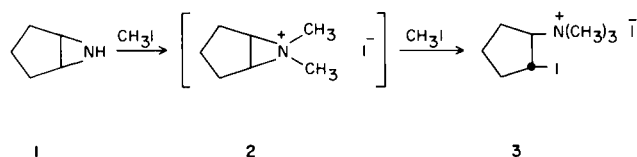


## Aziridines. XVII. Reactions of 6-Azabicyclo[3.1.0]hexane (1)

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As part of our continuing study of the chemistry of fused, bicyclic aziridines, we have examined some further reactions of cyclopentenimine, 6-azabicyclo[3.1.0]hexane (1) (3). In previous work, it had been found that the cycloalkenimines containing a 7,8,10, or 12-membered carbocyclic ring formed stable, crystalline, quaternary aziridinium salts on treatment with methyl iodide. When this reaction was attempted with compounds in which the aziridine ring was fused to a six-membered ring, as in cyclohexenimine, or a 5-membered ring, as in 3-oxa-6-azabicyclo[3.1.0]hexane, only ring-opened products were obtained (4). Similarly, we have now found that the attempted preparation of the quaternary aziridinium salt 2 by the reaction of 1 with methyl iodide gave only the ring-opened product 3.



In order to obtain a suitable heavy-element derivative for determination of the crystal and molecular structure by the X-ray diffraction technique, the *p*-bromobenzene-sulfonyl, *p*-iodobenzene-sulfonyl and *p*-bromobenzoyl derivatives of 1 were prepared and are now under investigation in the laboratory of Dr. L. M. Trefonas (5a).

In previous papers in this series, it was reported that ring size has a profound effect on the rate and course of the pyrolytic rearrangement of *N*-acylcycloalkenimines. When the carbocyclic ring had six or more members, the product of pyrolysis was primarily the isomeric, unsaturated amide homologous to 6. In contrast, pyrolysis of 6-benzoyl-3-oxa-6-azabicyclo[3.1.0]hexane, containing an aziridine ring fused to a five-membered ring, gave only the isomeric, bicyclic oxazoline (the oxygen analog of 9) (4).

We have now found that the pyrolysis of 6-(*p*-nitro

benzoyl)-6-azabicyclo[3.1.0]hexane (4) in toluene solution at 205-208° for eight hours gave a brown, solid product from which was isolated a 34% yield of the oxazoline (9) and a 35% yield of the isomeric, unsaturated amide (6). In a separate experiment it was found that 4 rearranged to give 9 in quantitative yield by refluxing with sodium iodide in acetone. Since the iodide-catalyzed ring-expansion undoubtedly occurs *via* an intermediate (7) involving two successive inversions at the substituted carbon atom, the oxazoline ring of 9 must be fused to the cyclopentane ring in the *cis*-configuration. The structure of 6 was independently demonstrated by synthesis from 3-amino-cyclopentene.

The possibility that the unsaturated amide (6) is an intermediate in the formation of the oxazoline (9), or that 9 is an intermediate in the formation of 6, was conclusively excluded by analysis of the products resulting from experiments in which samples of 6 and 9 were separately subjected to the same pyrolytic conditions which resulted in their formation from the acyl aziridine (4).

A reasonable interpretation of this evidence is that the steric and electronic factors favor about equally the attainment of the quasi-six-membered ring transition state 5, leading to the formation of 6, and the transition state or intermediate represented by the alternative formulations 8, leading to the oxazoline (9).

The results of the X-ray work of Trefonas (5b) support the view that in its ground state, compound 4 is in a puckered boat conformation represented by the perspective drawing 10, in which the bridgehead hydrogens are well-staggered relative to the hydrogens of the methylene group. Attainment of transition state 5 requires the bicyclic nucleus to assume a chair conformation as represented by the perspective drawing 11, which is more strained due to the eclipsing of the bridgehead hydrogens with the methylene group.

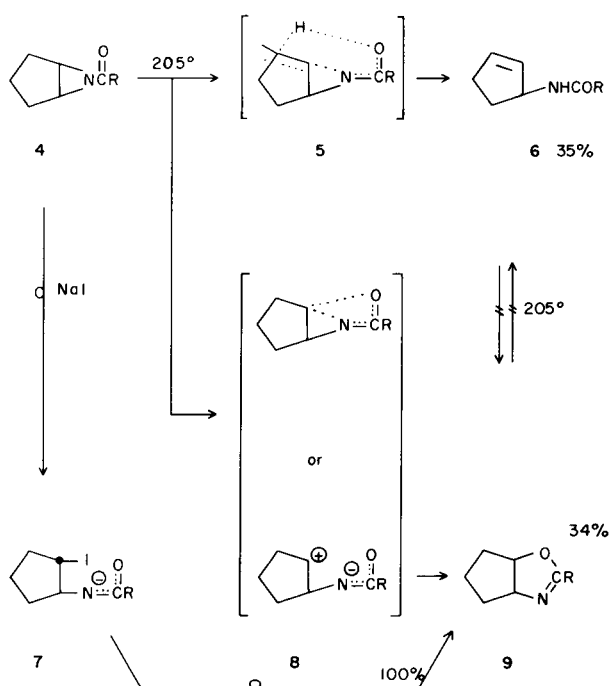
Pyrolysis of the unsubstituted analog of compound 4 ( $\text{R} = \text{C}_6\text{H}_5$ ) gave 60% of oxazoline and 6% of the unsaturated amide.

An attempt to cyclize the unsaturated amide 6 to the oxazoline (9) by treatment with concentrated sulfuric acid at room temperature gave instead a poor yield of *p*-nitrobenzamide.

TABLE I

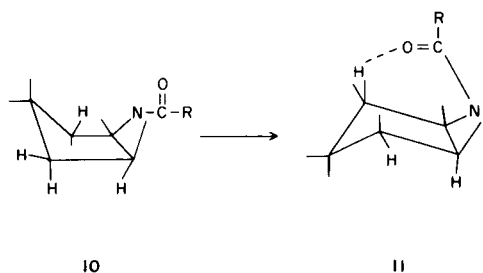
Properties of the 6-Substituted-6-azabicyclo[3.1.0]hexane Derivatives

6-Substituent	Formula	Yield, %	m.p. or b.p. °C	Calcd, %			Found, %		
				C	H	N	C	H	N
Benzoyl	C <sub>12</sub> H <sub>13</sub> NO	78	125-7/2 mm.	76.96	7.01	7.48	77.24	7.09	7.63
<i>p</i> -Nitrobenzoyl	C <sub>12</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	95	109-110	62.05	5.22	12.06	61.84	5.15	11.76
<i>p</i> -Bromobenzoyl	C <sub>12</sub> H <sub>12</sub> NOBr	93	72-73.5	54.15	4.54	5.27	54.15	4.44	5.14
<i>p</i> -Nitrobenzenesulfonyl	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> O <sub>4</sub> S	85	117-118	49.24	4.52	10.44	48.98	4.50	10.29
<i>p</i> -Bromobenzenesulfonyl	C <sub>11</sub> H <sub>12</sub> NO <sub>2</sub> SBr	97	70.5-71.5	43.72	4.00	4.63	43.52	3.82	4.60
<i>p</i> -Iodobenzenesulfonyl	C <sub>11</sub> H <sub>12</sub> NO <sub>2</sub> SI	95	98-99	37.83	3.47	4.01	38.30	3.57	4.25



Scheme I

R = -C<sub>6</sub>H<sub>4</sub>NO<sub>2</sub> (*p*) Hypothetical intermediates and transition states are in brackets.



## EXPERIMENTAL

Microanalyses were performed by Micro-Tech Laboratories, Skokie, Ill. Melting points were determined in a Thomas-Hoover capillary melting point apparatus. All melting points and boiling points are uncorrected. The n.m.r. spectra were obtained on a Varian A-60 Spectrophotometer using either neat samples or dilute solutions in deuteriochloroform (ca. 10% by weight). Chemical shifts are given on the  $\delta$ -scale in ppm. with tetramethylsilane as an internal standard ( $\delta = 0.00$ ). Infrared spectra were recorded in chloroform solutions using a Perkin-Elmer Model 137 Spectrophotometer with sodium chloride optics.

6-Azabicyclo[3.1.0]hexane was prepared by slight modification of the previously described procedure (3). The sulfate ester was prepared in 89% yield by treatment of *trans*-2-aminocyclopentanol (6) with chlorosulfonic acid in carbon tetrachloride, and cyclized to the imine in 75% yield with aqueous sodium hydroxide. The infrared spectrum of the imine had a medium intensity band 3300 cm<sup>-1</sup> (NH), and the n.m.r. spectrum of the compound (neat liquid) had a sharp singlet at 2.27 (2 H, bridgehead protons), a complex multiplet centered at about 1.54 (6 H, ring methylene protons), and a broad singlet at 0.77 (1 H, NH).

*trans*-*N,N,N*-Trimethyl-2-iodocyclopentylammonium Iodide (3).

A solution of 0.01 moles of imine 1 and 0.056 moles of methyl iodide in 30 ml. of dry benzene was stirred at room temperature under a nitrogen atmosphere. A white solid began to separate after 0.5 hour. After 30 hours, the solid was collected and recrystallized from ethanol to give 33% of fine, white crystalline product, m.p. 161-162° dec. A similar result was obtained when 0.01 mole of methyl iodide was used. An infrared spectrum of the product revealed no band at about 3500 cm<sup>-1</sup>.

Anal. Calcd. for C<sub>8</sub>H<sub>17</sub>Nl<sub>2</sub>: C, 25.21; H, 4.51; N, 3.68. Found: C, 25.60; H, 4.64; N, 3.69.

Aroyl and Arenesulfonyl Derivatives of 6-Azabicyclo[3.1.0]hexane.

These derivatives were prepared by treatment of the imine with the corresponding acid chloride in benzene solution in the presence of triethylamine. All derivatives, except the benzoyl, were solids and were recrystallized from ethanol or benzene-hexane. The n.m.r. spectra of all derivatives had a sharp 2H singlet at 3.1-3.5 (bridgehead H) and a 6H multiplet centered at 1.68-1.80 (carbocyclic methylene H). Other data are summarized in Table I.

Pyrolysis of 6-(*p*-Nitrobenzoyl)-6-azabicyclo[3.1.0]hexane (4).

A solution of 0.80 g. of compound 4 in 30 ml. of dry toluene

was heated in a glass-lined steel bomb for 8 hours at 205-208°. Evaporation of the solvent left a solid, brown residue which was extracted with 2 x 150 ml. of hot hexane. Removal of the solvent gave 0.27 g. (34%) of white solid, m.p. 128-134°, which formed fine, white crystals, m.p. 134-136° upon recrystallization from ethanol. (Lit. m.p. 137.5-139.5° (7)). This compound did not decolorize permanganate, and its n.m.r. spectrum was consistent with the oxazoline structure **9**, with a quartet at 8.15 (4H, aromatic protons) a pair of multiplets at 5.17 and 4.77 (1H each, bridgehead protons), and a multiplet centered at 1.70-1.80 (6H, ring protons).

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: C, 62.05; H, 5.22; N, 12.06. Found: C, 61.98; H, 5.16; N, 12.14.

The hexane-insoluble residue was recrystallized from benzene giving 0.28 g. (35%) of fine, yellow needles, m.p. 167-169°. A second recrystallization raised the melting point to 169-170.5°. This substance instantaneously decolorized methanolic potassium permanganate, and the spectral data supported the unsaturated amide structure **6**. The infrared absorption spectrum had a medium intensity NH band at 3500 cm<sup>-1</sup> and a strong C=O band at 1670 cm<sup>-1</sup>. The n.m.r. spectrum had a quartet at 8.08 (4H, aromatic protons), a multiplet centered at 6.39 (1H, NH), a pair of multiplets at 6.01 and 5.78 (1H each, -HC=CH-), a multiplet at 5.18 (1H, H-CN), and a multiplet centered at 2.20 (4H, ring protons). Compound **6** was also independently synthesized by the reaction of 3-aminocyclopentene (**8**) with *p*-nitrobenzoyl chloride and triethylamine in benzene solution. The two samples were found to be identical by melting point, mixture melting point, and the infrared and n.m.r. spectra.

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>: C, 62.05; H, 5.22; N, 12.06. Found: C, 62.04; H, 5.23; N, 12.14.

When the pyrolysis was conducted for 15 hours at 204-212°, the yield of oxazoline (**9**) was 41% and 14% of the unsaturated amide (**6**) was isolated. When a solution of 1.0 g. of compound **4** and 2.5 g. of sodium iodide in 100 ml. of acetone was refluxed for 5 hours, oxazoline (**9**) was obtained in quantitative yield.

#### Pyrolysis of Amide (**6**) and Oxazoline (**9**).

When a solution of 1.0 g. of the amide (**6**) in 40 ml. of toluene was heated in a glass-lined steel bomb for 8 hours at 205-208°, the oxazoline (**9**) could not be isolated from the residue. Similarly, heating 0.50 g. of the oxazoline (**9**) in toluene for 20 hours at 210° gave material from which the amide (**6**) could not be isolated.

#### Reaction of the Amide (**6**) with Sulfuric Acid.

A total of 1.0 g. of the amide (**6**) was added in small portions with stirring to 10 ml. of ice-cold, concentrated sulfuric acid. After stirring overnight at room temperature, the solution was poured into crushed ice and neutralized by addition of aqueous sodium hydroxide solution. A dark brown precipitate was collected and recrystallized from benzene to give 0.15 g. (21%) of *p*-nitrobenzamide, white needles, m.p. 199-201° (lit., 201° (9)).

Pyrolysis of 6-Benzoyl-6-azabicyclo[3.1.0]hexane (**4**, R = C<sub>6</sub>H<sub>5</sub>).

The benzoyl derivative (1.60 g.) was gradually heated neat in a small flask provided with a thermometer immersed in the liquid. At 150°, an exothermic reaction occurred and the temperature rose to 250°. After a further 10 minutes at 220°, the product was distilled to give a pale yellow, viscous liquid, b.p. 94-98°/0.3 mm., which solidified on standing at room temperature. Sublimation of this solid at 0.1 mm. pressure gave 0.96 g. (60%) of translucent, white prisms of the isomeric oxazoline, m.p. 47-49° (lit. (10) m.p. 50-51°). The n.m.r. spectrum was similar to that of **9**.

*Anal.* Calcd. for C<sub>12</sub>H<sub>13</sub>NO: C, 76.96; H, 7.01; N, 7.48. Found: C, 76.81; H, 6.98; N, 7.23.

The oxazoline formed a crystalline picrate, yellow needles from ethanol, m.p. 166-167° (1).

*Anal.* Calcd. for C<sub>18</sub>H<sub>16</sub>N<sub>4</sub>O<sub>8</sub>: C, 51.92; H, 3.88; N, 13.46. Found: C, 52.02; H, 3.99; N, 13.23.

The residue from the sublimation of the oxazoline consisted of 0.09 g. (6%) of pale yellow solid, m.p. 112-113°. Recrystallization from hexane gave fine, white crystals, m.p. 114-115°. The compound gave a positive permanganate test for unsaturation and the infrared spectrum had a strong NH band 3340 cm<sup>-1</sup>, in agreement with the structure of **6** (R = C<sub>6</sub>H<sub>5</sub>).

*Anal.* Calcd. for C<sub>12</sub>H<sub>13</sub>NO: C, 76.96; H, 7.01; N, 7.48. Found: C, 76.66; H, 6.99; N, 7.77.

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