Alkylation Reactions at the Benzo Moiety of 2,4-Dimethoxy-3-(phenylsulfonyl)benzo[*a*]heptalenes – Model Compounds of Colchicinoids

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Dedicated to *Albert Eschenmoser* on the occasion of his 85th birthday

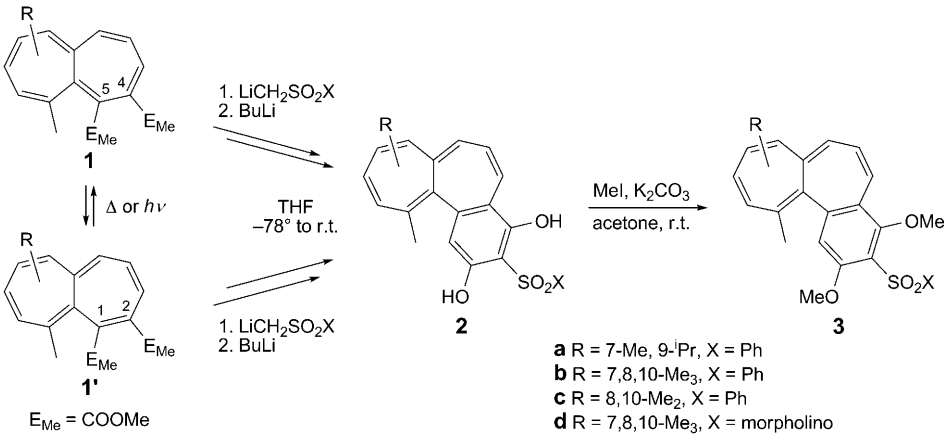
The times change, along with fashions,
ways of being and of trust change;
all the world's made up of change,
consistent only in alteration.
Everything we see seems novel
and altered from all we ever dreamed;
evil endures as grief remembered,
good, if one finds it, as fond recall.
Luís de Camões [1]

Alkylation reactions of 3-(X-sulfonyl)benzo[*a*]heptalene-2,4-diols (X = Ph, morpholin-4-yl) and their dimethyl ethers were studied. The diols form with K_2CO_3/MeI in aqueous media the 1-methylated benzoheptalenes, but in yields not surpassing 20% (*Table 1*). On the other hand, 2,4-dimethoxybenzo[*a*]heptalenes can easily be lithiated at C(3) with BuLi and then treated with alkyl iodides to give the 3-alkylated forms in good yield (*Table 2*). Surprising is the reaction with two equiv. or more of *t*-BuLi since the alkylation at C(4) is accompanied by the reductive elimination of the X-sulfonyl group at C(3) (*Table 3*). Most exciting is also the course of 2,4-dimethoxy-3-(phenylsulfonyl)benzo[*a*]heptalenes in the presence of an excess of MeLi. After the expected exchange of MeO against Me at C(4) (*Scheme 6*), rearrangement takes place under formation of 4-benzyl-2-methoxybenzo[*a*]heptalenes and concomitant loss of the sulfonyl group at C(3) (*Table 4*). In the case of X = morpholin-4-yl, rearrangement cannot occur. However, the intermediate benzyl anions of Type **E** (*Scheme 8*) react easily with O_2 of the air to build up corresponding benzo[*a*]heptalene-4-methanols (*Table 6*).

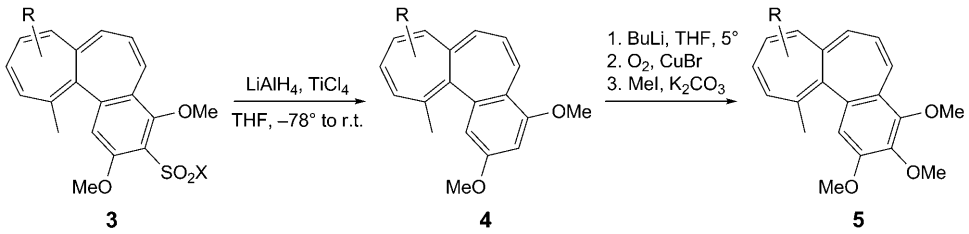
1. Introduction. – Just 15 years ago, on the occasion of *Albert Eschenmoser*'s 70th birthday, we reported in this journal on the transformation of colchicine and some of its 4-alkyl analogs into their underlying heptalene structure, *i.e.*, 1,2,3,9,10-pentamethoxybenzo[*a*]heptalenes [2]. About two years later, we found by chance a new benzo-fusion reaction of dimethylheptalene-4,5- and -1,2-dicarboxylates with (sulfonylmethyl)lithiums as C_1 carrier in the presence of an excess of BuLi to yield 3-(X-sulfonyl)benzo[*a*]-heptalene-2,4-diols [3]. We have improved this new 'one-pot access' to benzo[*a*]heptalenes in the meantime continuously (see [4] and lit. cit. therein), so that colchicine-like compounds of type **2** and **3** – with the non-natural position of the O-functionalities as compared with colchicine – became available in yields of >80% (*Scheme 1*). A

slight modification of our procedure gave also access to 4-methyl-2-(X-sulfonyl)benzo[*a*]heptalenes with the MeO groups in the natural 1,3-position [5]. The sulfonyl groups of these compounds can be removed reductively [5][6] and the missing third MeO group thus introduced by lithiation and catalyzed air oxidation and then methylation of the formed OH group (see **3** → **4** → **5** in *Scheme 2*) [7].

Scheme 1



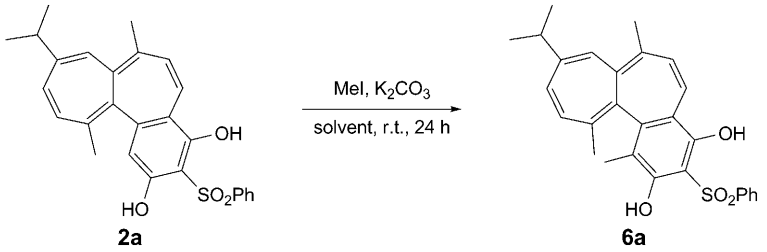
Scheme 2



The ease of the availability of compounds of type **2**–**4** inspired us to study in more detail alkylation reactions with these heptaleno-fused resorcinols and their methyl ether – what in some cases led to astonishing results.

2. C-Alkylation Reactions. – 2.1. *Methylation of C(1) of 3-(Phenylsulfonyl)benzo[*a*]heptalene-2,4-diol* **2a**. The benzo-fusion products **2** can be O-methylated almost quantitavely with MeI under *Claisen*'s standard conditions of methyl ether formation of phenols (*Scheme 1*). On the other hand, a sluggish methylation of C(1) is observed in protic media such as acetone/H_2O, EtOH/H_2O, or H_2O alone, in general agreement with O- *vs.* C-alkylation of phenols (see, *e.g.*, [8]). But, the yields of 1-methylbenzo[*a*]heptalene-2,4-diol **6a**, resulting from **2a** as model compound, did not exceed 20% (*Table 1*), possibly due to a steric screening effect by Me–C(12) on the methylation of C(1) (see [5] for the X-ray crystal structure of **6a**). Fortunately, the one-pot step-by-step benzo-fusion of 8-isopropyl-3,3-dimethoxy-6,11-dimethylheptaleno[1,2-*c*]furan-

Table 1. *Methylation of C(1) of 3-(Phenylsulfonyl)benzo[*a*]heptalene-2,4-diol* **2a**[a])



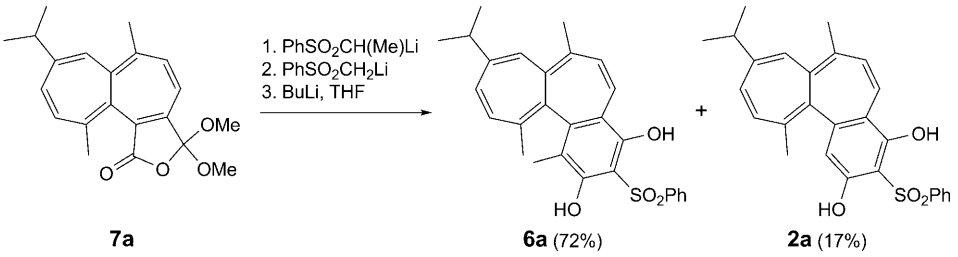
2a **6a**

Aqueous system[b])	Yield [%]
Acetone (5)/H_2O (20)	7
EtOH (5)/H_2O (30)	20[c])
H_2O (15)	3

[a]) For details, see *Exper. Part.* [b]) In parentheses ml, applied for 0.22 mmol of **2a**. [c]) The reaction in pure EtOH gave the O- and C-methylated product in 5% yield.

1(3*H*)-one (**7a**), one of the two possible pseudoesters of **1′a** (R = 5-Me, 7-^{i}Pr) [9], at first with [1-(phenylsulfonyl)ethyl]lithium and then with [(phenylsulfonyl)methyl]-lithium and BuLi gives **6a** in a yield of 72% besides 17% of **2a** (*Scheme 3*) [5].

Scheme 3[a])



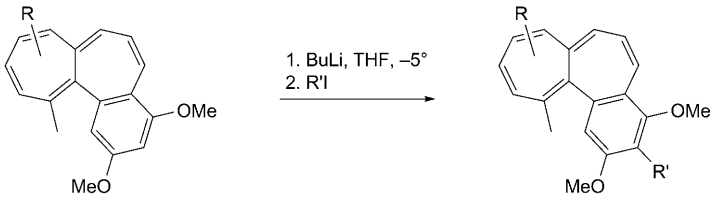
7a **6a** (72%) **2a** (17%)

[a]) For details, see [5].

2.2. *Alkylation of C(3) of 2,4-Dimethoxybenzo[*a*]heptalenes.* These compounds can easily and in good yields be alkylated with MeI and EtI after lithiation with BuLi (*Table 2*). The yield of the 3-Me products **8aa**, **8ba**, and **8ca** is in all cases higher (65–81%) than that of the corresponding 3-Et analogues **8ab**, **8bb**, and **8cb** (46–70%).

We performed X-ray crystal-structure analyses of **8ca** and **8bb**. The stereoprojection of the crystal structure of 3-ethyl-2,4-dimethoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene (**8bb**) is displayed in *Fig. 1*. It is of interest to note that the three-dimensional arrangement of the 2,3,4-substituents is the same as for all colchicinoids of this type, and it corresponds with that of the 1,2,3-pattern of colchicine-like compounds (*cf.* [2][5] and lit. cit. therein). These spatial arrangements are not influenced – at best accentuated – by further substituents at the heptalene part. *Fig. 2*, which shows the stereoprojection of the AM1-calculated and energetically relaxed structure of the four

Table 2. *Alkylation of 2,4-Dimethoxybenzo[*a*]heptalenes* **4**[a])



4 **8**

Reactant	R	R′	Product	Time [h]	Yield [%]
4a	7-Me, 9-^{i}Pr	Me	**8aa**	2	81
4a		Et	**8ab**	6	70
4b	7,8,10-Me_3	Me	**8ba**	5	65
4b		Et	**8bb**	20	46
4c	8,10-Me_2	Me	**8ca**	5	73
4c		Et	**8cb**	12	54

[a]) See *Exper. Part* for details.

possible (*P*)-configured benzo[*a*]heptalenes, carrying three MeO groups at the benzo moiety and alternatively at C(4) or C(1), respectively, a Me group, illustrates the steric constrains that determine the spatial arrangements at the benzo moiety (the steric substituent interactions are quite similar to those of 1,2,3-trimethoxynaphthalenes).

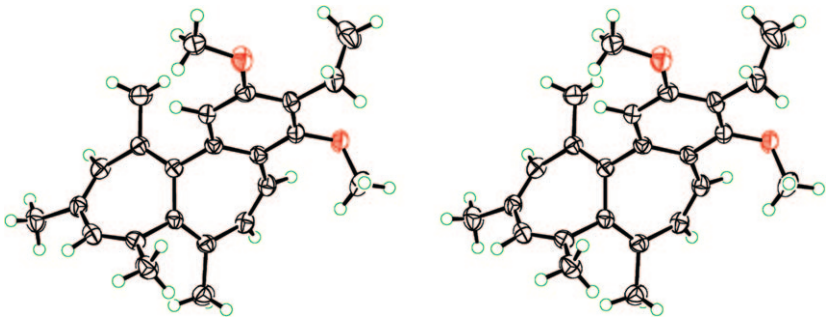


Fig. 1. *Stereoscopic view of the X-ray crystal structure of 3-ethyl-2,4-dimethoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene* (**8bb**) (50% probability ellipsoids)

Fig. 2,*a*, demonstrates that the heptalene fragment C(12a)=C(12)–H forces the MeO group at C(1) in an out-of-plane *anti*-position with respect to the fragment. As a consequence, MeO–C(2) takes the out-of-plane *anti*-position with respect to MeO–C(1). Only MeO–C(3) lies in an in-plane orientation with respect to the benzo moiety. An additional Me group at C(4) drives also MeO–C(3) in the out-of-plane position with respect to its MeO neighbor at C(2) (*Fig. 2*,*b*). The spatial arrangement is quite similar for the 2,3,4-substitution pattern (*Fig. 2*,*c*). Here, it is MeO–C(4) that takes an out-of-plane *anti*-position with respect to the heptalene

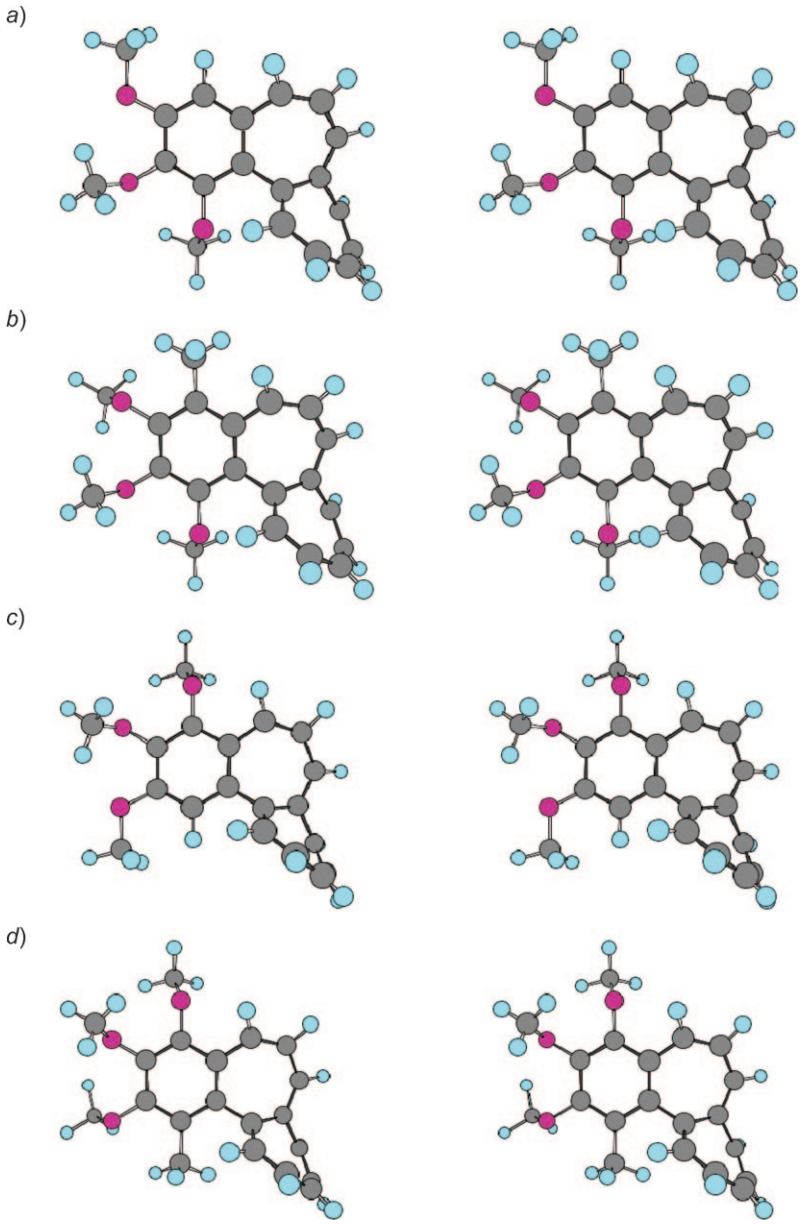


Fig. 2. *Stereoscopic view of AM1-calculated structures of benzo[*a*]heptalenes with three MeO and one Me substituent at the benzo moiety*

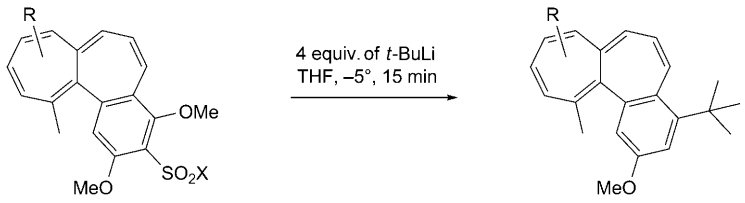
fragment H–C(5)=C(6). And, again, as a consequence, MeO–C(3) occupies the out-of-plane *anti*-site with respect to MeO–C(4). The nonoccupied C(1) allows MeO–C(2) to be in-plane with the benzo moiety. An additional Me group at C(1)

changes the spatial arrangement in that MeO–C(2) is now in an out-of-plane position with respect to MeO–C(3) (*Fig. 2*, *d*). In other words, it is the fused heptalene part that determines the 'up and down' of two-atom chains at the benzo moiety of benzo[*a*]heptalenes, a situation, which is also verified in the X-ray crystal structure of **8bb** (*Fig. 1*) and **8ca** and which may also be of biological relevance (see [2] and lit. cited therein).

2.3. *Reaction of 2,4-Dimethoxy-3-(X-sulfonyl)benzo[*a*]heptalenes with* t-*BuLi*. The *ortho*-position of the two MeO groups in relation to the electron-attracting X-sulfonyl group of compounds **3** should facilitate principally their nucleophilic exchange by metal alkanides. Therefore, we investigated the behavior of **3** in the presence of an excess of *t*-BuLi in THF. The result was surprising in that indeed the MeO group at C(4) was exchanged by a *t*-Bu group; however, the X-sulfonyl group at C(3) was eliminated also (*Table 3* and *Fig. 3*). The yield of the products **9** was good as long as at least two equiv. of *t*-BuLi were applied. We also observed that the yields of **9**, starting with the corresponding 3-(phenylsulfonyl)benzo[*a*]heptalenes, were in all cases higher than those from the 3-(morpholinosulfonyl)benzo[*a*]heptalenes. Moreover, in the case of the reaction of **3e** with *t*-BuLi, we performed a careful chromatographic separation of the crude product. By this way, we found the 2-methoxy-4-morpholinobenzo[*a*]heptalene **10a** as a second product (*Scheme 4*). The position of the substituents at the benzo moiety was secured by an X-ray crystal-structure determination (see *Exper. Part*).

We performed a number of control experiments to understand mechanistically the reductive elimination of the X-sulfonyl group, which accompanies the substitution reaction of compounds **3** with *t*-BuLi. We envisaged two principal possibilities, which are displayed in *Scheme 5*, thereby taking into account that an H-atom (or in an alternative view, a hydride ion) had to be transferred to C(3) of the benzo moiety carrying the X-sulfonyl group, so that this group could be eliminated as X-sulfinate.

Table 3. *4-(*tert-*Butyl)-2-methoxybenzo[*a*]heptalenes* **9** *from 2,4-Dimethoxy-3-X-sulfonylbenzo[*a*]heptalenes* **3** *and* t-*BuLi*



3 **9**

Entry	Reactant	R	X[a])	Product	Yield [%][b])
1	**3a**	7-Me, 9-^{i}Pr	Ph	**9a**	94
2	**3e**		Mor	**9a**	79[c])
3	**3b**	7,8,10-Me_3	Ph	**9b**	72
4	**3d**		Mor	**9b**	66
5	**3c**	8,10-Me_2	Ph	**9c**	65
6	**3f**		Mor	**9c**	59

[a]) Mor = morpholino. [b]) Yield of crystallized products. [c]) See text and *Scheme 4*.

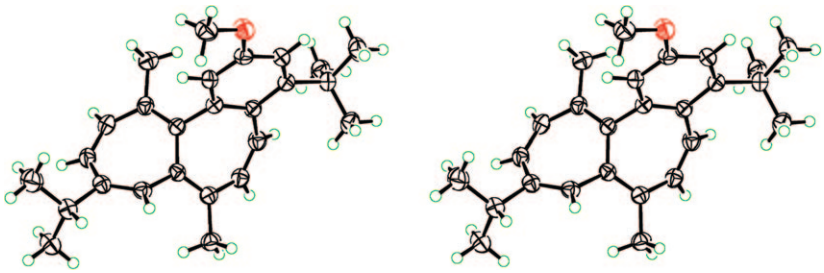
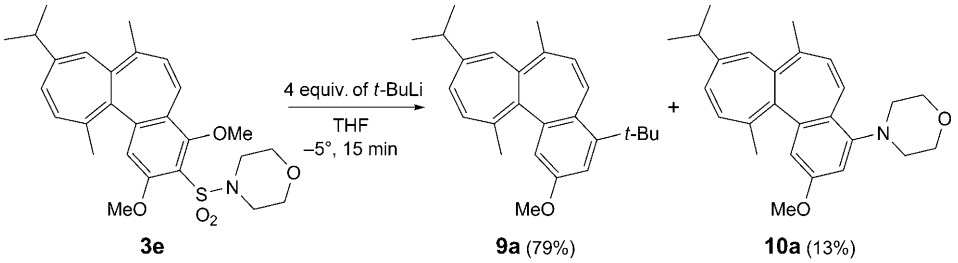


Fig. 3. *Stereoscopic view of the X-ray crystal structure of 4-*(tert-*butyl)-9-isopropyl-2-methoxy-7,12-dimethylbenzo[*a*]heptalene* (**9a**) (50% probability ellipsoids)

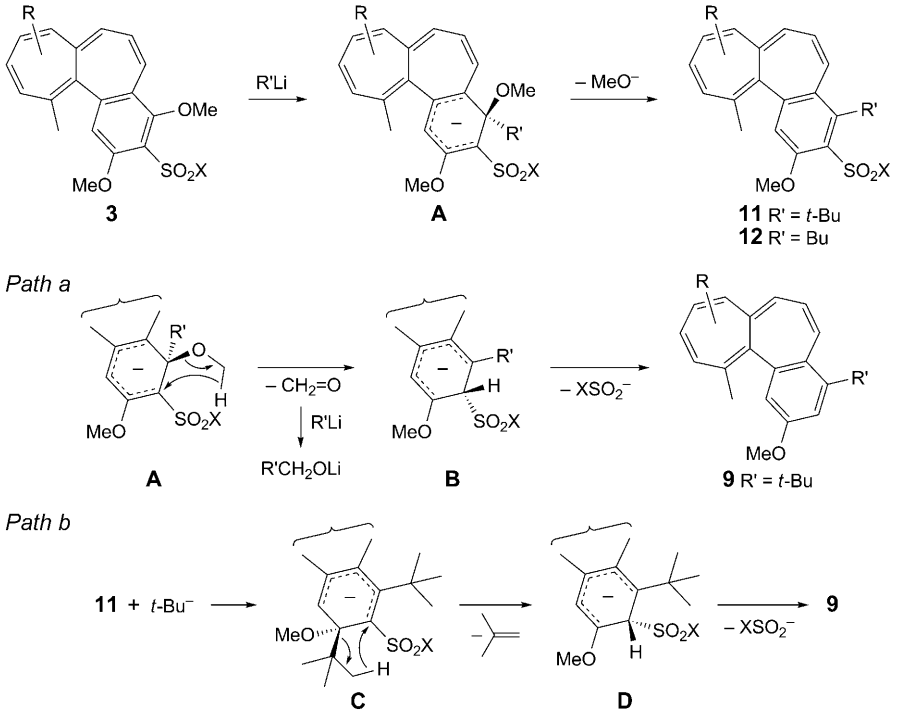
Scheme 4



There is little doubt that nucleophiles enter compounds **3** first at C(4) due to the reduction of *peri*-strain (C(4)–OMe ↔ H–C(5)) in the intermediates **A** (*Scheme 5*). The elimination of MeO^- leads thus to the primary products **11**. Indeed, the reaction of **3a** with *t*-BuLi gave small isolable amounts of **11a** (R = 7-Me, 9-^{i}Pr, X = Ph). On the other hand, when we used BuLi instead of *t*-BuLi the corresponding 4-butyl-2-methoxy-3-(phenylsulfonyl)benzo[*a*]heptalene **12a** was found in a yield of 82% (see *Exper. Part*), but no possible follow-up products comparable with **9a**. In addition, we found that quenching the reaction of **3a** and *t*-BuLi with D_2O did not lead to any D-incorporation at C(3) of **9a** according to its ^{2}H-NMR analysis. This means that compounds **9**, lithiated at C(3), are not intermediates of the elimination of the X-sulfonyl group in the course of the discussed reaction.

The intermediates **A** would have principally the structural prerequisite for a pericyclic H-shift by elimination of formaldehyde and formation of intermediate **B** – in analogy to the thermal *retro*-ene reaction of allyl methyl ethers (*Scheme 5*, *Path a*). Intermediates **B** would be ideally disposed for the elimination of X-sulfinate under formation of compounds **9**. The second molecule of alkyllithium would then be necessary for the trapping of formaldehyde as primary lithium alkoxide. In someway more realistic seems to be, however, the uptake of a second molecule of *t*-BuLi at C(2) of the primary products **11**. This will result in the formation of intermediates **C**, which also can undergo an anionic *retro*-ene fragmentation under formation of intermediates **D** and 2-methylprop-1-ene (*Scheme 5*, *Path b*). Now, elimination of X-sulfinate can take place under formation of the final products **9**. This second pathway would also

Scheme 5

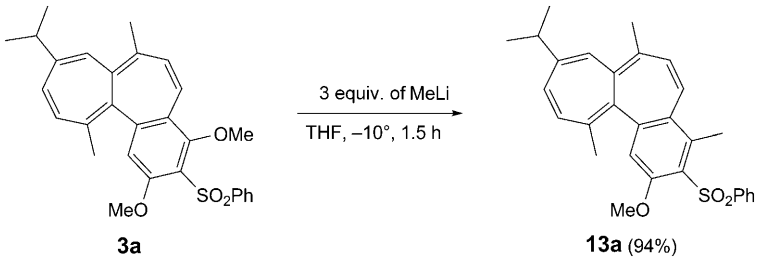


explain the appearance of by-product **10a** in case of the reaction of the 3-(morpholinosulfonyl)benzo[*a*]heptalene **3e** with *t*-BuLi – we suppose that similar by-products were also present in the product mixtures obtained from **3d** and **3f** (*cf. Table 3*), but we looked not specifically for them. Lithium morpholinosulfinate, formed in the elimination reaction of the corresponding intermediate **D**, seems to decompose under the reaction conditions into morpholinolithium and SO_2. The morpholinolithium, on the other hand, seems to act as competitor for *t*-BuLi in the substitution reaction at C(4) of **3e**. Indeed, the reaction of **3a** with piperidinolithium in THF at $-5°$ gives smoothly the corresponding 2,4-dipiperidino-3-(phenylsulfonyl)benzo[*a*]heptalene in a yield of 89% [10]. The further steps of intermediate **11** (R = 7-Me, 9-^{i}Pr, R' = X = morpholino) to **10a** would then follow the path of reduction by *t*-BuLi as sketched in *Scheme 5*, *Path b*.

A last point, worth to be investigated, was the question whether *Path a* in *Scheme 5* contributes to the global reductive elimination of the X-sulfonyl group at C(3) or not or to what extent. To clarify this point, we synthesized **3a** with [$^2H_3$]MeO–C(4), following an established pathway [6], and treated it in the usual manner with *t*-BuLi. The result of this experiment was unequivocal. We found neither by ^{2}H-NMR spectroscopy nor by mass spectrometry any ^{2}H incorporation in product **9a**. This result means that *Path a* (*Scheme 5*) has no relevance for the formation of the products **9**.

2.4. *Reaction of 2,4-Dimethoxy-3-(phenylsulfonyl)benzo[*a*]heptalenes with MeLi.* The reaction of the model compound **3a** with three equiv. of MeLi in THF at $-5°$ offered no surprise. We isolated the expected 2-methoxy-4-methyl-3-(phenylsulfonyl)-benzo[*a*]heptalene **13a** after crystallization from AcOEt/hexane in 94% yield (*Scheme 6*).

Scheme 6

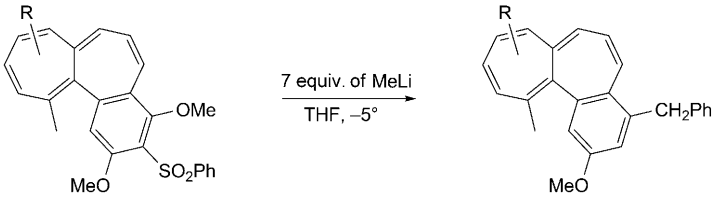


3a **13a** (94%)

However, the chemical scene changed completely when we applied 7 equiv. of MeLi on **3a** and its analogs **3b** and **3c** (*Table 4*). We isolated from the product mixtures in good to excellent yields the 4-benzyl-2-methoxybenzo[*a*]heptalenes **14a**–**14c**. In the case of the reaction of **3b**, we isolated by column chromatography a second unusable product **15b** (*Scheme 7*). Its structure was solved by an X-ray crystal-structure determination (*Fig. 4*). It revealed the relation of **15b** to other dibenzothiophene derivatives, which we had found after treatment of **3a** with lithium diisopropylamide (LDA) [10].

Treatment of **13a** with MeLi or other alkyllithiums gave **14a** in high yields (*Table 5*). The formal elimination of SO_2 in the course of the rearrangement **13** to **14** must therefore follow a quite different path as compared with the transformation **3** to **9** caused specifically by *t*-BuLi, despite the fact that the products look quite similar.

Table 4. *Reaction of 2,4-Dimethoxy-3-(phenylsulfonyl)benzo[*a*]heptalenes* **3** *with an Excess of MeLi*[a])

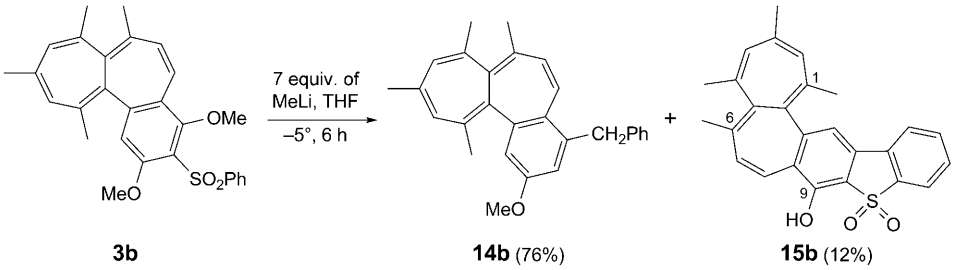


3 **14**

Reactant	R	Time [h]	Product	Yield [%][b])
3a	7-Me, 9-^{i}Pr	1.5	**14a**	91
3b	7,8,10-Me_3	6	**14b**	76[c])
3c	8,10-Me_2	2.5	**14c**	84

[a]) For details, see *Exper. Part.* [b]) Yield of purified product. [c]) A second product, **15b**, was isolated in this case; see text.

Scheme 7



3b **14b** (76%) **15b** (12%)

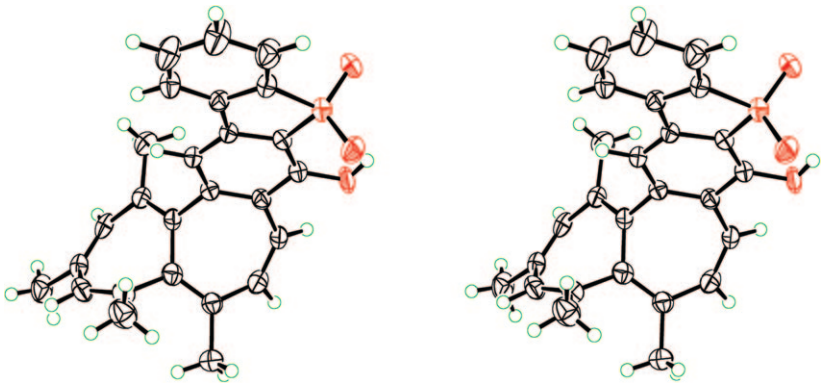
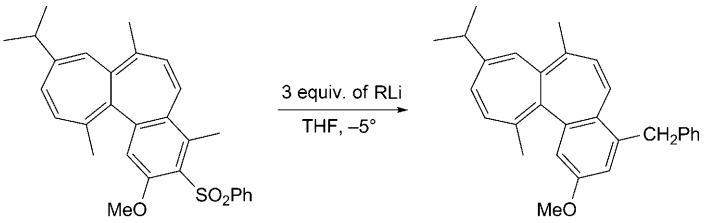


Fig. 4. *Stereoscopic view of the X-ray crystal structure of the heptaleno-fused dibenzothiophene* **15b** (50% probability ellipsoids)

Table 5. *Rearrangement of 2-Methoxy-4-methyl-3-(phenylsulfonyl)benzo[*a*]heptalene* **13a**



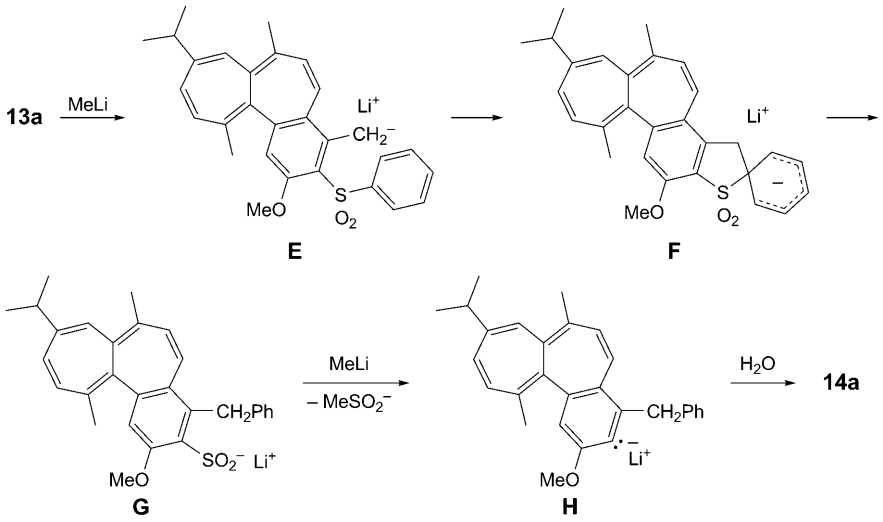
13a **14a**

Base	Time [min][a])	Yield [%]
MeLi	90	83
BuLi	10	65
t-BuLi	30	68

[a]) Time at r.t., after addition of RLi and 15 min at −5°.

A possible mechanism of the surprising rearrangement **13a** → **14a**, driven by MeLi or other alkyllithiums and accompanied by the formal loss of SO_2, is shown in *Scheme 8*. It starts with the deprotonation (lithiation) of Me–C(4) by MeLi to give intermediate **E**. The cyclization of **E** to intermediate **F** profits by the better stabilization of the negative charge as cyclohexadienyl anion. The latter shifts the negative charge by ring opening to the sulfinate structure **G**. The sulfinate substituent of **G** takes up MeLi (in general, RLi; see *Table 5*) in the same way as carboxylates react with RLi to form finally ketones. In the present case, fragmentation to methanesulfinate and the corresponding phenyl anion takes place, followed by protonation in the course of workup.

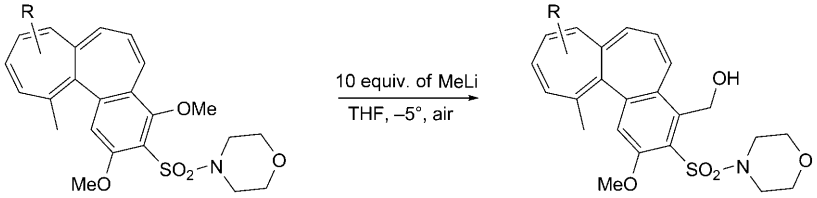
Scheme 8



A last point of concern was the question how 2,4-dimethoxy-3-(morpholinosulfonyl)benzo[*a*]heptalenes **3** would behave in the presence of an excess of MeLi. The expected benzyl anion of type **E** (*cf. Scheme 8*; morpholinoSO_2 instead of PhSO_2) showed as expected no further reactions. However, traces of air led to the formation of the corresponding benzyl alcohols **16** in good yield (*Table 6*). The necessity of air for the formation of **16** excludes the possibility that MeLi deprotonates (lithiates) MeO–C(4) of **3** (X = morpholino), so that the formed anion undergoes a three-atom *Smiles* rearrangement to the corresponding benzyl oxides of **16**.

The most interesting spectroscopic feature of the new compounds **16** is that the benzylic H-atoms of the primary alcohol function at C(4) are diastereotopic. Their ^{1}H-NMR signals ($CDCl_3$) appear as *AB* system, for **16e** for example, at δ(H) 5.09 and 4.83, with $J_{AB} = 12.7$ Hz, whereby both signals are further split by a vicinal coupling ($J = 9.7$ and 5.9 Hz, resp.) with the H-atom of the OH group. These findings, together with the observation of a strong reciprocal NOE effect between one of the CH_2–C(4) proton (δ(H) 4.83, $^3J = 9.7$ Hz) and H–C(5) speaks for a relatively fixed arrangement of the CH_2OH group in **16e** due to H-bonding of the H-atom of the OH group and one

Table 6. *Reaction of 2,4-Dimethoxy-3-(morpholinosulfonyl)benzo[*a*]heptalene* **3** *with an Excess of MeLi in the Presence of Air*



3 **16**

Reactant	R	Time [h]	Product	Yield [%][a])
3e	7-Me, 9-^{i}Pr	4	**16e**	78
3d	7,8,10-Me_3	8	**16d**	63
3f	8,10-Me_2	5	**16f**	69

[a]) Yield of purified and recrystallized product.

of the O-atoms of the SO_2 group. The same is true for **16d** and **16f**. The structure of **16e** was finally established by an X-ray crystal-structure determination, which revealed an intramolecular H-bond with a distance of 206 pm between the H-atom of the OH group and one of the O-atoms of the SO_2 group (*Fig. 5*).

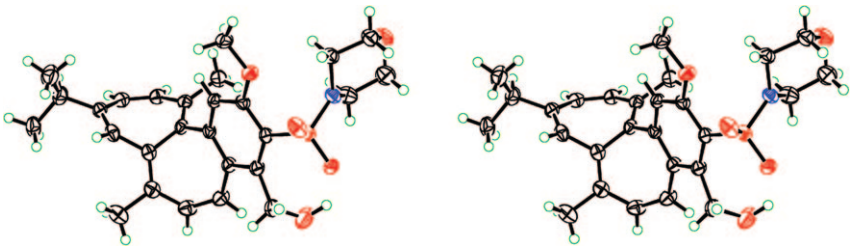


Fig. 5. *Stereoscopic view of the X-ray crystal structure of 9-isopropyl-2-methoxy-7,12-dimethyl-3-(morpholinosulfonyl)benzo[*a*]heptalene-4-methanol* (**16e**) (50% probability ellipsoids)

In conclusion, we can say that the synthesis of benzo[*a*]heptalenes, starting with heptalene-1,2- or -4,5-dicarboxylates or their derivatives, allows the entrance to colchicinoids with substituents at the benzo moiety, which can be changed at will to optimize possible biological activities.

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

Experimental Part

General. For the synthesis of the benzo[*a*]heptalene derivatives as starting material, see [4] and ref. cit. therein. All solvents (Et_2O, THF) were purified by refluxing over Na benzophenone. They were distilled just before use. All reactions with carbanions were performed under Ar. Melting points: *Büchi-FP5* melting-point apparatus; uncorrected. Column chromatography (CC): silica gel *60* (SiO_2; 40–63 μm; *Chemie Uetikon AG*). TLC: aluminium sheets coated with SiO_2 *60* F_{254} (*Merck*). ^{1}H- and ^{13}C-NMR Spectra: *Bruker-ARX300*, *-AMX-500*, or *-AMX-600* spectrometers; in $CDCl_3$; δ in ppm rel. to internal $SiMe_4$ (=0 ppm) at 300 K and internally adjusted to the solvent signals δ(H) 7.26 and δ(C) 77.00), *J* in Hz; assignment by additional DEPT 90, DEPT 135, COSY, NOESY, NOE, HSQC, HMBC, TOCSY, and ^{2}H-NMR measurements; for most of the benzo[*a*]heptalenes, only the signals for the benzo moiety (C(1)–C(4)) are given since the position of the signals of the heptalene part and its substituents do not vary very much (see, *e.g.*, [3][5][9][11]). Mass spectra: CI: *Finnigan-MAT-95* mass spectrometer; at 70 eV and 250°, with NH_3; EI: at 70 eV ionization energy on a GC/MS *Carlo-Erba* instrument (*GC-8000-Top* gas chromatograph; *OV-5* capillary column (15 m × 0.25 mm), coated with 95% dimethyl- and 5% diphenylpolysiloxane); oily compounds showed correct MS; in *m/z* (rel. %). Elemental analyses: all crystalline compounds gave correct elemental analyses.

1. *Alkylation Reactions.* 1.1. *Methylation of 9-Isopropyl-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]-heptalene-2,4-diol* (**2a**). 1.1.1. *General Procedure.* To a soln. of K_2CO_3 (0.5 g, 3.6 mmol) in H_2O (30 ml), a soln. of **2a** (0.100 g, 0.22 mmol) in EtOH (5 ml) was added, and the mixture was stirred for 1 h at −5°. Then, MeI (1 ml, 7 mmol) was added. The mixture was stirred for 24 h at r.t. The mixture was treated with HCl/ice, and the product was extracted with Et_2O. The org. phase was washed with brine and dried (Na_2SO_4). The residue of the org. phase was purified by CC (hexane/AcOEt 8:1) to give, after crystallization from CH_2Cl_2, 0.021 g (20%) of *9-isopropyl-1,7,12-trimethyl-3-(phenylsulfonyl)benzo[*a*]-heptalene-2,4-diol* (**6a**). Yellow plates. M.p. 207.1–208.3° ([5]: 208.6–209.5° (CH_2Cl_2/hexane)). Spectra: identical with those reported in [5].

1.1.2. *C- and O-Methylation of* **2a**. Heptalene **2a** (0.100 g, 0.22 mmol) was added to a suspention of K_2CO_3 (0.5 g, 3.6 mmol) in EtOH (20 ml). The mixture was stirred for 1 h at −5°. MeI (1 ml, 7 mmol) was added, and stirring was continued for 24 h at r.t. After addition of H_2O, the product was extracted with Et_2O, the Et_2O phase dried (Na_2SO_4), the solvent evaporated, and the product purified by CC (hexane/AcOEt 8:1). The product was crystallized from Et_2O with a drop of CH_2Cl_2 to give 5.4 mg (5%) of *9-isopropyl-2,4-dimethoxy-1,7,12-trimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene.* Yellow crystals. M.p. 179.9–180.4°. R_f (hexane/AcOEt 3:1) 0.49. ^{1}H(^{13}C)-NMR: 3.92 (63.42) (*Me*O–C(4)); 3.86 (62.46) (*Me*O–C(2)); 1.98 (12.86) (*Me*–C(1)).

1.2. *Alkylation of 2,4-Dimethoxybenzo[*a*]heptalenes* **4**: *General Procedure.* To a soln. of 2,4-dimethoxybenzo[*a*]heptalene **4** (0.50 g) in dry THF (10 ml), 2.5M BuLi (2.5 equiv. per equiv. of **4**) was slowly added at −5°. The mixture was stirred for 2 h, then MeI or EtI (20 equiv. per equiv. of **4**) was slowly added, and stirring was continued for the time indicated in *Table 2*. The mixture was treated with ice/4N HCl and then extracted with AcOEt. The org. phase was washed with brine and dried (Na_2SO_4). The yellow products were purified by CC (hexane/AcOEt 10:1), followed by crystallization from a Et_2O/hexane mixture. For yields, see *Table 2*.

*9-Isopropyl-2,4-dimethoxy-3,7,12-trimethylbenzo[*a*]heptalene* (**8aa**): M.p. 118.0–121.6°. R_f (hexane/AcOEt 4:1) 0.74. ^{1}H(^{13}C)-NMR: 6.30 (106.35) (H–C(1)); 3.80 (55.73) (*Me*O–C(2)); 3.74 (60.71) (*Me*O–C(4)); 2.17 (8.89) (*Me*–C(3)).

*2,4-Dimethoxy-3,7,8,10,12-pentamethylbenzo[*a*]heptalene* (**8ba**): M.p. 106.0–108.3°. R_f (hexane/AcOEt 4:1) 0.70. ^{1}H(^{13}C)-NMR: 6.28 (105.54) (H–C(1)); 3.78 (55.71) (*Me*O–C(2)); 3.77 (60.74) (*Me*O–C(4)); 2.19 (8.92) (*Me*–C(3)).

*2,4-Dimethoxy-3,8,10,12-tetramethylbenzo[*a*]heptalene* (**8ca**): M.p. 129.2–130.8°. R_f (hexane/AcOEt 4:1) 0.78. ^{1}H(^{13}C)-NMR: 6.31 (106.46) (H–C(1)); 3.79 (55.73) (*Me*O–C(2)); 3.75 (60.67) (*Me*O–C(4)); 2.19 (8.92) (*Me*–C(3)). For the X-ray crystal structure of **8ca**, see *Table 7*.

*3-Ethyl-9-isopropyl-2,4-dimethoxy-7,12-dimethylbenzo[*a*]heptalene* (**8ab**): Yellow oil. R_f (hexane/AcOEt 4:1) 0.77. ^{1}H(^{13}C)-NMR: 6.32 (106.70) (H–C(1)); 3.81 (55.63) (*Me*O–C(2)); 3.78 (61.67)

Table 7. *Crystallographic Data for Compounds* **8bb**, **9a**, **15b**, **16e**, **10a**, *and* **8ca**

	8bb	**9a**	**15b**	**16e**	**10a**	**8ca**
Crystallized from	petroleum ether	petroleum ether/hexane	AcOEt/Et_2O	hexane/Et_2O	Et_2O/hexane	Et_2O
Empirical formula	$C_{24}H_{28}O_2$	$C_{26}H_{32}O \cdot 0.5\ C_6H_{14}$	$C_{26}H_{22}O_3S$	$C_{27}H_{33}NO_5S$	$C_{26}H_{31}NO_2$	$C_{22}H_{24}O_2$
M_r	348.48	403.63	414.52	483.62	389.54	320.43
Crystal color, habit	yellow, prism	yellow, plate	yellow, needle	yellow, prism	yellow, plate	yellow, plate
Crystal dimensions [mm]	$0.07 \times 0.10 \times 0.17$	$0.05 \times 0.12 \times 0.22$	$0.02 \times 0.07 \times 0.20$	$0.12 \times 0.20 \times 0.25$	$0.05 \times 0.25 \times 0.30$	$0.03 \times 0.17 \times 0.22$
Temperature [K]	160(1)	160(1)	160(1)	160(1)	160(1)	160(1)
Crystal system	monoclinic	triclinic	triclinic	monoclinic	triclinic	monoclinic
Space group	$P2_1/n$	$P\bar{1}$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$	$P2_1$
Z	4	2	2	4	2	4
Reflections for cell determination	3559	4234	3567	5934	4820	8214
2θ Range for cell determination [°]	4–50	4–50	4–50	4–55	2–55	4–55
Unit cell parameters:						
a [Å]	11.1112(3)	7.9518(4)	8.1535(2)	10.4922(1)	10.0291(2)	9.1729(1)
b [Å]	15.1469(5)	12.8196(7)	11.3186(3)	14.1062(2)	10.5444(2)	16.5246(2)
c [Å]	12.0368(3)	12.9619(8)	12.6501(3)	16.8196(2)	12.2887(3)	12.1549(1)
α [°]	90	73.438(2)	111.5853(8)	90	70.034(1)	90
β [°]	107.291(2)	77.515(2)	97.450(1)	91.5108(4)	66.9947(9)	103.6462(6)
γ [°]	90	81.009(4)	102.228(1)	90	69.0172(9)	90
V [Å^3]	1934.3(1)	1230.2(1)	1032.88(5)	2488.52(5)	1085.73(4)	1790.41(3)
$F(000)$	752	442	436	1032	420	688
D_x [g cm^{-3}]	1.197	1.090	1.333	1.291	1.191	1.189
$\mu(\mathrm{Mo}K_\alpha)$ [mm^{-1}]	0.0740	0.0634	0.182	0.168	0.0741	0.0743
Scan type	ϕ and ω	ϕ and ω	ω	ϕ and ω	ϕ and ω	ϕ and ω
$2\theta_{(\max)}$ [°]	50	50	50	55	55	55
Total reflections measured	26505	17010	11534	55280	24447	68932
Symmetry-independent reflections	3427	4347	3616	5706	4959	8220
R_{int}	0.087	0.078	0.066	0.074	0.044	0.064
Reflections with $I > 2\sigma(I)$	2258	2863	2454	4250	3696	5852
Parameters refined	236	290	275	307	263	432
$R(F)$ ($I > 2\sigma(I)$ reflections)	0.0531	0.0625	0.0526	0.0523	0.0511	0.0502
$wR(F)$ ($I > 2\sigma(I)$ reflections)	0.0536	0.1779[a])	0.0550	0.0530	0.0565	0.0497
Goodness of fit	1.995	1.023	1.874	3.056	2.654	2.218
Secondary extinction coefficient	$1.2(2) \cdot 10^{-6}$	0.021(5)	–	–	$4.5(10) \cdot 10^{-6}$	$1.5(2) \cdot 10^{-6}$
Final Δ_{max}/σ	0.0002	0.001	0.0003	0.0004	0.0002	0.0007
$\Delta\rho$ (max; min) [e Å^{-3}]	0.25; −0.22	0.40; −0.33	0.29; −0.34	0.40; −0.37	0.36; −0.21	0.21; −0.29

[a]) Refined on F^2; $wR(F^2)$ using all data.

(*Me*O–C(4)); 2.74, 2.67 (17.21) (*AB* of ABX_3, $^2J_{AB}$ = 12.9, Me*CH*$_2$–C(3)); 1.18 (14.42) ($^3J_{AX}$ = $^3J_{BX}$ = 7.1, *Me*CH$_2$–C(3)).

*3-Ethyl-2,4-dimethoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene* (**8bb**): M.p. 154.0–158.5°. R_f (hexane/AcOEt 4:1) 0.74. ^{1}H(^{13}C)-NMR: 6.29 (105.94) (H–C(1)); 3.77 (55.66) (*Me*O–C(2)); 3.80 (61.70) (*Me*O–C(4)); 2.73, 2.69 (17.27) (*AB* of ABX_3, $^2J_{AB}$ = 12.9, Me*CH*$_2$–C(3)); 1.19 (14.43) ($^3J_{AX}$ = $^3J_{BX}$ = 7.5, *Me*CH$_2$–C(3)). For the X-ray crystal structure of **8bb**, see *Fig. 1* and *Table 7*.

*3-Ethyl-2,4-dimethoxy-8,10,12-trimethylbenzo[*a*]heptalene* (**8cb**): Yellow oil. R_f (hexane/AcOEt 4:1) 0.81. ^{1}H(^{13}C)-NMR: 6.31 (106.88) (H–C(1)); 3.78 (55.66) (*Me*O–C(2)); 3.77 (61.70) (*Me*O–C(4)); 2.73, 2.67 (17.29) (*AB* of ABX_3, $^2J_{AB}$ = 12.9, Me*CH*$_2$–C(3)); 1.18 (14.41) ($^3J_{AX}$ = $^3J_{BX}$ = 7.5, *Me*CH$_2$–C(3)).

1.3. *Reaction of 2,4-Dimethoxy-3-(X-sulfonyl)benzo[*a*]heptalenes* **3** *with* t-*BuLi: General Procedure.* To a soln. of heptalene **3** (0.50 g) in dry THF (10 ml) was added slowly at –5° 1.6M *t*-BuLi (4 equiv. per equiv. of **3**). The mixture was stirred at –5° for 15 min. Then, the mixture was treated with ice/4N HCl, followed by extraction with AcOEt. The org. phase was washed with brine and dried (Na_2SO_4), the solvent evaporated, and the residue subjected to CC (hexane/AcOEt 5:1). Finally, the products were crystallized from hexane/petroleum ether. See *Table 3* and *Scheme 4* for yields.

*4-(*tert-*Butyl)-9-isopropyl-2-methoxy-7,12-dimethylbenzo[*a*]heptalene* (**9a**): M.p. 89.9–91.0°. R_f (hexane/AcOEt 4:1) 0.74. ^{1}H(^{13}C)-NMR: 159.90 (C(2)); 149.06 (C(4)); 7.03 (113.08) (J_m = 2.7, H–C(3)); 6.40 (109.98) (J_m = 2.9, H–C(1)); 3.80 (55.19) (*Me*O–C(2)); 1.51 (35.95, 31.39) (*Me*$_3$*C*–C(4)). For the X-ray crystal structure of **9a**, see *Fig. 3* and *Table 7*.

*4-(*tert-*Butyl)-9-isopropyl-2-methoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[a]heptalene* (**11a**): R_f (hexane/AcOEt 3:1) 0.59. ^{1}H-NMR (300 MHz): 7.54 (*m*, H$_o$ of Ph); 7.42 (*m*, H$_p$ of Ph); 7.33 (*m*, H$_m$ of Ph; *d*, ^3J(5,6) = 12.1, H–C(5)); 6.44 (*AB*, H–C(10), H–C(11)); 6.26 (*d*, ^3J(6,5) = 12.1, H–C(6)); 6.12 (*s*, H–C(1)); 5.81 (*s*, H–C(8)); 3.00 (*s*, MeO–C(2)); 2.53 (*sept.*, Me$_2$*CH*–*C*(9)); 1.80 (*s*, Me$_3$C–C(4)); 1.71 (*s*, Me–C(7)); 1.49 (*s*, Me–C(12)); 1.14, 1.13 (2*d*, ^3J = 6.9, 6.8, *Me*$_2$CH–C(9)).

*9-Isopropyl-7,12-dimethyl-4-(morpholin-4-yl)benzo[*a*]heptalene* (**10a**): Yellow crystals. M.p. 199.9–202.0° (Et_2O/hexane). R_f (hexane/AcOEt 3:1) 0.56. ^{1}H(^{13}C)-NMR: 161.06 (C(2)); 151.88 (C(4)); 6.58 (105.11) (J_m = 2.5, H–C(3)); 6.28 (107.80) (J_m = 2.4, H–C(1)); 3.89, 3.82, 3.18, 2.77 (67.34, 52.60) (O(*CH*$_2$*CH*$_2$)$_2$N–C(4)); 3.79 (55.40) (*Me*O–C(2)). EI-MS ($C_{26}H_{31}NO_2$; 389.20): 390.2 (75, $[M+1]^+$), 389.2 (100, $M^{+\cdot}$), 374.1 (84, $[M-Me]^+$), 349.1 (50, $[M-MeC{\equiv}CH]^{+\cdot}$). For the X-ray crystal structure of **10a**, see *Table 7*.

*4-(*tert-*Butyl)-2-methoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene* (**9b**): M.p. 127.3–129.8°. R_f (hexane/AcOEt 4:1) 0.77. ^{1}H(^{13}C)-NMR: 159.78 (C(2)); 149.10 (C(4)); 7.00 (108.88) (J_m = 2.7, H–C(3)); 6.34 (112.99) (J_m = 2.6, H–C(1)); 3.76 (55.24) (*Me*O–C(2)); 1.50 (35.97, 31.44) (*Me*$_3$*C*–C(4)).

*4-(*tert-*Butyl)-2-methoxy-8,10,12-trimethylbenzo[*a*]heptalene* (**9c**): M.p. 68.9–70.8°. R_f (hexane/AcOEt 4:1) 0.75. ^{1}H(^{13}C)-NMR: 160.22 (C(2)); 149.14 (C(4)); 7.01 (113.31) (J_m = 2.7, H–C(3)); 6.36 (109.81) (J_m = 2.7, H–C(1)); 3.77 (55.27) (*Me*O–C(2)); 1.48 (35.98, 31.48) (*Me*$_3$*C*–C(4)).

1.4. *Reaction of 9-Isopropyl-2,4-dimethoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene* (**3a**) *with BuLi.* To a soln. of **3a** (0.5 g, 1.05 mmol) in dry THF (15 ml), 2.5M BuLi (0.55 ml, 1.37 mmol) was added slowly at –40°. The mixture was stirred for 10 min. Then, the mixture was treated with ice/4N HCl and extracted with AcOEt. The org. phase was washed with brine and dried (Na_2SO_4). The residue of the extract was purified by CC (hexane/AcOEt 8:1). The product was crystallized from Et_2O/hexane to give 0.43 g (82%) of pure *4-butyl-9-isopropyl-2-methoxy-7,12-dimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene* (**12a**): Yellow crystals. M.p. 92.1–94.0°. R_f (hexane/AcOEt 4:1) 0.42. ^{1}H-NMR (600 MHz): 7.89 (*dd*, J_o = 7.3, J_m = 1.3, H$_o$ of Ph); 7.51 (*m*, H$_p$ of Ph); 7.46 (*m*, H$_m$ of Ph); 7.05 (*d*, ^3J(5,6) = 12.1, H–C(5)); 6.40 (*d*, ^3J(11,10) = 11.9, H–C(11)); 6.36 (*dd*, ^3J(10,11) = 11.9, ^4J(10,8) = 1.1, H–C(10)); 6.32 (*s*, H–C(1)); 6.30 (*d*, ^3J(6,5) = 12.2, H–C(6)); 5.74 (*s*, H–C(8)); 3.50, 3.34 (2*m*, MeCH$_2$CH$_2$C*H*$_2$–C(4)); 3.47 (*s*, MeO–C(2)); 2.53 (*sept.*, Me$_2$C*H*–*C*(9)); 1.82, 1.74 (2*m* MeCH$_2$C*H*$_2$CH$_2$–C(4)); 1.71 (*s*, Me–C(7)); 1.62 (*s*, Me–C(12)); 1.57 (*m*, MeC*H*$_2$CH$_2$CH$_2$–C(4)); 1.14, 1.13 (2*d*, ^3J = 6.8, 6.7, *Me*$_2$CH–C(9)); 1.02 (*t*, ^3J = 7.4, *M*eCH$_2$CH$_2$CH$_2$–C(4)). ^{13}C-NMR (150 MHz): 158.39 (*s*, C(2)); 147.18 (*s*, C(9)); 144.79 (*s*, C$_{ipso}$ of Ph); 144.56 (*s*, C(12b)); 144.13 (*s*, C(4)); 135.44 (*d*, C(11)); 135.08 (*s*, C(12a)); 134.15 (*s*, C(7a)); 132.97 (*d*, C(6)); 132.06 (*d*, C$_p$ of Ph); 131.60 (*d*, C(10)); 131.05 (*s*, C(12)); 130.11 (*s*, C(4a)); 128.37 (*d*, C(5)); 128.16 (*s*, C(7)); 128.13 (*d*, C$_m$ of Ph); 126.99 (*s*, C(3)); 126.87 (*d*, C$_o$ of Ph); 121.96 (*d*, C(8)); 110.88 (*d*,

C(1)); 55.85 (*q*, *Me*O–C(2)); 34.45 (*d*, Me_2CH–C(9)); 29.14 (*t*, $MeCH_2CH_2CH_2$–C(4)); 33.70 (*t*, $MeCH_2CH_2CH_2$–C(4)); 23.29 (*t*, $MeCH_2CH_2CH_2$–C(4)); 22.69, 22.78 (2*q*, Me_2CH–C(9)); 19.65 (*q*, Me–C(12)); 16.57 (*q*, Me–C(7)); 13.85 (*q*, $MeCH_2CH_2CH_2$–C(4)). EI-MS ($C_{12}H_{36}O_3S$; 500.71): 501.2 (33, $[M+1]^+$), 500.1 (100, $[M]^{+\cdot}$), 485.06 (30, $[M-Me]^+$), 460.1 (12, $[M-MeC\equiv CH]^{+\cdot}$).

1.5. *Reaction of 2,4-Dimethoxy-3-(X-sulfonyl)benzo[*a*]heptalenes* **3** *with MeLi.* 1.5.1. *2,4-Dimethoxy-3-(phenylsulfonyl)benzo[*a*]heptalenes* **3a**–**3c**: *General Procedure.* To a soln. of 0.50 g of the 3-(phenylsulfonyl)benzo[*a*]heptalene **3** in dry THF (10 ml) was added slowly at $-5°$ a soln. of 1.6M MeLi (7 equiv. per equiv. of **3**) in portions of 2 equiv. of MeLi. The mixture was stirred at $-5°$ for 15 min, and then stirring was continued at r.t. for the time indicated in *Table 4*. Ice/4N HCl was added, and the product was extracted with AcOEt. The org. phase was washed with brine and dried (Na_2SO_4). The yellow oily products were purified by CC (hexane/AcOEt 4:1).

*4-Benzyl-9-isopropyl-2-methoxy-7,12-dimethylbenzo[*a*]heptalene* (**14a**): R_f (hexane/AcOEt 4:1) 0.76. $^1H(^{13}C)$-NMR: 160.62 (C(2)); 140.15 (C(4)); 6.66 (115.82) ($J_m = 2.6$, H–C(3)); 6.44 (111.39) ($J_m = 2.8$, H–C(1)); 4.12, 4.07 (39.75) (*AB*, $^2J_{AB} = 15.9$, PhCH_2–C(4)); 3.75 (55.27) (*Me*O–C(2)).

*9-Isopropyl-2-methoxy-4,7,12-trimethyl-3-(phenylsulfonyl)benzo[*a*]heptalene* (**13a**): Yellow crystals. M.p. 216.7–218.2° (hexane/AcOEt). R_f (hexane/AcOEt 1:1) 0.70. $^1H(^{13}C)$-NMR: 158.48 (C(2)); 139.21 (C(4)); 127.80 (C(3)); 6.33 (110.81) (H–C(1)); 2.92 (16.59) (*Me*–C(4)). EI-MS ($C_{29}H_{30}O_3S$; 458.62): 459.1 (31, $[M+1]^+$), 458.0 (100, $M^{+\cdot}$), 423.0 (39, $[M-Me]^+$), 418.0 (35, $[M-MeC\equiv CH]^{+\cdot}$).

Rearrangement of **13a** *with Alkyl Lithium* (RLi) *Bases:* To a soln. of **13a** (0.50 g, 1.09 mmol) in dry THF (10 ml), kept under stirring at $-5°$, were added slowly in portions 3.27 mmol of the corresponding RLi soln. (R = Me, Bu, and *t*-Bu). Stirring was continued at $-5°$ for additional 15 min and then at r.t. for the time indicated in *Table 5* to give **14a**.

*4-Benzyl-2-methoxy-7,8,10,12-tetramethylbenzo[*a*]heptalene* (**14b**): R_f (hexane/AcOEt 4:1) 0.81. $^1H(^{13}C)$-NMR: 160.53 (C(2)); 139.53 (C(4)); 6.49 (115.74) ($J_m = 2.7$, H–C(3)); 6.40 (110.32) ($J_m = 2.7$, H–C(1)); 4.15, 4.05 (39.83) (*AB*, $^2J_{AB} = 15.9$, PhCH_2–C(4)); 3.73 (55.26) (*Me*O–C(2)).

*1,3,5,6-Tetramethylbenzo[*b*]heptaleno[2′,1′:4,5]benzo[1,2-*d*]thiophen-9-ol 10,10-Dioxide* (**15b**): Yellow needles. M.p. 304.9–307.3° (AcOEt/Et_2O). R_f (hexane/AcOEt 2:1) 0.48. ^{1}H-NMR (600 MHz): 7.80 (*d*, $J_o = 7.6$, H–C(11)); 7.69 (*d*, $J_o = 7.5$, H–C(14)); 7.61 (*td*, $J_o = 7.4$, $J_m = 1.1$, H–C(13)); 7.50 (*td*, $J_o = 7.6$, $J_m = 1.1$, H–C(12)); 7.07 (*d*, $^3J(8,7) = 11.9$, H–C(8)); 6.93 (*s*, H–C(15)); 6.33 (br. *s*, HO–C(9); 6.45 (*d*, $^3J(7,8) = 11.9$, H–C(7)); 6.21 (struct. *s*, H–C(2)); 6.08 (struct. *s*, H–C(4)); 2.05 (*d*, ^4J(Me,H–C(2)) = 1.1, Me–C(3)); 1.95 (*d*, ^4J(Me,H–C(4)) = 1.1, Me–C(5)); 1.75 (*s*, Me–C(6)); 1.69 (*s*, Me–C(1)). ^{13}C-NMR (125 MHz): 149.74 (C(9)); 145.33 (C(15a)); 139.27 (C(3)); 138.12 (C(10a)); 137.75 (C(5a)); 135.96 (C(7)); 133.86 (C(13)); 133.33 (C(14b)); 131.81 (C(14a)); 131.17 (C(1)); 130.45 (C(2)); 130.14 (C(5), C(12)); 113.88 (C(15)); 120.70 (C(9a)); 121.95 (C(11)); 121.79 (C(14)); 129.16 (C(15b)); 128.85 (C(4)); 128.35 (C(8a)); 127.86 (C(6)); 123.25 (C(8)); 25.09 (*Me*–C(3)); 22.97 (*Me*–C(5)); 19.07 (*Me*–C(1)); 17.82 (*Me*–C(6)). CI-MS ($C_{26}H_{22}O_3S$; 414.52): 434.3 (21), 433.3 (32), 432.3 (100, $[M+NH_4]^+$), 414 (5, $M^{+\cdot}$). For the X-ray crystal structure of **15b**, see *Fig. 4* and *Table 7*.

*4-Benzyl-2-methoxy-8,10,12-trimethylbenzo[*a*]heptalene* (**14c**): R_f (hexane/AcOEt 4:1) 0.83. $^1H(^{13}C)$-NMR: 160.94 (C(2)); 139.52 (C(4)); 6.69 (116.11) ($J_m = 2.7$, H–C(3)); 6.45 (111.29) ($J_m = 2.7$, H–C(1)); 4.14, 4.08 (39.83) (*AB*, $^2J_{AB} = 15.9$, PhCH_2–C(4)); 3.75 (55.26) (*Me*O–C(2)).

1.5.2. *2,4-Dimethoxy-3-(morpholin-4-ylsulfonyl)benzo[*a*]heptalenes* **3d**–**3f**: *General Procedure.* To a soln. of 3-(morpholin-4-ylsulfonyl)benzo[*a*]heptalene **3** (0.50 g) in dry THF (10 ml) at $-5°$ was added slowly at $-5°$ a soln. of 1.6M MeLi (10 equiv. per equiv. of **3**) in portions of 2 equiv. After 15 min of each addition of MeLi, the flask was opened and the mixture exposed to air for 30 s. After the last exposure to air, stirring was continued at r.t. for the time indicated in *Table 6*. Ice and 4N HCl were added. The yellow products were extracted with AcOEt, purified by CC (hexane/AcOEt 3:1), and finally recrystallized from hexane/Et_2O.

*9-Isopropyl-2-methoxy-7,12-dimethyl-3-(morpholin-4-ylsulfonyl)benzo[*a*]heptalene-4-methanol* (**16e**): Yellow prisms. M.p. 194.0–197.7°. R_f (hexane/AcOEt 1:1) 0.59. $^1H(^{13}C)$-NMR: 157.51 (C(2)); 139.97 (C(4)); 127.24 (C(3)); 6.58 (112.64) (H–C(1)); 5.09 (*A* of *ABX*, $^2J_{AB} = 12.7$, $^3J_{AX} = 5.9$, HOCH_2–C(4)); 4.83 (*B* of *ABX*, $^2J_{AB} = 12.6$, $^3J_{BX} = 9.7$, HOCH_2–C(4)); 3.90 (56.72) (*Me*O–C(2)); 3.35 (OH, partially covered by $O(CH_2CH_2)_2NSO_2$–C(3)). For the X-ray crystal structure of **16e**, see *Fig. 5* and *Table 7*.

*2-Methoxy-7,8,10,12-tetramethyl-3-(morpholin-4-ylsulfonyl)benzo[*a*]heptalene-4-methanol* (**16d**): Yellow prisms. M.p. 215.2–216.7°. R_f (hexane/AcOEt 1:1) 0.44. ^{1}H(^{13}C)-NMR: 157.42 (C(2)); 140.12 (C(4)); 127.20 (C(3)); 6.56 (111.69) (H–C(1)); 5.12 (*A* of *ABX*, $^2J_{AB}$ = 12.7, $^3J_{AX}$ = 5.7, HOCH_2–C(4)); 4.84 (*B* of *ABX*, $^2J_{AB}$ = 12.8, $^3J_{BX}$ = 9.7, HOCH_2–C(4)); 3.87 (56.73) (*Me*O–C(2)); 3.41 (OH, partially covered by O(CH$_2$CH_2)$_2$NSO$_2$–C(3)).

*2-Methoxy-8,10,12-trimethyl-3-(morpholin-4-ylsulfonyl)benzo[*a*]heptalene-4-methanol* (**16f**): Yellow prisms. M.p. 225.1–226.3°. R_f (hexane/AcOEt 1:1) 0.42. ^{1}H(^{13}C)-NMR: 157.64 (C(2)); 140.05 (C(4)); 127.52 (C(3)); 6.58 (112.66) (H–C(1)); 5.11 (*A* of *ABX*, $^2J_{AB}$ = 12.8, $^3J_{AX}$ = 5.7, HOCH_2–C(4)); 4.82 (*B* of *ABX*, $^2J_{AB}$ = 12.7, $^3J_{BX}$ = 9.5, HOCH_2–C(4)); 3.88 (56.72) (*Me*O–C(2)); 3.36 (OH, partially covered by O(CH$_2$CH_2)$_2$NSO$_2$–C(3)).

2. Crystal-Structure Determination of **8bb**, **9a**, **15b**, **16e**, **10a**, *and* **8ca** (*Table 7* and *Figs. 1* and *3–5*)[1]). All measurements were conducted on a *Nonius KappaCCD* area detector diffractometer [12][13] by using graphite-monochromated MoK_α radiation (λ 0.71073 Å) and an *Oxford-Cryosystems-Cryostream-700* cooler. The data collection and refinement parameters are given in *Table 7*, while views of the molecules of **8bb**, **9a**, **15b**, and **16e** are shown in *Figs. 1* and *3–5*. The intensities were corrected for *Lorentz* and polarization effects but not for absorption. Each structure was solved by direct methods with either SIR92 [14] or SHELXS97 [15], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. The OH H-atom of **15b** was placed in the position indicated by a difference-electron-density map, and its position was allowed to refine together with an isotropic displacement parameter. All of the remaining H-atoms were placed in geometrically calculated positions, and each H-atom was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent atom (1.5 U_{eq} for the Me groups of **9a**). The orientation of the hydroxy O–H vector in **16e** was based on the position of a peak located in a difference-electron-density map. The refinement of each structure was carried out on F (F^2 for **9a**) by using full-matrix least-squares procedures. A correction for secondary extinction was applied in the cases of **8bb**, **9a**, **10a**, and **8ca**.

The asymmetric unit of **9a** contains one molecule of the heptalene plus one half of a hexane molecule. The hexane molecule sits across a crystallographic center of inversion and is disordered. Two positions were defined for the central two C-atoms of the hexane molecule. The site-occupation factors of the two conformations were held fixed at a ratio of 0.8/0.2. Bond-length restraints were applied to the bonds of the hexane molecule so as to maintain reasonable geometry. Compound **8ca** crystallized in a noncentrosymmetric polar space group with two symmetry-independent molecules in the asymmetric unit. These molecules are almost perfectly related to one another by a local center of inversion; however, no additional crystallographic symmetry could be found. The absolute direction of the polar axis was chosen arbitrarily.

Neutral-atom scattering factors for non-H-atoms were taken from [16a], and the scattering factors for H-atoms were taken from [17]. Anomalous dispersion effects were included in F_c [18]; the values for f' and f'' were those of [16b]. The values of the mass-attenuation coefficients are those of [16c]. All calculations were performed with the teXsan crystallographic software package [19] (SHELXL97 [14] for **9a**). The crystallographic diagrams were drawn with ORTEPII [20].

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