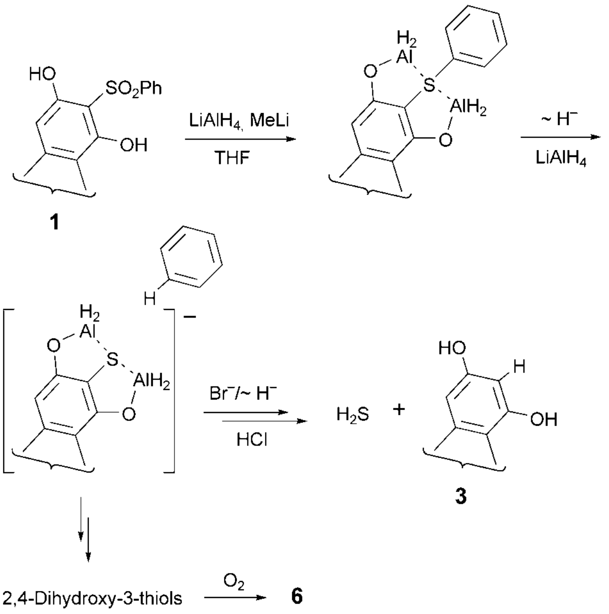


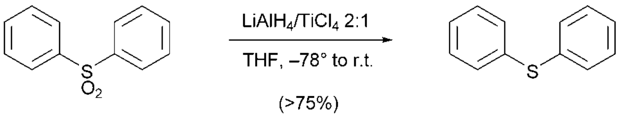
Fig. 1. *DFT-Calculated structures of binary aluminum hydrido complexes of* a) *2-(phenylthio)benzene-1,3-diolate and* b) *1,3-dioxidobenzene-2-thiolate as model compounds for the reduction of* **2** *with LiAlH$_4$*

Scheme 8

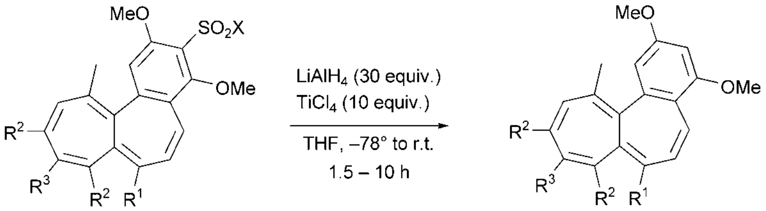


Several years ago, *Akgün et al.* reported that the inertness of diphenyl sulfone against LiAlH$_4$ can be overcome in the presence of TiCl$_4$ [20]. At low temperature, it is reduced by a preformed 2:1 mixture of LiAlH$_4$/TiCl$_4$ to the diphenyl sulfide in excellent yield (*Scheme 9*). The formation of diphenyl sulfide under these conditions encouraged us to run the reduction with the dimethyl ethers **2** of our sulfonylated substrates **1**, but using a LiAlH$_4$/TiCl$_4$ ratio of 3:1, and a 10-fold molar excess with respect to **2** (*Scheme 10*)[6]). The yields of the expected products **7** were good-to-excellent for the (phenylsulfonyl)-substituted dimethoxy derivatives **2a**–**2c**. Also, the sulfonamide **2d** still gave an acceptable yield of **7a** (51%) on reduction with $LiAlH_4$/$TiCl_4$[7]). The procedure has been successfully applied to other 1,3- and 1,2-dimethoxybenzo[*a*]heptalenes bearing a phenylsulfonyl group in 2- and 3-position, respectively [4][21].

Scheme 9



Scheme 10



2a	R^1 = Me, R^2 = H, R^3 = i-Pr, X = Ph	**7a** (91%)
2b	R^1 = R^3 = H, R^2 = Me, X = Ph	**7b** (84%)
2c	R^1 = R^2 = Me, R^3 = H, X = Ph	**7c** (76%)
2d	R^1 = Me, R^2 = H, R^3 = i-Pr, X = morpholino	**7a** (51%)

We have not undertaken any mechanistically oriented experiments or searched for the other cleavage products, since we concentrated on the benzo[*a*]heptalenes **7**, which could easily be identified by chromatographic separation on silica gel due to their intense yellow color. Nevertheless, it is known that $LiAlH_4$ reduces $TiCl_4$ at low temperature in THF to low-valent Ti species such as TiH_2 (see literature cited in [20]), and that these species, due to their oxophilicity, reduce sulfones [20] and sulfoxides [22] at the S-atom to sulfides. Diaryl sulfides are cleaved by alkali metals – in liquid NH_3 or $MeNH_2$ [8][23], or in etheral solvents [24] – to yield the corresponding aryl thiolates and arenes, just as discussed for diaryl sulfones (*cf. Scheme 2*)[8]). Therefore, it is reasonable to assume that our sulfonyl compounds **2**, under the conditions applied here, are first deoxygenated to the sulfides, which are then cleaved reductively to the

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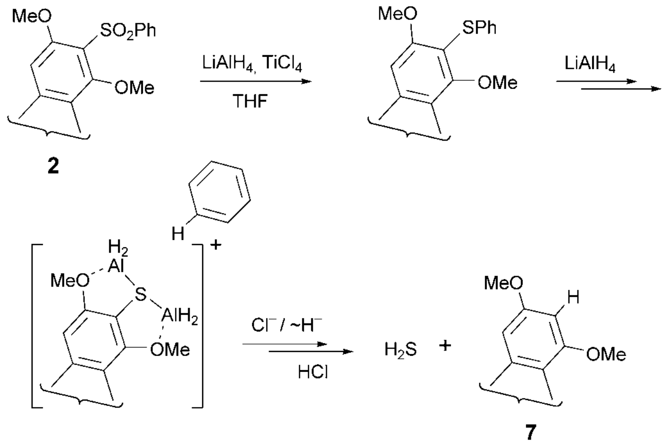
[6]) Lower molar ratios of the reducing system and **2** gave lower yields of the desulfonylated products **7**.

[7]) The structure of **7a** was secured by X-ray analysis (see *Table 4* in the *Exper. Part*). Moreover, all compounds of this type exhibited *J*(1,3) values of 2.4 Hz in their ^{1}H-NMR spectra ($CDCl_3$; *cf. Table 2* in the *Exper. Part*).

[8]) The reductive cleavage of diaryl sulfides can also be induced by anions *via* charge-transfer (CT) complex formation in the excited state [25].

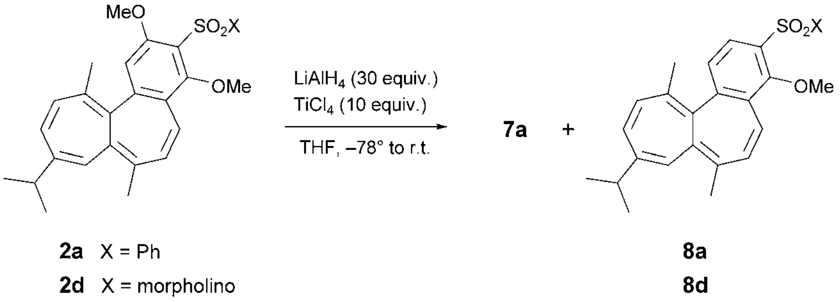
desulfonylated compounds **7**[9]. We suppose that a similar sequence of complexes of bicyclic aluminum hydrido species, as discussed before (*Scheme 8*), are responsible for the smooth desulfonylation of **2** with $LiAlH_4/TiCl_4$, whereby, in this case, Cl^- ions induce the intramolecular hydride transfer (*Scheme 11*). A totally different mechanism is followed when diaryl sulfones are cleaved by strong bases such as lithium triphenylsilanide [27] or sodium piperidinide [28].

Scheme 11



In the search for the corresponding sulfides, we stopped the reduction before completion of the reaction (*Scheme 12*). However, we found no sulfides in the reaction mixtures. Instead, we isolated small amounts of the 2-demethoxy sulfones **8a** and **8d**,

Scheme 12



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[9] A single-electron-transfer (SET) reaction, as discussed above, can be excluded due to the reduction potential Ti^{2+}/Ti^{3+} of -0.368 V [26], which is too small for an electron transfer to a diaryl sulfide. For diphenyl sulfone, a reduction potential of -2.16 V is listed [26].

respectively, in addition to **7a**. The structures of **8a** and **8d** were established spectroscopically (^{1}H-NMR: $J(1,2) = 8.2$ Hz) and by an X-ray crystal-structure analysis of **8d** (*Fig. 2*).

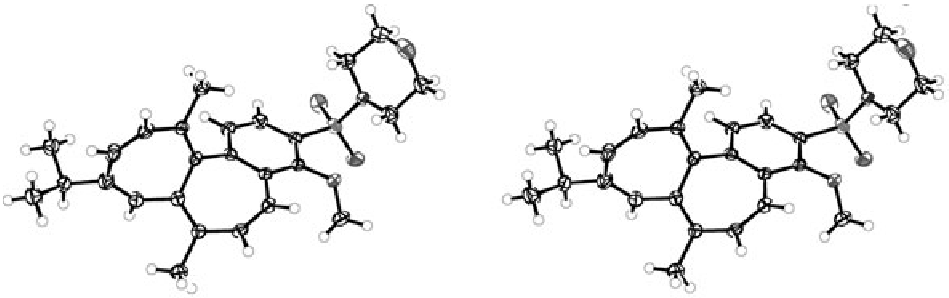

Fig. 2. *Stereoscopic view of the X-ray crystal structure of* **8d**

The structures of the by-products speak for a nucleophilic substitution of the MeO group at C(2) by hydride ions, possibly delivered by intramolecular complexes of Al or Ti hydrides with the two O-atoms of the sulfonyl group and the two adjacent MeO groups at C(2) and C(4). Indeed, the X-ray crystal structures of 3-(X-sulfonyl)benzo[*a*]heptalenes of type **1** typically show quite short O ⋯ O distances between the 2-O- as well as the 4-O-atoms and their adjacent 3-sulfonyl O-atom neighbors (*Table 1*) [4]. It is, therefore, possible that cyclic, six-membered Al or Ti complexes can also be formed with the dimethyl ethers **2**, in which hydride transfer can take place to substitute, in a side-process, the 2-MeO group. Additional experiments would be necessary to clarify this situation.

Table 1. *Shortest Intramolecular C–O ⋯ O=S Distances* (in pm) *in* **1c**, **8d**, *and* **9c**

	1c	**8d**	**9c**
C(2)–O ⋯ OS(O)–C(3)	295.4(2)	–	297.0(2)
C(4)–O ⋯ OS(O)–C(3)	259.0(2)	293.2(2)	258.3(2)

We mentioned in the introduction that the 3-sulfonyl group of the dimethyl ethers of **1** could not directly be substituted by MeO$^-$ in a nucleophilic-displacement reaction. Indeed, the reaction in boiling THF takes another path. When **2a** or **2c** was heated under anhydrous conditions with MeONa (8 mol-equiv.) in THF, a regioselective demethylation of the 4-MeO group took place (*Scheme 13*)[10]. The structure of **9c** was unequivocally established by X-ray crystal-structure determination (*Fig. 3*). It showed, as expected, a short intramolecular H-bond between the 4-OH group and one of the O-atoms of the adjacent sulfonyl group. This H-bond was also present in solution, as

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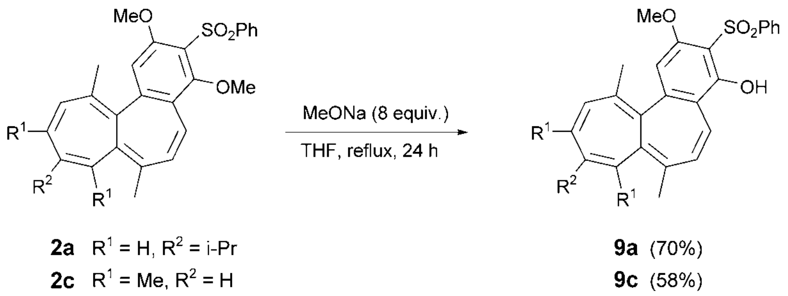
[10] The selective demethylation of **2a** could also be realized with a mixture of MeONa/TiCl$_4$ at –78 to 20° in THF (for details, see *Exper. Part*).

Scheme 13



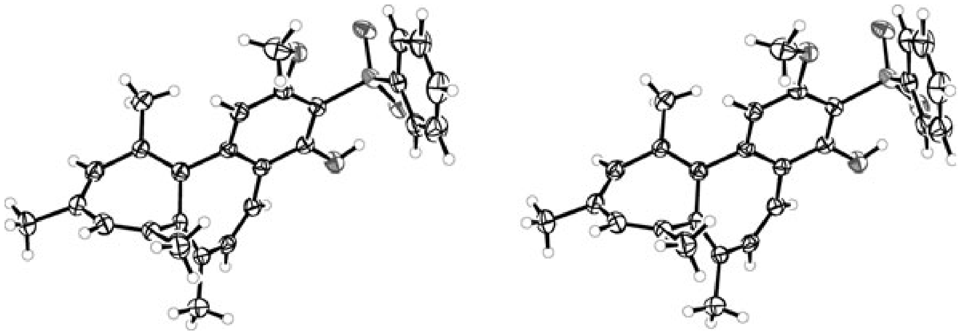


Fig. 3. *Stereoscopic view of the X-ray crystal structure of* **9c**

deduced from the corresponding ^{1}H-NMR (CDCl$_3$) chemical shift (δ(H) 11.01 (OH); for other examples, see [4]).

We thank the NMR laboratory, University of Zurich, for specific NMR measurements, the MS laboratory for recording mass spectra, and the micro-analytical laboratory for elemental analyses. Financial support of this work by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. See [1–3].

1. *Formation of 3-(X-sulfonyl)benzo[*a*]heptalene-2,4-diols* **1**. 1.1. *Improved General Procedure* (*GP 1*, *cf.* [3]). To a soln. of methyl phenyl sulfone (4.00 g, 25.64 mmol) or methyl morpholino sulfone (3.83 g, 25.64 mmol) in THF (15 ml), a 2.5M soln. of BuLi in hexane (10.75 ml, 25.96 mmol) was added at – 5°. After stirring for 20 min, a yellow precipitate was formed. The suspension was cooled to – 78°, and a soln. of the corresponding 3,3-dimethoxyheptaleno[1,2-*c*]furan-1-one (6.40 mmol) in THF (3 ml) was added. Stirring was continued for 3 h at – 78°. Then, the mixture was allowed to warm to – 5°, and a second portion of a 2.5M BuLi soln. in hexane (10.75 ml, 25.96 mmol) was added slowly. The color of the mixture changed immediately to a dark reddish-brown. Stirring was continued for 12 h at r.t. The mixture was treated with ice/HCl, and the product was extracted with AcOEt. The org. phase was washed with brine, and dried (Na$_2$SO$_4$). The solvent was distilled off, and the product was purified by CC (SiO$_2$; hexane/AcOEt 3 : 1). The products were crystallized from Et$_2$O. Yield: 82% of **1a** [3], 94% of **1b** [1], 76% of **1c** [2], and 58% of **1d** [3]. Compound **1c** was re-crystallized from Et$_2$O/CH$_2$Cl$_2$. The crystals contained Et$_2$O, but were suitable for an X-ray crystal-structure analysis (see *Table 4*).

1.2. O-*Methylation of Compounds* **1**. *General Procedure* (*GP 2*): The diol **1** and K_2CO_3 (13 mol-equiv.) were stirred in acetone at $-5°$ for 20 min. MeI (13 mol-equiv.) was added, and stirring was continued for 12 h at r.t. The product was extracted with AcOEt, and the org. phase was dried ($MgSO_4$). The solvent was distilled off, and the product was purified by CC (hexane/AcOEt 3 : 1). The yellow products were crystallized from Et_2O/CH_2Cl_2. Yield (m.p.): 97% (190.9 – 191.8°) for **2a**; 98% (184.7 – 186.3°) for **2b**; 92% (169.1 – 171.3°) for **2c**, and 95% (201.0 – 202.0°) [1] for **2d**. The MeO ^{1}H-NMR signals are characteristic, appearing, in $CDCl_3$, at δ(H) 3.64 – 3.68 (2-MeO) and 3.98 – 4.00 (4-MeO) for **2a** – **2c**, and at 3.86 (2-MeO) and 3.89 (4-MeO) [1] for **2d**.

1.3. O-*Demethylation of 9-Isopropyl-2,4-dimethoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene* (**2a**). To a soln. of **2a** (0.25 g, 0.53 mmol) in THF (10 ml), a 1.0M soln. of $LiEt_3BH$ in hexane (5.3 ml, 5.3 mmol) was added. The mixture was heated at reflux during 4 h, until all **2a** had been transformed into a salt (TLC). The mixture was carefully added to ice/HCl. After extraction with AcOEt, washing with brine, drying ($MgSO_4$), and evaporation of the solvent, the residue was purified by CC (SiO_2; hexane/AcOEt 2 : 1), which gave pure **1a** (0.22 g, 93%).

2. *Reductive Cleavage of 3-(Phenylsulfonyl)benzo[*a*]heptalene-2,4-diols* **1**. 2.1. *With NaH/LiEt$_3$BH/BuLi.* 2.1.1. A soln. of **1a** (0.50 g, 1.12 mmol) in THF (10 ml) was heated at reflux with NaH (0.06 g, 2.50 mmol) for 1 h. Then, a 1.0M soln. of $LiEt_3BH$ in hexane (11.2 ml, 11.2 mmol) was added. The mixture was refluxed for 7 h, and a 2.5M soln. of BuLi in hexane (2.24 ml, 5.6 mmol) was added. After 8 h at reflux, another portion of a 2.5M BuLi soln. (2.24 ml, 5.6 mmol) was added, and heating was continued for a further 8 h. After cooling, the mixture was carefully added to ice/HCl, and the products were extracted with AcOEt. The org. phase was washed with brine and dried ($MgSO_4$). The solvent was distilled off, followed by separation of the products **3a** and **4a** by CC (SiO_2; hexane/AcOEt 2 : 1).

*Data of 9-Isopropyl-7,12-dimethylbenzo[*a*]heptalene-2,4-diol* (**3a**). Yield: 0.15 g (45%). Yellow oil. R_f (hexane/AcOEt 1 : 1) 0.71. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.93 (*d*, $^3J = 11.8$, H–C(5)); 6.40 (*d*, $^3J = 11.8$, H–C(11)); 6.36 (*dd*, $^3J = 12.3$, $^4J = 0.8$, H–C(10)); 6.32 (*d*, $^4J = 2.4$, H–C(3)); 6.23 (*d*, $^3J = 11.8$, H–C(6)); 6.10 (*d*, $^4J = 2.3$, H–C(1)); 5.70 (*s*, H–C(8)); 5.08 (*s*, HO–C(4)); 4.88 (*s*, HO–C(2)); 2.54 (*sept.*, Me$_2$C*H*–C(9)); 1.69 (*s*, Me–C(7,12)); 1.14, 1.13 (2*d*, $^3J = 6.9$ and 6.8, *Me*$_2$CH–C(9)). ^{1}H-NMR (300 MHz, (D$_6$)acetone): 8.45 (br. *s*, HO–C(4)); 8.19 (br. *s*, HO–C(2)); 7.06 (*d*, $^3J = 11.9$, H–C(5)); 6.42 (*d*, $^4J = 2.3$, H–C(3)); 6.37 (*m*, H–C(10,11)); 6.03 (*d*, $^3J = 11.9$ H–C(6)); 6.02 (*d*, $^4J = 2.2$, H–C(1)); 5.70 (*s*, H–C(8)); 2.56 (*sept.*, Me$_2$C*H*–C(9)); 1.65 (*s*, Me–C(7)); 1.64 (*s*, Me–C(12)); 1.14, 1.13 (2*d*, $^3J = 6.9$ and 6.8, *Me*$_2$CH–C(9)). ^{13}C-NMR (75 MHz, (D$_6$)acetone): 160.43 (*s*, C(2)); 156.32 (*s*, C(4)); 147.67 (*s*, C(9)); 140.97 (*s*, C(12b)); 137.07 (*s*, C(12)); 136.59 (*d*, C(11)); 132.98 (*s*, C(7a)); 131.52 (*d*, C(10)); 130.40 (*s*, C(12a)); 130.17 (*d*, C(6)); 128.49 (*s*, C(7)); 127.32 (*d*, C(5)); 122.92 (*d*, C(8)); 117.93 (*s*, C(4a)); 107.52 (*d*, C(1)); 101.86 (*d*, C(3)); 35.13 (*d*, Me$_2$*C*H–C(9)); 23.09, 23.13 (2*q*, *Me*$_2$CH–C(9)); 19.90 (*q* , *Me*–C(12)); 17.23 (*q*, *Me*–C(7)). EI-MS ($C_{21}H_{22}O_2$; 306.41): 307.1 (25, $[M + 1]^+$); 306.1 (100, M^+); 291.1 (26, $[M - Me]^+$); 266.9 (56, $[M - Me-C{\equiv}CH]^+$); 251.0 (39); 238.0 (27, $[M - Me_2CH-C{\equiv}CH]^+$); 189.0 (48); 165.0 (51).

Data of 3-Ethyl-9-isopropyl-7,12-dimethylbenzo[a]heptalene-2,4-diol (**4a**). Yield: 4 mg (1%). Yellow oil. R_f (hexane/AcOEt 1 : 1) 0.82. ^{1}H-NMR (300 MHz; $CDCl_3$): 7.03 (*d*, $^3J = 11.8$, H–C(5)); 6.75 (*s*, HO–C(4)); 6.40 (*d*, $^3J = 11.9$, H–C(11)); 6.36 (*m*, H–C(10)); 6.34 (*s*, H–C(1)); 6.29 (*s*, HO–C(2)); 6.21 (*d*, $^3J = 11.8$, H–C(6)); 5.70 (*s*, H–C(8)); 2.66 (*q*, $^3J = 7.4$, MeC*H*$_2$–C(3)); 2.54 (*sept.*, Me$_2$C*H*–C(9)); 1.70 (*s*, Me–C(7)); 1.69 (*s*, Me–C(12)); 1.26 (*t*, $^3J = 7.4$, *Me*CH$_2$–C(3)); 1.14, 1.13 (2*d*, $^3J = 6.8$ and 6.9, *Me*$_2$CH–C(9)).

2.2. *With LiAlH$_4$/MeLi · MeBr. General Procedure* (*GP 3*): Compound **1** and $LiAlH_4$ (30 mol-equiv.) were heated at reflux in THF for 2 h. Then, a 1.6M soln. of MeLi · LiBr in hexane (2 mol-equiv.) was added. After 24 h of heating, a second portion of MeLi · LiBr (2 mol-equiv.) was added, and heating was continued for a further 24 h. The cooled mixture was carefully added to ice/HCl and the products were extracted with AcOEt. The org. phase was washed with brine and dried (Na_2SO_4). After evaporation of the solvent, the residue was subjected to CC (SiO_2; hexane/AcOEt 5 : 1).

2.2.1. *9-Isopropyl-7,12-dimethylbenzo[*a*]heptalene-2,4-diol* (**3a**). Compound **1a** (1.00 g, 2.25 mmol) and $LiAlH_4$ (2.60 g, 68.4 mmol) in THF (20 ml) were reacted with MeLi · LiBr according to *GP 3*. After CC, pure **3a** (0.49 g, 71%) and a small amount of *9-isopropyl-7,12-dimethyl-3-(phenylsulfanyl)benzo[*a*]heptalene-2,4-diol* (**5a**; 46 mg, 5%) were obtained.

Data of **3a**. See *Sect. 2.1.1.*

Data of **5a**. Yellow oil. R_f (hexane/AcOEt 2 : 1) 0.83. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.57 (*m*, H_o of PhS); 7.38 (*m*, H_p and H_m of PhS); 6.95 (*d*, $^3J = 11.9$, H–C(5)); 6.39 (*d*, $^3J = 11.9$, H–C(11)); 6.37 (*dd*, $^3J = 11.9$, $^5J = 1.2$, H–C(10)); 6.27 (*s*, HO–C(4)); 6.21 (*s*, HO–C(2)); 6.19 (*d*, $^3J = 11.9$, H–C(6)); 5.74 (*s*, H–C(1)); 5.59 (*s*, H–C(8)); 2.54 (*sept.*, Me$_2$C*H*–C(9)); 1.7 (br. *s*, Me–C(7,12)); 1.14, 1.13 (2*d*, $^3J = 6.9$ and 6.8, *Me*$_2$CH–C(9)). ^{1}H-NMR (600 MHz, (D$_6$)acetone): 8.61 (br. *s*, HO–C(4)); 7.96 (br. *s*, HO–C(2)); 7.66 (*m*, H_o of PhS); 7.34 (*m*, H$_m$ of PhS); 7.31 (*m*, H$_p$ of PhS); 7.00 (*d*, $^3J = 11.9$, H–C(5)); 6.39 (br. *s*, H–C(10,11)); 6.15 (*s*, H–C(1)); 6.10 (*d*, $^3J = 11.9$, H–C(6)); 5.72 (*s*, H–C(8)); 2.56 (*sept.*, Me$_2$*CH*–C(9)); 1.64 (*s*, Me–C(7,12)); 1.13, 1.12 (2*d*, $^3J =$ 6.9 and 6.8, *Me*$_2$CH–C(9)). ^{13}C-NMR (150 MHz, (D$_6$)acetone): 160.84 (*s*, C(2)); 156.92 (*s*, C(4)); 148.28 (*s*, C(9)); 142.88 (*s*, C(12b)); 138.03 (*s*, C$_{ip}$ of PhS); 136.41 (*d*, C(11)); 136.09 (*s*, C(12a)); 133.20 (*s*, C(7a)); 132.08 (*d*, C(10)); 131.46 (*d*, C(6)); 131.13 (*s*, C(12)); 130.65 (*d*, C$_o$ of PhS); 129.88 (*d*, C$_m$ of PhS); 128.88 (*s*, C(7)); 128.65 (*d*, C$_p$ of PhS); 127.02 (*s*, C(5)); 123.07 (*d*, C(8)); 118.03 (*s*, C(4a)); 107.74 (*d*, C(1)); 107.65 (*s*, C(3)); 35.15 (*d*, Me$_2$*C*H–C(9)); 23.03/23.07 (2*q*, *Me*$_2$CH–C(9)); 19.83 (*q*, *Me*–C(12)); 17.13 (*q*, *Me*–C(7)).

2.2.2. *8,10,12-Trimethylbenzo[*a*]heptalene-2,4-diol* (**3b**). Compound **1b** (1.00 g, 2.39 mmol) and LiAlH$_4$ (2.72 g, 71.7 mmol) in THF (20 ml) were reacted with MeLi · LiBr according to *GP 3*. CC afforded pure **3b** (0.45 g, 68%). Yellow oil. R_f (hexane/AcOEt 1 : 1) 0.61. ^{1}H-NMR (500 MHz, (D$_6$)acetone): 8.50 (*s*, HO–C(4)); 8.31 (*s*, HO–C(2)); 7.11 (*d*, $^3J = 11.7$, H–C(5)); 6.44 (*d*, $^4J = 2.4$, H–C(3)); 6.13 (*dd*, $^3J = 11.7$, 5.8, H–C(6)); 6.11 (*s*, H–C(11)); 6.02 (*d*, $^4J = 2.4$, H–C(1)); 5.93 (*s*, H–C(9)); 5.67 (*d*, $^3J = 5.8$, H–C(7)); 1.98 (*d*, $^4J = 1.2$, Me–C(8)); 1.94 (*d*, $^4J = 1.2$, Me–C(10)); 1.60 (*s*, Me–C(12)). ^{13}C-NMR (125 MHz, (D$_6$)acetone): 160.82 (*s*, C(2)); 156.47 (*s*, C(4)); 142.54 (*s*, C(7a)); 141.19 (*s*, C(12b)); 136.91 (*s*, C(8)); 135.39 (*s*, C(10)); 132.23 (*d*, C(11)); 131.62 (*s*, C(12a)); 131.59 (*s*, C(12)); 129.03 (*d*, C(9)); 128.02 (*d*, C(5)); 125.43 (*d*, C(6)); 122.73 (*d*, C(7)); 118.71 (*s*, C(4a)); 107.55 (*d*, C(1)); 102.10 (*d*, (C(3)); 25.30 (*q*, *Me*–C(10)); 24.96 (*q*, *Me*–C(8)); 20.3 (*q*, *Me*–C(12)). EI-MS ($C_{19}H_{18}O_2$, 278.35): 279.1 (22, $[M+1]^+$); 278.1 (100, M^+); 263.1 (51, $[M-\mathrm{Me}]^+$); 238.1 (64, $[M-\mathrm{Me}-\mathrm{C{\equiv}CH}]^+$); 223.0 (33); 207.0 (46); 189.0 (23); 165.0 (29).

2.3. *With LiAlH$_4$/MeLi. General Procedure* (*GP 4*): The benzo[*a*]heptalene-2,4-diol and LiAlH$_4$ (30 mol-equiv.) in THF were heated at reflux for 2 h. Then, a 1.6M soln. of MeLi in hexane (5 mol-equiv.) was added. After 24 h at reflux, a second portion of 1.6M MeLi in hexane (5 mol-equiv.) was added. Heating was continued for a further 24 h. The cooled mixture was carefully added to ice/HCl. The products were extracted with AcOEt. The org. phase was washed with brine, and dried (Na$_2$SO$_4$). After evaporation of the solvent, the residue was subjected to CC (SiO$_2$; hexane/AcOEt 5 : 1).

2.3.1. *3,3′-Dithiobis(9-isopropyl-7,12-dimethylbenzo[*a*]heptalene-2,4-diol)* (**6a**). Compound **1a** (1.00 g, 2.25 mmol) and LiAlH$_4$ (2.60 g, 68.4 mmol) in THF (20 ml) were reacted with MeLi according to *GP 4*. CC afforded **6a** (0.50 g, 40%; 1 : 1 mixture of *meso*- and *rac*-forms), **3a** (0.048 g, 7.0%), and **5a** (0.040 g, 4.3%). When the reaction was performed with **1d** (1.00 g, 2.20 mmol), a 1 : 1 mixture of *meso*- and *rac*-**6a** (0.53 g, 71%) was obtained exclusively.

Data of **6a**. Yellow oil. R_f (hexane/AcOEt 2 : 1) 0.75. ^{1}H-NMR (300 MHz, CDCl$_3$): 6.90, 6.89 (2*d*, $^3J = 11.9$ each, H–C(5,5′)); 6.45, 6.43 (2*s*, HO–C(4,4′)); 6.40 (*d*, $^3J = 11.9$, H–C(11,11′)); 6.37 (*d*, $^3J = 11.9$, H–C(10,10′)); 6.24, 6.22 (2*s*, H–C(1,1′)); 6.19, 6.17 (2*d*, $^3J = 11.9$ each, H–C(6,6′)), 5.98 (2*s*, HO–C(2,2′)); 5.70 (*s*, H–C(8,8′)); 2.53 (*sept.*, Me$_2$*CH*–C(9,9′)); 1.714, 1.711 (2*s*, Me–C(12,12′)); 1.696, 1.692 (2*s*, Me–C(7,7′)); 1.14, 1.13 (2*d*, $^3J = 6.9$, 6.8, *Me*$_2$CH–C(9,9′)). ^{13}C-NMR (75 MHz, CDCl$_3$): 158.26 (*s*, C(2,2′)); 154.84 (*s*, C(4,4′)); 147.16 (*s*, C(9,9′)); 144.86 (*s*, C(12b,12b′)); 135.50 (*d*, C(11,11′)); 134.37 (*s*, C(12a,12a′)); 132.86 (*s*, C(7a,7a′)); 131.90 (*d*, C(6,6′)); 131.69 (*d*, C(10,10′)); 131.31 (*s*, C(12,12′)); 128.44 (*s*, C(7,7′); 125.19 (*d*, C(5,5′)); 122.41 (*d*, C(8,8′)); 117.92 (*s*, C(4a,4a′)); 107.52 (*d*, C(1,1′)); 104.21 (*s*, C(3,3′)); 34.49 (*d*, Me$_2$*C*H–C(9,9′)); 22.76 (*q*, *Me*$_2$CH–C(9,9′)); 19.67 (*q*, *Me*–C(12,12′)); 17.07 (*q*, *Me*–C(7,7′)).

2.3.2. *3,3′-Dithiobis(7,12-dimethylbenzo[*a*]heptalene-2,4-diol)* (**6c**). Compound **1c** (1.00 g, 2.31 mmol) and LiAlH$_4$ (2.63 g, 69.3 mmol) in THF (20 ml) were reacted with MeLi according to *GP 4*. CC afforded **6c** (0.49 g, 36%) as a 1 : 1 mixture of the *meso*- and *rac*-forms. Yellow oil. R_f (hexane/AcOEt 2 : 1) 0.66. ^{1}H-NMR (600 MHz, CDCl$_3$): 6.927, 6.903 (2*d*, $^3J = 11.9$ each, H–C(5,5′)); 6.48, 6.43 (2 br. *s*, HO–C(4,4′)); 6.190, 6.175 (2*s*, H–C(1,1′)); 6.173, 6.154 (2*d*, $^3J = 11.7$ each, H–C(6,6′)); 6.157 (br. *s*, H–C(11,11′)); 6.05, 5.98 (2 br. *s*, HO–C(2,2′)); 6.006 (br. *s*, H–C(9,9′)); 2.017 (*s*, Me–C(10,10′)); 1.918, 1.909 (2*s*, Me–C(8,8′)); 1.714, 1.708 (2*s*, Me–C(7,7′)); 1.696, 1.690 (2*s*, Me–C(12,12′)). ^{13}C-NMR (150 MHz, CDCl$_3$): 158.21, 158.11 (2*s*, C(2,2′)); 154.98, 154.84 (2*s*, C(4,4′)); 144.98, 144.90 (2*s*, C(12b,12b′)); 138.68, 138.65 (2*s*, C(10,10′)); 136.11, 136.03 (2*s*, C(7a,7a′)); 134.19, 134.16 (2*s*, C(8,8′)); 131.72, 131.64 (2*d*, C(6,6′)); 130.54 (*d*, C(11,11′)); 130.37 (*s*, C(12,12′)); 129.96 (*s*, C(12a,12a′)); 128.41 (*d*, C(9,9′)); 127.49, 127.48 (2*s*, C(7,7′)); 125.44, 124.42 (2*d*, C(5,5′)); 117.79, 117.77 (2*s*, C(4a,4a′)); 106.76, 106.72 (2*d*, C(1,1′)); 103.67, 103.60 (2*s*, C(3,3′)); 25.04 (*q*, Me–C(10,10′)); 22.81 (*q*, Me–C(8,8′)); 19.34, 19.31 (2*q*, Me–C(12,12′)); 17.93, 17.92 (2*q*, Me–C(7,7′)). ESI-MS: 650.2/649.3/648.3/647.2 (2/8/17/33, $[M+1]^+$); 326.2/325.2/324.2/323.2 (8/48/100/88, $[\frac{1}{2}M+2]^+$). CI-MS ($[M+1]^+$ not obs.): 363.2 (51, $[C_{23}H_{22}O_2S+1]^+$); 325.2 (100, $[\frac{1}{2}M+2]^+$); 293.2 (21).

3. *Reductive Cleavage of 2,4-Dimethoxy-3-(X-sulfonyl)benzo[*a*]heptalenes* **2**. *General Procedure* (*GP 5*): At −78°, fresh TiCl$_4$ (10 mol-equiv.) was dissolved in THF under Ar gas, and LiAlH$_4$ (30 mol-equiv.) in THF was added slowly through a dropping funnel. The mixture was allowed to warm to −10°, so that a vigorous reaction accompanied by the development of a yellow vapor took place, turning the mixture into a dark-blue

suspension. The mixture was cooled again to – 78°, and a soln. of **2** (1 mol-equiv.) in THF was slowly added, whereby effervescence of the mixture was observed. The mixture was allowed to warm slowly to r.t., and stirring was continued for 1.5 – 10 h. The mixture was added to an aq. sat. soln. of NH_4Cl, and stirred for 1 h. Then, the products were extracted with AcOEt (3 ×), and the org. phase was dried (Na_2SO_4). After evaporation of the solvent, the residue was subjected to CC (hexane/AcOEt 3 : 1). The desulfonylated products **7a** – **7d** were crystallized from hexane/Et_2O.

3.1. *9-Isopropyl-2,4-dimethoxy-7,12-dimethylbenzo[*a*]heptalene* (**7a**) *and 9-Isopropyl-4-methoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene* (**8a**). According to *GP 5*, $TiCl_4$ (8.0 ml, 42.1 mmol) in THF (10 ml) and $LiAlH_4$ (4.80 g, 126.3 mmol) in THF (5 ml) were combined, and then reacted with **2a** (2.00 g, 4.21 mmol) in THF (5 ml) for 1.5 h at r.t. Yield of crystallized **7a**: 1.30 g (91%). Its structure was secured by an X-ray crystal-structure analysis (*cf. Table 4*). When the reduction of **2a** was interrupted after 45 min, the mixture contained **7a** and a small amount of **8a**.

Data of **7a**. Yellow crystals. M.p. 163.0 – 163.6°. R_f (hexane AcOEt 4 : 1) 0.57. ^1H- and ^{13}C-NMR: see *Tables 2* and *3*, resp. EI-MS: 335.0 (25, $[M+1]^+$); 334.0 (100, M^+); 319.0 (32, $[M-\text{Me}]^+$); 294.0 (55, $[M-\text{Me}-\text{C}{\equiv}\text{CH}]^+$); 279.0 (49, $[M-(\text{Me}+\text{Me}-\text{C}{\equiv}\text{CH})]^+$); 266 (33, $[M-{}^i\text{Pr}-\text{C}{\equiv}\text{CH}]^+$); 261.0 (16); 202.0 (26); 189 (21). Anal. calc. for $C_{23}H_{26}O_2$ (334.46): C 82.60, H 7.84; found: C 82.49, H 7.67.

Data of **8a**. Yellow crystals. M.p. 212.7 – 213.6° (hexane/AcOEt). ^1H-NMR (300 MHz, $CDCl_3$): 8.11 (*d*, ^3J = 8.3 H–C(2)); 8.00 (*m*, H_o of Ph); 7.56 (*m*, H_p of Ph); 7.50 (*m*, H_m of Ph); 6.94 (*d*, ^3J = 7.8, H–C(1)); 6.89 (*d*, ^3J = 12.1, H–C(5)); 6.40 (*AB*, H–C(10,11)); 6.34 (*d*, ^3J = 11.9, H–C(6)); 5.72 (*s*, H–C(8)); 3.87 (*s*, MeO–C(4)); 2.55 (*sept.*, Me_2CH–C(9)); 1.61 (*s*, Me–C(7,12)); 1.16, 1.14 (2*d*, ^3J = 6.9, 6.8, Me_2CH–C(9)). EI-MS ($C_{28}H_{28}O_3S$; 444.60): 445.1 (62, $[M+1]^+$); 444.1 (100, M^+); 429.01 (76, $[M-\text{Me}]^+$); 404.0 (71, $[M-\text{Me}-\text{C}{\equiv}\text{CH}]^+$); 376.0 (23, $[M-{}^i\text{Pr}-\text{C}{\equiv}\text{CH}]^+$); 288.0 (17); 256.0 (29); 245.0 (30); 229.0 (25); 214.9 (40); 201.9 (45); 188.9 (30); 76.8 (37).

Table 2. *^1H-NMR Data for Compounds* **7a** – **7c**. At 500 or 600 MHz in $CDCl_3$; δ in ppm, *J* in Hz.

	7a	**7b**	**7c**
H–C(1)	6.14 (*d*, ^4J = 2.4)	6.14 (*d*, ^4J = 2.4)	6.12 (*d*, ^4J = 2.4)
2-MeO	3.79 (*s*)	3.78 (*s*)	3.78 (*s*)
H–C(3)	6.42 (*d*, ^4J = 2.4)	6.43 (*d*, ^4J = 2.4)	6.43 (*d*, ^4J = 2.4)
4-MeO	3.85 (*s*)	3.85 (*s*)	3.87 (*s*)
H–C(5)	7.08 (*d*, ^3J = 11.9)	7.15 (*d*, ^3J = 11.8)	7.13 (*d*, ^3J = 11.9)
H–C(6)	6.20 (*d*, ^3J = 11.9)	6.30 (*dd*, ^3J = 11.8, 5.8)	6.21 (*d*, ^3J = 12.0)
7-Me[a])	1.70 (*d*, ^4J = 0.9)	5.73 (*d*, ^3J = 5.8)	1.73 (*s*)
H–C(8)[b])	5.70 (*s*)	2.04 (*d*, ^4J = 0.9)	1.94 (*d*, ^4J = 1.2)
H–C(9)[c])	2.56 (*sept.*); 1.16, 1.15 (2*d*, ^3J = 6.9 and 6.8)	5.95 (*s*)	6.05 (*s*)
H–C(10)[d])	6.36 (*dd*, ^3J = 11.9, ^4J = 1.3)	2.00 (*d*, ^4J = 1.0)	2.04 (*d*, ^4J = 1.1)
H–C(11)	6.41 (*d*, ^3J = 11.7)	6.18 (*s*)	6.19 (*s*)
12-Me	1.67 (*s*)	1.65 (*s*)	1.67 (*s*)

[a]) H–C(7) for **7b**. [b]) 8-Me for **7b** and **7c**. [c]) 9-(i-Pr) for **7a**. [d]) 10-Me for **7b** and **7c**.

3.2. *2,4-Dimethoxy-8,10,12-trimethylbenzo[*a*]heptalene* (**7b**). According to *GP 5*, $TiCl_4$ (8.55 ml, 44.8 mmol) in THF (10 ml) and $LiAlH_4$ (5.11 g, 134.4 mmol) in THF (5 ml) were combined and then reacted with **2b** (2.00 g, 4.48 mmol) in THF (5 ml) for 2.5 h at r.t. Yield of crystallized **7b**: 1.15 g (84%). Yellow crystals. M.p. 172.0 – 173.1°. R_f (hexane/AcOEt 4 : 1) 0.70. IR (KBr): 2965*m*, 2935*m*, 2907*m*, 1599v*s*, 1561*s*, 1543*m*, 1476*m*, 1462*s*, 1437v*s*, 1344*m*, 1318v*s*, 1258*m*, 1219*m*, 1196v*s*, 1161v*s*, 1115*s*, 1025v*s*, 810s. ^1H- and ^{13}C-NMR: see *Tables 2* and *3*, resp. EI-MS: 307.0 (22, $[M+1]^+$); 306.0 (100, M^+); 291.0 (52, $[M-\text{Me}]^+$); 266.0 (69, $[M-\text{Me}-\text{C}{\equiv}\text{CH}]^+$); 252.0 (26); 250.9 (33); 201.9 (27); 188.9 (32). Anal. calc. for $C_{21}H_{22}O_2$ (306.41): C 82.32, H 7.24; found: C 82.20, H 7.37.

3.3. *2,4-Dimethoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene* (**7c**). According to *GP 5*, $TiCl_4$ (8.29 ml, 42.1 mmol) in THF (10 ml) and $LiAlH_4$ (4.95 g, 129.3 mmol) in THF (5 ml) were reacted with **2c** (2.00 g, 4.34 mmol) in THF (5 ml) for 6 h at r.t. Yield of crystallized **7c**: 1.06 g (76%). Yellow crystals. M.p. 151.5 – 153.1°. R_f (hexane/AcOEt 3 : 1) 0.73. ^1H- and ^{13}C-NMR: see *Tables 2* and *3*, resp. EI-MS: 321.00 (24, $[M+1]^+$),

Table 3. *^{13}C-NMR Data of Compounds* **7a**–**7c**. At 125 or 150 MHz in $CDCl_3$; δ in ppm.

	7a	**7b**	**7c**
C(1)	104.29	104.25	103.40
C(2)	161.86	162.16	161.76
C(3)	97.27	97.40	97.07
C(4)	157.55	157.60	157.59
C(4a)	119.68	120.35	119.51
C(5)	25.79	126.80	125.98
C(6)	131.04	126.10	130.71
C(7)	128.19	121.94	127.09
C(7a)	132.85	142.33	136.10
C(8)	122.17	136.61	134.20
C(9)	146.99	128.45	128.26
C(10)	131.25	138.19	138.10
C(11)	135.69	131.62	130.76
C(12)	130.51	131.81	131.46
C(12a)	135.66	130.47	129.55
C(12b)	139.69	139.88	140.41
2-MeO	55.46	55.47	55.45
4-MeO	55.60	55.57	55.51
7-Me	17.01	–	19.40
8-Me	–	24.88	22.89
9-(i-Pr)		34.43, 22.89, 22.77	–
–			
10-Me	–	25.38	25.02
12-Me	19.74	20.16	19.86

320.0 (100, M^+); 305.0 (87, $[M - Me]^+$); 290.0 (29, $[M - CH_2O]^+$); 280.0 (38, $[M - Me{-}C{\equiv}CH]^+$); 266.0 (42); 265.0 (21); 201.9 (12); 188.9 (12); 144.4 (19); 100.9 (10). Anal. calc. for $C_{22}H_{24}O_2$ (320.44): C 82.46, H 7.55; found: C 82.28, H 7.47.

3.4. *9-Isopropyl-2,4-dimethoxy-7,12-dimethylbenzo[*a*]heptalene* (**7a**) *and 9-Isopropyl-4-methoxy-7,12-dimethyl-3-(morpholinosulfonyl)benzo[*a*]heptalene* (**8d**). Following *GP 5*, $TiCl_4$ (7.90 ml, 41.4 mmol) in THF (10 ml) and $LiAlH_4$ (4.72 g, 124.2 mmol) in THF (5 ml) were reacted with **2d** (2.00 g, 4.14 mmol) in THF (5 ml). The mixture was finally stirred for 6 h at r.t. Yield of crystallized **7a**: 0.73 g (51%). When the reduction of **2d** was interrupted after 5 h, the mixture contained **7a** and a small amount of **8d**, which was isolated by CC.

Data of **7a**. See *Sect. 3.1.*

Data of **8d**. Yellow crystals. M.p. 219.4–222.1° (Et_2O/hexane). R_f (hexane/AcOEt 1:1) 0.59. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.83 (*d*, $^3J = 8.3$, H–C(2)); 7.03, (*d*, $^3J = 12.0$, H–C(5)); 6.85 (*d*, $^3J = 8.2$, H–C(1)); 6.42 (*m*, H–C(6,10,11)); 5.74 (*s*, H–C(8)); 3.91 (*s*, MeO–C(4)); 3.73, 3.21 (2*m*, 8 morpholino H); 2.56 (*sept.*, Me_2CH–C(9)); 1.73 (*s*, Me–C(7)); 1.63 (*s*, Me–C(12)); 1.16, 1.15 (2*d*, $^3J = 6.9$, 6.8, Me_2CH–C(9)). EI-MS ($C_{26}H_{31}NO_4S$; 453.61): 455.1 (26, $[M+2]^+$); 454.1 (29, $[M+1]^+$); 453.1 (100, M^+); 438.1 (30, $[M - Me]^+$) 413.0 (33, $[M - Me{-}C{\equiv}CH]^+$); 412.0 (24); 385.0 (10, $[M - {}^iPr{-}C{\equiv}CH]^+$); 271.0 (19): 245.0 (25); 215.0 (33); 201.0 (35); 189.0 (21); 86.0 (52); 56.0 (84).

4. *Selective Demethylation of Compounds* **2**. *General Procedure* (*GP 6*): Compound **2** (1.10 mmol) and anh. MeONa (8.7 mmol; freshly prepared from Na and MeOH) were heated at reflux for 24 h in THF (20 ml). After usual workup, the products were purified by CC (SiO_2; hexane/AcOEt 5:1) and crystallized from Et_2O/hexane.

4.1. *Data of 9-Isopropyl-2-methoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]heptalen-4-ol* (**9a**). Yield: 70%. Yellow crystals. M.p. 217.3–218.2°. R_f (hexane/AcOEt 3:1) 0.42. ^{1}H-NMR (600 MHz, $CDCl_3$): 10.98 (*s*, HO–C(4)); 7.98 (*m*, H_o of Ph); 7.59 (*m*, H_p of Ph); 7.17 (*t*, $^3J = 7.6$, H_m of Ph); 7.13 (*d*, $^3J = 11.9$, H–C(5)); 7.11 (*d*, $^3J = 11.9$, H–C(11)); 6.37 (*dd*, $^3J = 11.9$, $^4J = 1.0$, H–C(10)); 6.29 (*d*, $^3J = 12.0$, H–C(6)); 5.96 (*s*, H–C(1)); 5.69 (*s*, H–C(8)); 3.63 (*s*, MeO–C(2)); 2.52 (*sept.*, Me_2CH–C(9)); 1.70 (*s*, Me–C(7)); 1.63 (*s*, Me–C(12)); 1.14/1.13 (2*d*, $^3J = 6.5$ each, Me_2CH–C(9)). ^{13}C-NMR (150 MHz, $CDCl_3$): 158.68 (*s*, C(2)); 155.66 (*s*, C(4)); 147.48 (*s*, C(9)); 144.37 (*s*, C(12b)); 142.01 (*s*, C_{ip} of Ph); 135.51 (*d*, C(11)); 134.44 (*s*, C(12a)); 133.34 (*d*, C_p of

Ph); 132.44 (*s*, C(7a)); 132.34 (*d*, C(6)); 132.06 (*d*, C(10)); 131.42 (*s*, C(12)); 128.98 (*s*, C(7)); 128.51 (*d*, C_m of Ph); 127.84 (*d*, C_o of Ph); 125.14 (*d*, C(5)); 122.27 (*d*, C(8)); 120.45 (*s*, C(4a)); 109.97 (*s*, C(3)); 102.71 (*d*, C(1)); 56.03 (*q*, MeO–C(2)); 34.41 (*d*, Me_2*C*H–C(9)); 22.68, 22.78 (2*q*, *Me*$_2$CH–C(9)); 19.61 (*q*, *Me*–C(12)); 16.97 (*q*, Me–C(7)). EI-MS: 461.0 (33, $[M+1]^+$); 460.0 (100, M^+); 445.0 (27, $[M-\mathrm{Me}]^+$); 420.0 (49, $[M-\mathrm{Me}-\mathrm{C{\equiv}CH}]^+$); 405.0 (33); 392.0 (11, $[M-{}^i\mathrm{Pr}-\mathrm{C{\equiv}CH}]^+$); 281.0 (22); 191.0 (17); 96.0 (33); 77.0 (78); 73.0 (42). Anal. calc. for $C_{28}H_{28}O_4S$ (460.60): C 73.02, H 6.13, S 6.96; found: C 73.01, H 6.16, S 6.76.

4.2. *Data of 2-Methoxy-7,8,10,12-tetramethyl-3-(phenylsulfonyl)benzo[*a*]heptalen-4-ol* (**9c**). Yield: 58%. Yellow crystals. M.p. 206.6–208.8°. R_f (hexane/AcOEt 2:1) 0.74. ^{1}H-NMR (600 MHz, $CDCl_3$): 11.01 (*s*, HO–C(4)); 8.00 (*m*, H_o of Ph); 7.60 (*m*, H_p of Ph); 7.47 (*m*, H_m of Ph); 7.36 (*d*, $^3J = 11.9$, H–C(5)); 6.28 (*d*, $^3J = 12.0$, H–C(6)); 6.15 (*s*, H–C(11)); 6.01 (*s*, H–C(9)); 5.94 (*s*, H–C(1)); 3.60 (*s*, MeO–C(2)); 2.01 (*s*, Me–C(10)); 1.90 (*s*, Me–C(8)); 1.73 (*s*, Me–C(7)); 1.62 (*s*, Me–C(12)). ^{13}C-NMR (150 MHz, $CDCl_3$): 158.62 (*s*, C(2)); 155.91 (*s*, C(4)); 145.23 (*s*, C(12b)); 142.15 (*s*, C_{ip} of Ph); 139.07 (*s*, C(10)); 135.73 (*s*, C(7a)); 134.48 (*s*, C(8)); 133.35 (*d*, C_p of Ph); 132.19 (*d*, C(6)); 130.49 (*d*, C(11)); 130.47 (*s*, C(12)); 130.18 (*s*, C(12a)); 128.63 (*d*, C(9)); 128.53 (*d*, C_m of Ph); 128.03 (*s*, C(7)); 127.89 (*d*, C_o of Ph); 125.41 (*d*, C(5)); 120.28 (*s*, C(4a)); 109.82 (*s*, C(3)); 102.06 (*d*, C(1)); 56.10 (*q*, MeO–C(2)); 25.06 (*q*, *Me*–C(10)); 22.82 (*q*, *Me*–C(8)); 19.33 (*q*, *Me*–C(12)); 17.89 (*q*, *Me*–C(7)). EI-MS ($C_{27}H_{26}O_4S$; 446.57): 447.0 (32, $[M+1]^+$); 446.0 (100, M^+); 431.0 (81, $[M-\mathrm{Me}]^+$); 406.0 (36, $[M-\mathrm{Me}-\mathrm{C{\equiv}CH}]^+$); 290.0 (18); 275.0 (16); 215.0 (18); 202.0 (29); 189.0 (21); 78.0 (21); 77.0 (67).

4.3. *Alternative Procedure for the Selective Demethylation of* **2a**. At −78°, $TiCl_4$ (0.21 ml, 1.1 mmol) was added to THF (5 ml). Then, solid anh. MeONa, freshly prepared from Na (0.20 g, 8.7 mmol) and MeOH (3 ml), was added under Ar gas, whereby a yellow suspension was formed. A soln. of **2a** (50 mg, 0.105 mmol) in THF (15 ml) was slowly added, and the mixture was allowed to warm to r.t. Stirring was continued for 3 h. The mixture was added to a sat. aq. soln. of NH_4Cl, and stirred for 1 h. Usual workup afforded **9a** in 94% yield.

5. *X-Ray Crystal-Structures of Compounds* **1c**, **7a**, **8d**, *and* **9c** (see *Table 4*, and *Figs. 2* and *3*)[11]). All measurements were conducted at low temperature using graphite-monochromated MoK_α radiation ($\lambda = 0.71073$ Å). A *Rigaku AFC5R* diffractometer on a 12-kW rotating anode generator was used for **7a**, and a *Nonius KappaCCD* diffractometer [29][30] fitted with a *Cryostream-700* cooler (*Oxford Cryosystems*) was used for **1c**, **8d**, and **9c**. The data collection and refinement parameters are given in *Table 4*, and views of the molecules of **8d** and **9c** are shown in *Figs. 2* and *3*. The intensities were corrected for *Lorentz* and polarization effects, and equivalent reflections were merged. An absorption correction was applied only in the case of **1c** based on the multi-scan method [31]. Each structure was solved by direct methods using either SHELXS97 [32] or SIR92 [33], which revealed the positions of all non-H-atoms. The asymmetric unit of **1c** contains one molecule of the heptalene derivative plus one disordered Et_2O molecule. Two positions were defined for each atom of the solvent molecule, and refinement of constrained site occupation factors for the two orientations yielded a value of 0.785(9) for the major conformation.

Similarity restraints were applied to the chemically equivalent bond lengths and angles involving all disordered atoms, while neighboring atoms within and between the disordered conformations were restrained to have similar atomic displacement parameters.

The non-H-atoms of each structure were refined anisotropically. The OH H-atom in **9c** was placed in the position indicated by a difference *Fourier* map, and its position was allowed to refine together with an isotropic displacement parameter. The positions of the OH H-atoms of **1c** were initially located in a difference *Fourier* map, then their positions were geometrically optimized, while retaining the direction of the O–H vector in line with that given by the peak in the map. All remaining H-atoms were fixed in geometrically optimized positions, and each was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent atom (1.5 U_{eq} for the Me and OH groups of **1c**). The structures of **7a**, **8d**, and **9c** were refined on F, using full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. For **1c**, the refinement was carried out on F^2 by minimizing the corresponding function based on F^2. A correction for secondary extinction was applied in the case of **1c**, **7a**, and **8d**. For **1c**, **8d**, and **9c**, one, four, and eight reflections, resp., whose intensities were considered to be extreme outliers, were omitted from the final refinement. Neutral-atom-scattering factors for non-H-atoms were taken from [34], and the scattering factors for H-atoms were taken from [35]. The values of

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[11]) CCDC-263001-263003 (for **7a**, **8d** and **9c**, resp.) and -263983 (for **1c**) contain the supplementary crystallographic data for this paper. These data can be obtained, free of charge, *via* www.ccdc.cam.ac.uk/data_request/cif, or from the *Cambridge Crystallographic Data Centre*, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

Table 4. *Crystallographic Data for Compounds* **1c**, **7a**, **8d**, *and* **9c**

	1c	**7a**	**8d**	**9c**
Crystallized from	CH_2Cl_2/Et_2O	hexane/Et_2O	hexane/Et_2O	hexane/Et_2O
Empirical formula	$C_{26}H_{24}O_4S \cdot C_4H_{10}O$	$C_{23}H_{26}O_2$	$C_{26}H_{31}NO_4S$	$C_{27}H_{26}O_4S$
Formula weight [g/mol]	506.65	334.46	453.59	446.56
Crystal color, habit	yellow, prism	yellow, prism	colorless, plate	yellow, tablet
Crystal dimensions [mm]	0.20 × 0.22 × 0.25	0.33 × 0.33 × 0.40	0.03 × 0.14 × 0.14	0.12 × 0.30 × 0.30
Temperature [K]	160(1)	173(1)	160(1)	160(1)
Crystal system	triclinic	orthorhombic	monoclinic	monoclinic
Space group	$P\bar{1}$	$Pbca$	$P2_1/n$	$P2_1/c$
Z	2	8	4	4
Refl. for cell determination	22904	25	5659	5403
2θ Range [°]	4–60	20–37	2–55	4–55
Unit-cell parameters: a [Å]	11.1409(2)	15.813(1)	16.9868(2)	8.6395(1)
b [Å]	12.0702(2)	23.724(6)	7.0230(1)	15.9392(2)
c [Å]	12.4394(3)	10.116(4)	19.3143(3)	16.5413(3)
α [°]	61.2531(9)	90	90	90
β [°]	76.7103(9)	90	95.9446(8)	94.1305(6)
γ [°]	68.663(1)	90	90	90
V [Å^3]	1362.98 (5)	3795(1)	2291.77(6)	2271.93(6)
$F(000)$	540	1440	968	944
D_x [g/cm^3]	1.234	1.171	1.315	1.305
$\mu(\text{Mo}K_\alpha)$ [mm^{-1}]	0.156	0.0728	0.174	0.174
Scan type	ϕ and ω	$\omega/2\theta$	ϕ and ω	ϕ and ω
2θ (max) [°]	60	55	55	55
Total refl.	40871	5639	47163	59600
Symmetry-independent refl.	7909	4357	4999	5205
R_{int}	0.105	0.099	0.077	0.060
Refl. with $I > 2\sigma(I)$	3893	2169	3427	3772
Parameters refined	382	227	290	293
Restraints	137	0	0	0
Refl. for refinement	7908	2169	3427	3772
Final $R(F)$	0.0596	0.0629	0.0494	0.0538
$wR(F)$	0.1777 (on F^2)	0.0542	0.0421	0.0604
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	[a])	0.005	0.005	0.005
Goodness-of-fit	0.977	2.062	1.940	3.283
Secondary extinction coefficient	0.011(3)	$1.8(3) \times 10^{-7}$	$5.6(8) \times 10^{-7}$	–
Final $\Delta_{\text{max}}/\sigma$	0.001	0.0002	0.0003	0.0003
$\Delta\rho$ (max; min) [e Å^{-3}]	0.35; –0.54	0.29; –0.28	0.67; –0.45	0.62; –0.32

[a]) $w^{-1} = \sigma^2(F_o^2) + (0.0903P)^2$, where $P = (F_o^2 + 2F_o^2)/3$.

the mass-attenuation coefficients were those of [36]. The calculations for **1c** were performed with the SHELXL97 program [37], while those for **7a**, **8d** and **9c** employed the teXsan crystallographic-software package [38]. The crystallographic diagrams were drawn with ORTEPII [39].

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