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REACTIVITY OF 3,6-DIMETHOXY-3,6-DIMETHYLCYCLOHEXA-1,4-DIENE: NUCLEAR *VERSUS* BENZYLIC NUCLEOPHILIC SUBSTITUTION

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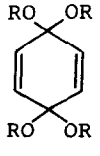
Summary: The treatment of cis/trans-3,6-dimethoxy-3,6-dimethylcyclohexa-1,4-diene (ca. 1/1 mixture; easily prepared electrochemically in multigram scale from p-xylene) under acidic conditions (acetic, trifluoroacetic, sulfuric, or a Lewis acid) yields almost exclusively 2-methoxy-1,4-dimethylbenzene **4**, through a transposition reaction. The use of aqueous hydrochloric or hydrofluoric acid gives 2,5-dimethylphenol **12**, and with hydrogen chloride a mixture of 2- and α-chloro-p-xylene (**13**, **14**) is isolated. Different oxygen-, nitrogen-, and sulfur-containing nucleophiles (alcohols, thiols, or hydrazoic acid) react with **3** under acid catalysis giving the corresponding products resulting from a nuclear or/and benzylic substitution on p-xylene (**15**-**20**). The reaction of compound **3** with organolithium reagents affords exclusively benzylic products **21** in a regiospecific manner. In all cases the mixtures of isomers are separated by column chromatography. The lithiation of compound **3** with lithium powder or lithium naphthalenide fails,giving p-xylene. A probable mechanism is proposed for the studied reactions.

Introduction

Quinone biketals of the type **1**, which are easily available by electrochemical oxidation[1] of the corresponding 1,4-dialkoxybenzene in alcoholic medium, are versatile intermediates in organic synthesis,[2] above all in the preparation of anthracyclinones.[3] However, the corresponding alkylated derivatives of the type **2**,[4] prepared also by the same methodology, have not been studied in relation to their reactivity. The possibility of obtaining substrates of the type **2** in ca. 10 g scale,[5] prompted us to study their application in organic synthesis. We report in this paper our results in this field.



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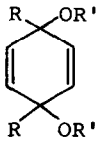

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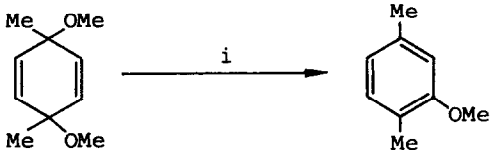
Results and Discussion

The treatment of a cis/trans-mixture of **3** (ca. 1/1)[4,5] with several Brönsted or Lewis acids under different reaction conditions led almost exclusively to 2,5-dimethylanisole **4** (Scheme 1 and Table 1). As by-products, compounds **5-7** could be characterized in yields lower than 7% (Table 1, entries 1, 4, and 6) by tandem g.l.c.-mass spectrometry (see Experimental).



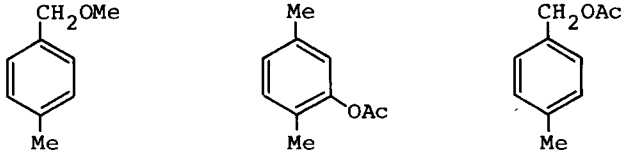
3 **4**

Scheme 1: i, H^+ or Lewis acid.

Table 1. Treatment of compound **3** with acids

Entry	Reagents and solvents	**4**, Yield (%)[a]
1	i, $BF_3 \cdot OEt_2$; ii HOAc gl.-THF	85 (4)[b,c]
2	i, HOAc gl.; $BF_3 \cdot OEt_2$-Et_2O	~100, 82[d]
3	i, HOAc gl.-NaOAc; ii, $BF_3 \cdot OEt_2$	98[d]
4	H_2SO_4 conc.-THF	97 (3)[b]
5	HOAc gl.-Ac_2O-H_2SO_4 conc.	89
6	CF_3CO_2H-CH_2Cl_2	98 (1)[b]
7	$AlCl_3$-Et_2O	~100
8	$BF_3 \cdot OEt_2$-Et_2O	95

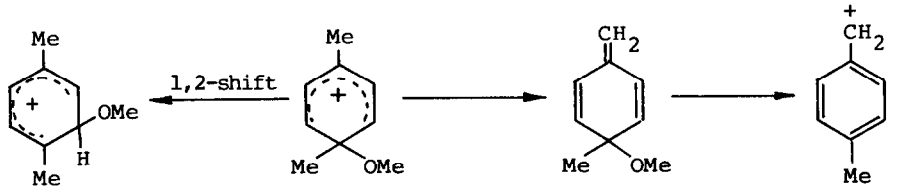
[a] Deduced by g.l.c. analysis using cyclohexanone as internal standard. [b] In parenthesis yield of compound **5**. [c] Compounds **6** (4%) and **7** (7%) were also obtained. [d] The reaction was performed at -78°C.



5 **6** **7**

The possible mechanism for this process has to involve a 1,2-migration of the methoxide group from the delocalized cation **8** to **9**. The final deprotonation yields the product **4**. The formation of by-product **6** can be explained

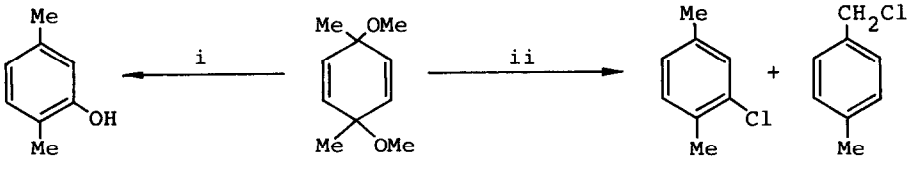
via a nucleophilic attack of acetic acid to the cation intermediate **8** followed by methanol elimination. In the case of compounds **5** and **7** the process can take place through the species **10** or **11** generated from **8** and further nucleophilic attack of the corresponding nucleophile (methanol or acetic acid) at the benzylic position (Scheme 2).



9 **8** **10** **11**

Scheme 2.

The use of aqueous hydracids such as hydrochloric or hydrofluoric acid yielded mainly 2,5-dimethylphenol **12**; in the last case the corresponding ether **4** was also obtained as by-product (Table 2, entry 2). In the absence of water and using hydrogen chloride in different solvents the corresponding chlorinated systems **13** and **14** were isolated (Scheme 3 and Table 2).



12 **3** **13** **14**

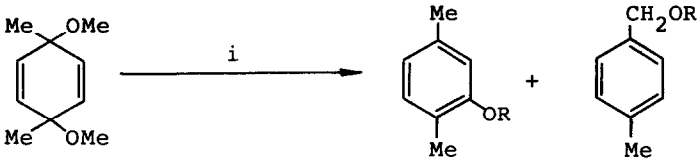
Scheme 3: i, 1 N HCl-Et_2O or 40% HF-Et_2O; ii, HCl (g)-solvent (Et_2O, HOAc, $^{i}PrOH$).

Table 2. Reaction of compound **3** with HHal

Entry	Reagents and solvents	Product, yield (%)[a]
1	1 N HCl-Et_2O	**12** (88)[b]
2	40% HF-Et_2O	**12** (63), **4** (33)[c]
3	HCl (g)-Et_2O	**13** (16), **14** (33)
4	HCl (g)-HOAc-THF	**13** (23), **14** (38)
5	HCl (g)-$Pr^{i}OH$	**13** (21), **14** (52)

[a] See footnote a in Table 1. [b] 90% isolated yield for a 10 mmol reaction. [c] 60% (**12**) and 30% (**4**) isolated yield for a 10 mmol reaction.

The possibility of obtaining different alkoxy-p-xylenes was tested by using an alcohol as solvent and concentrated sulfuric acid as catalyst. Thus, the expected products **15** and **16** were obtaining and separated by column chromatography (Scheme 4 and Table 3). It is worthy to note that in the case of using tert-butyl alcohol only the benzylic substitution took place due, probably, to steric effects (compare entries 2-4 in Table 3).



3 **15** **16**

Scheme 4: i, ROH (excess)-H_2SO_4 conc. (cat.).

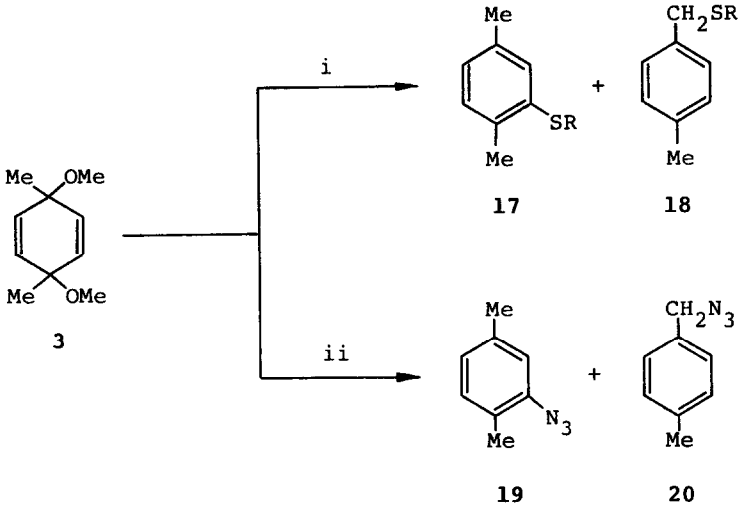
Table 3. Obtention of products **15** and **16**

Entry	R	Reagents and solvents	Products, yield (%)[a]	
1	Et	EtOH-H_2SO_4 conc.	**15a** (62)	**16a** (32)
2	Et	EtOH-$HC(OEt)_3$-H_2SO_4 conc.	**15a** (86)	**16a** (14)
3	Pr^i	Pr^iOH-H_2SO_4 conc.	**15b** (35)	**16b** (50)
4	Bu^t	Bu^tOH-THF-H_2SO_4 conc.	**15c** (-)	**16c** (62)[b]
5	$PhCH_2$	$PhCH_2OH$-Et_2O, H_2SO_4 conc.	**15d** (13)	**16d** (60)
6	CH_2=$CHCH_2$	CH_2=$CHCH_2OH$-Et_2O-H_2SO_4 conc.	**15e** (40)	**16e** (40)
7	CH≡CCH_2	CH≡CCH_2OH-Et_2O-H_2SO_4 conc.	**15f** (7)	**16f** (64)

[a] See footnote a in Table 1. [b] 65% isolated yield for a 10 mmol reaction.

When less nucleophilic oxygenated reagents such as phenol or benzoic acid were used in the reaction above described for alcohols (ether or THF as solvent and concentrated sulfuric acid as catalyst) the corresponding compound **4** was isolated as the major reaction product together with small amounts of the benzylic derivative **5**.

Sulfur-containing nucleophiles and hydrazoic acid gave similar results as for alcohols under acid catalysis and a mixture of compounds **17/18** or **19/20** were obtained (Scheme 5 and Table 4) and isolated by column chromatography. Other nitrogenated sustrates such as secondary amines (diethylamine, methylaniline), acetamide or acetonitrile did not give the expected products under the same reaction conditions or using zinc dichloride as catalyst; in all cases products **4** (major) and **5** (minor) were always obtained.



Scheme 5: i, RSH-Et_2O-H_2SO_4 conc.; ii HN_3-$HCCl_3$-H_2SO_4 conc.

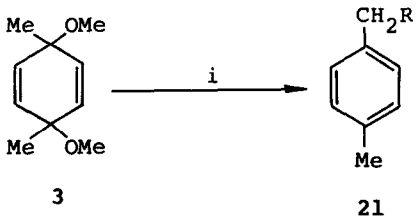
Table 4. Obtention of compounds **17-20**

Entry	R	Reagents and solvents	Products, yield (%)[a]	
1	Ph	PhSH-Et_2O-H_2SO_4 conc.	**17a** (54)	**18a** (16)[b]
2	$HS(CH_2)_3$	$HS(CH_2)_3SH$-Et_2O-H_2SO_4 conc.	**17b** (51)	**18b** (17)
3	-	HN_3-$HCCl_3$-H_2SO_4 conc.	**19** (35)	**20** (19)

[a] See footnote a in Table 1. [b] 58% (**17a**) and 15% (**18a**) isolated yields for a 10 mmol reaction.

From a mechanistic point of view, the obtention of compounds **12-20** can be easily explained considering the possible formation of intermediates **8** and **10** or **11** followed by nucleophilic attack at both nuclear and benzylic positions and final aromatization of the resulting system.

We have also studied the reaction of the starting material **3** with carbanionic reagents in order to create a carbon-carbon bond. Thus, the reaction of compound **3** with alkyl-lithium derivatives gave exclusively the product **21** resulting from a benzylic substitution (Scheme 6 and Table 5). Grignard reagents (i.e. methylmagnesium chloride in THF) even in the presence of a copper(I) salt [copper(I) iodide] does not react with compound **3** under the same reaction conditions as for alkyl-lithium reagents. Moreover, the reaction of **3** with diethyl malonate (THF, concentrated sulfuric acid) or its sodium salt (THF, boron trifluoride etherate-ether) led almost exclusively to the product **4** without formation of the expected carbon-carbon bond.



3 21

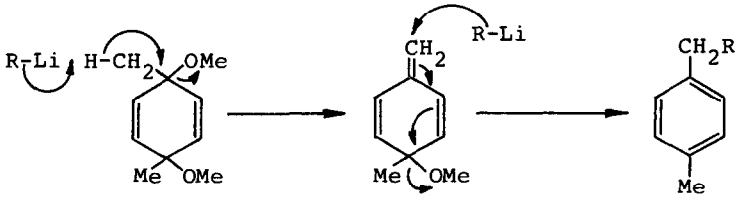
Scheme 6: i, RLi-THF.

Table 5. Obtention of compounds **21**

Entry	R	Product, yield (%)[a,b]
1	Bu^n	**21a** (95, *88*)
2	sec-Bu	**21b** (91, *85*)
3	Bu^t	**21c** (87, *76*)

[a] See footnote a in Table 1. [b] Isolated yields for 10 mmol reactions are given in italics.

In the case of the reaction with alkyl-lithium reagents, we have never observed the possible lithiation of the starting material **3**, which could afford the organolithium intermediate **22**. Instead of this process,a deprotonation at the methyl group takes probably place yielding the intermediate **10** (see above), which suffers nucleophilic attack by another molecule of the organometallic reagent (used in an 5/1 excess) giving the corresponding product **21** (Scheme 7). The absence of deprotonation at the nuclear position giving **22** and the only formation of products **21** can be justified taking in account that in the second case a very rapid β-elimination[6] yielding **10** may drive the reaction in that direction.

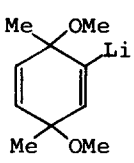


3 10 21

Scheme 7.

Finally, we have investigated the direct lithiation of compound **3** using lithium under different reaction conditions (lithium powder or lithium naph-

thalenide at -78°C or room temperature). In all cases p-xylene (23) was obtained in practically quantitative yield, so a Birch type reduction took place involving, probably, delocalized radical and carbanionic species 24 and 25. This reaction has no synthetic interest since p-xylene was the precursor of the starting material 3.[4,5]



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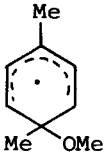

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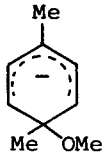

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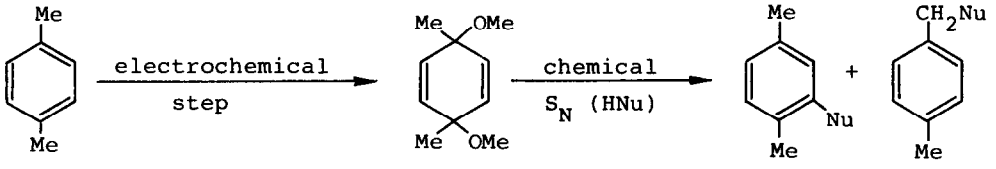
Conclusions

From the results described above we conclude that the tandem electrochemical/chemical nucleophilic substitution of p-xylene (23) allows the preparation of both nuclear or benzylic substituted systems (26 and 27, respectively) (Scheme 8). Since both type of products are easily separated by column chromatography (see Experimental) and the starting material is available in multigram scale,[5] this combined methodology represents an adequate route to introduce oxygen-, sulfur-, or carbon-containing nucleophiles both in the ring or at the benzylic position of p-xylene. The reaction seems to be more general because the electrochemical step works well also with other arenes.[7]



23 3 26 27

Scheme 8.

Experimental

General.- M.p.s are uncorrected and were measured on a Reichert thermovar apparatus. I.r. spectra were determined with a Pye Unicam SP3-200 spectrometer. ^1H n.m.r. spectra were recorded on a Varian EM-360L spectrometer with $SiMe_4$ as internal standard and using deuteriochloroform as solvent ;chemical shifts are given in δ (ppm) and the coupling constants are measured in Hz. M.s. (e.i.) were recorded with a Hewlett Packard EM/CG HP-5988A spectrometer. The purity of volatile distilled products and the chromatographic analysis (g.l.c.) were determined with a Hewlet Packard HP-5890 instrument equipped with a 25 m WCOT capillary column (0.22 mm diam., 0.2 μm film thickness OV-101 stationary phase) using nitrogen (2 ml/min) as the carrier gas, $T_{injector} = 250°C$, $T_{column} = 60°C$ (3 min) and 60-220°C (10°C/min); retention

times (t_r) are given under these conditions. Thin layer chromatography (t.l.c.) was carried out on aluminium backed plates coated with a 0.2 mm layer of silica gel 60H, using a mixture of hexane/ethyl acetate (95/5) as eluant; R_f values are given under these conditions. Starting material **3** was prepared according to the literature method.[4,5] The reagents used including organolithium compounds were commercially available (Aldrich). Solvents for the reactions with lithium or organolithium reagents were dried as usually.

Transformation of Compound 3 into 2,5-Dimethylanisole (4) under Acid Conditions. General Procedure.- 3,6-Dimethoxy-3,6-dimethylcyclohexa-1,4-diene (**3**) (0.17 g, 1 mmol) was dissolved in the corresponding solvent (2 ml, see Table 1) and to the resulting solution was added the Lewis acid (1 mmol) or/and the protic acid (10 mmol) at room temperature or at -78°C (see Table 1) under argon. After 1 h stirring the resulting mixture was hydrolyzed with water (1 ml), extracted with ether (2x3 ml) and the organic layer dried over anhydrous sodium sulfate. Solvents were evaporated (15 torr) and the residue analyzed by g.l.c. By-products **5-7** were characterized by tandem g.l.c/m.s. The main product **4** was purified by column chromatography (silica gel; hexane/ethyl acetate: 98/2).

2,5-Dimethylanisole (**4**) t_r=10.38 min, R_f=0.61 (lit.,[8] b.p. 194°C); ν_{max} (film) 3020, 1605, 1580, 1495 (HC=C), 1250, 1225, and 1035 cm^{-1} (C-O); δ_H 2.2, 2.25 (6 H, 2 s, 2x MeAr), 3.75 (3 H, s, MeO), and 6.55-7.0 (3 H, m, ArH); *m/z* 137 (M^++1, 7%), 136 (M^+, 85), 135 (12), 121 (100), 105 (15), 93 (11), 91 (68), 78 (14), 77 (65), 65 (16), and 51 (11).

α-Methoxy-p-xylene (**5**)[9] t_r=10.07 min; *m/z* 136 (M^+, 61%), 135 (36), 121 (83), 106 (15), 105 (100), 104 (27), 103 (18), 91 (50), 79 (17), 77 (35), 65 (17), and 51 (14).

2,5-Dimethylphenyl Acetate (**6**) t_r=12.94 min (lit.,[8] b.p. 237°C); *m/z* 165 (M^++1, 5%), 164 (M^+, 45), 122 (100), 107 (51), 105 (82), 104 (57), 103 (35), 93 (13), 91 (25), 79 (18), 78 (35), 77 (34), 65 (18), 63 (10), 51 (13), and 43 (29).

4-Methylbenzyl Acetate (**7**) t_r=12.43 min (lit.,[10] b.p. 118-119°C/20 torr); *m/z* 165 (M^++1, 2%), 164 (M^+, 15), 122 (100), 107 (47), 91 (11), 77 (15), and 43 (13).

Reaction of Compound 3 with Hydrochloric or Hydrofluoric Acid. General Procedure.- To a solution of compound **3** (1 mmol) in ether (10 ml) was added an aqueous solution of the corresponding acid (3 mmol of 1 N hydrochloric acid or 40% hydrofluoric acid) and the mixture was stirred for 30 min at room temperature. Then it was hydrolyzed and worked up as for compound **4**. The obtained mixture of **12/4** (Table 2, entry 2) was separated by column chromatography (silica gel; hexane/ethyl acetate: 98/2).

2,5-Dimethylphenol (**12**) t_r=10.98 min, R_f=0.22, m.p. 70-72°C (ethanol) (lit.,[8] m.p. 71-73°C); ν_{max} (KBr) 3400 (OH), 3020, 1620, 1590 (HC=C), and 1255 cm^{-1} (C-O); δ_H 2.1, 2.15 (6 H, 2 s, 2x Me), ~4.5 (1 H, br s, OH), and 6.45-6.85 (3 H, m, ArH); *m/z* 122 (M^+, 84%), 121 (36), 107 (100), 91 (19), 79 (18), and 77 (35).

Reaction of Compound 3 with Hydrogen Chloride. Isolation of Compounds 13 and 14.- Through a solution of compound **3** (1 mmol) in the corresponding solvent (4 ml; see Table 2, entries 3-5)* was bubbled hydrogen chloride for 30 min. The resulting mixture was then hydrolyzed and worked up as for compound **4**. Compounds **13** and **14** were isolated by column chromatography (silica gel; hexane/ethyl acetate: 98/2)

2,5-Dimethylchlorobenzene (**13**) t_r=9.56 min, R_f=0.76 (lit.,[11] b.p. 184-185°C, m.p. 2°C); ν_{max} (film) 3020, 1605, and 1580 cm^{-1} (HC=C); δ_H 2.3 (6 H, br s, 2x Me), and 6.8-7.15 (3 H, m, ArH); 142 (M^++2, 17%), 140 (M^+, 46), 125 (19), 105 (100), 103 (25), 89 (10), 78 (13), 77 (25), 63 (14), and 51 (19).

4-Methylbenzyl Chloride (**14**) t_r=10.52 min, R_f=0.56 (lit.,[12] b.p. 200-202°C); ν_{max} (film) 3040, 1610, and 1580 cm^{-1} (HC=C); δ_H 2.3 (3 H, s, Me), 4.5 (2 H, s, CH_2), and 6.95-7.3 (4 H, m, ArH); *m/z* 142 (M^++2, 7%), 140 (M^+, 23), 105 (100), 103 (17), 78 (10), 77 (16), and 51 (11).

Reaction of Compound 3 with Alcohols Catalyzed by Sulfuric Acid. Isolation of Compounds 15 and 16. General Procedure.- To a solution of compound **3** (1 mmol) in the corresponding alcohol (4 ml) was added a solution of sulfuric acid (0.01 mmol) in the same alcohol (2 ml) and the mixture was stirred for ca. 10 h at room temperature under argon. Then the mixture was hydrolyzed and worked up as for compound **4**. Products **15** and **16** were separated by column chromatography (silica gel; hexane/ethyl acetate: 98/2). In the case of tert-butanol, benzyl alcohol, or propargyl alcohol (Table 3, entries 4,5, and 7), THF or ether (4 ml) were also added as co-

(*) In the case of using glacial acetic acid as additive (Table 2, entry 4), 10 mmol of this compound were added.

solvent. When ethyl orthoformiate was used as reagent (Table 3, entry 2), 0.5 mmol of this compound was used.

2-Ethoxy-1,4-dimethylbenzene (**15a**) t_r= 11.30 min, R_f= 0.62 (lit.,[8] b.p. 199°C); ν_{max} (film) 3035, 1605, 1580 (HC=C), and 1250 cm^{-1} (C-O); δ_H 1.4 (3 H, t, J=7, $MeCH_2$), 2.15, 2.3 (6 H, 2 s, 2 x MeAr), 3.95 (2 H, q, J=7, CH_2), and 6.55-7.2 (3 H, m, ArH); *m/z* 151 (M^++1, 3%), 150 (M^+, 31), 122 (67), 121 (33), 107 (100), 94 (10), 92 (10), 91 (77), 79 (30), 78 (25), 77 (77), 65 (24), 63 (13), 53 (14), and 51 (19).

2-Isopropyloxy-1,4-dimethylbenzene (**15b**) t_r= 11.79 min, R_f=0.42; ν_{max} (film) 3030, 1605, 1580 (HC=C), and 1250 cm^{-1} (C-O); δ_H 1.3 (6 H, d, J=6, 2 x MeCH), 2.15, 2.25 (6 H, 2 s, 2 x MeAr), 4.4 (1 H, heptet, J=6, CHMe), and 6.5-7.0 (3 H, m, ArH); *m/z* 165 (M^++1, 4%), 164 (M^+, 22), 123 (10), 122 (100), 121 (27), 107 (95), 91 (53), 79 (22), 78 (19), 77 (58), 65 (21), 63 (10), 53 (10), 51 (17), 43 (12), and 41 (21).

2-Benzyloxy-1,4-dimethylbenzene (**15d**) t_r= 19.60 min, R_f= 0.36 (lit.,[13] b.p. 169-171°C/14 torr); ν_{max} (film) 3080, 3045, 1605, 1580 (HC=C), and 1260 cm^{-1} (C-O); δ_H 2.25, 2.3 (6 H, 2 s, 2 x Me), 5.0 (2 H, s, CH_2), 6.4-6.9 (3 H, m, xylylic H), and 7.35 (5 H, s, phenylic H); *m/z* 213 (M^++1, 1%), 212 (M^+, 5), 92 (11), 91 (100), 78 (12), 77 (40), 65 (44), 63 (16), and 51 (20).

2-Allyloxy-1,4-dimethylbenzene (**15e**) t_r= 13.34 min, R_f= 0.57 (lit.,[14] b.p. 63-64°C/~1 torr); ν_{max} (film) 3080, 3040, 1640, 1610, 1580 (HC=C), and 1260 cm^{-1} (C-O); δ_H 2.2, 2.3 (6 H, 2 s, 2 x Me), 4.45 (2 H, m, CH_2O), 5.15, 5.3 (2 H, 2 m, CH_2=C), 6.0 (1 H, m, CH=CH_2), and 6.5-7.0 (3 H, m, ArH); *m/z* 162 (M^+, 14%), 147 (21), 121 (24), 119 (18), 93 (16), 92 (19), 91 (100), 78 (24), 77 (70), 65 (22), 63 (11), 53 (13), 51 (19), and 41 (35).

1,4-Dimethyl-2-propargyloxybenzene (**15f**)[15] t_r = 12.75 min, R_f = 0.33; ν_{max} (film) 3280, 2100 (HC≡C), 3040, 1605, 1575 (HC=C), and 1250 cm^{-1} (C-O); δ_H 2.3 (6 H, br s, 2 x Me), 2.45 (1 H, t, J = 2.5, HC≡C), 4.65 (2 H, d, J= 2.5, CH_2), and 6.45-6.9 (3 H, m, ArH); *m/z* 160 (M^+, 46%), 159 (36), 145 (71), 121 (52), 117 (31), 115 (13), 93 (13), 92 (19), 91 (90), 78 (22), 77 (100), 65 (34), 63 (16), 53 (30), 52 (16), 51 (37), 50 (17), 43 (31), and 41 (25).

Ethyl 4-Methylbenzyl Ether (**16a**) t_r = 11.24 min, R_f = 0.59 (lit.,[16] b.p. 204°C); ν_{max} (film) 3035, 1605 (HC=C), and 1090 cm^{-1} (C-O); δ_H 1.2 (3 H, t, J = 7, $MeCH_2$), 2.35 (3 H, s, MeAr), 3.45 (2 H, q, J=7, CH_2Me), 4.4 (2 H, s, CH_2Ar), and 7.1 (4 H, s, ArH); *m/z* 151 (M^++1, 2%), 150 (M^+, 14), 135 (17), 107 (29), 106 (71), 105 (100), 104 (21), 103 (21), 93 (36), 91 (87), 79 (37), 78 (23), 77 (68), 65 (25), 63 (15), and 51 (20).

Isopropyl 4-Methylbenzyl Ether (**16b**) t_r = 12.12 min, R_f = 0.22 (lit.,[16] b.p. 65°C/5 torr); ν_{max} (film) 3035, 1610 (HC=C), and 1065 cm^{-1} (C-O); δ_H 1.15 (6 H, d, J = 6, 2 x MeCH), 2.3 (3 H, s, MeAr), 3.6 (1 H, heptet, J = 6, CHMe), 4.4 (2 H, s, CH_2), and 7.1 (4 H, s, ArH); *m/z* 164 (M^+, 5%), 107 (23), 106 (55), 105 (100), 104 (12), 103 (15), 93 (23), 91 (48), 79 (23), 78 (16), 77 (47), 65 (17), 63 (10), 51 (13), and 43 (16).

tert-Butyl 4-Methylbenzyl Ether (**16c**)[17] t_r = 13.37 min, R_f = 0.35; ν_{max} (film) 3025, 1605, 1570 (HC=C), and 1070 cm^{-1} (C-O); δ_H 1.25 (9 H, s, 3 x MeC), 2.3 (3 H, s, MeAr), 4.35 (2 H, s, CH_2), and 7.05 (4 H, s, ArH); *m/z* 178 (M^+, 13%), 122 (100), 93 (27), 91 (15), 79 (12), 77 (21), 57 (15), and 43 (12).

Benzyl 4-Methylbenzyl Ether (**16d**) t_r= 19.76 min, R_f = 0.33 (lit.,[18] b.p. 110°C/0.2 torr); ν_{max} (film) 3080, 3040, 1600 (HC=C), and 1070 cm^{-1} (C-O); δ_H 2.35 (3 H, s, Me), 4.45 (4 H, s, 2 x CH_2), 7.15 (4 H, s, xylylic H), and 7.3 (5 H, s, phenylic H); *m/z* 212 (M^+, 1%), 121 (29), 106 (36), 105 (45), 103 (10), 93 (17), 92 (38), 91 (100), 79 (19), 78 (15), 77 (56), 65 (35), 63 (12), and 51 (23).

Allyl 4-Methylbenzyl Ether (**16e**) t_r= 13.41 min, R_f = 0.54 (lit.,[19] b.p. 106-108°C/14 torr); ν_{max} (film) 3060, 3030, 1630, 1605 (HC=C), and 1080 cm^{-1} (C-O); δ_H 2.35 (3 H, s, Me), 3.95 (2 H, m, CH_2CH=C), 4.45 (2 H, s, CH_2Ar), 5.15, 5.2 (2 H, 2 m, CH_2=C), 5.95 (1 H, m, CH=CH_2), and 7.15 (4 H, s, ArH); *m/z* 162 (M^+, 4%), 120 (20), 119 (22), 106 (41), 105 (100), 103 (13), 93 (17), 91 (48), 79 (15), 78 (12), 77 (37), 65 (13), and 51 (10).

4-Methylbenzyl Propargyl Ether (**16f**)[20] t_r= 13.00 min, R_f = 0.32; ν_{max} (film) 3280, 2100 (HC≡C), 3040, 1610 (HC=C), and 1080 cm^{-1} (C-O); δ_H 2.35 (3 H, s, Me), 2.45 (1 H, t, J=2.5, HC≡C), 4.1 (2 H, d, J=2.5, CH_2C≡C), 4.55 (2 H, s, CH_2Ar), and 7.15 (4 H, s, ArH); *m/z* 160 (M^+, 13%), 145 (13), 130 (32), 129 (11), 121 (15), 120 (16), 119 (56), 115 (18), 106 (38), 105 (78), 104 (10), 103 (18), 93 (37), 92 (13), 91 (100), 79 (19), 78 (19), 77 (74), 65 (37), 63 (20), 53 (14), 52 (10), 51 (32), 50 (13), and 41 (12).

Reaction of Compound 3 with Thiols. Isolation of Compounds 17 and 18. General Procedure.- To a solution of compound **3** (1 mmol) in ether (3 ml) was added a solution of the corresponding thiol (1.5 mmol) and sulfuric acid (0.005 mmol) in ether (2 ml), and the mixture was stirred overnight. Then, the resulting mixture was hydrolyzed and worked up as for **4**. Compounds **17** and **18** were isolated by column chromatography (silica gel; hexane/ethyl acetate: 98/2).

1,4-Dimethyl-2-phenylthiobenzene (**17a**) t_r = 19.17 min, R_f = 0.42 (lit.,[21] b.p. 171°C/11 torr); ν_{max} (film) 3040, 1600, and 1580 cm^{-1} (HC=C); δ_H 2.25, 2.3 (6 H, 2 s, 2 x Me), 7.0 (3 H, m, xylylic H), and 7.1 (5 H, s, phenylic H); *m/z* 215 (M^++1, 16%), 214 (M^+, 100), 199 (16), 184 (14), 166 (11), 165 (16), 136 (28), 135 (30), 106 (13), 105 (41), 103 (23), 92 (16), 91 (32), 79 (18), 78 (28), 69 (14), 65 (31), 63 (18), 53 (15), 52 (11), 51 (64), 50 (20), and 45 (30).
1,4-Dimethyl-2-(3-mercaptopropylthio)benzene (**17b**) t_r = 19.54 min, R_f = 0.44; ν_{max} (film) 3040, 1595 (HC=C), and 2540 cm^{-1} (SH); δ_H 1.75-2.05 (2 H, m, CH_2CH_2S), 2.3 (6 H, s, 2 x Me), 2.4-2.85 (2 H, m, CH_2SH), 3.0 (2 H, m, CH_2SAr), and 6.85-7.1 (3 H, m, ArH); *m/z* 212 (M^+, 36%), 151 (13), 138 (73), 137 (24), 135 (18), 134 (13), 121 (20), 107 (10), 106 (21), 105 (89), 104 (15), 103 (35), 97 (13), 93 (16), 92 (12), 91 (81), 79 (32), 78 (38), 77 (94), 75 (14), 65 (29), 63 (22), 61 (10), 59 (17), 53 (20), 52 (12), 51 (36), 47 (83), 46 (20), 45 (100), and 41 (52).
4-Methylbenzyl Phenyl Thioether (**18a**) t_r = 19.76 min, R_f = 0.30, m.p. 66-68°C (hexane) (lit.,[22] m.p. 70°C); ν_{max} (KBr) 3040 and 1575 cm^{-1} (HC=C), δ_H 2.3 (3 H, s, Me), 4.05 (2 H, s, CH_2), 7.05 (4 H, s, xylylic H), and 7.2 (5 H, s, phenylic H); *m/z* 214 (M^+, 11%), 105 (100), and 77 (13).
3-Mercaptopropyl 4-Methylbenzyl Thioether (**18b**) t_r = 19.96 min, R_f = 0.43; ν_{max} (film) 3040, 1650, 1595 (HC=C), and 2540 cm^{-1} (SH); δ_H 1.75-2.0 (2 H, m, CH_2CH_2S), 2.3 (3 H, s, Me), 2.4-2.8 (4 H, m, 2 x CH_2S), 3.65 (2 H, s, CH_2Ar), and 7.1 (4 H, s, ArH); *m/z* 212 (M^+, 3%), 107 (15), 106 (39), 105 (100), 104 (10), 103 (20), 91 (15), 79 (35), 78 (20), 77 (48), 73 (16), 65 (13), 63 (11), 51 (17), 47 (35), 46 (11), 45 (48), and 41 (19).

Reaction of Compound 3 with Hydrazoic Acid. Isolation of Compounds 19 and 20.- To a solution of compound **3** (1 mmol) in chloroform (4 ml) was added a solution of hydrazoic acid[23] (1.8 mmol) and sulfuric acid (0.005 mmol) in chloroform (2 ml), and the mixture was stirred overnight. The resulting solution was hydrolyzed and worked up as for **4**. Compounds **19** and **20** were separated by column chromatography (silica gel; hexane/ethyl acetate: 98/2).
2-Azido-1,4-dimethylbenzene (**19**)[24] t_r = 12.58 min, R_f = 0.75; ν_{max} (film) 3040, 3010, 1570 (HC=C), 2110, and 1295 cm^{-1} (N_3); δ_H 2.15, 2.3 (6 H, 2 s, 2 x Me), and 6.65-7.0 (3 H, m, ArH); *m/z* 147 (M^+, 5%), 119 (42), 118 (100), 117 (11), 104 (36), 93 (34), 92 (13), 91 (67), 78 (14), 77 (38), 76 (12), 75 (11), 66 (10), 65 (24), 64 (11), 63 (25), 53 (10), 52 (23), 51 (36), and 50 (26).
4-Methylbenzyl Azide (**20**)[25] t_r = 12.46 min, R_f = 0.53; ν_{max} (film) 3040, 1610 (HC=C), and 2095 cm^{-1} (N_3); δ_H 2.35 (3 H, s, Me), 4.45 (2 H, s, CH_2), and 7.15 (4 H, s, ArH); *m/z* 119 (M^+-28, 20%), 106 (24), 105 (54), 104 (13), 103 (20), 93 (10), 91 (100), 88 (20), 79 (32), 78 (27), 77 (83), 65 (45), 63 (20), 53 (10), and 51 (20).

Reaction of Compound 3 with Organolithium Reagents. Isolation of Compounds 21. General Procedure.- To a solution of compound **3** (1 mmol) in THF (5 ml) was added the corresponding alkyl-lithium (see Table 5) (5 mmol) in 4 portions over a period of 8 h with stirring and under argon. The resulting mixture was then hydrolyzed and worked up as for **4**. Compounds **21** were purified by column chromatography (silica gel; hexane/ethyl acetate: 98/2).
4-Methyl-1-pentylbenzene (**21a**) t_r = 12.94 min, R_f = 0.83 (lit.,[26] b.p. 98.9-99.5°C/12 torr); ν_{max} (film) 3040 and 3010 cm^{-1} (HC=C); δ_H 0.8-1.5 [9 H, m, $Me(CH_2)_3$], 2.3 (3 H, s, MeAr), 2.55 (2 H, t, J = 7, CH_2Ar), and 7.0 (4 H, s, ArH); *m/z* 162 (M^+, 31%), 106 (22), 105 (100), 103 (15), 91 (18), 79 (14), and 77 (17).
4-Methyl-1-(2-methylbutyl)benzene (**21b**)[27] t_r = 12.25 min, R_f = 0.82; ν_{max} (film) 3030 and 3010 cm^{-1} (HC=C); δ_H 0.8 (3 H, d, J = 6, MeCH), 0.85 (3 H, t, J = 6, $MeCH_2$), 1.05-1.65 (3 H, m, $CHCH_2Me$), 2.3 (3 H, s, MeAr), 2.5 (2 H, d, J = 6, CH_2Ar), and 7.0 (4 H, s, ArH); *m/z* 162 (M^+, 14%), 117 (11), 115 (13), 106 (37), 105 (100), 103 (14), 91 (26), 79 (17), 78 (11), 77 (27), and 41 (10).
4-Methyl-1-(2,2-dimethylpropyl)benzene (**21c**)[28] t_r = 11.40 min, R_f = 0.72; ν_{max} (film) 3040 and 3010 cm^{-1} (HC=C); δ_H 0.9 (9 H, s, 3 x MeC), 2.25 (3 H, s, MeAr), 2.4 (2 H, s, CH_2Ar), and 6.95 (4 H, ArH); *m/z* 162 (M^+, 31%), 147 (12), 117 (12), 115 (20), 106 (100), 105 (88), 104 (14), 103 (24), 91 (47), 79 (24), 78 (20), 77 (48), 65 (14), 62 (13), 57 (28), 51 (17), and 41 (35).

Lithiation of Compound 3. General Procedure.- A solution of compound **3** (1 mmol) in THF (6 ml) was treated with lithium powder (20 mmol, room temperature) or with a solution of lithium naphthalenide[29] (3 mmol, -78°C) in THF. After ca. 10 h stirring at the same temperature the mixture was carefully hydrolyzed and worked up as for **4**. The resulting product was analyzed by g.l.c. (see General) using a commercial sample (Merck) of p-xylene for comparison, giving a ca. 100% yield of p-xylene (**23**).

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