

Reactions of Halogenated *o*-Quinol Acetates with Isopropylmagnesium Bromide and Di-isopropylmagnesium. Mechanisms for Formation of Ethers, Reduction Products, and *m*-Isopropylphenols

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A mechanism is proposed to account for the nature and the variations in yields of products from reactions of Grignard reagents with halogenated *o*-quinol acetates.

The mechanisms by which carbanionoid reagents react with unsaturated carbonyl compounds are of great current interest.¹ The factors that determine whether polar or single electron transfer (SET) processes will occur, or what reactions may follow initial SET, are far from well defined.

In earlier work from this laboratory it was demonstrated that formation of aryl ethers (E) and reduction products (R) from reactions of Grignard reagents with *o*-quinol acetates such as (**1a**) and (**1b**) proceeds by SET processes,^{2,3} in which the principal electron donors are dialkylmagnesium compounds, rather than the Grignard reagents themselves.² Formation of ethers was ascribed to combination of alkyl and phenoxy radicals, but details of the mechanism leading to

formation of reduction products were not established. In contrast to ether formation and reduction, *m*-alkylphenols (P) were formed principally, if not entirely, by polar mechanisms rather than SET.²

We have now found that *m*-alkylphenols are formed by SET processes in reactions of Grignard reagents with *o*-quinol acetates bearing halogen substituents. As a result of these studies, we can now specify the manner in which the radical anions formed by initial SET are transformed into the final reaction products.

Solutions of isopropylmagnesium bromide (0.5 M, prepared from triply sublimed magnesium) in ether were treated with solutions of the mono- and di-halogenated *o*-quinol acetates

Table 1. Reactions of *o*-quinol acetates with 0.5 M isopropylmagnesium bromide

<i>o</i> -Quinol acetate	Reaction products (mol %)			mol % (E) mol % (R)
	P	E	R	
(1b), A=B=Me ^a	23.5 ± 0.6	40.7 ± 0.4	34.4 ± 0.5	1.18
(1c), A=Me, B=Cl	12.5 ± 1.0	43.5 ± 0.7	43.9 ± 0.9	0.99
(1d), A=Me, B=Br	10.2 ± 0.2	42.1 ± 1.1	47.9 ± 0.8	0.88
(1e), A=Br, B=Me	14.8 ± 1.1	32.2 ± 0.3	53.1 ± 1.0	0.61
(1f), A=B=Cl	25.8 ± 0.8	11.1 ± 0.4	63.5 ± 0.5	0.18
(1g), A=B=Br	19.9 ± 0.8	8.0 ± 0.1	72.3 ± 0.4	0.11
(1h), A=B=Me ^b	0	27.7 ± 3.6	72.4 ± 3.7	0.38

^a Data from ref. 2b. ^b (**1h**) is substituted with bromine atoms at C-3 and C-5.

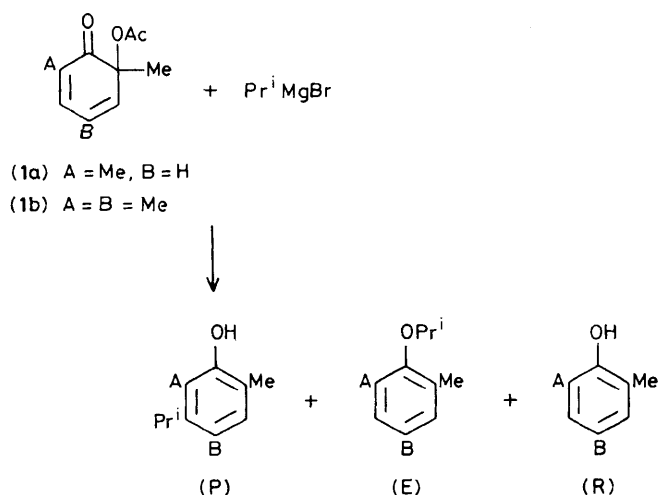


Table 2. Reactions of *o*-quinol acetates with di-isopropylmagnesium and dilute (0.05 M) isopropylmagnesium bromide solutions.

<i>o</i> -Quinol acetate	Reagent	Reaction products (mol %)		
		(P)	(E)	(R)
(1b)	Pr ₂ Mg ^{a,b}	2.18 ± 1.1	49.5 ± 1	49.4 ± 1
	Pr ⁱ MgBr ^b	6.1	54.0	38.8
(1c)	Pr ₂ Mg ^a	10.5	41.5	48.1
	Pr ⁱ MgBr	13.0	43.1	44.0
(1d)	Pr ₂ Mg ^a	9.1	37.3	53.6
	Pr ⁱ MgBr	12.1	39.9	48.0
(1g)	Pr ₂ Mg ^a	16.3	6.3	77.4
	Pr ⁱ MgBr	19.8	8.3	71.9

^a Solvent was diethyl ether–dioxane (70:30 v/v). ^b Ref. 2.

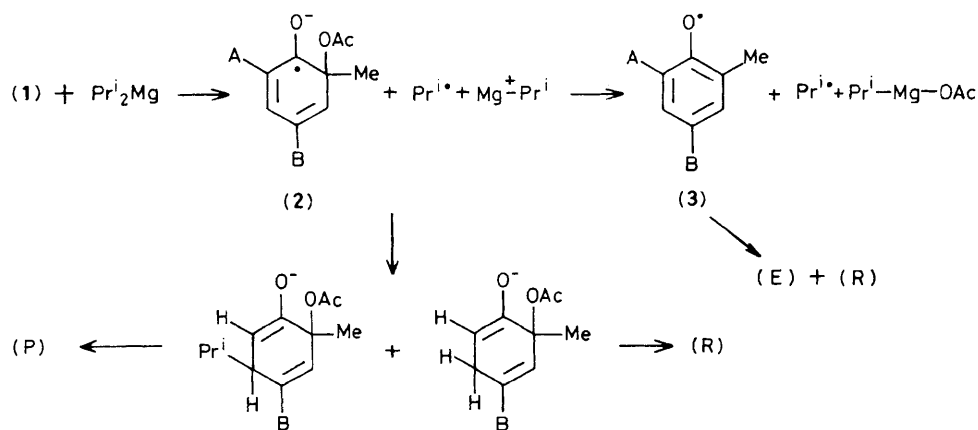
(1c)—(1h). All reactions proceeded cleanly to give three products, which were isolated and identified as (P), (E), and (R). No evidence was observed for the formation of isomeric alkylphenols resulting from attack of the Grignard reagent at C-5 of (1e)—(1g).

Table 1 shows that yields of (R) increase steadily with increasing numbers of halogen substituents, or with substitution of bromine for chlorine, while yields of (P) decrease sharply on halogen substitution, but then increase on disubstitution. [Reaction with the 3,5-dibrominated ketone (1h) is an exception.] Because of the decrease in yields of (P), the yields of (E) do not appear to be significantly changed by mono-halogenosubstitution. In comparison with yields of (R), however, yields of (E) decrease markedly with increasing halogen substitution.

Interpretation of the rather confusing data in Table 1 is aided by Table 2, which shows that nearly unchanged product mixtures are obtained from reactions of (1c), (1d), or (1g) with concentrated PrⁱMgBr or with Pr₂Mg or dilute PrⁱMgBr. In contrast, as has been previously observed,² yields of (P) from reaction with (1b) drop sharply on dilution of the Grignard solution, and drop even further on substitution of Pr₂Mg for PrⁱMgBr.

Since Pr₂Mg (and dilute solutions of PrⁱMgBr, which contain relatively high proportions of Pr₂Mg) are much better electron donors than concentrated solutions of PrⁱMgBr,² the invariance of product yields from reactions of halogenated *o*-quinol acetates on changing the organometallic reagent indicates that all products from reactions of these ketones are formed *via* SET. The variations in product ratios with degree (and type) of halogen substitution can be accounted for by a mechanism in which (R) is formed by hydrogen transfer to either the radical anion (2) or the phenoxyl radical (3), while (P) is formed solely from (2) and (E) solely from (3) (Scheme 1).

According to Scheme 1, the relative yields of the three products should depend, to a large extent, on the rate at which



Scheme 1

Table 3. Reactions of *o*-quinol acetates with 0.5 M hexadeuterioisopropylmagnesium bromide.

<i>o</i> -Quinol acetate	Reaction products (mol %)			%D at C-3 of (R)
	(R)	(P)	(E)	
(1b)	19.3	25.2	55.5	1 ± 3
(1d)	28.5	22.4	49.7	13 ± 4 ^a
(1g)	43.3	34.4	20.4	22 ± 2

^a %D at C-3 = 2[% (C-3 + C-5)].

(2) loses acetate anion to form (3). Polyhalogen substitution (or substitution by bromine rather than chlorine) should increase the stability of (2), and thus increase the relative yields of (P) and of (R) compared to (E), in agreement with the data in Table 1.

To test this mechanistic scheme, we studied the reactions of *o*-quinol acetates (1b), (1d), and (1g) with 1,1,1,3,3,3-hexadeuterioisopropylmagnesium bromide. In agreement with predictions from the proposed mechanism the yield of (R) from each reaction decreased when the deuteriated reagent was employed and the percentage of deuterium incorporated at C-3 increased with increasing bromine substitution, as shown in Table 3.

Scheme 1, therefore, appears to account completely for the products of reactions of halogenated *o*-quinol acetates with isopropylmagnesium bromide.

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