zinc, addition of the filtrate to 20 mL of saturated aqueous ammonium chloride, extraction with methylene chloride and chromatography of the dried solution ($CaCl_2$) on a short neutral alumina column, using methylene chloride as eluant. Chromatography was not necessary for the maleic anhydride adduct. Evaporation of CH_2Cl_2 after extraction gave an analytically pure sample. The other adducts were >95% pure (by NMR and GC) following chromatography. Our yields are based on quantities obtained after this step. Analytically pure samples were obtained by preparative gas chromatography. Structural assignments are based on NMR, IR, and mass spectral data and elemental analyses. The cis configuration of the product from the reaction of dimethyl maleate was assigned because it was the only product from that reaction and it was different from the single product obtained when dimethyl fumarate was used as the dienophile.

The production of **2** is strongly implied by these observations and, if so, ultrasound provides a convenient low-temperature route to this intermediate. That **1** is commercially available and inexpensive makes this procedure very attractive. Typically **2** is generated in synthetically useful quantities at high temperatures from intermediates requiring one or two synthetic steps.[9] Work is now in progress to broaden the scope of the reactions of **2** as well as to apply this technique to vicinal and geminal dihalides.

Acknowledgment. Fruitful discussions with Clayton H. Heathcock are gratefully acknowledged. We also thank the Air Force Office of Scientific Research for financial support through Grant No. AFOSR-80-0239.

Registry No. 1, 91-13-4; 2, 32796-95-5; 3, 1460-59-9; 2,5-furandione, 108-31-6; dimethyl (*Z*)-2-butenedioate, 624-48-6; methyl 2-propenoate, 96-33-3; 3-buten-2-one, 78-94-4; 3a,4,9,9a-tetrahydronaphtho[2,3-*c*]furan-1,3-dione, 29811-05-0; dimethyl *cis*-1,2,3,4-tetrahydro-2,3-naphthalenedicarboxylate, 80399-27-5; methyl 1,2,3,4-tetrahydro-2-naphthalenecarboxylate, 39246-30-5; 2-acetyl-1,2,3,4-tetrahydronaphthalene, 35060-50-5; zinc, 7440-66-6.

(9) Boekelheide, V.; Ewing, G. *Tetrahedron Lett.* **1978**, *19*, 4245-4248. Cava, M. P.; Deana, A. A. *J. Am. Chem. Soc.* **1959**, *81*, 4266-4268. Oliver, J. A.; Ongley, P. A. *Chem. Ind. (London)* **1965**, 1024-1025.

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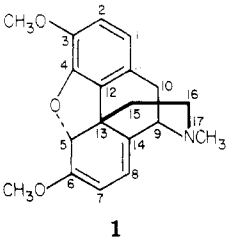
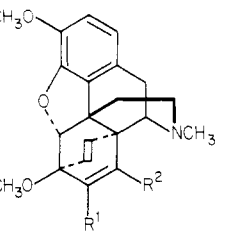
Thebaine and Acetylenic Dienophiles

Summary: Reaction of thebaine (**1**) with methyl propiolate (MP) in methanol gave the ketal **8** accompanied by the adduct **5**. Treatment of **8** with 1.5 equiv of a strong acid converted it to **5**. Larger amounts of acid gave the ketone **7**, whose structure was established by single-crystal X-ray structure determination. Prolonged hydrolysis of **8** with base gave the amine **9**, which when treated with MP gave the ketal **10** isomeric with **8**. The adduct **11** was obtained when **1** was treated with dimethyl acetylenedicarboxylate in methanol.

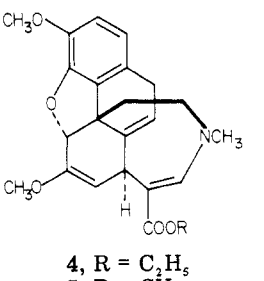
Sir: Rapoport and Sheldrick[1] reported that heating thebaine (**1**) and dimethyl acetylenedicarboxylate (DMAD) in benzene at 50 °C for 1 h gave the expected adduct **2** in 90% yield, but that under comparable conditions ethyl propiolate (EP) afforded **3** in only 6% yield. . In connection with our efforts to obtain opioids of biological interest from thebaine,[2] we had occasion to reexamine the reaction of **1** with acetylenic dienophiles. While our work was in progress, Hayakawa et al.[3] published a preliminary communication describing results of a similar study. They found, inter alia, that **1** and ethyl propiolate (EP) reacted at room temperature in acetonitrile to give the adduct **4** and that methyl propiolate (MP) furnished the corresponding methyl ester **5** in excellent yields. Mild acid hydrolysis of **4** and **5** gave the ketones **6** and **7**, respectively. The structural assignments were made primarily on the basis of spectroscopic data. We prepared **7** by a somewhat different route and established the structure by means of a single-crystal X-ray structure determination.[4] The structure and molecular geometry of **7** are shown in Figure 1.



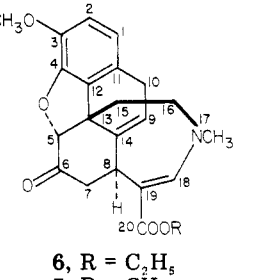
1



2, $R^1 = R^2 = COOCH_3$
3, $R^1 = COOC_2H_5$; $R^2 = H$



4, $R = C_2H_5$
5, $R = CH_3$



6, $R = C_2H_5$
7, $R = CH_3$

Some of our observations differ substantially from those of Hayakawa et al.[3] For example, these investigators

(1) H. Rapoport and P. Sheldrick, *J. Am. Chem. Soc.*, **85**, 1636 (1963).

(2) J. M. Bidlack, L. G. Abood, P. Osei-Gyimah, and S. Archer, *Proc. Natl. Acad. Sci.* U.S.A., **78**, 636 (1981).

(3) K. Hayakawa, S. Motohiro, I. Fujii, and K. Kanematsu, *J. Am. Chem. Soc.*, **103**, 4605 (1981). These investigators report that **5** melts at 160-162 °C and **7** at 231-233 °C.

(4) Crystal of **7** are orthorhombic with space group $P2_12_12_1$, $Z = 4$. The unit cell parameters are as follows: $a = 10.440$ (6) Å, $b = 11.915$ (4) Å, $c = 13.352$ (7) Å, $V = 1910$ (1) Å^3. The calculated density is 1.334 g/cm^3. Data were collected on a Syntex P2 diffractometer with graphite monochromated Cu Kα radiation ($\lambda = 1.5418$ Å) in the $\theta/2\theta$ mode to a maximum 2θ of 115°. Of the 1509 symmetry independent reflections measured, 1423 (94.3%) were considered observed at $I \geq 3\sigma(I)$. Data reduction, least-squares refinement procedures, and various electron density syntheses were calculated with the XRAY system (J. M. Stewart, G. Kruger, H. L. Ammon, C. Dickinson, and S. R. Hall, (1972). "The Xray system", June 1972 version Tech. Rep. TR-192, Computer Science Center, University of Maryland, College Park, MD) Initial phasing was performed by MULTAN 78 (P. Main, S. E. Huss, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, "MULTAN 78. A System of Computer Programs for the Automatic Solution of Crystal Structures from X-Ray Diffraction Data", Universities of York, England, and Louvain, Belgium, 1978). The trial set with the highest combined figure of merit indicated 24 correct atomic positions of the 28 nonhydrogen atoms. After refining the positional coordinates and isotropic temperature factors of this trial structure with full-matrix least-squares analyses, the remaining four atoms were found with a difference electron density synthesis. The final refinement, using anisotropic temperature factors for all nonhydrogen atoms, gave a residual index of 0.075. Crystallographic tables with atomic positional coordinates, temperature factors, bond distances, and angles and a list of observed and calculated structure factors can be obtained from J.H.

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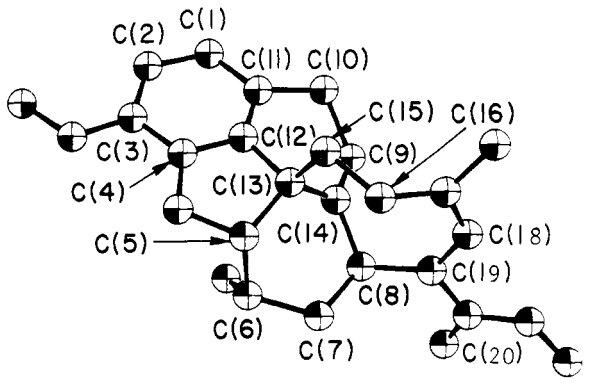
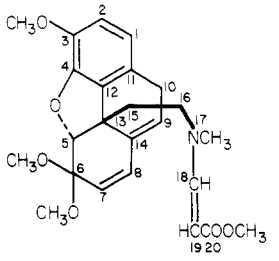
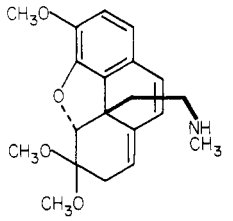


Figure 1. ORTEP drawing of 7.[4] The numbering of the carbon atoms is identical with that of the text.

claimed that the reaction of thebaine (1) with MP in CH_3OH gave the adduct **5** in quantitative yield. We found that when MP and 1 were allowed to stand in CH_3OH for 30 min, the ether-insoluble adduct,[5] **5**, mp 160–162 °C,[3] was obtained in 32% yield: $[\alpha]_D$ −325° ($CHCl_3$); UV(EtOH) λ_{max} 296 nm (log ϵ 4.31); IR (KBr) 1675 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.90 (m, 2 H, H-15), 2.92 (s, 3 H, NCH_3), 3.04–3.40 (m, 4 H, H-10, H-16), 3.58 (s, 3 H, 6-OCH_3), 3.74 (s, 3H, $COOCH_3$), 3.86 (s, 3 H, 3-OCH_3), 4.54 (d, 1 H, H-8, J = 5 Hz), 4.98 (s, 1 H, H-5), 5.25 (d, 1 H, H-7, J = 5 Hz), 5.92 (dd, 1 H, H-9), 6.65 (s, 2 H, H-1, H-2), 7.35 (s, 1 H, H-18). Our IR and NMR data are in substantial agreement with those reported.[3] The major product, **8**, obtained



8

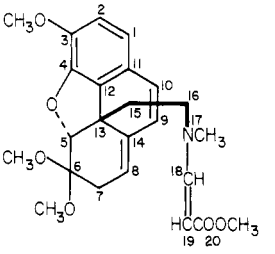


9

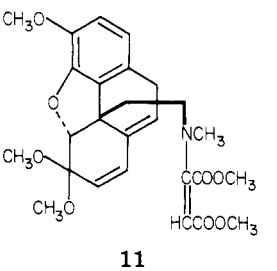
in 53% yield was an ether-soluble, white substance: mp 117–118 °C (methanol); $[\alpha]_D$ −155° ($CHCl_3$); UV(EtOH) λ_{max} 280 (log ϵ 4.49), 225 nm (sh, log ϵ 4.26). The mass spectrum (M^+, m/e 427) and the elementary analyses indicated that the empirical formula differed from that of the ether **5** by the elements of methanol. The IR (KBr) spectrum showed absorption at 1675 cm^{-1} characteristic of the NC=CCOOCH$_3$[3] functionality. The ^1H NMR spectrum ($CDCl_3$) exhibited signals at δ 1.83 (t, 2H), assigned to the methylene H-15 protons, an N-methyl group, δ 2.70 (s, 3H), four methoxyl groups, δ 2.92 (s, 3 H), 3.55 (s, 3 H), 3.64 (s, 3 H), and 3.90 (s, 3 H), the H-10 and H-16 protons at δ 3.00–3.50 (m, 4 H), the H-19 proton at δ 4.40 (d, 1 H, J = 13 Hz), the H-5 proton at δ 4.80 (s, 1 H), the H-7 proton at δ 5.62 (d, 1 H, J = 10 Hz), the H-8 proton at δ 6.60 (d, 1 H, J = 10 Hz), the vinyl proton at H-9, δ 5.94 (dd, 1 H), the two aromatic protons H-1, H-2, δ 6.65 (s, 2 H), and the H-18 proton, δ 7.35 (d, 1 H, J = 13 Hz). The coupling constants of the H-18 and H-19 protons (J = 13 Hz) indicated that the stereochemistry was trans.[6,7]

Brief exposure of **8** to either 1.5 equiv of 6 N HCl in H_2O–MeOH or to 1.5 equiv of *p*-toluenesulfonic acid in MeOH converted the ketal **8** to the adduct **5** in 55% yield. Treatment of **8** with 10 equiv of 6 N HCl for 5 min converted it probably via **5**, to the ketone **7** in 67% yield: mp 225 °C;[3] $[\alpha]_D$ −307° ($CHCl_3$); mass spectrum, m/e 381 (M^+); IR (KBr) 1725, 1665 cm^{-1}; ^1H NMR δ 1.70–2.13 (m, 2 H, H-15), 2.40–2.90 (m, 2 H, H-7), 3.03 (s, 3 H, NCH_3), 3.20 (d, 2 H, H-10), 3.48 (m, 2 H, H-16), 3.73 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 4.42 (br t, 1 H, H-8), 5.06 (s, 1 H, H-5), 5.90 (dd, 1 H, H-9), 6.68 (s, 2 H, H-1, H-2), 7.42 (s, 1 H, H-18). The stereostructure as determined by single-crystal X-ray and the relevant crystallographic data are shown in Figure 1.

When the ketal **8** was heated for several days with NaOH in EtOH, an oily base, **9**, was obtained in 53% yield; the IR spectrum of **9** showed the absence of carbonyl absorption, and the mass spectrum (M^+, m/e 343) and UV spectrum (λ_{max} (EtOH) 214 (log ϵ 4.29), 249 (log ϵ 3.98), 319 nm (log ϵ 3.90) suggested loss of the acrylate residue and double bond isomerization. The NMR spectrum also indicated that the diene system of **8** had shifted into conjugation with the aromatic ring and that the acrylic ester group had been lost. The ^1H NMR spectrum exhibited an NH signal at δ 1.20 (s, 1 H), which exchanged with D_2O, H-15 protons at δ 1.60–2.06 (br t, 2 H), an NCH_3 singlet and the H-7 and H-16 protons at δ 2.06–2.70 (m, 7 H), three methoxyl singlets at δ 2.91 (s, 3 H), 3.53 (s, 3 H), 3.90 (s, 3 H), the H-5 proton at δ 5.00 (s), the H-8 proton at δ 5.50–5.70 (dd, 1 H), the H-9 proton at δ 6.00 (d, 1 H, J = 10 Hz), the H-10 proton at δ 6.36 (d, 1 H, J = 10 Hz), and two aromatic protons at δ 6.61 (s, 2 H). The base furnished a crystalline fumarate, mp 205 °C (MeOH–THF). When **9** was allowed to react with MP in MeOH, a yellow crystalline solid, **10**, mp 125–127 °C, was obtained in 70% yield. The same compound was obtained



10



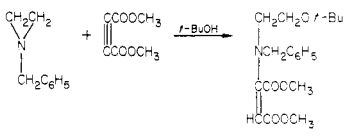
11

in 80% yield by treating **8** with NaOH in aqueous MeOH for 2 h: $[\alpha]_D$ +265° ($CHCl_3$); IR (KBr) 1685 cm^{-1}; UV(EtOH) λ_{max} 282 (log ϵ 4.49), 326 nm (log ϵ 3.81); ^1H NMR ($CDCl_3$) δ 1.66–2.08 (m, 2 H, H-15), 2.12–2.56 (dd, 2 H, H-7), 2.71 (s, 3 H, NCH_3), 2.94 (s, 3 H, OCH_3), 3.03–3.40 (m, 2 H, H-16), 3.58 (s, 3 H, OCH_3), 3.65 (s, 3 H, OCH_3), 3.92 (s, 3 H, OCH_3), 4.48 (d, 1 H, H-19, J = 13 Hz), 4.86 (s, 1 H, H-5), 5.68 (dd, 1 H, H-8), 6.12 (d, 1 H, H-9, J = 10 Hz), 6.40 (d, 1 H, H-10, J = 10 Hz), 6.64 (s, 2 H, H-1, H-2), 7.34 (d, 1 H, H-18, J = 13 Hz). It is clear from a

(5) Satisfactory elementary analyses were obtained for all new compounds. Combustion analyses were performed in the Spang Microanalytical Laboratory, Eagle Harbor, MI.

(6) F. E. Herkes and H. E. Simmons, *J. Org. Chem.*, **38**, 2845 (1973), found that tertiary amines added to methyl propiolate to give (carbomethoxy)vinylalkylammonium compounds in which the vinyl protons were trans (J = 13.8–14.0 Hz). Addition to DMAD took place in an analogous manner to give the corresponding maleate esters. See also ref. 7.

(7) E. Winterfeldt and H. J. Dillinger, *Chem. Ber.*, **99**, 1558 (1960). DMAD and *N*-benzylaziridine in *tert*-butyl alcohol at room temperature furnished the adduct i in 41% yield.



i

comparison of the spectroscopic data of both ketals that **10** differs from **8** only in the position of the diene system. When **10** was treated with 1.5 equiv of *p*-toluenesulfonic acid in methanol for 3 h, cyclization did not occur; instead, the acrylate ester group was lost, giving **9**, isolated as the known fumarate (40%).

When thebaine and DMAD were allowed to react for 15 min in MeOH, the ketal **11** was obtained in 35% yield: mp 172–174 °C: $[\alpha]_D$ −109°C ($CHCl_3$); UV(EtOH) λ_{max} 284 nm (log ϵ 4.09); IR (KBr) 1740, 1690 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.88 (t, 2 H, H-15), 2.74 (s, 3 H, NCH_3), 2.92 (s, 3 H, OCH_3), 3.05–3.45 (m, 4 H, H-10, H-16), 3.55 (s, 3 H, OCH_3), 3.61 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 3.90 (s, 3H, OCH_3), 4.51 (s, 1 H, H-19), 4.75 (s, 1 H, H-5), 5.62 (d, 1 H, H-7, J = 10 Hz), 5.94 (dd, 1 H, H-9), 6.59 (d, 1 H, H-8, J = 10 Hz), 6.67 (s, 2 H, H-1, H-2). The NMR spectrum of **11** was similar to that of **8** except for the presence of additional OCH_3 protons and the absence of an H- 18 proton signal. Accordingly, the signal for the H-19 proton appeared as a singlet at δ 4.51, characteristic of a dialkyl aminomaleate.[6] Hydrolysis of **11** with NaOH over a period of several days afforded **9**, the fumarate of which was identical with that obtained previously.

Preliminary experiments with EP and thebaine in MeOH suggested that a ketal corresponding to **8** was obtained. Thus, the condensation of acetylenic dienophiles with thebaine in methanol to produce ketals such as **8** and **11** seems to be general.

Acknowledgment. We thank Dr. Denis M. Bailey and Dr. Stephen M. Clemans of the Sterling-Winthrop Research Institute for some of the NMR and mass spectra and the National Institute on Drug Abuse for financial support. A. Singh thanks G.M.D.U., Amritsar, India for a grant of leave.

Registry No. **1**, 115-37-7; **5**, 78923-43-0; **7**, 78914-30-4; **8**, 80410-25-9; **9**, 80410-26-0; **9** fumarate, 80446-41-9; **10**, 80410-27-1; **11**, 80410-28-2; methyl propiolate, 922-67-8; dimethyl acetylenedicarboxylate, 762-42-5.

Supplementary Material Available: Tables I–III, listing fractional coordinates and temperature factors for **2** and bond distances and angles for **7** (4 pages). Ordering information is given on any current masthead page.

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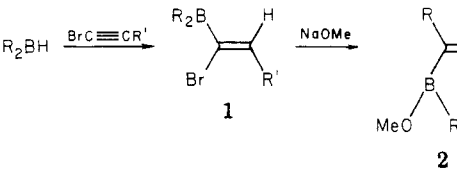
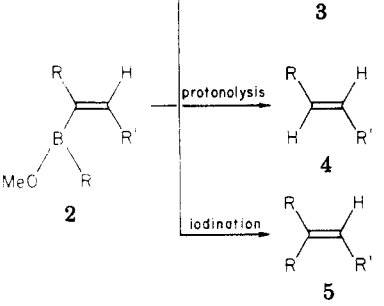
A General Synthesis of *B*-(*cis*-1-Bromo-1-alkenyl)dialkylboranes. Valuable Intermediates for the Synthesis of Ketones, Trans Alkenes, and Trisubstituted Alkenes

Summary: Dialkylboranes, generated in situ via hydridation of dialkylhaloboranes, hydroborate 1-bromo-1-alkynes to provide cleanly *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes. Treatment of these intermediates with sodium methoxide results in the migration of one of the alkyl groups on boron to the adjacent carbon, displacing the bromine, providing *B*-(*trans*-1-alkyl-1-alkenyl)alkylborinate esters. These intermediates provide ketones on oxidation, stereospecific trans alkenes on protonolysis, and trisubstituted alkenes on iodination, all in high yields.

Sir: Hydroboration of 1-halo-1-alkynes with dialkylboranes results in the formation of *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes (**1**).[1-3] As demonstrated by Zweifel and coworkers,[1-3] these vinylboranes are valuable synthetic intermediates. Thus, treatment with base induces migration of one of the alkyl groups from boron to the attached carbon, providing vinylboron intermediates (**2**) not available by direct hydroboration (eq 1). These intermediates (**2**) can be readily transformed into ketones (**3**)[1] via oxidation, into trans alkenes (**4**)[1,3] via protonolysis, and into trisubstituted alkenes (**5**)[2] via iodination (eq 2).



(1)



(2)

However, the applicability of this reaction sequence is presently restricted by the availablility of stable dialkylboranes. Only in the case of relatively hindered alkenes, such as cyclohexene, α-pinene, etc., does direct hydroboration lead cleanly to the formation of dialkylboranes. Consequently, this route has had limited application in organic synthesis.

Recently a convenient general method for the preparation of dialkylboranes via hydridation of dialkylhaloboranes has been developed in this laboratory.[4] We reported that these dialkylboranes hydroborate terminal and internal alkynes to provide the corresponding dialkylvinylboranes[5] which serve as valuable intermediates for the synthesis of cis alkenes[6] and trisubstituted alkenes,[7] greatly extending the generality of the Zweifel syntheses. We now report the utility of such dialkylboranes for a general synthesis of *B*-(*cis*-1-bromo-1-alkenyl)dialkylboranes and their transformations into ketones, trans alkenes, and trisubstituted alkenes.

Dialkylboranes, generated in situ via the hydridation of dialkylhaloboranes, hydroborate 1-bromo-1-alkynes cleanly to provide the corresponding *B*-(*cis*-1-bromo-1-alkenyl)-

(1) Zweifel, G.; Arzoumanian, H. *J. Am. Chem. Soc.* **1967**, *89*, 5086.
(2) Zweifel, G.; Fisher, R. P. *Synthesis* **1972**, 557.
(3) Zweifel, G.; Fisher, R. P.; Snow, J. T.; Whitney, C. C. *J. Am. Chem. Soc.* **1971**, *93*, 6309.
(4) Brown, H. C.; Kulkarni, S. U. *J. Organometal. Chem.* **1981**, *218*, 309.
(5) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Organometal. Chem.*, in press.
(6) Kulkarni, S. U.; Basavaiah, D.; Brown, H. C. *J. Organometal. Chem.*, in press.
(7) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, *47*, 171.

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