

THE SYNTHESIS AND NMR CHARACTERIZATION OF A SERIES OF 1,4-DIHYDRO-1,4- ETHANONAPHTHALENE EPOXIDES

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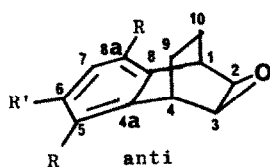
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Abstract—A series of *syn* and *anti* epoxides derived from 5,8-disubstituted-1,4-dihydro-1,4-ethanonaphthalenes have been prepared. The role of the solvent on epoxidation stereochemistry has been explored. The structures of the epoxides were assigned with the aid of proton NMR coupled with chemical shift reagents. The C-13 spectra have also been assigned, and an unusual γ -effect of the epoxide structure noted.

Recently we required a supply of an epoxide, derived from 5,8-dimethoxy-1,4-dihydro-1,4-ethanonaphthalene, in which the oxygen is *anti* to the aromatic ring (1a). In reaching this objective a related series of epoxides were prepared and characterized by NMR spectroscopy. The results of this study are germane to

Epoxidation of the parent 1,4-dihydro-1,4-ethanonaphthalene with *m*-chloroperoxybenzoic acid (MCPBA) had been reported some years ago to give the *anti* and *syn* epoxides in 1:1 ratio but in unreported yield.³ More recently, the same peroxyacid in chloroform has been reported to convert



anti

1a

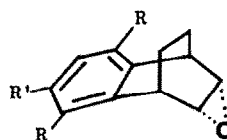
2a

3a

R=OCH₃, R'=H

R=OCH₃, R'=NO₂

R=OAc, R'=H



syn

1b

2b

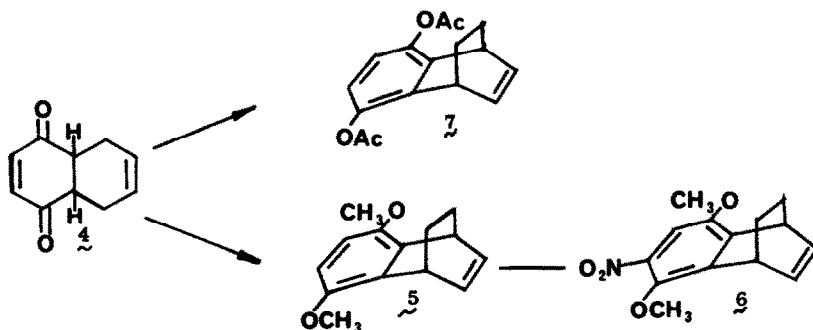
3b

work recently published from other laboratories, and so we wish to report our results here.

Convenient access to the series is offered by the Diels-Alder adduct (4) from *p*-benzoquinone and cyclohexadiene.¹ This material undergoes ready aromatization and derivatization to form the dimethoxy and diacetoxy compounds 5 and 7 respectively.

2-methyl-5,8-dimethoxy-1,4-dihydro-1,4-ethanonaphthalene to epoxides in 52% yield. The NMR determined ratio of *anti* to *syn* isomers was 0.59.

Initial results with 5 using MCPBA in methylene chloride appeared discouraging in that tlc showed seven or eight different spots of about equal intensity. Given that the crude product was dark brown other

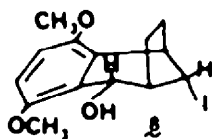


While these compounds have been reported previously,^{1,2} conditions were developed which allow their preparation more conveniently and in better yields. The conversion of 5 to 6 is readily accomplished at room temperature in a mixture of dilute nitric acid and dioxane.

pathways to the desired product were sought. It might be added parenthetically that C-13 NMR analysis of the crude product later showed that the desired epoxides were the major constituents. The conditions of Anderson and Veysoglu⁵ were applied using MCPBA in methylene chloride stirred with

dilute sodium bicarbonate. While the number of side products appeared to be curtailed, even with three equivalents of MCPBA only partial conversion to epoxides occurred. Analysis by C-13 NMR showed 25% *anti* and 33% *syn* epoxides with the balance starting olefin.

In an attempt to avoid these difficulties, 5 was reacted with iodine and iodic acid in the hope of gaining the iodohydrin.⁹ The resultant iodohydrin would not form an epoxide in base and was subsequently shown by NMR and chemical evidence to be the rearranged product 8. Carbocation rearrangements in the 1,2,3,4-tetrahydro-1,4-ethanonaphthalene system are well known and might be expected whenever a well developed carbocation intermediate is formed.⁷ Examples exist of similar



rearrangements upon electrophilic addition to the 1,4-dihydro-1,4-ethanonaphthalene double bond.⁸

In contrast to the results with 5, the diacetoxylefin 7 gave a quantitative yield of epoxides when treated with MCPBA in methylene chloride overnight. The two epoxides were readily separated by flash column chromatography.⁹ Their structures, as will be described shortly, were determined by NMR. The ratio of *anti* to *syn* isomers was 1.

When 7 in methylene chloride was treated with monoperoxyphthalic acid in ether the reaction was very much slower requiring three days to reach 70% completion. More encouraging was the fact that the *anti:syn* ratio was now 2.

Given these results, a more detailed examination of the reaction conditions was undertaken. The results of the epoxidation of 5, 6 and 7 with MCPBA in methylene chloride and with MPPA in ether are given in Table I. Under the latter conditions both 5 and 7 give *anti:syn* ratios of ca 3. With the nitrodimethoxy olefin 6, the *anti:syn* ratio is significantly improved by the change in conditions, but the *syn* isomer still predominates.

These changes are not due to the change in peroxyacid but rather to the change in solvent. Moreover, excellent material balances were obtained throughout excluding the possible effect of preferential destruction of one isomer. In Fig. 1 are shown the results for the epoxidation of 7 in a variety of solvents. As can be seen, as the hydrogen-bonding capability of the solvent increases there is a decrease in the reaction rate accompanied by a linear increase in the *anti:syn* ratio. Peroxyacids in solvents that do not readily form hydrogen bonds are thought to react¹⁰ in the internally hydrogen-bonded form *via* a transition state as shown (9). In solvents such as ether which can form hydrogen bonds, reaction is 1-2 orders of magnitude slower and there is evidence that another transition state may participate. Ewins *et al.*¹¹ found that the relatively unhindered 4-*t*-butyl-1-methylenecyclohexane (10) was epoxidized for preference (ca 4:1) by axial attack, and that the choice of solvent made little difference to this preference. When steric hindrance was introduced, as in 1-methylene-3,3,5-trimethylcyclohexane (11), the preference was reversed: equatorial attack predominated by ca 4:1 in benzene or dichloromethane, but by less than 2:1 in ether. This suggests that externally hydrogen-bonded peroxyacid, though intrinsically less reactive than the rather rigid internally bonded form as in 9, can adapt itself better to steric constraints in the transition state. Other influences then

Table I. Reaction products of olefins 5, 6 and 7 (1 mmol) with peroxyacids in two solvents at room temperature

(a) MCPBA (1.4 mmol) in 20 ml CH ₂ Cl ₂ for 7 hours	Dimethoxy (5) ^a	Nitrodimethoxy (6)	Diacetoxylefin (7)
	Olefin	77	31
<i>anti</i> Epoxide	8	16	32
<i>syn</i> Epoxide	15	53	14

^aThe relative rate here is misleading in that some unknown side reaction consumes peroxyacid and produces a small amount of tarry product which does not appear in the proton or C-13 NMR but which is clearly evident in the TLC. This was not important with the MPPA reaction below.

(b) MPPA (7.9 mmol) in 20 ml diethyl ether			
Olefin	51 (72 hrs)	75 (72 hrs)	66 (48 hrs)
<i>anti</i> Epoxide	36	9	27
<i>syn</i> Epoxide	13	16	-

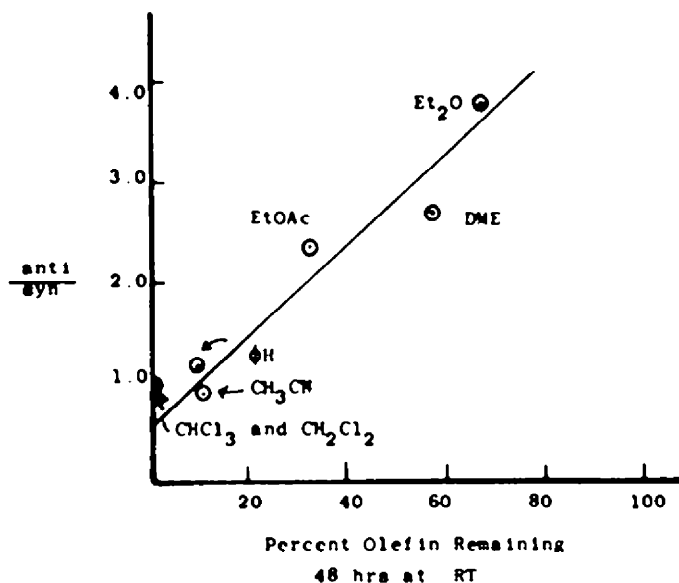
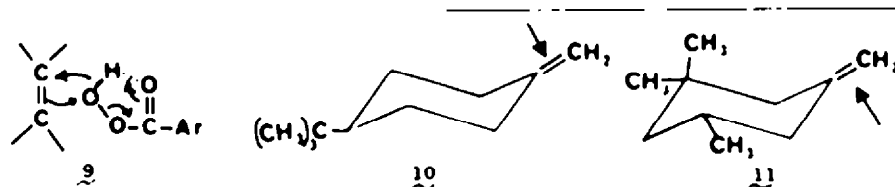


Fig 1 Reaction of 7 with MPPA a plot of the ratio of 3a to 3b vs the amount of unreacted 7 in a variety of solvents

become relatively more important in determining the direction of attack

homoconjugation in 6 is less important, and there is a clear swing to sterically preferred *syn* attack



Paquette *et al.*⁴ have discussed the implications of homoconjugative interactions between the aromatic ring and the olefinic π -electrons in the 1,4-dihydro-1,4-ethanonaphthalene system. Reactions of a number of weak electrophiles with 2-methyl-5,8-dimethoxy-1,4-dihydro-1,4-ethanonaphthalene and two related molecules were carried out. As mentioned above, epoxidation was with MCPBA in chloroform. Based on the stereochemistry of these additions, photoelectron spectroscopy data and theoretical calculations, they conclude that homoconjugation is unimportant in these systems. The steric bulk of the ethano bridge and a disrotation of the olefin σ -lobes (induced via a π - σ interaction through the framework of the bicyclic ring) favor attack of the electrophile *syn* to the aromatic ring.

The data in Table I and in Fig 1 bring us to the opposite conclusion with regard to the importance of homoconjugation in the epoxidations of 5, 6 and 7. When a solvent is used which acts as a hydrogen-bond acceptor, the reactivity of the peroxyacid is lowered because of the increased electron density at the peroxidic oxygen, making stabilization of the transition state more important. When a nonacceptor solvent is used, the peroxyacid does not need this stabilization and stereochemical factors predominate. The homoconjugative interaction seems particularly evident in comparing the data for the epoxidation of 5 and 6. With the reduction of electron density in the aromatic ring occasioned by the nitro group in 6

Catalytic deuteration, over Pd(C), of 5 was found to go exclusively to the *anti* side of the double bond. Since this result depended on the correct assignment of the proton chemical shifts in the saturated hydrocarbon,¹ the assignment was confirmed by the use of Eu(FOD)₃. While such hydrogenation reactions are not considered to be electrophilic processes, it would appear that homoconjugation in 5 leads to a lower energy pathway *anti* to the aromatic ring, steric interference by the ethano bridge notwithstanding.

The UV spectrum of 5 offers evidence of the homoconjugative interaction at least in the excited state. Both 5 and its saturated analog, 5,8-dimethoxy-1,2,3,4-tetrahydro-1,4-ethanonaphthalene, show broad absorbances in the region of 270–310 nm which can be resolved into a series of four peaks in the second derivative spectra. These appear in the olefin at 283, 290, 294 and 300 nm and are displaced by 4–6 nm towards the blue in the saturated counterpart. This is true in both methanol and hexane solutions. Filipescu and Chiang¹² have reported a "strong" homoconjugative coupling in 5,8-dimethoxy-1,4-dihydro-1,4-methanonaphthalene between the aromatic ring and the double bond which results in a 10 nm red shift compared to the saturated compound.

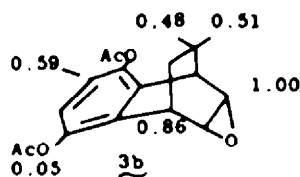
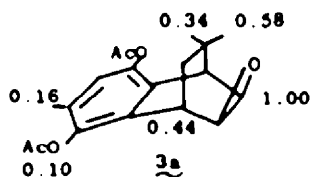
Finally, the diacetoxy olefin 7 was epoxidized by peroxyacetic acid generated *in situ* from hydrogen peroxide and acetic anhydride giving a quantitative yield of epoxides with an *anti*/*syn* ratio of 0.77. Acetic

acid, a stronger acid than peroxyacetic acid, suppresses ionization and external hydrogen-bonding in the peroxyacid, and may actually activate it by donating a hydrogen-bond to its carbonyl group. Consequently transition state stabilization is not so important as in previous examples and attack is preferentially on the *syn* face of the double bond.

While the isomeric epoxides **1** have been separated by preparative tlc, larger scale separations have not been so satisfactory no doubt due to the small difference in *R_f* values. Since a convenient conversion of the epoxides **3a, b** to the dimethoxy compounds was found to go quantitatively, it is probably better to go to **1a** from **3a** rather than the more direct route. The conversion is carried out by treating the diacetate epoxides with five equivalents of methyl lithium at -5° in ether. No opening of the epoxide ring occurs under these conditions as the presumed dilithio salt precipitates out. Treatment with methyl iodide and dimethyl sulfoxide then completes the conversion.

protons on the *anti* isomer are in the more shielded position than their counterparts in the *syn* isomer with regard to the aromatic ring. We repeated their calculation of the ring current effect by the method of Johnson and Bovey¹³ using dimensions taken from Dreiding models. The calculated difference in shielding was 0.2 ppm as against their experimental value of 0.08 ppm. Given the smallness of the effect and the uncertainties of the magnitudes to be expected in polysubstituted benzenes, we consider the ring current argument to be of suggestive value only.

A more direct assessment of epoxide stereochemistry can be gained from lanthanide induced chemical shifts (LIS). It has been ascertained that lanthanide complexation occurs on or near the line bisecting the carbon-carbon bond and the epoxide oxygen.^{14,15} Treatment of each of the diacetate epoxides by incremental additions of Eu(FOD)₃ produced a linear LIS with concentration. The relative LIS for each epoxide were as follows.



NMR results

The proton chemical shifts for the various olefins and epoxides in this study are given in Table 2. In their original configurational assignments for the 1,4-dihydro-1,4-ethanonaphthalene epoxides, Tori *et al.*¹ made use of the ring current argument applied to the protons attached to the epoxide carbons. The

From these data it was quite clear that the less polar (tlc), lower melting isomer had the *anti* configuration.

Tori *et al.*¹ had noted a perturbation of the chemical shifts of the ethano protons by the *anti* epoxide oxygen. Those protons *syn* to this oxygen were deshielded while the protons *anti* to the oxygen were shielded in respect to their counterparts in the olefin

Table 2 Proton chemical shifts for the 5,8-DiX-1,4-ethanonaphthalenes and epoxides

Compound	Chemical Shifts (ppm)						
	1,4	2,3	<u>9α-10α</u> ^a	<u>9β-10β</u> ^a	ArH	CH ₃	
(1s)	5,8-Dimethoxy	4.37	6.42	1.42	1.38	6.56	3.78
(1a)	5,8-Dimethoxy - <i>anti</i> -2,3-epoxide	3.80	3.25	1.92	0.96	6.62	3.70
(1b)	5,8-Dimethoxy - <i>syn</i> -2,3-epoxide	3.90	3.38	1.65	1.33	6.70	3.78
(2b)	6-Nitro-5,8-dimethoxy	4.40	6.42	1.52	1.40	7.10	3.80, 3.86
(2a)	6-Nitro-5,8-dimethoxy - <i>anti</i> -2,3-epoxide	3.90	3.32	2.06	1.05	7.33	3.85, 3.88
(2b)	6-Nitro-5,8-dimethoxy - <i>syn</i> -2,3-epoxide	3.96	3.44	1.90	1.38	7.34	3.82, 3.87
(3)	5,8-Diacetate	3.95	6.42	1.46	1.46	6.70	2.30
(3a)	5,8-Diacetate - <i>anti</i> -2,3-epoxide	3.39	3.28	1.96	1.04	6.87	2.28
(3b)	5,8-Diacetate - <i>syn</i> epoxide	3.50	3.34	1.70	1.39	6.93	2.28

^a *s*(*syn*) and *a*(*anti*) here mean *syn* or *anti* to the epoxide oxygen or to the olefinic bond, as appropriate.

Table 3 Carbon chemical shifts for the 5,8-DiX-1,4-ethanonaphthalenes and epoxides

Compound	Chemical Shift (ppm)						
	1,4	2,3	9,10	4a, 8a	5,8	6,7	CH ₃ - CO ₂
(5) 5,8-Dimethoxy	33.1	135.2	25.1	134.0	148.1	108.0	56.3
(1a) 5,8-Dimethoxy- anti-2,3-epoxide	30.8	58.0	22.8	133.5	149.8	109.2	56.3
(1b) 5,8-Dimethoxy- syn-2,3-epoxide	29.6	48.8	21.8	127.7	148.8	109.0	56.1
(6) ^a 6-Nitro-5,8-dimethoxy	33.4	134.8	25.0	140.0	142.5	140.7	63.1
(12a) ^a 6-Nitro-5,8-dimethoxy- anti-2,3-epoxide	34.4		24.5	140.3	149.2	104.5	56.1
(12b) ^a 6-Nitro-5,8-dimethoxy- syn-2,3-epoxide	31.1	57.1	22.3	139.2	143.9	141.5	63.5
(7) 5,8-Diacetoxy	32.2		22.7	140.2	151.0	105.4	57.1
(13a) 5,8-Diacetoxy- anti-2,3-epoxide	29.8	48.2	21.3	134.0	143.3	141.6	63.2
(13b) 5,8-Diacetoxy- syn-2,3-epoxide	30.4		21.6	134.9	150.3	105.4	56.0
(7) 5,8-Diacetoxy	34.5	134.7	24.6	137.7	142.3	118.8	20.7, 169.2
(13a) 5,8-Diacetoxy- anti-2,3-epoxide	32.6	57.1	22.2	136.9	144.1	120.2	20.7, 169.3
(13b) 5,8-Diacetoxy- syn-2,3-epoxide	31.3	48.4	21.3	131.5	143.4	120.2	20.8, 169.2

^a The second line in this entry refers to the carbon having (or in the case of methoxy groups, attached to) the higher-numbered position.

or to the *syn* epoxide. This observation was confirmed by Cristol *et al.*¹⁶ on a series of substituted epoxybicyclo[2,2,2]octanes. As shown in Table 2, the same is true for the diacetoxy epoxides. This is probably the single most useful criterion for the configurational assignments in the bicyclo[2,2,2]-octane epoxide series and was applied subsequently to the dimethoxy and nitrodimehoxy compounds here.

The C-13 NMR chemical shifts were assigned from considerations based on single frequency off-resonance decoupling (sford), known substituent additivity effects and the use of model compounds such as 1,4-dimethoxybenzene and 2-nitro-1,4-dimethoxybenzene. These data are given in Table 3.

Chemical shift effects for the C-13 data in this series are, with one exception, quite similar to those published recently by Cristol *et al.*¹⁶ They observed both the *syn* and *anti* γ -effects of the epoxide oxygen in the saturated bicyclo[2,2,2]octane system to be a small shielding effect on the ethano carbons corresponding to C-2 and C-3. In fact, both *syn* and *anti* γ -effects involving heteroatom C-H interactions have proven increasingly unreliable in making stereochemical assignments.^{17,18} However, in contrast to these observations our data show a substantial *syn* γ -effect for the interaction of the *syn* oxygen and carbons 4a, 8a of the aromatic ring. The steric interaction explanation evoked to explain hydrocarbon γ -effects can hardly apply here. More likely it is an electronic perturbation of the lone pair electrons on the oxygen upon the excitation term of the Ramsey shielding mechanism as applied to the aromatic carbons.¹⁹ Clearly this does not extend beyond carbons 4a and 8a in the ring. It does, however, provide a convenient stereochemical confirmation applicable to epoxides derived from the bicyclo[2,2,2]octadienes.

EXPERIMENTAL

All mps are uncorrected. All NMR spectra were determined in CDCl₃ with internal TMS. Proton spectra were taken on Varian T-60 and EM-390 instruments. C-13 spectra were determined either on a Bruker WP-80 or JEOL FX-60 instruments.

5,8-Dimethoxy-1,4-dihydro-1,4-ethanonaphthalene 5

A soln of 2.03 g (10.8 mmol) of 4 in 30 ml dimethyl sulfoxide was stirred with 4 ml MeI under N₂ at room temp as 1.5 g of powdered KOH was added in portions. After 3 hr, 2 ml additional MeI was added, and the mixture was allowed to stand overnight. The soln was poured into water and extracted with CH₂Cl₂ (three 50 ml portions). Upon evaporation to dryness, the residue weighed 3.1 g. This brown oil was passed through an alumina plug using petroleum ether as the eluant to give 2.31 g of colorless, crude 5. Crystallization from MeOH gave two crops of crystals totaling 2.26 g (96%). m.p. 55-57° (lit.² 56-57°).

6-Nitro-5,8-dimethoxy-1,4-dihydro-1,4-ethanonaphthalene 6

A mixture of 50 ml water, 50 ml dioxane and 50 ml 70% HNO₃ was prepared. To this mixture at room temp was added 2.0 g of 5, and the whole was stirred overnight. The workup followed the procedure above: water, extraction with CH₂Cl₂, washing with dil NaHCO₃ aq, evaporation to dryness and crystallization from MeOH, yield 1.95 g (80%), m.p. 77.5-79° (Found C, 64.26, H, 5.61, N, 5.39. Calc for C₁₂H₁₁NO₄: C, 64.36, H, 5.79, N, 5.36%).

5,8-Diacetoxy-1,4-dihydro-1,4-ethanonaphthalene 7

A soln of 2.20 g (12 mmol) of 4 in 15 ml dry benzene was treated with 2 ml Ac₂O and 2 ml Et₃N at room temp overnight. The soln was washed with dil HCl aq and evaporated to dryness. The residue was crystallized from 75% MeOH, m.p. 165-167° (lit.¹ m.p. 164°), yield 2.3 g (70%). On a larger scale yields in excess of 90% were achieved.

Epoxidation of 7 A soln of 0.50 g (1.8 mmol) of 7 in 5 ml CH₂Cl₂ was reacted with 5.5 mmol monopero-phthalic acid in 10 ml ether at room temp for 18 hr. Precipitated phthalic acid was removed by filtration, and the soln was washed with dil

NaHCO₃ aq. Evaporation of the solvent, and examination of the residue by PMR using the aromatic proton absorptions at 6.87 and 6.93 ppm indicated that a mixture of 2,3-epoxy-5,8-diacetoxy-1,4-dihydro-1,4-ethanonaphthalenes had been formed with *anti:syn* ratio of 2. These were separated by flash column chromatography⁹ over 230–400 mesh silica gel (E. Merck, Darmstadt) using toluene-EtOAc in the ratio 4:1. The predominant *anti* isomer eluted first.

The *anti* epoxide **3a** (0.17 g) was crystallized from MeOH, m.p. 185–187° (Found C, 66.82, H, 5.57. Calc for C₁₄H₁₀O, C, 66.66, H, 5.59%). The *syn* epoxide (0.170 g) was also crystallized from MeOH, m.p. 196–198° (Found C, 66.53, H, 5.63%).

In an analogous fashion, **7** was epoxidized in CH₂Cl₂ with 1.1 equiv of *m*-chloroperoxybenzoic acid (MCPBA) at room temp overnight. The yield of crude epoxides was quantitative, and the PMR analysis showed the two isomeric epoxides to be present in equal amounts.

Epoxidation of 7 with peroxyacetic acid. The olefin **7**, 272 mg (1 mmol) was dissolved in 20 ml Ac₂O and 5 ml 30% H₂O₂ were added in one portion. The mixture stood at room temp for 3 days. It was then poured into 200 ml water and extracted with several small portions of CH₂Cl₂. The combined extracts were washed with dil NaHCO₃ aq. Evaporation to dryness gave 260 mg (90%) crude residue which was shown by PMR and tlc to consist of 42% *anti* epoxide **3a** and 55% *syn* epoxide **3b**.

The preparation of the epoxides of **5**

(a) **Conversion from 3a and 3b.** A soln of 288 mg (1 mmol) of *anti* **3a** in 20 ml ether was chilled to –5° under a blanket of argon. To this stirred soln was added dropwise 5 mmol MeLi in ether (20 ml). The mixture was stirred at –5° for 2 hr, and 10 ml MeI was added. The mixture was brought to room temp, 20 ml DMSO was added and the mixture stirred overnight. A granular ppt had formed upon addition of MeLi. This became quite stiff after the addition of the DMSO, but subsequently passed mainly into soln. The product was worked up as usual. The crude **1a**, (0.27 g), was crystallized either from petroleum ether or 70% MeOH, yield 0.150 g (65%), m.p. 129–130° (Found C, 72.42, H, 7.01. Calc for C₁₄H₁₀O, C, 72.39, H, 6.94%). The residue from the crystallization was by NMR essentially pure epoxide.

The *syn* epoxide **1b** was prepared from the corresponding diacetoxy epoxide in a similar fashion, yield 90% from 70% MeOH, m.p. 132–133° (Found C, 72.15, H, 7.07%).

(b) **From the dimethoxy olefin 5.** A mixture of 416 mg (2 mmol) of **5** in 30 ml CH₂Cl₂ containing 350 mg MCPBA was rapidly stirred with 5 ml water containing 250 mg KHCO₃. After 3 hr the starch-iodide paper test for peroxide was negative. A check of the product by tlc showed the reaction to be far from complete so the entire procedure was repeated twice more. Thus, after three equivs of peracid C-13 NMR, using the ethano carbons, showed 42% of starting material and 25 and 33% of the *anti* and *syn* epoxides respectively. No attempt to isolate these was made.

Preparation of the epoxides from **6**

A soln of 261 mg (1 mmol) of **6** in 3 ml CH₂Cl₂ was reacted overnight with 250 mg MCPBA. The epoxide mixture was worked up as usual giving 0.33 g crude product. The latter was resolved into the two epoxides by preparative tlc over silica gel using toluene-EtOAc 4:1 as the eluant. The band following the small amount of starting material was extracted with CH₂Cl₂ and proved to be the *anti* epoxide **2a**, 0.08 g, recrystallized twice from MeOH, m.p. 137.5–139.5° (Found C, 60.72, H, 5.22, N, 5.08. Calc for C₁₄H₁₁NO, C, 60.65, H, 5.45, N, 5.05%).

The most polar band was the *syn* epoxide **2b**, extracted with CH₂Cl₂, 0.18 g, m.p. 117.5–118.5° from MeOH (Found C, 60.33, H, 5.22, N, 5.08%).

Small scale epoxidations

(a) The following operations were carried out separately on olefins **5**, **6** and **7**. One millimole olefin was taken up in 20 ml CH₂Cl₂ and allowed to react with 250 mg (1.4 mmol) MCPBA at room temp. The mixture was washed with dil NaHCO₃ aq, and the solvent evaporated to dryness under vacuum. Material balances were routinely 92–100%. Analyses were performed by PMR on the aromatic proton absorptions or by C-13 NMR on the ethano carbons. The latter technique assumes that relaxation effects are equal in these related series of molecules. Several checks by PMR confirmed this assumption. For the dimethoxy series the aromatic proton resonances were coincident for the epoxides. They could be cleanly resolved by adding a small portion of Eu(FOD), which always affects the *syn* isomer the most. The results of this study are given in Table 1.

(b) A standardized ether soln containing 7.9 mmol MPPA was evaporated under vacuum and 20 ml of the desired solvent was added. To each soln was added 272 mg (1 mmol) of **7**. Each reaction was allowed to stand for 48 hr at room temp (*ca* 23°) then worked up as above. Again material balances were in the range 95–100%. Analyses by NMR were performed as before. A list of the solvents and results are incorporated in Fig. 1.

Hydrogenation of the dimethoxy olefin **5**

A soln of 0.5 g of **5** in 25 ml of MeOH was stirred with 50 mg Pd/C while a soln of 78 mg NaBH₄ in 5 ml water was added dropwise. The apparatus was connected to a gas burette to contain the excess H₂ as it was generated. After stirring overnight, the mixture was filtered, poured into 100 ml water and extracted with 3 × 50 ml portions CH₂Cl₂. The solvent was evaporated, and the residue crystallized from MeOH, yield 0.4 g, m.p. 68–69°. Analysis was by high resolution mass spectroscopy (Found 218.1312. Calc for C₁₄H₁₄O, 218.1307).

The C-13 NMR (CDCl₃) showed carbons at 25.66(CH₂), 26.27(CH), 56.28(OCH), 108.18(Ar CH), 133.84(C₁₀), and 148.74(CO) ppm respectively. The PMR had absorptions at 1.35 and 1.70 (multiplets, 4H each) assigned to the *syn* and *anti* ethano protons respectively, 3.43(2H), 3.82(6H), and 6.63(2H) ppm respectively. The assignment of the ethano protons was confirmed by the addition of Eu(FOD), in small portions. The upfield ethano protons were shifted by a factor of about three over the downfield set.

In a second experiment, 1 mmol of **5** in 10 ml MeOD was reduced as above with NaBD₄ in 5 ml D₂O. Upon workup and NMR examination it was found that the absorption at 1.70 ppm had one half the intensity of the multiplet centered at 1.35 ppm. Comparison with the intensities at the OMe and aromatic proton positions confirmed that deuteration was exclusively at the *anti* position.

1,4-Dimethoxy-10-iodo-5,6,7,8-tetrahydro-5,8-methanobenzocyclohepten-9-ol (**8**)

A mixture of 1.20 g of **5**, 0.56 g iodine, 0.195 g iodic acid, 15 ml sulpholane and 3 ml water was stirred overnight. The crude product, precipitated by water, weighed 1.76 g. Recrystallization from MeOH gave 1.35 g well-formed prisms. Repeated recrystallization was necessary to remove a trace of impurity. The pure iodohydrin had m.p. 175° (Found C, 46.81, H, 4.72. Calc for C₁₄H₁₇IO, C, 46.67, H, 4.72%). The PMR gave 1.2–2.2 (m, 4H), 2.8 (bs, 1H), 3.23 (d, J 5 Hz, 1H), 3.78 (s, 3H), 3.82 (m overlapping s, 4H), 4.12 (t, J 5 Hz, 1H), 6.80 (s, 2H). C-13 NMR 23.0(d), 26.0(t), 29.7(t), 41.0(d), 43.4(d), 55.6(q), 56.4(q), 71.3(d), 108.4(d), 110.7(d), 123.9(s), 131.5(s), 149.5(s), 152.4(s). The IR spectrum (paraffin paste) showed unusually sharp peaks including the O–H stretching vibration at 3560 cm⁻¹. The PMR spectrum in CDCl₃ changed upon addition of D₂O, the doublet at 3.23 ppm disappeared and the broad doublet at 4.62 collapsed to a singlet. This determined the assignment of the 9-OH group to the *endo* position as shown in **8**, calculation

by Allinger's MM-2 program (kindly performed by Dr I D Entwistle of Sittingbourne Research Centre, Shell Research, Ltd) showed a torsional angle of 79° between H-9 and H-8 in **8** explaining the absence of detectable coupling. The assigned stereochemistry of the I atom, *anti* to the ethylene bridge, is based on the assumed stereochemistry of the skeletal rearrangement producing **8**.

1, 4-Dimethoxy-10-iodo-5, 6, 7, 8-tetrahydro-5, 8-methano-benzocyclohepten-9-one

A soln of 1.0 g CrO₃ in 1 ml water was added to 10 ml pyridine with stirring and cooling. The above iodohydrin (0.5 g) was then added. After 60 hr the neutral product was recovered in the normal manner and was then recrystallized from EtOAc. The ketone (0.34 g) formed large prisms, m.p. 174–175° (depressed below 150° by a mixture with iodohydrin (Found C, 46.95, H, 4.28. Calc for C₁₂H₁₅O₃, C, 46.95, H, 4.22%). The IR spectrum (paraffin paste) showed no C–H stretching band and a strong (C=O) at 1682 cm⁻¹. Conjugation of the new CO group with the aromatic ring was also shown by the UV absorption (in EtOH) λ 353 nm, ε 700, and by the formation of a deeply colored 2,4-dinitrophenylhydrazone scarlet needles from toluene light petroleum, m.p. 230–231° (Found C, 44.90, H, 3.83, N, 10.54. Calc for C₁₆H₁₁N₂O₅, C, 44.62, H, 3.56, N, 10.46%).

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