thioxanthene oxides which lack substituents at C-4 and C-9. For example, three intense absorptions are found in the sulfinyl region[2] of the infrared spectrum of 2-chlorothioxanthene 10-oxide (carbon tetrachloride): 1101, 1081, and 1044 cm^{-1}.[11] In going to chloroform[11] only the absorption at 1044 cm^{-1} disappears while a new, broader absorption appears at 1035 cm^{-1}.[12] This unequivocally[8] assigns the 1044-cm^{-1} absorption (carbon tetrachloride) to ν_{S-O}. The corresponding absorption in **5** occurs at 1041 cm^{-1}. Addition of iodine monochloride to **5** (carbon tetrachloride) causes the absorption at 1041 cm^{-1} to diminish in intensity and produces two new absorptions—at 992 and 953 cm^{-1}. This suggests that the complex formed between **5** and iodine monochloride exists as a mixture of conformers.[13]

Experimental Section

Infrared spectra were obtained on a Perkin-Elmer Model 621 spectrophotometer using solutions 0.02 M in solute and, where indicated, in complexing agent.

All of the compounds have been described by us or are available commercially.[4] No special purification procedures were employed in using iodine monochloride (commercially available).

Acknowledgments. We gratefully acknowledge the support of the Robert A. Welch Foundation through Grant Y-484 to A.L.T., including a postdoctoral fellowship for B.R.H.

References and Notes

(1) Presented at the VII International Symposium on Organic Sulphur Chemistry, Hamburg, 1976.
(2) L. J. Bellamy, "The Infrared Spectra of Complex Molecules", 2nd ed., Wiley, New York, N.Y., 1958, p 358.
(3) For an interesting example see M. Oki, I. Oka, and K. Sakaguchi, *Bull. Chem. Soc. Jpn.*, **42,** 2944 (1969).
(4) A. L. Ternay, Jr., and S. A. Evans, *J. Org. Chem.*, **39,** 2941 (1974).
(5) S. A. Evans and A. L. Ternay, Jr., *J. Org. Chem.*, **40,** 2993 (1975), and references cited therein.
(6) E. Augdahl and P. Klaeboe, *Acta Chem. Scand.*, **18,** 18 (1964); see also P. Klaeboe, *ibid.*, **18,** 27 (1964).
(7) Other, minor changes accompany complex formation (e.g., small changes in bandwidth at half-height). However, no other significant bands disappear from the sulfinyl region.[2]
(8) (a) D. Barnard, J. M. Fabian, and H. P. Koch, *J. Chem. Soc.*, 2442 (1949); (b) W. Otting and F. A. Neugebauer, *Chem. Ber.*, **95,** 540 (1962); (c) T. Gramstad, *Spectrochim. Acta*, **19,** 829 (1963); (d) J. H. S. Green, *ibid.*, **24A,** 1627 (1968).
(9) One would expect that thianthrene or thioxanthene sulfoxides which form particularly stable cations might also be better studied using iodine.
(10) A. L. Ternay, Jr., L. Ens, J. Herrmann, and S. Evans, *J. Org. Chem.*, **34,** 940 (1969).
(11) 0.02 M.
(12) The absorptions at 1101 and 1081 cm^{-1} diminish slightly in intensity, shift to lower frequency ($\Delta\nu = 3$ cm^{-1}), *but* diminish in bandwidth at half-height by approximately 15%. The bandwidth at half-height of the 1035 cm^{-1} absorption is 2.3 times as great as that of the 1044 cm^{-1} band in carbon tetrachloride.
(13) We have demonstrated that thioxanthene sulfoxide assumes a predominantly a′ conformation in trifluoroacetic acid, presumably owing to increased size of the sulfinyl group upon hydrogen bonding to the solvent: A. L. Ternay, Jr., J. Herrmann, and B. R. Hayes, submitted for publication.

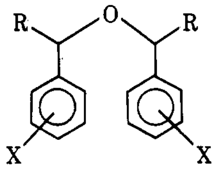
Synthesis of Dibenzyl Ethers via the Dehydration of Benzylic Alcohols in Dimethyl Sulfoxide

Jack Emert,* Merrill Goldenberg, Grace L. Chiu, and Anthony Valeri

Department of Chemistry, Polytechnic Institute of New York, Brooklyn, New York 11201

Received December 20, 1976

During the course of our investigations of intramolecular excimer formation of dibenzyl ethers,[1] we developed a general method of preparing substituted benzyl ethers of structure I in high yields from the respective alcohols using dimethyl sulfoxide as the dehydrating agent. The ethers could be prepared with either electron-donating or electron-withdrawing substituents X, and with R = H or alkyl. This method was preferable to the Williamson synthesis or simple acid catalyzed dehydration which often gave low yields or mixtures of products.[2]



R = H, alkyl

I

Dimethyl sulfoxide mediated dehydration of 1-alkylcycloalkanols and secondary and tertiary benzylic alcohols to olefins has been well documented by Traynelis and co-workers.[3,4] Me_2SO-catalyzed dehydration of diols to cyclic ethers has also been reported.[4,5] In both cases low ratios of alcohol to Me_2SO (1:3 to 1:12) were employed. When the ratio of alcohol to Me_2SO was raised to 1:1 or 3:1, more ether was produced at the expense of olefin, but the product still consisted of a complex mixture of olefin, ether, ketone, and starting material.[4]

We have observed that modification of earlier conditions[4] to very high ratios of alcohol:Me_2SO (16:1) completely suppresses the formation of olefins and oxidized products and provides high yields of ethers (Table I).

When lower ratios of alcohol to Me_2SO (12:1, 3:1) were tried, significant amounts of olefin and oxidized products were obtained. In general, secondary benzyl alcohols reacted faster than primary benzyl alcohols, and alcohols containing electron-donating groups on the ring reacted faster than those containing electron-withdrawing groups. Dehydration of *p*-methoxybenzyl alcohol proceeded smoothly in Me_2SO to give an 85% yield of ether, though it polymerized, rather than dehydrated, in the presence of sulfuric acid or $ZnCl_2$. An unsymmetrical cyclohexyl (α-methylbenzyl) ether also could be prepared if an excess of cyclohexanol were present in the reaction mixture.

A limitation of this method is indicated by the last entry in the table. No product was obtained upon heating *p*-nitrobenzyl alcohol in Me_2SO even after 22 h. It has been proposed that the radical decomposition of Me_2SO to strong acids is responsible for its apparent catalytic action in a variety of reactions.[6,7] The lack of reactivity of *p*-nitrobenzyl alcohol is therefore probably due to the presence of the radical quenching nitro group. In fact, addition of nitrobenzene was sufficient to significantly inhibit the reaction of *p*-methylbenzyl alcohol with Me_2SO presumably by preventing the production of strong acids.

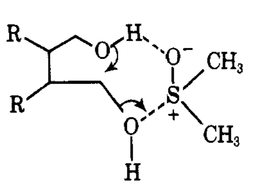
The reaction also appeared to be accelerated by oxygen. Thus, *p*-fluorobenzyl alcohol was unreactive in the presence of dimethyl sulfoxide at 175 °C under a nitrogen atmosphere, though it reacted completely after 8 h in air. This is consistent with other reports that oxygen is a requisite ingredient for the formation of strong acids from Me_2SO at elevated temperatures.[7,8]

The detailed mechanistic pathway of Me_2SO-catalyzed dehydrations has been the subject of some speculation. Traynelis has shown that a carbenium ion is implicated in the dehydration of alcohols to olefins in Me_2SO.[3,4] On the other hand, Gillis and Beck suggested an S_N2-type mechanism for the formation of tetrahydrofurans from 1,4-diols, where dimethyl sulfoxide aids in the removal of a proton from the attacking group while simultaneously stabilizing the leaving group (1).[5]

Table I. Dehydration of Benzyl Alcohols to Ethers in Dimethyl Sulfoxide[a]

Starting alcohol	Reaction time, h	Yield[b] of ether, %
α-Methylbenzyl alcohol	5[c]	99[d]
α-Methylbenzyl alcohol (+ fourfold excess of cyclohexanol)	3	65 (unsymmetrical ethers)
p-Methylbenzyl alcohol	3	89
p-Methoxybenzyl alcohol	0.5	85
p-Fluorobenzyl alcohol	8	99
p-Nitrobenzyl alcohol	22	

[a] Reactions were run using a 16:1 molar ratio of benzyl alcohol to Me_2SO. The reaction temperature was 175 °C. [b] Yields are for isolated, pure products. [c] Reaction was actually complete after 15–30 min. [d] Product consisted of a mixture of meso and *dl* ethers.



1

If the intermolecular reaction of benzyl alcohols were proceeding through a cyclic transition state analogous to **1**, the dehydration of optically active α-methylbenzyl alcohol should give only meso product. However, when *l*-α-methylbenzyl alcohol (91% optically pure), resolved via its brucine salt,[9] was reacted with Me_2SO for 5 min at 175 °C, the NMR spectrum of the product indicated that it consisted of a nearly 50:50 mixture of the meso and *dl* ethers. Recovered starting material was found to be 77% racemized. These results together with the observed substituent effects on the reaction rate rule out a transition state such as **1**. Instead, an unimolecular pathway is indicated, although alkoxysulfonium salts may be involved. Further mechanistic studies are necessary to clarify the exact nature of the intermediate.

Experimental Section

Reagents and Materials. Dimethyl sulfoxide was obtained from the Fisher Scientific Co. and was dried over Linde type 3A molecular sieves before use. The starting alcohols were all available commercially and were used without further purification. Silica gel 60F-254 TLC plates were purchased from Merck and used to monitor all reactions. Silica gel 60 (70–230 mesh) obtained from Merck was heated overnight to 160 °C before use in the chromatographic separation of alcohols and ethers.

Sample Procedure for the Dehydration of Benzyl Alcohols. Two grams (0.0164 mol) of *p*-methylbenzyl alcohol and 0.08 g (0.001 mol) of dimethyl sulfoxide (molar ratio of 16:1) were heated to 175 °C for 3 h. The disappearance of starting material and appearance of product were monitored conveniently by thin layer chromatography (50% ether/hexane). The reaction mixture was chromatographed directly on a silica gel column giving 1.65 g (0.0073 mol, 89%) of bis(*p*-methylbenzyl) ether after removing solvent and drying in vacuo. The ethers obtained were pure by TLC and NMR.

Properties of the Substituted Dibenzyl Ethers. Bis(*p*-methylbenzyl) ether, mp 62–63 °C, reported[10] 63–63.5 °C; bis(*p*-methoxybenzyl) ether, mp 38–38.7 °C, reported[11] 39–39.5 °C; Bis(α-methylbenzyl) ether, bp (10 Torr) 144–150 °C, n^{23}_{D} 1.540, reported[2] bp (10 Torr) 145 °C, n^{20}_{D} 1.539.

Bis(*p*-fluorobenzyl) ether was previously unreported. Combustion analysis of our product gave satisfactory results (±0.2%) for carbon, hydrogen, and fluorine.

Cyclohexyl (α-methylbenzyl) ether was previously unreported. The NMR spectrum of our product was consistent with the ether structure.

Acknowledgments. We are grateful to the National Science Foundation (GM-05811) and to the Mobil Foundation for their financial support.

Registry No.—Me_2SO, 67-68-5; *l*-α-methylbenzyl alcohol, 1445-91-6; cyclohexanol, 108-93-0; *p*-methylbenzyl alcohol, 589-18-4; *p*-methoxybenzyl alcohol, 105-13-5; *p*-fluorobenzyl alcohol, 459-56-3; *p*-nitrobenzyl alcohol, 619-73-8; bis-(*p*-methylbenzyl) ether, 38460-98-9; bis-(*p*-methoxybenzyl) ether, 5405-95-8; *dl*-bis-(α-methylbenzyl) ether, 53776-69-5; *meso*-bis-(α-methylbenzyl) ether, 53776-68-4; bis-(*p*-fluorobenzyl) ether, 61812-54-2; cyclohexyl (α-methylbenzyl) ether, 61812-55-3.

References and Notes

(1) Y.-C. Wang and H. Morawetz, *J. Am. Chem. Soc.*, **98,** 3611 (1975).
(2) See, for example, D. Braun and H. G. Keppler, *Monatsh. Chem.*, **94,** 1250 (1963).
(3) V. J. Traynelis, W. L. Hergenrother, J. R. Livingston, and J. A. Valicenti, *J. Org. Chem.*, **27**, 2377 (1962).
(4) V. J. Traynelis, W. L. Hergenrother, H. T. Hanson, and J. A. Valicenti, *J. Org. Chem.*, **29**, 123 (1964).
(5) B. T. Gillis and P. E. Beck, *J. Org. Chem.*, **28,** 1388 (1963).
(6) T. M. Santosusso and D. Swern, *Tetrahedron Lett.*, 4255 (1974).
(7) D. L. Head and C. G. McCarty, *Tetrahedron Lett.*, 1405 (1973).
(8) T. M. Santosusso and D. Swern, *Tetrahedron Lett.*, 4261 (1968).
(9) J. Kenyon and E. J. Downer, *J. Chem. Soc.*, Part II, 1156 (1939).
(10) A. Etienne, *Ann. Chim.* (*Paris*), **1,** 5 (1946).
(11) A. Sosa, *Ann. Chim.* (*Paris*), **14**, 5 (1940).

Fluoroisoprenyl Synthesis Using Ethyl 2-Fluoroacetoacetate[1]

Paul R. Ortiz de Montellano* and Wayne A. Vinson

Department of Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California 94143

Received November 5, 1976

Fluorine substituted isoprenyl derivatives have aroused interest as potential insect juvenile hormone substitutes,[2] hyperlipidaemic drugs,[3] and, most recently, cancer chemotherapeutic agents.[4] The study of fluorinated isoprenoids in these and other contexts, however, has been hindered by a lack of convenient methods for their synthesis. Although 3-trifluoromethyl-2-butenol[5] and the 3-trifluoromethyl analogue of methyl farnesoate[2] have recently been prepared from trifluoroacetone and ethyl 1,1,1-trifluoroacetoacetate, respectively, most fluorinated isoprenyl compounds have been synthesized via schemes involving perchloryl fluoride fluorination.[3,6,12] The detonation hazards associated with this reagent,[7] however, discourage its use outside of specially equipped laboratories. We have developed a route to monofluorinated isoprenols involving base-catalyzed condensations of ethyl 2-fluoroacetoacetate (**1**), illustrated here by the preparation of 4-fluorofarnesol (**5**), whose general applicability is suggested by the widespread utility of ethyl acetoacetate itself in the assembly of carbon skeletons. Analogous condensations with ethyl 2-fluoroacetoacetate have not, to our knowledge, been previously reported.[8]

Ethyl 2-fluoroacetoacetate is readily prepared from inexpensive precursors, albeit in moderate yield, by base-promoted condensation of ethyl fluoroacetate and acetyl chloride.[8] Ethyl fluoroacetate is toxic but not otherwise hazardous,[9] and therefore can be handled with care by conventional techniques. Addition of geranyl bromide[10] to a solution of **1** in sodium methoxide–methanol gave in 63% isolated yield, after in situ base hydrolysis, 3-fluorogeranylacetone (**3**). Wadsworth–Emmons[11] condensation of **3** with diethyl 1-carboethoxyethylphosphonate gave ethyl 4-fluorofarnesoate (**4**)