Facile oxidation of flavanones to flavones using [hydroxy(tosyloxy)iodo]benzene in an ionic liquid

Murugan Muthukrishnan,* Pratap S. Patil, Shivaji V. More and Ramesh A. Joshi*

Division of Organic Chemistry: Technology, National Chemical Laboratory, Pune 411008, India. E-mail: mmk@dalton.ncl.res.in

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A method for the oxidation of flavanones to flavones has been developed using [hydroxy(tosyloxy)iodo]benzene (HTIB) in the room-temperature ionic liquid 1,3-di-*n*-butylimidazolium bromide ([bbim]+Br-).

Ionic liquids are an attractive alternative to conventional organic solvents because of their negligible vapour pressure, high thermal stability and reusability. They are non hazardous and non explosive. Organic reactions such as Diels–Alder reaction,¹ Wittig reaction,² Friedel–Crafts reaction,³ Heck reaction,⁴ Suzuki coupling⁵ and many biotransformations⁶ have been successfully carried out in ionic liquids.⁷

Flavones are widespread phenolic compounds of plant origin.8 Flavones are of interest because of their pharmacological activities including antioxidant, anti-inflammatory, antiviral, antineoplastic and anticancer properties.⁹⁻¹¹ The biomimetic oxidation of flavanone to flavone was carried out using a variety of reagents such as thallium(III) acetate, CuCl2-DMSO, DDQ, nickel peroxide and pyrrolidone hydrotribromide in DMSO,¹² which are either hazardous or expensive. Prakash et al.13 reported the utility of hypervalent iodine as an oxidising agent for the conversion of flavanone to flavone. Even though hypervalent iodine-mediated oxidative reactions are mild and efficient, these methods are time-consuming and characterised by low yields and unwanted by-products such as 2-aryl-2,3-dihydrobenzofuran-3-carboxylates and cis-3-methoxy-flavanones. Here, we report the oxidation¹⁴ of flavanones to flavones using [hydroxy(tosyloxy)iodo]benzene (HTIB) in a room-temperature ionic liquid.[†] We obtained flavones in high yields within 2–4 h (Scheme 1).[‡]



To study the general applicability of this simple protocol, flavanones differently substituted at ring A and ring B were successfully oxidised to their corresponding flavones. Good to

Table 1 Oxidation of flavanones in an ionic liquid.

| Product | R, R' | Time/h | Yield ^a (%) |
|---------|----------------------|---------------------|------------------------|
| 2a | R = R' = H | $2(16)^{b}$ | 84 (68) ^b |
| 2b | R = H, R' = 4-Me | 3 | 82 |
| 2c | R = 4-Me, $R' = H$ | 2 | 91 |
| 2d | R = R' = 4-Me | 3 | 84 |
| 2e | R = 4-Cl, R' = 4-Me | 4 | 78 |
| 2f | R = 4-Cl, R' = H | $2(16)^{b}$ | 85 (70) ^b |
| 2g | R = H, R' = 4-Cl | 3 (16) ^b | $74 \ (65)^b$ |
| 2h | R = R' = 4-Cl | $3(16)^{b}$ | $75(75)^{b}$ |
| 2i | $R = H, R' = 3-NO_2$ | 2 | 90 |

^{*a*}Isolated and unoptimised yields. ^{*b*}Time and yield given in parentheses are reported for HTIB oxidation in methanol.^{13(*a*)}

excellent yields were obtained in all cases (Table 1). The products were characterized by IR and NMR spectroscopy.[§] No by-products were detected. To verify the reusability of the ionic liquid, water was completely removed from a used ionic liquid, which was recycled in subsequent reactions. Second and third reactions using the recovered ionic liquid afforded yields similar to those obtained in the first run.

In conclusion, we have developed an efficient methodology for the rapid oxidation of flavanones to flavones using HTIB in the ionic liquid [bbim]⁺Br⁻.

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[§] Spectroscopic data for **2e**: crystalline solid, mp 197–198 °C (lit.,¹⁷ 196 °C). ¹H NMR (200 MHz, CDCl₃) δ: 2.45 (s, 3 H), 6.79 (s, 1H), 7.33 (d, 2 H), 7.50 (q, 2 H), 7.82 (d, 2 H), 8.02 (s, 1 H). ¹³C NMR (75 MHz, CDCl₃) δ: 177.23, 163.92, 154.57, 142.60, 140.22, 133.84, 131.11, 129.84 (2 C), 127.24, 126.27 (2 C), 125.17, 119.77, 106.87, 21.55. Found (%): C, 69.22; H, 3.81. Calc. for C₁₆H₁₁ClO₂ (%): C, 70.99; H, 4.10.

 $^{^\}dagger$ The ionic liquid [bbim]+Br- was prepared according to ref. 15. All the flavanones used in this study were prepared according to the procedures described in ref. 16.

[‡] In a typical experiment, a flavanone was stirred with 2 equiv. of HTIB in 3 ml of [bbim]⁺Br⁻ at 60–70 °C for 2–4 h. The reaction was monitored by TLC. After completion of the reaction, 10 ml of water was added, and the reaction mixture was extracted with dichloromethane. The dichloromethane layer was seperated, washed with water and dried over Na₂SO₄. After filtration, the solvent was removed under reduced pressure to yield a flavone. The flavone thus obtained was further crystallised using petroleum ether in ethyl acetate. We performed few reactions with the ionic liquid [bbim]⁺BF₄⁻, but the yields were good only with [bbim]⁺Br⁻.

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