Pergamon

Tetrahedron Letters, Vol. 35, No. 2, pp. 231-232, 1994
Elsevier Science Ltd
Printed in Great Britain
0040-4039/94 $6.00+0.00

0040-4039(93)E0231-8

Stereoselectivities of Thermal and Lewis Acid Catalyzed Diels-Alder Reactions of 1,2,2-Trimethylpropyl Acrylate with Cyclopentadiene

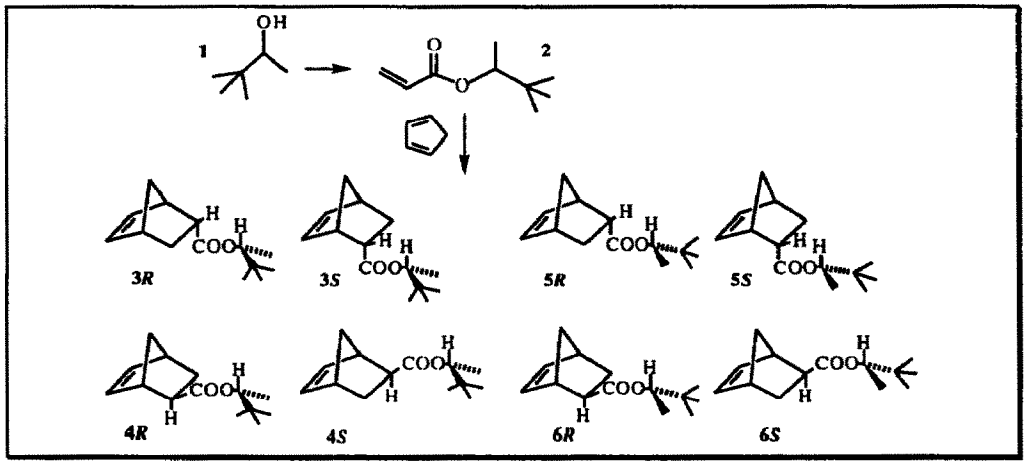
Beatriz de Pascual-Teresa and K. N. Houk*

Department of Chemistry and Biochemistry. University of California , Los Angeles
Los Angeles, California 90024-1569

Abstract. The Diels-Alder reaction of 1,2,2-trimethylpropyl acrylate with cyclopentadiene was carried out under Lewis acid catalyzed and thermal conditions. Results are in agreement with previous experimental work on the catalyzed process, and quantitate the lower thermal stereoselectivities.

The synthetic utility of the Diels-Alder reaction stems in part from its applications for the facile introduction of absolute stereochemistry.[1] The use of a chiral auxiliary in Lewis acid catalyzed Diels-Alder reactions was introduced by Walborsky and co-workers.[2] This concept has been widely used in organic synthesis.[3]

We have recently developed an ab initio-based force-field model for Lewis acid catalyzed asymmetric Diels-Alder reactions.[4] The theoretical and experimental study of the reaction of 1,2,2-trimethylpropyl acrylate, **2**, with cyclopentadiene is particularly basic to understanding of stereoselectivity, because **2** constitutes the simplest acrylate with small, medium and large alkyl groups differing only in steric bulk. We wished to verify the results for the catalyzed process and also to determine the asymmetric induction in the thermal reaction. We report here the addition of **2** to cyclopentadiene under thermal and Lewis acid catalyzed conditions.



The BF_3·Et_2O catalyzed Diels-Alder reaction of (*S*)-(+)-1,2,2-trimethylpropyl acrylate (*S*)-**2**, with cyclopentadiene has been reported to give a 97:3 endo:exo mixture and a diastereomeric excess of 80-85% in favor of **5*S***.[5] We carried out the reaction of (*R*)-(-)-trimethylpropyl acrylate (*R*)-**2**[6] with cyclopentadiene in the presence of BF_3·Et_2O in CH_2Cl_2 at -78°C. The Diels-Alder adduct was identified by ^1H and ^{13}C NMR and analyzed by GC/MS. A 98.5:1.5 endo:exo mixture was found, and a diastereomeric excess of 87% was obtained for the stereoisomer **3*S*** $[\alpha]^{20}_D$ =+24.1° (c 1.1, $CHCl_3$). A thermal reaction with the racemic alcohol was also carried out; a 73:27 endo:exo mixture was formed. This gave all four diastereomers, which allowed us to assign the peaks from the GC/MS for the different diastereomers. The Lewis acid catalyzed reaction with (*S*)-**1** was repeated, and the diastereomeric excess was determined by GC/MS. The results are summarized in the following table.

Acrylate	Catalyst/T(°C)	ENDO				EXO			
(*R*)-**2**	BF_3·Et_2O/-78	87.7	**3*R***	11.0	**3*S***	-		1.3	**4*S***
(*S*)-**2**	BF_3·Et_2O/-78	87.5	**5*S***	11.0	**5*R***	-		1.5	**6*R***
(*R*,*S*)-**2**	none/60	40	**3*R*+5*S***	33	**3*S*+5*R***	13	**4*R*+6*S***	14	**4*S*+6*R***

The relative activation free energies for the thermal reaction are 0, 0.13, 0.74 and 0.69 kcal/mol for the isomers in the table. The Lewis acid increases the differences to 0, 0.80, >20 and 1.62 kcal/mol. Thus, the increase in selectivity is due to both the lower temperature of the catalyzed reaction and the increased selectivity due to changes in transition state geometry in the catalyzed process.[4]

Acknowledgment. We are grateful to the National Institutes of Health for financial support of this research and to the Fundación Ramón Areces (Spain) for a Fellowship to BPT.

References and Notes

1. Carruthers,W."Cycloaddition Reactions in Organic Synthesis" Pergamon Press: Oxford, 1990.

2. Walborsky, H. M.; Barash, L.; Davis, T. C. *Tetrahedron* **1963**, *19*, 2333.

3. Oppolzer, W. *Angew. Chem. Int. Ed. Engl.* **1984**, *23*, 876. and references therein.

4. Pascual-Teresa, B. de; Gonzalez, J.; Houk, K. N., submitted for publication.

5. Sauer, J.; Kredel, J. *Tetrahedron Lett.* **1966**, 6359. Le Drian, C.; Greene, A. *J. Am. Chem. Soc.* **1982**, *104*, 5473.

6. (*R*)-(-)-3,3-dimethyl-2-butanol (*R*)-**1** was prepared via the hydrogen phtalate brucine salt,[7] and the enantiomeric excess was determined to be 99% by NMR with the use of [Eu(tfc)$_3$] as a shift reagent.[8] (*R*)-**1**(1g) was dissolved in 6 mL CH_2Cl_2 and 2 mL N-ethyldiisopropylamine were added. The temperature was fixed at -40°C, and 1 mL acryloyl chloride was added slowly. After 10 min., the usual work-up afforded 800 mg of (*R*)-(-)-1,2,2-trimethylpropyl acrylate (*R*)-**2** $[\alpha]^{20}_{D\ neat}$=-10.0°. ^1H and ^{13}C NMR were consistent with the structure, and enantiomeric purity was tested with the shift reagent.

7. Pickard, R.H.; Kenyon, J. *J. Chem. Soc.* **1911**, *99*, 45.

8. Parker, D. *Chem. Rev.* **1991**, *91*, 1442.

(*Received in USA* 20 *October* 1993; *accepted* 10 *November* 1993)