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Imidazolium salts as specific catalysts for Michael addition to nitroalkanes: a structure–catalyst efficiency relationship

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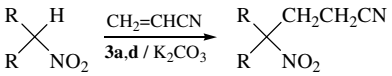
Imidazolium catalyst structures were optimised in relation to the Michael addition of acrylonitrile to secondary nitroalkanes.

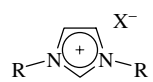
Traditionally, strong bases or their combinations with common phase-transfer reagents are employed as catalysts for the Michael addition to nitroalkanes. For example, potassium carbonate,[1] potassium fluoride,[2] cesium fluoride,[3] alkoxides[4] and amines[5] have been used in catalytic, stoichiometric or excess amounts. In connection with the synthesis of γ-aminobutyric acid, our interest was attracted to the specific reaction of acrylonitrile (or acrylates) with secondary nitroalkanes (2-nitropropane **1** and nitrocyclohexane **2**). Here, the efficiency of a particular catalyst can be easily monitored by measuring a temperature jump after the addition of a catalyst to the mixture of reagents (reaction is strongly exothermic). Evaluation of the traditional catalysts such as DBU, potassium isopropylate, potassium hydroxide–polypropylene glycol has shown some general features of these bases performance.

Really, common to all of these bases is the initiation of side reactions destroying the catalyst. In our practice, the addition of a catalyst (*e.g.* ~1 mol% DBU) to a mixture of **1a** or **1b** and acrylonitrile in acetonitrile as a solvent initiated an exothermal reaction (temperature rise *ca.* 20 °C above room temperature), which subsides after a short time (10–15 min). The addition of a fresh portion of the same catalyst resulted in a new temperature jump. Several repetitions of the procedure produced the same (but diminishing) effect. In a search for more adequate catalysts, we were pleased to find these to be the sterically crowded imidazolium salts–potassium carbonate combination.



1a R = Me
1b R + R = $(CH_2)_5$

2a R = Me
2b R + R = $(CH_2)_5$



3a R = Bu^t, X = Cl
3b R = CH_2COOBu^t, X = Cl
3c R = CH_2COBu^t, X = Br
3d R = $CH_2CH(OH)Bu^t$, X = Br

Scheme 1

The first experiments have shown that stirring the mixture of reagents containing acrylonitrile, nitroalkane (**1a** or **1b**), potassium carbonate and the solvent (acetonitrile) for a long time (1–2 h) resulted in no temperature change and no product formation. However, the addition of a small quantity of sterically crowded imidazolium salt **3a** produced an almost immediate temperature rise (up to the boiling point of the solvent). It is essential to control the temperature at the early stage to prevent an explosion-like process. If at the exothermal stage the temperature is controlled by cooling at 40–50 °C, the reaction is complete after additionally stirring for 1 h from the moment when the reaction subsides.†

A comparison of the thermal effects produced by the 'classical' phase-transfer reagent Bu^n_4NBr and imidazolium salt **3a** indicates that the efficiency of catalyst **3a** is incomparably higher. Moreover, besides a modest temperature rise, Bu^n_4NBr stops functioning short time after addition when most of the reagents are still unchanged. Dealkylation–neutralisation may be responsible for catalyst deactivation. Therefore, the assumption that imidazolium salts act only as phase-transfer reagents for potassium carbonate may be discarded.

The properties of other lipophilic imidazolium derivatives **3b** and **3c** support this argument.‡ Despite the similarities in the steric bulk with salt **3a**, diester **3b** and diketone **3c** are absolutely inactive as catalysts for the Michael addition of acrylonitrile to nitroalkanes **1a**,**b**.§ Moreover, **3b**,**c** block the activity of catalyst **3a**, *i.e.*, they act as effective inhibitors of catalyst **3a** when used together.

The reasons of this inhibitory activity of compounds **3b**,**c** may be the ionisation at the α-carbon atoms to the positively charged imidazolium ring with the formation of a neutral

† *Syntheses of addition products* **2a** *and* **2b**. Salt **3a** (0.5 g, 2.3 mmol) was added to the mixture of **1a** (13.5 ml, 0.15 mol), acrylonitrile (10 ml, 0.15 mol) and potassium carbonate (1 g, 7.2 mmol) in acetonitrile (10 ml), and the mixture was stirred with temperature control. After the completion of heat evolution and stirring for 1 h, filtration and rotary evaporation gave product **2a** as an oil, bp 101–102 °C (1 Torr), yield 85%. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.6 (s, 6H), 2.26 and 2.60 (2t, 2×2H, *J* 7 Hz).

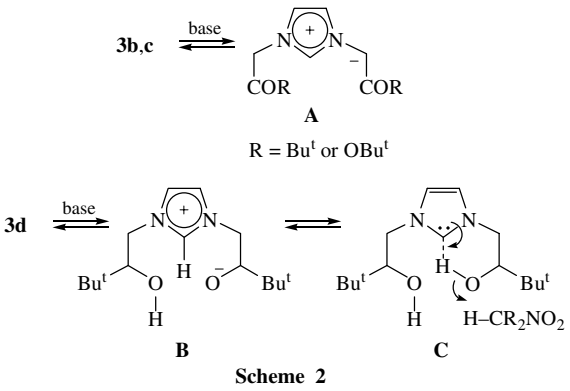
The same procedure was used for the synthesis of **2b** as a low melting solid, mp 42 °C, yield 90%. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.5–2.5 (m, 14H).

3a: ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.63 (s, 18H), 8.15 (s, 2H), 9.45 (s, 1H).

‡ *Imidazolium salts* **3b** *and* **3c**. The mixture of equimolar quantities of imidazole, *tert*-butyl chloroacetate and potassium carbonate was stirred in acetonitrile at 60 °C for 1 h. Fresh equivalents of the base and chloro ester were added and after heating at 90 °C for 2 h filtration and rotary evaporation left the product (glassy residue), which after crystallisation from acetonitrile–ethyl acetate gave imidazolium salt **3b**, yield 60%, mp 125–127°C. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.45 (s, 18H), 5.30 (s, 4H), 7.84 (s, 2H), 9.4 (s, 1H).

For the synthesis of salt **3c**, a one-stage procedure was used with one equivalent of imidazole and two equivalents of both bromopinacolone and potassium carbonate in acetonitrile (cooling at the exothermal stage and heating at 50 °C for 2 h), yield 60%. ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 1.23 (s, 18H), 5.76 (s, 4H), 7.72 (s, 2H), 9.20 (s, 1H).

§ *Michael additions.* All experiments were conducted in a round bottom flask with an overhead stirrer (1500 rpm).



Scheme 2

zwitterionic structure (Scheme 2, **A**).¶ This or a similar bipolar species could block the potassium carbonate surface thus preventing the catalytic action of salt **3a**.

As an argument in favour of this hypothesis, the extraordinarily high catalytic activity of reduced salt **3d** can be considered. In this compound, which is structurally similar to starting keto analogue **3c**, the acidity of methylene hydrogens is diminished but a new evidently active function is formed: a hydroxy group. Another interesting feature of this hydroxy salt **3d** in addition to its high catalytic activity is the ability to create deep blue colour of the reaction mixture in contrast to catalyst **3a** giving a yellow colour. This yellow colour is typical of reactions with the participation of nitro anions. At the same time, a blue colour is typical of monomeric nitroso species, anion radicals and some charge-transfer complexes. At present, it is unclear either this blue colour results from some side reactions or the formation of reactive intermediates.

The reaction pathway **3d** → **B** → **C**, as shown in Scheme 2, with the participation of stabilised carbenoic form **C** deserves consideration as an explanation of the greatly enhanced reactivity of salt **3d** as a catalyst. The equilibrium concentration of form **C**, as well as its ability to deprotonate a nitro compound molecule, seems to be increased due to stabilisation of this form.

¶ *Reduction of salt* **3c**. To a solution of salt **3c** (2.7 g, 7.8 mmol) in water (30 ml) sodium borohydride (0.7 g, 18.5 mmol) was added in portions with a small exothermal effect (room temperature to 30 °C) and the precipitation of borohydride salt of the starting imidazolium. This suspension when gradually heated to 80 °C gave with foaming a clear solution of intermediate borohydride complex. Finally, addition of aqueous HBr resulted in hydrogen evolution and the formation of salt **3d** as a mixture of *meso* and *rac* isomers (1:1). Evaporation of this solution and crystallisation from isopropanol–ethyl acetate gave hydroxy imidazolium salt **3d**, mp 190–194 °C (1.5 g, yield 55%). ^{1}H NMR (250 MHz, [$^2H_6$]DMSO) δ: 0.92 (s, 18H), 3.4–3.9 (m, 2H), 4.50 (d, 2H, *J* 7 Hz), 5.20 (d, 2H, *J* 7 Hz), 7.80 (s, 2H), 9.20 (s, 1H).

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