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Photoisomerization of Ionic Liquid Ammonium Cinnamates: One-Pot Synthesis−Isolation of *Z*-Cinnamic Acids

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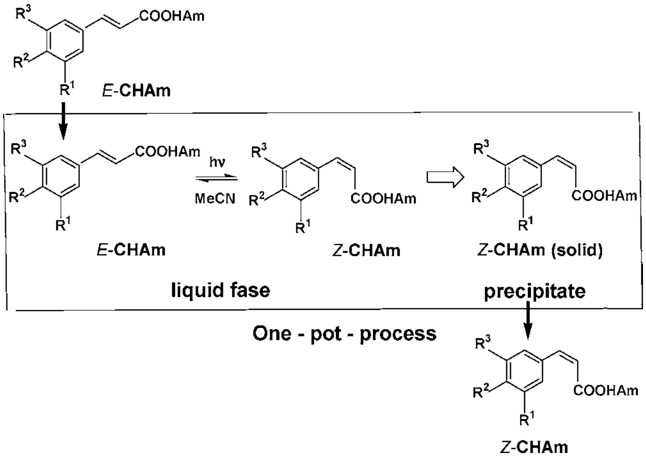
ABSTRACT



Photoisomerization presents the only direct method for contra-thermodynamic *E*−*Z* isomerization of olefins. Synthetic applications of this method have been limited by its reversible nature, which leads to a photostationary-state mixture of both isomers. For the first time, a highly efficient one-pot preparation−isolation of solid ionic liquid *Z*-cinnamic acids by photoisomerization in acetonitrile solution of ionic liquid *E*-cinnamic acids is described.

Ionic liquids (ILs) are nanostructured compounds whose properties can be tuned by variation of the cation and anion nature.[1] There are countless combinations possible, which make ILs well suited to creating tailor-made or "designed compounds" with different densities, viscosities, polarity, optical properties, etc.[1] As part of a project related to the study of the photochemical stability of ILs for application as matrixes in matrix-assisted laser desorption/ionization mass spectrometry,[2a,b] several ILs (*E*-CHAm) were prepared combining commercially available *E*-cinnamic acids (*E*-CH) (Scheme 1(a), *E*-**1**, *E*-**2**, *E*-**3**, *E*-**4**, and *E*-**5**) and organic bases (Am) (Scheme 1(b), Am = **a**−**i**), i.e., *E*-**1a**, *E*-**1b**, *E*-**2a**, and *E*-**2b**, etc. (*E*-CHAm; see Scheme 1(c)). The photostability of the *E*-CHAm was studied in MeCN solution. To our surprise and good luck, we found a one-pot method for the preparation−isolation as a solid, without any additional chemical manipulation, of the corresponding IL *Z*-CHAm (Scheme 2). From *Z*-CHAm, the

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[1] Wassescheid, P.; Keim, W. *Angew. Chem., Int. Ed. Engl.* **2000**, *39*, 3772.

[2] (a) Armstrong, D. W.; Zhang, L.-K.; He, L.; Gross, M. L. *Anal. Chem.* **2001**, *73*, 3679. (b) Crank, J. A.; Armstrong, D. W. *J. Am. Soc. Mass Secptrom.* **2009**, *20*, 1790.

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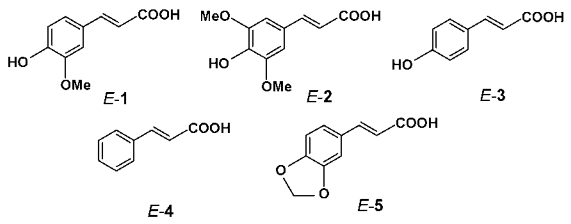
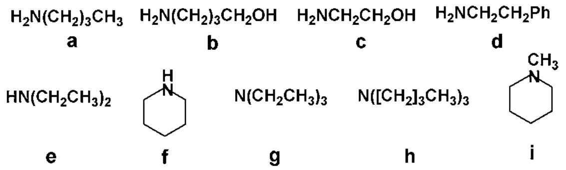
Scheme 1. Substrates Studied[a]

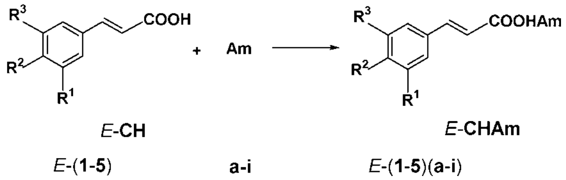
(a) – *E*-cinnamic acids (*E*-CH).



(b) – Amines (Am).



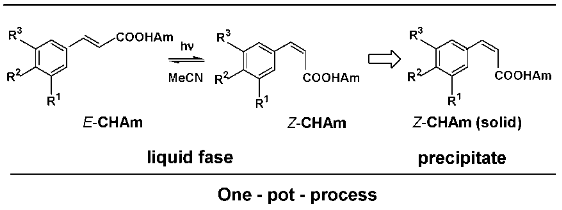
(c) – Ionic liquids of *E*-cinnamic acids (*E*-CHAm).[a]



[a] Detailed nomenclature, preparation, and charaterization of *E*-CHAm are described in the Supporting Information.

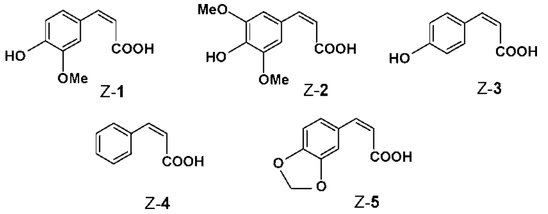
corresponding *Z*-cinnamic acid (*Z*-CH, Scheme 3) could be easily obtained by pH adjusting a *Z*-CHAm methanol solution.

Scheme 2. Photoreaction Studied



Cinnamic acids exists in both *E*- and *Z*-forms in nature. Thus, interest in both isomers has increased because they were detected in all kinds of plant-derived products: i.e., foods, herbs medicines, cosmetics, etc.[3a,b] The role of *E*-CH in plant and mammal cells has been extensively studied because they are commercially available.[3a−c] In contrast to exploring the possible physiological roles played by *Z*-CH that still are not known, it is essential to have these compounds commercially available and/or simple and friendly protocols for their preparation−isolation and purification.[3c]

Scheme 3. *Z*-Cinnamic Acids (*Z*-CH) Prepared[a]



[a] Characterization of *Z*-CH is described in the Supporting Information.

Photochemical *E*−*Z* isomerization is a major area of interest in modern photochemical research and is also studied, as a special tool for synthesis, in preparative organic photochemistry.[4a−c] It has a major role in many photobiological phenomena.[4a−c] It has practical application in industry[4d] and in many optoelectrical, optomechanical switching, storage devices, and light-driven chiroptical molecular motors.[4e,f] Synthetic applications of this method have been limited by its reversible nature, which, in the absence of other reactions, leads to a photostationary-state mixture of both isomers in solution (Scheme 2).[4a−c,5a,b] The composition of these mixtures is governed by different factors,[4a−c,5a,b] and there are few citations for the efficient photochemical *E* to *Z* one-way isomerization process.[4c,6a,b]

Herein we report for the first time a highly efficient one-pot preparation−isolation of solid *Z*-CHAm by photoisomerization in MeCN solution of the corresponding *E*-CHAm (Scheme 2).

Irradiation of 0.01 M *E*-**1** in acetonitrile solution with a Pyrex-filtered high-pressure mercury lamp (λ_{em} >300 nm) or monochromatic light (313 nm) results in the formation of a photostationary state consisting of 67% *E*-**1** and 33% *Z*-**1**. Photodimerization does not compete with *E*/*Z* isomer-

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(3) For selected examples of biosynthesis and plant physiology, studies of *trans*- and *cis*-cinnamic acids: (a) Caccamese, S.; Azzolina, R. *Chromatographia* **1979**, *12*, 545. (b) Wong, W. S.; Guo, D.; Wang, X. L.; Yin, Z. Q.; Xia, B.; Li, N. *Plant Physiol. Biochem.* **2005**, *43*, 929, and references therein. (c) Sun, F.-M.; Smith, J. L.; Vittimberga, B. M.; Traxler, R. W. *ACS Symp. Ser.* **2002**, *816*, 228.

(4) For selected reviews on *cis*−*trans* photoisomerization and its applications: (a) Mori, T.; Inoue, Y. In *C*=*C Photoinduced Isomerization Reactions*; Griesbeck, A. G., Mattay, J., Eds.; Synthetic Organic Photochemistry; Marcel Dekker: New York, 2005; p 417. (b) Arai, T. In *Photochemical cis-trans Isomerization in the Triplet State*; Ramamurthy, V., Schanze, K. S., Eds.; *Organic Molecular Photochemistry*, in the Series, *Molecular and Supramolecular Photochemistry*, 1999; Vol 3, p 131. (c) Rao, V. J. In *Photochemical cis-trans Isomerization from the Singlet State*, Ramamurthy, V.; Schanze, K. S., Eds.: *Organic Molecular Photochemistry*, in the Series, *Molecular and Supramolecular Photochemistry*, 1999; Vol 3, 169. (d) Braun, A. M.; Maurette, M. T.; Oliveros, E. *Photochemical Technology*; Wiley-Chichester, 1991; p 500. (e) Nieuwendaal, R. C.; Bertmer, M.; Hayes, S. E. *J. Phys. Chem. B* **2008**, *112*, 12920. (f) Feringa, B. L.; van Delden, R. A.; Koumura, N.; Geertsema, E. M. *Chem. Rev.* **2000**, *100*, 1789.

(5) (a) Klessinger, M.; Michl, J. *Excited States and Photochemistry of Organic Molecules*; VCH Publishers, Inc.: New York, 1995; p 362. (b) Turro, N. J.; Ramamurthy, V.; Scaiano, J. C. *Principles of Molecular Photochemistry: An Introduction* ; University Science Books: Sausalito, 2009; p 319.

(6) (a) Lewis, F. D.; Yang, J.-S. *J. Phys. Chem.* **1996**, *100*, 14560, and references therein. (b) Raj Gopal, V.; Mahipal, A.; Reddy, V.; Rao, J. *J. Org. Chem.* **1995**, *60*, 7966.

ization under these conditions. Similar values of the photostationary state are obtained in ethanol and methanol solution. Irradiation of 0.01 M *E*-**1a** (prepared with *E*-**1** and **a**, Scheme 1) in acetonitrile solution results in a photostationary state consisting of 57**%** *E*-**1a** and 37% *Z*-**1a** (Table 1, entry 1) together with a solid phase characterized as *Z*-**1a** in 20% yield (Table 1, entry 1).

Table 1. Results Obtained by UV-Irradiation of Ionic Liquids of *E*-Cinnamic Acids (*E*-CHAm) in MeCN Solution: Substrate Scope

		products in solution yield [%][a]		product precipitated yield [%][b]
entry	ionic liquid	*E*-CHAm	*Z*-CHAm	*Z*-CHAm
1	*E*-**1a**	57[c]	37	20
2	*E*-**1b**	73[c]	21	26
3	*E*-**1c**	55	45	30
4	*E*-**1c**[d]	93	7	68
5	*E*-**1d**	66	34	39[e]
6	*E*-**1f**	68[c]	26	33
7	*E*-**1i**	60[c]	35	–
8	*E*-**2a**	44[c]	51	–
9	*E*-**2b**	63[c]	34	12
10	*E*-**2b**[d]	45[c]	50	21
11	*E*-**2c**	78	15	26
12	*E*-**2c**[d]	75	25	56
13	*E*-**2d**	50[c]	46	25[e]
14	*E*-**2f**	29[c]	67	–
15	*E*-**2i**	50[c]	46	–
16	*E*-**3a**	57[c]	36	31
17	*E*-**3b**	69	31	32
18	*E*-**3c**	21	79	–
19	*E*-**3f**	40	60	19[e]
20	*E*-**4a**	93	7	29
21	*E*-**4b**	86	14	–
22	*E*-**4c**	94	6	–
23	*E*-**4f**	97	3	–
24	*E*-**5a**	58	42	40

[a] Determined by ^{1}H NMR spectroscopic analysis of the irradiated solution. [b] The yields are based on the conversion of the starting material (*E*-CHAm). [c] Low yield of the decarboxylated product (aryl–alkene, 3–7%) in solution is observed. [d] Reirradiation of the mother liquor after solid *Z*-CHAm was filtered off. [e] Solid *Z*-CHAm is obtained contaminated with *E*-CHAm.

The effect of varying the amine on the optimum conversion of *E*-**1** to *Z*-**1** in acetonitrile solution is shown in Table 1. Conversions of 26%, 30%, and 33% of the starting material *E*-**1Am** to *Z*-**1Am**, as a solid precipitate formed during the irradiation, were observed with *E*-**1b**, *E*-**1c**, and *E*-**1f** prepared with 4-amino-1-butanol (Scheme 1 and Table 1, entry 2), ethanolamine (Scheme 1 and Table 1, entry 3), and piperidine (Scheme 1 and Table 1, entry 6). This conversion increases noticeably (68%) when after filtering the solid in suspension, i.e., *Z*-**1c**, the transparent solution (mother liquor) was again irradiated until the solid phase formation was observed. Thus, the efficiency of one-pot IL *E* to IL *Z* photoconversion, yielding IL *Z* as a pure solid compound, could be optimized by recycling (reirradiating) the mother solution after the solid was filtered off (Table 1, entry 4). To our surprise, no solid phase was formed during the irradiation of the acetonitrile solution of *E*-**1e** (Scheme 1, **e** dielthylamine), *E*-**1g** (Scheme 1, **g** trielthylamine), *E*-**1h** (Scheme 1, **h** tributylamine), and *E*-**1i** (Scheme 1, **i** *N*-methylpiperidine). After irradiation, no solid phase was obtained, although several attempts to induce precipitation were made (i.e., irradiated solution kept at low temperature, partial evaporation of the solvent). As an exception, irradiation of the acetonitrile solution of *E*-**1d** (Scheme 1, **d** 2-phenylethylamine) afforded *Z*-**1d** contaminated with *E*-**1d** as precipitate (Table 1, entry 5).

As is depicted in Table 1, the photoisomerization IL *E*-**1**–IL *Z*-**1** is the major process that occurs in solution. A minor decarboxylation reaction was also observed in some cases with the aryl-ethene compound formed in solution remaining (Table 1, entries 1, 2, 6, and 7). The acetonitrile solution of each IL prepared with *E*-**1** and the above-mentioned bases (**a**–**i**; Scheme 1(b)) were shown to be stable kept in the dark at room temperature.

Furthermore, we have explored the substrate scope of the reaction using different *E*-cinnamic acids (*E*-CH, see details in Scheme 1 and Table 1). Irradiation of *E*-**2** in acetonitrile solution showed the formation of a photostationary state consisting of 53% *E*-**2** and 47% *Z*-**2**. Irradiation of *E*-**2a** in acetonitrile solution results in a photostationary state consisting of 44% *E*-**2a** and 51% *Z*-**2a** (Table 1, entry 8) together with 5% of the corresponding decarboxylated product. Any solid precipitated was obtained, although several attempts to induce it were made. Similar results were obtained by irradiation of *E*-**2Am** with **Am** = **e**–**i** (some results are listed in Table 1, entries 14 and 15). As shown in Table 1, conversion of *E*-**2Am** to solid *Z*-**2Am** in situ, during the irradiation process, was observed with *E*-**2b** and *E*-**2c**, showing the latter with optimum conversion value (Table 1, entries 9–12). As it was previously observed, irradiation of the acetonitrile solution of the *E*-CHAm containing **d** (2-phenylethylamine) in its structure, *E*-**2d** (Scheme 1), afforded *Z*-**2d** contaminated with *E*-**2d** as precipitate (Table 1, entry 13).

From the analysis of the above results, we envisioned that the basic character of the amine used to prepare the IL *E*-CHAm is not the only reason for the low solubility in the irradiated solution of the IL *Z*-CHAm formed and its specific precipitation as a pure solid compound (Scheme 2). The molecular structure of both the cinnamic acid (CH) and the amine (Am) would be the cause of this special behavior.

We hypothesized that the end terminal structure of the amine would approach the aromatic moiety (aryl group) of the cinnamic acid structure in a synclinal overlapping fashion to provide the required distance among functional groups to generate stabilizing intramolecular (intra-IL-molecular) interactions such as hydrogen bridge or hydrophobic–hydrophobic interactions. As is shown in Figures 1 and 2, after the *E* to *Z* photoisomerization, this approach can easily occur in one of the rotamers formed by the *Z*-CHAm (Figure 2, structure on the right; molecular modeling details are included in the Supporting Information). This is the first level of control of *E*-CHAm to *Z*-CHAm in a one-way photocon-

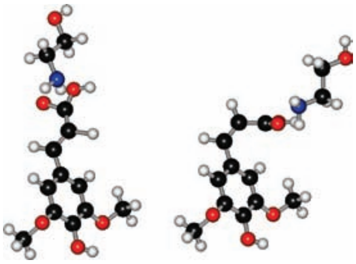

Figure 1. *E*−*Z* photoisomerization of ionic liquid cinamic acids (*E*-CHAm/*Z*-CHAm). As an example, *E*-**2c**/*Z*-**2c**.

version with selective *Z*-CHAm solid formation (precipitation) (Scheme 2). This level of control is imparted through the irradiated substrate itself. A second level of control of the process can be imparted through the medium itself; i.e., the capability of the solvent to compete, as a protic solvent, providing a source of intermolecular hydrogen bridge, would stabilize other rotamer structures of the *Z*-CHAm soluble in polar protic media. Soluble photostationary *E*-CHAm−*Z*-CHAm mixtures were obtained in methanol and in ethanol solution. Besides, *Z*-CHAm obtained as precipitate during irradiation requires acetontrile−methanol mixtures enriched in methanol (higher % of methanol) for complete dissolution. Furthermore, irradiation of this solution yielded the completely soluble photostationary state of a *Z*-CHAm−*E*-CHAm mixture from which any of the components could be isolated as a pure solid compound.

To explore the potential application of these principles to the one-pot preparation−isolation of *Z*-CHAm, we chose two cinnamic acids, *p*-coumaric acid *E*-**3** (Scheme 1(a)) with the hydroxyl group as the only substituent at the C-4 position and cinnamic acid itself, *E*-**4** (Scheme 1(a)), without any substituent in the aromatic ring. The experiments were conducted, and as expected the reactions proceeded for *E*-**3Am** similarly to what was observed for *E*-**1Am** and *E*-**2Am** (Table 1, entries 16−19), with the best results for *E*-**3a** and *E*-**3b**. To our delight, when we irradiated *E*-**4Am**, only pure solid *Z*-**4a** was obtained as precipitated from the irradiated solution in 29% yield (Table 1, entry 20) when butylamine as base was used (hydrophobic−hydrophobic stabilizing interaction). We then investigated the substrate scope of the reaction using *E*-**5**, the methylene-3,4-dioxy derivative of cinnamic acid (Scheme 1(a)). The methylene-3,4-dioxy group fixing the electron-donating groups at the *meta*- and *para*-positions creates in this portion of the cinnamic molecule an electronic environment similar to that of *E*-**1** (see structures in Scheme 1(a)). Thus, the *Z*-**5Am** as a pure solid precipitate was obtained by photoisomerization of *E*-**5a**, *E*-**5b**, and *E*-**5c**. The optimum conversion was obtained with *E*-**5a** (Table 1, entry 24).

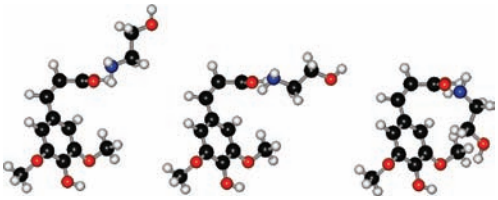

Figure 2. Proposed rotamer structure for *Z*-CHAm: soluble forms (left and middle) and lower soluble form (right). As an example, *Z*-**2c**.

In summary, we have developed the first one-pot preparation−isolation of a pure *Z*-cinnamic acid (*Z*-CH) precursor by simple *E*−*Z* photoisomerization of ionic liquids *E*-CHAm whose anion is the corresponding *E*-cinnamic acid (*E*-CH). The IL is prepared choosing a commercial simple primary amine (Am) with the proper end terminal group (i.e., butylamine, ethanolamine, etc.). This selection depends on the nature of the substituents located in *meta* or *para* positions, or both, in the *E*-CH structure. The selective formation of the solid pure *Z*-IL (*Z*-CHAm) during the irradiation only takes place if irradiation is conducted in MeCN. Both result in a strong outcome suggesting that an intra-IL-molecular interaction affected by the solvent nature is operating. We propose that within the different rotamer structures of *Z*-CHAm only few are stabilized by intramolecular hydrogen bonding. Because of this, closed rotamers show minimum interaction with the medium precipitate as pure *Z*-CHAm. Additional studies exploring this *E*/*Z* photochemical one-pot preparation−isolation of pure ionic liquid *Z* isomers in the field of 3-aryl-acrylic acids are currently underway, and the results will be reported in due course.

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Supporting Information Available: Experimental procedures, spectroscopic data for IL, ^{1}H NMR spectra, and full characterization data for *E*- and *Z*-cinnamic acids. This material is available free of charge via the Internet at http://pubs.acs.org.

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