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SELECTIVE NUCLEOPHILIC TRANSFORMATIONS OF CYCLOPENTADIENONE EPOXIDES

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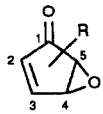
Abstract: Acid-catalysed solvolyses of cyclopentadienone epoxides lead to epoxide ring opening and take place regioselectively at C-4. The stereochemical outcome of the epoxide ring opening depends on the substitution pattern and the nature of the substituents. Trans *opening is preferred in most cases. Participation of the substituents in the transition state, however, leads to* cis *opened products. Selective reactions with the enone moiety,* i.e. *methanol addition and alkaline epoxidation, are described.*

Introduction

Cyclopentadienone epoxides **1** are challenging species to explore chemoselectivity and control of reactivity because the various functional groups present in these small molecules all are susceptible to the same reagents. A study of the chemical behaviour of these multifunctionalized compounds is of interest for general strategies in organic synthesis and for possible applications[1,2] in the synthesis of natural products, particularly highly oxygenated cyclopentenoids.

Until recently no practical synthesis of cyclopentadienone epoxides **1** was available and therefore their chemistry has but sporadically been described. Only their photochemistry was studied in some detail. Tri- and tetraphenyl substituted cyclopentadienone epoxides equilibrate with pyrylium oxides on irradiation[3,4]. Photochemical induced rearrangements to 2-pyrones were reported for the parent compound **1** (R=H)[5] and for the alkyl- and phenylsubstituted epoxides **1** (R=2,5-dimethyl; R=3,4-diphenyl; R=2,3,4,5-tetraphenyl)[6-8]. The postulated intermediacy of cyclopentadienone epoxides in the photo-isomerisation of 4-pyrones to 2-pyrones was unambiguously proven for **1** (R=2,5-dimethyl)[6]. Phenyl-, alkyl- and otherwise substituted cyclopentadienone epoxides rearrange to 2-pyrones on heating[3,5,9-13]. The parent compound **1** (R=H) decomposes in acidic or basic media[5]. Only a few reports deal with synthetic applications. These involve either a reaction with the enone moiety[14] or a reaction with the epoxide function[1,2].

A general synthesis of the cyclopentadienone epoxides **1**, using normal chemical procedures involving acid or basic reaction or work-up conditions, is frustrated by their inherent sensitivity to acids and bases. An alternative synthetic approach, in which these epoxides are generated by gas phase thermolysis (Flash Vacuum Thermolysis, FVT) of cyclopentadiene derived polycyclic epoxides **2** (X=CH_2,O) is limited by the thermal instability of **1**. These thermolyses of **2** (X=CH_2) often require rather high temperatures (430°-500°C), at which the thermal rearrangement of **1** to 2-pyrones hardly can be avoided[5,11,12]. Recently we demonstrated[13], however, that furan derived **2** (X=O) are excellent substrates for the FVT mediated synthesis of cyclopentadienone epoxides **1**. This type of polycyclic epoxides can efficiently be thermolysed at temperatures as low as



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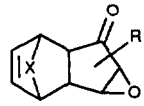

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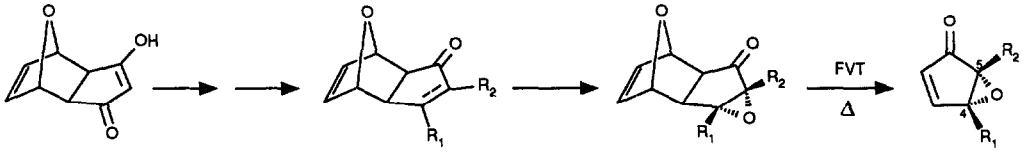
300-375°C, to give **1** without concomitant formation of pyrones. The polycyclic epoxides **2** (X=O),in turn, can conveniently be obtained from the Diels-Alder adduct **3** of furan and 2-cyclopentene-1,4-dione[13,15]. Starting from this adduct **3**, various 4- and 5-substituted cyclopentadienone epoxides **4** were prepared using the sequence of reactions shown in Scheme 1. These cyclopentadienone epoxides **4** were used to uncover the chemistry of this

Scheme 1



3 4

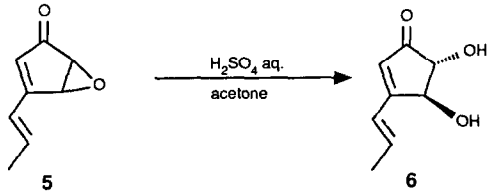
interesting class of compounds. In this report we focus on nucleophilic transformations of **4**, *viz.* hydrolyses, methanolyses and epoxidations, under acid, neutral and alkaline conditions. It will be shown that, depending on reaction conditions and substitution pattern, a highly selective reaction with either the epoxide function or the enone moiety can be accomplished. The regio- and stereochemistry of these reactions is analysed and mechanistic aspects are discussed.

Results and Discussion

Acid-catalysed hydrolysis of the epoxide function.

In a previous communication[1] we reported that selective hydrolysis of the epoxide function of **5** required more drastic acidic conditions than expected. In an ethereal solution, containing 10% 0.4N H_2SO_4aq, no reaction took place. It was found, after careful experimentation, that the desired epoxide ring opening could conveniently be achieved in acetone, containing 1% 0.5 N H_2SO_4 aq. Under these conditions the epoxide function of **5** was stereospecifically transformed into a *trans*-diol group, to give terrein **6** in 55% yield[1] (Scheme 2). When these

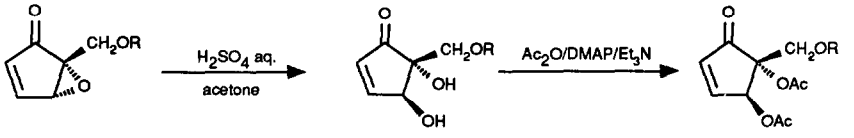
Scheme 2



5 6

same hydrolytic conditions were applied to the 5-alkoxymethyl substituted epoxides **7** and **8**, followed by an immediate acylation, the acyl-protected *epi*-pentenomycins **9** and **10** were obtained in 54% and 30% yield, respectively (Scheme 3). The *trans* configuration of these *epi*-pentenomycin diacetates **9** and **10** followed

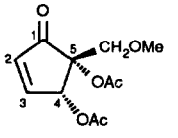
Scheme 3



7 R=Me
8 R=Et

9 R=Me
10 R=Et

unequivocally from comparison of their ^{1}H-NMR spectra with that of the epimer of **9**, *i.e.* **11**[12]. The signals for



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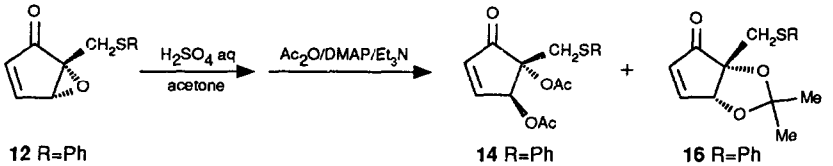
the ring protons, H_2, H_3 and H_4 of **9** and **10** were found at δ 6.47-6.45, δ 7.40-7.35 and δ 6.26-6.25 ppm, respectively, whereas the resonances of the corresponding protons of **11** were observed at δ 6.35, δ 7.25 and δ 5.75 ppm. The signals for H_4 in **9** and **10** were particularly indicative of the *trans* configuration. They were observed approximately 0.5 ppm downfield as compared with the resonance for H_4 in **11**.

Surprisingly, treatment of cyclopentadienone epoxides **12** and **13**, containing a phenyl- or benzyl-thiomethyl group instead of an alkoxymethyl group, with the same mixture of acetone and aqueous H_2SO_4, followed by acylation, also provided, in addition to the expected *trans*-diacetates **14** (36%) and **15** (38%), respectively, the acetonides **16** (32%) and **17** (32%) (Scheme 4). It should be emphasized that during the

Scheme 4



12 R=Ph
13 R=Bz

14 R=Ph
15 R=Bz

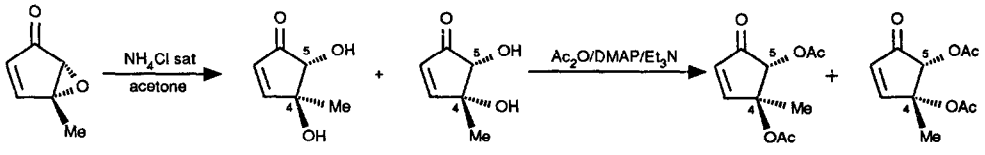
16 R=Ph
17 R=Bz

hydrolyses of **7** and **8** no such acetonides were observed.

Another unexpected result was obtained when cyclopentadienone epoxide **18** was subjected to these same hydrolysis conditions. After acylation of the resulting product mixture no identifiable compound was isolated. The spectral data of the crude mixture suggested that the initial products, despite the mild acidic conditions of the hydrolysis, were converted *in situ* into other unstable materials. The hydrolysis of **18** was therefore tried again, but now in the absence of acid, *viz.* in acetone only containing 5% of water. However,

under these conditions, epoxide **18** did not react. In a third attempt, epoxide **18** was stirred in a 10:1 mixture of acetone and saturated NH_4Cl aq. According to its ^{1}H-NMR spectrum, the product mixture now consisted of *trans*-diol **19** and *cis*-diol **20**, in a ratio of 1.8:1, and a trace of unreacted **18**. Subsequent acylation provided the corresponding diacetates **21** and **22**, in 22% overall yield (Scheme 5). These acetates were also obtained in the ratio of 1.8:1, implying that during the acylation no epimerisation had taken place. The formation of **20** by epimerisation of **19**, or *vice versa*, during the hydrolysis of epoxide **18** must therefore be considered as highly unlikely. During this hydrolysis of **18** a considerable amount of *cis*-diol was formed. Formation of an acetonide, similar to **16** and **17**, had, however, not occurred. This underlines the extremely mild acidic conditions needed to accomplish the opening of the epoxide ring of **18**. The configurations of **19** and **20** were deduced from the

Scheme 5

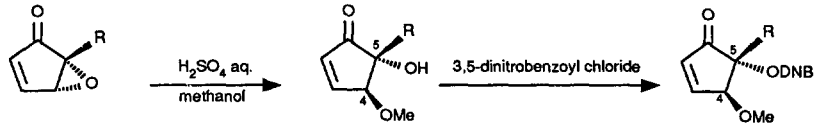


relative ^{1}H-NMR resonances of the respective H_5 protons. The most downfield H_5 signal, *viz.* at δ 4.30 ppm, was assigned to the *trans*-diol **19**, because in this isomer the C_4-OH group will exert a considerable deshielding effect on the adjacent, *cis*-orientated H_5 proton. Such an effect is obviously absent in *cis*-diol **20** and the H_5 signal of **20** is accordingly observed at higher field, *viz.* δ 3.87 ppm. A similar difference in chemical shift was found for the H_5 protons of the respective diacetates **21** and **22**, which were observed at δ 5.84 and δ 5.14 ppm, respectively.

Acid-catalysed methanolysis of the epoxide function.

Hydrolysis and methanolysis reactions of epoxides are usually mechanistically very similar. The latter, however, provide valuable information about the regiochemistry of these solvolyses. Methanolysis of the parent cyclopentadienone epoxide **23** was performed using the same concentration of acid as applied during the hydrolyses of the cyclopentadienone epoxides **5**, **7**, **8**, **12** and **13**. Under these conditions **23** was quantitatively converted into the *trans*-methoxyalcohol **24**. Subsequent treatment with 3,4-dinitrobenzoyl chloride gave product **25** (Scheme 6). Cyclopentadienone epoxide **7** similarly afforded the corresponding *trans*-products **26** (88% yield) and **27** (70% overall), respectively. No trace of the respective *cis*-methoxy epimers was observed in

Scheme 6



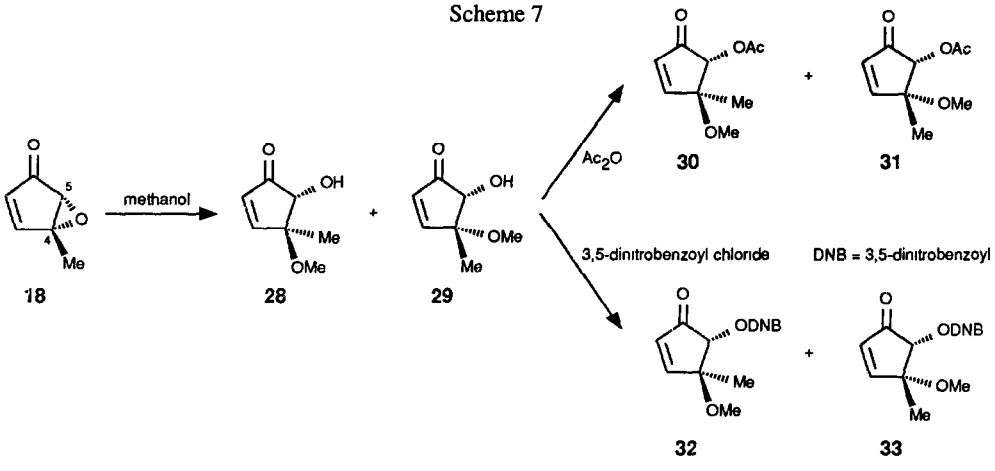
these cases. The ^{1}H-NMR spectra of **24-27** clearly established the 4-position of the methoxy group as well as the

trans relationship between the methoxy and the hydroxy group. The particular position of the methoxy group in **24-27** was deduced from the following ^{1}H-NMR data. Upon benzoylation the doublet for the H_5 proton of **24** shifted downfield by 1.32 ppm. Such a shift is characteristic for a proton attached to a hydroxylated carbon that is converted into a benzoate[16]. Benzoylation of **26** led to a downfield shift of 0.57 ppm for the H_4 proton, implying that this proton was not situated at a carbon, carrying a hydroxyl group. Both observations indicated that the methoxy group in **24-27** is present at C-4. The relatively small coupling constants of 2.7 Hz and 3.0 Hz, observed for H_4 and H_5 in the ^{1}H-NMR spectra of **24** and **25**, respectively, are indicative of a *trans* relationship between these vicinal protons. In terrein **6** this coupling is similar, *viz.* 2.5 Hz[1], whereas in its epimer, *iso*-terrein, a much larger coupling of 6 Hz is found[17] for the *cis* H_4 and H_5 protons . These data confirm the *trans* structure of **24** and **25**. The *trans* configurations of **26** and **27** followed from comparison of their ^{1}H-NMR spectra with those of **9** and its diol-precursor (Scheme 3).

Methanolyses under neutral conditions.

In view of the very mild acidic conditions required for the hydrolysis of **18**, methanolysis of **18** was attempted without acid catalysis. Stirring of this epoxide in a solution of methanol at room temperature resulted in a smooth cleavage of the epoxide ring affording a 3.3:1 mixture of the *trans*- and *cis*-methoxy-alcohols **28** and **29**, respectively, in almost quantitative yield (Scheme 7). Subsequent acylation gave acetates **30** and **31**, respectively, which failed to crystallize. Benzoylation with 3,5-dinitrobenzoyl chloride, however, afforded solid derivatives, *viz.* **32** and **33**, respectively. Crystals of the predominant isomer **32** were subjected to an X-Ray diffraction analysis. This structure determination unambiguously revealed that the methoxy group in **32** is located at C-4, *trans* to the C-5-dinitrobenzoate group[18]. With the spectral features of **32** as a reference, the structures of **28-33** could be established with certainty.

Scheme 7



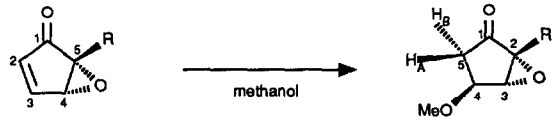
The acetates, **30** and **31**, as well as the benzoates, **32** and **33**, were obtained in the same ratio as the alcohols **28** and **29**, *viz.* 3.3:1, indicating that during acylation and benzoylation no epimerisation had taken place. Comparison of the *trans/cis* product ratios obtained in the hydrolysis and the methanolysis of **18** shows that the preference for *trans*-epoxide-opening in the latter case is slightly larger.

The above results show that the opening of the epoxide ring of **18** in neutral methanol takes place

regioselectively at C-4, with some preference for the *trans* stereochemistry.

The parent cyclopentadienone epoxide **23** and the 5-alkoxymethylsubstituted epoxides **7** and **34** were also subjected to methanolysis under neutral conditions. Stirring of **23** in methanol for one week at room temperature gave a single product, which, however, as ascertained by capillary GC, was not alcohol **24** but cyclopentenone epoxide **35** (Scheme 8). The rather low yield of 39% must be attributed to considerable loss of material during the removal of the solvent. Similar treatment of the cyclopentadienone epoxides **7** and **34** led to the correspon-

Scheme 8



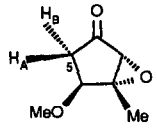
23 (R=H)
7 (R=CH_2OMe)
34 (R=CH_2OiPr)

35 (R=H)
36 (R=CH_2OMe)
37 (R=CH_2OiPr)

ding cyclopentenone epoxides **36** and **37**, in excellent yields of 82% and 100%, respectively.

The structures of the products **35-37** were deduced from their ^{1}H-NMR data. The splitting pattern of the signal for H_4 was particularly decisive for the assignment of the configurations. This proton has a medium range coupling of 5-6 Hz with one of the H_5 protons and a very small (for **35**) or even no (for **36, 37**) coupling with the other H_5 proton. In all cases no coupling was observed with H_3. The coupling of 5-6 Hz was attributed (Karplus equation) to spin-spin interaction of H_4 with the *cis*-orientated H_5 proton, *i.e* H_B. The absence of spin coupling between H_4 and H_3 indicates that H_3 is *trans*-orientated to H_4. The methoxy group and the epoxide ring were therefore also positioned *trans* to each other. The resonances for H_3 and H_2 in the ^{1}H-NMR spectrum of **35**, at δ 3.36 ppm and δ 3.94 ppm, respectively, were assigned by comparison with the positions of the H_3 signals of **36** and **37**, which were present at δ 4.00 ppm and δ 4.03 ppm.

The substrates, shown in Scheme 8, all gave, in fact unexpectedly, exclusive addition of methanol to the enone system leaving the epoxide group in tact. In view of these results the ^{1}H-NMR spectrum of the crude product mixture, obtained from **18** under neutral methanolysis conditions, was scrutinized for the presence of the methanol addition product **38**. A weak AB pattern in the 1.8 - 2.4 ppm region was indeed observed, which was



38

assigned to the H_5 protons of **38**, by comparison with the ^{1}H-NMR spectra of **35-37**. This means that also some conjugate addition of methanol to **18** had taken place to give **38** (yield ≤ 5%).

It is, in principle, conceivable that the products **28** and **29** from **18** (Scheme 7) are the result of an initial conjugative methanol addition to give **38**, followed by epoxide opening and elimination of methanol to produce the actual products isolated. A similar sequence can be envisaged for the formation of the products **24** and **26**, during the acid-catalysed methanolysis of **23** and **7** (Scheme 6). To test this hypothesis, compound **35** was treated with methanol containing a trace of acid. Instead of compound **24**, however, a fatty polymeric material was obtained (100%). This observation rules out the just mentioned involvement of an initial conjugative

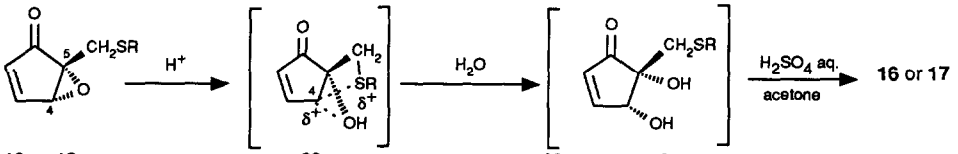
methanol addition. The epoxide opening and enone addition are clearly independent processes.

Mechanistic aspects of the (acid-catalyzed) opening of the epoxide ring.

In the discussion of the mechanism of the opening of the epoxide ring two aspects need to be covered, *viz.* the regiochemistry and the stereochemical course. The methanolysis reactions, shown in Schemes 6 and 7, clearly indicate that the nucleophilic solvent attacks at C-4. Because of the similarity in results between the above epoxide hydrolyses and methanolyses, it is justified to conclude that also the hydrolyses proceed by nucleophilic attack at C-4. It should be noted that this also holds for epoxide **18**, with a methyl substituent at C-4 (Scheme 5). The stereochemistry of the epoxide hydrolysis of the precursor **5** of terrein follows the general pattern[19-23] of epoxide opening reactions, implying exclusive formation of *trans*-diols (Scheme 2). Consistent herewith are the hydrolyses and methanolyses of the parent compound **23** and the 5-substituted cyclopentadienone epoxides **7** and **8**, which also proceed exclusively with *trans* stereochemistry (Schemes 3 and 6). This *trans* opening of the epoxide ring takes place with inversion of configuration at C-4. Confirming evidence for this stereo- and regio-chemistry is the observation[24] that the acid-catalysed hydrolysis and subsequent acylation of homochiral cyclopentadienone epoxide **7** lead to enantiomerically pure diacetate **9**.

This seemingly consistent picture of the stereochemistry of the epoxide opening needs reconsideration for the cyclopentadienone epoxides **12** and **13**. The formation of the acetonides **16** and **17** during the hydrolyses of these epoxides (Scheme 4) can only be reconciled by the involvement of *cis*-diols. In view of the exclusive C-4 epoxide opening, observed for the other cyclopentadienone epoxides, it is justified to assume that for these two compounds the epoxide opening also occurs at C-4. The interference of the sulphur containing substituent at C-5 allows a plausible explanation for *cis*-diol formation in these hydrolyses. The sulphur atom of this group can serve as an internal nucleophilic centre and assist in the opening of the epoxide ring[25]. Its role here is presumably restricted to anchimeric shielding of the cationic centre, that is generated at C-4 by stretching of the C-O bond in the protonated epoxide (see structure **39** in Scheme 9). The rear side of the epoxide function is in this manner

Scheme 9



12 or **13** **39** **40** (R = Ph) or **41** (R = Bz)

blocked for attack of the nucleophilic solvent molecule and, in consequence, *cis*-opened products, *i.e.* diols **40** or **41**, will be produced. Under the applied reaction conditions these diols are trapped by acetone to produce the acetonides **16** and **17**, respectively. This rationale in fact conforms with the generally accepted mechanism[26] of the acid-catalysed hydrolysis of epoxide rings, according to which this reaction has a considerable cationic character with the nucleophile entering rather late in the transition state, when the C-O bond cleavage has already progressed to a great extent (borderline A_2 mechanism).

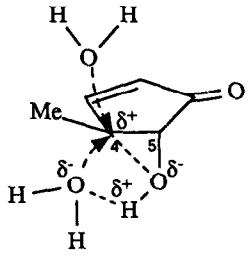
Alternatively, a four-membered thietanium ion, resembling structure **39**, can be envisaged as an actual intermediate. If this were the case, then the *cis*-diol formation is readily explained by a two stage process involving double inversion. However, a true four-membered thietane would involve considerable annelation

strain. Moreover, in that case the methylene carbon would *a priori* have been a more logical site for nucleophilic attack leading to entirely different products.

The anchimeric shielding is only partly effective as can be judged from the observed diacetate-acetonide ratio of *ca* 1:1 (Scheme 4). It is noteworthy that the alkoxymethyl substituents in the epoxides **7** and **8** are apparently ineffective in exerting an anchimeric shielding for nucleophilic epoxide opening from the rear side.

The formation of *cis*-diol **20** on hydrolysis of **18** (Scheme 5) can clearly not be explained by neighbouring group participation. On the basis of the general mechanism of the acid-catalysed hydrolysis of epoxides (*vide supra*), it is conceivable that the epoxide ring opening in this case has a high degree of S_N1 character, because the methyl substituent can stabilize the cationic centre at C-4. This implies that C-4 is close to sp^2 hybridisation and as a consequence thereof, the methyl group has moved towards the plane of the five membered ring. The nucleophilic solvent can now enter the transition state from either side of the five membered ring producing a mixture of *cis*- and *trans*-diols. The respective arrangements are shown in Figure 1.

Figure 1



Similar arrangements explain the formation of the *trans*- and *cis*-products, **28** and **29**, in the methanolysis of **18** (Scheme 7). In this case the solvated epoxide is involved in the transition state, rather than the protonated oxirane.

Comparison of the stereochemistry of the epoxide opening in the substrates **23** and **18** (see methanolysis reactions in Schemes 6 and 7, respectively) reveals that the methyl group at C-4 has a remarkable influence. When this group is lacking no *cis*-opening is observed. The extremely mild conditions under which the hydrolysis and methanolysis of this compound take place are also noteworthy. They illustrate the high reactivity of this particular cyclopentadienone epoxide.

In the literature sofar only a few examples of *cis*-epoxide-opening reactions, not involving double inversion are reported[19,27-30]. These epoxide openings were observed under acid-catalysed conditions for epoxides carrying alkenyl or aryl groups. Such unsaturated substituents can stabilize the incipient cationic centre resulting from the C-O bond stretching. This stabilizing effect apparently allows the introduction of the nucleophilic solvent from the front as well as the rear side.

The results obtained with the epoxide opening of the respective cyclopentadienone epoxides investigated here, clearly demonstrate the great influence of the substituents on the stereochemical course of the reaction. The regiochemistry on the other hand is the same for all substrates. It involves exclusive nucleophilic attack at C-4.

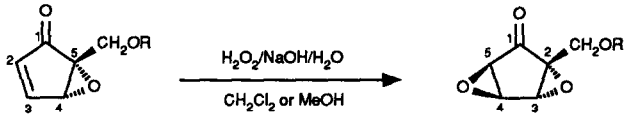
Alkaline epoxidation of the double bond.

The enone moiety in cyclopentadienone epoxides is considerably reactive as is demonstrated by the

conjugate addition of methanol (Scheme 8). It is of interest to investigate other reactions of the enone part. In view of the interesting structures of the expected products, the nucleophilic epoxidation was explored.

Treatment of the 5-substituted cyclopentadienone epoxides **7** and **8** with alkaline hydrogen peroxide in dichloromethane or methanol afforded the bis-epoxides **42** and **43** in 25% and 64% yield, respectively (Scheme 10). These bis-epoxides are rather labile compounds. They slowly decompose, even on storage in the freezer.

Scheme 10



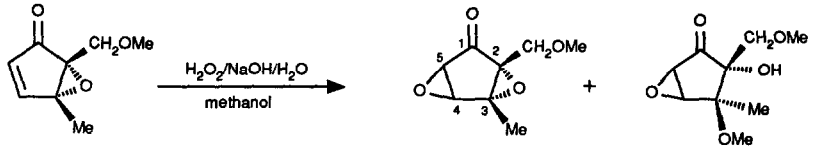
7 (R=Me) **42** (R=Me)

8 (R=Et) **43** (R=Et)

The IR spectra of the crude products sometimes displayed strong OH absorptions, indicating that epoxide opening already had occurred during the reaction.

The alkaline epoxidation of cyclopentadienone epoxide **44** in a mixture of dichloromethane and methanol provided a 3:1 mixture of the bis-epoxide **45** and the mono-epoxide **46**, in *ca* 50% yield (Scheme 11). The bis-epoxide could be obtained in pure state by filtration of the crude product over silicagel. In order to establish its intermediacy in the formation of mono-epoxide **46**, it was stirred in methanol. This led to a mixture of **45** and **46**, in a ratio of 1:3. An attempt to prepare the acyl derivative of **46** by treatment of this mixture with acetic anhydride, DMAP and triethylamine failed. Instead, a larger amount of the bis-epoxide **45** was obtained than initially had been introduced. Under the conditions of this acylation the mono-epoxide **46** was apparently reconverted into its precursor **45**.

Scheme 11

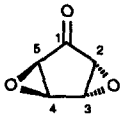


44 **45** **46**

Attempts to prepare the bis-epoxide, derived from **18**, were frustrated by the lability of the product. To avoid decomposition *in situ* of this bis-epoxide, less alkaline conditions than applied in the other epoxidations were tested. This however resulted only in the formation the diols **19** and **20**.

The parent compound **23** smoothly reacted with alkaline hydrogen peroxide in dichloromethane. The isolation of the resulting bis-epoxide **47**, however, was troublesome due to the high volatilty of this compound. So far, we only succeeded to obtain this bis-epoxide in solution.

The above epoxidations all afforded only one single diastereomer, *i.e* either the anti- or the syn-bis-epoxide. The configuration of **42** and **43** was deduced from the ^{1}H-NMR spectra of these compounds, which showed negligible spin coupling between H_4 and H_3, indicating the trans-orientation of these protons. For the *cis* orientated protons, H_5 and H_4, a distinct spin coupling of *ca.* 2.5 Hz was observed. In consequence, both epoxide rings in **42** and **43** are positioned in an anti fashion.



47

The spectral data of **45** and **47** did not reveal the relative position of the epoxide rings with certainty. It is reasonable to assume that the epoxidizing agent in the reaction with **23** approaches from the same side as methanol in the conjugate addition to this compound (Scheme 8). Therefore the anti-bis-epoxide structure is proposed for **47**. In the case of **44** the steric course of the epoxidation is unpredictable, because both sides of the five membered ring carry substituents of comparable size.

The ^{1}H-NMR positions of the protons H_3, H_4 and H_5 in all bis-epoxides could readily be assigned by comparison with the ^{1}H-NMR spectrum of the methanol adduct **35**. In this adduct the H_2 proton absorbs at higher field than H_3, *viz.* at δ 3.36 ppm and δ 3.94 ppm, respectively. Accordingly, for the bis-epoxides the high field resonance at *ca* 3.39 ppm was assigned to H_5 (and H_2 for **47**) and the low field resonances at *ca.* 4.0-4.2 ppm to H_3 and H_4.

The results of the alkaline epoxidation reactions of the investigated cyclopentadienone epoxides show that under basic conditions the enone moiety is more prone to react with nucleophiles than the epoxide function. This observation is consistent with the selective reaction of methanol with the cyclopentadienone epoxides **23**, **7** and **34** under neutral conditions, where preferential enone addition is observed (Scheme 8).

Concluding remarks

The results presented in this paper demonstrate that the epoxide function in cyclopentadienone epoxides allows a selective acid-catalysed hydrolysis or methanolysis reaction in which the nucleophilic solvent attacks at C-4. The stereochemical course of the epoxide ring opening strongly depends on the substitution pattern of the substrates and the nature of the substituents. Opening in *trans* fashion is usually preferred. However, depending on the substituents, considerable amounts of *cis*-opened products are obtained. These results can in part be explained by invoking a participation of the substituents in the solvolysis reaction. Selective reactions of the enone moiety of some substrates could be accomplished, *viz.* conjugate methanol addition under neutral and nucleophilic epoxidation under alkaline conditions.

Experimental

General remarks

Melting points were measured with a Reichert Thermopan microscope and are uncorrected. IR spectra were taken on a Perkin Elmer 298 infrared spectrophotometer. ^{1}H-NMR spectra were recorded on a Varian EM-390 or a Bruker WH-90 spectrometer using TMS as internal standard. For mass spectra a Varian SM-1B or a double focussing VG 7070E mass spectrometer was used. Column chromatography ("flash chromatography") was carried out at a pressure of *ca* 1.5 bar, a column length of *ca* 15 cm and a column diameter of 1-4 cm, using Merck Kieselgel 60 H. For preparative TLC precoated Kieselgel plates Merck 60-F254 were used.

The relative configurations of the products are specified by means of the prefixes R* and S*. The asterisks (*) indicate that the products consist of racemic mixtures[31].

(4S,5R*)-4,5-Diacetoxy-5-methoxymethyl-2-cyclopentenone* (**9**)[32].

A solution of cyclopentadienone epoxide **7**[13] (86 mg; 0.6 mmol) in acetone containing 1 vol. % 5N H_2SO_4aq (25 ml) was stirred at room temperature for 2 days. Then, $NaHCO_3$ (5g) and $MgSO_4$ (5g) were added and the resulting slurry was stirred overnight. The mixture was filtered. The solids were carefully washed with acetone and the combined filtrates were concentrated in vacuo to give 86 mg of crude *(4S*,5R*)-4,5-dihydroxy-5-methoxymethyl-2-cyclopentenone*, as a yellow oil. IR(film) ν: 3700-3040 (s;OH), 2980(m), 2920(m), 1710(s;C=O), 1635(s;C=C), 1100(s) cm^{-1}. ^{1}H-NMR($CD_3OD/CDCl_3$) δ: 3.33(3H,s;CH_2OCH_3), 3.57(2H,s;CH_2OCH_3), 4.73(1H,br s;H_4), 6.27(1H,br d,$J_{2,3}$=6Hz;H_2), 7.53(1H,dd,$J_{3,4}$=1.5Hz,$J_{3,2}$=6Hz;H_3). Without further purification, the crude diol was acylated in a mixture of dichloromethane (4 ml), Ac_2O (0.2 ml), DMAP (10 mg) and Et_3N (0.2 ml). After stirring at room temperature for 3 hrs, the reaction was quenched with water (10 ml). The aqueous layer was extracted with dichloromethane (3x5 ml). The combined organic solutions were successively washed with 3% HCl (3x5 ml) and water (3x5 ml), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2/ethyl acetate) to afford 78 mg (54% overall) of **9**, as a colourless oil. IR(CCl_4) ν: 1735(broad s;C=O), 1370(m), 1245(s), 1220(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.10(s)/2.13(s)(6H;2xCH_3CO), 3.33(3H,s;CH_2OCH_3), 3.55(2H,s;CH_2OCH_3), 6.26(1H,t,$J_{4,3}$=$J_{4,2}$=2Hz;H_4), 6.47(1H,dd,$J_{2,4}$=2Hz,$J_{2,3}$=6Hz;H_2), 7.40(1H,dd,$J_{3,4}$=2Hz,$J_{3,2}$=6Hz;H_3). MS(EI) m/e(%): 242(0.71;M^+), 158(10;-2xCH_2CO), 140(51;-CH_2CO,-CH_3COOH), 113(19;-2xCH_2CO,-CH_2OMe), 95(63;-CH_2CO,-CH_3COOH,-CH_2OMe), 45(43;CH_2OMe^+), 43(100;CH_3CO^+). HRMS(EI) m/e: 242.0787 (calc. for $C_{11}H_{14}O_6$(M): 242.0790).

(4S,5R*)-4,5-Diacetoxy-5-ethoxymethyl-2-cyclopentenone* (**10**).

The hydrolysis of cyclopentadienone epoxide **8**[13] (60 mg; 0.39 mmol) and subsequent acylation were carried out as described for the conversion of **7** into **9**. Crude **10** was purified by preparative TLC (SiO_2/ethyl acetate-petroleum ether 40°-60°(1:1)). Crystallization from ethyl acetate-petroleum ether 40°-60° provided analytically pure **10** (30 mg; 30%), mp: 48-52°C. IR(CCl_4) ν(s): 1740(C=O), 1550 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.11(3H,t,J=7Hz;OCH_2CH_3), 2.06(s)/2.08(s)(6H;2xCH_3CO), 3.50(q,J=7Hz)/3.58(s)(4H;OCH_2CH_3 and CH_2OEt), 6.25(1H,t,$J_{4,3}$=$J_{4,2}$=2Hz;H_4), 6.45(1H,dd,$J_{2,4}$=2Hz,$J_{2,3}$=6.5Hz;H_2), 7.35(1H,dd,$J_{3,4}$=2Hz,$J_{3,2}$=6.5Hz;H_3). MS(70eV) m/e: 256(M^+), 214(-CH_2CO), 197(257-CH_3COOH), 172(-2xCH_2CO), 154(-CH_2CO,-CH_3COOH), 126, 110, 95(-CH_2CO,-CH_3COOH,-CH_2OEt), 84, 68, 59(CH_2OEt^+). HRMS m/e: 256.0946 (calc. for $C_{12}H_{16}O_6$ (M): 256.0945). (Found: C 56.3, H 6.2. Calc. for $C_{12}H_{16}O_6$: C 56.25, H 6.29%.)

Acid-catalysed hydrolysis and subsequent acylation of **12**.

The hydrolysis of cyclopentadienone epoxide **12**[13] (55 mg; 0.25 mmol) and subsequent acylation were carried out as described for the conversion of **7** into **9**. Purification of the crude product by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) afforded 29 mg (36%) of *(4S*,5R*)-4,5-diacetoxy-5-phenylthiomethyl-2-cyclopentenone* (**14**), as a colourless oil. IR(CCl_4) ν: 1748(s;C=O), 1728(s;C=O), 1440(w), 1370(m), 1230/1215(broad;s), 1042/1022(broad;m), 690(w) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.00(6H,s;2xCH_3CO), 4.16/4.29/4.53/4.65(2H,ABq,J_{AB}=11.4Hz;CH_2SPh), 5.99(1H,dd,$J_{4,2}$=1.5Hz,$J_{4,3}$=2.6Hz;H_4), 6.31(1H,dd,$J_{2,4}$=1.5Hz,$J_{2,3}$=6Hz;H_2), 7.4(6H,m;5 ArH and H_3). MS(EI) m/e(%): 320(15;M^+), 211(5;-SPh), 169(38;-SPh,-CH_2CO), 110(23), 109(48;SPh^+), 91(6), 81(11), 65(11), 43(100;CH_3CO^+). HRMS(EI) m/e: 320.0716 (calc. for $C_{16}H_{16}O_5S$ (M): 320.0718).

Furthermore, 22 mg (32%) of *(4R*,5R*)-4,5-iso-propylidenedioxy-5-phenylthiomethyl-2-cyclopentenone* (**16**) was obtained, as a colourless oil. IR(CCl_4) ν: 2987(m), 1720(s;C=O), 1438(m), 1380/1370(s), 1260(m), 1220(s), 1187(s), 1168(m), 1105(s), 1025(m), 868(m), 692(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.31(3H,s)/1.42(3H,s) (2xCH_3), 3.85(2H,s;CH_2SPh), 4.76(1H,dd,$J_{4,2}$=1Hz,$J_{4,3}$=2.6Hz;H_4), 6.29(1H,dd,$J_{2,4}$=1Hz,$J_{2,3}$=6Hz;H_2), 7.41(6H,m;5 ArH and H_3); MS(EI) m/e(%): 276(6;M^+), 218(13;-$(CH_3)_2CO$), 123(10), 109(8;SPh^+), 95(100), 81(8), 77(6), 65(7), 45(11), 39(26). HRMS(EI) m/e: 276.0815 (calc. for $C_{15}H_{16}O_3S$ (M): 276.0820).

Acid-catalysed hydrolysis and subsequent acylation of **13**.

The hydrolysis of cyclopentadienone epoxide **13**[13] (86 mg; 0.37 mmol) and subsequent acylation were carried out as described for the conversion of **7** into **9**. Purification of the crude product by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) afforded 43 mg (38%) of *(4S*,5R*)-5-benzylthiomethyl-4,5-diacetoxy-2-cyclopentenone* (**15**), as a colourless oil. IR(CCl_4) ν: 1750(s;C=O), 1720(s;C=O), 1450(w), 1370(m), 1230(broad;s), 1042/1028(m), 702(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.00(3H,s)/2.08(3H,s)(2xCH_3CO), 3.95(2H,brs;SCH_2Ph), 4.16/4.27/4.60/4.73(2H,ABq,J_{AB}=12Hz;CH_2SCH_2Ph), 5.75(1H,dd,$J_{4,2}$=1.2Hz,$J_{4,3}$=2.6Hz;H_4), 6.37(1H,dd, $J_{2,4}$=1.2Hz,$J_{2,3}$=6Hz;H_2), 7.27(m)/7.40(dd,$J_{3,4}$=2.6Hz,$J_{3,2}$=6Hz)(6H;5 ArH and H_3, respectively). MS(EI) m/e(%): 334(0.21;M^+), 212(29;M+1-SCH_2Ph), 152(100;M+1-SCH_2Ph,-CH_3CO_2H), 123(30;SCH_2Ph), 110(100), 91(100;CH_2Ph), 82(14), 65(25), 45(24), 43(100;CH_3CO^+). HRMS(EI) m/e: 334.0868 (calc. for $C_{17}H_{18}O_5S$ (M): 334.0875).

Furthermore, 34 mg (32%) of *(4R*,5R*)-5-benzylthiomethyl-4,5-iso-propylidenedioxy-2-cyclopentenone* (**17**) was obtained as a colourless oil. IR(CCl_4) ν: 1715(s;C=O), 1450(w), 1381/1372(m), 1222(s), 1190(m), 1168(w), 1108(s), 1030(w), 870(w), 702(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.31(3H,s)/1.40(3H,s)(2xCH_3), 3.87 (4H,s;CH_2SCH_2Ph), 4.55(1H,dd,$J_{4,2}$=0.9Hz,$J_{4,3}$=2.6Hz;H_4), 6.38(1H,dd,$J_{2,4}$=0.9Hz,$J_{2,3}$=6Hz;H_2), 7.25(br s;5 ArH), 7.52(1H,dd,$J_{3,4}$=2.6Hz,$J_{3,2}$=6Hz;H_3). ^{13}C-NMR($CDCl_3$) δ: 23(q)/26(q)($(CH_3)_2$C), 32(t;CH_2SBz), 52(s;$(CH_3)_2$C), 61(t;SCH_2Ph), 77.6(d;C(4)), 100.4(s;C(5)), 126.8(d)/128.1(d)/128.8(d)(p-,m- and o-ArC, respectively), 135(d;C(2)), 136.6(s;qrt. ArC), 158.6(d;C(3)), 203(s;C(1)). MS(CI) m/e(%): no M+1 signal, 233(32;-$(CH_3)_2CO$), 215(77,-$(CH_3)_2C(OH)_2$), 119(14), 110(13), 91(96), 59(19;$(CH_3)_2COH^+$), 41(100). HRMS(EI, direct inlet) m/e: 290.0981 (calc. for $C_{16}H_{18}O_3S$ (M): 290.0977).

Acid-catalysed hydrolysis and subsequent acylation of **18**.

Cyclopentadienone epoxide **18**[13] (92 mg; 0.84 mmol) was stirred at room temperature in a mixture of acetone (5 ml) and satd NH_4Cl aq (0.5 ml) for ca 20 hrs. The reaction mixture was then diluted with dichloromethane (5 ml) and $MgSO_4$ (5 g) was added. Stirring was continued for 3 hrs, whereupon the mixture was filtered and concentrated in vacuo, leaving ca 71 mg of an oily residue, consisting of a 1.8:1 mixture of *(4S*,5R*)-* and *(4R*,5R*)-4,5-dihydroxy-4-methyl-2-cyclopentenone* (**19**) and (**20**). ^{1}H-NMR($CDCl_3$) δ: 1.37(s;CH_3(**19**)), 1.52(s;CH_3(**20**)), 3.87(s;H_5(**20**)), 4.30(s;H_5(**19**)), 6.16/6.23(overlapping doublets ($J_{2,3}$=6Hz) of H_2(**19**) and H_2(**20**)), 7.49(d,$J_{3,2}$=6Hz;H_3(**19**) and H_3(**20**)). Without further purification the diols **19** and **20** were subjected to acylation as usual, see the preparation of **9**. Purification of the crude product (82 mg) was carried out by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) to afford 39 mg (22% overall) of a colourless oil, consisting of a 1.8:1 mixture of the di-acetates *(4S*,5R*)-* and *(4R*,5R*)-4,5-diacetoxy-4-methyl-2-cyclopentenone* (**21**) and (**22**). IR(CCl_4) (**21** + **22**) ν: 1740(s;C=O), 1370(m), 1230(broad;s), 1095(m), 1055(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) (**21** + **22**) δ: 1.49(s;C(4)-CH_3(**21**)), 1.77(s;C(4)-CH_3(**22**)), 2.00(s;CH_3CO(**22**)), 2.07(s; CH_3CO(**21**)), 2.22(s;CH_3CO(**22**)), 2.23(s;CH_3CO(**21**)), 5.14(s;H_5(**22**)) 5.84(s;H_5(**21**)), 6.27(d,$J_{2,3}$=8Hz;H_2(**21**)),

6.34(d,$J_{2,3}$=6.5Hz;H_2(**22**)), 7.72(d,$J_{3,2}$=8Hz;H_3(**21**)), 7.86(d,$J_{3,2}$=6.5Hz;H_3(**22**)). GCMS(CI), 100°-150°C, 5°C.min^{-1}, m/e(%): **22** (rt 3'59"): 153(25;-AcOH), 139(5), 125(9), 111(100;-AcOH,-CH_2CO), 95(43), 83(12), 71(12), 69(15), 61(42;$AcOH_2^+$), 57(39), 55(28), 45(21); **21** (rt 4'20"): 153(54;-AcOH), 139(12), 125(24), 111(100;-AcOH,-CH_2CO), 95(53), 83(14), 71(13), 69(15), 61(76;$AcOH_2^+$), 57(39), 55(27), 45(25). MS(CI, direct inlet) m/e(%): 213(1.8;M+1$^+$), 153(46), 139(6), 125(10), 111(100), 95(19), 61(43). HRMS(CI, direct inlet) m/e: 213.0758 (calc. for $C_{10}H_{13}O_5$ (M+1): 213.0763). No attempts were made to separate **21** and **22**.

(4S,5R*)-5-(3,5-Dinitrophenylcarbonyloxy)-4-methoxy-2-cyclopentenone* (**25**).

A solution of cyclopentadienone epoxide **23**[13] (70 mg; 0.73 mmol) in methanol, containing 1 vol.% 5N H_2SO_4 aq (5 ml), was stirred at room temperature for 30 min. Then, $NaHCO_3$ (2 g) and $MgSO_4$ (2 g) were added and the resulting thick slurry was diluted with dichloromethane (14 ml). Stirring was continued overnight, whereupon the mixture was filtered and concentrated in vacuo to leave *ca* 100 mg (~100 %) of crude *(4S*,5R*)-5-hydroxy-4-methoxy-2-cyclopentenone* (**24**) as a colourless oil (purity ~ 90%). IR(CCl_4) ν: 3420(m;OH), 1750(m)/1728(s)(C=O), 1200(m), 1125(s), 982(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 3.58(3H,s;OCH_3), 4.18(1H,d,$J_{5,4}$=2.7Hz;H_5), 4.35(1H,m;H_4), 6.28(1H,dd,$J_{2,4}$=1.2Hz,$J_{2,3}$=6.0Hz;H_2), 7.48(1H,dd,$J_{3,4}$=2.0Hz, $J_{3,2}$=6.0Hz;H_3). Part of this material (85 mg; ~ 0.66 mmol) was dissolved in dichloromethane (7 ml) and at 0°C were successively added: 3,5-dinitrobenzoyl chloride (159 mg; 0.69 mmol), DMAP (15 mg) and Et_3N (100 mg; 1.0 mmol). The resulting mixture was stirred for 20 min, whereupon the cooling bath was removed. After an additional 2 hrs the reaction mixture was diluted with water (5 ml). The aqueous layer was extracted with dichloromethane (3x12 ml). The combined organic solutions were successively washed with 3% HCl (2x12 ml) and water (3x12 ml), dried ($MgSO_4$), filtered and concentrated in vacuo. The residue was purified by flash chromatography (SiO_2/hexane-ethyl acetate mixtures ranging from 3:1 to 1:1) to afford 108 mg (51%) of **25** as a thick oil. Attempts to crystallize this oil failed. IR(CCl_4) ν: 1745(m)/1735(s)(C=O), 1545(s;NO_2), 1340(s;NO_2), 1195(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 3.53(3H,s;OCH_3), 4.79(1H,m;H_4), 5.50(1H,d,$J_{5,4}$=3.0Hz;H_5), 6.45(1H,dd, $J_{2,4}$=1.4Hz,$J_{2,3}$=6.2Hz;H_2), 7.64(1H,dd,$J_{3,4}$=2.0Hz,$J_{3,2}$=6.2Hz;H_3), 9.2(m;3ArH). MS(EI) m/e(%): 322(48;M$^+$), 195(95;dinitrophenylcarbonyl$^+$), 149(32;195-NO_2), 127(60;-dinitrophenylcarbonyl), 110(18), 99(38;-dinitrophenylcarbonyl,-CO), 84(69), 75(52), 68(45), 49(97). HRMS(EI) m/e: 322.0448 (calc. for $C_{13}H_{10}O_8N_2$ (M): 322.0437).

(4S,5R*)-5-(3,5-Dinitrophenylcarbonyloxy)-4-methoxy-5-methoxymethyl-2-cyclopentenone* (**27**).

The acid-catalyzed methanolysis of cyclopentadienone epoxide **7**[13] (35 mg; 0.25 mmol) was carried out similar to that of **23** (see the preparation of **25**). This afforded 37 mg (88%) of *(4S*,5R*)-5-hydroxy-4-methoxy-5-methoxymethyl-2-cyclopentenone* (**26**), as a colourless oil (purity ~ 100% (capillary GC)): ^{1}H-NMR($CDCl_3$) δ: 3.33(3H,s;CH_2OCH_3), 3.53(2H,s;CH_2OCH_3), 3.57(3H,s;C(4)-OCH_3), 4.37(1H,br s;H_4), 6.30(1H,br d,$J_{2,3}$=6Hz; H_2), 7.63(1H,br d,$J_{3,2}$=6Hz;H_3). Benzoylation of this material with 3,5-dinitrobenzoyl chloride was performed as described for **24**, see the preparation of **25**. The purification of the crude product was carried out by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) yielding 56 mg (70%) of **27**. Recrystallization in hexane-ethyl acetate (3:1) provided an analytically pure sample, mp: 133-135°C. IR(CCl_4) ν(s): 1730(broad;C=O), 1548 (NO_2), 1342(NO_2), 1285, 1198, 1168 cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 3.44(3H,s;CH_2OCH_3), 3.60(3H,s;C(4)-OCH_3), 3.74/3.85/3.91/4.01(2H,AB_q,J_{AB}=10.3Hz;CH_2OCH_3), 4.94(1H,m;H_4), 6.49(1H,dd,$J_{2,4}$=1.7Hz,$J_{2,3}$=6.5Hz;H_2), 7.58(1H,dd,$J_{3,4}$=2.0Hz,$J_{3,2}$=6.5Hz;H_3), 9.2(m;3ArH). MS(EI) m/e(%): 366(12;M$^+$), 321(34;-CH_2OCH_3), 195(36;dinitrophenylcarbonyl$^+$), 171(4;-dinitrophenylcarbonyl), 154(8;-dinitrophenylcarbonyl,-CH_2OCH_3),

149(16;195-NO_2), 139(14), 123(6), 115(19), 98(12), 75(26), 45(100;$CH_2OCH_3^+$). (Found: C 49.18, H 3.90, N 7.54. Calc. for $C_{15}H_{14}N_2O_9$: C 49.19, H 3.85, N 7.67%.)

Methanolysis of **18**

A solution of cyclopentadienone epoxide **18**[13] (125 mg; 1.1 mmol) in 5 ml of methanol was stirred at room temperature for 2 days. (To avoid any acid-catalysis the reaction vessel used, had been rinsed with NH_4OHaq in order to remove possible traces of acid absorbed on the glass wall.) Subsequent concentration in vacuo left 180 mg (~ 100%) of a colourless oil consisting of a 3.3:1 mixture of *(4S*,5R*)-* and *(4R*,5R*)-5-hydroxy-4-methoxy-4-methyl-2-cyclopentenone* (**28**) and (**29**). ^{1}H-NMR($CDCl_3$) (**28** + **29**) δ: 1.28(s;C(4)-CH_3 (**28**)), 1.53(s;C(4)-CH_3(**29**)), 3.23(s;OCH_3(**29**)), 3.35(s;OCH_3(**28**)), 3.70(s;H_5(**29**)), 4.27(s;H_5(**28**)), 6.21(d,$J_{2,3}$=6.0Hz;H_2(**28**)), 6.38(d,$J_{2,3}$=6.0Hz;H_2(**29**)), 7.32(d,$J_{3,2}$=6.0Hz;H_3(**29**)), 7.48(d,$J_{3,2}$=6.0Hz;H_3(**28**)).

Acylation of **28** *and* **29**.

Part of the above mixture of alcohols **28** and **29** (80 mg; 0.56 mmol) was subjected to the acylation procedure described for the preparation of **9**. Purification of the resulting product by tedious flash chromatography (SiO_2/hexane-ethyl acetate mixtures ranging from 10:1-3:1) afforded 30 mg (29%) of *(4S*,5R*)-5-acetoxy-4-methoxy-4-methyl-2-cyclopentenone* (**30**) as a colourless oil. IR(film) ν: 2920(s), 2845(m), 1730(broad;s), 1455(m), 1440(m), 1375(m), 1230(broad;s), 1110(s), 1095(s), 1048(s), 908(w), 888(w), 800(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.35(3H,s;C(4)-CH_3), 2.20(3H,s;CH_3CO), 3.33(3H,s;C(4)-OCH_3), 5.63(1H,s;H_5), 6.27(1H,d,$J_{2,3}$=6.0Hz;H_2), 7.47(1H,d,$J_{3,2}$=6.0Hz;H_3). MS(CI) m/e(%): 185(15;M+1$^+$), 171(21), 153(59;-CH_3OH), 143(78;-H_2C=C=O), 142(25;-CH_3C=O), 125(23), 111(100;-CH_3OH,-H_2C=C=O), 95(13), 83(6), 61(17). HRMS(CI) m/e: 185.0810 (calc. for $C_9H_{13}O_4$ (M+1): 185.0814).

Furthermore, 9 mg (9%) of *(4R*,5R*)-5-acetoxy-4-methoxy-4-methyl-2-cyclopentenone* (**31**) was obtained: colourless oil; IR and mass spectra : nearly identical to those of **30**; ^{1}H-NMR(CCl_4) δ: 1.49(3H,s;C(4)-CH_3), 2.16(3H,s;CH_3CO), 3.03(3H,s;C(4)-OCH_3), 4.97(1H,s;H_5), 6.37(1H,d,$J_{2,3}$=6.0Hz;H_2), 7.20(1H,d,$J_{3,2}$=6.0Hz;H_3).

Each of these acetates **30** and **31** was stirred in methanol at room temperature during several weeks to investigate possible epimerisation. However, no reaction was observed; the acetates were recovered quantitatively.

Benzoylation of **28** *and* **29**.

Part of the above mixture of alcohols **28** and **29** (53 mg; 0.37 mmol) was treated with 3,5-dinitrobenzoyl chloride according to the procedure given for **25**. Purification of the resulting product mixture by flash chromatography (SiO_2/hexane-ethyl acetate (3:1)) afforded 41 mg of *(4S*,5R*)-5-(3,5-dinitrophenylcarbonyl-oxy)-4-methoxy-4-methyl-2-cyclopentenone* (**32**)[18] as a white solid. Crystallization from hexane-ethyl acetate (4:1) provided an analytically pure sample (fine needlets), mp: 133-135°C. IR(KBr) ν: 1742(s;C=O), 1720(s;C=O), 1550(s), 1538(s;NO_2), 1348(s;NO_2), 1285(s), 1178(s), 1120(m), 1042(m), 797(m), 738(s), 722(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.47(3H,s;C(4)-CH_3), 3.36(3H,s;C(4)-OCH_3), 5.91(1H,s;H_5), 6.36(1H,d,$J_{2,3}$=7.2Hz;H_2), 7.60(1H,d,$J_{3,2}$=7.2Hz;H_3), 9.17(m;3ArH). (Found: C 50.09, H 3.62, N 8.24. Calc. for $C_{14}H_{12}N_2O_8$: C 50.01, H 3.60, N 8.33%.). Furthermore, 57 mg of a 3:2 mixture of **32** and its epimer: *(4R*,5R*)-5-(3,5-dinitro-phenylcarbonyloxy)-4-methoxy-4-methyl-2-cyclopentenone* (**33**) was obtained. No further attempts were made to separate **33** from **32**. The ^{1}H-NMR resonances of **33** followed from comparison with the ^{1}H-NMR spectrum of

32: ^{1}H-NMR($CDCl_3$) δ: 1.66(3H,s;C(4)-CH_3), 3.18(3H,s;C(4)-OCH_3), 5.35(1H,s;H_5), 6.51(1H,d,$J_{2,3}$=6.7Hz;H_2), 7.46(1H,d,$J_{3,2}$=6.7Hz;H_3), 9.2(m;3ArH). The total yield of this benzoylation reaction ammounted to 98 mg (79%). The products **32** and **33** were obtained in a ratio of 3.3:1.

(2R,3R*,4S*)-2,3-Epoxy-4-methoxycyclopentanone* (**35**).

A solution of cyclopentadienone epoxide **23**[13] (20 mg; 0.2 mmol) in methanol (3 ml) was stirred at room temperature during 1 week. Subsequent concentration in vacuo left only 10 mg (39%) of **35**, as the only product. This low yield is probably due to the volatility of **35**. The product was obtained as a colourless oil. IR(CCl_4) ν: 2985(w), 2925(m), 2895(m), 2850(w), 2820(m), 1760(s;C=O), 1460/1455(w), 1398(w), 1342(m), 1202(m), 1172(m), 1152(m), 1108(s), 1088(s), 948(m), 860(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.94(br s)/2.16(br s)(1H,upfield half of ABX system,J_{AB}=18Hz;H_{5A}), 2.38(d,$J_{5B,4}$=6Hz)/2.60(d,$J_{5B,4}$=6Hz)(1H,downfield half of ABX system,J_{AB}=18Hz;H_{5B}), 3.36(4H,s+d($J_{2,3}$~3Hz);OCH_3+H_2), 3.94(1H,d,$J_{3,2}$=3.4Hz;H_3), 4.19(1H,br d,$J_{4,5B}$=6Hz;H_{4c}). MS(EI) m/e(%): 128(64;M^+), 101(37;-CO), 97(51;-OCH_3), 85(80), 74(29), 69(51), 66(64), 58(100), 41(96). HRMS(CI) m/e: 129.0559 (calc. for $C_6H_9O_3$ (M+1): 129.0552).

(2R,3R*,4S*)-2,3-Epoxy-4-methoxy-2-methoxymethylcyclopentanone* (**36**).

A solution of cyclopentadienone epoxide **7**[13] (59 mg; 0.42 mmol) in methanol (3 ml) was stirred at room temperature for 4 days. (To avoid any acid-catalysis, the reaction vessel used, had been rinsed with 25% NH_4OH in order to remove traces of acid adsorbed on the glass wall.) Subsequent concentration in vacuo afforded 59 mg (82%) of **36** as a colourless oil[33]. IR(CCl_4) ν: 2985(w), 2925(m), 2890(m), 2822(m), 1748(s;C=O), 1450(w), 1343(w), 1200(m), 1120(s)/1108(s)/1090(s), 992(w), 940(w) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 2.06(s)/2.26(s)(1H,upfield half of ABX system,J_{AB}=18.6Hz;H_{5A}), 2.50(d,$J_{5B,4}$=5Hz)/2.71(d,$J_{5B,4}$=5Hz)(1H,downfield half of ABX system,J_{AB}=18.6 Hz;H_{5B}), 3.37(6H,s;2xOCH_3), 3.67/3.80/3.83/3.98(2H,AB_q,J_{AB}=12.5Hz;CH_2OCH_3), 4.00(1H, s;H_3), 4.12(1H,d,$J_{4,5B}$=5Hz;H_4). MS(EI) m/e(%): 172(5;M^+), 140(17;-CH_3OH), 125(6), 110(13), 95(58;-CH_3OH, -CH_2OCH_3), 85(63), 68(59), 58(26), 45(100;$CH_2OCH_3^+$). HRMS(EI) m/e: 172.0731 (calcd. for $C_8H_{12}O_4$ (M): 172.0736).

(2R,3R*,4S*)-2,3-Epoxy-2-*iso*-propoxymethyl-4-methoxycyclopentanone* (**37**).

A solution of cyclopentadienone epoxide **34**[13] (41 mg; 0.24 mmol) in methanol (3 ml) was stirred at room temperature for 2.5 week. Subsequent concentration in vacuo afforded 53 mg (~ 100%) of **37** as a colourless oil[38]. IR(CCl_4) ν: 2970(s), 2925(m), 2885(m), 2824(w), 1750(s;C=O), 1467/1455(w), 1380(m), 1368(m), 1340(m), 1200(m), 1100(broad;s), 945(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.13(6H,d,J=6Hz;$CH(CH_3)_2$), 2.05(s)/2.26(s)(1H,upfield half of ABX system,J_{AB}=19Hz;H_{5A}), 2.53(d,$J_{5B,4}$=6Hz)/2.74(d,$J_{5B,4}$=6Hz)(1H,downfield half of ABX system,J_{AB}=19 Hz;H_{5B}), 3.38(3H,s;OCH_3), 3.62(1H,septet,J=6Hz;$CH(CH_3)_2$), 3.73/3.87/3.90/4.03(2H,AB_q,J_{AB}=12Hz;CH_2OiPr), 4.03(1H,s;H_3), 4.14(1H,d,J=$6_{4,5B}$Hz;H_4). MS(CI) m/e(%): 201 (100;M+1$^+$), 169(40;-CH_3OH), 159(63;-iPr), 141(50;-iPrOH), 131(32;-iPr,-CO), 127(49), 113(49), 109(18), 99(30), 95(8), 85(27), 81(71), 73(11), 71(45), 59(29), 55(11). HRMS(CI) m/e: 201.1117 (calc. for $C_{10}H_{17}O_4$ (M+1): 201.1127).

anti-*(2,3)-(4,5)-Bisepoxy-2-methoxymethylcyclopentanone* (**42**).

A mixture of cyclopentadienone epoxide **7**[13] (41 mg; 0.29 mmol), dichloromethane (8 ml), 35% H_2O_2

(0.9 ml) and 0.2 N NaOH (0.9 ml) was vigorously stirred at room temperature for 20 min. The aqueous phase was then carefully extracted with dichloromethane (4x). The combined organic layers were washed with water (2x), dried ($MgSO_4$), filtered and concentrated in vacuo to give 12 mg (~ 25%) of **42** as a colourless oil. The capillary GC diagram of this material indicated a purity of *ca* 88%. It also revealed a distinct contaminant (*ca* 4%), the amount of which gradually increased on storage, even in the freezer. An attempt to remove this impurity by flash chromatography (SiO_2/hexane-ethyl acetate mixtures ranging from 3:1 to 1:1) failed. IR(CCl_4) ν: 2930(m), 1760(s), 1740(m), 1370(w), 1240(m), 1190(s), 1125(m), 860(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 3.37(3H,s;OCH_3), 3.42(1H,d,$J_{5,4}$=2.6Hz;H_5), 3.59/3.73/3.87/4.00(2H,AB_q,J_{AB}=12Hz;CH_2OCH_3), 4.13(1H,d, $J_{4,5}$=2.7Hz;H_4), 4.25(1H,br s;H_3). MS(EI) m/e: 156(M^+), 139, 127, 111, 97, 85, 84, 71, 69, 55, 45. HRMS(EI) m/e: 156.0427 (calcd. for $C_7H_8O_4$ (M): 156.0422).

anti-*(2,3)-(4,5)-Bisepoxy-2-ethoxymethylcyclopentanone* (**43**).

A mixture of cyclopentadienone epoxide **8**[13] (52 mg; 0.33 mmol), dichloromethane (0.6 ml), methanol (0.6 ml), 35% H_2O_2 (0.05 ml) and 0.2 N NaOH (0.05 ml) was stirred for 30 min. Subsequent work up as described for **42** afforded 36 mg (*ca* 64%) of **43** as a colourless oil: purity *ca* 94% (capillary GC data). IR(film) ν: 2980(m), 2930(m), 2875(m), 1760/1750(s), 1445(m), 1380(m), 1305(m), 1200(m), 1115(s), 870(s), 810(s) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.16(3H,t,J=7Hz;OCH_2CH_3), 3.42(d,$J_{5,4}$=2.5Hz;H_5)/3.53(q,J=7Hz;OCH_2CH_3)(3H), 3.65/3.78/3.93/4.07(2H,AB_q,J_{AB}=12.5Hz;CH_2OEt), 4.16(1H,d,$J_{4,5}$=2.5Hz;H_4), 4.27(1H,br s;H_3). HRMS(CI) m/e: 171.0653 (calc. for $C_8H_{11}O_4$ (M+1): 171.0657). Compound **43** gradually decomposed, despite storage in the freezer.

Alkaline epoxidation of **44**.

A mixture of cyclopentadienone epoxide **44**[13] (61 mg; 0.40 mmol), dichloromethane (3 ml), methanol 0.5 ml, 35% H_2O_2 (0.2 ml) and 0.2 N NaOH (0.2 ml) was stirred for 30 min. Subsequent work up as described for **42** afforded 38 mg of a crude mixture, containing *(2,3)-(4,5)-bisepoxy-2-methoxymethyl-3-methylcyclopentanone* (**45**) and *(4,5)-epoxy-2-hydroxy-2-methoxymethyl-3-methoxy-3-methyl-cyclopentanone* (**46**) in a ratio of *ca* 3:1 (^{1}H-NMR data). Alcohol **46** and other contaminants could be removed by stirring the crude product for a few minutes in a CCl_4 solution, to which a pinch of SiO_2 was added. Subsequent filtration followed by concentration in vacuo provided pure **45**, as a colourless oil. IR(CCl_4) ν: 2920(m), 1762(s;C=O), 1195(m), 1130(m), 1100(m), 867(m) cm^{-1}. ^{1}H-NMR($CDCl_3$) δ: 1.73(3H,s;C(3)-CH_3), 3.36(4H,s+d($J_{5,4}$=2.7Hz);CH_2OCH_3 and H_5, respectively), 3.39/3.53(1H,upfield part of AB_q,J_{AB}=12Hz;$CH_AH_BOCH_3$), 3.93/4.07(downfield part of AB_q,J_{AB}=12Hz)/3.98(d,J=2.7Hz)(2H;$CH_AH_BOCH_3$ and H_4, respectively). MS(CI) m/e(%): 171(4;$M+1^+$), 155(15), 139(13;-CH_3OH), 125(16;-CH_3OCH_3), 111(40), 85(16), 83(15), 45(100;$CH_2OCH_3^+$). HRMS(CI) m/e: 171.0657 (calcd. for $C_8H_{11}O_4$ (M+1): 171.0657).

A methanolic solution of **45** was subsequently stirred at room temperature for 18 hrs and then concentrated in vacuo. This yielded an mixture of **45** and **46** in a ratio of 1:3. Since **46** now formed the main constituent, its ^{1}H-NMR pattern could easily be deduced by comparison of the ^{1}H-NMR spectrum of this mixture with that of **45**: ^{1}H-NMR($CDCl_3$) δ: 1.50(s;C(3)-CH_3), 3.08/3.19(upfield part of AB_q,J_{AB}=10Hz; $CH_AH_BOCH_3$), 3.24(d,$J_{5,4}$=3Hz;H_5), 3.38(s;CH_2OCH_3), 3.51(s;C(3)-OCH_3), 3.70(d,$J_{4,5}$=3Hz;H_4), 4.17/4.29 (downfield part of AB_q,J_{AB}=10Hz;$CH_AH_BOCH_3$).

(2,3)-(4,5)-Bisepoxy-cyclopentanone (47).

A mixture of cyclopentadienone epoxide **23**[13] (75 mg; 0.78 mmol), dichloromethane (4 ml), 35% H_2O_2 (0.12 ml) and 0.2 N NaOH (0.12 ml) was stirred at 0°C for 30 min. In view of the volatility of the product, the organic layer was, after the usual work-up (see **42**), only partially concentrated in vacuo. The yield could therefore not be established. ^{1}H-NMR ($CDCl_3/CH_2Cl_2$) δ: 3.37(t,J=2.0Hz;H_2 and H_5), 4.20(t,J=2.0Hz;H_3 and H_4), (5.3 (s) CH_2Cl_2). GCMS(CI) m/e: 113($M+1^+$), 97, 84, 69, 57, 49. HRMS(CI) m/e: 113.0243 (calc. for $C_5H_5O_3$ (M+1): 113.0239).

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32. Although the synthesis of **9** has been described previously[13], it is repeated here because the procedure is used as reference for the other syntheses.
33. A trace (*ca* 2.5%) of 6-methoxymethyl-2-pyrone was observed in the capillary GC output of the product. This pyrone arises most probably from a thermally induced rearrangement of **7**, see ref 13.
34. A trace (*ca* 4%) of 6-*iso*-propoxymethyl-2-pyrone was observed in the capillary GC output of the product. This pyrone arises most probably from a thermally induced rearrangement of **37**, see ref 13.