

<sup>13</sup>C NMR SPECTROSCOPY OF CARBONYL COMPOUNDS  
 2. CONFORMATIONAL AND CONFIGURATIONAL DEPENDENCE  
 OF THE (Z)-EPOXYENONE/FURAN ISOMERIZATION<sup>1</sup>

Klaus Müllen\*, Eleni Kotzamani and Hans Schmickler

Institut für Organische Chemie der Universität, D-5 Köln 41, Greinstr. 4, FR Germany

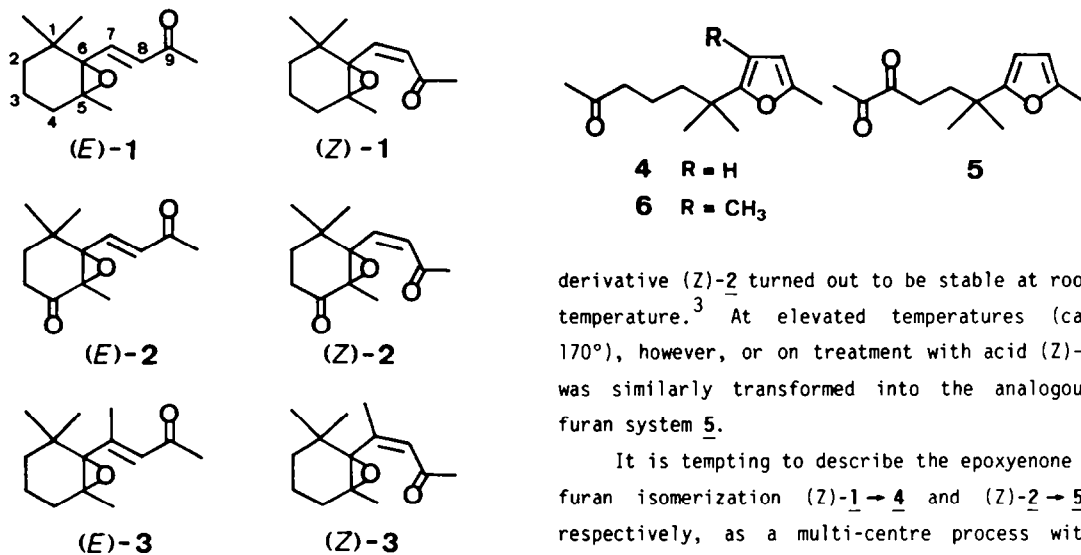
Bruno Frei

Laboratorium für Organische Chemie der ETH Zürich, CH-8092 Zürich, Switzerland

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**Abstract.** The furan derivative **4** which has been isolated upon photolysis of the epoxyenone compound (E)-**1** results from a thermal isomerization of the intermediate (Z)-isomer (Z)-**1**. The latter reaction can best be understood as a multi-centre process implying a nucleophilic attack of the carbonyl oxygen upon the oxirane ring. Inspection of related epoxyenones (e.g. **2** and **3**) reveals that the ease of the above isomerization sensitively depends upon the conformation with respect to the C-6/C-7 single bond.

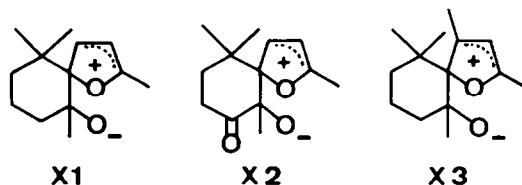
The conformational properties of a series of epoxyenones as well as of related dienones and epoxydienes have been studied by dynamic <sup>13</sup>C NMR spectroscopy. The chemical and spectroscopic information is combined to describe the stereochemical course of the epoxyenone/furan isomerization. As a consequence we can control the thermal reactivity of the title compounds by creating an appropriate conformational behaviour.



derivative (Z)-**2** turned out to be stable at room temperature.<sup>3</sup> At elevated temperatures (ca. 170°), however, or on treatment with acid (Z)-**2** was similarly transformed into the analogous furan system **5**.

It is tempting to describe the epoxyenone / furan isomerization (Z)-**1** → **4** and (Z)-**2** → **5**, respectively, as a multi-centre process with intermediate charge-separation as depicted by formulae **X1** and **X2**. Moreover, from the occurrence of a highly-ordered transition state, one would expect that the ease of the thermal reaction sensitively depends on steric factors.

**1. Introduction.** - It has been shown that, on  $\pi, \pi^*$ -excitation of epoxyenone (E)-**1**, an (E/Z)-isomerization to (Z)-**1** occurred as the main process.<sup>2</sup> Under these reaction conditions, however, (Z)-**1** could not be isolated but spontaneously underwent thermal or acid catalyzed rearrangement to the furan derivative **4**. The latter isomerization implies a nucleophilic attack of the carbonyl oxygen at centre C-6 of the oxirane ring. In contrast to (Z)-**1** the 4-oxo



As can be inferred from consideration of models, torsion around the C-6/C-7 single bond of (Z)-1 or (Z)-2 leads to two preferential conformations, only one of which allows a trans-diaxial arrangement of the incoming (carbonyl) and leaving (ring) oxygen atom in the course of the oxirane ring opening.

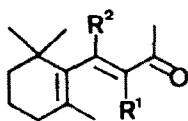
How can the conformational properties of the epoxyenones be influenced? It will be shown below that the conformational behaviour of dienones related to 1 and 2, e.g. compounds 7 and 8, depends on both the configuration of the C-7/C-8 double bond and the extent of (alkyl) substitution in the side chain: thus, increasing steric interaction between the enone moiety and the cyclohexane ring causes a substantial twist around the C-6/C-7 bond.

The present work is devoted to the study of such effects exerted upon the energy profiles of conformational interconversions within epoxyenones. Thereby,  $^{13}\text{C}$  NMR spectroscopy proved to be a most useful tool.<sup>1,4-6</sup> Conclusions drawn from the spectroscopic studies led us to conceive and prepare novel epoxyenone species with increased steric interference of the epoxy-cyclohexane ring and the enone side chain. We thus arrived at conformers, which do not interconvert at room temperature and which differ substantially in their isomerization reactions; as a consequence we can control the thermal reactivity by creating an appropriate conformational behaviour.

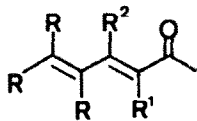
## 2. Conformational behaviour of dienones related to 1-3.

- Three conformational processes have to be considered, concerning the stereochemistry of  $\beta$ -ionone compounds 7 as well as of the acyclic dienones 8:

- s-cis/s-trans isomerism in the enone moiety,
- s-cis/s-trans isomerism in the diene fragment as well as
- cyclohexene ring inversion.



**7**    **a**     $\text{R}^1 = \text{R}^2 = \text{H}$   
          **b**     $\text{R}^1 = \text{CH}_3$      $\text{R}^2 = \text{H}$   
          **c**     $\text{R}^1 = \text{H}$      $\text{R}^2 = \text{CH}_3$



**8**     $\text{R} = \text{H, alkyl}$

By measuring  $^{13}\text{C}$  NMR spectra of the parent compound 7a at very low temperatures (below  $-130^\circ$ ) we could separately detect the s-cis and s-trans enone conformers and kinetically analyze their dynamic interconversion.<sup>1</sup> The diene mobility could not be frozen out. The relative weight of s-cis and s-trans diene isomers in 8, however, could be shown from NOE measurements to depend on the substituents R. These stereochemical features will be discussed in a forthcoming paper.<sup>7</sup>

Methyl substitution at C-8 or C-7 giving rise to compounds 7b and 8b or 7c and 8c, respectively, suppressed the dynamic equilibrium of enone conformers.<sup>8</sup> Thus, 7b and 8b exist as s-trans, and 7c and 8c as s-cis enone conformers.

The increased steric interaction of ring and side chain in 7b and 7c causes a substantial twist of the C-6/C-7 single bond; as a consequence, the cyclohexene ring and the enone unit are limited to a nearly orthogonal arrangement. At the same time the rotation around C-6/C-7 is slowed down in the NMR time scale which affects the line shape of the carbon signals of C-1a and C-1a'. The tendency toward slowly interconverting conformers with dihedral angles  $\varphi \pm 90^\circ$  was further enhanced upon going to the (Z)-configuration of the C-7/C-8 double bond. Not surprisingly, therefore, the diene rotation of compound (Z)-7b was seen to be slow within the NMR time scale even at  $+100^\circ$ .

## 3. Results and Discussion. 3.1. Conformational control of thermal reactivity.

The number of resonances in  $^{13}\text{C}$  NMR spectra of (E)-1<sup>9</sup> and (E)-2 at room temperature was in accord with the constitutional formulae. No exchange broadening was observed when lowering the temperature down to  $-80^\circ$ . The  $^{13}\text{C}$  NMR spectrum of (E)-3<sup>10</sup> at room temperature exhibited the "double" number of signals, the relative intensity of every pair being 65:35. Above  $70^\circ$  we observed severe line broadening effects indicating some dynamic process. Even at  $+155^\circ$ , the highest temperature at which  $^{13}\text{C}$  NMR spectra of (E)-3 were taken, the fast exchange domain is not yet reached (see Fig.1 and Table 1).

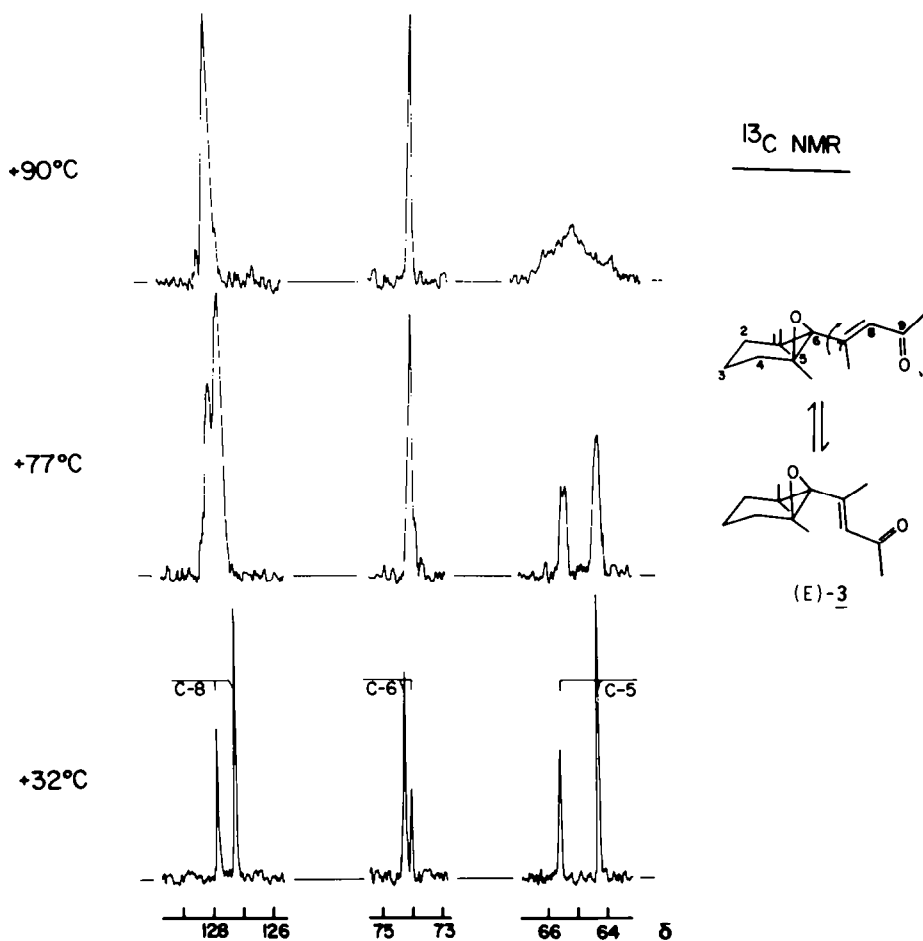


Figure 1.  $^{13}\text{C}$  NMR spectra (22 MHz, tetrachloroethane- $d_2$ ) of (E)-3 at different temperatures (selected signals only).

What is the process responsible for the observed exchange behaviour of (E)-3?

From a comparison with the dynamic properties of the reference compounds 7a-7c and 8a-8c (see Section 2), we learn that 7-methyl substituted dienones and enones are not expected to give rise to dynamic effects detectable by NMR. This finding, together with the failure of the parent epoxyenone (E)-1 to exhibit line broadening effects in the above temperature range, indicate that (E)-3 must exist as two conformers which differ by the torsional angle around the C-6/C-7 bond. It is significant in the present context that rotation around the C-6/C-7 bond in (E)-3 affects the magnetic sites of all nuclei within the molecule, while the s-cis/s-trans enone interconversion of 7a and 8a causes line broadening only for the signals of C-9a, C-9, C-8, C-7 and C-6 (and/or C-5).

If in (E)-3 the increased steric interaction between ring and side chain suffices to slow down the conformational isomerism, then this effect should also hold true for the (Z)-isomer (Z)-2. Indeed, dynamic  $^{13}\text{C}$  NMR measurements on (Z)-2 revealed an analogous exchange behaviour to (E)-3: a fast exchange spectrum with a number of signals corresponding to the constitution was only observed above  $+80^\circ$  (see Fig. 2). On lowering the temperature, every signal was broadened and finally split into two separate signals of relative intensity 3:2 (coalescence temperature between  $25^\circ$  and  $30^\circ$ ). The slow exchange domain was achieved below  $0^\circ$ . The  $^1\text{H}$  NMR spectrum of (Z)-2 at  $-20^\circ$  supports this interpretation: particularly characteristic are the olefinic signals (H-7, H-8; AB-system) of both conformers (see Fig. 3).

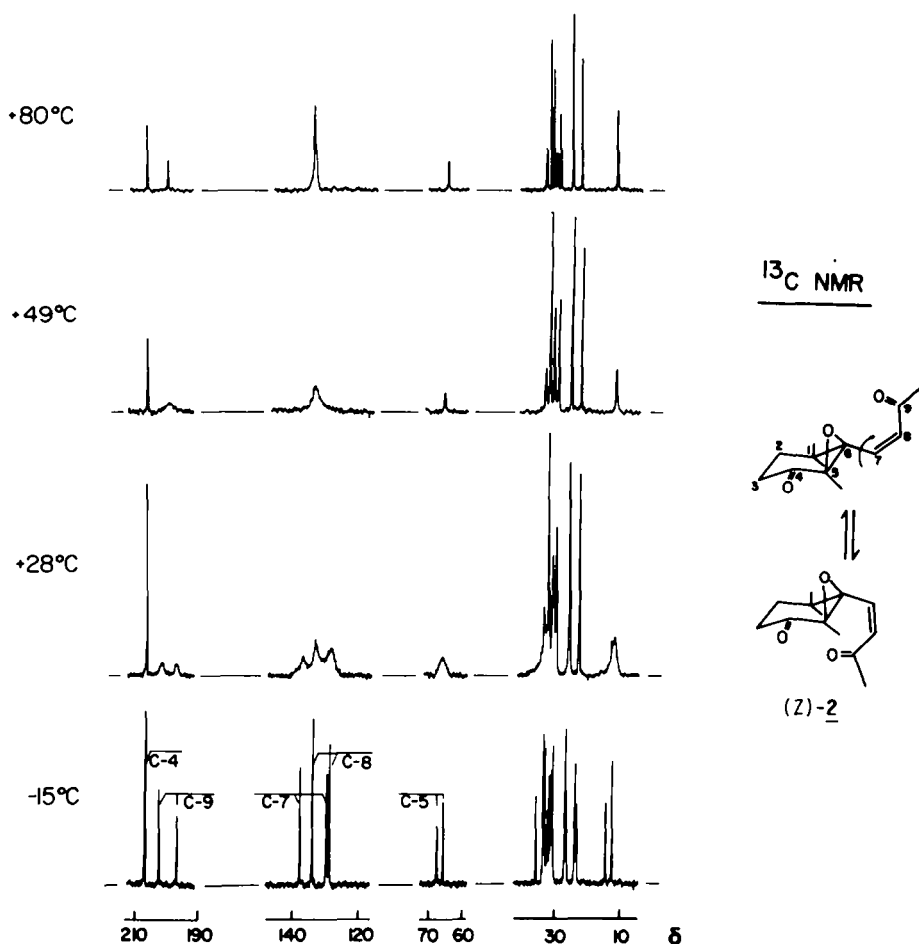
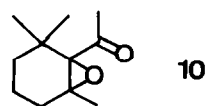


Figure 2.  $^{13}\text{C}$  NMR spectra (22 MHz, tetrachloroethane- $d_2$ ) of (Z)-2 at different temperatures.

The rate constants of the conformational process were determined via a line shape analysis of the exchange broadened  $^{13}\text{C}$  resonances.<sup>11</sup> From a subsequent Arrhenius plot we obtained activation parameters as given in Table 2. The free enthalpies of activation  $\Delta G^\ddagger(25^\circ)$  for the rotational interconversions in (Z)-2, (E)-3 and (E)-9 (see Experimental) are 14.9, 17.3 and 17.0 kcal/mol, respectively.

On comparing these values it appears significant that a methyl group in the (E)-enone unit contributes slightly more to the steric hindrance of the rotation around C-6/C-7 than a non-substituted (Z)-enone side chain. The steric influence of a methyl group at C-7 suggested the investigation of compound 10, where the enone moiety has been replaced by an acetyl group.

Down to a temperature of  $-80^\circ$  the epoxy system 10 did not show exchange broadened  $^{13}\text{C}$  resonances. We conclude that a methyl group alone is not sufficient to slow down the above conformational process.



In our attempt at further impeding the rotation around the C-6/C-7 bond of the epoxy-enone system we were interested in examining the corresponding (Z)-isomer (Z)-3. Such a compound, besides constituting a most promising substrate within the present conformational analysis, might also be prone to thermal oxirane ring opening.

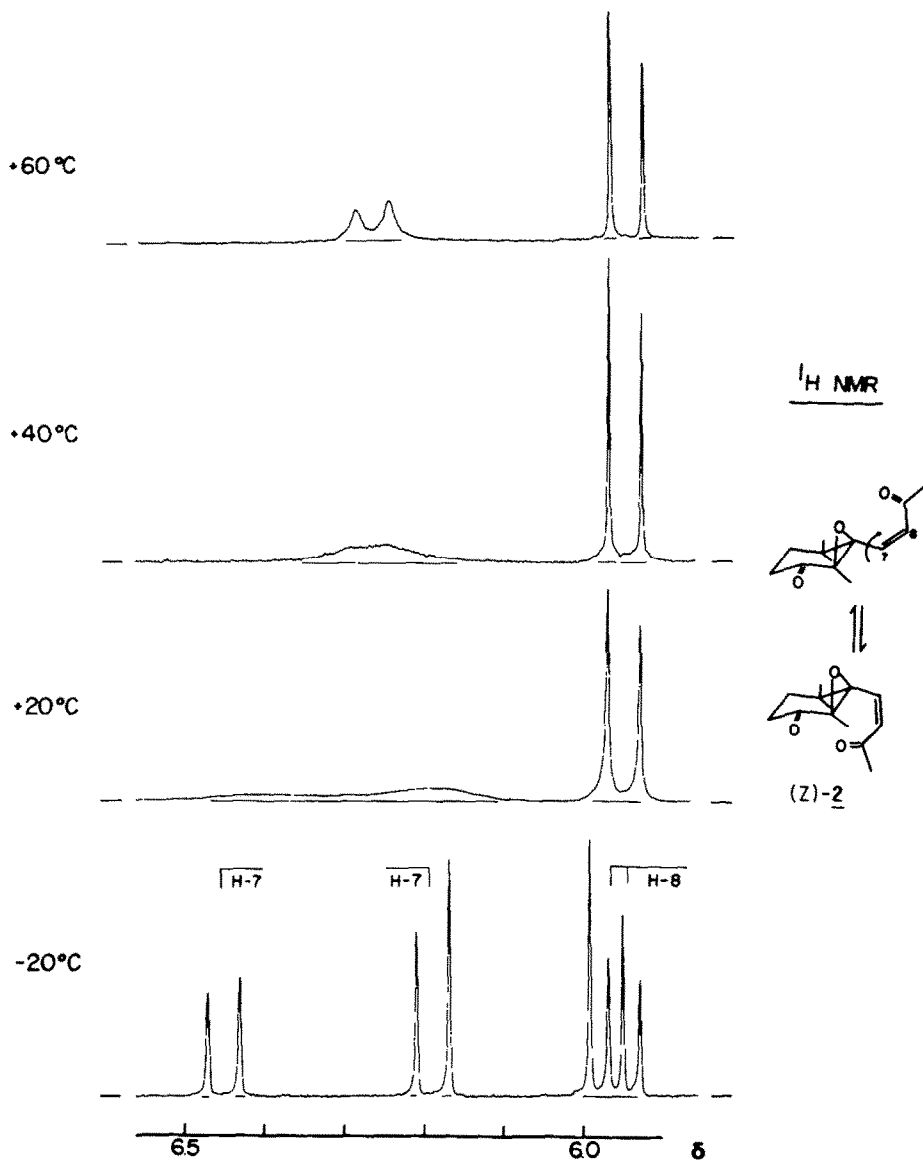


Figure 3.  $^1\text{H}$  NMR spectra (300 MHz, dichloro-methane- $\text{d}_2$ ) of (Z)-2 at different temperatures (olefinic part only).

Due to the combined effects of a (Z)-configured double bond and an alkyl substituent, the steric interaction between the enone side chain and the cyclohexane ring would be expected to become even more severe: within the present series (Z)-3 should exhibit the slowest conformational interconversion.

Upon photolysis of (E)-3 (see Experimental) one main product, (Z)-3', was obtained. Compound (Z)-3' was stable at room temperature. At about 80°, however, it was transformed into a novel species (Z)-3''. The structural proof of (Z)-3'

and (Z)-3'' is based upon the following: the NMR spectra of (E)-3, (Z)-3' and (Z)-3'' indicate that the constitution of the epoxyenone remained intact and that (Z)-3' and (Z)-3'', while having in common a (Z)-configured double bond, differ

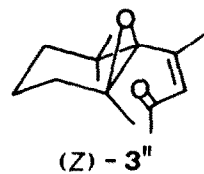
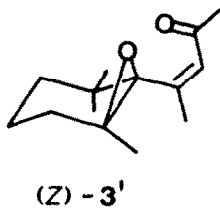


Table 1

 $^{13}\text{C}$  NMR chemical shifts (22 MHz,  $\text{CDCl}_3$ ,  $30^\circ$ )<sup>k</sup> of epoxyenones and related compounds

C-atoms	1	2	3	4	5	6	7	8	9	1a (1a')	5a	7a	9a	10
(E)- <u>1</u> <sup>a</sup>	33.5	35.6	17.0	29.8	65.6	70.4	142.4	132.7	196.7	25.9	20.8		27.9	
(E)- <u>2</u>	33.9	31.9	33.3	205.3	66.6	73.8	137.8	132.6	196.7	26.7 (23.3)	11.8		28.4	
(Z)- <u>2</u> <sup>b</sup>	33.4 <sup>d</sup>	31.0 <sup>g</sup>	33.7 <sup>g</sup>	206.7	65.2	73.9	127.9 <sup>f</sup>	133.7 <sup>f</sup>	202.4	26.6 (23.4)	11.6		30.6	
(Z)- <u>2</u> <sup>c</sup>	36.1	31.9	33.0	205.9	66.9	71.7	137.6 <sup>f</sup>	129.1	196.3	26.2 (22.7) <sup>g</sup>	13.6		31.5 <sup>d</sup>	
(E)- <u>3</u> <sup>b</sup>	33.5	36.7	17.1	30.0	64.4	74.6	155.0	126.5	197.9	26.7 (25.9)	21.8	21.0	32.1	
(E)- <u>3</u> <sup>c</sup>	34.0	35.5	16.9	29.4	65.6	74.1	152.9	126.7	197.6	25.1 (23.9)	h	18.2		
(Z)- <u>3</u>	33.7	36.9	16.6	29.6	63.6	72.9	142.3	131.5	201.8	27.5 (26.4)	20.8	23.4	30.4	
(Z)- <u>3</u> <sup>*</sup>	33.5	37.4	17.1	31.2	65.7	71.3	153.6	125.5	195.8	26.7 (26.0)	21.6	22.6	30.9	
(E)- <u>9</u> <sup>b</sup>	34.1	36.9	17.2	30.3	65.5	74.7	141.4	131.3	134.5	26.9 (26.9)	19.4	25.2 <sup>e</sup>	23.7 <sup>e</sup>	114.9
(E)- <u>9</u> <sup>c</sup>	34.4	35.8	17.1	29.9	64.1	i	141.3	131.0	133.0	26.3 (26.3)	16.7	23.9	21.7	114.7
(Z)- <u>9</u>	34.5	36.8	16.9	29.8	62.0	72.8	142.5	133.2	133.2	27.3 (27.2)	22.0	24.7 <sup>e</sup>	23.5 <sup>e</sup>	114.0
(Z)- <u>9</u> <sup>*</sup>	34.4	38.1	17.4	31.7	66.5	70.7	141.0	128.9	134.9	26.8 (27.4)	21.9	24.3 <sup>e</sup>	23.7 <sup>e</sup>	114.5
<u>10</u>	32.1	35.2	16.5	29.1	64.1	74.9			208.5	26.0 (24.9)	22.4		30.0	

<sup>a</sup>See reference 9. <sup>b</sup>Major conformer. <sup>c</sup>Minor conformer. <sup>d</sup>No assignment possible due to signal overlap. <sup>e</sup>The small shift difference of the corresponding proton signals (H-7a, H-9a) does not allow  $^{13}\text{C}$  signal assignments via selective decoupling experiments. <sup>f</sup>The assignment has been made from the exchange behaviour and from selective decoupling experiments. <sup>g</sup>Assignment made by analogy with (E)-2, see text. <sup>h</sup>Covered by signals of the major conformer. <sup>i</sup>Covered by the solvent signal. <sup>k</sup>(Z)-2 at  $-25^\circ$ .

by the torsion angle with respect to the C-6/C-7 single bond. In the case of the related dienone 7 the (E/Z)-isomerization caused an upfield shift of the resonance of the methyl protons H-7a. In (E)-3 the analogous signal (d, J=1.5 Hz) appeared at  $\delta=2.07$  and 2.02 (two conformers), while in (Z)-3<sup>i</sup> and (Z)-3<sup>\*</sup> the absorption was seen at  $\delta=1.80$  and 1.85. These shift differences can be ascribed to the fact that in the (E)-configured compound, which exists preferentially as the s-cis enone conformer, the methyl protons are deshielded by the carbonyl group.<sup>8,12</sup> This is not true for the (Z)-configuration (predominantly s-cis enone). A more detailed stereochemical description of these

systems is given in Section 3.2.

Supporting evidence in favour of the above structural assignment was obtained from the fact that (Z)-3<sup>\*</sup> was independently prepared from (Z)-7c via epoxidation with m-chlorperbenzoic acid. Since the enone side chain in (Z)-7c is twisted about  $90^\circ$  around the C-6/C-7 bond, it seems reasonable that the double bond would be attacked from the less hindered side (see Experimental).

Following the thermolysis (Z)-3<sup>i</sup>  $\rightarrow$  (Z)-3<sup>\*</sup> by time dependent  $^1\text{H}$  NMR measurements (see Experimental) [ $\Delta G^\ddagger(20^\circ) = 26.1$  kcal/mol], we obtained the relevant kinetic data which are included in Table 2.

Table 2.

Activation parameters of the rotation around the C-6/C-7 single bond in (Z)-2, (Z)-3 and (Z)-9<sup>a</sup>

	$E_a$ [kcal/mol]	$\Delta H^\ddagger(25^\circ)$ [kcal/mol]	$\Delta S^\ddagger(25^\circ)$ [eu]	$\Delta G^\ddagger(25^\circ)$ [kcal/mol]
(Z)- <u>2</u> <sup>b</sup>	14.3 $\pm$ 0.5	13.8 $\pm$ 0.7	-3.8 $\pm$ 1.8	14.9 $\pm$ 0.1
(Z)- <u>3</u> <sup>c</sup>	25.4 $\pm$ 1.7	24.8 $\pm$ 2.0	-4.2 $\pm$ 4.0	26.1 $\pm$ 0.1
(Z)- <u>9</u> <sup>c</sup>	23.9 $\pm$ 2.0	23.3 $\pm$ 2.0	-11.7 $\pm$ 4.0	26.7 $\pm$ 0.1

<sup>a</sup>The errors have been calculated as described in Section 5.2.

<sup>b</sup>Determined by dynamic <sup>13</sup>C NMR (see text), conversion of the major into the minor conformer.

<sup>c</sup>Determined by time dependent <sup>1</sup>H NMR (see text), conversion of (Z)-3' [(Z)-9'] into (Z)-3" [(Z)-9"].

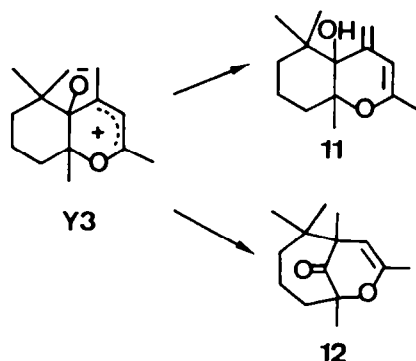
The predicted increase of the activation barrier of the dynamic process prevailing in compounds 1, 2 and 3 is obvious: while rotation around the C-6/C-7 single bond in (E)-3 and (Z)-2 occurs within the NMR time scale, the conversion is slowed down to a "chemical" time scale in the sterically most hindered epoxyenone (Z)-3; resulting in the stable conformers (Z)-3' and (Z)-3". This finding allowed us to test the above mentioned expectation concerning the conformational requirements of the valence isomerization.

While we have firmly established that (Z)-3' and (Z)-3" constitute conformational isomers, an assignment as to the actual torsional angle of each individual conformer is not straightforward from spectroscopic evidence. We recall, however, that only one of the molecules exhibits an arrangement suitable for the facile oxirane ring cleavage. The particular reactivities of (Z)-3' and (Z)-3" are, indeed, significant: - when solutions of (Z)-3" were heated to about 160°, the epoxyenone was transformed into the furan derivative 6; - conformers (Z)-3' and (Z)-3" also differ in their behaviour toward acids.<sup>10</sup> When one drop of trichloroacetic acid was added to a 0.1 molar solution of (Z)-3' in methylene chloride at -80°, the <sup>1</sup>H NMR spectrum remained essentially

unaffected. In the case of (Z)-3", however, we instantaneously observed the appearance of new resonances which from comparison with the spectrum of an authentic sample were assigned to compound 6. A similar experiment was performed under HCl-catalysis. Treatment of (Z)-3' and (Z)-3" with HCl at -20° in methylene chloride converted (Z)-3" to the furan 6 as main product, while (Z)-3' was recovered unchanged after workup.

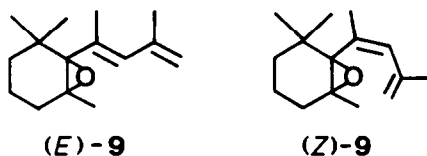
We have therefore firm evidence that (Z)-3" constitutes the "reactive" isomer whose conformation fulfils the stereoelectronic requirements for the facile oxirane ring opening, i.e. the trans diaxial arrangement of the two oxygen atoms involved.

A significant difference was observed between the thermolysis of (Z)-2 and (Z)-3". While (Z)-2 produced the furan 5 exclusively, thermolysis (170°, cyclohexane) of (Z)-3" afforded the furan 6, as well as the enol ethers 11 and 12.<sup>10</sup> These side reactions did not allow us to carry out a proper determination of the activation parameters for the reaction (Z)-3"  $\rightarrow$  6. The formation of 11 and 12 presumably proceeds by a nucleophilic attack of the carbonyl oxygen at C-5 via the intermediate Y3. Products of an intermediate of type Y were not observed on acid catalyzed or thermal reaction of (Z)-1 and (Z)-2 without a 7a-methyl group. This indicates that the interaction of the 7a-methyl group with the 1a,1a'-ring methyl groups is responsible for the C-5/O oxirane cleavage, presumably by causing an enhancement of the activation energy for the C-6/O cleavage.



The increasing activation barrier for the rotation around the C-6/C-7 bond within the series of compounds (Z)-2 - (E)-3 - (Z)-3 results essentially from steric features. That,

indeed, one does not have to invoke particular conjugational effects within the epoxyenone chromophores to explain this barrier, e.g. a polarization exerted by the carbonyl oxygen, can be demonstrated independently by examining the epoxydienes **9**. Wittig reaction of (E)-**3** and (Z)-**3'** with methylene triphenyl phosphorane in ether provided (E)-**9** and (Z)-**9'**, respectively, and subsequent photolysis of (E)-**9** afforded (Z)-**9''**. As anticipated from the thermally induced conversion (Z)-**3'**  $\rightarrow$  (Z)-**3''**, the epoxydiene (Z)-**9'** was smoothly transformed into (Z)-**9''** when warmed to about 80°. We conclude that (Z)-**9'** and (Z)-**9''** represent analogous conformers differing only by their torsional angle around the C-6/C-7 single bond.



Moreover, we have determined the relevant activation parameters of the conformational process by recording the time dependent  $^1\text{H}$  NMR spectra for different reaction temperatures. As becomes obvious from an inspection of Table 2, the data obtained for the epoxyenone and the epoxydiene case are quite similar. This finding supports our expectation that the conformational processes are, indeed, controlled by steric factors.

3.2.  $^{13}\text{C}$  NMR spectroscopic description of stereoisomerism in epoxyenones. Until now, the structural characterization of (E)- and (Z)-isomers has been restricted to the chemically most important feature, i.e. the torsional angle around the C-6/C-7 single bond. This rotational process creates a syn- and anti-arrangement of the carbonyl and oxirane oxygens. The stereodynamic situation, however, is expected to be more complex since structural changes such as methyl substitution or (E/Z)-isomerization affect the energy profile of both the C-8/C-9 as well as C-6/C-7 rotation. The  $^{13}\text{C}$  chemical shifts of the enone side chain within the title series (see Table 1) support this view: - The changes of  $^{13}\text{C}$  resonances observed upon (E/Z) -

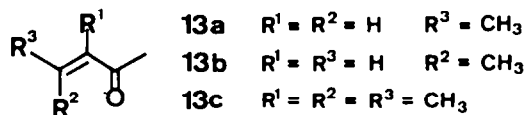
isomerization in either (E)-**2** or (E)-**3** do not correspond to those resulting from (E/Z)-isomerization of the reference compound **8a**.<sup>1</sup> - While rotation around the C-6/C-7 bond in (E)-**3** shifts the carbon resonances of C-1 to C-9 by not more than 2 ppm, the changes upon going from (E)-**3** to (Z)-**3'** and (Z)-**3''** are as follows:

			C-9	C-8	C-7
(E)- <b>3</b>	↗	(Z)- <b>3'</b>	$\Delta\delta =$	+3	+5
	↘	(Z)- <b>3''</b>	$\Delta\delta =$	-2	-1
				-11	0

(positive values indicate a downfield shift)

- Quite a similar relationship of chemical shifts is observed when comparing the data of (E)-**2** with those of the C-6/C-7 conformers in (Z)-**2** (see below).

We learn from the above  $^{13}\text{C}$  resonances that, apart from the effects of (E/Z)-isomerism and of C-6/C-7 rotation, another structural change must occur in (Z)-**3'**. Consideration of models indicate appreciable non-bonding interactions between the ring and the side chain. The resulting strain would be released if the s-cis conformer within the enone unit deviates from the coplanar arrangement. On the other hand, (Z)-**3''** is similar to (E)-**2** and (E)-**3** in that it possesses a planar enone moiety, consequently the severe non-bonding interactions in (Z)-**3''** do not allow a substantial twist around C-8/C-9.



Reference to the series of enone species **13** is revealing. It has been described by Stothers<sup>13</sup> that the  $^{13}\text{C}$  chemical shifts of the fully methylated derivative **13c** differ significantly from those of **13a** and **13b**: in the former the carbonylic carbon C-9 and the olefinic carbon C-7 are appreciably deshielded and shielded, respectively. This outcome indicates that due to a non-planar conformation, the transfer of the partial positive charge from C-9 to C-7 is less effective. From the observation of related shift increments in (Z)-**3'** one concludes the following: although in (Z)-**3'** the substituent at C-8 is  $\text{R}^1 = \text{H}$ , the large epoxy-cyclohexane moiety suffices to produce a similar twisting process as in **13c**.

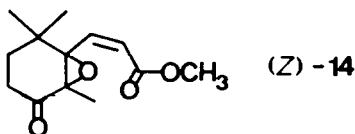


UV data of the stereoisomers (E)-3, (Z)-3' and (Z)-3'' are similarly indicative. It is anticipated that a twist around the enone single bond will shift the absorption to shorter wavelengths and decrease the extinction coefficients.<sup>14</sup> The experimental values are  $\lambda_{\text{max}}=241$  nm ( $\epsilon=12144$ ); 237 (7534) and 224 (4610) for (E)-3, (Z)-3'' and (Z)-3', respectively, and support the stereochemical interpretation of the  $^{13}\text{C}$  chemical shifts.

We recall that, as opposed to the situation in (Z)-3' and (Z)-3'', no structural assignment has yet been possible for the two rapidly interconverting conformers of (Z)-2. In analogy to the case of (Z)-3 we denote as (Z)-2' the C-6/C-7 conformer with the syn-arrangement of the two oxygens. Then, from an inspection of Table 1 and a comparison with the chemical shifts of (Z)-3' and (Z)-3'' we can identify the minor conformer of (Z)-2 as (Z)-2'' and the major as (Z)-2' (see Table 1).

**4. Electronic and steric requirements of the epoxyenone/furan isomerization.** We are now in a position to describe the structural features of epoxyenones which are necessary for the occurrence of the above valence isomerization:

- The (E)-isomers of compounds 1, 2 and 3 are all thermally stable. Only the (Z)-configuration of the C-7/C-8 double bond allows the carbonyl oxygen to approach the centre C-6 of the oxirane moiety.
- The thermal stability of the epoxydiene (Z)-9'' indicates the significance of a nucleophilic oxygen for the oxirane ring opening. Moreover, while (Z)-2 smoothly produced the furan isomer, its ester analogue (Z)-14 was recovered unchanged when being heated to 160° for 24 hours. Obviously, the carbonyl oxygen of the latter does not possess sufficient nucleophilicity.



- While at 130° (Z)-2 and (Z)-3'' rearrange with comparable rates, only the reaction of the former allowed a ready kinetic analysis to be made (see Section 3.1 and Experimental). The enthalpies of activation are 24.8 kcal/mol in acetonitrile- $\text{d}_3$  and 24.4 kcal/mol in cyclohexane- $\text{d}_{12}$ , while the activation entropies are  $\Delta S^\ddagger=-19$  e.u. and -25.7 e.u., respectively. The negative values of  $\Delta S^\ddagger$  can be explained by the occurrence of a highly ordered transition state with partial charge separation. Therefore, the intermediate formation of structures such as X1 and X3 appears reasonable. The bond cleavage within the latter is facilitated by the electronic stabilization of the furan moieties being formed.
- The combined chemical and  $^{13}\text{C}$  NMR spectroscopic evidence indicates that an additional steric requirement for the epoxyenone/furan isomerization is defined by the torsional angle around the C-6/C-7 bond, i.e. only conformers (Z)-2'' and (Z)-3'' with a trans-diaxial arrangement of carbonyl and oxirane oxygen are prone to undergo the isomerization.

## EXPERIMENTAL

**1. Synthesis of the compounds.** The epoxyenones (E)-1, (E)-2, (E)-3 and (Z)-2 were prepared as described previously.<sup>2,3,10</sup> On photolysis ( $\lambda > 347$  nm, acetonitrile) of (E)-3 the photoisomer (Z)-3' was obtained in 57% yield. The isomer (Z)-3' is stable at room temperature. Upon heating to 80° (cyclohexane) (Z)-3' transformed into (Z)-3'', the structure of which is discussed above. It is most indicative that (Z)-3'' was synthesized independently by epoxidation (m-chloroperbenzoic acid, ether/NaHCO<sub>3</sub>-solution) of (Z)-7c in 64% yield.<sup>10</sup> Wittig reaction of the epoxyenones (E)-3 and (Z)-3' (ca. 0.3 molar ethereal solution of methylene triphenyl phosphorane) afforded the corresponding epoxydienes (E)-9 (82%) and (Z)-9' (60%), respectively.<sup>15</sup> A 7:1-mixture of (Z)-9'' and (Z)-9' was obtained upon heating of a solution of (Z)-9' in cyclohexane- $\text{d}_{12}$  at 120° for 2 hours ( $^1\text{H}$  NMR analysis).<sup>15</sup>

(E)-**9** (ca. 1:1 mixture of two conformers).  $^1\text{H}$  NMR (chloroform-d): 0.98, 1.01, 1.02, 1.04 [4s, 6H, 3H-(C-1a,1a')]; 1.12, 1.18 [2s, 3H, 3H-(C-5a)]; 0.90-1.90 [m, 6H, 2H-(C-2,3,4)]; 1.80, 1.85 [2d, 3H,  $J=1$ , 3H-(C-7a), d at 1.85 overlapping with s]; 1.85 [s, 3H, 3H-(C-9a)]; 4.81, 4.97 [2m,  $w_{1/2}=6$ , 2H, 2H-(C-10)]; 5.57, 5.90 [2m,  $w_{1/2}=4$ , 1H, H-(C-8)]. -  $^{13}\text{C}$  NMR see Table 1.

(Z)-**9'** (contaminated with ca. 10% of (Z)-**9''**).  $^1\text{H}$  NMR (chloroform-d): 1.04, 1.10, 1.23 [3s, 9H, 3H-(C-1a,1a',5a)]; 1.20-1.90 [m, 6H, 2H-(C-2,3,4)]; 1.79, 1.82 [2m,  $w_{1/2}=3$ , 6H, 3H-(C-9a,7a)]; 4.89, 4.96 [2m,  $w_{1/2}=5$ , 2H, 2H-(C-10)]; 5.84 [m,  $w_{1/2}=4$ , 1H, H-(C-8)]. -  $^{13}\text{C}$  NMR see Table 1.

(Z)-**9''** (contaminated with ca 10% of (Z)-**9'**).  $^1\text{H}$  NMR (chloroform-d): 1.04, 1.10, 1.20 [3s, 9H, 3H-(C-1a,1a',5a)]; 1.20-1.90 [m, 6H, 2H-(C-2,3,4)]; 1.83 [m,  $w_{1/2}=3$ , 6H, 3H-(C-9a,-7a)]; 4.87, 5.04 [2m,  $w_{1/2}=5$ , 2H, 2H-(C-10)]; 5.78 [m,  $w_{1/2}=4$ , 1H, H-(C-8)]. -  $^{13}\text{C}$  NMR see Table 1.

2. **NMR measurements.**  $^{13}\text{C}$  NMR spectra were taken at 22.6 MHz on a Bruker HX-90 spectrometer. Sweep widths of 6000 Hz were used in order to include the carbonyl signals at low field. The scans were accumulated into an 8 K memory. The lock signal was taken from the deuterium resonance of the solvent. Chloroform-d and tetrachloroethane-d<sub>2</sub> were used as solvents, the concentrations being between 0.5 and 1.0 molar. In the course of the temperature-dependent studies the temperature, which was measured with a calibrated thermocouple, was taken before and after all runs and was constant within  $\pm 1.0^\circ$ .

Line shape analysis of exchange broadened signals of compound (Z)-**2** was achieved by means of the computer program DNMRIT,<sup>11</sup> and the rate constants obtained were used for Arrhenius plots. Care was taken to account for the temperature dependence of the signals by recording the chemical shifts in the slow exchange domain and extrapolating to the temperature under consideration. The latter procedure turned out to be essential in view of the small shift differences of related magnetic sites. Separate simulation procedures were performed for the

resonances of C-9, C-8, C-7 and C-5, respectively. The relative weight of the interconverting isomers, determined from integration of the signals in the slow exchange domain, was kept constant during kinetic analysis. Slight variation of the equilibrium constant, however, did not significantly affect the data. The error limits of the rate constants [ $p$ ] were determined by taking the closest  $p$ -value on both sides of the optimal value for which the visual fit obviously deviated from the experimental line shape. The resulting errors were 10% in the middle of the temperature range and up to 25% at the temperature extremes. The errors of the kinetic data quoted in Table 2 were calculated as described in reference 11.

$^{13}\text{C}$  signals assignments are based upon the following techniques and criteria.

- The spectra are clearly divided into four parts, the carbonylic, olefinic, "etheric" and aliphatic region. Consequently, detailed assignments have to be made for the olefinic signals of C-7/C-8, the signals of C-5/C-6 within the oxirane ring and the aliphatic ones.
- CW-offset  $^1\text{H}$  decoupling as well as the "attached proton test"<sup>16</sup> allow to identify the different types of carbons (quarternary, tertiary, secondary and primary). The differentiation of C-7 and C-8 in (E)-**3**, (Z)-**3'** and (Z)-**3''** follows immediately. In the same fashion, one recognizes the signal of the quarternary and secondary ring carbons C-1 and C-2, C-3, C-4, respectively, as well as those of the methyl groups.
- Selective decoupling helped us to assign the resonances of C-7 and C-8 in (E)-**1**, (E)-**2** and (Z)-**2** as well as those of the methyl signals in (E)-**1**, (E)-**2**, (Z)-**2**, (Z)-**3'** and **10**.
- The signal of C-7a in (E)-**3**, (Z)-**3'** and (Z)-**3''** was also identified with the help of a trideuterio derivative bearing a CD<sub>3</sub>-group at C-7.
- The  $^{13}\text{C}$  chemical shifts within the complete series of related compounds (see Table 1) were compared and structural changes were assessed. Among these effects are the incorporation of a 4-oxo group, the epoxydiene formation, the methyl substitution at C-7<sup>10</sup>

or the (E/Z)-isomerization. The substitution within the enone side chain and the configurational change are expected to affect the conformational properties, which therefore guide the course of the valence isomerization. These effects are considered in detail above (see Section 3.2).

The chemical shift differences  $\Delta\nu$  of exchanging magnetic sites in (E)-3 and (E)-9 are too small to allow for a line shape analysis with error limits similar to those in the case of (Z)-2 [(Z)-2:  $\Delta\nu=44\text{Hz}$ , (C-5); 100, 209 (C-7, C-8); 131 (C-9); (E)-3: 30 (C-5); 53 (C-7); 4 (C-8); 6 (C-9); (E)-9: 34 (C-5); 3 (C-7); 6 (C-8); 9 (C-9)]. A comparison of the conformational mobility of (Z)-2, (E)-3 and (E)-9 will, thus, be based on  $\Delta G^\ddagger$  values only (see text).

The thermal reactions (Z)-3'  $\rightarrow$  (Z)-3'' and (Z)-9'  $\rightarrow$  (Z)-9'' (degassed toluene- $d_8$  as solvent, NMR tubes sealed in vacuo) were monitored and kinetically analyzed by conventional methods. Thereby the time dependent concentrations of starting material and product (thermolysis temperatures; (Z)-3': 63°, 59°, 74.5°, 68°, 56°; (Z)-9': 86°, 92°, 76°, 81°, 72°) were determined from the signal intensity of the olefinic proton H-8. The resulting activation parameters are given in Table 2.

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