114. σ-Skeletal Rearrangement of Heptalenes: Thermal Transformation of Heptalene-1,2-dicarboxylates into Heptalene-1,3-dicarboxylates[1])

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Dedicated to Prof. *Albert Eschenmoser* on the occasion of his 60th birthday

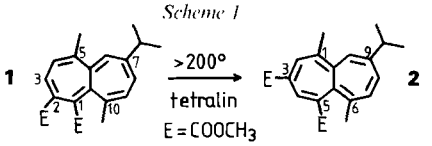
(1.IV.85)

It is shown that dimethyl heptalene-1,2-dicarboxylates undergo rearrangements at temperatures > 200° to yield the corresponding 1,3-dicarboxylates, which are isolated as the more stable 3,5-dicarboxylates. ^{2}H- and ^{13}C-labelling experiments with dimethyl 7-isopropyl-5,10-dimethylheptalene-1,2-dicarboxylate (**1**) which is rearranged into dimethyl 9-isopropyl-1,6-dimethylheptalene-3,5-dicarboxylate (**2**) indicate that the reaction occurs by interchange of C(2) and C(3) in the heptalene skeleton of **1**. Thus, the transformation of **1** into **2** represents the first thermal σ-skeletal rearrangement of heptalenes. The structures of **1** and **2** are discussed in terms of an X-ray analysis and the spectral data.

Introduction. – Heptalene-heptalene transformations may be subdivided in π-skeletal, σ-skeletal, and peripheral rearrangements. The first type involves double-bond shifts in heptalenes which can be induced photochemically [1] or thermally [1] [2]. The second mode of rearrangement depicts a thermal (or photochemical) reorganization of the heptalene skeleton by C-atom interchanges. We have already reported briefly on the thermal rearrangement of dimethyl 7-isopropyl-5,10-dimethylheptalene-1,2-dicarboxylate (**1**) into the corresponding 9-isopropyl-1,6-dimethylheptalene-3,5-dicarboxylate (**2**)[4]) at temperatures > 200° [3] *(Scheme 1)*. On the basis of experiments with ^{2}H- and ^{13}C-labelled **1**, we report here the characterization of this transformation as the first heptalene σ-skeletal rearrangement involving an interchange of C(2) and C(3).

To our knowledge, the third kind of the heptalene-heptalene rearrangements, *i.e.* the migration of substituents along the unaltered σ-skeleton has not been observed so far[5]).

Scheme 1



[1]) Presented in part by *H.-J. H.* in Basel (1980), Wien (1982), Berlin (1982), Lodz (1984), and Zurich (1985).

[2]) Part of the Ph. D. thesis of *W. B.*, No. 837, University of Fribourg/Switzerland, 1982. Present address: Eidg. Turn- und Sportschule, Hauptstr. 243–245, CH-2532 Magglingen.

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

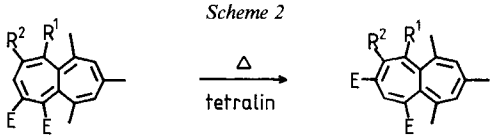
[4]) Numbering of the heptalene ring according to the IUPAC nomenclature rules.

[5]) In general, we can expect peripheral rearrangements to occur more easily in aromatic annulenes such as benzene with an energetically low-lying π-system (*cf.* the *Jacobsen* rearrangement and related processes [4]). For the same reason, aromatic annulenes should be less susceptible to the thermal σ-reorganization processes than non-aromatic annulenes (*cf.* [5]). On the other hand, it is well-known that aromatic annulenes undergo readily photochemical σ-skeletal rearrangements (*cf.* [6] for such rearrangements in benzene derivatives). Heptalenes as representatives of non-aromatic annulenoannulenes (*cf.* [7]) seem to be quite stable photochemically, and only light-induced double-bond shifts have so far been observed [1].

Thermal Rearrangement of Heptalene-1,2-dicarboxylates. – The rearrangement **1**→**2** *(Scheme 1)* most efficiently occurs in tetralin as solvent leading to yields of up to 25–40%. The yields are better than 90% with respect to consumed **1**. However, the high reaction temperature and the long reaction times of more than 70 h do not allow a complete conversion of **1**[6]). The irreversible transformation of **1** into **2** (*cf.* [3]) can easily be followed by a change in the colour of the tetralin solution from yellow (**1**) to red (**2**). The rearrangement of **1** takes also place in higher-boiling hydrocarbons such as dodecane and decalin, however, much slower. Attempts to perform the rearrangement in molten naphthalene at 230° failed. On the basis of these observations and the fact that traces of α-tetralone could be detected in the tetralin solution of **1** and **2** after the reaction, we assume that the rearrangement **1**→**2** is initiated by the addition of a radical (probably an alkoxy radical) to **1** (see below).

The rearrangement is not restricted to **1**. Dimethyl 5,6,8,10-tetramethylheptalene- (**3**) and dimethyl 4-isopropyl-6,8-10-trimethylheptalene-1,2-dicarboxylate (**4**) could also be rearranged into the corresponding 3,5-dicarboxylates **5** and **6**, respectively *(Scheme 2)*. Thus, the described type of rearrangement seems to be characteristic for alkyl-substituted heptalene-1,2-dicarboxylates.

Scheme 2

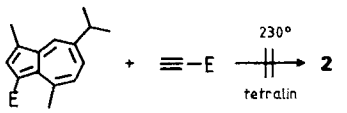


3 $R^1 = CH_3$, $R^2 = H$ 210°/9.5 d **5** (24%)[a])
4 $R^1 = H$, $R^2 = i\text{-}C_3H_7$ 210°/43 h **6** (17%)[b])

[a]) Yield with respect to consumed **3** at 21% conversion.
[b]) Yield with respect to consumed **4** at 8% conversion.

Rearrangement of ^{2}H- and ^{13}C-Labelled 1. – We assumed that only C(2) and C(3) of **1** are involved in the rearrangement into **2**. A simple mode for the interchange of C(2) and C(3) would be the formation of methyl propiolate and methyl 7-isopropyl-1,4-dimethylazulene-3-carboxylate (**7**) by thermal ring contraction of **1**[7]). However, the rearrangement **1**→**2** in tetralin is not dependent on dilution, and **7** [8] does not react with methyl propiolate at 230° to yield **2** *(Scheme 3)*. This implies that we have to consider an intramolecular pathway for the formation of **2** from **1**. To demonstrate that the rearrangement does not take place by a peripheral 1,2-migration of the methoxycarbonyl group at C(2) accompanied by a double-bond shift, we synthesized labelled derivatives of

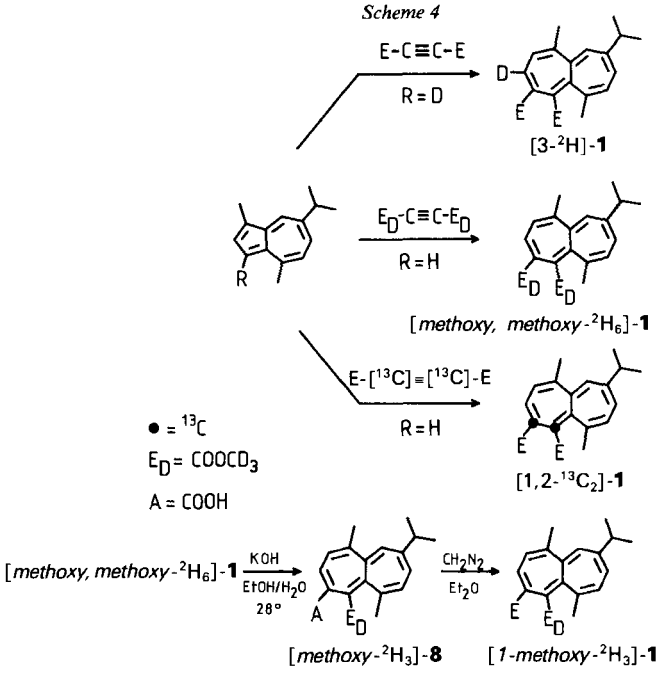
Scheme 3



7

[6]) The formation of several colourless side products becomes more dominant over longer heating periods. These products were not characterized.
[7]) This is one of the possible paths of fragmentation of M^+ of **1** in the mass spectrometer.

Scheme 4



1 by reaction of guajazulene with the appropriate acetylenedicarboxylates *(Scheme 4)*. [3-$^2H_1$]Guajazulene with 0.94 D at C(3) was prepared by deuteration of guajazulene with 50% [$^2H_2$]SO_4. About 20% loss of the deuterium label was observed in the reaction with dimethyl acetylenedicarboxylate (ADM) at 220° in tetralin. Specifically deuterated [*1-methoxy*-$^2H_3$]-**1** was obtained from the corresponding 2-acid [*methoxy*-$^2H_3$]-**8** by esterification with CH_2N_2 in Et_2O. The 2-acid was formed by selective saponification (*cf.* [9]) of the [$^2H_6$]dimethyl 1,2-dicarboxylate [*methoxy,methoxy*-$^2H_6$]-**1** which, in turn, was prepared by the reaction of guajazulene with [$^2H_6$]dimethyl acetylenedicarboxylate (see *Exper. Part*).

The doubly ^{13}C-labelled ADM, which reacted with guajazulene to yield [1,2-$^{13}C_2$]-**1**, has been obtained from 1,2-dibromo[$^{13}C_2$]ethane[8]) *via* [$^{13}C_2$]vinylbromid, dilithium [$^{13}C_2$]acetylide and [1,2-$^{13}C_2$]acetylenedicarboxylic acid (see *Exper. Part*).

The results of the thermal rearrangement of labelled **1** are outlined in *Scheme 5*. Heating of [3-^2H]-**1** resulted exclusively in the formation of [4-^2H]-**2** labelled between the two methoxycarbonyl groups.

The ^2H-NMR spectrum of [4-^2H]-**2** in $CHCl_3$ showed only one ^2H signal at 7.82 ppm which is in perfect agreement with the position of the ^1H signal of H–C(4) of **2** in the ^1H-NMR spectrum[9]). This finding is in agreement with an interchange of C(2) and C(3) in **1** but does not exclude a peripheral interchange of ^2H at C(3) and the $COOCH_3$ group at

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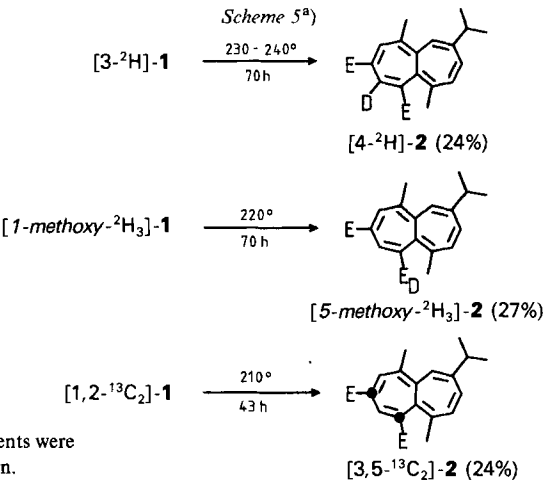
[8]) ^{13}C-Content at both C-atoms 99%. The material was diluted with the unlabelled compound to give a ^{13}C-content of ~ 14%.

[9]) The position of the label in [4-^2H]-**2** can also be deduced from its ^{13}C-NMR spectrum which shows for C(4) in the ^1H-decoupled mode a triplet, caused by the direct C, ^2H-coupling.

Scheme 5[a])

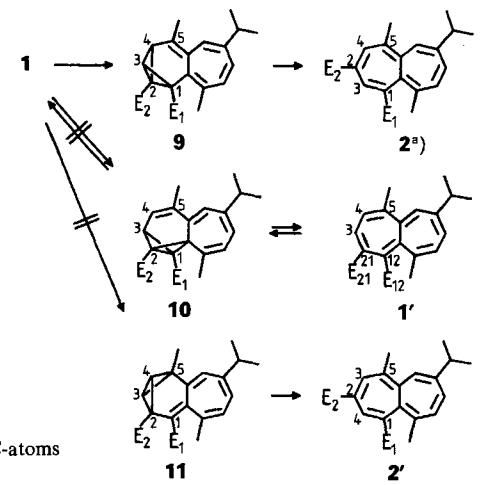


[a]) All heating experiments were carried out in tetralin.

C(2). That, indeed, solely the $COOCH_3$ group at C(2) is involved in the rearrangement, follows from the observation that the thermal reaction of [*1-methoxy*-$^2H_3$]-**1** leads to the exclusive formation of [*5*-methoxy-$^2H_3$]-**2**. This product showed only the signal of the $COOCH_3$ group at C(3) in its ^{1}H-NMR spectrum (*cf. Exper. Part* and [3]).

The occurrence of a skeletal rearrangement can unequivocally be deduced from the result of the thermal transformation of [1,2-$^{13}C_2$]-**1** which led to the formation of [3,5-$^{13}C_2$]-**2**. Whereas [1,2-$^{13}C_2$]-**1** exhibited $^1J(^{13}C(1),^{13}C(2)) = 61.0$ Hz and $^1J(^{13}C(2),^{13}C(3)) = 69.0$ Hz (*cf.* [1]), the rearranged product did not show such couplings. However, for C(4) beside a *singlet* (^{1}H-decoupled ^{13}C-NMR spectrum), a weak *'triplet'* with $^1J(C(4),C(5)) + {}^1J(C(4),C(3)) = 126$ Hz was observed indicating that the ^{13}C-label is located at C(3) and C(5)[10]).

Scheme 6

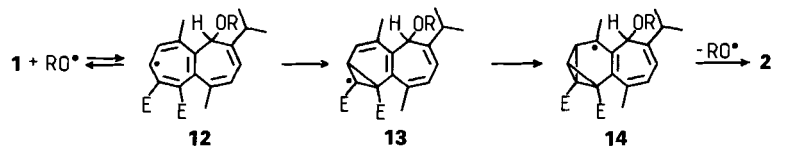


[a]) Numbering of the C-atoms as in **1**.

[10]) As a rule, in olefins $^2J(C, C) < 1$ Hz (*cf.* [10]).

Thus, there is no doubt that the rearrangement **1**→**2** occurs by skeletal interchange of C(2) and C(3), *i.e.* by cleavage of the C(1)–C(2) and C(3)–C(4) bonds and concomitant formation of the C(1)–C(3) and C(2)–C(4) bonds. This would imply that a 2,4-disubstituted bicyclobutane **9** is the intermediate in the rearrangement **1**→**2** *(Scheme 6)*[11]). Other bicyclobutane intermediates such as **10** or **11** can be excluded since **10** would lead to an interchange of C(1) and C(2) in the starting heptalene, and further reaction of **11** would result in the formation of **2** with the C-atom sequence 1,4,3,2 as compared to the starting material. 2,4-Disubstituted bicyclobutanes have also been postulated as intermediates in the thermal rearrangement of naphthalene, azulene, and related aromatic compounds (*cf.* [10]). In our case, however, we have evidence that the rearrangement **1**→**2** may be induced by reversible addition of a radical – possibly an alkoxy radical generated by thermal decomposition of an hydroperoxide of the solvent – to the heptalene skeleton. The radical addition at C(6) is demonstrated in *Scheme 7*[12]).

Scheme 7



12 **13** **14**

Formation of the methoxycarbonyl-stabilized cyclopropyl radical **13** (*cf.* [13]) can be postulated, since the cycloheptatrienyl radical **12** is energetically rather unfavourable. The rearrangement of **13** to the bicyclobutylmethyl radical **14** corresponds to the transformation of a homoallyl radical into a cyclopropylmethyl radical (*cf.* [14]). The final step consists of the radical cleavage of the C(1)–C(2) bond followed by loss of the added radical under rupture of the C(3)–C(4) bond and formation of **2**. Furthermore, the sequential bond cleavage in the final step can also start at the C(3)–C(4) bond. Alternatively, the radical **12** could undergo an electrocyclic ring closure (formation of the C(2)–C(4) bond) in analogy to the well-established interchange of cycloheptatriene and bicyclo[4.1.0]heptadiene. Subsequent bond formation between C(1) and C(3) would also lead to **14**. The experiments with labelled **1** exclude again the intermediate appearance of bicyclobutylmethyl radicals other than **14** (*cf.* radicals corresponding to **10** and **11** in *Scheme 6*). No doubt, there are ambiguities with respect to the operating mechanism of the observed σ-skeletal rearrangement of heptalene, as it is also the case in numerous σ-skeletal rearrangements of aromatic compounds (*cf.* [5]).

Structural Features and Spectroscopic Properties of 1 and 2. – The constitutions of **1** and **2** can unambiguously be deduced from the corresponding ^{1}H-, ^{13}C-NMR and mass

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[11]) For a bisbicyclobutane derivative as intermediate in the synthesis of heptalene, see [11]. The facility of thermal ring opening of alkoxycarbonyl-substituted bicyclobutanes to yield the corresponding 1,3-butadienes is well-documented (*cf.* [12] and lit. cited therein).

[12]) Comparable radical intermediates can be formulated if RO· or a similar radical is added at C(5), C(7), or C(8). An addition at C(2) can also be considered. In this case, the formulation of a bicyclobutane intermediate can be avoided, when we assume that the cyclopropylmethyl radical would undergo a rearrangement *via* cleavage of the C(1)–C(2) bond and formation of the new C(2)–C(4) bond. Elimination of the added radical from this intermediate under concomitant cleavage of the C(3)–C(4) bond would also lead to **2**.

spectra (see below and [3]). To get more insight into their structural features, we performed additionally an X-ray analysis of **1** as well as **2**, and tried to correlate the crystal data with the NMR data from solution.

X-Ray Analyses. – The triclinic yellow crystals of **1** as well as the monoclinic red crystals of **2** form a racemate (*cf.* [9])[13]. A stereoscopic view of the X-ray structures of **1** and **2** in the (*P*)-configuration is shown in *Fig. 1a* and *1b*. Bond lengths and angles in **1** and **2** are collected in *Table 1*. They clearly show that **2** possesses in the crystal the structure of a heptalene-3,5-dicarboxylate. This holds also for **2** in solution at temperatures $< 20°$ (*cf.* [3] and below). For both molecules, we recognize a clear alternation between C–C and C=C bonds around the perimeter. The three central σ-bonds in both molecules (aver. 1.483 and 1.480 Å) are slightly longer than the four remaining C–C bonds in the skeletons (aver. 1.448 and 1.449 Å). The C=C bonds (aver. 1.346 and 1.349 Å) are considerably shorter. The average ring bond angles (122.6 and 123.0°) are somewhat greater than 120° expected for an sp^2 hybridised C-atom but well smaller than the average value required (128.6°) to form a planar seven-membered ring. The two heptalene ring systems are, therefore, far from flat, and the largest distortions from planarity are found in the region where the two rings meet. Thus, the torsion angles of the three sequential single bond vectors in **1** and **2** are −112.7° and −123.2°, respectively, and it is in this region that the strain energy must be compensated. It is interesting to note that this difference of 10.5° is consistent with a reduction of strain in going from **1** to **2**, but one cannot exclude the possibility that it arises from the differences in packing forces in the two crystals.

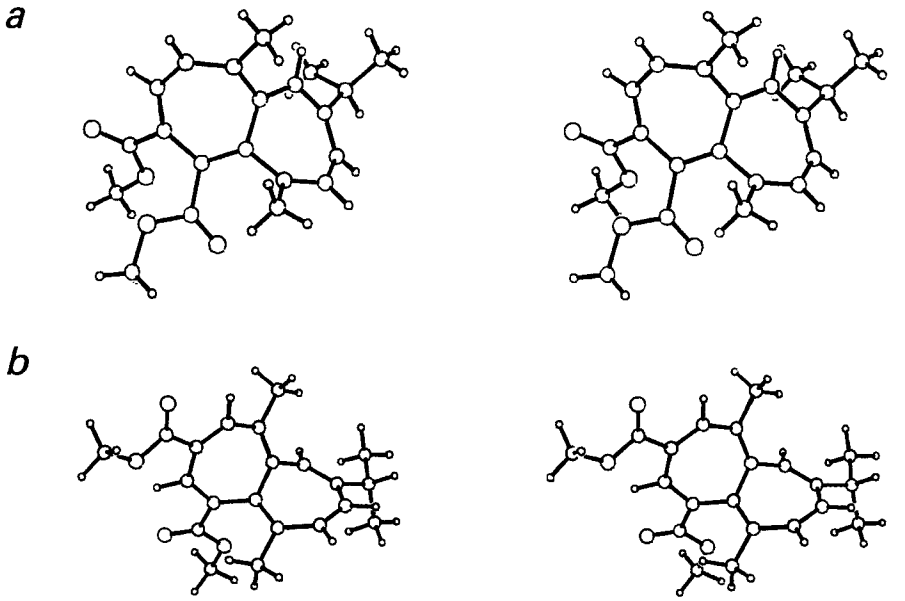
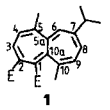
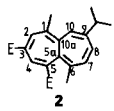


Fig. 1. *Stereoscopic projection of the X-ray structure of* **1** (a) *and* (b) *in the* (P)*-configuration*

[13] *Crystal Data of* **1**. Space group and cell dimensions: triclinic $P\bar{1}$, with $a = 9.470$ (2), $b = 9.916$ (2), $c = 10.684$ (2) Å, $\alpha = 95.36$ (3)°, $\beta = 97.13$ (3)°, $\gamma = 97.59$ (3)°; $D = 1.15$ Mgm^{-3}. $Z = 2$. *Data collection. Crystal size:* $0.4 \times 0.45 \times 0.45$ mm^3; temp. 293°K; wavelength: 0.71069 Å; total data measured: 3459 (excluding standards), total data observed: 2402. The structure was determined by direct methods. Refinement proceeded smoothly to convergence at $R = 0.058$ with anisotropic refinement of all non-H-atoms.
Crystal Data of **2**. Space group and cell dimensions: monoclinic, $P2_{1/n}$, with $a = 14.303$ (3), $b = 9.533$ (2), $c = 13.883$ (3) Å, $\beta = 91.86°$; $D = 1.19$ Mgm^{-3}, $Z = 4$. *Data collection. Crystal size:* $0.45 \times 0.45 \times 0.45$ mm^3; temp.: 293°K; wavelength: 0.71069 Å; total data measured: 3325 (excluding standards), total data observed: 2164. The structure was determined by direct methods. Refinement proceeded smoothly to convergence at $R = 0.055$ with anisotropic refinement of all non-H-atoms.

Table 1. *Bond Lengths and Valence Angles of the Heptalene Skeleton of* **1** *and* **2**

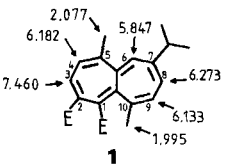

1


2

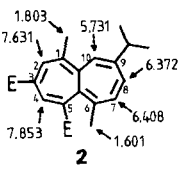
	Bond lengths [Å]			Valence angles [°]	
	1	**2**		**1**	**2**
C(1)–C(2)	1.473	1.443	C(1)–C(2)–C(3)	124.4	129.5
C(2)–C(3)	1.348	1.355	C(2)–C(3)–C(4)	128.6	124.1
C(3)–C(4)	1.441	1.446	C(3)–C(4)–C(5)	125.5	124.8
C(4)–C(5)	1.339	1.347	C(4)–C(5)–C(5a)	120.4	121.5
C(5)–C(5a)	1.481	1.486	C(5)–C(5a)–C(10a)	114.5	113.8
C(5a)–C(6)	1.343	1.347	C(5a)–C(10a)–C(1)	122.7	122.0
C(5a)–C(10a)	1.479	1.477	C(10a)–C(5a)–C(6)	122.2	123.3
C(6)–C(7)	1.447	1.452	C(5a)–C(6)–C(7)	127.2	122.4
C(7)–C(8)	1.358	1.340	C(6)–C(7)–C(8)	121.6	128.7
C(8)–C(9)	1.430	1.453	C(7)–C(8)–C(9)	127.5	128.0
C(9)–C(10)	1.338	1.345	C(8)–C(9)–C(10)	127.7	122.3
C(10)–C(10a)	1.488	1.477	C(9)–C(10)–C(10a)	119.4	123.7
C(1)–C(10a)	1.351	1.357	C(10)–C(10a)–C(5a)	111.4	115.4
			C(10a)–C(1)–C(2)	123.4	123.4

^{1}H-NMR Data. – Whereas the ^{1}H-NMR spectrum of **1** shows no temperature dependence up to 180°, the spectrum of **2** exhibits strong changes in the temperature range of 0° to +50° due to a rapid double-bond shift (*cf.* [1] [3]). The ^{1}H-NMR spectrum at 20° is only compatible with the structure of a heptalene-3,5-dicarboxylate as established also by the X-ray analysis. The most important chemical shifts and coupling constants of **1** and **2** are shown in *Scheme 8*. The ^{1}H-signals were assigned according to the observed position, coupling pattern, NOE, and G-values in the presence of Eu(fod)$_3$ (*cf.* [15]). The location of the double and single bonds of the heptalene skeleton is unequivocally given by the vicinal H,H-coupling constants. ^3J = 6.3 and 6.5 Hz in **1**, and 11.5 Hz in **2** is only compatible with the structures shown *(Scheme 8)*. If we assume that a hypothetical planar heptalene of type **1** with localized double bonds exhibits ^3J(–CH=CH–) ≈ 11.5 Hz and ^3J(=CH–CH=) ≈ 8.5 Hz[14]), we can calculate the torsional angle between

Scheme 8



1



2

δ [ppm] in $CDCl_3$

H,H-coupling constants [Hz]
^3J(3,4) = 6.3[a])
^3J(8,9) = 6.5
^4J(6,8) ≈ 1

H,CH$_3$-coupling constants [Hz]
^4J(4,5) = 1.4
^4J(9,10) = 1.3
^5J(3,5) = 1.0

H,H-coupling constants [Hz]
^3J(7,8) = 11.5
^4J(8,10) = 1.2
^4J(2,4) ~ 0.5

H,CH$_3$-coupling constants [Hz]
Not recognizable, *i.e.* ^4J < 0.5

[a]) Numbers in parentheses refer to the positions of the coupled protons and/or to the position of the CH_3 group.

[14]) Corresponds to ^3J(=CH–CH=) of 1,2-benzazulene in which ^3J(–CH=CH–) = 10.9 Hz (*cf.* [16]).

C(3),C(4) and C(8),C(9) applying the *Karplus* equation $^3J(H,H) = J^\circ \times \cos^2\theta - 0.3$ (*cf.* [17]) to be in the order 33 and 31°, respectively. This is in excellent agreement with the corresponding torsional angles (32.0 and 33.2°, respectively) determined by the X-ray analysis *(cf. Table 1)*.

Table 2. *^{13}C-NMR Data* ($CDCl_3$) *of* **1** *and* **2**[a])

C-Atom	δ [ppm]	G-value[b]) [ppm]	Coupling constants[c]) [Hz]
C(1)	123.24	10.9	^3J(H–C(3),C(1)) = 9.5
	128.05	6.9	
C(2)	132.23	19.9	^1J(H–C(3),C(2)) ≈ 4, ^3J(H–C(4),C(2)) ≈ 8–9
	146.01	16.5	^1J(H–C(2), C(2)) = 156, ^3J(H–C(4), C(2)) ≈ ^3J(CH_3–C(1),C(2)) ≈ 4
C(3)	139.76	14.6	^1J(H–C(3), C(3)) = 158.7
	129.23	24.0	
C(4)	125.58	4.2	^1J(H–C(4),C(4)) = 156
	137.34	16.2	^1J(H–C(4),C(4)) = 162, ^3J(H–C(2),C(4)) = 9
C(5)	144.06	3.1	
	125.12	12.4	
C(5a)	131.89	3.6	
	133.49	4.5	
C(6)	125.50	1.8	^1J(H–C(6),C(6)) = 156
	129.30	5.5	
C(7)	148.43	1.7	
	136.22	2.1	^1J(H–C(7),C(7)) = 154
C(8)	125.74	2.1	^1J(H–C(8),C(8)) = 152
	131.99	1.4	^1J(H–C(8),C(8)) = 156
C(9)	127.47	2.2	^1J(H–C(9),C(9)) = 154; ^3J(CH_3–C(10),C(9)) = 6.4
	150.39	1.7	
C(10)	143.75	5.6	
	121.35	2.4	^1J(H–C(10),C(10)) = 158; ^3J((CH_3)$_2$C*H*–C(9),C(10)) ≈ ^3J(H–C(8),C(10)) ≈ 5
C(10a)	128.60	3.2	^3J(H–C(6),C(10a)) ≈ ^3J(H–C(9), C(10a)) ≈ 7
	142.00	5.2	
CH_3–C(5)	25.36	1.4	^3J(CH_3–C(5),H–C(4)) = 6.0
CH_3–C(1)	17.73	0.95	^3J(CH_3–C(1),H–C(2)) = 4.5
CH_3–C(10)	22.34	2.5	^3J(CH_3–C(10),H–C(9)) = 6.4
CH_3–C(6)	17.63	4.1	^3J(CH_3–C(6),H–C(7)) = 3.5
(CH_3)$_2$CH–C(7)	35.67	0.9	^1J((CH_3)$_2$*C*H) = 127.5
(CH_3)$_2$CH–C(9)	35.09	1.0	^1J((CH_3)$_2$*C*H) = 128
(*C*H_3)$_2$CH–C(7)	23.09	0.6	
	22.48	0.6	
(*C*H_3)$_2$CH–C(9)	22.86	0.7	
	22.62	0.7	
CH_3OOC–C(1)	167.87	8.7	No coupling with H–C(3)
CH_3OOC–C(5)	165.89	19.7	
CH_3OOC–C(2)	167.33	47.1	^3J(H_3COOC–C(2),H–C(3)) = 7.5
CH_3OOC–C(3)	166.98	56.1	
CH_3OOC–C(1)	51.96	1.6	
CH_3OOC–C(5)	52.05	7.3	
CH_3OOC–C(2)	51.95	4.8	
CH_3OOC–C(3)	52.05	22.0	

[a]) 100.6-MHz ^{13}C-NMR spectra; first row: data of **1**, second row: data of **2**. [b]) Shift reagent: Yb(dpm)$_3$ (*cf.* [18]). [c]) From 'gated-decoupled' spectra.

The location of the double bonds follows also from the observed allylic coupling constants between the protons at the heptalene ring and the adjacent CH_3 groups. Thus, $^4J(4,5) = 1.4$ and $^4J(9,10) = 1.3$ *(cf. Scheme 8)* are in agreement with the locations of double bonds between C(4) and C(5), and C(9) and C(10), respectively. On the other hand, heptalene **2** does not show such coupling constants in agreement with the location of a single bond between C(1) and C(2), and C(6) and C(7).

The label in [3-^{2}H]-**1** and [4-^{2}H]-**2** could clearly be localized at C(3) and C(4), respectively, since the signal for H–C(3) in **1** was missing, H–C(4) showed no vicinal coupling with H–C(3), and in **2** the lowest field signal at 7.85 ppm was absent. The label could also be localized in the ^{13}C-NMR spectrum of [3-^{2}H]-**1** and [4-^{2}H]-**2** (see below).

The position of the label in [*1-methoxy*-$^2H_3$]-**1** follows from the synthesis of this compound (see *Scheme 4*) and from its ^{13}C-NMR spectrum (see below). In the ^{1}H-NMR spectrum, both $COOCH_3$ groups show identical ($CDCl_3$) or nearly identical (CCl_4) chemical shifts, but different G-values (Eu(fod)$_3$ in $CDCl_3$) of 2.28 (CH_3OCC–C(1)) and 5.64 (CH_3OOC–C(2)). In the rearranged product **2**, both $COOCH_3$ groups can easily be differentiated (CH_3OCC–C(3) at 3.83 and CH_3OOC–C(5) at 3.74 ppm). The $COOCH_3$ group at C(5) shows a NOE of 0.6% when the CH_3 group at C(6) is irradiated. The product obtained from the rearrangement of [*1-methoxy*-$^2H_3$]-**1** exhibited only the signal of the $COOCH_3$ group at C(3), *i.e.* at 3.83 ppm.

^{13}C-NMR Data. – The data for **1** and **2** are collected in *Table 2*. The ^1J(C,H) values are in the range of those of olefins (*cf.* propene with ^1J(C,H) = 152–157 Hz; see [18] and lit. cited therein). They easily allow to assign the C-atoms next to the $COOCH_3$ group carrying C-atoms since the electron-acceptor effect of the $COOCH_3$ group augments the ^1J(C,H) values (*cf. Table 3*, C(3) of **1** and C(4) of **2**; *cf.* [18]).

The ^3J(H,C) values of couplings between H- and C-atoms of the skeleton as well as those between H-atoms of the skeleton and the C-atom of CH_3 groups at the skeleton allow to locate the C,C single and double bonds. Thus, $^3J(CH_3$–C(5),H–C(4)) = 6.0 and $^3J(CH_3$–C(10),H–C(9)) = 6.4 Hz of **1** clearly show that a double bond is located between C(4) and C(5), and C(9) and C(10), respectively. On the other hand, the corresponding coupling constants of **2**, namely $^3J(CH_3$–C(1),H–C(2)) = 4.5 and $^3J(CH_3$–C(6),H–C(7))

Table 3. *^1J(^{13}C,^{13}C) Values in Heptalenes*

Heptalene[a])	^1J [Hz]			
	C(1),C(2) or C(4),C(5)[b])	C(2),C(3) or C(3),C(4)[b])	C(1),CH_3OOC–C(1)	C(2),CH_3OOC–C(2)
[1,2-$^{13}C_2$]-**1**	61.0	69	74	71
[1,2-$^{13}C_2$]-**3**	61.4	72	–[c])	–
[3,5-$^{13}C_2$]-**2**	> 63*[d])	68	–	–
[4,5-$^{13}C_2$]-**15**	74.3*	57*	–	–

[a])  and  (*cf.* [1]).

[1,2-$^{13}C_2$]-**3** [4,5-$^{13}C_2$]-**15**

[b]) Marked with *.

[c]) Not determined.

[d]) Only [^1J(C(3),C(4)) + ^1J(C(4),C(5))] = 126 could be determined.

= 3.5 are only compatible with the location of a single bond between C(1) and C(2), and C(6) and C(7), respectively[15]). For the coupling between H–C(2) and C(4) which corresponds to an olefinic *trans*-coupling constant (^3J(H,C)) (*cf.* [10] [18] [19]), we observed a value of 9 Hz, whereas the inverse ^3J(H,C) (coupling between H–C(4) and C(2)), which can be compared to ^3J(H,C) of an H-atom of an α-substituent of an olefin and C(β) of the olefin (*cf.* [10] [18]), is of the order of 4 Hz.

Table 4. *MS Data of* **1**, **2**, **3**, *and* **16** *at 70 eV*

Ion	*m/z* (rel.-%)			
	1[a])	**2**[a])	**3**[b])	**16**[c])
M^+	340 (73.5)	340 (100)	326 (93.5)	368 (100)
$M^+ - CH_3$	325 (16.5)	325 (22.5)	311 (19)	353 (24)
$M^+ - CH_3O^·$	309 (23)	309 (17.5)	295 (17.5)	337 (14)
$M^+ - CH_3OH$	308 (19.5)	308 (17)	294 (11)	?
$M^+ - CH_3C{\equiv}CH$	300 (12.5)	300 (23)	286 (8.5)	328 (4)
$M^+ - (CH_3^· + CH_3OH)$	293 (17.5)	293 (16)	279 (30.5)	321 (27)
$M^+ - CH_3OOC^·$	281 (26.5)	281 (22)	267 (22.5)	309 (21)
$M^+ - RC{\equiv}CH$[d])	272 (13)	272 (35)	286 (8.5)	286 (26)
$M^+ - (CH_3^· + CH_3OH + CO)$	265 (10)	265 (10.5)	251 (9.5)	?
$M^+ - HC{\equiv}CCOOCH_3$	256 (16)	256 (58)	242 (9)	284 (7)
$M^+ - CH_3C{\equiv}CCOOCH_3$	242 (31.5)	242 (91.5)	228 (31)	270 (28)
$M^+ - (H_3COOC^· + CH_3OH + CO)$	221 (16.5)	221 (9)	207 (25)	?
M^+ – ADM	198 (100)	–	184 (100)	226 (66)
$M^+ - (CH_3^· + ADM)$	183 (33)	–	169 (13.5)	?

[a]) *Cf.* [3]. [b]) *Cf.* [9]. [c]) *Cf.* [1]. [d]) **1**: R = i-Pr; **2**: R = i-Pr; **3**: R = Me; **16**: R = *t*-Bu.

Table 3 contains the $^1J(^{13}C,^{13}C)$ values which we found in the ^{13}C-labelled heptalenes. Again, they reflect the olefinic nature of the heptalenes (*cf.* [10] [18]) and, in addition, the position of a double or single bond between the corresponding C-atoms in the skeleton. Thus, ^1J(C,C) values of 60 ± 3 Hz are only compatible with a single bond between the coupled partner, whereas ^1J(C,C) values of 71 ± 3 Hz are found for C-atoms linked by a double bond.

Mass Spectra. – The MS behaviour of **1** and **2** are determined by the loss of acetylenic units and fragments of the ester groups. In *Table 4*, the mass spectra of **1**, **2**, **3**, and dimethyl 8-(*tert*-butyl)-5,6,10-trimethylheptalene-1,2-dicarboxylate (**16**) are compared [1]. It is of interest to note that the extent of the loss of the acetylenic component is correlated with the stability of the acetylenes. Thus, the intensity of the fragment ion ($M^+ - RC{\equiv}CH$) increase with R = CH_3 (8.5 rel.-%; **3**), *i*-C_3H_7 (13 rel.-%; **1**), and *t*-C_4H_9 (26 rel.-%; **16**). The same trend holds for the loss of methyl propiolate and ADM. The signal of the ($M^+ - HC{\equiv}CCOOCH_3$) ion is in MS of **2** roughly 3 times more intense than in that of **1**. This observation is in agreement with the statistically 3 times greater possibility in **2** to lose methyl propiolate [3]. The position of the label in [3-^{2}H]-**1** and [4-^{2}H]-**2** can easily be verified by their mass spectra: the first compound loses mainly

[15]) These differences in ^3J(H, C) which are in agreement with ^3J(H, C) observed in olefins and cyclic conjugated π-systems (*cf.* [10] [18]) are nicely demonstrated by the two ^3J(H, C) values observed for CH_3–C(8) in **3** and **15** (cf. *Table 3*) which are in the order of 7.0 and 7.4 (coupling with H–C(7)), and 3.5 and 3.8 (coupling with H–C(9)), respectively.

$[^2H]C{\equiv}CCOOCH_3$ and the latter more $[^2H]C{\equiv}CCOOCH_3$ than $HC{\equiv}CCOOCH_3$ in accordance with location of the ^2H label between the ester groups at C(3) and C(5). Similarly, [*5-methoxy*-$^2H_3$]-**2** loses preferentially $HC{\equiv}CCOOCH_3$ since the signal at *m/z* 259 is more than 5 times as intense as the signal at *m/z* 256 ($M^+ - HC{\equiv}CCOOC[^2H_3]$).

The loss of methyl tetrolate ($CH_3C{\equiv}CCOOCH_3$) from the parent ion is common to all heptalenes in *Table 4*. The rationalization of this fragmentation is not clear at the moment. In the case of **1** and **2** the loss of $C_5H_6O_2$ was secured by high-resolution MS which yielded signals at *m/z* 242.1328 and 242.1283, respectively, corresponding to an atomic composition of $C_{16}H_{18}O_2$ of the fragment ions [3]. The MS of [*1-methoxy*-$^2H_3$]-**1** and [*5-methoxy*-$^2H_3$]-**2** clearly show that the $COOC[^2H_3]$ group at C(1) and C(5), respectively, is involved in this fragmentation, since only the loss of $CH_3C{\equiv}CCOOC[^2H_3]$ is observed.

The basis signal in the mass spectrum of **6** *(cf. Scheme 2)* corresponds to the loss of $(CH_3)_2CHC{\equiv}CCOOCH_3$, whereas the signal for the loss of ADM is not observed. This is a good indication for the skeletal rearrangement also in the case of heptalene **5**.

We thank Dr. *P. Bischofberger*, Dr. *M. Cosandey*, and *F. Nydegger*, Institut de chimie organique de l'Université de Fribourg, and our colleagues in the department of physics of the Central Research Units of *F. Hoffmann-La Roche & Co., Ltd.*, Basle for IR, NMR, and mass spectra as well as for GC, HPLC and elemental analyses. We gratefully acknowledge partial support of this work by the *Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung*, and *P. B.* expresses his gratitude to the personnel department of *F. Hoffmann-La Roche & Co., Ltd.*, Basle for grant of a scholarship.

Experimental Part

General. See [1]. ^{13}C-NMR spectra at 100.6 and 25.2 MHz were registered on *Bruker-Spectrospin-WM-400* and *Varian-XL-100* instruments, respectively.

1. Syntheses of Labelled Heptalenes. – 1.1. *Dimethyl 7-Isopropyl-5,10-dimethyl-[3-^2H]heptalene-1,2-dicarboxylate* ([3-^2H]-**1**). 1.1.1. *[3-^2H]Guajazulene.* D_2O (5.0 ml) and D_2SO_4 (3.6 ml; 98% $[^2H]$) were mixed under ice cooling. To this mixture was added finely powdered guajazulene (1.0 g, 5.04 mmol). After 1 h stirring at r.t. all guajazulene was dissolved. The mixture was diluted with D_2O (14 ml) and the precipitated [3-^2H]guajazulene extracted with Et_2O. After washing with $NaHCO_3$ soln. and drying (Mg_2SO_4), the Et_2O was evaporated (RE). The residual blue oil (0.99 g) crystallized after 1 h at r.t.; m.p. 27–28°. ^1H-NMR (90 MHz, $CDCl_3$): 7.61 (*s*, 1.00 H, H–C(2)). No signal could be integrated at 7.21 (H–C(3)). ^{13}C-NMR (25.2 MHz, $CDCl_3$): All signals unchanged with respect to guajazulene except for C(3) at 112.8 which appeared as *t* in the 'off-resonance' spectrum. MS: 200 (17, $M^+ + 1$), 199 (100, M^+), 198 (14.5), 184 (97); *cf.* MS of guajazulene with: 199 (18, $M^+ + 1$), 198 (100, M^+), 197 (8.5). From this, the $[^2H]$content was estimated: 0.94 ^2H/molecule.

1.1.2. *Thermal Reaction of [3-^2H]Guajazulene with ADM.* The deuterated azulene (483.5 mg, 2.4 mmol) and ADM (0.34 ml) were dissolved in 9.7 ml freshly distilled tetralin and heated at reflux (220°). Over a period of 4.5 h, additional ADM (in total 0.23 ml) was added in two portions. Tetralin was evaporated (RE) and the brown residue was purified by chromatography on silica gel (hexane/Et_2O 7:3) to yield [3-^2H]-**1** (417 mg, 50.3%) and dimethyl 7-isopropyl-4-methyl-[3-^2H]azulene-1,2-dicarboxylate (65 mg, 9%; according to ^1H-NMR: 0.25 H at C(3)).

*[3-^2H]-***1**. M.p. 139–141°. ^1H-NMR (100 MHz, $CDCl_3$): At 7.46 (H–C(3)) 0.26 H was integrated taking H–C(6) (br. *s* at 5.85) as integration standard. ^{13}C-NMR (25.2 MHz, CCl_4): identical with that of the unlabelled compound *(cf. Table 3)* with the exception of the signals at 165.6 (*s*, CH_3OOC–C(2)), 138.3 (*t*, C(3)), and 132.4 (*s*, C(2)) which were distinctly reduced in their intensity as compared to those of **1**. MS[16]: 342/341/340 (26/90/23, M^+), 326 (22), 310 (28), 309 (26), 301 (14), 300 (5.5), 294 (17), 282 (35), 273 (13), 266 (22), 257 (8, $M^+ - HC{\equiv}CCOOCH_3$), 256 (19, $M^+ - [^2H]C{\equiv}CCOOCH_3$), 243 (37), 222 (17), 208 (15), 200 (21), 199 (100), 198 (30).

[16]) For interpretation see *Table 4*.

1.2. *Methyl 7-Isopropyl-1-[$^2H_3$]methoxycarbonyl-5,10-dimethylheptalene-2-carboxylate* ([*1-methoxy*-$^2H_3$]-**1**). 1.2.1. *Di[$^2H_3$]methyl Acetylenedicarboxylate* ([$^2H_6$]ADM). A mixture of acetylenedicarboxylic acid (12.5 g, 0.109 mol), [$^2H_4$]methanol (99.5% ^2H; 10.0 g, 0.277 mol), conc. H_2SO_4 (4.5 g) and benzene (25 ml) was heated during 5 h at reflux. Workup (dilution with sat. NaCl soln. extraction with Et_2O) yielded [$^2H_6$]ADM (13.0 g, 81%) after fractional distillation (30° at 0.04 Torr) as colourless, clear liquid. MS: 148 (5, M^+), 114 (100, $M^+ - CD_3O^\cdot$).

1.2.2. *Di[$^2H_3$]methyl 7-Isopropyl-5,10-dimethylheptalene-1,2-dicarboxylate* ([*methoxy,methoxy*-$^2H_6$]-**1**). Guajazulene (12.5 g, 63 mmol) and [$^2H_6$]ADM (9.3 g, 63 mmol) were dissolved in tetralin (39 ml) and heated during 4 h at reflux (220°). Workup (see. *1.1*) yielded *di[$^2H_3$]methyl 7-isopropyl-4-methylazulene-1,2-dicarboxylate* (680 mg, 3.5%) and [*methoxy,methoxy*-$^2H_6$]-**1** (8.93 g, 41%). ^{1}H-NMR (90 MHz, CCl_4): no signals could be integrated about 3.60 (CH_3OOC–C(1) and –C(2)). ^{13}C-NMR (25.2 MHz, $CDCl_3$): identical with that of **1** with the exception of the signal at 51.2 (CH_3OOC–C(1) and –C(2)) which appeared as *m* in the 'off-resonance' spectrum. MS[16]): 346 (86, M^+), 331 (12), 328 (6, $M^+ - C[^2H_3]$), 312 (22, $M^+ - C[^2H_3]O^\cdot$), 311 (21, $M^+ - C[^2H_3]OH$), 306 (13), 296 (13, $M^+ - (CH_3 + C[^2H_3]OH)$), 284 (27, $M^+ - C[^2H_3]OOC^\cdot$), 278 (15), 259 (15, $M^+ - HC{\equiv}CCOOC[^2H_3]$), 245 (31, $M^+ - CH_3C{\equiv}CCOOC[^2H_3]$), 221 (13), 213 (13), 198 (100).

1.2.3. *7-Isopropyl-1-[$^2H_3$]methoxycarbonyl-5,10-dimethylheptalene-2-carboxylic Acid* (*methoxy*-$^2H_3$]-**8**) (*cf.* [1]). KOH (25.8 g) was dissolved in EtOH/H_2O (120 ml each), and the diester [*methoxy,methoxy*-$^2H_6$]-**1** (5.0 g, 14.5 mmol) added to this soln. at 28°. The acid [*methoxy*-$^2H_3$]-**8** was isolated after 25 h, and recrystallized several times from Et_2O/hexane. IR (CCl_4): 1737, 1717, 1690 (COOH and COOR). ^{1}H-NMR (90 MHz, $CDCl_3$): no signal could be integrated at ~ 3.69 (CH_3OOC–C(1)). ^{13}C-NMR (25.2 MHz, [$^2H_6$]acetone)[17]): 168.0 (*s*); 148.9 (*s*); 144.7 (*s*); 143.3 (*s*); 140.1 (*d*); 133.3 (*s*); 132.8 (*s*); 129.4 (*s*); 127.9 (*d*); 126.2 (2*d*); 125.8 (*d*); 124.7 (*s*); 51.1 (*sept.*); 36.2 (*d*); 25.3 (*q*); 23.3 (*q*); 22.7 (*q*); 22.5 (*q*). MS: 330 (8), 329 (22, M^+), 326 (29), 294 (100, $M^+ - CD_3OH$), 250 (22), 235 (22), 226 (32).

1.2.4. *Esterification of* [*methoxy*-$^2H_3$]-**8** *with* CH_2N_2. The reaction was carried out as described in [1]. The mixed diester [*1-methoxy*-$^2H_3$]-**1** was recrystallized from Et_2O/hexane; m.p. 141–142°. IR (CCl_4): 2250/2190/2080 (C–H), 1725 (br., COOR). ^{1}H-NMR (90 MHz, CCl_4): 3.68 (*s*, CH_3OOC–C(1)); ~ 3.60 (CH_3OOC–C(2)) no signal > 0.01 H could be integrated, also after addition of Eu(fod)$_3$ (*cf.* [3]). ^{13}C-NMR (25.2 MHz, $CDCl_3$): the signal at 167.7 (*s*, C[$^2H_3$]OOC–C(1)) was reduced in its intensity by ~ 50% in comparison to the signal at 167.1 (*s*, CH_3OOC–C(2)). All other signals as given in *Table 2*. MS[16]): 343 (80), 328 (13), 325 (4), 312 (8), 311 (5), 309 (14), 308 (17), 303 (13), 296 (4), 293 (14), 284 (10), 281 (17), 275 (13), 259 (13, $M^+ - HC{\equiv}CCOOCH_3$), 256 (28, $M^+ - HC{\equiv}CCOOC[^2H_3]$), 221 (13), 210 (13), 198 (100).

1.3. *Dimethyl 7-Isopropyl-5,10-dimethyl-[1,2-$^{13}C_2$]heptalene-1,2-dicarboxylate* ([1,2-$^{13}C_2$]-**1**). 1.3.1. *Dimethyl [1,2-$^{13}C_2$]Acetylenedicarboxylate* ([$^{13}C_2$]ADM; *cf.* [20]). A mixture of 1,2-dibromoethane (11.0 g, 59 mmol) and 1,2-dibromo[$^{13}C_2$]ethane (2.0 g, 11 mmol; 99% 2H; from KOR isotopes) was added dropwise to a KOH soln. in 95% EtOH (15 g/75 ml) under vigorous stirring. The temp. raised to 50°. This temp. was maintained by heating until all formed [$^{13}C_2$]vinylbromide had been collected in a trap cooled with dry ice (reaction time *ca.* 1 h). The reaction apparatus was flushed with Ar, the distillate warmed up to 0°, washed 3× with ice water to remove EtOH, and, after drying, ($CaCl_2$) redistilled (2×). The purified [$^{13}C_2$]vinylbromide was dissolved in Et_2O (40 ml) and the soln. added at 0° under vigorous stirring to a 1.6M soln. of BuLi in hexane (44 ml) which had been diluted with Et_2O (85 ml). The milky mixture reacted for 1 h at 0° and then quenched with an excess of dry ice. 2N H_2SO_4 (55 ml) was added, the aq. phase saturated with NaCl and the [1,2-^{13}C]acetylenedicarboxylic acid extracted with Et_2O (3×). Evaporation of the solvent mixture (RE) yielded 2.0 g (22.6%) of the di-acid as residue which was dissolved in benzene (55 ml). To this mixture, MeOH (2.1 g, 66 mmol) and conc. H_2SO_4 (0.8 g) were added, and the mixture heated during 1.25 h under reflux. Workup yielded 1.73 g (17% overall yield with respect to 1,2-dibromo[$^{13}C_2$]ethane) of [$^{13}C_2$]ADM after bulb-to-bulb distillation. IR (film): 2145 (–C≡C–), 1724 (COOR). ^{13}C-content according to dilution: 16.4 atom-%.

1.3.2. *Thermal Reaction of [$^{13}C_2$]ADM with Guajazulene.* Freshly distilled guajazulene (1.15 g, 5.8 mmol) and [$^{13}C_2$]ADM (0.9 g, 6.3 mmol) were dissolved in tetralin (12 ml), and the blue soln. heated under Ar 1.5 h at 210°. The tetralin was evaporated (RE) and the oily brown residue separated with prep. TLC (Et_2O/hexane 1:1) to yield 4 fractions. The first fraction contained 0.32 g of starting azulene, the second yielded 93 mg (6.5%) of dimethyl (*E*)-1-(5′-isopropyl-3′,8′-dimethylazulen-1-yl)-[$^{13}C_2$]ethene-1,2-dicarboxylate[18]), and the third 0.59 g (41%) of [1,2-$^{13}C_2$]-**1** as well as 17 mg of dimethyl 7-isopropyl-4-methyl-[1,2-$^{13}C_2$]azulene-1,2-dicarboxylate[19]).

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[17]) *Cf. Table 2.*

[18]) MS: 342/341/340 (16.5/23/100, M^+) for the labelled and 342/341/340 (3.5/23/100, M^+), for the unlabelled compound.

[19]) MS: 302/301/300 (16.5/20/100, M^+) for the labelled and 302/301/300 (3/20/100, M^+), for the unlabelled compound.

[1,2-$^{13}C_2$]-1. M.p. 142–143° (Et_2O/hexane). ^{1}H-NMR (400 MHz, $CDCl_3$): identical with that of **1**, see *2.1.* ^{13}C-NMR (100.6 Hz, $CDCl_3$): identical with that of **1** *(cf. Table 2)* with the following exceptions: 123.24 (*d*, ^1J(C(1),C(2)) = 61.0, C(1)); 132.23 (*d*, ^1J(C(2),C(1)) = 61.0, C(2)); 139.76 (satellite *d*, ^1J(C(3),C(2)) = 69, C(3)); 167.33 (satellite *d*, ^1J(C(2'),C(2)) = 71, CH_3OOC(2')–C(2)); 167.87 (satellite *d*, ^1J(C(1'),C(1)) = 74 (CH_3OOC(1')–C(1)). MS: see *Table 5*. ^{13}C-content: 16.8 atom-%.

2. Thermal Rearrangement of Heptalene-1,2-dicarboxylates. – 2.1. *Rearrangement of* **1** (*cf.* [3]). Heptalene **1** (2.0 g, 5.9 mmol) was dissolved in freshly distilled tetralin (60 ml) and heated under Ar and stirring during 45 h at 210°[20]. Tetralin was evaporated (90°/0.05 Torr), and the red-to-brown coloured residue separated by prep. TLC (Et_2O/hexane 3:2) to yield 1.57 g (78.5%) of **1** and 0.43 g (21.5%) of *dimethyl 9-isopropyl-1,6-dimethylheptalene-3,5-dicarboxylate* (**2**) as red oil which crystallized upon standing over night. It was recrystallized from hexane/Et_2O to yield ruby crystals; m.p. 118–119°. UV (hexane): λ_{max} 210 (4.39), 279 (4.33), 334 sh (br., 3.50), 424 (br., 3.17); λ_{min} 244 (4.09), 376 (br., 3.14). IR (KBr): 1715/1708 (COOR). ^{1}H-NMR (400 MHz, $CDCl_3$; *cf.* [3]): 1.159 and 1.142 (*2d*, each 3H, ^3J((CH_3)$_2$CH–C(9)) = 6.3, (CH_3)$_2$CH–C(9)); 1.601 (*s*, CH_3–C(6)); 1.803 (*s*, CH_3–C(1)); 2.573 (*sept.*, ^3J((CH_3)$_2$CH–C(9)) = 6.3, (CH_3)$_2$CH–C(9)); 3.744 (*s*, CH_3OOC–C(5)); 3.829 (*s*, CH_3OOC–C(3)); 5.731 (br. *s*, H–C(10)); 6.372 (*dd*, ^3J(H–C(8),H–C(7)) = 11.5, ^4J(H–C(8),H–C(10)) = 1.2, H–C(8)); 6.408 (*d*, ^3J(H–C(7),H–C(8)) = 11.5, H–C(7)); 7.631 (br. *s*, H–C(2)); 7.853 (br. *d*, ^4J(H–C(4),H–C(2)) ≈ 0.5, H–C(4)). ^{1}H-DR-NMR: 1.601 (CH_3–C(6))→no effect; 1.803 (CH_3–C(1))→7.631 (H–C(2), signal sharpening); 2.573 ((CH_3)$_2$CH–C(9))→1.142 and 1.159 (2*s*, (CH_3)$_2$CH–C(9)); 5.731 (H–C(10))→6.372 (*d*, ^3J(H–C(8),H–C(7)) = 11.5, H–C(8)). ^{1}H-NOE: 1.601 (CH_3–C(6))→3.744 (CH_3OOC–(5), 0.6%), 6.408 (H–C(7), 5.1%), 6.372 (H–C(8), 5.1%), 7.853 (H–C(4), 2.3%); 1.802 (CH_3–C(1))→5.731 (H–C(10), 10%), 7.631 (H–C(2), 17%); 3.744 (CH_3OOC–C(5))→7.631 (H–C(2), no effect), 7.853 (H–C(4), 2.1%); 3.829 (CH_3OOC–C(3))→7.631 (H–C(2), 1.5%), 7.853 (H–C(4), 2.5%); 6.839 (H–C(8))→1.159 and 1.142 ((CH_3)$_2$CH–C(9), 32%), 2.573 ((CH_3)$_2$CH–C(9), 21%). ^{13}C-NMR (100.6 MHz, $CDCl_3$; *cf.* [3]): see *Table 2*. MS: see *Table 4* and *5*. Anal. calc. for $C_{21}H_{24}O_4$ (340.42): C 74.09, H 7.11; found: C 73.78, H 7.41.

Re-isolated **1**. M.p. 143–144° (Et_2O/hexane). ^{1}H-NMR (400 MHz, $CDCl_3$; *cf.* [3]): 1.054 and 1.092 (*2d*, each 3H, J((CH_3)$_2$CH–C(7)) = 6.8, (CH_3)$_2$CH–C(7)); 1.995 (br. *s*, CH_3–C(10)); 2.077 (br. *t*, ^4J(CH_3–C(5), H–C(4)) ≈ ^5J(CH_3–C(5), H–C(3)) ≈ 1.2, CH_3–C(5)); 2.482 (*sept.*, ^3J((CH_3)$_2$CH–C(7)) = 6.8, (CH_3)$_2$CH–C(7)); 3.707 (*s*, CH_3OOC–C(1) and –C(2)); 5.847 (br. *s*, H–C(6)); 6.133 (*dq*, ^3J(H–C(9),H–C(8)) = 6.5, ^4J(H–C(9),CH_3–C(10)) = 1.3, H–C(9)); 6.182 (*dq*, ^3J(H–C(4),H–C(3)) = 6.3, ^4J(H–C(4),CH_3–C(5)) = 1.4, H–C(4)); 6.273 (br. *d*, ^3J(H–C(8),H–C(9)) = 6.5, H–C(8)); 7.460 (*dq*, ^3J(H–C(3),H–C(4)) = 6.3, ^5J(H–C(3),CH_3–C(5)) = 1.0, H–C(3)). ^{1}H-DR-NMR: 1.995 (CH_3–C(10))→6.133 (*d*, ^3J(H–C(9),H–C(8)) = 6.5, H–C(9)); 6.273 (br. *d*, ^3J(H–C(8),H–C(9)) = 6.5, ^4J(H–C(8),H–C(6)) ≈ 1.0, H–C(8)); 2.077 (CH_3–C(5))→6.182 (*d*, ^3J(H–C(4),H–C(3)) = 6.3, H–C(4)); 7.460 (*d*, ^3J(H–C(3),H–C(4)) = 6.3, H–C(3)); 5.847 (H–C(6))→6.182 (signal sharpening, H–C(4)), 6.273 (signal sharpening, H–C(8)); 7.460 (H–C(3))→2.077 (*d*, ^4J(CH_3–C(5),C(4)) = 1.4, CH_3–C(5)); 6.182 (*q*-like *s*, ^4J(H–C(4), CH_3–C(5)) ≈ 1.4, H–C(4)). ^{1}H-NOE: 1.994 (CH_3–C(10))→6.133 (H–C(9), 11%); 2.077 (CH_3–C(5))→5.847 (H–C(6), 10%), 6.182 (H–C(4), 14%). ^{13}C-NMR (100.6 MHz, $CDCl_3$): see *Table 2*. MS: see *Table 4* and *5*. Anal. calc. for $C_{21}H_{24}O_4$ (340.42): C 74.09, H 7.11; found: C 74.09, H 7.14.

2.2. *Rearrangement of Dimethyl 5,6,8,10-Tetramethylheptalene-1,2-dicarboxylate* (**3**). The heptalene **3** (120 mg, 0.37 mmol) [1] was dissolved in tetralin (4 ml) and heated under Ar and stirring 9.5 d at 210°. Repeated prep. TLC (Et_2O/hexane 3:2) of the residue of the tetralin soln. yielded 95 mg (79%) of **3**, 12 mg (10%) of *dimethyl 1,6,8,10-tetramethylheptalene-4,5-dicarboxylate* (**15**; *cf.* [9]), and 6 mg (5%; or 24% with respect to reacted **3**) of *dimethyl 1,6,8,10-tetramethylheptalene-3,5-dicarboxylate* (**5**) as red-brown coloured oil. ^{1}H-NMR (270 MHz, $CDCl_3$): 1.593 (*s*, CH_3–C(6)); 1.844 (*s*, CH_3–C(1)); 1.986 (*s*, with f.s., ^4J(CH_3–C(8),H–C(7)) ≈ 1.3, CH_3–C(8)); 2.014 (*s*, with f.s., ^4J(CH_3–C(10),H–C(9)) ≈ 1.2, CH_3–C(10)); 3.746 (*s*, CH_3OOC–C(5)); 3.840 (*s*, CH_3OOC–C(3)); 6.094 and 6.128 (2 br. *s*, each 1H, H–C(7) and H–C(9)); 7.672 (splitted *s*, ^4J(H–C(2),H–C(4)) ≈ 0.5, H–C(2)); 7.872 (splitted *s*, ^4J(H–C(4),H–C(2)) ≈ 0.7, H–C(4)). MS[16]): 326 (100, M^+), 311 (26, $M^+ - CH_3$), 296 (8, $M^+ - CH_2O$), 295 (14, $M^+ - CH_3O^\cdot$), 286 (22, $M^+ - CH_3C{\equiv}CH$), 279 (24, $M^+ - (CH_3 + CH_3OH)$), 272 (17), 267 (27, $M^+ - CH_3OCC^\cdot$), 252 (20), 251 (17), 242 (18, $M^+ - HC{\equiv}CCOOCH_3$), 235 (13), 229 (17), 228 (100, $M^+ - CH_3C{\equiv}CCOOCH_3$), 208 (25), 207 (28), 206 (11), 205 (20), 193 (36), 192 (20), 191 (19), 190 (8), 189 (13), 184 (9), 165 (22).

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[20]) In our first experiments, we performed the rearrangement of **1** in tetralin in glass bombs at 230 ± 5° (*cf.* [3]). The procedure described here avoids the formation of colourless side products.

2.3. *Rearrangement of Dimethyl 4-Isopropyl-6,8,10-trimethylheptalene-1,2-dicarboxylate* (**4**). The heptalene **4** (80 mg, 0.23 mmol)[21]) was dissolved in tetralin (3 ml) and heated during 43 h at 210°. Repeated prep. TLC (Et_2O/hexane 1:1) of the residue of the tetralin soln. yielded 74 mg (92.5%) of **4** and 5 mg of a red-brown oil which was further purified to yield *ca.* 1 mg (1.3%; or 17% with respect to reacted **4**) of *dimethyl 2-isopropyl-6,8,10-trimethylheptalene-3,5-dicarboxylate* (**6**).

Re-isolated **4**. ^{1}H-NMR (270 MHz, $CDCl_3$): 1.157 and 1.169 (2*d*, each 3H, $^3J((CH_3)_2CH-C(4)) = 6.9$, $(CH_3)_2CH-C(4)$); 1.723 (*s*, $CH_3-C(6)$); 1.973 (*s*, with f.s., $^4J(CH_3-C(8),H-C(7)) \approx 1.2$, $CH_3-C(8)$); 2.014 (*s*, with f.s., $^4J(CH_3-C(10),H-C(9)) \approx 1.3$, $CH_3-C(10)$); 2.589 (*sept.*, $^3J((CH_3)_2CH-C(4)) = 6.9$, $(CH_3)_2CH-C(4)$); 3.688 and 3.718 (2*s*, each 3H, $CH_3OOC-C(1)$ and $-C(2)$); 5.809 (br. *s*, H–C(7)); 5.943 (br. *s*, with f.s., H–C(9)); 6.128 (br. *s*, H–C(5)); 7.558 (*s*, H–C(3)). MS: 354 (55, M^+), 339 (23, $M^+ - CH_3$), 323 (12, $M^+ - CH_3O^\cdot$), 322 (5, $M^+ - CH_3OH$), 307 (12, $M^+ - (CH_3 + CH_3OH)$), 295 (22, $M^+ - H_3COOC^\cdot$), 286 (7, $M^+ - (CH_3)_2CHC{\equiv}CH$), 279 (12), 265 (8), 263 (10), 254 (6), 251 (5), 235 (12), 228 (10, $M^+ - (CH_3)_2CHC{\equiv}CCOOCH_3$), 221 (12), 220 (8), 219 (6), 213 (20), 212 (100, $M^+ -$ ADM), 197 (27).

6. MS: 354 (19, M^+), 339 (7), 323 (6), 307 (5), 295 (8), 279 (9), 265 (5), 263 (6), 229 (17), 228 (100, $M^+ - (CH_3)_2CHC{\equiv}CCOOCH_3$), 221 (8), 220 (7), 205 (17), 197 (10), 193 (6).

2.4. *Rearrangement of [3-^2H]-***1**. The heptalene [3-^{2}H]-**1** (298 mg, 0.87 mmol; 0.74 ^{2}H at C(3)) was dissolved in tetralin (9 ml) and heated in an evacuated glass bomb at 230–240° during 70 h. Tetralin was removed by distillation and the residue separated by prep. TLC to yield 203 mg (68%) [3-^{2}H]-**1**[22]) and 73 mg (24.5%; or 77% with respect to reacted [3-^{2}H]-**1**) of [4-^{2}H]-**2** which was recrystallized from $CHCl_3$. ^{1}H-NMR (100 MHz, $CDCl_3$): integration of the region at 7.85 (H–C(2)) yielded 0.38 H (*i.e.* 0.62 ^{2}H) using H–C(6) at 5.74 for calibration. ^{2}H-NMR (15.35 MHz, $CDCl_3$): 7.82 (br. *s*, ^{2}H–C(2); no other ^{2}H signal recognizable!). ^{13}C-NMR (25.2 MHz, $C_2Cl_4D_2$): identical with that of **2** *(cf. Table 2)* with the exception that the signals at 137.1 (*t*, C(4)) and 124.6 (*s*, C(5)) were reduced in their intensity as compared to those of **2**. MS[16]): 342/341/340 (25/100/34, M^+), 326 (19), 310 (19), 309 (17), 301 (15), 300 (6), 294 (19), 293 (10), 282 (14), 281 (13), 273 (21), 272 (5), 257 (15, $M^+ - HC{\equiv}CCOOCH_3$), 256 (21, $M^+ - [^2H]C{\equiv}CCOOCH_3$), 243 (28).

2.5. *Rearrangement of [*1-methoxy-$^2H_3$*]-***1**. The heptalene [*1-methoxy*-$^2H_3$]-**1** (620 mg, 1.81 mmol) was dissolved in freshly distilled tetralin (24 ml) and heated in evacuated glass bombs during 70 h at 220°. Workup yielded 167 mg (27%) of crystalline [*5-methoxy*-$^2H_3$]-**2**. ^{1}H-NMR (100 MHz, CCl_4): 3.80 (*s*, $CH_3OOC-C(3)$); no H could be integrated in the range of 3.65 to 3.75 ($CH_3OOC-C(5)$). Both ester groups can be differentiated according to their G-values in the presence of Eu(fod)$_3$: $CH_3OOC-C(3)$ at 3.80 (G = 7.0), $CH_3OOC-C(5)$ at 3.71 (G = 5.0).

Table 5. *MS Data of* **1**, *[1,2-*$^{13}C_2$*]-***1**, **2**, *and [3,5-*$^{13}C_2$*]-***2**[a])

m/z	Rel. intensities of *m/z*, *m/z* + 1, *m/z* + 2											
	1			[1,2-$^{13}C_2$]-**1**			**2**			[3,5-$^{13}C_2$]-**2**		
340	73.5	17.5	2.5	68	16	11.5	100	23	3.5	100	24	16.5
325	16.5	3.5	1	15	3.5	2.5	22.5	5	1	24.5	3.5	2.5
309	23	7	1.5	20.5	8	4	17.5	7.5	1.5	19.5	8.5	2.5
300	12.5	2.5	0	11	2.5	2	23	4.5	1.5	25	3	3
293	17.5	4.5	2	14.5	3.5	3.5	16	4	2	17.5	3	3
281	26.5	7	1.5	23.5	7	4.5	22	6	6	25	4.5	11
272	13	2.5	1	11.5	2	2	35	6	2.5	39	4	4
265	10	6	3.5	8	5.5	8	10.5	8	3.5	12.5	9.5	4
256	16	–	–	13.5	–	–	58	12	2	67	23	3
242	31.5	6	1.5	27	8.5	1	91.5	16	2	103.5	32.5	3
227[b])	7	–	–	6	–	–	15.5	3	2.5	20	4	1
221	16.5	7	4	13	5.5	4.5	9	–	–	14.5	–	–
207[c])	16	4	4.5	13	4	4.5	15	4	8.5	22.5	4.5	14.5
198	100	16.5	1.5	100	17	1.5	–	–	–	–	–	–
191[c])	13.5	–	–	10.5	–	–	12.5	9	5.5	21.5	14	12.5
183	33	–	–	32	–	–	–	–	–	–	–	–
179[d])	–	–	–	–	–	–	17.5	8	5.5	29.5	14.5	11.5
178[e])	20.5	–	–	15.5	–	–	13	–	–	22.5	–	–
165[f])	23	–	–	16	–	–	20	7.5	7.5	37.5	13.5	16.5

[a]) At 70 eV. [b]) $C_{15}H_{15}O_2$; *cf.* [3]. [c]) Composition unknown. [d]) $C_{14}H_{11}$; *cf.* [3]. [e]) $C_{14}H_{10}$; *cf.* [3]. [f]) $C_{13}H_9$; *cf.* [3].

[21]) Obtained from the reaction of 2-isopropyl-4,6,8-trimethylazulene with ADM in tetralin at 210° during 1 h [21].

[22]) The ^{2}H-content of [3-^2H]-**1** was unaltered.

^{13}C-NMR (25.2 MHz, $CDCl_3$): identical with that of **2** with the following exceptions: 166.9 (*s*, CH_3OOC–C(3)); 165.8 (*s*, C[$^2H_3$]OOC–C(5)). The latter signal is distinctly reduced in intensity as compared to that of **2**. 52.1 (*q*, CH_3OOC–C(3)), 50.4 (*sept.*, C[$^2H_3$]OOC–C(5)). MS (25 eV)[16]: 344/343 (27/100, M^+), 328 (11), 303 (13), 293 (9), 275 (19), 259 (23, $M^+ - HC{\equiv}CCOOCH_3$), 256 (4, $M^+ - HC{\equiv}CCOOC[^2H_3]$), 242 (41, $M^+ - CH_3C{\equiv}CCOOC[^2H_3]$), no clear signal at *m/z* 245! MS (7 eV): 343 (100, M^+), 242 (4).

2.6. *Rearrangement of [1,2-$^{13}C_2$]-***1**. The heptalene [1,2-$^{13}C_2$]-**1** (300 mg, 0.88 mmol) was dissolved in dry tetralin (9 ml) and heated during 43 h at 210°. The tetralin was distilled off (95°/0.05 Torr) and the red-brown residue separated by prep. TLC to yield 170 mg (57%) of [1,2-$^{13}C_2$]-**1** and 130 mg (43%) of a red oil, from which 73 mg (24%) of [3,5-$^{13}C_2$]-**2** as ruby crystals were obtained (m.p. 117–118°). ^{1}H-NMR (400 MHz, $CDCl_3$): identical with that of **2**. ^{13}C-NMR (100.6 MHz, $CDCl_3$): identical with that of **2** with the following exceptions: 125.09 (strong *s*, C(5)); 129.19 (strong *s*, C(3); ^2J(C(3),C(5)) not recognizable, *i.e.* < 2 Hz); 137.34 (*s* with satellites, ^1J(C(4),C(5)) + ^1J(C(4),C(3)) ≈ 126); 146.01 (*s* with *d*-satellite, ^1J(C(2),C(3)) = 68, C(2)). MS: see *Table 5*. ^{13}C-content 16.5 atom-%.

REFERENCES

[1] W. Bernhard, P. Brügger, J. J. Daly, P., Schönholzer, R. H. Weber, H.-J. Hansen, *Helv. Chim. Acta* **1985,** *68,* 415.

[2] a) E. Vogel, H. Köngishofen, J. Wassen, K. Müllen, J. F. M. Oth. *Angew. Chem.* **1974,** *86,* 777, *ibid. Int. Ed.* **1974,** *13,* 732; b) E. Vogel, F. Hogrefe, *Angew. Chem.* **1974,** *86,* 779, *ibid. Int. Ed.* **1974,** *13,* 734; c) E. Vogel, D. Kerimis, N. T. Allison, R. Zellerhof, J. Wassen, *Angew. Chem.* **1979,** *91,* 579, *ibid. Int. Ed.* **1979,** *18,* 545; d) K. Hafner, G. L. Knaup, H. J. Lindner, H.-C. Flöter, *Angew. Chem.* **1985,** *97,* 209, *ibid. Int. Ed.* **1985,** *24,* 212.

[3] W. Bernhard, H.-R. Zumbrunnen, H.-J. Hansen, *Chimia* **1979,** *33,* 324.

[4] a) M. J. S. Dewar, in 'Molecular Rearrangements', Ed. P. de Mayo, Interscience Publ., New York, London, 1963, p. 295ff.; b) H. J. Shine, 'Aromatic Rearrangements', Elsevier Publ. Comp., Amsterdam–London–New York, 1967, p. 23ff.

[5] a) L. T. Scott, *Acc. Chem. Res.* **1982,** *15,* 52; b) K.-P. Zeller, *Angew. Chem.* **1982,** *94,* 448, *ibid. Int. Ed.* **1982,** *21,* 440; c) D. Lloyd, 'Nonbenzoid Conjugated Carbocyclic Compounds', Elsevier Publ. Comp., Amsterdam, 1984, p. 375ff.

[6] a) D. Bryce-Smith, A. Gilbert, *Tetrahedron* **1976,** *32,* 1309; b) D. Bryce-Smith, A. Gilbert, in 'Rearrangements in Ground and Excited States', Ed. P. de Mayo, Academic Press, Inc., New York, 1980, p. 349; c) G. Kaupp, *Angew. Chem.* **1980,** *92,* 245, *ibid. Int. Ed.* **1980,** *19,* 243.

[7] T. M. Cresp, F. Sondheimer, *J. Am. Chem. Soc.* **1975,** *97,* 4412, *ibid.* **1977,** *99,* 194; I. Agranat, B. A. Hess, Jr., L. J. Schad, *Pure Appl. Chem.* **1980,** *52,* 1399.

[8] W. Treibs, C. Vollrad, M. Reimann, *Liebigs Ann. Chem.* **1961,** *648,* 164.

[9] W. Bernhard, P. Brügger, P. Schönholzer, R. H. Weber, H.-J. Hansen, *Helv. Chim. Acta* **1985,** *68,* 429.

[10] J. L. Marshall, 'Carbon-Carbon and Carbon-Proton NMR Couplings', Verlag Chemie International, Deerfield Beach, Florida, 1983, p. 123ff.

[11] L. A. Paquette, A. R. Browne, E. Chamot, *Angew. Chem.* **1979,** *91,* 581, *ibid. Int. Ed.* **1979,** *18,* 546.

[12] I. A. D'yakonov, V. V. Razin, M. I. Komendantov, *Tetrahedron Lett.* **1966,** 1127 and 1135; R. B. Woodward, D. L. Dalrymple, *J. Am. Chem. Soc.* **1969,** *91,* 4612; K. B. Wiberg, *Adv. Alicycl. Chem.* **1968,** *2,* 185.

[13] R. Wehrli, H. Schmid, D. Bellus, H.-J. Hansen, *Helv. Chim. Acta* **1977,** *60,* 1325.

[14] J. Elzinga, H. Hagaveen, *J. Org. Chem.* **1979,** *44,* 2381; A. L. J. Beckwith, K. U. Ingold, in 'Rearrangements in Ground and Excited States', Ed. P. de Mayo, Academic Press, Inc. New York, 1980, Vol. 1, 220ff.

[15] R. W. Lang, H.-J. Hansen, *Helv. Chim. Acta* **1979,** *62,* 1025.

[16] D. J. Bertelli, in 'Aromaticity, Pseudo-Aromaticity, Anti-Aromaticity', Eds. E. D. Bergman and B. Pullman, Proc. of an Internat. Symposium held at Jerusalem, 1970, p. 326; D. J. Bertelli, in 'Topics in Nonbenzoid Aromatic Chemistry', Ed. T. Nozoe, J. Wiley & Sons, New York, 1973, Vol. 1, p. 29ff.

[17] L. Phillips, in 'Spectroscopy', Eds. B. P. Straughan and S. Walker, Chapman and Hall, London, 1976, Vol. 1, p. 110ff.

[18] H.-O. Kalinowski, S. Berger, S. Braun, '^{13}C-NMR-Spektroskopie', G. Thieme Verlag, Stuttgart – New York, 1984, p. 420ff.

[19] U. C. Vögeli, Ph. D. Thesis, University of Zurich, 1978.

[20] M. S. Kharasch, M. C. McNab, F. R. Mayo, *J. Am. Chem. Soc.* **1933,** *55,* 2521; H. Gilman, A. H. Haubein, *ibid.* **1945,** *67,* 1420; Y. J. Topper, *J. Biol. Chem.* **1949,** *177,* 303.

[21] D. Beer, Diploma Work, University of Fribourg, 1980.