132. Formation of Cyclic *'ortho'*-Anhydrides of Heptalene-1,2-dicarboxylic Acids

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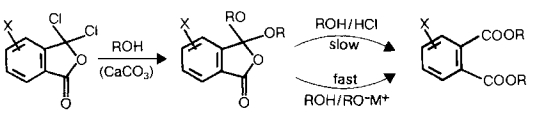
1-(Alkoxycarbonyl)heptalene-2-carboxylic acids as well as 2-(alkoxycarbonyl)heptalene-1-carboxylic acids react with the iminium salt formed from *N,N*-dimethylformamide (DMF) and oxalyl chloride, in the presence of an alcohol, to yield the corresponding cyclic *'ortho'*-anhydrides (ψ-esters; *cf. Schemes 2, 3, 6,* and *8*). When the alkoxy moiety of the acids and the alcohols is different, then diastereoisomeric *'ortho'*-anhydrides are formed due to the non-planarity of the heptalene skeleton. The approach of the alcohol from the β-side is strongly favored *(cf. Scheme 5* and *Table 1)*. This effect can be attributed to the bent topology of the heptalene skeleton which sterically hinders the approach of the nucleophile from the α-side of the postulated intermediates, *i.e.* the charged *O*-alkylated anhydrides of type **19** *(cf. Scheme 6)*. Whereas the *'ortho'*-anhydrides with four substituents in the 'peri'-positions of the heptalene skeleton are configurationally stable up to 100°, the *'ortho'*-anhydrides with only three 'peri'-substituents slowly epimerize at 100° *(cf. Scheme 7)* due to the thermally induced inversion of the configuration of the heptalene skeleton.

1. Introduction. – Cyclic *'ortho'*-anhydrides **2** of 1,2-dicarboxylic acids are known for over more than 70 years [1]. However, the only systematic investigations stem from *Kirpal,* who first characterized unequivocally this class of compounds and showed that 3,3-dichlorophthalides **1**, upon standing in alcoholic solutions at room temperature, form the corresponding *'ortho'*-anhydrides **2** [2] [3][3]). These 'asymmetric' phthalic esters, upon further standing in acidic alcoholic solution, are slowly transformed into the well-known symmetric phthalic esters **3**. This transformation instantaneously occurs in alcoholic solution in the presence of catalytic amounts of the corresponding alkoxide *(Scheme 1)*[4])[5]).

Scheme 1



1 X = H, Cl_n, $(MeO)_n$ **2** **3**

[1]) Part of the planned Ph. D. thesis of *R. H. W.*, University of Basel/Switzerland.

[2]) Part of the Ph. D. thesis of *P. B.*, No. 858, University of Fribourg/Switzerland, 1983.

[3]) In older literature *'ortho'*-anhydrides of type **2** are often called *pseudo*-esters (ψ-esters) or asymmetric esters [2–5].

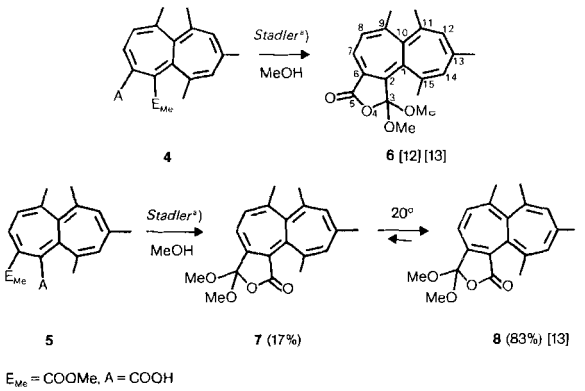
[4]) The existence of 'anhydride-like' ethers of type **2** has been postulated by *Graebe* as early as 1883 [4].

[5]) Acid-sensitive *'ortho'*-anhydrides like **2** (X = H) are only obtained in the presence of powdered $CaCO_3$ [3].

In the meantime, only few reports on *'ortho'*-anhydrides of type **2** and related structures have been published (*cf.* [5–7])[6]. An interesting access to spirocyclic *'ortho'*-anhydrides **2** (RR = C_2 moiety) has been discovered by *Greene* [10] in the course of investigations on the oxidation of olefins by phthaloyl peroxide.

We found that *'ortho'*-anhydrides of type **6** to **8** are formed, when half-esters **4** and **5** of heptalene-1,2-dicarboxylic acids are treated with the iminium salt obtained from DMF and $(COCl)_2$, followed by addition of an alcohol in pyridine according to a procedure described by *Stadler* [11] for a mild esterification of acids *(Scheme 2)*. In the cases investigated so far, the *'ortho'*-anhydrides of type **7** are in a thermal equilibrium with their double-bond-shifted (DBS) isomers **8** [13]. Since we found these transformations to be a new method for the synthesis of new *'ortho'*-anhydrides of 1,2-dicarboxylic acids, we here report on these reactions in detail. Furthermore, the nucleophilic addition of alcohols to heptalenes of type **4** under *Stadler* conditions also allows to characterize the topology of the non-planar, C_2-twisted heptalene skeleton (*cf.* [12] [14–15]) with respect to its reactivity on the α- and β-side.

Scheme 2



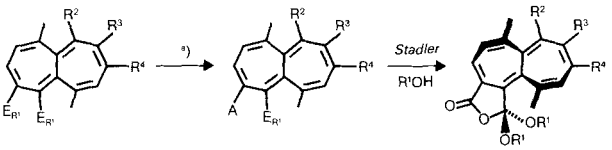
[a]) In this and the following schemes *'Stadler'* means. *1.* Formation of the iminium salt from DMF and $(COCl)_2$ in MeCN at $< 0°$. *2.* Addition of the corresponding half-ester of the heptalene-1,2-dicarboxylic acid at 0 to 10°. *3.* Addition of the corresponding alcohol in MeCN at 0°. Pyridine as a base may be omitted *(cf. Exper. Part)*.

2. Results. – 2.1. *Reaction of 1-(Alkoxycarbonyl)heptalene-2-carboxylic Acids with Alcohols under* Stadler *Conditions.* The acids can easily be obtained from the corresponding diesters by semi-saponification at room temperature (*cf.* [12–14]). Reaction according to *Scheme 3* gives the corresponding cyclic *'ortho'*-anhydrides in good yields. As by-products, small amounts of cyclic 1,2-anhydrides *(cf. Exper. Part)* and, in the case of sterically crowded alcohols, of open-chain 2,2'-anhydrides (*cf.* [12]) can be detected.

Photochemically stable, dark-yellow crystals of the racemic *'ortho'*-anhydrides **6** and **10–16** are obtained from Et_2O/hexane solutions. Dissolved in aprotic solvents, the *'ortho'*-

[6]) Recent investigations on ψ-esters and derivatives have been performed by *Fariña et al.* (*cf.* [8] and earlier lit. cit. therein) and the formation of a five-membered cyclic *'ortho'*-imide has been described [9].

Scheme 3



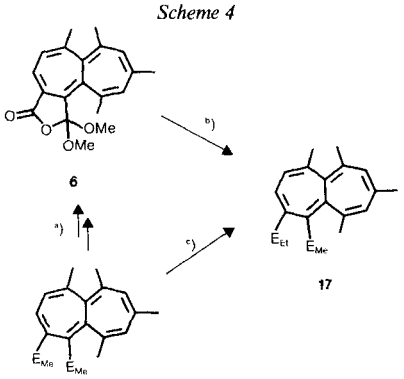
R^1, R^2, R^4 = Me, R^3 = H	**4**	**6** (83%)[b]	[12]
R^1 = Et, R^2, R^4 = Me, R^3 = H	**9**	**10** (46%)	
R^1 = $PhCH_2$, R^2, R^4 = Me, R^3 = H	**11**	**12** (57%)	
R^1, R^2 = Me, R^4 = *t*-Bu, R^3 = H	**13**	**14** (77%)	
R^1 = Me, R^2 = *i*-Pr, R^2, R^4 = H	**15**	**16** (63%)	[13]

[a]) Saponification with KOH in $EtOH/H_2O$ at 20–40° *(cf. Exper. Part)*.
[b]) In brackets, not-optimized yields of pure, crystallized material *(cf. Exper. Part)*.

anhydrides are stable in the dark. Exposure to light photochemically equilibrates them to the corresponding DBS isomers (*cf.* [13]). Day or laboratory light is sufficient to induce this equilibrium process. Thermally induced DBS isomerization is strongly dependent on the nature of R^2. For **16** (R^2 = H), thermal equilibration is observed at room temperature. However, **16** (98.7%; $\Delta G_{303} = -11$ kJ·mol^{-1}) is strongly favored over its DBS isomer (1.3%) (*cf.* [13]). In solution, the *'ortho'*-anhydrides with R^2 = Me are thermally stable up to 80°. Above this temperature, equilibrium slowly starts. For **6**, thermal equilibrium (100°, in tetralin; $\Delta G_{373} = -8.5$ kJ·mol^{-1}) mixture contains 94% of **6** and 6% of its DBS isomer [13]. Similar ΔG values may be expected for the other *'ortho'*-anhydrides with R^2 = Me[7]).

In alcoholic solution and in the presence of sodium alkoxide, the *'ortho'*-anhydride **6** is easily transformed into the mixed diester (*cf.* **17**, *Scheme 4*), which can also be obtained

Scheme 4



[a]) See *Scheme 3*. [b]) 1 mol-equiv. 0.06M EtONa in EtOH, 5 min at 20°. [c]) 1 mol-equiv. 0.06M EtONa in EtOH, 300 min at 40°.

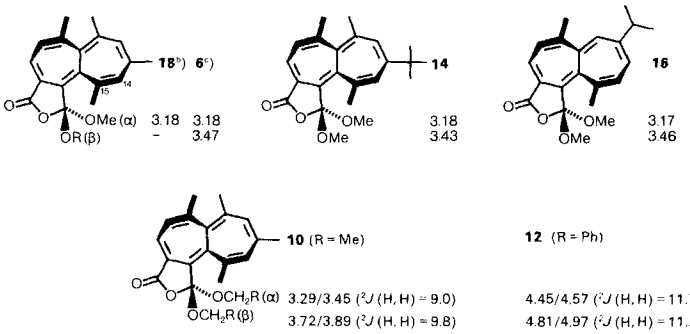
[7]) We have shown earlier that the DBS isomer of **4** *(Scheme 2)* exclusively yields **6** under *Stadler* conditions in the presence of MeOH [13]. Therefore, the DBS isomers of the *'ortho'*-anhydrides of type **6** can only be obtained by photochemical isomerization (*cf.* [13]).

by selective transesterification of the corresponding dialkyl heptalene-1,2-dicarboxylate (*cf.* also [15]). Under acidic conditions, the rearrangement **6**→**17** occurs only sluggishly, whereas the exchange of the alkoxy groups in **6** is fast (*cf.* [13]).

The structure of the *'ortho'*-anhydrides **6** and **10** to **16** follows from the typical $\tilde{\nu}$(C=O) value between 1760 and 1775 cm^{-1} in the IR, which is characteristic for unsaturated γ-lactones as well as for *'ortho'*-anhydrides of type **2** (*cf.* [10])[8]).

In the ^{1}H-NMR spectra ($CDCl_3$, 30°), the two alkoxy groups of the *'ortho'*-anhydrides are anisochronous, which demonstrates the stability of the configuration of the non-planar heptalene skeleton (*cf.* [13]). The stereographic representation of the *'ortho'*-anhydride **18** *(Scheme 5)*, isolated from the reaction of **4** with (±)-1-phenylethanol under *Stadler* conditions [12], clearly shows that the five-membered *'ortho'*-anhydride ring adopts an envelope conformation with the 1-phenylethoxy group at the top in a pseudo-axial position and correspondingly the MeO group in a pseudo-equatorial position *(cf. Fig. 1a)*. The latter position brings the α-MeO group in the shielding region of the C(14)=C(15) bond and allows the unambiguous assignment of the MeO groups in the *'ortho'*-anhydrides **6**, **14**, and **16**. Compared with the α-MeO group, the signal of the pseudo-axial β-MeO group is *ca.* 0.3 ppm at lower field (*cf.* [12] and *Scheme 5*)[9]). This effect is also observed in the *'ortho'*-anhydrides **10** and **12** carrying EtO and $PhCH_2O$ groups at the α- and β-side of the *'ortho'*-anhydride ring. The CH_2 groups at the α-side absorb at significantly higher field as compared to the CH_2 groups on the β-side. Interestingly, ^2J(H, H) of the diastereotopic H's of the CH_2 group in α- and β-position are slightly different. This effect is small, but relevant, and can also be used for the assignment of the relative configuration of alkoxy groups (see below).

Scheme 5[a])

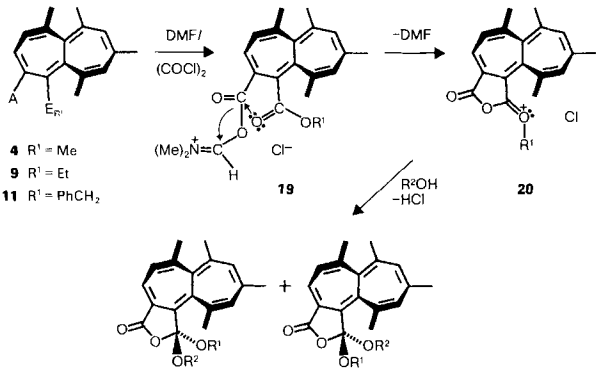


[a]) Only the (*P*)-configuration of the heptalene skeleton is shown; δ in ppm, J in Hz.
[b]) R = (*S*)-PhCH(Me).
[c]) R = Me.

[8]) For the angularly less strained heptalene *'ortho'*-anhydrides (R^2 = H, *Scheme 3*) such as **16**, $\tilde{\nu}$(C=O) is at lower frequency (about 1762 cm^{-1}). The position of the C=C bonds in the heptalene skeleton does not seem to influence the C=O absorption in the corresponding *'ortho'*-anhydrides (*cf. Exper. Part* and [13]).

[9]) That the high-field position of the signal of the pseudo-equatorial MeO group is indeed due to its orientation relative to the C(14)=C(15) bond can also be seen from the lower-field position of the corresponding signal in the spectrum of the DBS isomers. The difference is *ca.* 0.1 ppm (*cf.* [13] and *Exper. Part*).

Scheme 6[a])



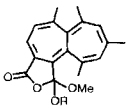
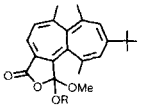
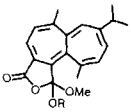
for α-attack	for β-attack		for α-attack	for β-attack
R^1 = Et, R^2 = Me	R^1 = Me, R^2 = Et	**21**	**22** R^1 = Me, R^2 = Et	R^1 = Et, R^2 = Me
R^1 = $PhCH_2$, R^2 = Me	R^1 = Me, R^2 = $PhCH_2$	**23**	**24** R^1 = Me, R^2 = $PhCH_2$	R^1 = $PhCH_2$, R^1 = Me
	R^1 = Me, R^2 = $[^2H_3]$Me	$[^2H_3]$-**6β**	$[^2H_3]$-**6α** R^1 = Me, R^2 = $[^2H_3]$Me	

[a]) For *'α'- and/or 'β'-attack*, see the text.

The unambiguous assignment of the α- and β-alkoxy groups by ^{1}H-NMR correlation based on an X-ray structure analysis of **18** (*cf.* [12]) allows a stereochemical analysis of the nucleophilic attack of alcohols on the activated heptalene-2-carboxylic acids under *Stadler* conditions (*cf. Scheme 6* and [13]). We assume that *O*-alkylated anhydrides such as **20** are intermediates. Otherwise, the electrophilic reactivity of the alkoxycarbonyl group at C(1) in the activated acid **19** would be hardly comprehensive. A β-attack of R^2OH on **20** derived from **4** would lead to the *'ortho'*-anhydrides **21**, **23**, or $[^2H_3]$-**6β** with the entered alkoxy group in the pseudo-axial position. Correspondingly, the α-attack would yield the diastereoisomeric *'ortho'*-anhydrides **22**, **24**, and $[^2H_3]$-**6α**.

The substitution pattern of the alkoxy groups can be reversed, if we exchange the sequence of R^1 and R^2; *e.g.* starting with the acid **9** or **11** the reaction under β-attack of **20** by MeOH would give **22** (R^1 = Et, R^2 = Me) or **24** (R^1 = $PhCH_2$, R^2 = Me). The results of the reaction of the 1-(Methoxycarbonyl)heptalene-2-carboxylic acids **4**, **13**, and **15** (*cf. Schemes 3* and *6*) with various alcohols ROH ($R \neq Me$) under *Stadler* conditions are collected in *Table 1*. The ratio of β/α attack could easily be determined by a ^{1}H-NMR measurement of the crude reaction mixtures (*cf. Tables 1* and *2*). A distinct dependence of the β/α ratio with respect to the structure of heptalene-2-carboxylic acid (horizontal ratios) as well as with respect to the degree of substitution at C(1) of the alcohol (vertical ratios) can be recognized. The degree of substitution at C(2) of the alcohol has no significant influence on the β/α ratio. The ratios are definitely kinetically controlled. The configuration of the heptalene skeleton is stable up to 100° for the tetramethyl- and (*tert*-butyl)-trimethyl-substituted *'ortho'*-anhydrides (*cf.* [12] [13]). However, optically active dimethyl 7-isopropyl-5,10-dimethylheptalene-1,2-dicarboxylate racemizes slowly at room temperature [12]. Indeed, when **27** and **28** as well as **29** and **30** were heated at 100° in $C_2D_2Cl_4$, they were slowly interconverted within 24–30 h to a *ca.* 1:1 mixture of both diastereoisomers (*Scheme 7*). The slowness of epimerization ($\tau_{1/2}(100°) \approx$ 4–6.5 h) clearly shows that the β/α ratios for the i-Pr-substituted *'ortho'*-anhydrides, are also kinetically controlled.

Table 1. *Formation of Diastereoisomeric* 'ortho'-*Anhydrides from 1-(Methoxycarbonyl)heptalene-2-carboxylic Acids* **4**, **13**, *and* **15**, *and Alcohols* (ROH) *under* Stadler *Conditions*[a])

ROH	Formed *'ortho'*-Anhydrides ([%])											
												
[$^2H_3$]MeOH	**6β**[b])	(88)	**6α**	(12)	**14β**	(94)	**14α**	(6)	**16β**	(84)	**16α**	(16)
EtOH	**21**[c])	(88)	**22**[c])	(12)	**25**	(98)	**26**	(2)	**27**	(80)	**28**	(20)
$PhCH_2OH$	**23**	(92)	**24**[d])	(8)	–[e])		–		**29**	(90)	**30**	(10)
i-BuOH	**31**	(92)	**32**	(8)	–		–		–		–	
Neopentyl alcohol	**33**	(92)	**34**	(8)	**35**	(100)[f])	–		–		–	
2-PhEtOH	**36**	(93)	**37**	(7)	–		–		–		–	
i-PrOH	**38**	(97)	**39**	(3)	–		–		**40**	(95)	**41**	(5)

[a]) See *Schemes 2, 3,* and *6*. β/α ratios were determined in the crude reaction mixture according to the integration of the MeO signals at *ca.* 3.18 ppm (β-isomer) and 3.46 ppm (α-isomer) in the ^{1}H-NMR spectrum. See also *Scheme 5* and *Table 2*.

[b]) [$^2H_3$]-**6β** *etc.*

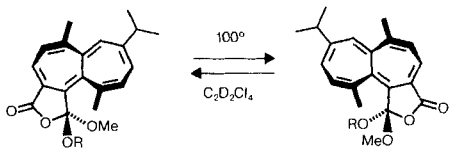
[c]) The reaction of the 1-(ethoxycarbonyl)heptalene-2-carboxylic acid **9** *(cf. Scheme 6)* with MeOH yielded 12% **21** (α-attack) and 88% **22** (β-attack).

[d]) The reaction of the 1-(benzyloxycarbonyl)heptalene-2-carboxylic acid **11** *(cf. Scheme 6)* with MeOH yielded **24** as main product (β-attack). Amount of **23** was not determined.

[e]) Reaction not performed.

[f]) Only the β-isomer was isolated in 61% yield.

Scheme 7



R = Et **27** (50%)[a]) $\tau_{1/2} \approx 230$ min **28** (50%)

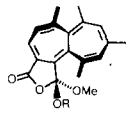
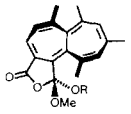
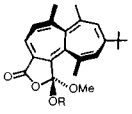
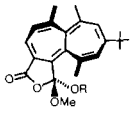
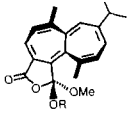
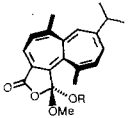
R = $PhCH_2$ **29** (51%)[a]) $\tau_{1/2} \approx 400$ min **30** (49%)

[a]) Percentages after 24 and 30 h, respectively, at 100°. The isomerizations were performed with the racemates.

2.2. *Reaction of 2-(Methoxycarbonyl)heptalene-1-carboxylic Acids with Alcohols under* Stadler *Conditions.* Reaction of heptalene-1,2-dicarboxylic 1,2-anhydrides with MeOH in the presence of a slightly more than equimolar amount of MeONa at 18–20° predominantly yields corresponding acids (*cf.* [12] [13] and *Scheme 8*), which can be purified by crystallization. Under *Stadler* conditions, heptalene-1-carboxylic acids **5** and **44**, in the presence of MeOH, form the corresponding *'ortho'*-anhydrides of type **7** (*cf. Scheme 2* and [13]), which are structurally isomeric with those discussed under *2.1*. As already mentioned, these new compounds are constitutionally labile and undergo already a rapid DBS even at room temperature (*cf. Scheme 2* and [13]). We could not assign signals of the MeO groups in the ^{1}H-NMR spectra (**7**: 3.30 [3.32] and 3.41 [3.44] ppm[10]); **8**:

[10]) In square brackets, chemical shifts of corresponding i-Pr-substituted *'ortho'*-anhydrides (*cf.* [13]).

Table 2. *Chemical Shifts and Geminal Coupling Constants* (^2J(H,H)) *of the Alkoxy Groups of the Diastereoisomeric* 'ortho'-*Anhydrides*[a])

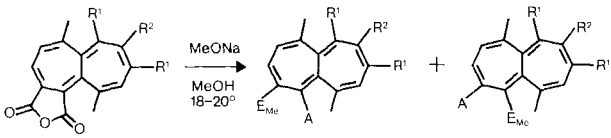
												
R	MeO	$R'CH_2O$	MeO	$R'CH_2O$	MeO	$R'CH_2O$	MeO	$R'CH_2O$	MeO	$R'CH_2O$	MeO	$R'CH_2O$
$[^2H_3]$Me	3.18	–	3.47	–	3.18	–	3.43	–	3.17	–	3.46	–
Et	3.16	3.75/3.90 (9.8)	3.46	3.30/3.47 (9.0)	3.16	3.69/3.85 (9.7)	3.39	b)	3.16	3.76/3.89 (9.8)	3.45	3.35/3.42 (9)
$PhCH_2$	3.23	4.77/4.90 (11.2)	3.52	4.40/4.53 (11.6)	–	–	–	–	3.22	4.77/4.89 (11.2)	3.53	4.36/4.61 (10.8)
i-Bu	3.16	3.50/3.54 (9.5)	3.45	~ 3.50/3.55 (9.2)	–	–	–	–	–	–	–	–
Neopentyl	3.17 [3.05]c)	3.41 [3.64/3.68] (9.0)	3.44	b)	3.17 [3.10]	3.35 [3.61/3.64] (9.1)	–	–	–	–	–	–
β-PhEt	3.15	3.93/4.05	3.41	–	–	–	–	–	–	–	–	–

a) ^{1}H-NMR chemical shifts in ppm ($CDCl_3$) and ^2J(H,H) in Hz in parentheses; see also *Exper. Part.*

b) Chemical shift and ^2J(H,H) could not be determined.

c) Chemical shifts in C_6D_6 in square brackets, ^2J(H,H) in parentheses.

Scheme 8



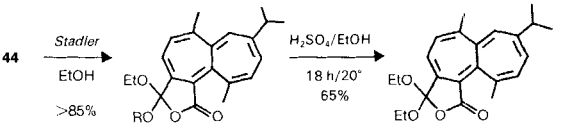
42 R^1 = Me, R^2 = H
43 R^1 = H, R^2 = i-Pr

5 (80%)
44 (89%)

4 (20%)
15 (11%)

3.432 [3.45] and 3.56 [3.49] ppm) to the pro-(*R*)- and pro-(*S*) positions of these groups. Furthermore, the reaction of **44** with EtOH under *Stadler* conditions led to the formation of a mixture of the corresponding ethoxymethoxy- and diethoxy-*'ortho'*-anhydride **45** and **46**, respectively *(cf. Scheme 9)*, in good yield. This observation indicates that the alkoxy groups in these *'ortho'*-anhydrides can easily be exchanged under acidic conditions. Indeed, when the above mentioned mixture of *'ortho'*-anhydrides was dissolved in H_2SO_4/EtOH (0.015M), it was completely transformed into the diethoxy-*'ortho'*-anhydride **46** *(Scheme 9)*. Obviously, dialkoxy-*'ortho'*-anhydrides such as **46** can generally be obtained from heptalene-1-carboxylic acids such as **5** and **44**.

Scheme 9[a])



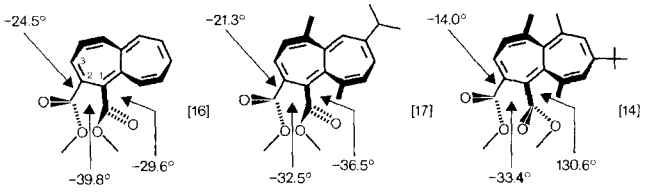
R = Me, Et **45/46**

46

[a]) Only one DBS isomer of **45** and **46** is shown. The ^{1}H-NMR spectrum of **46** in $CDCl_3$ at −50° indicated a mixture of 16% of **46** and 84% of its DBS isomer **47** *(cf. Exper. Part)*.

3. Discussion. – 3.1. *Formation of the* 'ortho'-*Anhydrides.* We postulated that charged *O*-alkylated anhydrides such as **20** *(cf. Scheme 6)* might be the crucial intermediates in the *'ortho'*-anhydride formation (*cf.* also [13]). In principle, a concerted attack of the alcohol upon the ester C=O group at C(1) in the activated intermediate **19** and ring closure would directly lead to the *'ortho'*-anhydrides. The structural setup in the 1-(alkoxycarbonyl)heptalene-2-carboxylic acids seems favorable for such a concerted reaction. *Scheme 10* shows the relevant torsion angles between the two ester C=O groups and the corresponding C(10a)=C(1) and C(2)=C(3) bonds as well as the torsion angle between

Scheme 10[a])



[a]) Torsion angles refering to the (*P*)-configuration of the heptalene skeletons.

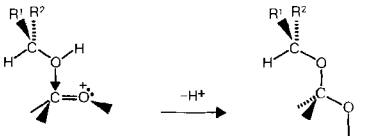
the two carbonyl-C-atoms including the C(1)–C(2) bond of the heptalene skeleton as established by the X-ray structure analysis of dimethyl heptalene-1,2-dicarboxylates.

According to *Scheme 10,* the ester C=O group at C(2) adopts in all three cases a slightly staggered s-*cis*-conformation with respect to the C(2)=C(3) bond. In contrast, the ester C=O group at C(1) seems to populate more variable conformations and seems to be forced into a s-*trans*-arrangement with respect to the C(10a)=C(1) bond in the case of the angularly most strained *t*-Bu-substituted heptalene. In an arrangement presented in *Scheme 10* (3rd example), acyloxyformamidinium intermediates of type **19** *(cf. Scheme 6)* would fulfill the stereochemical conditions for a concerted formation of *'ortho'*-anhydrides. Such an arrangement would, indeed, lead to an incorporation of the nucleophile from the *β*-side of the formed *'ortho'*-anhydride ring. However, it can be seen from *Scheme 10* or from molecular models that for any torsion angle between 90 and 180° of the molecular segment O=C–C(1), C(10a) – which would allow an accompanying ring closure – the trajectory for a nucleophilic attack (*cf.* [18]) at the ester C=O group at C(1) is severely hindered by the Me group at C(10). The observed trend, namely an enhanced *β*-attack selectivity with increased substitution at C(1) of the alcohols *(cf. Table 1)*, is in plain contradiction with this observation concerning the formation of the *'ortho'*-anhydrides. On the other hand, a structural constellation, as a consequence, as found in the *t*-Bu-substituted heptalene would be ideal for a cyclization of **19** to give *O*-alkylated 1,2-anhydrides of type **20** *(Scheme 6)*. Since one can expect a nearly unrestricted conformational freedom with respect to rotations around the C(1)–(C=O) and C(2)–(C=O) bond, there will always be an ideal constellation of both carboxyl moieties for ring closure to an anhydride structure, as long as there is a torsion angle in the O=C–C(1), C(2)–C=O segment imposed by the heptalene skeleton (*cf.* 30 to 40° in *Scheme 10*)[11]). These views are supported by our finding that the DBS isomer of **4** 5-(methoxycarbonyl)-1,6,8,10-tetramethylheptalene-4-carboxylic acid does not yield the expected *'ortho'*-anhydride, but exclusively its DBS isomer **6** under the usual *Stadler* conditions (*cf. Scheme 8* in [13]). Furthermore, we found that neither methyl hydrogenphthalate, nor hydrogenmaleate, nor hydrogensuccinate could be transformed into the corresponding *'ortho'*-anhydrides under *Stadler* conditions in the presence of MeOH. Instead, the normal dimethyl esters were obtained, while the maleate exclusively yielded dimethyl fumarate. So, there is good evidence that charged *O*-alkylated 1,2-anhydrides of type **20** *(cf. Scheme 6)* are intermediates in *'ortho'*-anhydride formation. Heptalene-1,2-dicarboxylic anhydrides may serve as structural models for these reactive intermediates. *Fig. 1b* shows the dotted *van der Waals* surface of 8,10-dimethylheptalene-1,2-dicarboxylic anhydride (**48**) in a stereoprojection modelled according to the X-ray-structure analysis of the i-Pr-substituted anhydride **43** *(Scheme 8)* [13]. The presentation clearly visualizes that the *β*-side of the molecule is suitable for a nucleophilic attack at the C=O group at C(1). The Me group at C(10) cannot hinder the approach of a nucleophile, because the trajectory of the nucleophile will be bent to the upper left part above the molecule[12]). Evidently, the *α*-side of the

[11]) According to molecular models, such 1,2-dicarboxylic structures should be governed by conformational directionality (*cf.* [19]) in a way that their torsional motions are not independent. These motions may take place like that of windscreen-wipers, thus, favoring 'in-out' (with respect to both C=O groups; *cf. Scheme 10*) constellations well-disposed for cyclization.

[12]) Nevertheless, the Me group at C(10) seems to exert a certain repulsion on the approaching nucleophiles, because the anhydrides **42** and **43** are mainly attacked by nucleophiles at the CO group at C(2) *(cf. Scheme 8)*.

Scheme 11



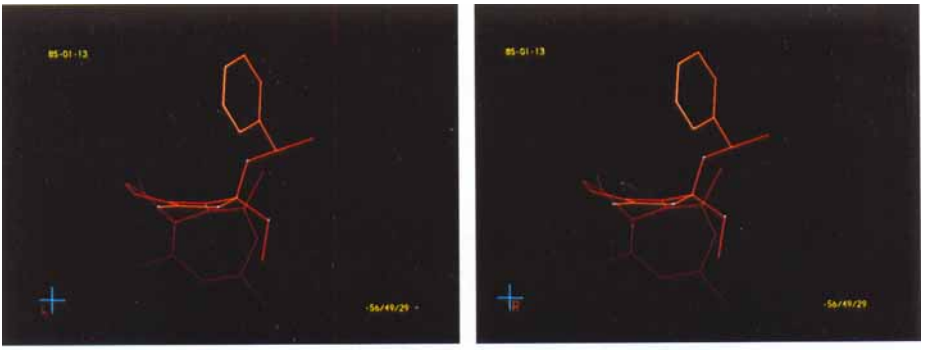
molecule is partially shielded by the bent heptalene skeleton, especially by the C(9)=C(10) bond and by the substituents at C(8). The C(9), C(10) segment is situated in a distance of about 3 Å to the assumed trajectory on the α-side of the heptalene-1,2-dicarboxylic anhydride. When the substituent at C(8) is a *t*-Bu group, then one of its Me groups always overlaps with the trajectory of the nucleophile at the α-side of the C=O group at C(1), in a distance of about 5 Å with respect to the C-atom of the C=O group. If the usual model for the nucleophilic approach of an alcohol to an activated C=O group *(cf. Scheme 11)* is assumed, then the observed β/α ratios in *Table 1* can well be understood. The best stereochemical probe is [$^2H_3$]MeOH, because the products should not be subjected to any diastereoisomeric discrimination. The observed amounts of product stemming from β-attack evidently decrease with increasing bulkiness of the substituent at C(8) in the heptalene-2-carboxylic acids: H (**15**) 16%, Me (**4**) 12%, and *t*-Bu (**13**) 6%. On the other hand, there is an abrupt change in the amount of products arising from β-attack, when there are two substituents ≠ H at C(1) of the alcohols (*cf.* **4** + RCH_2OH (R = Me, Ph, i-Pr, *t*-Bu, $PhCH_2$)→12 to 7% β-attack; however, **4** + R_2CHOH→3% β-attack as well as **15** + EtOH→20% β-attack and **15** + i-PrOH→5% β-attack!). These results are in perfect agreement with the discussed topology of the heptalene skeleton.

However, there might be a further intramolecular factor which would influence the β/α ratio of the *'ortho'*-anhydride formation and which might cooperate with the intermolecular 'steric' factors so far discussed. When a nucleophile approaches the C=O group at C(1) in our model anhydride **48** the C–O bond will start to bend (*cf.* [18]). This means that the O of the C=O group will move away from the Me–C(10) segment (β-attack) or towards it (α-attack). This is shown in a hypothetical model with two O-atoms attached to the C at C(1) in *Fig. 1c*. It clearly shows that the α-attack is unfavorable with respect to the induced bending mode of the C–O bond in opposite direction and towards the Me group at C(10). The final situation after the more favorable β-attack is visualized in *Fig. 1d* which shows the superposition of the structure of **48** with

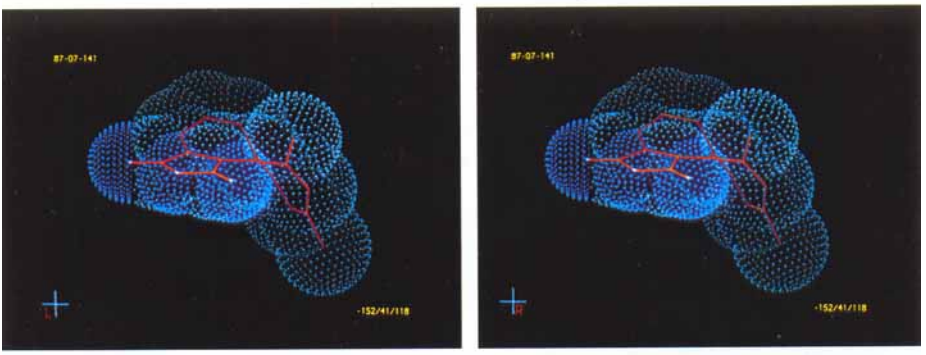
→

Fig. 1. a) *Stereoscopic projection of the X-ray-diffraction structure of racemic 3-methoxy-9,11,13,15-tetramethyl-3-(1'-phenylethoxy)-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**18**) *in the* (P,3R,1'S)*-configuration, showing the envelope conformation of the five-membered* 'ortho'*-anhydride ring and the pseudo-axial position of the β-oriented 1'-phenylethoxy group.* b) *Stereoscopic projection with dotted* van der Waals *surface of the structure of 6,8-dimethylheptalene-1,2-dicarboxylic anhydride* (**48**)*, derived from the X-ray-diffraction structure of racemic 7-isopropyl-5,10-dimethylheptalene-1,2-dicarboxylic anhydride* (**43**). Heptalene skeleton is shown in the (*P*)-configuration. c) *Hypothetical* 'ortho'*-anhydride model derived from* **48** *by computer-generated dioxy-group addition without modification of the conformation of the anhydride ring.* Heptalene skeleton is shown in the (*P*)-configuration with relevant interatomic distances. d) *Superposition of the structures of* **48** (yellow) *and* **18** (red) (*cf. Fig. 1a* and *b*) *showing the conformational changes in the five-membered ring segments with respect to the nearly unchanged heptalene skeletons.*

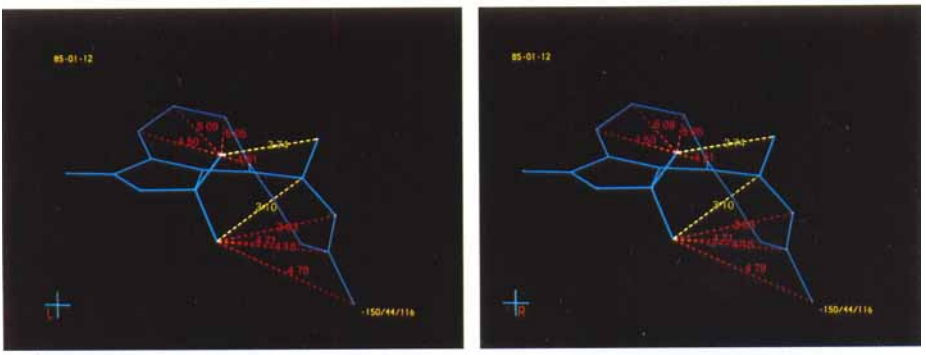
a)


85-01-13
85-01-13

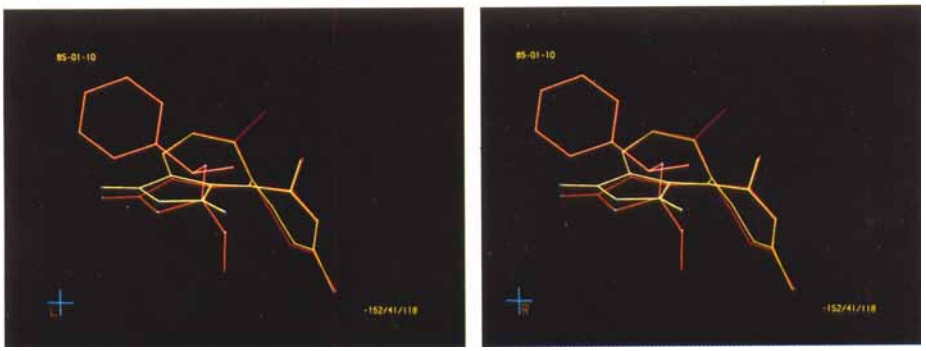
b)


87-07-141
87-07-141

c)


85-01-12
85-01-12

d)

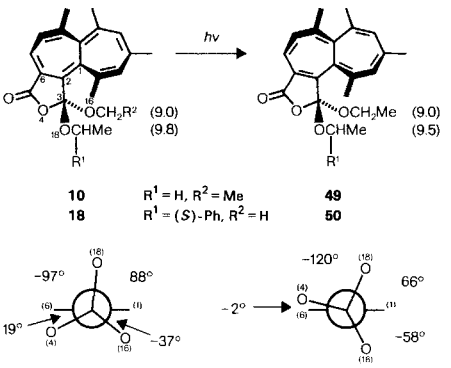

85-01-10
85-01-10

the structure of **18** (*cf. Scheme 5* and *Fig. 1a*). The superposition documents that the main changes are indeed in the five-membered ring and that the entering β-substituent is forced to the pseudo-axial position.

A dominance of the intramolecular steric repulsions over the intermolecular steric interactions should lead to β/α ratios which are largely insensitive to changes in the bulkiness of the attacking nucleophile. However, this is not observed[13]).

3.2. *Variation of the Geminal Coupling Constants of the Alkoxy Groups in the* 'ortho'-*Anhydrides.* It is well established that $^2J(H,H)$ of the CH_2 groups varies appreciably with changes of substituents and of the H–C–H bond angle (*cf.* [20]). σ-Acceptor substituents at the CH_2 group lead to an increase in $^2J(H,H)$, *i.e.* make it more positive. The same effect is observed when the s-character in the C–H bonds increases, *i.e.* when the H–C–H bond angle increases. Our measurements (*cf. Scheme 5* and *Table 2*) show that $^2J(H,H)$ of β-alkoxy groups in the pseudo-axial position is by *ca.* 0.8 Hz more negative than $^2J(H,H)$ of the corresponding α-alkoxy moiety in the pseudo-equatorial position. Two factors may influence $^2J(H,H)$, namely steric compression of the H–C–H bond angle of the β-alkoxy group due to the proximity of the Me group at C(10) and an anomeric effect in the *'ortho'*-anhydrides. The steric compression should slightly reduce the H–C–H bond angle and, therefore, the s-character in corresponding C–H bonds. This would lead to a more negative $^2J(H,H)$ in the pseudo-axial alkoxy group. However, the anomeric effect would act in the same direction, since the interaction between a lone-pair at the anhydride O-atom and the antibonding orbital of the pseudo-axial C–O bond will lead to a reduction of the electronegativity of the O-atom in pseudo-axial position in comparison to the O-atom in pseudo-equatorial positon[14]).

Scheme 12[a])



[a]) In parentheses $^2J(H,H)$ of the EtO groups. The torsion angles refer to the C(2)–C(3) bond in the (*P*)-configurated heptalenes. The X-ray-structure analysis of the dimethoxy-*'ortho'*-anhydride **6** (see *Exper. Part*) confirms the torsion angles given for **18**, *i.e.* the heavier 1-phenylethyl group in β-position at C(3) does not significantly influence the intrinsic torsion angles of the *'ortho'*-anhydride structure.

[13]) So far, we were not able to synthesize configurationally stable 1-(alkoxycarbonyl)heptalene-2-carboxylic acids without any substituent at C(10) and would, therefore, allow to differentiate more clearly the intra- and intermolecular factors.

[14]) According to the X-ray diffraction structure of **18**, the pseudo-equatorial MeO group occupies a conformation which prevents an anomeric contribution from the pseudo-equatorial O-atom. For further examples of the influence of the anomeric effect on *J*, see [21].

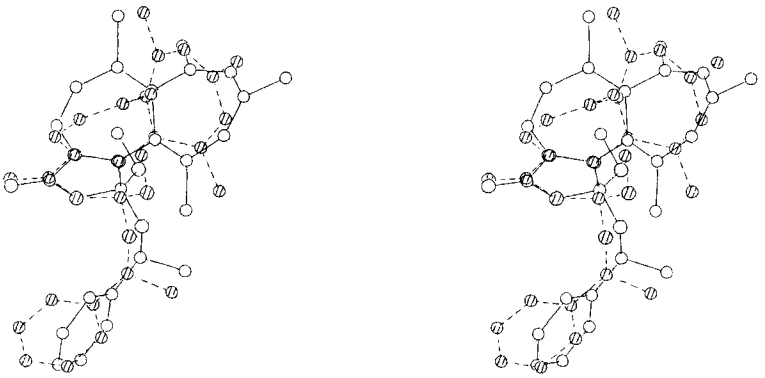


Fig. 2. *Stereographic presentation of the ideal superposition of racemic 3-methoxy-9,11,13,15-tetramethyl-3-(1'-phenylethoxy)-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14- and -2(6),7,9,11,13,15-hexaen-5-one* (**18** and **50**, respectively) *in their (*P,3R,1'S*)-configuration* (**18**: straight line, **50**: dotted line). Optimum superposition with respect to the molecular segment C(2), O(4), C(5), C(6)[15].

Can we differentiate between these two possible effects? Irradiation of the diethoxy-*'ortho'*-anhydride **10** leads to its DBS isomer **49** *(Scheme 12)*, whose β-alkoxy group exhibits a slightly more positive ^2J(H,H) than the *'ortho'*-anhydride **10**. The X-ray analyses of the related *'ortho'*-anhydrides **18** and **50** (*cf. Scheme 12* and *Fig. 2*) [12] [13] show that the DBS mainly changes the conformation of the five-membered ring. The distinct envelope conformation in **18** is flattened to a nearly planar pentagon structure in **50**. This can be recognized from the torsion angles around the C(2)–C(3) bond in **18** and **50** *(cf. Scheme 12)*. This means that in **49**, there is no preferred position of the two alkoxy groups at C(3) with respect to the ring O-atom and, therefore, an anomeric effect should vanish. On the other hand, *Fig. 2* shows that in **18** and **50** the β-substituent is in nearly the *same* spatial relation to the Me group at C(10). The slightly more positive ^2J(H,H) for the β-EtO group in **49** ($\Delta(^2J(H,H) \approx 0.3$ Hz) indicates that the contribution of a possible anomeric effect in **10** and related *'ortho'*-anhydrides (*cf. Scheme 5* and *Table 2*) cannot be more than a third of both discussed effects, and it cannot amount to more than 3% of ^2J(H,H).

We thank our colleagues in the physics department of the Central Research Units of *F. Hoffmann-La Roche & Co. AG*, Basel, for IR, NMR, and MS as well as for elemental analyses. Low-temperature ^{1}H-NMR measurements were kindly performed by Dr. *T.A. Jenny*, Institut de chimie organique de l'Université, CH-1700 Fribourg. *H.-J.H.* especially thanks PD Dr. *K. Müller, F. Hoffmann-La Roche & Co. AG*, Basel, for molecular-modeling and for stimulating discussions. We gratefully acknowledge partial support of this work by the *Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung*, and *R.H.W.* and *P.B.* express their gratitude to the personnel department of *F. Hoffmann-La Roche & Co. AG*, Basel, for scholarships.

[15]) The presentation also makes clear the changes of the atomic positions of the heptalene skeleton in space induced by the DBS. It exemplifies why the DBS would not occur in the crystalline state.

Experimental Part

General. See [12–14] [17].

1. Syntheses of the *'ortho'*-Anhydrides (*cf.* [12] [13]). – *General Procedure* (*cf.* [11]). The soln. of DMF in MeCN was kept at 0° under N_2 and $(COCl)_2$ in MeCN added within 2 min under stirring. CO_2 evolved after a short time and the iminium salt precipitated as a thick paste which was kept stirring by dilution with MeCN. After 5 min at 0°, the carboxylic acid was added and the mixture stirred until a clear soln. had been formed. To this soln., the alcohol in MeCN was added dropwise. After 15 min stirring at 0°, the mixture was poured into ice-water and extracted with Et_2O. The Et_2O extracts were washed with sat. $NaHCO_3$ soln. and H_2O. An ^{1}H-NMR was taken from the residue to determine the ratio of diastereoisomeric *'ortho'*-anhydrides and the residue further purified by prep. TLC to remove traces of the starting acid and of the formed cyclic anhydride.

1.1. *3,3-Dimethoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**6**). See [12] [13].

1.2. *(PM,3RS)- and (PM,3SR)-3-Methoxy-3-[$^2H_3$]methoxy-9,11,13,15-tetramethyl-4-oxatricyclo-[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* ([$^2H_3$]-**6β** and [$^2H_3$]-**6α**). DMF (0.48 ml, 6.3 mmol) in MeCN (4 ml) was reacted with $(COCl)_2$ (0.15 ml, 1.8 mmol) in MeCN (2 ml), and acid **4** (0.3 g, 0.96 mmol) [12] was added, followed by [$^2H_3$]MeOH (0.13 ml, 3.3 mmol; > 99.8% ^{2}H) in MeCN (1 ml). The crude product (0.29 g, 92%) was recrystallized from Et_2O/hexane: 0.18 g (56%) of dark yellow crystals. M. p. 171–172°. IR (KBr): 2257, 2191, 2129, 2070 ([$^2H_3$]MeO). ^{1}H-NMR (270 MHz): 3.181 (*s*, 2.64 H, MeO–C(3) of [$^2H_3$]-**6β**; 88%) and 3.465 (*s*, 0.36 H, MeO–C(3) of [$^2H_3$]-**6α**; 12%). Reference for integration: Me–C(9), Me–C(11), Me–C(13), or Me–C(15). MS: 329 (92, $M^{+\cdot}$), 314 (9, $M^{+\cdot}$ – Me$^\cdot$), 297 (46, $M^{+\cdot}$ – MeOH), 294 (47, $M^{+\cdot}$ – [$^2H_3$]MeOH), 289 (10, $M^{+\cdot}$ – $CH_3{\equiv}CH$), 282 (11, $M^{+\cdot}$ – (MeOH + Me$^\cdot$)), 279 (14, $M^{+\cdot}$ – ([$^2H_3$]MeOH + Me$^\cdot$)), 193 (100).

1.3. *(PM,3RS)-3-Ethoxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**21**). DMF (0.3 ml, 3.8 mmol) in MeCN (2 ml) was reacted with $(COCl)_2$ (0.11 ml, 1.3 mmol) in MeCN (1.5 ml), and **4** (0.2 g, 0.64 mmol) [12] was added, followed by EtOH (0.38 ml, 6.5 mol) in MeCN (1 ml). The crude product (^{1}H-NMR: 88% of **21** and 12% of **22** (*cf. 1.9.3*)) was purified by prep. TLC (hexane/Et_2O 2:1) and recrystallized from Et_2O/hexane: **21** (0.154 g, 71%) in orange crystals. M.p. 144–145°. R_f (Et_2O/hexane 1:1) 0.51. UV: Identical with that of **6** [12]. IR (KBr): 1774 (5-ring lactone). ^{1}H-NMR (270 MHz): Identical with that of **6** [12] except for 1.191 (*t*, ^3J = 7.15, β-CH_3CH_2); 3.164 (*s*, α-MeO); 3.751, 3.901 (each *dq*, ^2J = 9.8, β-CH_3CH_2). MS: 340 (64, $M^{+\cdot}$), 309 (14, $M^{+\cdot}$ – MeO$^\cdot$), 308 (26, $M^{+\cdot}$ – MeOH), 295 (25, $M^{+\cdot}$ – EtO$^\cdot$), 294 (40, $M^{+\cdot}$ – EtOH), 193 (100). Anal. calc. for $C_{21}H_{24}O_4$ (340.42): C 74.09, H 7.11; found: C 73.90, H 7.01.

1.4. *(PM,3RS)-3-Isobutoxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**31**). DMF (0.32 ml, 4.2 mmol) in MeCN (3 ml) was reacted with $(COCl)_2$ (0.1 ml, 1.2 mmol) in MeCN (1.5 ml), and **4** (0.2 g, 0.64 mmol) [12] added, followed by i-BuOH (0.16 g, 2.2 mmol) in MeCN (1 ml). The crude product (^{1}H-NMR: 92% of **31** and 8% of **32**) was purified by prep. TLC (hexane/Et_2O 7:3) to yield yellow crystals (0.18 g, 76%) which were recrystallized from Et_2O/hexane. M.p. 135–136°. R_f (hexane/Et_2O 7:3) 0.41. UV: Identical with that of **6** [12]. IR (KBr): 1769 (5-ring lactone). ^{1}H-NMR (250 MHz): Identical with that of **6** except for 0.864, 0.881 (2 *d*, ^3J = 6.7, β-$(CH_3)_2CHCH_2$); 1.815 (*sept.*-like, ^3J = 6.7, β-$(CH_3)_2CHCH_2$); 3.162 (*s*, α-MeO); 3.501, 3.542 (2*dd*, ^2J = 9.5, ^3J = 6.7, β-$(CH_3)_2CHCH_2$). MS: 368 (57, $M^{+\cdot}$), 337 (8, $M^{+\cdot}$ – MeO$^\cdot$), 336 (28, $M^{+\cdot}$ – MeOH), 295 (44, $M^{+\cdot}$ – i-BuO$^\cdot$), 294 (75, $M^{+\cdot}$ – i-BuOH), 193 (100). Anal. calc. for $C_{23}H_{28}O_4$ (368.17): C 74.97, H 7.66; found: C 74.90, H 7.75.

(PM,3SR)-Isomer **32**: characterized by its ^{1}H-NMR signal at 3.45 (*s*, β-MeO).

1.5. *(PM,3RS)-3-Methoxy-9,11,13,15-tetramethyl-3-neopentyloxy-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**33**). The *'ortho'*-anhydride formation was performed with 0.22 g (0.7 mmol) of **4** [12] and 0.2 g (2.2 mmol) of neopentyl alcohol (*cf. 1.4*). The crude product (^{1}H-NMR: 92% of **33** and 8% of **34**) was purified by prep. TLC (hexane/Et_2O 7:3) to yield red-orange crystals (0.22 g, 82%) which were recrystallized from Et_2O/hexane. M.p. 151–152°. R_f (hexane/Et_2O 7:3) 0.43. UV: Identical with that of **6** [12]. IR (KBr): 1768 (5-ring lactone). ^{1}H-NMR (250 MHz): Identical with that of **6** except for 0.868 (*s*, β-$(CH_3)_3CCH_2$); 3.166 (*s*, α-MeO); 3.414 (*s*, β-$(CH_3)_3CCH_2$). ^{1}H-NMR (250 MHz, C_6D_6): 0.840 (*s*, β-$(CH_3)_3CCH_2$); 1.499 (*s*, Me–C(11)); 1.673 (*d*-like *s*, $^4J \approx 0.7$, Me–C(13)); 1.747 (*d*-like *s*, $^4J \approx 1.3$, Me–C(9)); 2.315 (*d*-like *s*, $^4J \approx 1.3$, Me–C(15)); 3.050 (*s*, α-MeO); 3.640, 3.677 (2*d*, ^2J = 9.0, β-$(CH_3)_3CH_2$); 5.864 (br. *s*, H–C(8), H–C(14)); 5.983 (br. *s*, H–C(12)); 7.392 (*d*, ^3J = 6.2, H–C(7)). MS: 382 (46, $M^{+\cdot}$), 351 (4, $M^{+\cdot}$ – MeO$^\cdot$), 350 (16, $M^{+\cdot}$ – MeOH), 295 (51, $M^{+\cdot}$ – $Me_3CCH_2O^\cdot$), 294 (57, $M^{+\cdot}$ – Me_3CCH_2OH), 193 (100). Anal. calc. for $C_{24}H_{30}O_4$ (382.50): C 75.36, H 7.91; found: C 75.56, H 7.97.

(PM,3SR)-Isomer **34**: characterized by its ^{1}H-NMR signal at 3.44 (*s*, β-MeO).

1.6. *(PM,3RS)-3-Benzyloxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**23**). DMF (0.64 ml, 8.4 mmol) in MeCN (6 ml) was reacted with $(COCl)_2$ (0.2 ml, 2.4 mmol) in MeCN (3 ml), and acid **4** (0.4 g, 1.3 mmol) [12] was added, followed by $PhCH_2OH$ (0.47 g, 4.4 mmol) in MeCN (1.5 ml). The crude product (^{1}H-NMR: 92% of **23** and 8% of **24** (*cf. 1.12*)) was purified by prep. TLC to yield orange crystals (0.36 g, 69%) which were recrystallized from Et_2O. M.p. 170–171°. R_f (Et_2O/hexane 1:1) 0.48. UV (cyclohexane): λ_{max} 212 (4.39), 247 (4.26), 268 (4.23), 308 (3.71, sh), 398 (2.98, br.); λ_{min} 228 (4.12), 257 (4.19), 370 (2.91). IR (KBr): 1767 (5-ring lactone). ^{1}H-NMR (270 MHz): Nearly identical with that of **6** and **18** [12] except for 3.228 (*s*, α-MeO); 4.769, 4.904 (2*d*, ^2J = 11.2, β-PhCH_2O); 7.28–7.33 (struct. *s*, β-*Ph*CH_2O). MS: 402 (68, $M^{+\cdot}$), 371 (4, $M^{+\cdot}$ – MeO·), 370 (5, $M^{+\cdot}$ – MeOH), 295 (30, $M^{+\cdot}$ – $PhCH_2O$·), 294 (75, $M^{+\cdot}$ – $PhCH_2OH$), 91 (100, $PhCH_2^+$). Anal. calc. for $C_{26}H_{26}O_4$ (402,49): C 77.49, H 6.51; found: C 77.45, H 6.92.

1.7. *(PM,3RS)-3-Methoxy-9,11,13,15-tetramethyl-3-(2'-phenylethoxy)-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**36**). The *'ortho'*-anhydride formation was performed with 0.2 g (0.64 mmol) of **4** [12] and 0.27 g (2.2 mmol) of β-PhEtOH (*cf. 1.4*). The crude product (^{1}H-NMR: 93% of **36** and 7% of **37**) was purified with prep. TLC (hexane/Et_2O 7:3) to yield yellow crystals (0.19 g, 71%) which was recrystallized from Et_2O 7:3. M.p. 128–129°. R_f (hexane/Et_2O 7:3) 0.34. UV: Nearly identical with that of **6** [12] and **23**. IR (KBr): 1767 (5-ring lactone). ^{1}H-NMR (250 MHz): Nearly identical with that of **6** [12] except for 2.877 (*t*, ^3J = 7.5, β-PhC$H_2$$CH_2$); 3.153 (*s*, α-MeO); 3.927, 4.048 (2*dt*, ^2J = 9.6, ^3J = 7.7, β-PhCH_2CH_2); 7.15–7.31 (several signals, β-*Ph*CH_2CH_2, H–C(7)). MS: 416 (36, $M^{+\cdot}$), 385 (5, $M^{+\cdot}$ – MeO·), 384 (13, $M^{+\cdot}$ – MeOH), 295 (21, $M^{+\cdot}$ – β-PhEtO·), 294 (48, $M^{+\cdot}$ – β-PhEtOH), 105 (100, $PhEt^+$). Anal. calc. for $C_{27}H_{28}O_4$ (416.52): C 77.86, H 6.78; found: C 77.80, H 6.91.

(PM,3SR)-Isomer **37**: characterized by its ^{1}H-NMR signal at 3.41 (*s*, β-MeO).

1.8. *(PM,3RS)-3-Isopropoxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**38**). The *'ortho'*-anhydride formation was performed with 0.3 g (0.96 mmol) of **4** [12] and 0.2 g (3.3 mmol) of i-PrOH (*cf. 1.2*). The crude material (^{1}H-NMR: 97% of **38** and 3% of **39**) was purified by TLC (Et_2O/hexane 1:1) to yield orange crystals (0.22 g, 64%) which were recrystallized from Et_2O. M.p. 131–132°. R_f (hexane/Et_2O 7:3) 0.41. UV: Identical with that of **6** [12]. IR (KBr): 1767 (5-ring lactone). ^{1}H-NMR (270 MHz): Identical with that of **6** except for 1.169 and 1.237 (2*d*, ^3J = 6.3, β-$(CH_3)_2$CH); 3.142 (*s*, α-MeO); 4.542 (*sept.*, ^3J = 6.3, β-$(CH_3)_2$C*H*). MS: 354 (72, $M^{+\cdot}$), 323 (5, $M^{+\cdot}$ – MeO·), 322 (17, $M^{+\cdot}$ – MeOH), 295 (42, $M^{+\cdot}$ – i-PrO·), 294 (70, $M^{+\cdot}$ – i-PrOH), 193 (100). Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.38, H 7.53.

(PM,3SR)-Isomer **39**: characterized by its ^{1}H-NMR signal at 3.50 (*s*, β-MeO).

1.9. *(PM,3SR)-3-Ethoxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**22**). 1.9.1. *Diethyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate.* Diethyl acetylendicarboxylate (ADE, 14.7 g, 86.4 mmol) and 1,4,6,8-tetramethylazulene (9.5 g, 51.6 mmol) [12] were heated in distilled tetralin (115 ml) under N_2 and stirring at 180° during 4.5 h. Tetralin was removed (50°/0.01 Torr) and the residual dark blue oil (31 g) chromatographed (1 kg silica gel, hexane/Et_2O 7:3) to yield, after recrystallization from Et_2O/hexane, pure heptalene-1,2-dicarboxylate (3.5 g, 19%) in yellow crystals and diethyl 4,6,8-trimethylazulene-1,2-dicarboxylate (3.2 g, 19%) in blue-violet crystals.

Diethyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate. M.p. 122–124°. R_f (hexane/Et_2O 7:3) 0.23, R_f (hexane/Et_2O 1:1) 0.38. UV (hexane): λ_{max} 210 (4.40), 235 (4.19, sh), 253 (4.19, sh), 263 (4.22), 318 (3.48, sh), 362 (2.98, br. sh, tailing to longer λ); λ_{min} 242 (4.17). IR (KBr): similar to that of the corresponding dimethyl dicarboxylate [12]; 1738, 1716 (COOR). ^{1}H-NMR (80 MHz): nearly identical with that of the corresponding dimethyl dicarboxylate [12] except for 1.26 (*t*, ^3J = 7.3, 2 CH_3CH_2); 4.17 (*q*, ^3J = 7.3, CH_3CH_2OOC–C(1)); 4.19 (*q*, ^3J = 7.3, CH_3CH_2OOC–C(2)). MS: 354 (100, $M^{+\cdot}$), 329 (12), 325 (11, $M^{+\cdot}$ – Et·), 309 (23, $M^{+\cdot}$ – EtO·), 256 (9, $M^{+\cdot}$ – HC≡CCOOEt), 242 (23, $M^{+\cdot}$ – CH_3C≡CCOOEt), 184 (96, $M^{+\cdot}$ – ADE). Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.41, H 7.32.

Diethyl 4,6,8-Trimethylazulene-1,2-dicarboxylate. M.p. 104–106°. R_f (hexane/Et_2O 7:3) 0.14 R_f (Et_2O) 0.59. UV (hexane): λ_{max} 220 (4.13), 250 (4.50), 293 (4.74), 304 (4.79), 340 (3.79, sh), 351 (3.83), 368 (3.84); λ_{min} 224 (4.12), 267 (3.89), 297 (4.70), 324 (3.62), 362 (3.64). IR and ^{1}H-NMR are similar to those of the dimethyl dicarboxylate [12]. Anal. calc. for $C_{19}H_{22}O_4$ (314.38): C 72.59, H 7.05; found: C 72.37, H 7.17.

1.9.2. *1-(Ethoxycarbonyl)-5,6,8,10-tetramethylheptalene-2-carboxylic Acid* (**9**). The diethyl ester (1.2 g, 3.4 mmol) was suspended in EtOH (21 ml) and a soln. of KOH (4.2 g, 75 mmol) in H_2O (21 ml) added. After 6 h stirring at 40°, the diethyl ester had been consumed (TLC). The mixture was diluted with H_2O, extracted with Et_2O, and acidified with 25% aq. HCl. The precipitated acid **9** was extracted with CH_2Cl_2 and recrystallized from Et_2O: 0.85 g (77%) of pure material in yellow crystals. M.p. 186–188° (dec.). R_f (AcOEt/hexane/AcOH 50:50:1) 0.52. IR (KBr): 1722 (COOR), 1682 (COOH). ^{1}H-NMR (80 MHz): identical with that of **4** [12] except for 1.22 (*t*, ^3J = 7.1, CH_3CH_2); 4.16 (*q*, ^3J = 7.1, CH_3CH_2); HOOC–C(2) not determined. MS: 326 (100, $M^{+\cdot}$), 281 (32, $M^{+\cdot}$ – EtO·), 280 (85, $M^{+\cdot}$ – EtOH). Anal. calc. for $C_{20}H_{22}O_4$ (326.39): C 73.60, H 6.79; found: C 73.28, H 6.79.

1.9.3. *Formation of* **22**. The *'ortho'*-anhydride was formed from 0.4 g (1.23 mmol) of **9** and 0.18 ml (4.3 mmol) of MeOH *(cf. 1.6)*. The oily crude product (^{1}H-NMR: 88% of **22** and 12% of **21** *[cf. 1.3]*) was crystallized from Et_2O/hexane: 0.18 g (44%) of pure **22** in red crystals. M.p. 138–139°. R_f (Et_2O/hexane 1:1) 0.51. UV: identical with that of **6** [12]. IR (KBr): nearly identical with that of **21**; 1767 (5-ring lactone). ^{1}H-NMR (270 MHz): identical with that of **6** [12] and **21** except for 1.160 (*t*, ^3J = 7.06, α-CH_3CH$_2$O); 3.301, 3.468 (2*dq*, ^2J = 9.0, ^3J = 7.06, α-CH$_3$CH_2O); 3.458 (*s*, β-MeO). MS: 340 (86, $M^{+\cdot}$), 309 (25, $M^{+\cdot}$ – MeO·), 308 (36, $M^{+\cdot}$ – MeOH), 295 (23, $M^{+\cdot}$ – EtO·), 294 (54, $M^{+\cdot}$ – EtOH), 193 (100). Anal. calc. for $C_{21}H_{24}O_4$ (340.42): C 74.09, H 7.11; found: C 73.87, H 7.15.

1.10. *(PM)-3,3-Diethoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,10,12,14-hexaen-5-one* (**10**). DMF (0.57 ml, 7.5 mmol) in MeCN (5 ml) was reacted with $(COCl)_2$ (0.18 ml, 2.2 mmol) in MeCN (3 ml) and **9** (0.38 g, 1.16 mmol) added, followed by EtOH (0.24 ml, 4.1 mmol) in MeCN (1 ml). Product **10** (0.40 g, 97%) precipitated during the reaction. It was recrystallized from Et_2O to yield **10** (0.19 g, 46%) in dark yellow crystals. M.p. 161–162°. R_f (hexane/Et_2O 7:3) 0.40, R_f (Et_2O/hexane 1:1) 0.54. UV (cyclohexane): λ_{max} 212 (4.27), 246 (4.27), 268 (4.24), 310 (3.69, sh), 400 (2.96, br. tailing to longer λ); λ_{min} 227 (4.12), 257 (4.20), 370 (2.89). IR (KBr): 1769 (5-ring lactone). ^{1}H-NMR (270 MHz): identical with that of **6** [12] except for 1.147 (*t*, ^3J = 7.04, α-CH_3CH$_2$O); 1.191 (*t*, ^3J = 7.09, β-CH_3CH$_2$O); 3.296, 3.452 (2*dq*, ^2J = 9.0, ^3J = 7.04, α-CH$_3$CH_2O); 3.719, 3.888 (2*dq*, ^2J = 9.8, ^3J = 7.09, β-CH$_3$CH_2O). MS: 354 (86, $M^{+\cdot}$), 309 (57, $M^{+\cdot}$ – EtO·), 308 (100, $M^{+\cdot}$ – EtOH), 193 (89). Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.46, H 7.45.

1.11. *(PM)-3,3-Dibenzyloxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**12**). 1.11.1. *Dibenzyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate*. To $PhCH_2OH$ (5 ml) was added NaH (*ca.* 10 mg of a 80% dispersion in mineral oil) and the mixture stirred until the NaH had been dissolved under evolution of H_2. The corresponding dimethyl ester (0.5 g, 1.5 mmol) [12] was introduced and the mixture heated at 100° during 17 h under Ar and stirring. After cooling, Et_2O was added and the org. phase washed with 0.1N HCl, sat. $NaHCO_3$ soln., and H_2O. $PhCH_2OH$ was removed by distillation (120°/0.01 Torr) and the residue purified by prep. TLC (Et_2O/hexane 1:1) to yield, after crystallization from Et_2O, 0.40 (54%) of the corresponding dibenzyl dicarboxylate in yellow crystals. M.p. 124–125°. R_f (Et_2O/hexane 1:1) 0.57. UV (hexane): λ_{max} 207 (4.62), 263 (4.23), 314 (3.53, sh), 370 (2.91, br. tailing to longer λ); λ_{min} 245 (4.19). IR (KBr): 1712 (COOR). ^{1}H-NMR (250 MHz): nearly identical with that of the corresponding dimethyl ester [12] except for 4.917, 4.948 (2*d*, ^2J = 12.7, PhCH_2OOC–C(2)); 5.022, 5.091 (2*d*, ^2J = 12.5, PhCH_2OOC–C(1)); 7.25–7.35 (several signals, *Ph*CH$_2$OOC–C(1), *Ph*CH$_2$OOC–C(2)). MS: 478 (0.6, $M^{+\cdot}$), 387 (31, $M^{+\cdot}$ – PhCH$_2$·), 91 (100, PhCH$_2^+$). Anal. calc. for $C_{32}H_{30}O_4$ (478.59): C 80.31, H 6.32; found: C 80.19, H 6.41.

1.11.2. *1-Benzyloxy-5,6,8,10-tetramethylheptalene-2-carboxylic Acid* (**11**). The dibenzyl ester (0.35 g, 0.73 mmol) was suspended in EtOH (6 ml) and a soln. of KOH (0.9 g, 16 mmol) in H_2O (5 ml) added. The suspension had not been dissolved after 6 h stirring at 40°. Therefore, further EtOH (5 ml) was added and stirring continued for additional 23 h at 40°. Workup and crystallization from Et_2O yielded **11** (0.14 g, 49%) in dark-yellow crystals. M.p. 172–174° (decomp.) R_f (AcOEt/hexane/AcOH 50:50:1) 0.50. IR (KBr): 1721 (COOR), 1685 (COOH). ^{1}H-NMR (250 MHz): nearly identical with that of **4** [12] except for 5.088, 5.136 (2*d*, ^2J = 12.2, PhCH_2); 7.2–7.35 (several signals, *Ph*CH$_2$). MS: 388 (3, $M^{+\cdot}$), 297 (52, $M^{+\cdot}$ – PhCH$_2$·), 280 (100, $M^{+\cdot}$ – $PhCH_2OH$). Anal. calc. for $C_{25}H_{24}O_4$ (388.46): C 77.30, H 6.23; found: C 77.20, H 6.37.

1.11.3. *Formation of* **12**. Acid **11** (0.2 g, 0.51 mmol) was reacted with $PhCH_2OH$ (0.16 g, 1.5 mmol) in MeCN according to the *General Procedure*. The crude product was purified by TLC (Et_2O/hexane 1:1), whereby about 25 mg of anhydride **42** were removed. After recrystallization from Et_2O, pure **12** (0.14 g, 57%) was obtained in dark yellow crystals. M.p. 170–171°. R_f (hexane/Et_2O 7:3) 0.37, R_f (Et_2O/hexane 1:1) 0.66. UV (hexane): λ_{max} 205 (5.15), 247 (4.25), 270 (4.23), 314 (3.65, sh), 400 (2.94, br. tailing to longer λ); λ_{min} 232 (4.18), 258 (4.19), 370 (2.85). IR (KBr): 1770 (5-ring lactone). ^{1}H-NMR (250 MHz): nearly identical with that of **6** and **18** [12] except for 4.449, 4.572 (2*d*, ^2J = 11.7, α-PhCH_2O); 4.804, 4.972 (2*d*, ^2J = 11.2, β-PhCH_2O); 7.25–7.40 (several signals, 2 *Ph*CH$_2$, H–C(7)). MS: 478 (11, $M^{+\cdot}$), 371 (4, $M^{+\cdot}$ – PhCH$_2$O·), 370 (7, $M^{+\cdot}$ – $PhCH_2OH$), 91 (100, PhCH$_2^+$). Anal. calc. for $C_{32}H_{30}O_4$ (478.59): C 80.31, H 6.32; found: C 80.14, H 6.32.

1.12. *(PM,3SR)-3-Benzyloxy-3-methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**24**). Acid **11** (0.3 g, 0.77 mmol) was reacted with MeOH (0.11 ml, 2.7 mmol) in MeCN according to the *General Procedure*. The crude material was prepurified by TLC (Et_2O/hexane) and small amounts of **42** removed by crystallization from Et_2O/hexane. The pure *'ortho'*-anhydride **24** (0.10 g, 32%) was obtained in red-orange crystals. M.p. 132–133°. R_f (hexane/Et_2O) 0.39, R_f (Et_2O/hexane 1:1) 0.48. UV (cyclohexane): λ_{max} 210 (4.51), 229 (4.24), 244 (4.25, sh), 248 (4.26), 254 (4.23), 261 (4.23, sh), 270 (4.26), 314 (3.68, sh), 400 (3.03, br. tailing to longer λ); λ_{min} 225 (4.24), 236 (4.21), 253 (4.23), 258 (4.21), 370 (2.98). IR (KBr): 1768 (5-ring lactone). ^{1}H-NMR (250 MHz, *cf. 1.6*): nearly identical with that of **6** and **18** [12] except for 3.512 (*s*, β-MeO); 4.404, 4.525 (2*d*,

^2J = 11.6, α-PhCH_2O); 7.25–7.40 (several signals, α-*Ph*CH_2O, H–C(7)). MS: 402 (38, $M^{+\cdot}$), 371 (3, $M^{+\cdot}$ – MeO·), 370 (2, $M^{+\cdot}$ – MeOH), 295 (15, $M^{+\cdot}$ – PhCH_2O·), 294 (37, $M^{+\cdot}$ – PhCH_2OH), 193 (60), 91 (100, PhCH_2^+). Anal. calc. for $C_{26}H_{26}O_4$ (402.49): C 77.59, H 6.51; found: C 77.35, H 6.66.

1.13. *(*PM*)-13-(*tert*-Butyl)-3,3-dimethoxy-9,11,15-trimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**14**). 1.13.1. *13-(*tert*-Butyl)-1-(methoxycarbonyl)-9,11,15-trimethylheptalene-2-carboxylic Acid* (**13**). The corresponding dimethyl ester (1.2 g, 3.26 mmol) [12] was suspended in EtOH (20 ml) and semi-saponified in the presence of KOH (4.0 g, 71 mmol) in H_2O (20 ml) at 40° during 4 h. Usual workup yielded 1.1 g (95%) of crystallized crude **13**, a probe of which was recrystallized from Et_2O. M.p. 171–172° (decomp.). R_f (AcOEt/hexane/AcOH 50:50:1) 0.47. IR (KBr): 1730 (COOR), 1689 (COOH). ^{1}H-NMR (250 MHz): nearly identical with that of the dimethyl ester [12] except for 3.658 (*s*, MeOOC); 10.9 (br. *s*, COOH). MS: 354 (98, $M^{+\cdot}$), 339 (16, $M^{+\cdot}$ – Me·), 323 (22, $M^{+\cdot}$ – MeO·), 322 (64, $M^{+\cdot}$ – MeOH), 272 (25, $M^{+\cdot}$ – (t-Bu)C≡CH), 240 (100). Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.48, H 7.43.

1.13.2. *Formation of* **14**. The acid **13** (0.2 g, 0.56 mmol) was reacted with MeOH (0.082 ml, 2.0 mmol) in MeCN according to the *General Procedure*. The crude oily product was crystallized from Et_2O/hexane to yield **13** (0.16 g, 77%) as orange crystals. M.p. 140–141°. R_f (hexane/Et_2O 7:3; *cf.* R_f (**6**) 0.32) 0.36. UV (cyclohexane): λ_{max} 211 (4.29), 248 (4.28), 268 (4.23) 313 (3.70, sh), 400 (3.00, br. tailing to longer λ); λ_{min} 228 (4.04), 258 (4.20), 370 (2.97). IR (KBr): 1775 (5-ring lactone). ^{1}H-NMR (270 MHz): 1.178 (*s*, *t*-Bu); 1.760 (*s*, Me–C(11)); 2.073 (br. *s* with f.s., Me–C(9)); 2.193 (*d*-like *s*, ^4J = 1.1, Me–C(15)); 3.176 (*s*, α-MeO); 3.433 (*s*, β-MeO); 6.302 (br. *s*, H–C(12)); 6.339 (br. *s* with f.s., H–C(14)); 6.458 (*dq*, ^3J = 6.3, ^4J = 1.5, H–C(8)); 7.222 (*d*, ^3J = 6.3, H–C(7)). ^{1}H-DR (270 MHz): 2.073 (Me–C(9))→6.458 (*d*, ^3J = 6.3, H–C(8)); 2.193 (Me–C(15))→6.339 (*s*, H–C(14)). MS: 368 (100, $M^{+\cdot}$), 353 (19, $M^{+\cdot}$ – Me·), 337 (43, $M^{+\cdot}$ – MeO·); 336 (66, $M^{+\cdot}$ – MeOH); 286 (95, $M^{+\cdot}$ – (*t*-Bu)C≡CH). Anal. calc. for $C_{23}H_{28}O_4$ (368.47): C 74.97, H 7.66; found: C 74.92, H 7.69.

1.14. *(*PM,3RS*)- and (*PM,3SR*)-13-(*tert*-Butyl)-3-methoxy-3-[$^2H_3$]methoxy-9,11,15-trimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* ([$^2H_3$]-**14β** and [$^2H_3$]-**14α**). According to the *General Procedure* acid **13** (0.15 g, 0.42 mmol) and [$^2H_3$]MeOH (0.062 ml, 1.5 mmol; > 99.8% ^{2}H) were reacted in MeCN. The crude product crystallized from Et_2O/hexane to yield 0.134 g (85.2%) of pure material in orange crystals. M.p. 140–141°. IR (KBr): 2230, 2175, 2110, 2060 ([$^2H_3$]MeO); 1775 (5-ring lactone). ^{1}H-NMR (250 MHz): identical with that of **14** except for 3.176 (*s*, 2.82 H, α-MeO, 94%), 3.433 (*s*, 0.18 H, β-MeO, 6%). Reference for integration: Me–C(11). MS: 371 (100, $M^{+\cdot}$), 356 (17, $M^{+\cdot}$ – Me·), 340 (18, $M^{+\cdot}$ – MeO·), 337 (22, $M^{+\cdot}$ – [$^2H_3$]MeO·), 336 (31, $M^{+\cdot}$ – [$^2H_3$]MeOH), 289 (97, $M^{+\cdot}$ – (*t*-Bu)C≡CH). Anal. calc. for $C_{23}H_{25}{}^2H_3O_4$ (371.49): C 74.36, H 6.78, ^{2}H 1.63; found: C 74.29, H 6.82, ^{2}H 1.64.

1.15. *(*PM,3RS*)-13-(*tert*-Butyl)-3-ethoxy-3-methoxy-9,11,15-trimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**25**). Acid **13** (0.2 g, 0.56 mmol) was reacted with EtOH (0.12 ml, 2 mmol) in MeCN according to the *General Procedure*. The crude product (^{1}H-NMR: 98% of **25** and 2% of **26**) was recrystallized from Et_2O/hexane: 0.15 g (69%) red-orange crystals of pure **25**. M.p. 142–143°. R_f (hexane/Et_2O 7:3) 0.41. UV (cyclohexane): λ_{max} 211 (4.30), 248 (4.30), 268 (4.24), 312 (3.72, sh), 400 (3.03, br. tailing to longer λ); λ_{min} 228 (4.04), 258 (4.21), 370 (2.97). IR (KBr): 1770 (5-ring lactone). ^{1}H-NMR (250 MHz): nearly identical with that of **14** except for 1.189 (*t*, ^3J = 7.1, β-CH_3CH_2O); 3.162 (*s*, α-MeO); 3.692, 3.846 (2*dq*, ^2J = 9.7, ^3J = 7.1, β-CH$_3$CH_2O). MS: 382 (100, $M^{+\cdot}$), 367 (15, $M^{+\cdot}$ – Me·), 351 (22, $M^{+\cdot}$ – MeO·), 350 (37, $M^{+\cdot}$ – MeOH), 337 (37, $M^{+\cdot}$ – EtO·), 336 (57, $M^{+\cdot}$ – EtOH), 300 (64, $M^{+\cdot}$ – (*t*-Bu)C≡CH), 193 (47). Anal. calc. for $C_{24}H_{30}O_4$ (382.50): C 75.36, H 7.91; found: C 75.32, H 7.97.

*(*PM,3SR*)-Isomer* **26**: characterized by its ^{1}H-NMR signal at 3.39 (*s*, β-MeO).

1.16. *(*PM,3RS*)-13-(*tert*-Butyl)-3-methoxy-9,11,15-trimethyl-3-neopentyloxy-4-oxatricyclo[8.5.0.0^{2,6}]-pentadeca-1,6,8,10,12,14-hexaen-5-one* (**35**). Acid **13** (0.2 g, 0.56 mmol) was reacted with neopentyl alcohol (0.18 g, 2 mmol) in MeCN according to the *General Procedure*. The product was purified by prep. TLC (hexane/Et_2O 7:3) and then recrystallized from Et_2O: pure **35** (0.145 g, 61%) as orange crystals. M.p. 170–171°. R_f (hexane/Et_2O) 0.46. UV: identical with that of **25**. IR (KBr): 1771 (5-ring lactone). ^{1}H-NMR (250 MHz): nearly identical with that of **14** except for 0.873 (*s*, β-(CH_3)$_3$CCH$_2$O); 3.174 (*s*, α-MeO); 3.350 (*AB*-like br. *s*, $^2J \approx 9.2$, β-(CH$_3$)$_3$CCH_2O). ^{1}H-NMR (250 MHz, C_6D_6): nearly identical with that of **33** except for 0.852 (*s*, (CH_3)$_3$CCH$_2$O); 3.104 (*s*, α-MeO); 3.608, 3.644 (2*d*, ^2J = 9.1, β-(CH$_3$)$_3$CCH_2). MS: 424 (83, $M^{+\cdot}$), 409 (15, $M^{+\cdot}$ – Me·), 393 (7, $M^{+\cdot}$ – MeO·), 392 (21, $M^{+\cdot}$ – MeOH), 342 (46, $M^{+\cdot}$ – (*t*-Bu)C≡CH), 337 (85, $M^{+\cdot}$ – (CH$_3$)$_3$CCH$_2$O·), 336 (86, $M^{+\cdot}$ – (CH$_3$)$_3$CCHOH), 221 (65). Anal. calc. for $C_{27}H_{36}O_4$ (424.58): C 76.38, H 8.55; found: C 76.09, H 8.71.

1.17. *12-Isopropyl-3,3-dimethoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**16**). See [13].

1.18. *(*PM,3RS*)- and (*PM,3SR*)-12-Isopropyl-3-methoxy-3-[$^2H_3$]methoxy-9,15-dimethyl-4-oxatricyclo-[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* ([$^2H_3$]-**16β** and [$^2H_3$]-**16α**, resp.). DMF (0.25 ml, 3.3 mmol) in

MeCN (5 ml) was reacted with $(COCl)_2$ (0.15 ml, 1.8 mmol) in MeCN (3 ml), and **15** (0.3 g, 0.92 mmol) [12] was added, followed by $[^2H_3]$MeOH (0.1 ml, 2.5 mmol; > 99.8% ^2H) in MeCN (0.5 ml). The crude product was purified by prep. TLC (Et_2O/hexane 1:1) and crystallization from Et_2O yielded 0.18 g (56%) of the pure compound in ruby crystals. M.p. 121–122° (*cf.* [13]). IR (KBr): 2251, 2076 ($[^2H_3]$MeO). ^{1}H-NMR (250 MHz): 3.171 (*s*, 2.52 H, MeO of $[^2H_3]$-**16***β*; 84%) and 3.463 (*s*, 0.48 H, MeO of $[^2H_3]$-**16***α*; 16%). Reference for integration: Me–C(9) and Me–C(15). MS: 343 (100, $M^{+\cdot}$), 328 (12, $M^{+\cdot} - Me^{\cdot}$), 312 (45, $M^{+\cdot} - MeO^{\cdot}$), 311 (79, $M^{+\cdot} - MeOH$), 309 (47, $M^{+\cdot} - [^2H_3]MeO^{\cdot}$), 308 (74, $M^{+\cdot} - [^2H_3]MeOH$), 296 (14, $M^{+\cdot} - (MeOH + Me^{\cdot})$), 293 (15, $M^{+\cdot} - ([^2H_3]MeOH + Me^{\cdot})$), 275 (41, $M^{+\cdot}$ – (i-Pr)C≡CH), 207 (90).

1.19. *(PM,3RS)-3-Ethoxy-12-isopropyl-3-methoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**27**). Acid **15** (0.5 g, 1.53 mmol) was reacted with EtOH (0.24 ml, 4 mmol) in MeCN (8 ml in total) according to the *General Procedure*. Anhydride **43** [12], which was formed to an extent of 23% (0.11 g), was removed by prep. TLC (hexane/Et_2O 7:3), and the crude product (^{1}H-NMR: 80% of **27** and 20% of **28**) recrystallized from Et_2O/hexane: 0.17 g (31%) of brick-red crystals of pure **27**. M.p. 130–131°. R_f (Et_2O/hexane 1:1) 0.54. UV: Identical with that of **16** [13]. IR (KBr): 1764 (5-ring lactone). ^{1}H-NMR (270 MHz): nearly identical with that of **16** [13] except for 1.191 (*t*, ^3J = 7.14, *β*-CH_3CH_2O); 3.156 (*s*, α-MeO); 3.763, 3.887 (2*d*, ^2J = 9.8, ^3J = 7.14, *β*-CH_3CH_2O). MS: 354 (92, $M^{+\cdot}$), 339 (4, $M^{+\cdot} - Me^{\cdot}$), 323 (39, $M^{+\cdot} - MeO^{\cdot}$), 322 (77, $M^{+\cdot} - MeOH$), 309 (20, $M^{+\cdot} - EtO^{\cdot}$), 308 (100, $M^{+\cdot} - EtOH$), 207 (66). Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.34. H 7.64.

(PM,3SR)-Isomer **28**: characterized by its ^{1}H-NMR signal at 3.45 (*s*, *β*-MeO); see also *2.6*.

1.20. *(PM,3RS)-3-Benzyloxy-12-isopropyl-3-methoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**29**). According to the *General Procedure*, **15** (0.3 g, 0.92 mmol) [12] was reacted with $PhCH_2OH$ (0.26 ml, 2.5 mmol) in MeCN (6 ml in total). The by-product **43** was removed by prep. TLC (hexane/Et_2O 7:3), and the brown-red oil (0.30 g, 78%; ^{1}H-NMR: 90% of **29** and 10% of **30**) was crystallized from hexane: 0.16 g (41%) of **29** in brown-red crystals. M.p. 114–115°. R_f (hexane/Et_2O 7:3) 0.40. UV (cyclohexane): λ_{max} 212 (4.41), 249 (4.31), 261 (4.22, sh), 279 (4.11, sh), 320 (365, sh), 410 (2.93, br. tailing to longer λ); λ_{min} 230 (4.16). IR (KBr): 1760 (5-ring lactone). ^{1}H-NMR (250 MHz): nearly identical with that of **16** [13] except for 3.221 (*s*, α-MeO); 4.775, 4.886 (2*d*, ^2J = 11.2, *β*-PhCH_2O); 7.25–7.40 (several signals, *β*-*Ph*CH_2O). MS: 416 (28, $M^{+\cdot}$), 385 (2, $M^{+\cdot} - MeO^{\cdot}$), 384 (< 1, $M^{+\cdot} - MeOH$), 325 (7, $M^{+\cdot} - PhCH_2^{\cdot}$), 309 (22, $M^{+\cdot} - PhCH_2O^{\cdot}$), 308 (46, $M^{+\cdot} - PhCH_2OH$), 207 (42), 91 (100, $PhCH_2^+$). Anal. calc. for $C_{27}H_{28}O_4$ (416.52): C 77.86, H 6.78; found: C 77.74, H 6.90.

(PM,3SR)-Isomer **30**: characterized by its ^{1}H-NMR signal at 3.53 (*s*, *β*-MeO); see also *2.7*.

1.21. *(PM,3RS)-3-Isopropoxy-12-isopropyl-3-methoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**40**). Acid **15** (0.4 g, 1.2 mmol) [12] was reacted with i-PrOH (0.26 ml, 3.3 mmol) in MeCN (9 ml in total) according to the *General Procedure*. Traces of **43** were removed by prep. TLC (Et_2O/hexane 1:1), and the crude product (0.27 g, 59%; ^{1}H-NMR: 95% of **40** and 5% of **41**) was recrystallized from Et_2O: 0.16 g (35%) of pure **40** in ruby crystals. M.p. 140–141°. R_f (Et_2O/hexane 1:1) 0.57. UV: identical with that of **16** [13]. IR (KBr): 1764 (5-ring lactone). ^{1}H-NMR (250 MHz): nearly identical with that of **16** except for 1.168, 1.239 (2*d*, ^3J = 6.2, *β*-$(CH_3)_2CHO$); 3.136 (*s*, α-MeO); 4.534 (*sept.*, ^3J = 6.2., $(CH_3)_2CHO$). MS: 368 (63, $M^{+\cdot}$), 337 (8, $M^{+\cdot} - MeO^{\cdot}$), 336 (25, $M^{+\cdot} - MeOH$), 309 (65, $M^{+\cdot}$ – i-PrO$^{\cdot}$), 308 (100, $M^{+\cdot}$ – i-PrOH), 207 (82). Anal. calc. for $C_{23}H_{28}O_4$ (368.47): C 74.97, H 7.66; found: C 75.26, H 7.68.

(PM,3SR)-Isomer **41**: characterized by its ^{1}H-NMR signal at 3.38 (*s*, *β*-MeO).

1.22. *5,5-Diethoxy-12-isopropyl-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-3-one* (**46**) *and 5,5-Diethoxy-12-isopropyl-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-2(6),7,9,11,13,15-hexaen-3-one* (**47**). Acid **44** (0.5 g, 1.53 mmol) was reacted with EtOH (0.24 ml, 4 mmol) in MeCN (9.5 ml in total) according to the *General Procedure*. Purification by prep. TLC (Et_2O/hexane 1:1) afforded 0.46 g (82%) of a red to brown oil which proved to be a mixture **46**/**47** and the 3-ethoxy-3-methoxy-*'ortho'*-anhydride **45** *(cf. Scheme 7)* according to MS.

This mixture (51 mg; *ca.* 0.14 mmol) was dissolved in 5 ml of EtOH, and 0.5 ml of a 0.014M soln. of H_2SO_4/EtOH was added. After 18 h at r.t., only **46**/**47** could be detected by TLC. Workup yielded 39 mg (76%) of the pure diethoxy compounds which were crystallized from a small amount of pentane. M.p. 106–108°. R_f (hexane/Et_2O 4:1) 0.51. UV: identical with that of the corresponding 5,5-dimethoxy compound [13]. IR (KBr): 1770 (5-ring lactone). ^{1}H-NMR (250 MHz, 30°): 1.095 (*d*, ^3J = 6.8, $(CH_3)_2CH$); 1.228 (*t*, $^3J \approx 7.2$, CH_3CH_2O); 1.257 (*t*, $^3J \approx 7.2$, CH_3CH_2O); 1.6–1.9 (br. *s*, Me–C(9), Me–C(15)); 2.489 (*sept.* ^3J = 6.8, $(CH_3)_2CH$); 3.50–3.85 (several *q*-like signals, $^3J \approx 7.2$, 2 CH_3CH_2O); 5.47–5.63 (br. *s*, H–C(11)); 6.3–6.4 (several signals, H–C(8), H–C(13), H–C(14)); 6.62–6.80 (br. *s*, H–C(7)). ^{1}H-NMR (360 MHz, –50°): signals of **46** (16%) which are not covered by the signals of **47** (84%): 1.026 (*d*, ^3J = 7.0, $(CH_3)_2CH$); 1.155 (*t*, ^3J = 7.0, CH_3CH_2O); 2.138, 2,272 (2*s*,

Me–C(9), Me–C(15)); 3.475 (*t*-like signals, ^3J = 7.3, CH_3CH_2O); 5.858 (*s*, H–C(11)); 6.225 (br. *s*, H–C(8), H–C(13), H–C(14)); 6.485 (*d*, ^3J = 6.7, H–C(7)). Signal of **47** (84%): 1.066, 1.094 (2*d*, ^3J = 6.7, $(CH_3)_2CH$); 1.223, 1.271 (2*t*, ^3J = 7.1, 2 CH_3CH_2O); 1.639 (*s*, Me–C(15)); 1.717 (*s*, Me–C(9)); 2.478 (*sept.*, ^3J = 6.7, $(CH_3)_2CH$); 3.566 (*sext.*, $^3J \approx 7.1$, CH_3CH_2O); 3.730, 3.830 (2 *quint.*-like, $^3J \approx 7.1$, CH_3CH_2O); 5.468 (*s*, H–C(11)); 6.300 (*d*, ^3J = 11.4, H–C(8)); 6.315 (*AB*, $^3J(AB)$ = 12.0, H–C(13), H–C(14)); 6.800 (*d*, ^3J = 11.4, H–C(7)). MS: 368 (30, $M^{+\cdot}$); 339 (69, $M^{+\cdot}$ – Et$^\cdot$), 323 (16, $M^{+\cdot}$ – EtO$^\cdot$), 311 (20), 294 (29), 269 (100), 267 (36), 251 (19), 241 (24), 221 (35), 207 (30), 191 (26). Anal. calc. for $C_{23}H_{28}O_4$ (368.47): C 74.97, H 7.66; found: 75.18, H 7.68.

2. Reactions with the *'ortho'*-Anhydrides (*cf.* [13]). – 2.1. *Photochemical Formation of (*PM*)-3,3-Diethoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-2(6),7,9,11,13,15-hexaen-5-one* (**49**) *from* **10**. *'ortho'*-Anhydride **10** (0.10 g, 0.28 mmol) was dissolved in 250 ml of *t*-BuOMe and irradiated under Ar during 2 h (*cf.* [13]). *t*-BuOMe was evaporated and the residue dissolved in a small amount of Et_2O to yield 24 mg of a first crop of crude **49**. The mother liquor was separated by prep. TLC (hexane/Et_2O 4:1) to yield, besides 30 mg of **10**, a second crop of 52 mg of crude **49**. Recrystallization of the crude **49** from Et_2O/hexane yielded 22 mg (22%) of pure **49** in dark yellow crystals. M.p. 140–141°. R_f (hexane/Et_2O 7:3; *cf.* R_f (**10**) 0.40) 0.49. UV (cyclohexane): λ_{max} 202 (4.34), 230 (4.16, sh), 269 (4.29), 307 (3.56, sh), 380 (2.64, broad); λ_{min} 247 (4.05), 360 (2.56). IR (KBr): 1766 (5-ring lactone). ^{1}H-NMR (250 MHz): 1.190 (*t*, ^3J = 7.1, α-CH_3CH_2O); 1.232 (*t*, ^3J = 7.1, β-CH_3CH_2O); 1.755 (*s*, Me–C(15)); 1.827 (*s*, Me–C(9)); 1.933 (br. *s*, Me–C(11), Me–C(13)); 3.488, 3.611 (2*dq*, ^2J = 9.0, ^3J = 7.1, α-CH_3CH_2O); 3.879, 3.991 (2*dq*, ^2J = 9.5, ^3J = 7.1, β-CH_3CH_2O); 6.021 (br. *s*, H–C(14)); 6.107 (br. *s*, H–C(12)); 6.601, 6.631 (2*d*, ^3J = 11.6, H–C(7), H–C(8)). MS: identical with that of **10**. Anal. calc. for $C_{22}H_{26}O_4$ (354.45): C 74.55, H 7.39; found: C 74.49. H 7.29.

2.2. *Photochemical Formation of (*PM,*3*RS*)- and (*PM,*3*SR*)-3-Methoxy-3-[$^2H_3$]methoxy-9,11,13,15-tetramethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-2(6),7,11,13,15-hexaen-5-one* ([$^2H_3$]-**51β** and [$^2H_3$]-**51α**, resp.) *from the Mixture [$^2H_3$]-**6β**/[$^2H_3$]-**6α**].* The mixture (0.070 g, 0.21 mmol; *cf. 1.2*) was irradiated in 250 ml of *t*-BuOMe during 2 h. Prep. TLC (hexane/Et_2O 7:3) yielded, besides the mixture [$^2H_3$]-**6β**/[$^2H_3$]-**6α** (0.025 g, 36%), 46 mg (66%) of [$^2H_3$]-**51β**/[$^2H_3$]-**51α** which were recrystallized from Et_2O/hexane. M.p. 113–114° (*cf.* [13]). ^{1}H-NMR (250 MHz): identical with that of the DBS isomer of **6** [13] except for 3.294 (*s*, 2.40 H, MeO–C(3) of [$^2H_3$]-**51β**; 80%) and 3.566 (*s*, 0.60 H, MeO–C(3) of [$^2H_3$]-**51α**; 20%). Reference for integration: Me–C(11) and Me–C(13).

2.3. *Photochemical Formation of (*PM,*3*RS,*1'*SR*)-3-Methoxy-9,11,13,15-tetramethyl-3-(1'-phenylethoxy)-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-2(6),7,9,11,13,15-hexaen-3-one* (**50**) *from* **18**. See [13].

2.4. *Base-Catalyzed Rearrangement of* **6** *into 2-Ethyl 1-Methyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate* (**17**). 2.4.1. *Transesterification of Dimethyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate into* **17**. The dimethyl ester (0.10 g, 0.3 mmol) was dissolved in 15 ml of EtOH containing 0.9 mmol of EtONa and stirred during 5 h at 40°. After that time, no starting material could be detected by TLC. Workup including prep. TLC (Et_2O/hexane 1:1) yielded **17** (0.083 g, 80%) as a yellow oil which was crystallized from hexane with a trace of Et_2O. M.p. 104–105°, R_f (Et_2O/hexane 1:1; starting material R_f 0.43) 0.50. IR (KBr): 1706 (COOR). ^{1}H-NMR (80 MHz): identical with that of the starting material except for 1.25 (*t*, ^3J = 7.0, CH_3CH_2); 3.71 (*s*, MeOOC); 4.18, 4.20 (2*q*, ^3J = 7.0, CH_3CH_2). MS: 340 (100, $M^{+\cdot}$), 325 (13, $M^{+\cdot}$ – Me$^\cdot$), 300 (7, $M^{+\cdot}$ – Me–C≡CH), 242 (26, $M^{+\cdot}$ – MeC≡CCOOMe), 228 (5, $M^{+\cdot}$ – MeC≡CCOOEt), 184 (91, $M^{+\cdot}$ – MeOOC–C≡C–COOEt). Anal. calc. for $C_{21}H_{24}O_4$ (340.42): C 74.09, H 7.11; found: C 73.83, H 7.13.

2.4.2. *Rearrangement of* **6**. *'ortho'*-Anhydride **6** (0.045 g, 0.14 mmol) was dissolved in EtOH (7 ml), and a soln. of Na (*ca.* 5 mg, 0.22 mmol) in EtOH (1 ml) was added. After 20 min at 20°, *ca.* half of **6** had already been reacted to yield **17**. After 60 min, the transformation was complete. Workup yielded **17** (0.0295 g, 63%) identical in all aspects (R_f, mixed m.p., ^{1}H-NMR, and MS) with the material described above *(2.4.1)*.

2.5. *Acid-Catalyzed Reaction of* **6**. See [13].

2.6. *Thermal Equilibration of (*PM,*3*RS*)- and (*PM,*3*SR*)-3-Ethoxy-12-isopropyl-3-methoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,14-hexaen-5-one* (**27** and **28**, resp.). *'ortho'*-Anhydride **27** (*ca.* 7 mg) was dissolved in 1,1,2,2-tetrachloro-[1,2-$^2H_2$]ethane ($C_2D_2Cl_4$; *ca.* 0.1 ml filtrated over basic alumina) and heated in an oil bath at 100°. After heating, the probes were diluted with $CDCl_3$, and the amount of **27** and **28** was determined by ^{1}H-NMR according to the integral of the signals at 3.154 (*s*, α-MeO in **27**) and at 3.464 (*s*, β-MeO in **28**). Results: 0.5. h 96/4%, 1 h 94/6%, 4 h 69/31% and 24 h 50/50% of **27**/**28**. These data yield for the equilibrium kinetics (k(**27**) + k(**28**)) $\approx 5 \cdot 10^{-5} s^{-1}$ or $\tau_{½} \approx 230$ min. ^{1}H-NMR (250 MHz, $C_2D_2Cl_4$ + $CDCl_3$) of **28** (extracted from the ^{1}H-NMR of the 1:1 mixture of **27** and **28**): 1.031, 1.049 (2*d*, ^3J = 6.9, $(CH_3)_2CH$); 1.119 (*t*, ^3J = 7.0, α-CH_3CH_2O); 2.187 (br. *s*, Me–C(9)); 2.200 (br. *s*, Me–C(15)); 2.437 (*sept.*, $^3J \approx 7$, $(CH_3)_2CH$); 3.316, 3.428 (2*dq*, ^2J = 8.9,

^3J = 7.0, α-CH_3CH_2O)[16]; 3.464 (*s*, β-MeO); 5.699 (br. *s*, H–C(11)); 6.09–6.21 (several signals, H–C(13), H–C(14)); 6.304 (*dquint.*-like, ^3J(8,7) = 6.6, ^4J(8, CH_3–C(9)) ≈ 1.3, H–C(8)); 7.143 (*dq*-like, ^3J(7,8) = 6.5, ^5J(7, CH_3–C(9)) ≈ 0.7, H–C(7)).

2.7. *Thermal Equilibration of (*PM,*3*RS*)- and (*PM,*3*SR*)-3-Benzyloxy-12-isopropyl-3-methoxy-9,15-dimethyl-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-1,6,8,10,12,14-hexaen-5-one* (**29** and **30**, resp.). *'ortho'*-Anhydride **29** (*ca.* 5 mg) was dissolved in $C_2D_2Cl_4$ (filtrated over basic alumina) and heated in an oil bath at 100°. After heating, the probes were diluted with $CDCl_3$ and the amount of **29** and **30** determined by ^{1}H-NMR according to the integral of the signals at 3.220 (*s*, α-MeO in **29**) and at 3.525 (*s*, β-MeO in **30**). Results: 0.5 h 99/3%, 1 h 95/5%, 4 h 84/16%, 24 h 52/48% and 30 h 51/49% of **29**/30; *i.e.* (k(**29**) + k(**30**)) ≈ $2.9 \cdot 10^{-5}$s^{-1} or $\tau_{½}$ ≈ 400 min. ^{1}H-NMR (250 MHz, $C_2D_2Cl_4$ + $CDCl_3$) of **30** (extracted from the ^{1}H-NMR of the 52:48 mixture of **29** and **30**): 1.021, 1.046 (2*d*, ^3J = 6.6, $(CH_3)_2CH$); 2.19 (br. *s*, Me–C(9)); 2.227 (br. *s*, Me–C(15)); 2.423 (*sept.*, ^3J = 6.6, $(CH_3)_2CH$); 3.525 (*s*, β-MeO); 4.356, 4.459 (2*d*, ^2J = 11.1, α-PhCH_2O)[17]; 5.718 (*d*-like *s*, ^4J(11, 13) ≈ 1.1, H–C(11)); 5.959, 6.080 (2*dq*, ^3J(13, 14) = 6.6, ^4J(14, CH_3–C(15)) = 1.4, H–C(13), H–C(14)); 6.329 (*dq*, ^3J(8,7) = 6.6, ^4J(8, CH_3–C(9)) ≈ 1.4, H–C(8)); 7.190 (*dq*-like, ^3J(7,8) = 6.6, ^5J(7, CH_3–C(9)) ≈ 0.5, H–C(7)); 7.2–7.4 (*m*, α-PhCH_2O).

2.8. *Crystal Data of (*PM,*3*RS,*1'*SR*)-3-Methoxy-9,11,13,15-tetramethyl-3-(1'-phenylethoxy)-4-oxatricyclo[8.5.0.0^{2,6}]pentadeca-2(6),7,9,11,13,15-hexaen-3-one* (**49**; see [13]). *Space group and cell dimensions:* monoclinic $P2_1/n$, with a = 6.853(2), b = 22.264(7), c = 14.954(4) Å, β = 101.09(2)°; D = 1.24 Mg m^{-3}, Z = 4. *Data collection. Crystal size:* 0.21 × 0.33 × 0.60 mm^3; temp. 170 K; wavelength: 0.71069 Å; total data measured: 4407 (excluding standards), total data observed: 3197. The structure was determined by direct methods using 32 starting phase permutations. Refinement proceeded smoothly to convergence at R = 0.0389 with anisotropic refinement of all non-H-atoms. Coordinates and thermal parameters have been deposited with the *Crystallographic Data Centre*, Cambridge, University Chemical Lab., Cambridge CB2 1EW, England.

2.9. *Crystal Data of* (PM)-**6**. *Space group and cell dimensions:* triclinic $P\bar{1}$ with a = 8.292, b = 9.192, c = 12.845 Å, α = 89.27°, β = 72.63°, γ = 69.32°; D = 1.25 Mgm^{-3}, Z = 2. *Data collection. Crystal size:* 0.33 × 0.33 × 0.33 mm^3; temp. 170 K; wavelength: 0.71069 Å; total data measured: 3049 (excluding standards), total data observed: 2234. The structure was determined by direct methods using 32 starting phase permutations. Refinement proceeded smoothly to convergence at R = 0.0526 with anisotropic refinement of all non-H-atoms. Coordinates and thermal parameters have been deposited with the *Crystallographic Data Centre*, Cambridge, University Chemical Lab., Cambridge CB2 1EW, England. The torsion angles related to *Scheme 12* are: O(4)–C(3)–C(2)–C(6) = 18.6°, C(1)–C(2)–C(3)–O(α) = –39.9°, C(1)–C(2)–C(3)–O(β) = 84.0°, C(6)–C(2)–C(3)–O(β) = –98.6°.

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[16]) The corresponding signals of **27** appeared at 3.759 and 3.884 (2 *dq*, ^2J = 9.6, ^3J = 7.1, β-CH_3CH_2O; *cf. 1.19*).
[17]) The corresponding signals of **29** appeared at 4.774 and 4.885 (2*d*, ^2J = 11.1, β-PhCH_2O; *cf. 1.20*).

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