

Perfluorinated sulfonic acid resin (Nafion-H) catalysed Ritter reaction of benzyl alcohols

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Perfluorinated sulfonic acid resin (Nafion-H) catalyst found to be effective in promoting the Ritter reaction of benzyl alcohols with nitriles such as acetonitrile, acrylonitrile and benzonitrile to give the corresponding *N*-benzylamides.

Keywords: solid superacid, Nafion-H, Ritter reaction, benzyl alcohols, *N*-benzylamides

The application of polymer supported reagents in organic synthesis such as acidic ion exchange resins and ionomer membranes as strong acid catalysts is well-known.² Nafion-H,³ a perfluorinated sulfonic acid resin has been used as a superacidic catalyst to carry out a variety of acid catalysed transformations.

We have utilised Nafion-H as a versatile acid catalyst and this has been reviewed.³ Thus, we have found that Nafion-H catalyst is effective in a wide range of liquid and gas phase systems, including electrophilic aromatic substitution transalkylation, and condensation reactions.⁴

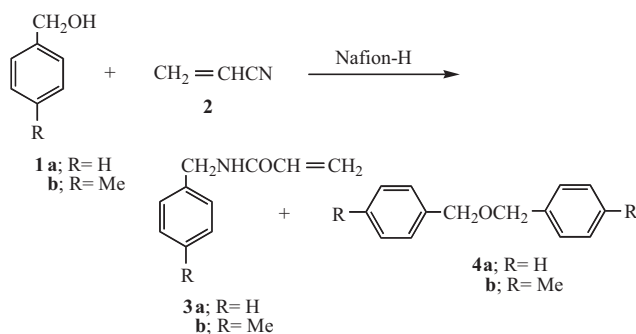
Nitrogen functionality can readily be introduced by the Ritter reaction which involves treatment of alkenes or alcohols with nitriles in the presence of sulfuric acid.⁵ The mechanism involves electrophilic alkylation of nitriles. Several modifications of the Ritter type reaction have appeared in the literature⁶ which either start from alkyl halides or alkanes to generate the potential electrophilic alkylation species. It is often carried out with a large excess of protic acid, such as concentrated sulfuric acid² or trifluoromethane sulfonic anhydride.^{5c} Although these procedures are usually very effective, the methodology is frequently tedious and the reaction conditions are generally quite critical. The reaction requires either prolonged periods of standing or elevated temperatures for completion. In addition, the environmental difficulties that arise from using a large excess of acid are serious problems. Thus there is substantial interest in developing an efficient and convenient procedure for the Ritter reaction. Prompted by the strongly acidic nature of Nafion-H catalyst, we now report the mild Nafion-H catalysed reactions of benzyl alcohols with nitriles to obtain the corresponding *N*-benzyl amides.

Results and discussion

The attempted condensation reaction of 4-methylbenzyl alcohol (**1b**) with 15 equiv. of acrylonitrile (**2**), performed under refluxing for 36 h in the presence of 30 wt% Nafion-H, failed. Only starting material was recovered. However, when the reaction was performed at 100°C for 6 h in sealed

tube, the desired product, *N*-(4-methylbenzyl)acrylamide (**3b**) was obtained in 39% yield along with 4-methylbenzyl ether (**4b**) in 41% yield (Table 1). When the reaction time was increased to 24 h and the temperature raised to 120°C the yield of **3b** increased to 75%. Product **3b** was isolated simply by filtering the hot reaction mixture and distilling off the unreacted acrylonitrile. The reaction was very clean. The amount of catalyst required, as a function of the amount of 4-methylbenzyl alcohol (**1b**), was between 10 and 30 wt%. Optimum yields of amide **3b** were obtained with 30 wt% of catalyst. The use of 10 wt% of catalyst gave lower yields. Similar result was obtained in the reaction of benzyl alcohol (**1a**) with acrylonitrile to afford *N*-benzylacrylamide (**3a**) in 56% yield.

The formation of 4-methylbenzyl ether (**4b**) can be expected to be attributed to the self-condensation reaction of 4-methylbenzyl alcohol (**1b**). In fact, treatment of **1b** in diethylene glycol dimethyl ether in the presence of Nafion-H for 6 h under the conditions described above afforded 4-methylbenzyl ether (**4b**) in quantitative yield. Thus comparing the reaction products as shown in Table 1, runs 3 and 4, the 4-methylbenzyl cation generated from the 4-methylbenzyl ether (**4b**) might react with acrylonitrile in a Ritter reaction under these conditions to form *N*-(4-methylbenzyl)acrylamide (**3b**). In fact, the reaction of



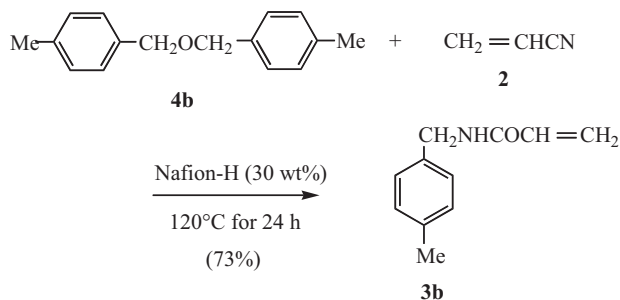
Scheme 1

Table 1 Ritter reaction of benzyl alcohols **1** with acrylonitrile **2**^a

Run	Benzyl alcohol	Temp./°C	Time/h	Yield/% ^b	
				3	4
1	1b	100	6	39	41
2	1b	100	24	49	36
3	1b	120	6	43	38
4	1b	120	24	90 (75) ^c	<1
5	1a	120	24	67 (56) ^c	31

^aReaction conditions: [Benzyl alcohol **1**]/[acrylonitrile **2**] = 1:15; Nafion-H: 30 wt%; ^bYields were determined by GLC analysis. ^cIsolated yields are shown in parenthesis.

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4-methyldibenzyl ether (**4b**) with acrylonitrile in the presence of 30 wt% Nafion-H under the same conditions as those used with 4-methylbenzyl alcohol (**1b**) afforded *N*-(4-methylbenzyl)acrylamide (**3b**) in 73% yield (Scheme 2).

As shown in Table 2, the present method gives good yields, and the products are easily isolated. No acid-catalysed polymerisation of acrylonitrile was observed under the reaction conditions in contrast to the protic acid (CF₃SO₃H) or Lewis acid Sc(OTf)₂ catalysed Ritter reaction. Thus, the Ritter reaction of 4-methylbenzyl alcohol (**1b**) with acrylonitrile in the presence of CF₃SO₃H or Sc(OTf)₂ afforded *N*-(4-methylbenzyl)acrylamide (**3b**) in only 30 and 5% yields, respectively, along with a large amount of intractable mixture of products. Oi *et al.* reported⁷ the synthesis of *N*-substituted acrylamide by the reaction of benzyl alcohol with acrylonitrile in the presence of cationic palladium(II) catalyst, Pd(CH₃CN)₂(PPh₃)₂(BF₄)₂. Reactive systems like *tert*-butyl alcohol gave corresponding amides in 45% yield. The reaction, however, did not occur with alcohols such as benzyl alcohol or *iso*-propyl alcohol.

In conclusion, the major advantage in the above discussed reactions with Nafion-H in the simple work-up procedure, wherein the product is isolated by filtration of the catalyst followed by evaporation. Furthermore, the ready regeneration of the catalyst without the loss of catalytic activity offers an advantage over previously reported methods.

Experimental

¹H NMR spectra were recorded at 300 MHz on a Nippon Denshi JEOL FT-300 NMR spectrometer in deuteriochloroform with Me₄Si

as an internal reference. IR spectra were measured as KBr pellets on a Nippon Denshi JIR-AQ20M spectrometer. Mass spectra were obtained on a Nippon Denshi JMS-01SA-2 spectrometer at 75 eV using a direct-inlet system. GLC analysis was carried out by Shimadzu gas chromatograph, GC-14A (conditions: Silicone OV-1, 2 m; programmed temperature rise, 12°C/min; carrier gas nitrogen, 25 cm³/min.).

Materials

Nafion-H catalyst was prepared from commercially available (Du Pont) Nafion-K resin, as previously described.³

General procedure for the Nafion-H catalysed Ritter reaction of nitriles with benzyl alcohols

Typical procedure. A mixture of benzyl alcohol (**1**) (5 mmol) and Nafion-H (200 mg, 30 wt%) in acrylonitrile (**2**) (4 g, 75 mmol) was heated in the Pyrex sealed tube at 120°C till completion of the reaction, as monitored by GLC analysis (OV 101 column) (reaction time listed in Table 1). The solid resin-sulfonic acid was then filtered and the solvent evaporated. The crude product was washed with a small amount of hexane (10 cm³) to give the respective amides. The yields are given in Table 2.

N-Benzylacrylamide (**3a**): White solid, m.p. 110–111°C (lit.⁸ m.p. 109–110°C); δ_H(CDCl₃): 4.47 (2H, d, *J* = 5.4 Hz, CH₂), 5.68 (1H, d, *J* = 10 Hz, =CH_a), 6.10 (1H, broad s, NH), 6.13 (1H, dd, *J* = 10, 14 Hz, CH_c=CH₂), 6.31 (1H, d, *J* = 14 Hz, =CH_b), 7.2–7.4 (5H, m, ArH).

N-(4-Methylbenzyl)acrylamide (**3b**): White solid, m.p. 68–69°C (lit.⁹ m.p. 68–69°C); δ_H(CDCl₃): 2.31 (3H, s, Me), 4.46 (2H, d, *J* = 5.4 Hz, CH₂), 5.68 (1H, d, *J* = 10 Hz, =CH_a), 5.90 (1H, broad s, NH), 6.12 (1H, dd, *J* = 10, 14 Hz, CH_c=CH₂), 6.32 (1H, d, *J* = 14 Hz, =CH_b), 7.24 (2H, d, *J* = 8 Hz, ArH), 7.12–7.20 (4H, m, ArH).

N-Benzylacetamide (**5a**): White solid, m.p. 61–62°C (lit.^{5d} m.p. 60–62°C).

N-(4-Methylbenzyl)acetamide (**5b**): White solid, m.p. 114–116°C (lit.^{5d} m.p. 115–116°C).

N-(4-Methylbenzyl)benzamide (**6a**): White solid, m.p. 137–138°C (lit.¹⁰ m.p. 137°C); δ_H(CDCl₃): 2.34 (3H, s, Me), 3.60 (2H, s, CH₂), 4.59 (2H, d, *J* = 5.4 Hz, CH₂), 6.48 (1H, broad s, NH), 7.14–7.79 (9H, m, ArH).

N-(4-Methylbenzyl)-4-methylbenzamide (**6b**): White solid, m.p. 165–166°C (lit.¹¹ m.p. 164–166°C); δ_H(CDCl₃): 2.34 (3H, s, Me), 2.38 (3H, s, Me), 4.57 (2H, d, *J* = 5.4 Hz, CH₂), 6.43 (1H, broad s, NH), 7.01–7.7 (8H, m, ArH).

Preparation of 4-methylbenzyl ether (**4b**)

A mixture of 4-methylbenzyl alcohol (6.1 g, 50 mmol) and NaH (4.0 g, 100 mmol, 60%) in dry tetrahydrofuran (THF) (10 cm³) and dimethylformamide (DMF) was heated at reflux for 1 h under N₂. Then a solution of 4-methylbenzyl chloride (7.1 g, 5.56 mmol) in THF (10 cm³) was added at room temperature and the mixture heated

Table 2 Ritter reaction of benzyl alcohols with nitriles^a

Run	Benzyl alcohols	Nitriles	Product	Yield/% ^b
1	1a	CH ₃ CN		5a (82)
2	1a	CH ₂ =CHCN		3a (56)
3	1b	CH ₃ CN		5b (86)
4	1b	CH ₂ =CHCN		3b (75)
5	1b			6a (81)
6	1b			6b (62)

^aReaction conditions: [benzyl alcohol 1]/[nitrile] = 1:15; Nafion-H 30 wt%. ^bIsolated yields are shown.

under reflux for an additional 3 h. After cooling the reaction mixture to room temperature, it was acidified with 1 N HCl (10 cm³) and extracted with CH₂Cl₂ (100 cm³ × 2). The combined extracts were washed with water (50 cm³ × 2), dried (Na₂SO₄) and condensed under reduced pressure to give a colourless solid. Recrystallisation from hexane afforded **4b** (9.0 g, 80%) as colourless prisms, m.p. 61–62°C (lit.¹² m.p. 60–62°C); δ_H(CDCl₃): 2.34 (6H, s, Me), 4.49 (4H, s, CH₂), 7.14 (2H, d, J = 8 Hz, ArH), 7.24 (2H, d, J = 8 Hz, ArH).

Nafion-H catalysed Ritter reaction of acrylonitrile (2) with 4-methylbenzyl ether (4b)

A mixture of 4-methylbenzyl ether (**4b**) (565 mg, 2.5 mmol) and Nafion-H (30 wt%, 200 mg) in acrylonitrile (**2**) (4 g, 75 mmol) was heated in the pyrex sealed tube at 120–125°C for 24 h. The solid resin-sulfonic acid was then filtered and the solvent evaporated. The crude product was washed with a small amount of hexane (10 cm³) to give *N*-(4-methylbenzyl)acrylamide (**3b**) (640 mg, 73%) as a white solid.

Sc(OTf)₃ catalysed Ritter reaction of acrylonitrile (2) with 4-methylbenzyl alcohol (1b)

To a mixture of 4-methylbenzyl alcohol (**1b**) (610 mg, 5 mmol) and acrylonitrile (**2**) (4 g, 75 mmol) was added Sc(OTf)₃ (492 mg, 1 mmol) at room temperature. After the reaction mixture was stirred at room temperature for 6 h, it was quenched with ice-water and extracted with CH₂Cl₂ (10 cm³ × 2). The combined extracts were washed with water (5 cm³ × 2), dried (Na₂SO₄) and condensed under reduced pressure. The crude product was washed with a small amount of hexane (5 cm³) to give *N*-(4-methylbenzyl)acrylamide (**3b**) (44 mg, 5%) as a white solid.

Similarly, when the same reaction was carried out in the presence of CF₃SO₃H, *N*-(4-methylbenzyl)acrylamide (**3b**) was obtained in 30% yield.

Regeneration of Nafion-H catalyst

The spent catalyst was washed several times with acetone and deionised water, then it was dried at 105°C for 10 h. The activity of the regenerated catalyst was the same as that of fresh catalyst.

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