BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN VOL. 41 221—225 (1968)

The Reaction of Benzylic Alcohols with Dimethyl Sulfoxide-Polyphosphoric Acid

Takeo SATO, Akihiko TAKATSU, Yoshitaka SAITO,
Takafumi TOHYAMA and Kazuo HATA

Department of Chemistry, Faculty of Science, Tokyo Metropolitan University, Setagaya-ku, Tokyo

(Received July 25, 1967)

The reaction of dimethyl sulfoxide-polyphosphoric acid mixture with benzylic alcohols has been shown to afford a complex mixture of the products; this is in contrast to the case of aliphatic alcohols, which yield the corresponding acetal as the major product. By carrying out reactions using several benzylic alcohols and a series of benzyl alcohols, it was found that, in addition to the acetal formation reaction, dehydration and oxidation reactions, as well as a methyl thioether-formation reaction, were occurring. Possible pathways for the formation of these products are presented.

In continuing our work[1] aimed at the development of a new use of dimethyl sulfoxide (DMSO) in organic reactions, this paper will record the reactions of benzylic alcohols with DMSO, polyphosphoric acid (PPA), or a DMSO-PPA mixture.

In another study, a facile dehydration reaction of α-(bromomesityl)benzyl alcohol to give the corresponding ether has been achieved[2] by treatment with PPA. Current interest in DMSO as an efficient dehydrating agent[3] has led us to investigate the ether formation reaction of benzylic alcohols in DMSO.[2] By heating benzhydrol (IIId) in a DMSO solution, bis(diphenylmethyl) ether (IVd) was isolated in a 88% yield. Likewise, α-(bromomesityl)benzyl alcohol afforded an ether. Similar results have concurrently been reported by Traynelis and his co-worker.[4] In contrast, 9-hydroxyfluorene produced only a 14% yield of bis(9-fluorenyl) ether under similar conditions, the major product being 9-fluorenone, which was obtained in a yield of up to 56%. An attempted dehydration reaction of benzyl alcohol with either DMSO or PPA, however, resulted in the formation of only a small amount of benzaldehyde or of a polymeric material respectively.

Recently considerable interest has arisen in the reaction in which DMSO is used as a reactant as well as a solvent in acidic media. A novel oxidation method developed by Moffatt and his co-workers[5] utilizes DMSO-dicyclohexylcarbodiimide (DCC)-orthophosphoric acid for the selective oxidation of primary alcohols to aldehydes. It has also been reported from our laboratories[6] that a new reagent, a DMSO-PPA mixture, reacts even with aliphatic primary alcohols to form the corresponding acetal I in a 50—90% yield. These alcohols, which are inert toward DMSO, are known to produce only polymeric hydrocarbons on reaction with PPA.[6,7]

---

1) For the previous paper of this series, see T. Sato, H. Inoue and K. Hata, This Bulletin, **40**, 1502 (1967).

2) T. Sato, A. Takatsu and K. Hata, *ibid.*, **37**, 902 (1964).

3) T. Sato, *Yuki Gosei Kagaku Kyokaishi (J. Soc. Org. Synth. Chem. Japan)*, **23**, 768, 867 (1965).

4) V. J. Traynelis, W. L. Hergenrother, H. T. Hanson and J. A. Valicenti, *J. Org. Chem.*, **29**, 123 (1964); V. J. Traynelis and W. L. Hergenrother, *J. Am. Chem. Soc.*, **86**, 298 (1964).

5) A. H. Fenselau and J. G. Moffatt, *ibid.*, **88**, 1762 (1966) and earlier papers in this series.

6) T. Sato, Y. Saito, M. Kainosho and K. Hata, This Bulletin, **40**, 391 (1967).

7) H. R. Snyder and J. X. Werber, *J. Am. Chem. Soc.*, **72**, 2965 (1950); J. W. Jean, U. S. Pat. 2373475 (1945).

TABLE 1. THE REACTION OF BENZYLIC ALCOHOLS III WITH DMSO-PPA

Benzylic alcohol	Product, %				
	IV	V	VI	VII	others
IIIa	10	16	8.5	13[a]	
IIIb, X=NO_2	—	46	20	4.9	
IIIc	27	—	0.5	—	styrene, 19
IIId	53	—	13	20	

a) Determined by gas chromatography using Carbowax-1500 on celite-408 column at 199°C.

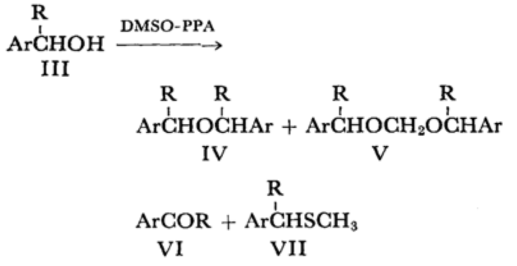
TABLE 2. NMR AND IR SPECTRA DATA

Compound	NMR,[a] δ(ppm)				IR, cm^{-1}
	OCH_2O	OCH_2S	ArCH(or CH_2)	SCH_3	
II, R=cyclohexyl		4.58(2)		2.08(3)	1323, 1065
II, R=(−)-menthyl		4.62(2)		2.08(3)	1320, 1060, 1050
IVa			4.50(4)		1200, 1095
IVc			4.37(2)		1085
IVd			5.35(2)		1050
Va	4.68(2)		4.53(4)		1163, 1101, 1045, 1023
Vb, X=NO_2	4.94(2)		4.78(4)		1170, 1125, 1105, 1060, 1010
VIIa			3.58(2)	1.87(3)	1325, 675
VIIb, X=NO_2			3.75(2)	1.96(3)	1325, 675
VIId			4.97(1)	1.91(3)	1325, 675

a) Determined on Varian A-60 spectrometer as a carbon tetrachloride solution except for Vb and VIIb (X=NO_2) which were dissolved in deuteriochloroform. All the signals, relative to TMS (δ=0.0 ppm), appeared as a singlet except for IVc, which were consisted of a pair of quartets. Numerals in parentheses denote the number of protons.

The treatment of benzylic alcohols with this DMSO-PPA mixture at a water-bath temperature for 2—5 hr produced a complex mixture of the ether IV, the acetal V, the carbonyl compound VI, and the methylthio compound VII. In contrast to the aliphatic series, acetal was no longer the main product, and no methylthiomethyl ether corresponding to II was detectable. Among the benzylic alcohols studied, 1-phenylethanol (IIIc) behaved differently and afforded only dehydration products, styrene and bis(1-phenylethyl) ether (IVc).[8] The results of representative examples are shown in Table 1. The reaction products were analyzed either by column chromatography on alumina or by gas chromatography. The carbonyl compounds were determined as 2, 4-dinitrophenylhydrazones. The pertinent NMR and IR data used for the identification of the materials are compiled in Table 2.

$$ROH \xrightarrow{\text{DMSO-PPA}} \underset{\text{I}}{ROCH_2OR} + \underset{\text{II}}{ROCH_2SCH_3}$$



$$\underset{\text{III}}{Ar\overset{R}{C}HOH} \xrightarrow{\text{DMSO-PPA}} \underset{\text{IV}}{Ar\overset{R}{C}HO\overset{R}{C}HAr} + \underset{\text{V}}{Ar\overset{R}{C}HOCH_2O\overset{R}{C}HAr}$$

$$\underset{\text{VI}}{ArCOR} + \underset{\text{VII}}{Ar\overset{R}{C}HSCH_3}$$

	Ar	R
a	C_6H_5	H
b	p-X-C_6H_4	H
c	C_6H_5	CH_3
d	C_6H_5	C_6H_5

As a typical example, the reaction products from benzyl alcohol (IIIa) were analyzed in the following manner. By gas chromatographical analyses using Carbowax-1500 on celite column, benzaldehyde (VIa), benzyl methyl sulfide (VIIa), unreacted alcohol (IIIa), dibenzyl ether (IVa), and dibenzyloxymethane (Va) (listed in the order of the retention time) were identified. Column chromatography on alumina using *n*-hexane containing an increasing amount of ether as an eluent furnished VIIa, IVa, Va, and IIIa, in that order. The treatment of IIIa with DMSO-85% orthophosphoric acid resulted in the recovery of the starting material, while the mixture made from DMSO and phosphorus pentoxide decomposed

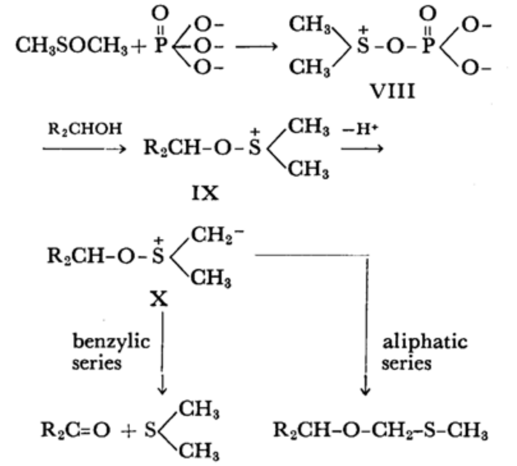
---

[8] Dehydration of 1-phenylethanol to styrene required much drastic conditions when carried out in DMSO alone, see V. J. Traynelis, W. L. Hergenrother and J. A. Valicenti, *J. Org. Chem.*, **27**, 2377 (1962).

vigorously before it could be brought into the reaction.[9]

The formation of the ether IV, which is absent in the aliphatic series[6] but is formed in as high as a yield as 53% with IIId, is favored in benzylic alcohols, since the reaction proceeds through a carbonium ion mechanism. This may also explain the formation of VII, by assuming the reaction of benzylic carbonium ion either with methyl mercaptan, one of the possible decomposition products of DMSO in acidic media, or with any species capable of generating it.[10]

The yields of benzaldehydes derived from a series of *p*-substituted benzyl alcohols (IIIb) are shown in Table 4 (see the Experimental section). It is apparent that the presence of an electron-withdrawing group favors the formation of the oxidation products. The fact that aliphatic alcohols do not produce any oxidation product, but instead afford the methylthiomethyl ether II, which is absent in the benzyl series, suggests that the formation of VI from benzylic alcohols and that of II from aliphatic alcohols share a common intermediate X. The reaction of DMSO with PPA produces VIII, which, upon an attack from the back by an alcohol, is converted to the alkoxysulfonium compound IX. Further reactions of the ylide X derived from IX are dependent on the nature of the alkyl residues. In the case of aliphatic compounds, carbanion preferentially attacks oxygen to produce methylthiomethyl ether, while in the benzyl series the ylide decomposes into a carbonyl compound and dimethyl sulfide. The benzyl alcohol bearing an electron-withdrawing group is more easily oxidized, since the benzyl hydrogen becomes more acidic, thus facilitating the attack by the carbanion. The intermediacy of X in a number of reactions in which DMSO serves as an oxident has been well established.[5] Further, relevant examples found in recent papers include the formation of II by the reaction of alcohol with DMSO containing DCC,[11,12] or acid anhydride.[13,14]



Experimental

α-(Bromomesityl)benzyl Alcohol. Benzoylbromomesitylene[15] was reduced with lithium aluminum hydride in the usual manner. Colorless prisms, mp 65—67°C, were then obtained in a 95% yield by recrystallization from benzene - petroleum ether.

Found: C, 62.77; H, 5.51%. Calcd for $C_{16}H_{17}OBr$: C, 62.96; H, 5.61%.

IR (KBr): 3450 and 1150 cm^{-1}.

Acetylation with acetic anhydride containing pyridine afforded an acetate as colorless prisms, mp 99—100°C.

Found: C, 62.07; H, 5.21%. Cacld for $C_{18}H_{19}O_2Br$: C, 62.25; H, 5.51%.

Bis[α-(Bromomesityl)benzyl] Ether. To 32 g of PPA, 2.0 g (6.6 mmol) of the above alcohol was added, after which the mixture was heated on a water bath for 15 min. The reaction mixture was then diluted with water, and the crystalline material was recrystallized from benzene - ethanol to give 1.5 g (77% yield) of colorless prisms, mp 147—149°C. After five successive recrystallizations, the melting point was raised to 176—177°C.

Found: C, 64.51; H, 5.51%. Calcd for $C_{32}H_{32}OBr_2$: C, 64.87; H, 5.45%.

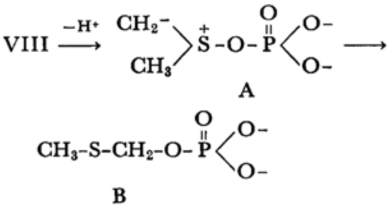
The combined mother liquors were evaporated, and the residue was passed through an alumina column, using petroleum ether as an eluent; thereby we obtained another compound, mp 152—154°C which was assumed to be a structural isomer.

The Reaction with DMSO. *a) Bis(diphenylmethyl) Ether (IVd).* A mixture of IIId in DMSO was heated at 165—170°C under various conditions, summarized in Table 3. After the reaction was over, the mixture was diluted with water and the resulting IVd was recrystallized from ethanol; mp 108—109°C (lit. 108°C).

---

[9] Recently, however, DMSO-P_2O_5 was used for the oxidation of carbohydrates, see K. Onodera, S. Hirano and N. Kashimura, *J. Am. Chem. Soc.*, **87**, 4651 (1965).

[10] Compound B which arose *via* A may be responsible for the origin of methylthio group as well as formaldehyde.



[11] J. B. Jones and R. C. Wigfield, *Tetrahedron Letters*, **1965**, 4103.

[12] K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5670 (1965).

[13] J. D. Albright and L. Goldman, *ibid.*, **87**, 4214 (1965).

[14] An alternative mechanism[12,13] which postulates the intermediacy of $CH_3\overset{+}{S}=CH_2$ has also been advanced, see also K. E. Pfitzner and J. G. Moffatt, *J. Am. Chem. Soc.*, **87**, 5661 (1965).

[15] J. F. Hyde and R. Adams, *ibid.*, **50**, 2503 (1928).

TABLE 3. BIS(DIPHENYLMETHYL) ETHER (IVd) FORMATION REACTION AT 165—170°C

IIId mol	DMSO mol	Time hr	Yield of IVd, %
0.03	0.6	4	63
0.03	0.6	8	88
0.02	0.02	8	68
0.08	0.4	8	66
0.03	0.6	24	82

No ether formation was observed when IIId itself or a diethylene glycol solution was heated at 165—170°C for 11—18 hr.

b) Bis[α-(bromomesityl)benzyl] Ether. A mixture of 3.0 g (0.01 mol) of α-(bromomesityl)benzyl alcohol and 15.6 g (0.2 mol) of DMSO was heated at 165—170°C for 16 hr. Colorless prisms, mp 156.5—158°C, were thus obtained (0.6 g). The IR spectra agreed with the product obtained by the PPA dehydration reaction described above.

c) Bis(9-fluorenyl) Ether. A mixture of 3.6 g (0.02 mol) of 9-hydroxyfluorene and 31.2 g (0.4 mol) of DMSO was heated at 165—170°C for 24 hr. The recrystallization of the product from ethanol afforded 0.2 g of bis(9-fluorenyl) ether, mp 223—225°C (lit. 228°C). The rest of the material was analyzed by column chromatography on alumina, using benzene-chloroform-ethanol as an eluent; this afforded 0.2 g of an unidentified yellow solid, mp 232—237°C, 0.3 g of bis(9-fluorenyl) ether (total yield 14.3%), and 1.2 g (33.4%) of 9-fluorenone, mp 73—76°C, together with the starting material (14.3% recovery).

The same experiment carried out at 165—185°C for 25 hr afforded a 56% yield of 9-fluorenone.

d) Attempted Reaction of Benzyl Alcohol. A mixture of 5.4 g (0.05 mol) of benzyl alcohol and 78 g (1.0 mol) of DMSO was heated at 160—170°C for 20 hr. A part of the reaction mixture was then treated with a 2, 4-dinitrophenylhydrazine solution to give a 15.7% yield of the benzaldehyde hydrazone, mp 231.5—234°C. About 60% of the starting alcohol was recovered by simple distillation.

Methylthiomethyl Ether (II). *a) Cyclohexyl Methylthiomethyl Ether (II, R=Cyclohexyl).* The treatment of cyclohexanol with DMSO-PPA afforded,6) in addition to a 44% yield of dicyclohexyloxymethane (I, R=cyclohexyl), a fraction which boiled at 97—99°C/15 mmHg. From its IR and NMR spectra it was identified as II (R=cyclohexyl), it was obtained in a 8.6% yield.

NMR (CCl_4): δ 4.58 (2H), 3.60 (1H), 2.08 (3H) and 1.1—1.8 (10H).

Found: C, 60.85; H, 10.10%. Calcd for $C_8H_{16}OS$: C, 59.98; H, 10.07%.

b) (−)-Menthyl Methylthiomethyl Ether (II, R=Menthyl). The same reaction as above but using (−)-menthol furnished a 28.9% yield of dimenthyloxymethane (I, R=menthyl), bp 207°C/23 mmHg, mp 58°C and a 4.5% yield of II (R=menthyl), bp 138—140°C/17 mmHg.

NMR (CCl_4): δ 4.62 (2H), 3.45 (1H), 2.08 (3H) and 0.7—2.3 (18H).

Found: C, 67.15; H, 11.26%. Calcd for $C_{12}H_{24}OS$: C, 66.63; H, 11.18%.

The Reaction with DMSO-PPA. *a) Benzyl Alcohol (IIIa).* To a mixture which had been prepared under cooling by adding 78 g (1.0 mol) of DMSO to 54 g of 80% PPA, 21.6 g (0.2 mol) of IIIa was added. After the reaction mixture had then been heated on a water bath for 5 hr, it was diluted with water and extracted with diisopropyl ether. A part of the extract was treated with a 2, 4-dinitrophenylhydrazine solution to give the benzaldehyde hydrazone in a 9.5% yield. The rest of the material was chromatographed through an alumina column, using *n*-hexane containing an increasing amount of ether; this eluted VIIa, IVa (10% yield), Va (16% yield), and unreacted IIIa successively. All the compounds had satisfactory NMR and IR spectra compared with the authentic specimens (Table 2). By gas chromatography using Carbowax-1500 on celite-408 column, VIa, VIIa, IIIa, IVa, and Va (in the order of the retention time) were identified. As VIIa tended to co-distill with *n*-hexane, the yield for this material (13% yield) was obtained from the gas chromatographical measurements.

b) p-Nitrobenzyl Alcohol (IIIb, X=NO_2). A mixture of 7.6 g (0.05 mol) of IIIb (X=NO_2), 19.5 g (0.25 mol) of DMSO, and 13.5 g of PPA was heated at water-bath temperature for 5 hr. A 20% yield of aldehyde VIb (X=NO_2) was then attained by converting it to 2, 4-dinitrophenylhydrazone.

Column chromatography on alumina using benzene as an eluent furnished sulfide VIIb (X=NO_2) in a yield of 4.9%.

Found: C, 52.51; H, 4.85; N, 7.28%. Calcd for $C_8H_9O_2NS$: C, 52.46; H, 4.95; N, 7.65%.

No ether formation was observed, and the next fraction contained acetal Vb (X=NO_2) as colorless needles mp 98—99°C; it was isolated in a 46% yield.

Found: N, 8.70%. Calcd for $C_{15}H_{14}O_6N_2$: N, 8.80%.

In one experiment, benzaldehyde bis(*p*-nitrobenzyloxy) acetal was isolated from the reaction mixture as a colorless, amorphous material, mp 202—206°C.

Found: N, 9.52%. Calcd for $C_{21}H_{17}O_8N_3$: N, 9.56%.

c) p-Substituted Benzyl Alcohols (IIIb). The same reaction was applied to a series of IIIb. The yields of the benzaldehydes formed are tabulated in Table 4.

TABLE 4. THE FORMATION OF BENZALDEHYDES (VIb) FROM *p*-SUBSTITUTED BENZYL ALCOHOLS (IIIb)

IIIb	Yield of VIb, %
X: CH_3O	11
CH_3	9.4
H	8.5
Cl	39a)
NO_2	20

a) Including *p*-chlorobenzoic acid.

d) 1-Phenylethanol (IIIc). A mixture of 24 g (0.2 mol) of IIIc, 120 g (1.5 mol) of DMSO, and 50 g of PPA was heated on a water bath for 5 hr. The diisopropyl ether extract was then distilled to give a 19% yield of styrene, bp 63—70°C/70 mmHg, and a 27% yield of the ether IVc, bp 158—162°C/70 mmHg,

n_D^{21} 1.5375. From the intermediate fraction, acetophenone (VIc) was isolated as 2, 4-dinitrophenylhydrazone (0.5% yield).

e) Benzhydrol (IIId). A mixture of 4.8 g (0.025 mol) of IIId, 9.8 g (0.125 mol) of DMSO, and 6.8 g of PPA was brought into the reaction as above. When water was then added to the reaction mixture, IVb was isolated as colorless plates, mp 102—104°C. From the filtrate, benzophenone was isolated as 2, 4-dinitrophenylhydrazone in a 13% yield. The diisopropyl ether extract of the filtrate was analyzed by alumina-column chromatography.

n-Hexane eluted VIId, mp 33—33.5°C, in a yield of 20%. The sulfide VIId was also isolated, together with benzophenone, by the direct distillation of the reaction mixture.

Found: C, 78.59; H, 6.34; S, 14.82%. Calcd for $C_{14}H_{14}S$: C, 78.48; H, 6.59; S, 15.00%.