to −0.05 V relative to a saturated calomel electrode. The appropriate correction factor was applied to the experimentally determined $E_{p/2}$ [$E_{p/2}$ is the potential on the oxidation wave where the current is half the maximum (peak) current]. The reference electrode was inserted in a salt bridge (1.0 M tetramethylammonium chloride) which tapered to a capillary tip. This was placed within 0.5 mm of the platinum disk (Beckman Instruments) working electrode. A short piece of platinum wire was used as the auxiliary electrode. Solutions were prepared by using acetonitrile distilled successively from calcium hydride and phosphorus pentoxide and stored under nitrogen over molecular sieves. Tetra-*n*-butylammonium perchlorate (0.05 M) was used as the supporting electrolyte, and the compound was (1–2) × 10^{-3} M. The potentials reported are those obtained with a scan rate of 0.1 V/s. The oxidations were not completely reversible at this scan rate, and for certain compounds, other oxidation waves were seen at higher potentials (≤2.0 V). Accuracy of the $E_{p/2}$ values reported is estimated to be ±0.05 V.

Acknowledgment. We gratefully acknowledge partial support from the National Science Foundation (Grant No. CHE76-80381 A81) and the National Institutes of Health (Grant No. CA17712-01A2). We thank Dr. Michael Manning and Mr. Jeffrey Weidenhamer for preliminary studies of the oxidation of **29** and **37** and Professor L. Eberson for calling our attention to ref 8d.

Registry No. **8**, 25245-34-5; **8a**, 60316-51-0; **9**, 2674-34-2; **9a**, 65400-01-3; **10**, 24599-58-4; **10a**, 60736-94-9; **11**, 72054-75-2; **11a**, 72054-78-5; **12**, 4537-09-1; **12a**, 72205-69-7; **13**, 72054-77-4; **13a**, 72054-80-9; **14**, 72054-76-3; **14a**, 72054-79-6; **15**, 41038-40-8; **15a**, 72205-70-0; **16**, 33538-81-7; **16a**, 72205-71-1; **17**, 19754-22-4; **17a**, 72054-81-0; **18**, 10075-62-4; **18a**, 37972-49-9; **19**, 53772-19-3; **19a**, 64648-82-4; **20**, 60683-53-6; **20a**, 72205-72-2; **21**, 35896-55-0; **21a**, 72214-02-9; **22**, 72205-73-3; **22a**, 72205-74-4; **23**, 3467-59-2; **23a**, 72205-75-5; **24**, 62397-61-9; **24a**, 72205-75-5; **25**, 72205-76-6; **25a**, 72205-77-7; **26**, 72205-78-8; **26a**, 72205-79-9; **27**, 28689-10-3; **27a**, 72205-80-2; **28**, 93-02-7; **28a**, 72205-81-3; **29**, 64648-81-3; **29a**, 64648-84-6; **30**, 53772-33-1; **30a**, 64648-85-7; **31**, 72214-03-0; **31a**, 72214-04-1; **32**, 72205-82-4; **33**, 1201-38-3; **36**, 72205-83-5; **38**, 72205-84-6; 2,5-dimethoxybenzoic acid, 2785-98-0; trimethylsilyl chloride, 75-77-4; methyl iodide, 74-88-4; ethylene glycol, 107-21-1; 2-hydroxy-1,4-naphthoquinone, 83-72-7; 3-(2,5-dimethoxyphenyl)propionic acid, 10538-49-5; 2,3-dibromo-1,4-naphthoquinone, 13243-65-7; *p*-diethoxybenzene, 122-95-2.

Organocopper Chemistry of Quinone Bisketals. Application to the Synthesis of Isoprenoid Quinone Systems

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The reactions of organocuprates of 1,4-benzoquinone and 1,4-naphthoquinone bisketals are reported. These reagents, formed from the corresponding lithium reagent, cuprous iodide, and dimethyl sulfide react efficiently with allylic bromides (allyl, prenyl, geranyl, and phytyl), often with utilization of greater than one R group of the R_2CuLi. Their reactions with acid chlorides and benzyl bromide proceed with acceptable efficiency, but they are unreactive toward a number of other substrates. The utility of this chemistry in the synthesis of menaquinone-2, phylloquinone, cymopol, and cymopol methyl ether is described.

Whereas the quinone moiety is present in numerous natural-product systems, methods for carbon–carbon bond formation to quinones[3] have been limited to alkylation via a radical addition–oxidation sequence,[4] arylation using diazonium salts,[5] and functionalization of hydroquinone ethers followed by oxidation.[6] Recently there has been renewed interest in synthetic procedures for carbon–carbon bond formation at the quinone nucleus. Sequences involving allylation via π-allylnickel complexes[7] and allyltin reagents[8] and isoprenylation via protected quinones[9] and the utility of 2,5-dimethoxybenzoquinone[10] in effecting this objective have been published. Several years ago we noted that lithioquinone bisketals, readily available from the corresponding bromo derivatives by metal–halogen exchange, allowed introduction of carbon functionality into protected quinones.[2,11] Acid hydrolysis could be controlled to afford either the quinone or its monoketal in most cases.[12] Whereas **1** gave functionalized quinone bisketals in good yields with difficultly enolized ketones, aryl esters, and aryl aldehydes, it gave either no yields or poor yields

(1) (a) Ohio State University Graduate Fellow, 1977–1978. (b) Camille and Henry Dreyfus Teacher-Scholar, 1972–1977.

(2) Part of this work has appeared in preliminary form: Raynolds, P. W.; Manning, M. J.; Swenton, J. S. *J. Chem. Soc., Chem. Commun.* **1977**, 499–500.

(3) For an excellent review of hydroquinone and *p*-benzoquinone chemistry, see: (a) Eastman Publication No. D-146; Eastman Chemical Products, Inc., Industrial Chemicals Division, B-280: Kingsport, TN, Aug 1977. (b) Patai, S., Ed. "The Chemistry of the Quinonoid Compounds", Wiley-Interscience: New York, 1974; Vol. 1 and 2.

(4) (a) Jacobsen, N.; Forssel, K. *Justus Liebigs Ann. Chem.* **1972**, *763*, 135–48. (b) *Acta Chem. Scand.* **1973**, *27*, 3211–6.

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(10) Moore, H. W.; Sing, Y. L.; Sidhu, R. S. *J. Org. Chem.* **1977**, *42*, 3320–1.

(11) For leading references, see: Swenton, J. S.; Jackson, D. K.; Manning, M. J.; Raynolds, P. W. *J. Am. Chem. Soc.* **1978**, *100*, 6182–8.

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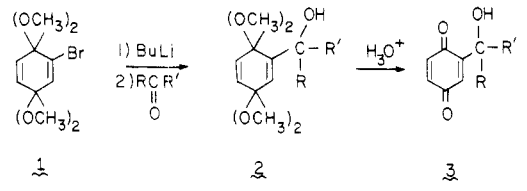
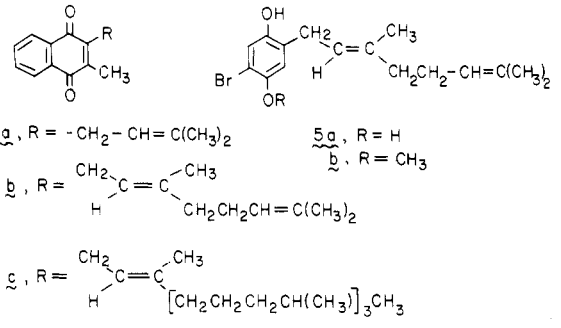


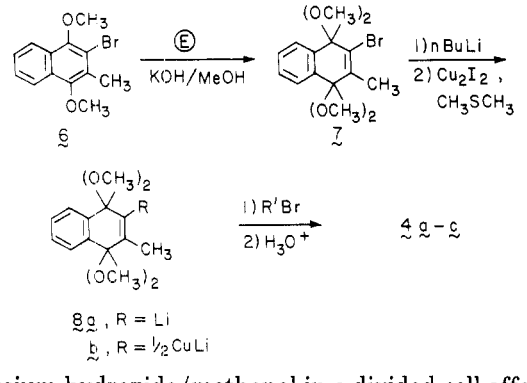
of adduct with alkyl and allylic bromides, enolizable ketones and aldehydes, and certain acid chlorides.[11] The low reactivity with allylic halides was especially unfortunate because of the wide range of naturally occurring isoprenoid quinones.

We report here the chemistry of lithium organocuprates of quinone bisketals. These reagents react efficiently (transfer of greater than one R group of R_2CuLi) with allylic bromides to afford high yields of functionalized bisketals. The reaction of these cuprates with acid chlorides is acceptable for synthetic purposes while conjugate additions to cyclohexenone are of little value. This chemistry has been applied to the synthesis of **4a**, menaquinone-2 (**4b**),[6b] phylloquinone (**4c**),[6a,d,13] cymopol (**5a**),[14] and cymopol methyl ether (**5b**).[14]



Isoprenoid Naphthoquinone Synthesis

In view of the extensive interest in vitamin K[6a,d,13] chemistry, we first examined the utility of the organocuprate chemistry of the bisketals in synthesizing isoprenoid naphthoquinones. Thus, anodic oxidation of **6** in 2%



potassium hydroxide/methanol in a divided cell afforded the respective bisketal **7** in 85% yield. The lithium organocuprate **8b** was generated by addition of the lithiated bisketal **8a** (generated at −60 °C by metalation of **7** with *n*-butyllithium in a glass-jacketed addition funnel) to a slurry of cuprous iodide and dimethyl sulfide in dry tetrahydrofuran followed by stirring for 0.5 h (all operations conducted at −60 °C).[15] Addition of prenyl, geranyl, or phytyl bromide and stirring of the mixture for 0.5 h at −60 °C, followed by stirring for several hours at ambient temperature, afforded the functionalized bisketals. These compounds were not purified but hydrolyzed directly to the isoprenoid quinones **4a–c** in overall yields for the sequence of 92, 96, and 93% (based on halide). An interesting observation was also noted concerning the stoichiometry of these cuprate reactions. When **8b** was treated with either 2 equiv or 1 equiv of prenyl or geranyl bromide, the same yield (~47% based on bisketal) of **4a** or **4b** resulted. However, when 2 equiv of phytyl bromide was used per 1 equiv of **8b**, 93% of **4c** was obtained. Thus, in the reaction of the cuprate with phytyl bromide, both bisketal units are utilized.

As noted by Rapoport[6b] the maintenance of the trans configuration about the double bond in menaquinone-2, **4b**, and phylloquinone, **4c**, is a major concern in an acceptable route to these compounds. The NMR spectra of **4b,c** as well as mixtures of these compounds with their cis isomers have been extensively studied.[13f] By comparing our compounds with the literature spectra, we could detect none of the cis isomer where 5% could have easily been noted. Thus, these bisketal cuprates react in the same manner as the 2-magnesio- or 2-cupro-3-methyl-1,4-dimethoxynaphthalene reagents, allowing carbon–carbon bond formation without isomerization of olefin stereochemistry.[6b]

Cymopol and Cymopol Methyl Ether

Recently, ether extracts from a green algae, *Cymopolia barbata*, have been shown to possess antibiotic and antifungal properties.[14] Several of the components of the extracts have been identified, among them the prenylated hydroquinone cymopol, **5a**, and its monomethyl ether **5b**. While the synthesis of **5a** would appear straightforward by conventional procedures, the regiochemical problem in **5b** did not seem amenable to a classical solution. However, utilization of the organocuprate chemistry and the regioselective monohydrolysis of bisketals to monoketals[12] offered a potentially regioselective synthesis of **5b**.

Anodic oxidation of **9** gave the bisketal **10** in 58–65% yield which was then converted to the cuprate and coupled to geranyl bromide to form **11** in 84% yield (see Scheme I). Monohydrolysis of **11** under mild conditions cleanly afforded a mixture of **12** and **13** in the ratio 4:1. The minor product is assigned as **13** on the basis of its NMR signals at δ 7.22 (s, 1 H), 6.17 (m, 1 H), 3.42 (s, 6 H). Since these two products were inseparable by a variety of methods, the mixture was hydrolyzed under more vigorous conditions to give **12** and **14**. Separation was then easily effected on neutral alumina since **12** was the only material eluted, the quinone **14** being decomposed on the column.

The structure assigned **12** was supported by its combustion analysis and IR and NMR spectra. Definitive evidence for the regioselectivity of this hydrolysis product was obtained from the NMR spectrum of its sodium borohydride reduction product.[12b] Thus, protons H^2 and H^5 in **11** and **12** can be readily differentiated since allylic coupling renders H^5 a distorted triplet ($J \approx 1.5$ Hz) while H^2 appears as a sharp singlet. Comparison of the chemical shifts of H^2 and H^5 for compounds **11**, **12**, and **15** (Scheme II) indicates only a small downfield shift for H^2 in **12**, while H^5 (distorted t, $\Delta\nu_{1/2}$ = 4 Hz) experiences the expected large downfield shift when it is β to a carbonyl group. In **15**, H^2 appears as a clean doublet (J = 3.5 Hz) while H^5

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(14) Högberg, H. E.; Thomson, R. H.; King, J. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1696–701 and references cited therein.

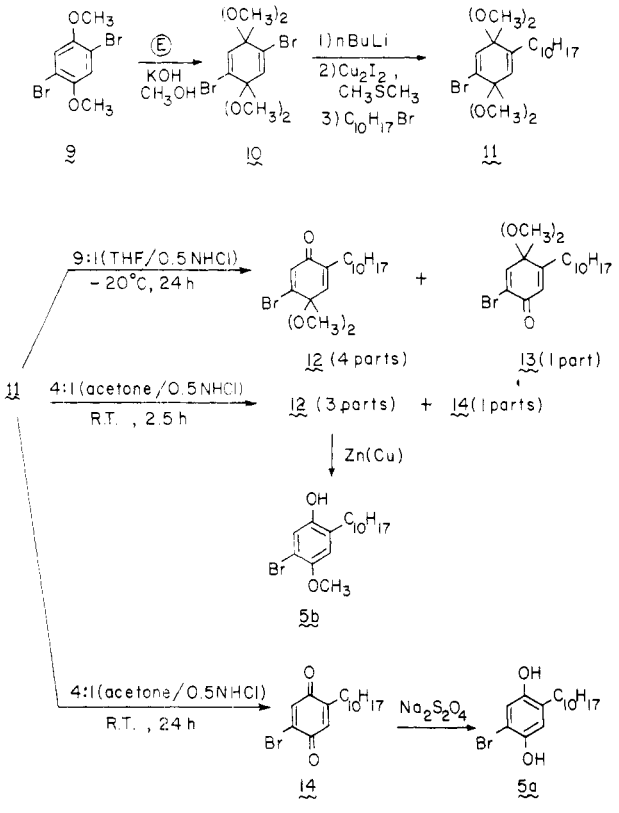
(15) This is essentially the procedure of Heathcock: Chavdarian, C. G.; Heathcock, C. H. *J. Am. Chem. Soc.* **1975**, *97*, 3822–3.

Table I. Reaction of 16 and 17 with Various Substrates[a]

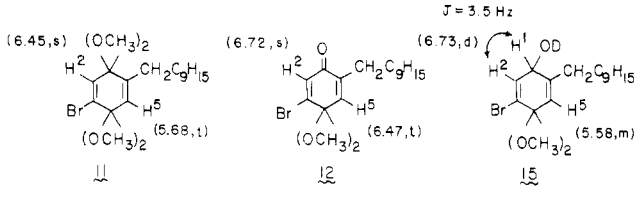
entry	substrate	product	% yield[b] regular	% yield[b] inverse	via 17
1	$CH_2=CHCH_2Br$	$RCH_2CH=CH_2$	(78)[c]	58[c]	
2	c-$C_6H_{13}C(O)Cl$	$RC(O)$-c-C_6H_{13}	0	79	0
3	$PhC(O)Cl$	$RC(O)Ph$	76 (88)	81	
4	$PhCH_2Br$	RCH_2Ph	67		
5	$BrCH_2CO_2Me$	$RCH_2CO_2CH_3$	31 (38)	32 (47)	

[a] Substrates unreactive to functionalization: $PhCH_2Cl$,[d] $ClC(O)OCH_3$,[d,e] PhHC(-CH_2-O),[d,e] $CH_3C(O)H$,[d] n-BuBr,[d] n-BuI,[d,e] n-BuOTs,[d,e] cyclohexenone.[d-f] [b] Yields based on transfer of one R group of the cuprate. VPC yields given in parentheses. [c] Yields based on transfer of both R groups of the cuprate. [d] Regular addition. [e] Inverse addition. [f] Via 17.

Scheme I. Synthesis of Cymopol and Cymopol Methyl Ether



Scheme II. NMR Shifts of 11, 12, and 15



appears as a broad singlet ($\Delta\nu_{1/2}$ = 4 Hz). These data rigorously establish **12** as the major hydrolysis product.

With the monoketal now available, reduction with a zinc/copper couple[12b] proceeded smoothly to cymopol methyl ether. Although the molecularly distilled product appeared pure by GLC, TLC, ^1H NMR, and ^{13}C NMR, it gave a combustion analysis 0.67% high in carbon and 0.10% high in hydrogen. Since debromination with a zinc/copper couple is a reasonable possibility,[16] it is assumed that the slight error in the combustion analysis is due to some contamination (~1%) with the debrominated compound. Rather than attempt further purification of the somewhat unstable **5b**, it was converted to its 3,5-dinitrobenzoate, and proper analytical data were obtained on this crystalline derivative.

Since cymopol, **5a**, was previously prepared via Friedel–Crafts alkylation of bromohydroquinone,[14] an opportunity was available to compare this standard method (which gave an 11% yield of product) with the bisketal entry into these systems. Thus, hydrolysis of **11** to the quinone followed by reduction with sodium dithionite gave a 92% yield of cymopol, **5a**, after recrystallization. Finally, it is worth noting that an alternate route involving appending the hydrocarbon side chain before anodic oxidation was considered. We were successful in forming the aromatic counterpart of **11** in about the same yield from the 2,5-dibromo-1,4-dimethoxybenzene and geranyl bromide. However, the compound, an oil, could not be conveniently freed from impurities by column chromatography; thus, this route was abandoned.

Scope and Limitation of the Bisketal Cuprates

In view of the success noted in the reaction of the bisketal cuprates with allylic bromides, we have investigated two general aspects of this chemistry: first, the range of substrates which react with these reagents and, second, the reactivity of a mixed cuprate.[17] The fact that reagents of the type R_2CuLi usually efficiently utilize only one of the R groups is an undesirable feature of cuprate chemistry. This is especially important in the bisketal systems since the untransferred bisketal and the functionalized bisketal are often only difficultly separable by chromatography. Mixed cuprates have been developed to overcome this problem; however, this is often at the expense of lower reactivity of the reagent.[18] To assess these features in this system, we have conducted the following study.

The reactivity of the cuprate **16** has been investigated under three sets of conditions. First, cuprous iodide and dimethyl sulfide were added to a −60 °C solution of the lithio bisketal. Warming to −10 °C for a few minutes generated the cuprate to which the substrate was added for a one-pot reaction (regular addition). Second, **16**, generated as above, was transferred under nitrogen pressure to a glass-jacketed addition funnel (−60 °C) and added dropwise to a tetrahydrofuran solution of the substrate

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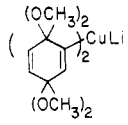
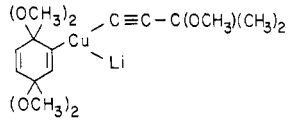


16



17

(inverse addition). Third, in selected cases, the mixed cuprate 17 was examined.[18f]

The results recorded in Table I further support the synthetic utility of the cuprate additions to allylic bromides. More than one R group is transferred with allyl bromide under either regular or inverse addition conditions to afford the functionalized bisketal in good yield. While benzoyl chloride and cyclohexylcarboxylic acid chloride afford good yields based on acid chloride (transfer of only one R group), the order of addition was critical in the latter case. Furthermore, separation of the adducts from the 1 equiv of untransferred R group detracts from the synthetic utility of the process. Finally, benzyl bromide affords acceptable yields of the functionalized system, but methyl bromoacetate affords only a low yield of a difficultly purified adduct. The structure for this adduct was rigorously established by an alternate synthesis from anodic oxidation from the dimethoxy aromatic compound (see Experimental Section). Unfortunately, this cuprate reagent, when employed in stoichiometric amounts, is synthetically of no value with a range of other substrates.

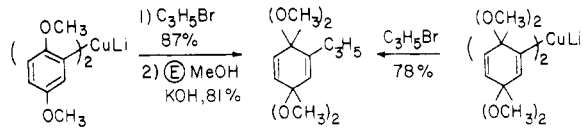
Discussion

The results noted here demonstrate that bisketal cuprates react efficiently with allylic bromides (i.e., allyl, prenyl, geranyl, and phytyl) to afford functionalized bisketals and then by hydrolysis to afford functionalized quinones. Thus, the cuprates nicely complement the reactivity of the lithio bisketals which are unreactive toward a variety of allylic derivatives. While the cuprates afford good yields of adducts with acid chlorides, they are unfortunately unreactive toward a wide range of less reactive substrates.

Since the inception of this work, we have explored the anodic oxidation of a variety of substituted 1,4-dimethoxybenzenes to assess the stability of functional groups to the electrolysis conditions.[19] It is appropriate now to compare the two alternate routes to the functionalized bisketals: first, a sequence of functionalization of a 1,4-dimethoxyaromatic via its cuprate or organolithium reagent, as per Rapoport,[6b,20] followed by anodic oxidation and, second, functionalization of a cuprate of the bisketal. In fact, the two methods often complement each other. Thus, for aromatics having groups which are unstable or complicate the anodic oxidation reaction (i.e., PHC=O, HC(OH)R), functionalization of the bisketal via the lithio or cuprate derivative is available. In other cases, the choice is indicated by experimental convenience. Thus, in the preparation of cymopol methyl ether, isoprenylation of the bisketal proceeded cleanly while the monocuprate of 2,5-dibromo-1,4-dimethoxybenzene, 18, reacted with geranyl bromide to afford a difficultly purified product. In the case of 19, either option can be easily executed. Finally, as in the case of appending the CH_2CO_2Me linkage, neither route is acceptable.

(19) Henton, D.; McCreery, R.; Swenton, J. S. *J. Org. Chem.*, preceding paper in this issue.

(20) Although Rapoport[6b] reported a low yield in attempting to couple the lithium (dinaphthyl) cuprate of 2-bromo-3-methyl-1,4-dimethoxynaphthalene with geranyl bromide, we have observed that by changing the reaction solvent from ether to tetrahydrofuran and using dimethyl sulfide, a 60% yield of product on the basis of transfer of both naphthyl groups was recorded.



18 19 20

Experimental Section[21]

4a. The organolithium compound was formed by adding 430 μL of 2.14 M *n*-butyllithium to a −60 °C solution of 0.313 g (0.912 mmol) of 7 in 15 mL of dry tetrahydrofuran in a glass-jacketed addition funnel. This solution was added over 5 min to a −60 °C suspension of 0.087 g (0.456 mmol) of purified cuprous iodide and 0.133 g (1.82 mmol) of dimethyl sulfide in 10 mL of dry tetrahydrofuran. After the mixture was stirred for 0.5 h at −60 °C, 0.068 g (0.456 mmol) of 1-bromo-3-methyl-2-butene dissolved in 1 mL of dry tetrahydrofuran was added dropwise via syringe, and the mixture was stirred for 15 min at −60 °C and for an additional 4 h at 0 °C. The reaction was quenched with 5 mL of saturated ammonium chloride and worked up in the usual manner to afford a light yellow oil. The oil was dissolved in 5 mL of tetrahydrofuran; 5 mL of 1 N HCl was added and the mixture stirred at room temperature for 5 h. The solution was then neutralized with saturated sodium carbonate and worked up as usual to afford an orange oil. The crude product was chromatographed on silica gel (25 × 1 cm column). Elution with 3% E/PE[21] proceeded as follows: 10 mL, nil; 50 mL, 0.030 g of an impurity; 60 mL, 0.100 g (92% based on the allyl bromide) of **4a** as a yellow oil homogeneous on TLC; 50 mL, 0.025 g of 2-methyl-1,4-naphthoquinone; IR (neat) 2920 (s), 1655 (s), 1595 (s), 1295 (s), 715 cm^{-1} (s); NMR δ 1.62 (s, 3 H), 1.71 (s, 3 H), 2.13 (s, 3 H), 3.22 (d, 2 H, J = 7 Hz), 4.86 (t, br, 1 H, J = 7 Hz), 7.4–7.7 (m, 2 H), 7.7–8.0 (m, 2 H); exact mass analysis calcd m/e 240.115 02, obsd m/e 240.115 54, difference 0.0005.

Menaquinone-2 (4b). In a manner identical to that for **4a**, the lithium organocuprate formed from 430 μL of 2.14 M *n*-butyllithium, 0.313 g (0.912 mmol) of 7, 0.087 g (0.456 mmol) of cuprous iodide, and 0.113 g (1.82 mmol) of dimethyl sulfide was reacted with 0.100 g (0.456 mmol) of geranyl bromide to afford a yellow oil after workup. Hydrolysis as in **4a** but for 18 h afforded an orange oil which was chromatographed on silica gel (25 × 1 cm column). Elution with 5% E/PE proceeded as follows: 15 mL, nil; 50 mL, 0.135 g (96% based on geranyl bromide) of pure yellow quinone [mp 51–53 °C (lit.[6b] mp 52–53 °C)]; 50 mL, 0.035 g of 2-methyl-1,4-naphthoquinone.

Phylloquinone (4c). The organolithium compound was generated by adding 430 μL of a 2.1 M solution of *n*-butyllithium to a cooled (−60 °C) solution of 0.313 g (0.912 mmol) of 7 in 15 mL of dry tetrahydrofuran in a glass-jacketed dropping funnel. This was added over 5 min to a stirred, cooled (−60 °C) solution of 0.087 g (0.456 mmol) of purified cuprous iodide and 0.113 g (1.82 mmol) of dimethyl sulfide in 10 mL of dry tetrahydrofuran,

(21) All melting points were taken with a Thomas-Hoover capillary melting point apparatus and are uncorrected. Measurements of standard samples indicated that the observed melting points were probably 1–2 °C lower than the corrected values. Infrared spectra were recorded on a Perkin-Elmer Model 467 grating spectrometer. ^1H NMR spectra were taken at 60 MHz (in CCl_4 unless otherwise noted) with Varian EM-360 or A-60A instruments, with the latter being used for all critical work. ^{13}C NMR spectra were recorded on a Bruker HX-90 instrument by Dr. Charles Cottrell. Mass spectra and exact mass measurements were obtained by Mr. C. R. Weisenberger on a Consolidated Electronics MS-9 double-focusing mass spectrometer. Analytical samples were determined by Scandinavian Microanalytical Laboratory, Herlev, Denmark. Aluminum oxide and silica gel were from E. Merck Co. Tetrahydrofuran was distilled from benzophenone ketyl directly into the reaction flask. Reactions run in an inert atmosphere made use of a three-way stopcock with a $^{14}/_{20}$ ⊽ joint which allowed the flask to be flame dried under vacuum and filled with purified nitrogen. Butyllithium in hexane (Ventron) was titrated in tetrahydrofuran with 1,10-phenanthroline or HMPA–Ph_3CH (−78 °C) as indicator. Cuprous iodide was obtained from Fisher Scientific, purified by extraction in a Soxhlet apparatus with boiling tetrahydrofuran for 24 h followed by drying in vacuo (24 h), and stored over copper sulfate. Procedures for the anodic oxidations are described in the accompanying paper.[19] Workup as usual refers to extraction with ether, washing of the ether layers with saturated brine solution, drying over calcium sulfate, and concentration in vacuo. In chromatography, E refers to ether, while PE refers to petroleum ether (bp 35–50 °C).

and the entire system was maintained under nitrogen. After the mixture was stirred for 0.5 h at −60 °C, 0.330 g (0.912 mmol) of phytyl bromide dissolved in 1 mL of dry tetrahydrofuran was added dropwise via syringe, and the mixture was stirred for 15 min at −60 °C and for an additional 4 h at 0 °C. The reaction was quenched with 5 mL of saturated ammonium chloride solution and worked up as usual to afford a light yellow oil. The oil was dissolved in 5 mL of tetrahydrofuran; 5 mL of 1 N HCl was added and the mixture stirred at 70 °C for 12 h. Workup afforded an orange oil which was chromatographed on silica gel (25 × 1 cm column). Elution with 3% E/PE proceeded as follows: 20 mL, nil; 80 mL, 0.380 g (93% based on phytyl bromide) of **4c** as a yellow oil, homogeneous on TLC; 100 mL, 0.020 g of 2-methyl-1,4-naphthoquinone.

1,4-Dibromo-2,5-dimethoxybenzene (9). Following the outline of a briefly reported procedure,[22] we treated 50 g (0.35 mol) of 1,4-dimethoxybenzene and 78 g (0.080 mol) of anhydrous potassium acetate in 400 mL of acetic acid with 122 g (0.76 mol) of bromine in 100 mL of acetic acid over a period of 2 h. The precipitate was filtered, triturated with 300 mL of methanol, and crystallized once from methylene chloride/ethanol to give material melting at 143–144 °C with sweating from 138 °C. One more recrystallization from 75 mL of methylene chloride (boiled down from the 250 mL which is required for solution) gave 77.2 g (72%) of compact white crystals: mp 143–144 °C (lit.[23] mp 142 °C).

1,4-Dibromo-2,2,5,5-tetramethoxycyclohexa-1,4-diene (10). A slurry of 20.09 g (67.87 mmol) of **9** and 4.66 g of potassium hydroxide was oxidized at a platinum anode under constant current conditions in 700 mL of methanol at 0° C (12 h) by using power supply A.[19] The progress of the reaction was monitored by the decrease in the UV maximum at 301 nm. About 300 mL of solvent was removed at reduced pressure below room temperature, and the residue was diluted with 600 mL of water. Filtration afforded 23.37 g of a light yellow crystalline solid which was triturated with 25 mL of methanol and crystallized from methanol, yielding a white solid, mp 130–140 °C. Two crystallizations from 7 mL of methylene chloride and 25 mL of PE gave 14.16 g (58%) of **10**: mp 139–141 °C; IR (KBr) 1648 (m), 1359 (m), 1220 (m), 1116 (s), 1068 (s), 1017 (m), 982 (s), 969 (s), 731 cm^{-1} (m); NMR ($CDCl_3$) δ 6.55 (s, 2 H), 3.30 (s, 12 H); mass spectrum, molecular ion not observed; fragments containing the typical two-bromine splitting pattern were observed centered at m/e 343 (weak, P − 15) and 327 (strong, P − 31, OCH_3).

Anal. Calcd for $C_{19}H_{14}Br_2O_4$: C, 33.54; H, 3.94. Found: C, 33.58; H, 4.00.

11. A solution of 2.00 g (5.59 mmol) of **10** in a flask equipped with a gas inlet, a rubber septum, a thermometer, and a mechanical stirrer was cooled to −95 °C with a dry ice/liquid nitrogen/mixed hydrocarbon bath, and 2.54 mL (5.59 mmol) of *n*-butyllithium was added via syringe over a period of 5 min. A light yellow color developed, and 0.7093 g (3.72 mmol, 0.67 equiv) of cuprous iodide was added rapidly through one of the necks of the flask, while maintaining a steady stream of nitrogen to exclude atmosphere. After 2.0 mL of dimethyl sulfide was syringed in, the temperature was allowed to rise by holding the flask in the air until most of the cuprous iodide dissolved at −20 °C. The solution was cooled to −60 °C and 0.6065 g (2.80 mmol) of geranyl bromide was added neat. The solution was stirred for 2 h at 3 °C and quenched by adding 10 mL of saturated ammonium chloride solution. Most of the tetrahydrofuran was removed under reduced pressure, and the hexane-soluble portion of the residue was filtered into a separatory funnel, washed once with water, and dried by being passed through a cone of calcium sulfate. Removal of solvent gave 1.9117 g of an orange oil which was chromatographed on 30 g of alumina. The only product to elute with 200 mL of hexane was 0.9715 g (84%) of **11** as an analytically pure, off-white oil which decomposed upon attempted molecular distillation: IR (film) 2950 (s, br), 2835 (m), 1643 (m), 1454 (s), 1378 (m), 1327 (m), 1225 (s), 1174 (m), 1075 (s, br), 1022 (s), 981 (s), 912 (m), 745 cm^{-1} (m); NMR δ 6.45 (s, 1 H), 5.68 (distorted t, $J \simeq 2$ Hz, 1 H), 5.4–4.3 (mostly between 5.4 and 4.9, m, 2 H), 3.18 (s, 6 H), 3.16 (s, 6 H), 2.80 (br d, J = 8 Hz, 2 H), 2.3–2.0 (m, 4 H), 1.8–1.5 (m, 9 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 144.4, 138.8, 135.3, 131.7, 130.2 (additional shoulder present), 126.1, 124.1, 119.5, 97.6, 95.5, 51.1 (probably 4 OCH_3), 39.7, 26.6, 26.4, 25.7, 17.7, 16.0; exact mass analysis calcd m/e 414.140 61, obsd m/e 414.141 44, difference 0.0008; UV (CH_3OH) no maximum observed.

Anal. Calcd for $C_{20}H_{31}O_4Br$: C, 57.83; H, 7.83. Found: C, 57.83; H, 7.65.

12. The hydrolysis of 0.7727 g (1.86 mmol) of **11** was carried out in 75 mL of a 4:1 mixture of acetone/2 N hydrochloric acid for 2.5 h at room temperature. A majority of the acetone was removed at reduced pressure, and the yellow product was extracted with ether and dried with calcium sulfate. Removal of solvent gave 0.6529 g of a yellow oil whose NMR spectrum only contained peaks which could be attributed to two products in a 3:1 ratio: the desired monoketal (see below) and what is believed to be the quinone **13** showing a singlet, δ 7.17, and a triplet, δ 6.57; all other NMR signals for this compound would be expected to be obscured by those of the major product. Chromatography on 20 g (1 × 20 cm column) of alumina conveniently destroyed the unwanted quinone, leaving the column black and allowing elution of 0.5186 g of a yellow oil (73%) with 2% ether in hexane without the necessity of collecting fractions. The analytical sample was molecularly distilled from a 90–100 °C bath at 3×10^{-5} torr: IR (film) 1669 (s), 1650 (sh), 1614 (m), 1248 (m), 1098 (s), 1075 cm^{-1} (s); NMR δ 6.72 (s, 1 H), 6.47 (distorted t, J = 1.5 Hz, 1 H), 5.4–4.5 (m, 2 H), 3.22 (s, 6 H), 2.98 (br d, J = 7 Hz, 2 H), 2.05 (m, 4 H), 1.65 (m, 9 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 183.1, 146.3, 142.3, 139.4, 138.6, 135.8, 131.8, 124.0, 118.9, 95.8, 51.3 (probably 2 OCH_3), 39.6, 26.9, 26.5, 25.7, 17.7, 16.1; exact mass analysis calcd m/e 368.098 74, obsd m/e 368.099 38, difference 0.0006; UV (CH_3OH) 242 nm (ϵ 8170).

Anal. Calcd for $C_{18}H_{25}BrO_3$: C, 58.54; H, 6.82. Found: C, 58.53; H, 6.81.

5b. A mixture of 0.4012 g (1.08 mmol) of **12** and 0.1413 g of zinc/copper couple in 10 mL of a mixture of tetrahydrofuran/acetic acid/water (6:3:1) was refluxed under argon for 2 h and cooled. Solvent was removed under reduced pressure, and the residue was partitioned between water and methylene chloride. From the organic layer was obtained virtually pure product (NMR) which was freed of a trace of very low R_f material by chromatography on 15 g of alumina (1 × 30 cm column, 10% E/hexane), yielding 0.3214 g of **5b** as an oil (88%). Molecular distillation from a 110 °C bath at 3×10^{-5} torr gave the analytical sample: IR (film) 3440 (s, br), 2960 (s), 2910 (s), 2850 (m), 1492 (s), 1465 (s), 1451 (s), 1402 (s), 1201 (s), 1056 cm^{-1} (s); NMR δ 6.87 (s, 1 H), 6.58 (s, 1 H), 5.3–4.6 (m, 3 H, including a br s at 5.09 which disappears with C_2H_5OD), 3.75 (s, 3 H), 3.23 (d, J = 7 Hz, 2 H), 2.05, 2.02 (overlapping br s, 4 H), 1.68, 1.62, and 1.55 (br s, 9 H); ^{13}C NMR ($CDCl_3$, 20 MHz) δ 150.2, 148.7, 139.0, 132.1, 127.5, 123.9, 121.1, 120.7, 114.3, 109.2, 57.1, 39.7, 29.8, 26.5, 25.7, 17.8, 16.3; exact mass analysis calcd m/e 338.088 18, obsd m/e 338.088 81, difference 0.0006; UV (CH_3OH) 297 nm (ϵ 5440), shifting to 310 nm with a trace of sodium hydroxide.

Anal. Calcd for $C_{17}H_{23}BrO_2$: C, 60.18; H, 6.82. Found: C, 60.85; H, 6.95.

The 3,5-dinitrobenzoate of **5b** was prepared from freshly crystallized 3,5-dinitrobenzoyl chloride in the usual manner. Purification of the initially pure product was complicated by decomposition, and the derivative, mp 99–100 °C, was obtained only after extensive loss of product: IR (KBr) 1743 (s), 1628 (w), 1539 (s), 1349 (s), 1260 (s), 1195 (s), 1185 (s), 1153 cm^{-1} (s); NMR δ 9.28 (s, 3 H), 7.28 (s, 1 H), 6.73 (s, 1 H), 5.5–4.6 (m, 2 H), 3.88 (s, 3 H), 3.23 (d, J = 6.5 Hz, 2 H), 1.95 (m, 4 H), 1.58 (m, 9 H); exact mass analysis calcd m/e 532.084 55, obsd m/e 532.085 87, difference 0.001.

Anal. Calcd for $C_{24}H_{25}N_2O_5Br$: C, 54.04; H, 4.72. Found: C, 53.86; H, 4.73.

5a. The bisketal **11** (0.4422 g, 1.07 mmol) was hydrolyzed at room temperature for 24 h in a solution of 40 mL of acetone and 10 mL of 2 N hydrochloric acid. The solution was neutralized with 5% sodium bicarbonate, and most of the acetone was removed at reduced pressure. Sodium dithionite (1 g) was added to the suspension of product in water, and vigorous shaking caused the disappearance of the yellow color. Extraction with methylene chloride and drying yielded, after removal of solvent, 0.3511 g of a crude orange oil. This material was chromatographed to

(22) Misra, G. C.; Pande, L. M.; Jashi, G. C. *Chem. Abstr.* **1971**, *74*, 111681.

(23) Hesse, J. *Ber. Dtsch. Chem. Ges.* **1878**, *11*, 1031–4.

remove a very low R_f impurity from otherwise pure material, yielding 0.3301 g (95%) of **5a** as a faintly yellow oil which gave a white solid: mp 59–61 °C (lit.[15] mp 59–61 °C); IR (KBr) 3240 (s, br), 2930 (m), 1432 (s), 1197 cm^{-1} (s); NMR ($CDCl_3$ δ 6.95 (s, 1 H), 6.82 (s, 1 H), 5.5–4.7 (m, 4 H), 3.28 (d, J = 7 Hz, 2 H) 2.13, 2.08 (overlapping br s, 4 H), 1.75, 1.72, 1.70, and 1.62 (overlapping signals, 9 H); exact mass analysis calcd m/e 324.072 53, obsd m/e 324.072 94, difference 0.0004.

15. A small sample of **12** in methanol was reduced with an excess of sodium borohydride at room temperature. All solvent was removed, and the residue was partitioned between water and methylene chloride. The organic layer was dried with calcium sulfate, giving an oil which was only characterized by the NMR spectrum: NMR ($CDCl_3$) δ 6.73 (d, J = 3.5 Hz, 1 H), 5.58 (m, 1 H), 5.4–4.6 (m, 2 H), 4.42 (br d, J = 3.5 Hz, 1 H), 3.23 (s, 3 H), 3.15 (s, 3 H), 3.02 (br d, J = 8 Hz, 2 H), 2.2–2.0 (m, 4 H), 1.8–1.6 (m, 9 H). Except for traces of methylene chloride and methanol which were not removed in the workup, there was no indication of more than one product arising in this reaction.

Reactions of the Lithium Cuprate of 1,1,4,4-Tetramethoxy-2,4-cyclohexadiene with Various Substrates. Allyl Bromide. To a −60 °C solution of 0.5 g (1.79 mmol) of **1** in 15 mL of dry tetrahydrofuran was added 0.813 mL of 2.2 M *n*-butyllithium in hexane. After 5 min CuI (0.171 g, 0.9 mmol) and dimethyl sulfide (0.2 mL) were added, and the resulting suspension was warmed to −5 °C for 10 min and then cooled to −60 °C. To the gray-black solution was added 0.155 mL (1.79 mmol) of allyl bromide dropwise followed by stirring for 30 min at −60 °C and then warming to room temperature for 1 h. Saturated sodium carbonate (10 mL) was added, the mixture was stirred for 1 h, the tetrahydrofuran was removed at reduced pressure, ether (25 mL) was added, and the inorganics were filtered. Workup yielded 358 mg of yellow oil which was purified by preparative GLC (1 ft × 0.25 in. column, 20% SE-30, 110 °C). GLC analysis (methyl 2,5-dimethoxyphenylacetate as internal standard) gave a yield of 78%: IR (neat) 2935 (s, br), 2830 (s), 1640 (m), 1470 (m), 1400 (s), 1210 (m), 1110 (s, br), 1070 (s, br), 965 cm^{-1} (s); NMR δ 5.95 (AB, J = 10 Hz, $\Delta\nu$ = 16 Hz, lower field signal meta coupled, J = 2 Hz, 2 H), 5.82–5.45 (m, 2 H), 5.24–4.8 (m, 2 H), 3.20 (s, 6 H), 3.10 (s, 6 H), 2.80 (br d, $J \simeq 7$ Hz, 2 H); exact mass for $C_{13}H_{20}O_4$ calcd m/e 240.136 15, obsd m/e 240.136 78, difference 0.0006.

Cyclohexanecarboxylic Acid Chloride. The cuprate formed as in the previous example was pressure-gradient transferred to a dry-ice-jacketed addition funnel at −60 °C and added over 10 min to a stirred −60 °C solution of 0.24 mL (1.79 mmol) of the acid chloride in 15 mL of dry tetrahydrofuran. Stirring and workup as for allyl bromide afforded 416 mg of a yellow oil which was chromatographed on neutral alumina (activity III, 1.5 × 22 cm column). Elution proceeded as follows: 1% E/PE (800 mL), nil; 1% E/PE (300 mL) and 5% E/PE (210 mL), 100 mg of the *p*-benzoquinone bisketal; 5% E/PE (270 mL) and 10% E/PE (200 mL), 205 mg (79%) of the product as an off-white solid: mp 49–50 °C; IR (KBr) 2938 (s), 2860 (m), 1695 (m), 1672 (m), 1642 (m), 1451 (m), 1400 (m), 1317 (m), 1255 (m), 1210 (m), 1166 (m), 1125 (s), 1110 (s), 1062 (s), 1022 (m), 978 (s), 909 cm^{-1} (m); NMR δ 6.58 (d, J = 3 Hz, 1 H), 5.92 (AB, J = 10 Hz, $\Delta\nu$ = 16 Hz, low-field signal meta coupled, J = 2 Hz, 2 H), 3.27 (s, 6 H), 3.20 (s, 6 H); exact mass for $C_{17}H_{26}O_5$ calcd m/e 310.178 01, obsd m/e 310.178 77, difference 0.0008.

Benzoyl Chloride. The organocuprate was formed in the usual manner from 5 g (17.9 mmol) of **1**, 7.39 mL of 2.42 M *n*-butyllithium, cuprous iodide (1.71 g, 9 mmol), and dimethyl sulfide (2.64 mL) in 50 mL of tetrahydrofuran. To this solution was added dropwise 1.05 mL (9 mmol) of benzoyl chloride followed by workup in the usual manner to afford 4.4 g of a yellow oil which was chromatographed on activity III neutral alumina (2.5 × 28 cm column). Elution proceeded as follows: 10% E/PE (60 mL), nil; 10% E/PE (180 mL), 1.93 g of *p*-benzoquinone bisketal as a white solid; 10% E/PE (220 mL) and 25% E/PE (450 mL), 2.07 g of product as a light yellow oil; chloroform (500 mL), 0.471 g of a reddish brown oil, unknown. The product fractions were triturated with E/PE to yield 1.30 g of product. The mother liquors were rechromatographed to yield 0.437 g of material for a total yield of 1.75 g (65%), mp 66–67 °C (lit.[11] mp 66–67 °C).

Benzyl Bromide. To the cuprate at −60 °C prepared as for allyl bromide was added 0.213 mL (1.79 mmol) of benzyl bromide dropwise. After the mixture was stirred for 1 h at −60 °C and then warmed to room temperature for 2.5 h, workup afforded 517 mg of a yellow oil which was chromatographed on activity III neutral alumina (2 × 19 cm column). Elution with 5% E/PE proceeded as follows: 70 mL, benzyl bromide, 111 mg; 70 mL, *p*-benzoquinone bisketal, 7.5 mg; 280 mL, unsubstituted bisketal and product, 324 mg. This material was triturated with E/PE to afford 174 mg (67%) of product: mp 55–56.5 °C; IR (KBr) 2923 (m), 2820 (m), 1124 (s), 1114 (s), 1060 (s), 1039 (s), 974 (s), 957 cm^{-1} (s); NMR δ 7.17 (s, 5 H), 5.96 (AB, J = 11 Hz, $\Delta\nu$ = 15 Hz, lower field component meta coupled, J = 2.5 Hz, 2 H), 5.4 (m, 1 H), 3.37 (d, J = 2 Hz, 2 H), 3.13 (s, 6 H), 3.10 (s, 6 H); exact mass for $C_{17}H_{22}O_4$ calcd m/e 290.151 80, obsd m/e 290.152 18, difference 0.0003.

Methyl α-Bromoacetate. The procedure was essentially that used for cyclohexanecarboxylic acid chloride. The cuprate formed from 0.5 g of **1** was added dropwise to a stirred −60 °C solution of methyl bromoacetate (0.15 g, 1.79 mmol in 10 mL of tetrahydrofuran). Stirring and workup as for allyl bromide afforded 324 mg of a yellow oil which was chromatographed on activity III neutral alumina with elution as follows: 5% E/PE (300 mL), 106 mg of *p*-benzoquinone bisketal, 10% E/PE (300 mL), 60.8 mg of product greater than 85% pure by NMR. VPC analysis (1 ft × $^1/_8$ in. column, 3% SE-30 on 100/120 Chromosorb G at 110 °C) using octadecane as internal standard gave a yield of 47.2% based on transfer of one R group. Since decomposition occurs during chromatography, a purified sample was isolated via preparative VPC (1 ft × 0.25 in., 20% SE-30, 135 °C) in >95% purity: NMR δ 6.62 (minor impurity), 6.20–5.72 (m, 3 H), 3.62 (s, 3 H), 3.38 (minor impurity), 3.22 (s, 6 H), 3.08 (s, 6 H), 2.99 (br s, 2 H); exact mass for $C_{13}H_{20}O_6$ calcd m/e 272.1259, obsd m/e 272.1266, difference 0.0007.

2-Allylbenzoquinone. The cuprate formed from 5.0 g (17.9 mmol) of **1**, 11.0 mL of 1.63 M *n*-butyllithium, 1.71 g of cuprous iodide, and 2 mL of dimethyl sulfide in 100 mL of tetrahydrofuran was reacted with allyl bromide (1.55 mL, 17.9 mmol) in the usual manner. The crude product (3.9 g) was hydrolyzed in tetrahydrofuran (25 mL) and 1 M HCl (15 mL) for 24 h at room temperature. Filtration of the material through silica gel (2.5 × 45 cm column) with 2% E/PE as eluent afforded 1.25 g (47% overall) of the known quinone.[25]

2-Benzylbenzoquinone. The product from a run identical with that already described was dissolved in 10 mL of 1:1 water/acetone and 0.5 mL of trifluoroacetic acid. After the mixture was stirred for 6 h at room temperature, workup afforded 362 mg of a dark oil which was chromatographed on silica gel (2 × 18 cm column). Elution proceeded as follows: 2% E/PE (100 mL), 36.1 mg of benzyl bromide; 5% E/PE (100 mL), 198 mg (56%) of the known quinone which solidified on standing, mp 40.5–42 °C (lit.[26] mp 43 °C).

Electrolysis of Methyl (2,5-Dimethoxyphenyl)acetate.[24] Anodic oxidation of the title compound under our standard conditions afforded little of the bisketal, and this alternative was then developed. A methanolic (30 mL) solution of 1% tetrabutylammonium perchlorate (TBAP) and 0.3 g of methyl (2,5-dimethoxyphenyl)acetate was electrolyzed at 20 °C, with the potential being raised from 1.3 to 2.0 V vs. a Pt electrode to maintain a current of 0.4–0.5 A which decreased to 0.1 A at the end of the electrolysis. The reaction was monitored by UV at 290 nm and terminated when the absorbance dropped to 10% of its original value (700 C, 40% current efficiency). The solution was concentrated to dryness in vacuo, ether (25 mL) was added, and the solid TBAP was filtered. Workup in the usual manner yielded 284 mg of a yellow oil which was analyzed by GLC (32% yield). Preparative VPC produced a light yellow oil showing a VPC retention time and IR and NMR spectra in agreement with the product from the cuprate reaction.

2-Allyl-1,4-dimethoxybenzene.[27] A solution of 2-bromo-1,4-dimethoxybenzene (2.6 mL, 17.9 mmol) in 100 mL of dry tetrahydrofuran was cooled to −60 °C and 11 mL of 1.63 M *n*-butyllithium in hexane added. The solution was warmed to

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(26) Stollé, R.; Moring, W. *Chem. Ber.* **1904**, *37*, 3486–8.
(27) Mauthner, A. *J. Prakt. Chem.* **1921**, *210*, 41–4.

0 °C for 15 min, 1.71 g (9.0 mmol) of cuprous iodide added, and the suspension warmed to room temperature and stirred for 15 min (solution becomes homogeneous). After the mixture cooled to 0 °C, allyl bromide (1.55 mL, 17.9 mmol) was added dropwise and the solution stirred at 0 °C (1 h) followed by warming to room temperature (1 h). Water (30 mL) was added, the tetrahydrofuran was removed in vacuo, ethyl ether (50 mL) was added, and the inorganics were filtered. Standard workup afforded 3.21 g of crude product which gave 2.78 g (87%) of the product on short-path distillation (bath temperature 50–55 °C, 0.5 torr).

Electrolysis of 2-Allyl-1,4-dimethoxybenzene. The aromatic compound (0.5 g, 2.81 mmol) was dissolved in 40 mL of 1% methanolic potassium hydroxide and electrolyzed at 0 °C by using power supply C[19] at a potential of 1.95 V (760 C, 71% current efficiency) vs. a Pt electrode. Standard workup afforded 627 mg of yellow oil which on short-path distillation (bath temperature 50–55 °C, 0.1 torr) gave 546 mg (81%) of the bisketal as a colorless liquid which showed an NMR spectrum identical with that of the material prepared via the cuprate.

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Registry No. 1, 60316-51-0; **4a**, 957-78-8; **4b**, 7421-23-0; **4c**, 84-80-0; **5a**, 62008-14-4; **5b**, 62008-01-9; **5b** 3,5-dinitrobenzoate, 72205-63-1; **7**, 64648-85-7; **8a**, 72205-64-2; **8b**, 72207-14-8; **9**, 2674-34-2; **10**, 65400-01-3; **11**, 65372-74-9; **12**, 65372-76-1; **13**, 65372-77-2; **15**, 72205-65-3; **16**, 72207-15-9; **17**, 72207-16-0; **18**, 72207-17-1; **19**, 72054-81-0; 2-(cyclohexylcarbonyl)-1,1,4,4-tetramethoxy-2,5-cyclohexadiene, 72205-66-4; 2-benzoyl-1,1,4,4-tetramethoxy-2,5-cyclohexadiene, 60316-59-8; 2-benzyl-1,1,4,4-tetramethoxy-2,5-cyclohexadiene, 72205-67-5; methyl 3,3,6,6-tetramethoxy-1,4-cyclohexadiene-2-acetate, 72205-68-6; 1-bromo-3-methyl-2-butene, 870-63-3; phytyl bromide, 4444-13-7; 1,4-dimethoxybenzene, 150-78-7; geranyl bromide, 6138-90-5; allyl bromide, 106-95-6; cyclohexanecarboxylic acid chloride, 2719-27-9; benzoyl chloride, 98-88-4; benzyl bromide, 100-39-0; methyl α-bromoacetate, 96-32-2; methyl (2,5-dimethoxyphenyl)acetate, 6202-39-7; 2-allyl-1,4-dimethoxybenzene, 19754-22-4; 2-bromo-1,4-dimethoxybenzene, 25245-34-5.

Hydroboration. 54. New General Synthesis of Alkyldihaloboranes via Hydroboration of Alkenes with Dihaloborane–Dimethyl Sulfide Complexes. Unusual Trends in the Reactivities and Directive Effects[1]

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The reactions of alkenes with the dimethyl sulfide complexes of the dihaloboranes ($HBX_2 \cdot SMe_2$; X = Cl, Br, I) have been studied in detail. Dichloroborane–dimethyl sulfide ($HBCl_2 \cdot SMe_2$) hydroborates representative olefins relatively slowly and requires the presence of a strong Lewis acid, such as boron trichloride, to complete the hydroboration reaction rapidly. Unexpectedly, dibromoborane–dimethyl sulfide ($HBBr_2 \cdot SMe_2$) and diiodoborane–dimethyl sulfide ($HBI_2 \cdot SMe_2$) react readily with olefins, even in the absence of such Lewis acids. This is contrary to the trend expected on the basis of the strengths of these methyl sulfide adducts and a hydroboration mechanism involving a prior dissociation of the addition compound. The hydroboration of olefins with these reagents, followed by distillation under reduced pressure, affords alkyldihaloborane–dimethyl sulfide complexes in good yields. These are readily converted by hydrolysis into the boronic acids or by methanolysis to the corresponding esters. Oxidation with alkaline hydrogen peroxide utilizing sufficient sodium hydroxide to neutralize the hydrogen halide readily provides the corresponding alcohols. $HBBr_2 \cdot SMe_2$ and $HBI_2 \cdot SMe_2$ exhibit an unusual directive effect in the hydroboration of trisubstituted olefins, giving unexpected enhanced amounts of the Markovnikov (tertiary) derivatives.

Monochloroborane etherate ($H_2BCl \cdot OEt_2$) hydroborates representative olefins cleanly and completely, providing pure dialkylchloroboranes in high yields.[3] The methyl sulfide complexes of monohaloboranes ($H_2BX \cdot SMe_2$; X = Cl, Br, I) possess a number of advantages over the etherates.[4] These reagents have provided the first general route for the synthesis of dialkylhaloboranes from olefins. In view of the synthetic utilities of trialkylboranes (R_3B) and dialkylboron halides (R_2BX), it is anticipated that the alkyldihaloboranes (RBX_2) should also find valuable applications in organic synthesis.

We recently reported the preparation of a series of alkyldichloroboranes via the hydroboration of alkenes with dichloroborane etherate ($HBCl_2 \cdot OEt_2$).[5] However, this reagent suffers from some practical difficulties. The reagent itself is not stable over long periods of time, cleaving the ether solvent at a significant rate, even with storage at 0 °C. The reaction of $HBCl_2 \cdot OEt_2$ with alkenes in ether or in pentane is slow and incomplete. The hydroboration goes to completion when neat reagents are allowed to react, but the resulting product is predominantly the dialkylchloroborane (R_2BCl) and not the desired alkyldichloroborane ($RBCl_2$). In the presence of 1 molar equiv of BCl_3 in pentane, however, $HBCl_2 \cdot OEt_2$ reacts with alkenes quantitatively and cleanly to give the desired $RBCl_2$ (eq 1).[5] This development provided for the first

$$\text{alkene} + HBCl_2 \cdot OEt_2 + BCl_3 \xrightarrow{\text{pentane}} RBCl_2 + BCl_3 \cdot OEt_2\downarrow \quad (1)$$

time a convenient low-temperature procedure for the general synthesis of alkyldichloroboranes.

Since the development of this procedure, many valuable applications of $RBCl_2$ have been uncovered.[6-9] However,

(1) For preliminary reports on some aspects of this study, see: (a) Brown, H. C.; Ravindran, N. *J. Org. Chem.* **1977**, *42*, 2533. (b) Brown, H. C.; Ravindran, N. *J. Am. Chem. Soc.* **1977**, *99*, 7097.

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