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Confined space and cations enhance the power of a chiral auxiliary: photochemistry of 1,2-diphenylcyclopropane derivatives†

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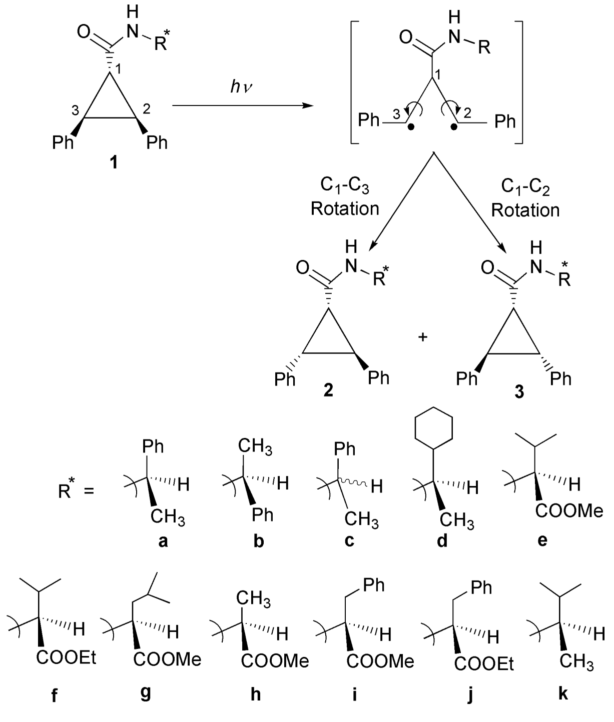
Received (in Cambridge, UK) 21st January 2002, Accepted 5th March 2002
First published as an Advance Article on the web 20th March 2002

Alkali ion-exchanged Y-zeolites significantly enhance asymmetric induction in the photoisomerization of a number of *cis*-1,2-diphenylcyclopropane derivatives containing a distant chiral auxiliary.

The unique nature of organized media is nowhere more evident than in their ability to control the formation of enantiomerically enriched photoproducts.[1] We report below the photoisomerization of several *cis*-1,2-diphenylcyclopropane derivatives to the chiral *trans* forms in which asymmetric induction has been enhanced with the use of a confined medium. 1,2-Diphenylcyclopropane itself has played a central role in the quest for new methods of asymmetric induction in organic photochemistry.[2] Following the original report by Hammond and Cole (ee 6.7%),[2a] asymmetric induction during the isomerization of *cis*-1,2-diphenylcyclopropane to the *trans* isomer has been investigated by at least five groups, and the best ee obtained thus far is only 10%.[2b–f] Our interest in the parent system in the context of asymmetric induction faded when *cis*-1,2-diphenylcyclopropane failed to isomerize to the *trans* form within alkali cation-exchanged Y zeolite.[3]

We now report that introduction of a third substituent, such as a carboxamide group onto the cyclopropane ring (*e.g.*, amides of 2β,3β-diphenylcyclopropane-1α-carboxylic acid, Scheme 1) solves the problem of lack of reactivity, and the chiral *trans* isomers were obtained upon irradiation of the 2β,3β-diphenylcyclopropane-1α-carboxamides within alkali cation-exchanged Y zeolites. The structure and energy of Li^+ ion binding to the *cis* isomer of amide **1b** calculated at the *ab-initio* level (RHF/3-21G, Gaussian 98)[4] accounted for the difference in the photobehavior between the parent *cis*-1,2-diphenylcyclopropane and its amides **1a–k**. The site of Li^+ ion binding is different in these two types of molecules (Fig. 1). While in the parent molecule, the cation binds to the *cis*-phenyl groups *via* a cation–π interaction,[5] in the amide derivative the Li^+ ion binds to the carboxamide group *via* a dipolar interaction.[6] Thus, while a cation-imposed barrier for *cis* to *trans* conversion is likely in the parent system, such is not the case for the amide derivative. This key observation permitted us to investigate asymmetric induction during the isomerization of optically pure amides of 2β,3β-diphenylcyclopropane-1α-carboxamide to the *trans* form. The distal amide substituent serves as the chiral auxiliary. Upon excitation of these amides, the C2–C3 bond cleaves resulting in free rotation of the C1–C2 and/or C1–C3 bond. The absolute configuration of the final product depends on which of these two bonds rotates (Scheme 1).

In this communication, we report the results on eleven chiral amides of 2β,3β-diphenylcyclopropane-1α-carboxylic acid (Scheme 1). When the amides **1a–k** were irradiated in hexane–methylene chloride solution the corresponding *trans* isomers



Scheme 1

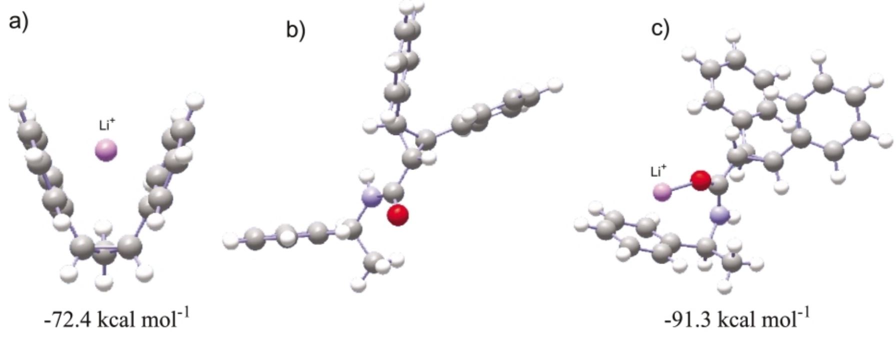


Fig. 1 Structures of Li^+ complex of *cis*-1,2-diphenylcyclopropane (A), (−)-1-phenylethylamide of 2β,3β-diphenylcyclopropane-1α-carboxylic acid (B), and its Li^+ complex (C) as calculated by RHF/3-21G. Computed cation interaction energies are also shown.

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† Electronic supplementary information (ESI) available: experimental details of irradiation, extraction and analysis of products, and representative synthesis and spectral data of reactant *cis* and product *trans* isomers; total number of pages 21. See http://www.rsc.org/suppdata/cc/b2/b200640e/

DOI: 10.1039/b200640e

were obtained in ±2% diastereomeric excess (de; except **1f** where the de is 20%). In stark contrast to the solution results, photolysis of amides **1a**–**j** as adsorbed on zeolites LiY, NaY or KY afforded the *trans* isomers with de′s. in the range of 20–83% (Table 1).

The amides **1a**–**c** and **1e** gave the highest de′s. (80–83%) of any of the systems examined thus far in zeolites.[7] The results for these two systems are highlighted below. Irradiation of 1-phenylethylamide **1a**–**c** in hexane–methylene chloride solution gave the *trans* isomers in ∼2% de. As illustrated in Table 1, when 1-phenylethylamide included in LiY was irradiated, the *trans* isomer was obtained in 80% de. The fact that the same chiral auxiliary failed to effect asymmetric induction during solution irradiation suggests that the confined space of the zeolite is essential to force a chirally significant interaction between the amide auxiliary and the site of reaction on the 3-membered ring. Similarly, the amino acid-derived chiral auxiliary **1e** gave excellent results in LiY (de 83%) but not in solution (de 2%). The following three observations suggest that, in addition to the confined space, the cations present in a zeolite play a crucial role in the asymmetric induction process: (a) for amides **1a**–**c** and **1e**, the extent of de as well as the identity of the isomer being enhanced is dependent on the cation. For example, in the case of amide **1a** the de observed in LiY, NaY and KY are 80%, 28%, 14% respectively. More importantly, while LiY favoured the formation of isomer B (the second of the two diastereomeric peaks eluted from GC; SE-30 column), NaY and KY gave some A in excess. A similar observation was made with amide **1e**: LiY gave 83% of isomer B while KY led to an 80% excess of isomer A. (b) The extent of de within LiY depends on the water content. For example, in the case of amide **1a**, saturating the LiY with water dramatically reduced the de from 80% (dry) to 8% (wet). We believe that co-ordination of water to the cation reduces the influence of the cation on the reaction. (c) Adsorbing the amides on a silica surface, which does not contain cations, gave low de′s. (8%). Silica surface differs from zeolites in terms of cavity size as well as silica–alumina content.

The role of cations in controlling asymmetric induction within a zeolite is supported by various experimental and computational results on cation–amino acid complexation reported in recent years.[6,8] We believe that the most likely factor responsible for the changes in diastereoselectivity observed upon irradiation of the amide derived from phenylalanine methyl ester and 2β,3β-diphenylcyclopropane-1α-carboxylic acid between solution and KY zeolite (de: 2% *vs.* 53%) is the conformational preference for the reactant molecule in these two media. The interaction between the cation present in a zeolite and the reactant most likely aids a conformation in which the asymmetric center of the chiral auxiliary is closer to the reaction site. Recently, as expected, the computed conformations of free and Na$^+$ bound phenylalanine have been reported to be different.[6b–d] Cation–π, dipolar cation–O=C and cation–nitrogen lone pair interactions control the conformation of Na$^+$ bound phenylalanine. Results of our computation on **1b** is consistent with this reasoning. A comparison of the structure of free and Li$^+$-complexed **1b** (Fig. 1) suggests that the Li$^+$ ion causes the chiral auxiliary to move closer to the 2,3-diphenyl portion of the molecule. A comparison of the structures of cation-bound and cation-free **1b** reveals that in the former the two phenyl groups will experience different extents of steric hindrance upon rotation to the *trans* geometry. We recognize that the calculated conformation may not be applicable in zeolites, but as a working hypothesis this appears to be a good starting point. It appears that presence of either a phenyl or carboalkoxy or both is required in the chiral auxiliary to obtain significant asymmetric induction. For example **1k** which does not contain any of these groups gives a very low de.

Table 1 Diastereomeric excess obtained upon direct irradiation of amides **1a**–**k** included within MY zeolites[a]

Compound	Solution	Li$^+$	Na$^+$	K$^+$
1a	2-B	80-B	25-A	14-A
1b	0	82-B	22-A	13-A
1c	1-B	77-B	27-A	13-A
1d	2-B	29-B	24-A	26-A
1e	2-A	83-B	21-A	80-A
1f	20-A	39-B	31-A	61-A
1g	3-A	26-B	22-A	46-A
1h	5-B	34-B	22-A	31-A
1i	2-A	10-A	32-A	53-A
1j	1-A	21-A	40-A	44-A
1k	2-B	7-A	7-A	3-A

[a] Analyses were performed by GC using an SE-30 column. The first diastereomeric peak eluted from the GC column is arbitrarily assigned as A.

As presented in Table 1 the cations not only control the extent of diastereoselectivity but also the isomer that is being enhanced. Based on density functional calculations and low energy collisionally activated and thermal radiative dissociation experiments a difference in binding pattern between Li$^+$ and K$^+$ ions with glycine and valine has been proposed.[8] Such a phenomenon may likely be involved within a zeolite and could be the cause for the observed cation controlled diastereomer switching within a zeolite.

The examples provided here demonstrate convincingly that the influence of a chiral center present as a chiral auxiliary can be enhanced significantly when the photoreaction is carried out within a zeolite. Examination of the zeolite interior, in which the reactant molecule is held, suggests that the most likely factor responsible for the change in de between solution and zeolite is the difference in conformational preference for the reactant molecule in these two media. In solution the influence of cations are wiped out by solvation of cations by the solvent molecules. Cations present in zeolites being only partially co-ordinated to the surface oxygen are free to interact with included guest molecules. X and Y zeolites contain high concentrations (∼5 M) of exchangable cations making them seemingly open structures of alkali salts with zeolite framework as the anion. We believe that cations present in zeolites can be cleverly exploited to control the chemical behaviour of organic molecules.

VR thanks the National Science Foundation for support of the research (CHE-9904187). JRS thanks the National Sciences and Engineering Research council of Canada for financial support.

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