



Research Article

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One-Pot, Four-component Synthesis of Oxime ethers from Cinnamaldehyde, Crotonaldehyde, Hydroxylamine Salt, Potassium carbonate and Alkyl halides

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ABSTRACT

Oxime ethers were synthesised in a one-pot, four-component reaction from cinnamaldehyde crotonaldehyde, hydroxylamine hydrochloride, anhydrous sodium carbonate and some alkyl halides. Alkyl halides also served as the solvent of the reaction. The reactions were completed in about 1 hour with yields of 57 to 84%.

Key words: Oxime ether, One-pot synthesis, four-component system, aldoximes

INTRODUCTION

The importance of oxime ethers in medicine, agriculture and organic synthesis is emphasised by the numerous references in literature [1-4]. The usual method for the preparation of oxime ethers involves a two-step reaction in which the first step is the reaction of aldehyde or ketone with hydroxylamine in the presence of a base to give aldoximes or ketoximes which are subsequently, in the second step, reacted with alkyl halides in the presence of a base such as sodium alkoxides, NaH, K₂CO₃, KOH, NaHCO₃ etc [1, 3]; in solvents like acetone, DMSO, DMF, THF *etc* to give the corresponding oxime ethers. We have previously reported a one-pot synthesis of oxime ethers from crotonaldehyde and cinnamaldehyde, hydroxylamine hydrochloride, anhydrous sodium carbonate and alkyl halides in Tetrahydrofuran. We present a more efficient one-pot and four-component procedure in which the alkyl halides served as the solvent of reaction with yields between 57- 84%.

EXPERIMENTAL SECTION

General

The infrared spectra were recorded on Perkin-Elmer Model 1310 spectrophotometer. The ¹H and ¹³C-NMR spectra of **a**, **b**, **e** and **f** were run at 250 MHz while ¹H, ¹³C, ¹³C-DEPT, ¹H-¹H coupling correlation, ¹H-¹³C ¹J correlations were run at 400 MHz for products **c** and **d**, the *O*-alkyl cinnamaldoxime ethers, using deuterated chloroform (or carbontetrachloride) as solvent and tetramethylsilane (TMS) as internal standard. The chemical shifts are given on the δ (ppm) scale. Elemental analysis was determined on a Yanaco CHN Corder Elemental analyzer. Cinnamaldehyde, crotonaldehyde, benzaldehyde, *p*- methoxybenzaldehyde and hydroxylamine hydrochloride were purchased from Aldrich. Product, **e**, was purified by column chromatography which was performed using silica gel 60 (230–400 mesh, Merck). All the liquid oxime ethers were purified by redistillation under reduced pressure. All chemical compounds used were, where possible, redistilled before use but all solid reagents were used with melting points uncorrected.

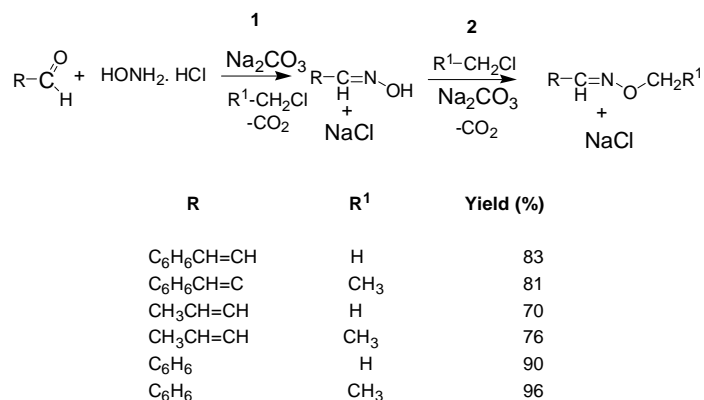
Typical procedure for preparation of oxime ethers:

Excess anhydrous Sodium carbonate (5.6 mMol) was added to a mixture of hydroxyl amine hydrochloride (3.60 mMol), redistilled cinnamaldehyde (3.60 mMol) in redistilled ethyl bromide (100mL). The resulting mixture was allowed to reflux for 1 hour. The reaction was monitored by TLC and IR. The mixture was allowed to cool to room temperature and poured into cold water (100mL). The product is extracted from the mixture trice with 25mL of

chloroform, washed once with water and the chloroform evaporated off under vacuum and the oxime ether is purified by vacuum distillation.

RESULTS AND DISCUSSION

The reactions were carried out by adding 2.5 equivalents of potassium carbonate to the aldehyde and hydroxylamine hydrochloride in ethyl bromide (100mL) without the use of a separate solvent since the alkyl halide also serves as the solvent (Scheme 1). The product, **e**, was passed through a column of silica gel with ethyl acetate/hexane (1:2) mixture to eliminate traces of nitron; while **a-d** and **f** were redistilled under reduced pressure.



Scheme 1

It is easy to monitor and confirm the transformations as the reaction proceeds from the aldehydes through the oximes to the corresponding oxime ethers. The absence of the C=O band of the carbonyl compounds (Cinnamaldehyde and crotonaldehyde) and the existence of a broad =N-OH band centred on 3166 cm⁻¹ in the IR spectrum of the oximes is the evidence the aldehydes were transformed into the oximes. The -OH proton appears as a broad singlet at around 13.0 ppm in the ¹H-NMR spectrum. This peak disappears upon alkylation or acylation of the oxime.

3-Phenylpropenal *o*-ethyl oxime (**a**)

Oil, b.p. 100-102 °C (10 mmHg) 5.55 cm³ (78%), d 0.994g/mL, IR(cm⁻¹, neat): 2820-2920, 1613(C=N), 1030 (N-O); ¹H-nmr (CDCl₃): δ 1.25 (t, *J* = 12.5Hz, 3H, Me), 4.05-4.20(q, *J* = 12.5Hz, 2H, CH₂O), 6.7-6.8 (m, 2H, CH=CH), 7.1-7.4 (m, 5H, ArH), 7.8 (d, *J* = 12.5Hz, 1H, N=CH). ¹³C-nmr (CDCl₃): δ 150.5, 138.0, 136.0, 129.0, 127.5, 127.0, 122.0, 70.0, 16.0. Anal. Calc. (%) for C₁₁H₁₃NO: C, 75.40; H, 7.48; N, 7.99; O, 9.13. Found: C, 75.60; H, 7.20, N, 7.54; O, 9.20.

N-Methoxy-4-phenyl-1-azabutadiene or 3-Phenylpropenal *O*-methyl oxime ether (**b**)

Oil, b.p. 103 °C (10 mmHg), Yield: 1.75g (70%), d 0.994g/mL, IR (cm⁻¹, neat): 2820-2920, 1613, 1030; ¹H-nmr (CDCl₃): δ 4.1 (s, 3H, MeO), 6.8-6.9 (m, 2H, CH=CH), 7.3-7.5(m, 5H, Ar-H), 7.9 (d, *J* = 10.0Hz, 1H, N=CH), ¹³C-nmr (CDCl₃): δ 150.5, 140.0, 138.5, 129.0, 128.0, 127.0, 122.0, 63.0. Anal. Calc. (%) for C₁₀H₁₁NO: C, 74.51; H, 6.88; N, 8.69; O, 9.93. Found: C, 74.20; H, 6.99; N, 8.88; O, 9.61.

But-2-enal *O*-methyl oxime (**c**).

Oil, b.p. 103 °C (10 mmHg), d 0.894g/mL, Yield: 2.8mL 77.8%; IR (cm⁻¹, neat): 2820-2920, 1613 (C=N), 1030; ¹H-NMR (CDCl₃): δ 1.4 (dd, *J*₁ = 7Hz, *J*₂ = 1Hz, 3H, Me); 4.0 (s, 3H, MeO-) 5.4-5.9 (m, 2H, CH=CH); 7.9 (d, *J* = 7Hz, 1H, N=CH); ¹³C-NMR (CDCl₃) δ 163.0, 137.0, 124.0, 55.0, 17.0; Anal. Calc (%) for C₅H₉NO: C, 60.58; H, 9.15; N, 14.13, O, 16.14. Found: C, 60.42; H, 9.11; N, 14.08; O, 16.50.

But-2-enal *O*-ethyl oxime (**d**).

Oil, b.p. 107-110 °C (12 mmHg); Yield: 1.30 mL (78%), d 0.901g/mL; IR (cm⁻¹): 2820-2920, 1613, 1030; ¹H-NMR (CDCl₃): δ 1.4 (m, 6H, Me); 4.1, (q, *J* = 8Hz, 2H, CH₂O); 5.5-5.8 (m, 2H, CH=CH); 7.9 (d, *J* = 7Hz, 1H, N=CH); ¹³C-NMR (CDCl₃) δ 164.0, 137.0, 124.0, 64.0, 17.0, 12.0. Anal. Calc. (%) for C₆H₁₁NO: C, 63.68; H, 9.80; N, 12.38; O, 14.14. Found: C, 63.40; H, 9.30; N, 12.20; O, 14.10.

Benzyl cinnamaldoxime ether (**e**)

Yield: 6.8g, 84%. m.p. 101-102° C. IR (cm⁻¹ CHCl₃ film): 2820-2920, 1613, 1030. ¹H-NMR (CCl₄): δ 4.80(s, 2H, CH₂), 6.7-6.8(m, 2H, CH=CH), 7.14-7.50(m, 10H, Ar-H), 7.80 (*J* = 12.5Hz, d, 1H, N=CH). ¹³C-nmr (CDCl₃)

δ :163.7, 140.9, 140.1, 134.9, 128.7, 128.4, 127.7, 127.4, 127.3, 126.2, 120.6,76.8. Anal. Calc. (%) for C₁₆H₁₅NO: C, 80.98; H, 6.37; N, 5.90; O, 6.74. Found: 80.79; H, 6.31; N, 5.92; O, 6.77.

Benzyl crotonaldoxime ether (f)

Yield: 57%, Oil (b.p. 114°C, 12 mmHg). IR (cm⁻¹, neat):2820-2925, 1615, 1035. ¹H-nmr (CDCl₃): δ 1.71 (m, 3H, 5.0-5.7 (m, 2H, CH=CH), 4.80 (s, 2H, CH₂), 7.14-7.50(m, 5H, Ar-H), 7.80 (*J* = 12.5Hz, d, 1H, N=CH). ¹³C-NMR (CDCl₃): δ 163.7, 140.90, 137.00, 127.30, 127.30, 128.70,128.7, 127.40, 124.20, 17.50. Anal.Cal. (%) for C₁₁H₁₃NO: C, 75.48; H, 7.48; N, 7.99; O, 9.13. Found: C, 75.33; H, 7.44; N, 7.83; O, 9.10.

CONCLUSION

The synthesis of O-alkylated α , β -unsaturated oxime ethers derived from cinnamaldehyde and crotonaldehyde has been achieved. The structures and configurations of these compounds were confirmed with the aid of IR, ¹H-NMR, ¹³C-NMR as well as elemental analysis.

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