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A Convenient and Efficient Procedure for Oxime Ethers

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Abstract: Acetophenone oxime and benzaldehyde oxime were converted to oxime ethers in the presence of alkyl halide or methyl sulfate and KOH in aqueous DMSO in 5 to 70 min. The yields of oxime ethers were 70 - 96%.

Keywords: Oxime ethers**,** synthesis.

In connection with our asymmetric reduction research, we are of interest to synthesize ketoxime ethers because they give good enantioselectivty in the reduction system of Lewis acid-$NaBH_4$-Ligand[1]. In the literature the oxime ethers were made under anhydrous conditions using strong base such as NaH or sodium alkoxides to realize the substitution reaction between alkyl halide and oxime[2]. The reaction has also been performed under PTC conditions[3]. There were cases where the yields were low[4] or the side products such as nitrones were formed as well[5].

We wish to report a convenient and very simple procedure for the preparation of oxime ethers. A mixture of aqueous DMSO, KOH, alkyl halide (or methyl sulfate) and oxims was stirred at room temperature for 5 to 70 min which on work-up gave oxime ethers in 70 to 96% yields. The results are summarized in **Table 1**.

Table 1 Yield (%) and reaction time in min (in bracket) of oxime ethers

RX	acetophenone oxime	benzaldehyde oxime
CH_3I	87 (5)	77 (5)
Me_2SO_4	76 (5)	81 (10)
EtBr	72 (10)	96 (35)
BuBr	82 (30)	70 (5)
$CH_3(CH_2)_6Br$	74 (5)	83 (15)
$Br(CH_2)_3Br$	72 (10)	70 (15)
iPrBr	80 (60)	76 (50)
BzlCl	85 (70)	96 (60)

Acetophenone oxime and benzaldehyde oxime were used as representative. The amounts of halides and methyl sulfate used were 1.2 equivalents and 1.6 equivalents respectively. 0.5 g of KOH were used for 1 mmol of oxime. Bisoxime ether, a potential bidentate ligand, was formed in high yield by reacting 1, 3-dibromopropane with oximes. The bisoxime ethers were filtered through silica gel eluted with petroleum ether and ether (3:1) for purification. Other oximes were purified by bulb to bulb distillation.

Replacing KOH with NaOH and DMSO with DMF gave similar results as checked between benzaldehyde oxime and ethyl bromide.

The reaction between benzaldehyde oxime and ethyl bromide may serve as a typical procedure. To the stirred mixture of 0.50 g of benzaldelyde oxime (4.127 mmol), 2.00 g of KOH, 5 mL of DMSO and 2 mL of H_2O were added 0.54 g (4.953 mmol) of ethyl bromide. The reaction was monitored by TLC and was completed in 35 min. Brine (20 mL) was added to the reaction followed by extraction with ethyl acetate (80 mL). The organic layer was washed with brine (20 mL) 3 times. The extract was concentrated in vacuum. The residue was purified through bulb to bulb distillation to give oxime ether as colorless oil (0.588 g), yield 96%.

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