

THE CLEAVAGE OF ETHERS BY BENZYNE

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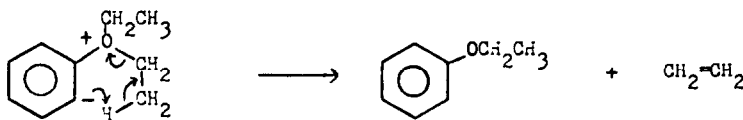
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(Received in USA 30 August 1973; received in UK for publication 4 October 1973)

Recently, reports have appeared which describe the cleavage of diethyl ether with highly electrophilic tetrachlorobenzynes and tetrafluorobenzynes to give ethylene and the corresponding 2,3,4,5-tetrahalophenetole.<sup>1,2</sup> Although unsubstituted benzyne is thought to undergo nucleophilic attack by ethers to form betaines, no cleavage products have been isolated in the absence of betaine-trapping reagents.<sup>2,3</sup> In contrast we wish to report the facile cleavage of ethers by benzyne in a solvent medium other than the ether itself.

When benzenediazonium-2-carboxylate (0.13m), isolated as a slurry in 200 ml of chloroform containing diethyl ether (0.26m), was heated at 45° for 1.5 hours, phenetole was isolated in 40% distilled yield. Lower yields were obtained in solvents in which the benzyne precursor was more poorly solvated and its rate of decomposition was slower.<sup>4a</sup> Yields of phenetole using 1,2-dichloroethane, dichloromethane, carbon tetrachloride, and diethyl ether as solvents were 14%, 12%, 0%, and 0%, respectively. Apparently decomposition of benzenediazonium-2-carboxylate in solution favors the formation of benzyne and benzyne derived products, whereas decomposition as a solid leads to a higher ratio of polymeric material.<sup>4b</sup>

By analogy to ether cleavage by tetrahalobenzynes and the cleavage of thioethers and certain tertiary amines by benzyne,<sup>5</sup> the probable mechanism is nucleophilic attack by the ether on benzyne followed by E1 collapse of the initially formed betaine through a six-membered transition state.<sup>6</sup>



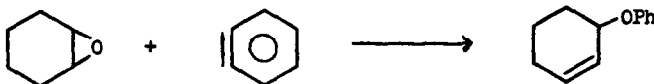
Results obtained with other ethers are summarized in the following table.

Benzynes Cleavage of Ethers in Chloroform<sup>7</sup>

<u>Ether</u>	<u>Products</u>	<u>% Yield</u>
diethyl ether	$\text{PhOC}_2\text{H}_5 + \text{CH}_2=\text{CH}_2$	40
diisopropyl ether	$\text{PhOCH}(\text{CH}_3)\text{CH}_3 + \text{CH}_2=\text{CHCH}_3$	14
phenetole	No Cleavage	0
methyl cyclohexyl ether	$\text{PhOCH}_3 + \text{cyclohexene}$	18
cyclohexene oxide	3-phenoxy-cyclohexene	23
ethyl isobutyl ether (1)	$\text{PhOC}_2\text{H}_5 + \text{CH}_2=\text{C}(\text{CH}_3)_2$ (22%) $\text{PhOCH}_2\text{CH}(\text{CH}_3)_2 + \text{CH}_2=\text{CH}_2$ (78%)	24
ethyl cyclohexyl ether(2)	$\text{PhOC}_2\text{H}_5 + \text{cyclohexene}$ (62%) Cyclohexyl phenyl ether + $\text{CH}_2=\text{CH}_2$ (38%)	23

The cleavage is sensitive to both steric and electronic factors in the reacting ethers. The former is indicated by the lower yield from diisopropyl ether, in line with the favored addition of diethyl amine over diisopropyl amine to benzyne.<sup>8</sup> The anticipated lower nucleophilicity of phenyl ethers versus aliphatic ethers<sup>9</sup> can account for the failure of initially produced alkyl phenyl ethers to undergo subsequent cleavage. Under identical conditions phenetole does not cleave to give diphenyl ether.

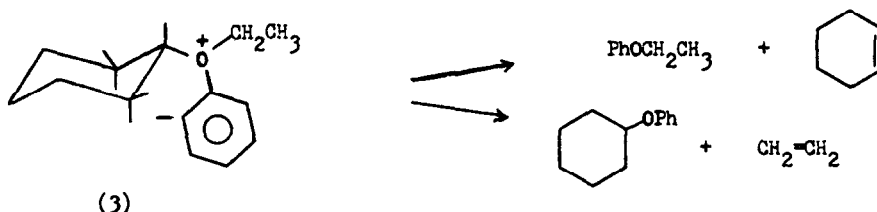
Alkene elimination was confirmed by the gas chromatographic detection of cyclohexene as a cleavage product from methyl cyclohexyl ether and the formation of 3-phenoxy-cyclohexene<sup>10</sup> from cyclohexene oxide.



A statistical orientation for alkene formation (rather than Hofmann or Saytzeff) was determined by an analysis of the product distribution from the cleavage of unsymmetrical dialkyl ethers. As shown, the cleavage of ethyl isobutyl ether, (1), gives phenetole (plus isobutylene) and isobutyl phenyl ether (plus ethylene) in a ratio close to the 25% and 75% distribution of the numbers of competing  $\beta$ -hydrogens. Similarly, benzyne cleavage of

ethyl cyclohexyl ether, (2), forms phenetole (plus cyclohexene) and cyclohexyl phenyl ether (plus ethylene) in yields approximating the 4:3 statistically expected ratio.<sup>11</sup> That these results are not fortuitous is indicated by the observation that (1) gives predominantly the less stable alkene with abstraction of the more acidic hydrogen (primary vs. tertiary), whereas with (2) the favored alkene is the more stable one resulting from abstraction of the less acidic hydrogen (secondary vs. primary). Orientation thus resembles the randomness found in many pyrolytic eliminations ( $\Delta 1$ ).<sup>12</sup> The product distribution argues for a  $\beta$ - as opposed to an  $\alpha$ -elimination process.

With (3) as the most highly populated conformation of the benzyne adduct from (2),<sup>13</sup>



statistical orientation of elimination implies not only that both cis and trans eliminations are occurring from the cyclohexyl group, but also that cyclohexene formation is not inhibited by a six-membered transition state which is not completely coplanar. Analogous mechanistic features have been found in other E1 reactions.<sup>12, 14</sup>

A future paper will deal with the reaction of benzyne with other epoxides and ethers, including tetrahydrofuran.

Acknowledgment. Appreciation is expressed to Grand Valley State Colleges for a research grant which supported this investigation.

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4. a) R.W. Hoffmann, Dehydrobenzene and Cycloalkynes, Academic Press, N.Y., 1967, p. 74.;  
b) Decomposition of benzenediazonium-2-carboxylate (.065M) was incomplete after two days in refluxing diethyl ether containing methanol (0.13M). No detection of carbon dioxide evolution or anisole formation indicated the absence of benzyne generation.
  5. V. Franzen, H.I. Joscheck, and C. Mertz, Ann., 654, 82 (1962); H. Hellmann and D. Eberle, ibid., 662, 188 (1963); Reference 4, p. 164, 171.
  6. At this point  $\alpha$ -elimination with initial loss of a carbene cannot be ruled out.
  7. Ether products were identified by a comparison of physical and spectral properties with those of authentic samples. For the last two entries ether product distributions, given in parentheses, were determined by gas chromatography (1% Carbowax 20M) using known mixtures as standards. The percent yields in all reactions are based upon benzenediazonium-2-carboxylate as the limiting reagent and represent total ether yields for the last two entries. Unreacted higher boiling ethers could be recovered almost quantitatively from the two-fold molar amounts used.
  8. The competition constant for amine addition is 18. T. Kauffmann, H. Fischer, R. Nuernberg, M. Vestweber, and R. Wirthwein, Tetrahedron Letters, 2911 (1967).
  9. The basicity constants for phenyl ethers are about 1000 times smaller than for aliphatic ethers. E.M. Arnett and C.Y. Wu, Chem. Ind. (London), 1488 (1959).
  10. NMR confirmed the presence of vinylic hydrogens. An authentic sample was prepared from 3-bromocyclohexene and sodium phenoxide.
  11. In contrast N-ethylpiperidine has been reported to react with benzyne to give only N-ethylpiperidine and ethylene. See reference 4, p. 171.
  12. C.H. DePuy and R.W. King, Chem. Rev., 60, 431 (1960).
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