Tetraalkylammonium and 1,3-Dialkylimidazolium Salts with Fluorinated Anions as Recoverable Phase-Transfer Catalysts in Solid Base-Promoted Cross-Aldol Condensations

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Tetraalkylammonium and 1,3-dialkylimidazolium tetrafluoroborates and hexafluorophosphates were employed for the first time as recoverable phase-transfer catalysts in multiphase reactions of CH-acids, in particular in solid base-promoted cross-aldol condensations. The catalysts retained their catalytic activity over several reaction cycles.

Introduction

Low melting salts of bulky organic bases with weakly solvating fluorinated anions, integral components of ionic liquids,[1] have been intensively studied as solvents and as catalysts for chemical reactions.[2] They enhance reaction rates and selectivity and possess properties attractive for processing, such as nonvolatility, noninflammability, and recoverability.[3] Heterogeneous catalysts, homogeneous catalysts,[4] and biocatalysts[5] immobilized in the liquid salt medium retain catalytic activity (turnover factor; TOF) over several reaction cycles.

Salts of bulky nitrogen bases with fluorinated anions would appear to offer extensive and so far unexplored opportunities for multiphase organic reactions. Voluminous cations similar to those present in conventional phase-transfer catalysts (PTCs)[6] facilitate phase transfer and enhance reaction rates. Weakly solvating anions reduce PTC solubility,[7] thereby improving recoverability. It is worth mentioning that conventional PTCs with Hal^- anions (Hal = Cl, Br) are usually soluble in both organic and water phases and their recovery is a difficult and so far unsolved problem.[8] Recoverable heterogeneous polymer-bound PTCs are expensive and have not found wide application.[6]

There are a few reports on the use of salts with BF_4^- and PF_6^- anions as PTCs, particularly in alkylation reactions.[9] The authors, however, did not focus on their recovery and did not compare their efficacy with that of conventional halide-based PTCs.

Here we describe the first application of tetraalkylammonium and 1,3-dialkylimidazolium perfluoroborates and -phosphates as recoverable PTCs in solid base-promoted cross-aldol condensations. This reaction is common in organic chemistry as one of the most convenient and simple methods for C–C bond formation.[10,11] Highly efficient solid–liquid heterogeneous systems containing solid alkali have previously been demonstrated in CH-acid alkylation[12a] and condensation reactions.[12b] Salts with fluorinated anions, employed recently as solvents in self-aldol condensations[13] and related reactions,[14,15] have never been used as PTCs in aldol-like reactions up to now.

Results and Discussion

As a test system we chose a reaction between methyl 4-formylbenzaldehyde (**1a**), containing two base-sensitive functional groups, and propanal (**2**). The reaction product, methyl 4-(2-methyl-3-oxoprop-1-enyl)benzoate (**3a**), is a convenient building block for the synthesis of *para*-(*nor*-polyprenyl)benzoic acid derivatives[16] possessing antitumor,[17a] hypolipidemic,[17b] and anticoagulant[17c] activities. The reaction between **1a** and **2** was studied in the ionic liquid 1-butyl-3-methylimidazolium tetrafluoroborate (**4a**) and in multiphase (solid base/PTC/benzene) systems. Solid KOH, NaOH, or LiOH (0.025–1.0 equiv. with respect to aldehyde **1a**, depending on the experimental procedure) were used as the base, and imidazolium and ammonium-based tetrafluoroborates **4a** and **5a**, hexafluorophosphates **4b, 5b,** and **6b**—and also, for comparison, the corresponding bromides **4c** and **5c** and the chlorides **4d** and **6d**—as the PTCs (Scheme 1).

Salts **5a**, **5b**, and **6b** were synthesized from the corresponding halides **5c** and **6d** by anion metathesis with 50% HBF_4 or 60% HPF_6. Being water-insoluble, they are easy to isolate by filtration.

Aldehyde **1a** reacts with propanal (**2**) in a mixture of KOH (1.0 equiv.) and liquid salt **4a** (5.0 equiv.) to yield a condensation product **3a**, though in a moderate (52%) yield

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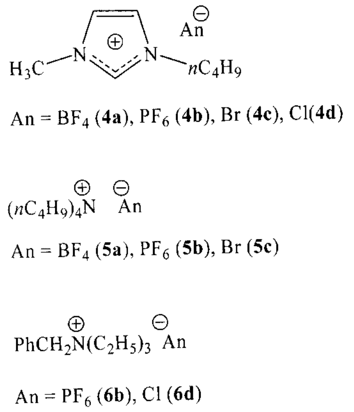


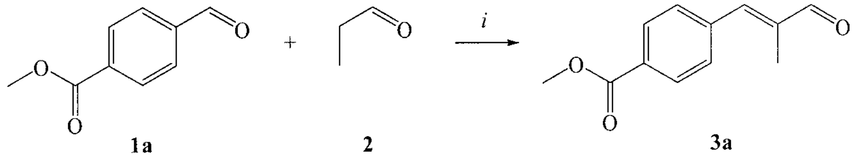
Scheme 1. 1,3-Dialkylimidazolium and tetraalkylammonium tetrafluoroborates, hexafluorophosphates, bromides, and chlorides used as solvents or PTCs.

(Table 1, entry 1). Use of a “milder” base ($LiOH·H_2O$ instead of KOH) did not give a higher product yield but increased the reaction time (Table 1, entry 2). The yield of compound **3a** dropped to 5% when the base amount was reduced to 0.15 equiv. (Table 1, entry 3). It is believed that the moderate yields of **3a** obtained in the liquid salt medium were the result of self-condensation and oligomerization of propanal (**2**) that reportedly occurred in the melt,[13a] an assumption consistent with the presence of aldehyde **1a** and 4-formylbenzoic acid, the product of ester group hydrolysis in **1a**, in the reaction mixture after the complete consumption of propanal (TLC and GLC monitoring).

Noticeably higher enal **3a** yields were obtained in a KOH(s)/PTC/benzene multiphase system (Table 1, entries 4–16). The efficacy of the process depended on the amounts of base and PTC, their ratio, and the two ions making up the PTC. Suitable amounts of base and PTC were found to be at least 0.075 and 0.05 equiv. (with respect to aldehyde **1a**), respectively. To obtain a higher product yield (Table 1, entries 10–13) the base should be present in excess with respect to the PTC. The yield remained the same when a corresponding amount of NaOH was used as a base instead of KOH, but the reaction time increased from 2.0 to 6.0 hours (Table 1, entry 13).

The KOH(s) (0.15 equiv.)/PTC (0.10 equiv.)/benzene system, which had proven to be the most efficient, was employed to compare PTCs **4**–**6**. Yields of enal **3a** in the catalytic systems containing imidazolium-based PTCs **4a**–**d** were found to increase over the following anion series: $BF_4^- > PF_6^- > Br^- > Cl^-$ (Table 1, entries 4–7), but in the cases of the ammonium-based PTCs **5a**–**c** and **6b** and **6d** the sequences were different ($PF_6^- > Br^- > BF_4^-$ and $Cl^- > PF_6^-$, respectively) (Table 1, entries 8, 9, 14–16). Despite the complicated picture, the obtained data show that PTCs with weakly solvating BF_4^- and PF_6^- anions possess efficacies in cross-aldol condensations similar to or even higher than those of conventional halide-based PTCs . Of the nine salts studied, PTC **5b** was shown to be the most efficient, en-

Table 1. Cross-aldol condensations of methyl 4-formylbenzoate (**1a**) and propanal (**2**) in catalytic multiphase systems with solid alkali in the presence of 1,3-dialkylimidazolium (**4a**–**d**) and tetraalkylammonium (**5a**–**5c**, **6b, 6d**) salts.



1a **2** **3a**

Reagents and conditions: *i*) **1a** (10 mmol), **2** (12 mmol), PhH (15 mL), 20 °C

Entry	Salt **4**–**6** [mmol]	Cation	Anion	Base [mmol]	*t* [h]	Yield of **3a** [%][a]
1[b]	**4a** [50]	bmim+	BF_4^-	KOH [10]	4.0	52
2[b]	**4a** [50]	bmim+	BF_4^-	$LiOH·H_2O$ [10]	24	49
3[b]	**4a** [50]	bmim+	BF_4^-	KOH [1.5]	4.0	5
4	**4a** [1.0]	bmim+	BF_4^-	KOH [1.5]	2.0	88
5	**4b** [1.0]	bmim+	PF_6^-	KOH [1.5]	2.0	81
6	**4c** [1.0]	bmim+	Br^-	KOH [1.5]	4.0	64
7	**4d** [1.0]	bmim+	Cl^-	KOH [1.5]	5.0	57
8	**5a** [1.0]	nBu_4N^+	BF_4^-	KOH [1.5]	2.0	88
9	**5b** [1.0]	nBu_4N^+	PF_6^-	KOH [1.5]	2.0	98
10	**5b** [0.5]	nBu_4N^+	PF_6^-	KOH [0.75]	2.0	94
11	**5b** [0.25]	nBu_4N^+	PF_6^-	KOH [0.38]	2.0	47
12	**5b** [0.25]	nBu_4N^+	PF_6^-	KOH [0.25]	2.0	10
13	**5b** [1.0]	nBu_4N^+	PF_6	NaOH [1.5]	6.0	88
14	**5c** [1.0]	nBu_4N^+	Br^-	KOH [1.5]	2.0	93
15	**6b** [1.0]	$BnEt_3N^+$	PF_6^-	KOH [1.5]	2.0	78
16	**6d** [1.0]	$BnEt_3N^+$	Cl^-	KOH [1.5]	2.0	82 (88–90[12])[c]
17	–	–	–	nBu_4NOH [1.5]	0.5	96
18	–	–	–	nBu_4NOH [0.75]	2.0	95
19	None	None	None	KOH [1.5]	4	30

[a] Yield of crystallized compound (**3a**). [b] No PhH was added. [c] A minor discrepancy with the reported data [12] (in brackets) is probably due to a different purity and dispersion of the PTC and base.

abling enal **3a** to be produced in 98% yield and with 100% selectivity.

The scope of PTC **5b** was estimated in solid–liquid phase cross-aldol condensations between aromatic (heteroaromatic) aldehydes and various carbonyl compounds. Benzaldehyde derivatives **1b–g** bearing both electron-releasing and electron-withdrawing groups in the aromatic ring, as well as aldehydes of the pyridine (**1h**), furan (**1i**), and thiophene (**1j**) series, were used as electrophiles. Propanal (**2**), pentanal (**7**), 3-methylbutanal (**8**), acetophenone (**9**), and acetylcyclopropane (**10**) were studied as cross-components. In all the cases the corresponding products **3b–q** were obtained in yields comparable to or higher than those reported in the literature (Table 2).

The reactions were influenced by the electronic and steric properties of aldehydes **1a–g**: electron-releasing groups in the aromatic ring decreased the product **3** yield, while electron-withdrawing ones increased it. Bulky groups *ortho* to the aldehyde group hampered the condensation: 2-nitrobenzaldehyde, unlike 3- or 4-nitrobenzaldehyde, did not noticeably react with propanal (**2**) under the studied conditions.

The condensation products **3** each consisted of a single stereoisomer (GLC and ^{1}H NMR monitoring). (*E*) Configurations were assigned to the enals **3a–c**, **3e–k**, and **3n–q** by comparison of their physicochemical and spectral properties with the reported data (see Table 2)[12,18,19] and to compounds **3d**, **3l**, and **3m** by analogy (see also ref.[20]).

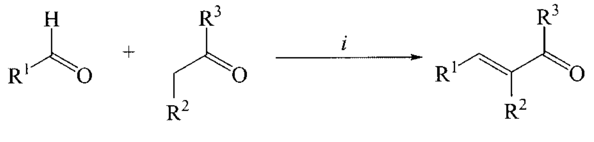
We took advantage of the poor solubilities of salts **4b**, **5a**, **5b**, and **6b** in organic and water phases by multiply repeated use of these catalysts in the condensation process. After each condensation cycle, a benzene solution of product **3a** was separated and replaced with a fresh solution of the starting compounds **1a** and **2**. Catalytic systems containing the PTCs **4b**, **5a**, and **6b** retained their activities over at least three reaction cycles, and the system containing salt **5b** for more than five cycles (Table 3). In the last case replenishment of the system with base was required in the fifth cycle to compensate for its loss due to gradual conversion into K_2CO_3 and/or to "washing" out into the benzene solution by eliminated water. A fresh portion of the base may also be required to bind eliminated water that gradually dilutes the solid phase. Recoverability of the PTC **5b**/KOH catalytic system was also demonstrated in cross-aldol condensations of other aldehydes **1b–j** and carbonyl compounds **2**, **10** (Table 2). Unlike the poorly soluble salts **4b**, **5a**, **5b**, **6b**, the PTCs **4a**, **4c**, **4d**, and **5c**, with good solubilities in benzene, could not be used repeatedly due to losses during product isolation and purification (Table 3).

Table 3. Recovery of PTCs **4b**, **5a**, **5b**, and **6b** in cross-aldol condensations between **1a** and **2** in the PTC (0.10 equiv.)/KOH(s) (0.15 equiv.)/PhH catalytic system.

PTC	Yield of **3a** [%]				
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 5
4b	81	75	66	–	–
5a	88	80	73	–	–
5b	98	97	98	88	98[a]
5c	93	40	–	–	–
6b	78	75	70	–	–

[a] A fresh portion of solid KOH (0.15 equiv.) was added.

Table 2. Cross-aldol condensations of aromatic (heteroaromatic) aldehydes **1a–j** with carbonyl compounds **2** and **7–10** in the nBu$_4$NPF$_6$/KOH(s)/PhH catalytic system.



1a–j **2, 7–10** **3a–q**

Reagents and conditions: *i*) **1a–j** (10 mmol), **2**, **7–10** (12 mmol), [nBu$_4$N][PF$_6$] (1 mmol), KOH(s) (1.5 mmol), PhH (15 mL), 20 °C.

	R^1	R^2	R^3	*t* [h]		M.p. or b.p. [°C]	n_D^{20}	Yield [%] (cycle)
1a, 2	4-$C_6H_4CO_2CH_3$	CH_3	H	2	**3a**	93–94 (93–94[12])	–	98 (1)[a] (90[12])
1b, 2	Ph	CH_3	H	4	**3b**	115–117 (6 Torr) [135–138 (15 Torr)[12]]	1.5885 (1.5880[12])	75 (1), 73 (2) (62[12])
1c, 2	4-C_6H_4Cl	CH_3	H	4	**3c**	39–40 (38–39[12])	–	81 (1), 81 (2) (73[12])
1d, 2	2-C_6H_4Cl	CH_3	H	6	**3d**	80–82 (0.5 Torr)	1.5970	76 (1), 75 (2)
1e, 2	4-$C_6H_4OCH_3$	CH_3	H	20	**3e**	127–129 (0.7 Torr) [120–122 (0.5 Torr)[12]]	–	38 (1), 37 (2) (29[12])
1f, 2	4-$C_6H_4NO_2$	CH_3	H	2	**3f**	97–98 (98–99[12])	–	89 (1), 87 (2) (84[12])
1g, 2	3-$C_6H_4NO_2$	CH_3	H	3	**3g**	84–85 (83[18])	–	97 (1), 95 (2) (30[18])
1h, 2	2-pyridyl	CH_3	H	3	**3h**	124–126 (6 Torr) [130–132 (10 Torr)[12]]	1.6015 (1.6020[12])	76 (1), 76 (2) (72[12])
1i, 2	2-furyl	CH_3	H	3	**3i**	110–112 (10 Torr) [106–108 (9 Torr)[12]]	1.6110 (1.6100[12])	82 (1), 81 (2) (70[12])
1j, 2	2-thienyl	CH_3	H	2	**3j**	130–132 (8 Torr) [132–134 (10 Torr)[12]]	1.6502 (1.6510[12])	76 (1), 74 (2) (69[12])
1b, 7	Ph	nC_3H_7	H	4	**3k**	140–142 (1 Torr) [107–110 (0.5 Torr)[12]]	1.5703 (1.5710[12])	69 (62[12])
1g, 7	3-$C_6H_4NO_2$	nC_3H_7	H	3	**3l**	52–53	–	90
1g, 8	3-$C_6H_4NO_2$	iC_3H_7	H	5	**3m**	49–50	–	82
1b, 9	Ph	H	Ph	4	**3n**	54–55 (55[19])	–	95 (90[19])
1g, 9	3-$C_6H_4NO_2$	H	Ph	2	**3o**	140–142 (141–142[19])	–	96 (94[19])
1b, 10	Ph	H	cC_3H_7	3	**3p**	51–53 (52.8–53.0[10a])	–	76 (1), 76 (2) (72[10a])
1e, 10	4-$C_6H_4OCH_3$	H	cC_3H_7	6	**3q**	72–73 (70–72[20])	–	56 (1), 53 (2) (50[20])

[a] Yields obtained in recycling experiments with compounds **1a** and **2** are given in Table 3.

Cross-aldol condensations in the solid–liquid systems studied are assumed to proceed according to Makosza's scheme,[21a,21b] which consists of CH-acid deprotonation on the solid base surface, followed by carbanion interception with a PTC and its transfer into the organic phase, where the reaction with an electrophile takes place. The reaction with an electrophile may also occur within the interfacial region (so-called "omega phase"[21c,21d]), followed by the extraction of the condensation products into the organic phase. The important role of the solid–liquid interfacial region is consistent with a strong influence exerted by the solid base metal cation on the condensation process: use of a "milder" deprotonating agent (NaOH) gave a slower reaction rate than use of KOH. The solid base surface should also not be covered completely with adsorbed PTC ions (the base should be present in excess with respect to the PTC), or it will not be able to deprotonate the CH-acid.

A commercially available organic base ($n\mathrm{Bu_4NOH}$), used in amounts as high as 0.075–0.15 equiv. with respect to aldehyde **1a**, was also shown to act as an efficient homogeneous catalyst (Table 1, entries 17, 18). This catalysis is assumed to be formed in the last step of the reaction sequence (the reaction of carbanion tetrabutylammonium salt with electrophile), but its direct formation on the solid base surface by the metathesis of PTC and solid alkali hydroxide should be thermodynamically unfavorable, due to high crystal lattice energy of the solid base and low solvation energy of ions in the nonpolar solvent. It is also unlikely that two solid phases, in particular the fluorinated PTC and base, both with low solubilities in benzene (we have shown that the solubility of hexafluorophosphate **5b** in benzene at 20 °C is $< 10^{-1}$ wt.-%, whereas the solubility of the corresponding bromide **5c** in toluene is as high as 52 wt.-% under the same conditions[22]), would contact efficiently enough to produce the required amount of the quaternary base under the reaction conditions.

Conclusions

Tetraalkylammonium and 1,3-dialkylimidazolium tetrafluoroborates and hexafluorophosphates represent a new class of efficient recoverable PTCs for reactions including the formation of CH-acid carbanions. They allow the base-promoted cross-aldol condensation to be performed repeatedly in high yield and with high selectivity. The salts are now being studied as PTCs for other base-promoted multiphase reactions of CH-acids.

Experimental Section

General Remarks: ^{1}H NMR spectra were recorded on Bruker AM 300 (300.13 MHz {^{1}H}) and Bruker DRX 500 (500.13 {^{1}H}, 125.76 {^{13}C}, 470.4 {^{19}F}, 202.4 MHz {^{31}P}) instruments in $\mathrm{CDCl_3}$ and [D$_6$]DMSO. ^{1}H, ^{13}C, ^{19}F, and ^{31}P chemical shifts are relative to $\mathrm{Me_4Si}$, [D$_6$]acetone, $\mathrm{CFCl_3}$, and $\mathrm{H_3PO_4}$, respectively. Reactions were monitored by TLC (silufol plates, eluent: ethyl acetate/PhH 1:19, visualization by I_2) and GLC (LKhM-80 chromatograph with a flame ionization detector, N_2, 1.5 × 0.003 m glass column with 5% SE-30 on Chromaton N–AW–DMCS). Salts **5c** and **6d** and $n\mathrm{Bu_4NOH}$ toluene solution (0.1 N) were purchased from Acros and were used without further purification. Imidazolium-based salts **4a–d** were synthesized by the reported methods.[23,24] The ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra of the salts **4a–d** were identical to those reported previously.[25,26]

Tetraalkylammonium Tetrafluoroborate 5a and Hexafluorophosphates 5b and 6b. General Procedure: Aqueous solutions of $\mathrm{HBF_4}$ (50%, 3.5 mL, 20.0 mmol) or $\mathrm{HPF_6}$ (60%, 4.8 mL, 20.0 mmol) were added dropwise at 0 °C to stirred solutions of tetra(*n*-butyl)ammonium bromide (**5c**) or benzyltriethylammonium chloride (**6d**) (20.0 mmol) in water (30 mL). The reaction mixture was stirred for 15–20 min at 20 °C. The precipitate was filtered off, washed successively with water (3 × 10 mL) and diethyl ether (2 × 10 mL), and dried under reduced pressure (10 Torr) at 40 °C to afford compounds **5a**, **5b** and **6b**.

Tetra(butyl)ammonium Tetrafluoroborate (5a): Yield 90%, m.p. 158–159 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 0.80 (t, 12 H, 4 × $\mathrm{CH_3}$), 1.17 (m, 8 H, 4 × $\mathrm{CH_2}$), 1.43 (m, 8 H, 4 × $\mathrm{CH_2}$), 3.03 (m, 8 H, 4 × $\mathrm{CH_2}$) ppm. ^{13}C NMR: δ = 13.5 ($\mathrm{CH_3}$), 19.5 ($\mathrm{CH_2}$), 23.4 ($\mathrm{CH_2}$), 57.9 ($\mathrm{CH_2}$) ppm. ^{19}F NMR: δ = –149.2 ppm. $\mathrm{C_{16}H_{36}BF_4N}$: calcd. C 58.36, H 11.02, F 23.08, N 4.25; found C 58.55, H 11.13, F 22.91, N 4.19.

Tetra(butyl)ammonium Hexafluorophosphate (5b): Yield 93%, m.p. 243–246 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 1.00 (t, 12 H, 4 × $\mathrm{CH_3}$), 1.35 (m, 8 H, 4 × $\mathrm{CH_2}$), 1.60 (m, 8 H, 4 × $\mathrm{CH_2}$), 3.15 (m, 8 H, 4 × $\mathrm{CH_2}$) ppm. ^{13}C NMR: δ = 13.4 ($\mathrm{CH_3}$), 19.2 ($\mathrm{CH_2}$), 23.0 ($\mathrm{CH_2}$), 57.5 ($\mathrm{CH_2}$) ppm. ^{19}F NMR: δ = –70.7 (d, $^1J_{\mathrm{P,F}}$ = 708 Hz) ppm. ^{31}P NMR: δ = –142.4 (sept, $^1J_{\mathrm{P,F}}$ = 708 Hz) ppm. $\mathrm{C_{16}H_{36}F_6NP}$: calcd. C 49.60, H 9.37, F 29.42, N 3.62, P 7.99; found C 49.82, H 9.29, F 29.27, N 3.55, P 7.81.

Benzyltriethylammonium Hexafluorophosphate (6b): Yield 87%, m.p. 176–177 °C. ^{1}H NMR ([D$_6$]DMSO): δ = 1.30 (t, 9 H, 3 × $\mathrm{CH_3}$), 3.15 (q, 6 H, 3 × $\mathrm{CH_2}$), 4.50 (s, 2 H, $\mathrm{CH_2}$), 7.53–7.60 (m, 5 H, Ph) ppm. ^{13}C NMR: δ = 7.7 ($\mathrm{CH_3}$), 52.3 ($\mathrm{CH_2}$), 59.8 ($\mathrm{CH_2}$), 128.1, 129.4, 130.6, 132.8 (Ph) ppm. ^{19}F NMR: δ = –70.6 (d, $^1J_{\mathrm{P,F}}$ = 708 Hz) ppm. ^{31}P NMR: δ = –142.8 (sept, $^1J_{\mathrm{P,F}}$ = 708 Hz) ppm. $\mathrm{C_{13}H_{22}F_6NP}$: calcd. C 46.29, H 6.57, F 33.80, N 4.15, P 9.18; found C 46.18, H 6.42, F 33.64, N 4.03, P 9.11.

Condensation of Methyl 4-Formylbenzoate (1a) with Propanal (2) in Ionic Liquid 4a. General Procedure: Aldehyde **1a** (1.64 g, 10 mmol) and then, gradually, propanal (**2**, 0.70 g, 12 mmol) were added successively at 20 °C to a vigorously stirred suspension of powdery KOH or $\mathrm{LiOH{\cdot}H_2O}$ (10 mmol) in the ionic liquid **4a** (50 mmol). The reaction mixture was stirred at 20 °C until the condensation was complete (TLC and GLC monitoring) and extracted with diethyl ether (3 × 10 mL). The combined ether extracts were washed with water (2 × 5 mL) and dried over anhydrous $\mathrm{MgSO_4}$. The solvent was evaporated under reduced pressure, and the residue was crystallized from hexane to afford methyl *trans*-4-(2-methyl-3-oxoprop-1-enyl)benzoate (**3a**), m.p. 93–94 °C (lit.[12] m.p. 93–94 °C).

Cross-Condensations between Aromatic (Heteroaromatic) Aldehydes 1a–j and Carbonyl Compounds 2 and 7–10 in the PTC (4a–d, 5a–c, 6 b, 6d)/Solid Base/PhH System. General Procedure: Solutions of aldehydes **1a–j** (10 mmol) in benzene (5 mL) and then, dropwise, of alkanals **2**, **7**, **8** (12 mmol) or ketones **9**, **10** (10 mmol) in benzene (5 mL) were added successively at 20 °C to vigorously stirred suspensions of the appropriate amounts of powdery KOH or NaOH and PTC (**4a**–**d**, **5a**–**c**, or **6b**/**6d**) (Table 1 and Table 2) in benzene (5 mL). The reaction mixture was vigorously stirred at the same temperature until the condensation was complete (TLC and GLC monitoring). The organic solution was decanted from the wet PTC/KOH solid phase, and the residue was extracted with benzene (10 mL). The combined benzene extracts were washed with water (2 × 5 mL) and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure, and the residue was distilled in vacuo or crystallized from hexane. The yields, melting (boiling) points, and refractive indexes of the enals **3a**–**q**, as well as the ^{1}H NMR spectroscopic data for compounds **3a**–**c**, **3e**–**k**, and **3n**–**q**, were in accordance with those reported in the literature (Table 2).

***trans*-2-Chloro-β-methylcinnamaldehyde (3d):** B.p. 80–82 °C (0.5 Torr); n_D^{20} = 1.5970. ^{1}H NMR ($CDCl_3$): δ = 1.95 (s, 3 H, CH_3), 7.20–7.45 (m, 5 H, CH=C and $4\times H^{Ar}$), 9.63 (s, 1 H, CHO) ppm. $C_{10}H_9ClO$: calcd. C 66.49, H 5.02, Cl 19.63; found C 66.67, H 5.11, Cl 19.39.

***trans*-3-Nitro-β-propylcinnamaldehyde (3l):** M.p. 52–53 °C. ^{1}H NMR ($CDCl_3$): δ = 1.00 (t, J = 7.0 Hz, 3 H, CH_3), 1.52 (m, 2 H, CH_2), 2.50 (t, J = 7.0 Hz, 2 H, CH_2–C=), 7.25 (s, 1 H, CH=C), 7.60–7.80 (m, 2 H, $2\times H^{Ar}$), 8.20–8.30 (m, 2 H, $2\times H^{Ar}$), 9.58 (s, 1 H, CHO) ppm. $C_{12}H_{13}NO_3$: calcd. C 65.74, H 5.98, N 6.39; found C 65.90, H 6.06, N 6.21.

***trans*-β-Isopropyl-3-nitrocinnamaldehyde (3m):** M.p. 49–50 °C. ^{1}H NMR ($CDCl_3$): δ = 1.25 (d, 6 H, $2\times CH_3$, J = 7.2 Hz), 3.00 (m, 1 H, $CH(CH_3)_2$), 7.22 (s, 1 H, CH=C), 7.50–7.65 (m, 2 H, $2\times H^{Ar}$), 8.20–8.30 (m, 2 H, $2\times H^{Ar}$), 9.58 (s, 1 H, CHO) ppm. $C_{12}H_{13}NO_3$: calcd. C 65.88, H 6.01, N 6.39; found C 65.90, H 6.06, N 6.47.

In the cases of salts **4b**, **5a**, **5b**, and **6b** as PTCs and KOH as a base the reactions were performed repeatedly with a PTC/solid base mixture ("wet solid phase") that remained after the first condensation cycle, with addition of fresh aldehyde/alkanal (ketone)/benzene solutions (Table 2 and Table 3).

***n*Bu₄NOH-Promoted Condensation of Methyl 4-Formylbenzoate (1a) with Propanal (2):** A solution of aldehyde **1a** (1.64 g, 10 mmol) and propanal (**2**; 0.70 g, 12 mmol) in benzene (10 mL) was added at 20 °C with stirring to the appropriate amount of commercially available nBu_4NOH toluene solution (0.1 N) (Table 1, entries 17, 18). The reaction mixture was stirred at the same temperature for 0.5–2.0 hours (TLC and GLC monitoring), washed with water (2 × 5 mL), and dried over anhydrous $MgSO_4$. The solvent was evaporated under reduced pressure to afford enal **3a**.

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[1] a) T. Welton, *Chem. Rev.* **1999**, *99*, 2071–2083; b) P. Wasserscheid, T. Welton (Editors), *Ionic Liquids in Synthesis*, Wiley-VCH, **2003**, p. 363.

[2] a) D. Zhao, M. Wu, Y. Kou, E. Min, *Catal. Today* **2002**, *74*, 157–189; b) H. Olivier-Bourbigou, L. Magna, *J. Mol. Catal.* **2002**, *182–183*, 419–437.

[3] a) M. Freemantle, *Science/Technology* **2000**, *78*, 37–50; b) M. J. Earle, K. R. Seddon, *Pure Appl. Chem.* **2000**, *72*, 1391–1398.

[4] a) P. Wasserscheid, W. Keim, *Angew. Chem. Int. Ed.* **2000**, *39*, 3772–3789; b) J. Dupont, R. F. de Souza, P. A. Z. Suarez, *Chem. Rev.* **2002**, *102*, 3667–3692; c) U. Kragl, M. Eckstein, N. Kaftzic, *Current Opinion Biotech.* **2002**, *13*, 565–571.

[5] a) R. A. Sheldon, R. M. Lau, M. J. Sorgedrager, F. van Rantwijk, K. R. Seddon, *Green Chem.* **2002**, *4*, 147–151; b) P. Lozano, T. De Diego, D. Carrie, M. Vaultier, J. L. Iborra, *J. Mol. Catal. B: Enzymatic* **2003**, *21*, 9–13.

[6] E. V. Dehmlov, S. S. Dehmlov, "Phase Transfer Catalysis", 3rd ed., VCH Verlagsgesellschaft, Weinheim, **1993**.

[7] a) R. Hagiwara, Y. Ito, *J. Fluorine Chem.* **2000**, *105*, 221–227; b) S. Cadra-Broch, A. Berthod, D. W. Armstrong, *Anal. Bioanal. Chem.* **2003**, *375*, 191–199; c) P. Bonhôte, A. P. Dias, N. Papageorgiu, K. Kalyanasundaram, M. Grätzel, *Inorg. Chem.* **1996**, *35*, 1168–1178.

[8] Y. Sasson, G. Rothenberg, in "*Handbook of Green Chemistry and Technology*", Eds. J. Clark, D. Macquarrie, Blackwell Science Ltd., **2002**, pp. 206–257.

[9] a) T. Tanaka, T. Mukaiama, *Chem. Lett.* **1976**, 1259–1262; b) R. N. M. T. Lourenço, C. A. M. Afonso, *Tetrahedron* **2003**, *59*, 789–794.

[10] a) A. T. Nielsen, W. J. Houlihan, *Org. Reactions* **1968**, *16*, 1; b) S. M. Makin, I. E. Mikerin, E. K. Dobretsova, O. A. Shavrygina, *Russ. J. Org. Chem.* **1993**, *29*, 572–575; c) M. L. Kantam, B. M. Choudary, C. V. Reddy, K. K. Rao, F. Figueras, *Chem. Commun.* **1998**, 1033–1034.

[11] a) J. Lopez, J. S. Valente, J. M. Clacens, F. Figueras, *J. Catal.* **2002**, *208*, 30; b) S. Abello, F. Medina, X. Rodriguez, Y. Cesteros, P. Salagre, J. E. Sueiras, D. Tichit, B. Coq, *Chem. Commun.* **2004**, 1096–1097.

[12] a) C. Wheeler, K. N. West, C. L. Liotta, C. A. Eckert, *Chem. Commun.* **2001**, 887–888; b) G. V. Kryshtal′, G. M. Zhdankina, E. P. Serebryakov, *Russ. J. Org. Chem.* **1994**, *30*, 777–779.

[13] a) C. P. Mehnert, N. C. Dispenziere, R. A. Cook, *Chem. Commun.* **2002**, 1610–1611; b) C. P. Mehnert, N. C. Dispenziere, *WO 03/002502 A1*, **2003**; c) J. Ha, T. Suzuki, T. Hoshi, K.-i. Shimizu, Y. Kitayama, H. Hagiwara, *SynLett.* **2003**, 873–875.

[14] a) A. A. Shestopalov, L. A. Rodinovskaya, A. M. Shestopalov, S. G. Zlotin, V. Nesterov, *Synlett SynLett.* **2003**, 2309–2312; b) A. M. Shestopalov, S. G. Zlotin, A. A. Shestopalov, V. Yu. Mortikov, L. A. Rodinovskaya, *Russ. Chem. Bull., Int. Ed.* **2004**, *53*, 573–579; c) C. Su, Z.-C. Chen, Q.-G. Zheng, *Synthesis* **2003**, 555–559.

[15] a) T.-P. Loh, L.-C. Feng, H.-Y. Yang, J.-Y. Yang, *Tetrahedron Lett.* **2002**, *43*, 8741–8743; b) N. S. Chowdari, D. B. Ramachary, C. F. Barbas III, *Synlett SynLett.* **2003**, 1906–1909.

[16] a) G. V. Kryshtal′, G. M. Zhdankina, E. P. Serebryakov, *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1993**, *42*, 2039–2041; b) G. V. Kryshtal′, E. P. Serebryakov, *Bull. Acad. Sci. USSR Div. Chem. Sci. (Engl. Transl.)* **1995**, *44*, 1785–1804.

[17] a) *Ger. Offen*. DE 3320544 // *Chem. Abstr.* **1984**, *101*, 7482; b) *Eur. Pat. Appl*. EP 0194693 // *Chem. Abstr.* **1989**, *111*, 5730; c) *Eur. Pat. Appl*. EP 110397 // *Chem. Abstr.* **1985**, *102*, 6974.

[18] G. Heller, H. Lanth, A. Buchwaldt, *Ber. Dtsch. Chem. Ges.* **1922**, *55*, 483–489.

[19] S. V. Tsukerman, Yu. N. Surov, V. F. Lavrushin, *Zh. Obshch. Khim* **1968**, *38*, 524–529; *Chem. Abstr.* **1968**, *69*, 6536a.

[20] D. G. Diana, U. J. Salvador, E. S. Zalay, R. E. Johnson, J. C. Collins, D. Johnson, W. B. Hinshaw, R. R. Lorenz, W. N. Thielking, F. Pancic, *J. Med. Chem.* **1977**, *20*, 750–756.

[21] a) M. Makosza, I. Krylova, *Tetrahedron* **1999**, *55*, 6395–6402; b) M. Makosza, in: "*Phase-Transfer Catalysis: Mechanisms and Synthesis*" (Ed.: M. E. Halpern), ACS Symposium Series 659, **1997**, 41–51; c) C. L. Liotta, J. Berkner, J. Wright, B. Fair, in: "*Phase-Transfer Catalysis: Mechanisms and Synthesis*" (Ed.: M. E. Halpern), ACS Symposium Series 659, **1997**, 29–40; d) S. S. Yufit, G. V. Kryshtal, I. A. Esikova, in: "*Phase-Transfer Catalysis: Mechanisms and Synthesis*" (Ed.: M. E. Halpern), ACS Symposium Series 659, **1997**, 52–67.

[22] D. Mason, S. Magdassi, Y. Sasson, *J. Org. Chem.* **1991**, *56*, 7229–7232.

[23] P. A. Z. Suarez, J. E. L. Dullius, S. Einloft, R. F. De Souza, J. Dupont, *Polyhedron* **1996**, *15*, 1217–1219.

[24] S. Chun, S. V. Dzyuba, R. A. Bartsch, *Anal. Chem.* **2001**, *73*, 3737–3741.

[25] S. G. Zlotin, G. V. Kryshtal, G. M. Zhdankina, P. A. Belyakov, E. P. Serebryakov, *Russ. Chem. Bull., Int. Ed.* **2004**, *53*, 659–664.

[26] G. V. Kryshtal, G. M. Zhdankina, I. V. Astakhova, S. G. Zlotin, *Russ. Chem. Bull., Int. Ed.* **2004**, *53*, 647–651.

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