The Effect of Hydrogen Bonding on Allylic Alkylation and Isomerization Reactions in Ionic Liquids

James Ross and Jianliang Xiao*[a]

Abstract: Neutral allylic alkylation reactions, in which a base is generated in situ and which hence require no external bases, can significantly be retarded when carried out in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]). Evidence suggests that the base or base precursor enters into hydrogen bonding with the imidazolium cation and is thus made less readily available for deprotonation of pre-nucleophiles. However, the reaction proceeds well in the presence of stronger bases that are capable of deprotonation. Whilst the phenomenon of hydrogen bonding in ionic liquids can be detrimental to reactions such as allylic alkylation, it can be exploited to suppress unwanted allylic isomerization.

Keywords: allylation · homogeneous catalysis · hydrogen bonds · ionic liquids · palladium

Introduction

Hydrogen bonding embraces many important areas of chemistry and biochemistry.[1] The effect of hydrogen bonding on reaction chemistry in common molecular solvents is well documented and understood.[1, 2] Hydrogen bonding in solvents based on room-temperature ionic liquids is a relatively new subject. In fact, the perception of hydrogen bonding in imidazolium ionic liquids, the most extensively investigated ionic liquids to date, was still controversial in the mid 1980s.[3] Thanks to the pioneering studies of several research groups,[3] it is now well established that imidazolium cations and their associated anions form hydrogen bonds both in the solid state and in solution.[4] The H^2, H^4 and H^5 ring protons of the 1,3-dialkylimidazolium cation can act as hydrogen bond donors and interact with counteranions such as Cl^-, OTf^-, and BF_4^-, which act as hydrogen-bond acceptors and can also enter into hydrogen bonding with external hydrogen donors such as H_2O. Of the three imidazolium ring protons, the H^2 proton appears to form the strongest hydrogen bond. This feature has been exploited for the assembly of a new class of anion receptors based on imidazolium cations,[5] and has been invoked to explain the selective transport/separation of amines by membrane-supported imidazolium ionic liquids.[6]

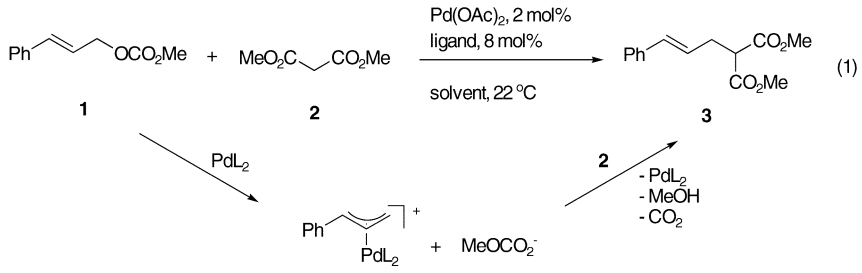
Whilst the concept of hydrogen bonding in ionic liquids has generally been accepted and explosive growth in research on reaction chemistry in these solvents has been witnessed in the past few years, little attention has been paid to the potential effects of hydrogen bonding on catalyzed reactions in ionic liquids.[7] Only recently have Diels–Alder and nucleophilic substitution reactions with no added catalysts been investigated in this context in imidazolium ionic liquids.[8] Following on from our earlier studies into Pd-catalyzed reactions in ionic liquids,[9] we have found that the capability of imidazolium ionic liquids for hydrogen bonding can exert a remarkable effect on neutral allylic alkylation reactions and, interestingly, the effect can be harnessed to suppress Pd^0-catalyzed allylic isomerization,[10] a reaction that may diminish the stereoselectivity of asymmetric allylic substitution.[11] The details of our results are herein described.

[a] Dr. J. Xiao, J. Ross
Leverhulme Centre for Innovative Catalysis
Department of Chemistry, University of Liverpool
Liverpool L69 7ZD (UK)
Fax: (+44) 151 794-3589
E-mail: j.xiao@liv.ac.uk

Results and Discussion

Our previous investigation shows that Pd^0-catalyzed allylic alkylation or Tsuji–Trost reactions with a variety of active methylene compounds can be readily carried out in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate ([bmim][BF_4]) under basic conditions.[9a,d] Similar results have been reported from other laboratories.[12] In an effort to determine the scope of reaction, the room-temperature allylic alkylation of phenylallyl carbonate **1** with dimethyl malonate **2** catalyzed by Pd^0–PAr_3 was investigated in [bmim][BF_4] [Eq. (1)]. The catalytically active Pd^0 species is expected to be generated in situ from the starting $Pd(OAc)_2$ upon reduction with PAr_3.[13] This is a neutral Tsuji–Trost reaction; it requires no external base, as decarboxylation of $MeOCO_2^-$, which results from the oxidative addition of **1** to Pd^0, generates CO_2 and a strong base MeO^-.[10, 11] Although methanol has a higher

DOI: 10.1002/chem.200304895

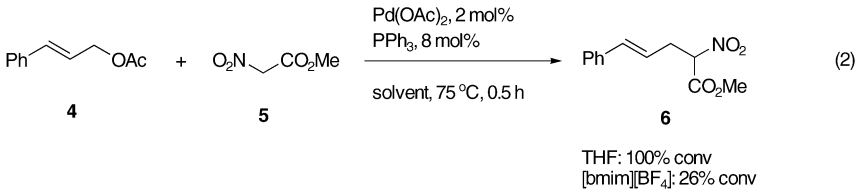


pK_a than a dialkylimidazolium ion (29 versus ca. 24 in DMSO),[14] the methoxide is expected to preferentially deprotonate the malonate, which is about eight orders of magnitude more acidic than the imidazolium cation.[15] Furthermore, even if deprotonation of the solvent cations took place, the so generated dialkylimidazol-2-ylidene would readily deprotonate the malonate to give the required nucleophile to attack the Pd–allyl intermediate and complete the catalytic cycle,[14b,c] unless it forms inactive palladium complexes (vide infra).

After first confirming the reaction to be rapid in THF, reaching complete conversion within 20 min,[16] we carried out the same reaction in [bmim][BF_4] under otherwise identical conditions (Table 1, entries 1–5). Surprisingly, the reaction in [bmim][BF_4] was considerably slower, affording less than 1% conversion after 1 h and complete conversion in a prolonged time of about 30 h. PPh_3 was found to be the best ligand out of several phosphines tested in the ionic liquid. For example, changing the ligand to the more ionic liquid-soluble and more electron-rich $P(4-MeOC_6H_5)_3$ under the same conditions gave a negligible conversion after 1 h and only 9% conversion after 5 h (Table 1, entries 6 and 7). For comparison, the same ligand in THF brought about a nearly complete reaction in 25 min (Table 1, entry 8). Even more strikingly, the reaction in THF was significantly inhibited by the addition of a small quantity of [bmim][BF_4] and the rate was progressively decreased by introducing more [bmim][BF_4] (Table 1, entries 9–11), indicating that some key intermediate in the catalytic cycle is involved in a pre-equilibrium with the imidazolium additive.

It was possible to accelerate the reaction by external bases. This is clearly seen from the results obtained in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or OAc^- (Table 1, entries 12 and 13). However, the role of the two bases must be different (vide infra); unlike the more basic DBU, the acetate cannot deprotonate **2**.[15, 17] A very revealing experiment is the comparison of the reaction performed in [bmim][BF_4] with that in 1-butyl-2,3-dimethylimidazolium tetrafluoroborate ([bdmim][BF_4]), in which the H^2 ring proton is replaced with a methyl group (Table 1, entries 14 and 15). The reaction in the latter was considerably faster, suggesting that the retarding effect of [bmim][BF_4] relates to its H^2 proton.

The allylic alkylation of phenylallyl acetate **4** with methyl nitroacetate **5** was similarly retarded when conducted in the ionic liquid [Eq. (2)]. This is again a neutral reaction requiring no external bases, because the OAc^- ion generated in the oxidative addition of **4** to Pd^0 is basic enough to deprotonate **5**



(pK_a 8.0 in DMSO),[18] which is much more acidic than **2**. Indeed, the reaction in THF was complete within 0.5 h when catalyzed by Pd^0–PPh_3 at 75 °C. Repeating this reaction in [bmim][BF_4], only 26% conversion was reached after 0.5 h and complete conversion after an extended reaction time of 24 h.

According to the generally accepted mechanism for allylic substitution, the oxidative addition of **1** or **4** to Pd^0–PPh_3 leads to two ionic species, $MeOCO_2^-$ or OAc^- and a Pd-allyl cation [Eq. (1)], and as such should not be slowed down on going from THF to an ionic medium. Therefore it is probably the nucleophilic attack step that is affected in the ionic liquid. Amatore, Jutand, and co-workers have recently shown that the oxidative addition of allylic acetate to Pd^0 is reversible, and in the less polar THF, the resulting acetate anion and Pd–allyl cation form tight ion pairs rather than free ions as in DMF.[19] The formation of such ion pairs could diminish the positive charge on Pd^{II} and enhance the steric hindrance around the metal atom, thus leading to a slower nucleophilic attack. In the polar [bmim][BF_4],[20] the formation of tight ion

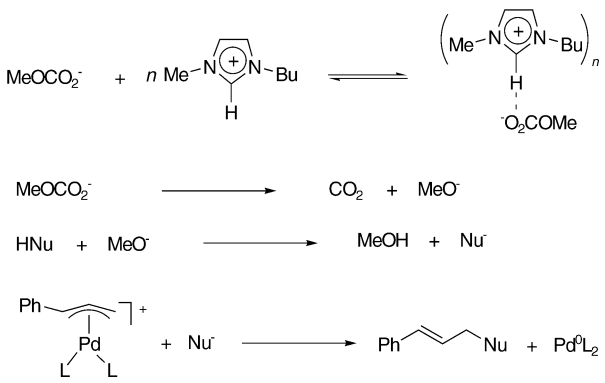
Table 1. Effect of solvents on the neutral Tsuji–Trost reaction between **1** and **2**.[a]

Entry	Solvent	Additive (mol%)[b]	Ligand	Time [h]	Conv[c] [%]
1	THF	-	PPh_3	0.33	100
2	[bmim][BF_4]	-	PPh_3	1	< 1
3	[bmim][BF_4]	-	PPh_3	5	38
4	[bmim][BF_4]	-	PPh_3	16	75
5	[bmim][BF_4]	-	PPh_3	30	100[d]
6	[bmim][BF_4]	-	$P(4-MeOC_6H_5)_3$	1	< 1
7	[bmim][BF_4]	-	$P(4-MeOC_6H_5)_3$	5	9
8	THF	-	$P(4-MeOC_6H_5)_3$	0.42	99
9	THF	[bmim][BF_4] (4)	$P(4-MeOC_6H_5)_3$	0.90	63
10	THF	[bmim][BF_4] (10)	$P(4-MeOC_6H_5)_3$	0.90	46
11	THF	[bmim][BF_4] (20)	$P(4-MeOC_6H_5)_3$	0.90	33
12	[bmim][BF_4]	DBU (200)	PPh_3	0.33	100
13	[bmim][BF_4]	[nBu$_4$N][OAc] (100)	$P(4-MeOC_6H_5)_3$	0.83	71
14[e]	[bdmim][BF_4]	-	$P(4-MeOC_6H_5)_3$	0.50	89
15[e]	[bmim][BF_4]	-	$P(4-MeOC_6H_5)_3$	5	48

[a] All reactions were performed on a 1 mmol scale, 2 mol% $Pd(OAc)_2$, and 8 mol% phosphine in [bmim][BF_4] (2 mL) or THF (2 mL) at room temperature unless otherwise indicated. [b] Relative to palladium catalyst. [c] Determined by ^1H NMR spectroscopy of the crude reaction mixture. [d] Isolated yield for **3**: 90%. [e] At 50 °C.

pairs between Pd–allyl and acetate ions is less likely, as the acetate would interact more favorably with the much more abundant, less bulky solvent cations. Therefore, the sluggish reaction in the ionic liquid could be due to the availability of nucleophiles rather than a high barrier in the nucleophilic attack step. This is of course consistent with the reaction being fast when an external base is added, which could make the deprotonated **2** more readily available (Table 1, entry 12).

In a very recent, detailed study, Welton and co-workers reported that the nucleophilicity of halides in a noncatalyzed S_N2 reaction in [bmim][Tf_2N] [Tf_2N = bis(trifluoromethylsulfonyl)amide] follows the order $Cl^- < Br^- < I^-$.[4h] This is explained by the chloride forming the strongest hydrogen bond to the imidazolium cations, in particular the H^2 ring protons, and so being made least available to undergo nucleophilic attack. The observed inhibition of the neutral Tsuji–Trost reaction by [bmim][BF_4] could be accounted for in a similar manner by assuming that the $MeOCO_2^-$ or OAc^- ions generated in the oxidative addition are strongly solvated or "trapped" by hydrogen bonding with the imidazolium cations and are thus made unavailable to deprotonate the hydrocarbon acids **2** or **5** to give the required nucleophile for subsequent nucleophilic attack (Scheme 1). OAc^- is known to



Scheme 1. Proposed role of [bmim][BF_4] as hydrogen-bond donor in preventing efficient deprotonation of HNu, thus inhibiting nucleophilic attack by Nu^-.

form a strong hydrogen bond to the H^2 proton of imidazolium ring in both solution and solid states.[21] To confirm this, a ^1H NMR titration experiment was carried out, in which the concentration of [nBu$_4$N][OAc] was kept constant while that of [bmim][BF_4] was varied in $CDCl_3$. The titration revealed that the H^2 proton chemical shift moved to lower field in a sigmoid fashion with increasing acetate/bmim molar ratios until a value of about 2, thereafter the H^2 chemical shift was little affected (Figure 1).[22] Only insignificant changes were observed for the H^4 and H^5 ring protons. These observations suggest that the H^2 proton hydrogen bonds to OAc^- and a 1:2 stoichiometric complex could be formed between the imidazolium and OAc^- ions in $CDCl_3$.[23] NMR spectroscopy has been most frequently used in probing hydrogen bonding involving imidazolium ionic liquids,[3–5, 21b] and in the case of the imidazolium receptors mentioned earlier, similar observations have been made.[5] However, the nature of hydrogen bonding complex in [bmim][BF_4] shown in Scheme 1 is less

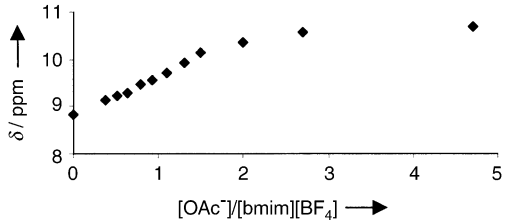


Figure 1. ^1H NMR titration profile for addition of [bmim][BF_4] (26–323 mM) to [nBu$_4$N][OAc] (123 mM) in $CDCl_3$ at 21 °C, the first point on the chemical shift axis corresponding to 680 mM in [bmim][BF_4].

clear, although it has bee suggested that chloride is surrounded by six imidazolium cations in related ionic liquids.[4h]

Titrating [bmim][BF_4] with [$MeOCO_2$][HDBU][21c] in $CDCl_3$ gave similar results (Figure 2). Although the change in H^2 chemical shift is less significant, indicating a weaker interaction, it is clear that methyl carbonate forms hydrogen

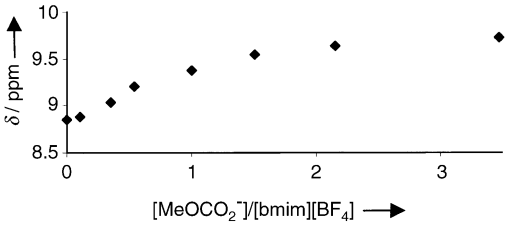


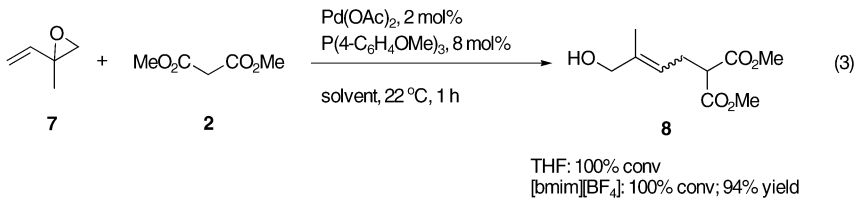
Figure 2. ^1H NMR titration profile for addition of [$MeOCO_2$][HDBU] (0–112 mM) to [bmim][BF_4] (32.2 mM) in $CDCl_3$ at 21 °C.

bonds to the imidazolium cations. Hence, one can reasonably assume that it is this hydrogen bonding that prevents the carbonate ions from decomposing readily to form the base necessary for deprotonation of **2**. A recent study by Amatore, Jutand, and co-workers shows that the oxidative addition of allylic carbonates to Pd^0 is reversible and the resulting carbonate anion does not decarboxylate as fast as previously thought.[11] Hydrogen bonding should certainly enhance its stability. Indeed, it is known that decarboxylation can dramatically be decelerated by using dipolar protic solvents.[24] In line with the hydrogen bonding assertion, the imidazolium H^2 ring proton moved immediately from $\delta =$ 8.6 ppm to $\delta = 10.4$ ppm in the ^1H NMR spectrum upon the addition of Pd^0–PPh_3 to a NMR tube containing a 1/1 mixture of **1** and [bmim][BF_4] in $CDCl_3$ [$Pd(OAc)_2$, 10 mg; ratio of Pd/PPh_3/**1** = 1/4/1]. As aforementioned, methyl carbonate would be generated from the oxidative addition of **1** to Pd^0 under these conditions. The major contribution to the downfield shift comes probably from the acetate of $Pd(OAc)_2$, however. This experiment also indicates that the neutral allylic alkylation in [bmim][BF_4] is not limited by the oxidative addition step and supports the proposition that it is the nucleophilic attack that is affected by the ionic liquids.

The notion that $MeOCO_2^-$ could not function efficiently as a base precursor due to hydrogen bonding explains the effects of the added [bmim][BF_4] on the reaction of **1** with **2** in THF. The more imidazolium cations added, the easier the formation of the hydrogen bonding complex, and hence the lower the concentration of base. Consequently, the concentration of

nucleophile will be lowered, thus leading to slower nucleophilic addition (Scheme 1).

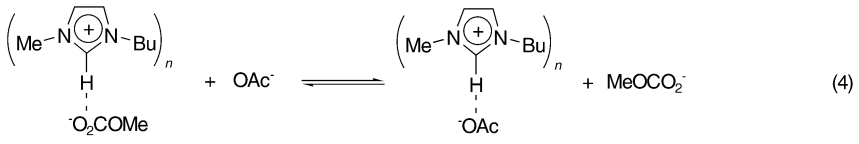
It is also clear why DBU as an external base could bring about an efficient reaction. DBU is a stronger base[17] than OAc^- and $MeOCO_2^-$ (pK_a 5.6 in water).[25] It does not form stable hydrogen bonds with the acidic H^2 proton of imidazolium in the presence of the much more acidic **2**; rather, as expected, it deprotonates **2**.[26] This is further supported by a reaction involving an alkoxide base. Alkoxides are even stronger bases; as such they are not expected to form a stable hydrogen bond with [bmim][BF_4] in the presence of **2**. This is clearly seen in the allylic alkylation of 2-methyl-2-vinyloxirane **7** with **2**, which generates in situ an alkoxide base by oxidative addition to Pd^0 and proceeds fast to give **8** as a mixture of *E*,*Z*-isomers ($E/Z = 3/2$) in room temperature [bmim][BF_4] or THF, reaching completion within 1 h in either solvent under otherwise identical conditions [Eq. (3)].[27]



(3)

These results also show that, unlike Welton's nucleophilic substitution,[4h] it is the basicity of oxy anions, rather than the uncleophilicity of hydrocarbon anions, that is primarily affected by hydrogen bonding in the reactions involving **1** or **4** in [bmim][BF_4]. The underlining mechanism for the observed effects in the two different types of reactions is the same, however, that is the nucleophiles or bases are made less available for subsequent reactions due to hydrogen bonding with the ionic liquid cations.

Acetate plays a different role. As indicated above, it cannot deprotonate the acid **2** due to its low basicity. The accelerating effect of acetate on the reaction of **1** and **2** most probably results from the equilibrium shown in Equation (4), which

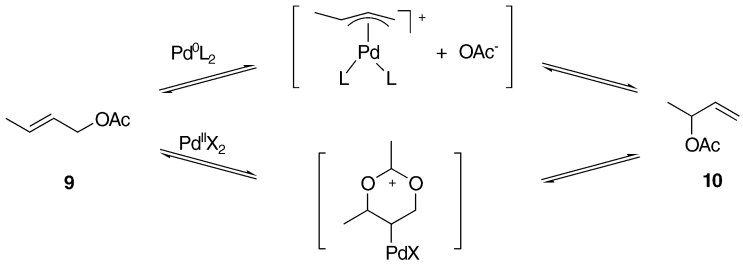


(4)

increases the concentration of free carbonate and hence the probability of its decomposition into the base MeO^-. This is reminiscent of some S_N2 reactions carried out in protic solvents, which can be accelerated upon introducing a basic additive. The base competes with nucleophiles for hydrogen bonding with the solvent and thus frees the former from strong solvation by the latter.[2]

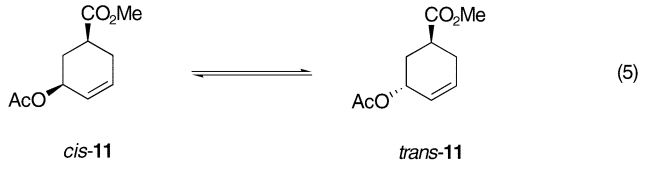
There exists a possibility that the sluggish reaction between **1** and **2** in [bmim][BF_4] could stem from the formation of some inactive dialkylimidazol-2-ylidene complexes of palladium by deprotonation of the imidazolium cation by MeO^-.[9b, 28] This appears to be unlikely. First, the reaction of **7** and **2**, which involves an in situ generated alkoxide, proceeds equally well in THF and the ionic liquid, suggesting that either *N*-heterocyclic carbenes are not formed or they have no effect on the palladium catalysis if formed. Second, the fact that **1** reacts with **2** much faster in the presence of DBU is inconsistent with this hypothesis, because DBU would not be expected to inhibit the formation of carbenes through deprotonation by MeO^-. Third, the effect of [bmim][BF_4] on the allylic alkylation in THF also casts doubts on this possibility (Table 1), since the activity of the hypothesized Pd–carbene species would not be affected by additional imidazolium cations. Indeed, no Pd-carbene complexes were ever detected by NMR spectroscopy in the stoichiometric reaction of Pd^0–PPh_3 with **1** in the presence of [bmim][BF_4] at room temperature. However, when the catalyst preparation was performed with DBU present at 80 °C rather than being introduced upon cooling the Pd^0-PPh_3-ionic liquid mixture to room temperature,[9a,d] the resulting mixture became colorless as opposed to the more usual pale yellow. This catalyst mixture did not promote the reaction between **1** and **2** and it is probable that the acidic H^2 proton in [bmim][BF_4] is being deprotonated at elevated temperature, leading to inactive Pd–carbene formation.

Applying the hydrogen bonding proposition, it was possible to suppress the Pd^0-catalyzed isomerization of allylic acetates, a reaction that can lead to the loss of regio- and stereochemistry in stereospecific allylic substitution.[11] The isomerization is thought to be due to the key oxidative addition step being reversible, and unequivocal evidence for this has recently been laid out.[11] As OAc^- can be trapped by hydrogen bonding with [bmim][BF_4], allylic isomerization resulting from reversible attack by the acetate would be expected to be retarded when the isomerization is carried out in an imidazolium ionic liquid. This is indeed the case. Treating **9** with 5 mol% Pd^0–PPh_3 in CH_2Cl_2 afforded 35% of product **10** after 1 h, comparable with the equilibrium value reported in the literature (Scheme 2).[29] However, the same reaction appears to be completely suppressed in [bmim][BF_4]. Thus, **10** was not detected in the crude reaction mixture even after 20 h. The isomerization of **9** in CH_2Cl_2 was even inhibited by a substoichiometric quantity of [bmim][BF_4]. Thus, in the presence of only 0.15 equivalents of [bmim][BF_4] relative to **9**, only 12% of **10** was formed after 3 h. These observations are again consistent with the acetate ion being involved in equilibrium with imidazolium cations.



Scheme 2. Isomerization of **9** and **10** by mechanistically distinct Pd^0/Pd^{II} catalysis.

Similar inhibition of isomerization was observed starting from **10**. Thus, while 58% of **9** was formed after 1 h in CH_2Cl_2, **10** remained intact in [bmim][BF_4] even after 20 h. This is not surprising, as the equilibrium constant K is close to 1 and so the rate constant $k_- \approx k_+$. Similar observations have been made with other allylic acetates in our laboratory. For instance, the isomerization of **11**, whilst not observed at room temperature, proceeded smoothly at 50 °C in molecular solvents [Eq. (5)]. Thus, exposing **11** to 5 mol% Pd^0-PPh_3



in CH_2Cl_2 lowered its initial cis/trans ratio from 87/13 to 43/57 after 1 h. An equilibrium value of 34/66 was measured after an extended reaction time of 22 h. The same reaction was suppressed in [bmim][BF_4], though not entirely, probably due to weakening of the hydrogen bonding interactions at elevated temperature. Thus, the initial cis/trans ratio of **11** was lowered from 87/13 to only 76/24 after 1 h and to a value of 54/46 that is still far from equilibrium after 22 h.

Remarkably, the isomerization can be brought about when a Pd^{II} catalyst is employed. Thus, treatment of **9** with [$PdCl_2(MeCN)_2$] in [bmim][BF_4] afforded **10** in 20% yield in 1 h reaction time; the same reaction in CH_2Cl_2 gave **10** in 33% yield (Scheme 2). As is known in the literature, this reaction proceeds intramolecularly via a cyclic intermediate and involves no ionized acetate ions;[30] therefore it should not be suppressed by hydrogen bonding. Differences between CH_2Cl_2 and [bmim][BF_4] in other solvent properties possibly account for the different extent of isomerization in these solvents. These results show that if the isomerization of an allylic acetate is to be carried out in imidazolium ionic liquids, Pd^{II}, rather than Pd^0, should be the catalyst of choice.

Conclusion

In summary, neutral allylic alkylation reactions can be considerably retarded in dialkylimidazolium ionic liquids and our results suggest that this is due to hydrogen bonding between the H^2 proton of [bmim][BF_4] and OAc^- or $MeOCO_2^-$ ions. Being strongly solvated by the ionic liquid via hydrogen bonding, the anions could not function as effective bases to deprotonate a HNu nucleophile, thus rendering slow the nucleophlic attack at the Pd^{II}–allyl intermediate. However, this retarding effect can be alleviated when a relatively strong base, either generated in situ or added externally, is used, which favors deprotonation rather than hydrogen bonding with the solvent. We further showed that the phenomena of hydrogen bonding in the imidazolium ionic liquids could be exploited to suppress unwanted, Pd^0-catalyzed isomerization of allylic acetates. Taken together, these results highlight the potential effects of imidazolium cations as hydrogen bond donors on catalytic reactions in imidazolium ionic liquids and corroborate that "The more a solvent blocks up by hydrogen bond or otherwise the active centers which take part in a chemical reaction, the less will be the speed in it".[31]

Experimental Section

General: All reactions were carried out in oven-dried glassware under argon, using standard Schlenk and vacuum line techniques. [bmim][BF_4] and [bdmim][BF_4] were prepared according to published procedures and vacuum-dried and stored under argon.[32] THF and CH_2Cl_2 were freshly distilled from sodium benzophenone and calcium hydride, respectively, under nitrogen immediately prior to use. Phenylallyl carbonate **1** was synthesized according to a literature method.[33] The synthesis of compound **10** was adapted from a literature method.[34] [$MeOCO_2$][HDBU] was prepared according to a recent procedure.[21c] Compounds **2**, **4**, **5**, **7** and **9**, [nBu_4N][OAc], $Pd(OAc)_2$, and PPh_3 were purchased from commercial suppliers and used as received without further purification.

Typical neutral Tsuji–Trost reaction in [bmim][BF_4] as exemplified for the allylic alkylation between 1 and 2: $Pd(OAc)_2$ (4.5 mg, 2 mol%) and PPh_3 (21.0 mg, 8 mol%) were stirred in [bmim][BF_4] (2 mL) at 80 °C for 20 min under an atmosphere of argon and then allowed to cool to room temperature. Compounds **1** (192.2 mg, 1.0 mmol) and **2** (198.2 mg, 1.5 mmol) were added and the mixture stirred vigorously under argon for 30 h. The reaction was not complete within a reaction time of 20 h, as judged by ^1H NMR monitoring. Upon completion, the reaction was quenched with distilled water and the product extracted with EtOAc. The organic layer was washed with water and brine and dried over $MgSO_4$ to give **3**, which was isolated in 90% yield upon purification by flash column chromatography (silica gel, eluent: *n*-hexane/EtOAc = 10/1). The same reaction was repeated in THF following a reported literature procedure.[16] Starting with the same quantity of catalyst and reactants in 2 mL of THF, the reaction was complete in 20 min. ^1H NMR spectroscopy was used to confirm the identity of the product by comparison with the literature.

The reaction of **4** and **5** in [bmim][BF_4] on the same scale as above was performed at 75 °C for an extended reaction time of 24 h to give a complete conversion to **6**. The reaction between **7** and **2** in [bmim][BF_4] was complete within 1 h reaction time furnishing **8**, which was isolated in 94% yield following purification by flash column chromatography (silica gel, eluent: *n*-hexane/EtOAc = 4/1). ^1H NMR was used to confirm the identity of the products by comparison with the literature, but in the case of **8**, more data are supplied, which do not appear to have been reported.

(*E*)-5-Phenyl-2-methoxycarbonyl-4-enoic acid methyl ester 3:[35] ^1H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 2.79$ (dd, $J = 7.6$, 7.2 Hz, 2H; CH_2), 3.54 (d, $J = 7.6$ Hz, 1H; CH), 3.71 (s, 6H; CH_3), 6.12 (dt, $J = 15.8$, 7.2 Hz, 1H; CH=C*H*CH_2), 6.46 (d, $J = 15.8$ Hz, 1H; C*H*=CHCH_2), 7.31 ppm (m, 5H; C_6H_5).

(*E*)-5-Phenyl-2-nitropent-4-enoic acid methyl ester 6:[18] ^1H NMR (250 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 3.12$ (m, 2H; CH_2), 3.85 (s, 3H; CH_3), 5.22 (dd, $J = 8.9$, 5.8, Hz, 1H; CH), 6.08 (dt, $J = 15.8$, 7.2 Hz, 1H; CH=C*H*CH_2), 6.56 ppm (d, $J = 15.8$ Hz, 1H; C*H*=CHCH_2).

(*E*)/(*Z*′)-2-(4-hydroxy-3-methyl-but-2-enyl)-malonic acid dimethyl ester 8: ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.67$ (br s, 3H; CH_3), 1.79 (br s, 3H; CH_3'), 2.65 (br m, 4H; CH_2CCH_3, CH_2CCH_3'), 3.42 (m, 2H; CH′, CH), 3.74 (s, 12H; OCH_3, OCH_3'), 3.96 (br s, 2H; CH_2), 4.10 (br s, 2H; CH_2'), 5.19 (br t, $J = 7.7$ Hz, 1H; C=CH′), 5.35 ppm (br t, $J = 7.2$ Hz, 1H; C=CH); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 13.9$, 21.8, 27.4, 27.4, 51.9, 52.0, 52.8, 52.9, 61.5, 68.3, 120.4, 122.9, 138.7, 138.8, 169.8, 169.9 ppm; MS (I.C./NH_3): *m*/*z* (%): 234 $[M + NH_4]^+$ (80); elemental analysis calcd (%) for $C_{10}H_{16}O_5$: C 55.55, H 7.47; found: C 55.55, H 7.54. The *E*/*Z* ratio for **8** was 3/2 for the reaction in [bmim][BF_4] and in THF based on ^{1}H NMR integration.

Typical Pd^0-catalyzed isomerization reaction in [bmim][BF_4] as exemplified for 9: [Pd(dba)$_2$] (28.7 mg, 5 mol%) and PPh_3 (26.2 mg, 10 mol%) were stirred in [bmim][BF_4] (2 mL) at 80 °C for 20 min and then allowed to cool to room temperature. **9** (114.2 mg, 1.0 mmol) was added and the mixture stirred vigorously under an atmosphere of dry argon. ^{1}H NMR monitoring showed no formation of **10** after 20 h. The reaction was then quenched with distilled water and the product extracted with Et_2O. The organic layer was washed with water and brine and dried over $MgSO_4$ to give **9** quantitatively. The same reaction in THF followed a reported procedure,[29] with the ratio of **9** and **10** determined by ^{1}H NMR spectroscopy.

(*E*)-1-Acetoxy-but-2-ene (9):[36] ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.73$ (dd, $J = 6.1$, 1.1 Hz, 3H; CH_3), 2.05 (s, 3H; CH_3CO_2), 4.50 (d, $J = 6.6$ Hz, 2H; CH_2), 5.59 (td, $J = 15.4$, 6.6, 1.1 Hz, 1H; C*H*CH_2), 5.80 ppm (br dq, $J = 15.4$, 6.1 Hz, 1H; CH_3C*H*).

3-Acetoxy-but-1-ene (10):[36] ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C, TMS): $\delta = 1.31$ (d, $J = 6.6$ Hz, 3H; CH_3), 2.06 (s, 3H; CH_3CO_2), 5.15 (dd, $J = 10.4$, 1.1 Hz, 1H; CH=C*H*$_2$), 5.25 (dd, $J = 17.3$, 1.1 Hz, 1H; CH=C*H*$_2$), 5.35 (br quintet, $J = 6.6$ Hz, 1H; CH_3C*H*), 5.85 ppm (ddd, C*H*=CH_2).

Acknowledgement

We thank the EPSRC for a studentship (J.R.) and the industrial partners of the Leverhulme Centre for Innovative Catalysis for support. We are also grateful to Professor Don Bethell and Dr. Richard Bonar-Law for helpful discussions. Johnson Matthey is gratefully acknowledged for the loan of palladium.

[1] a) G. A. Jeffrey, *An Introduction to Hydrogen Bonding*, Oxford University Press, New York, **1997**; b) S. Schreiner, *Hydrogen Bonding*, Oxford University Press, New York, **1997**. For some recent publications concerning hydrogen bonding and catalysis, see: c) S. P. de Visser, F. Ogliaro, P. K. Sharma, S. Shaik, *Angew. Chem.* **2002**, *114*, 2027–2031; *Angew. Chem. Int. Ed.* **2002**, *41*, 1947–1951; d) Y. Huang, V. H. Rawal, *J. Am. Chem. Soc.* **2002**, *124*, 9662–9663; e) R. D. Bach, *J. Phys. Chem. B* **2002**, *106*, 4325–4335; f) C. E. Cannizzaro, K. N. Houk, *J. Am. Chem. Soc.* **2002**, *124*, 7163–7169.

[2] C. Reichardt, *Solvents and Solvents Effects in Organic Chemistry*, 2 ed., VCH, Weinheim, **1990**.

[3] a) A. A. Fannin, L. A. King, J. A. Levisky, J. S. Wilkes, *J. Phys. Chem.* **1984**, *88*, 2609–2614; b) S. Tait, R. A. Osteryoung, *Inorg. Chem.* **1984**, *23*, 4352–4360; c) A. K. Abdul-Sada, A. M. Greenway, P. B. Hitchcock, T. J. Mohammed, K. R. Seddon, J. A. Zora, *J. Chem. Soc. Chem. Commun.* **1986**, 1753–1754; d) K. M. Dieter, C. J. Dymek, Jr., N. E. Heimer, J. W. Rovang, J. S. Wilkes, *J. Am. Chem. Soc.* **1988**, *110*, 2722–2726; e) A. G. Avent, P. A. Chaloner, M. P. Day, K. R. Seddon, T. Welton, *J. Chem. Soc. Dalton Trans.* **1994**, 3405–3413, and references therein.

[4] For recent examples, see: a) L. Cammarata, S. G. Kazarian, P. A. Salter, T. Welton, *Phys. Chem. Chem. Phys.* **2001**, *3*, 5192–5200; b) L. M. J. Muldoon, C. M. Gordon, I. R. Dunkin, *J. Chem. Soc. Perkin Trans. 2*, **2001**, 433–435; c) A. Elaiwi, P. B. Hitchcock, J.-F. Huang, P.-Y. Chen, I.-W. Sun, S. P. Wang, *Inorg. Chim. Acta* **2001**, *320*, 7–11; d) A. D. Headley, N. M. Jackson, *J. Phys. Org. Chem.* **2002**, *15*, 52–55; e) A. E. Bradley, C. Hardacre, J. D. Holbrey, S. Johnston, S. E. J. McMath, M. Nieuwenhuyzen, *Chem. Mater.* **2002**, *14*, 629–635; f) C. G. Hanke, N. A. Atamas, R. M. Lynden-Bell, *Green Chem.* **2002**, *4*, 107–111; g) S. N. Baker, G. A. Baker, F. V. Bright, *Green Chem.* **2002**, *4*, 165–169; h) N. L. Lancaster, P. A. Salter, T. Welton, G. B. Young, *J. Org. Chem.* **2002**, *67*, 8855–8861; i) C. Hardacre, J. D. Holbrey, S. E. J. McMath, D. T. Bowron, A. K. Soper, *J. Chem. Phys.* **2003**, *118*, 273–278.

[5] a) K. Sato, S. Arai, T. Yamagishi, *Tetrahedron Lett.* **1999**, *40*, 5219–5222; b) J.-L. Thomas, J. Howarth, K. Hanlon, D. McGuirk, *Tetrahedron Lett.* **2000**, *41*, 413–416; c) Y. Yuan, G. Gao, Z. L. Jiang, J. S. You, Z. Y. Zhou, D. Q. Yuan, R. G. Xie, *Tetrahedron* **2002**, *58*, 8993–8999, and references therein.

[6] L. C. Branco, J. G. Crespo, C. A. M. Afonso, *Chem. Eur. J.* **2002**, *8*, 3865–3871.

[7] For recent reviews, see: a) T. Welton, *Chem. Rev.* **1999**, *99*, 2071–2084; b) P. Wasserscheid, W. Keim, *Angew. Chem.* **2000**, *112*, 3926–3945; *Angew. Chem. Int. Ed.* **2000**, *39*, 3772–3789; c) M. J. Earle, K. R. Seddon, *Pure Appl. Chem.* **2000**, *72*, 1391–1398; d) R. Sheldon, *Chem. Commun.* **2001**, 2399–2407; e) C. M. Gordon, *Appl. Catal. A: General* **2001**, *222*, 101–117; f) H. Olivier-Bourbigou, L. Magna, *J. Mol. Catal. A: Chemical* **2002**, *182–183*, 419–437; g) D. Zhao, M. Wu, Y. Kou, E. Min, *Catal. Today* **2002**, *74*, 157–189; h) C. C. Tzschucke, C. Markert, W. Bannwarth, S. Roller, A. Hebel, R. Haag, *Angew. Chem.* **2002**, *114*, 4136–4173; *Angew. Chem. Int. Ed.* **2002**, *41*, 3964–4000.

[8] a) T. Fischer, A. Sethi, T. Welton, J. Woolf, *Tetrahedron Lett.* **1999**, *40*, 793–796; b) C. W. Lee, *Tetrahedron Lett.* **1999**, *40*, 2461–2464; c) A. Aggarwal, N. L. Lancaster, A. R. Sethi, T. Welton, *Green Chem.* **2002**, *4*, 517–520; d) S. V. Dzyuba, R. A. Bartsch, *Tetrahedron Lett.* **2002**, *43*, 4657–4659; e) O. Acevedo, J. D. Evanseck, *Abstr. Pap. Amer. Chem. Soc.* **2002**, *224*, 028-IEC.

[9] a) W. Chen, L. Xu, C. Chatterton, J. Xiao, *Chem. Commun.* **1999**, 1247–1248; b) L. Xu, W. Chen, J. Xiao, *Organometallics* **2000**, *19*, 1123–1127; c) L. Xu, W. Chen, J. Ross, J. Xiao, *Org. Lett.* **2001**, *3*, 295–297; d) J. Ross, W. Chen, L. Xu, J. Xiao, *Organometallics* **2001**, *20*, 138–142; e) J. Ross, J. Xiao, *Green. Chem.* **2002**, *4*, 129–133.

[10] J. Tsuji, *Palladium Reagents and Catalysts-Innovations in Organic Synthesis*, Wiley, Chichester, **1995**.

[11] a) C. Amatore, S. Gamez, A. Jutand, G. Meyer, M. Moreno-Manas, L. Morral, R. Pleixats, *Chem. Eur. J.* **2000**, *6*, 3372–3376, and references therein; b) C. Amatore, S. Gamez, A. Jutand, *Chem. Eur. J.* **2001**, *7*, 1273–1280.

[12] a) C. de Bellefon, E. Pollet, P. Grenouillet, *J. Mol. Catal. A: Chemical* **1999**, *145*, 121–126; b) S. Toma, B. Gotov, I. Kmentová, E. Solcániová, *Green. Chem.* **2000**, *2*, 149–151; c) I. Kmentová, B. Gotov, E. Solcániová, Š. Toma, *Green. Chem.* **2002**, *4*, 103–106.

[13] C. Amatore, E. Carré, A. Jutand, M. A. M′Barki, *Organometallics* **1995**, *14*, 1818–1826.

[14] a) W. N. Olmstead, Z. Margolin, F. G. Bordwell, *J. Org. Chem.* **1980**, *45*, 3295–3299; b) R. W. Alder, P. R. Allen, S. J. Williams, *J. Chem. Soc. Chem. Commun.* **1995**, 1267–1268; c) Y.-J. Kim, A. Streitwieser, *J. Am. Chem. Soc.* **2002**, *124*, 5757–5761.

[15] The pK_a of closely related diethyl malonate in DMSO is 16.4: F. G. Bordwell, *Acc. Chem. Res.* **1988**, *21*, 456–463.

[16] a) J. Tsuji, I. Minami, *Acc. Chem. Res.* **1987**, *20*, 140–145; b) J. Tsuji, *Tetrahedron* **1986**, *42*, 4361–4401.

[17] The pK_a of DBU is 12.9 in H_2O and 23.9 in CH_3CN: W. Galezowski, A. Jarczewski, M. Stanczyk, B. Brzezinski, F. Bartl, G. Zundel, *J. Chem. Soc. Faraday Trans.* **1997**, *93*, 2515—2518, and references therein. The pK_a of HOAc is 4.8 in H_2O and 12.3 in DMSO.[15]

[18] G. Giambastiani, G. Poli, *J. Org. Chem.* **1998**, *63*, 9608–9609.

[19] C. Amatore, A. Jutand, G. Meyer, L. Mottier, *Chem. Eur. J.* **1999**, *5*, 466–473.

[20] J. L. Anderson, J. Ding, T. Welton, D. W. Armstrong, *J. Am. Chem. Soc.* **2002**, *124*, 14247–14254, and references therein.

[21] a) J. S. Wilkes, M. J. Zaworotko, *J. Chem. Soc. Chem. Commun.* **1992**, 965–967; b) P. Bonhôte, A.-P. Dias, N. Papageorgiou, K. Kalyanasundaram, M. Grätzel, *Inorg. Chem.* **1996**, *35*, 1168–1178. Methyl carbonate forms a stable salt with protonated DBU, probably due to hydrogen bonding: c) P. Munshi, A. D. Main, J. C. Linehan, C.-C. Tai, P. G. Jessop, *J. Am. Chem. Soc.* **2002**, *124*, 7963–7971.

[22] The chemical shift of the imidazolium H^2 proton moved upfield by only 0.07 ppm when the concentration of [bmim][BF_4] changed from 0.014 to 0.68 M in $CDCl_3$ in the absence of [nBu$_4$N][OAc], showing that

the variation depicted in Figure 1 results primarily from interactions with the acetate not from changes in the concentration of [bmim][BF_4].[3e]

[23] a) S. N. Vinogradov, R. H. Linnell, *Hydrogen Bonding*, Van Nostrand Reinhold, New York, **1971**; b) D. H. Williams, I. Fleming, *Spectroscopic Methods in Organic Chemistry*, McGraw-Hill, London, **1996**. Assuming that the imidazolium and acetate ions are in equilibrium with a 1:2 complex, the chemical shift of the imidazolium H^2 proton would vary in a sigmoid manner with the concentration of acetate ion.

[24] D. S. Kemp, D. D. Cox, K. G. Paul, *J. Am. Chem. Soc*. **1975**, *97*, 7312 – 7318.

[25] G. Gattow, W. Behrendt, *Angew. Chem.* **1972**, *84*, 549 – 550; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 534 – 535.

[26] In contrast to the behavior of acetate salts, addition of DBU to a CD_2Cl_2 solution of [bmim][BF_4] caused an upfield shift of the H^2 resonance in the ^{1}H NMR spectrum, suggesting that imidazolium ring stacking rather than hydrogen bonding could be in operation.[3e] However, weaker bases such as DABCO have been proposed to be capable of deprotonating dialkylimidazolium salts in the presence of an aldehyde.[28d]

[27] J. Tsuji, H. Kataoka, Y. Kobayashi, *Tetrahedron Lett.* **1981**, *22*, 2575 – 2578.

[28] a) D. S. McGuinness, K. J. Cavell, B. F. Yates, *Chem. Commun*. **2001**, 355 – 356; b) C. J. Mathews, P. J. Smith, T. Welton, A. J. P. White, D. J. Williams, *Organometallics* **2001**, *20*, 3848; c) M. Hasan, I. V. Kozhevnikov, M. R. H. Siddiqui, C. Femoni, A. Stenier, N. Winterton, *Inorg. Chem.* **2001**, *40*, 795 – 800; d) V. K. Aggarwal, I. Emme, A. Mereu, *Chem. Commun*. **2002**, 1612 – 1613.

[29] D. C. Braddock, A. J. Wildsmith, *Tetrahedron Lett.* **2001**, *42*, 3239 – 3242.

[30] S. Bouquillon, J. Muzart, *Eur. J. Org. Chem.* **2001**, 3301 – 3305.

[31] S. R. Palit, *J. Org. Chem*. **1947**, *12*, 752 – 759.

[32] J. D. Holbrey, K. R. Seddon, *J. Chem. Soc. Dalton Trans.* **1999**, 2133 – 2140.

[33] J. Lehmann, G. C. Lloyd-Jones, *Tetrahedron* **1995**, *51*, 8863 – 8874.

[34] T. Hayashi, A. Yamamoto, Y. Ito, E. Nishioka, H. Miura, K. Yanagi, *J. Am. Chem. Soc*. **1989**, *111*, 6301 – 6311.

[35] F. Glorius, M. Neuburger, A. Pfaltz, *Helv. Chim. Acta.* **2001**, *84*, 3178 – 3196.

[36] A. L. J. Beckwith, A. A. Zavitsas, *J. Am. Chem. Soc.* **1986**, *108*, 8230 – 8234.

Received: February 28, 2003 [F4895]
Revised: June 6, 2003