SHORT PAPER

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Efficient imidazolium catalysts for the benzoin condensation†

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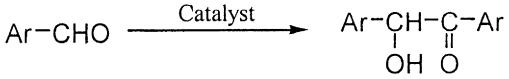
The benzoin condensation occurred easily within minutes when imidazolium salts **7–9** were used as catalysts at low concentrations (1 mol%) in tetrahydrofuran with 50% aqueous sodium hydroxide, and the benzoin yield rose to 91% on catalysis by **7c**, *N*-methyl-*N* 'benzylimidazolium hexafluorophosphate.

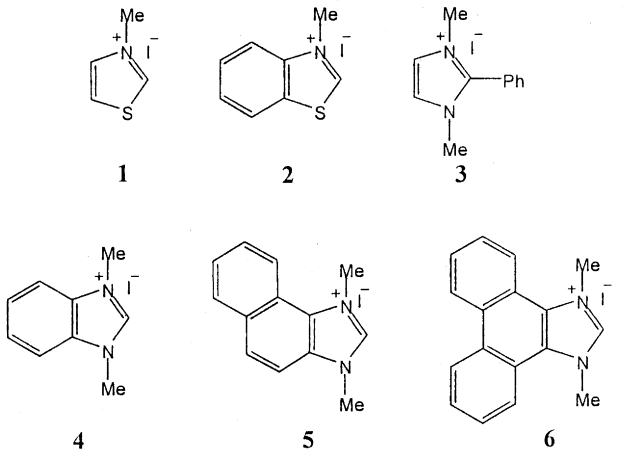
Keywords: benzoin condensation, imidazolium catalysts

Benzoins (2-hydroxy-1,2-diphenylethanones) are important intermediates for organic synthesis. Among several preparative methods, the self-condensation of aromatic aldehydes (benzoin condensation) is an easy and simple procedure. Two molecules of an aromatic aldehyde condense in the presence of a catalyst, resulting in the formation of benzoins (Scheme 1). It is well known that cyanide ion was the original catalyst.[1] However, the cyanide ion is highly toxic and new catalysts are therefore desirable. So far, several other catalysts have been investigated, for example, thiazolium and benzothiazoliun salts (**1,2**),[2,3] imidazolium salts (**3,7a**),[4–6] and a benzimidazolium salt and its analogues (**4-6**)[5,6] (Scheme 2 and 3). The catalytic ability of thiazolium salts is due to thiazolium-2-ylide generated by the removal of the C-2 hydrogen by base. This acts as well as cyanide in the benzoin condensation. Although thiazolium salts show good catalytic ability for the benzoin condensation, their use is limited because the thiazolium ring is easily destroyed by oxygen in the presence of base. Imidazolium is far more stable than thiazolium and it can endure strong acids, bases and heating. Its C-2 hydrogen is removed by bases to form imidazolium-2-ylide, and this was also found to catalyse the benzoin condensation. Obviously, 1,3-dimethyl-2-phenylimidazolium iodide (**3**) cannot catalyse the benzoin condensation because its 2-position is substituted.[6] Therefore, imidazolium salts with no substituents at the 2-position should be good alternatives to thiazolium salts as catalysts for the benzoin condensation. During our continuous research on imidazolium and multi-imidazolium compounds,[8,9] we are interested in seeking simple but highly efficient catalysts for the benzoin condensation based on imidazolium.



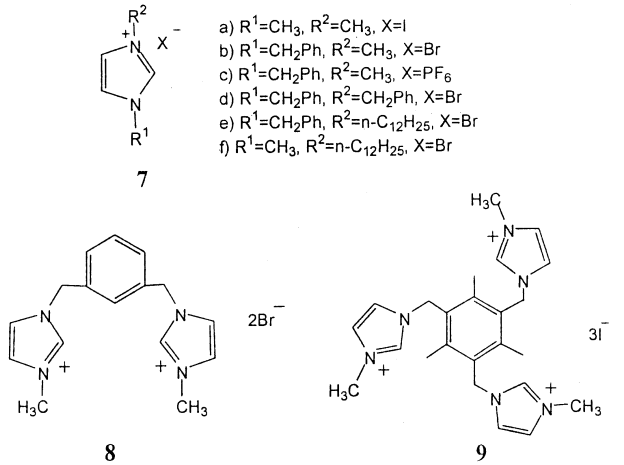
Scheme 1

Here we report efficient imidazolium catalysts **7–9** (Scheme 3) for the benzoin condensation. They were all easily synthesised by quaternisation of the corresponding *N*-substituted imidazole derivatives with halohydrocarbons. In our catalysis experiments we selected tetrahydrofuran (THF) as the solvent and 50% aqueous sodium hydroxide (NaOH) as the base. This reaction system proved to be very efficient for the benzoin condensation. When using THF with sodium hydride (NaH)



Scheme 2

or methanol (MeOH) with 50% aqueous NaOH,[5] we gained hardly any benzoin under our reaction conditions. We also selected trichloromethane ($CHCl_3$) as a solvent, which is non-hydroxylic and has a similar boiling point to THF, but we gained no benzoin. The presumptive actual catalyst imidazolium-2-ylide was formed after NaOH removed the C-2 hydrogen imidazolium. Then the reaction mixture rapidly turned brown and solidified within minutes. Benzoin was gained in good yield as shown in Table 1. All the catalysts exhibited good catalytic activity at low catalyst concentrations (1 mol%) compared to the concentrations of other catalysts reported (5–20 mol%)[2-7] as effective.



Scheme 3

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Synthesis of benzoin catalysed by imidazolium salts **7–9**

Run	Catalyst	Amount of catalyst (mol%)	Time/min	Yield[a]/%
1	**7a**	1	2	86
2	**7b**	2	2	86
3	**7b**	1	2	81
4	**7c**	1	2	91
5	**7c**	0.3	2	52
6	**7d**	1	1	80
7	**7e**	1	2	86
8	**7f**	1	2.5	72
9	**8**	1	25	87
10	**9**	2	120	74

[a] Yields are all isolated yields and the benzoin gained was characterised by comparison with an authentic sample.

Different substituents on the nitrogen of the imidazolium ring did not show large influences on the catalytic ability of the catalysts. The catalytic activity of *N*-methyl-*N*' -benzylimidazolium bromide (**7b**) and *N*-methyl-*N*' -benzylimidazolium hexafluorophosphate (**7c**) decreased along with the reduction of their concentrations (runs 2, 3 and 4, 5). The solubility of **7b** in THF was greatly improved after it was transformed to hexafluorophosphate (**7c**), and its catalytic ability was greatly improved too. We gained the best benzoin yield (91%) using 1 mol% of **7c** as catalyst after two minutes refluxing in THF. We considered that the greater contact between the catalyst and benzaldehyde led to a better benzoin condensation. **7c** even catalysed benzoin condensation at a very low concentration (0.3 mol%) to give benzoin in 52% yield after only two and a half minutes.

We then synthesised the di- and tri- imidazolium salts **8** and **9** to catalyse the benzoin condensation. Both showed good catalytic activity and benzoin was gained in 87% and 74% yields respectively. Nevertheless, their catalytic abilities are not as great as the catalysts having only one imidazolium moiety. A larger concentration or a longer reaction time was necessary for them to catalyse the benzoin condensation. The steric hindrance increase due to the increase of imidazolium rings may be perhaps responsible for the decrease of their catalytic ability.

Moreover, we also carried out the benzoin condensation using 1,3-dimethylimidazolium iodide (**7a**) as catalyst. It exhibited excellent catalytic activity under our reaction conditions (1 mol% **7a**, 86% benzoin yield after two minutes refluxing in THF), and the benzoin yield was increased 10% over that reported under Miyashita's reaction conditions (5 mol% **7a**, 78% benzoin yield).[5]

In summary, we have synthesised imidazoliun (**7b** and **7c**), di-imidazolim (**8**) and tri-imidazolium **9** compounds, three kinds of new highly efficient catalysts for the benzoin condensation for the first time. These catalysts were of significance for their low effective concentrations, short reaction times and high yields for the benzoin condensation. In particular *N*-methyl-*N*'-benzylimidazolium hexafluorophosphate (**7c**) catalysed the benzoin condensation in up to 91% yield, which is the best yield ever reported for the benzoin condensation by an imidazolium analogue as catalyst.

Experimental

N-methyl-N'-benzylimidazolium bromide[10] (**7b**): *N*-methylimidazole was quaternized by an equimolar amount of benzyl bromide in acetonitrile under reflux. After removal of acetonitrile under reduced pressure, the residue was purified by chromatography with ethanol/ethyl acetate 1:3 on silica gel to afford **7b** as a colourless oil in 83% yield, δ_H (D_2O, 300 MHz) 3.87 (3H, s), 5.38 (2H, s), 7.45 (7H, m), 8.7 (1H, s) in accordance with the literature values: δ_H (D_20) 3.90 (3H,s) 5.40 (2H,s), not reported 7H, s(broad), 8.89 1H,s).

N-methyl-N'-benzylimidazolium hexafluorophosphate (**7c**): Ammonium hexafluorophosphate was dissolved in water to saturation. Then this solution was added dropwise to an aqueous solution of **7b** until no precipitate was seen to form. **7c** was gained as colourless needles after filtration and water wash. The yield was over 90%, m.p. 132–134 °C. Anal. calcd. for $C_{11}H_{13}N_2PF_6$: C, 41.50; H, 4.12; N, 8.80. Found: C, 41.44; H, 4.23; N, 8.67%.

1,3-bis(N-(N'-methyl) imidazoliummethyl)benzene bromide (**8**): refluxing solution of 1,3-bis(bromomethyl)benzene (528 mg, 2 mmol) in 30 ml acetonitrile was added to a *N*-methylimidazole (0.32 ml, 4 mmol) and then reflux was continued for 2 h. The reaction was followed by thin layer chromatography. Then the reaction mixture was concentrated to about 10 ml under reduced pressure and filtered. The filter cake was washed with acetonitrile and petroleum ether to give a crude product. The crude product was recrystallised from methanol to give **8** (735 mg, 86%) as colourless crystals, m.p. 228–230 °C. δ_H (D_2O, 300 MHz) 3.88 (6H, s), 5.42 (4H, s), 7.44 (8H, m), 8.74 (1H, s); Anal. calcd. for $C_{16}H_{20}N_4Br_2$: C, 44.88; H, 4.71; N, 13.09. Found: C, 44.84; H, 4.83; N, 12.73%.

1,3,5-tris(N-(N'-methyl)imidazoliummethyl)-2,4,6-trimethylbenzene iodide (**9**): Prepared from 1,3,5-tris(*N*-imidazolylmethyl)-2,4,6-trimethylbenzene and iodomethane using the literature method[9] in 83% yield as colourless crystals, m.p. 294 °C (lit[9] m.p.294°C)

General procedure of imidazolium catalysed benzoin condensation: To a well stirred and refluxing structure of 15ml THF with the catalyst, the freshly distilled benzaldehyde 0.5 ml (4.9 mmol) and 50% NaOH aqueous solution 0.5 ml were added sequentially. After a few minutes of reaction, the reaction mixture solidified. Then THF was removed under reduced pressure and water (10ml) was added to the residue. The mixture was extracted with dichloromethane (10 ml×3). The extract was washed with water (10 ml), was dried over anhydrous magnesium sulfate and the dichloromethane was removed under reduced pressure to give the crude benzoin Then benzoin was isolated by recrystallisation from ethanol and column chromatography on silica gel, m.p. 133–135°C (lit[11] m.p. 129°C), identical (^{1}H NMR and MS spectra) with an authentic sample.[11]

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References

1 (a) W.S. Ide and J.S. Buck, *Org. React*., 1948, **4**, 269;(b) D.A. White and M.M. Baizer, *J. Chem. Soc*., *Perkin Trans.* 1, 1973,2230.
2 T, Ugai, R. Tanaka and S. Dokawa, *Yakugaku Zasshi,* 1943, **63**, 296.
3 Y. Yano, Y. Tamura and W. Tagaki, *Bull. Chem. Soc. Jpn*., 1980, **53**, 740.
4 T, Ugai, S. Dokawa and S. Tsubokawa, *Yakugaku Zasshi,* 1944, **64**, A7, 3.
5 A. Miyashita, Y. Suzuki, K-i. Iwamoto and T. Higashino, *Chem. Pharm. Bull.,* 1994, **42**, 2633.
6 A. Miyashita, Y. Suzuki, M. Kobayashi, N. Kuriyama and T. Higashino, *Heterocycles,* 1996, **43**, 509.
7 M.F. Lappert and R.K. Maskell, *J. Chem. Soc., Chem. Commun.,* 1982, 580
8 (a) Y. Yuan, J.M. Yan, A.S.C. Chan, Z.L. Jiang, G. Gao and R.G. Xie, *Synth. Commun.,* 2000, **30**, 4555; (b) Z.C. Liu, C.H. Zhou, X.Y. Su and R.G. Xie, *Synth. Commun.,* 1999, **29**, 2979; (c) M.M. Luo, R.G. Xie, D.Q. Yuan, W. Lu, P.F. Xia and H.M. Zhao, *Chin. J. Chem.,* 1999, **17,** 384; (d) Z.C. Liu, C.H. Zhou and R.G. Xie, *Chin. Chem. Lett.,* 1997, **8**, 387.
9 Y. Yuan, Z.L. Jiang, G. Gao and R.G. Xie, *Chin. J Chem.,* in press.
10 B.K.M. Chan, N.-H. Chang and M.R. Grimmett, *Aust. J Chem.,* 1977, **30**, 2005.
11 R. Adams and C.S. Marvel, *Org. Synth*., Coll. Vol. I, 1932, p.88.