Synthesis of 2*H*-Chromenes in Ionic Liquid Solvents

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Received 31 January 2003

Abstract: Vinylboronic acids react with *o*-hydroxyaryl aldehydes in room temperature ionic liquids in the presence of secondary amines to generate 2*H*-chromenes.

Key Words: ionic liquid, chromenes, Petasis reaction, boronic acid, green chemistry

The past few years have witnessed a growing interest in ionic liquids as solvent systems for organic syntheses.[1] Reactions carried out in ionic liquids often exhibit different thermodynamic and kinetic behaviors than those run in conventional solvents. In addition, ionic liquids are air and moisture stable and possess other properties that are of importance in industrial applications.[2] Their lack of vapor pressure is most notable and their use in a wide variety of environmentally friendly organic transformations (green chemistry) has been widely reported.[3]

Chromene and chroman ring systems are important oxygen heterocycles[4] occurring widely in nature. In view of the recent interest in green chemistry in industrial applications employing room temperature ionic liquids, we wish to report the synthesis of 2*H*-chromenes using boronic acids, amines, and *o*-hydroxyaryl aldehydes.[5] The reaction is complementary to one reported by Wang and Finn[6] who utilized 40 mol% of resin-bound amine at 90 °C for 24 hours in dioxane. Reaction yields are comparable to those obtained by Wang and Finn, using the resin bound amine. The new ionic liquid reaction was developed as part of our investigation of boron reactions in non-traditional media.[5d,7]

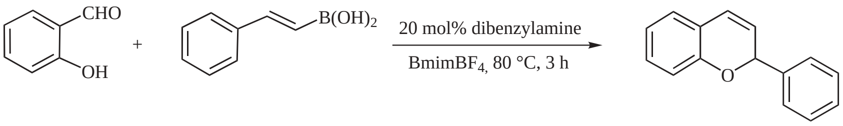
Many of the readily available imidazolium-based ionic liquids can be utilized in the reaction. These include butylmethylimidazolium bromide (BmimBr), butylmethylimidazolium tetrafluoroborate ($BmimBF_4$), and ethylmethylimidazolium tetrafluoroborate ($EmimBF_4$). Using some of these solvents, 2-phenyl-2*H*-chromene can be obtained in high yield in the presence of 20 mol% of dibenzylamine. $BmimPF_6$, an acidic ionic liquid, appeared to degrade the starting reagents and produced lower yields (Scheme 1, Table 1). Because $BmimBF_4$ is a liquid at room temperature and is simple to prepare, it was used in the remainder of the study. It is important to note that the product is easily separated from the ionic liquid by simple diethyl ether extraction or by distillation. A variety of salicylaldehyde derivatives and vinyl boronic acids were used to prepare the corresponding 2-substituted 2*H*-chromenes. All the products were obtained in high yields in $BmimBF_4$ (Table 2).

Table 1 Reaction of Salicylaldehyde and Styrenylboronic Acid in the Presence of 20 mol% Dibenzylamine in Ionic Liquids

Entry	Ionic Liquid	Isolated yield (%)
1	$BmimBF_4$	92
2	$EmimBF_4$	91
3	BmimBr	89
4	$BmimPF_6$	7

Although $BmimBF_4$, $EmimBF_4$ and BmimBr are easily prepared,[3b] they are expensive, and recycling becomes important. We found that the ionic liquid solvent could be used repeatedly by dissolving them in acetone and filtering off the solid reaction by-products.[8] Generally, after four cycles product yields were decreased by an average of only 5%. NMR analyses indicated that the ionic liquids are recovered essentially unchanged.

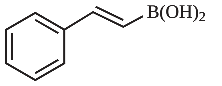
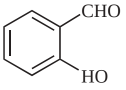
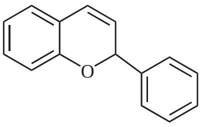
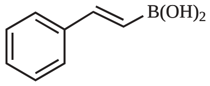
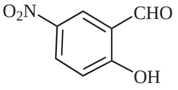
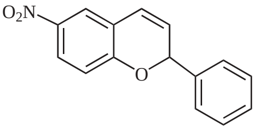
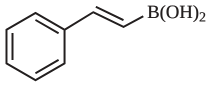
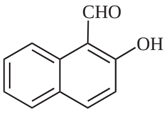
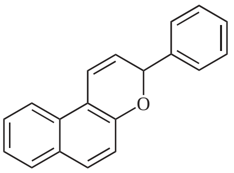
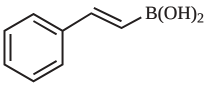
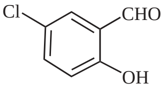
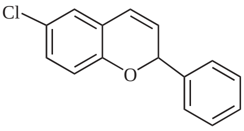
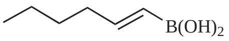
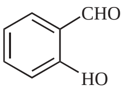
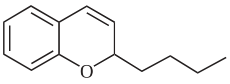
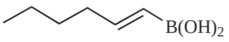
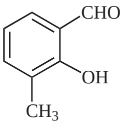
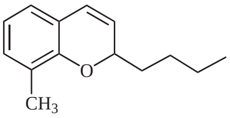
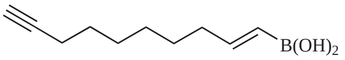
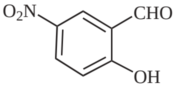
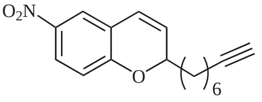
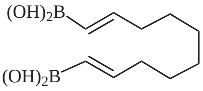
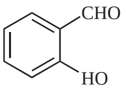
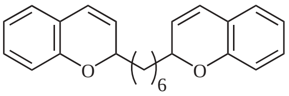
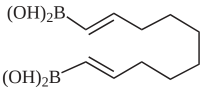
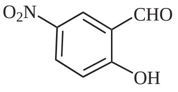
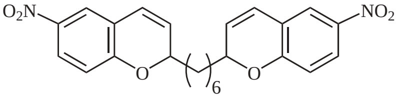
In summary, ionic liquids are excellent as solvents for preparing 2*H*-chromenes. The reactions do not require long reaction times and the isolation procedures are straightforward.



Scheme 1

SYNLETT 2004, No. 12, pp 2194–2196
Advanced online publication: 21.09.2004
DOI: 10.1055/s-2004-832823; Art ID: S01203ST

Table 2 Synthesis of 2*H*-Chromenes from Vinylboronic Acids and *o*-Hydroxyaryl Aldehydes in the Presence of 20 mol% Dibenzylamine in $BmimBF_4$

Vinylboronic acid	Aldehyde	Product[a]	Yield (%)[b]
			92
			91
			90
			88
			94
			87
			91
			88[c]
			87[c]

[a] All products exhibited ^1H NMR and ^{13}C NMR characteristics in accord with assigned structures and literature values (for known compounds). New products were analyzed by C, H, N analysis.

[b] Isolated yields, based on boronic acid.

[c] Two equivalents of aldehyde were utilized.

General Procedure:
o-Hydroxyaryl aldehyde (1 mmol), vinylboronic acid (1 mmol) and dibenzylamine (20 mol%) was added to $BmimBF_4$ (400 mg) and the solution stirred at 80 °C for 3 h. The mixture was then washed with Et_2O (4 × 6 mL), the combined ether extracts concentrated under reduced pressure, and the product purified by silica gel column chromatography.

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(8) After extracting the product from the ionic liquid, the ionic liquid was diluted with acetone; a white solid precipitated and was removed by filtration. The acetone was evaporated under reduced pressure, and the ionic liquid was then reused.