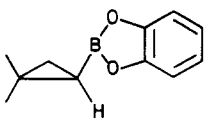
1.0 equiv of *n*-BuLi and then 1.0 equiv of catecholborane (THF, −100 °C → 25 °C) produced the cyclopropylborane **1** in 91% yield after distillation.[7]



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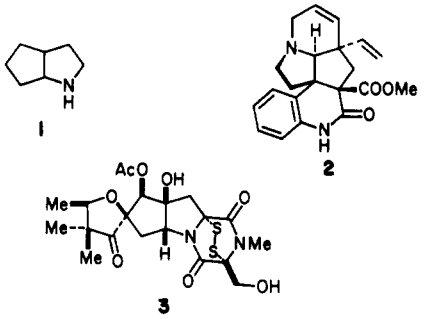
Stereocontrolled Synthesis of Substituted *cis*-Cyclopenta[*b*]pyrrolidines[1]

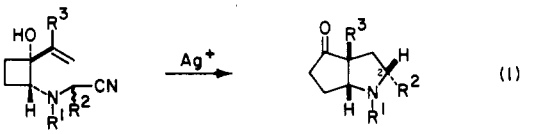
Summary: Substituted *cis*-4-oxooctahydrocyclopenta[*b*]pyrroles are formed in good yield by tandem cationic aza-Cope rearrangement–Mannich cyclization of *trans*-2-amino-1-vinylcyclobutanols.

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}

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(7) Bloomfield, J. J.; Nelke, J. M. *Org. Synth.* **1977**, *57*, 1.

(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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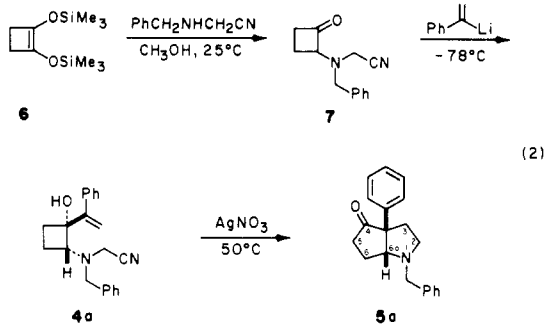


(0.07–0.52 M in CCl_4). Tandem cationic aza-Cope rearrangement–Mannich cyclization was triggered by treatment of **4a** at 50 °C with 1.1 equiv of $AgNO_3$ to give a single product, **5a**[8] (IR 1741 cm^{-1}), in 93% yield. *cis*-Octahydrocyclopenta[*b*]pyrrole **5a** (mp 78 °C, after recrystallization from pentane) showed a characteristic doublet (J = 3.9 Hz) at δ 3.47 for H_{6a} and an AB quartet for the benzyl methylene group centered at δ 3.74 (J_{AB} = 13.5 Hz, $\Delta\nu_{AB}$ = 196 Hz). The stereochemistry of **5a** was established by single-crystal X-ray diffraction analysis[9] of the maleate salt (mp 127–128 °C), and an ORTEP drawing of the molecular model is shown in Figure 1. The cyclopentane conformation observed in the crystal nicely rationalizes the observation of H_{6a} as a doublet in the ^1H NMR spectrum, since the estimated[9b] dihedral angle between H_{6a} and the trans H_6 hydrogen is 103°.

In a similar fashion, a variety of *trans*-2-[alkyl(cyanoalkyl)amino]cyclobutanols **4**[8] were prepared from **6** and transformed to cyclopentapyrrolidines **5**[8] upon treatment with $AgNO_3$ in EtOH (see eq 1 and Table I). With the exception of **4d**, the rearrangement step was very clean and afforded a *single* product. In the case of cyclopentapyrrolidines **5e**[8] and **5f**[8] that have an additional methyl substituent at C-2, the 250-MHz ^1H NMR spectrum of the crude reaction product showed only a *single* methyl doublet (**5e**: δ 1.02, J = 6.1 Hz; **5f**: δ 1.08, J = 6.0 Hz). Debenzylation[10] of **5e** to give **5** (R^1 = H, R^2 = Me, R^3 = Ph) established the fact that the methyl group was oriented on the sterically more congested concave face of the *cis*-azabicyclo[3.3.0]octane ring system. Comparison of the ^1H NMR signals for H_2 (δ 3.38, m) and H_{6a} (δ 4.13, d) of this latter material with the corresponding signals of **5f** (H_2 δ 2.50, m; H_{6a} δ 3.25, m) showed that the *N*-methyl group caused an upfield shift of 0.88 ppm for *both* of these hydrogens. *cis*-Cyclopenta[*b*]pyrroldine **5f** should exist preferentially in a conformation with the *N*-Me group on the β face (trans to C_6 and the C_2-Me) and, thus, the cis C_{6a} and C_2 hydrogens should be identically shielded[4a,11] by the syn *N*-Me group and the anti electron pair.

The facile rearrangement of iminium ions derived from **4** should be contrasted with the thermal rearrangement of *trans*-1,2-divinylcyclobutane which requires high temperature and proceeds via a diradical pathway to give primarily products of a 1,3-shift.[12] In the iminium ion rearrangement reported here, the preferential formation of the less stable *trans*-2-methyl-*cis*-cyclopentapyrrolidines

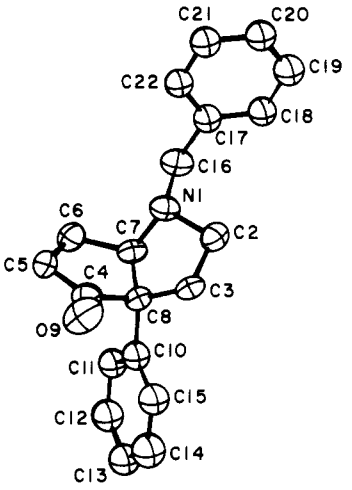


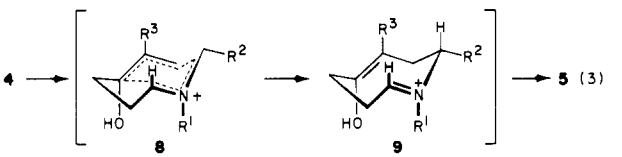
Figure 1.

Table I

	cyclobutanol 4				cyclopentapyrrolidine 5	
	R^1	R^2	R^3	yield,[a] %	rearrg cond	yield, %
a	CH_2Ph	H	Ph	58	50 °C, 2 h	93
b	CH_3	H	Ph	65	50 °C, 4 h	78
c	CH_2Ph	H	CH_3	65	50 °C, 15 h	88
d	CH_2Ph	H	H	52	50 °C, 14 h	31
e	CH_2Ph	CH_3	Ph	70	25 °C, 25 h	85
f	CH_3	CH_3	Ph	68	60 °C, 15 min	66

[a] From the corresponding 2-[alkyl(cyanoalkyl)amino]cyclobutanone. In all cases only a single stereoisomer was produced from addition of the vinyllithium reagent.

5e and **5f** must result from kinetic control in the conversion **4** → **5**. The simplest explanation for the stereoselectivity we observe is that the iminium ions derived from **4** undergo [3,3]-sigmatropic rearrangement in a chair geometry to give the *trans,trans*-1,5-azacyclooctadiene intermediates **9**.[13] Rapid intramolecular Mannich cyclization of **9** would then lead to **5** (eq 3). For rearrangements of acetaldehyde



iminium ions, the observed trans orientation of the C-2 methyl group in the bicyclic product would result from preferential rearrangement of the *E* iminium ion isomer **8** in which the R^2 substituent is oriented in a favored[14] quasi-equatorial fashion. The rapid rearrangement of iminium ions derived from **4** suggests the possibility that the observed transformations occur via initial isomerization to *cis*-divinylcyclobutanol intermediates, which then undergo rapid [3,3]-sigmatropic rearrangement. However, this explanation is inconsistent with the formation of **5e** and **5f**, since preferential rearrangement of the *E* iminium ion **10**[15] in the favored boat sense[12] (eq 4) would lead to a bicyclic product with a cis-oriented substituent at C-2.

In summary, the sequence summarized in eq 1 and 2 provides an efficient and stereocontrolled method for

(9) (a) The structure was solved by direct methods, using the MULTAN77 system of programs. The final unweighted and weighted *R* values were 0.063 and 0.078, respectively. (b) Hydrogen atoms were treated in calculated tetrahedral positions.

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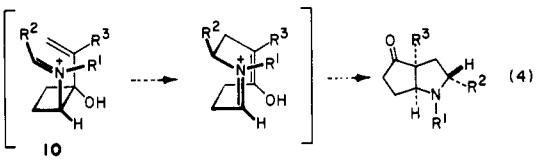
(15) The *Z* iminium ion related to **10** would experience serious repulsive interactions between R^2 and the cyclobutane ring.



10 (4)

preparing substituted *cis*-cyclopenta[*b*]pyrrolidines. Moreover, the facile rearrangement observed in these *trans*-"divinyl"-cyclobutane systems provides, perhaps, the best illustration to date of the powerful accelerating effect on [3,3]-sigmatropic rearrangements provided by the positively charged iminium ion grouping.

Acknowledgment. The financial support of the National Institutes of Health (NS-12389) is gratefully acknowledged. We particularly thank Professor R. J. Doedens for his invaluable assistance with the X-ray experiment. NMR and mass spectra were determined at Irvine with spectrometers purchased with the assistance of NSF departmental instrumentation grants.

Registry No. **4a**, 96617-23-1; **4b**, 96617-24-2; **4c**, 96617-25-3; **4d**, 96617-26-4; **4e**, 96617-27-5; **4f**, 96617-28-6; **5a**, 96617-29-7; **5a**·$^1/_2C_4H_4O_4$, 96617-36-6; **5b**, 96617-30-0; **5c**, 96617-31-1; **5d**, 96617-32-2; **5e**, 96617-33-3; **5f**, 96617-34-4; **6**, 17082-61-0; **7**, 96617-35-5; $PhCH_2NHCH_2CN$, 3010-05-7; $MeNHCH_2CN$, 5616-32-0; $PhCH_2NHCH(CH_3)CN$, 3010-09-1; $MeNHCH(CH_3)CN$, 16752-54-8; $PhCLi{=}CH_2$, 45680-22-6; $CH_3CLi{=}CH_2$, 6386-71-6; $CHLi{=}CH_2$, 917-57-7.

Supplementary Material Available: Tables I–VII of atomic positional and thermal parameters, bond distances, and bond angles (7 pages). Ordering information is given on any current masthead page.

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Methyl- and Ethylvinylhalonium Ions[1]

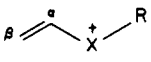
Summary: The first hitherto unknown alkylvinylhalonium ions, the methyl- and ethylvinylbromonium and -chloronium ions, have been prepared by the alkylation of the corresponding vinyl halides with $CH_3F(C_2H_5F)$–SbF_5 in SO_2 or SO_2ClF solution and characterized by ^{13}C NMR spectroscopy.

Sir: The only known divinylhalonium ion is the bis(*trans*-2-chlorovinyl)iodonium chloride (**1**) prepared by Nesmeyanov[2] in 6% yield by reacting (*trans*-2-chlorovinyl)mercuric chloride with iodine trichloride. Several

$(ClCH{=}CH)_2I^+Cl^-$ (1)

$(ClCH{=}CH)I^+C_6H_5Cl^-$ (2)

$(C_6H_5ClC{=}CH)I^+C_6H_5BF_4^-$ (3)



4, X = Cl, Br; R = CH_3, C_2H_5

vinylaryliodonium ions such as the chlorovinylphenyliodonium chloride (**2**) and (α-chlorostyrylphenyl)iodonium tetrafluoroborate (**3**) have been prepared.[3,4] To date, however, no alkylvinylhalonium ions **4** have been reported.

We are now able to prepare alkylvinylhalonium ions **4**-R (X = Br, Cl) by alkylating vinyl halides with methyl and ethyl fluoride–antimony pentafluoride complexes in either SO_2 or SO_2ClF solvent. A solution of vinyl bromide in SO_2ClF at −78 °C was slowly added with stirring to a fourfold excess of freshly prepared CH_3F:SbF_5 complex in SO_2ClF at −78 °C to obtain a light yellow colored solution whose ^{13}C NMR spectrum at −90 °C showed three absorptions at $\delta^{13}C$ 132.9 (triplet, J_{C-H} = 170.0 Hz), 120.9 (doublet, J_{CH} = 227.0 Hz) and 44.1 (quartet, J_{CH} = 163.0 Hz). The observed chemical shifts and multiplicities are consistent with the ion being the methylvinylbromonium ion **4**-CH_3 (X = Br). Similarly, the ethylvinylbromonium ion **4**-C_2H_5 (X = Br) was prepared by using the $CH_3CH_2F \rightarrow SbF_5$ complex in SO_2 solution. The ion **4**-C_2H_5 (X = Br) exhibited four ^{13}C NMR absorptions at $\delta^{13}C$ 136.0 (triplet, J_{C-H} = 169.4 Hz), 116.9 (doublet, J_{CH} = 225.0 Hz), 72.3 (triplet, J_{C-H} = 164.0 Hz), and 15.1 (quartet). It is interesting to compare the ^{13}C NMR chemical shifts of **4**-CH_3 (X = Br) and **4**-C_2H_5 (X = Br) with those of progenitor vinyl bromide [observed at $\delta^{13}C$ 122.4 (triplet, J_{C-H} = 161.9 Hz) and 114.3 (doublet, J_{C-H} = 198.0 Hz)]. Apparently in the bromonium ions the β-methylene carbons are much more deshielded [10.5 ppm for **4**-CH_3 (X = Br) and 13.6 ppm for **4**-C_2H_5 (X = Br)] than the α-methine carbons [6.6 ppm for **4**-CH_3 (X = Br) and 2.6 ppm for **4**-CH_2CH_3 (X = Br)]. Relatively less deshielding of the α-methine carbon in **4**-C_2H_5 (X = Br) compared to that in **4**-CH_3 (X = Br) can be rationalized by a γ-CH_3 substituent effect in the former.[5] The best evidence for the formation of the alkylvinylbromonium ion comes from the change in the carbon–hydrogen coupling constant in the α-methine carbons compared to that in the progenitor vinyl bromide [the difference is 29.0 Hz in **4**-CH_3 (X = Br) and 27.0 Hz in **4**-C_2H_5 (X = Br)]. Such large increase in coupling constant can only occur by the placement of positive charge on the bromine (effect of a strongly electron-withdrawing group). It is, however, not clear why the β-methylene carbons in these alkylvinylbromonium ions get much more deshielded than α-methine carbons similar to those observed in regular allyl cations,[6] although in the latter such phenomenon can be readily rationalized by allyl delocalization. The methyl- and ethylvinylhalonium ions were stable at −78 °C for only several hours (~4 h) after which polymerization sets in.

Compared to the alkylvinylbromonium ions, the corresponding alkylvinylchloronium ions were found to be less stable. In fact, we were able to prepare only the methylvinylchloronium ion by methylating vinyl chloride using $CH_3F \rightarrow SbF_5$ in SO_2ClF solution at −90 °C. The ion **4**-CH_3 (X = Cl) was stable at −78 °C for less than an hour. In the ^{13}C NMR spectrum at −90 °C it showed three resonances at $\delta^{13}C$ 131.7 (triplet, J_{C-H} = 168.9 Hz), 127.2 (doublet, J_{C-H} = 220.0 Hz), and 50.4 (quartet, J_{C-H} = 161.0 Hz). Compared to the ^{13}C NMR chemical shifts of vinyl chloride (Table I) the β-methylene carbon in **4**-CH_3 (X = Cl) is much more deshielded (14.5 ppm) than the α-mthine

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(4) (a) Beringer, F. M.; Galton, S. A. *J. Org. Chem.* **1965**, *30*, 1930. (b) Nesmeyanov, A. M.; Tolstaya, T. P.; Soklova, N. F.; Varfolomessva, V. N.; Petrakov, A. V. *Dokl. Akad. Nauk. USSR* **1971**, *198*, 115; *Chem. Abstr.* **1971**, *75*, 48576t. (c) For recent related work, see: Ochiai, M.; Sumi, K.; Nagao, Y.; Fujita, E. *Tetrahedron Lett.* **1985**, *26*, 2351.
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(6) Olah, G. A.; Spear, R. J. *J. Am. Chem. Soc.* **1975**, *97*, 1539.

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