ORGANIC LETTERS

2002
Vol. 4, No. 24
4221−4224

Reactive-State Spin-Dependent Diastereoselective Photoisomerization of *trans,trans*-2,3-Diphenylcyclopropane-1-carboxylic Acid Derivatives Included in Zeolites

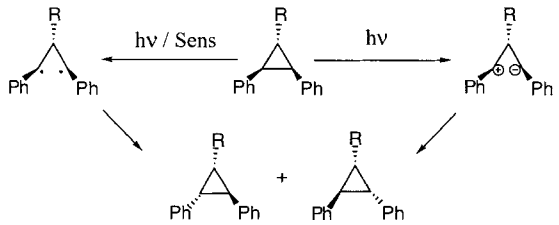
J. Sivaguru, Tetsuya Shichi, and V. Ramamurthy*

Department of Chemistry, Tulane University, New Orleans, Louisiana 70118

murthy@tulane.edu

Received August 7, 2002

ABSTRACT



The asymmetric induction facilitated by a chiral auxiliary during the photoisomerization of *trans,trans*-2,3-diphenylcyclopropane derivatives depends on the medium (solution vs zeolite) and the reactive state (singlet vs triplet). Within zeolites, direct excitation most likely proceeds via a zwitterionic intermediate, while triplet sensitization most likely proceeds via a diradical intermediate.

In establishing the power of zeolites in enhancing chiral induction, the choice of 1,2-diphenylcyclopropane and its derivatives as the model system is justified by their important role in the development of concepts such as triplet sensitization,[1] asymmetric induction,[2] heterolytic cleavage in the excited state,[3] and spin−orbit coupling in 1,3-diradicals.[4] Recently, we have shown that a diastereomeric excess (de) > 80% could be achieved in the product trans,cis isomer upon excitation of *trans,trans*-2,3-diphenylcyclopropane-1-carboxamides included in alkali cation-exchanged zeolites.[5] The observed >80% de in zeolites in comparison to the <2% de in solution has opened up new opportunities in chiral photochemistry.[5b] In this report, we show that an equally high de is obtained during triplet-sensitized geometric isomerization of *trans,trans*-2,3-diphenylcyclopropane-1-carboxamides within zeolites and, more importantly, that the enhanced diastereomer upon triplet sensitization is different, at least in one case, from the one obtained through direct excitation.[6] By examining the photochemistry of pure diastereomers of *trans,cis*-2,3-diphenylcyclopropane-1-carboxamide of 1-phenylethylamine in solution as well as in zeolite, we show that zeolites bring about diastereoselectivity by

(1) Hammond, G. S.; Wyatt, P.; DeBoer, C. D.; Turro, N. J. *J. Am. Chem. Soc.* **1964**, *86*, 2532−2533.

(2) (a) Hammond, G. S.; Cole, R. S. *J. Am. Chem. Soc.* **1965**, *87*, 3256−3257. (b) Inoue, Y.; Yamasaki, N.; Shimoyama, H.; Tai, A. *J. Org. Chem.* **1993**, *58*, 1785−1793.

(3) (a) Hixson, S. S. In *Organic Photochemistry*; Padwa, A., Ed.; Marcell Dekker: New York, 1979; Vol. 4, pp 191−260. (b) Hixson, S. S.; Garrett, D. W. *J. Am. Chem. Soc.* **1974**, *96*, 4872−4879. (c) Hixson, S. S. *J. Am. Chem. Soc.* **1974**, *96*, 4866−4871.

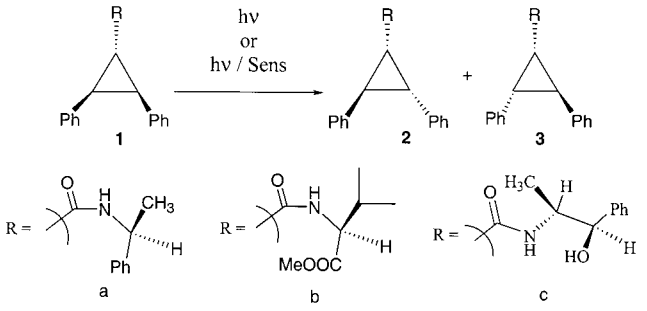
(4) (a) Ichinose, N.; Mizuno, K.; Otsuji, Y.; Caldwell, R. A.; Helms, A. M. *J. Org. Chem.* **1998**, *63*, 3176−3184. (b) Mizuno, K.; Ichinose, N.; Yoshimi, Y. *J. Photochem. Photobio. C* **2000**, *1*, 167−193.

(5) (a) Sivaguru, J.; Scheffer, J. R.; Chandrasekhar, J.; Ramamurthy, V. *J. Chem. Soc., Chem. Commun.* **2002**, 830−831. (b) Sivaguru, J.; Shailaja, J.; Uppili, S.; Ponchot, K.; Joy, A.; Arunkumar, N.; Ramamurthy, V. In *Organic Solid State Reactions*; Toda, F., Ed.; Kluwer Academic Press: Amsterdam, 2002; pp 159−188.

(6) Triplet sensitization in zeolites has been established previously: (a) Pitchumani, K.; Gamlin, J. N.; Ramamurthy, V.; Scheffer, J. R. *J. Chem. Soc., Chem. Commun.* **1996**, 2049−2050. (b) Wada, T.; Shikimi, M.; Inoue, Y.; Lem, G.; Turro, N. J. *J. Chem. Soc., Chem. Commun.* **2001**, 1864−1865.

10.1021/ol026695l CCC: $22.00
Published on Web 11/05/2002

Scheme 1



influencing the relative energies of the diastereomeric intermediates and that the diastereomer enhanced under the direct and triplet-sensitized conditions differ possibly due to the difference in nature of the intermediates involved.

Acetone sensitization of chiral amides of *trans,trans*-2,3-diphenylcyclopropane-1-carboxylic acid (**1a**−**c**) in solution gave the corresponding trans,cis isomers **2** and **3** (Scheme 1) with de values varying between 0 and 15%. Triplet sensitization with 4′-methoxyacetophenone in hexane−dichloromethane also gave similar results. Although direct excitation resulted in several other products, triplet sensitization both in solution as well as in zeolites gave mainly the products of geometric isomerization and the photostationary state was achieved within 12 h in zeolites. As seen in Table 1, the de values obtained under direct excitation and

Table 1. Percentage of Diastereoselectivity in Product Trans,Cis Isomers upon Direct Excitation and Triplet Sensitization of Chiral Amides of *trans,trans*-2,3-Diphenylcyclopropane-1-carboxylic Acid (**1a**−**c**)[a−c]

cmpd	mode	solution	LiY	NaY	KY	RbY	CsY
1a	direct	2-B	80-B	28-A	14-A	5-A	5-A
1a	sens	15-A	33-B	40-A	61-A	15-A	2-A
1b	direct	2-A	83-B	21-A	80-A	47-A	5-A
1b	sens	0-A	52-B	18-A	81-A	45-A	13-A
1c	direct	30-A	25-B	60-A	13-A	2-A	0
1c	sens	7-A	23-B	59-B	43-B	17-B	1-B

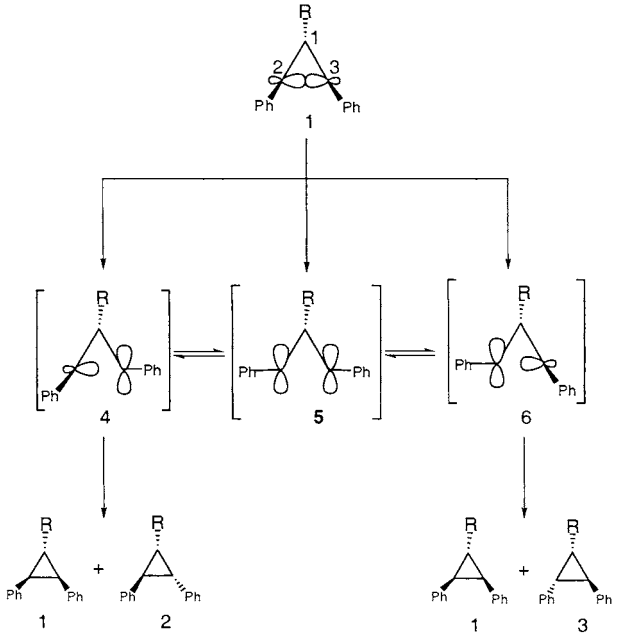
[a] 4′-Methoxyacetophenone was used as the sensitizer within zeolites. [b] Acetone was used as the solvent and triplet sensitizer in solution. [c] Products of **1a** and **1b** were separated on an SE-30 GC column; products of **1a** were also separated on a Chiralpak AD-RH HPLC column to verify the de. Products of **1c** were separated on a Chiralpak AD-RH. Diastereomeric excess in the case of **2c**/**3c** was verified by injecting on two different columns (Chiralpak AD-RH and Chiralpak AD).

4′-methoxyacetophenone sensitization were different; however, between the three examples, no clear pattern resulted.[7] In these irradiations, 4′-methoxyacetophenone primarily absorbs the light and serves as a triplet sensitizer.

The following observations emerge from the data presented in Table 1. (a) During triplet sensitization, the de obtained within zeolites was much higher than that obtained in solution (acetone).[8] (b) In two out of three examples (**1a** and **1c**), within a given zeolite, direct excitation and triplet sensitization resulted in different amounts of de. In the case of **1b**, the de is nearly the same during direct irradiation and triplet sensitization. (c) Remarkably, within NaY, direct excitation of **1c** resulted in diastereomer A in 60% excess, whereas upon triplet sensitization, diastereomer B was obtained in 59% excess (diastereomers are labeled A and B on the basis of their elution time in GC or HPLC). To our knowledge, such a switch in diastereoselectivity between S_1 and T_1 reactions has not been reported earlier. (d) The de obtained depends slightly upon the substituent on the triplet sensitizer acetophenone (ACP). For example, with **1b** in KY, the de values obtained with acetophenone, 4′-methoxy ACP, 4′-methyl ACP, and 4′-chloro ACP as sensitizers are 85, 81, 78, and 71%, respectively. Generally, we have preferred to use 4′-methoxyacetophenone as the sensitizer within zeolites.

Triplet-sensitized geometric isomerization of **1** is likely to follow the reaction sequence shown in Scheme 2.[4] As per

Scheme 2 [a]



this model, the cleavage of C_2-C_3 bond (β-cleavage) results from the mixing of the $\sigma\sigma^*$ state of C_2-C_3 bond with the $\pi\pi^*$ state of the phenyl chromophore. The triplet diradical formed (**4** or **6**) will be determined by the phenyl ring that can better overlap with the C_2-C_3 σ bond. In a symmetrical molecule such as 1,2-diphenylcyclopropane (**1**, R = H), in the absence of a chiral influence both phenyl rings would be able to equally overlap with the C_2-C_3 σ bond, and therefore the triplet diradicals **4** and **6** would be formed in

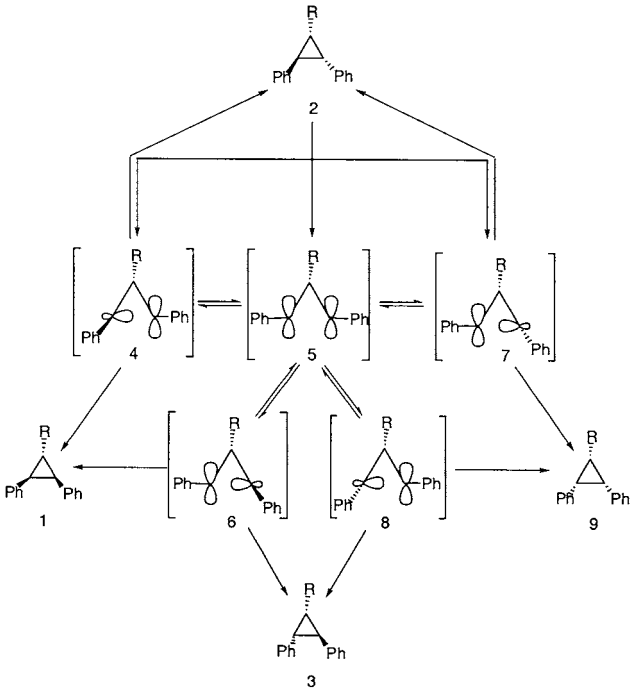
(7) See Supporting Information for details.

(8) The de did not depend on the duration of irradiation (12−72 h) and on the loading level of the sensitizer (from 1 in 10 to 1 in 1 supercage).

equal amounts. These triplet diradicals of equal energies would give the final products **2** and **3** in equal amounts (ee = 0). In all molecules investigated here, a chiral center is present as a chiral auxiliary (R = chiral auxiliary), although at a remote location. This could influence the isomerization process by either altering the rates of formation of the diasteromeric intermediates **4** and **6** or tilting the equilibrium (if **4** and **6** establish equilibrium prior to crossing to singlet diradicals) in favor of one of the two intermediates.

Better insight into the mechanism of the isomerization process of **1** can be obtained by examining the photochemistry of pure diasteromers **2** and **3** (R = chiral auxiliary). As shown in Scheme 3, triplet sensitization of diastereomer **2**

Scheme 3 [a]



could result in three products, diastereomer **3**, *trans,trans*-**1**, and *cis,cis*-**9**. Since in no case did we detect *cis,cis*-**9**, we believe that this is not formed as the product from **1**−**3**. In the absence of equilibrium between the diradical intermediates **4** and **7** via **5**, only **1** is expected. However, if there was equilibrium of the diradicals **4** and **7** via **5**, diastereomer **3** would also be formed as the primary photoproduct. Isolating pure diasteromers of *trans,cis*-2,3-diphenylcyclopropane-1-carboxamide of 1-phenylethylamine by preparative HPLC using Chiralcel OD allowed the photochemistry of individual diasteromers to be examined in solution and in alkali cation-exchanged Y zeolites.

In the absence of knowledge of the absolute configuration of the two diastereomers, we labeled them **A** and **B** (since the isomers were not crystalline, we could not obtain the absolute configuration of isomers **A** and **B**, but for mechanistic discussion, this information is not essential). As

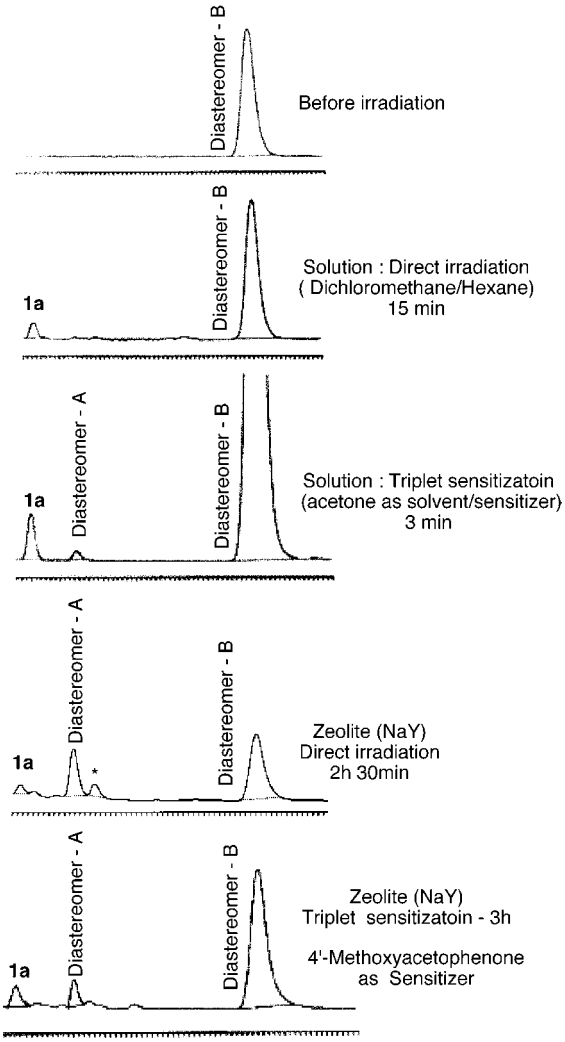


Figure 1. Product distribution upon direct irradiation and triplet sensitization of diasteromer **B** of *trans,cis*-2,3-diphenylcyclopropane-1-carboxamide of 1-phenyl ethylamine under various conditions. Peak positions and duration of irradiation are marked on the trace. The major peaks **1a** and diasteromers **A** and **B** have been identified by co-injecting pure samples. The second trace from the bottom has an impurity next to diasteromer **A**, and this was not identified.

illustrated in Figure 1, triplet sensitization of the diastereomer **B**, even at very early times, gave both the cis isomer **1a** and diastereomer **A**, suggesting that the triplet diradicals **4**−**8** (Scheme 3) establish an equilibrium prior to closing to give products.[9]

Extending this observation to **1**, we believe that the triplet diradicals **4** and **6** (Scheme 2) formed upon sensitization of **1a** would be in equilibrium before they intersystem-cross to the corresponding singlet diradicals and close to diastereomeric products **2** and **3**. Accordingly, the observed de within

(9) During acetone-sensitized isomerization of optically pure methyl 1-(*R*)-cyano-2-(*R*)-phenylcyclopropanecarboxylate, involvement of open-chain trimethylene diradical capable of undergoing multiple rotations at both chiral centers has been established: Howe, N. E.; Yankee, E. W.; Cram, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 4230−4237.

zeolites must result from the ability of zeolites to alter the relative energies of the triplet diradicals **4** and **6** and thereby tilt the equilibrium in favor of one of the two diradicals. Even if the chiral auxiliary influences the rate of formation of the two diradicals (**4** and **6**), when there is equilibrium it would have no consequence on the diastereoselectivity of the product trans,cis isomers.

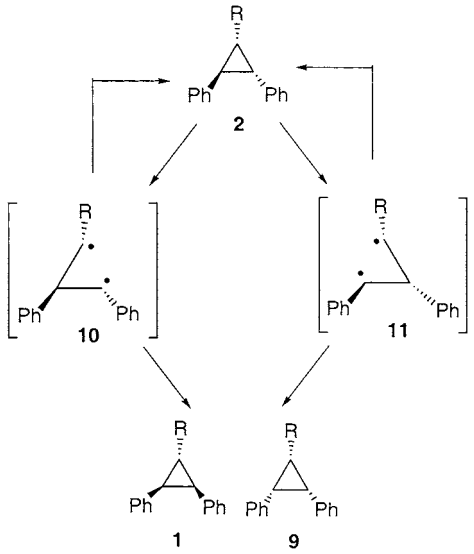
The final discussion relates to the observed diastereomeric switch between excited singlet and triplet reactions in the case of **1c**. In this context, examination of the time-dependent product study upon direct excitation of pure diasteromers of *trans,cis*-2,3-diphenylcyclopropane-1-carboxamide of 1-phenylethylamine has been very valuable. In Figure 1, the HPLC traces of the product distribution obtained upon direct excitation of the pure diastereomer **B** are shown. Clearly in solution (dichloromethane−hexane), the only product obtained upon 15 min of irradiation was the trans,trans isomer **1a**, suggesting that there was no equilibrium between diradicals **4**−**8** (Scheme 3; singlet diradicals). Examination of Figure 1 indicates that within zeolite, even after 2 h and 30 min, the major product is diastereomer **A**. This suggests that the mechanisms of isomerization upon direct excitation in solution and within zeolites are not the same.

In the discussion above, we have assumed that the isomerization occurs via cleavage of the 2,3-bond. In principle, isomerization could also result from cleavage of the 1,2- or 1,3-bond.[10] As illustrated in Scheme 4 this process would not allow interconversion between the diastereomers. The fact that upon sensitized irradiations in solution and within zeolite the diastereomeric interconversion occurs suggests that cleavage of the 2,3-bond does occur.

At this stage, we cannot exclude the possibility of 1,2- or 1,3-bond cleavage being responsible for the formation of *cis*-**1** upon irradiation of diastereomers **2** and **3**. The 1,2- or 1,3-bond cleavage has been postulated during the photoisomerization of *trans,trans*-2,3-diphenyl-1-benzoyl cyclopropane derivatives.[11]

1,2-Diarylcyclopropanes, upon direct excitation, are known to undergo homolytic cleavage in nonpolar media and heterolytic cleavage in polar media.[3] Within the established

Scheme 4



highly polarizable environment of the zeolite,[12] isomerization via a heterolytic pathway is quite likely. We speculate that the character of intermediates **4** and **6** formed upon direct excitation of **1a** within LiY and NaY is zwitterionic, and that upon triplet sensitization is triplet diradical. The observed switch in the favored diastereomer in the case of **1c** under the two conditions is most likely due to variations in the ability of the chiral auxiliary in stabilizing the intermediates with different characters, namely, diradical and zwitterionic. We are continuing our investigations to understand and exploit this novel observation.

Acknowledgment. The authors thank the National Science Foundation for support of the research (CHE-9904187 and CHE-0212042).

Supporting Information Available: Photolysis methods, control experiments, and analytical techniques used in asymmetric induction studies. This material is available free of charge via the Internet at http://pubs.acs.org.

OL026695L

(10) We thank one of the referees for suggesting that we consider this possibility.

(11) (a) Chong, K. C. W.; Sivaguru, J.; Shichi, T.; Yoshimi, Y.; Ramamurthy, V.; Scheffer, J. R. *J. Am. Chem. Soc.* **2002**, *124*, 2858−2859. (b) Zimmerman, H. E.; Flechtner, T. W. *J. Am. Chem. Soc.* **1970**, *92*, 6931−6935.

(12) (a) Ortiz, W.; Cozens, F. L.; Schepp, N. P. *Org. Lett.* **1999**, *1*, 531−534. (b) Uppili, S.; Thomas, K. J.; Crompton, E. M.; Ramamurthy, V. *Langmuir* **2000**, *16*, 265−274.