Tetrahedron Letters, Vol. 33, No. 6, pp. 753-756, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press plc

Evidence for Stereoelectronic Control in the Epoxidation of Sterically Unbiased 3,3-Diarylcyclopentenes

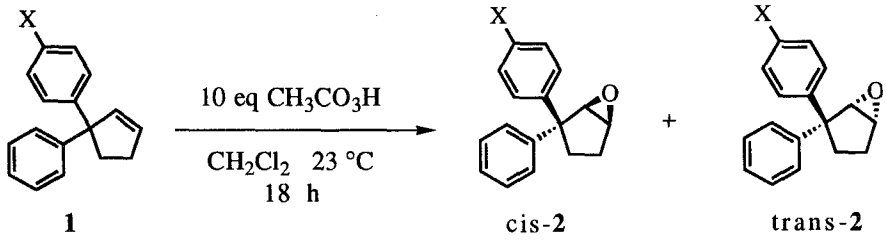
Ronald L. Halterman* and Marjorie A. McEvoy

Department of Chemistry, Boston University, Boston, Massachusetts 02215

Summary: Epoxidations of the sterically unbiased olefin, 3-(4-X-phenyl)-3-phenylcyclopentene (X = NO_2, Br, Cl, OCH_3) with peracetic acid have been found to proceed with up to 73:27 stereoselectivity. Stereochemistry of the products was determined by lanthanide shift studies, COSY and 1D NOE ^1H NMR spectroscopic techniques and chemical correlation to the known 2,2-diarylcyclopentanols.

Control of facial selectivity is crucial to many asymmetric transformations, and can be accomplished by utilizing either a sterically or electronically based diastereomeric bias. The role of stereoelectronic factors in determining facial selectivity, however, is not well understood due to insufficient suitable experimental evidence. For the synthetically important epoxidation reaction, the effect of stereoelectronics has been recently studied by Srivastava and le Noble who report that for the epoxidation of 5-fluoro-2-methyleneadamantane approach of the electrophile syn to the best electron acceptor leads to the major isomer[1], and by Cieplak and Johnson who observed that for the epoxidation of methylenecyclohexane derivatives the amount of axial attack increased as the 3-substituent became more electron withdrawing[3] and by Mehta using a methylenenorbonane system.[4] In each of these studies, the results are in agreement with the facial selectivity predicted by Cieplak's theory of stereoelectronic control in asymmetric reactions.[5] Vedejs and Dent have examined the epoxidation of 4-tertbutylmethylenecyclohexane derivatives, but concluded that stereoelectronic factors were not the primary forces involved in determining stereoselectivity.[2] Further research with sterically unbiased olefins should help identify the role of stereoelectronics in determining selectivity for the epoxidation reaction. In order to provide more data on stereoelectronic effects in the epoxidation reaction we undertook the study of the epoxidation of the sterically unbiased 3-(4-X-phenyl)-3-phenylcyclopentene **1** (X = NO_2, Br, Cl, OCH_3). The use of this conformationally flexible cyclopentyl system avoids any inherent steric bias of the cyclohexyl system[5] while placing the electronically non-equivalent phenyl groups closer to the center of reactivity than in the adamantane case.

*To whom correspondence should be addressed at: Department of Chemistry, 620 Parrington Oval, University of Oklahoma, Norman, OK 73019-0370.



1 cis-**2** trans-**2**

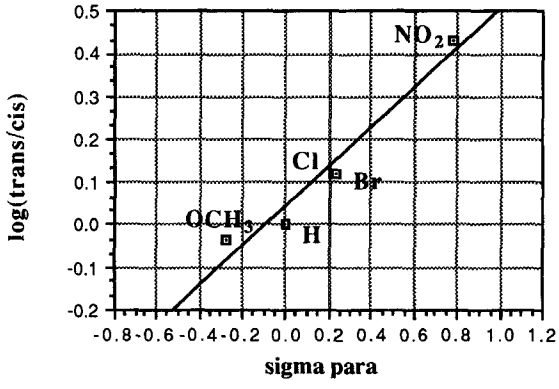
X = NO_2 (**a**), Br (**b**), Cl (**c**), OCH_3 (**d**)

The cyclopentene substrates, **1a-d**, were generated from the elimination of the tosyl hydrazone[6] of the corresponding 2,2-diarylcyclopentanones **3**, the synthesis of which we have described in previous reports.[7,8] Treatment of the four electronically different cyclopentenes, **1a-d**, with 10 equivalents of aqueous peracetic acid in methylene chloride at room temperature for 18 h generated the corresponding epoxides **2** in high yield.[9] In all cases the ^1H and ^{13}C NMR spectra were recorded of the crude epoxides and diastereomeric ratios were determined from these spectra. The results of the epoxidations are shown in Table 1.[10] Stereoselectivity as high as 73:27 was observed for the epoxidation of the strongly electron withdrawing nitro-substituted diarylcyclopentene, **1a**. A graph of selectivities (expressed as log(cis/trans)) versus the σ_p values for the substituents can be linearly correlated with a coefficient of 0.95 as seen in Figure 1.

Table 1. Ratio of Epoxidation Products

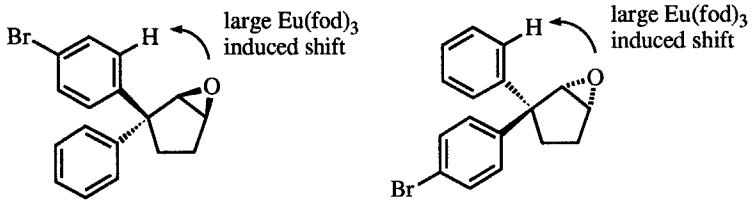
X	Epoxide	σ_p	% cis	% trans	log(cis/trans)
NO_2	**2a**	0.778	73	27	0.432
Br	**2b**	0.232	57	43	0.122
Cl	**2c**	0.227	57	43	0.12
(H)	**2d**	0.0	(50	50)	0.0
OCH_3	**2e**	-0.268	48	52	-0.035

Figure 1. Selectivity vs. Sigma Para Values



The diastereomers of oxiranes, **2a-c**, could be separated by SiO_2 preparative thin layer chromatography. The major and minor diastereomers of each were then analyzed by ^1H NMR COSY[11] experiments, and 1D NOE[12] studies performed to assign the stereochemical nature of the products. For each of the epoxides, irradiation of the proton geminal to the oxirane oxygen and alpha to the aryl rings showed an NOE effect consistent with the stereochemistry indicated in Table 1. Spectra of each diastereomer were also obtained in the

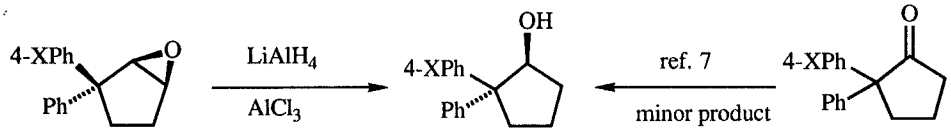
presence of the lanthanide shift reagent, $Eu(fod)_3$. As shown in Figure 2 for the bromo-substituted product **2c**, the major isomer showed a larger shift of the signals due to the ortho hydrogens on the substituted arene, while the minor isomer showed a complimentary effect on the unsubstituted phenyl group, supporting our assignments.



2b-major **2b**-minor

Figure 2. Determination of Stereochemistry by Lanthanide Shift Reagent

Since the stereochemistry of each diastereomer of the corresponding 2,2-diarylcyclopentanols was ascertained in our study of the reduction of 2-(4-X-phenyl)-2-phenylcyclopentanone, **3**, (X = NO_2, Br, Cl, OCH_3, OH, NH_2),[7] chemical correlation to these known alcohols was performed on both the nitro-substituted epoxide, **2a**, and the chloro-substituted epoxide, **2c**, to verify the structural assignments made with respect to the NMR experiments. In each case, Lewis acid catalyzed opening of the major diastereomer from the product mixture with lithium aluminum hydride gave either 2-(4-nitrophenyl)-2-phenylcyclopentanol or 2-(4-chlorophenyl)-2-phenylcyclopentanol, in 68% and 15% yields respectively (1.5 eq $AlCl_3$, 3.0 eq LAH, THF, reflux 4 h).[13] The ^1H NMR and ^{13}C NMR spectra of our products derived from the *major* epoxide, **2a** or **2c**, were identical to those of the *minor* isomers of the known 2,2-diarylcyclopentanols generated in the reduction of the corresponding cyclopentanones, **3a** or **3c**. Thus the facial selectivity in the epoxidation of cyclopentenes **1** must be *identical* to that observed in the reduction of the cyclopentanones **3**.



2 major **3**

We have shown that the epoxidation of the sterically unbiased 3,3-diarylcyclopentenes occurs in a Cieplak fashion where the major product arises from approach of the electrophile opposite the best electron donor and proceeds in up to 73:27 selectivity.

Acknowledgement. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for support of this research (21260-G1).

References

1. Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1987**, *109*, 5874-5875.

2. (a) Vedejs, E.; Dent, W. H. III *J. Am. Chem. Soc.* **1989**, *111*, 6861-6862. (b) Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094-1096.

3. Johnson, C. R.; Tait, B. D.; Cieplak, A. S. *J. Am. Chem. Soc.* **1987**, *109*, 5875-5876.

4. Mehta, G.; Khan, F. A. *J. Chem. Soc., Chem. Commun.* **1991**, 18.

5. Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

6. Buchs, B. *Top. Stereochem.* **1968**, *10*, 1. Legon, A. C. *Chem. Rev.* **1980**, *80*, 231. Lambert, J. B.; Papay, J. J.; Khan, S. A.; Kappauf, K. A.; Magyar, E. S. *J. Am. Chem. Soc.* **1974**, *96*, 6112. Adams, W. J.; Geise, H. J.; Bartell, L. S. *Ibid.* **1970**, *92*, 5013.

7. Halterman, R. L.; McEvoy, M. A. *J. Am. Chem. Soc.* **1990**, *112*, 6690-6695.

8. Halterman, R. L.; McEvoy, M. A. *J. Am. Chem. Soc.* in press.

9. Korach, M.; Nielsen, D. R.; Rideout, W. H. *J. Am. Chem. Soc.* **1960**, *82*, 4328.

10. The value of the nondiastereomeric diphenyl product, necessarily 50/50, has been added to the experimental data set.

11. Bax, A.; Freeman, R.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 164.

12. Noggle, J. H.; Schirmer, R. E. *The Nuclear Overhauser Effect*; Academic Press: New York, 1971.

13. Murphy, D. K.; Alumbaugh, R. L.; Rickborn, B. *J. Am. Chem. Soc.* **1969**, *91*, 2649-2653.

(Received in USA 12 June 1991; accepted 24 October 1991)