

Reactivity in Cleavage of Dimethoxybenzenes by Sodium in Liquid Ammonia

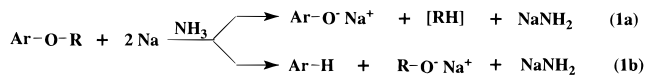
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The sodium/liquid ammonia cleavage of the dimethoxybenzenes and related substances, reported in large part by Birch in 1947, has been re-examined with use of improved techniques. Remarkable patterns of reactivity (e.g., *ortho* > *meta* ≫ *para*) that he described are confirmed and extended. They are agreeably rationalized by means of a simple, approximate adaptation from MO theory.

Alkyl aryl ethers are readily cleaved by alkali metals, forming (after hydron² acquisition) a hydrocarbon and an alcohol (eq 1b) or phenol (eq 1a). Constitutional and environmental influences on this seemingly simple reaction have consequences that differ from familiar patterns of reactivity. The consequences may be spectacular effects on reaction rate or switches between aryl–oxygen and alkyl–oxygen bond rupture. Rate effects are our chief interest.



The literature on this topic is scattered, but a reader is assisted by the reviews of Burwell³ and of Maercker.⁴ In recent years Melloni and co-workers^{5–10} have made numerous important contributions, relevant in particular to the matter of which bond ruptures. Some of the reactions they have discovered are of considerable utility in synthesis. A number of experiments of Ohsawa et al.¹¹ are also relevant to our study.

Our interest was aroused by a 1947 paper by Birch,¹² who studied the cleavage of the three dimethoxybenzenes by sodium metal in ammonia/diethyl ether. He observed substantial cleavage of the *o*- and *m*-dimethoxybenzenes to the corresponding methoxyphenols, but much less of the *para* isomer. His experimental techniques were unsophisticated. We felt his observations to be of such value that the experiments should be repeated with use of refinements, some not available before 1947.

Birch¹² combined 15 mL of a diethyl ether solution of the alkyl aryl ether with 150 mL of liquid ammonia in a Dewar flask, added sodium metal (3.6 equiv), stirred for 15 min, and let the mixture stand for 7 h before workup. Workup was by extraction, distillation, and crystalliza-

Table 1. Cleavage of Dimethoxybenzenes by Sodium in Ammonia^a

isomer	yield of methoxyphenol cleavage product, % ^b	
	in neat ammonia	in 83% ammonia/17% THF
<i>ortho</i>	95.0 ± 1.8	92.4 ± 5.3
<i>meta</i>	63.6 ± 0.8	70.8 ± 2.1
<i>para</i>	<10% ^c	8.4 ± 0.8

^a During 3.5 h at reflux. ^b Standard deviations are shown. ^c Preliminary experiment by Anne De Jarnatt.

tion. (Gas chromatography was unknown). Under those conditions he observed 89% cleavage of *o*-dimethoxybenzene,¹³ 71% of the *meta* isomer, and only 2.5% cleavage of the *para*. He recognized that “the small yield in the last case may be due partly to low solubility”, but offered an argument that low solubility was not primarily responsible.

Results

Our experiments were conducted in round-bottom glass flasks equipped with well-type reflux condensers cooled by solid carbon dioxide. That gave us an advantage: we could see the reacting system. Initial experiments, sketched in Table 1, concerned cleavage of the three dimethoxybenzenes in neat ammonia at reflux. We observed the same reactivity order as did Birch: *ortho* > *meta* ≫ *para*. Like him, we saw that the *para* isomer is not very soluble in ammonia and speculated that its apparent low reactivity might stem from that factor. Accordingly, we determined the reactivity order in 83% ammonia/17% tetrahydrofuran (THF), in which solvent all isomers are soluble at the concentrations involved in our experiments. Again, the *para* isomer was the least reactive; see the right column in Table 1.

In Table 2, we present further experimental data on cleavage of the dimethoxybenzenes plus observation that anisole is cleaved more readily than *p*- but not so readily as *o*- and *m*-dimethoxybenzenes. Noteworthy is that as much as 5% of anisole, representing aryl–oxygen scission, was obtained from the *meta* isomer, and traces from the other two.

Presented in Table 3 are observations concerning cleavage of two dimethoxytoluenes and 3,4-(methylene-dioxy)toluene. All but 2,5-dimethoxytoluene had been studied by Birch. Our results are similar to his, but our use of gas chromatography to examine reaction products

(13) In the quaint language of those times, “veratrole gave guaiacol, 89%”.

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- (1) Based in part on the B. A. thesis of J. Jenvey, August 1982.
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Table 2. Products from Cleavage of Diverse Ethers by Sodium in Ammonia/THF^a

substrate	solvent	no. of expts	product ^b	mol % of substrate ^c
anisole	NH ₃	1	anisole	54.4
			phenol	25.6
<i>o</i> -C ₆ H ₄ (OMe) ₂	NH ₃	2	benzene	1.8
			<i>o</i> -C ₆ H ₄ (OMe) ₂	1.3 ± 0.5
			<i>o</i> -MeOC ₆ H ₄ OH	95.0 ± 1.8
<i>m</i> -C ₆ H ₄ (OMe) ₂	NH ₃	3	anisole	<i>d</i>
			<i>m</i> -C ₆ H ₄ (OMe) ₂	29.2 ± 2.5
			<i>m</i> -MeOC ₆ H ₄ OH	63.6 ± 0.8
<i>m</i> -C ₆ H ₄ (OMe) ₂ ^e	NH ₃	3	anisole	4.9 ± 1.1
			<i>m</i> -C ₆ H ₄ (OMe) ₂	20.4 ± 4.9
			<i>m</i> -MeOC ₆ H ₄ OH	82.4 ± 4.8
<i>o</i> -C ₆ H ₄ (OMe) ₂ ^g	NH ₃ /THF	1	anisole	<i>f</i>
			<i>o</i> -C ₆ H ₄ (OMe) ₂	0.8
<i>o</i> -C ₆ H ₄ (OMe) ₂	NH ₃ /THF	2	<i>o</i> -MeOC ₆ H ₄ OH	99.7
			<i>o</i> -C ₆ H ₄ (OMe) ₂	0.66 ± 0.25
<i>m</i> -C ₆ H ₄ (OMe) ₂	NH ₃ /THF	2	<i>o</i> -MeOC ₆ H ₄ OH	92.4 ± 5.3
			anisole	0.58 ± 0.05
			<i>m</i> -C ₆ H ₄ (OMe) ₂	26.2 ± 4.5
<i>p</i> -C ₆ H ₄ (OMe) ₂	NH ₃ /THF	2	<i>m</i> -MeOC ₆ H ₄ OH	70.8 ± 2.1
			anisole	3.5 ± 1.7
			<i>p</i> -C ₆ H ₄ (OMe) ₂	80.8 ± 2.8
			<i>p</i> -MeOC ₆ H ₄ OH	8.4 ± 0.8

^a At reflux; reaction time 3.5 h, except as noted. ^b Or recovered substrate. ^c Standard deviations are shown. ^d Anisole observed (1.6%) in one experiment. ^e Reaction time 7 h. ^f Anisole observed, but not determined, in two experiments. ^g Reaction time 1 h.

enabled detection and quantification of minor byproducts that Birch did not report.

Prominent trends of reactivity revealed or confirmed by our data are these: (a) in the solvents employed, alkyl-oxygen scission predominates except in the case of 3,4-(methylenedioxy)toluene, which afforded exclusively products of aryl-oxygen rupture; (b) a methyl substituent resembles methoxy in tending to reduce scission *para* to itself, whether of the alkyl-oxygen or aryl-oxygen linkage; (c) 2,5-dimethoxytoluene has low cleavage reactivity virtually equal to that of *p*-dimethoxybenzene; its methyl group neither accelerates nor retards, but does somewhat favor cleavage of the methoxy group *ortho* to it over the one that is *meta*.

Discussion

The species that rupture during cleavage of alkyl aryl ethers by alkali metals are radical anions of the ethers.¹⁴⁻¹⁷ Two steps are involved: transfer of an electron to the ether from an electron donor, generally an equilibrium process, and scission of the radical anion. Although solvated electrons in ammonia have high negative redox potential,¹⁸ studies of Birch reduction¹⁹ kinetics indicate that neither benzene²⁰ nor anisole²¹ is fully electronated in liquid ammonia solutions of alkali metals.

Significant differences of cleavage reactivity are differences in the extent of electronation of the ethers.

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Methoxy groups tend to increase the electron affinity of a benzene derivative through their electron-attracting inductive effect, but to decrease it by π -donation of p electrons into aromatic LUMOs, as discussed below. Among the dimethoxybenzenes, these effects should cause the *para* isomer to have the highest electron affinity because (*vide infra*) it should be little troubled by the π -donation effect. Inasmuch as an introduced methoxy group has little effect on the electron affinity of benzene,^{22,23} the extent of electronation of *p*-dimethoxybenzene should resemble that of anisole.

There is some resemblance of our cleavage reactivity observations with those by ESR spectroscopists. Brown et al.²⁴ prepared the radical anions of the dimethoxybenzenes by the action of potassium metal in ether solvent (tetrahydrofuran or 1,2-dimethoxyethane). The ESR spectrum of the *para* radical anion was observable, as of a stable species, -80 to -20 °C, but the *ortho* and *meta* isomers did not give observable spectra. Similar behavior was reported by Bowers.²⁵

Sodium in hexamethylphosphorotriamide, during 2-4 h at 100 °C, efficiently demethylates all three dimethoxybenzenes to the corresponding methoxyphenols, in high yield.²⁶ Although useful for syntheses, that reagent under those conditions does not reveal the orientation effects of present interest.

We shall employ a simple, qualitative rationalization of many of our data, one similar to that used by Bowers²⁵ in his interpretation of ESR spectra of anisole and related ethers. It stems from molecular orbital treatment of the benzene π system, which generates six π MOs, the three lower in energy being bonding and the upper three antibonding in character. In the benzene molecule, the three bonding π MOs are occupied by six electrons. Two degenerate antibonding LUMOs, Ψ_4 and Ψ_5 , depicted in Figure 1, are respectively symmetric and antisymmetric. Since they are at equal energy levels for benzene itself, the "extra" electron of the benzene radical anion resides with equal probability in one or the other. In a substituted benzene, however, interactions of substituents with Ψ_4 and Ψ_5 influence their characteristics, including their relative energy levels.

For discussion purposes, Bowers assumed the approximation that substituents such as methyl and methoxy make only small perturbations to the benzene MOs, mainly to remove the degeneracy between Ψ_4 and Ψ_5 , raising or lowering the energy level of one (when singly occupied by the "extra" electron of a radical anion) with respect to the other. For a substituted benzene, he aligned Ψ_4 and Ψ_5 with respect to substituents so that a plane of symmetry (perpendicular to the plane of the ring) of the molecule coincided with a symmetry or antisymmetry plane of the MO. In the radical anion, the SOMO (Ψ_4 or Ψ_5 occupied by an electron) of lower energy was considered more likely to contain the "extra" electron and to make a larger contribution in the linear combination of Ψ_4 and Ψ_5 for the species.

In our application of the Bowers approach, we presume that the interaction of substituents with Ψ_4 or Ψ_5 is stronger the larger the atomic orbital coefficient at the

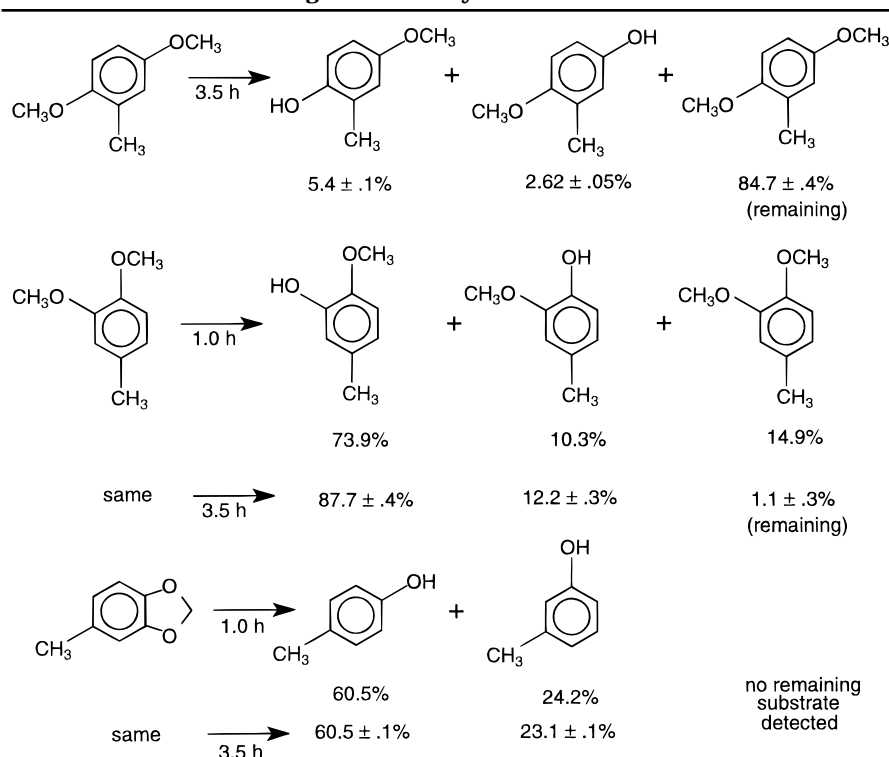
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Table 3. Cleavages Effected by Sodium in Ammonia/THF^a

^a Those for 1 h duration were single experiments; those for 3.5 h were duplicates.

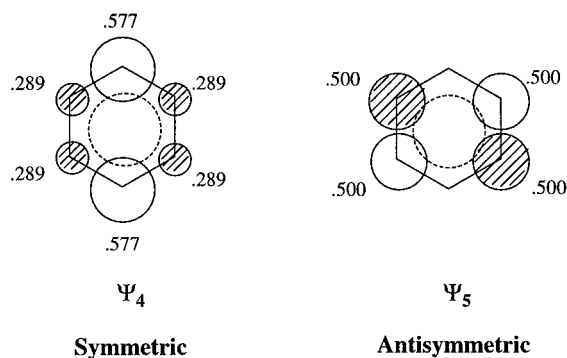


Figure 1. The two (antibonding) LUMOs of benzene.^{22,27} Atomic orbital coefficients at the ring positions are indicated by numbers and represented approximately by the diameters of the circles.

site of attachment of the substituent. That interaction may be of two sorts: (1) since both methoxy and methyl groups have π -donating capability, their interaction with a SOMO is unfavorable, raising its energy level; and (2) electron shift from the π -system to the alkoxy group of an ether is necessary for scission. In considering the latter interaction, we give principal attention to the SOMO that mainly accommodates the "extra" electron.

This qualitative approach is less rigorous than proper MO calculations, but has the advantage that it can be invoked in reading or conversation without recourse to a computer. It may be likened to qualitative resonance theory as widely used by organic chemists. One must however note that π -electron-attracting substituents, such as nitro and cyano, which interact preferentially with Ψ_4 , greatly distort its shape. This is shown by the ESR spectra of nitrobenzene and benzonitrile radical anions.²⁵

Our interpretation of why cleavage of *o*- and *m*-dimethoxybenzenes is faster than of the *para* isomer resembles that of Zimmerman.²⁸ He suggested that

cleavage rate is greater the greater the π^* electron density in a radical anion at a methoxy site. His LCAO MO calculations²⁹ showed no π^* electron density at the methoxy-bearing carbon atoms in *p*-dimethoxybenzene radical anion, plus significant (but low) electron density on the methoxy-bearing carbons for the *ortho* and *meta* isomers. Recent calculations by Wenzel³⁰ give similar results.

Our simple, approximate treatment leads to conclusions remarkably similar to those from Zimmerman's calculations. Allowable LUMO alignments for the dimethoxybenzenes are shown in Figure 2. Whether the methoxy groups make Ψ_4 or Ψ_5 more energetic is determined by the fact that methoxy is electronically a π -donor group and our presumption that the strength of interaction is greater the greater the atomic orbital coefficients at the carbons where they are attached. Placement of an electron in an antibonding orbital increases molecular energy, and π -donation of electrons by methoxy groups increases it further. The more favorable alignment of Ψ_4 or Ψ_5 has methoxy groups attached to carbons with lower atomic coefficients.

Among the dimethoxybenzene radical anions, the lowest energy alignment is that of antisymmetric Ψ_5 to the *para* isomer, at lower right in Figure 2. In this case, the atomic coefficients at the methoxy positions are zero. In contrast, Ψ_4 of the *para* isomer has both methoxy groups on carbons with relatively high (0.577) coefficients, for high energy in the radical anion. For the *ortho* and *meta* isomers, as shown in Figure 2, the disfavored alignments both have methoxy groups on carbons with relatively high (0.500) coefficients. The favored alignments have the methoxy groups on carbons with coefficients 0.289.

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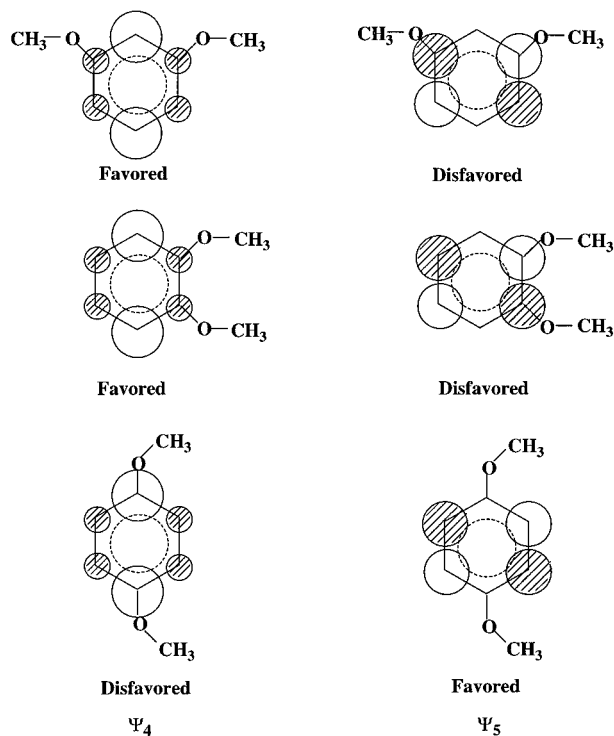


Figure 2. The two π LUMOs of benzene "fitted" to the dimethoxybenzenes. Diameters of the circles around benzene carbon atoms indicate approximately the magnitudes of their atomic orbital coefficients. Electronic interactions between occupied p orbitals of the methoxy groups and Ψ_4 and Ψ_5 cause "disfavored" MOs, when occupied by an electron, to be at higher energy levels than "favored".

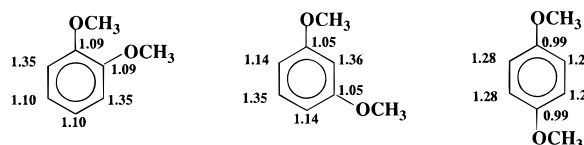


Figure 3. Electron densities at aromatic carbon atoms of the dimethoxybenzene radical anions as calculated by Zimmerman.^{28,29} To obtain the electrical charge at any carbon, subtract 1.00 from the electron density.

The probability of an electron being at any site is, in theory, the square of its atomic orbital coefficient. For *o*-dimethoxybenzene radical anion, with the "extra" electron in Ψ_4 , this simple approach predicts LUMO electron densities at the 2-, 3-, and 4-positions of 0.08, 0.33, and 0.08, respectively. The electron densities that Zimmerman²⁸ calculated are displayed in Figure 3. Subtraction of 1.00 (the average π electron density per carbon in the neutral molecule) from each gives net charges at the 2-, 3-, and 4-positions in the radical anion of 0.09, 0.35, and 0.10, respectively. Thus the results from the simple, approximate approach agree rather well with Zimmerman's LCAO MO calculations.^{28,29} The charges calculated for the 1-, 2-, and 3-carbon atoms of *m*-dimethoxybenzene by the approximate approach, namely, 0.08, 0.33, and 0.08, agree with Zimmerman's values not quite so well.

If an ether linkage is more likely to rupture the higher the electron density at its aromatic carbon, these considerations predict moderate reactivity for the *o*- and *m*-dimethoxybenzenes and very low reactivity for the *para* isomer, as observed (Table 2). Indeed, the fact that the *para* isomer ruptures at all indicates that disfavored Ψ_4 is occupied to some extent.

Other Alkyl Aryl Ethers. That the cleavage reactivity of anisole is low but higher than that of *p*-dimethoxy-

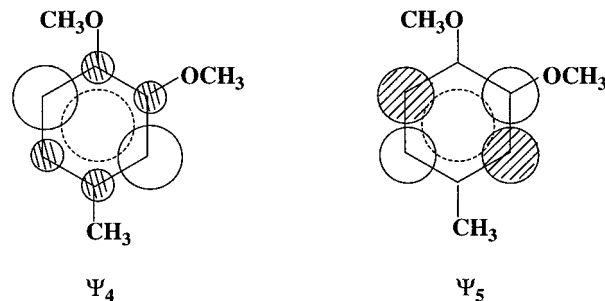


Figure 4. Alignments of benzene LUMOs Ψ_4 and Ψ_5 to 3,4-dimethoxytoluene.

benzene finds interpretation in the same qualitative theory. For anisole, the favored alignment is Ψ_5 , like that of *p*-dimethoxybenzene in Figure 2, but without the second methoxy group. Because of the absence of the latter, partial utilization of Ψ_4 involves less of an energetic penalty in the case of anisole.

2,5-Dimethoxytoluene (top line in Table 3) is methyl-substituted *p*-dimethoxybenzene. Very likely the more favored MO alignment for it is like that of *p*-dimethoxybenzene in Figure 2, with the methoxy groups at sites of zero atomic orbital coefficient. Its total cleavage reactivity is nearly the same as that of *p*-dimethoxybenzene. That it ruptures at all is probably due, again, to partial utilization of Ψ_4 . Why, however, is the methoxy group *ortho* to methyl cleaved twice as fast as that *meta* to methyl?

Inasmuch as 3,4-dimethoxytoluene is methyl-substituted *o*-dimethoxybenzene, one might expect its total cleavage reactivity to be of similar magnitude. Our data from 1 h exposure to sodium in ammonia/THF indicate it however to be somewhat less reactive. Noteworthy is that the remote methyl group, *meta* to one methoxy and *para* to the other, exerts a substantial influence on which alkyl-oxygen linkage ruptures; that *meta* to methyl breaks about seven times as fast as the one *para* to methyl.³¹ These behaviors become intelligible if the radical anion has its "extra" electron shared between symmetric Ψ_4 and antisymmetric Ψ_5 (Figure 4). Neither alignment is perfect. Experimental fact suggests that the methyl group, a π donor resembling methoxy,³² makes Ψ_4 in this case somewhat less favorable than for *o*-dimethoxybenzene and at the same time Ψ_5 more attractive because it has the methyl and one methoxy group both at zero atomic orbital coefficient positions. To the extent that the extra electron resides in Ψ_5 , the methoxy group *meta* to methyl is disposed to rupture. The Ψ_4 alignment would suggest more or less equal rates of scission of the two methoxy groups.

A case that can be similarly rationalized is cleavage of 1,2,4-trimethoxybenzene by sodium in hexamethylphosphorotriamide to afford 2,5-dimethoxyphenol in 65% yield.²⁶

Aryl-Oxygen Scission. 3,4-(Methylenedioxy)toluene (Table 3, bottom line) has the same substituent orientation as 3,4-dimethoxytoluene and on reaction with sodium in ammonia/THF likewise shows much greater scission *meta* than *para* to the methyl group. A major difference is, however, that now the aryl-oxygen bonds

(31) Somewhat similar behavior is shown by 3,4-dimethoxytoluene on exposure to Na/K alloy in THF or dimethoxyethane at very low temperature (ref 17). Cleavage to *p*-methoxytoluene (aryl-oxygen scission!) occurs readily.

(32) There are suggestions also in studies of ESR spectra of radical anions that a methyl group is almost as strong a π -donor as is a methoxy group; see refs 17 and 25.

are the ones that break. A key difference between the two substrates is that, whereas 3,4-dimethoxytoluene is a true diether, the two oxygen atoms of 3,4-(methylenedioxy)toluene are in acetal functionality. Others^{12,33} have observed that acetals of phenols, when cleaved by alkali metals, tend to suffer rupture of aryl-oxygen bonds.

In seeking to understand this remarkable change, let us note that change from alkyl-oxygen to aryl-oxygen scission can also be caused by change of solvent.⁴ For example, anisole is mainly cleaved to phenol in ammonia (this work) and in hexamethylphosphorotriamide³⁴ but to phenylpotassium in heptane.³⁵ The trend is for less polar solvents more to favor aryl-oxygen scission. Melloni and co-workers^{5,7} have made good use of the solvent effect in synthesis.

A plausible interpretation is that two major factors affect the sense of scission: (a) the basicity and (b) solvation or ion-pairing of the oxyanion released. Release of the less basic (aryloxide) anion is favored if solvation is good, but if solvation is poor the exceptionally tight ion-pairing of a highly basic (alkoxide) ion with an alkali metal ion is energetically favored and alkyl-oxygen scission occurs. For acetals, two influences of an α -alkoxy substituent increase the likelihood of aryl-oxygen scission: it diminishes the basicity of an alkoxide ion (significant for polar solvents) and probably increases ion-pairing with an alkali metal cation (relevant especially to nonpolar solvents). Lesser basicity for ROCH_2O^- is suggested by the fact that $\text{p}K_a$ for HOCH_2OH in water is 13.3³⁶ vs 15.5 for CH_3OH .³⁷ An α -alkoxy group may help ion-pairing by chelation of the cation by the bridging oxygen atom.

Experimental Section

Materials. **3,4-Dimethoxytoluene** was synthesized, according to the Huang-Minlon-modified Wolff-Kishner method,³⁸ from 3,4-dimethoxybenzaldehyde: yield 46%, >99% pure by GC analysis; n_D^{25} 1.5263 (lit.³⁹ n_D^{25} 1.5257); $^1\text{H NMR}$ (60 MHz, CCl_4) δ 2.2 (s, 3H), 3.6 (s, 6H), 6.3 (s, 3H); MS m/z 152 (M^+). **4-Methoxy-2-methylphenol** was prepared from *m*-cresol by Elbs persulfate oxidation, methylation, and hydrolysis, after Baker and Brown.⁴⁰ Distillation (95–127 °C/5 Torr) afforded the crude product (18.1%), which was purified by flash chromatography (silica gel column, dichloromethane) and recrystallization from toluene and hexanes: white needles: yield 8.1%; mp 69–71 °C (lit.⁴¹ 70.5–71.5 °C); $^1\text{H NMR}$ (60 MHz, CCl_4) δ 2.2 (s, 3H), 3.6 (s, 3H), 5.2 (s, 1H), 6.4 (m, 3H). Shrinkage of the δ 5.2 signal on exposure to D_2O and broad IR absorbance at 3350 cm^{-1} both indicate a phenol. **2-Methoxy-5-methylphenol** was prepared via diazotization of 2-methoxy-5-methylaniline and ensuing hydroxydediazotization;⁴² orange plates; >99% pure by GC analysis; yield 16.3%; $^1\text{H NMR}$ (60 MHz, CCl_4) δ 2.2 (s, 3H), 3.7 (s, 3H), 5.2 (broad s, 1H), 6.4 (m, 3H); MS m/z 138 (M^+). **2-Methoxy-4-methylphenol** was prepared from vanillin according to Martin's modified Clemmensen reduction;^{43,44} yield 44%; bp 70–77 °C/4–5 Torr (lit.⁴⁴ 105–106 °C/15 Torr); after redistillation, >99% pure by GC analysis; bp 68–74 °C/4.5 Torr; $^1\text{H NMR}$ (60 MHz,

CCl_4) δ 2.2 (s, 3H), 3.5 (m, 3H), 5.5 (broad s, 1H), 6.3 (m, 3H); MS m/z 138 (M^+). **4-Methoxy-3-methylphenol** was prepared from *o*-cresol by a method identical to that described above for 4-methoxy-2-methylphenol. After distillation (bp 115–135 °C/4.5 Torr) and purification by flash chromatography, the product, which solidified after a few minutes in the freezer, was recrystallized three times from toluene and light petroleum ether; separation of an oil was avoided by chilling the warm solution quickly by means of a salt/ice/water bath: small white needles; yield 1.4%; mp 45–46 °C (lit.⁴¹ 46–46.5 °C); $^1\text{H NMR}$ (60 MHz, CCl_4) δ 2.0 (s, 3H), 3.6 (s, 3H), 5.8 (broad s, 1H), 6.3 (m, 3H). The δ 5.8 signal shrank on addition of one drop of D_2O and shifted upfield to δ 4.5. **3,4-(Methylenedioxy)toluene** was synthesized from piperonal in a Huang-Minlon-modified Wolff-Kishner reduction identical to that described above for 3,4-dimethoxytoluene: yield 56%; bp 42 °C/4 Torr (lit.⁴⁵ 196 °C/740 Torr); $^1\text{H NMR}$ (60 MHz, CCl_4) δ 2.2 (s, 3H), 5.6 (s, 2H), 6.3 (m, 3H); MS m/z 136 (M^+); >99% pure by GC analysis. All other reagents used were purchased.

Standard Procedure for Cleavage Experiments. Steps 1–4 were performed under an atmosphere of nitrogen and with constant stirring. (1) Approximately 100 mL of ammonia was distilled from sodium metal into a three-necked round-bottom flask fitted with a well-type reflux condenser cooled by solid carbon dioxide. For reactions in which THF was used as a cosolvent, about 20 mL of THF, freshly distilled, was added. (2) Approximately 6.7 mmol of substrate was added to the flask. (3) Approximately 27 mmol of sodium metal was added to the flask. (4) The mixture was allowed to react under reflux for the specified length of time. (5) The reaction mixture was quenched with a minimum amount of sodium benzoate (usually 1–2 g). A color change from blue to orange signaled completion of this addition. (6) The excess base was neutralized with ammonium nitrate (usually 1–2 g). A color change from orange to colorless signaled completion of this addition. (7) Approximately 3 mmol of an appropriate GC internal standard was added to the flask. The internal standards found to be most useful were, for anisole, *m*-dimethoxybenzene; for *m*-dimethoxybenzene, phenol, *o*-dimethoxybenzene, or *p*-methoxyphenol, or a combination thereof; for *o*-dimethoxybenzene, *m*-dimethoxybenzene; for *p*-dimethoxybenzene, *o*-dimethoxybenzene and *m*-methoxyphenol; for 2,5-dimethoxytoluene, 3,4-dimethoxytoluene; for 3,4-dimethoxytoluene, 2,5-dimethoxytoluene; for 3,4-(methylenedioxy)toluene, 2,5-dimethoxytoluene. (8) After the addition of 100 mL of chilled diethyl ether and with the condenser (from which all the carbon dioxide had sublimed) left attached to the flask, the ammonia was allowed to evaporate, a process that took approximately 3 h after the carbon dioxide had all sublimed. The purpose of having diethyl ether present was to reduce entrainment of more volatile compounds, such as benzene, with the evaporating ammonia. (9) Enough 5% aqueous sodium bicarbonate solution (usually 50–75 mL) was added to dissolve all solid material. (**CAUTION:** If particles of sodium metal had clung to the upper walls or necks of the flask, fire might result.) (10) The ether and aqueous layers were separated, and the aqueous phase extracted three times with 25 mL portions of diethyl ether. All the ether extracts were combined and dried over magnesium sulfate. (11) The ether solution was analyzed by a Hewlett-Packard 5840A gas chromatograph (GC) equipped with either a 10 m methyl silicone capillary column or a 20 m carbowax capillary column. A reference solution of authentic samples was used to calibrate the GC; product identifications were by GC retention time analysis.

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