Introduction of Adjacent Oxygen-Functionalities in Dimethyl Heptalenedicarboxylates

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Dedicated to *Heinz Heimgartner* on the occasion of his 70th birthday

The bromination of dimethyl 8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate (**6**; *Scheme 2*) with *N*-bromosuccinimide (NBS) in *N*,*N*-dimethylformamide (DMF) leads in acceptable yields to the corresponding 9-bromoheptalenedicarboxylate **10** (*Table 1*). Ether cleavage of **6** with chlorotrimethylsilane (Me_3SiCl)/NaI results in the formation of oxoheptalenedicarboxylate **13** in good yield (*Scheme 4*). The latter can be acetyloxylated to the (acetyloxy)oxoheptalenedicarboxylate **14** with $Pb(OAc)_4$ in benzene (*Scheme 5*). Oxo derivative **14**, in turn, can be selectively *O*-methylated with dimethyl sulfate (DMS) in acetone to the (acetyloxy)methoxyheptalenedicarboxylates **15** and **15′** (*Scheme 6*). The AcO group of the latter can be transformed into a benzyl or methyl ether group by treatment with MeONa in DMF, followed by the addition of benzyl bromide or methyl iodide (*cf. Scheme 9*). Reduction of the ester groups of dimethyl 7,8-dimethoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate (**25′**) with diisobutylaluminium hydride (DIBAH) in tetrahydrofuran (THF) leads to the formation of the corresponding dimethanol **26′**, which can be cyclized oxidatively (IBX, dimethyl sulfoxide) to 8,9-dimethoxy-6,7,11-trimethylheptaleno[1,2-*c*]furan (**27**; *Scheme 11*).

1. Introduction. – Over the past 15 years, we have developed two main approaches to the synthesis of benzo[*a*]heptalenes as possible colchicinoid candidates starting with dimethyl heptalene-4,5-dicarboxylates **1** or their double-bond-shifted (DBS) isomers, *i.e.*, dimethyl heptalene-1,2-dicarboxylates (*Scheme 1*; see [1] and lit. cit. therein). Intermediates of the first approach are heptaleno[1,2-*c*]furans **2** [2], which easily undergo thermal *Diels–Alder* reactions with a broad variety of dienophiles [3][4]. The cycloadducts rearrange on base or acid catalysis to benzo[*a*]heptalenes, capable to be further modified to **4** or those with other substitution patterns at the benzo moiety. The second approach starts with **1** or its DBS isomer, which on treatment with 1-(phenylsulfonyl)ethyllithium yield directly benzo[*a*]heptalenes of type **3** [5], which again can be simply modified to **4** [6]. However, it would chemically be difficult to introduce O-functions at C(9) and C(10) of **4** to arrive at the tropolone ring *C* of colchicines **5**. Therefore, we investigated the introduction of adjacent O-functions already in dimethyl heptalenedicarboxylates **1** and report on these experiments in the following part.

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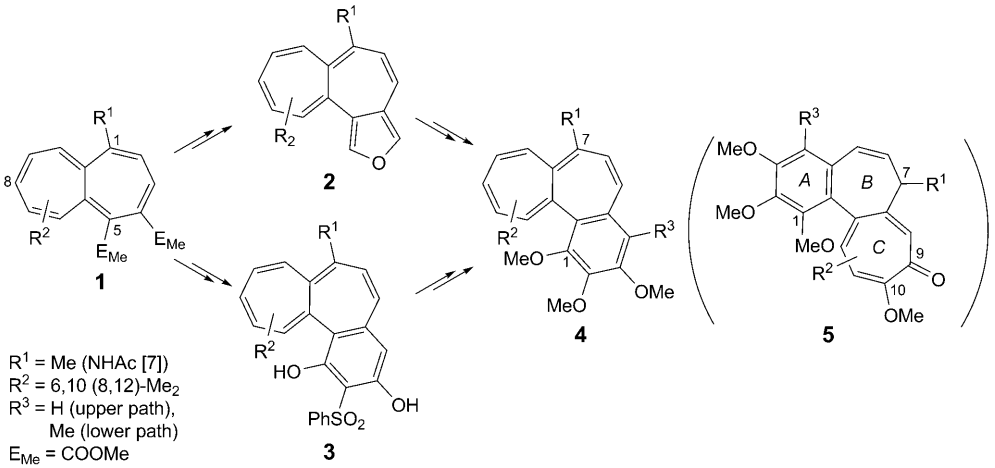
[1]) Part of the M.S. work of *F. R.*, University of Zürich, 2002.

[2]) Part of the M.S. work of *D. S.*, University of Zürich, 2004.

Scheme 1

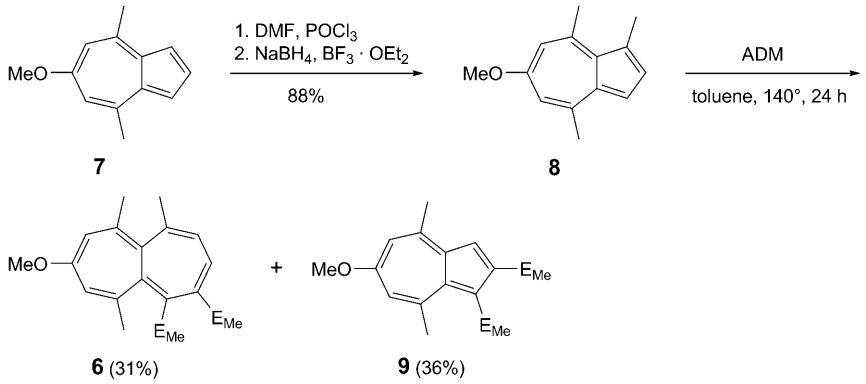


2. Syntheses. – 2.1. *Dimethyl 8-Methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**6**) *and Its DBS Isomer* **6′**. Since heptalenedicarboxylates of type **1** are accessible by thermal reaction of azulenes and acetylenedicarboxylates following *Hafner*'s general method (see [1][8]), we decided to incorporate the first O-function as methyl ether already in the azulene reactant. The 6-methoxy-4,8-dimethylazulene (**7**) is available from 4-methoxy-2,6-dimethylpyrylium tetrafluoroborate and sodium cyclopentadienide [9]. The transformation of **7** into 6-methoxy-1,4,8-trimethylazulene (**8**) *via* the reduction of the intermediate azulene-1-carboxaldehyde, following earlier work of us [10], could be managed in a yield of 88% over both steps (*Scheme 2*). The reaction of **8** with 3 equiv. of dimethyl acetylenedicarboxylate (=dimethyl but-2-ynedioate; ADM) in toluene at 140° gave crystalline **6** as yellow needles in average yields of 31%, accompanied by almost equal amounts of the azulene-1,2-dicarboxylate **9** as *retro-Diels–Alder* product (*cf.* [1]). The DBS isomer **6′** could also be identified in minor amounts by TLC in the original toluene solution after heating (see below). The yield of **6** could be slightly enhanced to 37% when **8** was treated with 5 equiv. of ADM in DMF (*N*,*N*-dimethylformamide) at 140° for 24 h[3]). The structure of **6** was securely confirmed by an X-ray crystal-structure analysis (see *Exper. Part*).

It was difficult to isolate the minor amounts of the DBS isomer **6′**, *i.e.*, of dimethyl 8-methoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate, from the original mixture of products. However, when a 0.1M solution of pure **6** in MeCN was exposed for 8 h to normal daylight at room temperature, a photostationary mixture of 52% of **6** and 48% of **6′** was formed (*cf.* [11a] for former similar results), from which **6′** could be isolated almost quantitatively and characterized. The two isomers are clearly differentiated by the vicinal coupling constant of their two adjacent H-atoms at the heptalene skeleton,

[3]) In one experiment (**8** + 3.1 equiv. of ADM, toluene, 120°, 22 h), we isolated a mixture of **6** and **6′** in a yield of 66%. Unfortunately, we could not repeat a yield of 66% in further experiments.

Scheme 2



which amount to 5.8 Hz for **6** and 11.8 Hz for **6′**, in agreement with those of other heptalene isomers of this type (*cf.* [11]).

Heptalene-1,2-dicarboxylate **6′** in MeCN solution in the dark at room temperature is quite stable and isomerizes to its DBS form **6** only very slowly with $\tau_{1/2}$ *ca.* 42 d. However, in $CDCl_3$ solution in the dark at room temperature, $\tau_{1/2}$ amounts to 2 h, whereby a final equilibrium mixture of 9% of **6′** and 91% of **6** is formed, in good agreement with the calculated ratio of 94 : 6 of dimethyl 1,6,8,10-tetramethylheptalene-4,5-dicarboxylate and its DBS isomer in tetralin [11a]. We suppose that traces of HCl in $CDCl_3$ catalyze the thermal DBS process of **6′** and **6** (see [12] for similar observations).

2.2. *Bromination Experiments with Dimethyl 8-Methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**6**). The fixed C=C bonds in heptalene **6** should make it possible to introduce a Br-substituent at C(9) due to the π-donor effect of the adjacent MeO group at C(8). *N*-Bromosuccinimide (NBS) in $CHCl_3$ or CH_2Cl_2 at low temperature has been successfully applied in electrophilic bromination reactions [13]. Therefore, we investigated the bromination of **6** with NBS in CH_2Cl_2. The results are listed in *Table 1*. We observed the formation of four products, **10**–**13**, in nearly equal amounts which all could be separated chromatographically and identified spectroscopically. Only one of them, namely **10**, represented the expected 9-bromoheptalene-4,5-dicarboxylate. Two other heptalene-4,5-dicarboxylates, namely **11** and **12**, carried a $BrCH_2$ group at C(6), and **12**, in addition, a second Br-substituent at C(9). The fourth compound contained no Br-substituent and was characterized as the ether-cleavage product of **6**, namely dimethyl 8,9-dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate[4]) (**13**).

The structures of **10** and **13** were verified by an X-ray crystal-structure analysis (see *Exper. Part* and below). Characteristic for **11** and **12** is the missing of the Me–C(6) signal in their NMR spectra. Instead of it, one finds in the ^{1}H-NMR spectra of both

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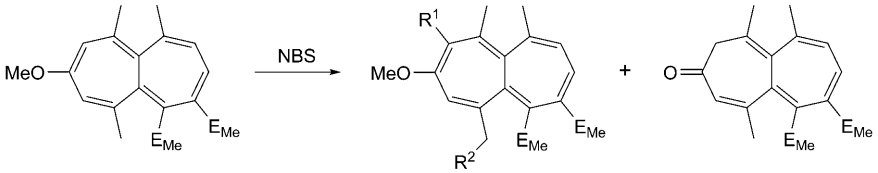
[4]) Since the two ester substituents are the locant-determining groups, the correct name of **13** would be dimethyl 7,8-dihydro-5,6,10-trimethyl-8-oxoheptalene-1,2-dicarboxylate. However, for the sake of comparison and to avoid confusion, we use the locants of the original heptalene core (see also below). The same applies to **14**.

Table 1. *Bromination of Heptalene-4,5-dicarboxylate* **6** *with* N-*Bromosuccinimide* (NBS)



6 **10** R^1 = Br, R^2 = H; **11** R^1 = H, R^2 = Br; **12** R^1 = R^2 = Br **13**

Solvent	NBS [equiv.]	Additive [equiv.]	Time [h]	Temp. [°]	Yield [%][a])			
					10	**11**	**12**	**13**
CH_2Cl_2	2	5 (Na_2CO_3)	7	– 78	26	23	12	37
CH_2Cl_2	2	–	4	– 78	22	17	19	24
DMF	1.1	–	1	– 15	67	21	6	5

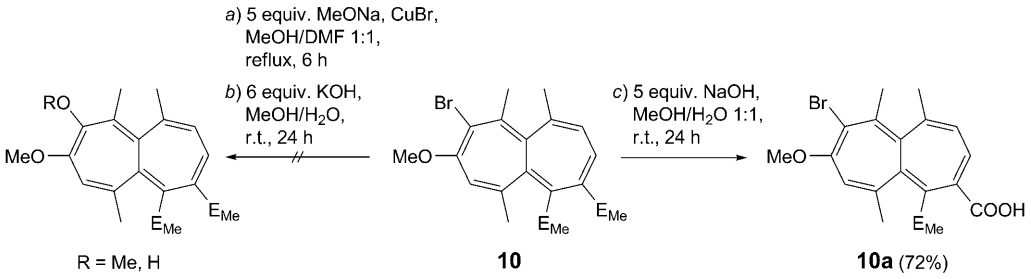
[a]) Yield of isolated products.

compounds an *AB* system for a $BrCH_2$ group at C(6) with $^2J_{AB} = 10.4$ and 10.7 Hz, respectively.

The bromination-product composition did not alter very much in the presence or absence of Na_2CO_3. Therefore, we reduced the amount of NBS and tried DMF as polar solvent. Under these conditions, we got finally an acceptable yield of **10**. However, the formation of product **11** and its follow-up product **12**, resulting from the radical bromination of Me–C(6), could not be suppressed. On the other hand, the yield of the ether cleavage product **13** was distinctly reduced.

The Br-substituent of **10** could not be exchanged against OH or MeO under strong basic condition, and with NaOH in MeOH/DMF at room temp., only cleavage of the sterically less hindered ester group at C(4) was observed (→ **10a**; *Scheme 3*). Therefore, we had to look for other ways for the introduction of O-functionalities at C(9) of heptalenedicarboxylate **6**.

Scheme 3

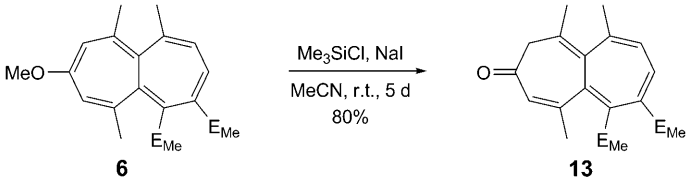


R = Me, H **10** **10a** (72%)

2.3. *Acetyloxylation of Dimethyl 8,9-Dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate*[4]) (**13**). The appearance of nearly equal amounts of **10** and **13** as the result

of the ionic reaction path of **6** and NBS in CH_2Cl_2 (*Table 1*) shows that the ether function of **6** can be cleaved quite easily by H^+ catalysis. Moreover, the CH_2 group in α-position to the keto group of **13** pointed to the possibility that this favorable structural situation could be utilized for the direct insertion of an O-function in **13**. But first of all, we had to look for a productive ether cleavage of **6**. *Olah* and co-workers have described an efficient procedure for the selective cleavage of esters, ethers, and other O-functions with chlorotrimethylsilane (Me_3SiCl) in the presence of NaI [14]. When we exposed **6** over 5 days to these conditions, we obtained **13** in a yield of 80%, whereby 14% of **6** could be recovered, so that the chemical yield of **13** amounted to 93% (*Scheme 4*).

Scheme 4



Onishi and *Osawa* have described a radical α-acetyloxylation of steroidal ketones with $Pb(OAc)_4$ in boiling benzene [15], a procedure, which seemed to us very promising, because an AcO group at C(9) can be modified easily to other O-functionalities. The X-ray crystal structure of **13** (*Fig. 1*) as well as its AM1-calculated structure show $H_{pro\text{-}S}$–C(9) in the (*P*)-configuration of the heptalene skeleton in a close to 90° position with respect to the π-plane of the adjacent π-bonds as indicated by the torsion angles Θ ($H_{pro\text{-}S}$–C(9)–C(10)=C(10a)) = 50.9° and Θ ($H_{pro\text{-}S}$–C(9)–C(8)=O) = 115.2°, whereas $H_{pro\text{-}R}$–C(9) occupies a more or less in-plane position with respect to the adjacent π-bonds (Θ ($H_{pro\text{-}R}$–C(9)–C(10)=C(10a)) = 168.3° and Θ ($H_{pro\text{-}R}$–C(9)–C(8)=O) = −2.2°).

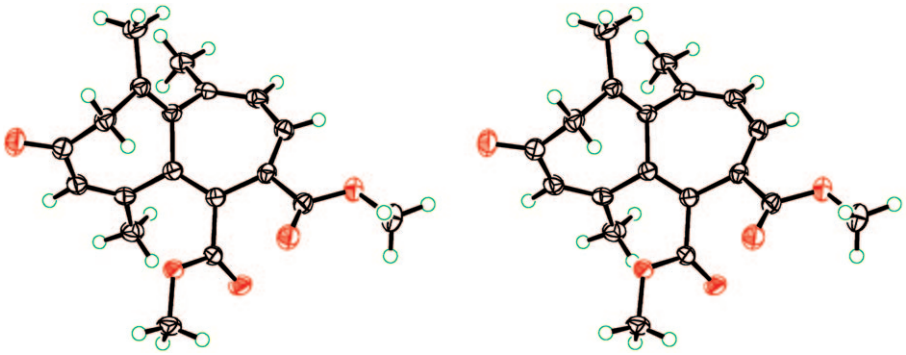
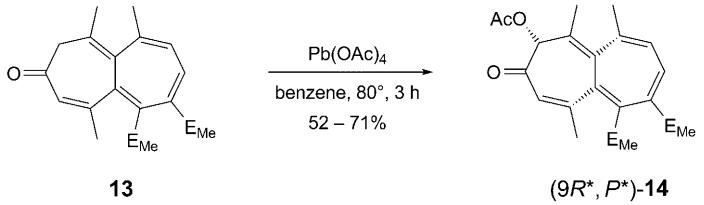


Fig. 1. *Stereoscopic view of dimethyl 8,9-dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate*[4]) (**13**) (50% probability ellipsoids)

Therefore, we were quite optimistic that $H_{pro\text{-}S}$ could easily be attacked and removed by AcO$^\bullet$ and the thus formed π-stabilized radicals of **13** then combine with

further acetyloxy radicals (see also below). Instead of 8.7 equiv. of $Pb(OAc)_4$ per equiv. of ketone [15], we used only 1.1 equiv. of $Pb(OAc)_4$, and the reaction time in boiling benzene was reduced from 48 h to 3 h. By this modified procedure, we obtained the expected 9-(acetyloxy)heptalene-4,5-dicarboxylate[4]) **14** in yields of 52 to 71%, depending on the purity of the applied $Pb(OAc)_4$ (*Scheme 5*). By crystallization from a mixture of hexane/AcOEt/Et_2O, we obtained **14** in yellow tablets, suitable for an X-ray crystal-structure analysis, which allowed determining the relative configuration of **14**. The (9*R**,*P**)-configuration was thus established for **14** (*Fig. 2*). Since the axis of chirality of (9*R**,*P**)-**14** could switch principally by double-ring inversion to the (*M**)-configuration of the diastereoisomer of **14** with (9*R**,*M**)-configuration, we calculated with AM1 ΔH_f° of both diastereoisomers. It turned out that (9*R**,*P**)-**14** is with $\Delta\Delta H_f^\circ = -1.83$ kcal mol^{-1} the thermodynamically favored product (see later).

Scheme 5



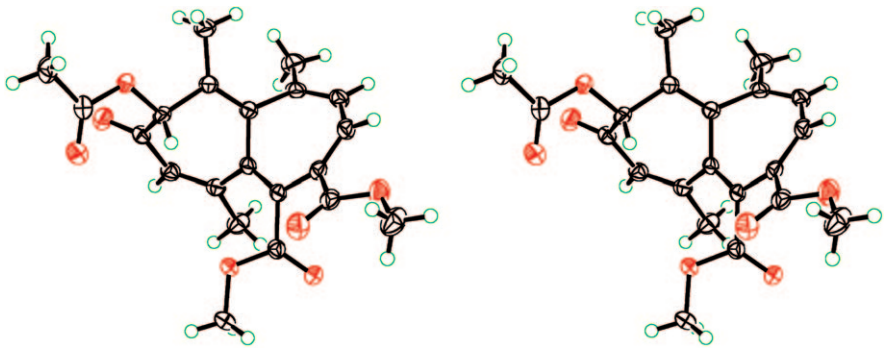
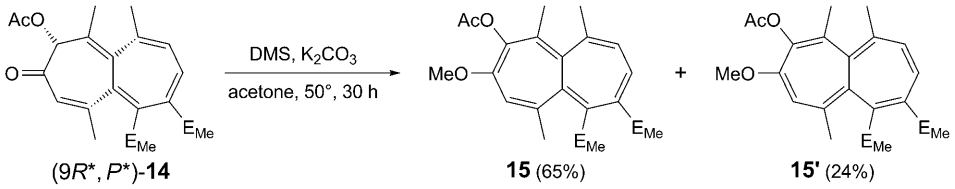


Fig. 2. *Stereoscopic view of dimethyl 9-(acetyloxy)-8,9-dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate*[4]) (**14**) (50% probability ellipsoids)

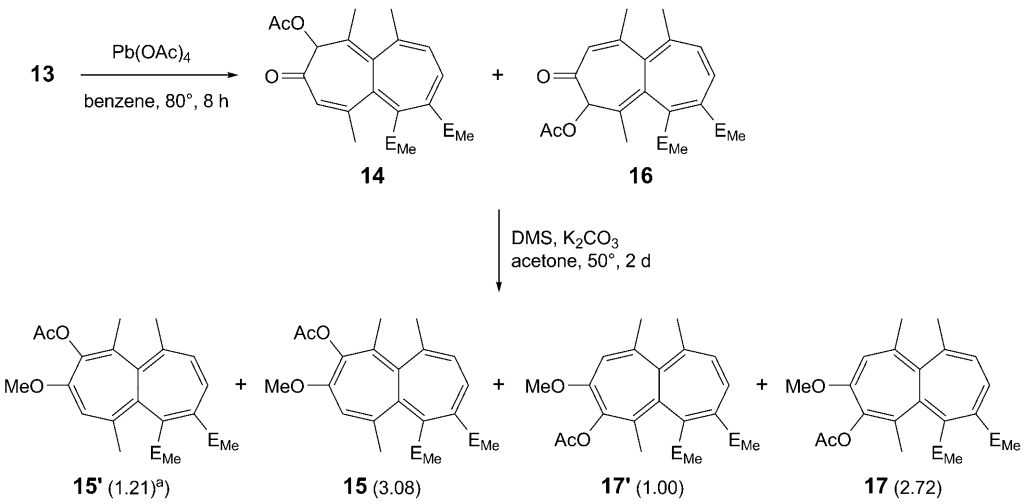
The formation of enol ether derivatives of **14** by *O*-alkylation would allow the re-entrance in the world of multi-functionalized 12e-heptalenes for further modifications (*cf. Scheme 1*). First attempts to alkylate **14** (in analogy to [16]) with MeI in the presence of K_2CO_3 failed completely. No defined product at all was formed. The situation changed when we applied the stronger methylating agent dimethyl sulfate (DMS) in acetone (in analogy to [17]). Now, we found after 30 h at 50° the expected heptalene-4,5-dicarboxylate **15** in a yield of 65% accompanied by its DBS isomer **15′** established in 24% yield (*Scheme 6*). The X-ray crystal analysis of **15′** established unequivocally its structure (see *Exper. Part*).

Scheme 6



The excellent yield of **15** and **15′** together led us to a reproving experiment, stimulated by the fact that we found in the ^{1}H-NMR spectra of not fully purified **14** weak signals of a further compound, which could possibly belong to an isomer of **14**. Crude **14** was therefore methylated according to *Scheme 6*, whereby the reaction time was prolonged to two days. The HPLC analysis of the crude product mixture indicated the presence of four heptalenedicarboxylates, which could be cleanly separated by prep. HPLC (*Scheme 7*). Peak 2 and 4 represented **15′** and **15**, respectively, whereas Peak 1 and 3 belonged to the new heptalenedicarboxylates **17′** and **17**, respectively. The latter two were fully identified by their ^{1}H-NMR spectra (see *Exper. Part*). The ratio of (**15′** + **15**)/(**17′** + **17**) amounted to 8 : 1. The origin of the DBS isomers **17** and **17′** must be the oxoheptalenedicarboxylate **16**.

Scheme 7



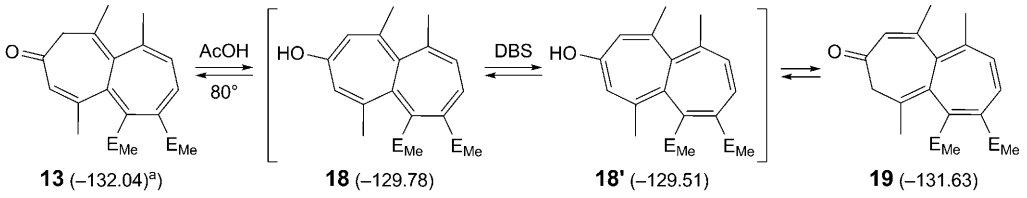
a) In parentheses, the relative retention times (t_R) on the *Spherisorb CN* column. Actual t_R of **17'** was 4.12 min.

We suppose that under the conditions of the acetyloxylation of **13** (80°, benzene) and favored by the presence of AcOH in the reaction mixture[5]), an H^+-catalyzed equilibrium mixture of **13** and its isomer **19** is established *via* their corresponding enol

[5]) AcOH is formed in the course of the reaction; however, more important is the fact that purchased $Pb(OAc)_4$ contains for stabilization up to 15% AcOH.

forms **18** and **18′** (*Scheme 8*)[6]). The ΔH_f° values of the four components of the postulated equilibrium lie quite close together with a maximum difference of 2.5 kcal mol^{-1}, whereby the two oxoheptalenedicarboxylates show $\Delta\Delta H_f^\circ = 0.41$ kcal mol^{-1} in favor of **13**, in general agreement with the fact that we found 8 times more heptalenedicarboxylates **15**/**15′** in comparison to the amount of **17**/**17′**.

Scheme 8



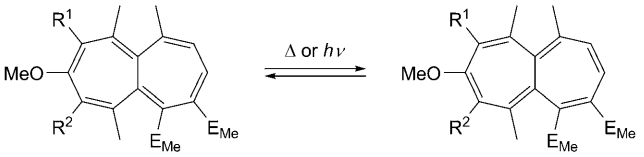
a) In parentheses, the AM1-calculated ΔH_f° [kcal mol^{-1}] values.

Since **15**/**15′** and **17**/**17′** are new and represent positional isomers with respect to the AcO substituent, we determined the thermal and photochemical equilibrium ratio of the two DBS pairs. The results are listed in *Table 2* together with those of **6**/**6′**. The ratios of the latter are in good agreement with those of the corresponding 8-methylheptalenedicarboxylates (ratio on Δ (tetralin, calc. for 25°), 15:1; ratio on *hν* (^{t}BuOMe, high-pressure mercury lamp), 1.2:1) [11a]. On the other hand, selective irradiation into heptalene band I of the (acetyloxy)-substituted heptalenedicarboxylates **15**/**15′** and **17**/**17′** favors strongly the 1,2-dicarboxylates in the photochemical equilibrium, in agreement with the slight differences in the absorption of these heptalenes (see *Table 3*). The UV/VIS spectra of heptalenes with the same π-bond pattern like the 8-methoxyheptalene-4,5-dicarboxylates **6**, **10**, and **15** show almost no differences in the long-wavelength region of the heptalene band I despite different substituents (H, Br, AcO) at C(9) (see *Fig. 3*). On the other hand, it is also of interest to note that the position of the AcO substituent of the two pairs of heptalenedicarboxylates influences the thermal-equilibrium ratio markedly. Whereas heptalenedicarboxylates **17**/**17′** exhibit a 'normal' thermal behavior in that it shows a preponderance of the 4,5-dicarboxylate in the thermal equilibrium in quite good agreement with the AM1-calculated difference of the ΔH_f° values of 0.51 kcal mol^{-1}, the AcO substituent in **15**/**15′** favors the 1,2-dicarboxylate, again in good accordance with the AM1-calculated difference of the ΔH_f° values of 0.43 kcal mol^{-1}.

The AcO group at C(9) of **15** (at C(7) of **15′**, resp.) should ideally be suited for base-catalyzed alkylation reactions without touching the two adjacent ester functions at the other heptalene-ring moiety. We tested this possibility by the reaction of **15** with benzyl bromide (BnBr) in the presence of MeONa in DMF (in analogy to [18]) with the idea that a BnO group could later on be cleaved by hydrogenolysis (*cf.* [19]). The result was that we got, after chromatography, a 1:2 mixture of the 9-(benzyloxy)hep-

6) It might be that the enol forms **18** and **18′** themselves are the important intermediates, which are oxidized by Pb^{IV} to the corresponding radical cations, which combine with AcO$^\bullet$ and formation of $Pb(OAc)_2$ and AcOH (*cf.* [15]).

Table 2. *Thermal and Photochemical Equilibrium Ratios of 8-Methoxyheptalenedicarboxylates* **6**/**6′**, **15**/**15′**, *and* **17**/**17′**

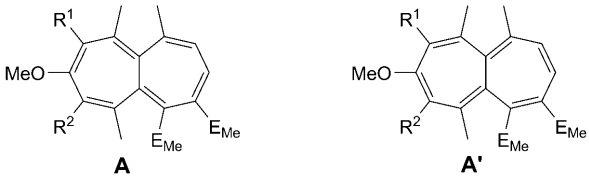


A **A'**

	R^1	R^2	Conditions Δ	**A**/**A′**	Conditions *hν*	**A**/**A′**
6/**6′**	H	H	$CDCl_3$, r.t., 20 h	10 : 1	MeCN[a]), daylight, 8 h	1.1 : 1
15/**15′**	AcO	H	C_6D_6, 75°, 3 d	1 : 2.8	CH_2Cl_2[b]), 366 nm[c]), 5 min	1 : 4.3
17/**17′**	H	AcO	C_6D_6, 75°, 3 d	1.5 : 1	CH_2Cl_2[b]), 366 nm[c]), 5 min	1 : 1.6

[a]) $c = 0.1$M. [b]) $c = 0.01$M. [c]) Light of a fluorescence tube with λ_{emiss} at 366 nm.

Table 3. *UV/VIS Maxima of Some 8-Methoxyheptalenedicarboxylates*[a])



A **A'**

	R^1	R^2	Type	Solvent	Heptalene band			
					I	II	III	IV
6	H	H	**A**	MeCN	390 (sh, 0.04)	330 (sh, 0.20)	272 (0.81), 290 (sh, 0.63)	238 (sh, 1.00)
6′	H	H	**A′**	MeCN	387 (sh, 0.03)	327 (sh, 0.15)	275 (1.00)	231 (0.93)
10	Br	H	**A**	MeCN	385 (0.05)	338 (sh, 0.15)	269 (sh, 0.72), 297 (sh, 0.43)	252 (1.00)
15	AcO	H	**A**	MeCN	387 (sh, 0.05)	327 (sh, 0.19)	268 (0.89), 290 (sh, 0.54)	240 (1.00)
15′	AcO	H	**A′**	MeCN	387 (sh, 0.03)	328 (sh, 0.10)	275 (1.00)	236 (sh, 0.91)
17	H	AcO	**A**	[b])	*ca.* 380 (sh, 0.06)	329 (sh, 0.15)	279 (0.61)	241 (1.00)
17′	H	AcO	**A′**	[b])	*ca.* 380 (sh, 0.04)	*ca.* 329 (0.16)	272 (1.00)	225 (0.87)
28[c])	H	H	**A**	[d])	*ca.* 370 (sh, 0.06)	*ca.* 320 (sh, 0.17)	261 (1.00), *ca.* 280 (sh, 0.87)	236 (sh, 1.00)
28′[c])	H	H	**A′**	[d])	390 (0.03)	318 (sh, 0.13)	268 (1.00)	233 (sh, 0.81)

[a]) Wavelength λ [nm], sh = shoulder, in parentheses relative band intensities; band numbering according to [20]. [b]) Hexane/(CH_2Cl_2 + 0.5% MeOH) 9 : 1. [c]) 8-Me instead of 8-MeO. Values are taken from [20]. [d]) Hexane/^{i}PrOH 25 : 1.

talene-4,5-dicarboxylate **20** and its DBS isomer **20′** in a combined yield of 48%. The starting material **15** was recovered in a yield of 26% accompanied by 16% of its DBS isomer **15′** (*Scheme 9*). The total chemical yield of **20** and **20′** corresponds thus to 90%.

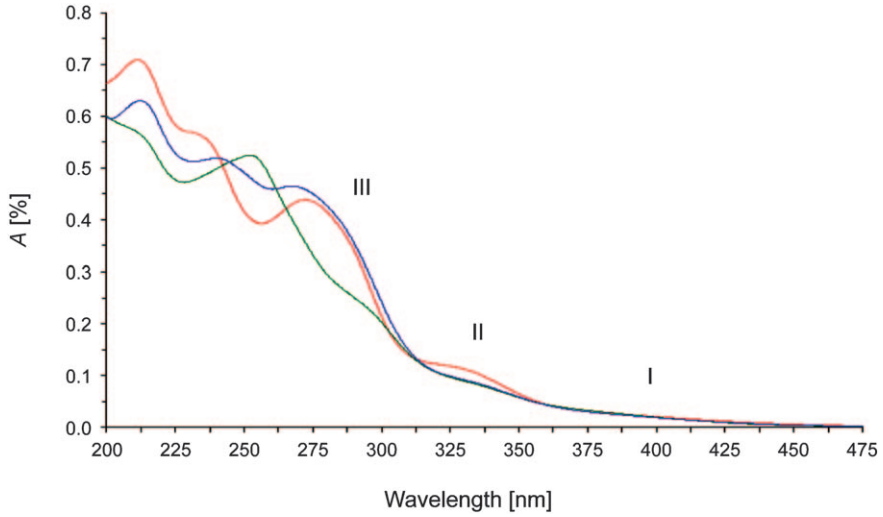
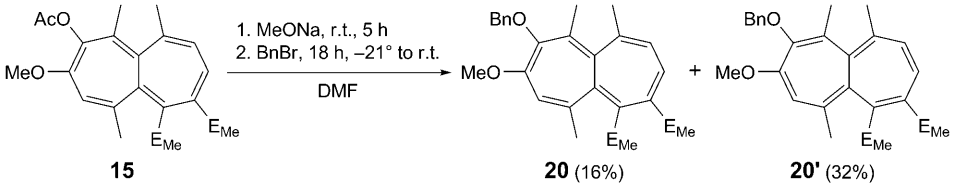


Fig. 3. *UV/VIS Spectra* (MeCN) *of 8-methoxyheptalene-4,5-dicarboxylate* **6** (red curve), *9-bromo-8-methoxyheptalene-4,5-dicarboxylate* **10** (green curve), *and 9-(acetyloxy)-8-methoxyheptalene-4,5-dicarboxylate* **15** (blue curve)

Scheme 9



15 **20** (16%) **20'** (32%)

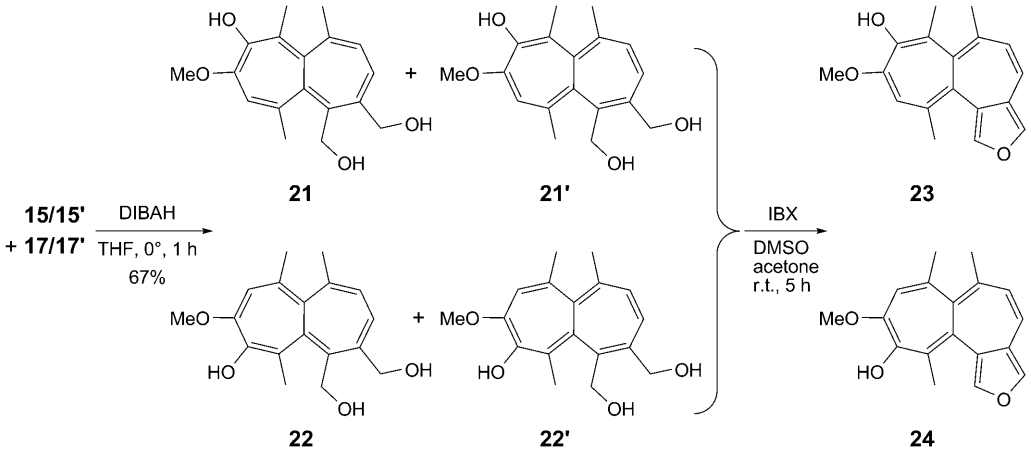
[a]) 26% of **15** and 16% of **15'** were recovered.

The reaction was performed without protection against daylight. Therefore, we suppose that the DBS isomers of **15** and **20** are formed under the influence of the laboratory light (see later), because the temperature did not exceed room temperature, which is in the present cases too low for a thermal DBS process.

2.4. *Heptaleno[1,2-c]furan Formation.* Furans of type **2** (*Scheme 1*) are available by reduction of the ester groups of heptalene-1,2- or -4,5-dicarboxylates to the corresponding heptalenedimethanols, which are then oxidatively cyclized to heptaleno[1,2-*c*]furans [2]. We tested, therefore, in some preliminary experiments with the original heptalenedicarboxylate mixture **15**/**15′**/**17**/**17′** (*Scheme 7*) the possibility of heptaleno[1,2-*c*]furan formation. The reduction was performed with diisobutylaluminium hydride (DIBAH) in tetrahydrofuran (THF), whereby also the AcO group was cleaved reductively (*Scheme 10*). The formation of the heptalenedimethanols **21** and **22** and their respective DBS isomers was established by the presence of the signals of the diastereotopic H-atoms of the 8 different CH_2OH groups in the ^{1}H-NMR spectrum of

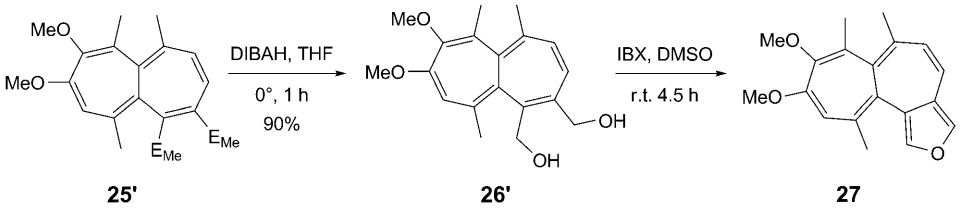
the mixture. The mixture was then taken up in acetone and added to a solution of IBX (1-hydroxy-1,2-benziodoxol-3(1*H*)-one 1-oxide) in DMSO at room temp. Chromatography (silica gel, hexane/^{t}BuOMe 2 : 3) gave a pure fraction of **23** (35%) and a mixture **23**/**24**. The compounds were unstable so that only **23** could be fully characterized by its ^{1}H-NMR spectrum in C_6D_6.

Scheme 10



We supposed that the OH group of **23** and **24** was responsible for their instability. Therefore, we synthesized dimethyl 7,8-dimethoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate (**25′**) by methylation of the acetyloxy precursor **15**, in analogy to the benzylation reaction of **15** (*Scheme 9*). The 1,2-dicarboxylate **25′** was isolated from the mixture of products by chromatography (silica gel, hexane/AcOEt 2 : 1). The reduction of the ester groups of **25′** caused no problems (*Scheme 11*), so that the dimethanol **26′** was not further characterized. Reaction of **26′** with IBX in DMSO led to the formation of the expected 8,9-dimethoxy-6,7,11-trimethylheptaleno[1,2-*c*]furan (**27**). The ^{1}H-NMR spectrum of **27** (600 MHz, C_6D_6) was in full agreement with its structure. Typical are the coupling patterns and chemical shifts of H–C(1) (*d*-like) at δ(H) 7.11, H–C(3) (*dd*-like *m* due to coupling with H–C(1) and H–C(4) or H–C(5)) at δ(H) 6.94, and H–C(4) and H–C(5) at δ(H) 6.42 and 5.86, respectively, with $J_{vic} = 11.4$ Hz. H–C(10) appeared as a sharp *s* at δ(H) 5.54. The position of the signals of the Me and MeO groups followed unambiguously from ^{1}H-NOE measurements.

Scheme 11



Finally, it can be said that our investigations showed that in *Scheme 1* the upper path *via* **2** as well as the lower path *via* **3** are principally realizable for the synthesis of colchicine structures of type **5**.

We are thankful to our NMR laboratory for specific NMR measurements, our MS laboratory for mass spectra, and our laboratory for microanalysis for elemental analyses. Financial support of this work by the *Swiss National Science Foundation* is gratefully acknowledged.

Experimental Part

General. M.p.: Homemade apparatus with heating table and microscope; uncorrected. TLC: Aluminium sheets coated with silica gel *60 F_{254}* (SiO_2; *Merck*) or plastic sheets coated with Al_2O_3 *N/UV$_{254}$* (*Polygram®*; *Macherey–Nagel*); spot visualization with UV light (254 or 366 nm) or with appropriate spray reagents. Prep. TLC: SiO_2 *60 F_{254}* plates (2 mm) or Al_2O_3 *150 F_{254}* plates (1.5 mm). Column chromatography (CC) and flash chromatography (FC): SiO_2 *C-560* (0.040–0.063 mm; *Chemie Uetikon AG*) or Al_2O_3, type *5016A*, basic (0.05–0.15 mm; *Fluka*). HPLC: *Spherisorb CN* (3 μ), 4 × 125 mm column. Semi-prep. HPLC: *Spherisorb CN* (5 μ), 20 × 250 mm column. UV/VIS Spectra: *Lambda 19* UV/VIS/NIR spectrophotometer (*Perkin–Elmer*); λ_{max} and λ_{min} in nm; molar extinction coefficients ε [1000 cm^2 mol^{-1}] in log ε, or in rel. intensities with a *Jasco MD-910* detector in the course of HPLC separations. IR Spectra: *Spectrum-One* FT-IR spectrophotometer (*Perkin–Elmer*) in KBr pills (*ca.* 1 mg of substrate/150 mg of KBr); absorption bands in cm^{-1}; intensities as residual transmission. ^{1}H- and ^{13}C-NMR Spectra: *Bruker* instruments (*ARX 300*, *DRX-500*, and *AMX 600*); in $CDCl_3$ if not otherwise stated and $SiMe_4$ as internal standard; chemical shifts δ in ppm, coupling constants *J* in Hz; assignments by NOESY and COSY measurements; DEPT for the determination of the multiplicities of the ^{13}C signals. Mass Spectra: *MAT-95* instrument (*Finnigan*), EI at 70 eV, source temp. 250°, CI with NH_3; in *m*/*z* (rel. peak intensities in %).

1. *Dimethyl 8-Methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**6**). 1.1. *4-Methoxy-2,6-dimethylpyrylium Tetrafluoroborate.* Under N_2, 2,6-dimethyl-4*H*-pyran-4-one (100 g, 0.806 mol; prepared from dehydracetic acid [21]) and dimethyl sulfate (161 g, 1.276 mol) were stirred for 18 h at 60°. The orange suspension was then cooled to *ca.* −3° and 50% aq. HBF_4 soln. (144 g, 0.82 mol) was slowly added under vigorous stirring. After the addition, stirring was continued at −3° for 2 h. Then, ^{t}BuOMe (100 ml) was added and stirring continued for 15 min. The yellow suspension was filtered over a glass frit under a slight pressure of N_2. The yellow filter cake was washed several times (CH_2Cl_2) and dried under h.v.: tetrafluoroborate (118.5 g, 65%). M.p. 173–175° ([22]: 174–175°).

1.2. *6-Methoxy-4,8-dimethylazulene* (**7**). NaH (60 g, 1.36 mol; 55–65% in mineral oil) was placed in a flame-dried flask under N_2. The mineral oil was removed by washing 3 times with hexane, and the NaH was then suspended in THF (600 ml). The suspension was cooled to −15°, and cyclopentadiene (90 g, 1.36 mol) was slowly added dropwise taking care that the temp. did not exceed −10°. After the addition, the thus prepared sodium cyclopentadienide soln. was stirred for 1 h at 0°. Then, 4-methoxy-2,6-dimethylpyrylium tetrafluoroborate (77 g, 0.341 mol; see *1.1*) was added under vigorous stirring and cooling at −10°. After the addition, the temp. was raised to 0° and the mixture then heated under reflux for 24 h. The volume of the brown-red soln. was reduced to 100 ml, poured onto crashed ice, and then extracted with AcOEt (5×). The combined extract was washed with brine, dried (Na_2SO_4), and concentrated and the residue filtered with hexane several times over Al_2O_3 to give **7** (30.27 g, 48%) after evaporation. Red powder. For characterization, a small quantity of **7** (0.10 g) was sublimed (90°/h.v.) to yield **7** as wine-colored plates. M.p. 101–103° ([9]: 100–101°). R_f (SiO_2, hexane/toluene 2:1) 0.48. IR: 3424*w*, 3103*w*, 3071*w*, 3010*w*, 2967*w*, 2935*w*, 2839*w*, 2778*w*, 2725*w*, 2561*w*, 2474*w*, 2418*w*, 2304*w*, 2208*w*, 2108*w*, 2021*w*, 1899*w*, 1790*w*, 1738*w*, 1717*w*, 1694*w*, 1578v*s*, 1541*m*, 1497*m*, 1463*m*, 1455*m*, 1426*m*, 1409*m*, 1373*w*, 1335v*s*, 1275*w*, 1215v*s*, 1190*m*, 1174*m*, 1151*m*, 1102*s*, 1083*w*, 1063v*s*, 1019*m*, 965*m*, 937*w*, 919*w*, 896*w*, 860*m*, 829*m*, 800*w*, 742*s*, 712*m*, 609*w*, 528*w*, 412*w*. ^{1}H-NMR (C_6D_6): 7.68 (*t*, ^3J = 3.9, H–C(2)); 7.44 (*d*, ^3J = 3.9, 2 H, H–C(1,3)); 6.64 (*s*, 2 H, H–C(5,7)); 3.28 (*s*, MeO–C(6)); 2.63 (*s*, 6 H, Me–C(4,8)). ^{13}C-NMR (C_6D_6): 164.42 (*s*, C(6)); 145.45 (*s*, C(4,8)); 134.37 (*s*, C(3a,8a)); 130.47 (*d*, C(2)); 117.58 (*d*,

C(1,3)); 112.82 (*d*, C(5,7)); 55.10 (*q*, *Me*O–C(6)); 25.18 (*q*, *Me*–C(4,8)). EI-MS: 187 (15), 186 (100, $M^{+\cdot}$), 185 (5), 171 (11), 155 (7), 143 (28), 142 (9), 141 (22), 129 (7), 128 (38), 127 (9), 115 (15). Anal. calc. for $C_{13}H_{14}O$ (186.26): C 83.83, H 7.58; found: C 83.84, H 7.55.

1.3. *6-Methoxy-1,4,8-trimethylazulene* (**8**). 1.3.1. *6-Methoxy-4,8-dimethylazulene-1-carboxaldehyde.* The *Vilsmeier* reagent was prepared at 0° from DMF (5 ml) and $POCl_3$ (1 ml, 11.36 mmol). The reagent was added through a syringe under stirring to a cooled soln. (3°) of **7** (1.863 g, 10.00 mmol) in DMF (8.2 ml). An intermediately formed orange solid was re-dissolved by addition of further DMF (10 ml). Stirring was continued for 30 min. The mixture was then poured into ice water what led to a dark red soln., which was brought to pH 9 with 4N aq. NaOH. H_2O was added, and the mixture was extracted 4 times with CH_2Cl_2 and finally with Et_2O. The combined org. phase was washed 3 times with brine, dried (Na_2SO_4) and concentrated. FC (SiO_2, hexane/CH_2Cl_2/AcOEt 2:2:1) gave the azulene-1-carboxaldehyde (1.994 g, 96%). Orange needles. M.p. 128–129°. R_f (SiO_2, AcOEt/hexane 2:1) 0.58. IR: 3441*w*, 3215*w*, 3106*w*, 3051*w*, 3011*w*, 2981*w*, 2939*w*, 2907*w*, 2839*w*, 2730*w*, 2652*w*, 2588*w*, 2517*w*, 2440*w*, 2400*w*, 2294*w*, 2212*w*, 2160*w*, 2129*w*, 2069*w*, 2035*w*, 2011*w*, 1801*w*, 1619v*s*, 1585v*s*, 1558*m*, 1527*w*, 1501*m*, 1465*m*, 1455*m*, 1445*m*, 1434*m*, 1413*w*, 1376*m*, 1355*m*, 1330v*s*, 1313*m*, 1223v*s*, 1196*m*, 1180*m*, 1105*m*, 1068*s*, 1033*w*, 1000*w*, 969*w*, 939*w*, 907*w*, 895*w*, 864*w*, 845*w*, 787*m*, 774*w*, 721*m*, 714*m*, 672*w*, 655*w*, 621*w*, 540*w*, 485*w*. ^{1}H-NMR: 10.56 (*s*, CH=O); 8.08 (*d*, $^3J = 4.5$, H–C(2)); 7.22 (*d*, $^3J = 4.5$, H–C(3)); 7.01 (*s*, H–C(7)); 7.00 (*s*, H–C(5)); 3.95 (*s*, MeO–C(6)); 3.10 (*s*, Me–C(8)); 2.86 (*s*, Me–C(4)). ^{13}C-NMR: 187.04 (*t*, CH=O); 164.95 (*s*, C(6)); 148.57 (*s*, C(8)); 148.46 (*s*, C(4)); 139.61 (*s*, C(3a)); 135.15 (*d*, C(2)); 134.04 (*s*, C(8a)); 130.70 (*s*, C(1)); 118.79 (*d*, C(7)); 117.47 (*d*, C(2)); 117.42 (*d*, C(5)); 55.95 (*q*, *Me*O–C(6)); 31.10 (*q*, *Me*–C(8)); 26.51 (*q*, *Me*–C(4)). CI-MS: 216 (15), 215 (100, $[M+1]^+$), 201 (6). Anal calc. for $C_{14}H_{14}O_2$ (214.27): C 78.48, H 6.59; found: C 78.90, H 6.52.

1.3.2. *Reduction.* Under N_2, $NaBH_4$ (3.00 g, 78.08 mmol) was suspended in diglyme (30 ml) in a flame-dried flask. Concurrently, a soln. of $BF_3 \cdot Et_2O$ (3.8 ml, 34.81 mmol) in Et_2O (60 ml) and a suspension of the aldehyde (5.50 g, 25.67 mmol; see *1.3.1*) in diglyme (60 ml) were added dropwise (→ violet suspension already after a few drops). Stirring was continued for 1 h at r.t. after addition of the reactants. The dark violet mixture was then poured into ice water (250 ml), and stirring was pursued until the frothing had ceased. The formed azulene **8** was extracted with hexane (3×), the extract washed with brine, dried (Na_2SO_4), and concentrated, and the residue dried at 60–65°/h.v. until it solidified. FC (Al_2O_3, hexane/AcOEt 20:1) gave pure **8** (4.70 g, 92%). Dark violet crystals. M.p. 99–100°. R_f (SiO_2, hexane/toluene 2:1) 0.48. IR: 3442*w*, 3065*w*, 3007*w*, 2973*w*, 2952*m*, 2940*w*, 2919*w*, 2864*w*, 2839*w*, 2780*w*, 2731*w*, 2640*w*, 2532*w*, 2458*w*, 2407*w*, 2377*w*, 2305*w*, 2257*w*, 2229*w*, 2155*w*, 2106*w*, 2081*w*, 2026*w*, 1922*w*, 1901*w*, 1746*w*, 1704*w*, 1636*w*, 1579v*s*, 1560*s*, 1531*m*, 1513*s*, 1453*m*, 1441*m*, 1407*m*, 1390*m*, 1365*m*, 1343*s*, 1302*s*, 1267*w*, 1217v*s*, 1205*s*, 1192*m*, 1171*s*, 1145*m*, 1105*m*, 1066*s*, 1033*m*, 957*w*, 942*w*, 872*m*, 834*m*, 777*s*, 720*m*, 714*m*, 707*m*, 691*w*, 531*w*. ^{1}H-NMR (C_6D_6): 7.40 (*d*, $^3J = 3.9$, H–C(2)); 7.33 (*d*, $^3J = 3.9$, H–C(3)); 6.49 (*d*, $^4J = 2.5$, H–C(7)); 6.47 (*d*, $^4J = 2.5$, H–C(5)); 3.30 (*s*, MeO–C(6)); 2.76 (*s*, Me–C(1)); 2.70 (*s*, Me–C(8)); 2.60 (*s*, Me–C(4)). ^{13}C-NMR (C_6D_6): 164.07 (*s*, C(6)); 147.02 (*s*, C(8)); 144.94 (*s*, C(4)); 135.22 (*s*, C(3a)); 134.82 (*d*, C(2)); 131.33 (*s*, C(8a)); 128.09 (*s*, C(1)); 116.33 (*d*, C(3)); 113.61 (*d*, C(7)); 111.32 (*d*, C(5)); 54.97 (*q*, *Me*O–C(6)); 27.91 (*q*, *Me*–C(8)); 25.67 (*q*, *Me*–C(4)); 20.03 (*q*, *Me*–C(1)). EI-MS: 201 (14), 200 (100, $M^{+\cdot}$), 199 (70), 185 (31), 157 (8), 156 (7), 155 (9), 153 (8), 152 (8), 143 (7), 142 (20), 141 (26), 128 (9), 115 (14), 57 (7). Anal. calc. for $C_{14}H_{16}O$ (200.28): C 83.96, H 8.05; found: C 84.00, H 7.99.

1.4. *Reaction of Azulene* **8** *with Dimethyl Acetylenedicarboxylate* (ADM). 1.4.1. *Dimethyl 8-Methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**6**) *and Dimethyl 6-Methoxy-4,8-dimethylazulene-1,2-dicarboxylate* (**9**). To a soln. of **8** (1.00 g, 5.00 mmol) in toluene (12 ml) in a flame-dried *Schlenk* vessel under N_2, ADM (0.62 ml, 15.0 mmol) was added through a syringe. The vessel was closed and the violet soln. heated at 140° for 24 h. After cooling, the now yellow-red soln. was poured on ice/water (10 ml) and further extracted with Et_2O (3×). The combined extract was washed with brine, dried (Na_2SO_4), and concentrated and the red-brown residue dried at 60° and then subjected to FC (SiO_2, hexane/AcOEt 3:1): **6** as yellow prisms (0.528 g, 31%), followed by **9**, as blood-red rhombs (0.545 g, 36%).

Data of **6**: M.p. 179–180°. R_f (SiO_2, hexane/AcOEt 2:1) 0.47. UV/VIS (MeCN; see also *Table 3* and *Fig. 3*): max. 211 (4.37), 238 (sh, 4.26), 272 (4.17), 290 (sh, 4.06), 331 (sh, 3.57), 390 (sh, 2.91); min. 196

(4.34), 256 (4.12). IR: 3444*w*, 3399*w*, 3016*w*, 2989*w*, 2950*m*, 2932*w*, 2911*w*, 2846*w*, 2832*w*, 1734v*s*, 1708v*s*, 1668*w*, 1649*m*, 1627*w*, 1597*m*, 1569*m*, 1535*m*, 1461*m*, 1434*s*, 1393*m*, 1374*w*, 1345*w*, 1296*m*, 1267v*s*, 1248v*s*, 1214*s*, 1197v*s*, 1175*s*, 1151*m*, 1109*m*, 1089*s*, 1052*s*, 1025*w*, 991*m*, 959*m*, 927*w*, 864*w*, 851*w*, 842*m*, 827*m*, 793*w*, 783*m*, 772*m*, 717*w*, 705*w*, 683*w*, 646*w*, 629*w*, 610*w*, 585*w*, 569*w*, 535*w*, 519*w*, 511*w*, 476*w*, 437*w*. ^{1}H-NMR: 7.52 (*d*, $^3J = 5.8$, H–C(3)); 6.25 (*dd*, $^3J = 5.8$, $^4J = 1.0$, H–C(2)); 6.00 (*s*, H–C(7)); 5.51 (*d*, $^4J = 1.1$, H–C(9)); 3.69 (*s*, MeOOC–C(4)); 3.69 (*s*, MeOOC–C(5)); 3.61 (*s*, MeO–C(8)); 1.99 (*s*, Me–C(1)); 1.95 (*s*, Me–C(6)); 1.77 (*s*, Me–C(10)). ^{13}C-NMR: 167.78 (*s*, *C*O–C(5)); 167.52 (*s*, *C*O–C(4)); 159.24 (*s*, C(8)); 145.19 (*s*, C(5a)); 143.98 (*s*, C(1)); 139.36 (*d*, C(3)); 133.49 (*s*, C(6)); 131.17 (*s*, C(4)); 129.81 (*s*, C(10)); 125.67 (*d*, C(2)); 123.63 (*d*, C(7)); 122.85 (*s*, C(10a)); 122.45 (*s*, C(5)); 105.94 (*d*, C(9)); 54.56 (*q*, *Me*O–C(8)); 51.98 (*q*, *Me*OOC–C(5)); 51.94 (*q*, *Me*OOC–C(4)); 23.58 (*q*, *Me*–C(1)); 22.07 (*q*, *Me*–C(6)); 19.11 (*q*, *Me*–C(10)). EI-MS: 343 (22), 342 (100, $M^{+\bullet}$), 327 (31, $[M - Me]^+$), 311 (12, $[M - MeO]^+$), 295 (33), 283 (34), 268 (12), 251 (29), 244 (24, $[M - MeC{\equiv}CCOOMe]^{+\bullet}$), 224 (12), 223 (14), 209 (15), 201 (11), 200 (69, $[M - ADM]^{+\bullet}$), 199 (12), 166 (10), 165 (27). Anal. calc. for $C_{20}H_{22}O_5$ (342.40): C 70.16, H 6.48; found: C 70.13, H 6.49.

The structure of **6** was finally established by an X-ray crystal-structure analysis (*Table 4*).

Data of **9**: M.p. 124–125°. R_f (SiO_2, hexane/AcOEt 1:1) 0.47. IR: 3388*w*, 3042*w*, 2988*w*, 2953*m*, 2916*w*, 2850*w*, 1727v*s*, 1702v*s*, 1662*w*, 1637*w*, 1586v*s*, 1554*m*, 1529*m*, 1511*m*, 1485*s*, 1455*m*, 1443*m*, 1430*s*, 1415*m*, 1388*m*, 1378*m*, 1371*m*, 1350*s*, 1277*s*, 1250v*s*, 1222v*s*, 1211v*s*, 1198v*s*, 1139*s*, 1098*s*, 1070*s*, 1054*s*, 1038*m*, 985*m*, 966*w*, 950*w*, 934*m*, 919*w*, 873*m*, 847*m*, 819*w*, 805*w*, 780*m*, 731*m*, 668*w*, 655*w*, 632*w*, 541*w*, 447*w*. ^{1}H-NMR: 7.69 (*s*, H–C(3)); 6.80 (*s*, H–C(5), H–C(7)); 3.99 (*s*, MeOOC–C(1)); 3.96 (*s*, MeO–C(6)); 3.91 (*s*, MeOOC–C(2)); 2.87 (*s*, Me–C(8)), 2.84 (*s*, Me–C(4)). ^{13}C-NMR: 171.30 (*s*, *C*O–C(1)); 167.45 (*s*, C(6)); 165.50 (*s*, *C*O–C(2)); 151.83 (*s*, C(8)); 151.13 (*s*, C(4)); 132.53 (*s*, C(8a)); 129.31 (*s*, C(2)); 129.07 (*s*, C(4a)); 123.26 (*s*, C(3)); 117.94 (*d*, C(1)); 116.81 (*d*, C(7)); 114.12 (*d*, C(5)); 56.02 (*q*, *Me*O–C(6)); 52.63 (*q*, *Me*OOC–C(1)); 51.80 (*q*, *Me*OOC–C(2)); 26.28 (*q*, *Me*–C(4)); 26.19 (*q*, *Me*–C(8)). CI-MS: 303 (50, $[M + 1]^+$), 271 (100, $[M - MeOH]^{+\bullet}$). Anal. calc. for $C_{17}H_{18}O_5$ (302.33): C 67.54, H 6.00; found: C 67.42, H 5.96.

1.4.2. *Dimethyl 8-Methoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate* (**6′**). A soln. of **6** (0.342 g, 1.00 mmol) in MeCN (10 ml) was exposed for 8 h to normal laboratory light. TLC indicated the presence of almost equal amounts of **6** and **6′**. FC (SiO_2, hexane/AcOEt 2:1) gave **6′** (0.156 g, 42%) as orange powder, followed by **6** (0.177 g, 52%).

Data of **6′**: M.p. 123–124°. R_f (SiO_2, hexane/AcOEt 4:1) 0.40. UV/VIS (MeCN; see also *Table 3*): max. 191 (sh, 4.40), 231 (4.24), 275 (4.27), 327 (sh, 3.44), 387 (sh, 2.78); min. 226 (4.24), 366 (2.75). IR: 3016*w*, 3005*w*, 2983*w*, 2957*m*, 2950*m*, 2912*w*, 2856*w*, 2834*w*, 1728v*s*, 1650*w*, 1622*w*, 1608*m*, 1567*s*, 1466*m*, 1451*m*, 1431*s*, 1401*w*, 1368*w*, 1319*m*, 1261v*s*, 1232*s*, 1204*s*, 1191*s*, 1167*s*, 1123*m*, 1094*s*, 1053*m*, 1036*m*, 1010*w*, 995*m*, 969*w*, 948*w*, 935*w*, 914*w*, 874*w*, 836*m*, 820*m*, 811*w*, 794*w*, 781*w*, 751*m*, 732*w*, 710*w*, 678*w*, 640*w*, 630*w*, 607*w*, 580*w*, 553*w*, 532*w*. ^{1}H-NMR (CD_3CN): 6.59 (*d*, $^3J = 11.8$, H–C(4)); 6.54 (*d*, $^3J = 11.8$, H–C(3)); 6.04 (*t*, $^4J = 1.4$, H–C(7)); 5.54 (*d*, $^4J = 1.7$, H–C(9)); 3.75 (*s*, MeOOC–C(2)); 3.65 (*s*, MeOOC–C(1)); 3.57 (*s*, MeO–C(8)); 2.00 (*d*, $^4J = 1.3$, Me–C(6)); 1.76 (*s*, Me–C(5)); 1.64 (*s*, Me–C(10)). ^{13}C-NMR (CD_3CN): 168.64 (*s*, *C*O–C(2)); 167.73 (*s*, *C*O–C(1)); 160.68 (*s*, C(8)); 140.11 (*d*, C(4)); 139.49 (*s*, C(5a)); 138.14 (*q*, C(2)); 137.34 (*s*, C(6)); 132.81 (*s*, C(10)); 130.39 (*s*, C(1)); 130.03 (*s*, C(5)); 127.31 (*d*, C(3)); 125.35 (*d*, C(7)); 121.27 (*s*, C(10a)); 106.48 (*d*, C(9)); 55.16 (*q*, *Me*O–C(8)); 53.17 (*q*, *Me*OOC–C(2)); 53.02 (*q*, *Me*OOC–C(1)); 22.62 (*q*, *Me*–C(6)); 18.31 (*q*, *Me*–C(10)); 17.86 (*q*, *Me*–C(5)). CI-MS: 361 (7), 360 (31, $[M + NH_4]^+$), 345 (6), 344 (18), 343 (100, $[M + 1]^+$), 342 (7), 313 (7), 312 (23), 311 (96, $[(M + 1) - MeOH]^+$).

2. *Bromination of Heptalene-4,5-dicarboxylate* **6** (see also *Table 1*). 2.1. *Formation of* **10**–**13**. To a soln. of **6** (0.450 g, 1.31 mmol) in dry DMF (9 ml) cooled to −15°, a pre-cooled soln. of NBS (0.234 g, 1.31 mmol) in DMF (2 ml) was added *via* a syringe. The mixture was stirred in the dark for an additional hour at −15°. The soln. was then poured on to ice and extracted with AcOEt (3×), the extract washed with H_2O (5×), dried (Na_2SO_4), and concentrated, and the residue subjected to CC (Al_2O_3, hexane/AcOEt 3:1), followed by a second CC (SiO_2, hexane/AcOEt 3:1): *dimethyl 6-(bromomethyl)-8-methoxy-1,10-dimethylheptalene-4,5-dicarboxylate* (**11**) as yellow powder (0.113 g, 21%), *dimethyl 9-bromo-8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**10**)/*dimethyl 9-bromo-6-(bromomethyl)-8-methoxy-1,10-dimethylheptalene-4,5-dicarboxylate* (**12**) as greenish yellow oil, and heptalenone **13**

Table 4. *Crystallographic Data of Compounds* **6**, **10**, **13**, **14**, *and* **15′**

	6	**10**	**13**	**14**	**15′**
Crystallized from	AcOEt/hexane/ DMF	Et_2O/hexane/ MeOH	AcOEt/hexane	EtOAc/hexane/ Et_2O	Et_2O/hexane/ MeCN
Empirical formula	$C_{20}H_{22}O_5$	$C_{20}H_{21}BrO_5$	$C_{19}H_{20}O_5$	$C_{21}H_{22}O_7$	$C_{22}H_{24}O_7$
M_r	342.39	421.28	328.36	386.40	400.42
Crystal color, habit	yellow, prism	yellow, needle	yellow, prism	yellow, tablet	orange, prism
Crystal dimensions [mm]	$0.17 \times 0.17 \times 0.25$	$0.05 \times 0.12 \times 0.25$	$0.12 \times 0.12 \times 0.20$	$0.10 \times 0.22 \times 0.23$	$0.10 \times 0.25 \times 0.28$
Temperature [K]	160 (1)	160 (1)	160 (1)	160 (1)	160 (1)
Crystal system	triclinic	monoclinic	triclinic	triclinic	orthorhombic
Space group	$P\bar{1}$	$P2_1/n$	$P\bar{1}$	$P\bar{1}$	*Pbca*
Z	2	4	2	2	8
Reflections for cell determination	3946	30307	3652	5624	4514
2θ Range for cell determination [°]	4 – 55	4 – 60	4 – 55	4 – 60	4 – 52
Unit cell parameters:					
a [Å]	8.3037(2)	6.3696(1)	8.2544(2)	6.9962(1)	8.6940(1)
b [Å]	8.4419(2)	19.6306(3)	10.0085(2)	11.2043(2)	21.1417(2
c [Å]	12.6946(4)	15.1721(2)	11.2872(3)	13.2844(3)	22.1651(3)
α [°]	94.448(2)	90	68.919(1)	75.8277(9)	90
β [°]	94.164(2)	96.1237(5)	87.505(1)	87.3942(8)	90
γ [°]	91.583(1)	90	71.1181(9)	76.450(1)	90
V [Å^3]	884.36(4)	1886.28(5)	820.45(3)	981.45(3)	4074.08(8)
$F(000)$	364	864	348	408	1696
D_x [g cm^{-3}]	1.286	1.483	1.329	1.307	1.306
$\mu(\text{Mo}K_\alpha)$ [mm^{-1}]	0.0917	2.213	0.0957	0.0982	0.0971
Scan type	ϕ and ω	ϕ and ω	ϕ and ω	ϕ and ω	ϕ and ω
$2\theta_{(\max)}$ [°]	55	60	55	60	52
Transmission factors (min; max)	–	0.675; 0.909	–	–	–
Total reflections measured	20292	47441	19837	29289	46911
Symmetry-independent reflections	4036	5512	3745	5701	4013
R_{int}	0.041	0.076	0.039	0.048	0.058
Reflections with $I > 2\sigma(I)$	2999	4144	2964	2930	
Parameters refined	226	236	223	254	263
$R(F)$ ($I > 2\sigma(I)$ reflections)[a])	0.0521	0.0399	0.0515	0.0498	0.0472
$wR(F)$ ($I > 2\sigma(I)$ reflections)[a])	0.0565	0.0407	0.1458[a])	0.0505	0.0475
Goodness of fit	2.985	1.844	1.075	2.218	2.673
Secondary extinction coefficient	–	$3(1) \cdot 10^{-7}$	0.050(8)	$2.9(9) \cdot 10^{-6}$	$5(1) \cdot 10^{-7}$
Final $\Delta_{\max}/\sigma$	0.0004	0.002	0.001	0.0004	0.0005
$\Delta\rho$ (max; min) [e Å^{-3}]	0.24; −0.28	0.64; −0.42	1.42; −0.19	0.26; −0.26	0.29; −0.28

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

(0.021 g, 5%), in this order. Treatment of the oil **10**/**12** with hexane/AcOEt/MeOH gave pure **10** as yellow needles (0.363 g, 67%) and pure **12** as deep yellow crystals (0.039 g, 6%).

Data of **10***:* M.p. 143–144°. R_f (SiO_2, hexane/AcOEt 2:1) 0.37. UV/VIS (MeCN; see also *Table 3* and *Fig. 3*): max. 193 (sh, 4.40), 213 (sh, 4.34), 252 (4.32), 269 (sh, 4.18), 297 (sh, 3.94), 338 (sh, 3.49), 3.85 (3.04); min. 228 (4.27). IR: 3412*w*, 2994*w*, 2974*w*, 2949*m*, 2918*w*, 2840*w*, 1717vs, 1675*w*, 1643*m*, 1621*w*, 1585*w*, 1548*m*, 1519*w*, 1440*m*, 1382*w*, 1370*w*, 1358*w*, 1342*w*, 1268vs, 1216*m*, 1194*m*, 1157*m*, 1116*w*, 1091*s*, 1072*m*, 1056*m*, 1040*w*, 1027*w*, 1007*w*, 984*w*, 965*w*, 955*w*, 919*w*, 880*w*, 853*w*, 841*w*, 831*w*, 801*w*, 788*w*, 767*m*, 727*w*, 696*w*, 676*w*, 646*w*, 630*w*, 573*w*, 521*w*, 476*w*, 459*w*. ^{1}H-NMR: 7.58 (*dd*, $^3J = 5.8$, $^5J = 0.5$, H–C(3)); 6.30 (*dd*, $^3J = 6.0$, $^4J = 1.3$, H–C(2)); 6.07 (*d*, $^4J = 1.3$, H–C(7)); 3.80 (*s*, MeO–C(8)); 3.74 (*s*, MeOOC–C(4)); 3.70 (*s*, MeOOC–C(5)); 2.05 (*s*, Me–C(1)); 1.96 (*s*, Me–C(10)); 1.94 (*d*, $^4J = 1.3$, Me–C(6)). ^{13}C-NMR: 167.34 (*s*, *C*O–C(5)); 167.10 (*s*, *C*O–C(4)); 155.64 (*s*, C(8)); 142.22 (*s*, C(5a)); 141.35 (*s*, C(1)); 139.07 (*d*, C(3)); 137.19 (*s*, C(6)); 130.69 (*s*, C(4)); 129.18 (*s*, C(10)); 127.01 (*s*, C(10a)); 125.84 (*d*, C(2)); 122.77 (*s*, C(5)); 120.76 (*d*, C(7)); 112.17 (*s*, C(9)); 58.47 (*q*, *Me*O–C(8)); 52.14 (*q*, *Me*OOC–C(4)); 52.08 (*q*, *Me*OOC–C(5)); 23.17 (*q*, *Me*–C(1)); 21.85 (*q*, *Me*–C(6)); 18.66 (*q*, *Me*–C(10)). CI-MS: 441, 439 (21, 23, $[M + NH_4]^+$), 440, 438 (100, 98), 423, 421 (23, 22, $M^{+\cdot}$), 422 (7), 391, 389 (17, 17), 358 (6), 343 (8), 311 (7), 281 (10), 209 (9).

The structure of **10** was finally established by an X-ray crystal-structure analysis (*Table 4*).

Data of **11***:* M.p. 177–178°. R_f (SiO_2, hexane/AcOEt 2:1) 0.46. IR: 3398*w*, 3016*w*, 2950*m*, 2931*w*, 2911*w*, 2845*w*, 2832*w*, 1734vs, 1708vs, 1668*w*, 1649*m*, 1627*w*, 1597*m*, 1569*m*, 1535*m*, 1461*m*, 1434*s*, 1392*m*, 1374*w*, 1345*w*, 1296*m*, 1267vs, 1248vs, 1213*s*, 1197vs, 1175*s*, 1151*s*, 1109*m*, 1089*s*, 1052*s*, 1024*w*, 991*m*, 959*m*, 927*w*, 864*w*, 851*w*, 842*m*, 827*m*, 793*w*, 783*m*, 772*m*, 717*w*, 705*w*, 683*w*, 646*w*, 629*w*, 610*w*, 584*w*, 570*w*, 535*w*, 511*w*, 476*w*, 437*w*. ^{1}H-NMR: 7.55 (*d*, $^3J = 6$, H–C(3)); 6.30 (*d*, $^4J = 1.6$, H–C(7)); 6.29 (*dd*, $^3J = 5.9$, $^4J = 1.3$, H–C(2)); 5.59 (*d*, $^4J = 1.5$, H–C(9)); 4.21, 3.96 (*AB*, $^2J_{AB} = 10.4$, $BrCH_2$–C(6)); 3.70 (*s*, MeOOC–C(4)); 3.67 (*s*, MeOOC–C(5)); 3.62 (*s*, MeO–C(8)); 2.14 (*s*, Me–C(1)); 1.79 (*s*, Me–C(10)). ^{13}C-NMR: 167.44 (*s*, *C*O–C(4)); 167.41 (*s*, *C*O–C(5)); 157.92 (*s*, C(8)); 145.12 (*s*, C(1)); 141.97 (*s*, C(5a)); 140.22 (*d*, C(3)); 134.01 (*s*, C(6)); 130.98 (*s*, C(4)); 130.28 (*s*, C(10)); 128.45 (*d*, C(7)); 126.28 (*d*, C(2)); 124.92 (*s*, C(10a)); 123.88 (*s*, C(5)); 108.44 (*d*, C(9)); 54.70 (*q*, *Me*O–C(8)); 52.06 (*q*, *Me*OOC–C(4), *Me*OOC–C(5)); 34.36 (*t*, Br*C*H_2–C(6)); 24.62 (*q*, *Me*–C(1)), 19.55 (*q*, *Me*–C(10)).

Data of **12***:* M.p. 148–149°. R_f (SiO_2, hexane/AcOEt 2:1) 0.37. IR: 3045*w*, 3000*w*, 2973*w*, 2950*m*, 2920*w*, 2846*w*, 1714vs, 1707vs, 1635*m*, 1615*m*, 1586*m*, 1547*m*, 1502*m*, 1431*s*, 1382*m*, 1341*w*, 1284*s*, 1268vs, 1245*s*, 1229*s*, 1216*m*, 1196*m*, 1162*s*, 1145*m*, 1106*w*, 1087*s*, 1073*m*, 1052*m*, 1030*m*, 987*w*, 971*m*, 945*w*, 911*w*, 896*w*, 874*w*, 860*w*, 828*m*, 807*w*, 788*w*, 766*m*, 732*m*, 709*w*, 696*w*, 681*w*, 637*w*, 593*w*, 576*w*, 515*w*, 495*w*. ^{1}H-NMR: 7.61 (*dd*, $^3J = 6.1$, $^5J = 0.9$, H–C(3)); 6.42 (*s*, H–C(7)); 6.34 (*dd*, $^3J = 6.1$, $^4J = 1.4$, H–C(2)); 4.21, 3.88 (*ABX*, $^2J_{AB} = 10.9$, $^4J_{AX} = {}^4J_{BX} = 0.7$, $BrCH_2$–C(6)); 3.79 (*s*, MeO–C(8)); 3.74 (*s*, MeOOC–C(4)); 3.69 (*s*, MeOOC–C(5)); 2.20 (*d*, $^4J = 1.0$, Me–C(1)); 1.99 (*s*, Me–C(10)). ^{13}C-NMR: 167.10 (*s*, *C*O–C(4)); 166.97 (*s*, *C*O–C(5)); 154.48 (*s*, C(8)); 142.53 (*s*, C(1)); 139.98 (*d*, C(3)); 138.62 (*d*, C(5a)); 137.28 (*s*, C(6)); 130.47 (*s*, C(4)); 130.03 (*s*, C(10)); 128.86 (*s*, C(10a)); 126.56 (*d*, C(2)); 125.72 (*d*, C(7)); 124.47 (*s*, C(5)); 115.73 (*s*, C(9)); 58.67 (*q*, *Me*O–C(8)), 52.25 (*q*, *Me*OOC–C(5)); 52.22 (*q*, *Me*OOC–C(4)), 32.78 (*t*, Br*C*H_2–C(6)), 24.48 (*q*, *Me*–C(1)), 19.06 (*q*, *Me*–C(10)). EI-MS: 502 (12), 500 (24), 422 (44), 405 (13), 390 (100), 375 (22), 361 (20), 348 (37), 340 (23), 325 (20), 309 (25), 281 (57), 266 (43), 251 (24), 235 (16), 178 (23), 165 (30), 157 (92), 151 (27), 129 (20), 106 (20), 91 (67), 75 (28), 44 (23).

2.2. *Attempts to Exchange the 9-Bromo Substituent of* **10** *by an Oxy Group* (see *Scheme 3*). The conditions that we applied gave no results, except for the saponification of the sterically less hindered ester group at C(4) of **10** resulting in the formation of *5-methyl 4-hydrogen 9-bromo-8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**10a**). To a suspension of **10** (0.050 g, 0.119 mmol) in MeOH/H_2O 1:1 (5 ml) was added NaOH (0.024 g, 0.60 mmol). The mixture was stirred at r.t. (24 h). The usual workup and FC (SiO_2, AcOEt/hexane 3:1) gave **10a** (0.035 g, 72%). Fine yellow needles. M.p. 182° (dec.)[7]). R_f (SiO_2, AcOEt) 0.30. IR: 3078*w*, 2988*w*, 2950*m*, 2925*w*, 2909*w*, 2851*w*, 2760–2390 (br.), 1718vs, 1636*m*, 1614*w*, 1584*w*, 1547*m*, 1514*w*, 1436*m*, 1376*m*, 1359*m*, 1344*m*, 1274vs, 1259vs, 1221*s*, 1210*s*, 1197*s*, 1165*m*, 1115*m*, 1084*m*, 1073*m*, 1053*m*, 1025*w*, 1009*w*, 970*m*, 953*w*, 939*w*, 923*w*, 857*w*, 832*w*, 794*m*, 734*m*, 702*w*, 688*w*, 663*w*, 628*w*, 590*w*, 570*w*, 543*w*, 523*w*, 464*w*, 439*w*. ^{1}H-NMR: 7.67 (*dd*, $^3J = 6.0$, $^5J = 0.8$,

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[7]) The cyclic anhydride was formed by loss of MeOH (*cf.* [11b]).

0.9, H–C(3)); 6.33 (*dd*, $^3J = 5.9$, $^4J = 1.4$, H–C(2)); 6.08 (*d*, $^4J = 1.4$, H–C(7)); 3.80 (*s*, MeO–C(8)), 3.70 (*s*, MeOOC–C(5)); 2.06 (*s*, Me–C(1)); 1.97 (*s*, Me–C(10)); 1.95 (*d*, $^4J = 1.3$, Me–C(6)). ^{13}C-NMR: 171.38 (*s*, HOO*C*–C(4)); 167.22 (*s*, *C*O–C(5)); 155.77 (*s*, C(8)); 142.79 (*s*, C(5a)); 142.51 (*s*, C(1)); 140.80 (*d*, C(3)); 137.11 (*s*, C(6)); 129.98 (*s*, C(4)); 129.49 (*s*, C(10)); 126.85 (*s*, C(10a)); 125.88 (*d*, C(2)); 122.51 (*s*, C(5)); 121.01 (*d*, C(7)); 112.23 (*s*, C(9)); 58.61 (*q*, *Me*O–C(8)); 52.26 (*q*, *Me*OOC–C(5)); 23.34 (*q*, *Me*–C(1)); 21.83 (*q*, *Me*–C(6)); 18.74 (*q*, *Me*–C(10)). CI-MS: 426, 424 (20, 20, $[M + NH_3]^+$), 409, 407 (6, 6, M^+), 394, 392 (100, 97), 377, 375 (44, 40), 359 (6), 314 (11), 297 (15).

3. *Introduction of an O-Functionality at C(9) of* **6**. 3.1. *Dimethyl 8,9-Dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate*[4]) (**13**). To the dark yellow soln. of **6** (0.100 g, 0.305 mmol) in DMF (3 ml) were added dry NaI (0.069 g, 0.467 mmol) and then Me_3SiCl (0.6 µl, 0.47 mmol). The mixture was stirred for 5 d at r.t. Thereafter, the mixture was poured on ice and extracted with Et_2O (3×). The combined Et_2O phase was washed with aq. sat. $Na_2S_2O_3$ soln. and brine, dried ($MgSO_4$), and concentrated, and the residue subjected to FC (SiO_2, hexane/AcOEt 3:1): **6** (0.014 g, 14%), followed by a yellow oil which slowly crystallized from AcOEt/hexane to give **13** (0.077 g, 80%). Yellow prisms. M.p. 151–153°. R_f (SiO_2, hexane/AcOEt 2:1) 0.32. UV/VIS (MeCN): max. 195 (sh, 4.34), 223 (sh, 4.05), 261 (4.27), 276 (sh, 4.19), 299 (sh, 3.90), 335 (sh, 3.44), 390 (sh, 2.90); min. 229 (4.04). IR: 3393*w*, 3289*w*, 3020*w*, 3009*w*, 2980*w*, 2953*m*, 2908*w*, 2879*w*, 2849*w*, 1728v*s*, 1706v*s*, 1655*s*, 1610*m*, 1600*w*, 1576*w*, 1520*w*, 1437*s*, 1394*w*, 1378*m*, 1342*w*, 1274v*s*, 1242*s*, 1211*m*, 1198*m*, 1187*m*, 1155*m*, 1137*m*, 1114*w*, 1092*m*, 1054*s*, 988*w*, 971*m*, 962*w*, 944*w*, 929*w*, 911*w*, 874*w*, 861*m*, 839*w*, 822*w*, 800*w*, 781*m*, 772*m*, 724*w*, 707*w*, 663*w*, 629*w*, 504*w*, 450*w*. ^{1}H-NMR: 7.57 (*dd*, $^3J = 6.2$, $^5J = 0.8$, H–C(3)); 6.30 (*dd*, $^3J = 6.2$, $^4J = 1.4$, H–C(2)); 5.95 (*t*, $^4J = 1.4$, 1.5, H–C(7)); 3.77 (*s*, MeOOC–C(5)); 3.76 (*s*, MeOOC–C(4)); 3.66 (*d*, $^2J = 13.1$, H–C(9)); 2.85 (*dd*, $^2J = 13.7$, $^4J = 1.8$, H–C(9)); 2.09 (*d*, $^4J = 1.0$, Me–C(1)); 1.92 (*d*, $^4J = 1.3$, Me–C(6)); 1.77 (*d*, $^4J = 0.5$, Me–C(10)). ^{13}C-NMR: 196.30 (*s*, C(8)); 168.02 (*s*, *C*O–C(5)); 166.98 (*s*, *C*O–C(4)); 153.33 (*s*, C(6)); 145.14 (*s*, C(1)); 141.66 (*s*, C(5a)); 138.45 (*d*, C(3)); 135.74 (*s*, C(10a)); 131.99 (*d*, C(7)); 129.70 (*s*, C(4)); 129.33 (*s*, C(10)); 127.48 (*s*, C(5)); 123.29 (*d*, C(2)); 52.64 (*q*, *Me*OOC–C(5)); 52.29 (*q*, *Me*OOC–C(4)); 50.07 (*t*, C(9)); 24.81 (*q*, *Me*–C(6)); 23.40 (*q*, *Me*–C(1)); 19.02 (*q*, *Me*–C(10)). EI-MS: 328 (40, $M^{+\bullet}$), 313 (15), 296 (35, $[M - MeOH]^{+\bullet}$), 281 (63, $[M - (MeOH + Me]^+$), 269 (100, $[M - (MeO + CO)]^+$), 253 (34), 237 (78), 231 (50), 209 (62), 195 (26), 181 (34), 165 (62), 152 (37), 141 (19), 115 (20), 89 (6), 77 (7), 59 (11), 43 (9). Anal. for $C_{19}H_{20}O_5$ (328.37): C 69.50, H 6.14; found: C 69.10, H 5.88.

The structure of **13** was finally established by an X-ray crystal-structure analysis (*Table 4* and *Fig. 1*).

3.2. *Acetyloxylation of* **13**. To a soln. of **13** (0.250 g, 0.761 mmol) in benzene (20 ml) under N_2, $Pb(AcO)_4$[8]) (0.480 g, 0.914 mmol) was added (yellow soln. → brownish). The mixture was heated under reflux for 3 h. After cooling, the benzene soln. was washed with brine, aq. sat. $NaHCO_3$ soln., and then again brine, dried (Na_2SO_4), and concentrated and the residue subjected to FC (SiO_2, hexane/AcOEt 3:1), which gave, after crystallization from hexane/AcOEt/Et_2O, *dimethyl 9-(acetyloxy)-8,9-dihydro-1,6,10-trimethyl-8-oxoheptalene-4,5-dicarboxylate*[4]) (**14**; 0.208 g, 71%). Pale greenish yellow tablets. M.p. 186–188°. R_f (SiO_2, hexane/AcOEt 1:1) 0.47. UV/VIS (MeCN): max. 195 (sh, 4.33), 221 (sh, 4.01), 266 (4.29), 273 (sh, 4.27), 300 (sh, 3.96), 338 (sh, 3.44), 383 (sh, 3.00); min. 229 (3.98). IR: 3405*w*, 3348*w*, 2986*w*, 2955*m*, 2911*w*, 2852*w*, 1756v*s*, 1729*s*, 1714v*s*, 1686v*s*, 1603*m*, 1578*w*, 1525*w*, 1440*s*, 1377*m*, 1343*w*, 1287v*s*, 1256v*s*, 1227v*s*, 1174*m*, 1143*m*, 1113*m*, 1088*s*, 1053*s*, 1029*m*, 992*w*, 970*w*, 945*w*, 934*w*, 912*w*, 863*w*, 857*w*, 802*w*, 789*m*, 771*m*, 745*w*, 716*w*, 685*w*, 667*w*, 646*w*, 626*w*, 597*w*, 562*w*, 536*w*, 518*w*, 476*w*, 452*w*. ^{1}H-NMR: 7.62 (*dd*, $^3J = 6.2$, $^5J = 0.9$, H–C(3)); 6.37 (*dd*, $^3J = 6.2$, $^4J = 1.4$, H–C(7)); 6.07 (*d*, $^4J = 1.3$, H–C(2)); 6.02 (*d*, $^4J = 1.1$, H–C(9)); 3.80 (*s*, MeOOC–C(5)); 3.76 (*s*, MeOOC–C(4)); 2.19 (*s*, AcO–C(9)); 2.09 (*t*, $^4J \approx 1.0$, Me–C(1)); 1.94 (*d*, $^4J = 1.3$, Me–C(6)); 1.73 (*d*, $^4J = 1.1$, Me–C(10)). ^{13}C-NMR: 190.13 (*s*, C(8)); 169.08 (*s*, Me*C*OO–C(9)); 167.73 (*s*, *C*O–C(5)); 166.64 (*s*, *C*O–C(4)); 152.69 (*s*, C(6)); 143.77 (*s*, C(1)); 138.57 (*d*, C(3)); 138.54 (*s*, C(5a)); 134.35 (*s*, C(10)); 130.47 (*d*, C(7)); 129.87 (*s*, C(4)); 129.39 (*s*, C(10a)); 128.61 (*d*, C(5)); 123.85 (*d*, C(2)); 77.94 (*d*, C(9)); 52.82 (*q*, *Me*OOC–C(5)); 52.37 (*q*, *Me*OOC–C(4)); 24.77 (*q*, *Me*–C(6)); 23.14 (*q*, *Me*–C(1)); 20.58 (*q*, *Me*COO–C(9)); 12.59 (*q*, *Me*–C(10)). CI-MS (CI): 405 (24), 404 (100, $[M + NH_4]^+$), 372 (11), 347 (8), 346 (39), 329 (15). Anal. calc. for $C_{21}H_{22}O_7$ (386.41): C 65.28, H 5.74; C 65.08, H 5.81.

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[8]) Contained 15% AcOH.

The relative (9*R**,*P**)-configuration of **14** was confirmed by an X-ray crystal-structure analysis (*Table 4*, *Fig. 2*).

3.3. O-*Methylation of* **14**. 3.3.1. *Dimethyl 7-Acetyloxy-8-methoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate* (**15′**) *and Dimethyl 9-(Acetyloxy)-8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**15**). To a suspension of dry and finely powdered K_2CO_3 (0.028 g, 0.20 mmol) in dry acetone (1 ml) under N_2, **14** (0.050 g, 0.129 mmol) was added, followed by $1.68 \cdot 10^{-3}$ M DMS in dry acetone (1 ml). The yellow mixture was stirred for 30 h at 50°. After usual workup, the residue was purified by FC (SiO_2, hexane/AcOEt 3:1): **15′** (0.013 g, 24%) as orange prisms, followed by **15** (0.035 g, 65%), as yellow tablets.

Data of **15**: M.p. 131–132°. R_f (SiO_2, hexane/AcOEt 1:1) 0.46. UV/VIS (MeCN, see also *Table 3* and *Fig. 3*): max. 190 (sh, 4.81), 212 (4.38), 240 (4.29), 268 (4.24), 327 (sh, 3.56), 387 (sh, 297); min. 202 (4.35), 231 (4.29), 260 (4.24). IR: 3400*w*, 3003*w*, 2983*w*, 2950*m*, 2910*w*, 2844*w*, 1760*s*, 1713v*s*, 1670*w*, 1645*m*, 1618*w*, 1593*w*, 1563*m*, 1523*w*, 1502*w*, 1438*s*, 1393*w*, 1375*m*, 1363*m*, 1349*w*, 1323*w*, 1297*m*, 1277v*s*, 1258v*s*, 1226*s*, 1210v*s*, 1198*s*, 1159*m*, 1128*s*, 1108*s*, 1095*m*, 1073*s*, 1054*s*, 1030*m*, 1010*m*, 970*m*, 942*w*, 930*w*, 897*m*, 874*w*, 855*w*, 838*w*, 812*w*, 798*w*, 786*m*, 771*m*, 734*w*, 705*w*, 692*w*, 677*w*, 643*w*, 612*w*, 584*w*, 568*w*, 481*w*, 456*w*. ^{1}H-NMR: 7.56 (*dd*, $^3J = 6.0$, $^5J = 0.8$, 0.7, H–C(3)); 6.30 (*dd*, $^3J = 6.0$, $^4J = 1.4$, H–C(2)); 6.17 (*d*, $^4J = 1.4$, H–C(7)); 3.72 (*s*, MeOOC–C(4)); 3.71 (*s*, MeO–C(8)); 3.70 (*s*, MeOOC–C(5)); 2.20 (*s*, MeCOO–C(9)); 2.02 (*s*, Me–C(1)); 1.97 (*d*, $^4J = 1.4$, Me–C(6)); 1.70 (*s*, Me–C(10)). ^{13}C-NMR: 168.60 (*s*, Me*C*OO–C(9)); 167.41 (*s*, *C*O–C(5)); 167.26 (*s*, *C*O–C(4)); 149.65 (*s*, C(8)); 143.05 (*s*, C(5a)); 142.00 (*s*, C(1)); 139.19 (*d*, C(3)); 136.55 (*s*, C(9)); 133.31 (*s*, C(6)); 130.95 (*d*, C(4)); 126.66 (*s*, C(10)); 126.17 (*s*, C(2)); 125.27 (*d*, C(10a)); 122.74 (*d*, C(5)); 120.41 (*d*, C(7)); 58.46 (*q*, *Me*O–C(8)); 52.11 (*q*, *Me*OOC–C(4)); 52.03 (*q*, *Me*OOC–C(5)); 23.18 (*q*, *Me*–C(1)); 21.94 (*q*, *Me*–C(6)); 20.37 (*q*, *Me*COO–C(9)); 13.27 (*q*, *Me*–C(10)). EI-MS: 400 (22, $M^{+\bullet}$), 358 (59), 343 (13), 326 (8), 311 (14), 299 (12), 297 (13), 283 (14), 267 (15), 260 (33), 238 (15), 216 (46), 211 (9), 195 (15), 181 (10), 165 (24), 152 (28), 141 (10), 128 (7), 115 (9), 77 (6), 59 (7), 43 (100). Anal. calc. for $C_{22}H_{24}O_7$ (400.43): C 65.99, H 6.04; found: C 65.90, H 5.79.

Data of **15′**: M.p. 162–163°. R_f (SiO_2, hexane/AcOEt 2:1) 0.37. UV/VIS (MeCN; see also *Table 3*): max. 194 (sh, 4.40), 208 (sh, 4.35), 236 (sh, 4.23), 275 (4.27), 328 (sh, 3.43), 387 (2.78); min. 252 (4.04), 366 (2.75). IR: 3007*w*, 2956*m*, 2919*m*, 2852*w*, 2837*w*, 1759v*s*, 1730v*s*, 1712v*s*, 1631*m*, 1605*m*, 1588*m*, 1565*m*, 1513*w*, 1506*w*, 1494*w*, 1455*m*, 1440*m*, 1400*m*, 1369*m*, 1334*w*, 1281v*s*, 1262v*s*, 1235*s*, 1212v*s*, 1141*s*, 1111*s*, 1095*s*, 1080*s*, 1033*m*, 1014*m*, 971*m*, 947*w*, 932*w*, 899*m*, 849*w*, 828*m*, 805*w*, 793*w*, 783*w*, 752*w*, 743*m*, 717*w*, 683*w*, 665*w*, 635*w*, 597*w*, 577*m*, 533*w*, 501*w*, 476*w*, 462*w*, 420*w*. ^{1}H-NMR: 6.62 (*d*, $^3J = 11.8$, H–C(3)); 6.59 (*d*, $^3J = 11.8$, H–C(4)); 5.51 (*s*, H–C(9)); 3.83 (*s*, MeOOC–C(2)); 3.72 (*s*, MeOOC–C(1)); 3.61 (*s*, MeO–C(8)); 2.24 (*s*, MeCOO–C(7)); 1.85 (*s*, Me–C(6)); 1.84 (*s*, Me–C(5)); 1.74 (*s*, Me–C(10)). ^{13}C-NMR: 168.46 (*s*, Me*C*OO–C(7)); 167.73 (*s*, *C*O–C(2)); 166.82 (*s*, *C*O–C(1)); 154.12 (*s*, C(8)); 139.46 (*s*, C(7)); 138.74 (*d*, C(4)); 135.65 (*s*, C(2)); 135.57 (*s*, C(5a)); 131.81 (*s*, C(5)); 131.27 (*s*, C(10)); 130.21 (*s*, C(1)); 126.41 (*d*, C(3)); 125.24 (*s*, C(6)); 122.80 (*s*, C(10a)); 106.89 (*d*, C(9)); 54.94 (*q*, *Me*O–C(8)); 52.55 (*q*, *Me*OOC–C(2)); 52.34 (*q*, *Me*OOC–C(1)); 20.52 (*q*, *Me*COO–C(7)); 18.11 (*q*, *Me*–C(10)); 18.01 (*q*, *Me*–C(5)); 16.75 (*q*, *Me*–C(6)). CI-MS: 419 (10), 418 (39, $[M + NH_4]^+$), 403 (13), 401 (10), 386 (23), 370 (23), 369 (100, $[(M + H) - MeOH]^+$]). Anal. calc. for $C_{22}H_{24}O_7$ (400.43): C 65.99, H 6.04; found: C 65.84, H 5.77.

The structure of **15′** was finally established by an X-ray crystal-structure analysis (*Table 4*).

3.3.2. O-*Methylation of Non-Crystallized* **14**. To a soln. of **13** (1.49 g, 4.50 mmol) in benzene (130 ml), $Pb(AcO)_4$[9]) (2.82 g, 6.00 mmol) was added and the mixture heated under reflux overnight. The usual workup and a short FC gave crude **14** (0.86 g, 49%). This material was added to a stirred suspension of finely powdered dry K_2CO_3 (0.48 g, 3.50 mmol) in acetone (20 ml), DMS (0.45, 360 mmol) was then added with a syringe. The mixture was heated at 50° and stirred at 50° during a weekend. The usual workup procedure gave *O*-methylated raw material (0.36 g, 41%), which showed by HPLC the presence of **15** and **15′** and two further heptalenedicarboxylates, namely *dimethyl 7-(acetyloxy)-8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**17**) and *dimethyl 9-(acetyloxy)-8-methoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate* (**17′**). All four heptalenedicarboxylates were finally separated by HPLC (*Spherisorb CN* (3 μ), 4 × 125 mm column, hexane/(CH_2Cl_2 + 0.5% MeOH 9:1), flow rate 0.8 ml/min): *cf. Scheme 7*.

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[9]) Content of AcOH was 5%.

Data of **15**: See *3.3.1*. ^{1}H-NMR (C_6D_6): 7.66 (*dd*, $^3J = 5.9$, $^5J = 0.8$, H–C(3)); 5.96 (*d*-like, $^4J = 1.4$, H–C(7)); 5.86 (*dd*, $^3J = 5.9$, $^4J = 1.4$, H–C(2)); 3.43 (*s*, MeOOC–C(4)); 3.39 (*s*, MeOOC–C(5)); 3.27 (*s*, MeO–C(8)); 1.88 (*d*-like, $J = 1.3$, Me–C(1)); 1.85 (*s*, MeCOO–C(9)); 1.72 (br. *s*, Me–C(6)); 1.69 (*s*, Me–C(10)).

Data of **15′**: See *3.3.1*. ^{1}H-NMR (C_6D_6): 6.79 (*d*, $^3J = 11.8$, H–C(3)); 6.29 (*d*, $^3J = 11.8$, H–C(4)); 5.31 (*s*, H–C(9)); 3.47 (*s*, MeOOC–C(2)); 3.41 (*s*, MeOOC–C(1)); 3.03 (*s*, MeO–C(8)); 1.90 (*s*, Me–C(5)); 1.83 (*s*, MeCOO–C(7)); 1.78 (*s*, Me–C(6)); 1.68 (*s*, Me–C(10)).

Data of **17**: UV/VIS: *Table 3*. ^{1}H-NMR (C_6D_6): 7.66 (*dd*, $^3J = 5.8$, $^5J = 0.9$, H–C(3)); 6.09 (*d*-like, J(H–C(9), Me–C(6)) ≈ 0.6, H–C(9)); 5.83 (*dd*, $^3J = 5.8$, $^4J = 1.4$, H–C(2)); 3.44 (*s*, MeOOC–C(4)); 3.35 (*s*, MeOOC–C(5)); 3.16 (*s*, MeO–C(8)); 1.86 (*d*-like, $^4J = 1.4$, Me–C(1)); 1.83 (*s*, MeCOO–C(7)); 1.67 (*s*, Me–C(10)); 1.64 (*d*-like, Me–C(6)).

Data of **17′**: UV/VIS: *Table 3*. ^{1}H-NMR (C_6D_6): 6.73 (*d*, $^3J = 11.8$, H–C(3)); 6.32 (*d*, $^3J = 11.8$, H–C(4)); 6.00 (br. *s*, H–C(7)); 3.44 (*s*, MeOOC–C(2)); 3.38 (*s*, MeOOC–C(1)); 3.36 (*s*, MeO–C(8)); 2.01 (*s*, Me–C(5)); 1.75 (*s*, MeCOO–C(9)); 1.73 (*s*, Me–C(6)); 1.70 (*s*, Me–C(10)).

3.4. *Base-Catalyzed Benzylation of* **15**. MeONa (0.009 g, 0.167 mmol) was added to dry DMF (2 ml), followed by **15** (0.050 g, 0.125 mmol) (→ dark violet). The soln. was stirred for 5 h at r.t., and then it was cooled to −21°. BnBr (21 µl, 0.175 mmol) was added and stirring continued for 18 h, whereby the soln. slowly warmed up to r.t. The now brownish yellow soln. was poured on to ice. After the usual workup, the residue was subjected to FC (SiO_2, hexane/AcOEt 3:1): *dimethyl 7-(benzyloxy)-8-methoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate* (**20′**) as yellow oil (0.018 mg, 32%), *dimethyl 9-(benzyloxy)-8-methoxy-1,6,10-trimethylheptalene-4,5-dicarboxylate* (**20**) as yellow oil (0.009 g, 16%), **15′** (0.008 g, 16%), and the starting material **15** (0.013 g, 26%), in this order. It was not tried to crystallize the two new heptalenedicarboxylates **20** and **20′** due to the small amounts of available material.

Data of **20**: R_f (SiO_2, hexane/AcOEt 3:1) 0.32. IR ($CHCl_3$): 3527*w*, 3026*m*, 3015*m*, 3012*m*, 2952*m*, 2841*w*, 1720v*s*, 1648*w*, 1603*m*, 1565*m*, 1497*w*, 1455*m*, 1436*m*, 1398*w*, 1376*m*, 1263v*s*, 1223*w*, 1217*w*, 1199*m*, 1163*m*, 1140*m*, 1093*m*, 1077*m*, 1055*m*, 1026*m*, 1009*w*, 986*m*, 947*w*, 910*m*, 859*w*, 845*w*, 823*w*, 806*w*. ^{1}H-NMR (500 MHz): 7.59 (*dd*, $^3J = 5.9$, $^5J = 0.9$, H–C(3)); 7.30–7.25 (*m*, Ph); 6.31 (*dd*, $^3J = 5.9$, $^4J = 1.4$, H–C(2)); 6.03 (*d*, $^4J = 1.4$, H–C(7)); 4.75, 4.45 (*AB*, $^2J_{AB} = 11.4$, PhCH_2O–C(9)); 3.75 (*s*, MeOOC–C(4)); 3.72 (*s*, MeOOC–C(5)); 3.34 (*s*, MeO–C(8)); 2.04 (*s*, Me–C(1)); 1.93 (*d*, $^4J = 1.4$, Me–C(6)); 1.79 (*s*, Me–C(10)). ^{13}C-NMR (125 MHz): 167.53 (*s*, *C*O–C(5)); 167.42 (*s*, *C*O–C(4)); 149.91 (*s*, C(8)); 144.53 (*s*, C(9)); 143.90 (*s*, C(5a)); 141.99 (*s*, C(10a)); 139.25 (*d*, C(3)); 137.18 (*s*, 1 C of Ph), 132.82 (*s*, C(6)); 130.81 (*s*, C(4)); 129.02 (*d*, 2 C of Ph); 128.13 (*d*, 2 C of Ph; *s*, C(10)); 127.82 (*d*, 1 C of Ph); 126.94 (*s*, C(1)); 125.73 (*s*, C(2)); 122.34 (*s*, C(5); *d*, C(7)); 74.71 (*t*, Ph*C*H_2O–C(9)); 58.62 (*q*, *Me*O–C(8)); 52.14 (*q*, *Me*OOC–C(4)); 52.00 (*q*, *Me*OOC–C(5)); 23.06 (*q*, *Me*–C(1)); 21.80 (*q*, *Me*–C(6)); 13.73 (*q*, *Me*–C(10)). CI-MS: 466 (100, $[M + NH_4]^+$), 449 (40, $[M + H]^+$), 417 (60, $[(M + H) - MeOH]^+$), 403 (6), 385 (13), 369 (37), 357 (15), 346 (47), 343 (12), 329 (18), 311 (7), 297 (20).

Data of **20′**: R_f (SiO_2, hexane/AcOEt 3:1) 0.45. IR ($CHCl_3$): 3025*m*, 3019*m*, 1723*s*, 1603*m*, 1567*m*, 1497*m*, 1456*m*, 1435*m*, 1324*m*, 1264*m*, 1231*m*, 1200*m*, 1177*m*, 1159*m*, 1123*m*, 1097*m*, 980*m*, 946*m*, 909*s*, 843*m*, 822*m*. ^{1}H-NMR (500 MHz): 7.37–7.27 (*m*, Ph); 6.60 (*d*, $^3J = 11.8$, H–C(3)); 6.57 (*d*, $^3J = 11.8$, H–C(4)); 5.56 (*s*, H–C(9)); 4.83, 4.64 (*AB*, $^2J_{AB} = 11.4$, PhCH_2O–C(7)); 3.82 (*s*, MeOOC–C(2)); 3.70 (*s*, MeOOC–C(1)); 3.69 (*s*, MeO–C(8)); 1.82 (*s*, Me–C(6)); 1.77 (*s*, Me–C(5)); 1.74 (*s*, Me–C(10)). ^{13}C-NMR (150 MHz): 168.04 (*s*, *C*O–C(2)); 167.09 (*s*, *C*O–C(1)); 156.03 (*s*, C(8)); 146.41 (*s*, C(7)); 139.01 (*d*, C(4)); 137.75 (*s*, 1 C of Ph); 137.54 (*s*, C(5a)); 135.04 (*s*, C(2)); 131.19 (*s*, C(5)); 130.80 (*s*, C(10a)); 130.20 (*s*, C(1)); 128.77 (*d*, 2 C of Ph); 128.49 (*d*, 2 C of Ph); 128.10 (*d*, 1 C of Ph); 126.01 (*d*, C(3)); 124.65 (*s*, C(10)); 123.77 (*s*, C(6)); 108.24 (*d*, C(9)); 73.58 (*t*, Ph*C*H_2O–C(7)); 55.07 (*q*, *Me*O–C(8)); 52.80 (*q*, *Me*OOC–C(2)); 52.54 (*q*, *Me*OOC–C(1)); 18.28 (*q*, *Me*–C(10)); 18.18 (*q*, *Me*–C(5)); 16.50 (*q*, *Me*–C(6)). CI-MS: 466 (38, $[M + NH_4]^+$), 449 (87, $[M + H]^+$), 434 (7), 417 (100, $[(M + H) - MeOH]^+$), 392 (8), 385 (24), 357 (16), 313 (6), 299 (13), 282 (12), 256 (8), 218 (12), 206 (12).

4. *9-Methoxy-6,7,11-trimethylheptaleno[1,2-c]furan-8-ol and -9-ol* (**23** and **24**, resp.). To the original mixture of the heptalenedicarboxylates **15**/**15′** and **17**/**17′** (0.460 g, 1.10 mmol; see *3.3.2*) in THF (25 ml) cooled with an ice bath, 1M DIBAH in hexane (7.5 ml, 7.50 mmol) was added dropwise under stirring. Stirring was continued for 30 min at 0° and then for 30 min at r.t. Then H_2O (200 ml) was added slowly and dropwise. The mixture was then extracted with AcOEt (2×), the org. layer washed with H_2O, dried

($MgSO_4$), and concentrated, and the residue subjected to FC (SiO_2, Et_2O/hexane 5:1): mixture of the four hydroxy-heptalenedimethanols **21**/**21′** and **22**/**22′** (0.234 g, 67%), which was not further characterized (see *Scheme 10* and text).

IBX (0.113 g, 0.40 mmol)[10]) was added to DMSO (2 ml) and the mixture stirred for 2 h at r.t. To the thus formed clear and colorless soln. was added the above dimethanol mixture (0.039 g, 0.10 mmol), dissolved in acetone (0.4 ml). Stirring was continued for 5 h at r.t. Then, Et_2O (2 ml) and 1M TsOH in acetone (0.1 ml) were added. The mixture was poured into H_2O and extracted with Et_2O (2×). The Et_2O extract was washed with H_2O, dried, and concentrated and the residual glutinous yellow material subjected to CC (SiO_2, ^{t}BuOMe/hexane 3:2): **23** (0.013 g, 35%) and **23**/**24**. Both fractions were not very stable.

Data of **23**: ^{1}H-NMR (C_6D_6): 7.14 (*d*, ^4J = 1.6, H–C(1)); 6.99 (*dd*, ^4J = 1.6, ^5J = 0.7, H–C(3)); 6.30 (*d*, ^3J = 11.5, H–C(4)); 5.72 (*d*, ^3J = 11.5, H–C(5)); 5.45 (*s*, H–C(10)); 3.13 (*s*, MeO–C(9)); 2.01 (*s*, Me–C(6)); 1.62 (*s*, Me–C(7)); 1.46 (*s*, Me–C(11)).

5. *8,9-Dimethoxy-6,7,11-trimethylheptaleno[1,2-c]furan* (**27**). 5.1. *Dimethyl 7,8-Dimethoxy-5,6,10-trimethylheptalene-1,2-dicarboxylate* (**25′**). In analogy to *3.4*, a mixture of the four (acetyloxy)heptalenedicarboxylates **15**/**15′** and **17**/**17′** (0.102 g, 0.255 mmol) was added to a soln. of MeONa (0.032 g, 0.59 mmol) in DMF (6 ml). After 6 h stirring of the violet soln. at r.t., it was cooled to −25° and MeI (31 µl, 0.50 mmol) was added. Stirring was continued for 24 h, whereby the temp. slowly rose to r.t. The usual workup and CC (SiO_2, hexane/AcOEt 3:1) gave **25′** (0.022 g, 23%) as a pure fraction. ^{1}H-NMR (C_6D_6): 6.80 (*d*, ^3J = 11.8, H–C(3)); 6.30 (*d*, ^3J = 11.8, H–C(4)); 5.40 (*s*, H–C(9)); 3.47 (*s*, MeOOC–C(2)); 3.45 (*s*, MeO–C(7)); 3.41 (*s*, MeOOC–C(1)); 3.17 (*s*, MeO–C(8)); 2.08 (*s*, Me–C(10)); 1.81 (*s*, Me–C(6)); 1.55 (*s*, Me–C(5)).

5.2. *7,8-Dimethoxy-5,6,10-trimethylheptalene-1,2-dimethanol* (**26′**). To **25′** (0.0095 g, 0.03 mmol) in THF (2 ml) cooled with an ice bath, 1M DIBAH, in hexane (0.2 ml, 0.20 mmol) was added with a syringe, (→ reddish soln.). After 25 min, the ice bath was removed and stirring continued for 20 min. H_2O (2 ml) was added to the mixture, which was extracted thereafter with AcOEt. The extracts were washed with H_2O, dried ($MgSO_4$), and concentrated. Purification of the residue was performed with prep. TLC (SiO_2, hexane/AcOEt 2:1): **26′** (0.0073 g, 90%). Yellow solid. ^{1}H-NMR (C_6D_6): 6.31, 6.30 (superimp. *AB*, H–C(3), H–C(4)); 5.48 (*s*, H–C(9)); 4.44, 4.05 (*AB*, $^2J_{AB}$ = 12.5, HOCH_2–C(1)); 4.18, 4.00 (*AB*, $^2J_{AB}$ = 11.9, HOCH_2–C(2)); 3.54 (*s*, MeO–C(7)); 3.24 (*s*, MeO–C(8)); 2.10 (*s*, Me–C(6)); 1.66 (*s*, Me–C(10)); 1.65 (*s*, Me–C(5)).

5.3. *Formation of* **27**. IBX (0.0095 g, 0.03 mmol) was added to DMSO (0.3 ml). The soln. was stirred for 2 h at r.t. To the colorless soln. was added **26′** (0.0043 g, 0.01 mmol). The mixture was stirred for 4.5 h at r.t., and was then poured into H_2O (1 ml). The product was extracted with Et_2O (2×), the Et_2O phase washed with H_2O, dried (Na_2SO_4), and concentrated, and the residual glutinous yellow mass, purified by prep. TLC (SiO_2, hexane/AcOEt 1:1): **27** (*ca.* 2 mg, 68%). Yellow solid. ^{1}H-NMR (C_6D_6): 7.11 (*d*-like, H–C(1)); 6.94 (*dd*-like, H–C(3)); 6.42 (*d*, ^3J = 11.4, H–C(4)); 5.86 (*d*, ^3J = 11.5, H–C(5)); 5.54 (*s*, H–C(10)); 3.53 (*s*, MeO–C(8)); 3.25 (*s*, MeO–C(9)); 2.00 (*s*, Me–C(6)); 1.81 (*s*, Me–C(7)); 1.66 (*s*, Me–C(11)).

6. *X-Ray Crystal-Structure Determinations of Compounds* **6**, **10**, **13**, **14**, *and* **15′**[11]). All measurements were conducted with a *Nonius KappaCCD* area detector diffractometer [24][25], 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 4*, while views of the molecules of **13** and **14** are shown in *Figs. 1* and *2*. The intensities were corrected for *Lorentz* and polarization effects. A numerical

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[10]) Following an established procedure [23], a soln. of *Oxone*® (18.17 g, 29.10 mmol; *Aldrich*) in H_2O (65 ml) was added to 2-iodobenzoic acid (5.40 g, 28.10 mmol). The mixture was heated under stirring at 70° for 3 h. After cooling by an ice bath, stirring was continued for additional 1.5 h. The formed suspension was filtered through a glass frit and the filter cake washed with acetone to yield IBX as colorless powder (3.92 g, 65%).

[11]) CCDC-820692 – 820696 contain the supplementary crystallographic data for this article. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre via* www.ccdc.cam.ac.uk/data_request/cif.

absorption correction [26] was applied in the case of **13**. Each structure was solved by direct methods with SIR92 [27], which revealed the positions of all non-H-atoms. The non-H-atoms were refined anisotropically. All of the 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 **13**). The refinement of each structure was carried out on F (F^2 for **13**) by full-matrix least-squares procedures. A correction for secondary extinction was applied, except for **6**. For **6**, **10**, **13**, and **14**, five, two, four, and four reflections, resp., whose intensities were considered to be extreme outliers, were omitted from the final refinement.

For **13**, one significant peak of residual electron density remained (1.42 e Å^{-3}). The peak is *ca.* 1.52 Å from C(7) and is in approximately the correct position (distance and angles) that might be expected if it represented a C-atom bonded to C(7). Attempts were made to include this peak in the model by defining it as the C-atom of a Me group and the refinement could be carried out successfully. The site occupation factor of the Me group refined to *ca.* 0.20 and the C(7)–C bond length remained at 1.52 Å. With the model defined in this way, the *R*-factor decreased by *ca.* 0.01. A similar result was obtained if it is assumed that the group is an OH or an NH_2 group. As the group, if real, exists in only *ca.* 20% of the molecules, it was not possible to locate any of the H-atoms of the group, and the bond length to C(7) is quite imprecise. Therefore, no definitive conclusion can be drawn about what type of substituent this might be, but on the crystallographic evidence alone, the assumption that this residual electron density peak is due to a small amount of a C(7)-substituted compound in the crystal is not entirely unreasonable. Data were collected from two different crystals, and the same feature was observed in both cases. An examination of the diffraction patterns did not reveal any evidence of twinning. In the absence of supporting chemical evidence for a minor by-product, the final refinement was conducted without including this additional unknown group in the model. This leads to a significant peak of residual electron density, slightly higher *R*-factors, and a lower precision of the geometric parameters than for the model where the group was included.

Neutral-atom scattering factors for non-H-atoms were taken from [28a], and the scattering factors for H-atoms were taken from [29]. Anomalous dispersion effects were included in F_c [30]; the values for f' and f'' were those of [28b]. The values of the mass attenuation coefficients are those of [28c]. All calculations were performed with the teXsan crystallographic software package [31] (SHELXL97 [32] for **13**). The crystallographic diagrams were drawn with ORTEPII [33].

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