

injected into the HRGC. Column: RSL-300 (polyphenylmethylsiloxane) (10 m × 0.53 mm i.d.) bonded FSOT (1.2 μm film). Temperature: 90 °C for 2 min, then to 230 °C at 25 °C/min. Flow rate: 4 mL/min He. Detector: FID 250 °C. Injector: splitter 1:40, 250 °C.

**Detection of NO Gas in Equilibrium with the Reaction Solution.** The oxidation of *n*-Bu<sub>2</sub>S was performed as described above. At the end of the reaction the GC-MS analysis of the gaseous phase [HP 5988A spectrometer, HP Ultra 1 (cross-linked methyl silicone) column (25 m × 0.32 mm, 0.17 μm film thickness), 70 °C, He carrier] revealed the presence of a discrete amount of NO and the absence of oxygen and other nitrogen oxides. Under strictly analogous conditions but in the absence of the sulfide as reducing agent, no NO formation was observed.

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**Registry No.** 1, 622-38-8; 1', 4170-80-3; 2, 622-38-8; 2',

114045-22-6; 3, 13865-49-1; 3', 114045-23-7; 4, 831-91-4; 4', 833-82-9; 5, 3019-20-3; 5', 4170-69-8; 6, 7570-92-5; 6', 3324-82-1; 7, 107-47-1; 7', 2211-92-9; 8, 7205-60-9; 8', 114129-36-1; 9, 3795-79-7; 9', 114129-35-0; 10, 50910-13-9; 10', 114045-25-9; 11, 123-09-1; 11', 934-73-6; 12, 100-68-5; 12', 1193-82-4; 13, 623-13-2; 13', 934-72-5; 14, 1879-16-9; 14', 3517-99-5; 15, 2388-73-0; 15', 38452-13-0; 16, 2388-74-1; 16', 13150-72-6; 17, 3393-77-9; 17', 1774-36-3; 18, 3561-67-9; 18', 114129-34-9; 19, 17241-04-2; 19', 83212-58-2; 20, 124461-76-3; 20', 124461-77-4; 21, 54091-78-0; 21', 124461-78-5; 22, 6937-97-9; 22', 114045-26-0; 23, 63-68-3; 23' (isomer 1), 3226-66-2; 23' (isomer 2), 23631-84-7; TBA<sup>+</sup>AuBr<sub>4</sub><sup>-</sup>, 17769-65-2; TBA<sup>+</sup>AuCl<sub>4</sub><sup>-</sup>, 17769-64-1; TBA<sup>+</sup>AuBr<sub>2</sub><sup>-</sup>, 50481-01-1; TBA<sup>+</sup>Br<sup>-</sup>, 1643-19-2; thiophenol, 108-98-5; 1,3-dibromopropane, 109-64-8; L-(-)-ephedrine [(1*R*,2*S*)-2-(methylamino)-1-phenyl-1-propanol], 299-42-3; tetrabromoauric acid, 17083-68-0; 3-bromopropyl phenyl sulfide, 3238-98-0.

**Supplementary Material Available:** Figure 1, HPLC and HRGC chromatograms for the oxidation of di-*tert*-butyl sulfide catalyzed by TBA<sup>+</sup>AuBr<sub>4</sub><sup>-</sup> (2 pages). Ordering information is given on any current masthead page.

## A New Rearrangement of Alkoxybenzyl Anions

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Alkyl groups migrate from oxygen to carbon in alkyl aryl ethers which have been metalated in benzylic positions. 2,6-Dimethylanisole provides a variety of 2,6-dialkylphenols and their ethers in 45–80% yields. Rearrangement products are obtained in 10–30% yields from other dimethylanisoles and from methylanisoles. The reactions appear to proceed, like Wittig rearrangements, by homolytic cleavage of the alkyl–oxygen bond followed by recombination of the resulting radical pair in a different way. The rearrangements can be avoided by using *methyl* ethers and working at or below room temperature.

In attempting to prepare dianion 1 by refluxing 2,6-dimethylanisole (**6d**) with 2 equiv of Lochmann's base (*n*-BuLi/KO-*t*-Bu)<sup>1</sup> in heptane, we obtained products from dianion 2 instead which indicated that the methyl group migrates from oxygen to benzylic carbon in at least 70% yield. We have studied the scope and mechanism of this unexpected rearrangement to learn where it is synthetically useful and also how it can be avoided, permitting reactions of alkoxybenzyl anions without rearrangement. Some products and yields obtained in this study are given in Chart I and Table I.

**Methylanisoles.** Since the simplest mechanisms for this rearrangement do not require a second methyl group on the ring, we tried methylanisoles (**3a–c**) as starting materials (reactions 1, 3, and 5). Rearrangement products were obtained in every case, but the total yields of rearrangement products (14–29%) were much lower than with 2,6-dimethylanisole (**6d**), with the simple rearrangement products **4d–f**, obtained in 11–14% yields, being accompanied by products containing *s*-Bu groups (**4j,k**, formed by benzylic metalation of ethyl groups followed by alkylation with diethyl sulfate) and *i*-Pr groups (**4i**, derived by benzylic metalation of ethyl groups followed by methylation via *intermolecular* rearrangement). That these further reactions were not observed in the para case is consistent with it being more difficult in general to met-

alate alkyl groups para to alkoxy groups than either ortho (favored by chelation<sup>2-5</sup>) or meta (favored by resonance effects). This generalization also explains why the main nonrearrangement products come from dealkylation–metalation–dialkylation in the ortho and meta cases (**4g,h**) but from dealkylation–monoalkylation in the para case (**4c**). Since ring metalation ortho to methoxyl groups is well known,<sup>6</sup> the formation of a small amount of **7b** in the para case is not surprising.

It should be noted that in these reactions in refluxing heptane, the methyl groups are completely lost from the starting anisoles **3a–c**. When these reactions were repeated at room temperature (reactions 2, 4, and 6), the methyl groups were largely retained in the products. The yields of propylanisoles **3f–h** from metalation–alkylation were 49, 80, and 26%, respectively. In the ortho case, dealkylation–metalation–dialkylation gave an additional 25% of the propylphenetol **4g**, and small amounts of rearrangement products were observed, but from these and examples below involving di- and trimethylanisoles, *the rearrangement can be avoided by working with methyl*

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(3) Majewski, M.; Green, J. R.; Snieckus, V. *Tetrahedron Lett.* 1986, 27, 531.

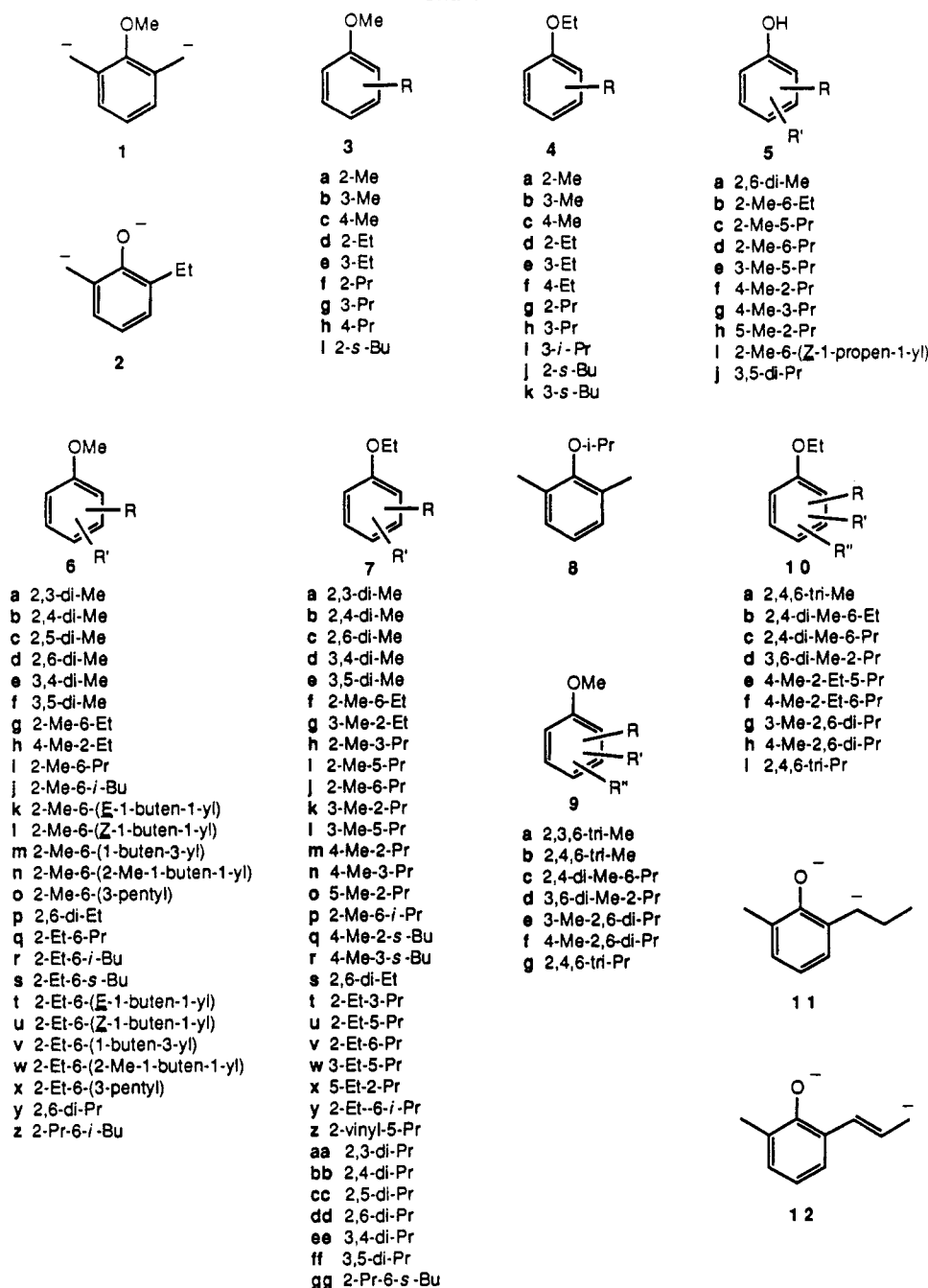
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(5) Harris, F. L.; Weiler, L. *Tetrahedron Lett.* 1985, 26, 1939.

(6) Gilman, H.; Webb, F. J.; *J. Am. Chem. Soc.* 1940, 62, 987; 1949, 71, 4062.

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Chart I



ethers at or below room temperature.

**Dimethylanisoles.** Rearrangement products were then sought from all six dimethylanisoles (6a-f) in refluxing heptane using enough base to make dianions. Since the total yields of rearrangement products obtained from the other five dimethylanisoles (Table I, reactions 7-9, 14, 15) are only 10-20%, there is clearly something special favoring rearrangement in the 2,6-dimethyl case (6d), which gives 60-71% under the same conditions (reactions 10,12). What this is will be seen below. First, it should be noted that the rearrangement products from the dimethylanisoles (6a-f) in no case arise from metalation at a para position (more difficult than at the other positions, as noted above) followed by rearrangement to the para position; para metalation products are observed from 2,4- and 3,4-dimethylanisoles (6b,e), and the example of 4-methylanisole (3c) above shows that rearrangement can occur to the para position, but apparently the slowness of para metalation

in the dimethylanisole cases means that the methyl group on oxygen has rearranged to the ortho or meta position or been lost through a dealkylation mechanism before it has a chance to rearrange to the para position. Four of the cases thus become relatively straightforward: In reaction 8, 2,4-dimethylanisole (6b) gives 4-methyl-2-sec-butylphenetole (7q) through an ortho metalation-ortho rearrangement-ortho metalation-dialkylation sequence; in reaction 12, 2,6-dimethylanisole (6d) gives 2-ethyl-6-propylphenetole (7v), perhaps by the same sequence, with the second metalation occurring as expected at the benzylic methyl rather than the benzylic methylene; in reaction 14, 3,4-dimethylanisole (6e) gives 3-sec-butyl-4-methylphenetole (7r) by a similar sequence involving the meta position rather than the ortho position; and in reaction 15, 3,5-dimethylanisole (6f) gives 3-ethyl-5-propylphenetole (7w) by an all-meta sequence with the second metalation again occurring at methyl rather than methylene.

Table I. Products and Yields in Reactions of Aryl Alkyl Ethers with Lochmann's Base Followed by Dialkyl Sulfates

rxn	SM <sup>a</sup>	equiv <i>t</i> -BuOK/ <i>n</i> - BuLi	time, h/temp	R <sub>2</sub> SO <sub>4</sub>	rearrangement products (% yield)	nonrearrangement products (% yield)
1	3a	1.5/1.8	4.5/rflx	Et	4j (12), 4d (11)	4g (42), 4a (18)
2	3a	1.0/1.0	2/rt	Et	4d (5), 4j (4), 3i (4), 3d (1)	3f (49), 4g (25), 6q (2), 4a (1)
3	3b	1.5/1.8	4.5/rflx	Et	4e (14), 4i (10), 4k (5)	4h (35), 4b (12)
4	3b	1.0/1.0	2/rt	Et	3e (1)	3g (80), 3b (5), 4h (5), 4b (2)
5	3c	1.5/1.8	4.5/rflx	Et	4f (14)	4c (56), 7b (4)
6	3c	1.0/1.0	2/rt	Et	none	3c (33), 3h (26), 6h (14), 4c (6)
7	6a	3.5/4.0	20/rflx	Et	7s (20), 7g (2)	7h (35), 7k (15), 7aa (12), 7a (2)
8	6b	2.5/3.0	20/rflx	Et	7q (11)	7m (50), 7bb (15), 5f (6), 7b (5)
9	6c	2.5/3.0	20/rflx	Et	7u (7), 7x (4), 7z (4)	7i (28), 7o (28), 7cc (28), 5c (8), 5h (3)
10	6d	2.5/3.0	20/rflx	Et	7f (61), 7p (4), 7s (3), 7v (3)	7c (24), 7j (3)
11	6d	2.5/3.0	20/rt	Et	7v (6), 6q (3), 7f (2), 7gg (1)	6y (62), 6i (12), 7dd (5), 7j (3)
12	6d	3.5/4.0	20/rflx	Et	7v (34), 7f (26)	7j (11), 7c (10), 7dd (8)
13	6d <sup>b</sup>	2.5/3.0	20/rflx	c	5b (52), 5d (5) <sup>d</sup>	5a (20) <sup>d</sup>
14	6e	3.5/4.0	20/rflx	Et	7r (10)	7n (44), 5g (11), 10e (6), 7ee (3), 7d (2)
15	6f	3.5/4.0	20/rflx	Et	7w (12)	7ff (35), 7l (15), 5j (10), 5e (8), 7e (2)
16	6p	4.0/4.5	20/rflx	Et	7y (45)	7s (18)
17	7c	2.5/3.0	20/rflx	Me	6i (55), 6o (6), 6k (4), 6l (tr), 6m (tr)	6d (27), 6p (tr)
18	7c	3.0/3.5	25/rflx	Me	6q (41), 6x (5), 6t (2), 6u (2), 6v (2)	6p (23), 6g (19)
19	7c	2.5/3.0	20/rt	Me	6q (28), 6s (3), 6i (2), 6x (1)	7s (30), 6p (23), 6g (8), 7f (1.5)
20	7c <sup>e</sup>	2.5/3.0	20/rflx	c	5d (49), 5b (8), 5i (4)	5a (30)
21	8	2.0/2.5	20/rflx	Me	6r (55), 6j (21), 6w (2), 8 (2), 6n (1)	6g (14)
22	8	2.5/3.0	40/rt	Me	6r (66), 6j (9)	6g (16), 8 (2)
23	8	2.5/3.0	40/rt	f	6z (50)	
24	9a	2.5/3.0	20/rt	Et	none	9e (50), 9d (20), 10d (18), 10g (5)
25	9b	2.0/3.0	20/rflx	Et	10b (50), 10f (13)	10a (19), 10c (13), 10h (2)
26	9b	2.5/3.0	20/rflx	Et	10f (28), 10b (26)	10c (21), 10a (12), 10h (9)
27	9b	3.0/3.5	20/rt	Et	none	9f (58), 9c (14), 10c (10), 9g (6), 10h (3), 10i (1)

<sup>a</sup> 1 equiv (10 mmol). <sup>b</sup> Equimolar mixture with phenetole. <sup>c</sup> H<sub>2</sub>O. <sup>d</sup> Products derived from 6d only. <sup>e</sup> Equimolar mixture with anisole. <sup>f</sup> 1.8 equiv of EtBr/300 mL, of THF/5 h, then 3.6 equiv of Me<sub>2</sub>SO<sub>4</sub>/15 h.

The 2,3- and 2,5-dimethylanisole cases (6a and 6c) each bring an ortho methyl group into competition with a meta methyl group, with the following results: In the former case, the sole rearrangement product (2-ethyl-3-propylphenetole, 7t) comes from rearrangement to the ortho position. In the latter case, the meta rearrangement product (2-propyl-5-ethylphenetole, 7x) is obtained in 4% yield along with 7% of the ortho rearrangement product (2-ethyl-5-propylphenetole, 7u) and 4% of 2-vinyl-5-propylphenetole (7z), which we believe arises from 7u by ortho metalation followed by elimination of hydride.

In reactions 10 and 12, run on 2,6-dimethylanisole (6d) with varying amounts of base, the simple rearrangement product 2-methyl-6-ethylphenetole (7f) from the monoanion is also formed; in reaction 10, with smaller amounts of base, its yield is 61%. We interpret this (along with other examples below) to indicate that *rearrangements go in good yield to an ortho position only when the other ortho position is occupied*, i.e., a dianion such as 1 is not required for a good rearrangement yield as long as there is some ortho substituent on the other side. A likely reason for this is given in the mechanism section below.

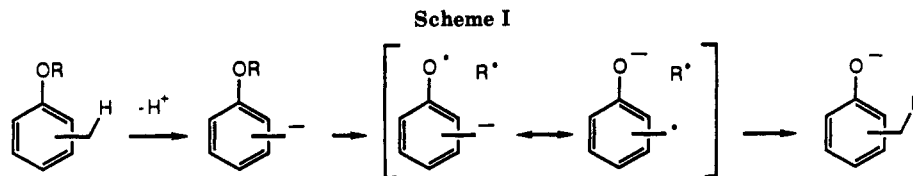
The major nonrearrangement products from the dimethylanisoles (6a-f) are easily explained. 7h-o are methylpropylphenetoles which apparently come from dianions obtained by metalation-demethylation-diethylation sequences. The small amounts of phenols 5 obtained in some reactions probably resulted from partial deethylation of phenetoles 7 during the reflux with methanolic KOH, which was used to destroy excess diethyl sulfate. Reaction 11 on 6d shows that the rearrangement of a methyl ether of a dianion can be almost totally suppressed by working at room temperature; the expected nonrearrangement product 2,6-dipropylanisole (6y) from dianion 1 was formed in 62% yield.

**Variations in the Migrating Group.** To establish whether groups other than methyl can migrate, reactions 17-19 starting from 2,6-dimethylphenetole (7c) and reac-

tions 21 and 22 starting from 2,6-dimethylphenyl isopropyl ether (8) were carried out; in these cases, *dimethyl* sulfate was used for the quench. Both ethyl and isopropyl groups migrated in good yield (52-81%) in refluxing heptane (reactions 17, 18, and 21; the first involved rearrangement predominantly from monoanion and the others, from dianions). As shown by reactions 19 and 22, ethyl and isopropyl groups (especially the latter) migrate appreciably *even at room temperature*. Some consequences of these findings are discussed in the mechanism section below.

In the case of an ethyl migrating to produce a propyl group (e.g., 6i from reaction 17 and 6q from reaction 18), minor side products from metalation of the propyl group are: the 3-pentyl derivative (6o and 6x), from intermolecular ethylation of the anion (11); the (*E*)- (6k, 6t) and (*Z*)-1-buten-1-yl (6l, 6u) and 1-buten-3-yl (6m, 6v) derivatives, formed when anion 11 eliminates hydride and then metalates further to give anion 12, which gives the observed products on quenching with dimethyl sulfate. Analogously, when an isopropyl group migrates to give an isobutyl group (e.g., 6j and 6r, reactions 21 and 22), the metalation-hydride elimination-methylation sequence gives small amounts of 2-methyl-1-buten-1-yl derivatives (6n, 6w).

**Further Substrates.** 2,6-Diethylanisole (6p) and 2,4,6-trimethylanisole (9b) were also shown to give rearrangement products in 45-63% yields (reactions 16, 25, and 26). The former shows that the reaction is not limited to migration of alkyl groups to methyl positions only, and the latter reveals that a *p*-methyl group does not compete significantly with two *o*-methyl groups for the migrating group. Reactions 24 and 27 on 2,3,6- and 2,4,6-trimethylanisoles (9a and 9b) show that rearrangements of methyl groups can be avoided in these systems by working at room temperature, and the usual dianion dialkylation products (9e and 9f) obtained in 50-58% yields; in the former case, a preference for ortho,ortho' dimetalation over ortho,meta dimetalation is observed.



**Mechanism of the Rearrangement.** Several findings rule out alternative mechanisms and suggest that these rearrangements, like the Wittig rearrangement, proceed by a homolytic dissociation-recombination mechanism (Scheme I). These include:

(1) The relative migration rates for alkyl groups are *i*-Pr > Et > Me, paralleling radical stability and ruling out  $S_N2$  mechanisms.

(2) While largely intramolecular (cross-over reaction 13, with equimolar amounts of 2,6-dimethylanisole (6d) and phenetole, gave 52% of the intramolecular rearrangement product 5b and only 5% of the intermolecular rearrangement product 5d, and its counterpart, reaction 20, with 2,6-dimethylphenetole (7c) and anisole, gave 49% of the intramolecular rearrangement product 5d and only 8% of the intermolecular product 5b), the reaction has a small intermolecular component (reaction 10, product 7p; reaction 13, 5c; reaction 17, 6o; reaction 20, 5b).

(3) Symmetrical coupling products  $ArCH_2CH_2Ar$  expected from dianion radicals, though not isolated, were observed by NMR ( $\delta$  CH<sub>2</sub>, 2.9) as minor byproducts in some of these rearrangements.

(4) Rearrangements occur to ortho, meta, and para positions, with a general decrease in yield as the distance the migrating group must move increases.

Substituents in the 2- and 6-positions are needed for good yields, probably because *this twists the methoxyl methyl group to a position nearly perpendicular to the aromatic ring, and gets it closer to the position to which it rearranges.* In terms of the mechanism in Scheme I, the alkyl radical R<sup>•</sup> must move a much shorter distance in a 2,6-disubstituted case, and is more likely to undergo the rearrangement than some other reaction.

**Dealkylation Mechanisms.** In all of the reactions in refluxing heptane, the alkyl groups of alkyl aryl ethers were completely lost. At room temperature overnight, isopropyl groups were almost completely lost, ethyl groups about one-third retained, and methyl groups largely retained. Thus the ease of dealkylation under these conditions, like the rearrangement, parallels the stability of radicals. Though many mechanisms are possible and more than one is probably occurring, we think a major one to be intimately connected to the rearrangement mechanism shown in Scheme I: In the second step, the alkyl-oxygen bond of the starting monoanion cleaves, resulting sometimes in rearrangement but also leading to other dealkylation products.

**Synthetic Utility of the Rearrangement.** These rearrangements should find use in the preparation of 2,6-dialkylated phenols and derivatives thereof. 2,6-Dialkylphenols are widely used as ligands for transition metals, and the availability of a variety of such phenols should allow fine tuning of the properties of some transition-metal complexes.<sup>8</sup> As a further example of the use of the rearrangement (reaction 23), 2-propyl-6-isobutylanisole (6z) was prepared in 50% yield in a one-pot reaction from isopropyl 2,6-dimethylphenyl ether (8) by (1)

dimetalation at room temperature (with rearrangement), (2) ethylation at carbon with ethyl bromide, and (3) methylation at oxygen with dimethyl sulfate.

## Experimental Section

For general techniques, see ref 9.

**Metalation of Alkyl Aryl Ethers.** The metalation procedure will be illustrated with 2,6-dimethylanisole (6d). Heptane (125 mL) in a 250-mL round-bottom flask was degassed with argon for 10 min, and KO-*t*-Bu (2.81 g, 25 mmol, Aldrich) and 18.8 mL of 1.6 M (30 mmol) *n*-BuLi in hexane (Aldrich) were added. After the mixture was stirred for 10 min, 2,6-dimethylanisole (6d, 1.36 g, 10 mmol) was added, causing a bright yellow color. Refluxing for 40 h gave the anion salt as a dark brown solid. After being cooled to 0 °C, the mixture was filtered (Schlenk), the solid was washed with 100 mL of pentane, and residual pentane was blown off with argon.

**Reactions of Anions with Diethyl Sulfate.** The anion salt was suspended by stirring at 0 °C in 150 mL of precooled THF. Diethyl sulfate (5.2 mL, 40 mmol) was added, turning the mixture greenish-brown. After the mixture was stirred for 18 h, KOH (2.8 g, 50 mmol) and 50 mL of methanol were added, and the solution was refluxed for 2 h to destroy excess diethyl sulfate. The solution was added to 200 mL of water and acidified with 6 M HCl. After extracting with 3 × 200 mL of pentane, drying (MgSO<sub>4</sub>), filtering, and evaporating off solvent, the products were separated by GC on SE-30 silicone oil. Yields estimated from GC and the NMR spectrum of the crude product using 100  $\mu$ L of CH<sub>2</sub>Cl<sub>2</sub> as an internal standard are given in Table I. Literature searches indicated most of these reaction products to be new.<sup>10</sup> Satisfactory elemental analyses were obtained on 6i,q,z,7f, and 10b; all compounds were characterized by their <sup>1</sup>H NMR parameters (CDCl<sub>3</sub>, TMS), which are given below if we did not find a literature reference to the compound.<sup>12</sup>

**2-Ethylphenetole (4d):**  $\delta$  7.15 (m, H-3, H-5), 6.88 (t,  $J$  = 7.4 Hz, H-4), 6.82 (d,  $J$  = 8.4 Hz, H-6), 4.03 (q,  $J$  = 7.0 Hz, 1-CH<sub>2</sub>), 2.65 (q,  $J$  = 7.5 Hz, 2-CH<sub>2</sub>), 1.42 (t,  $J$  = 7.0 Hz, 1-Me), 1.19 (t,  $J$  = 7.5 Hz, 2-Me).

**3-Ethylphenetole (4e):**  $\delta$  7.19 (t,  $J$  = 7.7 Hz, H-5), 6.76 (m, H-2, H-4, H-6), 4.03 (q,  $J$  = 7.0 Hz, 1-CH<sub>2</sub>), 2.62 (q,  $J$  = 7.6 Hz, 3-CH<sub>2</sub>), 1.41 (t,  $J$  = 7.0 Hz, 1-Me), 1.23 (t,  $J$  = 7.6 Hz, 3-Me).

**4-Ethylphenetole (4f):**  $\delta$  7.10 (br d,  $J$  = 8.6 Hz, H-3), 6.82 (br d,  $J$  = 8.6 Hz, H-2), 4.01 (q,  $J$  = 7.0 Hz, 1-CH<sub>2</sub>), 2.59 (q,  $J$  = 7.6 Hz, 4-CH<sub>2</sub>), 1.40 (t,  $J$  = 7.0 Hz, 1-Me), 1.21 (t,  $J$  = 7.6 Hz, 4-Me).

**3-Isopropylphenetole (4i):**  $\delta$  7.20 (t,  $J$  = 8.4 Hz, H-5), 6.81 (br d,  $J$  = 9.0 Hz, H-4), 6.78 (br s, H-2), 6.71 (br d,  $J$  = 8.1 Hz, H-6), 4.03 (q,  $J$  = 7.0 Hz, 1-CH<sub>2</sub>), 2.87 (heptet,  $J$  = 6.9 Hz, CH),

(9) Bates, R. B.; Siahaan, T. *J. Org. Chem.* 1986, 51, 1432.

(10) Registry Numbers or references for the known compounds are: 3a, 578-58-5; 3b, 100-84-5; 3c, 104-93-8; 3d, 14804-32-1; 3e, 10568-38-4; 3f, 13629-73-7; 3g, 62103-69-9; 3h, 104-45-0; 3i, 18272-71-4; 4a, 614-71-1; 4b, 621-32-9; 4c, 622-60-6; 4g and 4h, ref 9; 5b, 1687-64-5; 5d, 26615-74-7; 6a, 13651-14-4; 6b, 16308-92-2; 6c, 27129-87-9; 6d, 1004-66-6; 6e, 4685-47-6; 6f, 874-63-5; 6g and 6h, ref 11; 6p, 2944-51-6; 6y, 52489-57-3; 7c, 26620-08-6; 7e, 18102-49-3; 7f, 18102-07-3; 7v, ref 9; 7ff, ref 11; 8, 30718-66-2; 9a, 21573-36-4; 9b, 4028-66-4.

(11) Bates, R. B.; Siahaan, T. J.; Suvannachut, K.; Vasey, S. K.; Yager, K. M. *J. Org. Chem.* 1987, 52, 4605.

(12) <sup>1</sup>H NMR spectra of the new compounds in this study are reproduced in the supplementary material. The compounds were purified via preparative GC, and many were contaminated with substances from adjacent fractions. Compounds obtained in 90+% purity were 4e,f,i,k; 6o,q,r,t,x,z; 7a,d,s,y,bb,dd; 9c,d; 10a,b. In 80-90% purity: 4d,j; 5c,j; 7b,g,h,k,m,n,p,t,w,aa,gg; 9ef; 10f,g,h. In 70-80% purity: 6j,k,n,s,u,w; 7j,q,ee; 10c,e,i. In 60-70%: 7u,cc; 10d. In 50-60%: 5e,f,g; 7i,o. In 40-50%: 7x. In 30-40%: 7r,z. In 20-30%: 5h,i; 9g. In trace amounts: 6l,m,v.

(7) Schuster, I. I.; Parvez, M.; Freyer, A. J. *J. Org. Chem.* 1988, 53, 5819.

(8) E.g.: Ballard, K. R.; Gardiner, I. M.; Wigley, D. E. *J. Am. Chem. Soc.* 1989, 111, 2159.

1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.24 (d,  $J = 6.9$  Hz, 3-Me).

**2-sec-Butylphenetole (4j):**  $\delta$  7.15 (br d,  $J = 7.4$  Hz, H-3), 7.13 (td,  $J = 8.0, 1.8$  Hz, H-5), 6.90 (td,  $J = 7.4, 1.0$  Hz, H-4), 6.83 (br d,  $J = 8.0$  Hz, H-6), 4.02 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 3.11 (sextet,  $J = 7.0$  Hz, CH), 1.63 and 1.55 (m, 2-CH<sub>2</sub>), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.19 (d,  $J = 7.0$  Hz, CHMe), 0.84 (t,  $J = 7.4$  Hz, 2-CH<sub>2</sub>Me).

**3-sec-Butylphenetole (4k):**  $\delta$  7.19 (br t,  $J = 7.5$  Hz, H-5), 6.76 (br d,  $J = 7.8$  Hz, H-4), 6.73 (br s, H-2), 6.72 (br d,  $J = 7.7$  Hz, H-6), 4.03 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.55 (sextet,  $J = 7.0$  Hz, CH), 1.58 (pentet,  $J = 7.3$  Hz, 3-CH<sub>2</sub>), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.22 (d,  $J = 7.0$  Hz, CHMe), 0.82 (t,  $J = 7.4$  Hz, 3-CH<sub>2</sub>Me).

**2-Methyl-5-propylphenol (5c):**  $\delta$  7.01 (d,  $J = 7.4$  Hz, H-3), 6.66 (br d,  $J = 7.4$  Hz, H-4), 6.60 (br s, H-6), 4.57 (s, OH), 2.50 (t,  $J = 7.7$  Hz, ArCH<sub>2</sub>), 2.21 (s, 2-Me), 1.57 (sextet,  $J = 7.5$  Hz, CH<sub>2</sub>Me), 0.92 (t,  $J = 7.3$  Hz, 5-Me).

**3-Methyl-5-propylphenol (5e):**  $\delta$  6.59 (br s, H-4), 6.46 (br s, H-2, H-6), 4.59 (s, OH), 2.49 (t,  $J = 7.9$  Hz, ArCH<sub>2</sub>), 2.27 (s, 3-Me), 1.61 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 0.93 (t,  $J = 7.3$  Hz, 5-Me).

**4-Methyl-2-propylphenol (5f):**  $\delta$  6.92 (br s, H-3), 6.87 (br d,  $J = 8.0$  Hz, H-5), 6.66 (br d,  $J = 8.0$  Hz, H-6), 4.48 (s, OH), 2.54 (t,  $J = 7.7$  Hz, ArCH<sub>2</sub>), 2.25 (s, 4-Me), 1.63 (sextet,  $J = 7.5$  Hz, CH<sub>2</sub>Me), 0.97 (t,  $J = 7.3$  Hz, 2-Me).

**4-Methyl-3-propylphenol (5g):**  $\delta$  6.98 (d,  $J = 8.1$  Hz, H-5), 6.63 (d,  $J = 2.7$  Hz, H-2), 6.57 (dd,  $J = 8.1, 2.7$  Hz, H-6), 4.51 (s, OH), 2.51 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.21 (s, 4-Me), 1.60 (sextet,  $J = 7.5$  Hz, CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 3-Me).

**5-Methyl-2-propylphenol (5h):**  $\delta$  6.99 (d,  $J = 7.4$  Hz, H-3), 6.66 (br d,  $J = 7.4$  Hz, H-4), 6.60 (br s, H-6), 4.57 (s, OH), 2.54 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.26 (s, 5-Me), 1.61 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 0.96 (t,  $J = 7.4$  Hz, 2-Me).

**2-Methyl-6-((Z)-1-propen-1-yl)phenol (5i):**  $\delta$  7.00 (br d,  $J = 7.4$  Hz, H-3, H-5), 6.80 (t,  $J = 7.4$  Hz, H-4), 6.39 (br d,  $J = 12.4$  Hz, CH=CHMe), 6.04 (dq,  $J = 12.4, 6.9$  Hz, CHMe), 5.02 (br s, OH), 2.27 (s, 2-Me), 1.71 (dd,  $J = 6.9, 1.7$  Hz, 6-Me).

**3,5-Dipropylphenol (5j):**  $\delta$  6.58 (br s, H-4), 6.48 (br s, H-2), 4.57 (br s, OH), 2.50 (t,  $J = 7.7$  Hz, ArCH<sub>2</sub>), 1.61 (sextet,  $J = 7.5$  Hz, CH<sub>2</sub>Me), 0.93 (t,  $J = 7.3$  Hz, Me).

**2-Methyl-6-propylanisole (6i):**  $\delta$  7.02 (d,  $J = 7.4$  Hz, H-3, H-5), 6.96 (t,  $J = 7.4$  Hz, H-4), 3.73 (s, OMe), 2.62 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.30 (s, 2-Me), 1.64 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 6-Me).

**2-Methyl-6-isobutylanisole (6j):**  $\delta$  6.99 (m, ArH), 3.72 (s, OMe), 2.49 (d,  $J = 7.2$  Hz, CH<sub>2</sub>), 2.29 (s, 2-Me), 1.92 (nonet,  $J = 6.9$  Hz, CH), 0.91 (d,  $J = 6.6$  Hz, 6-Me).

**2-Methyl-6-((E)-1-buten-1-yl)anisole (6k):**  $\delta$  7.30 (br d,  $J = 7.4$  Hz, H-5), 7.04 (br d,  $J = 7.4$  Hz, H-3), 6.97 (t,  $J = 7.4$  Hz, H-4), 6.66 (d,  $J = 16.1$  Hz, CH=CHCH<sub>2</sub>), 6.26 (dt,  $J = 16.1, 6.6$  Hz, CHCH<sub>2</sub>), 3.71 (s, OMe), 2.28 (s, 2-Me), 2.26 (pentet,  $J = 7.3$  Hz, CH<sub>2</sub>), 1.10 (t,  $J = 7.5$  Hz, 6-Me).

**2-Methyl-6-((Z)-1-buten-1-yl)anisole (6l):**  $\delta$  6.52 (br d,  $J = 11.8$  Hz, CH=CHCH<sub>2</sub>), 5.71 (dt,  $J = 11.8, 7.4$  Hz, CHCH<sub>2</sub>), 2.28 (p,  $J = 7.4$  Hz, CH<sub>2</sub>), 1.03 (t,  $J = 7.5$  Hz, 6-Me).

**2-Methyl-6-(1-buten-3-yl)anisole (6m):**  $\delta$  6.04 (ddd,  $J = 17.0, 10.1, 7.0$  Hz, CH=C), 5.05 (br d,  $J = 17.0$  Hz, CH<sub>2</sub>), 5.03 (br d,  $J = 10.1$  Hz, CH<sub>2</sub>), 3.07 (p,  $J = 7.0$  Hz, CHMe), 1.33 (d,  $J = 7.0$  Hz, CHMe).

**2-Methyl-6-(2-methyl-1-buten-1-yl)anisole (6n):**  $\delta$  7.04 (br d,  $J = 8.8$  Hz, H-5), 7.01 (br d,  $J = 6.2$  Hz, H-3), 6.97 (t,  $J = 7.5$  Hz, H-4), 6.30 (br s, CH=C), 3.68 (s, OMe), 2.28 (s, 2-Me), 2.20 (q,  $J = 7.5$  Hz, CH<sub>2</sub>), 1.90 (d,  $J = 1.1$  Hz, C=CMe), 1.06 (t,  $J = 7.5$  Hz, CH<sub>2</sub>Me).

**2-Methyl-6-(3-pentyl)anisole (6o):**  $\delta$  7.00 (s, ArH), 3.71 (s, OMe), 2.88 (tt,  $J = 8.8, 5.7$  Hz, CH), 2.29 (s, 2-Me), 1.68 (dp,  $J = 13.4, 6.6$  Hz, CH<sub>2</sub>), 1.52 (dp,  $J = 13.4, 7.0$  Hz, CH<sub>2</sub>), 0.80 (t,  $J = 7.4$  Hz, 6-Me).

**2-Ethyl-6-propylanisole (6q):**  $\delta$  7.03 (m, ArH), 3.74 (s, OMe), 2.68 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 2.61 (t,  $J = 7.8$  Hz, 6-ArCH<sub>2</sub>), 1.64 (sextet,  $J = 7.6$  Hz, 6-CH<sub>2</sub>Me), 1.24 (t,  $J = 7.6$  Hz, 2-Me), 0.98 (t,  $J = 7.3$  Hz, 6-Me).

**2-Ethyl-6-isobutylanisole (6r):**  $\delta$  7.01 (m, ArH), 3.73 (s, OMe), 2.68 (q,  $J = 7.5$  Hz, 2-CH<sub>2</sub>), 2.50 (d,  $J = 7.3$  Hz, 6-CH<sub>2</sub>), 1.94 (nonet,  $J = 6.9$  Hz, CH), 1.24 (t,  $J = 7.5$  Hz, 2-Me), 0.92 (d,  $J = 6.6$  Hz, 6-Me).

**2-Ethyl-6-sec-butylanisole (6s):**  $\delta$  7.05 (s, ArH), 3.73 (s, OMe), 3.07 (sextet,  $J = 7.0$  Hz, CH), 2.69 (q,  $J = 7.5$  Hz, 2-CH<sub>2</sub>), 1.58 (pentet,  $J = 7.2$  Hz, 6-CH<sub>2</sub>), 1.25 (t,  $J = 7.5$  Hz, 2-Me), 1.21

(d,  $J = 7.0$  Hz, CHMe), 0.85 (t,  $J = 7.4$  Hz, 6-CH<sub>2</sub>Me).

**2-Ethyl-6-((E)-1-buten-1-yl)anisole (6t):**  $\delta$  7.31 (dd,  $J = 7.4, 2.0$  Hz, H-5), 7.07 (dd,  $J = 7.4, 2.0$  Hz, H-3), 7.01 (t,  $J = 7.4$  Hz, H-4), 6.65 (d,  $J = 16.0$  Hz, CH=CHCH<sub>2</sub>), 6.26 (dt,  $J = 16.0, 6.5$  Hz, CHCH<sub>2</sub>), 3.72 (s, OMe), 2.67 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 2.26 (p,  $J = 7.5$  Hz, 6-CH<sub>2</sub>), 1.23 (t,  $J = 7.6$  Hz, 2-Me), 1.10 (t,  $J = 7.4$  Hz, 6-Me).

**2-Ethyl-6-((Z)-1-buten-1-yl)anisole (6u):**  $\delta$  7.09 (br d,  $J = 7.5$  Hz, H-3, H-5), 7.03 (t,  $J = 7.5$  Hz, H-4), 6.51 (d,  $J = 11.7$  Hz, CH=CHCH<sub>2</sub>), 5.71 (dt,  $J = 11.7, 7.4$  Hz, CHCH<sub>2</sub>), 3.71 (s, OMe), 2.68 (q,  $J = 7.5$  Hz, 2-CH<sub>2</sub>), 2.28 (pentet,  $J = 7.4$  Hz, 6-CH<sub>2</sub>), 1.23 (t,  $J = 7.5$  Hz, 2-Me), 1.03 (t,  $J = 7.5$  Hz, 6-Me).

**2-Ethyl-6-(1-buten-3-yl)anisole (6v):**  $\delta$  6.04 (ddd,  $J = 17.0, 10.1, 7.0$  Hz, CH=C), 5.05 (br d,  $J = 17.0$  Hz, C=CH<sub>2</sub>), 5.03 (br d,  $J = 10.1$  Hz, C=CH<sub>2</sub>), 3.07 (p,  $J = 7.0$  Hz, CHMe), 1.33 (d,  $J = 7.0$  Hz, CHMe).

**2-Ethyl-6-(2-methyl-1-buten-1-yl)anisole (6w):**  $\delta$  7.04 (m, ArH), 6.30 (br s, CH=C), 3.69 (s, OMe), 2.67 (q,  $J = 7.5$  Hz, 2-CH<sub>2</sub>), 2.21 (q,  $J = 7.5$  Hz, 6-CH<sub>2</sub>), 1.91 (d,  $J = 1.4$  Hz, C=CMe), 1.23 (t,  $J = 7.5$  Hz, 2-Me), 1.06 (t,  $J = 7.5$  Hz, 6-CH<sub>2</sub>Me).

**2-Ethyl-6-(3-pentyl)anisole (6x):**  $\delta$  7.03 (m, ArH), 3.71 (s, OMe), 2.87 (tt,  $J = 8.7, 5.7$  Hz, CH), 2.69 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 1.68 (dp,  $J = 13.4, 6.8$  Hz, 6-CH<sub>2</sub>), 1.51 (dp,  $J = 13.4, 7.0$  Hz, 6-CH<sub>2</sub>), 1.25 (t,  $J = 7.6$  Hz, 2-Me), 0.81 (t,  $J = 7.4$  Hz, 6-Me).

**2,3-Dimethylphenetole (7a):**  $\delta$  7.03 (t,  $J = 7.6$  Hz, H-5), 6.76 (br d,  $J = 7.6$  Hz, H-4), 6.71 (br d,  $J = 7.6$  Hz, H-6), 4.01 (q,  $J = 7.0$  Hz, CH<sub>2</sub>), 2.26 (s, 3-Me), 2.15 (s, 2-Me), 1.42 (t,  $J = 7.0$  Hz, 1-Me).

**2,4-Dimethylphenetole (7b):**  $\delta$  6.95 (br s, H-6), 6.93 (br d,  $J = 8.1$  Hz, H-5), 6.71 (d,  $J = 8.1$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, CH<sub>2</sub>), 2.25 (s, 4-Me), 2.19 (s, 2-Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me).

**3,4-Dimethylphenetole (7d):**  $\delta$  7.01 (d,  $J = 8.2$  Hz, H-5), 6.70 (d,  $J = 2.7$  Hz, H-2), 6.63 (dd,  $J = 8.2, 2.7$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, CH<sub>2</sub>), 2.23 (s, 3-Me), 2.19 (s, 4-Me), 1.39 (t,  $J = 7.0$  Hz, 1-Me).

**2-Methyl-6-ethylphenetole (7f):**  $\delta$  7.03 (m, H-3, H-5), 6.96 (t,  $J = 7.0$  Hz, H-4), 3.84 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.67 (q,  $J = 7.6$  Hz, 6-CH<sub>2</sub>), 2.28 (s, 2-Me), 1.42 (t,  $J = 7.0$  Hz, 1-Me), 1.22 (t,  $J = 7.6$  Hz, 6-Me).

**3-Methyl-2-ethylphenetole (7g):**  $\delta$  7.02 (t,  $J = 7.6$  Hz, H-5), 6.75 (br d,  $J = 7.6$  Hz, H-4), 6.69 (br d,  $J = 7.6$  Hz, H-6), 4.01 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.67 (q,  $J = 7.5$  Hz, 2-CH<sub>2</sub>), 2.30 (s, 3-Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 1.09 (t,  $J = 7.5$  Hz, 2-Me).

**2-Methyl-3-propylphenetole (7h):**  $\delta$  7.06 (t,  $J = 7.7$  Hz, H-5), 6.75 (br d,  $J = 7.7$  Hz, H-4), 6.69 (br d,  $J = 7.7$  Hz, H-6), 4.01 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.58 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.18 (s, 2-Me), 1.58 (sextet,  $J = 7.6$  Hz, 3-CH<sub>2</sub>Me), 1.42 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.3$  Hz, 3-Me).

**2-Methyl-5-propylphenetole (7i):**  $\delta$  7.03 (d,  $J = 7.0$  Hz, H-3), 6.69 (m, H-4), 6.64 (br s, H-6), 4.02 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.55 (t,  $J = 7.6$  Hz, ArCH<sub>2</sub>), 2.18 (s, 2-Me), 1.62 (sextet,  $J = 7.5$  Hz, 5-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 0.94 (t,  $J = 7.3$  Hz, 5-Me).

**2-Methyl-6-propylphenetole (7j):**  $\delta$  7.02 (m, H-3, H-5), 6.95 (t,  $J = 6.8$  Hz, H-4), 3.83 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.60 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.29 (s, 2-Me), 1.64 (sextet,  $J = 7.6$  Hz, 6-CH<sub>2</sub>Me), 1.42 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.3$  Hz, 6-Me).

**3-Methyl-2-propylphenetole (7k):**  $\delta$  7.03 (t,  $J = 7.7$  Hz, H-5), 6.74 (br d,  $J = 7.7$  Hz, H-4), 6.69 (br d,  $J = 7.7$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.62 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.30 (s, 3-Me), 1.51 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.4$  Hz, 2-Me).

**4-Methyl-2-propylphenetole (7m):**  $\delta$  6.93 (m, H-3, H-5), 6.72 (d,  $J = 8.8$  Hz, H-6), 3.99 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.55 (t,  $J = 7.6$  Hz, ArCH<sub>2</sub>), 2.26 (s, 4-Me), 1.60 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me), 1.39 (t,  $J = 7.0$  Hz, 1-Me), 0.94 (t,  $J = 7.4$  Hz, 2-Me).

**4-Methyl-3-propylphenetole (7n):**  $\delta$  7.01 (d,  $J = 8.2$  Hz, H-5), 6.70 (d,  $J = 2.7$  Hz, H-2), 6.63 (dd,  $J = 8.2, 2.7$  Hz, H-6), 3.40 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.53 (t,  $J = 7.7$  Hz, ArCH<sub>2</sub>), 2.22 (s, 4-Me), 1.60 (sextet,  $J = 7.5$  Hz, 3-CH<sub>2</sub>Me), 1.38 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.3$  Hz, 3-Me).

**5-Methyl-2-propylphenetole (7o):**  $\delta$  7.00 (d,  $J = 7.3$  Hz, H-3), 6.69 (m, H-4), 6.64 (br s, H-6), 4.01 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.54 (t,  $J = 7.6$  Hz, ArCH<sub>2</sub>), 2.31 (s, 5-Me), 1.60 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 0.93 (t,  $J = 7.3$  Hz, 2-Me).

**2-Methyl-6-isopropylphenetole (7p):**  $\delta$  7.03 (m, ArH), 3.83 (q,  $J = 7.0$  Hz, CH<sub>2</sub>), 3.34 (heptet,  $J = 6.9$  Hz, CH), 2.29 (s, 2-Me),

1.43 (t,  $J = 7.0$  Hz, 1-Me), 1.22 (d,  $J = 6.9$  Hz, 6-Me).

**4-Methyl-2-sec-butylphenetole (7q):**  $\delta$  6.93 (m, H-3, H-5), 6.73 (d,  $J = 8.1$  Hz, H-6), 3.99 (q,  $J = 6.9$  Hz, 1-CH<sub>2</sub>), 3.07 (sextet,  $J = 7.0$  Hz, CH), 2.27 (s, 4-Me), 1.58 (m, 2-CH<sub>2</sub>), 1.39 (t,  $J = 6.9$  Hz, 1-Me), 1.18 (d,  $J = 7.0$  Hz, CHMe), 0.84 (t,  $J = 7.4$  Hz, 2-CH<sub>2</sub>Me).

**4-Methyl-3-sec-butylphenetole (7r):**  $\delta$  7.01 (d,  $J = 8.2$  Hz, H-5), 6.74 (d,  $J = 2.7$  Hz, H-2), 6.63 (dd,  $J = 8.2, 2.7$  Hz, H-6), 3.40 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.84 (sextet,  $J = 6.9$  Hz, CH), 2.23 (s, 4-Me), 1.59 (pentet,  $J = 7.1$  Hz, 3-CH<sub>2</sub>), 1.39 (t,  $J = 7.0$  Hz, 1-Me), 1.18 (d,  $J = 6.9$  Hz, CHMe), 0.85 (t,  $J = 7.4$  Hz, 3-CH<sub>2</sub>Me).

**2,6-Diethylphenetole (7s):**  $\delta$  7.04 (m, ArH), 3.83 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.67 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 1.43 (t,  $J = 7.0$  Hz, 1-Me), 1.24 (t,  $J = 7.6$  Hz, 2-Me).

**2-Ethyl-3-propylphenetole (7t):**  $\delta$  7.06 (t,  $J = 8.1$  Hz, H-5), 6.75 (br d,  $J = 7.6$  Hz, H-4), 6.69 (br d,  $J = 8.6$  Hz, H-6), 4.01 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.67 (q,  $J = 7.0$  Hz, 2-CH<sub>2</sub>), 2.58 (t,  $J = 7.9$  Hz, 3-ArCH<sub>2</sub>), 1.60 (sextet,  $J = 7.6$  Hz, 3-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.12 (t,  $J = 7.4$  Hz, 2-Me), 0.98 (t,  $J = 7.3$  Hz, 3-Me).

**2-Ethyl-5-propylphenetole (7u):**  $\delta$  7.04 (d,  $J = 7.5$  Hz, H-3), 6.70 (m, H-4), 6.65 (br s, H-6), 4.02 (q,  $J = 6.9$  Hz, 1-CH<sub>2</sub>), 2.61 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 2.55 (t,  $J = 7.5$  Hz, 5-ArCH<sub>2</sub>), 1.62 (sextet,  $J = 7.5$  Hz, 5-CH<sub>2</sub>Me), 1.41 (t,  $J = 6.9$  Hz, 1-Me), 1.18 (t,  $J = 7.6$  Hz, 2-Me), 0.94 (t,  $J = 7.5$  Hz, 5-Me).

**3-Ethyl-5-propylphenetole (7v):**  $\delta$  6.61 (br s, H-4), 6.57 (br s, H-2), 6.55 (br s, H-6), 4.02 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.59 (q,  $J = 7.6$  Hz, 3-CH<sub>2</sub>), 2.53 (t,  $J = 7.6$  Hz, 5-ArCH<sub>2</sub>), 1.63 (sextet,  $J = 7.5$  Hz, 5-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 1.22 (t,  $J = 7.6$  Hz, 3-Me), 0.82 (t,  $J = 7.4$  Hz, 5-Me).

**5-Ethyl-2-propylphenetole (7x):**  $\delta$  7.03 (d,  $J = 7.4$  Hz, H-3), 6.70 (m, H-4), 6.65 (br s, H-6), 4.02 (q,  $J = 6.9$  Hz, 1-CH<sub>2</sub>), 2.61 (q,  $J = 7.6$  Hz, 5-CH<sub>2</sub>), 2.54 (t,  $J = 7.5$  Hz, 2-ArCH<sub>2</sub>), 1.59 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me), 1.41 (t,  $J = 6.9$  Hz, 1-Me), 1.22 (t,  $J = 7.6$  Hz, 5-Me), 0.94 (t,  $J = 7.4$  Hz, 2-Me).

**2-Ethyl-6-isopropylphenetole (7y):**  $\delta$  7.05 (m, ArH), 3.82 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 3.33 (heptet,  $J = 6.9$  Hz, CH), 2.68 (q,  $J = 7.6$  Hz, 2-CH<sub>2</sub>), 1.44 (t,  $J = 7.0$  Hz, 1-Me), 1.24 (t,  $J = 7.6$  Hz, 2-Me), 1.22 (d,  $J = 6.9$  Hz, 6-Me).

**2-Vinyl-5-propylphenetole (7z):**  $\delta$  7.37 (d,  $J = 7.8$  Hz, H-3), 7.03 (dd,  $J = 17.8, 11.1$  Hz, CH=CH<sub>2</sub>), 6.74 (br d,  $J = 7.8$  Hz, H-4), 6.67 (br s, H-6), 5.71 (dd,  $J = 17.8, 1.7$  Hz, C=CH<sub>2</sub>), 5.19 (dd,  $J = 11.1, 1.7$  Hz, C=CH<sub>2</sub>), 4.05 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.59 (t,  $J = 7.5$  Hz, ArCH<sub>2</sub>), 1.64 (sextet,  $J = 7.5$  Hz, 5-CH<sub>2</sub>Me), 1.43 (t,  $J = 7.0$  Hz, 1-Me), 0.94 (t,  $J = 7.5$  Hz, 5-Me).

**2,3-Dipropylphenetole (7aa):**  $\delta$  7.06 (t,  $J = 8.1$  Hz, H-5), 6.75 (br d,  $J = 7.6$  Hz, H-4), 6.68 (br d,  $J = 8.6$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.61 (t,  $J = 7.9$  Hz, 2-ArCH<sub>2</sub>), 2.58 (t,  $J = 7.9$  Hz, 3-ArCH<sub>2</sub>), 1.60 (sextet,  $J = 7.6$  Hz, 3-CH<sub>2</sub>Me), 1.52 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me, 3-Me).

**2,4-Dipropylphenetole (7bb):**  $\delta$  6.94 (m, H-3, H-5), 6.73 (d,  $J = 8.8$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.54 (t,  $J = 7.7$  Hz, 2-ArCH<sub>2</sub>), 2.51 (t,  $J = 7.7$  Hz, 4-ArCH<sub>2</sub>), 1.61 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me), 1.58 (sextet,  $J = 7.5$  Hz, 4-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me), 0.96 (t,  $J = 7.3$  Hz, 4-Me).

**2,5-Dipropylphenetole (7cc):**  $\delta$  7.02 (d,  $J = 7.4$  Hz, H-3), 6.68 (br d,  $J = 7.4$  Hz, H-4), 6.65 (br s, H-6), 4.02 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.55 (t,  $J = 7.5$  Hz, 5-ArCH<sub>2</sub>), 2.54 (t,  $J = 7.5$  Hz, 2-ArCH<sub>2</sub>), 1.60 (sextet,  $J = 7.5$  Hz, 5-CH<sub>2</sub>Me), 1.59 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me), 0.94 (t,  $J = 7.5$  Hz, 2-Me, 5-Me).

**2,6-Dipropylphenetole (7dd):**  $\delta$  7.02 (m, ArH), 3.82 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.60 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 1.64 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 1.43 (t,  $J = 7.0$  Hz, 1-Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me).

**3,4-Dipropylphenetole (7ee):**  $\delta$  7.01 (d,  $J = 8.2$  Hz, H-5), 6.70 (d,  $J = 2.7$  Hz, H-2), 6.63 (dd,  $J = 8.2, 2.7$  Hz, H-6), 4.00 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.56 (t,  $J = 7.6$  Hz, 3-ArCH<sub>2</sub>), 2.49 (t,  $J = 7.6$  Hz, 4-ArCH<sub>2</sub>), 1.60 (sextet,  $J = 7.5$  Hz, 2-CH<sub>2</sub>Me, 3-CH<sub>2</sub>Me), 1.39 (t,  $J = 7.0$  Hz, 1-Me), 0.94 (t,  $J = 7.3$  Hz, 3-Me), 0.93 (t,  $J = 7.3$  Hz, 4-Me).

**2-Propyl-6-sec-butylphenetole (7gg):**  $\delta$  7.03 (m, ArH), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 3.06 (sextet,  $J = 6.9$  Hz, CH), 2.61 (t,  $J = 7.4$  Hz, ArCH<sub>2</sub>), 1.65 (sextet,  $J = 7.4$  Hz, 2-CH<sub>2</sub>Me), 1.57 (pentet,  $J = 7.2$  Hz, 6-CH<sub>2</sub>), 1.43 (t,  $J = 7.0$  Hz, 1-Me), 1.20 (d,  $J = 6.9$  Hz, CHMe), 0.98 (t,  $J = 7.3$  Hz, 2-Me), 0.85 (t,  $J = 7.4$  Hz, 6-CH<sub>2</sub>Me).

**2,4-Dimethyl-6-propylanisole (9c):**  $\delta$  6.83 (br s, ArH), 3.70 (s, OMe), 2.56 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.26 (br s, 2-Me, 4-Me), 1.62 (sextet,  $J = 7.7$  Hz, CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 6-Me).

**3,6-Dimethyl-2-propylanisole (9d):**  $\delta$  6.91 (d,  $J = 7.6$  Hz, H-5), 6.83 (d,  $J = 7.6$  Hz, H-4), 3.72 (s, OMe), 2.59 (t,  $J = 8.0$  Hz, ArCH<sub>2</sub>), 2.26 (s, 3-Me, 6-Me), 1.52 (sextet,  $J = 7.7$  Hz, CH<sub>2</sub>Me), 1.01 (t,  $J = 7.3$  Hz, 2-Me).

**3-Methyl-2,6-dipropylanisole (9e):**  $\delta$  6.93 (d,  $J = 7.8$  Hz, H-5), 6.86 (d,  $J = 7.8$  Hz, H-4), 3.72 (s, OMe), 2.61 (t,  $J = 7.6$  Hz, 6-ArCH<sub>2</sub>), 2.56 (t,  $J = 8.0$  Hz, 2-ArCH<sub>2</sub>), 2.27 (s, 3-Me), 1.63 (sextet,  $J = 7.5$  Hz, 6-CH<sub>2</sub>Me), 1.53 (sextet,  $J = 7.7$  Hz, 2-CH<sub>2</sub>Me), 1.00 (t,  $J = 7.4$  Hz, 2-Me), 0.97 (t,  $J = 7.4$  Hz, 6-Me).

**4-Methyl-2,6-dipropylanisole (9f):**  $\delta$  6.83 (br s, ArH), 3.70 (s, OMe), 2.57 (t,  $J = 7.9$  Hz, ArCH<sub>2</sub>), 2.26 (s, 4-Me), 1.63 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 4-Me).

**2,4,6-Tripropylanisole (9g):**  $\delta$  6.83 (br s, ArH), 3.71 (s, OMe), 2.57 (t,  $J = 7.8$  Hz, 2-ArCH<sub>2</sub>), 2.49 (t,  $J = 7.7$  Hz, 4-ArCH<sub>2</sub>), 1.63 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.60 (sextet,  $J = 7.5$  Hz, 4-CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me), 0.93 (t,  $J = 7.4$  Hz, 4-Me).

**2,4,6-Trimethylphenetole (10a):**  $\delta$  6.81 (br s, ArH), 3.81 (q,  $J = 7.0$  Hz, CH<sub>2</sub>), 2.23 (s, 2-Me, 4-Me), 1.40 (t,  $J = 7.0$  Hz, 1-Me).

**2,4-Dimethyl-6-ethylphenetole (10b):**  $\delta$  6.84 (br s, H-5), 6.83 (br s, H-3), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.62 (q,  $J = 7.6$  Hz, ArCH<sub>2</sub>), 2.25 (s, 4-Me), 2.24 (s, 2-Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.21 (t,  $J = 7.6$  Hz, 6-Me).

**2,4-Dimethyl-6-propylphenetole (10c):**  $\delta$  6.82 (br s, ArH), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.55 (t,  $J = 7.8$  Hz, ArCH<sub>2</sub>), 2.24 (s, 2-Me, 4-Me), 1.62 (sextet,  $J = 7.6$  Hz, 6-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.3$  Hz, 6-Me).

**3,6-Dimethyl-2-propylphenetole (10d):**  $\delta$  6.91 (d,  $J = 7.8$  Hz, H-5), 6.81 (d,  $J = 7.8$  Hz, H-4), 3.81 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.59 (t,  $J = 8.0$  Hz, ArCH<sub>2</sub>), 2.26 (s, 3-Me, 6-Me), 1.52 (sextet,  $J = 7.7$  Hz, 2-CH<sub>2</sub>Me), 1.42 (t,  $J = 7.0$  Hz, 1-Me), 1.00 (t,  $J = 7.5$  Hz, 2-Me).

**4-Methyl-2-ethyl-5-propylphenetole (10e):**  $\delta$  6.90 (s, H-3), 6.62 (s, H-6), 4.01 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.58 (q,  $J = 7.5$  Hz, 2-ArCH<sub>2</sub>), 2.51 (t,  $J = 7.8$  Hz, 5-ArCH<sub>2</sub>), 2.21 (s, 4-Me), 1.60 (sextet,  $J = 7.6$  Hz, 5-CH<sub>2</sub>Me), 1.39 (t,  $J = 7.0$  Hz, 1-Me), 1.17 (t,  $J = 7.5$  Hz, 2-Me), 0.98 (t,  $J = 7.3$  Hz, 5-Me).

**4-Methyl-2-ethyl-6-propylphenetole (10f):**  $\delta$  6.83 (m, ArH), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.63 (q,  $J = 7.6$  Hz, 2-ArCH<sub>2</sub>), 2.56 (t,  $J = 7.7$  Hz, 6-ArCH<sub>2</sub>), 2.27 (s, 4-Me), 1.60 (sextet,  $J = 7.5$  Hz, 6-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 1.22 (t,  $J = 7.6$  Hz, 2-Me), 0.98 (t,  $J = 7.3$  Hz, 6-Me).

**3-Methyl-2,6-dipropylphenetole (10g):**  $\delta$  6.93 (d,  $J = 7.8$  Hz, H-5), 6.85 (d,  $J = 7.8$  Hz, H-4), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.61 (t,  $J = 7.6$  Hz, 6-ArCH<sub>2</sub>), 2.56 (t,  $J = 8.0$  Hz, 2-ArCH<sub>2</sub>), 2.27 (s, 3-Me), 1.62 (sextet,  $J = 7.6$  Hz, 6-CH<sub>2</sub>Me), 1.52 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.43 (t,  $J = 7.0$  Hz, 1-Me), 1.01 (t,  $J = 7.7$  Hz, 2-Me), 0.97 (t,  $J = 7.7$  Hz, 6-Me).

**4-Methyl-2,6-dipropylphenetole (10h):**  $\delta$  6.83 (br s, ArH), 3.79 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.56 (t,  $J = 7.9$  Hz, ArCH<sub>2</sub>), 2.27 (s, 4-Me), 1.63 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me).

**2,4,6-Tripropylphenetole (10i):**  $\delta$  6.82 (br s, ArH), 3.80 (q,  $J = 7.0$  Hz, 1-CH<sub>2</sub>), 2.56 (t,  $J = 7.8$  Hz, 2-ArCH<sub>2</sub>), 2.49 (t,  $J = 7.7$  Hz, 4-ArCH<sub>2</sub>), 1.63 (sextet,  $J = 7.6$  Hz, 2-CH<sub>2</sub>Me), 1.60 (sextet,  $J = 7.6$  Hz, 4-CH<sub>2</sub>Me), 1.41 (t,  $J = 7.0$  Hz, 1-Me), 0.97 (t,  $J = 7.4$  Hz, 2-Me), 0.93 (t,  $J = 7.5$  Hz, 4-Me).

**Reaction of the Dianion from 8 with Ethyl Bromide Followed by Dimethyl Sulfate.** A suspension of dianion in pentane was cannulated into ethyl bromide (1.3 mL, 18 mmol) in 300 mL of THF at 0 °C. The solution was stirred at 25 °C for 5 h and then cooled to 0 °C, and 1.7 mL (18 mmol) of dimethyl sulfate was added. After stirring at 25 °C for 15 h, workup gave 2-propyl-6-isobutylanisole (6z) in 50% yield.

**2-Propyl-6-isobutylanisole (6z):**  $\delta$  7.00 (m, ArH), 3.72 (s, OMe), 2.61 (t,  $J = 7.8$  Hz, 2-ArCH<sub>2</sub>), 2.50 (d,  $J = 7.2$  Hz, 6-CH<sub>2</sub>), 1.94 (nonet,  $J = 6.9$  Hz, CH), 1.62 (sextet,  $J = 7.6$  Hz, CH<sub>2</sub>Me), 0.98 (t,  $J = 7.3$  Hz, 2-Me), 0.91 (d,  $J = 6.6$  Hz, 6-Me).

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**Registry No.** 3a, 578-58-5; 3b, 100-84-5; 3c, 104-93-8; 3d, 29643-62-7; 3e, 10568-38-4; 3f, 13629-73-7; 3g, 62103-69-9; 3h, 104-45-0; 3i, 18272-71-4; 4a, 614-71-1; 4b, 621-32-9; 4c, 622-60-6;



4d, 29643-62-7; 4e, 103386-84-1; 4f, 1585-06-4; 4g, 101144-90-5; 4h, 101144-93-8; 4i, 124267-89-6; 4j, 124268-42-4; 4k, 124267-90-9; 5a, 576-26-1; 5b, 1687-64-5; 5c, 7786-21-2; 5d, 3520-52-3; 5e, 36186-96-6; 5f, 4074-46-8; 5g, 61783-87-7; 5h, 31143-55-2; 5i, 124268-23-1; 5j, 85244-23-1; 6a, 2944-49-2; 6b, 6738-23-4; 6c, 1706-11-2; 6d, 1004-66-6; 6e, 4685-47-6; 6f, 874-63-5; 6g, 124268-22-0; 6h, 79744-78-8; 6i, 124268-14-0; 6j, 124268-25-3; 6k, 124268-16-2; 6l, 124268-06-0; 6m, 124268-17-3; 6n, 124268-27-5; 6o, 124268-15-1; 6p, 2944-51-6; 6q, 124267-88-5; 6r, 124268-24-2; 6s, 124268-22-0; 6t, 124268-19-5; 6u, 124268-20-8; 6v, 124268-21-9; 6w, 124268-26-4; 6x, 124268-18-4; 6y, 52489-57-3; 6z, 124268-28-6; 7a, 61808-02-4; 7b, 35338-30-8; 7c, 26620-08-6; 7d, 61808-04-6; 7e, 18102-49-3; 7f, 124268-03-7; 7g, 124267-91-0; 7h, 124267-92-1; 7i, 124268-40-2; 7j, 124268-04-8; 7k, 124267-93-2; 7l, 18102-07-3; 7m,

124267-96-5; 7n, 124268-09-3; 7o, 124268-01-5; 7p, 33641-87-1; 7q, 124267-95-4; 7r, 124268-08-2; 7s, 91763-69-8; 7t, 124268-41-3; 7u, 124267-98-7; 7v, 101144-91-6; 7w, 124268-12-8; 7x, 124267-99-8; 7y, 124268-13-9; 7z, 124268-00-4; 7aa, 124267-94-3; 7bb, 124267-97-6; 7cc, 124268-02-6; 7dd, 124268-07-1; 7ee, 124268-11-7; 7ff, 18102-08-4; 7gg, 124268-05-9; 8, 54350-31-1; 9a, 21573-36-4; 9b, 4028-66-4; 9c, 124268-37-7; 9d, 124268-30-0; 9e, 124268-29-7; 9f, 124268-36-6; 9g, 124268-38-8; 10a, 61248-63-3; 10b, 124268-33-3; 10c, 124268-36-6; 10d, 124268-31-1; 10e, 124268-10-6; 10f, 124268-34-4; 10g, 124268-32-2; 10h, 124268-35-5; 10i, 124268-39-9.

**Supplementary Material Available:**  $^1\text{H}$  NMR spectra for new compounds 4-10 (31 pages). Ordering information is given on any current masthead page.

## Proximate Charge Effects. 8. Ion Pair Formation as an Assembly Process in Ester Aminolysis<sup>1</sup>

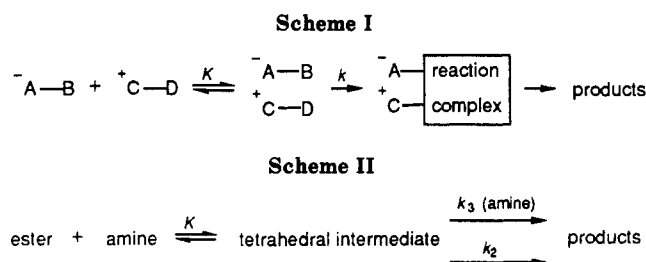
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The rate of aminolysis of *p*-nitrophenyl hexanoate by benzylamine in 95.3 mol % dioxane-water was compared to the rate of this reaction when the *n*-pentyl group in the ester was replaced by a  $(\text{CH}_3)_3^+\text{NCH}_2\text{CH}_2\text{CH}_2$  group, and the benzyl group in the amine by a  $^-\text{O}_3\text{SCH}_2\text{CH}_2$  group. The second-order rate constant of the first reaction was  $4.21 \times 10^{-3} \text{ L mol}^{-1} \text{ s}^{-1}$ , whereas the first-order rate constant for the reacting ion pair was  $1.88 \times 10^{-2} \text{ s}^{-1}$ , yielding an "effective molarity" of  $4.47 \text{ mol L}^{-1}$  as the measure of the rate acceleration caused by this preassembly of the reactants by electrostatic attraction. Further evidence for the intermediacy of an ion pair in the reaction between the oppositely charged reactants was the observation of a special salt effect, the addition of an inert salt causing a decrease in the aminolysis rate.

Catalysis by enzymes is generally believed to proceed through the formation of an enzyme-substrate complex, which then reacts further to form products, either directly or by way of one or more intermediates.<sup>2</sup> In this complex the substrate is held in juxtaposition with key functional groups comprising the enzyme. Proximity and orientation of these groups is believed to make a major contribution to the efficiency of the enzyme.<sup>3-6</sup> The importance of this juxtaposition has been examined by studies designed to mimic enzymatic catalysis by means of intramolecular catalysis.<sup>7</sup> Enlightening though many of these studies are, they nevertheless suffer from the difficulty that at best they mimic covalent enzyme-substrate complexes. In general, however, enzyme-substrate complexes are not covalent but involve forces of electrostatic attraction or apolar complexes such as  $\pi$  complexes and inclusion complexes. There are a number of studies of catalysis via apolar complexes.<sup>8</sup> Electrostatic catalysis has been observed in cases of substrate binding to polymeric catalysts<sup>9-12</sup> and to micelles and similar charged aggregates.<sup>13-15</sup>



In a medium of sufficiently low polarity it should be possible to look for the electrostatic assembly of two molecules in solution by the charges proximate to their reaction centers. Thus if A and C are (oppositely) charged inert groups on two molecules, and B and D are reactive sites proximate to A and C, respectively, then the reaction might take the course shown in Scheme I. The work described below endeavors to evaluate the extent to which complex formation via electrostatic attraction (ion pair formation) between reactant molecules in solution will facilitate a subsequent reaction between them.

### Results and Discussion

**Rates.** The reaction selected for study was the aminolysis of an ester in a the nonpolar solvent 95.3 mol % dioxane-water (dielectric constant = 2.53<sup>16</sup>). The active

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