

## 177. A 'One-Pot' Anellation Method for the Transformation of Heptalene-4,5-dicarboxylates into Benzo[*a*]heptalenes

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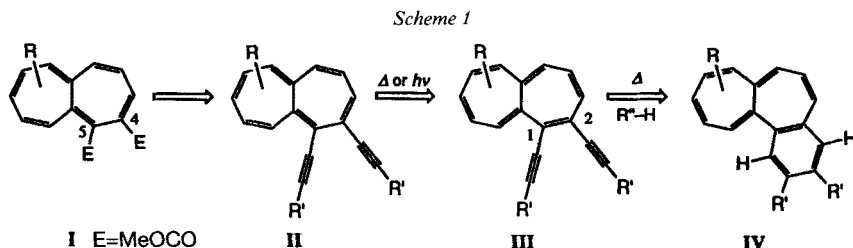
Dedicated to Wolfgang Pfeleiderer on the occasion of his 70th birthday

(22.X.97)

It has been found that dimethyl heptalene-4,5-dicarboxylates, when treated with 4 mol-equiv. of lithiated *N,N*-dialkylamino methyl sulfones or methyl phenyl sulfone, followed by 4 mol-equiv. of BuLi in THF in the temperature range of  $-78$  to  $20^{\circ}$ , give rise to the formation of 3-[(*N,N*-dialkylamino)sulfonyl]- or 3-(phenylsulfonyl)benzo[*a*]heptalene-2,4-diols (cf. Scheme 4, and Tables 2 and 3). Accompanying products are 2,4-bis{[(*N,N*-dialkylamino)sulfonyl]methyl}- or 2,4-bis{(phenylsulfonyl)methyl}-4,10a-dihydro-3*H*-heptaleno[1,10-*bc*]furan-3-carboxylates as mixtures of diastereoisomers (cf. Scheme 4, and Tables 2 and 3) which are the result of a Michael addition reaction of the lithiated methyl sulfones at C(3) of the heptalene-4,5-dicarboxylates, followed by (sulfonyl)methylation of the methoxycarbonyl group at C(5) and cyclization (cf. Scheme 5). It is assumed that the benzo[*a*]heptalene formation is due to (sulfonyl)methylation of both methoxycarbonyl groups of the heptalene-4,5-dicarboxylates (cf. Schemes 6 and 8). The resulting bis-enolates **35** are deprotonated further. The thus formed tris-anions **36** can then cyclize to corresponding tris-anions **37** of cyclopenta[*d*]heptalenes which, after loss of *N,N*-dialkylamido sulfite or phenyl sulfinat, undergo a ring-enlargement reaction by 1,2-C migration finally leading to the observed benzo[*a*]heptalenes (cf. Schemes 8 and 9). The structures of the new product types have been finally established by X-ray crystal-structure analyses (cf. Figs. 1 and 2 as well as *Exper. Part*).

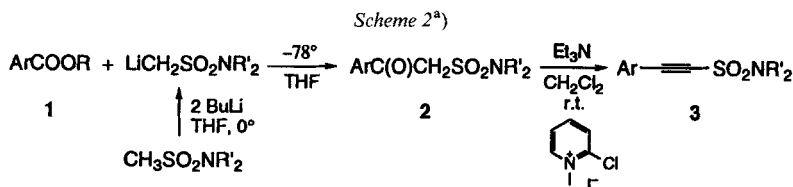
**1. Introduction.** – Recently we have shown that the thermally as well as photochemically inducible double-bond shifts (DBS) in heptalenes can be utilized for the generation of new thermo- and photochromic systems [1][2]. To test whether the DBS process of heptalenes could also be used for the formation of species of different chemical reactivity, we decided to transform the two ester groups of heptalene-4,5-dicarboxylates **I** into ethynyl groups (Scheme 1). The 4,5-di(ethynyl)heptalenes **II** can then be regarded as *proto*-forms of ene-diyne systems which could be activated by the thermal or photochemical DBS process leading to **III**. The Bergman rearrangement (cf. [3]) of **III** would give rise to benzo[*a*]heptalenes **IV** which may be viewed as *basal* forms of corresponding colchicinoid compounds. Cyclic ene-diyne substructures and their chemically triggered Bergman cyclization have been found responsible for the antibiotic and cytostatic properties of a number of complex natural products from different strains of *actinomycetes* (cf. [4]). In this context, the photochemical DBS process **II**  $\rightarrow$  **III** would allow a photo-triggering of the ene-diyne cyclization ( $\rightarrow$  **IV**), provided that the R' substituents represent members of a medium-size ring system [4] (cf. also [5]). We will return to these aspects in a forthcoming publication [6].

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There are several current methods for the transformation of Ac (*cf.*, *e.g.*, [7]) or aldehyde groups (*cf.*, *e.g.*, [8][9]) into ethynyl moieties which can also be applied to Ac- or CHO-substituted heptalenes [10] which are easily available from heptalene-4,5-dicarboxylates *via* *Tebbe* reaction [6][10] or selective reduction [2]. However, we were looking for simpler procedures allowing the direct conversion of alkoxycarbonyl into acetylenic groups.

Several years ago, *Leclercq* and *Brienne* [11] have reported on the transformation of substituted benzoates **1** into corresponding arylmethanesulfonamides **2** by reaction with lithiated methanesulfonamides, following a procedure originally developed by *Corey* and *Chaykovsky* [12] (Scheme 2). Formal dehydration of **2** to the (arylethynyl)sulfonamides **3** can readily be achieved by reaction of **2** with 2-chloro-1-methylpyridinium iodide in  $\text{CH}_2\text{Cl}_2/\text{Et}_3\text{N}$  at room temperature [11]. Therefore, we examined the applicability of the procedure of *Leclercq* and *Brienne* to the transformation of heptalene-4,5-dicarboxylates **I** into 4,5-di(ethynyl)heptalenes **II**.



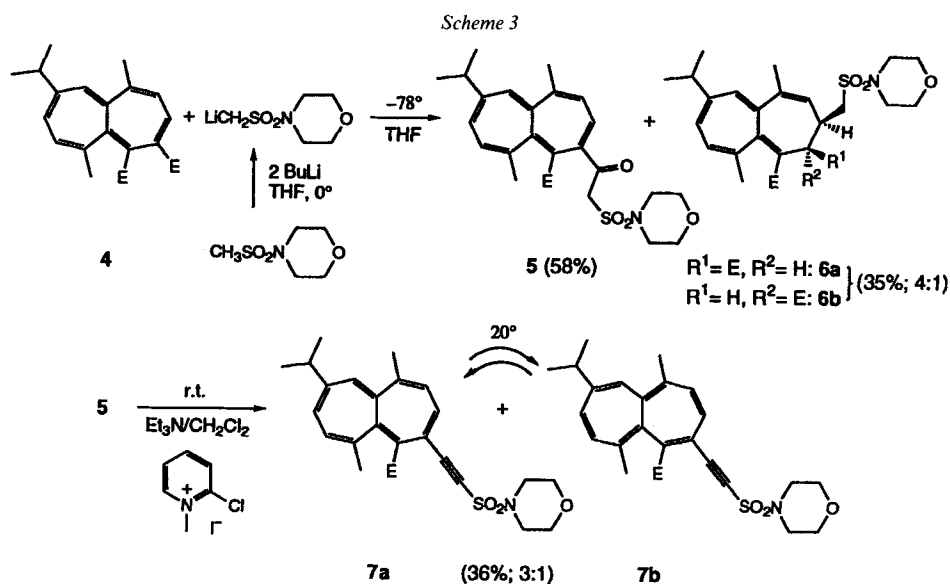
<sup>a)</sup> Procedure of *Leclercq* and *Brienne* [11];  $\text{R}'_2\text{N}$  = morpholino, 4-methylpiperazin-1-yl, or *N,N*-dimethylamino.

The reaction of dicarboxylate **4** with 1.1 mol-equiv. of lithiated methyl morpholino sulfone gave indeed the expected acylated sulfone **5** as main product, however, accompanied by a 4:1 mixture of the diastereoisomeric *Michael* adducts **6a** and **6b** (Scheme 3)<sup>2)</sup>.

That the lithiated methanesulfonamide had been acylated by **4** with the sterically less hindered MeOCO group at C(4) was not evident from the  $^1\text{H}$ -NMR spectrum ( $\text{CDCl}_3$ ) of **5** which displayed for H-C(3) a *doublet of quartets* ( $^3J(\text{H-C}(3), \text{H-C}(2)) = 6.3$  and  $^5J(\text{H-C}(3), \text{Me-C}(1)) \approx 0.7$  Hz) at 7.43 ppm, *i.e.*, the signal for H-C(3) showed nearly the same chemical shift as that for H-C(3) of the starting material **4**

<sup>2)</sup> The structure of **6a** was established by an X-ray crystal-structure analysis (see *Exper. Part*).

( $\delta(\text{H}-\text{C}(3)) = 7.46 \text{ ppm}$ ;  $\text{CDCl}_3$ )<sup>3</sup>). Nevertheless, the introduction of the  $\text{C}\equiv\text{C}$  bond (**5**  $\rightarrow$  **7a** + **7b**) revealed that  $\text{MeOCO}-\text{C}(4)$  had been alkylated by the lithiated methanesulfonamide, since **7a** showed in the  $^1\text{H}$ -NMR spectrum a high-field shift of the signal of  $\text{H}-\text{C}(3)$  (doublet of quartets with  $^3J(\text{H}-\text{C}(3), \text{H}-\text{C}(2)) = 6.4$  and  $^5J(\text{H}-\text{C}(3), \text{Me}-\text{C}(1)) \approx 1 \text{ Hz}$ ). It appeared at 6.96 ppm. At room temperature, **7a** is in thermal equilibrium with its DBS isomer **7b** of which  $\text{H}-\text{C}(3)$  appears as a doublet with  $^3J(\text{H}-\text{C}(3), \text{H}-\text{C}(4)) = 11.7 \text{ Hz}$  at 6.56 ppm<sup>4</sup>).



The realized reaction sequence **4**  $\rightarrow$  **5**  $\rightarrow$  **7a/7b** demonstrates that the procedure of *Leclercq* and *Brienne* can indeed be applied also to heptalene-4,5-dicarboxylates to transform at least the sterically less hindered carboxylate group at C(4) into an acetylenic function.

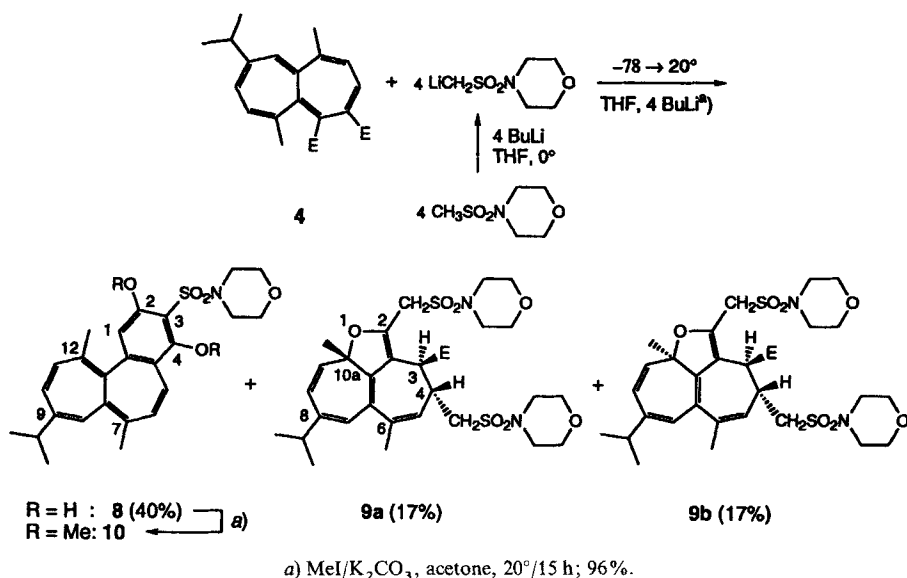
**2. Reaction of Heptalene-4,5-dicarboxylates with an Excess of Lithiated Methylsulfonyl Compounds.** – We concluded from the above mentioned results that it might be possible to transform both ester groups of heptalene-4,5-dicarboxylates **I** into 2-(aminosulfonyl)acetyl substituents, provided that the corresponding lithiated methanesulfonamides are applied in excess along with an increase in the reaction temperature to allow also the alkylation of the sterically more hindered  $\text{MeOCO}$  group at C(5). Therefore, we reacted **4** with a mixture of 4 mol-equiv. of lithiated methyl morpholino sulfone and 4 mol-equiv. of BuLi at  $-78^\circ$  in THF and raised the reaction temperature gradually in *ca.* 6 h to room temperature. The usual workup led to two main products, **8** and **9**,

<sup>3</sup>) Transformation of **4** into the corresponding *pseudo*-ester (3,3-dimethoxyheptaleno[1,2-*c*]furan-1-one) [13] and reaction of this derivative with the lithiated methanesulfonamide gives exclusively the isomer of **5** with exchanged functional groups at C(4) and C(5) [10]. It shows in the  $^1\text{H}$ -NMR spectrum for  $\text{H}-\text{C}(3)$  a doublet ( $^3J(\text{H}-\text{C}(3), \text{H}-\text{C}(2)) = 6.5 \text{ Hz}$ ) at 7.51 ppm. These observations demonstrate that the  $\pi$ - and  $\sigma$ -acceptor quality of the  $\text{MeOCO}$  group and the 2-(aminosulfonyl)acetyl substituent is almost the same in the studied heptalenes of type **5**.

<sup>4</sup>) The isomer **7a** is the only one that is present in the crystals (*cf. Exper. Part*).

whereby **9** turned out to be a *ca.* 1:1 mixture of two diastereoisomers (**9a** and **9b**; Scheme 4), which were difficult to separate chromatographically, whereas crystallization from AcOEt led to an enrichment of **9a**. In later experiments, we found that the yield of **8** could be improved to 40%, when 4 mol-equiv. of lithiated methanesulfonamide were prepared with an equimolar amount of BuLi, and the additional 4 mol-equiv. of BuLi were added to the reaction mixture of **4** and  $\text{LiCH}_2\text{SO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$  after the reaction temperature had reached  $-10^\circ$  to  $0^\circ$ .

Scheme 4



<sup>a)</sup> The additional amount of BuLi is added at  $-10$  to  $0^\circ$ ; then the temperature is slowly raised to  $20^\circ$ .

The  $^1\text{H}$ -NMR spectrum of **8** ( $\text{CDCl}_3$ ) revealed that a heptalene core with shifted  $\pi$ -bonds was still present in **8** as indicated by two vicinal coupling constants of four olefinic H-atoms in the order of 11.8 Hz and two *singlets* of two olefinic Me groups showing no allylic couplings. Moreover, the *i*-Pr group exhibited still diastereotopic Me groups. However, the signals of only one morpholino substituent were recognizable. Most astonishing was the fact that all other four H-signals appeared in the olefinic region as more or less sharp *singlets*. Two of them were shifted significantly to low field (8.77 and 8.22 ppm) and disappeared on treatment with  $\text{D}_2\text{O}$ , suggesting that two OH groups were present in **8**. This assumption was further supported by the IR spectrum of **8** ( $\text{CHCl}_3$ ) which displayed a broad absorption band at  $3382 \text{ cm}^{-1}$ , in agreement with intramolecularly chelated OH groups. Additional support for the presence of OH groups was provided by the UV spectrum of **8** in EtOH which exhibited the longest-wavelength absorption as a broad band at 313 nm which was bathochromically shifted by 37 nm in 1N KOH in EtOH. These observations allowed the conclusion that **8** might represent a fulvenoid or aromatic system, substituted with two OH groups and one morpholinosulfonyl residue. The  $^{13}\text{C}$ -NMR and UV spectrum of **8** clearly favored the second variant.

The structure of **8** was established by the X-ray crystal-structure analysis of its dimethyl ether **10** which was obtained in almost quantitative yield from **8** by methylation with MeI in the presence of  $\text{K}_2\text{CO}_3$  in acetone. The crystal structure (Fig. 1) disclosed

that **10** and, hence, **8** contained indeed a heptalene core with an [a]-annellated aromatic ring, substituted at C(2) and C(4) with MeO and OH groups, respectively, whereas the morpholinosulfonyl residue is attached to C(3).  $^1\text{H}$ -NOE Measurements allowed the assignment of the signal at 8.77 ppm to HO–C(4) and that at 8.22 ppm to HO–C(2). The residual *singlets* at 6.27 ppm and 5.74 ppm could be attributed to H–C(1) and H–C(8), respectively.

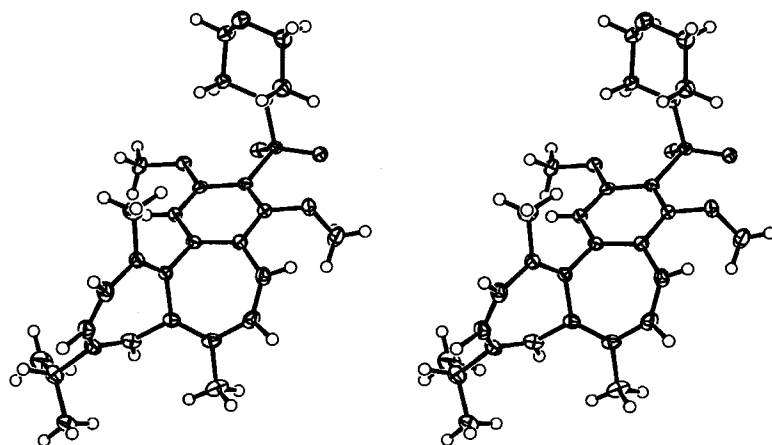


Fig. 1. Stereoscopic view of the X-ray crystal structure of 9-isopropyl-2,4-dimethoxy-7,12-dimethylbenzo[a]heptalen-3-yl morpholino sulfone (**10**)

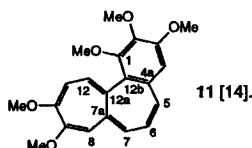
Table 1 gives a survey of the torsion angles of the benzo[a]heptalene skeleton of **10** and of 1,2,3,9,10-pentamethoxybenzo[a]heptalene (**11**) [14]. The torsion angles around the central C(7a)–C(12a) bond as well as those of the *s-cis*-buta-1,3-diene subunits of the heptalene perimeter are very similar for both compounds. The largest deviations are found for the torsion angles at the C(12a)–C(12b) bond which should reflect the steric interactions of the different substituents at the C-atoms of this bond. These angles are *ca.* 10° larger for **10**, which carries no substituent at C(1) and a Me group at C(12), than for **11** with a sterically less demanding MeO group at C(1) and no substituent at C(12).

The reaction with other lithiated methanesulfonamides and **4** (*cf.* Table 2), as well as with lithiated methyl phenyl sulfone and **4** and other dimethyl heptalene-4,5-carboxylates (*cf.* Table 3), showed that the formation of benzo[a]heptalenes and of 4,10a-dihydro-3*H*-heptaleno[1,10-*bc*]furans of type **13a** and **13b** as accompanying products is quite general. The structure of this second product type was established by an X-ray crystal-structure analysis of **13a** as well as of **19a** and **19b**. The latter two diastereoisomers crystallized as a *ca.* 1:1 mixture from AcOEt. Their crystal structure is shown in Fig. 2. All diastereoisomers of the *a*- and *b*-type exhibited in their  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra very similar chemical shifts and vicinal coupling constants of H–C(3) to H–C(5), in agreement with the *trans*-relation of the substituents at C(3) and C(4). For example, **19a** and **19b** showed  $^3J(\text{H}-\text{C}(3), \text{H}-\text{C}(4)) = 4.7$  and 4.8 Hz, and  $^3J(\text{H}-\text{C}(4), \text{H}-\text{C}(5)) = 9.2$

Table 1. Comparison of Some Skeletal Torsion Angles of **10** and of 1,2,3,9,10-Pentamethoxy-4-methylbenzo[a]heptalene (**11**)<sup>a)</sup>

Atoms	$\Theta [^\circ]^b)$		Remarks
	<b>10</b>	<b>11</b>	
C(7)–C(7a)–C(12a)–C(12)	–120.6(3)	–125.8(5)	Heptalene torsion angles around the central $\sigma$ -bond C(7a)–C(12a)
C(7)–C(7a)–C(12a)–C(12b)	59.9(3)	59.0(6)	
C(8)–C(7a)–C(12a)–C(12)	60.1(4)	58.5(6)	
C(8)–C(7a)–C(12a)–C(12b)	–119.5(3)	–116.7(5)	
C(7a)–C(12a)–C(12b)–C(1)	109.1(3)	117.8(5)	'Colchicinoid' torsion angles around the aromatic $\sigma$ -bond C(12a)–C(12b)
C(12)–C(12a)–C(12b)–C(1)	–70.5(4)	–57.3(6)	
C(7a)–C(12a)–C(12b)–C(4a)	–69.7(3)	–61.3(6)	
C(12)–C(12a)–C(12b)–C(4a)	110.7(3)	123.6(5)	
C(5)–C(6)–C(7)–C(7a)	–34.5(5)	–32.7(8)	s-cis-Buta-1,3-diene torsion angles of the heptalene perimeter benzo part
C(8)–C(9)–C(10)–C(11)	30.6(5)	32.6(7)	
C(10)–C(11)–C(12)–C(12a)	–31.3(5)	–32.8(7)	
C(12b)–C(4a)–C(5)–C(6)	35.6(5)	29.9(7)	

a)



b) In parentheses, e.s.d.'s.

Table 2. Reaction of Heptalene-4,5-dicarboxylate **4** with Various Lithiated Methanesulfonamides  $\text{CH}_3\text{SO}_2\text{NR}_2^a)$ 

Sulfonamide	Benzo[a]heptalenes <sup>b)</sup>		4,10a-Dihydro-3H-heptaleno[1,10-bc]furans <sup>c)</sup>	
	No.	Yield [%]	No.	Yield [%]
Morpholino	<b>8</b>	40.3	<b>9a/9b</b>	34.0
Piperidino	<b>12</b>	29.6	<b>13a/13b</b>	26.0
Pyrrolidino	<b>14</b>	25.6	<b>15a/15b</b>	25.8
Dimethylamino	<b>16</b>	25.2	<b>17a/17b</b>	28.9

<sup>a)</sup> Cf. Scheme 4. <sup>b)</sup> Yields are not optimized and refer to purified and crystallized material which resulted from the addition of 4 mol-equiv. of  $\text{LiCH}_2\text{SO}_2\text{NR}_2$  to **4** at  $-78^\circ$ , followed by additional 4 mol-equiv. of BuLi at  $-10$  to  $0^\circ$ . <sup>c)</sup> Yields of chromatographed 1:1 mixtures of both diastereoisomers; the two other possible diastereoisomers were present in amounts  $<1\%$  (see Table 3).

and 9.5 Hz, respectively, in full accordance with the observed torsion angles  $\Theta(\text{H}–\text{C}(3)–\text{C}(4)–\text{H}) = 55.6^\circ$  for **19a** and **19b**, as well as  $\Theta(\text{H}–\text{C}(4)–\text{C}(5)–\text{H}) = -2.9^\circ$  for **19a** and **19b** in their crystal structures<sup>5)</sup>. Moreover, the X-ray crystal-structure analysis of **13a** as well as of **19a** revealed the *trans*-relation of the  $\text{RSO}_2$ -carrying  $\text{CH}_2$

<sup>5)</sup> The X-ray crystal-structure data of **19a** and **19b** are of poor quality due to disorder in the crystals. However, the corresponding torsion angles in the crystal structure of **13a**, which gave much better and reliable results, are of the same size, namely  $53.5(3)^\circ$  and  $-5.5(3)^\circ$ , respectively.

Table 3. Reaction of Various Dimethyl Heptalene-4,5-dicarboxylates with Lithiated Methyl Phenyl Sulfone<sup>a)</sup>

Dimethyl Heptalene-4,5-dicarboxylates		Benzo[a]heptalenes <sup>b)</sup>		4,10a-Dihydro-3H-heptaleno[1,10-bc]furans <sup>c)</sup>	
R	No.	No.	Yield [%]	No.	Yield [%]
9-i-Pr, 1,6-Me <sub>2</sub>	<b>4</b>	<b>18</b>	37.7	<b>19a/19b</b>	30.8
6,8,10-Me <sub>3</sub>	<b>20</b>	<b>21</b>	20.0	<b>22a/22b</b>	16.6 <sup>d)</sup>
1,6,8,10-Me <sub>4</sub>	<b>23</b>	<b>24</b>	6.0 <sup>e)</sup>	<b>25a/25b</b>	36.6

<sup>a)</sup> Reaction conditions as indicated in Scheme 4 and Table 2. <sup>b)</sup> See Table 2. <sup>d)</sup> Yield of crystalline (3*R*\*,4*S*\*,10*aS*\*)-diastereoisomer **22b** which contained traces (< 1%) of **22a** as well as of the (3*R*\*,4*R*\*,10*aR*\*)- and (3*R*\*,4*R*\*,10*aS*\*)-diastereoisomers **22c** and **22d**, respectively. <sup>e)</sup> The yield of **24** can be improved to > 65% under concomitant suppression of the formation of **25a/25b** when the DBS isomer of **23** is chosen as starting material [15].

group at C(4) and the Me group at C(10a), and the corresponding *cis*-arrangement of these substituents at the heptalenofuran core in **19b** (Fig. 2). The **a**-forms belong accordingly to the series of heptalenofurans with (3*R*\*,4*S*\*,10*aR*\*)-configuration, whereas the **b**-compounds possess the (3*R*\*,4*S*\*,10*aS*\*)-configuration. The assignment of these relative configurations in solution is based on <sup>1</sup>H-NOE measurements. The bowl-like structure of the 4,10a-dihydro-3H-heptaleno[1,10-bc]furan skeleton of **19a** carries the Me groups at C(6) and C(10a) on the convex side of the molecule, *i.e.*, both groups are fairly close to each other<sup>6)</sup> and show, therefore, a weak reciprocal <sup>1</sup>H-NOE effect, whereas no effect is observed between XCH<sub>2</sub>–C(4) (X = PhSO<sub>2</sub>) and Me–C(10a) which are on the opposite sides of the molecule (*cf.* Fig. 2). The reverse situation is true for **19b**. In this case, no <sup>1</sup>H-NOE effect is observed between Me–C(6) and Me–C(10a). In turn, however, a weak-to-medium effect is observed between XCH<sub>2</sub>–C(4) (X = PhSO<sub>2</sub>) and Me–C(10a). The latter <sup>1</sup>H-NOE effect was also recognizable in the main isomer, **22b**, from the reaction of heptalene dicarboxylate **20** with lithiated methyl phenyl sulfone (*cf.* Table 3). Compound **22b** was obtained after one recrystallization of the mixture of **22a/22b**. A careful scrutiny of the <sup>1</sup>H-NMR spectrum of **22b** at 600 MHz (CDCl<sub>3</sub>) revealed that **22b** was accompanied – as expected – by traces (< 1%) of **22a**, but in addition, by two further isomers, also in amounts of ≤ 1%, as was evident, by small, but well interpretable satellite signals, close to those of **22b** (*cf.* Table 4). There is little doubt

<sup>6)</sup> The distance of the C-atoms of CH<sub>3</sub>–C(6) and CH<sub>3</sub>–C(10a) amounts to 529(2) pm in **19a** and to 577(2) pm in **19b**. On the other hand, a C,C distance of 423(3) pm is found for XCH<sub>2</sub>–C(4) and CH<sub>3</sub>–C(10a) in **19b**, and of 575(2) pm in **19a** according to their X-ray crystal-structure analyses (Fig. 2).

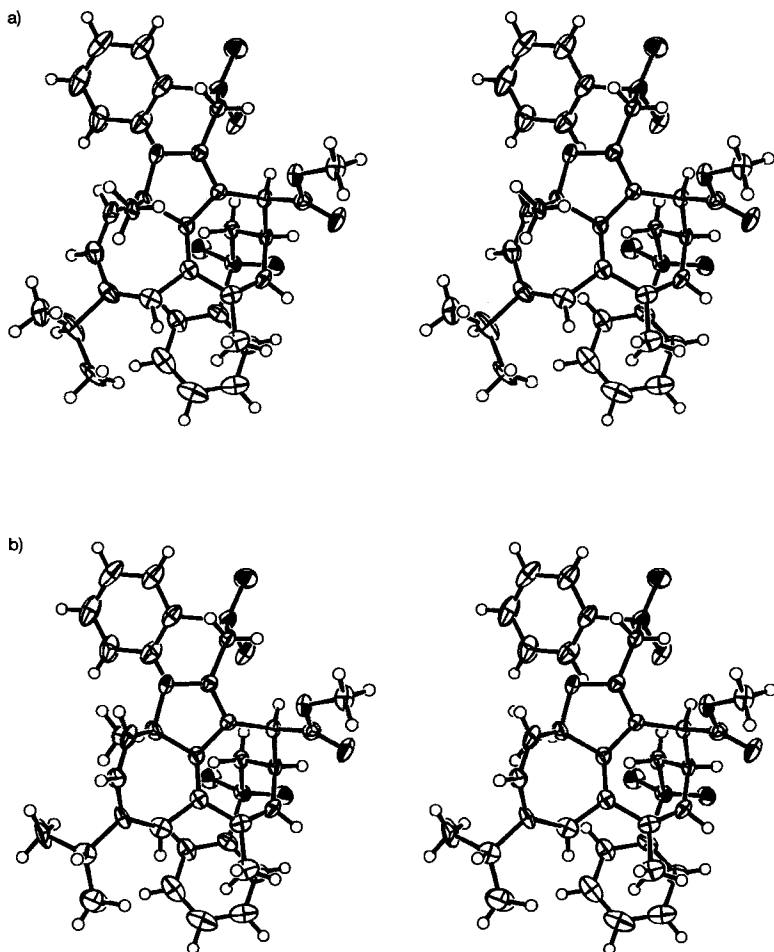


Fig. 2. Stereoscopic view of the X-ray crystal structures of methyl 4,10a-dihydro-8-isopropyl-6,10a-dimethyl-2,4-bis[(phenylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**19**). a) (3*R*\*,4*S*\*,10a*R*\*)-Diastereoisomer **19a** and b) (3*R*\*,4*S*\*,10a*S*\*)-diastereoisomer **19b**.

that these additional signals were caused by the other two possible diastereoisomers of **22a** and **22b**, namely **22c** and **22d**. Of diagnostic value is the observed smaller vicinal coupling constant  $^3J(\text{H}-\text{C}(4), \text{H}-\text{C}(5)) = 5.1 \text{ Hz}$  for **22c** and **22d** (cf. Table 4) due to the changed configuration at C(4) in comparison to **22a** and **22b**. Indeed, an interchange of the substituents at C(4) would lead to  $\theta(\text{H}-\text{C}(4)-\text{C}(5)-\text{H}) \approx 115^\circ$ , based on the X-ray crystal-structure analysis of **19a** or **19b** as reference, and taking into account the fact that the rigidity of the heptalenofuran system will not allow marked, substituent-dependent deviations of the torsion angles of its core structure. It is more difficult to define the relative configuration of **22c** and **22d** at C(3) or C(4) with respect to that at C(10a) on the basis of the observed additional



<sup>1</sup>H-NMR signals<sup>7)</sup>). However, the general trend in the chemical shifts of **22a** as compared to **22b** with established relative configurations (*cf.* Fig. 2 and Table 4) is also found for **22c** in comparison to **22d**. There is only one exception. The chemical shift of H–C(5) shows for **22c/22d** the opposite trend as for **22a/22b**. We assign, therefore, tentatively, on the basis of this trend analysis, the (3*R*\*,4*R*\*,10*aR*\*)-configuration to **22c** and the (3*R*\*,4*R*\*,10*aS*\*)-configuration to **22d**, *i.e.*, **22a** and **22c**, on one hand, and **22b** and **22d**, on the other, should possess the same relative configuration at C(10*a*).

Table 4. Observed <sup>1</sup>H-NMR Signals and Structural Assignment of the Four Possible Diastereoisomers of 4,10a-Dihydro-3H-heptaleno[1,10-*bc*]furan **22** from the Reaction of Heptalene-4,5-dicarboxylate **20** with Lithiated Methyl Phenyl Sulfone<sup>a)</sup>

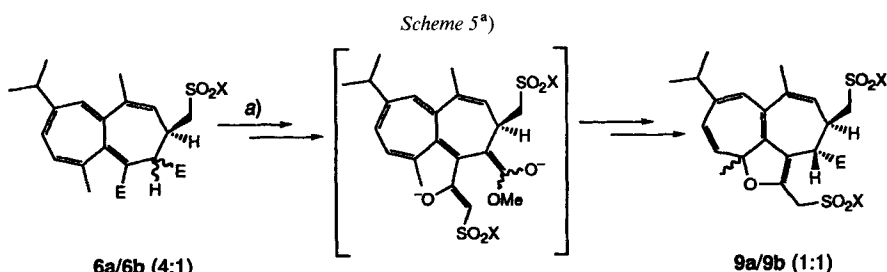
Assignment of <sup>1</sup> H position	$\delta(^1\text{H})$ [ppm] <sup>b)</sup>			
	<b>22a</b>	<b>22b</b>	<b>22c</b>	<b>22d</b>
MeOCO–C(3)	3.682 ( <i>s</i> )	3.642 ( <i>s</i> )	3.666 ( <i>s</i> )	3.618 ( <i>s</i> )
H–C(5)	5.575 ( <i>dd</i> , <i>J</i> = 8,6, 11.8)	5.656 ( <i>dd</i> , <i>J</i> = 8.9, 11.8)	5.523 ( <i>dd</i> , <i>J</i> = 5.1, 11.5)	5.491 ( <i>dd</i> , <i>J</i> = 5.1, 11.4)
Me–C(7)	1.983 ( <i>s</i> )	1.887 ( <i>s</i> )	2.073 ( <i>s</i> )	1.961 ( <i>s</i> )
H–C(8)	5.863 ( <i>s</i> )	5.963 ( <i>s</i> )	5.897 ( <i>s</i> )	5.953 ( <i>s</i> )
H–C(10)	5.068 ( <i>s</i> )	4.709 ( <i>s</i> )	4.807 ( <i>s</i> )	4.747 ( <i>s</i> )
Me–C(10 <i>a</i> )	0.770 ( <i>s</i> )	0.859 ( <i>s</i> )	0.760 ( <i>s</i> )	0.821 ( <i>s</i> )
Assignment of configuration	(3 <i>R</i> *,4 <i>S</i> *,10 <i>aR</i> *)	(3 <i>R</i> *,4 <i>S</i> *,10 <i>aS</i> *)	(3 <i>R</i> *,4 <i>R</i> *,10 <i>aR</i> *)	(3 <i>R</i> *,4 <i>R</i> *,10 <i>aS</i> *)

<sup>a)</sup> See also Table 3. <sup>b)</sup> <sup>1</sup>H-NMR spectrum (600 MHz, CDCl<sub>3</sub>); reference signal CHCl<sub>3</sub> at 7.270 ppm. The assignment of the relative configuration of **22c** and **22d** is tentative (see text).

We assume that traces of the *c*- and *d*-type diastereoisomers of the heptalenofurans are also present in the other product mixtures<sup>7)</sup>). However, we have not looked explicitly at signals of these diastereoisomers in the corresponding <sup>1</sup>H-NMR spectra. Nevertheless, a control experiment with the 4:1 mixture of the *Michael* adducts **6a** and **6b** (*cf.* Scheme 3) illustrated that these adducts are the precursor molecules of **9a** and **9b**, since they were formed quantitatively as *ca.* 1:1 mixture from **6a/6b** under the conditions of their formation in the 'one-pot' reaction (*cf.* Scheme 4). This observation demonstrates that the MeOCO group at C(4) of **6a** and **6b** is protected against the nucleophilic attack of the lithiated methanesulfonamides by ester-enolate formation due to the addition of LiCH<sub>2</sub>SO<sub>2</sub>NR<sub>2</sub> at C(3) of the heptalene-4,5-dicarboxylates (*cf.* Scheme 5). Further addition of LiCH<sub>2</sub>SO<sub>2</sub>NR<sub>2</sub> at the MeOCO group at C(5) leads to the corresponding 2-(aminosulfonyl)acetyl group which, in its enolate form, undergoes cyclization to the observed 4,10a-dihydro-3H-heptaleno[1,10-*bc*]furans (*cf.* Tables 2 and 3). The cyclization step can be regarded as 10*e* electrocyclization reaction which we have also observed

<sup>7)</sup> Based-catalyzed equilibration experiments with **22b** or the mixture **22a/22b** were not performed. We assume that the observed ratios of the heptalenofuran compounds in the reaction mixtures are kinetically controlled.

in neutral 5-acylheptalene systems (see [16] and the discussion there). The ratios of the amount of formed heptalenofurans and *Michael* adducts thus correspond to the proportion of the attack at C(3) to the attack at the ester C=O group at C(4) of the heptalene-4,5-dicarboxylates by the lithiated methanesulfonamides or methyl phenyl sulfone.



a) Reaction conditions as in Scheme 4.

<sup>a)</sup> In this and the following Schemes, X represents the morpholino moiety or one of the other amino groups (cf. Table 2) as well as the phenyl residue (cf. Table 3).

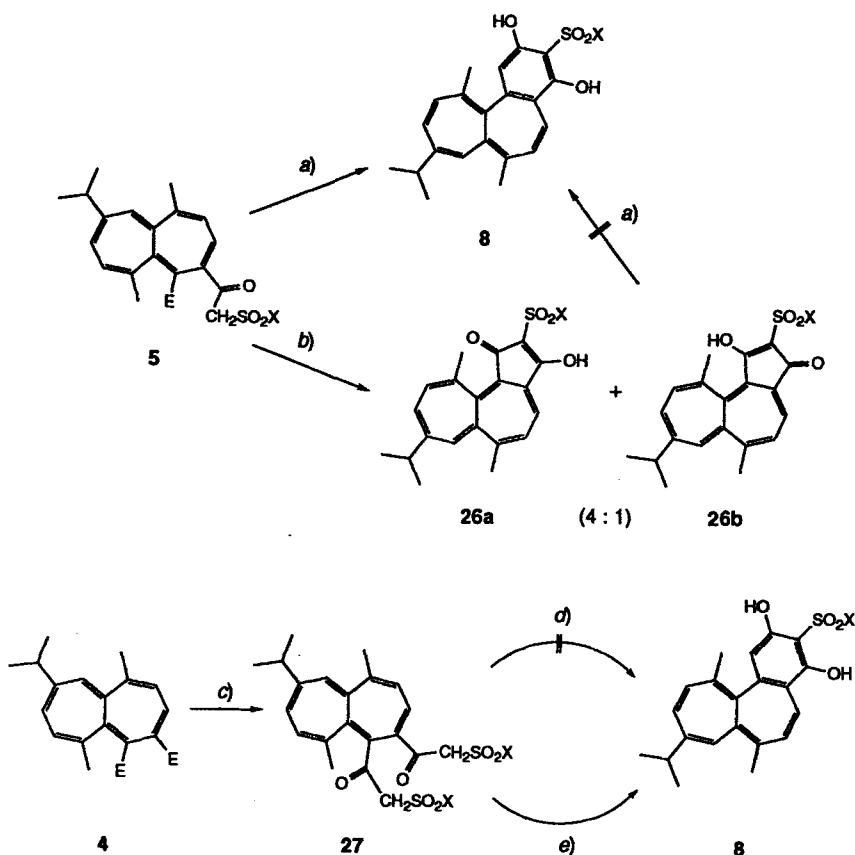
**3. On the Mechanism of Benzo[*a*]heptalene Formation.** – For the following discussion, it is necessary to mention some additional experiments and observations that we have conducted in the context with our benzo[*a*]heptalene syntheses.

a) When the mono[(aminosulfonyl)methylated] heptalene **5** (cf. Scheme 3) is treated under the conditions of benzo[*a*]heptalene formation, the corresponding benzo[*a*]heptalene **8** can be isolated in a yield of 68%, free of by-products. This result is in agreement with the fact that a maximum yield of 40% of **8** is obtained, when heptalene-4,5-dicarboxylate **4** is the starting material. Obviously, *ca.* one third of the heptalene-4,5-dicarboxylates is consumed by the discussed *Michael* addition leading finally to the mixture of diastereoisomers of the 4,10a-dihydro-3*H*-heptaleno[1,10-*bc*]furans (cf. Tables 2 and 3). Two third of the heptalene-4,5-dicarboxylates react *via* the mono[(aminosulfonyl)methylated] forms of type **5** to an extent of at maximum 70% to give finally the benzo[*a*]heptalenes. The other 30% are consumed by so far unknown side reactions (see, however, *d*).

b) On this understanding, it is tempting to postulate that the intermediates of type **5**, due to the increased acidity at their acylated CH<sub>2</sub> group and the present excess of base, undergo an intramolecular acylation reaction with the adjacent MeOCO group at C(5) under formation of cyclopenta[*d*]heptalene-1,3-diones in their enol or enolate forms. Indeed, when **5** was treated with KOH/MeOH at room temperature, the tautomeric cyclized enols **26a** and **26b** could be isolated in > 90% yield (Scheme 6). However, treatment of this mixture under the conditions of benzo[*a*]heptalene formation did not yield **8** in amounts worth mentioning.

c) On the other hand, when our model heptalene dicarboxylate **4** was reacted with only 2.2 mol-equiv. of methyl morpholino sulfone and 4 mol-equiv. of BuLi in the temperature range of –78 to 0°, we could isolate the bis[(aminosulfonyl)methylated] heptalene **27** as main product in a yield of > 50% (Scheme 6). Treatment of this com-

Scheme 6

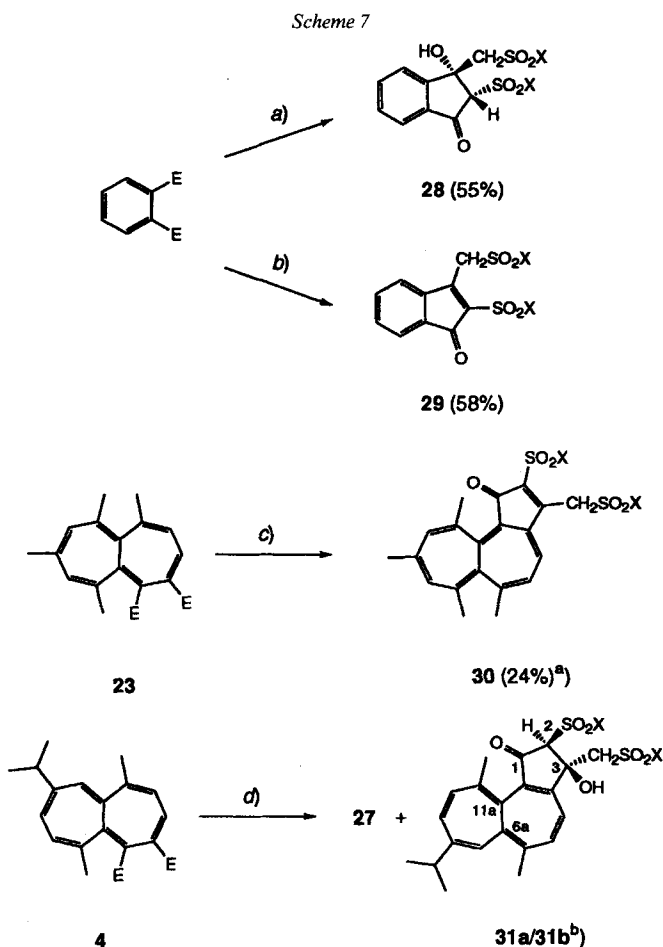


a) Reaction conditions as in Scheme 4. b) In 7 mol-equiv. of 0.75N KOH in MeOH, 20°/2.5 h; 93%. c) 2.2 mol-equiv.  $\text{MeSO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ /4 mol-equiv. BuLi/THF,  $-78 \rightarrow 0^\circ$ ; 53%. d) 2 mol-equiv.  $\text{MeSO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ /4 mol-equiv. BuLi/THF,  $-78 \rightarrow 0^\circ$ . e) See d) + 4 mol-equiv. BuLi at  $0^\circ$ , then gradual warming up to  $20^\circ$ .

pound with 2 mol-equiv. of methyl morpholino sulfone, followed by 4 mol-equiv. of BuLi in the temperature range of  $-78$  to  $0^\circ$ , did not lead to the formation of benzo-[a]heptalene **8** in noteworthy amounts. However, when additional 4 mol-equiv. of BuLi were added at  $0^\circ$ , and the temperature was then raised to room temperature, **8** turned out to be the main product in the mixture.

d) The reaction of dimethyl phthalate, as model compound for an unsaturated vicinal dicarboxylate, with lithiated methyl morpholino sulfone led, depending upon of the reaction conditions, to the indanone derivatives **28** and **29** (Scheme 7). The structure and configuration of **28** was established by an X-ray crystal-structure analysis (see *Exper. Part*). We assume that anellated five-membered ring structures of type **28** play also an important role on the pathway to the benzo[a]heptalenes, whereas **29** may stand for compounds representing 'dead ends' on the way to the 2,4-dihydroxybenzo[a]heptalenes,

since they miss one of the necessary O functions. This conjecture is substantiated by the fact that the reaction of heptalene-4,5-dicarboxylate **23**, which is a bad benzo[*a*]heptalene precursor (*cf.* Table 3), gave with methyl morpholino sulfone under the usual conditions, according to TLC analysis, beside the expected 4,10a-dihydro-3*H*-heptaleno[1,10-



a) 1.1 mol-equiv.  $\text{MeSO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ /2.2 mol-equiv.  $\text{BuLi/THF}$ ,  $-20 \rightarrow 20^\circ$ . b) 3 mol-equiv.  $\text{MeSO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ /6 mol-equiv.  $\text{BuLi/THF}$ ,  $-78 \rightarrow 0^\circ$ . c) Reaction conditions as in Scheme 4 (see also *Exper. Part*). d) 2.05 mol-equiv.  $\text{MeSO}_2\text{N}(\text{CH}_2\text{CH}_2)_2\text{O}$ /2.05 mol-equiv.  $\text{BuLi/THF}$ ,  $-78 \rightarrow -10^\circ$ ; 3 h.

<sup>a</sup>) The corresponding heptaleno[1,10-*bc*]furans of type **25a/25b** were also present in equal amounts according to TLC analysis. However, the mixture was not isolated.

<sup>b</sup>) A cyclopenta[*d*]heptalene, corresponding to **30** ( $^1\text{H-NMR}$  evidence), was also present in minor amounts as well as an unknown product type which was not isolated.

bc]furans<sup>8)</sup>, only traces of the corresponding benzo[a]heptalene. However, a deeply orange-colored compound could be isolated from the product mixture in a yield of 24% (Scheme 7). NMR Analyses including <sup>1</sup>H-NOE measurements (see *Exper. Part*) showed it to have structure **30** which is comparable to that of **29**.

e) On the search of the above mentioned product types in the reaction mixture of **4** and lithiated methyl morpholino sulfone, we reacted **4** once more with 2 mol-equiv. of lithiomethyl morpholino sulfone in the temperature range of  $-78$  to  $-10^{\circ}$ , *i.e.*, we avoided in this experiment any excess of BuLi, but prolonged the reaction time. After 3 h, the reaction mixture showed (TLC analysis) the presence of the expected bis[(aminosulfonyl)methylated] heptalene **27**, however, only in minor amounts. A further spot on the TLC plate indicated the presence of a cyclopenta[d]heptalene analogous to **30**<sup>9)</sup>. Furthermore, we found a new main spot, followed by a less intense spot which we had failed to recognize in our other experiments. The compound, hidden under the main spot, could be isolated and purified. A complete analysis of its <sup>1</sup>H- and <sup>13</sup>C-NMR spectra showed it to be a 3:1 mixture of the diastereoisomeric cyclopenta[a]heptalen-1-ones **31a** and **31b** (Scheme 7). Both isomers possess the same relative *trans*-configuration at the C(2)–C(3) bond. The diastereoisomerism is attributable to a different relative configuration at the helical heptalene axis C(6a)–C(11a), *i.e.*, **31a** possess the (2*R*\*,3*S*\*,6a*M*\*)- and **31b** the (2*R*\*,3*S*\*,6a*P*\*)-configuration. These assignments follow unequivocally from the <sup>1</sup>H-NOESY spectrum (C<sub>6</sub>D<sub>6</sub>) at 600 MHz of the 3:1 mixture<sup>10)</sup>.

The *trans*-configuration at the C(2)–C(3) bond of both isomers is evidenced by strong reciprocal <sup>1</sup>H-NOE effects between H–C(2) and the H-atoms of the CH<sub>2</sub> group at C(3). Most important for the relative configuration at the helical heptalene axis is a reciprocal <sup>1</sup>H-NOE effect of weak-to-medium intensity between H–C(2) and Me–C(11) which is only present in the minor diastereoisomer **31b**. Since a *cisoid*-vicinity of H–C(2) and Me–C(3)<sup>11)</sup> is only given in a (*P*\*)-configuration of the heptalene part, **31b** must possess the given (2*R*\*,3*S*\*,6a*P*\*)-configuration. Important are also <sup>1</sup>H-NOE effects that are observed between H–C(4) and the H-atoms of the CH<sub>2</sub> group as well as the OH group at C(3). In the minor diastereoisomer **31b**, the H–C(4) and the CH<sub>2</sub>–C(3) bonds are pointing in almost parallel directions, whereas the HO–C(3) and the H–C(4) bonds are more or less perpendicular to each other. As a result, we observe for this isomer strong reciprocal and medium <sup>1</sup>H-NOE effects between H–C(4) and the two H-atoms of the CH<sub>2</sub> group at C(3) and no effect between H–C(4) and HO–C(3). Just the reverse is true for the major diastereoisomer **31a**. The H–C(4) bond is in this isomer

<sup>8)</sup> All heptalenofurans of the described type show an intense blue fluorescence on TLC plates which allows to detect them unequivocally.

<sup>9)</sup> The cyclopenta[d]heptalene, analogous to **30**, was identified by its color on TLC as well as by the <sup>1</sup>H-NMR spectrum of the crude product which was not further purified.

<sup>10)</sup> The structure of a cyclopenta[a]heptalen-1-one of both diastereoisomers is not only supported by the described <sup>1</sup>H-NOE effects but also by the long-range <sup>1</sup>H, <sup>13</sup>C-COSY spectrum (600 MHz, C<sub>6</sub>D<sub>6</sub>) which displays, for the two isomers, two signals at 192.10 and 190.5 ppm indicating the cyclopent-2-en-1-one substructure. The position of the oxo function at C(1) is indicated by the absence of a <sup>3</sup>J(<sup>1</sup>H–C(4), <sup>13</sup>C=O) coupling and the presence of a corresponding <sup>3</sup>J(<sup>1</sup>H–C(4), <sup>13</sup>C(3)) coupling.

<sup>11)</sup> A *Dreiding* model of **31b** indicates a nearest interatomic distance in the *cisoid*-arrangement of H–C(4) and Me–C(11) of 320–330 pm, whereas the corresponding *transoid*-arrangement in **31a** reveals a distance of 400–410 pm for the mentioned atoms.

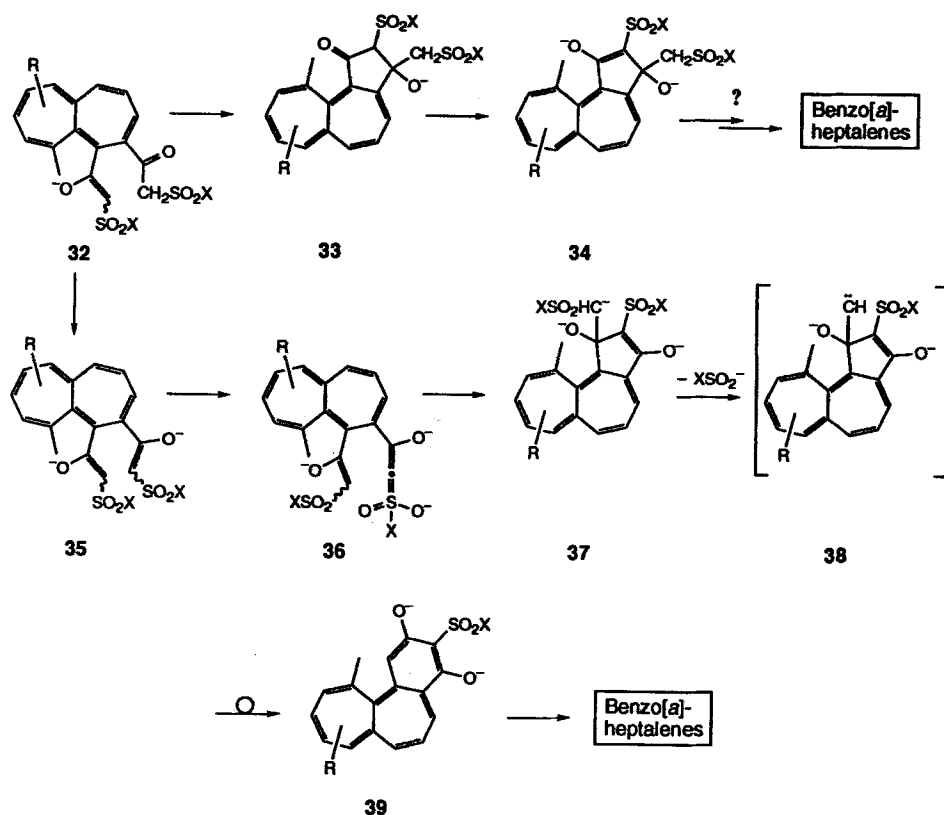
ion a nearly parallel orientation with respect to the O–C(3) bond, and the CH<sub>2</sub>–C(3) bond is found in a corresponding *quasi*-perpendicular orientation. Here, we observe a strong reciprocal <sup>1</sup>H-NOE effect between H–C(4) and HO–C(3), whereas the effects between H–C(4) and the H-atoms of the CH<sub>2</sub> group at C(3) are distinctly weaker than those observed for **31b**.

f) In all mixtures leading finally to the formation of the benzo[*a*]heptalenes, we observed the appearance of a red color in the temperature range of –20 to 0°. The addition of the excess of BuLi at this stage (*cf. Scheme 4*) accelerated and improved markedly the benzo[*a*]heptalene formation at 0 to 20°, whereby the red color changed to dark yellow.

For a tentative complete view of the reaction path that starts with the heptalene-4,5-dicarboxylates and ends at the specifically substituted benzo[*a*]heptalene-3-sulfonamides or benzo[*a*]heptalen-3-yl phenyl sulfones, we can add two further obvious informations as a consequence of the product structures. First of all, the unsubstituted C(1)-atom of the formed benzo moiety must arise from the C-atom of a sulfonylmethyl unit. Its specific position speaks for an insertion reaction between C(5) and the corresponding C=O C-atom of the heptalene-4,5-dicarboxylates. It can be explained by a 1,2-C migration under ring enlargement of a five-membered ring intermediate (*cf. [17]* for a general discussion of ring enlargements by one C-atom). Finally, the location of a aminosulfonyl group at C(3), flanked by OH groups at C(2) and C(4), is in agreement with the transitory appearance of a cyclopenta[*d*]heptalene derivative or its DBS isomer, *i.e.*, a cyclopenta[*a*]heptalene intermediate, that is alkylated by the lithiated methylsulfonyl reagent at C(1). The crucial step in the whole reaction sequence would then be the loss of a corresponding lithium *N,N*-dialkylamido sulfite or lithium phenylsulfinate by concomitant migration of C(11b) to the *exo*-C-atom at C(1) (*cf. Scheme 8*). The question concerns, however, the real nature and structure the five-membered ring intermediate that undergoes the ring-enlargement reaction. The necessity of the presence of an excess of a strong base, *e.g.*, BuLi, in the reaction mixture to induce the formation of benzo[*a*]heptalenes speaks for highly anionized species that are responsible for product formation.

The simplest way to explain product formation under these circumstances would be to assume the cyclization of the mono-enolates **32** of the bis[(X-sulfonyl)methylated] heptalenes (see **27**, *Scheme 6*, for a specific example) to give the five-membered-ring intermediates **33** which are the precursor of **31a/31b** (*Scheme 7*). However, these types of intermediates can at best lead to the formation of benzo[*a*]heptalenes with OH groups at C(1) and C(3), and the X-sulfonyl moiety at C(2) (*cf. Scheme 7*), a product type that has not been observed under the applied reaction conditions (*Scheme 4*). We assume, therefore, that the bis-enolates **35**, which may be responsible for the red color of the reaction mixtures at –20 to 0°, are incumbent for the progress of the reaction. Their further deprotonation will lead to the reactive tris-anions **36** which may cyclize to the cyclopenta[*d*]heptalene intermediates **37**. Loss of *N,N*-dialkylamido sulfite (or phenyl sulfinate) in an *E*<sub>1</sub> step will result in the formation of a carbene-like species **38**, prone to the discussed 1,2-C migration under formation of the decisive bis-anions **39** of the observed 2,4-dihydroxybenzo[*a*]heptalene-3-sulfonamides and 2,4-dihydroxybenzo[*a*]heptalen-3-yl phenyl sulfones, respectively. The necessary DBS process of the heptalene core may

Scheme 8



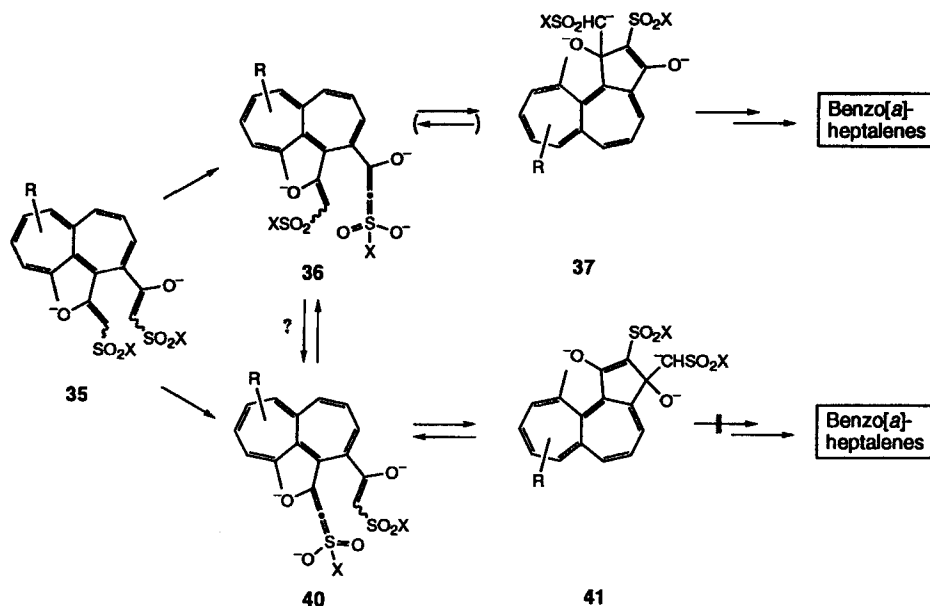
then take place as the very last step or already at any earlier stage of the reaction sequence<sup>12)</sup>.

There is one point left for discussion. It is the high site-selectivity or – more precisely – loco-selectivity of the observed benzanellation reaction. As already mentioned, in none of the cases, examined so far, we have found, in the reaction mixtures, benzo[*a*]heptalenes carrying the OH groups in 1,3-positions and the X-sulfonyl substituent at C(2), indicating an insertion process that took place at C(4), following otherwise the general route depicted in Scheme 8. There is no perceivable reason why the deprotonation of the bis-enolates 35 should not occur also at the enolate group at C(5), at least to a certain extent, followed by cyclization of the thus formed isomeric tris-anions 40 (Scheme 9). Therefore, to be consistent within our speculations, we have to postulate that the cyclization reactions are reversible, and that it is only the higher  $E_1$  reactivity of 37 as compared to its isomeric pendant 41, due to the bigger steric encumbrance at C(1) of 37 in relation to C(3) of 41, that pushes the overall reaction completely towards the formation of the

<sup>12)</sup> Indeed, heptalene-1,2-dicarboxylates can also be subjected to our ‘one-pot’ procedure of benzo[*a*]heptalene formation [15].

observed (2,4-dihydroxybenzo[*a*]heptalen-3-yl)sulfonyl derivatives<sup>13</sup>). Of course, it might also be that the two postulated tris-anions are in equilibrium *via* intramolecular proton shifts (*cf.* Scheme 9).

Scheme 9



We hope that further experiments will clarify this still vague picture of benzo[*a*]heptalene formation.

We are grateful to Dr. A. Linden who performed the X-ray crystal-structure analyses. We thank Prof. M. Hesse and his coworkers for mass spectra, Prof. W. von Philipsborn and his coworkers for NMR support and <sup>1</sup>H-NOE measurements, Mrs. J. Kessler for elemental analyses, and cand. chem. M. Lutz for assistance in the experiments with diethyl phthalate. The financial support of this work by the Swiss National Science Foundation is gratefully acknowledged.

#### Experimental Part

**General.** Solvents and reagents of the grade *puriss.* were used without further purification. Solvents of the grade *purum* were distilled and, where necessary, dried (Et<sub>2</sub>O and hexane over NaH; CH<sub>2</sub>Cl<sub>2</sub> over CaH<sub>2</sub>) before distillation. THF and toluene were freshly distilled from Na. BuLi: 2.5M soln. in hexane from Aldrich. TLC: Al sheets pre-coated with silica gel 60 F<sub>254</sub> from Merck; visualization by UV light. Column chromatography (CC) and flash chromatography (FC): on silica gel 60 (40–63 μm) Chemie Uetikon AG. M.p.: Mettler-FP5/52 apparatus. UV/VIS: Perkin-Elmer spectrophotometer, model Lambda 9, λ in nm (log ε). IR: Perkin-Elmer spectrophotometer, model FT-IR 1600; ν<sub>max</sub> in cm<sup>-1</sup>. <sup>1</sup>H-NMR: Bruker ARX 300 and Bruker AMX 600 spectrometer; δ in ppm rel. to internal Me<sub>4</sub>Si (= 0 ppm). J in Hz. <sup>13</sup>C-NMR: Bruker ARX 300 and Bruker AMX 600 spectrometer; δ in ppm rel. to CDCl<sub>3</sub> (δ(C) = 77.0 ppm, <sup>1</sup>J(C,D) = 31.5 Hz), assignments were confirmed by <sup>1</sup>H, <sup>13</sup>C-correlation data (HMBC). MS: Finnigan MAT 90 (Cl, NH<sub>3</sub>), SSQ 700 (EI, 70 eV), and TSQ/SSQ 700 (ESI, NaI); m/z (rel. %). Elemental analyses were performed by the Mikroanalytisches Laboratorium of the Organisch-chemisches Institut of the Universität Zürich and of the Laboratorium für Organische Chemie of ETH-Zürich.

<sup>13</sup>) More detailed studies on the reaction mechanism(s) of the benzo[*a*]heptalene formation are in progress.



**1. Synthesis of Dimethyl Heptalene-4,5-dicarboxylates.** – 1.1. *Dimethyl 9-Isopropyl-1,6-dimethylheptalene-4,5-dicarboxylate (4)* [18]. *Improved Procedure (IP)* [2]: Guaiazulene (14.85 g, 0.075 mol) and dimethyl acetylenedicarboxylate (ADM) (27.65 ml, 0.225 mol) were placed, together with toluene (70 ml), in a *Schlenk* reaction vessel. The vessel was stoppered and heated at 130° for 24 h in an oil bath. The mixture was cooled to r.t., diluted with Et<sub>2</sub>O, and washed with H<sub>2</sub>O (3 × 200 ml). After drying (MgSO<sub>4</sub>), the solvent was distilled off in a rotatory evaporator and the dark yellow oil dried in high vacuum to remove the rest of ADM. The dark yellow residue was recrystallized from Et<sub>2</sub>O (18.12 g, 71 %): yellow crystals. M.p. 147°.

1.2. *Dimethyl 6,8,10-Trimethylheptalene-4,5-dicarboxylate (20)* [19][20]. Following the *IP* (cf. 1.1), 4,6,8-trimethylazulene (12.77 g, 0.075 mol) [21] was reacted with ADM (27.65 ml, 0.225 mol) in toluene. Workup led to 13.35 g (57 %) of pure **20** and its DBS isomer as a dark yellow oil.

1.3. *Dimethyl 1,6,8,10-Tetramethylheptalene-4,5-dicarboxylate (23)* [20][22]. Following the *IP* (cf. 1.1), 1,4,6,8-tetramethylazulene (13.82 g, 0.075 mol) [22] was reacted with ADM (27.65 ml, 0.225 mol) in toluene. Workup led to 11.12 g (45 %) of pure crystalline **23**. M.p. 137–138° (Et<sub>2</sub>O); 124–125° (Et<sub>2</sub>O/hexane) [22].

**2. Reaction of the Heptalene-4,5-dicarboxylates with Lithiated Methylsulfonyl Compounds.** – 2.1. *Diester 4 with Methyl Morpholino Sulfone. Optimized Procedure:* Under Ar, a 2.5M soln. of BuLi (4.75 ml, 11.8 mmol) was added dropwise to a soln. methyl morpholino sulfone [11][12] (1.95 g, 11.8 mmol) in dry THF (60 ml), cooled to 0°. After stirring for 30 min at 0°, the mixture was cooled to –78°, and a soln. of **4** (1.00 g, 2.94 mmol) in THF (5 ml) was rapidly added. After 2.5 h, the mixture was allowed to warm to 0° within 1.5 h. At this temp. BuLi soln. (4.75 ml, 11.8 mmol) was added within 5 min. The reaction temp. was raised to r.t. within 30 min. The mixture was treated with ice water (50 ml), acidified with 1N aq. HCl soln., and extracted with AcOEt (100 ml). The org. phase was washed with 1N aq. HCl soln. (100 ml) and with brine (2 × 50 ml). After drying (MgSO<sub>4</sub>), the solvent was distilled off in a rotatory evaporator. The solid residue, chromatographed on silica gel with hexane/AcOEt 2:1, gave two main fractions. The first fraction, represented 9-isopropyl-7,12-dimethyl-3-(morpholinosulfonyl)benzo[a]heptalene-2,4-diol (**8**; 0.54 g, 40%). Yellow crystals. M.p. 198–199° (Et<sub>2</sub>O).

The second main fraction consisted of a ca. 1:1 mixture of the two diastereoisomers methyl (3*RS*,4*SR*,10*aRS*)- and methyl (3*RS*,4*SR*,10*aSR*)-4,10*a*-dihydro-8-isopropyl-6,10*a*-dimethyl-2,4-bis[(morpholinosulfonyl)methyl]-3*H*-heptaleno[1,10-*bc*]furan-3-carboxylate (**9a** and **9b**, resp.; 0.630 g, 34%). Yellow crystals.

*Data of 8:* *R<sub>f</sub>* (hexane/AcOEt 1:1) 0.58. UV/VIS (EtOH): λ<sub>max</sub> 224 (4.43), 261 (4.35), 313 (4.00), 380 (sh, 3.10). λ<sub>min</sub> 245 (4.28), 298 (3.94). UV/VIS (0.1N KOH/EtOH): λ<sub>max</sub> 221 (4.50), 251 (sh, 4.39), 278 (sh, 4.27), 350 (4.01), 435 (sh, 3.51). λ<sub>min</sub> 243 (4.38), 318 (3.89). IR (KBr): 3316vs, 2966s, 2853s, 1643w, 1602vs, 1552vs, 1456vs, 1416vs, 1262vs, 1185vs, 1115vs, 1055m, 951vs, 870w, 797m, 736m, 635s, 571w, 554m. <sup>1</sup>H-NMR: Table 5. <sup>13</sup>C-NMR: Table 6. CI-MS: 456 (100, [M + H]<sup>+</sup>), 415 (4), 390 (10), 304 (18), 236 (19). Anal. calc. for C<sub>25</sub>H<sub>29</sub>NO<sub>5</sub>S (455.58): C 65.91, H 6.42, N 3.07; found: C 65.79, H 6.44, N 3.03.

*Data of the Mixture 9a/9b:* *R<sub>f</sub>* (hexane/AcOEt 1:1) 0.24. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): Table 7. <sup>13</sup>C-NMR (75.5 MHz, CDCl<sub>3</sub>): Table 8. CI-MS: 656 (48, [M + NH<sub>4</sub>]<sup>+</sup>), 639 (100, [M + H]<sup>+</sup>), 490 (30), 355 (9), 222 (18). Anal. calc. for C<sub>30</sub>H<sub>44</sub>N<sub>2</sub>O<sub>9</sub>S<sub>2</sub> (638.81): C 56.41, H 6.63, N 4.39; found: C 56.44, H 6.47, N 4.44.

2.1.1. *O-Methylation of 8.* K<sub>2</sub>CO<sub>3</sub> (0.50 g) was suspended in dry acetone (5 ml). The mixture was cooled to 0°, and **8** (0.13 g, 0.29 mmol) was added under stirring. To the above mixture, MeI (0.5 ml) was added dropwise, and stirring was continued at r.t. overnight. TLC showed that all **8** has been consumed. The mixture was diluted with H<sub>2</sub>O (20 ml) and extracted with Et<sub>2</sub>O (2 × 20 ml). The org. layer was separated and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of Et<sub>2</sub>O by evaporation in vacuum left pure yellow crystalline **10** (0.133 g, 96%). Compound **10** was recrystallized to give yellow needles. M.p. 201–202° (Et<sub>2</sub>O).

*Data of 9-Isopropyl-2,4-dimethoxy-7,12-dimethyl-3-(morpholinosulfonyl)benzo[a]heptalene (10):* *R<sub>f</sub>* (hexane/AcOEt 1:1) 0.55. IR (KBr): 2951m, 2843m, 1576m, 1542s, 1458s, 1379s, 1344w, 1294w, 1259w, 1175s, 1094m, 947m, 792w, 718w, 590w, 518w. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 3.886, 3.862 (2s, 2 MeO). The chemical shifts for all the other signals are very similar to those of **8** (see Table 5). CI-MS: 484 (100, [M + H]<sup>+</sup>), 335 (16), 88 (9). Anal. calc. for C<sub>27</sub>H<sub>33</sub>NO<sub>5</sub>S (483.63) C 67.06, H 6.88, N 2.90; found: C 67.53, H 6.71, N 2.61.

The final structure of **10** was established by an X-ray crystal-structure analysis (cf. Fig. 1 and Table 9).

2.2. *Diester 4 with Methyl Piperidino Sulfone.* Following the optimized procedure (cf. 2.1), methyl piperidino sulfone (1.92 g, 11.8 mmol) was reacted as usual with BuLi soln. and **4** (1.00 g, 2.94 mmol) in THF. The usual workup and FC on silica gel with hexane/AcOEt 2:1 gave two main fractions. The first fraction yielded 9-isopropyl-7,12-dimethyl-3-(piperidinosulfonyl)benzo[a]heptalene-2,4-diol (**12**; 0.39 g, 30%). Pure yellow crystals. M.p. 207.5–208.5° (Et<sub>2</sub>O). The second main fraction consisted of a ca. 1:1 mixture of methyl (3*RS*,4*SR*,10*aRS*)- and methyl (3*RS*,4*SR*,10*aSR*)-4,10*a*-dihydro-8-isopropyl-6,10*a*-dimethyl-2,4-bis[(piperidinosulfonyl)methyl]-3*H*-heptaleno[1,10-*bc*]furan-3-carboxylate (**13a** and **13b**, resp.; 0.48 g, 26%). Yellow crystals. Recrystallization of **13a/13b** from Et<sub>2</sub>O/hexane gave pure **13a**. M.p. 155.5–156.5°.

Table 5. <sup>1</sup>H-NMR Data of Benzo[a]heptalenes<sup>a)</sup>

Position of H-atoms and/or alkyl groups	8	12	14	16	18	21	24
	(J[Hz]) <sup>b)</sup>						
H–C(1)	6.273 (s)	6.251 (s)	6.254 (s)	6.266 (s)	6.222 (s)	6.199 (s)	6.175 (s)
HO–C(2)	8.215 (s)	8.308 (s)	8.431 (s)	8.300 (s)	8.624 (s)	8.640 (s)	8.647 (s)
XSO <sub>2</sub> –C(3)	3.76, 3.15 (2m)	3.15, 1.67, 1.51 (3m)	3.35, 1.89 (2m)	2.835 (s)	8.00–7.50 (5 arom. H)	8.00–7.50 (5 arom. H)	8.00–7.50 (5 arom. H)
HO–C(4)	8.766 (s)	8.858 (s)	8.979 (s)	8.846 (s)	9.220 (s)	9.226 (s)	9.231 (s)
H–C(5)	7.002 (d, J=11.9)	7.019 (d, J=11.9)	7.028 (d, J=11.9)	7.022 (d, J=11.9)	7.003 (d, J=11.9)	7.056 (d, J=11.8)	7.024 (d, J=11.9)
H–C(6)	6.241 (d, J=11.9)	6.229 (d, J=11.9)	6.229 (d, J=12.0)	6.231 (d, J=12.0)	6.215 (d, J=11.9)	6.312 (dd, J=11.9, 5.8)	6.207 (d, J=12.0)
H– or Me–C(7)	1.712 (d, J=0.5)	1.709 (s)	1.710 (s)	1.705 (s)	1.671 (s)	5.707 (d, J=5.8)	1.702 (s)
H– or Me–C(8)	5.738 (s)	5.731 (s)	5.728 (s)	5.727 (s)	5.68 (s)	1.995 (d, J=1.1)	1.892 (d, J=1.3)
H– or i-Pr–C(9)	2.547 (sept.); 1.150, 1.139 (2d)	2.549 (sept.); 1.154, 1.133 (2d)	2.543 (sept.); 1.153, 1.131 (2d)	2.540 (sept.); 1.151, 1.131 (2d)	2.511 (sept.); 1.131, 1.108 (2d)	5.898 (br. s)	5.990 (br. s)
H– or Me–C(10)	6.389 (dd, J=11.9, 1.1)	6.382 (dd, J=11.9, 1.1)	6.386 (dd, J=11.9, 1.1)	6.387 (dd, J=11.9, 1.1)	6.367 (dd, J=11.9, 1.2)	1.972 (d, J=1.1)	2.001 (d, J=1.3)
H–C(11)	6.400 (d, J=11.9)	6.397 (d, J=11.9)	6.391 (d, J=11.9)	6.396 (d, J=11.9)	6.372 (d, J=11.9)	6.135 (br. s)	6.126 (br. s)
Me–C(12)	1.699 (s)	1.691 (s)	1.690 (s)	1.695 (s)	1.671 (s)	1.624 (s)	1.635 (s)

<sup>a)</sup> Spectra at 300 or 600 MHz; CDCl<sub>3</sub>, CHCl<sub>3</sub> at 7.260 ppm. <sup>b)</sup> X Groups are morpholino (for 8), piperidino (for 12), pyrrolidino (for 14), dimethylamino (for 16), and phenyl (for 18, 21, and 24).

Table 6.  $^{13}\text{C}$ -NMR Data of Some of the Benzo[a]heptalenes<sup>a)</sup>

Position of C-atoms and alkyl groups	$\delta[\text{ppm}]$						
	8 <sup>b)</sup>	12	14	16	18	21	24 <sup>b)</sup>
C(1)	109.59	109.40	109.42	109.46	109.78	109.91	109.07
C(2)	156.21	156.22	156.27	156.31	156.40	156.70	156.35
C(3)	102.90	104.40	105.38	103.64	107.90	107.96	107.70
C(4)	152.94	152.86	152.92	152.99	153.19	153.25	153.34
C(4a)	119.52	119.28	119.30	119.36	119.65	120.35	119.55
C(5)	124.71	124.87	125.02	124.91	124.65	125.63	124.84
C(6)	132.47	132.18	132.13	132.26	132.41	133.09	132.26
C(7)	128.77	128.73	128.72	128.74	128.80	122.23	127.80
C(7a)	133.72	133.92	133.91	133.84	133.66	136.62	136.11
C(8)	122.44	122.41	122.38	122.38	122.36	142.49	134.27
C(9)	145.56	145.01	144.91	145.18	146.18	127.51	128.55
C(10)	132.04	131.94	131.91	131.95	132.04	139.11	139.11
C(11)	135.37	135.45	135.45	135.42	135.48	128.75	130.33
C(12)	132.70	132.60	132.58	132.61	132.57	131.21	130.76
C(12a)	131.60	131.51	131.51	131.56	131.64	129.57	129.40
C(12b)	147.32	147.30	147.31	147.24	147.36	146.54	146.91
Me–C(7)	17.02	17.10	17.07	17.05	17.01	–	17.92
Me–C(8)	–	–	–	–	–	24.78	22.82
i-Pr–C(9)	34.72, 22.74	34.48, 22.76	34.38, 22.75	34.49, 22.57	34.44, 22.71	–	–
Me–C(10)	–	–	–	–	–	25.40	25.05
Me–C(12)	19.60	19.64	19.65	19.62	19.59	20.10	19.35
X–SO <sub>2</sub> –C(3)	65.73, 45.61	46.58, 24.88, 23.20	47.76, 25.21	37.68	126.16, 134.32, 129.58, 141.25	126.19, 134.32, 129.57, 141.20	126.20, 134.30, 129.60, 141.27

<sup>a)</sup> Spectra at 75 or 150 MHz;  $\text{CDCl}_3$ ,  $\text{CDCl}_3$  at 77.00 ppm. <sup>b)</sup> Assignments of all C-signals via long-range  $^1\text{H}$ ,  $^{13}\text{C}$ -COSY spectra.

Data of **12**:  $R_f$  (hexane/AcOEt 1:1) 0.82.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): Table 5.  $^{13}\text{C}$ -NMR (75.5 MHz,  $\text{CDCl}_3$ ): Table 6. CI-MS: 454 (100,  $[M + \text{H}]^+$ ), 350 (5), 307 (15). Anal. calc. for  $\text{C}_{26}\text{H}_{31}\text{NO}_4\text{S}$  (453.60): C 68.85, H 6.89, N 3.09; found: C 68.98, H 6.95, N 3.09.

Data of the Mixture **13a/13b**:  $R_f$  (hexane/AcOEt 1:1) 0.56.  $^1\text{H}$ -NMR (600 MHz,  $\text{CDCl}_3$ ): Table 7.  $^{13}\text{C}$ -NMR (150 MHz,  $\text{CDCl}_3$ ): Table 8. CI-MS: 652 (17,  $[M + \text{NH}_4]^+$ ), 635 (100,  $[M + \text{H}]^+$ ), 571 (13), 488 (44), 265 (6). Anal. calc. for  $\text{C}_{32}\text{H}_{46}\text{N}_2\text{O}_7\text{S}_2$  (634.87): C 60.54, H 7.30, N 4.41, S 10.10; found: C 60.17, H 6.97, N 4.43, S 10.41.

The final structure of **13a** was established by an X-ray crystal-structure analysis (cf. Table 9).

2.3. Diester **4** with Methyl Pyrrolidino Sulfone. Following the optimized procedure (cf. 2.1), methyl pyrrolidino sulfone (1.76 g, 11.8 mmol) was reacted as usual with BuLi soln. and **4** (1.00 g, 2.94 mmol) in THF. The usual workup and after FC on silica gel with hexane/AcOEt 3:2 gave two main fractions. The first fraction yielded 9-isopropyl-7,12-dimethyl-3-(pyrrolidinylsulfonyl)benzo[a]heptalene-2,4-diol (**14**; 0.33 g, 26%). Yellow crystals. M.p. 178–170° (Et<sub>2</sub>O). The second main fraction consisted of a ca. 1:1 mixture of methyl (3RS,4SR,10aRS)- and methyl (3RS,4SR,10aSR)-4,10a-dihydro-8-isopropyl-6,10a-dimethyl-2,4-bis[(pyrrolidinylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**15a** and **15b**, resp.; 0.46 g, 26%). Yellow crystals.

Data of **14**:  $R_f$  (hexane/AcOEt 3:2) 0.62.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): Table 5.  $^{13}\text{C}$ -NMR (75.5 MHz,  $\text{CDCl}_3$ ): Table 6. CI-MS: 457 (4,  $[M + \text{NH}_4]^+$ ), 440 (15,  $[M + \text{H}]^+$ ), 372 (8), 89 (12), 72 (37). Anal. calc. for  $\text{C}_{25}\text{H}_{29}\text{NO}_4\text{S}$  (439.58): C 68.31, H 6.65, N 3.19; found: C 68.51, H 6.64, N 3.19.

Data of the Mixture **15a/15b**:  $R_f$  (hexane/AcOEt 3:2) 0.25.  $^1\text{H}$ -NMR (600 MHz,  $\text{CDCl}_3$ ): Table 7.  $^{13}\text{C}$ -NMR (150 MHz,  $\text{CDCl}_3$ ): Table 8. CI-MS: 624 (10,  $[M + \text{NH}_4]^+$ ), 607 (100,  $[M + \text{H}]^+$ ), 591 (4), 543 (13), 472 (37). Anal. calc. for  $\text{C}_{30}\text{H}_{42}\text{N}_2\text{O}_7\text{S}_2$  (606.81): C 59.38, H 6.98, N 4.62; found: C 59.61, H 7.00, N 4.89.

Table 7. <sup>1</sup>H-NMR Data of the Two Main Diastereoisomers of the Methyl 4,10a-Dihydro-3H-heptaleno[1,10-bc]furan-3-carboxylates<sup>a)</sup>

Position of H-atoms and/or alkyl groups	9a <sup>c)</sup>	9b	13a	13b	15a	15b	17a
$\delta$ [ppm] ( $J$ [Hz]) <sup>b)</sup>							
XSO <sub>2</sub> -CH <sub>2</sub> -C(2)	n.a.	n.a.	4.032, 3.960 (AB, $J=14.5$ )	4.037, 4.005 (AB, $J=14.6$ )	4.066 (s) ( $J_2$ )	4.095, 4.054 (AB, $J=14.6$ )	4.067, 3.999 (AB, $J=14.6$ )
H-C(3)	n.a.	n.a.	3.993 (d, $J=4.8$ )	4.006 (d, $J=4.8$ )	4.038 (d, $J=4.7$ )	4.026 (d, $J=4.9$ )	4.004 (d, $J=4.7$ )
H-C(4)	n.a.	n.a.	3.501 (m)	3.551 (m)	3.56 (m)	3.52 (m)	3.53 (m)
XSO <sub>2</sub> -CH <sub>2</sub> -C(4)	n.a.	n.a.	2.914 (dd, $J=14.2, 7.1$ ); 2.756 (dd, $J=14.2, 6.8$ )	3.136 (dd, $J=14.0, 7.2$ ); 2.971 (dd, $J=14.0, 6.6$ )	2.984 (dd, $J=14.4, 6.0$ ); 2.876 (dd, $J=14.4, 7.7$ )	3.214 (dd, $J=14.1, 6.0$ ); 3.081 (dd, $J=14.1, 7.4$ )	2.932 (dd, $J=14.2, 7.1$ ); 2.838 (dd, $J=14.2, 7.1$ )
H-C(5)	5.68 (dq, $J=9.0, 1.2$ )	5.80 (dq, $J=9.2, 1.1$ )	5.670 (dq, $J=9.0, 1.1$ )	5.819 (d, $J=9.0$ )	5.692 (dq, $J=9.0, 1.2$ )	5.847 (dq, $J=9.1, 1.2$ )	5.679 (dq, $J=9.0, 1.1$ )
H- or Me-C(6)	2.04 (d, $J=1.1$ )	1.91 (d, $J=1.3$ )	2.035 (d, $J=1.0$ )	1.911 (d, $J=1.1$ )	2.032 (d, $J=1.2$ )	1.909 (d, $J=1.2$ )	2.04 (d, $J=1.2$ )
H- or Me-C(7)	6.61 (s)	6.39 (s)	6.609 (s)	6.397 (s)	6.610 (s)	6.389 (s)	6.613 (s)
H- or i-Pr-C(8)	2.505 (sept.); 1.13, 1.09 (2d)	2.50 (sept.); 1.12, 1.08 (2d)	2.504 (sept.); 1.121, 1.086 (2d)	~2.50 (sept.); 1.125, 1.091 (2d)	2.49 (sept.); 1.115, 1.079 (2d)	2.48 (sept.); 1.119, 1.085 (2d)	2.498 (sept.); 1.113, 1.087 (2d)
H- or Me-C(9)	~6.04 (dd, $J=10.8, 1.0$ )	~6.04 (dd, $J=10.8, 1.0$ )	6.021 (d, $J=10.7$ )	6.013 (d, $J=10.7$ )	6.028 (dd, $J=10.7, 0.8$ )	6.003 (dd, $J=10.8, 0.8$ )	6.022 (d, $J=10.6$ )
H-C(10)	5.73 (d, $J=10.7$ )	5.87 (d, $J=10.8$ )	5.723 (d, $J=10.7$ )	5.829 (d, $J=10.7$ )	5.679 (d, $J=10.6$ )	5.763 (d, $J=10.8$ )	5.718 (d, $J=10.7$ )
Me-C(10a)	1.13 (s)	1.09 (s)	1.123 (s)	~1.10 (s)	1.090 (s)	1.095 (s)	1.124 (s)
MeOOC-C(3)	3.68 (s)	3.61 (s)	3.676 (s)	3.612 (s)	3.674 (s)	3.607 (s)	3.68 (s)

Table 7 (cont.)

Position of H-atoms and/or alkyl groups	$\delta$ (ppm) ( $^1\text{H}$ NMR) <sup>a)</sup>		19b	22a <sup>d)</sup>	22b	25b <sup>e)</sup>
	17b	19a				
XSO <sub>2</sub> -CH <sub>2</sub> -C(2)	n.a.	4.297, 4.186 (AB, $J=14.6$ )	4.291, 4.220 (AB, $J=14.6$ )	4.271, 4.065 (AB, $J=14.2$ )	4.359, 4.233 (AB, $J=14.5$ )	4.208, 4.144 (AB, $J=14.6$ )
H-C(3)	n.a.	4.050 (d, $J=4.7$ )	4.080 (d, $J=4.8$ )	n.a.	4.223 (d, $J=4.6$ )	3.971 (d, $J=4.5$ )
H-C(4)	3.48 (m)	3.474 (dt)	3.40 (dt)	3.483 (dt, $\Sigma J=26.6$ )	3.545 (dt, $\Sigma J=27.2$ )	3.393 (m)
XSO <sub>2</sub> -CH <sub>2</sub> -C(4)	3.147 (dd, $J=14.0, 7.3$ );	3.133 (dd, $J=14.6, 6.9$ );	3.331 (dd, $J=14.4, 7.1$ );	3.202 (dd, $J=14.4, 7.5$ );	3.319 (dd, $J=14.4, 7.6$ );	3.300 (dd, $J=14.4, 7.1$ );
	3.035 (dd, $J=14.5, 6.5$ )	3.013 (dd, $J=14.6, 7.2$ )	3.199 (dd, $J=14.4, 7.0$ )	3.011 (dd, $J=14.4, 6.5$ )	3.093 (dd, $J=14.4, 6.1$ )	3.278 (dd, $J=14.4, 6.4$ )
H-C(5)	n.a.	5.353 (d, $J=9.2$ )	5.566 (d, $J=9.5$ )	5.575 (dd, $J=11.8, 8.6$ )	5.656 (dd, $J=11.8, 8.9$ )	5.510 (d, $J=9.0$ )
H- or Me-C(6)	1.913 (d, $J=1.3$ )	1.772 (s)	1.716 (s)	6.114 (d, $J=11.9$ )	5.979 (d, $J=11.8$ )	1.611 (s)
H- or Me-C(7)	6.396 (s)	6.400 (s)	6.150 (s)	1.983 (s)	1.887 (s)	1.781 (s)
H- or i-Pr-C(8)	~2.49 (sept.);	2.435 (sept.);	2.409 (sept.);	5.863 (s)	5.963 (s)	5.942 (s)
	1.121, 1.097 (2d)	1.081, 1.024 (2d)	1.056, 1.018 (2d)			
H- or Me-C(9)	6.009 (d, $J=10.8$ )	5.915 (d, $J=10.8$ )	5.845 (d, $J=10.8$ )	1.842 (s)	1.772 (s)	1.745 (s)
H-C(10)	5.817 (d, $J=10.7$ )	5.317 (d, $J=10.7$ )	5.153 (d, $J=10.8$ )	5.068 (s)	4.709 (s)	5.084 (s)
Me-C(10a)	1.076 (s)	0.848 (s)	0.728 (s)	0.770 (s)	0.859 (s)	0.932 (s)
MeOOC-C(3)	3.614 (s)	3.676 (s)	3.620 (s)	3.682 (s)	3.642 (s)	3.654 (s)

<sup>a)</sup> Spectra at 300 or 600 MHz; CDCl<sub>3</sub>, C<sub>6</sub>H<sub>5</sub>Cl<sub>3</sub> at 7.260 ppm; n.a.: not assignable due to overlapping of signals in the spectra of mixtures. <sup>b)</sup>  $\delta$  of the X residues: morpholino and phenyl; not determined; piperidino: 3.30 (m), 3.05 (m), 1.75–1.45 (m); pyrrolidino: 3.45–3.20 (m), 2.00–1.80 (m); dimethylamino: 2.93, 2.69 (9a); 2.92, 2.83 (9b). <sup>c)</sup> The diastereoisomers 9c and 9d were also present in the mixture of 9a (43%) and 9b (48%) in amounts of 5.5% and 3.5%. <sup>d)</sup> For details, see Table 4 and remarks in the text. <sup>e)</sup> Unfortunately, no <sup>1</sup>H-NMR spectrum of the ca. 1:1 mixture 25a/25b was measured. Therefore, only the data of purified 25b are available.

Table 8.  $^{13}\text{C}$ -NMR Data of Some of the Two Main Diastereoisomers of the Methyl 4,10a-Dihydro-3H-heptaleno[1,10-bc]furan-3-carboxylates<sup>a)</sup>

Position of C-atoms and alkyl groups	$\delta$ [ppm] <sup>b)</sup>									
	9a	9b	13a	13b <sup>c)</sup>	15a	15b	19a	19b	22b	25b
C(2)	153.63	153.16	154.25	n.a.	154.32	153.80	153.17	152.73	153.66	153.14
C(2a)	112.85	113.12	112.71	n.a.	112.74	112.98	113.25	113.44	112.79	111.95
C(3)	45.28	46.07	45.35	n.a.	45.51	46.55	45.29	46.30	46.00	47.51
C(4)	33.34	33.77	33.68	33.94	33.78	33.98	33.56	33.69	34.29	33.29
C(5)	123.79	124.86	124.06	n.a.	124.20	125.65	123.00	122.44	120.29	n.a.
C(6)	136.68	136.67	136.39	n.a.	136.08	135.76	136.87	136.52	n.a.	135.66
C(6a)	121.36	121.94	121.18	n.a.	121.27	121.68	121.32	121.78	120.29	n.a.
C(7)	124.83	126.39	125.00	n.a.	125.00	126.66	124.72	126.29	n.a.	n.a.
C(8)	142.44	144.34	142.65	n.a.	142.66	143.94	142.82	144.19	n.a.	n.a.
C(9)	123.30	123.65	123.18	n.a.	123.31	123.47	123.15	123.04	n.a.	n.a.
C(10)	123.71	123.86	123.91	n.a.	123.56	124.08	124.01	124.37	n.a.	124.18
C(10a)	88.79	88.84	88.69	n.a.	88.59	88.71	88.44	88.49	88.19	88.69
C(10b)	140.66	143.02	141.18	n.a.	141.04	143.94	141.07	142.68	145.39	146.51
XSO <sub>2</sub> –CH <sub>2</sub> –C(2)	48.40	48.51	48.48	n.a.	48.87	49.10	55.49	55.58	55.63	55.46
MeOOC–C(3)	170.81	170.37	171.16	170.73	171.13	170.76	170.69	170.32	170.37	170.70
	52.12	52.00	52.13	52.06	52.13	52.07	52.12	52.07	52.20	52.18
X–SO <sub>2</sub> –CH <sub>2</sub> –C(4)	48.16	48.10	48.62	n.a.	48.58	48.44	55.53	55.90	56.34	55.94
Me–C(6)	24.08	26.73	24.25	26.85	24.27	26.86	24.06	26.61	–	24.15
Me–C(7)	–	–	–	–	–	–	–	–	24.64	24.09
i-Pr–C(8)	36.77	36.67	36.85	36.74	36.88	36.70	36.72	36.55	–	–
	22.66	22.65	22.81	22.78	22.78	22.76	22.69	22.64	–	–
	21.92	21.70	22.04	21.81	22.06	21.79	21.89	21.45	–	–
Me–C(9)	–	–	–	–	–	–	–	–	21.98	21.78
Me–C(10a)	17.53	17.80	17.60	17.85	17.56	17.69	17.03	17.40	17.86	17.89

<sup>a)</sup> Spectra at 75 or 150 MHz;  $\text{CDCl}_3$ ,  $\text{CDCl}_3$  at 77.00 ppm; n.a.: not assigned. <sup>b)</sup>  $^{13}\text{C}$  Signals of the morpholino moieties in **9a/9b**: 66.61, 66.56, 66.45, 45.79, 45.63, 45.39; piperidino moieties of **13a**: 46.75, 46.33, 25.75, 25.65, 23.84, 23.82; pyrrolidino moieties in **15a/15b**: 48.03, 47.85, 47.73, 47.46, 27.74, 25.91, 25.87, 25.81; Ph residues of **19a**: 138.90/138.63 (C(1')/C(1'')), 133.99/133.39 (C(4')/C(4'')), 129.22/129.06 (C(3',5')/(3'',5'')), 128.71/127.92 (C(2',6')/C(2'',6'')); **19b**: 138.90/139.81, 133.90/133.53, 129.17/129.22, 128.71/127.95 (C(X',X'') for  $\text{PhSO}_2\text{CH}_2\text{--C}(2)/\text{PhSO}_2\text{CH}_2\text{--C}(4)$ ); **22b**: 138.81/139.36, 133.85, 129.12/129.24, 128.83/128.05 (C(X',X'') for  $\text{PhSO}_2\text{CH}_2\text{--C}(2)/\text{PhSO}_2\text{CH}_2\text{--C}(4)$ ); **25b**: 138.89/139.38, 134.08/133.71, 129.26/129.30, 128.67/128.20 (C(X',X'') for  $\text{PhSO}_2\text{CH}_2\text{--C}(2)/\text{PhSO}_2\text{CH}_2\text{--C}(4)$ ). <sup>c)</sup> Only to 13% in the mixture with **13a**.

**2.4. Diester 4 with N,N-Dimethylmethanesulfonamide.** Following the optimized procedure (cf. 2.1), *N,N*-dimethylmethanesulfonamide (1.45 g, 11.8 mmol) was reacted as usual with BuLi soln. and **4** (1.00 g, 2.94 mmol) in THF. The usual workup and FC on silica gel with hexane/AcOEt 1:1 gave two main fractions. The first fraction represented 3-(dimethylaminosulfonyl)-9-isopropyl-7,12-dimethylbenzo[*a*]heptalene-2,4-diol (**16**; 0.31 g, 25%). Yellow crystals. M.p. 145.5–146.5° (Et<sub>2</sub>O). The second main fraction consisted of a ca. 1:1 mixture of methyl (3*RS*,4*SR*,10*aRS*)- and methyl (3*RS*,4*SR*,10*aSR*)-2,4-bis[(dimethylaminosulfonyl)methyl]-4,10a-dihydro-8-isopropyl-6,10a-dimethyl-3H-heptaleno[1,10-bc]furan-3-carboxylate (**17a** and **17b**, resp.; 0.47 g, 29%). Yellow crystals.

**Data of 16:** *R*<sub>f</sub> (hexane/AcOEt 1:1) 0.55.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): Table 5.  $^{13}\text{C}$ -NMR (75.5 MHz,  $\text{CDCl}_3$ ): Table 6. CI-MS: 414 (100,  $[M + \text{H}]^+$ ), 310 (5). Anal. calc. for  $\text{C}_{23}\text{H}_{27}\text{NO}_4\text{S}$  (413.54): C 66.80, H 6.58, N 3.39; found: C 66.77, H 6.52, N 3.41.

**Data of the Mixture 17a/17b:** *R*<sub>f</sub> (hexane/AcOEt 1:1) 0.30.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ): Table 7. CI-MS: 572 (48,  $[M + \text{NH}_4]^+$ ), 555 (100,  $[M + \text{H}]^+$ ), 446 (20), 141 (27). Anal. calc. for  $\text{C}_{26}\text{H}_{38}\text{N}_2\text{O}_7\text{S}_2$  (554.74): C 56.30, H 6.91, N 5.05, S 11.56; found: C 56.04, H 6.59, N 5.04, S 12.00.

Table 9. Crystallographic Data of 6a, 10, 13a, 18, 19a, 19b, and 28

Substance	6a	10	13a	18	19a/19b	28
Crystallized from	CH <sub>2</sub> Cl <sub>2</sub> /Et <sub>2</sub> O	Et <sub>2</sub> O	Et <sub>2</sub> O/hexane	Et <sub>2</sub> O	Et <sub>2</sub> O/hexane	Acetone
Empirical formula	C <sub>26</sub> H <sub>33</sub> NO <sub>7</sub> S	C <sub>27</sub> H <sub>33</sub> NO <sub>5</sub> S	C <sub>32</sub> H <sub>46</sub> N <sub>2</sub> O <sub>7</sub> S <sub>2</sub>	C <sub>27</sub> H <sub>26</sub> O <sub>4</sub> S	C <sub>34</sub> H <sub>36</sub> O <sub>7</sub> S <sub>2</sub>	C <sub>18</sub> H <sub>24</sub> N <sub>2</sub> O <sub>8</sub> S <sub>2</sub> ·C <sub>3</sub> H <sub>8</sub> O
Formula weight	505.62	483.62	634.84	446.56	620.77	518.59
Crystal color, habit	colorless, prism	yellow, prism	yellow, prism	yellow, plate	yellow, prism	colorless, prism
Crystal dimensions [mm]	0.10–0.25–0.43	0.20–0.30–0.33	0.18–0.35–0.38	0.07–0.25–0.27	0.12–0.20–0.23	0.33–0.40–0.43
Temperature [K]	173(1)	173(1)	173(1)	173(1)	173(1)	173(1)
Crystal system	monoclinic	monoclinic	triclinic	triclinic	triclinic	triclinic
Space group	<i>P</i> 2 <sub>1</sub> / <i>c</i>	<i>P</i> 2 <sub>1</sub> / <i>c</i>	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$	<i>P</i> $\bar{1}$
<i>Z</i>	4	4	2	2	2	2
Reflections for cell determination	25	25	25	25	24	25
2 $\theta$ range for cell determination [°]	20–33	38–40	38–40	36–40	22–25	39–40
Unit cell parameters						
<i>a</i> [Å]	10.384(3)	10.423(3)	12.637(3)	9.990(2)	12.696(4)	9.850(1)
<i>b</i> [Å]	10.265(3)	13.755(3)	14.059(4)	13.012(2)	13.379(5)	12.976(4)
<i>c</i> [Å]	24.879(3)	17.145(2)	10.661(3)	9.501(2)	11.418(3)	9.677(2)
$\alpha$ [°]	90	90	111.21(2)	96.19(2)	107.37(3)	100.83(2)
$\beta$ [°]	100.32(2)	91.92(1)	94.29(2)	108.16(1)	113.79(2)	92.90(2)
$\gamma$ [°]	90	90	66.10(2)	74.25(1)	62.54(2)	87.37(2)
<i>V</i> [Å <sup>3</sup> ]	2609(1)	2456.7(7)	1608.6(8)	1129.0(4)	1560(1)	1212.5(5)
<i>F</i> (000)	1080	1032	680	472	656	548
<i>D<sub>x</sub></i> [g cm <sup>-3</sup> ]	1.287	1.307	1.311	1.313	1.322	1.420
$\mu$ (MoK $\alpha$ ) [mm <sup>-1</sup> ]	0.169	0.170	0.215	0.175	0.219	0.273
Scan type		$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$	
2 $\theta$ <sub>max</sub> [°]	55	55	55	55	50	55
Total reflections measured	6666	6184	7715	5460	5754	5885
Symmetry independent reflections	5988	5633	7383	5163	5481	5564
<i>R</i> <sub>int</sub>	0.025	0.055	0.016	0.032	0.033	0.016
Reflections used [ <i>I</i> > 2 $\sigma$ ( <i>I</i> )]	4178	3786	5105	3596	3051	4537
Parameters refined	456	439	434	393	451	445
Reflection/parameter ratio	9.16	8.62	11.8	9.15	6.76	10.2
Final <i>R</i>	0.0453	0.0515	0.0502	0.0464	0.0567	0.0406
<i>wR</i>	0.0412	0.0494	0.0447	0.0434	0.0474	0.0422
Weights:	0.005	0.0075	0.005	0.005	0.005	0.005
<i>p</i> in $w=[\sigma^2(F_o)+(pF_o)^2]^{-1}$						
Goodness of fit	1.563	1.758	1.982	1.531	1.684	2.505
Final $\Delta_{\max}/\sigma$	0.0005	0.0004	0.0006	0.0006	0.0004	0.0006
$\Delta\rho(\max; \min)$ [e Å <sup>-3</sup> ]	0.38; -0.35	0.63; -0.40	0.64; -0.41	0.35; -0.40	0.29; -0.32	0.31; -0.55
Range of $s(\delta(C-C))$ [Å]	0.003–0.004	0.003–0.005	0.003–0.005	0.003–0.005	0.006–0.05	0.003–0.01

**2.5. Diester 4 with Methyl Phenyl Sulfone.** Following the optimized procedure (*cf.* 2.1), methyl phenyl sulfone (1.84 g, 11.8 mmol) was reacted as usual with BuLi soln. and **4** (1.00 g, 2.94 mmol) in THF. The usual workup, after FC on silica gel with hexane/AcOEt 3:2, gave two main fractions. The first fraction yielded 9-isopropyl-7,12-dimethyl-3-(phenylsulfonyl)benzo[a]heptene-2,4-diol (**18**; 0.495, 38%). Yellow crystals. M.p. 207–208° (Et<sub>2</sub>O/hexane). The second main fraction consisted of a ca. 1:1 mixture of methyl (3RS,4SR,10aRS)- and methyl (3RS,4SR,10aSR)-4,10a-dihydro-8-isopropyl-6,10a-dimethyl-2,4-bis[(phenylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**19a** and **19b**, resp.; 0.56, 31%). Yellow crystals.

*Data of 18:* *R<sub>f</sub>* (hexane/AcOEt 3:2) 0.58. <sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>): *Table 5*. <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>): *Table 6*. CI-MS: 447 (100, [M + H]<sup>+</sup>), 307 (17). Anal. calc. for C<sub>27</sub>H<sub>26</sub>O<sub>4</sub>S (446.57): C 72.62, H 5.87; found: C 72.67, H 5.86.

The final structure of **18** was established by an X-ray crystal-structure analysis (*cf.* *Sect. 4* and *Table 9*).

*Data of the Mixture 19a/19b:* *R<sub>f</sub>* (hexane/AcOEt 3:2) 0.37. <sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>): *Table 7*. <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>): *Table 8*. CI-MS: 638 (100, [M + NH<sub>4</sub>]<sup>+</sup>), 621 (35, [M + H]<sup>+</sup>), 481 (25). Anal. calc. for C<sub>34</sub>H<sub>36</sub>O<sub>7</sub>S<sub>2</sub> (620.78): C 65.78, H 5.85; found: C 65.78, H 5.60.

The final structures of **19a** and **19b** in the mixed crystals, which contained according to <sup>1</sup>H-NMR in average 56% of **19a** and 44% of **19b**, were established by an X-ray crystal-structure analysis (*cf.* *Fig. 2, a* and *b*, as well as *Sect. 4* and *Table 9*).

**2.6. Diester 20 with Methyl Phenyl Sulfone.** Under Ar, a 2.5M soln. of BuLi (6.4 ml, 16 mmol) was added dropwise to a soln. of methyl phenyl sulfone (2.00 g, 12.8 mmol) in dry THF (60 ml), cooled to 0°. After 30 min stirring at 0°, the mixture was cooled within 15 min to –78°, and a soln. of **20** (1.00 g, 3.20 mmol) in THF (5 ml) was added within 5 min. After additional stirring at –78° for 1.5 h, the reaction temp. was raised within 45 min to 0° and kept at this temp. for 2 h. In a second flask, lithium diisopropylamide (LDA) was generated from (i-Pr)<sub>2</sub>NH (1.35 ml, 9.5 mmol) and BuLi soln. (3.8 ml, 9.5 mmol) in THF (10 ml) at 0° for 15 min. This soln. was added dropwise via a cannula to the above mixture at 0°. The yellow-brown soln. was warmed up within 1 h to r.t. and stirring continued for additional 45 min and then poured onto ice and 10% aq. HCl soln. (100 ml). The org. layer was extracted with AcOEt (2 × 50 ml), washed with brine (2 × 50 ml), and dried (MgSO<sub>4</sub>). Removal of AcOEt by evaporation in vacuum left a crude solid mixture which was chromatographed on silica gel (FC) with hexane/AcOEt 3:1 and gave two main fractions. The first fraction provided 8,10,12-trimethyl-3-(phenylsulfonyl)benzo[a]heptene-2,4-diol (**21**; 0.27 g, 20%). Yellow crystals. M.p. 111–112° (Et<sub>2</sub>O). The second fraction consisted of a ca. 1:1 mixture of methyl (3RS,4RS,10aRS)- and methyl (3RS,4SR,10aSR)-4,10a-dihydro-7,9,10a-trimethyl-2,4-bis[(phenylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**22a** and **22b**, resp.; 0.32 g, 17%). Yellow crystals. Recrystallization of this mixture from Et<sub>2</sub>O/hexane gave **22b** which was contaminated with small amounts (ca. 0.6–1%) of **22a** and of methyl (3RS,4RS,10aRS)- and methyl (3RS,4SR,10aSR)-4,10-dihydro-7,9,10a-trimethyl-2,4-bis[(phenylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**22c** and **22d**, resp.) according to <sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>, see also *Table 4* and remarks in the text).

*Data of 21:* *R<sub>f</sub>* (hexane/AcOEt 2:1) 0.36. <sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>): *Table 5*. <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>): *Table 6*. CI-MS: 419 (100, [M + H]<sup>+</sup>), 279 (13), 177 (22), 160 (17), 69 (32). Anal. calc. for C<sub>25</sub>H<sub>22</sub>O<sub>4</sub>S (418.51): C 71.75, H 5.30, S 7.66; found: C 72.02, H 5.25, S 7.51.

*Data of 22b:* *R<sub>f</sub>* (hexane/AcOEt 2:1) 0.15. <sup>1</sup>H-NMR (600 MHz, CDCl<sub>3</sub>): *Table 7*. <sup>13</sup>C-NMR (150 MHz, CDCl<sub>3</sub>): *Table 8*. CI-MS: 610 (16, [M + NH<sub>4</sub>]<sup>+</sup>), 593 (100, [M + H]<sup>+</sup>), 453 (33), 258 (9). Anal. calc. for C<sub>32</sub>H<sub>32</sub>O<sub>7</sub>S<sub>2</sub> (592.74): C 64.85, H 5.44, S 10.82; found: C 65.47, H 5.44, S 10.56.

Selected <sup>1</sup>H-NMR signals of **22a**, **22c**, and **22d**: see *Tables 4* and *7*.

**2.7. Diester 23 with Methyl Phenyl Sulfone.** Under Ar, a 2.5M soln. of BuLi (2.14 ml, 5.4 mmol) was added dropwise to a soln. of methyl phenyl sulfone (0.67 g, 4.29 mmol) in dry THF (20 ml), cooled to 0°. After stirring for 30 min at 0°, the mixture was cooled within 15 min to –78°, and a soln. of **23** (0.35 g, 1.07 mmol) in THF (5 ml) was added within 5 min. After additional stirring at –78° for 2 h, the reaction temp. was raised within 1 h to 0° and kept at this temp. for 1 h. In another flask, LDA was generated from (i-Pr)<sub>2</sub>NH (0.45 ml, 3.18 mmol) and BuLi soln. (1.27 ml, 3.18 mmol) in THF (5 ml) at 0° for 15 min. This soln. was added dropwise via a cannula to the above mixture at 0°. The yellow-red soln. was warmed up within 1 h to r.t. and after stirring for additional 45 min, poured onto ice and 10% aq. HCl soln. (100 ml). The usual workup (*cf.* 2.6) gave two main fractions. The first fraction yielded 7,8,10,12-tetramethyl-3-(phenylsulfonyl)benzo[a]heptene-2,4-diol (**24**, 0.028 g, 6%). Yellow crystals. M.p. 198–199° (Et<sub>2</sub>O). The second fraction consisted of a ca. 1:1 mixture of methyl (3RS,4SR,10aRS)- and methyl (3RS,4SR,10aSR)-4,10a-dihydro-6,7,9,10a-tetramethyl-2,4-bis[(phenylsulfonyl)methyl]-3H-heptaleno[1,10-bc]furan-3-carboxylate (**25a** and **25b**, resp.; 0.24 g, 37%). Yellow crystals. Recrystallization from Et<sub>2</sub>O/hexane gave almost pure **25b**. M.p. 201–202°.



**Data of 24:**  $R_f$  (hexane/AcOEt 2:1) 0.39.  $^1\text{H-NMR}$  (600 MHz,  $\text{CDCl}_3$ ): Table 5.  $^{13}\text{C-NMR}$  (150 MHz,  $\text{CDCl}_3$ ): Table 6. CI-MS: 433 (100,  $[M + H]^+$ ). Anal. calc. for  $\text{C}_{26}\text{H}_{24}\text{O}_4\text{S}$  (432.54): C 72.20, H 5.59; found: C 72.36, H 5.78.

**Data of 25b:**  $R_f$  (hexane/AcOEt 2:1) 0.22.  $^1\text{H-NMR}$  (600 MHz,  $\text{CDCl}_3$ ): Table 7.  $^{13}\text{C-NMR}$  (150 MHz,  $\text{CDCl}_3$ ): Table 8. CI-MS: 624 (47,  $[M + \text{NH}_4]^+$ ), 607 (100,  $[M + H]^+$ ). Anal. calc. for  $\text{C}_{33}\text{H}_{34}\text{O}_7\text{S}_2$  (606.77): C 65.33, H 5.65, N 10.57; found: C 65.64, H 5.75, N 10.90.

**2.8. Diester 23 with Methyl Morpholino Sulfone.** The BuLi soln. (3.06 ml, 7.66 mmol) was added at  $0^\circ$  to a soln. of methyl morpholino sulfone (1.01 g, 6.13 mmol) in THF (30 ml). After 30 min, the mixture was cooled to  $-78^\circ$  within 15 min, and a soln. of **23** (0.5 g, 1.53 mmol) in THF (5 ml) was added dropwise within 5 min. After additional stirring at  $-78^\circ$  for 2 h, the mixture was warmed up within 2 h to  $0^\circ$ . Then, BuLi soln. (1.53 ml, 3.83 mmol) was added. The mixture was warmed up within 45 min to r.t. and then poured onto ice and 10% aq. HCl soln. (100 ml). The mixture was extracted with AcOEt ( $2 \times 50$  ml), the org. phase washed with brine ( $2 \times 50$  ml) and dried ( $\text{MgSO}_4$ ). Removal of AcOEt by evaporation in vacuum left a solid residue which, after chromatography on silica gel (FC) with hexane/AcOEt 1:1, gave, as main product, 6,7,9,11-tetramethyl-2-(morpholinosulfonyl)-3-[(morpholinosulfonyl)methyl]-1H-cyclopenta[d]heptalen-1-one (**30**; 0.21 g, 24%). Orange crystals. M.p. 261.5–262.5° (AcOEt).

**Data of 30:**  $R_f$  (hexane/AcOEt 1:1) 0.28.  $^1\text{H-NMR}$  (600 MHz,  $\text{CDCl}_3$ ): 6.978 (*d*,  $^3J = 6.6$ , H–C(4)); 6.409 (*dd*,  $^3J = 6.7$ ,  $^5J = 1.4$ , H–C(5)); 6.262 (*s*, H–C(10)); 6.177 (*s*, H–C(8)); 4.860, 4.632 (*AB*,  $J_{AB} = 12.4$ ,  $\text{CH}_2$ ); 3.79–3.33 (*m*, 16 H of two morpholino residues); 2.221 (*s*, Me–C(11)); 2.053 (*s*, Me–C(6)); 2.033 (*s*, Me–C(9)); 1.868 (*s*, Me–C(7)).  $^1\text{H-NOE}$  (600 MHz,  $\text{CDCl}_3$ ): 6.972 (*d*, H–C(4))  $\rightarrow$  6.409 (H–C(5)) and 4.860/4.632 (*AB*,  $\text{SO}_2\text{CH}_2$ –C(3)); 4.860 (*A* of  $\text{SO}_2\text{CH}_2$ )  $\rightarrow$  6.978 (H–C(4)); 4.632 (*B* of  $\text{SO}_2\text{CH}_2$ )  $\rightarrow$  6.978 (H–C(4)).  $^{13}\text{C-NMR}$  (150 MHz,  $\text{CDCl}_3$ ): 182.63 (O=C(1)); 153.83 (C(2)); 145.50 (C(11a)); 140.15 (C(9)); 139.11 (C(6)); 137.28 (C(3a)); 136.81 (C(11b)); 133.19 (C(7)); 132.15 (C(11)); 130.72 (C(4/8)); 130.36 (C(10)); 126.94 (C(5)); 126.16 (C(6a)); 124.54 (C(3)); 66.87, 66.44 (4 C atoms of two morpholino residues); 46.15, 46.00 (4 C atoms of two morpholino residues), 45.58 ( $\text{CH}_2\text{SO}_2$ ); 25.04 (Me–C(9)); 24.20 (Me–C(6)); 23.80 (Me–C(11)); 19.86 (Me–C(7)). CI-MS: 575 (100,  $[M + H]^+$ ), 426 (27). Anal. calc. for  $\text{C}_{28}\text{H}_{34}\text{N}_2\text{O}_7\text{S}_2$  (574.71): C 58.52, H 5.96; found: C 58.10, H 5.83.

**3. Additional Experiments.** – **3.1. Synthesis of Methyl 9-Isopropyl-1,6-dimethyl-4-[(morpholinosulfonyl)ethynyl]heptalene-5-carboxylate (7a).** **3.1.1. Methyl 9-Isopropyl-1,6-dimethyl-4-[(morpholinosulfonyl)acetyl]heptalene-5-carboxylate (5).** The BuLi soln. (2.56 ml, 6.4 mmol) was added at  $0^\circ$  to a soln. of methyl morpholino sulfone (0.54 g, 3.2 mmol) in THF (50 ml). After 30 min, the mixture was cooled to  $-78^\circ$ , and a soln. of **4** (1.0 g, 2.94 mmol) in THF (5 ml) was added dropwise within 5 min. After additional stirring at  $-78^\circ$  to  $-40^\circ$  for 4 h, the mixture was poured onto ice and 5% aq. HCl soln. (100 ml). After extraction with  $\text{Et}_2\text{O}$  ( $3 \times 50$  ml), the org. layer was washed with  $\text{H}_2\text{O}$  (50 ml) and dried ( $\text{MgSO}_4$ ). Removal of  $\text{Et}_2\text{O}$  by evaporation *in vacuo* left a solid residue which, by TLC (hexane/ $\text{Et}_2\text{O}$  1:5), showed two main spots with  $R_f$  0.43 and 0.33, and another spot close to the starting line. By column chromatography on silica gel with hexane/ $\text{Et}_2\text{O}$  1:4, a ca. 4:1 mixture of dimethyl (3RS,4SR)- and dimethyl (3RS,4RS)-3,4-dihydro-9-isopropyl-1,6-dimethyl-3-[(morpholinosulfonyl)methyl]heptalene-4,5-dicarboxylate (**6a** and **6b**, resp.; 0.52 g, 35%) as colorless crystals, and **5** (0.81 g, 58%) could be isolated. The material producing on TLC the spot next to the starting line was later identified as a 4:1 mixture **26a/26b** (cf. 3.3).

**Data of 5:**  $R_f$  (hexane/ $\text{Et}_2\text{O}$  1:5) 0.33. M.p. 152.5–153.5° ( $\text{Et}_2\text{O}$ /hexane). Yellow crystals.  $^1\text{H-NMR}$  (300 MHz,  $\text{CDCl}_3$ ): 7.411 (*dd*,  $^3J = 6.4$ ,  $^5J = 0.7$ , H–C(3)); 6.271 (*dd*,  $^3J = 6.3$ ,  $^5J = 1.2$ , H–C(2), H–C(8)); 6.127 (*dd*,  $^3J = 6.4$ ,  $^5J = 1.2$ , H–C(7)); 5.874 (*s*, H–C(10)); 4.388, 4.222 (*AB*,  $^2J_{AB} = 13.9$ ,  $\text{CH}_2\text{SO}_2$ ); 3.695 (*s*, MeOOC); 3.67 (*m*, 4 H of morpholino residues); 3.28 (*m*, 4 H of morpholino residues); 2.474 (*sept.*,  $J = 6.9$ ,  $\text{Me}_2\text{CH}$ ); 2.102 (*s*, Me–C(1)); 1.986 (*s*, Me–C(6)); 1.07 (*d*,  $^3J = 7.0$ , 3 H,  $\text{Me}_2\text{CH}$ ); 1.03 (*d*,  $^3J = 6.8$ , 3 H,  $\text{Me}_2\text{CH}$ ).  $^{13}\text{C-NMR}$  (75.5 MHz,  $\text{CDCl}_3$ ): 189.09 (O=C–C(4)); 166.20 (O=C–C(5)); 148.28, 147.26 (2*s*); 143.65 (*d*, CH); 140.02, 131.27, 128.56 (3*s*); 127.30, 126.09, 125.81, 125.42 (4*d*, 4 CH); 122.50 (*s*); 66.59 (*t*, 2  $\text{CH}_2$  of morpholino residues); 57.31 (*t*,  $\text{CH}_2\text{SO}_2$ ); 52.13 (*q*, MeOOC); 46.07 (*t*, 2  $\text{CH}_2$  of morpholino residues); 35.52 (*d*,  $\text{Me}_2\text{CH}$ ); 25.67, 23.04, 22.37, 22.34 (4*q*, 4 Me). CI-MS: 491 (100,  $[M + \text{NH}_4]^+$ ), 474 (43,  $[M + H]^+$ ), 410 (15), 378 (9), 323 (18). Anal. calc. for  $\text{C}_{25}\text{H}_{31}\text{NO}_6\text{S}$  (473.60): C 63.40, H 6.60, N 2.96, S 6.77; found: C 63.33, H 6.47, N 2.99, S 6.64.

**Data of 6a and 6b:**  $R_f$  (hexane/ $\text{Et}_2\text{O}$  1:5) 0.43.  $^1\text{H-NMR}$  (300 MHz,  $\text{C}_6\text{D}_6$ ): Table 10. ESI-MS: 528 (100,  $[M + \text{Na}]^+$ ), 506 (9,  $[M + H]^+$ ), 446 (12).

The final structure of recrystallized, pure **6a** (m.p. of **6a** 167.5–168.5° ( $\text{CH}_2\text{Cl}_2/\text{Et}_2\text{O}$ )) was established by an X-ray crystal-structure analysis (cf. Table 9).

Table 10.  $^1\text{H}$ -NMR Data of **6a** and **6b** ( $\text{C}_6\text{D}_6$ )

Atom/group at C(X)	$\delta[\text{ppm}]$ ( $J[\text{Hz}]$ )	
	<b>6a</b>	<b>6b</b>
H–C(2)	6.59 ( <i>dd</i> , $J = 5.8$ , 0.9)	5.86 ( <i>br. s</i> )
H–C(10)	6.31 ( <i>s</i> )	6.34 ( <i>s</i> )
H–C(7)	6.15 ( <i>d</i> , $J = 6.5$ )	6.20 ( <i>d</i> , $J = 6.5$ )
H–C(8)	6.02 ( <i>dd</i> , $J = 6.5$ , 1.0)	6.09 ( <i>dd</i> , $J = 6.6$ , 1.1)
$\text{XCH}_2\text{–C}(3)$	4.30 ( <i>dd</i> , $J = 14.0$ , 1.9)	3.44 ( <i>dd</i> , $J = 14.1$ , 6.2)
$\text{XCH}_2\text{–C}(3)$	3.09 ( <i>dd</i> , $J = 14.0$ , 11.5)	3.26 ( <i>dd</i> , $J = 14.1$ , 5.7)
H–C(4)	3.88 ( <i>d</i> , $J = 2.3$ )	4.78 ( <i>d</i> , $J = 2.4$ )
Morpholino residue	$\sim 3.35$ ( <i>m</i> , 4 H) $\sim 3.80$ ( <i>m</i> , 4 H)	3.25 ( <i>m</i> ) 3.87, 3.83 (each <i>dt</i> , $J = 12.0$ , 4.7 $\Delta\delta = 27$ Hz)
$\text{MeOOC–C}(4,5)$	3.31/3.23 ( <i>s/s</i> )	3.36/3.24 ( <i>s/s</i> )
H–C(3)	3.4–3.2	3.4–3.2
$\text{Me}_2\text{CH–C}(9)$	2.32 ( <i>sept.</i> , $J = 6.9$ )	2.29 ( <i>sept.</i> , $J = 6.9$ )
$\text{Me–C}(6)$	1.84 ( <i>s</i> )	2.03 ( <i>s</i> )
$\text{Me–C}(1)$	1.76 ( <i>t</i> , $J = 1.2$ )	1.80 ( <i>t</i> -like, $J = 2.0/1.5$ )
$\text{Me}_2\text{CH–C}(9)$	0.99 ( <i>d</i> , $J = 7.5$ )	1.02 ( <i>d</i> , $J = 6.8$ )
	0.98 ( <i>d</i> , $J = 7.1$ )	0.99 ( <i>d</i> , $J = 7.5$ )

3.1.2. *Formation of 7a*. Freshly distilled (from  $\text{CaH}_2$ )  $\text{Et}_3\text{N}$  (2 ml) was added dropwise to a cooled (ice-bath) mixture of **5** (0.24 g, 0.5 mmol) and 2-chloro-1-methylpyridinium iodide (0.26 g, 1 mmol) in  $\text{CH}_2\text{Cl}_2$  (7 ml). The suspension was stirred at r.t. for 2 d, then 1N aq. NaOH soln. (2 ml) was added. After 5 min, the mixture was extracted with  $\text{CH}_2\text{Cl}_2$ . The org. phase was successively washed with 1N aq. NaOH soln. and  $\text{H}_2\text{O}$ , dried ( $\text{MgSO}_4$ ), evaporated, and the residue chromatographed on silica gel with hexane/ $\text{Et}_2\text{O}$  1:4 to give **7a** (0.105 g, 46%) which was recrystallized from  $\text{Et}_2\text{O}$ /hexane. M.p. 122–123°.

*Data of 7a*:  $R_f$  (hexane/ $\text{AcOEt}$  1:1) 0.64. When the crystals of **7a** are dissolved at  $-20^\circ$  in  $\text{CDCl}_3$ , only **7a** is present in solution. However, at r.t., a thermal equilibrium of 74% of **7a** and 26% of its DBS isomer **7b** is established.  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ , taken from the 3:1 mixture with **7b**): 6.958 (*dd*,  $^3J = 6.4$ ,  $^5J = 0.8$ , H–C(3)); 6.276 (*d*,  $^3J = 6.6$ , H–C(7)); 6.153 (*dd*,  $^3J = 6.6$ ,  $^5J = 1.3$ , H–C(8)); 6.01 (*dd*,  $^3J = 6.4$ ,  $^5J = 1.4$ , H–C(2)); 5.862 (*s*, H–C(10)); 3.788 (*s*,  $\text{MeOOC}$ ); 3.78 (*m*, 4 H of morpholino residue); 3.13 (*m*, 4 H of morpholino residue); 2.513 (*sept.*,  $J = 6.7$ ,  $\text{Me}_2\text{CH}$ ); 2.024 (*d*,  $^5J = 1.1$ ,  $\text{Me–C}(1)$ ); 1.993 (*s*,  $\text{Me–C}(6)$ ); 1.119 (*d*,  $^3J = 6.9$ , 3 H,  $\text{Me}_2\text{CH}$ ); 1.102 (*d*,  $^3J = 6.9$ , 3 H,  $\text{Me}_2\text{CH}$ ).  $^{13}\text{C}$ -NMR (300 MHz,  $\text{CDCl}_3$ , taken from the 3:1 mixture with **7b**): 166.87 (*s*,  $\text{O=C–C}(5)$ ); 149.05, 144.29 (2*s*); 143.86 (*d*, CH); 135.46, 131.33 (2*s*); 128.28, 126.64, 125.73, 125.38 (4*d*, 4 CH); 124.04, 121.76, 119.25 (3*s*); 92.12, 80.24 (2*s*); 65.72 (*t*,  $\text{CH}_2$  of morpholino residue); 52.43 (*q*,  $\text{MeO}$ ); 46.11 (*t*,  $\text{CH}_2$  of morpholino residue); 35.70 (*d*,  $\text{Me}_2\text{CH}$ ); 25.48, 23.07, 22.57, 22.48 (4*q*, 4 Me). CI-MS: 456 (100,  $[\text{M} + \text{H}]^+$ ), 307 (26), 88 (15). Anal. calc. for  $\text{C}_{25}\text{H}_{29}\text{NO}_5\text{S}$  (455.58): C 65.91, H 6.48, N 3.07; found: C 65.80, H 6.31, N 3.10.

*Data of Methyl 7-Isopropyl-5,9-dimethyl-2-[(morpholinosulfonyl)ethynyl]heptalene-1-carboxylate (7b)*:  $^1\text{H}$ -NMR (300 MHz,  $\text{CDCl}_3$ ; taken from the 3:1 mixture with **7a**): 6.567 (*d*,  $^3J = 11.7$ , H–C(3)); 6.45 (*m*, H–C(4), H–C(8), H–C(9)); 5.87 (*s*, H–C(6)); 3.84 (*m*, 4 H of morpholino residue); 3.722 (*s*,  $\text{MeOOC}$ ); 3.31 (*m*, 4 H of morpholino residue); 2.51 (*sept.*); 1.765, 1.632 (2*s*,  $\text{Me–C}(5)$ ,  $\text{Me–C}(10)$ ); 1.15, 1.14 (2*d*,  $^3J = 6.7$ ,  $\text{Me}_2\text{CH}$ ).

3.2. *Formation of 8 from 5*. A soln. of BuLi (0.88 ml, 2.2 mmol) was added dropwise to a soln. of methyl morpholino sulfone (0.315 g, 1.9 mmol) in THF (30 ml), stirred, and cooled at  $0^\circ$ . After 30 min, the colorless suspension was cooled to  $-40^\circ$ , and a soln. of **5** (0.3 g, 0.63 mmol) in THF (5 ml) was added within 5 min, and the reaction temp. raised within 2 h to  $0^\circ$ . After stirring for an additional 1 h at  $0^\circ$ , a second portion of BuLi soln. (0.76 ml, 1.9 mmol) was added. The color of the reaction changed from red to yellow-red. The mixture was allowed to warm to r.t. within ca. 30 min and poured onto ice and 10% aq. HCl soln. (50 ml). The product was extracted with  $\text{AcOEt}$  ( $2 \times 50$  ml), and the org. layer washed with brine (50 ml) and dried ( $\text{MgSO}_4$ ). Removal of  $\text{AcOEt}$  by evaporation *in vacuo* left a solid residue which, chromatographed on silica gel with hexane/ $\text{AcOEt}$  2:1, gave pure **8** (0.195 g, 68%). For data, cf. 2.1.

3.3. *Synthesis of the 4:1 Mixture of 3-Hydroxy-8-isopropyl-6,11-dimethyl-1-oxocyclopenta[a]heptalen-2-yl Morpholino Sulfone (26a) and Its 1-Hydroxy-3-oxo Tautomer 26b.* To a soln. of KOH (0.34 g, 6 mmol) in MeOH (8 ml) was added **5** (0.4 g, 0.85 mmol) at r.t. After stirring for 2.5 h, the mixture was poured into ice-water and acidified to pH 1 with 20% aq. H<sub>2</sub>SO<sub>4</sub> soln. to give a yellow precipitate. The mixture was extracted with AcOEt (5 × 20 ml). The AcOEt extracts were washed with brine, dried (MgSO<sub>4</sub>), and the solvent was removed. The solid residue which consisted of the 4:1 mixture **26a/26b** was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>/Et<sub>2</sub>O (0.347 g, 93%) as yellow powder.

*Data of 26a:* M.p. > 300°. *R*<sub>f</sub> (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 9:1) 0.30. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>; taken from the 4:1 mixture with **26b**) 10.075 (s, HO–C(3)); 6.826 (d, <sup>3</sup>*J* = 7.0, H–C(4)); 6.34–6.21 (m, H–C(5), H–C(9), H–(10)); 6.034 (s, H–C(7)); *ca.* 3.74 (m, 4 H of morpholino residue); *ca.* 3.29 (m, 4 H of morpholino residue); 2.485 (*sept.*, <sup>3</sup>*J* = 6.8, Me<sub>2</sub>CH); 2.243, 2.177 (2s, Me–C(6), Me–C(11)); 1.109, 1.086 (2d, <sup>3</sup>*J* = 6.8, Me<sub>2</sub>CH). <sup>13</sup>C-NMR (75.5 MHz, CDCl<sub>3</sub>; taken from the 4:1 mixture with **26b**): 177.80 (s, O=C(1)); 148.44, 141.80, 140.74, 133.44, 132.44, 131.85 (6s); 129.23, 127.93, 127.28, 125.81 (4d, 4 CH); 124.55, 108.84 (2s); 66.26, 45.82 (2t, 4 CH<sub>2</sub> of morpholino residue); 35.97 (d, Me<sub>2</sub>CH); 26.01, 24.51, 23.03, 22.70 (4g, 4 Me). CI-MS: 442 (100, [M + H]<sup>+</sup>), 293 (25), 88 (17). Anal. calc. for C<sub>24</sub>H<sub>27</sub>NO<sub>5</sub>S (441.55): C 65.29, H 6.16, N 3.17; found: C 65.06, H 6.21, N 3.21.

*Data of 26b:* <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>; taken from the 4:1 mixture with **26a**; only characteristic signals): *ca.* 10.56 (s, HO–C(1)); *ca.* 6.95 (d, H–C(4)); 6.02 (s, H–C(7)).

3.3.1. *Attempted Transformation of 26a/26b into 8.* A soln. of BuLi (0.20 ml, 0.50 mmol) was added dropwise to a soln. of methyl morpholino sulfone (0.076 g, 0.46 mmol) in THF (10 ml) at 0°. After 30 min, the colorless suspension was cooled to –20°, and a soln. of **26a/26b** (0.1 g, 0.23 mmol) in THF (5 ml) was added within 5 min. The reaction temp. was raised within 1 h to 0°. A second portion of BuLi soln. (0.20 ml, 0.50 mmol) was added. The mixture was allowed to warm to r.t. within *ca.* 30 min and poured onto ice and 10% aq. HCl soln. (40 ml). The usual workup and TLC of the product mixture revealed only the presence of traces of **8**.

3.4. *Synthesis of 9-Isopropyl-1,6-dimethyl-4,5-bis[(morpholinosulfonyl)acetyl]heptalene (27).* Methyl morpholino sulfone (0.54 g, 3.20 mmol) was dissolved in THF (30 ml) at 0°, and BuLi soln. (2.6 ml, 6.4 mmol) was added. After 30 min, the mixture was cooled to –78°, and a soln. of **4** (0.5 g, 1.47 mmol) in THF was added dropwise within 5 min. The mixture was warmed up within 2 h to –10° and then stirred for 1 h at –5 to 0°, and poured onto ice and 10% aq. HCl soln. (100 ml). The mixture was extracted with AcOEt. The AcOEt extracts were washed with brine and dried (MgSO<sub>4</sub>). The solvent was evaporated and the residue subjected to CC on silica gel with hexane/Et<sub>2</sub>O 1:5 yielding a yellowish powder of **27** (0.47 g, 53%).

*Data of 27:* M.p. 162–163° (Et<sub>2</sub>O). *R*<sub>f</sub> (hexane/Et<sub>2</sub>O 1:10) 0.28. <sup>1</sup>H-NMR 6.966 (d, <sup>3</sup>*J* = 7.2, H–C(3)); 6.284 (m, H–C(2), H–C(8)); 6.253 (dd, <sup>3</sup>*J* = 6.9, <sup>4</sup>*J* = 1.0, H–C(7)); 6.160 (s, H–C(10)); 4.839, 4.689 (AB, <sup>2</sup>*J*<sub>AB</sub> = 12.5, SO<sub>2</sub>CH<sub>2</sub>); 3.77–3.35 (m, 8 CH<sub>2</sub> of two morpholino residues, SO<sub>2</sub>CH<sub>2</sub>); 2.511 (*sept.*, <sup>3</sup>*J* = 6.6, Me<sub>2</sub>CH); 2.229, 2.157 (2s, Me–C(1), Me–C(6)); 1.100, 1.077 (2d, <sup>3</sup>*J* = 6.6, Me<sub>2</sub>CH). ESI-MS: 629 (100, [M + Na]<sup>+</sup>); 607 (5, [M + 1]<sup>+</sup>). Anal. calc. for C<sub>29</sub>H<sub>39</sub>N<sub>2</sub>O<sub>8</sub>S<sub>2</sub> (606.77): C 57.41, H 6.31, N 4.62; found: C 57.85, H 6.68, N 4.88.

3.4.1. *Transformation of 27 into 8.* A soln. of BuLi (0.4 ml, 1 mmol) was added dropwise to a soln. of methyl morpholino sulfone (0.076 g, 0.46 mmol) in THF (10 ml) at 0°. After 30 min, the mixture was cooled to –20°, and a soln. of **27** (0.14 g, 0.23 mmol) in THF (5 ml) was added. After 15 min, a second portion of BuLi soln. (0.4 ml, 1 mmol) was added. The mixture was allowed to warm to r.t. within 30 min, and poured onto ice and 10% aq. HCl soln. (40 ml). The usual workup and TLC control of the product mixture revealed the presence of **8** in distinct amounts.

3.5. *Synthesis of a Mixture of (2RS,3SR,6aMP)- and (2RS,3SR,6aPM)-3-Hydroxy-7-isopropyl-6,11-dimethyl-2-(morpholinosulfonyl)-3-[(morpholinosulfonyl)methyl]cyclopenta[a]heptalen-1-one (31a and 31b, resp.).* A soln. of BuLi (0.36 ml, 0.9 mmol) was added dropwise to a soln. of methyl morpholine sulfone (0.15 g, 0.9 mmol) in THF (10 ml) at 0°. After 30 min, the suspension was cooled to –78°, and a soln. of **4** (0.15 g, 0.44 mmol) in THF was added. The reaction temp. was raised within 3 h to –10°. TLC Control of the product mixture showed the presence of small spots for a cyclopenta[*d*]heptalene, analogous to **30** (<sup>1</sup>H-NMR evidence) and for **27**, followed by an intense spot and again a much smaller spot for two unknown products. The mixture was poured onto ice and 10% aq. HCl soln. (50 ml). The usual workup and chromatography on silica gel gave, beside small amounts of the compound, analogous to **30**, a *ca.* 3:1 mixture **31a/31b** (0.047 g, 18%) as brown oil. *R*<sub>f</sub> (hexane/AcOEt 1:1) 0.18.

*Data of 31a/31b:* IR (CHCl<sub>3</sub>): 3494m, 3024s, 3015s, 2966s, 2924s, 2865s, 1702s, 1616w, 1453s, 1347vs, 1329s, 1156vs, 1114vs, 1074s, 958vs, 787m, 780m, 766s, 758s, 721vs, 672vs, 550s, 500s, 470m. <sup>1</sup>H-NMR (600 MHz, C<sub>6</sub>D<sub>6</sub>; signals in the order **31a/31b**): 6.658/6.562 (d, <sup>3</sup>*J*(4,5) = 11.5/11.5, H–C(4)); 6.517/6.618 (d, <sup>3</sup>*J*(5,4) = 11.6/11.5, H–C(5)); 6.298/6.255 (d, <sup>3</sup>*J*(10,9) = 11.8/11.8, H–C(10)); 6.212/6.174 (dd, <sup>3</sup>*J*(9,10) = 11.9/11.8, <sup>4</sup>*J*(9,7) ≈ 1/1.2, H–C(9)); 5.574/5.444 (s, H–C(7)); 5.219/5.367 (s, H–C(2)); 5.193/4.830 (s, HO–C(3)); 3.236,

2.546/3.18, 3.58<sup>14</sup>) (*AB*,  $^2J_{AB}$  = 13.9/ca. 14<sup>14</sup>), SO<sub>2</sub>CH<sub>2</sub>); 3.64–3.16, 2.83–2.73, 2.69–2.63 (*m*, regions of the two morpholino groups in **31a** and **31b**); 2.278/2.266 (*sept.*, Me<sub>2</sub>CH); 1.867/1.746 (*s*, Me–C(11)); 1.606/1.512 (*s*, Me–C(6)); 0.980, 0.961/0.957, 0.945 (*2d*, *J* = 6.9, 6.8/7.0, Me<sub>2</sub>CH). <sup>13</sup>C-NMR (75 and 150 MHz, C<sub>6</sub>D<sub>6</sub>; signals in the order **31a/31b**): 192.10/190.50 (C(1)); 170.2/170.6 (C(3a)); 150.76/150.30 (C(8)); 145.12/145.31 (C(5)); 138.94/138.90 (C(6a)); 157.05/137.05 (C(10)); 135.66/136.80 (C(11)); 136.3/ca. 133.2 (C(11b)); 133.19/133.04 (C(9)); 130.72/131.16 (C(6)); 124.62/124.62 (C(11a)); 123.11/123.38 (C(4)); 122.31/122.74 (C(7)); 74.92/75.15 (C(3)); 71.11/70.78 (C(2)); 56.08/54.11 (SO<sub>2</sub>CH<sub>2</sub>); 35.22/35.22 (Me<sub>2</sub>CH); 22.67, 22.55/22.67, 22.55 (Me<sub>2</sub>CH); 19.30/19.12 (Me–C(11)); 18.28/18.28 (Me–C(6));  $\delta$  of the two morpholino groups: 66.78 (**31a**), 66.38 (**31b**), 66.11 (**31a/31b**), 46.69 (**31a**), 46.42 (**31b**), 45.58 (**31a/31b**). ESI-MS: 629.3 (100, [*M* + Na]<sup>+</sup>).

3.6. (2*RS*,3*SR*)-3-Hydroxy-2-(morpholinosulfonyl)-3-[(morpholinosulfonyl)methyl]indan-1-one (**28**). A soln. of BuLi (4.0 ml, 10 mmol) was added dropwise to a soln. of methyl morpholino sulfone (0.826 g, 5 mmol) in THF (40 ml) at 0°. After 30 min, the suspension was cooled to –20°, and a soln. of diethyl phthalate (1.0 g = 0.90 ml, 4.5 mmol) in THF (5 ml) was added. The reaction temp. was raised within 2 h to r.t. The mixture was poured onto ice and 10% aq. HCl soln. (50 ml). The mixture was extracted with AcOEt. The org. phase was washed with brine and dried (MgSO<sub>4</sub>). After evaporation, the residue was chromatographed on silica gel with hexane/AcOEt 1:3 to give as a main product **28** (1.15 g, 55%).

*Data of 28*: Colorless crystals. M.p. 183–184° (acetone). *R*<sub>f</sub> (hexane/AcOEt 1:3) 0.31. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 7.84–7.57 (*m*, 4 arom. H); 5.183 (*s*, H–C(2)); 4.667 (br. *s*, HO–C(3)); 3.81–3.70, 3.63–3.20 (*2m*, 16 H of two morpholino residues); 3.662, 3.191 (*AB*,  $^2J_{AB}$  = 14.2, CH<sub>2</sub>). <sup>13</sup>C-NMR (75.5 MHz, CDCl<sub>3</sub>): 192.19 (*s*, C=O); 154.16 (*s*); 136.62 (*d*, CH); 134.37 (*s*); 130.87, 124.47, 124.29 (*3d*, 3 CH); 75.27 (*s*); 71.74 (*d*, CH); 66.82, 66.37 (*2t*, 4 CH<sub>2</sub> of one morpholino residue); 57.09 (*t*, CH<sub>2</sub>SO<sub>2</sub>); 46.30, 45.61 (*2t*, 4 CH<sub>2</sub> of one morpholino residue). CI-MS: 460 (100, *M*<sup>+</sup>), 443 (45), 311 (39), 294 (25), 88 (45). Anal. calc. for C<sub>18</sub>H<sub>24</sub>N<sub>2</sub>O<sub>8</sub>S<sub>2</sub> (460.54): C 46.95, H 5.25, N 6.08; found: C 46.99, H 5.22, N 5.99.

The final structure of **28** was established by an X-ray crystal-structure analysis (*cf.* Table 9).

3.7. 2-(Morpholinosulfonyl)-3-[(morpholinosulfonyl)methyl]inden-1-one (**29**). A soln. of BuLi (8.1 ml, 20.25 mmol) was added dropwise to a soln. of methyl morpholino sulfone (1.67 g, 10.13 mmol) in THF (60 ml) at 0°. After 30 min, the suspension was cooled to –78°, and a soln. of diethyl phthalate (0.75 g = 0.67 ml, 3.38 mmol) in THF (5 ml) was added. The reaction temp. raised within 3 h to 0°. After additional stirring for 1 h at r.t., the mixture was worked up by addition of ice and 10% aq. HCl soln. The mixture was extracted with AcOEt (3 × 50 ml), the org. phase washed with brine and dried (MgSO<sub>4</sub>). The residue of the AcOEt extracts was chromatographed on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/MeOH 98:2 to give as main product **29** (0.87 g, 58%).

*Data of 29*: Yellow crystals. M.p. 199–200° (AcOEt). *R*<sub>f</sub> (CH<sub>2</sub>Cl<sub>2</sub>/MeOH 40:1) 0.55. <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>): 7.62–7.43 (*m*, 4 arom. H); 4.802 (*s*, CH<sub>2</sub>); 3.81–3.40 (*m*, 16 H of two morpholino residues). <sup>13</sup>C-NMR (75.5 MHz, CDCl<sub>3</sub>): 189.47 (*s*, C=O); 154.78, 141.34 (*2s*); 134.73 (*d*, CH); 133.90 (*s*); 132.09 (*d*, CH); 128.72 (*s*); 124.51, 123.73 (*2d*, 2 CH); 66.7, 66.40 (*2t*, 4 CH<sub>2</sub> of one morpholino residue); 46.46 (*t*, CH<sub>2</sub>); 46.17, 45.86 (*2t*, 4 CH<sub>2</sub> of one morpholino residue). CI-MS: 460 (100, [*M* + NH<sub>4</sub>]<sup>+</sup>), 443 (57, [*M* + H]<sup>+</sup>), 311 (44), 294 (36), 88 (66). Anal. calc. for C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>O<sub>7</sub>S<sub>2</sub> (442.52): C 48.86, H 5.01, N 6.33; found: C 48.80, H 4.97, N 6.07.

3.8. Transformation of the 4:1 Mixture **6a/6b** into the 1:1 Mixture **9a/9b**. A soln. of BuLi (0.12 ml, 0.3 mmol) was added dropwise to a soln. of methyl morpholino sulfone (0.05 g, 0.3 mmol) in THF (5 ml) at 0°. After 30 min, the suspension was cooled to –78°, and a soln. of the 4:1 mixture **6a/6b** (0.05 g, 0.1 mmol) in THF (2 ml) was added. The reaction temp. was raised within 1 h to 0°. A second portion of BuLi soln. (0.12 ml, 0.3 mmol) was added. The mixture was allowed to warm to r.t. in ca. 30 min, and poured onto ice and 10% aq. HCl soln. (20 ml). The usual workup and chromatographic purification gave a ca. 1:1 mixture **9a/9b** (<sup>1</sup>H-NMR evidence; *cf.* 2.1).

4. Crystal Structure Determinations of **6a**, **10**, **13a**, **18**, **19a/19b**, and **28**<sup>15</sup>. – All measurements were conducted on a Rigaku AFC5R diffractometer using graphite-monochromated MoK<sub>α</sub> radiation ( $\lambda$  = 0.71069 Å) and a 12-kW rotating anode generator. Except for **10**, the intensities of three standard reflections, which were measured after every 150 reflections, remained stable throughout each data collection. For **10**, the intensities of the standard reflections increased in a nonlinear fashion by ca. 12%, and a 5th-order polynomial correction factor was applied

<sup>14</sup>) The signals for **31b** are buried under *m* of the morpholino groups. Therefore, their  $\delta$  and *J* values were taken from the <sup>1</sup>H-NOESY spectrum of the 3:1 mixture **31a/31b**.

<sup>15</sup>) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-10/63. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: + 44-(0)1223-336033 or email: deposit@ccdc.cam.ac.uk).

to the intensities to correct for this. For each data set, the intensities were also corrected for Lorentz and polarization effects, but not for absorption.

Each structure was solved by direct methods using SHELXS86 [23] which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. For **6a**, **10**, **18**, and **28**, the H-atoms were located in difference-electron-density maps, and their positions were refined together with individual isotropic displacement parameters. For **13a** and **19a/19b**, the H-atoms were fixed in geometrically calculated positions ( $d(\text{C}-\text{H}) = 0.95 \text{ \AA}$ ) and in **19a/19b** they were assigned fixed isotropic displacement parameters with a value equal to  $1.2U_{\text{eq}}$  of the parent C-atom, while for **13a**, their isotropic displacement parameters were allowed to refine freely. No corrections were made for secondary extinction. All refinements were carried out on  $F$  using full-matrix least-squares procedures which minimized the function  $\sum W(|F_o| - |F_c|)^2$ . The data collection and refinement parameters for each compound are listed in Table 9.

Neutral atom scattering factors for non-H-atoms were taken from [24a] and the scattering factors for H-atoms from [25]. Anomalous dispersion effects were included in  $F_c$  [26]; the values for  $f'$  and  $f''$  were taken from [24b]. All calculations were performed using the TEXSAN [27] crystallographic software package, and the figures were produced with ORTEPII [28].

In **18**, the OH group at C(2) forms an intramolecular H-bond with one of the sulfoxide O-atoms ( $\text{O}(2) \cdots \text{O}(5) = 2.624(3) \text{ \AA}$ ,  $\text{H}(2) \cdots \text{O}(5) = 1.87(3) \text{ \AA}$ ,  $\text{O}(2) \cdots \text{O}(5) = 153(3)^\circ$ ). The OH group at C(4) forms an intermolecular H-bond with the other sulfoxide O-atom and thereby links the molecules into dimeric units situated across centers of inversion ( $\text{O}(4) \cdots \text{O}(6') = 2.792 \text{ \AA}$ ,  $\text{H}(4) \cdots \text{O}(6') = 2.01(3) \text{ \AA}$ ,  $\text{O}(4)-\text{H}(4) \cdots \text{O}(6') = 158(3)^\circ$ , where O(6') is in the molecule at  $-x, 1-y, -z$ ).

The crystal of **19a/19b** was quite small, which resulted in a smaller number of observed reflections than usual. The crystal contains a racemic mixture of each of the two diastereoisomers, **19a** and **19b**, namely the (3*RS*,4*SR*,10*aRS*)- and (3*RS*,4*SR*,10*aSR*)-isomers. The two diastereoisomeric configurations occupy the same locations within the unit cell, which results in the appearance of a disordered structure in which the heptalene ring with the *i*-Pr substituent has two conformations with inversion at C(10a). Disordered positions were assigned to the heptalene ring atoms C(8) to C(10), the Me group at C(10a) and the *i*-Pr group. The site occupation of each orientation was refined and yielded an occupation ratio of 0.56:0.44. All other atoms from these diastereoisomers overlap exactly in the structure. The positions for some of the disordered atoms, particularly C(10) and  $\text{CH}_3-\text{C}(10a)$ , which nearly overlap with their inverted counterparts, as well as those of the *i*-Pr group, do not refine very well and should be considered to be only approximate. This is evident in the large estimated standard deviations and distorted displacement ellipsoids for these atoms. As a result, some of the C–C bond lengths involving these atoms appear to be quite long, while others may be unduly short.

For **28**, the asymmetric unit also contains one disordered acetone molecule. Two positions were defined for the carbonyl C- and O-atoms of the acetone molecule with the two orientations having relative populations of 0.56:0.44. The OH group forms an intramolecular H-bond with one of the sulfoxide O-atoms of the sulfoxide group attached to the same C-atom at the OH group ( $\text{O}(1) \cdots \text{O}(12) = 2.915(2) \text{ \AA}$ ,  $\text{H}(1) \cdots \text{O}(12) = 2.15(3) \text{ \AA}$ ,  $\text{O}(1)-\text{H}(1) \cdots \text{O}(12) = 133(3)^\circ$ ).

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