Synthesis of Adamantane Derivatives. 32.[1] The Beckmann Rearrangement and Fragmentation Aptitude of Noradamantan-2-one Oxime

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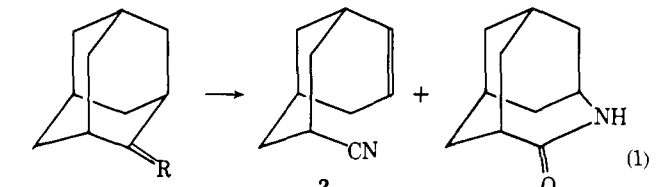
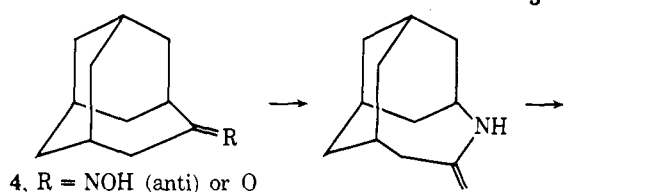
The Beckmann rearrangement of noradamantan-2-one oxime (syn and anti ratio 33:67) by polyphosphate ester afforded 4-azaprotoadamantan-5-one (**9**) and 5-azaprotoadamantan-4-one (**10**) as normal ring-expansion products and 3-cyanobicyclo[3.2.1]oct-6-ene (**11**), 6-cyano- (**12**), and 7-cyanobicyclo[3.2.1]oct-2-ene (**13**) as fragmentation products. The product distribution was time dependent, and **9** and **10** were converted to **11**–**13** under the reaction conditions. The fragmentation aptitude of noradamantan-2-one oxime and lactams **9** and **10** was rationalized from antiperiplanarity in the units H–C–C–C=N$^+$ or H–C–C–N=C$^+$ and strain considerations.

In the Beckmann and Schmidt reactions, the adamantanone (**1**) gives mainly the fragmentation product **2**[2] accompanied by the normal rearrangement product **3** (eq 1).[3] By comparison homoadamantan-4-one (**4**) affords exclusively normal rearrangement product **5** (or its regioisomer) which is, however, not stable under the reaction conditions and gives nitrile **6** in the Beckmann rearrangement by polyphosphate ester (PPE), and tetrazole derivatives in the Schmidt reaction (eq 2).[4] In view of this interesting behavior of caged ketone systems in the Beckmann and Schmidt reactions we were interested in the behavior of the noradamantan-2-one (**7**) system. This paper describes the results of the Beckmann rearrangement of **7**-oxime.



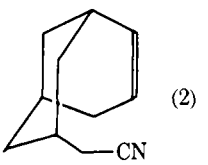
1, R = NOH or O

2 3 (1)



4, R = NOH (anti) or O

5



6 (2)

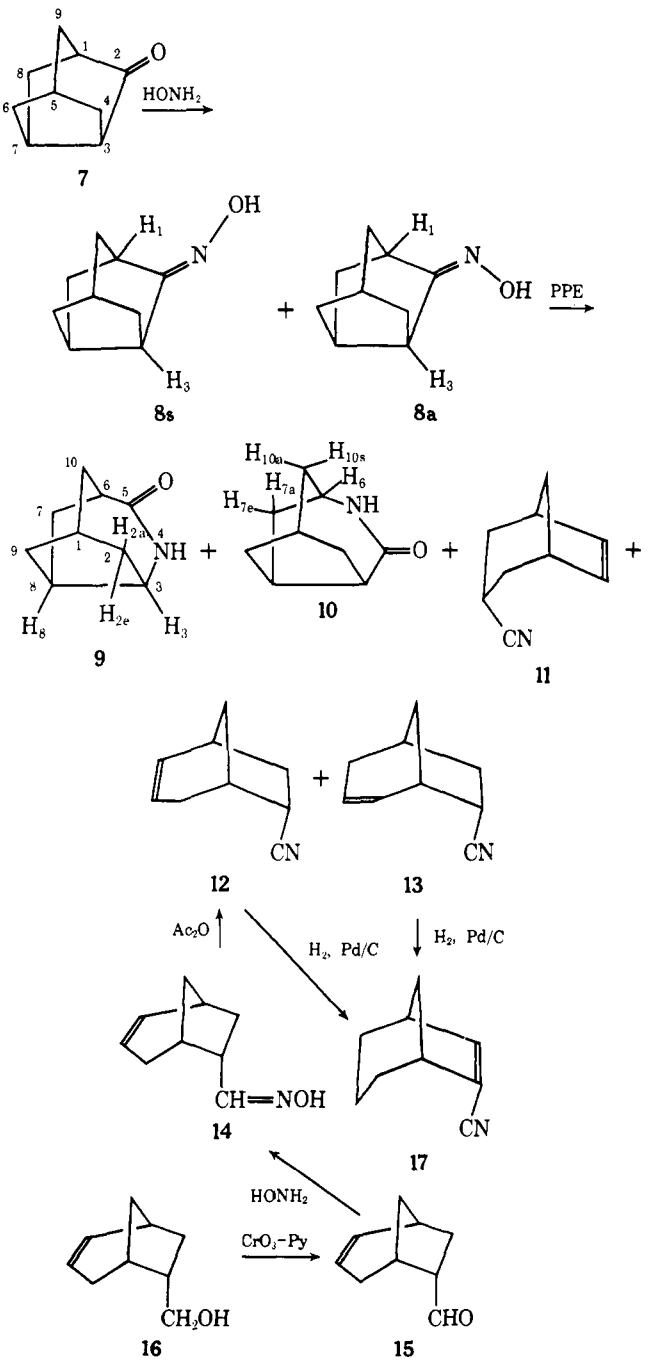
Results and Discussion

Oximation of noradamantan-2-one (**7**)[5] in 50% aqueous ethanol in the presence of excess potassium hydroxide afforded a 33:67 mixture of syn (**8s**) and anti oxime (**8a**)[6] in 74% yield after one recrystallization. The syn and anti ratio was determined by NMR data in the presence of a shift reagent, Eu(dpm)$_3$ (see Experimental Section).[7]

Treatment of **8s** and **8a** (33:67) in chloroform with a large excess of PPE under reflux afforded products **9**–**13** in a 23.4:40.0:4.3:16.9:15.6 ratio on GLC analysis (99.6% conversion). These products were isolated after chromatography (silica gel) and preparative GLC, and their structures were determined as summarized in Scheme I.

Both **9** and **10** were obtained as crystalline solids. In the ir

Scheme I



spectra (KBr), **9** had strong absorptions at 3200 (NH) and 1665 cm^{-1} (C=O) and **10** at 3220 (NH) and 1644 cm^{-1}

Table I. Observed and Calculated Coupling Constants for H_3 of 9 and H_6 of 10

H_3 of 9	Obsd, Hz	Calcd, Hz	(Dihedral angle)	H_6 of 10	Obsd, Hz	Calcd, Hz	(Dihedral angle)
$J_{2e,3}$	7.5	6.7	(25°)	$J_{6,7e}$	0	0.3	(75°)
$J_{2a,3}$	0	0	(95°)	$J_{6,7a}$	3.0	3.8	(45°)
$J_{3,8}$	7.5	7.9	(10°)	$J_{6,10s}$	0	0	(80°)
				$J_{6,10a}$	3.0	3.8	(45°)

Table II. Product Distributions of the Beckmann Rearrangement of 8s + 8a[a]

Reagent (amount)	Solvent	Temp °C	Time, min	Conversion, %[b]	Product distribution, %[b] 9	10	11	12	13	Others
PPE (20 w/w)	$CHCl_3$	Reflux	0.5	8.9	34.1	44.2	0.7	11.0	10.0	0
			5	42.3	31.6	43.7	1.7	12.8	10.2	0
			20	66.6	30.0	42.8	3.0	13.4	10.8	0
			50	87.9	30.5	45.1	3.5	14.6	13.1	0
			100	99.3	27.9	36.5	4.3	17.8	13.5	0
				(99.8)[c]	(25.7)	(41.7)	(4.0)	(16.2)	(12.4)[c]	Trace[d]
TsCl (1.2 mol)	$HCONMe_2$	80	240	17.8	1.2	25.8	3.9	50.0	10.1	8.9[d]
PCl_5 (4.0 mol)	Et_2O	r.t.[e]	2400	87.6	0.5	1.2	9.8	20.3	7.3	60.9[d]
NaN_3[f] (2.0 mol)	$MeSO_3H$–AcOH[g]		240	93.8	25.4	15.4	9.9	43.5	3.1	2.8[d]

[a] A 33:67 mixture was used. [b] GLC analysis. [c] Isolated yield. [d] Unidentified. [e] Ca. 25 °C. [f] The Schmidt reaction of 7. [g] 1:9 v/v ratio.

(C=O), indicating that **9** and **10** are isomeric lactams and normal rearrangement products. In the NMR spectra, **9** had a characteristic double triplet (J = 5.0 and 7.5 Hz) at δ 3.85 (1 H) assignable to CHNHCO–, which changed to a triplet (J = 7.5 Hz) on deuteration, while **10** had a pentet (J = 3.0 Hz) at δ 3.45 (1 H) which became a triplet (J = 3.0 Hz) on deuteration. The observed coupling constants and those calculated for H_3 of **9** and H_6 of **10** based on a Karplus relationship[8] and dihedral angles for C_3–H_3 and C_6–H_6 (on a Dreiding stereomodel) are summarized in Table I. From comparison of these values **9** was assigned as 4-azatricyclo[4.3.1.$0^{3,8}$]decan-5-one (or trivially 4-azaprotoadamantan-5-one) and **10** as 5-azatricyclo[4.3.1.$0^{3,8}$]decan-4-one (or 5-azaprotoadamantan-4-one).

Compounds **11–13** were obtained as volatile, oily materials after purification on preparative GLC, and had the same formula $C_9H_{11}N$. Ir spectra of **11–13** exhibited absorptions at 2245, 2240, and 2240 cm^{-1}, respectively, due to a nitrile function, suggesting that these compounds are the Beckmann fragmentation products. Treatment of **9** with PPE in chloroform under reflux for 600 min gave nitrile **11** (1.5%); the same reaction with **10** gave **12** and **13** (36.2%, 97:3 ratio).

Nitrile **11** had NMR signals at δ 6.55 (broad s, 2 H), 4.65–3.75 (m, 3 H), and 1.6–1.1 (m, 6 H), and hence the structure was assigned as 3-*endo*-cyanobicyclo[3.2.1]oct-6-ene. The endo configuration of the 3-CN group was assigned on the basis of its formation from **9** and the appearance of two vinyl proton signals at somewhat lower field than that of norbornene derivatives (δ 6.25–5.85)[9] (due to the anisotropy effect of the CN group).[10]

Nitriles **12** and **13** had very similar NMR spectra which revealed two vinylic protons signals at δ 5.4–5.9 and other protons signals at δ 3.3–1.0. Both **12** and **13** afforded the same dihydro derivative **17** on catalytic hydrogenation (Pd/C), indicating that both **12** and **13** have the same carbon skeleton. Their formation from **10** suggested that **12** and **13** are 6-*endo*- or 7-*endo*-cyanobicyclo[3.2.1]oct-2-ene. Finally, **12** was determined as 6-*endo*-cyanobicyclo[3.2.1]oct-2-ene and hence **13** as 7-*endo*-cyanobicyclo[3.2.1]oct-2-ene by an alternative synthesis of **12** via **14** and **15** starting from **16**, which has been reported previously by us[11] (Scheme I).

The material balance observed in the Beckmann rearrangement of **8s + 8a** (33:67) was in accord with the well-known fact that the trans group with respect to oxime hydroxyl group migrates to afford lactams in the Beckmann rearrangement,[12] and hence it can be concluded that **9** and **11** originate from **8s**, while **10, 12,** and **13** arise from **8a**, respectively (eq 3 and 4).

$$\mathbf{8s} \rightarrow \mathbf{9} + \mathbf{11} \quad (3)$$

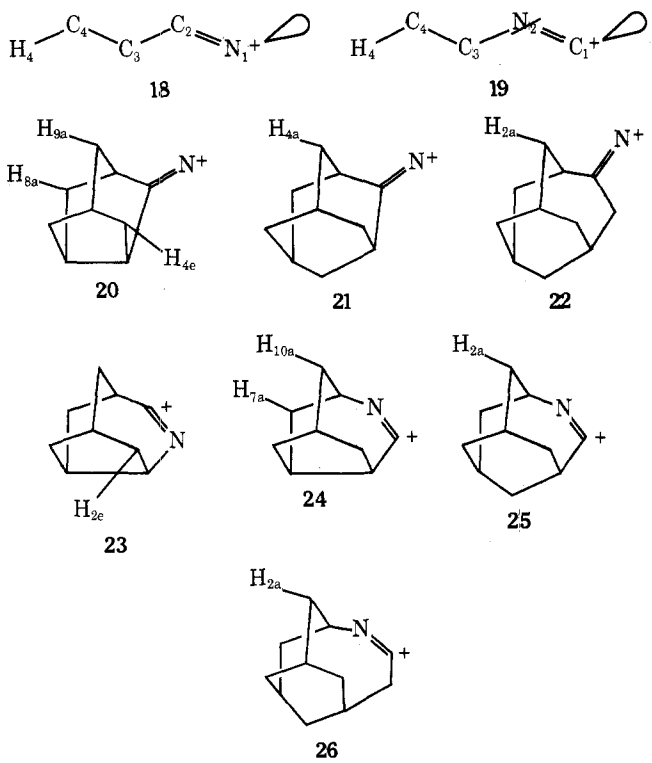
$$\mathbf{8a} \rightarrow \mathbf{10} + \mathbf{12} + \mathbf{13} \quad (4)$$

Since fragmentation to nitriles was observed extensively in the Beckmann rearrangement of **8s** and **8a** even with PPE, some other conditions were also examined and the results are summarized in Table II as well as the product distributions at various reaction times. The rearrangement with *p*-toluenesulfonyl chloride (TsCl) in dimethylformamide at 80 °C gave only very low conversion, but fragmentation products were produced extensively. Phosphorus pentachloride in ether also did not improve the results. For comparison, one example of the Schmidt reaction of **7** under very mild conditions is also shown in Table II. Extensive fragmentation was also observed.[13] In the reaction with PPE the fragmentation products **11–13** were produced even at very short reaction time, indicating that synchronous fragmentation paths as well as rearrangement–fragmentation paths are involved.[14] However, as the relative ratio of products in Table II shows, the fragmentation aptitudes of **8s** and **8a** as well as those of lactams **9** and **10** or their corresponding iminium cations[15] are quite different. Such difference may be ascribable to the degree of deviation from the antiperiplanarity of the participating bonds in the H–C–C–C=N moiety as postulated by Grob[14] and in a recent theoretical study.[16] For the indirect fragmentation, inductive and steric effects may be important factors.[14] As a simple method for expression of the deviation from the ideal antiperiplanarity, we measured values defined by $(180 - \phi) + \theta$ for each hydrogen, in which ϕ is the dihedral angle defined by bonds C_2–C_3 (or N_2–C_3) and C_4–H_4, and θ is the angle between bond C_4–H_4 and a plane involving bond C_2–C_3 (or N_2–C_3) and vertical to a C_2, C_3, C_4 (or N_2, C_3, C_4) plane in **18** and **19**.[17] The values for related hydrogens in **20–26** were

Table III. Deviations from Antiperiplanarity on Dreiding Stereomodel

Model str	20	20	20	21	22[c]	23	24	24	25	26[c]
Hydrogen	H_{4e}	H_{8a}	H_{9a}	H_{4a}	H_{2a}	H_{2e}	H_{7a}	H_{10a}	H_{2a}	H_{2a}
180-φ, deg[a]	17	14	6	0	22	37	14	17	18	36
θ, deg[a]	10	5	7	0	6	7	7	0	5	0
Deviation, deg[b]	27	19	13	0	28	44	21	13	23	36

[a] For the definition, see text. [b] $(180 - \varphi) + \theta$. [c] Assuming an untwisted conformation.



measured on a Dreiding stereomodel by using an imine component for $C{=}N^+$ or $N{=}C^+$ and are summarized in Table III. For example, H_{4e} in **20** is the hydrogen to be lost in the **8s** → **11** conversion. Of two hydrogens such as H_{4e} and H_{4a} in **20**, only H_{4e}, having a smaller deviation from antiperiplanarity, is shown in Table III. Comparison of the deviation for H_{4e}, H_{8a}, and H_{9a} in **20** indicates that the fragmentation should decrease in the order **8a** → **12** > **8a** → **13** > **8s** → **11**, as observed (Table II). H_{4a} in **21** (adamantanone system) has the ideal geometrical arrangement as postulated previously, and in fact, its large fragmentation aptitude is well known.[3,18] For the homoadamantan-4-one system with a flexible ethano bridge[19] an accurate value for the deviation could not be measured but approximate values for $(180 - \phi)$ and θ are 22 and 6° assuming an untwisted conformation (**22**). These deviations are considerably larger, in accord with their corresponding negative fragmentation aptitude.[4]

For the indirect fragmentation, the degree of deviation does not seem an important factor for determining the fragmentation aptitude: H_{2e} in **23** has a considerably larger deviation value but its fragmentation (**9** → **11**) was observed, while H_{2a} in **25** has much less deviation and yet the fragmentation of 4-azahomoadamantan-5-one (**3**) to 7-*endo*-cyanobicyclo-[3.3.1]non-2-ene (**2**) was not observed with PPE.[4b] There is a possibility that the fragmentation may be facilitated by inductive effects in the derived olefins;[20] the double bond in **11** (from **23**) is substituted by two secondary alkyl groups, while that in **2** (from **25**, if formed) is substituted by one secondary alkyl and one primary alkyl group, and hence **23** (or **9**) → **11** conversion becomes possible despite the larger "deviation" value. However, a facile fragmentation of **5** to **6** (eq 2)[4b] with PPE cannot be rationalized by such differences in inductive effects since both **2** and **6** have the same primary and secondary substituents for the double bond. Examination of **26** assuming an untwisted conformation[21] (Table III) indicates that the deviation value is considerably larger than that for **25**. In these indirect fragmentations, another important factor may be ring strain because the most fragmentable intermediate (**26**) is considered to involve the largest ring strain and the fragmentable intermediates **23** and **24** have less strains based on values reported for saturated carbocyclic analogues.[22] On the other hand, the observed large regioselectivity in the fragmentation of **10** (eq 4), i.e., almost exclusive formation of the 6-cyano derivative **12** rather than the 7-cyano **13**, should be ascribable to the deviation values because inductive and strain factors are the same.

In summary the deviation values from antiperiplanarity of H_4–C and C_2–C_3 in **18** are useful for estimation of the direct Beckmann fragmentation aptitude of rigid caged ketone systems, while those of H_4–C_4 and N_2–C_3 in **19** are important for determining the regioselectivity of the indirect fragmentation.

Experimental Section[23]

Noradamantan-2-one (7). This was prepared by the method of Nickon and his co-workers.[5] Deltacyclane[5c] (1.472 g, 12.3 mmol) in *n*-pentane (5 ml) was treated with 96% sulfuric acid (77 ml) at −10 to 5 ° for 16 min. Hydrolysis of the mixture and sublimation afforded noradamantan-2-ol (1.496 g, 88.4%), mp 218–219 °C (lit.[5a] 221–222 °C), which was oxidized to noradamantan-2-one (**7**), mp 214–215 °C (lit.[5a] 214.5–215 °C) with the Brown reagent[24] in 85% yield.

Noradamantan-2-one Oxime (8s + 8a). A mixture of **7** (1.686 g, 12.4 mmol) and hydroxylamine hydrochloride (1.034 g, 14.9 mmol) in ethanol (20 ml) and aqueous KOH [85%, 4.18 g in water (20 ml)] was refluxed for 3 h. The cooled mixture was concentrated to ca. 30 ml and neutralized with 5% hydrochloric acid to afford crude oxime as colorless precipitates which was recrystallized from water to give a 33:67 mixture of syn (**8s**) and anti oxime (**8a**) (1.388 g, 74.2%): mp 107.5–109.5 °C; ir (KBr) 3230, 3140, 2930, 2870, 1681, 1472, 1456, 1080, 970, 950, 910, 794, and 775 cm^{-1}; NMR ($CDCl_3$, 100 MHz) δ 8.65 (broad s, 1 H, disappeared on shaking with D_2O), 3.50 (d, d, $J_{3,7} = 7.0$, $J_{2,3} = 6.0$ Hz, 0.67 H, H_3 of **8a**), 2.60 (broad s, 0.33 H, H_1 of **8s**), 2.30 (m, 2 H), and 2.0–1.2 (m, 8 H); in the presence of Eu(dpm)$_3$ [the mole ratio of Eu(dpm)$_3$ to **8s** + **8a** = 0.140], H_3 of **8a** and **8s** appeared at δ 5.45 and 4.41 in 2:1 ratio as the similar unsymmetrical triplet (J = ca. 6.5 Hz), and H_1 of **8a** and **8s** at δ 4.29 and 5.10, respectively, as a broad singlet (in 2:1 ratio);[7] mass spectrum m/e 151 (M^+).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.33; H, 8.64; N, 9.06.

Beckmann Rearrangement of 8s and 8a with PPE. A 33:67 mixture of **8s** and **8a** (0.860 g, 5.63 mmol) and PPE[25] (17.2 g, 20 w/w times to the oxime) in chloroform (15 ml) was refluxed for 100 min. The cooled mixture was diluted with water (50 ml) and stirred for 24 h at room temperature. After neutralization with 10% KOH, the mixture was extracted with CH_2Cl_2 (7 × 10 ml). The combined extracts were dried (Na_2SO_4) and concentrated to ca. 1 ml. GLC analysis (Silicone SE-30 column, 100 and 170 °C) revealed seven peaks in the ratio 23.3:39.8:4.3:0.4:16.8:15.5:trace corresponding to lactams **9** and **10**, nitrile **11**, ketone **7**, nitriles **12** and **13**, and oxime, respectively. Chromatography on a silica gel column eluting with *n*-hexane–CH_2Cl_2 afforded **3-*endo*-cyanobicyclo[3.2.1]oct-6-ene (11)** as the first fractions (32 mg, ca. 5% of **7** was contaminated, 4.0%). Pure **11** was obtained as a semisolid after preparative GLC (30% Silicone SE-30 on 45/60 mesh Chromosorb W, at 120 °C): ir ($CDCl_3$) 3000, 2940, 2920, 2245, 1280, 1037, 984, and 890 cm^{-1}; NMR, see text; mass spectrum mol wt 133.0885 (calcd for $C_9H_{11}N$, 133.0889). The second fractions were a 57:43 mixture of **6-*endo*-cyano-(12)** and **7-*endo*-cyanobicyclo[3.2.1]oct-2-ene (13)** (214 mg) which was purified by prepar-

ative GLC. **12** was obtained as an oil: $n^{24}D$ 1.5027; ir (neat) 3033, 2920, 2882, 2850, 2240, 1460, and 741 cm^{-1}; NMR ($CDCl_3$) δ 5.97 (m, 1 H), 5.50 (m, 1 H), and 3.3–1.0 (m, 9 H); mass spectrum *m/e* (rel intensity) 134 (10.2), 133 (M^+, 50.2), 132 (35.6), 104 (10.7), 93 (13.6), 92 (16.7), 91 (22.2), 81 (15.6), 80 (100), and 79 (74).

Anal. Calcd for $C_9H_{11}N$: C, 81.16; H, 8.31; N, 10.52. Found: C, 81.31; H, 8.15; N, 10.56.

Nitrile **13** was obtained as a semisolid: ir (neat) 3030, 2920, 2880, 2850, 2240, 1460, 1445, and 710 cm^{-1}; NMR ($CDCl_3$) δ 5.86 (m, 1 H), 5.42 (m, 1 H), and 3.25–1.2 (m, 9 H); mass spectrum *m/e* (rel intensity) 134 (4.5), 133 (M^+, 30.2), 132 (17.8), 91 (14.6), 80 (100), and 79 (8.5).

Anal. Calcd for $C_9H_{11}N$: C, 81.16; H, 8.31; N, 10.52. Found: C, 81.35; H, 8.40; N, 10.35.

The third fractions gave a trace of unreacted oxime and the fourth fractions afforded **4-azaprotoadamantan-5-one (9)** as a hygroscopic solid (218 mg, 25.6%) which was purified by recrystallization from *n*-hexane–CH_2Cl_2: mp 274–276 °C; ir (KBr) 3200, 3100, 3050, 2940, 2910, 2860, 1665, 1482, 1458, 1445, 1415, 1344, 1308, 1283, 1177, 1148, 834, 818, 792, and 660 cm^{-1}; NMR ($CDCl_3$) δ 6.25 (broad s, 1 H, disappeared on shaking with D_2O, NH), 3.85 (t, d, J = 7.5 and 5.0 Hz, t on deuteration, 1 H), 2.50 (m, 2 H), 2.25 (m, 1 H), and 2.0–1.5 (m, 8 H); mass spectrum *m/e* (rel intensity) 152 (15.2), 151 (66.7), 150 (16.7), 124 (21.2), 123 (85.0), 122 (27.3), 119 (15.2), 111 (13.0), 110 (18.4), 109 (31.8), 108 (30.3), 106 (15.2), 105 (21.2), 104 (12.1), 97 (18.3), 96 (21.2), 95 (27.3), 94 (23.2), 93 (24.2), 92 (10.9), 91 (25.8), 85 (21.2), 83 (23.2), 82 (35.4), 81 (42.5), 80 (100), and 79 (45.5).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.47; H, 8.68; N, 9.26.

The fifth fractions gave **5-azaprotoadamantan-4-one (10)** as a hygroscopic solid (354 mg, 41.6%) which was purified by sublimation and recrystallization from *n*-hexane: mp 251–253 °C; ir (KBr) 3220, 3040, 2930, 2870, 1644, 1445, 1330, 1290, 1277, 1225, 1162, 1138, 1110, 1070, 993, 978, 910, 854, 763, 738, and 660 cm^{-1}; NMR ($CDCl_3$) δ 6.80 (broad s, disappeared on shaking with D_2O, 1 H, NH), 3.45 (pentet, J = 3.0 Hz, t on deuteration, 1 H), 2.65 (m, 2 H), 2.35 (m, 1 H), and 2.1–1.5 (m, 8 H); mass spectrum *m/e* (rel intensity) 152 (15.0), 151 (M^+, 62.1), 150 (14.5), 136 (20.8), 134 (12.0), 133 (12.5), 123 (22.3), 122 (16.1), 121 (14.7), 110 (16.5), 109 (86.3), 108 (56.0), 104 (29.1), 97 (13.0), 96 (18.6), 95 (32.0), 93 (22.0), 91 (23.8), 83 (15.0), 81 (44.0), 80 (48.5), and 40 (100).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.65; H, 8.81; N, 9.08.

The product distributions at various reaction times were determined by GLC after extractions with CH_2Cl_2 of the hydrolyzed and neutralized reaction mixtures at appropriate reaction times.

In another run, nitrile mixture was directly purified on preparative GLC.

Beckmann Rearrangement of 8s and 8a with *p*-Toluenesulfonyl Chloride. A 33:67 mixture of **8s** and **8a** (15 mg, 0.10 mmol) and *p*-toluenesulfonyl chloride (23 mg, 1.2 mmol) in dimethylformamide (1.0 ml) was stirred at 80 °C for 4 h. The cooled mixture was diluted with water (10 ml) and extracted with methylene chloride (5 × 3 ml). The combined extracts were washed with water and dried (Na_2SO_4) and concentrated to ca. 1 ml which was analyzed on GLC.

Beckmann Rearrangement of 8s and 8a with Phosphorus Pentachloride. The oxime mixture (15 mg, 0.10 mmol) and phosphorus pentachloride (110 mg, 0.40 mmol) in ether (5 ml) was stirred for 40 h at room temperature. The mixture was washed with water and dried (Na_2SO_4) and analyzed on GLC (Table II).

Synthesis of 6-*endo*-Cyanobicyclo[3.2.1]oct-2-ene (12) from 6-*endo*-Hydroxymethylbicyclo[3.2.1]oct-2-ene (16). 6-*endo*-Hydroxymethylbicyclo[3.2.1]oct-2-ene (**16**,[11] 1.38 g, 10.0 mmol) was oxidized with the Sarett reagent[26] prepared from chromic anhydride (2.00 g, 20.0 mmol) and pyridine (30 ml) for 100 min at room temperature. The reaction mixture was diluted with ether (100 ml) and the resulting precipitates were removed by filtration. The filtrate was washed with water (20 ml), 10% hydrochloric acid (3 × 20 ml), and 5% aqueous sodium bicarbonate (10 ml) successively, and dried (Na_2SO_4). Removal of the solvent under reduced pressure afforded crude aldehyde **15** as an oil (1.0 g, 73%), ir (neat) 2700, 1710, and 1630 cm^{-1}, which was treated with hydroxylamine hydrochloride (2.1 g, 30 mmol) in 95% ethanol (50 ml) containing KOH (3.4 g, 60 mmol) under refluxing for 1 h. The cooled mixture was concentrated to ca. 20 ml, diluted with water (100 ml), and extracted with methylene chloride (3 × 30 ml). The combined extracts were dried (Na_2SO_4) and evaporated to give curde oxime **14** as an oil (0.8 g). Chromatography on a silica gel column eluting with $CHCl_3$–MeOH afforded pure oxime **14** as an oil (0.605 g, 40.0% from **16**): $n^{22}D$ 1.5268; ir (neat) 3260, 3100, 3030, 1640, 1450, 1320, 930, 905, 755, and 710 cm^{-1}; NMR ($CDCl_3$) δ 7.45 and 6.82 (each d, J = 7.0 Hz, 0.6 and 0.4 H, CH=NOH), 6.15–5.25 (m, 3 H, 2 H after shaking with D_2O, OH and CH=CH), 3.65 (d, J = 7.0 Hz, CHCH=NOH), and 3.1–0.9 (m, 8 H, other protons).

Anal. Calcd for $C_9H_{13}NO$: C, 71.49; H, 8.67; N, 9.26. Found: C, 71.36; H, 8.78; N, 8.99.

A mixture of **14** (180 mg, 1.19 mmol) and acetic anhydride (3 ml) was refluxed for 15 h. The cooled mixture was diluted with water (10 ml), stirred for 5 h at room temperature, and extracted with ether (3 × 20 ml). The combined extracts were washed with 5% aqueous sodium bicarbonate (2 × 10 ml) and dried (Na_2SO_4). Evaporation of the solvent gave crude nitrile **12** which on chromatography (silica gel, *n*-hexane) afforded **12** as an oil (110 mg, 69.5%). GLC retention times, nD value, and spectral (ir and NMR) data were identical with those of the sample obtained from the Beckmann fragmentation reaction of **8a**.

Hydrogenation of 12 and 13 to 6-*endo*-Cyanobicyclo[3.2.1]octane (17). Nitrile **12** (30 mg, 0.23 mmol) was hydrogenated in methanol (3 ml) with 10% Pd/C (12 mg) for 5 h under atmospheric pressure at room temperature. After removal of the catalyst by filtration, the methanol solution was evaporated to dryness under reduced pressure to give **17** as colorless crystals, which were purified by sublimation (80 °C, 25 mm) (22 mg, 72.0%): mp 85–88 °C; ir (KBr) 2930, 2860, 2230, and 1460 cm^{-1}; NMR ($CDCl_3$) δ 2.80 (m, 1 H), 2.30 (m, 2 H), and 2.1–0.6 (m, 10 H).

Anal. Calcd for $C_9H_{13}N$: C, 79.95; H, 9.69; N, 10.36. Found: C, 80.23; H, 9.89; N, 10.15.

Nitrile **13** (20 mg, 0.15 mmol) was hydrogenated under similar conditions to afford **17** (15 mg, 74.0%) which was identical with the sample from **12** on the basis of GLC retention times, ir, and NMR spectra.

Fragmentations of Lactam 9 → 11 and of 10 → 12 + 13. Each lactam **9** or **10** was treated with 20 w/w PPE in $CHCl_3$ under reflux for appropriate times, and the products were analyzed on GLC after workup as above. A 41.6:58.4 mixture of **9** and **10** was also treated similarly in order to compare the relative reactivity (see text).

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Registry No.—**7**, 17931-67-8; **8s**, 58408-37-0; **8a**, 58408-38-1; **9**, 58408-39-2; **10**, 58408-40-5; **11**, 58408-41-6; **12**, 58408-42-7; **13**, 58408-43-8; **14**, 58408-44-9; **15**, 58408-45-0; **16**, 39837-57-5; **17**, 58408-46-1.

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Solvolysis of Benzobicyclo[3.2.1]octenylmethyl Tosylates

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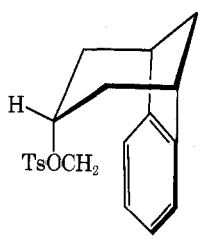
exo- and *endo*-benzobicyclo[3.2.1]octenylmethyl tosylates (**1** and **11**) were synthesized from the pyrrolidine enamine of 2-indanone using methyl-β,β'-dibromoisobutyrate (**3**) in an α,α' annelation reaction. The endo hydroxymethyl tosylate **1** undergoes acetolysis at 75 °C with a rate of 2.3×10^{-5} s^{-1}, 58 times that of the exo methyl tosylate (**11**). The products of the acetolysis of **1** were completely rearranged having a benzobicyclo[3.3.1]nonane skeleton (acetate **13** and olefin **12**).

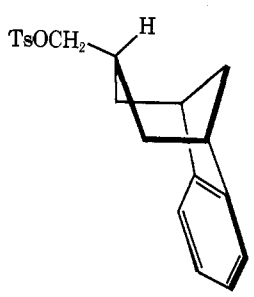
Participation of an aromatic moiety to the site of a developing cation is an area of organic chemistry which continues to be a source of fascinating and informative investigations.[1] Included among those structural factors which affect the contribution of aryl π-participation are the orientation of the aromatic ring with respect to the leaving group, the nature of the substituents on the aromatic ring, and the number and type of bonds in the chain between the aromatic ring and leaving group as well as the number of degrees of freedom in that chain. In spite of many extensive studies, there are few examples of systems in which a remote, developing primary cation is constrained to the face of an aromatic ring.[2] The benzobicyclo[3.2.1]octenyl-*endo*-methyl tosylate structure (**1**) contains this advantageous characteristic.



1

The synthetic design for a molecule such as **1** in which only a single mode of participation was likely to occur and in which the essential configurational and steric relationships were maintained was facilitated by the demonstrated ability of our α,α' annelation reaction[3] to provide unstable endo stereoisomers in the construction of bicyclic frameworks. Annelation of the pyrrolidine enamine of 2-indanone[4] **2** with β,β'-dibromoisobutyrate **3** yielded crystalline benzobicyclo[3.2.1]octenyl ester **5** by way of the intermediate enamine acrylate **4**.[5] The endo stereochemistry of the ester function in bicyclic **5** was supported by its conversion to exo epimer **6** with sodium methoxide–methanol, accompanied by a shift in the ^1H NMR resonance of the ester methyl to lower field. The ester methyl of endo ester **5** lies in the shielding cone of the benzene ring and resonates at 0.5 ppm higher field in the ^1H NMR than the methyl of exo ester **6**. Keto ester **5** was converted to its tosylhydrazone and reduced with lithium aluminum hydride.[6] The resulting endo alcohol **7** was characterized as acetate **8**. Starting from exo ester **6**, an identical route yielded alcohol **9** and acetate **10**. The ^1H NMR data of alcohols **7** and **9** and acetates **8** and **10** indicated that the stereochemistry of esters **5** and **6** was maintained during the transformations. The *p*-toluenesulfonates **1** and **11** were prepared from the corresponding alcohols in the usual manner.[7]

The severe diaxial interactions in the endo methyl tosylate **1** might cause it to have a significant population of the boat conformation **1a**, destroying the geometry appropriate for



1a

participation. Such a conformation is developed in the corresponding bicyclo[3.3.1]nonanone methyl derivatives.[3c] Nevertheless both the solvolytic data and ^1H NMR of endo tosylate **1** at room temperature and low temperature suggest that it exists predominantly in the chair form **1**. Protons of the methylene bearing the tosylate, in endo epimer **1**, occur 1.1 ppm upfield of those in the epimeric exo tosylate **11** and are unchanged to −80 °C in acetone. There is also evidence from lactonization experiments on other members of the benzobicyclo[3.2.1]octenyl series that the chair form is the predominant conformation.[3b]

The suitability of the architecture of endo tosylate **1** for participation was reflected by both its enhanced rate and by its products of acetolysis which were completely rearranged. Acetolysis of bicyclic endo methyl tosylate **1** at 75 °C proceeded with a rate of 2.3×10^{-5} s^{-1}, 58 times faster than the corresponding exo methyl tosylate **11** and 100 times faster than isobutyl tosylate.[8] The products of endo methyl tosylate