3-Chloro-1,1,2-trimethyl-2-indene[13] **(3a)**: colorless oil; 100 °C (5 mbar) [bulb-to-bulb distillation], obtained in pure state from a mixture of **3a**, **3f**, and **3g**; ^{1}H NMR ($CDCl_3$) δ 1.25 (6 H, s), 1.98 (3 H, s), 7.40 (4 H, s); ^{13}C NMR ($CDCl_3$) δ 9.84 (2-Me), 23.70 (1-Me), 49.13 (1-C), 118.45 (CH), 120.88 (CH), 125.45 (CH), 126.77 (CH); MS (70 eV), *m/e* (relative intensity) 194 (14), 192 (41), 179 (6.3), 177 (23), 165 (13), 163 (40), 158 (14), 157 (100), 142 (39), 141 (21), 129 (23), 128 (59), 127 (44), 126 (13), 115 (18), 105 (16), 101 (6), 77 (17), 71 (18), 70 (23), 63 (15), 55 (13)), 51 (19), 39 (11), 29 (18), 27 (25).

3-Chloro-1,1,2,6-tetramethyl-2-indene[14] **(3b)**: colorless oil; 95 °C (5 mbar) [bulb-to-bulb distillation]; ^{1}H NMR ($CDCl_3$) δ 1.22 (6 H, s), 1.93 (3 H, s), 2.38 (3 H, s), 7.06 (1 H, d, J_{AB} = 7.5 Hz), 7.11 (1 H, s), 7.2 (1 H, d, J_{AB} = 7.5 Hz); ^{13}C nmr ($CDCl_3$) δ 9.73 (2-Me), 21.52 (*p*-Me), 23.83 (1-Me), 49.32 (1-C), 118.24 (CH), 121.90 (CH), 127.48 (CH), 127.27 (CCl), 135.28 (2-C), 137.71 (MeC), 145.75 (3a-C), 151.54 (7a-C); MS (70 eV), *m/e* (relative intensity) 208 (7), 206 (24), 179 (12), 177 (39), 170 (13), 171 (100), 157 (22), 156 (33), 142 (47), 141 (56), 139 (13), 128 (15), 127 (12), 115 (42), 91 (3), 77 (9), 76 (8), 63 (18), 51 (15).

3-Chloro-6-fluoro-1,1,2-trimethyl-2-indene (3c): colorless oil, 110 °C (4.5 mbar) [bulb-to-bulb distillation]; ^{1}H NMR ($CDCl_3$) δ 1.21 (6 H, s), 1.92 (3 H, s), 6.90–7.03 (2 H, m), 7.22 (1 H, dd); ^{13}C NMR ($CDCl_3$) δ 9.78 (2-Me), 23.58 (1-Me), 49.62 (1-C), 108.95 (CH, J = 24 Hz), 113.45 (CH, J = 23 Hz), 119.25 (CH, J = 8 Hz), 124 (CCl), 136.0 (2-C), 146.46 (3a-C), 153.42 (7a-C), 162.0 (CF, J = 244 Hz); MS (70 eV), *m/e* (relative intensity) 212 (11), 210 (34), 195 (10.5), 176 (14), 175 (100), 106 (62), 159 (41), 157 (10), 147 (16), 133 (26), 125 (2), 107 (2), 79 (4), 69 (6), 51 (4), 39 (8), 27 (5).

3,6-Dichloro-1,1,2-trimethyl-2-indene (3d): colorless oil; 110–115 °C (4.5 mbar) [bulb-to-bulb distillation]; ^{1}H NMR ($CDCl_3$) δ 1.16 (6 H, s), 1.89 (3 H, s), 7.19 (1 H, d), 7.20 (1 H, s), 7.24 (1 H, d); ^{13}C NMR ($CDCl_3$) δ 9.75 (2-Me), 23.36 (1-Me), 49.55 (1-C), 119.31 (C-H), 121.55 (CH), 124.23 (CCl), 126.89 (CH), 131.60 (ClC_{aryl}), 135.57 (2-C), 147.25 (3a-C), 152.77 (7a-C); MS (70 eV), *m/e* (relative intensity) 228 (26), 226 (41), 213 (7), 211 (12), 193 (40), 192 (17), 191 (100), 178 (11), 177 (11), 176 (36), 163 (8), 156 (41), 155 (11), 141 (37), 139 (32), 115 (19), 99 (4), 77 (9), 76 (12), 75 (12), 63 (20), 51 (13).

3-Chloro-6-methoxy-1,1,2-trimethyl-2-indene (3e): colorless oil isolated by liquid chromatography on silica (eluent heptane/dichloromethane, 70:30) (R_f 0.44) from the 130 °C (4 mbar) fraction of the bulb-to-bulb distillation; ^{1}H NMR ($CDCl_3$) δ 1.28 (6 H, s), 1.92 (3 H, s), 3.75 (3 H, s), 6.69 (1 H, d), 6.82 (1 H, s), 7.12 (1 H, d); ^{13}C NMR ($CDCl_3$) δ 9.79 (2-Me), 23.94 (1-Me), 49.39 (1-C), 55.48 (MeO), 108.28 (CH), 111.31 (CH), 118.93 (CH), 124.37 (CCl), 133.27 (2-C), 144.50 (3a-C), 152.98 (7a-C), 158.62 (MeOC); MS (70 eV), *m/e* (relative intensity) 224 (26), 222 (75), 209 (11), 207 (34), 188 (23), 187 (100), 172 (65), 157 (11), 141 (9), 128 (30), 115 (10), 93 (3), 77 (6), 63 (8), 51 (8).

3-Chloro-5(6)-*tert*-amyl-1,1,2-trimethyl-2-indene (3f): colorless oil obtained together with **3a** in the 110 °C/(1 mbar) [bulb-to-bulb distillation] fraction and purified by preparative GLC; ^{1}H NMR ($CDCl_3$) δ 0.68 (3 H, t), 1.25 (6 H, s), 1.31 (6 H, s), 1.60 (2 H, q), 1.96 (3 H, s), 7.40 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 9.72 (2-Me), 23.85 (1-Me), 28.33, 28.40, 28.55, 36.80, 49.44 (1-C), 51.97, 117.78 (CH), 118.58 (CH), 124.38 (CH), 126.94 (CCl), 137.56 (2-C), 146.05 (3a-C), 147.29 (5-C or 6-C), 151.07 (7a-C); MS (70 eV), *m/e* (relative intensity) 264 (5), 262 (14.5), 247 (4), 235 (35), 233 (100), 218 (10), 205 (3), 198 (3), 183 (4), 165 (6), 155 (5), 141 (6), 128 (3), 115 (4), 99 (3), 77 (4), 71 (3).

5(6)-Benzoyl-3-chloro-1,1,2-trimethyl-2-indene (3g): white solid (mp 88 °C); obtained together with part of **3f** in the 120–160 °C (0.5–0.3 mbar) fraction during bulb-to-bulb distillation and purified by preparative TLC (eluent heptane/dichloromethane, 50:50); ^{1}H NMR ($CDCl_3$) δ 1.3 (6 H, s), 2.01 (3 H, s), 7.3–7.96 (8 H, complex); ^{13}C NMR ($CDCl_3$) δ 10.25 (2-Me), 23.49 (1-Me), 49.92 (1-C), 117.97 (CH), 122.33 (CH), 124.92 (CCl), 128.23 (CH), 129.34 (CH), 130.44 (CH), 132.06 (CH), 134.9 (5- or 6-C), 138.40 (2-C), 144.51 (3a-C), 151.35 (7a-C), 196.57 (C=O); MS (70 eV), *m/e* (relative intensity) 298 (11), 296 (34), 281 (3), 262 (13), 261 (67), 141 (10), 105 (100), 77 (55), 63 (4), 51 (12).

3-Chloro-6-methoxy-5-(*p*-methoxybenzoyl)-1,1,2-trimethyl-2-indene (3h). White solid (mp 132 °C) isolated by liquid chromatography of the bulb-to-bulb distillation residue yielding **3e** (eluent benzene/methyl *tert*-butyl ether, 70:30) (R_f 0.28); ^{1}H NMR ($CDCl_3$) δ 1.28 (6 H, s), 1.95 (3 H, s), 3.76 (3 H, s), 3.85 (3 H, s), 6.90 (2 H, d), 6.98 (1 H, s), 7.26 (1 H, s), 7.82 (2 H, d); ^{13}C NMR ($CDCl_3$) δ 9.84 (2-Me), 23.89 (1-Me), 49.93 (1-C), 105.79 (CH), 113.56 (CH), 119.05 (CH), 124.19 (CCl), 128, 131, 132.29 (CH), 133.07 (2-C), 145.57 (3a-C), 154.98 (7a-C), 156.54, 163.6, 195.09 (C=O); MS (70 eV), *m/e* (relative intensity) 356 (18), 341 (2), 339 (2), 321 (9), 189 (66), 135 (100), 77 (55); IR 1640 (C=O), 1590 cm^{-1} (C=C).

(b) Indenyl Benzoates 8a and 8b. Methanesulfonic acid (19.5 mL, 0.3 mol) was added rapidly to 271.2 g (1.2 mol) of benzoyl anhydride warmed at 60 °C. The temperature increased to 70 °C, and the mixure became brownish. The mixture was warmed to 115 °C for 30 min and then cooled to 75 °C. 2-Methyl-2-butanol (10.8 mL, 0.1 mol) was added dropwise for 30 min. The mixture became thick, and it was warmed to 100 °C for 18 h. On cooling, the mixture became very thick. It was dissolved into 300 mL of diethyl ether, and 100 mL of water was added. The ethereal layer yielded, after standing one night at 0 °C, a pink precipitate (11.3 g) which gave, after recrystallization in acetone, 9.8 g of 5(6)-benzoyl-3-indenyl benzoate (**8b**) (25% yield from 2-methyl-2-butanol) (mp 190–192 °C). The filtrate was neutralized with 200 mL of aqueous ammonia and extracted with dichloromethane. Liquid chromatography on silica (eluent pentane/dichloromethane, 80:20) yielded 4.8 g of 3-indenyl benzoate **8a** (17% yield from 2-methyl-2-butanol).

1,1,2-Trimethyl-3-indenyl benzoate (8a): pale yellow oil; ^{1}H NMR ($CDCl_3$) δ 1.30 (6 H, s), 1.80 (3 H, s), 7.0–8.3 (9 H, complex figure); ^{13}C NMR ($CDCl_3$) δ 8.30 (2-Me), 23.79 (1-Me), 47.24 (1-C), 117.56, 121.2, 125.11, 126.46, 128.64, 130.23, and 133.56 (CH), 129.31 (CCO_2), 142.29 (2-C), 137.46 (3a-C), 151.16 (7a-C), 163.94 (ester); MS (70 eV), *m/e* (relative intensity) 278 (1), 106 (6), 105 (100), 77 (22), 51 (5); IR 1730 cm^{-1} (C=O).

5(6)-Benzoyl-1,1,2-trimethyl-3-indenyl benzoate (8b): pink crystals; mp 190–192 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 (6 H, s), 1.90 (3 H, s), 7.0–8.20 (15 H, complex figure); ^{13}C NMR ($CDCl_3$) δ 8.74 (2-Me), 23.56 (1-Me), 47.67 (1-C), 117.12, 122.7, 128.2, 128.75, 129.94, 130.25, 132.01, 133.91, and 134.4 (CH) and 128.95 (CCO_2), 138.4, 141.95 (1-C), 142.35 (2-C), 142.09 (3a-C), 151.24 (7a-C), 163.94 (ester), 196.81 (C=O); MS (70 eV), *m/e* (relative intensity) 382 (7), 106 (8), 105 (100), 77 (23), 51 (4); IR 1730 and 1640 cm^{-1} (C=O).

Registry No. 1 (R = H), 98-88-4; 1 (R = Me), 874-60-2; 1 (R = F), 403-43-0; 1 (R = Cl), 122-01-0; 1 (R = MeO), 100-07-2; **2**, 594-36-5; **3a**, 111976-94-4; **3b**, 111976-95-5; **3c**, 111976-96-6; **3d**, 111976-97-7; **3e**, 111976-98-8; **3f**, 111977-01-6; **3g**, 111977-02-7; **3h**, 111976-99-9; **8a**, 111977-00-5; **8b**, 111977-03-8; benzoyl anhydride, 93-97-0; 2-methyl-2-butanol, 75-85-4.

(13) Isomeric 2-chloro-1,1,3-trimethyl indene has been reported recently: Anke, L.; Weyerstahl, P. *Chem. Ber.* **1985**, *118*, 613.
(14) Quoted in: Neth. Appl. 7802, 38, 1979; *Chem. Abstr.* **1979**, *90*, 71951e.

Transition-State Geometry of [3,3]-Sigmatropic Rearrangements of Iminium Ions[1]

Robert J. Doedens, Guy P. Meier,[2] and Larry E. Overman*

Department of Chemistry, University of California, Irvine, California 92717

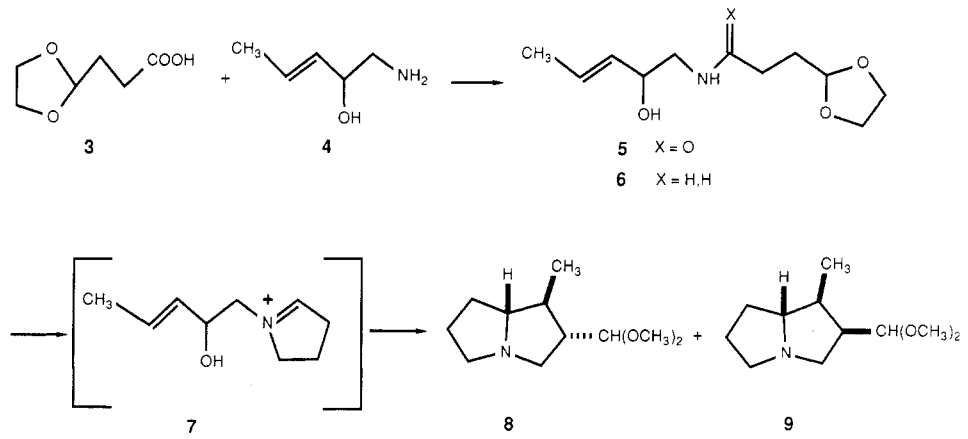
Received March 6, 1987

The tandem 2-aza-Cope rearrangement–Mannich cyclization reaction (eq 1) has been demonstrated to provide

(1) (a) Part 17 in the series "Synthesis Applications of Cationic Aza-Cope Rearrangements". For part 16, see: Overman, L. E.; Okazaki, M. E.; Jacobsen, E. J. *J. Org. Chem.* **1985**, *50*, 2403.
(2) (a) NIH Postdoctoral Fellow (GM 08155), 1981–1983. (b) Current address: Department of Medicinal Chemistry, University of Washington, Seattle, WA 98195.

0022-3263/88/1953-0685$01.50/0

Scheme I



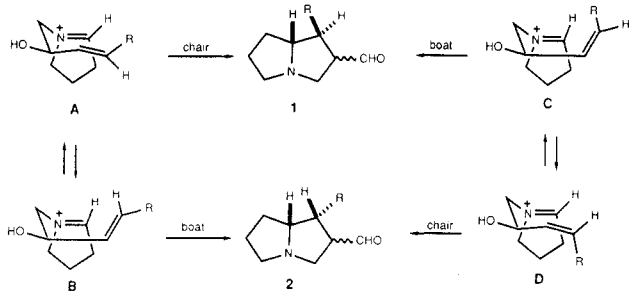
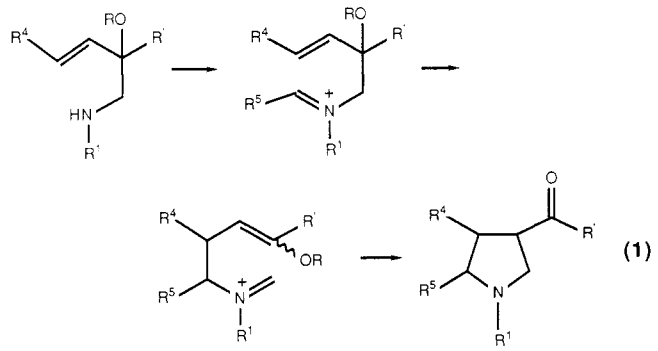


Figure 1.

a potent solution to several difficult problems in alkaloid synthesis.[1] Although the reaction scope and several ste-



(1)

reochemical and mechanistic features have been outlined,[1,3] the inherent transition-state topography of the [3,3]-sigmatropic rearrangement of iminium ions[4] has not been defined.[5] Herein we report experiments that demonstrate that cationic aza-Cope rearrangements (2-azonia-[3,3]-sigmatropic rearrangements) occur preferentially via chair geometries. We also report that the stereochemical preference is higher for *E* than for *Z* alkenes and that the sigmatropic rearrangement of the former also occurs considerably more rapidly. These studies illustrate also a new method for the stereocontrolled preparation of pyrrolizidines structurally related to some of the natural pyrrolizidine alkaloids.[6]

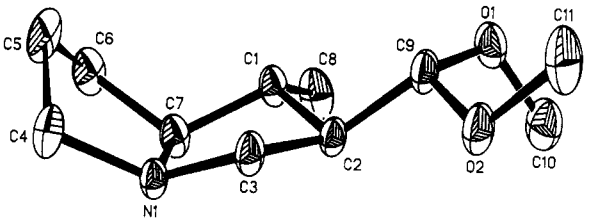


Figure 2. View of the molecular structure of 8. Thermal ellipsoids are drawn at the 50% probability level. The oxalate counterion and oxalic acid solvate are omitted for clarity.

Results

In order to define unambiguously the stereochemistry of the iminium ion double bond, the system shown in Figure 1 was chosen for study. With the "starting" iminium ion locked in the *E* configuration, rearrangement of an *E* alkene would lead to formyl pyrrolizidine **1** via a chair topography and formyl pyrrolizidine **2** if rearrangement occurred in a boat topography. Conversely, rearrangement of the *Z* alkene via chair or boat geometries would lead to formyl pyrrolizidines **2** and **1**, respectively.[5] From the outset, we realized that incorporation of the C–N double bond into a ring could bias the test system toward a boat geometry.[7]

As a precursor of the required Δ^1-pyrroline cation we chose a 4-amino acetal, which in the case of the *E* alkene substrate was prepared as summarized in Scheme I. Treatment of 4-dioxalanylbutyric acid (**3**)[8] with carbonyldiimidazole, followed by addition of (*E*)-1-amino-3-penten-2-ol (**4**),[9] provided amide **5** in essentially quanti-

(3) Jacobsen, E. J.; Levin, J.; Overman, L. E. *J. Am. Chem. Soc.*, in press.

(4) For brief reviews of iminium ion sigmatropic rearrangements, see: Winterfeldt, T. *Fortschr. Chem. Forsch.* **1971**, *16*, 75. Heimgartner, H.; Hansen, H.-J.; Schmidt, H. In *Iminium Salts in Organic Chemistry*; Bohme, H., Viehe, H. G., Eds.; Wiley: New York, 1979; Part 2, p 655.

(5) (a) Aliphatic Cope and Claisen rearrangements proceed predominately via a chairlike topography; see: Hansen, H.-J.; Schmid, H. *Tetrahedron* **1974**, *18*, 1959. Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227. (b) Some aza- and diaza-Cope rearrangements have been shown to proceed preferentially via boat topographies: Brombach, D.; Vögtle, F. *Synthesis* **1977**, 800. Vögtle, F.; Goldschmitt, E. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 767. Vögtle, F.; Goldschmitt, E. *Chem. Ber.* **1976**, *109*, 1. (c) The [3,3]-sigmatropic rearrangement of a *N*-acyliminium ion has in one case been demonstrated to proceed preferentially in a chair sense: Hart, D. J.; Yang, T.-K. *J. Org. Chem.* **1985**, *50*, 235. (d) The aza-Cope rearrangement of 2-alkenyl-2*H*-oxazol-5-ones has also been shown to occur by both chair and boat topographies depending upon the structure and stereochemistry of the alkene group: Steglich, W. *IUPAC, Chemistry for the Future*; Grünewald, H., Ed.; Pergamon: Oxford, 1984; pp 211–218.

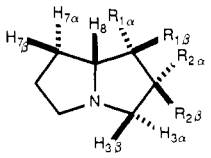
(6) Wrobel, J. T. *Alkaloids (N.Y.)* **1985**, *26*, 327.

(7) It has previously been shown that [3,3]-sigmatropic rearrangements in which one olefin partner is constrained to a ring (five- or six-membered) often occur via a boat topographies, see, inter alia: Bartlett, P. A.; Tanzella, D. J.; Barstow, J. F. *Tetrahedron Lett.* **1982**, *23*, 619–622. Bartlett, P. A.; Barstow, J. F. *Tetrahedron Lett.* **1982**, *23*, 623–626. Bartlett, P. A.; Barstow, J. F. *J. Org. Chem.* **1982**, *47*, 3933–3941. Ireland, R. E.; Varney, M. D. *J. Org. Chem.* **1983**, *48*, 1829–1833.

(8) Shea, K. J.; Wada, E. *J. Am. Chem. Soc.* **1982**, *104*, 5715.

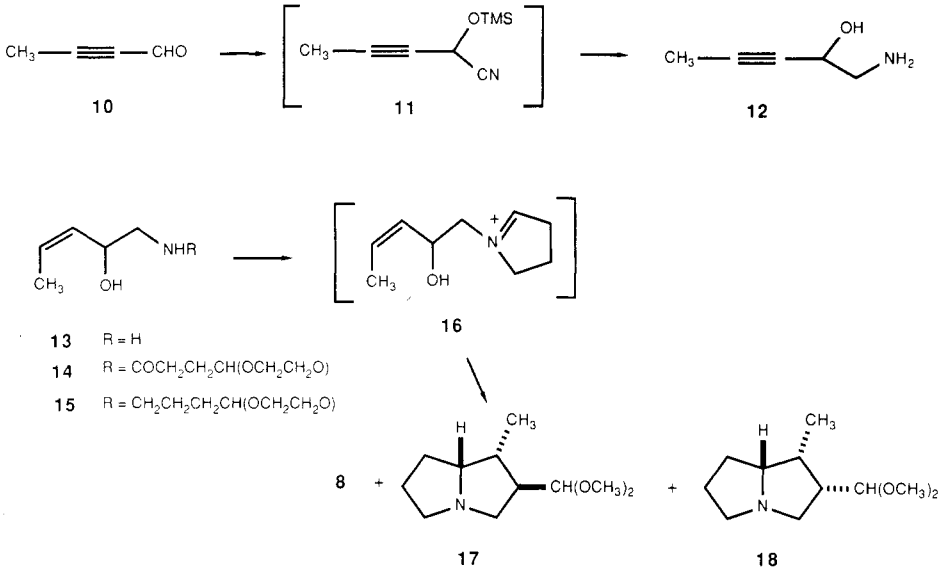
(9) Overman, L. E.; Kakimoto, M.; Okazaki, M. E.; Meier, G. P. *J. Am. Chem. Soc.* **1983**, *105*, 6622.

Table I. NOEDS Data on Pyrrolizidine Products



		R_1		R_2			% NOE				
entry	compd	α	β	α	β	irrid	H_1	H_2	H_8	$CH(OMe)_2$	other
1	8	H	Me	$CH(OMe)_2$	H	C-1 Me	3	2	3	<1	$H_{7\beta}$(1)
2	8	H	Me	$CH(OMe)_2$	H	$CH(OMe)_2$	6	4		irr	$H_{3\alpha}$(3), OMe (10)
3	9	H	Me	H	$CH(OMe)_2$	C-1 Me	3		1.5	5	OMe (1)
4	9	H	Me	H	$CH(OMe)_2$	$CH(OMe)_2$		3		irr	C_1-Me (4), $H_{3\beta}$(2), OMe(10)
5	17	Me	H	H	$CH(OMe)_2$	C-1 Me	3	1.5		<1	$H_{7\alpha}$(4), OMe (<1)
6	17	Me	H	H	$CH(OMe_2$	$CH(OMe)_2$	5	3		irr	$H_{3\alpha}$(5), OMe (14)
7	18	Me	H	$CH(OMe)_2$	H	C-1 Me	3			1	$H_{7\alpha}$(3), OMe (1)
8	18	Me	H	$CH(OMe)_2$	H	$CH(OMe)_2$		3		irr	C_1-Me(4), $H_{3\alpha}$(2), $H_{7\alpha}$(2)

Scheme II



tative yield. Reduction of **5** with $LiAlH_4$ gave the crystalline amino acetal **6** (mp 40–43 °C) in 76%–91% yield. The key rearrangement of **6** was cleanly accomplished by heating a 0.20 M solution of **6** in 0.25 M methanolic HCl at 65 °C for 6 h to give two epimeric pyrrolizidine acetals, **8** and **9**, in 84% and 6% yields, respectively, after chromatographic separation.

The gross structural assignment for **8** followed from its ^1H NMR and mass spectrum; however, the stereochemistry at C-1, C-2, and C-8 could not be determined unambiguously from coupling constants.[10] The stereostructure of **8** was initially secured by the NOEDS technique,[10,11] and the results are summarized in Table I. The key observations were that irradiation of the methyl doublet resulted in NOE enhancement of the signals for the hydrogens at C-2 and C-8, while irradiation of the methine hydrogen of the acetal group resulted in NOE enhancement of the hydrogen at C-1. This stereochemical assignment was confirmed by a single-crystal X-ray diffraction study of the oxalate salt of **8**, which crystallized as an oxalic acid solvate. A drawing of the molecular structure is shown in Figure 2. The stereochemical assignment for the minor pyrrolizidine acetal **9** followed in a similar fashion from NOEDS experiments. The NOE enhancement observed between the methyl group at C-1 and the methine hydrogen at C-8 for each isomer establishes that the two pyrrolizine products derived from **6** differ only in the configuration of the acetal substituent.

To examine what effect alkene stereochemistry would have on the stereoselectivity of the 2-azonia-[3,3]-sigmatropic rearrangement, as well as explore the utility of this reaction for the stereoselective synthesis of pyrrolizidines with either spatial arrangement of substituents at C-1 and C-8, the isomeric *Z* alkene amino acetal **15** was prepared (see Scheme II). The sequence began with 2-butynal (**10**), which was converted to the unstable trimethylsilyl cyanohydrin **11** in the presence of a catalytic amount of KCN.[12] Reduction with $LiAlH_4$ as described by Evans[13] gave alkyne amino alcohol **12** in 42%–62% overall yield from 2-butynal. Semihydrogenation (Pd–$BaSO_4$/pyridine) gave the corresponding *Z* alkene, judged to be >95% *Z* by ^1H NMR analysis, in excellent (91%–98%) yield. Conversion of **13** to amino acetal **15** was accomplished as before to give **15** in 71%–77% yield.

(10) For references to the difficulty in unambiguously assigning stereochemistry about five-membered rings from coupling constant data, see: Kakanishi, K.; Schooley, D. A.; Koreeda, M.; Kiura, I. *J. Am. Chem. Soc.* **1972**, *94*, 2865.

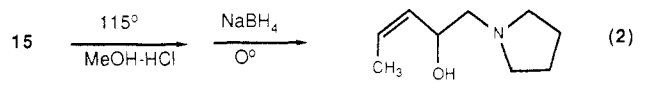
(11) See e.g.: Nauhaus, D.; Sheppard, R. N.; Bick, I. R. C. *J. Am. Chem. Soc.* **1983**, *105*, 5996.

(12) Utimoto et al. have used Lewis acid catalysis to generate the (trimethylsilyl)cyanohydrins of ynones: Utimoto, K.; Miwa, H.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 4177 and references therein.

(13) Evans, D. A.; Carroll, G. L.; Truesdale, L. K. *J. Org. Chem.* **1974**, *39*, 915.

Treatment of **15** with acid (0.20 M in 0.24 M methanolic HCl) at 65 °C, as employed for the rearrangement of **6**, did not afford any isolable pyrrolizidine products. However, rearrangement did occur at 115 °C (12 h, sealed tube) to give a mixture of pyrrolizidines **17**, **18**, and **8** in yields of 42%, 15%, and 20%, respectively. These isomers were separated by preparative GC, and the identity of **8** was confirmed by direct comparison with the major pyrrolizidine product formed from the isomeric *E* alkene amino acetal **6**. The trans stereorelationship of the hydrogen and methyl substituents at C-1 and C-8 of pyrrolizidines **17** and **18** was fairly secure, since **8** and **9** had been shown to have the cis relationship of these groups. This fact was confirmed, and the relative stereochemistry of the acetal substituents of **17** and **18** was assigned on the basis of ^{1}H NMR and NOEDS spectra (see Table I).

The stereochemical leakage observed in the rearrangement of the *Z* alkene amino acetal **15** could result from competitive rearrangement of **16** via a boat topography, from *Z* → *E* isomerization of the alkene double bond prior to rearrangement, or from thermodynamic equilibration of the product pyrrolizidine acetals. That **8** was a kinetic product of the rearrangement of **15** was established by showing that rearrangements of **15** conducted for 24 h led to no increase in the proportion of **8**: 53 ± 3% **17**, 21 ± 1% **18**, 26 ± 2% **8** at 12 h (two experiments); 59% **17**, 18% **18**, 23% **8** at 24 h. Since **8** also was recovered unchanged when subjected to the high-temperature rearrangement conditions (0.20 M in 0.24 M methanolic HCl, 115 °C, 12 h), the time-independent ratio of products formed from **15** cannot reflect thermodynamic equilibrium. To pursue the possibility that the *Z* alkene group of **15** underwent *Z* → *E* isomerization *prior* to rearrangement, rearrangements of **15** were carried out to partial completion and then quenched with $NaBH_4$ (eq 2). Analysis by capillary GC



(2)

19

(~1% detection limit) and ^{1}H NMR spectroscopy indicated the presence of *only* the *Z* pyrrolidine alcohol **19**. This result, while consistent with stereochemical crossover occurring during the rearrangement (i.e. by competitive rearrangement via a boat transition state) does not rigorously rule out isomerization prior to rearrangement since the *E* iminium cation **7** rearranges significantly faster than the *Z* isomer **16**.

Discussion

The formation of only pyrrolizidines **8** and **9** from the rearrangement of *E* alkene iminium ion **7** is consistent with the sigmatropic rearrangement occurring via chair transition state A (see Figure 1). Since the capillary GC analysis employed in this study would have been capable of detecting 1% of the alternate pyrrolizidine stereoisomers (i.e. **17** and **18**), we can estimate that the chair preference for the rearrangement of **7** is >3 kcal/mol. A chair preference (at least 3:1 at 115 °C) was observed also for the rearrangement of the *Z* alkene iminium ion **16**. These are the first demonstrations[5] that [3,3]-sigmatropic rearrangements of iminium ions occur preferentially in the same topographical sense as the Cope rearrangement of acyclic 1,5-dienes.

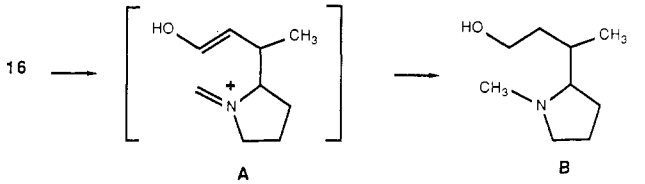
The temperature required for aza-Cope–Mannich rearrangement of the *Z* alkene acetal **15** was significantly higher (50 °C) than that required for the rearrangement of **6**. This result could arise from a slower rate of [3,3]-sigmatropic rearrangement of iminium ion **16** than **7**[14] and/or from a lower equilibrium concentration in methanolic HCl of the former iminium ion. Since iminium ion **7** is formed readily in methanolic HCl at 65 °C, it is difficult to ascribe the reluctance of **15** to rearrange to the inability of forming the isomeric iminium ion **16** under similar conditions. On the other hand, it is reasonable that [3,3]-sigmatropic rearrangement of **16** via a chair transition state (see D, Figure 1) should be inhibited by destabilizing steric interactions between the (*Z*)-methyl substituent and the azacyclopentene ring.[15] That **16** would rearrange at least partially via a boat topography (see C, Figure 1) is, therefore, not surprising.

Although detailed mechanistic interpretations of the rate and stereoselectivity differences observed in the rearrangement of the iminium ion intermediates **7** and **16** are prevented by the lack of quantitative kinetic data, the studies reported here do have practical implications for the use of aza-Cope rearrangements in synthesis. These investigations illustrate the *large* effect that alkene stereochemistry can exert on the rate and stereoselectivity of 2-azonia-[3,3]-sigmatropic rearrangements. An even more dramatic effect has been described by Steglich and coworkers[5d] for aza-Cope rearrangement of cinnamyl substrates where a complete preference for the *E* and *Z* isomers to rearrange via chair and boat topographies, respectively, is observed. Our studies highlight the potential advantage of synthesis designs involving iminium ion rearrangements of *E* alkenes. During the course of our studies in this area, Hart and Yang reported[5c] the use of the [3,3]-sigmatropic rearrangement of *N*-acyliminium ions for the enantioselective synthesis of the pyrrolizidine diols (−)-hastanecine and (−)-heliotridine. An *E* alkene was employed in these studies and high chair stereoselectivities were observed.[5c]

Experimental Section[16]

***N*-[(*E*)-2-Hydroxy-3-pentenyl]-3-(1,3-dioxolan-2-yl)-propanamide (5).** A solution of acid **3**[8] (1.14 g, 7.80 mmol) in 5 mL of dry THF was added via cannula to a cold (0 °C) slurry of 1,1-carbonyldiimidazole (1.56 g, 9.68 mmol) in 5.0 mL of dry THF under an argon atmosphere. This solution was warmed to 24 °C for 1 h and cooled to 0 °C, and a solution of amino alcohol **4**[9] (0.783 g, 7.74 mmol) in 5 mL of dry THF was added via cannula. The reaction mixture was stirred at 24 °C for 6 h and then concentrated to a tan oil. This oil was purified by flash chromatography (50 g, SiO_2, 95:5 ether/triethylamine) to give **5** (1.74 g, 98% yield) as a clear colorless oil: IR (film) 3360, 1660, 1560, 1150, 1060, 1045, 970, 730 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$) δ 6.73 (t, *J* = 5.3 Hz, N*H*), 5.62 (dqd, *J* = 0.9, 6.5, 15.3 Hz, CH_3CH=CH), 5.32 (qdd, *J* = 1.5, 5.2, 15.3 Hz, CH_3CH=C*H*), 4.79 (t, *J* = 4.4 Hz, OCHO), 4.0 (br m, C*H*OH), 3.75 (m, OCH_2CH_2O and OH), 3.31 (dd AB, *J* = 3.7, 5.3, 13.7 Hz, C*H*HNH), 3.02 (dd AB, *J* = 5.2, 7.6, 13.7 Hz, CH*H*NH), 2.21 (t, *J* = 7.2 Hz,

(14) A referee has suggested that the rate differences may occur in the Mannich step rather than the sigmatropic rearrangement. This possibility is precluded by the experiments illustrated in eq 2, since product B which would have resulted from reduction of a rearranged, but uncyclized, iminium cation A was not seen in the ^{1}H NMR spectrum (no N–CH_3 singlet) of the crude reduced product mixture.



(15) For a recent careful analysis of substituted effects on enolate Claisen rearrangements, see: Wilcox, C.; Badston, R. E. *J. Am. Chem. Soc.* **1986**, *108*, 6636.

(16) General experimental details have been described. See: Overman, L.e.; Sugai, S. *Helv. Chim. Acta* **1985**, *68*, 745.

$COCH_2$), 1.86 (dt, J = 4.4, 7.2 Hz, CH_2CH_2CH), 1.57 (dd, J = 1.5, 6.5 Hz, CH_3CH=CH); ^{13}C NMR (63 MHz, $CDCl_3$) 173.5 (C=O), 131.1 (CH=C), 127.4 (CH=C), 103.3 (OCHO), 71.3 (CHOH), 64.8 (OCH_2CH_2O), 53.4 (CH_2N), 30.3 ($COCH_2$), 29.3 (CH_2CH_2CH), 17.6 (CH_3); MS (EI, 100 eV), m/z 229.1309 (229.1313 calcd for $C_{11}H_{19}NO_4$).

(*E*)-1-[[3-(1,3-Dioxolan-2-yl)propyl]amino]-3-penten-2-ol (6). A solution of amide **5** (1.325 g, 5.78 mmol) in 5 mL of dry THF was added via cannula to a rapidly stirring slurry of $LiAlH_4$ (0.38 g, 10.0 mmol) and 5 mL of dry THF at 0 °C under an atmosphere of Ar. The resulting mixture was heated to reflux for 4 h, cooled to 0 °C, and slowly quenched by adding 6 N NaOH (20 mL). The resulting mixture was extracted with THF (4 × 10 mL), and the organic phases were dried (K_2CO_3), filtered, and concentrated to give a tan foam. Crystallization from hot ether/hexane (80:20) gave **6** as white crystals (mp 40–43 °C, 1.13 g, 91% yield): IR (film) 3600–3300, 1460, 1410, 1240, 1140, 1090, 1040, 970 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.73 (dqd, J = 1.0, 6.3, 15.5 Hz, CH_3CH=CH), 5.42 (q dd, J = 1.3, 5.0, 15.5 Hz, CH_3CH=C*H*), 4.83 (t, J = 5.1 Hz, OC*H*O), 4.08 (br m, C*H*OH), 3.80 (m, OCH_2CH_2O), 2.8–2.5 (m, CH_2NCH_2, OH, NH), 1.70 (dd, J = 1.3, 6.3 Hz, CH_3CH=CH), 1.60 (m, $CH_2CH_2CH_2CH$); ^{13}C NMR (63 MHz, $CDCl_3$) δ 132.3 (CH=CH), 127.0 (CH=CH), 104.3 (OCHO), 70.3 (CHOH), 64.8 (OCH_2CH_2O), 55.2 (CH_2N), 49.2 (CH_2N), 31.4 (CH_2), 24.3 (CH_2), 17.7 (CH_3CH=); MS (isobutane CI), m/z 216.1595 (216.1600 calcd for $C_{11}H_{22}NO_3$).

1-Amino-3-pentyn-2-ol (12). A solution of butynal (2.29 g, 33.7 mmol; freshly distilled) and 20 mL of dry CH_2Cl_2 was treated with trimethylsilyl cyanide (6.7 mL, 50.5 mmol) and a catalytic amount (10 mg) of the potassium cyanide/18-crown-6 ether complex, following the general procedure of Evans.[13] The solvent and excess trimethylsilyl cyanide were removed under vacuum (10 mm) at 24 °C to provide the crude silyl cyanohydrin **11**. A slurry of $LiAlH_4$ (1.92 g, 50.5 mmol) in 200 mL of dry ether was cooled to 0 °C, and thermally unstable crude **11** was added via cannula as a solution in dry ether (50 mL). The resulting brown mixture was heated to reflux for 4 h, cooled to 0 °C, and quenched with 6 N NaOH (25 mL), and the aqueous phase was extracted with THF (4 × 20 mL). The combined organic phase was dried (K_2CO_3) and filtered, and the solvent was evaporated to give a brown semisolid. The crude product was distilled (Kugelrohr; 100–110 °C, 20 mm) to give a colorless oil (2.43 g), which was shown to be a mixture of acetylene **12** (91%) and *E* alkene **4** (9%) by ^1H NMR spectroscopy. Crystallization of the crude mixture from ether/pentane at −20 °C gave the pure acetylene **12** (2.07 g, 62%) as white crystals (mp 31–33 °C): IR (CH_2Cl_2) 3700–2500, 3600, 2920, 2850, 2200, 1580, 1075, 1020 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 4.19 (qdd, J = 2.1, 4.8, 5.8 Hz, C*H*OH), 3.03 (br s, NH_2 and OH), 2.70 (d AB, J_{AB} = 13.1 Hz, J_A = 4.8 Hz, J_B = 5.8 Hz, $\Delta\nu_{AB}$ = 8.2 Hz, CH_2NH_2), 1.75 (d, J = 2.1 Hz, CH_3); ^{13}C NMR (63 MHz, $CDCl_3$) δ 81.1 ($CH_3C{\equiv}C$), 79.1 ($CH_3C{\equiv}C$), 63.1 (CHOH), 48.2 (CH_2N), 3.5 (CH_3); MS (isobutane CI), m/z 100.0759 (100.0762 calcd for $C_5H_{10}NO$).

(*Z*)-1-Amino-3-penten-2-ol (13). A mixture of 5% palladium on barium sulfate (0.030 g) and pyridine (20 mL) was saturated with hydrogen at room temperature and atmospheric pressure until the catalyst turned black. Alkyne **12** (0.304 g, 3.07 mmol) was added with vigorous stirring, and the uptake of hydrogen was monitored. After 45 min, the rate of hydrogen uptake decreased sharply [70 mL of hydrogen was consumed at 21 °C (760 mm)], the mixture was filtered through Celite, and the Celite was washed with additional methanol. The methanolic eluent was concentrated and the resulting brown oil was bulb-to-bulb distilled (bp 100–110 °C at 20 mm) to give 0.304 g of **13** (98%), a colorless oil which was >95% isomerically pure by ^1H NMR analysis: IR (film) 3700–3200, 1655, 1600, 1450 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.56 (dqd, J = 1.0, 6.8, 11.0 Hz, CH_3CH=C), 5.32 (qdd, J = 1.7, 8.4, 11.0 Hz, C=C*H*CH_2), 4.34 (app q, C*H*OH), 2.60 (m, NH_2), 1.64 (dd, J = 1.7, 6.8 Hz, CH_3); ^{13}C NMR (63 Hz, $CDCl_3$) δ 131.6 (CH=CH), 125.6 (CH=CH), 67.5 (CHOH), 47.1 (CH_2N), 12.9 (CH_3C=C); MS (CH_4 CI), m/z 102.0919 (102.0919 calcd for $C_5H_{12}NO$).

***N*-[(*Z*)-2-Hydroxy-3-penentyl]-3-(1,3-dioxolan-2-yl)propanamide (14).** Amino alcohol **13** (0.392 g, 3.87 mmol) was condensed with acid **3**, as described for the preparation of **5**. Purification of the crude product by flash chromatography (35 g SiO_2, 95:5 ether/triethylamine) gave **14** as a clear colorless oil (0.90 g, 99% yield): IR (film) 3360, 1660, 1570, 1140, 1055, 1050, 980 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 6.53 (t, J = 3.5, N*H*), 5.62 (dqd, J = 1.1, 6.9, 11.0 Hz, CH_3CH=CH), 5.37 (ddq, J = 1.7, 8.3, 11.0 Hz, CH_3CH=C*H*), 4.90 (t, J = 4.5 Hz, OCHO), 4.48 (br m, CHOH), 3.91 (m, OCH_2CH_2O), 3.29 (dd AB, J = 3.5, 5.8, 12.7 Hz, CHC*H*HN), 3.00 (dd AB, J = 4.3, 5.8, 12.7, CHCH*H*N), 2.18 (t, J = 7.0 Hz, $COCH_2CH_2$), 1.90 (dt, J = 5.0, 7.1 Hz, CH_2CHCH), 1.69 (dd, J = 1.1, 6.7 Hz, CH_3); MS (EI,100 eV), m/z 229.1310 (229.1313 calcd for $C_{11}H_{19}NO_4$).

(*Z*)-1-[[3-(1,3-Dioxolan-2-yl)propyl]amino]-3-penten-2-ol (15). Amide **14** (0.662 g, 2.89 mmol) was reduced with $LiAlH_4$ as described for the preparation of **6**. Purification of the crude product by flash chromatography (30 g of SiO_2, 95% ether, 5% triethylamine) gave pure **15** as a colorless oil, which could not be induced to crystallize: IR (film) 3460, 1670, 1410, 1130, 1070, 1035, 940 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.62 (dqd, J = 1.1, 6.9, 11.0 Hz, CH_3CH=CH), 5.37 (qdd, J = 1.7, 9.2, 11.0 Hz, CH_3=CH=C*H*CH), 4.87 (t, J = 4.4 Hz, OCHO), 4.48 (app dt, J = 3.8, 9.1 Hz, C=CHC*H*CH_2), 3.92 (m, OCH_2CH_2O), 2.68 (m, $NHCH_2O$), 2.68 (m, $NHCH_2$ and C*H*HNH), 2.53 (dd, J = 9.1, 12.1 Hz, CH*H*NH), 2.1 (br m, NH and OH), 1.69 (dd, J = 1.7, 6.9 Hz, CH_3); MS (CH_4 CI), m/z 216.1589 (216.1599 calcd for $C_{11}H_{22}NO_3$).

Rearrangement of (*E*)-Alkenyl Amino Acetal 6 to Pyrrolizidine Acetals 8 and 9. A solution of acetal amino alcohol **6** (0.217 g, 1.01 mmol) and 7 mL of anhydrous methanol was deoxygenated by bubbling dry Ar under the surface of the solution via a glass capillary for 15 min (the final volume was 5.2 mL). Aqueous HCl (38%, 0.10 mL, 1.20 mmol) was added via syringe, and the mixture was heated at 65 °C for 6 h under an atmosphere of Ar. The reaction mixture was cooled to 24 °C, quenched into 20 mL of saturated aqueous $NaHCO_3$, and extracted with dichloromethane (5 × 5 mL). The organic phase was washed (1 × 5 mL of H_2O, 1 × 5 mL of saturated aqueous NaCl), dried (K_2CO_3), filtered, and concentrated to give a dark oil. The residue was bulb-to-bulb distilled (50–100 °C, 2 mm) to give an impure mixture of the pyrrolizidines **8** and **9** (0.183 g, a 13:1 ratio of diastereomers by ^1H NMR spectroscopy and GC analysis). The mixture was separated by gas chromatography (20% FFAP on Supelcoport, 10 ft × $^3/_8$ in.) to give pure pyrrolizidine **8** (0.167 g, 84%) and **9** (0.012 g, 6%).

***rac*-(1*R*,2*R*,8*S*)-4-Aza-2-(dimethoxymethyl)-1-methylbicyclo[3.3.0]octane (8):**[21] IR (film) 1185, 1120, 1075, 1045, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$)[17] δ 4.25 (d, J = 6.5 Hz, MeOC*H*OMe), 3.36 (s, OCH_3), 3.32 (s, OCH_3), 3.19 (dd, J = 7.1, 10.0 Hz, H-3), 3.05 (ddd, J = 5.0, 6.8, 7.1 Hz, H-8), 2.90 (td, J = 6.3, 10.5 Hz, H-5), 2.54 (td, J = 6.4, 10.5, H-5), 2.38 (app t, 10.0 Hz, H-3), 2.22 (m, H-2), 1.95–1.75 (m, 2 H-6), 1.75–1.65 (m, H-7), 1.48 (m, H-1 and H-7), 1.08 (d, J = 7.2 Hz, CH_3); MS (100 eV EI), m/z 199.1568 (199.1572 calcd for $C_{11}H_{21}NO_2$).

A 29-mg (0.14-mmol) sample of **8**, 0.8 mL of methanol and 15 μL (0.17 mmol) of concentrated HCl was heated for 12 h at 115 °C in a sealed ampule. ^1H NMR analysis of this crude product showed that pyrrolizidines **17** and **18** had not been formed.

***rac*-(1*R*,2*S*,8*S*)-4-Aza-2-(dimethoxymethyl)-1-methylbicyclo[3.3.0]octane (9):** IR ($CHCl_3$) 1178, 1122, 1077, 1035 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$)[17] δ 4.53 (d, J = 7.4 Hz, MeOC*H*OMe), 3.55 (m, H-8), 3.50 (s, OCH_3), 3.30 (s, OCH_3), 3.19 (dd, J = 7.8, 10.8 Hz, H-3), 2.80 (m, H-2), 2.54 (m, H-5), 2.40 (dd, J = 8.6, 10.8 Hz, H-3), 2.25 (m, H-1), 1.98 (m, H-5 and H-7), 1.74–1.65 (m, H-7 and 2 H-6), 1.20 (d, J = 7.6 Hz, CH_3); MS (100 eV EI), m/z 199.1571 (199.1572 calcd for $C_{11}H_{21}NO_2$).

Rearrangement of (*Z*)-Alkenylamino Acetal 15 to Pyrrolizidine Acetals 17, 18, and 8. A glass ampule was charged with a solution of (*Z*)-alkenylamino alcohol **15** (0.214 g, 1.00 mmol) and 7 mL of dry methanol and deoxygenated by bubbling Ar under the surface of the solution via a glass capillary for 15 min (the final volume was 5.0 mL). Concentrated aqueous HCl (38%, 0.10 mL, 1.20 mmol) was added via syringe, and the ampule was cooled to −78 °C under Ar and sealed. The ampule was placed in an oil bath and then brought to 115 °C for 12 h. After being cooled to 24 °C, the sample was quenched into saturated aqueous $NaHCO_3$ (20 mL) and extracted with dichloromethane (5 × 5 mL).

(17) ^1H NMR assignments were confirmed by homonuclear decoupling experiments.

The organic phase was washed (1 × 5 mL of H_2O, 1 × 5 mL of saturated aqueous NaCl), dried (K_2CO_3), filtered, and concentrated to give a dark brown oil. The residue was bulb-to-bulb distilled (50–100 °C, 2 mm) to give an impure mixture of pyrrolizidines **17**, **8**, and **18** (0.191 g, 2.8:1.2:1 ratio, respectively, by GC analysis). This mixture was separated by preparative gas chromatography (10% SP-2100 on Supelcoport, 6 ft × $^1/_4$ in.) to give pure pyrrolizidines **17** (0.084 g, 42%), **8** (0.040 g, 20%), and **18** (0.030 g, 15%).

***rac*-(1*S*,2*S*,8*S*)-4-Aza-2-(dimethoxymethyl)-1-methylbicyclo[3.3.0]octane (17)**: IR ($CHCl_3$) 1185, 1122, 1075, 1035 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$)[17] δ 4.78 (d, J = 7.5 Hz, MeOC*H*OMe), 3.45 (m, H-8), 3.35 (s, OCH_3), 3.30 (s, OCH_3), 3.12 (ddd, J = 3.1, 6.0, 10 Hz, H-5), 2.94 (dd, J = 8.0, 10.8 Hz, H-3), 2.68 (dd, J = 8.1, 10.8 Hz, H-3), 2.54 (ddd, J = 7.1, 8.2, 10 Hz, H-5), 2.20 (m, H-1), 2.08 (app quintet, J = 6.8 Hz, H-3), 1.90 (m, H-6), 1.68 (m, H-6 and H-7), 1.42 (m, H-7), 1.08 (d, J = 7.3 Hz, CH_3); MS (CH_4 CI), m/z 200.165 0 (200.165 0 calcd $C_{11}H_{22}NO_2$).

***rac*-(1*S*,2*R*,8*S*)-4-Aza-2-(dimethyoxymethyl)-1-methylbicyclo[3.3.0]octane (18)**: IR ($CHCl_3$) 1178, 1120, 1077, 1045 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$)[17] δ 4.40 (d, J = 7.7 Hz, MeOC*H*OMe), 3.80 (m, H-8), 3.35 (s, OCH_3), 3.30 (s, OCH_3), 3.20 (dd, J = 7.7, 9.8 Hz, H-3), 2.84 (m, H-2), 2.52 (m, H-5), 2.45 (dd, J = 8.5, 9.8 Hz, H-3), 2.25 (m, H-1), 1.98 (m, H-5 and H-7), 1.74 (m, 2 H-6 and H-7), 0.88 (d, J = 7.7 Hz, CH_3); MS (CH_4 CI), m/z 200.165 0 (200.165 0 calcd for $C_{11}H_{22}NO_2$).

Exploration of Possible Alkene Isomerization in the Rearrangement of *Z* Alkene Amino Acetal 15. Three reaction samples of **15** (1.0 mmol) were prepared as previously described, and the ampules were heated at 115 °C for 3, 4, or 8 h. At the end of each reaction period, the sample was cooled to 0 °C and quenched with an excess of solid $NaBH_4$ (0.04 g, 1 mmol). Comparison of these samples with authentic samples of the (*Z*)- and (*E*)-pyrrolidine alcohols **19** and **20**, by capillary GC (30 m DB-5 column) and 250-MHz ^1H NMR analyses indicated the presence of only **19**.

(*Z*)-1-Pyrrolidino-3-penten-2-ol (19). To a solution of amino alcohol **13** (0.301 g, 2.98 mmol) and dry THF (10 mL) was added anhydrous K_2CO_3 (2.5 g, 18 mmol). The slurry was stirred, and a solution of 1,4-dibromobutane (0.36 mL, 3.0 mmol) in dry THF (10 mL) was added via cannula over a 45-min period. The resulting mixture was stirred at 24 °C for 12 h and filtered, and the solvent was evaporated. Flash chromatography (30 g, SiO_2, 95:5 ether/Et_3N) gave **19** as a colorless oil (0.333 g, 72% yield): IR (film) 3600–3200, 1660, 1605, 1450, 1115 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) δ 5.54 (dqd, J = 1.0, 6.7, 11.2 Hz, CH_3CH=), 5.35 (qdd, J = 1.6, 8.3, 11.2 Hz, =C*H*CH), 4.45 (pseudo dt, J = 4.0, 9.1 Hz, C*H*OH), 2.8–2.4 (m, 6 H, CH_2N), 1.66 (dd, J = 1.6, 6.7 Hz, CH_3CH), 1.45 (m, CH_2CH_2); MS (CH_4 CI), m/z 155.1311 (155.1310 calcd for $C_9H_{17}NO$).

(*E*)-1-Pyrrolidino-3-penten-2-ol (20). Amino alcohol **4** (1.002 g, 9.92 mmol) was alkylated with 1,4-dibromobutane (1.20 mL, 10.0 mmol) as described in the preparation of **19** to give **20** (1.169 g, 76%) as a colorless oil after purification on SiO_2: IR (film) 3600–3200, 1610, 1445, 1110, 1060 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$) 5.70 (dqd, J = 15.2, 6.8, 1.0 Hz, CH_3CH=), 5.44 (qdd, J = 1.6, 6.5, 15.2 Hz, CH_3CH=C*H*), 4.10 (br m, C*H*OH), 2.8–2.4 (m, 6 H, CH_2N), 1.72 (dd, J = 1.6, 6.8 Hz, CH_3CH=), 1.45 (m, CH_2CH_2); MS (CH_4CI), m/z 155.1309 (155.1310 calcd for $C_9H_{17}NO$).

Crystallography. Single crystals were prepared by slow crystallization from hexane. The crystals were found to belong to the triclinic system with unit cell dimensions at 22 °C: a = 8.453 (3) Å, b = 9.803 (3) Å, c = 11.513 (4) Å; α = 74.25 (2)°, β = 94.18 (2)°, γ = 112.23 (2)°. Intensity statistics favored the centrosymmetric space group P_1^-. A density of 1.30 g cm^{-3} was calculated for Z = 2 formula units per unit cell. Three-dimensional intensity data were collected on a Syntex $P2_1$ automated diffractometer, using monochromatized Mo Kα radiation (λ = 0.709 30 Å). The $\theta/2\theta$ scan technique was used to measure the intensities of 2215 independent reflections within the range 0° < 2θ < 55°.[18] Of these, 1815 had $F^2 > 3\sigma(F^2)$ and were used in subsequent calculations.

The structure was solved in a straightforward fashion by direct methods, with MULTAN 77 system of programs.[19] The oxalic acid of crystallization was revealed at this stage. Refinement was by full-matrix least-squares methods.[20] Hydrogen atoms were included at their idealized positions (C–H = 0.95 Å) with fixed isotropic temperature factors of 5.0 Å^2. The final unweighted and weighted R values were 0.047 and 0.064, respectively. A final difference map showed no significant residue.

Acknowledgment. Financial support from the National Science Foundation (Grant CHE-82-03366) is gratefully acknowledged. We particularly thank R. Marquis for carrying out control experiments with **8**. NMR and mass spectra were determined with spectrometers purchased with the assistance of NSF Shared Instrumentation Grants. We thank also Dr. Joseph Ziller for assistance with the crystallographic data.

Registry No. **3**, 4388-56-1; (±)-**4**, 112069-72-4; (±)-**5**, 112069-73-5; (±)-**6**, 112069-74-6; (±)-**8**, 112069-75-7; (±)-**8**·oxalate, 112069-82-6; (±)-**9**, 112069-76-8; **10**, 1119-19-3; (±)-**11**, 112069-77-9; (±)-**12**, 112069-78-0; (±)-**13**, 112069-79-1; (±)-**14**, 112069-80-4; (±)-**15**, 112069-81-5; (±)-**17**, 112069-83-7; (±)-**18**, 112069-84-8; (±)-**19**, 112069-85-9; (±)-**20**, 112069-86-0; TMS-CN, 7677-24-9; $Br(CH_2)_4Br$, 110-52-1.

Supplementary Material Available: Experimental data for X-ray diffraction study of pyrrolizidine acetal **8** and tables of positional parameters, anisotropic temperature factors, bond angles, and interatomic distances (4 pages). Ordering information is given on any current masthead page.

(18) General procedures for data collection and processing have been given in: Sams, D. B.; Doedens, R. J. *Inorg. Chem.* **1979**, *18*, 153.

(19) Main, P.; Lessinger, L.; Woolfson, M. M.; Germain, G.; Declercq, J. P. MULTAN 77, University of York, England, 1977.

(20) All computations were carried out on a VAX 11/780 computer by use of a modified version of the UCLA Crystallographic Computing Package (C. E. Strouse, personal communication). Major programs in this package are derived from the MULTAN system and from the Oak Ridge ORFLS/ORFFE/ORTEP programs.

(21) The numbering of the bicyclo compounds in this paper does not follow IUPAC recommendations.

Base-Induced Reactions of Polynitroarenes with Methyl 2-Chloropropionate

G. Patrick Stahly,* Barbara C. Stahly, and John R. Maloney

Ethyl Corporation, Ethyl Technical Center, P.O. Box 14799, Baton Rouge, Louisiana 70898

Received July 14, 1987

The alkylation of nitro aromatic compounds by leaving group substituted carbanions, a method pioneered by Makosza and co-workers, has proven to be one of the few general processes accomplishing formal nucleophilic aromatic substitution for hydrogen.[1] Our study of one such system showed that methyl 2-chloropropionate (MCP) reacts with a variety of nitro aromatic compounds under the influence of 2 equiv of strong base (NaH, Me_3COK, or Me_3CONa) in *N*,*N*-dimethylformamide (DMF) to give methyl 2-(4-nitrophenyl)propionates in good yields.[2] While reactions of this type are thought to proceed via Meisenheimer salt formation followed by elimination of HCl to give product anion (Scheme I), there is little direct evidence to support this mechanism.

Makosza and Glinka studied the mechanism of nitrobenzene alkylation by chloromethyl phenyl sulfone and

(1) Makosza, M.; Golinski, J.; Baran, J. *J. Org. Chem.* **1984**, *49*, 1488 and references cited therein.

(2) Stahly, G. P.; Stahly, B. C.; Lilje, K. C. *J. Org. Chem.* **1984**, *49*, 578.

0022-3263/88/1953-0690$01.50/0