Protic, Imidazolium Ionic Liquids as Media for (*Z*)- to (*E*)-Alkene Isomerization

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The quantitative isomerization of (*Z*)- to (*E*)-alkene in protic, imidazolium ionic liquids is demonstrated. The isomerization parameters were determined. The mechanism on the addition of the protic imidazolium species to carbon–carbon double bond is presented.

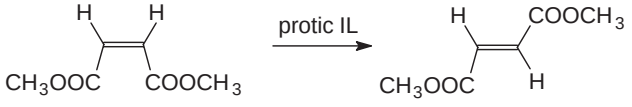
Nucleophilic catalysis of cis–trans isomerization has been observed in the case of dialkyl maleate and fumarate. Dimethyl maleate is readily isomerized to dimethyl fumarate through the catalytic action of primary and secondary amines[1–4] but not by tertiary amines. Aminals also catalyze this isomerization.[5] The amine moiety of aminals adds to dimethyl maleate via azomethine yield intermediates. Isomerization of dimethyl maleate to the corresponding fumarate is usually catalyzed by bromine. This bromine-catalyzed reaction is attributed to the reversible addition of a bromine radical at the site of the double bond.[6] The NBS-bromination condition is sufficient for (*Z*)- to (*E*)-alkene isomerization.[7] Dimethyl maleate on treatment with NBS-AIBN (*N*-bromosuccinimide dibenzoyl peroxide-azobisisobutyronitrile) reagent in reflux in CCl_4 gave dimethyl fumarate in 98% yield. Isomerization of the carbon–carbon double bond took place via an in situ addition–elimination of the bromine radical.

In nature, maleyl acetoacetate cis–trans isomerase (MAAI) catalyses an important stage of the phenylalanine and tyrosine metabolic degradation, being rather an example of "catalytic promiscuity," as it is also capable of performing oxygenation, dehalogenation, peroxidation, and some transferase activity.[8,9]

Ionic liquids (ILs) have recently found increasing applicability as solvents. Their unique properties are determined by the structure of and interaction between the individual ions. ILs have been demonstrated to be good alternative reaction media to organic volatile solvents in various chemical processes, biocatalytical transformations, and various electrochemical disciplines. This has resulted from their physical and chemical properties (good thermal, chemical, and electrochemical stability, large liquids range, negligible vapor pressure, non-flammable character, and good solvation properties for both polar and nonpolar compounds, due to the unique spatial heterogeneity[10]).

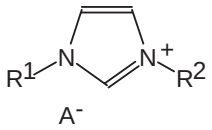
We herein report the isomerization of dimethyl maleate to dimethyl fumarate in imidazolium ILs. (Scheme 1).

Protic and aprotic imidazolium salts which were used as ILs are presented in Table 1. Lactates and salicylate were prepared



Scheme 1. Isomerization of dimethyl maleate to dimethyl fumarate.

Table 1. Protic imidazolium (**1**–**3**) and aprotic imidazolium (**4**) RTILs used



IL	R^1	R^2	A	Density /g mL^{-1}	T_{onset} /°C	Conv /%
1a	CH_3	H	DL-lactate	1.123	245	100
1b	C_4H_9	H	DL-lactate	1.060	265	100
1c	C_6H_{13}	H	DL-lactate	1.037	260	100
1d	$C_{10}H_{21}$	H	DL-lactate	0.991	245	90
1e	$C_6H_{13}OCH_2$	H	DL-lactate	1.025	230	31
2	$C_6H_{13}OCH_2$	H	salicylate	1.096	220	42
3	CH_3	H	BF_4			100
4a[a]	CH_3	C_2H_5	BF_4		412[b]	0
4b[a]	CH_3	C_4H_9	BF_4	1.12[b]	403[b]	0

[a]**4a** and **4b** Merck product, T_{onset}–temp. onset for decomposition, Conv.–conversion at 70 °C for 24 h. [b]Ref. 12.

according to the published method.[11] 1-Methylimidazole was protonated by HBF_4 to form **3**, which was characterized by ^{1}H and ^{13}C NMR spectra and elemental analysis [^{1}H NMR, $CDCl_3$, δ 12.24 (s, 1H, N^+-H), 8.18 (s, 1H, imid.), 7,27 (s, 2H, imid.), 3.79 (s, 3H, N-CH_3); ^{13}C NMR δ 137.2, 123.7, 122.9, and 35.4 (N-CH_3)]. Aprotic imidazolium salts **4** are commercially available (Merck).

Dimethyl maleate dissolved readily in the employed ILs but (*Z*)- to (*E*)-alkene isomerization was found to take place only in protic imidazolium ILs.

Alkyl or alkoxymethyl substituents on the imidazolium ring as well as the type of anion were found to significantly affect the course of the isomerization. The best results were obtained in protic lactates **1a**–**1c** and tetrafluoroborate **3**. Isomerization was found to develop slowly at room temperature. 100% conversion at a temperature of 90 °C was reached after 4 h and 63% conversion after 96 h at room temperature. Molar ratio of the IL to substrate was found to be of importance. At 50 °C and a molar ratio of 1, the conversion of maleate to fumarate stabilized at the level of 90% while at 25 °C it did not reach 85% until the molar ratio of 2 was attained. The extent of the conversion was determined using GC analysis of reactive mixtures, employing the internal standard (cyclohexanone). The conversion curves (Figure 1) demonstrate the degree to which the studied isomerization depended on the temperature and duration of the reaction. The newly formed dimethyl fumarate precipitated from protic imidazolium ILs (**1a**–**1d** and **3**) in the form of crystals (needles of melting point = 102–104 °C), easily separated by filtration. Solubility of dimethyl fumarate in protic imidazolium lactates

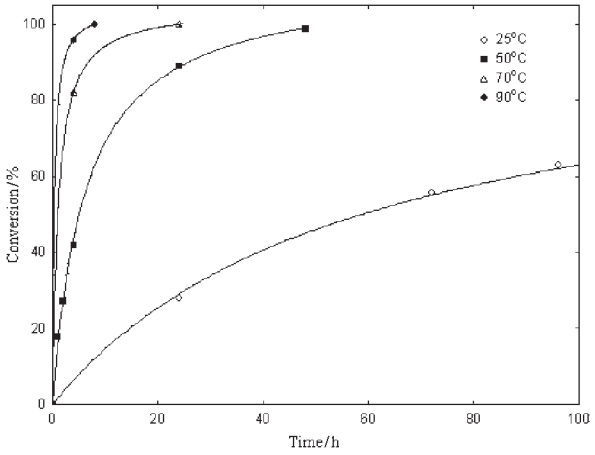


Figure 1. Variation in conversion (%) for 1 mmol dimethyl maleate isomerization in 1 mmol **1c** with respect to time at various reaction temperatures.

depended upon the length of alkyl substituent. For **1a** the lowest solubility was noted. ILs **1a**–**1d** and **3** could be recovered and reused several times with no decrease in the extent of the conversion. The isomerization was conducted in laboratory without necessity to ensure anhydrous conditions.

The formation of a reactive adduct of the 1-methylimidazolium cation with the carbon–carbon double bond of dimethyl maleate is thought to explain the cis–trans isomerization. The presence of the 1-methylimidazolium cation results in the formation of a non-reactive complex (because of cis maleate configuration, stabilized by hydrogen bonding toward two carbonyl oxygen atoms). However, the same cation might protonate a less nucleophilic double bond and could reversibly add its heterocyclic moiety to the alpha carbon atom of maleate. Boron tetrafluoride anion seems to be an exceedingly poor nucleophile to form a stable, covalent product. Instead of the adduct of IL and maleate as an ion pair undergoes rotation around the $C^{2'}$–$C^{3'}$ single bond and then dissociates itself releasing the dimethyl fumarate as the final product.

The mechanistic considerations advanced above require at least spectroscopic proof. In the first experiment dimethyl maleate with the BF_4^- protic IL were maintained at 25 °C and after 48 h extracted with ether and after ether evaporation the EI mass spectrum was recorded. In the ES+ scan, only the relatively intense peak at m/z 227 was displayed. Indeed, the atomic composition of 1-methylimidazolium cation adduct was confirmed by EI high-resolution mass spectrometry (for $C_{10}H_{15}O_4N_2$ calcd. 227.1032, obsd. 227.1020).

When dimethyl maleate was subjected to the reaction in 1-methylimidazolium lactate, the products were quite different and revealed numerous EI-MS peaks with the lack of the signal typical for the above mentioned adduct (m/z 227.1118 and so cannot represent the formula of $C_{10}H_{15}O_4N_2$). Instead of this, we observed the m/z 235, which could be easily interpreted as protonated lactic acid adduct of methyl maleate (for $C_9H_{15}O_7$ calc. 235.0818, obsd. 235.0826).

We have modeled both dimethyl maleate complexes: first as a hydrogen-bonded species and the second as an ion-pair adduct of imidazolium to the carbon–carbon double bond. The assumptions in the modeling process were that the most acidic 3H imidazolium proton forms a hydrogen bond (HB) with the two most basic carbonyl oxygens of maleate and that in the intermediate the 2H proton forms the 6- or 7-membered C–H intra-molecular HB. The last structures are more stable than the first ones of 1.4–1.5 kcal/mol for ion and 3.4–5.1 kcal/mol for ion-pair, depending on conformation and both conformation and/or counter-ion position, respectively (Figure 2). Thus, the EI-MS spectra, following the DFT calculations provide a molecular basis to easily explain (*Z*)- to (*E*)-isomerization in protic imidazolium ILs.

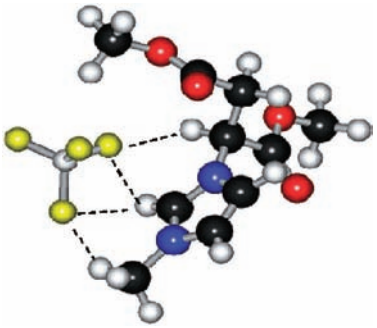


Figure 2. The DFT (B3LYP/6-31+G** level) structure of the most stable imidazole isomerization intermediate. The regard of counter-ion BF_4^- leads to intramolecular HB (see text) reorganization: Hydrogen atom contacts of C–H bonds of both imidazole ($^1CH_3$ and ^2H) and fumarate ($^{2'}H$) with fluorine are seen as dashed lines.

We have established the feasibility of a quantitative cis–trans isomerization of dimethyl maleate to fumarate. The suggested mechanism relies on the addition of the protic imidazolium species to carbon–carbon double bond, followed by rotation and final imidazolium elimination. Our protocol utilizes easily prepared ILs and compares well with the best methodologies currently available. The attained success relies on the use of (i.e. not purified or dried) RTILs employing a mild heating and simple water dilution in neutral and non-toxic reaction conditions.

References

1 G. R. Clemo, S. B. Graham, *J. Chem. Soc.* **1930**, 213.
2 K. Nozaki, *J. Am. Chem. Soc.* **1941**, *63*, 2681.
3 M. Davies, F. P. Evans, *Trans. Faraday Soc.* **1955**, *51*, 1506.
4 Z. Rappoport, C. Degani, S. Patai, *J. Chem. Soc.* **1963**, 4513.
5 A. G. Cook, A. B. Voges, A. E. Kammrath, *Tetrahedron Lett.* **2001**, *42*, 7349.
6 M. Kodomari, T. Sakamoto, S. Yoshitomi, *Bull. Chem. Soc. Jpn.* **1989**, *62*, 4053.
7 M. M. Baag, A. Kar, N. P. Argade, *Tetrahedron* **2003**, *59*, 6489.
8 K. Anandarajah, P. M. Kiefer, Jr., B. S. Donohoe, S. D. Copley, *Biochemistry* **2000**, *39*, 5303.
9 S. D. Copley, *Curr. Opin. Chem. Biol.* **2003**, *7*, 265.
10 Y. Wang, G. A. Voth, *J. Am. Chem. Soc.* **2005**, *127*, 12192.
11 J. Pernak, I. Goc, *Pol. J. Chem.* **2003**, *77*, 975.
12 J. G. Huddleston, A. E. Visser, W. M. Reichert, H. D. Willauer, G. A. Broker, R. D. Rogers, *Green Chem.* **2001**, *3*, 156.

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