(6) L. Horner, H. Hoffmann, H. G. Wippel, and G. Hassel, *Chem. Ber.*, **91**, 52 (1958).
(7) M. Zanger, C. A. VanderWerf, and W. E. McEwen, *J. Am. Chem. Soc.*, **87**, 3948 (1965).
(8) R. Alexander, C. Eaborn, and T. G. Traylor, *J. Organomet. Chem.*, **21**, 65 (1976).
(9) J. R. Corfield and S. Trippett, *Chem. Commun.*, 1267 (1970).
(10) G. F. Lanneau, R. J. Wikholm, C. T. Lin, and W. E. McEwen, *J. Organomet. Chem.*, **85**, 179 (1975).
(11) W. E. McEwen, G. H. Briles, and B. E. Giddings, *J. Am. Chem. Soc.*, **91**, 7079 (1969).
(12) J. W. Knapczyk, C. C. Lai, W. E. McEwen, J. L. Calderon, and J. J. Lubinkowski, *J. Am. Chem. Soc.*, **97**, 1188 (1975).
(13) C. C. Lai and W. E. McEwen, *Tetrahedron Lett.*, 3271 (1971).
(14) J. W. Knapczyk and W. E. McEwen, *J. Am. Chem. Soc.*, **91**, 145 (1969).
(15) G. H. Wiegand and W. E. McEwen, *J. Org. Chem.*, **33**, 2671 (1968).
(16) J. J. Lubinkowski, J. W. Knapczyk, J. L. Calderon, L. R. Petit, and W. E. McEwen, *J. Org. Chem.*, **40**, 3010 (1975).
(17) W. E. McEwen, J. J. Lubinkowski, and J. W. Knapczyk, *Tetrahedron Lett.*, 3301 (1972).
(18) J. J. Lubinkowski, M. Gomez, J. L. Calderon, and W. E. McEwen, Abstracts, 182d National Meeting of the American Chemical Society, San Francisco, Calif., Aug 29–Sept 3, 1976.
(19) M. C. Caserio, D. L. Glusker, and J. D. Roberts, *J. Am. Chem. Soc.*, **81**, 336 (1959).
(20) G. Wittig and K. Clauss, *Justus Liebigs Ann. Chem.*, **577**, 26 (1952).
(21) W. E. McEwen and C. T. Lin, *Phosphorus*, **3**, 229 (1974).
(22) When more than 1 equiv of water is present, the yield of benzene rises to well over 100%, and the residue obtained by evaporation of the solution consists mainly of the polymeric form of triphenylstibine oxide.[23] Evidently, the excess water catalyzes the conversion of hydroxytetraphenylantimony to benzene plus triphenylstibine oxide.
(23) D. L. Venezky, C. W. Sink, B. A. Nevett, and W. F. Fortescue, *J. Organomet. Chem.*, **35**, 131 (1972).
(24) H. E. Affsprung and H. E. May, *Anal. Chem.*, **32**, 1164 (1960).
(25) K. D. Moffett, J. R. Simmler, and H. A. Potratz, *Anal. Chem.*, **23**, 1356 (1956).
(26) A. L. Beauchamp, M. J. Bennett, and F. A. Cotton, *J. Am. Chem. Soc.*, **91**, 297 (1969).

Attack of Grignard and Lithium Reagents at Carbonyl Oxygens of *o*-Quinol Acetates[1]

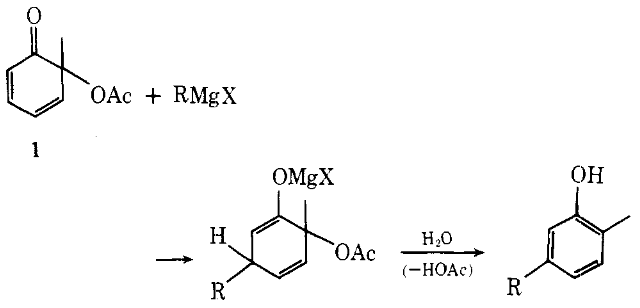
Bernard Miller

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01002

Received July 29, 1976

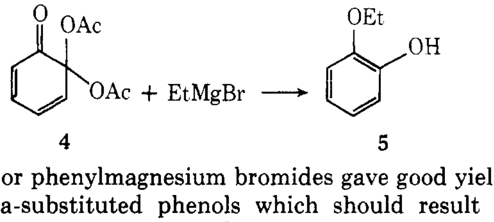
Grignard and lithium reagents react with *o*-quinol acetates (6-acetoxycyclohexa-2,4-dien-1-ones) to give alkyl aryl ethers resulting from formal attack at the "wrong ends" of the ketone carbonyls, as well as the normal reduction products and products arising from 1,2 and 1,4 addition to the conjugated carbonyls. Formation of ethers is not catalyzed by the presence of trace metals, which simply increases the yields of reduction products. Benzyl- and *tert*-butylmagnesium halides give exceptionally high relative yields of ethers, with secondary, primary, and methyl Grignards giving progressively lower yields of ethers. The yields of ethers appear to correlate well with the expected ease of oxidation of the Grignard reagents. These results are explained by assuming initial electron transfer from the organometallic reagent to the quinol acetate, giving a ketyl which then loses an acetate ion to give a phenoxy radical. The ethers are then formed by combination of phenoxy and alkyl radicals. This mechanism explains the occasional formation of 4-alkylphenols, which can arise by reaction of the alkyl radical at C-4 of the phenoxy radical, rather than at oxygen.

In an extensive series of papers, Wessely and his co-workers at the University of Vienna reported that reaction of Grignard reagents (including methyl-, ethyl-, and phenylmagnesium halides) with *o*-quinol acetates (6-acetoxycyclohexa-2,4-dien-1-ones) such as **1** gave 3-alkyl- or 3-arylphenols (e.g., **3**) as well as a variety of products apparently resulting from 1,2 addition of the Grignards to the ketone carbonyl.[2-6] This reaction has appreciable synthetic utility as a method for preparing meta-substituted phenols, which may otherwise be accessible only by multistep paths.[1,7] Formation of meta-substituted phenols presumably proceeds by initial conjugate addition of the Grignard reagent to the unsaturated carbonyls to give intermediates such as **2**, which then lose acetic acid, either during the reaction or during workup, to give **3**.



1 2 3

In one paper, Wessely and Kotlan reported that ethylmagnesium bromide reacted with the quinol diacetate **4** to give the ethyl ether, **5**, as the principal product[3]—a unique example of a Grignard reagent attacking the "wrong end" of a carbonyl group. Similar products were not observed in reactions of other quinol acetates,[2,4-6] while reaction of **4** with methyl- or phenylmagnesium bromides gave good yields of the meta-substituted phenols which should result from "normal" conjugate addition.[3]



4 5

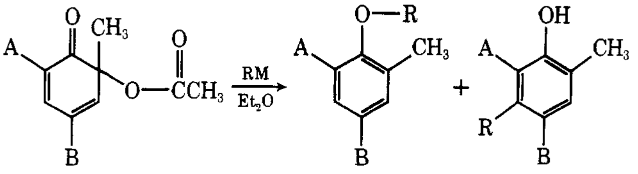
While attempting to prepare meta-substituted phenols by reactions of Grignard and lithium reagents with *o*-quinol acetates, we discovered that attack of the carbanionoid reagents at the oxygen atoms of carbonyls to give ethers is a very common result of these reactions.[1,8] This paper discusses the effect of changes in the structures of the organometallic reagents in determining the extent of attack at carbonyl oxygen atoms, and suggests a mechanism for these unusual reactions.

Results

Solutions of Grignard Reagents (1 M, prepared from >99.99% pure magnesium) were added rapidly to equal volumes of solutions of the quinol acetates in ether. To assure

Table I

a, A = B = CH_3
b, A = CH_3; B = H
c, A = *t*-Bu; B = H



6a–c **7a–c** **8a–c**

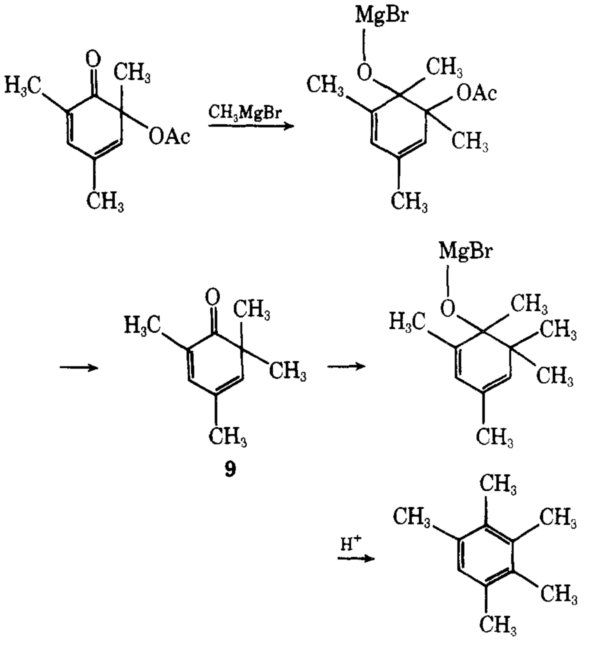
Ketone[d]	Organometallic reagent[e]	**7**, %	**8**, %	Redn product (**8**, R = H), %	Other products (%)	Additives	% **7**/% **8**
6a	CH_3MgBr	<0.1	39	4	Pentamethylbenzene (42) Unidentified ketones (15)		<0.003
6a	C_2H_5MgBr	4	52	7	2,5-Diethyl-2,4,6-trimethylcyclohex-3-en-1-one (31)		0.08
6a	C_2H_5MgBr	1	11	67	2,5-Diethyl-2,4,6-trimethylcyclohex-3-en-1-one (10)	Cu_2Cl_2 (0.1 g)	0.09
6a	*sec*-BuMgBr	67	16	17			4.2
6a	*sec*-BuMgBr	58[a]	15	28			3.9
6a	*sec*-BuMgBr	16	3	81		Cu_2Cl_2 (0.1 g)	5.3
6a	*sec*-BuMgBr	6	2	92		$CoCl_2$ (0.1 g)	3.0
6a	*sec*-BuMgBr	18	3	79		$FeCl_3$ (0.1 g)	6.0
6a	*t*-BuMgBr	28	<0.1	72			>280
6a	*t*-BuLi	15	<0.1	85			>150
6a	$PhCH_2MgCl$	91	<0.2	9			>450
6a	$PhCH_2MgCl$[a]	83	<0.2	17			>415
6b	*sec*-BuMgBr	46	27	32			
6b	*t*-BuMgBr	38	4	58	4-*tert*-Butyl-2,6-dimethylphenol (0.4)		1.7 9.5
6b	*t*-BuMgBr	38	3	60	4-*tert*-Butyl-2,6-dimethylphenol (0.4)		12.7[b]
6c	*sec*-BuMgBr	16	<1[c]	73	4-*sec*-Butyl-2-*tert*-butyl-6-methylphenol (11)		>16
6c	*t*-BuMgBr	<0.1	<0.1	86	2,4-Di-*tert*-butyl-6-methylphenol (14)		
6c	*sec*-BuMgBr	14	<1[c]	79	4-*sec*-Butyl-2-*tert*-butyl-6-methylphenol (8)		>14[b]
6c	$PhCH_2MgCl$	64	<1[c]	22	3-Benzyl-6-*tert*-butyl-2-methylphenol (2.0) 4-Benzyl-2-*tert*-butyl-6-methylphenol (12.5)		>64
6c	CH_3MgBr	0.1		39	1-*tert*-Butyl-2,3,5-trimethylbenzene (14) Unidentified ketones (39) (15)		

[a] Reagent prepared from "Grignard grade" magnesium. [b] Reaction time 30 s. [c] Estimated from NMR spectra of isomeric phenols. [d] Registry no.: **6a**, 4906-82-5; **6b**, 7218-21-5; **6c**, 51067-62-0. [e] Registry no.: CH_3MgBr, 75-16-1; C_2H_5MgBr, 925-90-6; *sec*-BuMgBr, 922-66-7; *t*-BuMgBr, 2259-30-5; *t*-BuLi, 594-19-4; $PhCH_2MgCl$, 6921-34-2.

complete reaction, ca. 7 mol of Grignard reagent was used for each mole of quinol acetate. The reactions were normally allowed to continue for 30 min, but two runs in which the reactions were worked up only 30 s after addition of the Grignard reagents was started gave identical results with those employing the longer reaction times. The results of the various reactions are summarized in Table I.

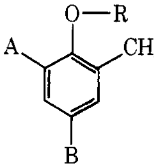
Reaction of quinol acetate **6a** with methylmagnesium bromide gave the conjugate addition product, 2,3,4,6-tetramethylphenol, and pentamethylbenzene as the principal addition products. A ketone with a camphorlike odor, which was presumably identical with the product which Wessely's group obtained from reaction of **6a** with methylmagnesium iodide,[2] was also obtained. The spectra of this product were quite complex, with several NMR peaks at other than integral ratios (see Experimental Section). We believe this product to be a mixture, despite failure to separate it on several GLC columns.

The major product, pentamethylbenzene, was presumably formed by 1,2 addition of the Grignard reagent to the ketone carbonyl, followed by a pinacol rearrangement, a second 1,2 addition, and a Wagner–Meerwein rearrangement, which may have occurred during the workup procedure (eq 1). The ke-



(1)

Table II. NMR Spectra of Ethers

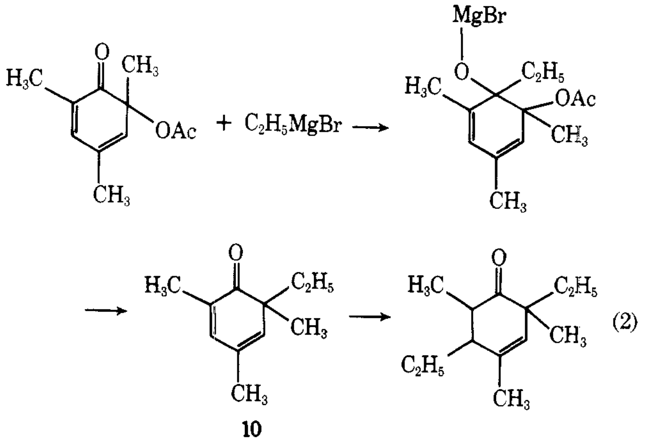


Registry no.		A	B	R	Chemical shifts, δ, ppm			
					ArCH$_3$	Other	ArH	R
61248-61-1	[a]	CH$_3$	CH$_3$	*t*-Bu	2.27 (s, 9 H)		6.83 (s, 2 H)	1.37 (s, 9 H)
19578-76-8	[a]	CH$_3$	CH$_3$	PhCH$_2$	2.21 (s, 9 H)		6.83 (s, 2 H) 6.97–7.55 (m, 5 H)	4.75 (s, 2 H)
61248-62-2	[a]	CH$_3$	CH$_3$	*sec*-Bu	2.23 (s, 9 H)		6.79 (s, 2 H)	0.99 (t, J = 6 Hz, 3 H) 1.20 (d, J = 6 Hz, 3 H) 3.8–4.1 (m, 1 H)
61248-63-3		CH$_3$	CH$_3$	C$_2$H$_5$	2.20 (s, 9 H)		6.79 (s, 2 H)	0.82 (t, J = 7 Hz, 3 H) 3.82 (q, J = 7 Hz, 2 H)
4028-66-4		CH$_3$	CH$_3$	CH$_3$	2.21 (s, 9 H)		6.80 (s, 2 H)	3.52
61248-64-4	[a]	CH$_3$	H	*sec*-Bu	2.19 (d, J = 0.5 Hz, 6 H)		6.7–6.9 (m, 3 H)	1.00 (t, J = 6 Hz, 3 H) 1.20 (d, J = 6 Hz, 3 H) 3.8–4.1 (m, 1 H)
54350-32-2	[a]	CH$_3$	H	*t*-Bu	2.29 (s, 6 H)		6.7–6.9 (m, 3 H)	1.38 (s, 9 H)
61248-65-5	[a]	*t*-Bu	H	*sec*-Bu	2.28 (d, J = 1 Hz, 3 H)	1.39 (s, 9 H)	6.8–7.3 (m, 3 H)	1.01 (t, J = 6 Hz) 1.14 (d, J = 5 Hz) 6 H total 4.3–4.8 (m, 1 H)
61248-66-6	[a]	*t*-Bu	H	PhCH$_2$	2.25 (s, 3 H)	1.35 (s, 9 H)	6.8–7.3 (m, 8 H)	4.83 (s, 2 H)
60772-80-7		*t*-Bu	H	CH$_3$	2.33 (s, 3 H)	1.35 (s, 9 H)	6.25–7.28 (m, 3 H)	3.21 (s, 3 H)

[a] Compound not previously reported. Satisfactory analytical data were obtained for C, H.

tonic products are also most likely formed by initial 1,2 addition to **6a** (possibly followed by a conjugate addition to ketone **9**), so that reaction of **6a** with methylmagnesium bromide appears to proceed principally by initial 1,2 addition. No evidence for any attack at carbonyl oxygen could be observed.

Reaction of **6a** with ethylmagnesium bromide gave, in addition to the conjugate addition product 3-ethyl-2,4,6-trimethylphenol, a 31% yield of a ketone, whose NMR spectrum was in excellent agreement with the structure 2,5-diethyl-2,4,6-trimethylcyclohex-3-en-1-one, which Wessely and his group assigned to the neutral product they isolated from this reaction.[4] Formation of this product can be rationalized by a mechanism (eq 2) identical with that previously suggested for formation of pentamethylbenzene by reaction of **6a** with methylmagnesium bromide, except that the ethyl Grignard gives only 1,4 rather than 1,2 addition to the cyclohexadienone **10**. The absence of 1,2 addition can readily be accounted for by steric interference with addition of ethylmagnesium bromide to the hindered carbonyl group of **10**.



10

(2)

The most interesting difference between reactions of **6a** with ethyl- and with methylmagnesium bromide is that reaction with ethylmagnesium bromide gave a 4% yield of ether **7a** (R = C$_2$H$_5$), which could be isolated and identified by comparison with the product obtained from a Williamson synthesis.

On changing from primary Grignard reagents to *sec*-butylmagnesium bromide the ether became the principal product, and the "normal" conjugate addition product was obtained in only 16% yield. No evidence for any 1,2 addition was observed, presumably owing to steric effects.

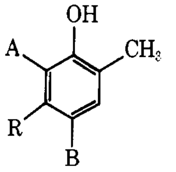
With *tert*-butylmagnesium bromide or *tert*-butyllithium, no evidence could be obtained for any conjugate addition products from reaction with **6a**. Reduction of the quinol acetate to mesitol was the major process in both reactions, but *tert*-butyl 2,4,6-trimethylphenyl ether was obtained in moderate yields. Not surprisingly, attempts to synthesize the ether by a Williamson procedure or by addition of the phenol to isobutylene failed. However, the structure of the ether was clearly established from its spectrum and from the fact that refluxing in acetic acid–sulfuric acid gave a quantitative yield of mesitol.

Reaction of benzylmagnesium chloride with **6a** gave a 91% yield of benzyl 2,4,6-trimethylphenyl ether. No 3-benzyl-2,4,6-trimethylphenol could be detected in the reaction mixture by GLC.

Reaction of quinol acetate **6b** with *sec*-butylmagnesium bromide again gave a mixture of the ether and the conjugate addition product, 3-*sec*-butyl-2,6-dimethylphenol. The somewhat higher yield of conjugate addition from this reaction compared to reaction of *sec*-butylmagnesium bromide with **6a** can readily be accounted for by the lesser steric interference with conjugate addition to **6b**. Reaction of **6b** with *tert*-butylmagnesium bromide, unlike reaction of **6a**, did give some of the conjugate addition product, 3-*tert*-butyl-2,6-dimethylphenol, in addition to the ether and the reduction product, 2,6-dimethylphenol. In this reaction, however, an additional reaction product, 4-*tert*-butyl-2,6-dimethylphenol, was obtained in trace quantities.

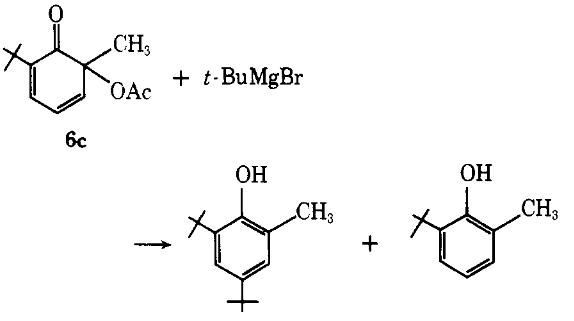
When attack at oxygen and conjugate addition were both inhibited by the presence of a *tert*-butyl group at C-2 in quinol acetate **6c**, reaction with *tert*-butylmagnesium bromide gave reduction and attack at C-4 to give phenol **11** as the only detectable processes. Reaction of **6c** with *sec*-butylmagnesium

Table III. NMR Spectra of Phenols



Registry no.		A	B	R	Chemical shift, δ, ppm ArCH$_3$	ArH	OH	R[B]
3238-38-8	[b]	CH$_3$	CH$_3$	CH$_3$	2.11 (s)	6.76 (s, 1 H)	4.45	2.11 (s)
3180-05-0	[c]	CH$_3$	CH$_3$	C$_2$H$_5$	2.15 (s, 9 H)	6.73 (s, 1 H)	4.52	1.03 (t, J = 8 Hz, 3 H) 2.55 (q, J = 8 Hz, 2 H)
61248-67-7	[a]	CH$_3$	CH$_3$	*sec*-Bu	2.20 (d, J = 1 Hz, 3 H)	6.77 (s, 1 H)	4.49	0.89 (t, J = 7 Hz, 3 H) 1.32 (d, J = 7 Hz, 3 H) 1.8 (m, 2 H)
61248-68-8	[a]	CH$_3$	H	*sec*-Bu	2.26 (s, 6 H)	6.77 (d, J = 7.5 Hz, 1 H) 7.01 (d, J = 7.5 Hz, 1 H)	4.63	0.90 (t, J = 8 Hz, 3 H) 1.26 (d, J = 7 Hz, 3 H) 1.6 (m 2 H) 2.9 (m, 1 H)
61248-69-9	[a]	CH$_3$	H	*t*-Bu	2.22 (s, 3 H) 2.42 (s, 3 H)	6.94 (s, 2 H)	4.61	1.42 (s, 9 H)
51067-63-1	[a]	*t*-Bu	*sec*-Bu	H	2.22 (s, 3 H)	6.79 (d, J = 7 Hz) 6.93 (d, J = 7 Hz)	4.56	[0.82 (t, J = 7 Hz, 3 H) 1.20 (d, J = 7 Hz, 3 H)]
616-55-7		*t*-Bu	*t*-Bu	H	2.22 (s, 3 H)	7.01 (s, 2 H)	4.53	[1.28 (s, 9 H)]

[a] Compound not previously reported. Satisfactory analytical data were obtained for C, H. [b] Mp 78–80 °C [reported [Hey, *J. Chem. Soc.*, 1581 (1931)], mp 79–81°]. [c] Mp 96–98 °C (reported[4] mp 96–97 °C).

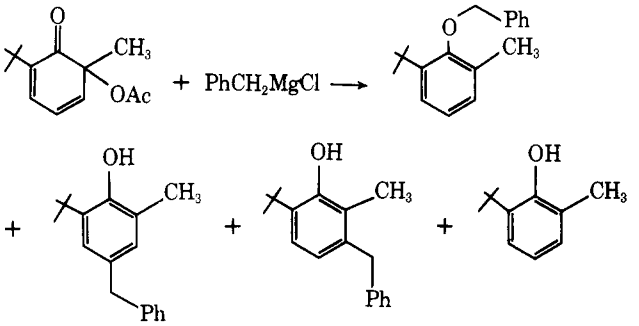


6c

11

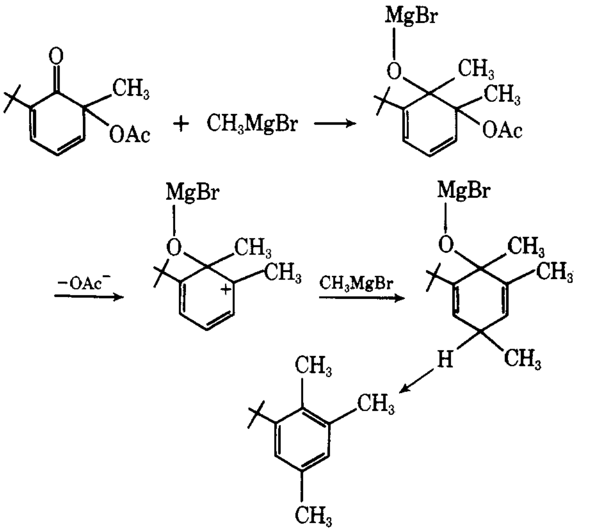
bromide gave reduction as the major process, together with a greatly reduced yield of ether. No conjugate addition was observed. However, a significant yield of 4-*sec*-butyl-2,6-dimethylphenol was obtained.

Not surprisingly, benzylmagnesium chloride, a primary Grignard, was less affected by the presence of a *tert*-butyl group at C-2. The principal product was again the ether, now accompanied by the product of attack at C-4 and by phenol **12**, resulting from conjugate addition at C-5. (Whether addition at C-5 is unique for reaction with **6c** cannot now be determined, since identical products would be obtained from reaction at C-3 or at C-5 in quinol acetates **6a** and **6b**.)



12

Reaction of **6c** with methylmagnesium bromide gave principally the reduction product, together with several ketones whose structures could not be determined and an aromatic hydrocarbon whose NMR spectrum showed the presence of a *tert*-butyl group, three methyl singlets, one of which was significantly downfield from the other two and was therefore presumably ortho to the *tert*-butyl group, and two aromatic protons showing meta coupling, one of which appeared to be ortho to the *tert*-butyl group. It was therefore assigned the structure 1-*tert*-butyl-2,3,5-trimethylbenzene. It was presumably formed by a mechanism similar to that shown in eq 3.



(3)

No evidence for either conjugate addition or ether formation could be detected in this reaction.

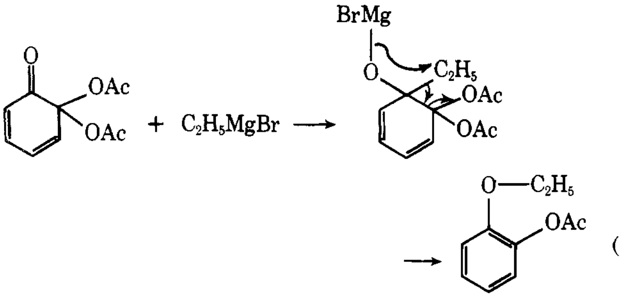
The addition of salts of copper, cobalt, and iron to the reactions was investigated, to see whether the presence of these metals favored conjugate addition or ether formation. In all cases, however, these additives simply gave marked increases in yields of reduction products. Similarly, the use of commercial "Grignard grade" magnesium resulted in an increase in reduction, but did not significantly affect the ratios of other products.

Discussion

The yields of ethers, relative to those of conjugate addition products, obtained from reactions of Grignard reagents with *o*-quinol acetates decrease sharply as the structures of the Grignard reagents are changed from benzyl or tertiary to secondary, primary, and finally methyl Grignards. With the exception of the benzyl Grignard, this sequence parallels the decrease in size of the carbanionoid reagents. Since attack at the exocyclic carbonyl oxygen should be less subject to steric hindrance by substituents at C-2 and C-6 than attack at either C-1 or C-3 of the ring, it might be argued that the effects of changes in the nature of the aliphatic Grignard reagents are principally steric in nature. Indeed, the data in Table I do suggest that the ratio of ether formation to conjugate addition is affected by the size of the substituents on the cyclohexadienone ring, although the effects do not seem to be very large.

However, steric effects cannot account for the remarkably high yields of ethers obtained from benzylmagnesium chloride, a primary Grignard reagent. Furthermore, no ether formation is observed in the reaction of methylmagnesium bromide with quinol acetate **6c.** Instead, all the products observed appear to arise from initial 1,2 addition to the carbonyl group, despite the fact that normal addition to the carbonyl in this molecule must be extremely hindered even for a methyl Grignard reagent.

It thus seems that some factor other than steric effects must be invoked to account for the high yields of ethers from tertiary and, particularly, from benzylic Grignard reagents. Does the suggestion of Wessely and Kotlan[3] that the ethyl ether from reaction of **4** with ethylmagnesium bromide is formed by initial 1,2 addition, followed by rearrangement of the ethyl group from carbon to oxygen (a sort of reverse Wittig rearrangement, as in eq 4), help account for these facts? This mechanism requires that the ratio of 1,2 to 1,4 addition of Grignard reagents to unsaturated ketones should increase markedly as the structure of the Grignard changes from primary to secondary and then to tertiary. The available evidence suggests that the opposite is true—that the ratio of 1,2 to 1,4 addition *decreases* as the degree of substitution at the carbanionoid center increases.[9] This is supported by the data in Table I, since ethylmagnesium bromide gives a significantly higher yield of the conjugate addition product than does methylmagnesium bromide. Furthermore, this mechanism would require that *tert*-butylmagnesium bromide should add readily to the very hindered carbonyl group of **6b,** in preference to the relatively unhindered β carbon of the double bond, and that the *tert*-butyl Grignard add to the carbonyl of **6b,** and the *sec*-butyl Grignard add to the carbonyl of **6c,** within a total reaction time of at most 30 s. (The actual reaction period seems to be significantly lower than that, since the yellow color of the quinol acetates has disappeared by the time addition of the Grignard is complete—some 5–6 s.) Finally, this mechanism offers no explanation for attack of the Grignard reagents at C-4 of the quinol acetate. While this reaction may proceed by a mechanism which is different from that for ether formation, it would be satisfying to be able to account for both anomalous reactions by a single mechanism, rather than require a fundamentally different, ad hoc, explanation for each.



(4)

We suggest that ether formation proceeds by initial electron transfer from the Grignard or lithium reagents to the quinol acetates—a reaction which has ample precedent in other reactions of Grignard reagents with ketones.[10] The fact that the stability of alkyl radicals increases in the order primary < secondary < tertiary is well known, as is the greater reactivity of tertiary and secondary Grignard and lithium reagents, compared to the primary reagents.[11] (Insofar as organometallic reagents can be considered to resemble carbanions, this order of reactivity follows directly from the greater stability of the less substituted carbanions.[12]) The ease of electron donation by Grignard and lithium reagents should therefore be in the order tertiary > secondary > primary > methyl.

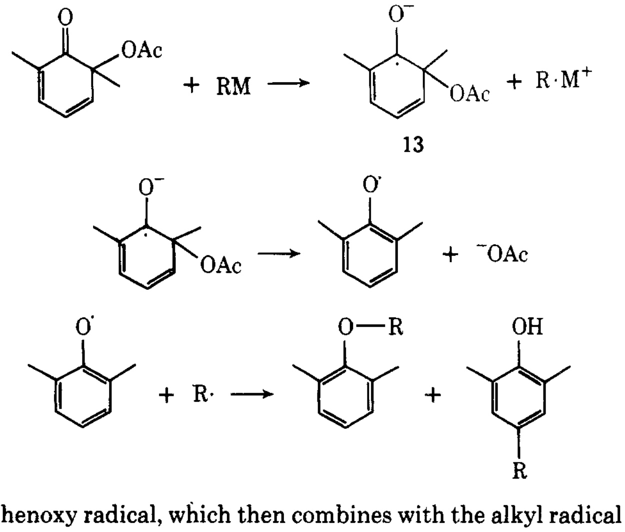
It seems probable that benzyl Grignard reagents are similarly more easily oxidized to free radicals than are other primary Grignards. The benzyl radical has been reported to have a lower electron affinity than the methyl radical (18.4 kcal/mol for the benzyl radical, compared to 24.8 kcal/mol for the methyl radical).[13,14] This is presumably due to the fact that placing a second electron into the p orbital of a benzyl radical should be less exothermic than placing it into the orbital of an alkyl radical, which would rehybridize to form the more stable hybrid anion.

Unfortunately, there seems to be no available evidence which would allow comparison of the electron affinities of benzyl radicals with those of alkyl radicals other than the methyl radical. However, it does not seem unreasonable to assume that the benzyl anion is among the more easily oxidized of hydrocarbon anions, in view of the relatively large (ca. 35%) reported difference in electron affinities between benzyl and methyl radicals.

On this assumption, the expected order of ease of electron transfer by Grignard and lithium reagents parallels the relative yields of ethers obtained from them in reactions with *o*-quinol acetates. The benzyl and tertiary Grignards, being the best electron donors, give the highest yields of ethers, while the methyl Grignard gives the lowest yield.

The hypothesis that ether formation proceeds by electron transfer explains why phenylmagnesium bromide and phenyllithium give no ethers, even from reaction with **4**,[3] since the phenyl radical has an exceptionally high electron affinity.[13]

We can thus write a simple mechanism for formation of ethers from reaction of *o*-quinol acetates with Grignard reagents. Initial electron transfer to give the ketyl **13** and an alkyl radical is followed by loss of an acetate anion to give a phenoxy radical, which then combines with the alkyl radical to give the ether.

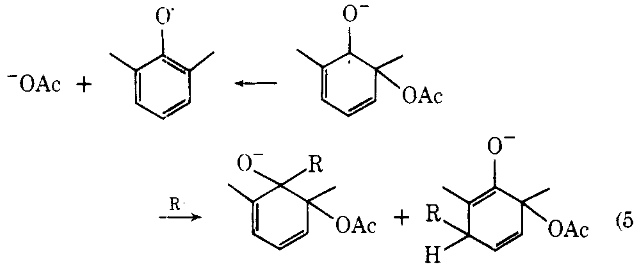


13

This mechanism has the virtue of providing an obvious mechanism for formation of *p*-alkylphenols from the reactions of quinol acetates with Grignard reagents.

The hypothesis that there is a close relationship between the mechanisms for formation of ethers and of *p*-alkylphenols is supported by the fact that reaction of methylmagnesium bromide with **6c** gives no trace of either the ether or of 2,4-dimethyl-6-*tert*-butylphenol, even though addition to the carbonyl must be highly hindered.

We have not attempted to suggest mechanisms for normal or conjugate additions to the carbonyl groups of *o*-quinol acetates. Perhaps the simplest hypothesis is that both 1,2 and 1,4 additions proceed by processes independent of electron transfer. However, it is conceivable that electron transfer is the initial step in all the reactions, but that combination of the more reactive primary radicals with the ketyl is very much faster than loss of an acetate anion (eq 5). Attempts to distinguish between these possibilities are now in progress.



(5)

Experimental Section

General. NMR spectra were taken on Perkin-Elmer R12A or Varian A-60 spectrometers in deuteriochloroform solutions, using Me$_4$Si as an internal standard. ir spectra were taken on a Perkin-Elmer 237B spectrometer. Mass spectra were taken on a Hitachi Perkin-Elmer RMU-6L instrument. Melting points were taken on a Mel-Temp apparatus, and are uncorrected. Microanalyses were carried out by the University of Massachusetts Microanalytical Laboratory, Amherst, Mass. GLC analyses were carried out on a Varian Model 202c gas chromatograph, using a 6 ft × 0.25 in. column packed with 5% SE-30 on Chromosorb W. Preparative runs were carried out on a 6 ft × 0.375 in. column with the same packing.

***o*-Quinol Acetates. 6-Acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one (6a),** mp 87.5–89 °C (reported[16] mp 84 °C), and **6-acetoxy-2,4-dimethylcyclohexa-2,4-dien-1-one (6b),** mp 36–38 °C (reported[17] mp 36 °C), were prepared as described in the literature.

6-Acetoxy-2-*tert*-butyl-6-methylcyclohexa-2,4-dien-1-one (6c). A suspension of lead tetraacetate (45 g, ca. 90% pure, 0.09 mol) in 50 ml of chloroform was cooled in ice. A solution of 2-*tert*-butyl-6-methylphenol (16.4 g, 0.10 mol) in 20 ml of chloroform was added slowly while the mixture was vigorously stirred, at a rate such that the temperature of the reaction did not give rise above 25 °C. After completion of the addition, the reaction mixture was allowed to stand at room temperature for 1 h and the yellow precipitate filtered off. Water was added to the filtrate, and the precipitated lead dioxide filtered off. The layers were separated, the organic layer dried over magnesium sulfate, and the solvent evaporated to give 16.9 g (0.76 mol, 85%) of a reddish oil which crystallized on standing in the refrigerator. Recrystallization from ether (−20 °C) gave yellow needles, mp 77–79 °C. Their IR spectrum showed a carbonyl peak at 1670 cm^{-1}. The NMR spectrum had peaks at δ 1.23 (s, 9 H), 1.37 (s, 3 H), 2.09 (s, 3 H), 6.19 (s) and 6.27 (d, J = 1 Hz) (totaling 2 H for the two signals), and 6.81 (dd, J = 4, 3 Hz, 1 H). Anal. Calcd for C$_{13}$H$_{18}$O$_3$: C, 72.2; H, 5.6. Found: C, 72.2; H, 5.7.

Preparation of Grignard Reagents. Grignard reagent solutions (ca. 1 M) were prepared by slowly dropping a solution of 0.050 mol of the alkyl halide in 25 ml of anhydrous ether into a flask containing 25 ml of ether and 1.2 g (0.050 mol) of magnesium. The mixture was stirred continuously and kept under nitrogen until reaction was apparently complete, and then refluxed for an additional 15 min. The mixture was then filtered under nitrogen pressure through a sintered glass filter, and stored under nitrogen for no longer than 3 days.

When not otherwise specified, the Grignard reagent was prepared using magnesium chips of >99.99% purity (grade m4N) obtained from the Ventron Corp. Reactions indicated in Table I as carried out with "Grignard grade magnesium" employed magnesium turnings obtained from the General Chemical Division of the Allied Chemical Co.

***tert*-Butyllithium.** Solutions of *tert*-butyllithium in *n*-pentane (2 M) were obtained from the Ventron Corp.

Reactions of Grignard Reagents with *o*-Quinol Acetates. In the general procedure, a ca. 0.50-g (2.1–2.7 mmol) sample of *o*-quinol acetate was dissolved in 15 ml of anhydrous ether under a nitrogen atmosphere. The Grignard solution (15 ml, ca. 15 mmol) was added rapidly from an equalizing addition funnel. The reaction mixture was stirred for 0.5 h (except where otherwise indicated) and a dilute solution of ammonium chloride in water was added. The ether layer was separated, and the aqueous layer was extracted with ether. The combined ether layers were washed with water and dried over magnesium sulfate, and the solvent was evaporated under vacuum. The product was weighed and analyzed by GLC, and then dissolved in hexane and extracted twice with Claisen alkali. The base-insoluble fraction was washed with water and dried over magnesium sulfate, and the solvent was evaporated. The base-soluble fraction was acidified with dilute hydrochloric acid and extracted twice with methylene chloride, the methylene chloride solution was washed with water and dried over magnesium sulfate, and the solvent was evaporated. Both base-soluble and base-insoluble products were weighed and analyzed by GLC. Corrections for differences in thermal conductivity of the products were made by analyzing standard mixtures of the products.

In synthetic runs, all products were isolated by preparative GLC. Reaction of *tert*-butyllithium with quinol acetate **6a** was carried out in precisely the same manner as reactions with Grignard reagents, except that a 10-ml aliquot of the lithium reagent was employed.

Reaction of Quinol Acetate 6a with Methylmagnesium Bromide. The base-insoluble fraction contained pentamethylbenzene, identified by comparison with a sample obtained from the Aldrich Chemical Co., and a ketone with IR peaks at 1670 and 1720 cm^{-1}. Its NMR spectrum had peaks at δ 1.08 (s, 2.3 H), 2.20 (s, 3 H), 2.6 (m, 8 H), 2.85 (dd, J = 6, 1 Hz, 4 H), 3.35 (m, 0.8 H), 4.45 (m, 1 H), 5.25 (bs, 0.7 H), 5.85 (bs, 1 H), 6.35 (bs, 1 H). Its mass spectrum showed peaks at *m/e* 166 (M$^+$) and 153.

Reaction of 6a with Ethylmagnesium Bromide. The base-insoluble fraction contained a ketone assigned the structure 2,5-diethyl-2,4,6-trimethylcyclohex-3-en-1-one.[3] Its NMR spectrum had peaks at δ 1.25 and 1.28 (triplets, J ca. 7 Hz, totaling 6 H), a singlet and a doublet (J = 7 Hz) at 1.04, totaling 6 H, 1.80 (s, 3 H), 2.15–2.45 (m, 1 H, proton at C-5), 2.65–3.15 (m, 1 H, proton at C-6), 5.31 (bs, 1 H). Its IR spectrum had a carbonyl peak at 1720 cm^{-1}.

Reaction of 6c with Benzylmagnesium Chloride. The alkali-soluble fraction contained 3-benzyl-5-*tert*-butyl-2-methylphenol and 4-benzyl-2-*tert*-butyl-6-methylphenol, which were identified by comparison of their IR and NMR spectra and GLC retention times with those of samples previously prepared.[18]

Reaction of 6c with Methylmagnesium Bromide. The alkali-insoluble fraction contained three components, with retention times (at 120 °C) of 4.0, 5.0, and 6.4 min. The component with the highest retention time was assigned the structure 1-*tert*-butyl-2,3,5-trimethylbenzene. Its NMR spectrum had peaks at δ 1.40 (s, 9 H), 2.23 (s, 3 H), 2.27 (s, 3 H), 2.35 (s, 3 H), 6.91 (d, J = 2 Hz, 1 H), and 7.08 (d, J = 2 Hz, 1 H). Its mass spectrum had peaks at *m/e* 176 (M$^+$) and 161. Anal. Calcd for C$_{13}$H$_{20}$: C, 88.6; H, 11.4. Found: C, 88.3; H, 11.5.

The component with intermediate retention time had a peak in its IR spectrum at 1675 cm^{-1}. Its NMR spectrum had peaks at δ 1.04 (s, 6 H), 1.24 (s, 9 H), 1.33 (s, 3 H), 2.22 (m, 1 H), and 5.60 (m, 2 H). Its mass spectrum had a peak at *m/e* 192 (M$^+$). Anal. Found: C, 92.4; H, 10.2.

The peak with lowest retention time could not be completely separated from the adjacent peak. Its IR spectrum had a peak at 1730 cm^{-1}, in addition to a smaller peak at 1675 cm^{-1}.

Synthesis of Alkyl Aryl Ethers. Potassium *tert*-butoxide (6.55 g, 0.05 mol) was dissolved in 30 ml of dimethyl sulfoxide. The appropriate phenol (0.05 mol) was added to the solution, which was shaken until a homogeneous solution was obtained. The alkyl halide (0.05 mol) was added, and the solution allowed to stand at room temperature for 15 min. Water was then added, and the mixture extracted with pentane. The organic layer was extracted with Claisen alkali, washed with water, and dried over magnesium sulfate. The solvent was evaporated to give the ether, which was essentially pure. Analytical samples were purified by preparative GLC.

Acknowledgment. I thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, for a grant in partial support of this work.

Registry No.—2-*tert*-Butyl-6-methylphenol, 36078-59-8; 2,2,4,5,6-pentamethylcyclohex-3-en-1-one, 61248-70-2; 2,5-diethyl-

2,4,6-trimethylcyclohex-3-en-1-one, 61248-71-3; 1-*tert*-butyl-2,3,5-trimethylbenzene, 61248-72-4.

References and Notes

(1) Reactions of Cyclohexadienones. 37. For part 36, see B. Miller and M. R. Saidi, *J. Am. Chem. Soc.*, **98**, 2227 (1976).

(2) F. Wessely, L. Holzer, and H. Vilcsek, *Monatsh. Chem.*, **83**, 1253 (1952); **84**, 655 (1953).

(3) F. Wessely and J. Kotlan, *Monatsh. Chem.*, **84**, 124 (1953).

(4) F. Wessely, L. Holzer, F. Langer, E. Schinzel, and H. Vilcsek, *Monatsh. Chem.*, **86**, 831 (1955).

(5) F. Wessely and E. Zbiral, *Justus Liebigs Ann. Chem.*, **605**, 98 (1957).

(6) F. Wessely and J. Leitich, *Monatsh. Chem.*, **92**, 1004 (1961).

(7) E.g., J. Borgulya, R. Madeja, P. Fahrni, H.-J. Hansen, H. Schmid, and R. Barner, *Helv. Chim. Acta*, **56**, 14 (1973).

(8) B. Miller, *J. Am. Chem. Soc.*, **95**, 8458 (1973).

(9) P. G. Stevens, *J. Am. Chem. Soc.*, **56**, 1425 (1934); **57**, 1112 (1935); F. C. Whitmore and G. W. Pedlow, Jr., *ibid.*, **63**, 758 (1941); E. R. Alexander and G. R. Coraor, *ibid.*, **73**, 2721 (1951); H. O. House, D. D. Traficante, and R. A. Evans, *J. Org. Chem.*, **28**, 348 (1963).

(10) See E. C. Ashby, J. Laemmle, and H. M. Neumann, *Acc. Chem. Res.*, **7**, 272 (1974), for leading references.

(11) E.g., P. D. Bartlett, S. Friedman, and M. Stiles, *J. Am. Chem. Soc.*, **75**, 1771 (1953).

(12) D. J. Cram, "Fundamentals of Carbanion Chemistry", Academic Press, New York, N.Y., 1965.

(13) A. F. Gaines and F. M. Page, *Int. J. Mass. Spectrom. Ion Phys.*, **1**, 315 (1968); *Trans. Faraday Soc.*, **59**, 1266 (1963).

(14) J. H. Richardson, L. M. Stephenson, and J. I. Brauman, *J. Chem. Phys.*, **63**, 74 (1975), similarly report an upper limit of 20.4 ± 1.5 kcal/mol for the electron affinity of the benzyl radical.

(15) D. K. Bohme and L. B. Young, *Can. J. Chem.*, **49**, 2918 (1971).

(16) F. Wessely and F. Sinwel, *Monatsh. Chem.*, **81**, 1055 (1950).

(17) H. Budzciewicz, G. Schmidt, P. Stockhammer, and F. Wessely, *Monatsh. Chem.*, **90**, 609 (1959).

(18) B. Miller, *J. Am. Chem. Soc.*, **92**, 6252 (1970).

Substituent Effects on Reactions of Benzylmagnesium Chlorides with *o*-Quinol Acetates[1]

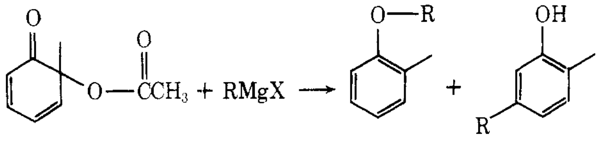
Bernard Miller

Department of Chemistry, University of Massachusetts, Amherst, Massachusetts 01002

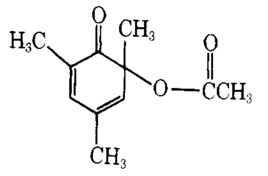
Received July 29, 1976

Reaction of 6-acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one with a series of meta- and para-substituted benzylmagnesium chlorides gave decreasing yields of benzyl aryl ethers and increasing yields of *m*-benzylphenols as the electron-withdrawing powers of the substituents increased. Reaction of 6-acetoxy-2,4-dimethylcyclohexa-2,4-dien-1-one with the same Grignard reagents yielded *p*-benzylphenols in addition to aryl benzyl ethers and *m*-benzylpherols. While the ratio of ethers to *m*-benzylphenols increased sharply when more electron-donating substituents were present on the Grignard reagents, the ratio of ethers to *p*-benzylphenols remained almost constant. These results support a mechanism for formation of ethers and of *p*-benzylphenols involving initial electron transfer from the Grignard to the ketone to form phenoxy radicals, and combination of phenoxy and benzyl radicals to form the products.

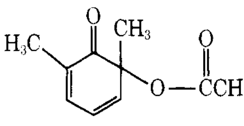
Grignard and lithium reagents normally react with α,β-unsaturated ketones by addition to the carbon atoms of the carbonyl groups or by conjugate addition to the double bonds. In the preceding paper, however, it was shown that Grignard and lithium reagents react with *o*-quinol acetates (6-acetoxycyclohexa-2,4-dien-1-ones) to give aromatic ethers resulting from attack at the carbonyl oxygen atoms, as well as the "normal" 1,4 and (for primary Grignard reagents) 1,2 addition to the unsaturated carbonyl systems.[2] While primary Grignard reagents gave only traces of ethers, tertiary and benzylic Grignards yielded ethers as the primary or only addition products. Secondary Grignards gave significant yields of the products of attack at both oxygen and carbon. The relative yields of ethers to those of the "normal" addition products appeared to roughly parallel the expected order of electron-donating abilities of the organometallic reagents. However, the relative importance of the sizes of the carbanionoid reagents and of their electron-donating abilities were difficult to evaluate, since changes in these factors parallel each other for simple alkyl Grignard reagents.[1]



In order to determine whether Grignard attack at oxygen atoms of *o*-quinol acetates is indeed a function of the electron-donating abilities of the Grignards, rather than their steric requirements, we have studied the products obtained from reaction of 6-acetoxy-2,4,6-trimethylcyclohexa-2,4-dien-1-one (**1**) and 6-acetoxy-2,6-dimethylcyclohexa-2,4-dien-1-one (**2**) with benzylic Grignard reagents bearing substituents in the meta and para positions.



1



2

Results

A solution of **1** (ca. 2 mmol) in 10 ml of ether was added rapidly to 10 mmol of the Grignard reagent in 10 ml of ether, and the products were analyzed by GLC. Each reaction was carried out two times, using a freshly prepared Grignard solution for each run. The results of these reactions are summarized in Table I.

Benzyl 2,4,6-trimethylphenyl ethers (**3**), which were readily identified by their NMR spectra and by comparison with synthetic samples, were obtained as major products from each reaction. However, neither reaction with benzylmagnesium chloride nor with 4-methylbenzylmagnesium chloride gave a detectable yield of a *m*-benzylphenol. The results obtained with benzylmagnesium chloride agree with those reported in the preceding paper,[2] which differ from those reported here only in that the Grignard reagent was added to the quinol acetate, rather than vice versa.