pounds 7, 10, and 12. General procedure: A solution of 3-(diethylamino)-2(1*H*)-pyrazinone (1 mmol) in freshly dried toluene (10 mL) containing 3 equiv of dienophile was heated at 60 °C until all starting material had disappeared. The solvent was evaporated under reduced pressure, and the residue was purified by chromatography (ethyl acetate–chloroform) on a silica gel column. The product was then recrystallized from hexane–chloroform.

Dimethyl 2-Cyano-5-(diethylamino)-1,6-dihydro-6-oxo-1-phenyl-3,4-pyridinedicarboxylate (7a). After reaction for 3 h followed by chromatography this compound was obtained from **5a** and dimethyl butynedioate in a yield of 363 mg (95%): mp 118–119 °C; IR (KBr) 2230 (CN), 1720 (ester), 1665 (lactam) cm^{-1}; ^1H NMR δ 1.3 (t, 6 H, NCH_2CH_3), 3.45 (q, 4 H, NCH_2CH_3), 4.0 (s, 6 H, CO_2CH_3), 7.4 (m, 5 H, ArH); MS (*m/z*) 383 (M^+, 54), 368 ($M^+ - CH_3$, 100), 351 ($M^+ - CH_3OH$, 65), 322 (91); HRMS calcd for $C_{20}H_{21}N_3O_5$ (M^+), 383.1481, found 383.1490. Anal. Calcd for $C_{20}H_{21}N_3O_5$: C, 62.66; H, 5.52; N, 10.96. Found: C, 62.28; H, 5.43; N, 10.71.

Dimethyl 2-Cyano-5-(diethylamino)-1,6-dihydro-1-methyl-6-oxo-3,4-pyridinedicarboxylate (7b). After reaction for 3 h this compound was obtained from **5b** in a yield of 299 mg (93%): mp 87–88 °C; IR (KBr) 2220 (CN), 1740 (ester), 1720 (ester), 1665 (lactam) cm^{-1}; ^1H NMR δ 1.3 (t, 6 H, NCH_2CH_3), 3.3 (q, 4 H, NCH_2CH_3), 3.8 (s, 3 H, CH_3), 3.9 (s, 3 H, CO_2CH_3), 3.95 (s, 3 H, CO_2CH_3); ^{13}C NMR δ 13.7 (q, NCH_2CH_3), 35.3 (q, NCH_3), 46.3 (t, NCH_2CH_3), 52.6 (q, OCH_3), 53.1 (q, OCH_3), 111.8 (s, CN), 116.8 (q, C-2, ^3J = 4), 118.3 (s, C-3), 132.0 (s, C-4), 143.6 (m, C-5, ^3J = 3), 159.8 (q, C-6, ^3J = 2), 163.0 (q, C=O, ^3J = 5), 165.6 (q, C=O, ^3J = 5); MS (*m/z*) 321 (M^+, 30), 306 ($M^+ - CH_3$, 100), 290 ($M^+ - OCH_3$, 26), 260 (46), 246 (39); HRMS calcd for $C_{15}H_{19}N_3O_5$ (M^+) 321.1325, found 321.1322. Anal. Calcd for $C_{15}H_{19}N_3O_5$: C, 56.07; H, 5.96; N, 13.08. Found: C, 55.76; H, 5.87; N, 13.00.

Ethyl 6-Cyano-3-(diethylamino)-1,2-dihydro-2-oxo-1-phenyl-4-pyridinecarboxylate (7c). After reaction for 8 h this compound was obtained from **5a** and ethyl propynoate in a yield of 288 mg (85%): mp 84 °C; IR (KBr) 2230 (CN), 1735 (ester), 1665 (lactam) cm^{-1}; ^1H NMR δ 1.25 (t, 6 H, NCH_2CCH_3), 1.4 (t, 3 H, $CO_2CH_2CH_3$), 3.5 (q, 4 H, NCH_2CH_3), 4.3 (q, 2 H, $CO_2CH_2CH_3$), 7.1 (s, 1 H, H-5), 7.4 (m, 5 H, ArH); ^{13}C NMR δ 13.5 (NCH_2CH_3), 14.1 (OCH_2CH_3), 46.4 (NCH_2CH_3), 61.4 (OCH_2CH_3), 109.4 (d, C-6, ^2J = 3), 113.2 (d, CN, ^3J = 5), 117.8 (d, C-5, ^1J = 174), 120.6 (s, C-4), 127.5, 128.3, 129.5 (C-Ar), 137.8 (C-ipso), 146.3 (m, C-3), 160.1 (C-2), 164.7 (C=O); MS (*m/z*) 339 (M^+, 43), 324 ($M^+ - CH_3$, 56), 310 ($M^+ - C_2H_5$, 100), 264 (73); HRMS calcd for $C_{19}H_{21}N_3O_3$ (M^+) 339.1583, found 339.1586. Anal. Calcd for $C_{19}H_{21}N_3O_3$: C, 67.24; H, 6.24; N, 12.38. Found: C, 67.20; H, 6.22; N, 12.40.

5-(Diethylamino)-1,6-dihydro-6-oxo-1,4-diphenyl-2-pyridinecarbonitrile (7d). After reaction for 12 h this compound was obtained from **5a** and phenylacetylene in a yield of 305 mg (89%): mp 140–141 °C; IR (KBr) 2220 (CN), 1660 (lactam) cm^{-1}; ^1H NMR δ 1.0 (t, 6 H, NCH_2CH_3), 3.05 (q, 4 H, NCH_2CH_3), 6.85 (s, 1 H, H-3), 7.6–7.15 (m, 10 H, ArH); ^{13}C NMR δ 13.6 (q, NCH_2CH_3), 45.9 (t, NCH_2CH_3), 112.4 (d, C-2, ^2J = 2.6), 113.5 (d, CN, ^3J = 5), 120.3 (d, C-3, ^1J = 171), 127.7, 127.8, 128.6, 129.3, 129.5, 129.6 (m, CAr), 136.7 (m, C-4), 138.0, 138.3 (2 × C-ipso), 143.1 (m, C-5), 161.1 (s, C-6); MS (*m/z*) 343 (M^+, 55), 328 ($M^+ - CH_3$, 59), 314 ($M^+ - C_2H_5$, 100), 299 (73); HRMS calcd for $C_{22}H_{21}N_3O$ (M^+) 343.1685, found 343.1686. Anal. Calcd for $C_{22}H_{21}N_3O$: C, 76.94; H, 6.16; N, 12.24. Found: C, 76.64; H, 6.02; N, 11.93.

Methyl 3-(Diethylamino)-1,2-dihydro-6-methyl-2-oxo-1-phenyl-4-pyridinecarboxylate (10). After reaction of compound **9** with methyl propynoate for 8 h, this compound was isolated in a yield of 47 mg (15%): mp 85–86 °C; IR (KBr) 1740 (ester), 1665 (lactam) cm^{-1}; ^1H NMR δ 1.05 (t, 6 H, NCH_2CH_3), 1.95 (s, 3 H, CH_3), 3.15 (q, 4 H, NCH_2CH_3), 3.9 (s, 2 H, CO_2CH_3), 6.1 (s, 1 H, H-5), 7.4 (m, 5 H, ArH); ^{13}C NMR 21.2 (qd, 6-CH_3), 103.5 (dq, C-5, ^1J = 168) MS (*m/z*) 314 (M^+, 100), 299 ($M^+ - CH_3$, 97), 285 ($M^+ - C_2H_5$, 85), 271 (35); HRMS calcd for $C_{18}H_{22}N_2O_3$ (M^+) 314.1630, found 314.1627.

Dimethyl 5-(Diethylamino)-1,6-dihydro-6-oxo-1-phenyl-3,4-pyridinedicarboxylate (12). After reaction of **11** with dimethyl butynedioate for 3 h, this compound was isolated in a yield of 305 mg (85%): mp 89–90 °C; IR (KBr) 1730 (ester), 1665 (lactam) cm^{-1}; ^1H NMR δ 1.0 (t, 6 H, NCH_2CH_3), 3.1 (q, 4 H, NCH_2CH_3), 3.75 (s, 3 H, CO_2CH_3), 3.9 (s, 3 H, CO_2CH_3), 7.4 (m, 5 H, ArH), 8.2 (s, 1 H, H-2); MS (*m/z*) 358 (M^+, 89), 329 ($M^+ - C_2H_5$, 21), 327 ($M^+ - OCH_3$, 47), 299 ($M^+ - CO_2CH_3$, 100); HRMS calcd for $C_{19}H_{22}N_2O_5$ (M^+) 358.1529, found 358.1533. Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.68; H, 6.19; N, 7.82. Found: C, 63.54; H, 6.15; N, 7.75.

Reactions of 5-Chloro-3-(diethylamino)-2*H*-1,4-oxazin-2-one 6 with Acetylenic Compounds: Generation of Compounds 8. General procedure: A solution of compound **6** (1 mmol) in neat acetylenic compound (3 mL) was stirred at room temperature until compound **6** had disappeared. Workup and purification of compounds **8** was done as for compound **7** using silica gel plates and chloroform as eluent.

Methyl 6-Cyano-3-(diethylamino)-2-oxo-2*H*-pyran-4-carboxylate (8a). After reaction for 1 h compound **8a** was obtained as an oil from **6** and methyl propynoate in a yield of 188 mg (75%): IR (KBr) 2225 (CN), 1740 (CO) cm^{-1}; ^1H NMR δ 1.2 (t, 6 H, NCH_2CH_3), 3.5 (q, 4 H, NCH_2CH_3), 3.9 (s, 3 H, CO_2CH_3), 7.2 (s, 1 H, H-5); ^{13}C NMR δ 13.4 (CH_2CH_3), 47.4 (CH_2CH_3), 52.5 (OCH_3), 112.4 (d, CN, ^3J = 4), 116.4 (s, C-4), 118.3 (d, C-5, ^1J = 175), 121.6 (d, C-6, ^2J = 4), 141.8 (m, C-3), 158.1 (C-2), 163.6 (CO_2CH_3); MS (*m/z*) 250 (M^+, 100); HRMS calcd for $C_{12}H_{14}N_2O_4$ (M^+) 250.0954, found 250.0950.

3-(Diethylamino)-4-phenyl-2-oxo-2*H*-pyran-6-carbonitrile (8b). After reaction for 40 h compound **8b** was obtained from compound **6** and phenyl acetylene in a yield of 91 mg (34%): mp 84 °C; IR (KBr) 2218 (CN), 1724 (CO) cm^{-1}; ^1H NMR δ 1.0 (t, 6 H, NCH_2CH_3), 3.0 (q, 4 H, NCH_2CH_3), 6.8 (s, 1 H, H-5), 7.5–7.3 (m, 5 H, ArH); ^{13}C NMR δ 13.4 (q, NCH_2CH_3), 46.0 (t, NCH_2CH_3), 112.6 (d, CN, ^3J = 4), 121.1 (d, C-5, ^1J = 171), 125.0 (d, C-6, ^2J = 4), 127.5, 128.8 (C-Ar), 135.0 (m, C-4), 136.5 (C-ipso), 137.3 (m, C-3), 159.3 (s, C-2); MS (*m/z*) 268 (M^+, 100); HRMS calcd for $C_{16}H_{16}O_2N_2$ (M^+) 268.1212, found 268.1207.

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Registry No. 1 (R^1 = Ph, R^3 = Cl), 87486-37-1; 1 (R^1 = Me, R^3 = Cl), 87486-33-7; **2** (R^3 = Cl), 125850-02-4; **5a**, 139706-32-4; **5b**, 139706-33-5; **6**, 139706-34-6; **7a**, 139706-35-7; **7b**, 139706-36-8; **7c**, 139706-37-9; **7d**, 139706-38-0; **8a**, 139706-39-1; **8b**, 139706-40-4; **9**, 139706-43-7; **10**, 139706-41-5; **11**, 139706-44-8; **12**, 139706-42-6; diethylamine, 109-89-7; dimethyl acetylenedicarboxylate, 762-42-5; ethyl propiolate, 623-47-2; phenylacetylene, 536-74-3.

Supplementary Material Available: ^1H and ^{13}C NMR spectra of **8a** and **8b** (9 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

An Asymmetric Synthesis of Crobarbatic Acid

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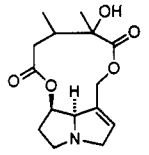
The knowledge that pyrrolizidine alkaloids are highly biologically active[1] has ensured that the synthesis[2] of such

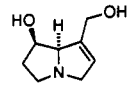
(1) For recent reviews, see: (a) Robins, D. J. In *Fortsch. Chem. Org. Naturstoffe/Progr. Chem. Org. Nat. Prod.*; Herz, W., Grisebach, H., Kirby, G. W., Eds.; Spring-Verlag: Vienna, 1982; Vol. 41. (b) Robins, D. J. *Nat. Prod. Rep.* **1989**, 221.

0022-3263/92/1957-2937$03.00/0

compounds continues to be the goal of much effort. Crobarbatine (1) is an 11-membered dilactone which incorporates a necine base (retronecine, 2) and 2-hydroxy-2,3-dimethylglutaric acid (3).[3] The hydrolysis of crobarbatine yields retronecine and crobarbatic acid (4), the product of the spontaneous lactonization of 2-hydroxy-2,3-dimethylglutaric acid. Crobarbatic acid has been shown to bear two trans methyl groups;[2a] however, its absolute configuration is still unknown.[2a,3]



1



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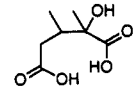


3

We have already described[4] an efficient method for preparing racemic crobarbatic acid via the reaction of ethyl pyruvate with the 2-propenyl-1,3-dithian-2-ylzinc reagent derived from 5 (Scheme I). The involvement of a chelate transition state (A) was hypothesized to account for the stereochemistry that is generated in the product. In addition to being a masked form of the dicarboxylic acid 3, the ketene dithioacetal 6 has the potential for regioselective elaboration to crobarbatine by esterification of retronecine at the allylic hydroxyl group[2a] and macrocyclization subsequent to hydrolysis of the ketenedithioacetal moiety.[5] Prior to the pursuit of this project, we investigated preparation of crobarbatic acid in optically pure form.

Attempts to kinetically resolve the ethyl ester 6 via enzymatic hydrolysis were unsuccessful. Treatment of 6 with a protease (Amanon) or any of nine lipases (AK, Ap 6, FAP 15, M-AP 10, N Conc, OF, P-Amano, Poncreo, and R-Amano 10) in phosphate buffer (pH 6.9) for as long as 1 week failed to effect any appreciable hydrolysis. The reluctance of 6 to undergo enzymatic hydrolysis is believed to be a consequence of the presence of the 3-methyl group for the structurally similar esters ethyl 2-methyl-3-(1,3-dithian-2-yl)propanoate and methyl 2-methyl-2-(benzyloxy)-4-pentenoate are readily hydrolyzed under the conditions described.

Since the first report[7] of its use in such a role, the (−)-8-phenylmenthoxy group has found wide employment as a chiral auxiliary.[8] Therefore, we decided to attempt an asymmetric synthesis of crobarbatic acid starting from (−)-8-phenylmenthyl pyruvate (7). Whitesell et al.[8b] showed that Grignard reagents attack the chiral pyruvate 7 at its *si*-diastereotopic face when the oxygen atoms of the two carbonyl groups are synclinally coordinated with the Mg^{2+} ion. From this observation and the inspection of molecular models, it was concluded that the addition to the ester 7 of a crotylmetal generated from 2-propenyl-1,3-dithiane 5 would proceed by way of a chelate transition state similar to A and would furnish a product

Scheme I

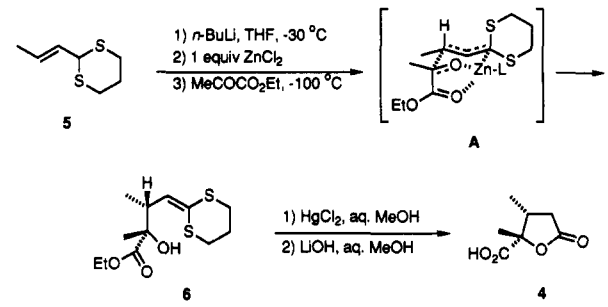


Table I. Results of the Addition of the Crotyllithium Derived from 2-Propenyl-1,3-dithiane (5) to the (−)-Phenylmenthyl Pyruvate 7 in the Presence of Various Additives

entry	additive (1 equiv)	reactn temp (°C)	product ratio[a] 8a:8b:8c:8d	total yield of 8a–d (%)	total yield of 9a–d[b] (%)
1		−78	30:20:30:20	82	68
2	$MgCl_2$[c]	−78	30:35:10:25	78	65
3	$ZnCl_2$	−78	20:30:30:20	68	
4	$ZnCl_2$	−78 to −40[d]	25:38:12:25	76	62
5	$ZnCl_2$ (3 equiv)	−78 to −40	23:34:16:27	57	
6	$ZnCl_2$	−100	26:35:18:21	84	70
7	$MgCl_2$; BF_3·OEt_2[e]	−78 to rt		28[f]	

[a] The ratio was calculated from the results of ^1H NMR analysis of the mixture of crude products. Both 8a and 8d could be isolated in pure form; however, 8b and 8c formed an inseparable mixture. The 8b:8c ratio was calculated from that of the corresponding hydrolysis products, 9b and 9c. [b] Overall yield (two steps) based on the dithiane 5. [c] Attempted direct deprotonation by treatment with MeMgCl at −30 °C was unsuccessful. [d] The pyruvate 7 was added at −78 °C. The mixture was then allowed to warm to −40 °C. The reaction was quenched 30 min later. [e] $MgCl_2$ (1 equiv) and BF_3·OEt_2 (1 equiv) were added in that order. The pyruvate 7 was added at −78 °C. The mixture was then allowed to warm to rt. The reaction was quenched 2 h later. [f] No reaction occurred at −78 °C. When the reaction temperature was raised to rt, the products 8 (28%), 5 (42%), and (−)-8-phenylmenthol (33%) were isolated.

which displays the desired stereochemistry. To our disappointment, the reaction of the pyruvate 7, unlike that of ethyl pyruvate, was not stereoselective (Table I). The reaction mediated by a divalent counterion such as Mg^{2+} or Zn^{2+} only showed a modest preference for the 2*S*-products (8a + 8b) and the relative 2,3-threo configuration (8b + 8d). The relative configurations of the four addition products, 8a–d (R* = (−)-8-phenylmenthyl), were established by ^1H NMR analysis of the corresponding γ-lactones (9a–d, respectively) as well as by an X-ray crystallographic analysis of 9a. The ^1H NMR spectra show that the protons of the 2-methyl group of both 9b (the 2*S*,3*S*-isomer) and 9d (the 2*R*,3*R*-isomer) are diamagnetically shielded by the adjacent 3-methyl group because they absorb at higher fields than the corresponding protons of 9a (the 2*S*,3*R*-isomer) and 9c (the 2*R*,3*S*-isomer).[5d,9] Likewise, dia-

(2) For leading references to the total synthesis of pyrrolizidine alkaloids, see: (a) Huang, J.; Meinwald, J. *J. Am. Chem. Soc.* **1981**, *103*, 861. (b) Brown, K.; Devlin, J. A.; Robins, D. J. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1819. (c) Narasaka, K.; Sakakura, T.; Uchimura, T.; Guedin-Vuong, D. *J. Am. Chem. Soc.* **1984**, *106*, 2954. (d) White, J. D.; Ohira, S. *J. Org. Chem.* **1986**, *51*, 5492. (e) Vedejs, E.; Ahmad, S.; Larsen, S. D.; Westwood, S. *J. Org. Chem.* **1987**, *52*, 3937. (f) Niwa, H.; Okamoto, O.; Yamada, K. *Tetrahedron Lett.* **1988**, *29*, 5139.

(3) Puri, R. L.; Sawhney, R. S.; Atal, C. K. *Experientia* **1973**, *29*, 390.

(4) Fang, J. M.; Hong, B. C. *J. Org. Chem.* **1987**, *52*, 3162.

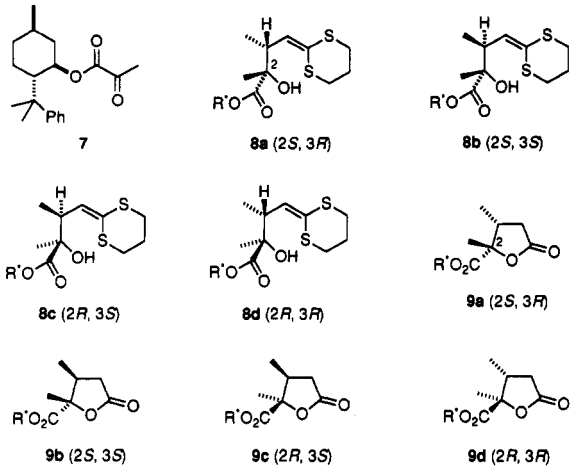
(5) (a) Corey, E. J.; Beams, D. J. *J. Am. Chem. Soc.* **1973**, *95*, 5829. (b) Seebach, D.; Kolb, M. *Liebigs Ann. Chem.* **1977**, 811. (c) Suzuki, K.; Masuda, T.; Fukazawa, Y.; Tsuchihashi, G.-I. *Tetrahedron Lett.* **1986**, *27*, 3661. (d) Fang, J. M.; Hong, B. C.; Liao, L. F. *J. Org. Chem.* **1987**, *52*, 855.

(6) (a) Gu, R. L.; Sih, C. J. *Tetrahedron Lett.* **1990**, *31*, 3283. (b) Sugai, T.; Kakeya, H.; Ohta, H. *J. Org. Chem.* **1990**, *55*, 4643.

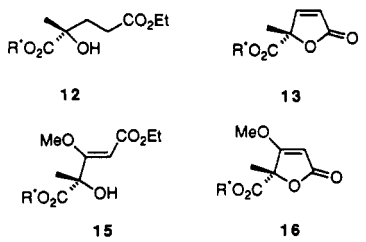
(7) Corey, E. J.; Ensley, H. E. *J. Am. Chem. Soc.* **1975**, *97*, 6908.

(8) For example, see: (a) Oppolzer, W. *Angew, Chem.* **1984**, *96*, 840; *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 876 and references cited therein. (b) Whitesell, J. K.; Bhattacharya, A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 988. (c) Grossen, P.; Herold, P.; Mohr, P.; Tamm, C. *Helv. Chim. Acta* **1984** *67*, 1625. (d) Weuthen, M.; Scharf, H.-D.; Runsink, J.; Vaßen, R. *Chem. Ber.* **1988**, *121*, 971. (e) Ihara, M.; Takahashi, M.; Nitsuma, H.; Taniguchi, N.; Yasui, K.; Fukumoto, K. *J. Org. Chem.* **1989**, *54*, 5413. (f) Hubscher, J.; Barner, R. *Helv. Chim. Acta* **1990**, *73*, 1068. (g) Solladie-Cavallo, A. *Tetrahedron* **1991**, *47*, 249.

magnetic shielding by the 2-methyl group causes the protons of the 3-methyl group of both **9b** and **9d** to resonate at higher fields than the corresponding protons of **9a** and **9c**.

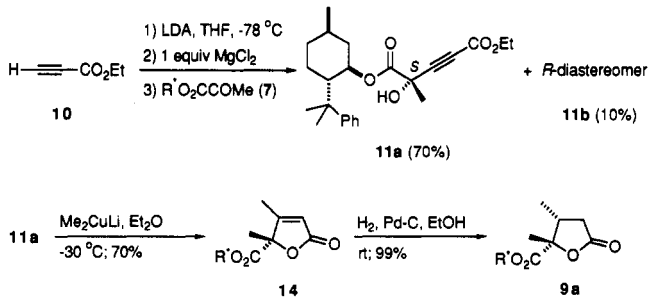


At this point, a different route to derivatives of crobarbatic acid was investigated. This first step involved the nucleophilic addition of the alkynyllithium generated from ethyl propiolate (**10**) to the chiral pyruvate **7**. In the presence of Mg^{2+}, the addition occurred stereoselectively to afford a 70% isolated yield of the (2*S*)-alcohol **11a**.[8b] To convert **11a** to crobarbatic acid, it was necessary to reduce the triple bond to a cis double bond and to introduce a methyl group at the 3-position. The hydrogenation of **11a** in the presence of Lindlar catalyst gave only **12**, a product of overreduction, which has served as an intermediate in a synthesis of (−)-frontalin.[10] Compound **11a** was not reduced at all when 5% $Pd/CaCO_3$ poisoned with quinoline was the catalyst. However, upon treatment with $Pd(OAc)_2(PPh_3)_2/HCO_2H$,[11] **11a** gave the furanone **13**. The addition of lithium dimethylcuprate to **13** yielded a 1:1 mixture of desired crobarbatate (**9a**) and its C-3 epimer (**9b**).[12] On the other hand, treatment of the alkynoate **11a** with lithium dimethylcuprate gave the furanone **14**, hydrogenation (10% Pd/C, EtOH) of which afforded, exclusively, the crobarbatate **9a**. In contrast, the reduction of **14** by treatment with magnesium[13] was less stereoselective than catalytic hydrogenation and gave a 1:2 mixture of **9a** and **9b**. Interestingly, if oxygen is not completely excluded during treatment of **11a** with lithium dimethylcuprate, only the methoxylated compounds **15** (27%) and **16** (32%) are isolated.



Thus, an expeditious synthesis of the crobarbatic acid ester **9a** (Scheme II), which involved (1) addition to the chiral pyruvate **7** of an alkynylmetal generated from ethyl propiolate, (2) addition to the alkynoate of lithium dimethylcuprate, and (3) the catalytic hydrogenation of the unsaturated lactone product, was achieved. Efforts directed toward a total synthesis of crobarbatine are now under way.

Scheme II



Experimental Section

Melting points are uncorrected. Electron impact mass spectra were recorded at an ionization voltage of 70 eV. Merck silica gel 60F sheets were used for analytical TLC. Column chromatography was performed with silica gel (70–230 mesh). Analytical and preparative HPLC were performed with a liquid chromatograph equipped with a refractive index detector. The column was a 1-cm i.d. × 25-cm stainless steel Hibar column packed with Lichrosorb Si 60 (7-μm particle size). A flow rate of 5 mL/min was maintained. Et_2O and THF were distilled under N_2 from sodium benzophenone ketyl. Anhydrous CuI, $MgCl_2$, and $ZnCl_2$ were heated in vacuo at 100 °C for 2 h before use. $Pd(OAc)_2(PPh_3)_2$ was prepared by a literature method.[11] (−)-8-Phenylmenthyl pyruvate (**7**) was prepared in 70% yield by the acid-catalyzed esterification of pyruvic acid and (−)-8-phenylmenthol. The latter was prepared from (*R*)-pulegone.[14]

5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 4-(1,3-Dithian-2-ylidene)-2-hydroxy-2,3-dimethylbutanoate (8a–d). The procedure described is typical of those that gave the results shown in Table I. *n*-BuLi (0.6 mmol, 0.375 mL of a 1.6 M solution in hexane) was added drop-by-drop to a cold (−40 °C) stirred solution of 2-propenyl-1,3-dithiane (80 mg, 0.5 mmol) in THF (5 mL) under N_2. After 15 min, anhydrous $ZnCl_2$ (68 mg, 0.5 mmol) was added to the solution of crotyllithium that resulted. After 15 min the mixture was cooled to −100 °C, and a solution of 8-phenylmenthyl pyruvate **7** (151 mg, 0.5 mmol) in THF (2 mL) was added drop-by-drop. Thirty min later, the reaction was quenched by adding a solution of HOAc (0.1 mL) in THF. The mixture was concentrated (rotary evaporator). The residue was taken up in EtOAc. The mixture was washed with brine, dried (Na_2SO_4), and filtered and then concentrated in vacuo. The residue was passed through a column of silica gel (EtOAc:hexane = 5:95) to give **8a–d** in 84% total yield. Compounds **8a** (the 2*S*,3*R*-isomer) and **8d** (the 2*R*,3*R*-isomer) were isolated by HPLC. However, **8b** (the 2*S*,3*S*-isomer) and **8c** (the 2*R*,3*S*-isomer) formed an inseparable mixture. **8a**: an oil, IR (neat) 3564, 1719, 1574 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.78–1.75 (6 H, m), 0.88 (3 H, d, *J* = 6.4 Hz, Me), 0.89 (3 H, d, *J* = 6.5 Hz, Me), 1.13 (3 H, s, Me), 1.24 (3 H, s, Me), 1.33 (3 H, s, Me), 1.77–2.23 (4 H, m), 2.70–2.95 (4 H, m, two SCH_2), 3.03 (1 H, dq, *J* = 10.0, 6.5 Hz), 4.93 (1 H, ddd, *J* = 10.6, 10.6, 4.4 Hz), 5.88 (1 H, d, *J* = 10.0 Hz), 7.10–7.38 (5 H, m, PhH); ^{13}C NMR ($CDCl_3$, 50 MHz, DEPT) δ 14.0 (q), 21.8 (q), 23.4 (q), 24.5 (q), 25.2 (t), 27.3 (t), 27.9 (t), 28.8 (t), 31.4 (d), 34.3 (q), 40.3 (s), 42.0 (t), 44.0 (d), 48.6 (t), 50.1 (d), 76.5 (d), 77.2 (s, C-2), 125.3 (d), 125.4 (d), 125.7 (d), 128.1 (two CH), 128.3 (d), 133.2 (s), 150.9 (s), 171.3 (s, CO_2R^*); MS *m/z* (rel intensity) 462 (1, M^+), 444 (3, $[M - 18]^+$), 214 (12), 203 (19), 199 (42), 159 (32), 145 (23), 119 (100). **8b**: ^1H NMR (partial) δ 0.85 (3 H, d, *J* = 6.4 Hz, Me), 0.97 (3 H, d, *J* = 6.5 Hz, Me), 1.13 (3 H, s, Me), 1.19 (3 H, s, Me), 1.33 (3 H, s, Me), 5.88 (1 H, d, *J* = 10.2 Hz). **8c**: ^1H NMR (partial) δ 0.85 (3 H, d, *J* = 6.4 Hz, Me), 0.86 (3 H, d, *J* = 6.5 Hz, Me), 1.18 (3 H, s, Me), 1.20 (3 H, s, Me),

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1.35 (3 H, s, Me), 3.05 (1 H, dq, J = 10.2, 6.5 Hz), 4.85 (1 H, ddd, J = 10.6, 10.6, 4.3 Hz), 5.87 (1 H, d, J = 10.2 Hz). **8d**: an oil; ^{1}H NMR (partial) δ 0.89 (3 H, d, J = 6.4 Hz), 0.91 (3 H, d, J = 6.5 Hz), 1.16 (6 H, s, two Me), 1.28 (3 H, s), 2.93 (1 H, dq, J = 10.6, 4.5 Hz), 4.82 (1 H, ddd, J = 10.6, 10.6, 4.5 Hz), 5.83 (1 H, d, J = 9.8 Hz).

5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2,3-Dimethyl-5-oxo-2,3,4,5-tetrahydrofuran-2-carboxylate (9). (A) By Hydrolysis of the Ketene Dithioacetals 8. A solution of **8a** (139 mg, 0.3 mmol) in 10% aqueous MeOH (10 mL) was treated with $HgCl_2$ (81.5 mg, 0.3 mmol). The mixture was refluxed for 5 h. MeOH was evaporated from the cooled mixture, and the residue was extracted with EtOAc. The extract was dried (Na_2SO_4) and then was concentrated in vacuo to give the lactone **9a**. Compounds **9b–d** were similarly obtained by the hydrolysis of **8b–d**, respectively.

(B) By the Addition of Lithium Dimethylcuprate to the Furanone 13. MeLi (2 mmol, 1.25 mL of a 1.6 M solution in Et_2O) was added drop-by-drop to a cold (−20 °C) stirred suspension of CuI (1 mmol, 190 mg) in Et_2O (5 mL) under N_2. After 20 min, the mixture was cooled to −30 °C, and a solution of the furanone **13** (67 mg, 0.19 mmol) in Et_2O (1 mL) was added drop-by-drop. Thirty min later saturated aqueous NH_4Cl was added. The mixture was filtered, and the two liquid phases of the filtrate were separated. The solid that was collected by filtration was washed with Et_2O (3 × 15 mL). The washings were added to the organic phases of the filtrate. The combined organic phases were washed with saturated aqueous NH_4Cl (2 × 15 mL), dried (Na_2SO_4), and concentrated. The residue was passed through a column of silica gel (EtOAc:hexane = 10:90) to give 22.6 mg (32%) of **9a** and 23.3 mg (33%) of **9b**.

(C) By Hydrogenation of the Furanone 14. A mixture of **14** (110 mg, 0.3 mmol) and a catalytic amount of 10% Pd/C and EtOH (5 mL) were stirred at rt for 6 h under H_2 (1 atm). The mixture was then filtered. The solvent was evaporated from the filtrate. The product, **9a** (110 mg, 99%), was obtained by passing the residue through a short column of silica gel (EtOAc:hexane = 10:90).

9a: colorless needles; mp 143–146 °C (hexane); TLC (EtOAc/hexane, 10:90) R_f = 0.15; $[\alpha]^{25}_D$ = +2.6° (c 2.0, $CHCl_3$); IR (neat) 1778, 1725, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.76–1.05 (3 H, m), 0.88 (3 H, d, J = 6.4 Hz, Me), 1.08 (3 H, d, J = 6.9 Hz, Me-3), 1.20 (3 H, s, Me), 1.24 (3 H, s, Me), 1.35 (3 H, s, Me-2), 1.36–1.65 (3 H, m), 1.90 (1 H, m), 2.09 (1 H, ddd, J = 10.5, 10.5, 4.4 Hz), 2.29–2.57 (3 H, m), 5.03 (1 H, ddd, J = 10.6, 10.6, 4.3 Hz), 7.11–7.36 (5 H, m, PhH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.3 (q), 20.9 (q), 21.8 (q), 26.7 (q), 26.9 (q), 27.3 (t), 31.4 (d), 34.2 (t), 35.8 (t), 40.0 (s), 42.0 (d), 42.2 (t), 49.9 (d), 77.1 (d), 86.9 (s), 125.4 (three CH), 128.3 (two CH), 150.8 (s), 169.9 (s, CO_2), 175.5 (s, CO_2R*); MS m/z (rel intensity) 372 (25, M$^+$), 307 (63), 292 (23), 214 (22), 159 (40), 119 (100), 105 (20), 91 (42). **9b**: an oil; TLC (EtOAc:hexane = 10:90) R_f = 0.17; $[\alpha]^{25}_D$ = +7° (c 0.3, $CHCl_3$); ^{1}H NMR (partial) δ 0.86 (3 H, d, J = 6.4 Hz), 1.05 (3 H, d, J = 6.9 Hz, Me-3), 1.19 (3 H, s), 1.25 (3 H, s), 1.33 (3 H, s, Me-2), 1.90 (1 H, m), 2.08 (1 H, ddd, J = 10.5, 10.5, 4.4 Hz), 2.12 (1 H, d, J = 17.1, 6.5 Hz), 2.42 (1 H, m), 2.66 (1 H, dd, J = 17.1, 8.7 Hz), 4.95 (1 H, ddd, J = 10.6, 10.6, 4.3 Hz). **9c**: an oil; TLC (EtOAc/hexane, 10:90) R_f = 0.19; $[\alpha]^{25}_D$ = −3.2° (c 1.1, $CHCl_3$); ^{1}H NMR (partial) δ 0.83 (3 H, d, J = 6.4 Hz), 1.10 (3 H, d, J = 6.9 Hz, Me-3), 1.25 (3 H, s), 1.29–1.77 (3 H, m), 1.31 (3 H, s), 1.40 (3 H, s, Me-2), 2.10 (1 H, dd, J = 17.0, 6.5 Hz), 2.41 (1 H, m), 2.67 (1 H, dd, J = 17.0, 8.7 Hz), 4.96 (1 H, ddd, J = 10.7, 10.7, 4.4 Hz). **9d**: an oil; TLC (EtOAc/hexane, 10:90) R_f = 0.21; $[\alpha]^{25}_D$ = −6.7° (c 1.33, $CHCl_3$); ^{1}H NMR (partial) δ 0.83 (3 H, d, J = 6.4 Hz), 1.01 (3 H, d, J = 7.0 Hz, Me-3), 1.23 (3 H, s), 1.29 (3 H, s), 1.33 (3 H, s, Me-2), 1.34–1.63 (3 H, m), 1.89 (1 H, m), 2.07 (1 H, ddd, J = 10.5, 10.5, 4.3 Hz), 2.12 (1 H, dd, J = 17.0, 4.9 Hz), 2.29 (1 H, m), 2.71 (1 H, dd, J = 17.0, 8.0 Hz), 4.86 (1 H, ddd, J = 10.7, 10.7, 4.4 Hz).

Ethyl 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2-Hydroxy-2-methyl-3-pentynedioate (11). To a cold (−78 °C) stirred solution of i-Pr_2NH (0.4 mL, 2.2 mmol) in THF (20 mL) under N_2 was added drop-by-drop n-BuLi (2 mmol, 1.34 mL of a 1.6 M solution in hexane). After 20 min, a solution of ethyl propiolate (1.96 mL, 2 mmol) in THF (1 mL) was added drop-by-drop. Twenty min later, anhydrous $MgCl_2$ (190 mg, 2 mmol) was added. Twenty min after that, a solution of the pyruvate **7** (604 mg, 2 mmol) in THF (2 mL) was added drop-by-drop. Twenty min later the reaction was quenched by adding saturated aqueous NH_4Cl. The mixture was concentrated and then was extracted with EtOAc. The extract was dried (Na_2SO_4) and then was concentrated in vacuo. The residue was purified by HPLC to give 560 mg (70%) of **11a** and 80 mg (10%) of **11b**. **11a**: an oil; HPLC (EtOAc/hexane (8:92)) t_R = 10.8 min; $[\alpha]^{25}_D$ = +11.1° (c 7.4, $CHCl_3$); IR (neat) 3533, 2959, 2253, 1715, 1444, 1241, 1140 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.86–1.15 (3 H, m), 0.89 (3 H, d, J = 6.4 Hz, Me), 1.21 (3 H, s, Me), 1.32 (3 H, s, Me), 1.32 (3 H, d, J = 7.2 Hz, Me), 1.40 (3 H, s, Me), 1.45–1.77 (3 H, m), 1.86 (1 H, m), 2.17 (1 H, dd, J = 10.6, 10.6, 3.9 Hz), 2.39 (1 H, br s, OH), 4.23 (2 H, q, J = 7.2 Hz), 4.89 (1 H, ddd, J = 10.6, 10.6, 4.0 Hz), 7.11–7.32 (5 H, m, PhH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.6 (q), 24.2 (q), 25.7 (q), 26.0 (q), 26.4 (q), 28.7 (q), 31.2 (d), 34.3 (t), 39.5 (s), 40.7 (t), 49.8 (d), 62.1 (t), 68.3 (s), 75.3 (s), 78.1 (d), 85.5 (s), 125.3 (two CH), 128.1 (d), 128.4 (two CH), 151.7 (s), 161.2 (s, CO_2), 169.6 (s, CO_2); MS m/z (rel intensity) 400 (1, M$^+$), 382 (1), 367 (2), 322 (1), 214 (42), 142 (13), 119 (100), 105 (87); HRMS calcd for $C_{24}H_{32}O_5$ 400.2250, found 400.2241. **11b**: an oil; HPLC (EtOAc/hexane (8:92)) t_R = 12.3 min; $[\alpha]^{25}_D$ = −5.9° (c 3.2, $CHCl_3$); ^{1}H NMR (partial) δ 0.88 (3 H, d, J = 6.4 Hz), 1.25 (3 H, s), 1.29 (3 H, d, J = 7.2 Hz), 1.30 (3 H, s), 1.38 (3 H, s), 4.20 (2 H, q, J = 7.2 Hz), 4.85 (1 H, ddd, J = 10.5, 10.5, 4.0 Hz).

Ethyl 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2-Hydroxy-2-methylpentanedioate (12). A mixture of **11a** (240 mg, 0.6 mmol), a small quantity of Lindlar catalyst (5% Pd/$CaCO_3$ poisoned with Pb), and MeOH (5 mL) were stirred at rt for 5 h under H_2 (1 atm). The mixture was then filtered, and the solvent was evaporated from the filtrate. The product, **12** (230 mg, 95%), was obtained by passing the residue through a short column of SiO_2 (EtOAc/hexane (10:90)). **12**: an oil; TLC (EtOAc/hexane (10:90)) R_f = 0.12; $[\alpha]^{25}_D$ = −4.6° (c 4.0, $CHCl_3$); IR (neat) 3519, 1731 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.83–1.13 (3 H, m), 0.88 (3 H, d, J = 6.4 Hz), 1.15 (3 H, s), 1.22 (3 H, s), 1.24 (3 H, d, J = 7.2 Hz), 1.31 (3 H, s), 1.42–1.71 (3 H, m), 1.81–1.99 (3 H, m), 2.11 (1 H, ddd, J = 10.6, 10.6, 7.0 Hz), 2.56 (1 H, br s, OH), 2.75 (1 H, dd, J = 16.0, 7.9 Hz), 2.92 (1 H, dd, J = 16.0, 7.0 Hz), 4.12 (2 H, q, J = 7.2 Hz), 4.86 (1 H, ddd, J = 10.5, 10.5, 4.2 Hz), 7.12–7.37 (5 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 14.2 (q), 21.7 (q), 24.8 (q), 26.9 (two CH_2), 27.0 (q), 28.7 (q), 31.3 (d), 34.3 (t), 34.4 (t), 39.8 (s), 41.3 (t), 49.6 (d), 60.4 (t), 73.6 (s), 77.1 (d), 125.4 (three CH), 128.2 (two CH), 151.0 (s), 173.3 (s), 175.6 (s); MS m/z (rel intensity) 404 (1, M$^+$), 387 (1), 358 (1), 285 (2), 214 (16), 191 (22), 145 (70), 119 (100); HRMS calcd for $C_{24}H_{36}O_5$ 404.2563, found 404.2537.

5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2,5-Dihydro-2-methyl-5-oxofuran-2-carboxylate (13). To solution of **11a** (100 mg, 0.25 mmol) in DMF (1 mL) was added Et_3N (0.12 mL, 0.9 mmol), $Pd(OAc)_2(PPh_3)_2$ (5 mg, 0.005 mmol), and HCO_2H (0.03 mL, 0.7 mmol). The mixture was gently refluxed at 60 °C for 6 h, and then it was cooled to rt. EtOAc (5 mL) and 0.1 N aqueous HCl (15 mL) were added. The two liquid phases were separated. The organic phase was washed with water, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (EtOAc/hexane (10:90)) to give 67 mg (0.19 mmol, 72%) of **13**: an oil; TLC (EtOAc/hexane, 10:90) R_f = 0.10; $[\alpha]^{25}_D$ = −47.6° (c 3.8, $CHCl_3$); IR (neat) 1778, 1730, 1601 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.73–1.10 (3 H, m), 0.86 (3 H, d, J = 6.4 Hz), 1.18 (3 H, s), 1.22–1.63 (3 H, m), 1.26 (3 H, s), 1.50 (3 H, s), 1.85 (1 H, m), 2.04 (1 H, ddd, J = 10.4, 10.4, 4.3 Hz), 4.88 (1 H, ddd, J = 10.6, 10.6, 4.4 Hz), 5.98 (1 H, d, J = 5.6 Hz), 6.92 (1 H, d, J = 5.6 Hz), 7.13–7.30 (5 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 21.6 (two CH_3), 26.8 (q), 26.8 (t), 27.0 (q), 31.2 (d), 34.4 (t), 39.9 (s), 41.3 (t), 49.6 (d), 77.5 (d), 87.1 (s), 121.3 (d), 125.4 (d), 125.5 (two CH), 128.1 (two CH), 150.9 (s), 155.5 (d), 167.0 (s), 171.5 (s); MS m/z (rel intensity) 356 (1, M$^+$), 414 (1), 339 (1), 279 (2), 237 (1), 214 (81), 118 (100), 105 (32), 98 (26); HRMS calcd for $C_{22}H_{28}O_4$ 356.1986, found 356.1956.

5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2,5-Dihydro-2,3-dimethyl-5-oxofuran-2-carboxylate (14). MeLi (2.0 mmol, 1.25 mL of a 1.6 M solution in Et_2O) was added drop-by-drop to a cold (−20 °C) stirred suspension of CuI (1 mmol, 190 mg) in Et_2O (5 mL). After 20 min, the mixture was cooled to −30 °C, and a solution of the furanone **11a** (160 mg, 0.4 mmol) in Et_2O

(2 mL) was added drop-by-drop. The mixture was stirred for 30 min, and then saturated aqueous NH_4Cl was added. The mixture was filtered, and the two liquid phases of the filtrate were separated. The solid that was collected by filtration was washed with Et_2O (3 × 15 mL). The washings were added to the organic phase of the filtrate. The combined organic phases were washed with saturated aqueous NH_4Cl (2 × 20 mL), dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel; (EtOAc/hexane = 10:90) to give 104 mg (70%) of **14**: an oil; TLC (EtOAc/hexane, 10:90) R_f = 0.15; $[\alpha]^{25}_D$ = −85.2° (*c* 2.9, $CHCl_3$); IR (neat) 1767, 1727, 1257 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.74–1.68 (3 H, m), 0.86 (3 H, d, *J* = 6.4 Hz, Me), 1.20–1.58 (3 H, m), 1.52 (3 H, s, Me), 1.88–1.99 (2 H, m), 2.06 (3 H, d, *J* = 1.4 Hz, Me), 4.87 (1 H, ddd, *J* = 10.4, 10.4, 4.5 Hz), 5.81 (1 H, d, *J* = 1.4 Hz), 7.12–7.32 (5 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.2 (q), 20.8 (q), 21.6 (q), 24.8 (q), 27.1 (q), 29.1 (t), 31.3 (t), 34.2 (t), 40.1 (s), 41.4 (d), 49.9 (d), 78.0 (d), 88.1 (s), 117.5 (d), 125.5 (two CH), 128.1 (two CH), 150.0 (s), 167.1 (s), 167.4 (s), 171.5 (s); MS *m/z* (rel intensity) 370 (49, M^+), 347 (11), 311 (5), 252 (3), 214 (20), 157 (30), 119 (100), 112 (44).

Ethyl 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2-Hydroxy-3-methoxy-2-methyl-3-pentenedioate (15) and 5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2,5-Dihydro-3-methoxy-2-methyl-5-oxofuran-2-carboxylate (16). Under an atmosphere of N_2, but without attempting to rigorously exclude O_2, MeLi (2 mmol, 1.25 mL of a 1.6 M solution in Et_2O) was added drop-by-drop to a cold (−20 °C) stirred suspension of CuI (1 mmol, 190 mg) in Et_2O (5 mL). After 20 min, the mixture was cooled to −30 °C, and a solution of the furanone **11a** (80 mg, 0.2 mmol) in Et_2O (1 mL) was added drop-by-drop. The mixture was allowed to warm to rt and was kept there for 3 h. Then saturated aqueous NH_4Cl was added, and the whole was extracted with EtOAc. The extract was washed with brine, dried (Na_2SO_4), and concentrated. The residue was passed through a column of silica gel (EtOAc:hexane = 10:90) to give compounds **15** (23.3 mg, 27%) and **16** (27.6 mg, 32%). **15**: an oil; HPLC (EtOAc/hexane, 10:90) t_R = 12.5 min; IR (neat) 3450, 2954, 1725, 1710, 1599, 1420 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.77–1.09 (3 H, m), 0.89 (3 H, d, *J* = 6.4 Hz), 1.24 (3 H, s), 1.30 (3 H, t, *J* = 6.7 Hz), 1.31 (3 H, s), 1.35 (3 H, s), 1.36–1.65 (3 H, m), 1.93 (1 H, m), 2.09 (1 H, ddd, *J* = 10.5, 10.5, 4.0 Hz), 3.12 (1 H, s, OH), 3.99 (3 H, s, OMe), 4.18 (1 H, q, *J* = 6.7 Hz), 4.94 (1 H, ddd, *J* = 10.6, 10.6, 4.1 Hz), 5.46 (1 H, s), 7.12–7.22 (1 H, m), 7.25–7.36 (4 H, m); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.8 (q), 19.0 (q), 19.2 (q), 21.7 (q), 22.3 (q), 26.0 (q), 27.0 (t), 27.8 (t), 30.7 (t), 32.0 (d), 34.4 (t), 40.0 (s), 41.1 (t), 49.9 (d), 63.9 (t), 76.4 (d), 95.2 (d), 125.4 (d), 125.5 (two CH), 128.2 (two CH), 150.8 (s), 165.5 (s), 169.3 (s), 172.5 (s); MS *m/z* (rel intensity) 432 (1, M^+), 389 (7), 313 (11), 269 (12), 243 (44), 218 (19), 173 (100), 105 (32); HRMS calcd for $C_{25}H_{36}O_6$ 432.2510, found 432.2522. **16**: an oil; HPLC (EtOAc:hexane = 10:90) t_R = 14.3 min; IR (neat) 1735, 1600 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 0.79–1.10 (3 H, m), 0.88 (3 H, d, *J* = 6.4 Hz), 1.22 (3 H, s), 1.32 (3 H, s), 1.36 (3 H, s), 1.40–1.67 (3 H, m), 1.95 (1 H, m), 2.06 (1 H, ddd, *J* = 10.4, 10.4, 3.9 Hz), 3.85 (3 H, s, OMe), 4.91 (1 H, ddd, *J* = 10.5, 10.5, 4.0 Hz), 5.11 (1 H, s), 7.13–7.25 (1 H, m), 7.28–7.42 (4 H, m); MS *m/z* (rel intensity) 374 (1, M^+), 343 (2), 328 (1), 214 (6), 199 (15), 142 (19), 119 (100), 105 (86).

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Registry No. **7**, 88292-41-5; **8a**, 139944-71-1; **8b**, 140147-00-8; **8c**, 140147-01-9; **8d**, 140147-02-0; **9a**, 139944-72-2; **9b**, 140147-03-1; **9c**, 140147-04-2; **9d**, 140147-05-3; **11a**, 139944-73-3; **11b**, 139944-79-9; **12**, 139944-74-4; **13**, 139944-75-5; **14**, 139944-76-6; **15**, 139944-77-7; **16**, 139944-78-8; 2-propenyl-1,3-dithiane, 51102-63-7; ethyl propiolate, 623-47-2.

Supplementary Material Available: X-ray crystallographic data for compound **9a** (ORTEP drawing, atomic coordinates, bond distances, and bond angles) and physical properties of compounds **8–9** and **11–16**, including ^1H and ^{13}C NMR spectra (35 pages). Ordering information is given on any current masthead page.

B-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane. A New Organoboron Reagent for the Preparation of Propargylic Alcohols†

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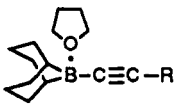
Introduction

Propargylic alcohols are key intermediates in the synthesis of many natural products including the prostaglandins,[1] steroids,[2] carotenoids,[3] and leukotrienes.[4] Researchers in this area have focused their attention mainly on the addition of alkynylmetals (Li, Na, K, Mg, Zn, and Al) to aldehydes as a means of preparing propargylic alcohols,[5] but these alkynylmetal reagents are not without limitations.

As an alternative to the alkynylmetals, Brown et al.[6,7] prepared a series of *B*-1-alkynyl-9-borabicyclo[3.3.1]nonanes as 1:1 complexes with THF (*B*-1-alkynyl-9-BBN, 1)



1; R= C_4H_9, $-CH(CH_3)_2$, $-C(CH_3)_3$, Ph
2; R= $Si(CH_3)_3$

and demonstrated their reaction with aldehydes and ketones to give the corresponding propargylic alcohols. These reagents were very mild, showing no reactivity toward a variety of functional groups[8] such as esters, nitriles, acetals, ketals, acid chlorides, alkyl halides, and amides, and perferentially react with aldehydes in the presence of ketones. Unfortunately, *B*-ethynyl-9-borabicyclo[3.3.1]nonane, the simplest member of this series, decomposed upon warming from −78 °C to room temperature and could not be isolated or studied.

We now wish to report the preparation of *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) and its reaction with aldehydes and ketones to give the corresponding trimethylsilyl-protected propargylic alcohols.[9]

Results and Discussion

B-[2-(Trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) was prepared from (trimethylsilyl)acetylene and *B*-methoxy-9-borabicyclo[3.3.1]nonane, using a modification of a literature procedure[7] (Scheme I), and isolated under a nitrogen atmosphere as a solid 1:1 complex with THF in 90% yield. Similar to the reagents reported by Brown et al.,[6-8] *B*-[2-(trimethylsilyl)ethynyl]-9-borabicyclo[3.3.1]nonane (**2**) reacted with a variety of aldehydes and ketones to afford the corresponding 2-(trimethylsilyl)ethynyl alcohols in excellent yields (Table I).

For example, when 1-octanal was added to a solution of **2** in pentane at 25 °C, a slight yellow color developed and dissipated within 30 min, indicating that the reaction was nearly complete. The reaction was complete in less than 1 h. Ethanolamine and methanol were added to the reaction at 0 °C, resulting in the precipitation of the 9-BBN-ethanolamine adduct **4**. Upon centrifugation and

† Dedicated to Professor Herbert C. Brown on the occasion of his 80th birthday.
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