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Silver Oxide-Mediated Oxime Ether Synthesis

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ABSTRACT

A series of oxime ethers were prepared from (E, E)-cinnamaldoxime, crotonaldoxime, (syn)-benzaldoxime and p-methoxybenzaldoxime by reaction with methyl iodide, ethyl bromide and benzyl chloride with silver oxide as base and catalyst. Excellent yields of the corresponding (E, Z isomers) ethers were obtained without the formation of nitrones or the use of undesirable solvents.

Keywords: silver oxide; oxime ether; catalysis; reactive solvent

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INTRODUCTION

The usual method for the preparation of oxime ethers is the reaction of aldehydes and ketones with alkyl halides in the presence of a base such as sodium alkoxides, NaH, K_2CO_3, KOH, $NaHCO_3$ etc [1, 3], in solvents like acetone, DMSO, DMF *etc*. These methods are usually complicated by the accompanying formation of nitrones as a side product [2-4]. We present a procedure in which the alkyl or aryl halide, aside from being the oximation agent, also serves as the solvent and the excess halide can be recovered from the reaction mixture by distillation and reused for further oxime alkylation/arylation or other uses. The silver oxide is also recoverable as silver metal which can be converted to silver nitrate. Another advantage of this procedure is that no nitrones are formed [2-4].

MATERIALS AND METHODS

3. Experimental

3.1. General

The infrared spectra were recorded on Perkin-Elmer Model 1310 spectrophotometer. The ^{1}H- and ^{13}C-NMR spectra of **a, b, e, f** and **g** were run at 250 MHz while ^{1}H, ^{13}C, ^{13}C-DEPT, ^{1}H-^{1}H coupling correlation, ^{1}H- ^{13}C ^{1}J correlations were run at 400 MHz for products **c** and **d,** the *O*-alkyl cinnamaldoxime ethers, using deuterated chloroform (or carbontetrachloride) in some cases as solvent and tetramethylsilane (TMS) as internal standard and 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. Column chromatography was performed using silica gel 60 (230–400 mesh, Merck). All the 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.

3.2. General Procedure for the Preparation of Oxime Ethers

Silver oxide (0.017mol) was added in small portions to a cooled solution of aldoxime ether (0.016 mol) in alkyl bromide (50 mL). The mixture was heated at reflux for 10 h. The resulting solution was filtered hot and the residue washed three times with chloroform (10 mL each time).

The filtrate was concentrated by distillation. The residue was vacuum-distilled to give the oxime ether.

3.3. Typical procedure: 3-Phenylpropenal o-ethyl oxime (**d**)

Silver oxide (3.94 g, 0.017mol) was added in small portions to a cooled solution of cinnamaldoxime (5.00 g, 0.016 mol) in ethyl bromide (50 mL). The mixture was heated at reflux for 12 h. The resulting mixture was filtered while still hot and the residue washed thrice with chloroform (10 mL), the filtrate was concentrated by distillation and the residue distilled under vacuum. Oil, b.p. 100-102 ºC (10 mmHg) 5.55 cm^3 (78%), d 0.994g/mL, IR(cm^{-1} , neat): 2820-2920, 1613, 1030; ^{1}H-nmr ($CDCl_3$): δ 1.25 (t, J = 12.5Hz, 3H, Me), 4.05-4.20(q, J = 12.5Hz, 2H, CH_2O), 6.7-6.8 (m, 2H, CH=CH), 7.1-7.4 (m, 5H, ArH), 7.8 (d, J = 12.5Hz, 1H, N=CH). ^{13}C-nmr ($CDCl_3$):δ 150.5,138.0, 136.0,129.0, 127.5,127.0,122.0, 70.0, 16.0. Anal. Calc. (%) for $C_{11}H_{13}NO$: 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.

3.4. Preparation of Silver Oxide

Dilute sodium hydroxide solution (0.2 mol/dm^3) was added gradually to 10% aqueous silver nitrate solution until the silver nitrate solution is alkaline. The product was washed thoroughly with distilled water.

But-2-enal O-methyl oxime (**a**). Oil, b.p. 103 ºC (10 mmHg), d 0.894g/mL, Yield: 3.6mL 73%; IR (cm^{-1} , neat): 2820-2920, 1613 (C=N), 1030; ^{1}H-NMR ($CDCl_3$): 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); ^{13}C-NMR ($CDCl_3$) δ 163.0, 137.0, 124.0, 55.0, 17.0; Anal. Calc (%) for C_5H_9NO: 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 (**b**). Oil, b.p. 107-110 ºC (12 mmHg); Yield: 3.20 mL (68%), d 0.901g/mL; IR (cm^{-1}): 2820-2920, 1613, 1030; ^{1}H-NMR ($CDCl_3$): δ 1.4 (m, 6H, Me); 4.1, (q, *J* = 8Hz, 2H, CH_2O); 5.5-5.8 (m, 2H, CH=CH); 7.9 (d, *J* = 7Hz, 1H, N=CH); ^{13}C-NMR ($CDCl_3$) δ164.0, 137.0, 124.0, 64.0, 17.0, 12.0. Anal. Calc. (%) for $C_6H_{11}NO$: 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.

3-Phenylpropenal O-methyl oxime ether (**c**). Oil, b.p. 103 ºC (10 mmHg), Yield: 3.60 cm^3 (70%), d 0.994g/mL, IR (cm^{-1} , neat): 2820-2920, 1613, 1030; ^{1}H-nmr ($CDCl_3$): 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),. ^{13}C-nmr ($CDCl_3$): δ 150.5,140.0,138.5,129.0, 128.0, 127.0, 122.0, 63.0. Anal Calc. (%) for $C_{10}H_{11}NO$: 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.

3-Phenylpropenal o-ethyl oxime **(d).** Oil, b.p. 100-102 ºC (10 mmHg). Yield: 5.55 cm^3 (78%), d 0.994g/mL, IR (cm^{-1} , neat): 2820-2920, 1613, 1030; ^{1}H-nmr ($CDCl_3$): δ 1.25 (t, J = 12.5Hz, 3H, Me), 4.05-4.20(q, J = 12.5Hz, 2H, CH_2O), 6.7-6.8 (m, 2H, CH=CH), 7.1-7.4 (m, 5H, ArH), 7.8 (d, J = 12.5Hz, 1H, N=CH). ^{13}C-nmr ($CDCl_3$):δ 150.5,138.0, 136.0,129.0, 127.5,127.0,122.0,

70.0, 16.0. Anal. Calc. (%) for $C_{11}H_{13}NO$: 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.

O-Ethylbenzaldoxime (**e**).Oil, b.p. 64 ºC/6 mmHg, Yield: 2.6 g, 46%, d 0.891g/mL, IR(cm^{-1}, neat): 1030,1620 (C=N-); 2925; H^1NMR ($CDCl_3$): δ8.0 (s, 1H, N=CH); 7.10-7.60 (m, 5H, ArH); 3.9-4.4 (q, J = 12.5Hz, 2H, CH_2O); 1.05-1.2 (t,12.5, 3H, Me); ^{13}C-nmr ($CDCl_3$) δ 163.0, 131.0, 129.0, 128.0,131.0, 64.0, 12.0. Anal. Calc. (%) for: $C_9H_{11}NO$: C, 72.46; H, 7.43; N, 9.39; O, 10.72. Found: C, 72.10; H, 7.10; N, 9.45; H, 11.10.

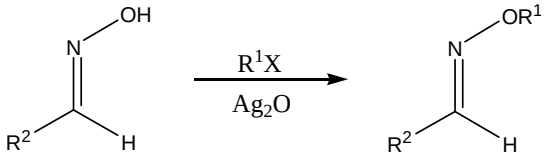
O-Ethyl-4-methoxybenzaldoxime (**f**). Oil, b.p.150 ºC/12mmHg, Yield: 68.7%, 5.7 g, d 0.992g/mL. IR (cm^{-1} , neat); 1030, 1620 (C=N-); 2900; ^{1}H-NMR(CCl_4: δ 8.2 (s, 1H, N=CH); 7.6-7.9 (d, 4H, ArH); 4.05-4.55 (s, 3H, MeO); 3.95 (q, J = 12.5Hz, 2H, CH_2O); 1.2-1-5(t, , J = 12.5Hz 3H, Me).; ^{13}C-nmr ($CDCl_3$) δ 164.0, 163.0, 130.0, 123.0, 114.0, 64.0, 56.0, 12.0. Anal. Calc. (%) for: $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82; O, 17.85. Found: C, 66.88; H, 7.11; N, 8.10; O, 17.77

3-Phenylpropenal-O-benzyl oxime (**g**). Brown solid, mp 98-100^{o}C, Yield: 2.8g, 69%**,** IR (cm^{-1} , neat): 2820, 1613, 1030, ^{1}H-NMR(CCl_4): δ 7.14-7.30 (m, 10H, Ar-H); 7.50 (d, J = 12.5Hz, 1H, N=CH); 5.6-6.60 (m, 2H, CH=CH); 4.20 (s, 2H, CH_2O).. ^{13}C-nmr (CCl_4) δ 164.0, 141.0, 140.0, 135.0, 126.0, 127.0, 127.5, 128.5, 129.0, 120.0, 77.0. Anal. Calc. (%) for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90; O, 6.74. Found: C, 81.11; H, 6.22; N, 5.56; O, 6.55.

RESULTS AND DISCUSSION

The oxime ethers were prepared from *E*, *E* cinnamaldoximes, crotonaldoxime, *syn* benzaldoxime and *p*-methoxybenazaldoxime (previously prepared and isolated by column chromatography) by the reaction of the aldoximes with the appropriate alkyl bromide or benzyl chloride in the presence of silver (I) oxide (Scheme 1).

Scheme 1. Alkylation of oximes



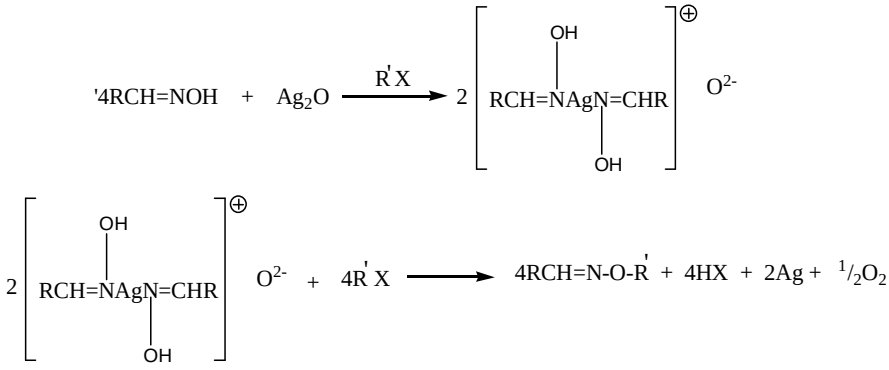
	R^1	R^2
a.	Me	MeCH=CH-
b.	Et	MeCH=CH-
c.	Me	PhCH=CH-
d.	Et	PhCh=CH-
e.	Et	Ph-
f.	Et	MeO-Ph-
g.	$PhCH_2$	PhCH=CH-

All products were obtained in good yields comparable to the yields of conventional procedures. We believe that the reaction involves silver (I) ion complex formation between silver and the oxime nitrogen, (Scheme 2) like in the silver mirror test reaction, a conversion occurs without attacking any double bonds. Silver ion is reduced while oxygen is released. In this case, the C=N double bond is not attacked, thereby preventing the alkylation of nitrogen that results in nitrone

formation. More studies are required to confirm the mechanism of the reaction. The reaction, like the silver mirror test, leaves a deposit of pure silver in the form of tiny pellets of silver metal and silver halide in the reaction mixture.

The compounds **a-d** and **g** are assigned *E, Z* configurations because the ^{1}H-NMR peak of C=N-OCH_2 or C=N-OCH_3 protons occurred at between δ3.9-4.2 ppm[5-7]. The *E, E*- isomers usually absorb downfield at higher δ ppm values than the *Z* isomers. For the same reasons, products **e** and **f** are assigned *Z* configuration. In addition, ^{1}H, ^{13}C, ^{13}C-DEPT, ^{1}H-^{1}H coupling correlation at 200 MHz, and ^{1}H- ^{13}C ^{1}J correlations at 400 MHz were used to confirm these assignments.

Scheme 2. Mechanism of silver ion catalyzed alkylation of oximes



The only drawback to the procedure is the use of the expensive silver oxide, but it can be recovered from the silver metal or silver halides which are the end products of the silver oxide in the reaction. The other disadvantage is that a solvent that is not one of the reagents is required if the alkyl or aryl halide is not a liquid.

CONCLUSIONS

The synthesis of oxime ethers from oximes and alkyl or aryl halides has been achieved with silver oxide as base and catalyst. No trace of nitrone formation was found, the oxime ethers were formed in good yields and liquid alkyl or aryl halides can also be the solvent of reaction. Both solvent and catalyst/base can be recovered and reused.

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