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# THE PREPARATION OF OXIME ETHERS UNDER PHASE TRANSFER CONDITION

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O-Butyloximes, O-allyloximes, O-2-chloroethyloximes, and O,O'-methylenedioximes were prepared from the corresponding oximes and halides under the phase transfer condition using sodium hydroxide and tetrabutylammonium bromide.

The reaction under phase transfer condition has become an usefull procedure in the preparation of the variety of compounds.[1] We are studying the convenient synthesis of oxime ethers under mild conditions using phase transfer catalyst. Here we report the synthesis of oxime ethers from oximes and halides using tetrabutylammonium bromide with a 10% solution of sodium hydroxide.

Alkylation of oximes has been known to occur both on oxygen to give oxime ethers and on nitrogen to give nitrons.[2] The chemo-selectivity and stereochemistry of the alkylation of oximes in phase transfer condition were studied by using syn-(Is) and anti-benzaldoxime (Ia).[3] As indicated below, syn-benzaldoxime (Is) gave syn-oxime ether (IIs) predominantly, whereas anti-oxime (Ia) yielded nitron (III) preferentially in the butylation by butyl bromide. The O/N ratio in the butylation (II/III) was 24 and 0.25 for syn- and anti-benzaldoxime, respectively. In contrast to our result, Buehler obtained the different O/N ratio, 6 and 0.05, for Is and Ia in the isopropylation of the oximes under homogeneous condition (EtONa/EtOH).[4] The observed differnce in the O/N ratio shows that the phase transfer condition is more sutable for O-alkylation

The stereochemistry of the oxime ethers was assigned by the chemical shift of the olefinec hydrogen in pmr spectra,[4] and clarified that the syn-anti isomerization did not take place under the present reaction condition.

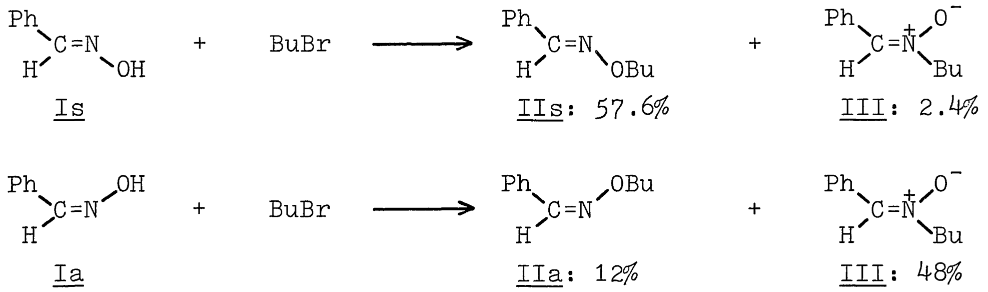
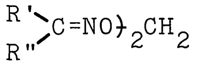


Table. Yield (%) of oxime ethers[a)]

| Oxime<br>Halide | $\mathrm{Ph(H)C{=}N{-}OH}$ | $\mathrm{Ph(H)C{=}N(OH)}$ | $\mathrm{Ph(CH_3)C{=}N{-}OH}$ | $\mathrm{(CH_2)_5C{=}NOH}$ | $\mathrm{C_6H_{13}(CH_3)C{=}NOH}$[b)] |
|---|---|---|---|---|---|
| $CH_3(CH_2)_3Br$ | 57.6 | 12[c)] | 84 | 60 | 80[e)] |
| $ClCH_2CH_2Cl$ | 91 | -- | 84 (78)[d)] | 91 | 76[e)] |
| $CH_2Cl_2$ | 81 | -- | 60 | 60 | 63[e)] |
| $CH_2{=}CHCH_2Br$ | 76 | -- | 86 | 78 | 83[e)] |

a) Yield were determined by pmr analyses. b) E:Z = 3:1 mixture; determined by cmr. c) Nitron was obtained as major product (48%). d) Carried out in 20 mmol scale and isolated yield. e) A mixture of E and Z-isomer.

We prepared other oxime ethers listed in the Table in 58-91% yield. The reaction of the oximes with dichloromethane yielded only O,O'-methylenedioxime (IV), whose synthesis was reported recently.[5)]



$(R'R''C{=}NO)_2CH_2$

IV

The preparation of O-butylacetophenone oxime serves as a typical example. To a solution of acetophenone oxime (0.268 g, 2.0 mmol), tetrabutylammonium bromide (0.10 g, 0.3 mmol), and butyl bromide (0.548 g, 4.0 mmol) in 2 ml of benzene was added dropwise 5 ml of a 10% aqueous sodium hydroxide.[6)] The mixture was stirred for 20 h at room temperature and then diluted with 5 ml of ether. The organic layer was washed with water and aqueous ammonium chloride, and dried over sodium sulfate. Concentration of the solution *in vacuo* afforded 0.32 g of essentially pure O-butylacetophenone oxime (84%). Pmr($CDCl_3$, $\delta$); 0.96 (3H, t, J=7 Hz), 1.08-1.88 (4H, m, $-CH_2CH_2-$), 2.22 (3H, s), 4.19 (2H, t, J=7 Hz) and 7.16-7.70 (5H, aromatic).

## References and Notes

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4) E. Buehler, J. Org. Chem., 32, 261 (1967).
5) S. J. Kirsch and H. Schelling, J. Org. Chem., 44, 3970 (1979); T. Hosokawa, T. Ohta, Y. Okamoto, and S. Murahashi, Tetrahedron Lett., 1980, 1259.
6) When 1 ml of 50% aqueous sodium hydroxide was used, the yield was diminished to 33% by the precipitation of sodium oximate.

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