BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (2), 627—628 (1979)

O-Methylation of Aromatic (*E*)-Oximes by Dimethylsulfonium Methylide

Shigeo TANIMOTO,* Takashi YAMADERA, Toyonari SUGIMOTO, and Masaya OKANO

Institute for Chemical Research, Kyoto University, Uji, Kyoto 611

(Received May 18, 1978)

Synopsis. The reactions of dimethylsulfonium methylide with (*E*)-aldoximes and (*E*)-ketoximes proceeded smoothly at room temperature and gave moderately good yields of *O*-methyl (*E*)-aldoximes and *O*-methyl (*E*)-ketoximes, respectively. A possible scheme for the formation of *O*-methyl (*E*)-oximes has been discussed.

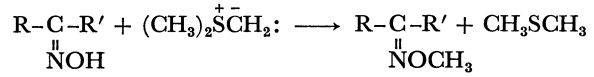
Metzger and coworkers[1] published a brief report on a facile methylation of nitrobenzene by dimethyloxosulfonium methylide. Additional methylation reactions with several substituted nitrobenzenes have been described by Traynelis and McSweeney.[2] Analogous *O*-methylation reactions with *o*-hydroxybenzaldehyde have been found by Holt and Lowe,[3] *i.e.*, when *o*-hydroxybenzaldehyde and dimethylsulfonium methylide (**1**) were allowed to react, *o*-methoxybenzaldehyde was isolated. The methylation reactions of anthracene and benzaldehyde phenylhydrazone with dimethyloxosulfonium methylide are also known.[1]

In this paper the facile *O*-methylation of (*E*)-aldoximes (**2a**—**2e**) and (*E*)-ketoximes (**2f**—**2k**) are reported employing **1** prepared *in situ* by the action of *t*-BuOK on trimethylsulfonium iodide in dimethyl sulfoxide (DMSO).

Hitherto, various *O*-methyl (*E*)-oximes (**3**) have been synthesized either by the reaction of a sodium (*E*)-oximate with methyl iodide[4,5] or by the action of methyl sulfate on an (*E*)-oxime under alkaline conditions.[6]

However, the above reactions proceeded with the accompanying formation of *N*-methylated oxime derivatives.[6] The present method provides an exclusive *O*-methylated (*E*)-oxime derivative (**3**). This reaction not only presents an alternative method[7] for the selective *O*-methylation of **2**, but is also of interest as an example of the utility of sulfur ylides.

When an (*E*)-oxime and **1** (generated *in situ* from trimethylsulfonium iodide and *t*-BuOK in DMSO) were allowed to react at room temperature, the corresponding *O*-methyl (*E*)-oxime (**3**) was formed in a moderately



2 **1** **3**

a: R=C_6H_5, R′=H
b: R=*p*-$CH_3C_6H_4$, R′=H
c: R=*p*-ClC_6H_4, R′=H
d: R=*p*-$CH_3OC_6H_4$, R′=H
e: R=*o*-ClC_6H_4, R′=H
f: R=C_6H_5, R′=CH_3
g: R=*p*-$CH_3C_6H_4$, R′=CH_3
h: R=*p*-ClC_6H_4, R′=CH_3
i: R=*p*-BrC_6H_4, R′=CH_3
j: R=C_6H_5, R′=C_6H_5
k: R–C(=)–R′=cyclo-C_6H_{10}=

good yield. The results are listed in Table 1.

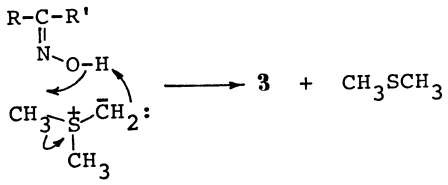
On the other hand, when a potassium (*E*)-oximate (prepared *in situ* by mixing 1 equivalent of an (*E*)-oxime

TABLE 1. *O*-METHYLATION OF (*E*)-OXIMES (**2**) BY DIMETHYLSULFONIUM METHYLIDE (**1**)

Run	(*E*)-Oxime	Product	Yield[a] (%)
1	**2a**	**3a**[b]	60
2	**2b**	**3b**[c]	51
3	**2c**	**3c**[d]	65
4	**2d**	**3d**[e]	54
5	**2e**	**3e**[f]	63
6	**2f**	**3f**[g]	91
7	**2g**	**3g**[h]	79
8	**2h**	**3h**[i]	84
9	**2i**	**3i**[j]	69
10[k]	**2j**[l]	**3j**[m]	77
11	**2k**[l]	**3k**[n]	32

a) Yield was based upon **2**, and was of the isolated product. b) Bp 86—88 °C/21 mmHg (lit,[8] 95 °C/20 mmHg). NMR ($CDCl_3$): δ 3.97 (s, 3H), 7.25—7.70 (m, aromatic 5H), 8.06 (s, 1H). c) Bp 80—83 °C/5 mmHg. Found: C, 72.32; H, 7.58; N, 9.42%. Calcd for $C_9H_{11}NO$: C, 72.45; H, 7.43; N, 9.39%. NMR ($CDCl_3$): δ 2.33 (s, 3H), 3.95 (s, 3H), 7.05—7.56 (m, aromatic 4H), 8.15 (s, 1H). d) Bp 92—94 °C/4 mmHg (lit,[6] mp 28 °C). NMR ($CDCl_3$): δ 3.95 (s, 3H), 7.20—7.58 (m, aromatic 4H), 8.00 (s, 1H). e) Bp 137—139 °C/22 mmHg (lit,[9] 129 °C/15 mmHg). NMR ($CDCl_3$): δ 3.77 (s, 3H), 3.92 (s, 3H), 6.75—7.62 (m, aromatic 4H), 8.00 (s, 1H). f) Bp 89—92 °C/6 mmHg. Found: C, 56.44; H, 4.62; N, 8.15%. Calcd for C_8H_8ClNO: C, 56.65; H, 4.75; N, 8.26%. NMR ($CDCl_3$): δ 3.97 (s, 3H), 7.12—7.98 (m, aromatic 4H), 8.49 (s, 1H). g) Bp 106—108 °C/21.5 mmHg (lit,[10] 132—135 °C/46 mmHg). NMR ($CDCl_3$): δ 2.19 (s, 3H), 3.98 (s, 3H), 6.86—7.96 (m, aromatic 5H). h) Bp 124—127.5 °C/23.5 mmHg. Found: C, 73.77; H, 8.19; N, 8.30%. Calcd for $C_{10}H_{13}NO$: C, 73.59; H, 8.03; N, 8.58%. NMR ($CDCl_3$): δ 2.16 (s, 3H), 2.29 (s, 3H), 3.95 (s, 3H), 6.96—7.68 (m, aromatic 4H). i) Bp 84—88 °C/2 mmHg. Found: C, 59.08; H, 5.42; N, 7.86%. Calcd for $C_9H_{10}ClNO$: C, 58.86; H, 5.49; N, 7.63%. NMR ($CDCl_3$): δ 2.16 (s, 3H), 4.00 (s, 3H) 7.20—7.79 (m, aromatic 4H). j) Bp 92—96 °C/2 mmHg. Found: C, 47.62; H, 4.34; N, 6.39%. Calcd for $C_9H_{10}BrNO$: C, 47.39; H, 4.42; N, 6.14%. NMR ($CDCl_3$): δ 2.16 (s, 3H), 3.98 (s, 3H), 7.33—7.68 (m, aromatic 4H). k) A considerable amount of DMSO was used as the solvent due to the small solubility of benzophenone oxime (**2j**). l) There is no geometrical isomerism. m) Purified by column chromatography on silica gel (eluent 25% ether–75% hexane). Mp 58—60 °C (lit,[11] 61—62 °C). NMR ($CDCl_3$): δ 3.97 (s, 3H), 7.17—7.65 (m, aromatic 10H). n) Bp 68—70 °C/21 mmHg (lit,[7] 50 °C/12 mmHg). NMR ($CDCl_3$): δ 1.38—2.64 (m, 10H), 3.78 (s, 3H).

and 1.5 equivalents of *t*-BuOK in DMSO) and 1.5 equivalents of trimethylsulfonium iodide were allowed to react at room temperature, the corresponding *O*-methyl (*E*)-oxime (**3**) was obtained, but the yield was very poor compared with the result in Table 1. For example, the yield of *O*-methyl (*E*)-benzaldoxime (**3a**) in this procedure was 25%. Consequently, it has to be assumed that the formation of an (*E*)-oximate anion and its subsequent attack on a trimethylsulfonium cation with the loss of neutral dimethyl sulfide occurs simultaneously in the reaction involving **1** and an (*E*)-oxime. Thus, the transition state might be represented as follows:



It has been reported that the methylation of sodium (*E*)-oximate by methyl iodide in ethanol always accompanies some degree of *N*-methylation, which is attributable to the ambifunctional nucleophilic character of the (*E*)-oximate anion.[8,12] However, **2** has been exclusively methylated on oxygen by the method described in this paper. The *N*-methylated oxime derivative could not be detected by NMR spectra. The selective *O*-methylation in the present reaction can be understood taking into consideration the formation of the cyclic transition state.

Experimental

Preparation of O-*Methyl* (E)-*Oximes* (*3*). *General Procedure*: A solution of trimethylsulfonium iodide (8.10 g, 39.6 mmol) in DMSO (20 ml) was placed in a 100 ml four-necked flask equipped with a reflux condenser, thermometer, gas-inlet tube, dropping funnel, and magnetic stirrer. Finely powdered *t*-BuOK (4.44 g, 39.6 mmol) was slowly added with efficient stirring at 5—10 °C, under a nitrogen atmosphere, to the solution. A DMSO solution (5 ml) of an (*E*)-oxime (26.4 mmol) was subsequently introduced dropwise at that temperature. The reaction mixture was then stirred for 5—6 h at room temperature, quenched with saturated aqueous Na_2SO_4 solution and extracted with ether. The organic extract was washed and dried over $MgSO_4$, the solvent evaporated and the residue distilled under reduced pressure.

References

1) H. Metzger, H. König, and K. Seelert, *Tetrahedron Lett.*, **1964**, 867.
2) V. J. Traynelis and Sr. J. V. McSweeney, O. P., *J. Org. Chem.*, **31**, 243 (1966).
3) B. Holt and P. A. Lowe, *Tetrahedron Lett.*, **1966**, 683.
4) S. G. Smith and D. V. Milligan, *J. Am. Chem. Soc.*, **90**, 2393 (1968).
5) W. R. Dunstan and E. Goulding, *J. Chem. Soc.*, **79**, 628 (1901).
6) O. L. Brady, F. P. Dunn, and R. F. Goldstein, *J. Chem. Soc.*, **1926**, 2386.
7) For the preparation of pure *O*-methyl (*E*)-oximes, the reaction of methoxyamine with either an aldehyde or a ketone has already been published: L. G. Donaruma, *J. Org. Chem.*, **22**, 1024 (1957).
8) E. Buehler, *J. Org. Chem.*, **32**, 261 (1967).
9) H. Lindemann and K. T. Tschang, *Chem. Ber.*, **60**, 1727 (1927).
10) G. W. Perold, A. P. Steyn, and F. V. K. Reiche, *J. Am. Chem. Soc.*, **79**, 462 (1957).
11) P. A. S. Smith and J. E. Robertson, *J. Am. Chem. Soc.*, **84**, 1197 (1962).
12) O. L. Brady and N. M. Chokshi, *J. Chem. Soc.*, **1929**, 2271.