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Quinol Intermediates in the Reaction of π-Allylnickel Bromides with Quinones

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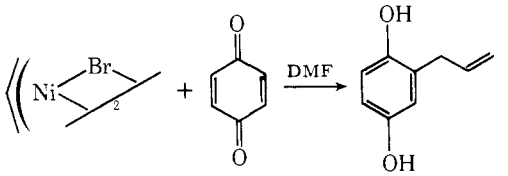
Abstract: The reaction of π-allylnickel bromide complexes with quinones was shown to proceed through relatively unstable allylquinol intermediates, which were isolated and characterized for the first time. Rearrangements of these allylquinols under a variety of conditions were studied, and their role in the production of allylquinones from the above reactions was elucidated.

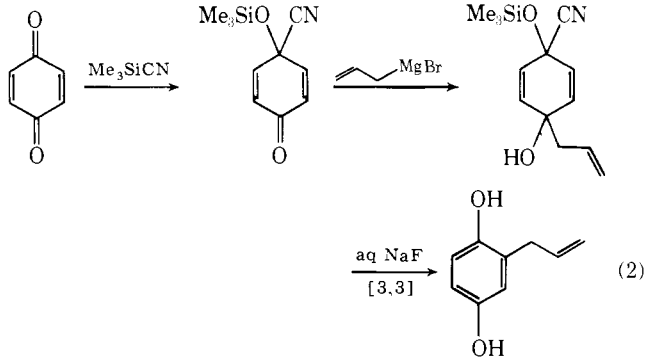
Introduction

The reaction of π-allylnickel bromide complexes with quinones produces allylhydroquinones in fair yield (eq 1).[1] With



(1)

unsymmetrical quinones under standardized reaction and isolation conditions high regioselectivity is observed, the allyl group being introduced at the ring site of highest spin density in the corresponding quinone radical anion.[2] However, alteration of reaction and isolation procedure leads to changes in the site of allylation, allowing a variety of differently substituted allylquinones and enediones to be prepared.[3] An alternate approach to allylquinones involving a protection, allylation, deprotection, and rearrangement sequence has recently been developed (eq 2).[4] Although allylquinols were never detected,



(2)

they were implicated as intermediates and were thought to proceed to products via a facile [3,3] sigmatropic rearrangement. Since π-allylnickel halide complexes are known to react with ketones to produce homoallylic alcohols,[5] and since the products from eq 1 and 2 are identical, evidence for the intermediacy of allylquinols in the reaction of eq 1 was sought.

Results and Discussion

Isolation and Characterization of Allylquinols from the Reactions of π-Allylnickel Bromide Complexes with Quinones. Since the standard reaction and isolation procedures for the reaction of π-allylnickel bromides with quinones involve stirring the reaction mixture for 12 h at 22 °C followed by partitioning between ether and 1.2 N HCl, quinols, if initially formed, would probably not survive these conditions. Hence the reactions were run under milder conditions (−10 to 0 °C) and isolated using a neutral partition between water and ether to facilitate detection of quinols. While no quinols were detectable in the reactions of simple alkyl quinones, quinols were *isolable* from reactions involving naphthoquinone, 2-methylnaphthoquinone, and 2,3-dimethoxy-5-methylbenzoquinone. This is the first time, to our knowledge, that allylquinols have been isolated and characterized. Once removed from the reaction mixture and purified these quinols were relatively stable, particularly those of dimethoxymethylbenzoquinone. Thus, treatment of this quinone with π-2-methylallylnickel bromide in DMF at −60 °C followed by slow warming to −10 °C, partitioning of the cold reaction mixture between ether and saturated NaCl solution, and separation by preparative layer chromatography gave both possible quinols (**1** and **2**) as well as rearrangement products thereof (eq 3). Quinols **1** and **2** had characteristic NMR spectra with well-separated signals for the two different OMe groups. They were differentiated by the relative chemical shifts of the ring methyl and hydrogen signals, δ 1.84 and 6.41, respectively, for **1** and δ 2.06 and 5.93 for **2**. In a similar fashion quinols **5–8** were prepared. All of these were relatively stable once purified, but underwent rapid rearrangement at 22 °C in the reaction mixture.

Quinol **1** was also prepared by the method described in eq 2. The protected quinol underwent deprotection *without* subsequent rearrangement upon treatment with aqueous NaF. The quinol of 2,5-dimethylbenzoquinone, prepared by the same route, was detected by NMR during the deprotection step but proved too unstable to isolate. Quinols **5** and **6** could not be prepared by this method since coupling of the allyl Grignard always occurred at the tertiary carbon of the allyl system,[4] in contrast to the primary coupling observed with π-allylnickel bromide complexes. Quinol **2** was also unavailable by eq 2 because of the regiospecificity of the protection reaction.

Behavior of the Pure Quinols. Isolation of substantial quantities of quinols from the above π-allylnickel bromide–quinone reactions suggests that quinols play an important role. To clarify this role, the behavior of the pure quinols was investigated first. Upon standing for periods (~2 weeks) at room

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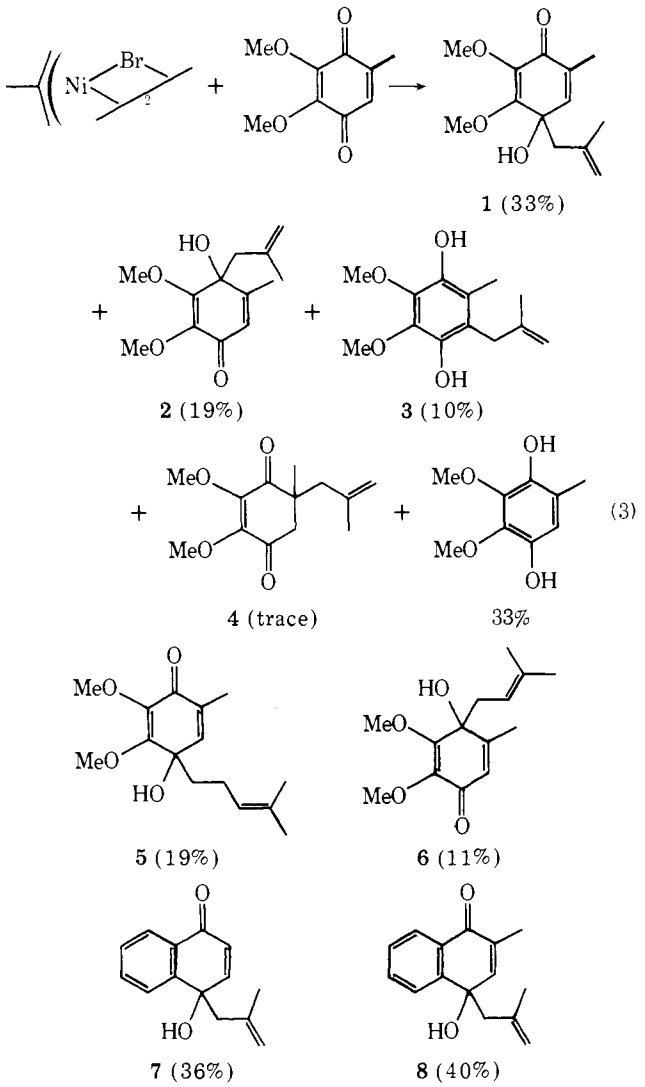
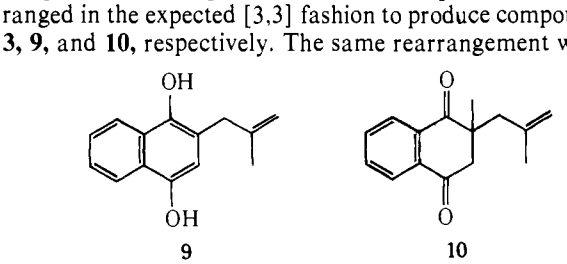
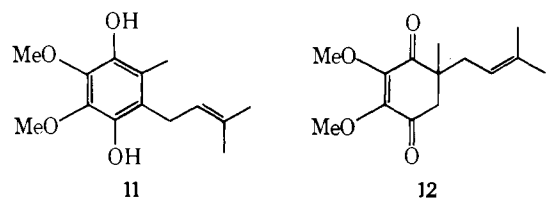
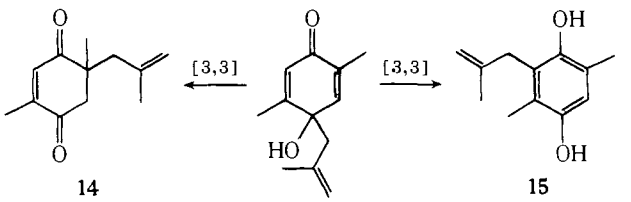


temperature, neat quinols **1, 2, 7,** and **8** quantitatively rearranged in the expected [3,3] fashion to produce compounds **4, 3, 9,** and **10,** respectively. The same rearrangement was observed by refluxing these quinols in CCl_4 for 16 h. Quinols **5** and **6** behaved in a significantly different fashion. A [3,3] rearrangement of either of these quinols would produce molecules with rather severe steric interactions. To circumvent this possibility quinols **5** and **6** undergo clean [1,2] rearrangement upon standing to produce **11** and **12,** respectively. Heating quinol **5** in CCl_4 led to the same [1,2] rearrangement in 45% yield, accompanied by 30% fragmentation (loss of allyl group to give unsubstituted hydroquinone).[6] In contrast, quinol **6** rearranged to **11** (in an apparent [1,3] rearrangement) in 11% yield, and also produced 23% fragmentation and a substantial amount of unidentified material. This behavior is in direct contrast to that of the quinols prepared by the Me_3SiCN protection route (eq 2). Use of the isoprenyl Grignard reagent results in coupling at the tertiary allylic terminus. These hindered quinols rearrange [3,3] spontaneously under the conditions required to remove the protecting group.[4] These [1,2] and [1,3] rearrangements may result from catalysis by adventitious traces of acid.



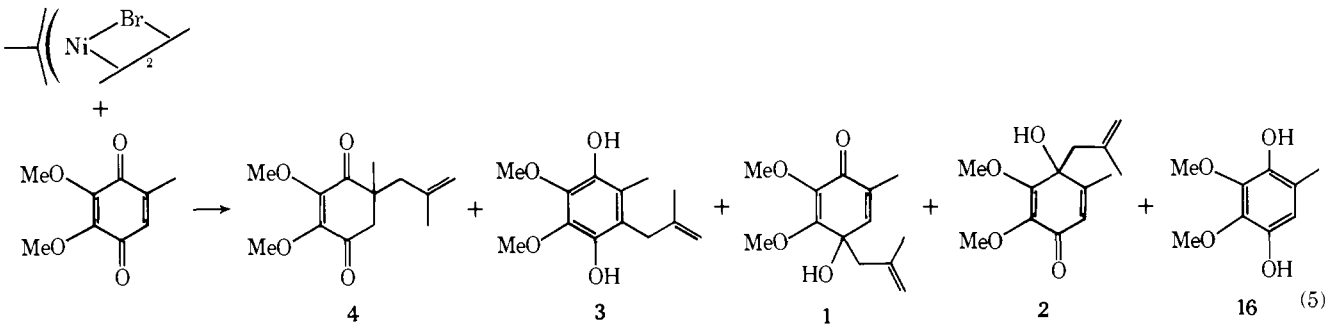


The behavior of the allylquinol from 2,5-dimethylbenzoquinone was of particular interest. It is capable of rearranging in two different ways, to produce either enedione **14** or allylhydroquinone **15** (eq 4). The reaction of π-2- methallylnickel bromide with 2,5-dimethylbenzoquinone produced **14** exclusively. (Quinol **13** could not be detected in this reaction under the mildest isolation conditions studied.) Treatment of the same quinone with Me_3SiCN, methallylmagnesium bromide, and finally aqueous NaF also produced **14** exclusively. Again **13** could not be isolated from this reaction. However, it was detected by NMR (signal at δ 6.00, H α to C=O in **13**) during the deprotection. Since this reaction must proceed via the quinol, and since the product formed is identical with that obtained from the nickel reaction, it is likely that both reactions involve quinol **13** as an intermediate. Why **14** is formed exclusively is not clear. The fact that rearrangement of **13** to **15** would involve eclipsing of a ring methyl group with the side chain methyl group in the pseudochair transition state accepted for [3,3] rearrangements is a possible factor. Alternatively, a homolytic rearrangement involving radical intermediates and migration to the site of highest spin density would also account for the observed product (vide infra).



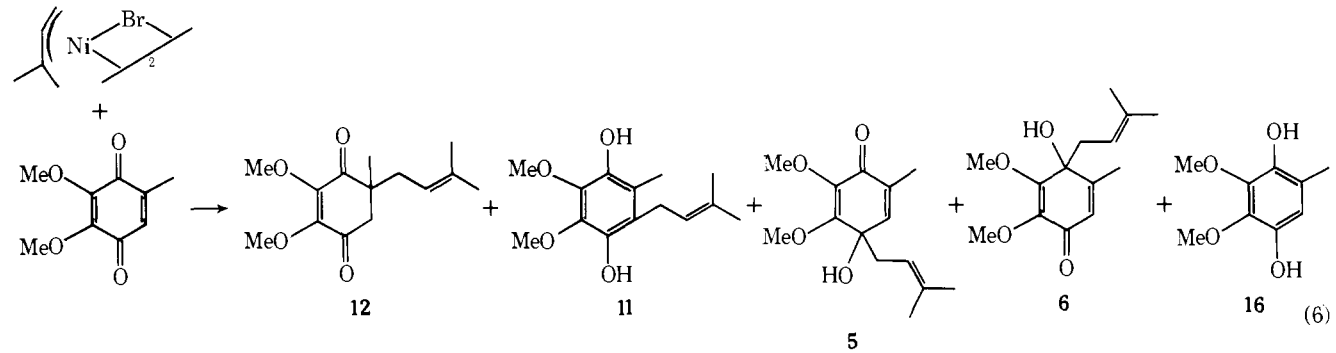
Since the π-allylnickel halide–quinone reaction mixtures were being exposed to acidic conditions during normal isolation,[3] and since the NaF cleavage of protected quinols generated NaCN in solution, the behavior of quinols **1, 2, 5,** and **6** under these conditions was examined next. Dissolution of quinol **1** in DMF followed immediately by partitioning between 1.2 N HCl and ether led to enedione **4** (40%) and allylhydroquinone **3** (33%) exclusively. Treatment of a solution of **1** in 1:1 THF–H_2O with 1 equiv of NaCN for 22 h produced 84% **4** and 16% **3.** Thus, both NaCN and especially aqueous HCl promote a significant amount of [1,2] rearrangement of this quinol. Similarly, quinol **2,** upon treatment with aqueous HCl as before, produced 30% **3,** 20% **4,** and 20% fragmentation to the unsubstituted hydroquinone. Treatment of quinol **5** with acid produced primarily **11** via a [1,2] rearrangement, although some fragmentation and secondary products were also observed. Treatment with NaCN in 1:1 THF–H_2O produced **11** exclusively in a very clean [1,2] rearrangement, while the same reaction in DMF was rather messy, producing 50% of enedione **12,** (a [1,3] rearrangement), no **11,** and substantial amounts of unidentified materials. Quinol **6** both rearranged [1,2] to **12** (40%) and fragmented (40%) upon treatment with acid, while exposure to NaCN in both 1:1 THF–H_2O and DMF produced **12** essentially quantitatively.

Summarizing these observations, allylquinols lacking substitution at C-1 of the allyl group undergo facile [3,3] or [1,3] rearrangements under neutral conditions. Under acid conditions [1,2] rearrangements become important. When C-1 is disubstituted [3,3] rearrangements are completely suppressed,



(5)

	4	3	1	2	16
"Standard" (22°C, H^+)[3]	33%				39% (a)
−4°C, neutral	20%	Trace	20%	10%	25% (b)
22°C, neutral	40%	~5%			30% (c)
−4°C, neutral, $NiBr_2$	Trace	10%	33%	19%	33% (d)
22°C, neutral, $NiBr_2$	Trace	10%	33%	19%	33% (e)



(6)

	12	11	5	6	16
"Standard" (22°C, H^+)[3]	60%				30% (a)
−10°C, neutral	40%		20%	10%	20% (b)
22°C, neutral	60%				30% (c)
−10°C, H^+	16%	31%			48% (d)
0°C, neutral, formamide	15%	10%	16%	16%	28% (e)
22°C, neutral formamide	30%	10%	10%	10%	20% (f)

and [1,2] rearrangement accompanied by fragmentation results under both neutral and acid conditions. Behavior of these quinols when treated with NaCN is unpredictable, and depends upon quinol structure, solvent, and specific rearrangement conditions.

The above discussion is not meant to imply specific mechanistic pathways for the observed rearrangements, but rather simply to denote the relation of products to precursors. Depending on the structure, substitution pattern, and reaction conditions, rearrangements of cyclohexadienones (and quinols) may proceed by many different pathways, including Cope-type rearrangements and both acid- and base-catalyzed dienone–phenol type rearrangements.[7] Cope ([3,3]) type rearrangements themselves may proceed by a concerted pathway involving either pericyclic (aromatic) or diradicaloid transition states or by a two-step process involving dissociation–recombination with the intervention of diradicals or zwitterions as intermediates.[8] Facile [1,3] sigmatropic rearrangements[9] and base-catalyzed acyloin rearrangements[10] are additional possibilities.

In the early stages of this study it was observed that the site of allyl group introduction in the quinone paralleled the site of highest spin density in the corresponding quinone radical anion when the reactions were run under a specified set of conditions.[2] This is consistent with a rearrangement mechanism involving radical intermediates. However, steric considerations for the pseudochair transition state for a [3,3] sigmatropic reaction lead to the same conclusions as do spin density arguments. Hence a judgment cannot be made from the existing experimental evidence.

The Role of Quinol Intermediates in the Reactions of π-Allylnickel Bromide Complexes with Quinones. Having demonstrated the intermediacy of quinols in the nickel–quinone reaction and having studied the behavior of the pure quinols involved, it remained to demonstrate the role of these quinols in the reaction as run, particularly in the response of product distribution to changes in reaction conditions. The reactions of dimethoxymethylbenzoquinone with 2-methallyl- and 1,1-dimethallylnickel bromide were chosen for study because of the stability of the quinols involved (eq 5 and 6). When run under standard conditions (DMF solvent, 22 °C for 12 h, acidic isolation), eq 5a produced only enedione **4** and reduced starting material.[3] In reactions 5b and 5c, one-half of the reaction mixture (5b) was subjected to neutral isolation at −4 °C. NMR analysis of the crude reaction mixture revealed a 2:1 ratio of quinol **1** to **2**. The predominance of quinol **1** is probably even greater since it is likely that enedione **4** is formed from **1**. The other half of the reaction (5c) was allowed to reach room temperature before being subjected to neutral isolation. Analysis of this reaction mixture shows no quinols, the predominant products being the enedione **4** and reduced starting material. This result is very similar to the results obtained under the standard reaction conditions (acidic workup). Reactions 5a–c therefore indicate that quinols are formed at low temperature and under the standard reaction conditions rearrange before the acidic product isolation. Thus, it appears that acid-catalyzed rearrangements are not a significant factor under the standard reaction conditions employed in the earlier synthetic studies.[3] Reactions 5d–e, identical with 5a–c except for added nickel bromide, were run and were also subjected to neutral isolation at low and room temperatures. In this case, the low-temperature isolation (eq 5d) results in less rearrangement of the quinols than in eq 5b. Also, the proportion of the more hindered quinol (**2**) is increased relative to eq 5b.

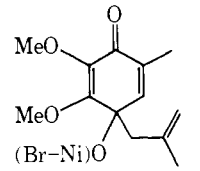
Room temperature isolation (eq 5e) reveals the major effect of added nickel bromide: only a small amount of rearrangement occurs. In this reaction added nickel bromide inhibits the thermal rearrangement so that the quinol survives long enough to undergo acid-catalyzed rearrangement during the standard isolation. It therefore appears that, in reactions with added nickel bromide, acid-catalyzed rearrangements are the major source of products, rather than thermal rearrangements.

In reactions 6b-d, π-1,1-dimethylallylnickel bromide was reacted with 2,3-dimethoxy-5-methylbenzoquinone and one-third of the reaction mixture was subjected to neutral isolation at low temperature (eq 6b). Analysis of this reaction mixture reveals a large amount of enedione **12** plus a considerable quantity of the two possible quinols **5** and **6**. Once again, the least hindered quinol (**5**) predominates. Low-temperature acidic isolation (eq 6d) produces a large amount of reduced starting material along with a considerable quantity of **11**. The quantity of enedione **12** is greatly reduced. Room temperature neutral isolation of the remaining third of the reaction (eq 6c) yields the same results as the standard (acidic) isolation procedure. The products are the enedione **12** and reduced starting material. No quinols and no allylquinones are present. A number of conclusions can be drawn from this experiment. Quinol **6** does not undergo a thermal [1,3] shift since no allylhydroquinone **11** (the [1,3] shift product) is observed in reaction 6c. As previously shown quinol **6** also does not undergo an acidic [1,3] rearrangement. Therefore, in reaction 6d, **11** must result from an acid-catalyzed [1,2] shift of quinol **5**. Rearrangement of **6** can then yield only the enedione **12** ([1,2] shift) or reduced starting material (fragmentation product). It appears that in reaction 6b a considerable amount of rearrangement has occurred during the neutral isolation to give the enedione **12**. In reaction 6d the acidic isolation conditions result in considerable suppression of enedione formation. The increase in reduced starting material from reaction 6b to 6c and 6d indicates that elimination is occurring to a significant degree. In reactions 6e and 6f, π-1,1-dimethylallylnickel bromide was reacted with the quinone in formamide and neutral isolations were carried out at 0 and 22 °C, respectively. NMR analysis of reaction 6e reveals that the quinols **5** and **6** are formed in approximately equal amounts. Analysis of reaction 6f indicates that a considerable amount of the quinols remains even at room temperature. Some of the rearranged products are probably due to rearrangement during the isolation procedure as was noted before.

To summarize these results, the least hindered quinol is the predominant quinol formed under the standard reaction conditions. In the absence of formamide or added nickel bromide, the quinols rearrange thermally at or below room temperature and acid-catalyzed rearrangements do not have a chance to occur. When the reaction is run in formamide or with added nickel bromide, the proportion of the more hindered quinol is increased and thermal rearrangement is inhibited. The quinols can then undergo acid-catalyzed rearrangements during the acidic product isolation. This stabilization and subsequent acid-catalyzed rearrangement of quinols can also be used to rationalize the results in the reactions of 2,5- and 2,6-dimethylbenzoquinones with π-2-methallylnickel bromide and added nickel bromide.[3]

One striking feature which arises from these studies is the relative stability of the isolated quinols when compared to the quinols in the unquenched reaction mixture under the standard conditions. In the absence of formamide or added nickel bromide, quinols in the crude reaction mixture will generally rearrange completely within several hours at room temperature. Once isolated the quinols appear to rearrange more slowly, requiring at least 1 week at room temperature to completely rearrange (vide supra).

When the quinols are initially formed, they must exist in the unquenched reaction mixture as quinol alkoxides, such as **17**.



17

Apparently, these quinol alkoxides are able to thermally rearrange much more rapidly than the corresponding protonated species. There is ample precedent in the literature for this behavior. The [3,3] sigmatropic rearrangement of 1,5-diene alkoxides was found to be 10^{10}–10^{17} faster than that of the corresponding protonated species.[11] Similarly the rates of [1,3] rearrangements of oxy-Cope systems were also greatly enhanced by generation of an alkoxide from the OH group.[9]

These studies now allow the rationalization of the observed changes in product distribution upon changes in reaction conditions previously cited.[3] Specific statements concerning the intimate mechanisms involved must await further experimental studies.

Experimental Section

General. The general experimental considerations and the preparation of starting materials are described elsewhere.[3] Exact mass measurements of the quinols were provided by the Department of Energy Facility, Laramie, Wyo.

Quinol Structural Assignments. The structural assignments for the quinols, protected quinones, and protected quinols were made from NMR and infrared spectral data and were based on similar structures reported by Evans[4] and others.

Preparation and Characterization of Quinols. A. Quinols 1 and 2. π-2-Methallylnickel bromide (0.42 g, 1.09 mmol) in 10 mL of DMF was added over 15 min to 2,3-dimethoxy-5-methylbenzoquinone (0.40 g, 2.18 mmol) and $NiBr_2 \cdot 3DMF$ (2.86 g, 6.52 mmol) in 10 mL of DMF at −60 °C. After addition was complete the reaction mixture was allowed to slowly warm to −8 °C, and 50 mL of cold, saturated NaCl solution was added. The resulting mixture was partitioned between ether and saturated NaCl solution, the aqueous phase washed with 3 × 50 mL of ether, and the combined organic extracts washed with 3 × 50 mL of saturated NaCl. After drying over anhydrous $MgSO_4$ and solvent removal, the crude material was separated by preparative layer chromatography (silica gel) developing three times with 1:1 petroleum ether/ether. The R_f 0.39 band contained quinol **1** (0.17 g, 0.70 mmol, 33%): NMR ($CDCl_3/Me_4Si$) δ 1.68 (m, 3, C=C-CH_3), 1.84 (d, J = 1 Hz, 3, ring CH_3), 2.33–2.83 (AB quartet, A = 2.43, B = 2.73, J = 13 Hz, -CH_2-), 3.58 (s, 1, OH), 3.70 (s, 3, CH_3O- ortho to OH), 4.18 (s, 3, CH_3O- meta to OH), 4.69 (m, 1, C=C-H), 4.83 (m, 1, C=C-H), 6.41 (m, 1, ring H); IR (neat) 2.93 (s, OH), 3.25 (w, *gem*-disubstituted alkene), 3.38 (s), 3.5 (w), 5.96 (m), 6.1 (s, C=O), 6.4 (s), 6.89 (m), 6.96 (s), 7.28 (m), 7.5 (m), 7.75 (m), 8.1 (s), 8.2 (m), 8.90 (w), 9.15 (w), 9.5 (s), 9.8 (w), 10.25 (m), 10.7 (m), 11.1 (w), 12.7 (w), 13.7 μ(m). NMR and IR data are consistent with the structure of 2,3-dimethoxy-6-methylcyclohexa-2,5-dien-1-on-4-(2-methyl-2-propenyl)-4-ol (**1**). Mass spectrum (70 eV) 238.1205 (calcd for $C_{13}H_{18}O_4$, 238.1205).

Quinol **2** (0.10 g, 0.040 mmol, 19%) was contained in the R_f 0.25 band: NMR ($CDCl_3/Me_4Si$) δ 1.66 (m, 3, C=C-CH_3), 2.06 (d, J = 2 Hz, 3 ring CH_3), 2.39–2.92 (AB quartet, A = 2.50, B = 2.82, J_{AB} = 14 Hz, -CH_2-), 3.73 (s, 3, CH_3O- ortho to OH), 3.90 (s, 1, OH), 4.20 (s, 3, CH_3O- meta to OH), 4.65 (m, 1, C=C-H), 4.80 (m, 1, C=C-H), 5.93 (m, 1, ring H); IR (neat) 2.95 (s, OH), 3.24 (w), 3.38 (s), 3.50 (w), 5.97 (s, unsaturated C=O), 6.09 (s), 6.21 (s), 6.86 (m), 7.25 (m), 7.40 (m), 7.70 (m), 8.23 (s), 8.58 (w), 8.77 (m), 9.09 (m), 9.34 (m), 9.76 (m), 10.00 (m), 11.1 (m), 11.14 (m), 13.70 (m), 14.6 (m); mass spectrum *m/e* (rel intensity) 238 (P, base), 221 (56, P − H_2O), 217 (60), 191 (53), 183 (67), 153 (44), 137 (33), 121 (37), 107 (33), 105 (40), 91 (83), 77 (100). NMR, IR, and mass spectral data are consistent with the structure of 2,3-dimethoxy-5-methylcyclohexa-2,5-dien-1-on-4-(3-methyl-3-propenyl)-4-ol (**2**). Mass spectrum (70 eV) 238.1203 (calcd for $C_{13}H_{18}O_4$, 238.1205).

In addition **3** (R_f 0.78, 0.020 g, 0.10 mmol, 10%) and reduced

starting quinone (R_f 0.67, 0.13 g, 0.70 mmol, 33%) were isolated from this reaction.

B. Quinols 5 and 6. A solution of π-1,1-dimethylallylnickel bromide (0.78 g, 1.88 mmol) in 24 mL of DMF was added over a 20-min period to a solution of dimethoxymethylbenzoquinone (0.68 g, 3.80 mmol) in 35 mL of DMF at −55 °C. After routine neutral isolation the crude material (1.92 g, yellow oil) was separated by preparative layer chromatography (silica gel) developing with 2:1 hexane/ether. The R_f 0.29 band (0.32 g, yellow oil) was rechromatographed, developing once with ether. The R_f 0.7 band contained quinol **5** (0.18 g, 0.71 mmol, 19%), a yellow oil: NMR ($CDCl_3$/Me_4Si) δ 1.67 (s, 6, C=C-$(CH_3)_2$), 1.90 (d, J = 1 Hz, 3, ring CH_3), 2.6 (m, 2, -CH_2-), 3.50 (s, 1, -OH), 3.70 (s, 3, CH_3O- ortho to OH), 4.17 (s, 3, CH_3O- meta to OH), 4.93 (m, 1, C=CH-), 6.40 (m, 1, ring H); IR (neat) 2.95 (s, OH), 3.44 (s), 6.12 (s, unsaturated C=O), 6.23 (s), 6.91 (s), 7.30 (m), 7.59 (m), 8.14 (s), 8.33 (s), 9.18 (m), 9.55 (m), 9.91 (m), 10.33 (m), 10.89 (m), 11.19 (w), 11.38 (w), 12.00 (w), 12.83 μ (m). NMR and infrared data are consistent with the structure of 2,3-dimethoxy-6-methylcyclohexa-2,5-dien-1-on-4-(2-methyl-2-butenyl)-4-ol (**5**). Mass spectrum (70 eV) 252.1360 (calcd for $C_{14}H_{20}O_4$, 252.1362).

Quinol **6** (0.10 g, 0.40 mmol, 11%) was contained in the R_f 0.6 band. NMR ($CDCl_3$/Me_4Si) δ 1.62 (s, 6, C=C-$(CH_3)_2$), 2.02 (d, J = 1 Hz, ring CH_3), 2.63 (m, 2, -CH_2-), 3.57 (s, 1, OH), 3.70 (s, 3, CH_3O- ortho to OH), 4.17 (s, CH_3O- meta to OH), 4.70 (m, 1, C=CH-), 6.00 (m, 1, ring H); IR (neat) 2.95 (s, OH), 3.42 (m), 3.50 (m), 5.98 (s, unsaturated C=O), 6.10 (s), 6.23 (s), 6.86 (m), 7.25 (w), 7.38 (w), 7.69 (m), 8.11 (m), 8.32 (m), 8.64 (w), 8.79 (m), 9.14 (m), 9.41 (m), 9.77 (m), 10.00 (m), 10.55 (w), 11.44 (w). NMR and infrared data are consistent with the structure of 2,3-dimethoxy-5-methylcyclohexa-2,5-dien-1-on-4-(2-methyl-2-butenyl)-4-ol (**6**). Mass spectrum (70 eV) 252.1362 (calcd for $C_{14}H_{20}O_4$, 252.1362).

C. Quinol 7. In a similar fashion, naphthoquinone (0.60 g, 3.82 mmol) was treated with π-2-methallylnickel bromide (0.37 g, 0.96 mmol) and the crude reaction mixture was separated by preparative layer chromatography (silica gel, 1:1 pentane/ether, three times). The R_f 0.6 band was rechromatographed, developing twice with 3:1 ether/pentane. The R_f 0.6 band contained quinol **7**, a tan solid (0.34 g, 36%). NMR (acetone-d_6) δ 1.4 (m, 3, C=C-CH_3), 2.7 (s, 2, -CH_2-), 4.46 (m, 1, C=C-H), 4.73 (m, 1, C=C-H), 6.3 (d, J = 10 Hz, ring H meta to OH), 7.13 (d, J = 10 Hz, ring H ortho to OH); IR (neat) 2.95 (s, OH), 3.38 (s), 3.5 (s), 5.9 (w), 6.02 (m), 6.26 (w), 6.90 (w), 7.22 (m), 7.4 (w), 7.7 μ (w). The NMR and infrared data are consistent with the structure of 4-(2-methyl-2-propenyl)-naphthoquin-4-ol (**7**). Mass spectrum (70 eV) 214.0998 (calcd for $C_{14}H_{14}O_2$, 214.0994).

D. Quinol 8. By the same procedure quinol **8** was prepared in 40% yield. NMR ($CDCl_3$/Me_4Si) δ 1.41 (s, 3, C=C-CH_3), 2.00 (d, 3, J = 2 Hz, ring CH_3), 2.68 (s, 2, -CH_2-), 4.40 (m, 1, C=CH), 4.75 (m, 1, C=CH), 6.80 (m, 1, ring H). Mass spectrum (70 eV) 228.1150 (calcd for $C_{15}H_{16}O_2$, 228.1150).

E. Synthesis of 2,3-Dimethoxy-5-methyl-4-cyano-4-trimethylsilyloxycyclohexa-2,5-dien-1-one.[4] 2,3-Dimethoxy-5-methylbenzoquinone (1.6 g, 8.8 mmol) was transferred to a 50-mL two-neck flask fitted with stir bar, stopcock, and rubber septum. The flask was degassed as before and trimethylsilyl cyanide (1.04 g, 1.22 mL, 10.5 mmol) was added via syringe. A catalytic amount of tetra-*n*-butylammonium cyanide was then added to the flask inside a nitrogen-filled glovebag. Within 0.5 h of addition of the catalyst, the reaction mixture became an oil. After stirring for 24 h, the red oil was dissolved in ether and filtered through a medium glass frit covered with Celite. Solvent removal produced a reddish oil (2.6 g): NMR (CCl_4/Me_4Si) δ 0.02 (s, 9, $(CH_3)_3SiO$-), 2.19 (d, J = 1 Hz, 3, ring CH_3), 3.8 (s, 3, CH_3O-, ortho to nitrile), 4.22 (s, 3, CH_3O-, meta to nitrile), 6.0 (m, 1, ring H). This material was used without further purification in the next step.

F. Synthesis of 2,3-Dimethoxy-5-methyl-1-(2-methyl-2-propenyl)-4-cyano-4-trimethylsilyloxycyclohexa-2,5-dien-1-ol.[4] A 250-mL flask fitted with a pressure-equalizing addition funnel and containing an excess of Rieke magnesium (approximately 0.8 g, 33 mmol) in 100 mL of dry THF was cooled to −60 °C. 2-Methallyl bromide (0.56 g, 4.14 mmol) and 2,3-dimethoxy-5-methyl-4-cyano-4-trimethylsilyloxycyclohexa-2,5-dien-1-one (0.88 g, 3.12 mmol) were dissolved in 65 mL of dry ether and added dropwise through the addition funnel to the Rieke magnesium mixture over a 70-min period at −60 °C. The reaction mixture was stirred for an additional 1.5 h at −60 °C. Then 30 mL of saturated aqueous NH_4Cl was added to this mixture and stirred for 5 min. This mixture was then poured onto Na_2SO_4 and stirred for 5 min. The mixture was then filtered and dried further over $MgSO_4$. The mixture was filtered and the solvents were stripped to yield a brownish-yellow oil (0.88 g). This oil was dissolved in hexane (20 mL) and washed with H_2O (6 × 30 mL) to remove 2,3-dimethoxy-4-cyano-5-methylphenol (apparently formed by reduction of the starting material by residual potassium). Concentration of the organic layer produced a yellow oil (0.64 g, 61%): NMR ($CDCl_3$/Me_4Si) δ 0.26 (s, 9, $OSi(CH_3)_3$), 1.73 (s, 3, C=C-CH_3), 1.95 (d, J = 1 Hz, 3 ring CH_3), 2.51 (m, 2, -CH_2-), 3.87 (s, 3, CH_3O-), 3.90 (s, 3, CH_3O-), 4.80 (m, 2, C=CH_2), 5.63 (m, 1, ring H). This compound is 2,3-dimethoxy-5-methyl-1-(2-methyl-2-propenyl)-4-cyano-4-trimethylsilyloxycyclohexa-2,5-dien-1-ol. This material was used without further purification in the next step.

G. Deprotection and Rearrangement.[4] To a stirred solution of the above material (0.33 g, 0.98 mmol) in 30 mL of THF at room temperature was added NaF (0.13 g, 3.14 mmol) in 30 mL of H_2O. After 3 days of stirring the reaction mixture at room temperature, no evidence of rearrangement was detectable by NMR. A reflux condenser was placed atop the reaction vessel and the mixture was refluxed overnight. The reaction mixture was then cooled to room temperature, poured into a separatory funnel, and extracted with chloroform until the organic layer was colorless. The chloroform extracts were combined, washed with H_2O (once, 10 mL), and evaporated to yield a yellow oil (0.19 g, 85%) of 2,3-dimethoxy-5-methyl-5-(2-methyl-2-propenyl)cyclohex-2-ene-1,4-dione (**4**) by comparison with authentic material.

H. Synthesis of 2,5-Dimethyl-4-cyano-4-trimethylsilyloxy-2,5-cyclohexadien-1-one.[4] This material was prepared as above, from 2,5-dimethylbenzoquinone (2.51 g, 18.43 mmol) and Me_3SiCN (2.01 g, 2.56 mL, 20.26 mmol) with tetra-*n*-butylammonium cyanide catalyst, producing 4.1 g (95%) of a yellow semisolid: NMR (CCl_4/Me_4Si) δ 0.2 (s, 9, $OSi(CH_3)_3$), 1.95 (d, J = 1 Hz, 3, ring CH_3 meta to nitrile), 2.2 (d, J = 1 Hz, 3, ring CH_3 ortho to nitrile), 6.17 (m, 1, ring H meta to nitrile), 6.72 (m, 1, ring H ortho to nitrile).

I. Synthesis of 2,5-Dimethyl-1-(2-methyl-2-propenyl)-4-cyano-4-trimethylsiloxycyclohexa-2,5-dien-1-ol. This material was prepared as above from Rieke magnesium (0.82 g, 33.6 mmol), methallyl bromide (0.56 g, 4.11 mmol), and the protected quinone (0.72 g, 3.12 mmol) producing a yellow oil (0.78 g, 86%): NMR ($CDCl_3$/Me_4Si) δ 0.2 (s, 9, $(CH_3)_3SiO$-), 1.7 (m, 3, C=C-CH_3), 1.91 (m, 6, ring CH_3's), 2.37 (s, 2, -CH_2-), 3.2 (s, 1, OH), 4.75 (m, 2, -C=CH_2), 5.7 (m, 2, ring H's). This compound is 2,5-dimethylcyclohexa-2,5-dien-1-on-4-(3-methyl-2-propenyl)-4-ol.

J. Deprotection and Rearrangement. To a stirred solution of the protected quinol (0.35 g, 1.2 mmol) in 30 mL of THF at room temperature was added NaF (0.15 g, 3.6 mmol) in 30 mL of H_2O. After 4 h, 20 mL of the reaction mixture was withdrawn, extracted with ether (2 × 20 mL), dried over anhydrous $MgSO_4$, and evaporated to dryness. The NMR spectrum of the crude material had, in addition to peaks due to protected quinol and rearranged product, two multiplets at δ 6.00 and 6.75, assigned to the ring protons of unrearranged quinol. Attempts to purify this quinol led to rearranged material instead. After 10 h of stirring, the remainder of the reaction mixture was poured into a separatory funnel and extracted with ether until the ether layers were colorless, and the ether layers were combined and dried over $MgSO_4$. Filtration and removal of the solvent were followed by separation of the crude reaction mixture via preparative layer chromatography. After developing twice with 2:1 petroleum ether/ether, 2,5-dimethyl-2-(2-methyl-2-propenyl)cyclohex-5-ene-1,4-dione (**14**) (R_f 0.50, 0.06 g, 60%) was obtained. It was identical in all respects with authentic material.[3]

Rearrangements of the Pure Quinols. Rearrangement products were identified by comparison of their NMR spectra with those of authentic material previously characterized.[3]

A. Thermal Rearrangement of 1. After 2 weeks at 25 °C, neat **1** had rearranged completely to **4** (100%) by NMR.

B. Thermal Rearrangement of 2. After 2 weeks at 25 °C, neat **2** had rearranged completely to **3** (100%) by NMR.

C. Thermal Rearrangement of 7. After 8 weeks at 25 °C, neat **7** had rearranged completely to **9** (100%) by NMR.

D. Thermal Rearrangement of 8. After 12 weeks at 25 °C, neat **8** had rearranged completely to **10** (100%) by NMR.

E. Thermal Rearrangement of 5. After 2 weeks at 25 °C, neat **5** had rearranged completely to **11** (100%) by NMR, a [1,2] rearrangement.

In contrast, refluxing a CCl_4 solution of **5** for 4 days led to 45% of **11** and 30% fragmentation to 2,3-dimethoxy-5-methylhydroquinone.

F. Thermal Rearrangement of 6. After 2 weeks at 25 °C, neat **6** had rearranged completely to **12** (100%) by NMR, a [1,2] rearrangement. In contrast, heating **6** at 75 °C for 2 days in DMF produced fragmentation (23%), a trace of enedione **12,** the [1,3] rearrangement product **11** (11%), and unrearranged quinol **6** (22%) as well as unidentified materials.

G. Acid-Catalyzed Rearrangement of 1. Quinol **1** (0.08 g, 0.35 mmol) was dissolved in 10 mL of DMF, then immediately partitioned between 1.2 N HCl and ether. The ether phase was dried over anhydrous $MgSO_4$, evaporated to dryness, and separated by preparative layer chromatography (silica gel, twice, 1:1 hexane/ether). The products obtained were **3** (R_f 0.6, 0.03 g, 33%) by a [1,2] rearrangement and **4** (R_f 0.44, 0.03 g, 40%) by a [3,3] rearrangement.

H. Sodium Cyanide Catalyzed Rearrangement of 1. A solution of NaCN (0.02 g, 0.4 mmol) in 7 mL of H_2O was added to a stirred solution of **1** (0.1 g, 0.41 mmol) in 7 mL of THF. The mixture was stirred for 22 h and then poured into a separatory funnel and extracted with chloroform until the organic layer was colorless. The organic layers were combined and washed (three times, 3 mL) with H_2O. Evaporation under reduced pressure produced a yellow-brown oil (0.05 g). NMR analysis of this oil indicates the presence of two compounds: **4** (84%) and **3** (16%).

I. Acid-Catalyzed Rearrangement of 2. Quinol **2** (0.05 g, 0.21 mmol) was dissolved in 10 mL of DMF and subjected to the standard acidic isolation procedure. A brown oil (0.06 g) was recovered. NMR analysis of this oil indicates the presence of four products: fragmentation (20%), **4** (20%), **1** (unrearranged starting material, 20%), and **3** (30%).

J. Reaction of 5 with NaCN in Aqueous THF. Quinol **5** (0.1 g, 0.41 mmol) was dissolved in 9 mL of THF with stirring. To this was added a solution of NaCN (0.02 g, 0.41 mmol) in 9 mL of H_2O. The resultant mixture quickly darkened. After 1 h, the reaction mixture was poured into a separatory funnel and extracted with ether until the organic layer was colorless. The ether extracts were combined and washed twice with saturated aqueous NaCl. Isolation as usual yielded a red oil (0.08 g). NMR analysis indicates the major product to be **11** (95%).

K. Reaction of 5 with NaCN in DMF. Quinol **5** (0.13 g, 0.52 mmol) was dissolved in 5 mL of DMF with stirring. To this was added a mixture of NaCN (0.024 g, 0.5 mmol) and 17 mL of DMF. After 3 h, the reaction mixture was isolated under neutral conditions. A brown oil was recovered (0.081 g). NMR analysis indicates that the major product is **12** (50%), as well as much unidentified material.

L. Acid-Catalyzed Rearrangement of 6. Quinol **6** (0.046 g, 0.18 mmol) was dissolved in 12 mL of DMF and the mixture was shaken in a separatory funnel for 5 min with 30 mL of 1.2 M HCl saturated with NaCl. The standard acidic product isolation procedure was conducted from this point. A light brown oil was isolated (0.044 g). NMR analysis of this oil indicates the presence of two compounds: **12** (40%) and reduced quinone (fragmentation).

M. Reaction of 6 with NaCN in Aqueous THF. A solution of NaCN (0.02 g, 0.36 mmol) in 9 mL of H_2O was added to a stirred solution of **6** (0.09 g, 0.35 mmol) in 9 mL of THF. The mixture was stirred for 3 days and then poured into a separatory funnel and extracted with ether until the organic layer was colorless. The organic layers were combined and washed twice with saturated aqueous NaCl and then dried over $MgSO_4$. Isolation as usual produced a brown oil (0.06 g). NMR analysis indicates the sole product to be **12** (100%).

N. Reaction of 6 with NaCN in DMF. A mixture of NaCN (0.01 g, 0.2 mmol) and 8 mL of DMF was added to a stirred solution of **6** (0.05 g, 0.21 mmol) in 2 mL of DMF. The mixture was stirred for 6 h and then isolated under neutral conditions as usual. NMR analysis of the product showed it to be **12** (100%).

Reaction of π-2-Methallylnickel Bromide with Dimethoxymethylbenzoquinone (Reaction 5). A solution of π-2-methallylnickel bromide (0.42 g, 1.1 mmol) in 10 mL of DMF was added over a 15-min period to a solution of dimethoxymethylbenzoquinone (0.4 g, 2.2 mmol) in 10 mL of DMF at −60 °C. After completion of addition, the reaction mixture was allowed to gradually warm up.

5b. When the reaction mixture reached −4 °C, 10 mL of the reaction mixture was withdrawn via syringe and subjected to neutral isolation. A red oil was recovered (0.26 g). NMR analysis of this reaction mixture reveals five products: **16** (25%), **1** (20%), **4** (20%), **2** (10%), and **3** (trace).

5c. The unquenched remainder of the reaction mixture was allowed to reach room temperature and was then isolated under neutral conditions. A red oil was recovered (0.22 g), containing **16** (30%), **4** (40%), and **3** (5%) by NMR.

A solution of π-2-methallylnickel bromide (0.42 g, 1.1 mmol) in 10 mL of DMF was added over a period of 15 min to a solution of dimethoxymethylbenzoquinone (0.4 g, 2.2 mmol) and $NiBr_2 \cdot 3DMF$ (2.9 g, 6.5 mmol) in 10 mL of DMF at −60 °. After completion of addition the reaction mixture was allowed to slowly warm up.

5d. When the reaction mixture reached −8 °C, 10 mL was withdrawn and subjected to the neutral isolation procedure. A red oil (0.25 g) was recovered, transferred to a preparative layer plate (silica gel), and developed three times with 1:1 petroleum ether/ether. Four compounds were isolated.

Compound 1: a red oil, R_f 0.78, 0.01 g; this compound is **3** (0.05 mmol, 10%).

Compound 2: a red oil, R_f 0.67, 0.064 g; this compound is **16** (0.35 mmol, 33%).

Compound 3: an oil, R_f 0.39, 0.085 g; this compound is **1** (0.35 mmol, 33%).

Compound 4: an oil, R_f 0.25, 0.048 g; this compound is **2** (0.35 mmol, 19%).

5e. The unquenched remainder of the reaction mixture was allowed to warm to room temperature and was then subjected to the neutral isolation procedure. A red oil was isolated (0.25 g). NMR analysis of this oil indicates the presence of five compounds: **16** (33%), **4** (trace), **1** (33%), **2** (19%), and **3** (10%).

Reaction of π-1,1-Dimethylallylnickel Bromide with Dimethoxymethylbenzoquinone (Reaction 6). A solution of π-1,1-dimethylallylnickel bromide (0.4 g, 0.95 mmol) in 16 mL of DMF was added over a 20-min period to a solution of dimethoxymethylbenzoquinone (0.35 g, 1.9 mmol) in 14 mL of DMF at −55 °C. After completion of addition, the reaction mixture was allowed to slowly warm up.

6b. When the reaction mixture reached −10 °C, 10 mL was withdrawn and subjected to neutral product isolation. A yellow oil was recovered (0.19 g). NMR analysis of this oil indicates the presence of four compounds. **16** (20%), **12** (40%), **5** (20%), and **6** (10%).

6d. A second 10-mL aliquot was withdrawn via syringe and subjected to the standard acidic product isolation procedures. A red oil was isolated (0.14 g). NMR analysis of this oil indicates the presence of three compounds: **16** (48%), **12** (16%), and **11** (31%).

6e. A solution of π-1,1-dimethylallylnickel bromide (0.22 g, 0.52 mmol) in 11 mL of formamide was added over a 17-min period to a solution of dimethoxymethylbenzoquinone (0.19 g, 1.04 mmol) in 10 mL of formamide at 0 °C. The reaction mixture was stirred for 5 min after completion of addition and then was subjected to the neutral isolation procedure. A brownish-red oil was isolated (0.27 g). NMR analysis of this oil indicates the presence of five compounds: **16** (28%), **12** (15%), **5** (16%), **6** (16%), and **11** (10%).

6f. A solution of π-1,1-dimethylallylnickel bromide (0.38 g, 0.46 mmol) in 12 mL of formamide was added over a 35-min period to a solution of dimethoxymethylbenzoquinone (0.33 g, 1.82 mmol) in 12 mL of formamide at 0 °C. After completion of addition, the reaction mixture was allowed to gradually warm to room temperature overnight. Neutral product isolation produced a yellow-brown oil (0.423 g). NMR analysis of this oil indicates the presence of five compounds: **16** (20%), **12** (30%), **5** (10%), **6** (10%), and **11** (10%).

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New Silicon–Phosphorus Reagents in Organic Synthesis. Carbonyl and Conjugate Addition Reactions of Silicon Phosphite Esters and Related Systems

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Abstract: The 1,2- and 1,4-addition reactions of organosilicon tervalent phosphorus esters, X_2POSiR_3(X = OMe, NMe_2, Ph), with saturated and α,β-unsaturated aldehydes and ketones have been studied. These addition reactions have been compared with the complementary reactions of alkyl phosphorus esters, X_2POCH_3, and R_3SiCl with carbonyl substrates. With α,β-unsaturated aldehydes, a judicious choice of reagent and conditions leads to the regioselective 1,2- or 1,4-addition mode. Some of the mechanistic details of these addition reactions have been elucidated.

Introduction

Over the last 5 years the general utility of the reaction of organosilanes,[1] R_3SiX, with carbonyl substrates has been widely recognized (eq 1).[2-8] Possibly the central explanation

(1)

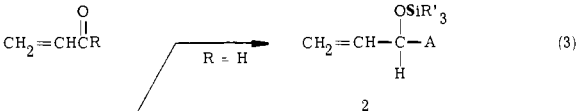
X = -CN,[2] $-N_3$,[3] -SR,[4] $-PR_2$,[5] $-C(N_2)CO_2Et$,[6] $-C{\equiv}CR$,[7] -H[8]

for the success in the development of such carbonyl insertion processes has been the recognition of specific modes of catalysis which facilitate such reactions.

In conjunction with our general interest in the development of synthetic operations which reverse the normal polar reactivity patterns of the carbonyl function, we have engaged in a general study of organosilane addition reactions to saturated and unsaturated aldehydes and ketones illustrated below (eq 2–4) where A is a potential carbanion-stabilizing function.[2a]

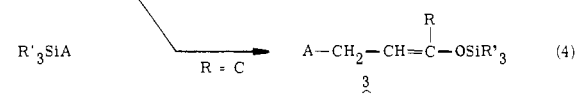
(2)

1



(3)

2



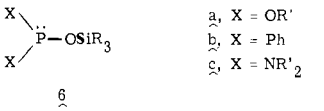
(4)

3

Upon strong-base metalation, adducts **1, 2,** and **3** should afford useful reversed polarity[9] equivalents such as carbonyl[2h,10] and homoenolate anions[11] **4** and **5.**

4 5

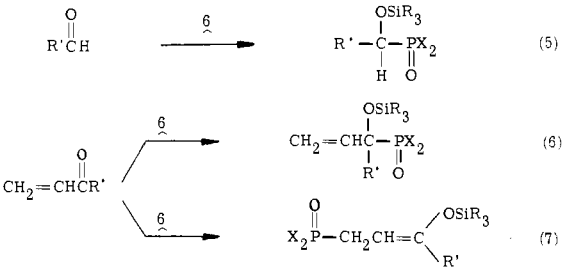
With the above objectives in mind we have undertaken a study of the 1,2- and 1,4-addition reactions of trialkylsilyl tervalent phosphorus esters **6.** The expected adducts derived



6

a, X = OR'
b, X = Ph
c, X = NR'_2

from **6** and aldehyde and ketone substrates are illustrated below (eq 5–7). In contrast to the alkyl tervalent phosphorus



(5)

(6)

(7)

esters **7,** X_2POY(Y = alkyl) which have been demonstrated to react with carbonyl derivatives by a manifold of reaction paths, it was anticipated the organosilicon esters **6** should undergo 1,2-addition with far greater facility based upon the mechanistic rationale presented in Scheme I. *In considering the addition of* **7** *(Y = SiR_3 or CR_3) to a carbonyl group, either a polar intermediate* **8** *or pericyclic transition state* **9** *is reasonable for Y = SiR_3 but not for Y = CR_3.* This prediction is based upon the fact that intramolecular migration of silicon via front-side displacement with retention of configuration is well documented.[12] In contrast, the analogous stepwise or concerted *intramolecular* alkyl transfer process (cf. **8** or **9,** Y = CR_3) is strongly disfavored.[13] In fact, when aliphatic aldehydes are heated in the presence of trialkyl phosphites, only a maximum of 24% of the carbonyl insertion product has been reported,[14] and these adducts have been suggested to be derived from *intermolecular* alkyl transfer.[15] Similar arguments *may* also apply to 1,4-addition reactions of X_2P–OY (Y = silicon vs. carbon) with unsaturated carbonyl substrates. It may thus be assumed that the carbonyl addition process of silyl phosphorus esters **6** might proceed by well-defined reaction paths

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