This salt was converted to the free acid in the usual manner to provide **7**: mp 36–37 °C; homogeneous; system CM51, R_f 0.56; $[\alpha]_D$ −14.7° (*c* 1.14, $CHCl_3$).

***N*-*tert*-Butyloxycarbonyl-*S*-trityl-L-cysteinyl-L-alanine Methyl Ester (8).** To a solution of 9.27 g (20.0 mmol) of **6** in 50 mL of dimethylformamide was added 2.2 mL of *N*-methylmorpholine and 2.6 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, this mixture was combined with a solution of 2.76 g (20.0 mmol) of L-alanine methyl ester hydrochloride[13] in 50 mL of dimethylformamide containing 2.2 mL of *N*-methylmorpholine at −15 °C. The mixture was stirred for 1 h at −15 °C and for 1 h at room temperature and then evaporated. A solution of the residue in ethyl acetate was washed with buffer solution (pH 2.0),[12] saturated $NaHCO_3$ solution, and water until neutral and then dried over Na_2SO_2. After removal of the solvent, the residue was crystallized from *n*-hexane. Recrystallization from hot methanol provided 8.85 g (73.3%) of the dipeptide derivative **8**: mp 184 °C; homogeneous; system CM91, R_f 0.90, and CMA, R_f 0.84; $[\alpha]_D$ +12.5° (*c* 1.03, $CHCl_3$).

Anal. Calcd for $C_{31}H_{36}N_2O_5S$: C, 67.85; H, 6.61; N, 5.11; S, 5.84. Found: C, 67.90; H, 6.70; N, 5.13; S, 5.90.

***N*-*tert*-Butyloxycarbonyl-*S*-benzyloxycarbonylsulfenyl-L-cysteinyl-L-alanine Methyl Ester (9). A. From *S*-Trityl Dipeptide 8.** To a solution of 1.60 g (2.92 mmol) of *S*-tritylcysteine derivative **8** in 30 mL of chloroform–ethyl acetate–methanol (2:2:1) was added 2.03 g (10.0 mmol) of SZ-Cl (**5**) with stirring at 0 °C. After 3 h, 2.9 mL of 1 N aqueous diethylamine was added and the mixture was stirred below 0 °C for 5 min. After evaporation of the solvent, the residue was dissolved in 200 mL of chloroform, followed by 100 mL of water to which 1 N aqueous diethylamine was added to pH 4. The organic phase was washed with water and dried over Na_2SO_4. After evaporation of the solvent, the residue was chromatographed on Lichroprep Si60 using system HEC111 as eluent to yield 0.92 g (66.6%) of oily product **9**: homogeneous; system HEC111, R_f 0.61; $[\alpha]_D$ −69.8° (*c* 1.06, $CHCl_3$).

Anal. Calcd for $C_{20}H_{28}N_2O_7S_2$: C, 50.83; H, 5.97; N, 5.93; S, 13.57. Found: C, 50.97; H, 6.02; N, 5.86; S, 13.33.

B. By the Mixed Anhydride Method. To a solution of 0.60 g (1.55 mmol) of SZ derivative **7** in 30 mL of tetrahydrofuran–dimethylformamide (5:1) was added 0.17 mL of *N*-methylmorpholine and 0.13 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, this solution was combined with a solution of 0.216 g (1.55 mmol) of L-alanine methyl ester hydrochloride[13] in 20 mL of the same solvent mixture containing 0.17 mL of *N*-methylmorpholine at −15 °C. The mixture was treated in the usual manner. Chromatography of the resulting gum provided 0.47 g (64.1%) of the dipeptide derivative **9**, identical with the material obtained in method A above.

***N*-*tert*-Butyloxycarbonyl-*S*-trityl-L-cysteinyl-L-glycine Benzyl Ester (11).** To a solution of 2.32 g (5 mmol) of **6** in 15 mL of dimethylformamide was added 0.55 mL of *N*-methylmorpholine and 0.65 mL of isobutyl chloroformate with stirring at −15 °C. After 3 min, the solution was combined with a solution of 1.69 g (5 mmol) of glycine benzyl ester toluene-*p*-sulfonate[14] in 20 mL of dimethylformamide, prepared by the addition of 0.55 mL of *N*-methylmorpholine at −15 °C. The mixture was treated in the manner previously described and crystallized from petroleum ether. Recrystallization from chloroform–*n*-hexane provided 2.55 g (83.5%) of the dipeptide derivative **11**: mp 56–57 °C; homogeneous; system CMA, R_f 0.66, and SBN, R_f 0.82; $[\alpha]_D$ +11.3° (*c* 1.08, $CHCl_3$).

Anal. Calcd for $C_{36}H_{38}N_2O_5S$: C, 70.79; H, 6.27; N, 4.59; S, 5.25. Found: C, 70.76; H, 6.36; N, 4.53; S, 5.40.

***N,N'*-Bis(*tert*-butyloxycarbonyl)-L-cystinyl-L-glycine Benzyl Ester (12).** To a solution of 611 mg (1 mmol) of the dipeptide **11** in 20 mL of ethyl acetate–methanol (2:1) was added 350 mg (1.1 mmol) of mercuric acetate with stirring. The mixture was stirred at room temperature for 4 h, and then hydrogen sulfide gas was bubbled through it for 10 min. The black precipitate was filtered off, and the filtrate was evaporated to dryness. The residue was washed four times with 10 mL of petroleum ether to provide a gum. A 385-mg (0.93 mmol) amount of **7** in 10 mL of chloroform–methanol (1:1) was added to a solution of the gum in 20 mL of the same solvent mixture with stirring at room temperature. After 2 h, the solvent was evaporated and the residue was triturated with *n*-hexane to provide a jelly-like product. This crude material was chromatographed on Sephadex LH-20 using methanol as eluent. Recrystallization from methanol–*n*-hexane provided 340 mg (62.2%) of unsymmetrical cystine derivative **12**: mp 45–47 °C; homogeneous; system CMA, R_f 0.52, HBP, R_f 0.11, and SBN, R_f 0.52; $[\alpha]_D$ −8.8° (*c* 1.12, $CHCl_3$). Amino acid ratio: cysteic acid 1.89 and glycine 1.00.

Anal. Calcd for $C_{25}H_{37}N_3O_9S_2$: C, 51.09; H, 6.35; N, 7.15; S, 10.91. Found: C, 51.18; H, 6.33; N, 6.98; S, 10.60.

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Registry No.—**1** (R_1 = *t*-Bu), 26555-38-4; **2**, 3693-95-6; **4**, 67951-99-9; **5**, 42734-93-0; **6**, 21947-98-8; **7**, 67952-00-5; **7** dicyclohexylamine salt, 67952-01-6; **8**, 52071-20-2; **9**, 67952-02-7; **10**, 67952-03-8; **11**, 67952-04-9; **12**, 67952-05-0; Boc-Cys(H)-Gly-OBzl, 67952-06-1; chlorocarbonylsulfenyl chloride, 2757-23-5; *tert*-butyl alcohol, 75-65-0; benzyl alcohol, 100-51-6; L-alanine methyl ester hydrochloride, 2491-20-5; glycine benzyl ester toluene-*p*-sulfonate, 1738-76-7.

References and Notes

(1) The following abbreviations have been utilized in the text: Boc = *tert*-butyloxycarbonyl; Z = benzyloxycarbonyl; Trt = trityl; SCM = methoxycarbonylsulfenyl; SCB = *tert*-butyloxycarbonylsulfenyl; SZ = benzyloxycarbonylsulfenyl; OMe = methyl ester; and OBzl = benzyl ester.
(2) On leave to Akiyama Laboratory, Department of Industrial Chemistry, Tokyo University of Agriculture and Technology, Nakamachi, Koganei, Tokyo 184, Japan.
(3) S. J. Brois, J. F. Pilot, and H. W. Barnum, *J. Am. Chem. Soc.*, **92**, 7629 (1970).
(4) B. Kamber, *Helv. Chim. Acta*, **56**, 1370 (1973).
(5) K. Nokihara, "The Use of the SCM Group for Thiol Protection of the B-Chain of Native Insulin", manuscript in preparation.
(6) R. G. Hiskey, N. Muthukumaraswamy, and R. R. Vunnam, *J. Org. Chem.*, **40**, 950 (1975).
(7) G. Zumach and E. Kühle, *Angew. Chem.*, **82**, 63 (1970).
(8) R. G. Hiskey, L. M. Beacham, and V. G. Matl, *J. Org. Chem.*, **37**, 2472 (1972).
(9) L. Zervas and I. Photaki, *J. Am. Chem. Soc.*, **84**, 3887 (1962).
(10) The reduction went to near completion, as shown by TLC.
(11) J. L. Bailey and R. D. Cole, *J. Biol. Chem.*, **234**, 1733 (1959).
(12) R. Spangenberg, P. Thamm, and E. Wünsch, *Z. Physiol. Chem.*, **352**, 655 (1971).
(13) H. Zahn and H. Schüssler, *Justus Liebigs Ann. Chem.*, **641**, 176 (1961).
(14) L. Zervas, M. Winitz, and J. P. Greenstein, *J. Org. Chem.*, **22**, 1515 (1957).

Reaction of Organoboranes with 2,5-Dihydroxy-1,4-benzoquinone and Related Compounds, and Its Application to the Synthesis of Rapanone

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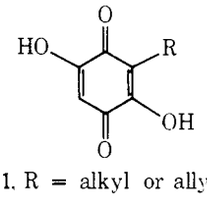
The wide occurrence of natural products having the 3-alkyl or 3-allyl substituted 2,5-dihydroxy-1,4-benzoquinone structure (**1**) and their application, e.g., as anthelmintic



1, R = alkyl or allyl

agents,[1] encouraged us to elaborate a general procedure for the introduction of alkyl groups into 2,5-dihydroxy-1,4-benzoquinone (**2**). Through the pioneering efforts of Hawthorne, alkylquinols may be formed by the reaction of trialkylboranes with 1,4-benzoquinone.[2] Kabalka[3] and Mikhailov[4] report that the reaction of trialkylboranes with 1,4-naphthaquinone gives the corresponding 2-alkyl-1,4-naphthalenediols. Consequently, we decided to explore the reaction of organoboranes with **2** in hope of developing a practical procedure which would

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Table I. Reaction of Boranes with Excess Amounts of 2[a]

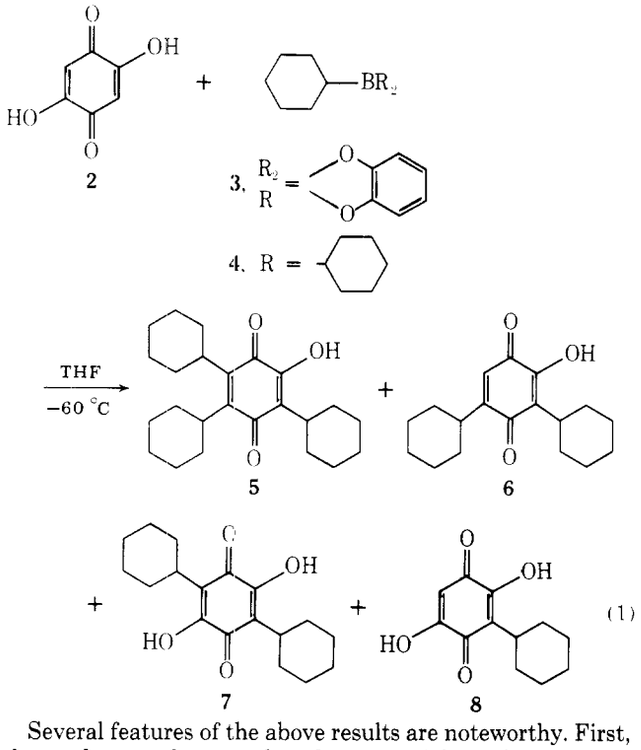
borane	2/borane (molar ratio)	solvent	yield,[b] % (isolated yield, %) 5	6	7	8
3	5[c]	THF	trace	(6)	(5)	(15)
4	15[c]	THF	trace	(22)	(8)	(111)
4	15	THF	*d*	29	*e*	132
4	9	THF	*d*	17	*e*	68
4	3	THF	*d*	43	(8)	61
4	15	Et_2O	*d*	35	*e*	125
4	15	DMF	*d*	*e*	*e*	172

[a] The borane was added at 0 °C and the yields were determined by analysis of ^1H NMR spectra, except where otherwise indicated. [b] Based upon the borane used. [c] The borane was added at −70 °C. [d] Not detected by TLC analysis. [e] Small amounts (<8%) were detected by TLC analysis.

permit the synthesis of naturally occurring 2,5-dihydroxy-1,4-benzoquinone derivatives.

Results and Discussion

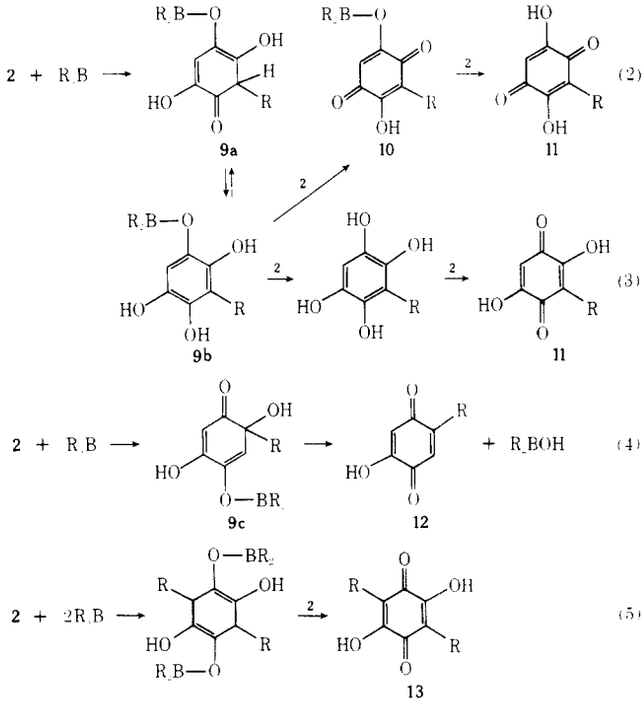
We initially investigated the reaction of **2** with cyclohexylcatecholborane (**3**) or tricyclohexylborane (**4**) in anticipation of facile introduction of the cyclohexyl group into the quinone. Contrary to expectation, a quite disappointing result was obtained; the polyalkylated quinones were isolated from among resinous substances (In the case of **3**: **5**, 1%; **6**, 5%; **7**, 1%; **8**, 1%. In the case of **4**: **5**, 10%; **6**, 30%; **7**, 1%; **8**, trace.) (eq 1). Hydroxyquinones undergo facile rearrangement to a number of compounds under various reaction conditions.[5] This may cause the tarry materials in the present reaction.



(1)

Several features of the above results are noteworthy. First, the products such as **5** and **6**, where one of the hydroxy groups is displaced by a cyclohexyl group, are obtained. Second, the polyalkylated quinones such as **5**, **6**, and **7** are formed in spite of the use of an equimolar amount of **3** (or **4**). Polyalkylated benzoquinones were not detected when 1,4-benzoquinone was treated with **4** under the present reaction conditions.[2] Finally, the quinones, instead of the corresponding quinols, are obtained without an oxidation process. As mentioned later, we reasoned that the formation of the undesirable polyalkylated quinones would be suppressed by the use of excess amounts of **2**. Actually, the desired quinone (**8**) was obtained as a major product (Table I). The best result is obtained in the reaction of **2** with **4** (**2**/**4** = 15:1) in DMF.

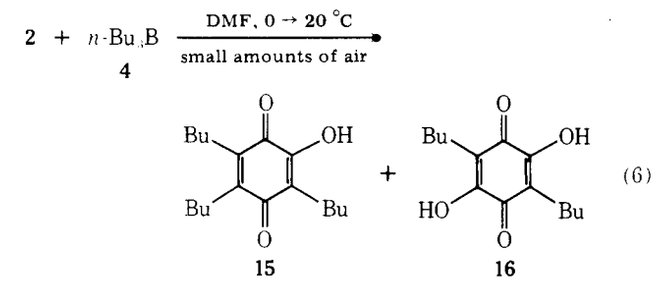
Hawthorne proposed 1,2-addition of R_3B to the carbonyl group followed the migration of an R group.[2] More recently, Kabalka demonstrated that the reaction proceeds in 1,4-addition manner via a free-radical chain mechanism.[3] It is known that the 1,4-addition reaction of normal organoboranes to α,β-unsaturated carbonyl groups proceeds via a free-radical mechanism,[6] and the highly reactive boranes such as triallylboranes undergo 1,2-addition to carbonyl groups.[7] In fact, the introduction of air into the reaction mixture caused the increased formation of alkylated 2,5-dihydroxy-1,4-benzoquinones, suggesting that the present reaction also proceeds via a free-radical mechanism. A plausible mechanism is shown in eq 2–5.



(2) (3) (4) (5)

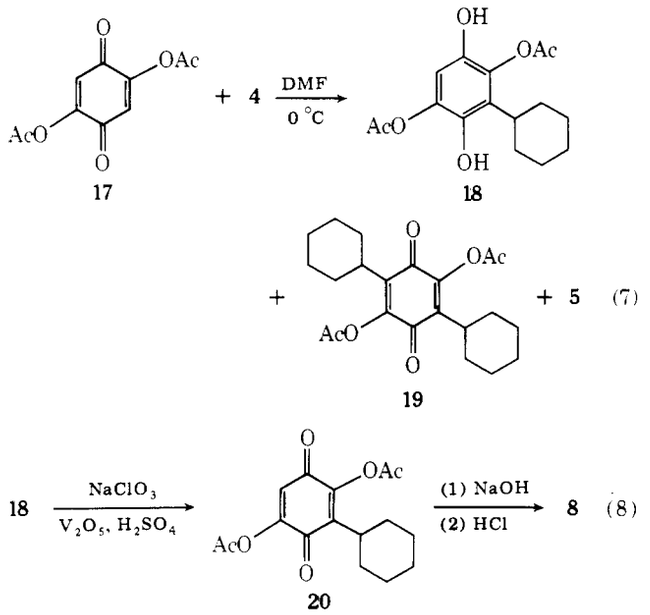
Conjugate addition of R_3B to **2** initially produces **9a**, which undergoes facile isomerization to **9b**. The starting material (**2**) exhibits a strong oxidizing property in comparison with simple benzoquinone.[8] Therefore, oxidation of **9b** by **2** leads to **10**. Because of the highly acidic characteristics of **2**,[9] **10** undergoes facile protonolysis to **11** (eq 2). Alternatively, protonolysis of **9b** by **2** followed by oxidation leads to **11** (eq 3). In any event, the quinone is directly produced without further treatment. Consequently, **11** again reacts with R_3B (or R_2BOH, R_2BO–, etc.), causing the formation of polyalkylated quinones.[10] Since the polyalkylation occurs even when an equimolar amount of cyclohexyl group is reacted, the oxidation and protonolysis steps must presumably proceed more rapidly than that of 1,4-addition. The displacement of hydroxy group via **9c** produces **12** (eq 4), which further suffers from the polyalkylation. In fact, similar displacement is known in the reaction of aminoquinones and related quinones with nucleophiles.[11] Finally, there is a possibility for double alkylation, leading to **13** (eq 5), since the double bond of **9a** is activated by the hydroxy group. These quinones (**11**, **12**, and **13**) further undergo 1,4-addition, oxidation, and protonolysis, causing the undesirable polyalkylation. A simple solution to this problem must involve the use of a large excess of **2** in order to accelerate the rate of 1,4-addition, and this proved to be the case (Table I). Alternatively, protection of the hydroxy group may alleviate these difficulties.

Since many naturally occurring compounds 1 possess normal alkyl chains, we examined the reaction of **2** with tri-*n*-butylborane (**14**) (molar ratio of **2**/**14** = 3) (eq 6). Although the similar polyalkylated quinones were isolated (**15**, 15%, and **16**, 16%), the desirable monoalkylated quinone was not obtained even under various reaction conditions. The marked difference between the reaction of **4** and that of **14** is rationalized as follows. Since secondary alkyl groups are more reactive toward a free-radical reaction of organoboranes than primary alkyl groups,[12] the 1,4-addition process of **14** is presumably more sluggish than that of **4**. Moreover, polyalkylation is more favorable for **14** than for **4** because of the steric factor. Consequently, we gave up an approach to the direct introduction of *n*-alkyl groups into **2**.

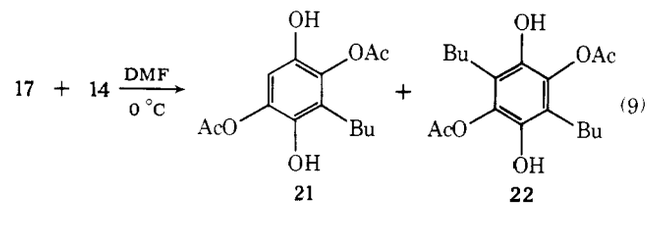


(6)

The equimolar reaction of 2,5-diacetoxy-1,4-benzoquinone (**17**) with **4** in DMF at 0 °C gave the desirable monoalkylated derivative (**18**) as a major product along with small amounts of polyalkylated materials (**19**, 2%, and **5**, < 1%) (eq 7). Oxidation of **18** by the known procedure[13] followed by hydrolysis produced **8** in an overall yield of 8% (eq 8). Formation of trace amounts of **5** must be due to the presence of **2** as an impurity or to the presence of small amounts of water. These results support the proposed reaction courses (eq 2 and 3), and the formation of **19** also suggests the involvement of the double alkylation process (eq 5). The similar reaction of **17** with **14** proceeded successfully to give the desired quinol (**21**; 25%) along with small amounts of the doubly alkylated quinol (**22**) (eq 9). Formation of quinone form **19** in the case of the cyclohexyl derivative is in striking contrast to that of quinol form **22** in the case of the *n*-butyl derivative. Probably the phenomenon might be a reflection of the delicate difference of oxidation reduction potentials.



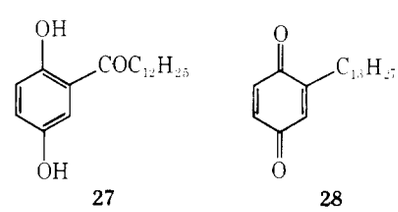
(7) (8)



(9)

The reaction of **17** with tri-*n*-tridecylborane (**23**) in THF proceeded quite sluggishly; the mixture was refluxed for 3 h to complete the reaction (eq 10). Oxidation of the quinol (**24**) followed by hydrolysis gave rapanone (**26**) in an overall yield of 17% (eq 10). Rapanone was first synthesized by Japanese workers.[14] Their route started from the ketone **27** obtained by Friedel–Crafts acylation of quinol dimethyl ether with tridecanoyl chloride. Clemensen reduction and oxidation to the quinone **28** was followed by reaction with dimethylamine and final hydrolysis of the 3,6-diamino derivative. Fieser's synthesis by decomposition of ditridecanoyl peroxide in a hot acetic acid solution of **2** is a far more convenient procedure, despite the low yield (overall 7%).[15] The present process provides an equally useful or even superior method. Consequently, the applicability of the present procedure for the synthesis of **1** appears general. If naturally occurring sec-alkylated quinones (**1**), such as 3,6-dihydroxythymoquinone[1] and helicobasidin,[1] are required, the direct reaction with excess amounts of **2** may provide an attractive synthetic alternative.

(10)



Experimental Section

^{1}H NMR spectra were recorded on a JEOL JNM-MH-100 instrument; chemical shifts (δ) are expressed in parts per million relative to Me_4Si. IR spectra were recorded on a JASCO IRA-1 spectrophotometer. Mass spectra were recorded on a Hitachi GC-M-52 instrument (22 eV). Elemental analyses were performed by the Kyoto University Microanalytical Laboratories, and the results are within the accepted limits (±0.3%). All temperatures were uncorrected. Reagent-grade solvents were purified by standard techniques and kept over a drying agent. Organoboranes (**3**, **4**, **14**, and **23**) were prepared by the reported procedures via hydroboration.[16] The quinone **2** was prepared by the method of Jones and Shonle,[17] and **17** was prepared by the method of Crosby and Lutz.[18]

Reaction of 2 with 3 and 4. In a 200-mL flask, equipped with a magnetic stirrer and maintained under N_2, were placed 1.40 g (10 mmol) of **2** and 50 mL of dry THF. A THF solution of the organoborane (10 mmol) was added. The color immediately changed from yellow to red-purple. Stirring was continued until this color faded away. The mixture was poured into a saturated NaCl solution and extracted with ether and ethyl acetate. The combined organic phase

was dried over anhydrous Na_2SO_4, and the solvents were removed under vacuum. $CHCl_3$ was added to the residue and the insoluble part (**2**) separated. The soluble part was filtered through a column of silica, and the products (**5**, **6**, **7**, and **8**) were isolated from among the tarry materials.

5: mp 159–160 °C (yellow crystals from acetone); IR (KBr) 3330, 1630 cm^{-1}; NMR (CCl_4) δ 1.0–2.0 (m, 30 H), 2.80 (m, 3 H), 6.97 (s, 1 H); mass spectrum, *m/e* 370.5 (M^+). Anal. Calcd for $C_{24}H_{34}O_3$: C, 77.80; H, 9.25. Found: C, 77.67; H, 9.30.

6: mp 77–79.5 °C (orange crystals from petroleum ether); IR (KBr) 3370, 1640 cm^{-1}; NMR (CCl_4) δ 1.0–2.0 (m, 20 H), 2.80 (m, 2 H), 6.28 (s, 1 H), 6.80 (s, 1 H); mass spectrum, *m/e* 288 (M^+). Anal. Calcd for $C_{18}H_{24}O_3$: C, 74.97; H, 8.39. Found: C, 74.72; H, 8.17.

7: mp 205–208.5 °C (orange crystals from acetone); IR (KBr) 3340, 1610 cm^{-1}; NMR ($CDCl_3$) δ 1.1–2.0 (m, 20 H), 2.80 (m, 2 H), 7.86 (s, 2 H); mass spectrum, *m/e* 304 (M^+). Anal. Calcd for $C_{18}H_{24}O_4$: C, 71.02; H, 7.95. Found: C, 68.83; H, 7.68.

8: mp 134.5–137.5 °C subl. (orange plates from CCl_4); IR (KBr) 3320, 1615 cm^{-1}; NMR (CCl_4) δ 1.0–2.0 (m, 10 H), 2.80 (m, 1 H), 5.91 (s, 1 H), 7.76 (s, 2 H); mass spectrum, *m/e* 222 (M^+). Anal. Calcd for $C_{12}H_{14}O_4$: C, 64.85; H, 6.35. Found: C, 64.54; H, 6.56.

The reactions of the boranes with excess amounts of **2** were carried out similarly; isolation was performed on a 5-mmol scale (borane), and excess **2** was recovered substantially. ^1H NMR analysis was performed on a 1-mmol scale (Table I). Dimethyl oxalate was used as an internal standard, and the yields were determined by the area ratio of its CH_3 signal to the olefinic signals of **6** and **8**. Although the yields of **5** and **7** could not be determined by this method, TLC analysis revealed that only small amounts of these quinones were formed.

Reaction of 2 with 14. To a DMF solution of **2** (0.84 g, 6 mmol) was added **14** (0.48 mL, 2 mmol) at 0 °C as described above. A similar isolation procedure using a column of silica gave **15** and **16**. **15**: mp 38–39 °C (yellow needles); IR (KBr) 3320, 1635 cm^{-1}; NMR ($CDCl_3$) δ 0.66–1.90 (m, 21 H), 2.10–2.70 (m, 6 H), 6.87 (s, 1 H); mass spectrum, *m/e* 292 (M^+). Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.97; H, 9.59. Found: C, 73.69; H, 9.68. **16**: mp 150–155 °C (sealed tube) (orange plates from $CHCl_3$); IR (KBr) 3320, 1620 cm^{-1}; NMR ($CDCl_3$) δ 0.80–1.14 (m, 6 H), 1.14–1.70 (m, 8 H), 2.34–2.60 (m 4 H), 7.58 (s, 2 H); mass spectrum, *m/e* 252 (M^+). Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.58; H, 8.10.

Reaction of 17 with Organoboranes. A THF solution of **4** (2 mmol) was added to a DMF (10 mL) solution of **17** (336 mg, 1.5 mmol) at 0 °C under N_2. The resulting mixture was stirred overnight and then heated at 50 °C for 30 min. A similar isolation method using a column of silica gave **5** (<1%), **19** (15 mg, 2%), and **18** (166 mg) contaminated with small amounts of 2,5-diacetoxyhydroquinone. Oxidation of **18** by the reported procedure[13] with $NaClO_3$ (0.03 g,), V_2O_5 (0.3 mg), and a 2% H_2SO_4 solution (0.54 mL) afforded **20** (39 mg) along with small amounts of **17** (<6 mg). Aqueous NaOH solution (2 N) was added to an acetone solution of **20**, and the resulting mixture was stirred for 2 h. The color changed from red-purple to yellow when the mixture was acidified with HCl. Extraction with ether gave **8** quantitatively. **19**: mp 182–192 °C subl. (light yellow crystals); IR (KBr) 1775, 1665, 1625 cm^{-1}; NMR (CCl_4) δ 1.0–2.1 (m, 20 H), 2.32 (s, 6 H), 2.75 (m, 2 H); mass spectrum, *m/e* 346, 304.

Hydrolysis of **19** gave **7**. **20**: mp 72–75 ° C (light yellow crystals from hexane); IR (KBr) 1780, 1675, 1620 cm^{-1}; NMR (CCl_4) δ 1.1–2.0 (m, 10 H), 2.31 (s, 3 H), 2.33 (s, 3 H), 2.76 (m 1 H), 6.44 (s, 1 H); mass spectrum, *m/e* 264, 222.

The reaction of **17** (1.6 mmol) with **14** (1.6 mmol) was carried out similarly. The isolation procedure was as follows. The insoluble part in $CHCl_3$ (**22**) was oxidized by the reported procedure[13] to give 2,5-diacetoxy-3,6-di-*n*-butyl-1,4-benzoquinone (30 mg, 6%): mp 115–118 °C (yellow crystals); IR (KBr) 1780, 1675, 1625 cm^{-1}; NMR ($CDCl_3$) δ 0.76–1.08 (m, 6 H), 1.08–1.60 (m, 8 H), 2.20–2.68 (m, 10 H), involving 2.33 (s, 6 H); mass spectrum, *m/e* 294, 252. Hydrolysis of this quinone gave **16**. The soluble part in $CHCl_3$ was filtered through a column of silica to afford **21** (106 mg, 25%): mp 104–108 °C (yellowish white crystals); IR (KBr) 3365, 1740, 1604 cm^{-1}; NMR ($CDCl_3$) δ 0.76–1.10 (m, 3 H), 1.10–1.64 (m, 4 H), 2.24–2.52 (m, 8 H) involving 2.34 (s, 6 H), 5.63 (s, 1 H), 6.59 (s, 2 H); mass spectrum, *m/e* 282 (M^+). Anal. Calcd for $C_{14}H_{18}O_6$: C, 59.56; H, 6.43. Found: C, 59.42; H, 6.49.

Synthesis of Rapanone (26). A THF solution of **17** (448 mg, 2 mmol) was added to a THF solution of **23** (2 mmol) at 0 °C. The color of the solution was still red-purple after 24 h and almost faded away by refluxing for 3 h. Extraction and a drying process were carried out as described above. Separation of the insoluble part of the residue in CCl_4 gave crude **24** (white precipitate, 384 mg). Oxidation of **24** (204 mg) by the standard procedure[13] ($NaClO_3$, 30 mg; V_2O_5, 0.3 mg; 2% H_2SO_4 solution, 0.5 mL), followed by filtration through a column of silica, gave **25** (62 mg) along with **17** (25 mg). Hydrolysis of **25** by the same procdure as described above gave **26** quantitatively. The total yield from **17** was 17%.

25: mp 52–54.5 °C (yellow crystals); IR (KBr) 1770, 1675, 1625 cm^{-1}; NMR ($CDCl_3$) δ 0.70–1.70 (m, 25 H), 2.27–2.52 (m, 8 H), involving 2.36 (s, 6 H), 6.62 (s, 1 H); mass spectrum, *m/e* 322.

26: mp 137–142 °C (lustrous orange plates from CCl_4) (lit. mp 139–142[14] and 141–142 °C[15]); IR (KBr) 3320, 1615 cm^{-1}; NMR ($CDCl_3$) δ 0.80–1.66 (m, 25 H), 2.48 (m, 2 H), 6.03 (s, 1 H), 7.70 (s, 2 H).

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References and Notes

(1) R. H. Thomson, "Naturally Occurring Quinones", 2nd ed., Academic Press, New York, 1971.
(2) M. F. Hawthorne and M. Reintjes, *J. Am. Chem. Soc.*, **86**, 951 (1964); **87**, 4585 (1965).
(3) G. W. Kabalka, *J. Organomet. Chem.*, **33**, C25 (1971).
(4) B. M. Mikhailov, G. S. T.-Sarkisyan, and N. A. Nikolaeva, *Zh. Obshch. Khim.*, **41**, 1721 (1971); *Chem. Abstr.*, **76**, 3934n (1972).
(5) H. W. Moore and R. J. Wikholm, *Chem. Quinoid Compd. 1974*, **1**, 425 (1974).
(6) H. C. Brown and M. M. Midland, *Angew. Chem., Int. Ed. Engl.*, **11**, 692 (1972).
(7) B. M. Mikhailov, G. S. T.-Sarkisyan, and N. A. Nikolaeva, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 527 (1968).
(8) H.-D. Becker, *Chem. Quinoid Compd. 1974*, **1**, 335 (1974).
(9) "Dictionary of Organic Compounds", Vol. 2, Maruzen, Tokyo, 1965, p 1058: $pK_1 = 5.18$, $pK_2 = 2.73$.
(10) There is a possibility that **10** instead of **11** reacts further with R_3B.
(11) K. T. Finley, *Chem. Quinoid Compd. 1974*, **2**, 877 (1974).
(12) H. C. Brown and E. Negishi, *J. Am. Chem. Soc.*, **93**, 3777 (1971).
(13) H. W. Underwood, Jr., and W. L. Walsh, "Organic Syntheses", Collect. Vol. 2, Wiley, New York, 1943, p 553.
(14) M. Asano and K. Yamaguchi, *Yakugaku Zasshi*, **60**, 585 (1940).
(15) L. F. Fieser and E. M. Chamberlin, *J. Am. Chem. Soc.*, **70**, 71 (1948).
(16) H. C. Brown, "Organic Synthesis via Boranes", Wiley-Interscience, New York, 1975.
(17) R. G. Jones and H. A. Shonle, *J. Am. Chem. Soc.*, **67**, 1034 (1945).
(18) A. H. Crosby and R. E. Lutz, *J. Am. Chem. Soc.*, **78**, 1233 (1956).

Convenient Two-Step Synthesis of Substituted 1-Azaadamantanes from α-Pinene[1]

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The solvomercuration–demercuration of olefins in the presence of acetonitrile provides a convenient technique for the Markownikoff amidation of carbon–carbon double bonds[2] or for allylic amidation.[3] Nevertheless, the treatment of α-pinene (**1**) with acetonitrile in the presence of mercuric nitrate followed by in situ borohydride reduction did not afford the expected amide, but led instead to azabicyclo[3.3.1]nonene **2** (Scheme I).

In imino olefinic structure **2**, the relative positions of the nitrogen atom and of the double bond permitted a one-step synthesis, via an iminium intermediate, of 1-azaadamantane of type **3** in virtually quantitative yield.

The 2,2,4,6-tetramethyl-3-azabicyclo[3.3.1]non-6-ene (**2**) was obtained in 51% yield as the hydrochloride. The racemic intermediate **4** was isolated when the reaction was carried out without borohydride reduction. Racemization of the imine **4**

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