thiobenzophenone-derived cycloadducts were obtained relative to the amount resulting from a trap with dimethyl fumarate.

Not suprisingly, a regiochemical mixture of fused cycloadducts was often obtained. Two interesting exceptions to this generalization are evident from entries 3 and 6. In the first, diethyl ketomalonate undergoes cycloaddition with the diprotio diyl **2b** leading to the isolation of **8** in 75% yield. In contrast, reaction of the same diylophile with the dimethyl diyl **2a** affords a mixture of regioisomers **5** and **6** in a ratio of 1.4:1. Interestingly, the former result is in accord with the principles of simple frontier molecular orbital theory.[4] Presumably the obtention of a mixture of products in the reaction with **2a** simply reflects the dominance of steric over electronic effects. In the second instance, formaldehyde, generated thermally from paraformaldehyde (in THF), proved unreactive unless zinc chloride was added. In addition to assisting in the depolymerization of the paraformaldehyde, the zinc chloride must also exert an electronic effect, since we were able to detect and isolate only one cycloadduct, **14**. We are presently investigating the generality of Lewis acid promoted diyl trapping reactions and the results will be reported on another occasion.

Finally, the last entry in Table I, illustrating the use of dimethyl acetylenedicarboxylate, deserves a brief comment. In previous reports, it was noted that polymeric products were obtained when acetylenes were used and it was suggested that this side reaction might be caused by the reaction of the acetylene and the diazene prior to deazetation.[5] Indeed, this is probably so. However, our results demonstrate that useful amounts (viz., 76%) of a fused cycloadduct *can* be obtained when the concentration of the diazene and diyl are maintained at a very low level through the use of syringe pump techniques.

In a typical experiment, 0.5 mmol of the diazene dissolved in 10 mL of dry, oxygen-free THF was added to a refluxing solution of the diylophile by using a syringe pump at a drop rate of 0.74 mL/h. An excess of the diylophile, also dissolved in THF, was used in each case.[6] Once the addition was complete, reflux was continued for an additional hour at which time the solvent was removed and the products were isolated using HPLC.

Acknowledgment. We are grateful to the National Institutes of Health (National Cancer Institute Grant CA 21144) for their continued support of our research. R.D.L. expresses gratitude to the Alfred P. Sloan Foundation for a fellowship, K.S. and H.B. to UCSB for fellowships, and O.W. to the Swiss National Fund for financial support during postdoctoral studies conducted at UCSB.

Registry No. **1a**, 31689-32-4; **1b**, 69442-65-5; **2a**, 32553-01-8; **2b**, 60743-11-5; **3a**, 96556-11-5; **3b**, 96614-13-0; **4a**, 96556-12-6; **4b**, 96614-14-1; **5**, 96556-13-7; **6**, 96556-14-8; **7**, 96556-15-9; **8**, 96556-16-0; **9**, 96556-17-1; **10**, 96556-18-2; **11**, 96556-19-3; **12a**, 96556-20-6; **12b**, 96614-15-2; **13**, 96556-21-7; **14**, 96556-22-8; **15**, 96556-23-9; PhCHO, 100-52-7; $(CO_2Et)_2C{=}O$, 609-09-6; $Ph_2C{=}S$, 1450-31-3; PhN=CHPh, 538-51-2; CH_2O, 50-00-0; $ZnCl_2$, 7646-85-7; $CH_3CO_2C{\equiv}CCO_2CH_3$, 762-42-5.

Supplementary Material Available: Listing of spectral data for each product (7 pages). Ordering information is given on any current masthead page.

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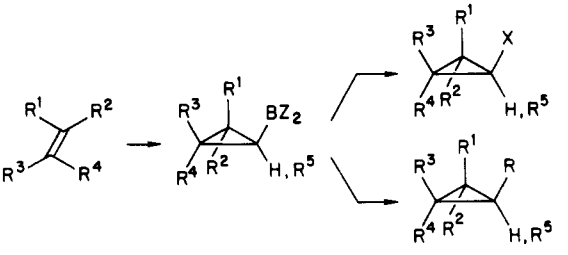
Applications of Cyclopropylboranes in Organic Synthesis. 1. A Stereocontrolled Route to Substituted Cyclopropanol Derivatives

Summary: Secondary and tertiary cyclopropanols are produced stereoselectively via the sequential treatment of 1,1-dibromocyclopropanes with *n*-butyllithium, catecholborane (or a trialkylborane), and alkaline hydrogen peroxide.

Sir: Cyclopropane derivatives are valuable synthetic intermediates, with considerable utility in the preparation of a variety of cyclic and acyclic organic compounds. Thus, we have recently reported a general [4 + 1] annulation approach to substituted cyclopentenes based on the accelerated rearrangement of 2-vinylcyclopropanol salts.[1] In connection with this methodology, we have recently been concerned with the development of new synthetic routes to both vinylcyclopropane and cyclopropanol derivatives, particularly the more highly substituted systems which are not available by employing existing methodology. In this paper we describe a general synthesis of cyclopropylboranes and demonstrate their potential utility for the preparation of a variety of highly substituted and functionalized cyclopropane derivatives.



The application of cyclopropylboranes in organic synthesis has received little attention previously, and few examples of this potentially valuable class of cyclopropane derivatives appear in the literature.[2] The most popular

(4) Berson, J. A. In "Diradicals"; Borden, W. T., Ed.; Wiley: New York, 1982; pp 151–194. Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976.

(5) Corwin, L. R.; McDaniel, D. M.; Bushby, R. J.; Berson, J. A. *J. Am. Chem. Soc.* **1980**, *102*, 276–287. The diyl generated thermally from 5-isopropylidenebicyclo[2.1.0]pentane adds smoothly to dimethyl acetylenedicarboxylate to give **15**. This result is reported in the Ph.D. Thesis of J. Mondo (1982) and A. Sabatelli (1984), Yale University. We are grateful to Professor Berson for informing us of this result and these references.

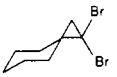
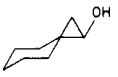
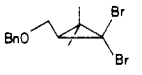
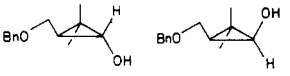
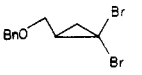
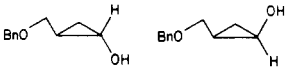
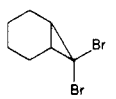
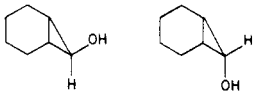
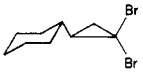
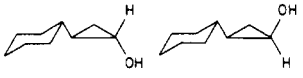
(6) The excesses ranged from 1.2- to 64-fold. Specifically, for benzaldehyde, 64.5 equiv at 9 M; for diethyl ketomalonate, 10 equiv at 4 M; for thiobenzophenone, 1.23 equiv at 0.18 M; for PhN=CHPh, 3.02 equiv at 4.6 M; and for dimethyl acetylenedicarboxylate, 20 equiv of 6.7 M. The concentrations listed above refer to that of the diylophile prior to the addition of the diazene.

(1) (a) Danheiser, R. L.; Martinez-Davila, C.; Auchus, R. J.; Kadonaga, J. T. *J. Am. Chem. Soc.* **1981**, *103*, 2443. (b) Danheiser, R. L.; Martinez-Davila, C.; Morin, J. M. *J. Org. Chem.* **1980**, *45*, 1340.

(2) (a) Binger, P.; Köster, R. *Angew Chem.* **1962**, *74*, 652. (b) Köster, R.; Arora, S.; Binger, P. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 205. (c) Cowley, A. H.; Furtsch, T. A. *J. Am. Chem. Soc.* **1969**, *91*, 39. (d) Brown, H. C.; Rhodes, S. P. *J. Am. Chem. Soc.* **1969**, *91*, 4306. (e) Utimoto, K.; Tamura, M.; Tanouti, M.; Sisido, K. *Tetrahedron* **1972**, *28*, 5697. (f) Dunkelblum, E. *Isr. J. Chem.* **1973**, *11*, 557. (g) Haubold, W.; Stanzl, K. *Chem. Ber.* **1978**, *111*, 2108. (h) Odom, J. D.; Szafran, Z.; Johnston, S. A.; Li, Y. S.; Durig, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 7173. (i) Mikhailov, B. M.; Bubnov, Yu. N. "Organoboron Compounds in Organic Synthesis"; Harwood: London, 1984; pp 402–406.

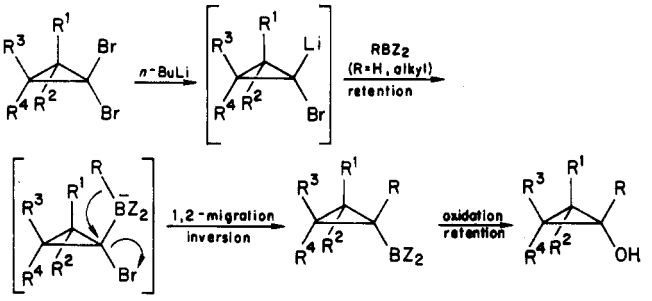
0022-3263/85/1950-2401$01.50/0

Table I. Synthesis of Secondary Cyclopropanols

entry	dibromocyclopropane	cyclopropanol(s)[a]	yield,[b] %	ratio[b]
1	 2[c]	 3[d]	82	
2	 4[e]	 5a 5b	79	>95:5
3	 6[e]	 7a 7b	57	93:7
4	 8[e]	 9a′ 9b′	84	94:6
5	 10[g]	 11a 11b	50	80:20

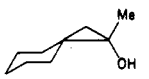
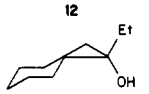
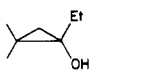
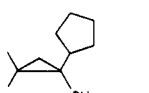
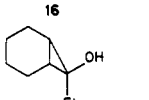
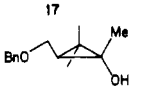
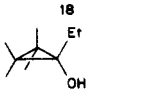
[a] In a typical reaction, 1.0–1.2 equiv of *n*-BuLi was added dropwise over 8 min (entry 1) or 1.0–1.5 h (entries 2–5) to the dibromide in THF at −100 °C. Catecholborane (2 equiv of a 1.0 M THF solution) was then added dropwise over 30 min, and after 15–60 min the reaction mixture was allowed to warm to 25 °C and then heated for 15–20 h at 50 °C. The resulting mixture was oxidized with excess 30% H_2O_2 and 10% NaOH at 25 °C for 3–4. [b] Isolated yields for major isomers purified by chromatography. Ratios were determined by ^1H NMR analysis of crude reaction products. [c] Reference 4a. [d] Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468. [e] Prepared by the method of ref 3a. [f] Schöllkopf, U.; Paust, J.; Al-Azrak, A.; Schumacher, H. *Chem. Ber.* **1966**, *99*, 3391. [g] Prepared by using the method of ref 3b.

Scheme I



route to organoboranes, hydroboration, unfortunately has limited utility in cyclopropylborane synthesis due to the relative inaccessibility of cyclopropene derivatives. Our two-step strategy for the preparation of cyclopropylboranes is outlined in Scheme I. First, stereospecific suprafacial addition of dibromocarbene to an olefin furnishes a dibromocyclopropane derivative,[3] which is then subjected to halogen–metal exchange with *n*-butyllithium in THF at −100 °C.[4] Addition of the resulting *gem*-lithiobromocyclopropane derivative to certain borane reagents next affords an ate complex, which upon warming undergoes 1,2-migration (Matteson–Pasto rearrangement)[5,6] to generate the desired cyclopropylborane. For example, treatment of 1,1-dibromo-2,2-dimethylcyclopropane with

Table II. Synthesis of Tertiary Cyclopropanols

entry	dibromocyclopropane	borane	cyclopropanol[a]	yield,[b] %
1	2	Me_3B	 12	81
2	2	Et_3B	 13	75
3	 14[c]	Et_3B	 15	71
4	14	$(c\text{-}C_5H_9)_3B$	 16	43
5	8	Et_3B	 17	50
6	4	Me_3B	 18	53
7	 19[c]	Et_3B	 20	35

[a] In a typical reaction, 1.0–1.1 equiv of *n*-BuLi (0.9 equiv in entry 5) was added dropwise over 5–70 min to the dibromide in THF at −100 °C. After 10–30 min, 1.5–5.0 equiv of R_3B was added dropwise, and the mixture was stirred at −100 °C for ca. 1 h and then allowed to warm to 0 °C or 25 °C. The resulting mixture was oxidized with excess 30% H_2O_2 and 10% NaOH at 25 °C (entries 1–3, 6) or 60 °C (entries 4–5, 7). [b] Isolated yields of products purified by chromatography or distillation. In entries 5 and 6, only a single cyclopropanol diastereomer was detected by TLC analysis of the crude reaction product. [c] Skell, P. S.; Garner, A. Y. *J. Am. Chem. Soc.* **1956**, *78*, 5430.

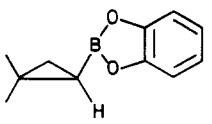
(3) Dibromocyclopropanes are conveniently prepared by the reaction of alkenes with (a) $CHBr_3$–KO-*t*-Bu (Parham, W. E.; Schweizer, E. E. *Org. React. (N.Y.)* **1963**, *13*, 55), (b) $CHBr_3$–NaOH–*n*-Bu_3N (Markosza, M.; Fedorynski, M. *Rocz. Chem.* **1976**, *50*, 2223), or (c) $PhHgCBr_3$ (Seyferth, D. *Acc. Chem. Res.* **1972**, *5*, 65).

(4) See: (a) Seyferth, D.; Lambert, R. L.; Massol, M. *J. Organomet. Chem.* **1975**, *88*, 255. (b) Kitatani, K.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1977**, *50*, 3288 and references cited therein.

(5) (a) Matteson, D. S.; Mah, R. W. H. *J. Am. Chem. Soc.* **1963**, *85*, 2599. (b) Pasto, D. J.; Miesel, J. L. *J. Am. Chem. Soc.* **1963**, *85*, 2118.

(6) See: (a) Matteson, D. S. "Organometallic Reaction Mechanisms"; Academic Press: New York, 1974; pp 161–171. (b) Pelter, A. In "Rearrangements in Ground and Excited States"; de Mayo, P., Ed.; Academic Press: New York, 1980; Vol. 2, pp 129–141. (c) Suzuki, A. *Top. Curr. Chem.* **1983**, *112*, 67, and other reviews cited therein.

1.0 equiv of *n*-BuLi and then 1.0 equiv of catecholborane (THF, −100 °C → 25 °C) produced the cyclopropylborane **1** in 91% yield after distillation.[7]



1

The in situ oxidation of these cyclopropylborane derivatives with alkaline hydrogen peroxide provides an efficient general route to secondary and tertiary cyclopropanols (Tables I and II). This strategy permits the synthesis of substituted cyclopropanols not easily prepared by alternative methods[8] and generally proceeds with a high degree of stereoselectivity. As outlined in Scheme I, the overall stereochemical outcome of these transformations is a consequence of well-established stereochemical features of the reactions of dibromocyclopropanes and organoboranes. Thus, halogen–metal exchange affords the *gem*-lithiobromocyclopropane in which the lithium atom is situated either syn to a chelating substituent or on the more sterically encumbered side of the cyclopropane ring.[4] Electrophilic substitution then occurs with retention of configuration at the carbon–metal bond[9] to afford an organoborate intermediate which undergoes 1,2-migration with inversion of configuration at the cyclopropyl carbon.[10] Finally, oxidation of the resulting cyclopropylborane proceeds with retention in the usual manner.

Further studies are under way in our laboratory to demonstrate the utility of cyclopropylboranes as intermediates for the synthesis of a variety of other cyclopropane derivatives. The application of this methodology in new annulation approaches to five- and seven-membered carbocycles is also under active investigation.

Acknowledgment. We thank the National Institutes of Health, Firmenich AG, and Eli Lilly and Co. for generous financial support.

Registry No. **2**, 56424-67-0; **3**, 90112-48-4; **4**, 96503-84-3; **5a**, 96503-85-4; **5b**, 96503-86-5; **6**, 96503-87-6; **7a**, 96503-88-7; **7b**, 96503-89-8; **8**, 2415-79-4; **9a**, 13830-44-9; **9b**, 931-31-7; **10**, 7087-57-2; **11a**, 96503-91-2; **11b**, 96503-92-3; **12**, 96503-93-4; **13**, 96503-94-5; **14**, 32264-50-9; **15**, 96503-95-6; **16**, 96503-96-7; **17**, 96503-97-8; **18**, 96532-45-5; **19**, 22715-57-7; **20**, 96503-98-9.

(7) IR (neat) cm^{-1}: 3075, 3000, 2950, 2875, 1480, 1440, 1420, 1290, 1240, 1200, 800, and 740. ^1H NMR (250 MHz, $CDCl_3$) δ: 0.26 (dd, J = 7.2, 9.0 Hz, 1 H), 0.86–0.92 (m, 2 H), 1.23 (s, 3 H), 1.27 (s, 3 H), and 7.02–7.19 (m, 4 H). ^{13}C NMR (67.9 MHz, $CDCl_3$) δ: 148.4, 122.2, 112.0, 27.9, 22.4, 21.8, and 20.7 (no signal is observed for the R_2CH–B carbon due to quadrupolar broadening, see: Odom, J. D. In "Comprehensive Organometallic Chemistry"; Wilkinson, G., Ed.; Pergamon Press: New York, 1982; Vol. 1, p 268 and references cited therein). MS: *m/e* 188 (M^+).

(8) (a) Girard, C.; Conia, J.-M. *J. Chem. Res., Suppl.* **1978**, 182. (b) Barber, G. N.; Olofson, R. A. *Tetrahedron Lett.* **1976**, 3783. (c) Gibson, D. H.; DePuy, C. H. *Chem. Rev.* **1974**, *74*, 605. (d) Longone, D. T.; Wright, W. D. *Tetrahedron Lett.* **1969**, 2859 and references cited therein.

(9) The stereochemical configuration of the intermediate *gem*-lithiobromocyclopropanes was confirmed in each case by protonolysis studies. Details will be included in the full report on this work.

(10) See ref 6 and Midland, M. M.; Zolopa, A. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 248.

(11) Alfred P. Sloan Research Fellow, 1981–1985.

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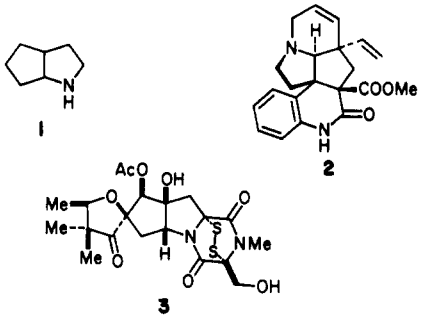
Stereocontrolled Synthesis of Substituted *cis*-Cyclopenta[*b*]pyrrolidines[1]

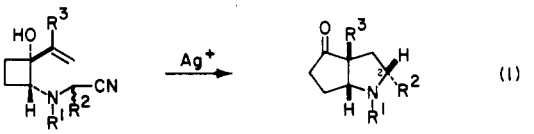
Summary: Substituted *cis*-4-oxooctahydrocyclopenta[*b*]pyrroles are formed in good yield by tandem cationic aza-Cope rearrangement–Mannich cyclization of *trans*-2-amino-1-vinylcyclobutanols.

Sir: The cyclopenta[*b*]pyrrolidine ring system (**1**) is found in a variety of natural products and pharmaceutical agents. Examples of the former include the *melodinus* alkaloids,[2] e.g., (+)-scandine (**2**) and the antibiotic sirodesmin A (**3**).[3]



1 **2** **3**

Recent publications from these laboratories have described the efficient preparation of substituted 4-oxooctahydroindoles[4] and 4-oxodecahydrocyclohepta[*b*]pyrroles[5] from 2-amino-1-vinylcyclopentanols and 2-amino-1-vinylcyclohexanols, respectively. In this paper, we report that the similar rearrangement of iminium ions derived from *trans*-2-amino-1-vinylcyclobutanols **4** provides a general synthesis of substituted *cis*-4-oxooctahydrocyclopenta[*b*]pyrroles **5** (eq 1). The key step in this sequence is an unusually facile [3,3]-sigmatropic rearrangement of a cationic *trans*-"divinyl"-cyclobutyl system.



4 **5** (1)

Reaction[6] of 1,2-bis[(trimethylsilyl)oxy]cyclobutene (**6**)[7] with 1.1 equiv of benzyl(cyanomethyl)amine[4a] gave cyclobutanone **7**[8] (IR 1790 cm^{-1}) in 75% yield (eq 2). The subsequent reaction of this intermediate with (1-phenylvinyl)lithium (2.5 equiv, −78 °C, THF) occurred completely from the side opposite the dialkylamino group to provide a single adduct, **4a**[8] (^1H NMR: δ 3.68, AB q, J_{AB} = 13.2 Hz, $\Delta\nu$ = 15.7 Hz, CH_2CN; 3.6–3.8, m, CHN), in 58% yield. The stereochemistry assigned to aminocyclobutanol **4a** was consistent with infrared studies that showed a strong intramolecular hydrogen-bonded OH absorption at 3446 cm^{-1}

(1) Part 16 in the series "Synthesis Applications of Cationic Aza-Cope Rearrangements". For part 15, see: Overman, L. E.; Angle, S. R. *J. Org. Chem.*, **1985**, in press.

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(8) New compounds showed IR, 250-MHz ^1H NMR, 63-MHz ^{13}C NMR, and mass spectra consistent with their assigned structures. Molecular composition was determined by elemental analysis or high-resolution mass spectroscopy.

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