Stereochemistry of Amino Ketone Rearrangements. Crystal Structure of 3-*N*-Methylamino-3-phenyl-2-bicyclo[3.2.1]octanone Hydrochloride[1,2]

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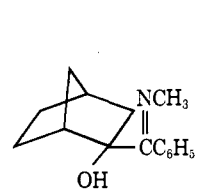
Abstract: A pair of diastereomeric α-hydroxyimines, *endo*-2-hydroxy-*exo*-2-(α-*N*-methylimino)benzylbicyclo-[2.2.1]heptane (**1**) and *exo*-2-hydroxy-*endo*-2-(α-*N*-methylimino)benzylbicyclo[2.2.1]heptane (**2**), and a pair of diastereomeric α-amino ketones, *endo*-2-*N*-methylamino-*exo*-2-benzoylbicyclo[2.2.1]heptane (**3**) and *exo*-2-*N*-methylamino-*endo*-2-benzoylbicyclo[2.2.1]heptane (**4**), were synthesized. Rearrangements of **1** and **2** under pyrolytic conditions gave *exo*-2-phenyl-*endo*-2-α-*N*-methylamino-3-bicyclo[3.2.1]octanone (**10**) and *exo*-3-*N*-methylamino-*endo*-3-phenyl-2-bicyclo[3.2.1]octanone (**15**), respectively. Similarly, rearrangement of **3** yielded *exo*-2-phenyl-*endo*-2-hydroxy-3-*N*-methyliminobicyclo[3.2.1]octane (**20**), but amino ketone **4** resisted rearrangement under pyrolytic conditions. However, **4** was obtained when *exo*-3-hydroxy-*endo*-3-phenyl-2-*N*-methyliminobicyclo[3.2.1]octane (**21**) was thermally rearranged. The structures of the rearrangement products were established by spectral and degradative data. The X-ray crystal structure of **15** as its hydrochloride is presented in detail and the stereochemical implications of the rearrangement are discussed. The hydrochloride of **15** crystallizes in the monoclinic system, space group $P2_1/n$, with four molecules per unit cell. Lattice constants were determined to be $a = 6.530$ (4) Å, $b = 13.755$ (9) Å, $c = 15.50$ (1) Å, and $\beta = 90.23$ (3)°. A total of 1359 reflections were examined with Mo Kα radiation on a card-controlled diffractometer. The phases were assigned *via* the Sayre equation, and the structure was refined by full matrix least squares to a final conventional discrepancy factor (R) of 0.054.

Mechanistic and kinetic studies on the thermal rearrangements of α-amino ketones[4] bearing dialkyl substituents at the α-carbon atom have indicated that these rearrangements are stereospecific and yield products predicted by a cyclic, concerted mechanism.[5] The rearrangements of steroidal D-ring tertiary α-hydroxy ketones of known configuration in the presence of methylamine or ammonia to D-homo α-amino ketones also showed that an intramolecular cyclic mechanism requiring a s-cis relationship between the hydroxyl and imine groups is operating in most cases.[6] However, experimentally verified explanations for the formation of several other products in these rearrangements are still lacking.[4] The only definitive evidence for the stereospecificity of amino ketone rearrangements has been the conversion of an optically active α-hydroxyimine to an optically active α-amino ketone.[7] We now report our findings on the stereochemistry of the rearrangements of a pair of diastereomeric α-hydroxyimines, **1** and **2**, and a pair of diastereomeric α-amino ketones, **3** and **4**. The norbornane ring system was chosen as it can incorporate the desired stereochemical properties and in addition can undergo facile carbon skeletal rearrangements.



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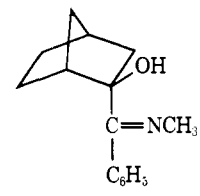

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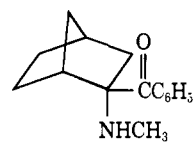

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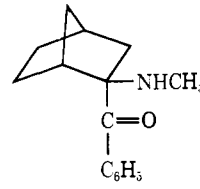

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In addition to the usual chemical and spectroscopic methods employed in structural characterization, the rearrangement product of **2** was subjected to a complete X-ray crystallographic analysis. This study was undertaken both to confirm the interpretation of the other, less direct measurements and to determine the

(1) Amino Ketone Rearrangements. VIII. For the previous paper in this series, see C. L. Stevens, A. Thuillier, K. G. Taylor, F. A. Daniher, J. P. Dickerson, H. T. Hanson, N. A. Nielsen, N. A. Tikotkar, and R. M. Weier, *J. Org. Chem.*, 31, 2601 (1966).

(2) A preliminary account on part of this work has been reported: C. L. Stevens and T. A. Treat, Abstracts, 158th National Meeting of the American Chemical Society, New York, N. Y., 1969, No. ORGN 62.

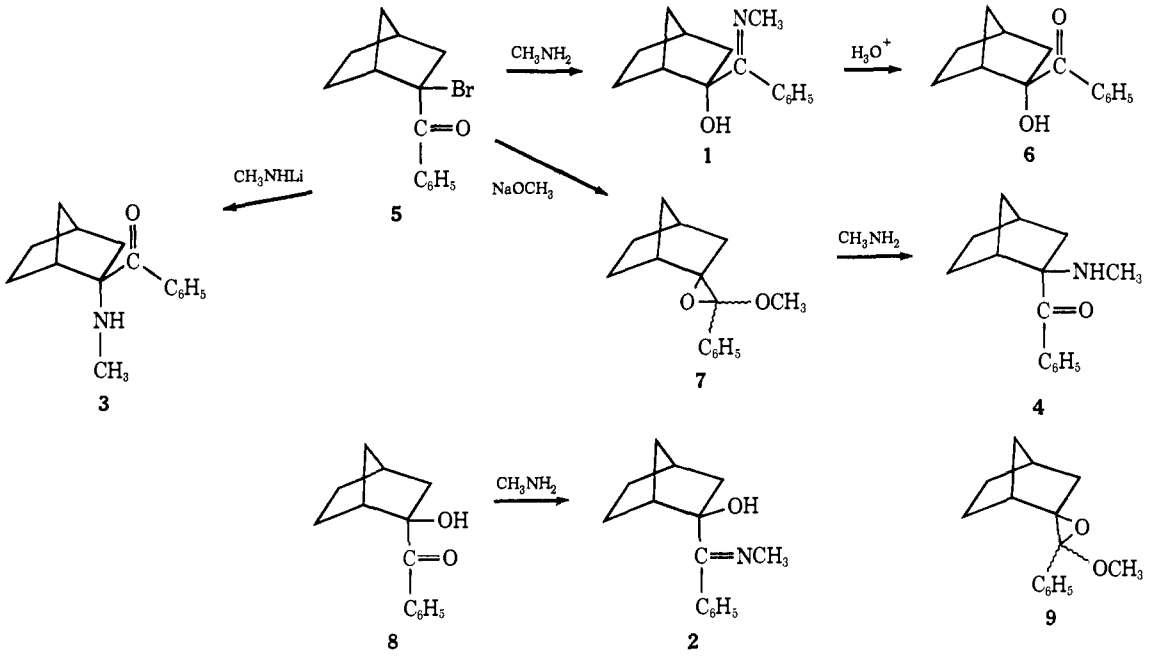
(3) Taken in part from the Ph.D. Dissertation of T. A. Treat, Wayne State University, 1969, and M. S. Thesis of W. Schmonsees, Wayne State University, 1971.

(4) For a recent review on amino ketone rearrangements, see C. L. Stevens, P. M. Pillai, M. E. Munk, and K. G. Taylor in "Mechanisms of Molecular Migrations," Vol. 3, B. S. Thyagarajan, Ed., Wiley, New York, N. Y., 1971, p 271.

(5) (a) C. L. Stevens, R. D. Elliott, B. L. Winch, and I. L. Klundt, *J. Amer. Chem. Soc.*, 84, 2272 (1962); (b) C. L. Stevens, R. D. Elliott, and B. L. Winch, *ibid.*, 85, 1464 (1963); (c) C. L. Stevens, A. Thuillier, and F. A. Daniher, *J. Org. Chem.*, 30, 2962 (1965); (d) C. L. Stevens, I. L. Klundt, M. E. Munk, and M. D. Pillai, *ibid.*, 30, 2967 (1965); (e) C. L. Stevens, H. T. Hanson, and K. G. Taylor, *J. Amer. Chem. Soc.*, 88, 2769 (1966).

(6) (a) D. F. Morrow, M. E. Brokke, G. W. Moersch, M. E. Butler, C. F. Klein, W. A. Neuklis, and E. C. Y. Huang, *J. Org. Chem.*, 30, 212 (1965); (b) D. F. Morrow, M. E. Butler, and E. C. Y. Huang, *ibid.*, 30, 579 (1965).

(7) S. Yamada, H. Mizuno, and S. Terashima, *Chem. Commun.*, 1058 (1967).



molecular parameters of the unusual bicyclo[3.2.1]-octanone system.

Results

Chemical. Hydroxyimine **1** was prepared in 72% yield by treatment of *exo*-2-bromo-*endo*-2-benzoylbicyclo[2.21]heptane[8] (**5**) with methylamine at −78°. The inversion of configuration at C-2 was expected on the basis of previous findings on the reaction of primary amines on α-halo ketones.[9] Further evidence for the structure of **1** was provided by its hydrolysis with 1.5 *M* hydrochloric acid to give *endo*-2-hydroxy-*exo*-2-benzoylbicyclo[2.2.1]heptane[8] (**6**). Hydroxyimine **2** was obtained from *exo*-2-hydroxy-*endo*-2-benzoylbicyclo[2.2.1]heptane[8] (**8**) in 74% yield by heating **8** with methylamine at 110° for 3 days. Hydrolysis of **2** back to **8** with 1.5 *M* hydrochloric acid furnished additional evidence for the structure of **2**. Synthesis and structural proof for hydroxy ketones **6** and **8** have been discussed previously.[8]

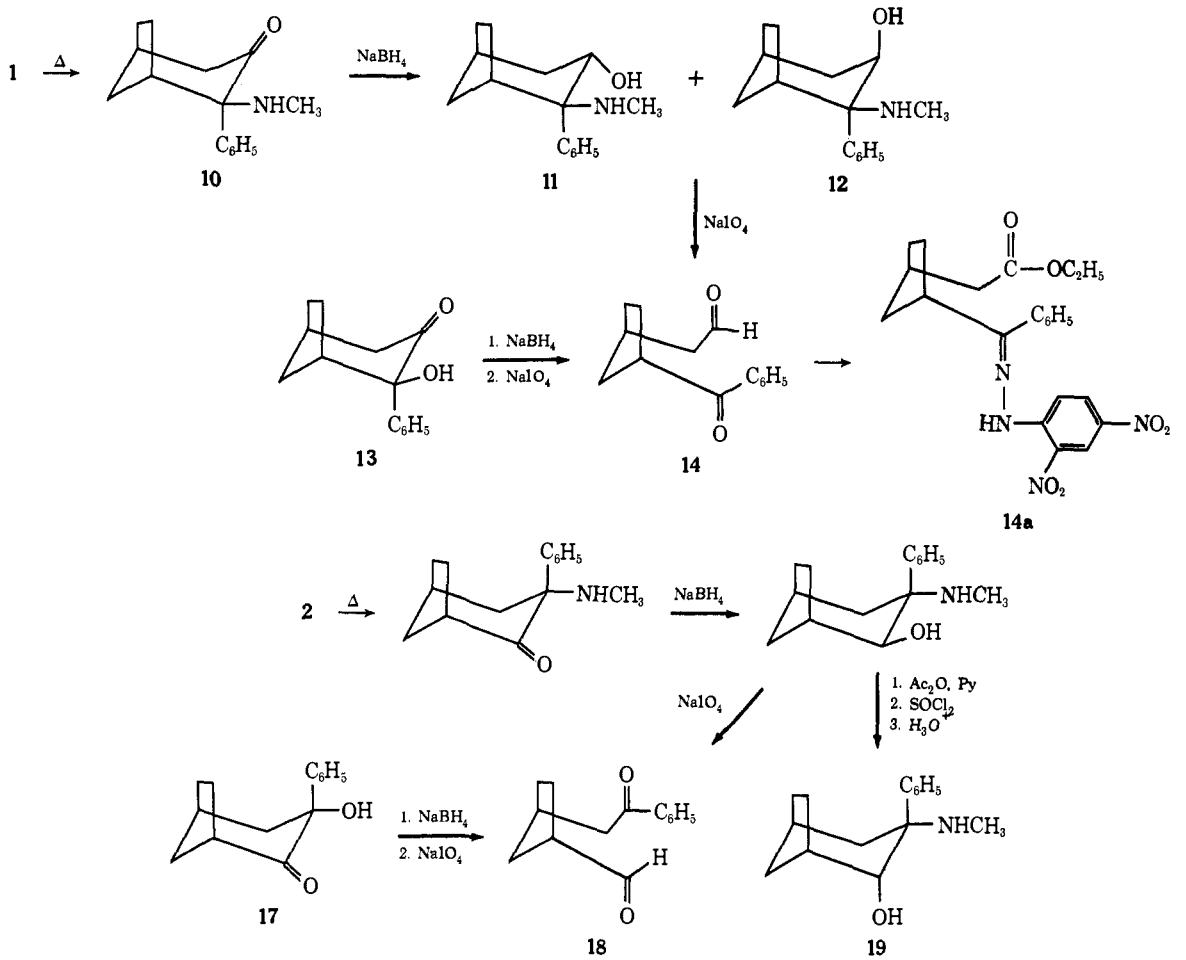
endo-2-Benzoyl-*exo*-2-*N*-methylaminobicyclo[2.2.1]-heptane (**4**) was prepared in 75% yield by heating a mixture of epoxy ether,[8] **7**, and methylamine in a sealed tube at 140° for 3 days.[10] As the epoxide ring in **7** is known to be endo oriented and the primary amine is expected to react by a SN2-type displacement at C-2, exo configuration is predicted for the *N*-methylamino group in **4**. The gross structure of **4** was confirmed by its reduction with sodium borohydride to a mixture of vicinal amino alcohols followed by cleavage with sodium metaperiodate to benzaldehyde and norcamphor which were isolated and characterized as their 2,4-dinitrophenylhydrazones.

The synthesis of *exo*-2-benzoyl-*endo*-2-*N*-methylaminobicyclo[2.2.1]heptane (**3**) could not be accomplished from epoxy ether **9**[11] as its reaction with methylamine was extremely slow. Thus, heating a mixture of methylamine and **9** at 100° for 2 days did not produce detectable amounts of **3** and practically all of **9** was recovered unchanged. The low reactivity of **9** toward methylamine may be due to steric hindrance against the approach of methylamine from the highly hindered endo side of the norbornane ring for a SN2-type displacement of the epoxide oxygen at carbon 2. Although higher temperature and longer time did cause some reaction between methylamine and **9**, the product obtained was not the amino ketone **3** but was its rearrangement product, **20**. This result was not unexpected as **3** itself was found to rearrange to **20** under those conditions as described later in this article. The preparation of **3** was achieved in low yield by the treatment of lithium methylamide with bromo ketone **5**. Amino ketone **3**, which was purified by preparative thin layer chromatography and characterized as the hydrochloride, had similar spectral characteristics as **4** and the same gross structure as shown by its reduction with sodium borohydride followed by degradation with sodium metaperiodate to benzaldehyde and norcamphor which were characterized as their 2,4-dinitrophenylhydrazones.

Rearrangement of Hydroxyimines. Both the α-hydroxyimines **1** and **2** rearranged when heated at 185° using *o*-dichlorobenzene as a solvent. The rearrangement of **1** was complete in 3 hr under those conditions and gave 96% of an amino ketone **10**, which was characterized as its hydrochloride. The minor product (4%) could not be separated and characterized but was shown to be different from all other compounds discussed here by means of its gas chromatographic retention time. The rearrangement of **2** was slower and required 14 hr of heating under reflux of an *o*-dichlorobenzene solution at 185° for completion. It gave a single product, *endo*-3-phenyl-*exo*-3-*N*-methylamino-2-bicyclo[3.2.1]octanone (**15**), which was isolated in 86% yield as its hydrochloride.

The position of the carbonyl group in **10** was determined by relating it to the known *exo*-2-phenyl-*endo*-2-hydroxy-3-bicyclo[3.2.1]octanone[8] (**13**). Both **10** and **13** were reduced with sodium borohydride and the reduction products were cleaved with sodium metaperiodate to give the same keto aldehyde **14** indicating the

(8) C. L. Stevens, T. A. Treat, and P. M. Pillai, *J. Org. Chem.*, 37, 2091 (1972).
(9) C. L. Stevens, P. Blumbergs, and M. E. Munk, *ibid.*, 28, 331 (1963).
(10) For formation of α-amino ketones from epoxy ethers, see C. L. Stevens and C. H. Chang, *ibid.*, 27, 4392 (1962).
(11) Unpublished work.



structure of **10** to be 2-phenyl-2-*N*-methylamino-3-bicyclo[3.2.1]octanone. Also an nmr spectrum of **14** showed that the aldehyde proton appeared as a triplet (J = 1.3 Hz) at δ 9.6 as expected.

The configuration at C-2 of **10** was established as follows. The mixture of amino alcohols **11** and **12** obtained by the reduction of **10** with sodium borohydride was separated into two pure components by fractional crystallization. Treatment of the *N*-acetate of the major component **11** with thionyl chloride followed by acid hydrolysis converted it to **12**, showing that **11** was the trans amino alcohol and **12** the cis isomer.[12] An examination of the nmr spectra of **11** and **12** indicated that the C-3 proton in **11** was axial as it appeared as a well-separated triplet (J = 9 Hz) at 248 Hz. On the other hand, the C-3 proton in **12** appeared as a broad singlet at 262 Hz as expected for an equatorial proton as axial–equatorial and equatorial–equatorial coupling constants are relatively small. Also the C-3 hydrogen in **11** appeared at a higher field than that in **12** agreeing with previous experience that generally the equatorial proton is more deshielded than the corresponding axial hydrogen.[13] Thus, as the C-3 hydrogen in **11** is axial, the C-3 hydroxyl must be equatorial, and as **11** has been shown to have trans hydroxyl and amine functions, the *N*-methylamino group in **11** and consequently in **10** must be equatorial.[14] Hence the structure of amino ketone **10** must be *exo*-2-phenyl-*endo*-2-*N*-methylamino-3-bicyclo[3.2.1]octanone.

Reduction of **15** with sodium borohydride gave a single crystalline amino alcohol, **16**, which on treatment with sodium metaperiodate yielded keto aldehyde **18**. As **18** was also obtained from the known hydroxy ketone[8] **17** by reduction with sodium borohydride followed by cleavage with sodium metaperiodate, the position of the keto group in **15** was shown to be at C-2. The appearance of the aldehyde hydrogen as a doublet (J = 2 Hz) at δ 9.6 in an nmr spectrum of **18** provided further evidence for the gross structure of **15**.

Amino alcohol **16** was shown to have trans hydroxyl and amine functions as its *N*-acetate on treatment with thionyl chloride followed by acid hydrolysis gave a new (cis) amino alcohol,[12] **19**. A comparison of the nmr spectra of **16** and **19** did not show any significant difference in the appearance of C-2 hydrogens, but they had considerably different chemical shifts. Thus, the C-2 proton of **16** appeared 26 Hz upfield from the C-2 hydrogen of **19** indicating that C-2 proton in **16** is axial and hence its C-2 hydroxyl equatorial.[14] As it was shown earlier that the amino group in **16** was trans to the hydroxyl, the amine function at C-3 must be equatorial both in **16** and in **15**. Consequently, **15** must have an *exo*-*N*-methylamino group. That **15** was in-

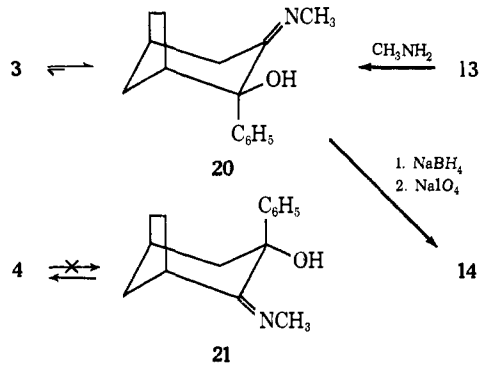
(12) For conversion of a trans amino alcohol (trans heteroatom substituents) to its cis isomer by the inversion of the hydroxyl group, see W. S. Johnson and E. N. Schubert, *J. Amer. Chem. Soc.*, 72, 2187 (1950).

(13) R. U. Lemieux, R. K. Kullning, H. J. Bernstein, and W. G. Schneider, *ibid.*, 80, 6098 (1958); R. U. Lemieux and J. D. Stevens, *Can. J. Chem.*, 43, 2059 (1965).

(14) Chair conformation is assumed here for the six-membered ring in the bicyclic system. Examination of molecular models indicated that the chair conformation has the least nonbonded interactions. Also similar systems have been shown to exist in the same conformation; see C. W. Jefford and B. Waegell, *Tetrahedron Lett.*, 1981 (1963).

deed *endo*-3-phenyl-*exo*-3-*N*-methylamino-2-bicyclo-[3.2.1]octanone was confirmed by X-ray crystallography as described later.

Rearrangement of Amino Ketones. Amino ketone **3**



rearranged readily to *exo*-2-phenyl-*endo*-2-hydroxy-3-*N*-methylimino[3.2.1]octane (**20**) when heated in *o*-dichlorobenzene at 152°, and after 21 hr the mixture contained 98% of **20** and 2% of **3** as shown by gas chromatography. Pyrolysis of **20** in *o*-dichlorobenzene at 185° for 12 hr also produced the same mixture showing that the rearrangement is reversible. Hydroxyimine **20** was characterized as its hydrochloride, and its structure was established by its formation from the known hydroxy ketone,[8] **13**. The structure of **20** was further confirmed by its reduction with sodium borohydride followed by cleavage with sodium metaperiodate to the ketoaldehyde, **14**.

Amino ketone **4** resisted rearrangement on heating in *o*-dichlorobenzene at 185° and in tridecane at 230°. Although some decomposition was observed on prolonged heating, no new product was detected, either by thin layer or by gas chromatography. Further, 75% of **4** was reisolated after heating it in *o*-dichlorobenzene at 185° for 4 days. However, when *exo*-3-hydroxy-*endo*-3-phenyl-2-*N*-methyliminobicyclo[3.2.1]octane[8] (**21**), which is the expected product from the rearrangement of **4**, was heated at 185° in *o*-dichlorobenzene as a solvent for 67 hr, it was converted almost exclusively to **4**, indicating that **4** is the thermodynamic product in this rearrangement.

Crystallographic. The data obtained from measurements on Weissenberg and precession photographs of a single crystal of the hydrochloride of **15** are given in Table I. The reported lattice constants have been refined by least squares from 19 diffractometer measurements. The structure determination indicated that the configuration at C(3) was, indeed, *endo*-phenyl-*exo*-methylamino, as expected from the rearrangement mechanism. Figure 1 is a projection of the octanone moiety viewed down the *a* axis. Table II lists the final atomic positions and anisotropic thermal parameters. The bond lengths, nonhydrogen bond angles, and their standard deviations are given in Table III.

Table I. Crystallographic Data

Formula:	$[C_{15}H_{20}NO]^+Cl^-$
Crystal system:	monoclinic
a =	6.530 ± 0.004 Å
b =	13.755 ± 0.009 Å
c =	15.497 ± 0.011 Å
β =	90.23 ± 0.03°
V =	1392 Å^3
Z =	4
Density (calcd) =	1.27 g/cm^3
Density (flotation) =	1.28 (3) g/cm^3
Absences:	$0k0$, $k = 2n + 1$
	$h0l$, $h + 1 = 2n + 1$
Space group:	$P2_1/n^a$
μ(Mo Kα):	2.67 cm^{-1}
F(000):	568

[a] The equivalent positions for this space group, with the center of symmetry chosen as the origin of the coordinate system, are x, y, z: $\bar{x} + 1/2, y + 1/2, \bar{z} + 1/2$; $\bar{x}, \bar{y}, \bar{z}$: $x + 1/2, \bar{y} + 1/2, \bar{z} + 1/2$.

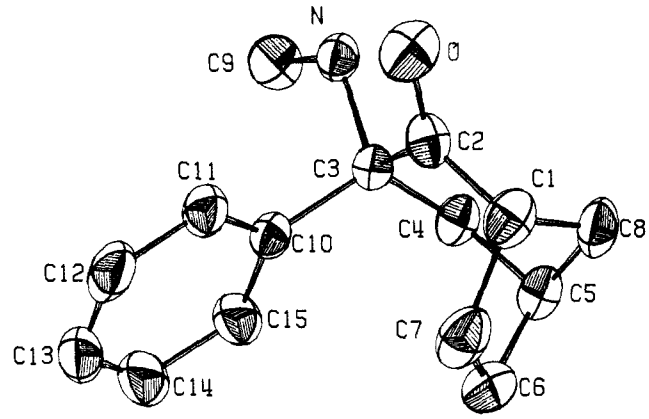


Figure 1. A projection of the 3-*N*-methylamino-3-phenyl-2-bicyclo[3.2.1]octanone cation on the *bc* plane, rotated 20° about *c*. The chloride counterion is not shown. The thermal ellipsoids contain the 40% probability region.

Discussion

Chemical. The thermal rearrangements of both the hydroxyimines and the amino ketones are stereospecific and yield products predicted by a cyclic, concerted mechanism. There are, however, a few points which require further comments. In the rearrangement of both **1** and **3**, it is the 1,2 bond that migrates as expected from electronic considerations, since the migrating aptitude of a trisubstituted carbon is usually greater than that of a disubstituted carbon to an electron-deficient center. But in the rearrangement of **2** to **15**, the less substituted carbon 3 migrates as in the thermal rearrangement of *exo*-2-hydroxy-*endo*-2-benzoylbicyclo[2.2.1]heptane[8] (**8**) to hydroxy ketone **17**. The reluctance of C-1 to migrate in this rearrangement has been explained as due to the steric repulsion between the bulky phenyl group and the hydrogens on the 2-carbon bridgehead in the transition state[8] (**2b**). Amino ketone **4** which also has an *endo*-benzoyl group as in **2** and **8** and an *exo*-*N*-methylamino group would have been expected to undergo rearrangement with the migration of the 3,2 bond to give the hydroxyimine **21**. But only the reverse rearrangement was found to occur. The resistance of **4** to undergo rearrangement may be partly due to the steric interaction between the phenyl group and the two carbon bridge in the transition state (**4a**) and partly due to the inherent greater stability of amino ketones over hydroxyimines.[15]

The rearrangements of **1** and **2** to **10** and **15**, respectively, are practically irreversible and can be expected to be so.[5c,e] But the rearrangements of α-amino ketones in general are known to involve a three-component equilibrium.[5e] The absence of phenyl migration in the

(15) The energy difference between the systems, C=N + C-O-H and C=O + C-N-H has been calculated to be 5-18 kcal favoring the amino ketone system.[5e]

Table II. Final Coordinates ($\times 10^4$) and Anisotropic Thermal Parameters ($\times 10^4$) for 3-*N*-Methylamino-3-phenyl-2-bicyclo[3.2.1]octanone Hydrochloride[a]

Atom	*X*	*Y*	*Z*	β_{11}	β_{22}	β_{33}	β_{12}	β_{13}	β_{23}
Cl	1500 (2)	5106 (1)	1468 (1)	314 (4)	58 (1)	32 (1)	7 (1)	−9 (1)	−1 (1)
C(1)	−858 (7)	1901 (3)	1152 (3)	248 (13)	72 (3)	47 (2)	−19 (5)	19 (5)	15 (2)
C(2)	−596 (7)	2699 (3)	505 (3)	195 (12)	60 (3)	34 (2)	−8 (5)	1 (4)	−4 (2)
C(3)	1511 (6)	2804 (3)	66 (2)	172 (11)	41 (2)	27 (2)	−5 (4)	−1 (3)	1 (2)
C(4)	3217 (6)	2599 (3)	743 (3)	207 (12)	54 (3)	33 (2)	−11 (5)	−11 (4)	5 (2)
C(5)	2682 (7)	1806 (3)	1397 (3)	292 (14)	63 (3)	33 (2)	7 (5)	−11 (4)	6 (2)
C(6)	2091 (8)	820 (3)	988 (3)	378 (17)	51 (3)	50 (2)	6 (6)	−1 (5)	8 (2)
C(7)	−179 (8)	902 (3)	783 (3)	386 (17)	62 (3)	52 (3)	−43 (6)	−14 (5)	17 (2)
C(8)	732 (8)	2085 (4)	1857 (3)	363 (16)	83 (4)	28 (2)	18 (6)	16 (5)	12 (2)
C(9)	3527 (7)	4140 (3)	−695 (3)	268 (13)	49 (3)	49 (2)	−29 (5)	25 (5)	1 (2)
C(10)	1595 (6)	2180 (3)	−747 (2)	238 (12)	44 (3)	44 (3)	−4 (4)	4 (5)	5 (2)
C(11)	−146 (7)	2119 (3)	−1271 (3)	348 (16)	54 (3)	54 (3)	−9 (5)	−27 (5)	1 (2)
C(12)	−74 (11)	1556 (4)	−2019 (3)	612 (23)	58 (4)	58 (4)	−33 (7)	−62 (6)	5 (2)
C(13)	1646 (13)	1074 (4)	−2263 (3)	783 (31)	51 (3)	51 (3)	−1 (9)	25 (7)	1 (2)
C(14)	3389 (9)	1142 (4)	−1760 (3)	521 (21)	58 (3)	58 (3)	7 (7)	63 (6)	1 (2)
C(15)	3361 (7)	1696 (3)	−1008 (3)	313 (15)	57 (3)	40 (2)	6 (5)	35 (5)	−1 (2)
N	1647 (5)	3858 (2)	−201 (2)	203 (9)	47 (2)	29 (2)	1 (3)	4 (3)	3 (1)
O	−1935 (5)	3295 (2)	359 (2)	194 (8)	88 (3)	61 (2)	19 (4)	15 (3)	17 (2)
H(1)	−2500	1900	1400						
H(4)	4500	2500	400						
H(4′)	3500	3300	1000						
H(5)	4000	1700	1800						
H(6)	2500	300	1400						
H(6′)	3000	700	400						
H(7)	−1000	500	1200						
H(7′)	−500	900	200						
H(8)	300	2900	2100						
H(8′)	500	1700	2400						
H(9)	3500	4900	−800						
H(9′)	3500	3700	−1200						
H(9″)	5000	3900	−200						
H(11)	−1500	2500	−1000						
H(12)	−1500	1500	−2400						
H(13)	2000	500	−2800						
H(14)	5000	900	−2000						
H(15)	5000	1700	−600						
H(N)	500	4100	−600						
H(N′)	1500	4300	400						

[a] Standard deviations are given in parentheses for least significant figures. Thermal motion was described by the relation $\exp[-(\beta_{11}h^2 + \beta_{22}k^2 + \beta_{33}l^2 + 2\beta_{12}hk + 2\beta_{13}hl + 2\beta_{23}kl)]$. Hydrogen atoms are identified by reference to the atom to which they are bonded. The hydrogen isotropic thermal parameter was set as 3.0.

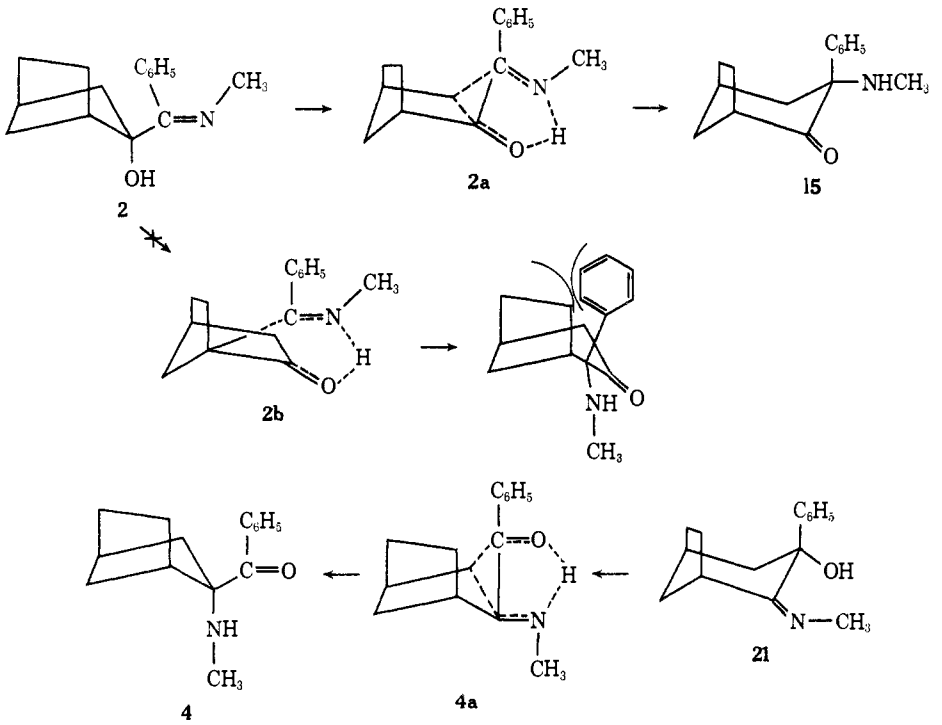


Table III. Bond Lengths and Nonhydrogen Angles for 3-*N*-Methylamino-3-phenyl-2-bicyclo[3.2.1]octanone Hydrochloride[a]

	Bond Lengths, Å		
C(1)–C(2)	1.498 (6)	C(1)–H(1)	1.14
C(2)–C(3)	1.544 (6)	C(4)–H(4)	1.00
C(3)–C(4)	1.552 (5)	C(4)–H(4′)	1.06
C(4)–C(5)	1.532 (6)	C(5)–H(5)	1.07
C(5)–C(6)	1.532 (6)	C(6)–H(6)	0.99
C(6)–C(7)	1.520 (7)	C(6)–H(6′)	1.10
C(7)–C(1)	1.554 (7)	C(7)–H(7)	1.01
C(1)–C(8)	1.526 (6)	C(7)–H(7′)	0.93
C(5)–C(8)	1.512 (6)	C(8)–H(8)	1.22
C(3)–C(10)	1.528 (5)	C(8)–H(8′)	1.00
C(10)–C(11)	1.397 (6)	C(9)–H(9)	1.05
C(11)–C(12)	1.396 (7)	C(9)–H(9′)	0.99
C(12)–C(13)	1.360 (9)	C(9)–H(9″)	1.27
C(13)–C(14)	1.382 (8)	C(11)–H(11)	1.11
C(14)–C(15)	1.394 (7)	C(12)–H(12)	1.10
C(15)–C(10)	1.394 (6)	C(13)–H(13)	1.17
C(2)–O	1.219 (5)	C(14)–H(14)	1.16
C(3)–N	1.511 (5)	C(15)–H(15)	1.24
C(9)–N	1.501 (5)	N–H(N)	1.02
N–Cl	3.105 (3)	N–H(N′)	1.12
Cl–H(N′)	1.99		
	Interior Angles, Deg		
C(7)–C(1)–C(2)	111.6 (4)	C(5)–C(6)–C(7)	105.1 (4)
C(7)–C(1)–C(8)	102.5 (4)	C(6)–C(7)–C(1)	105.6 (4)
C(8)–C(1)–C(2)	106.2 (4)	C(1)–C(8)–C(5)	101.1 (3)
C(1)–C(2)–C(3)	118.0 (4)	C(15)–C(10)–C(11)	118.5 (4)
C(2)–C(3)–C(4)	108.9 (3)	C(10)–C(11)–C(12)	119.0 (5)
C(3)–C(4)–C(5)	114.4 (3)	C(11)–C(12)–C(13)	122.1 (5)
C(4)–C(5)–C(6)	114.2 (3)	C(12)–C(13)–C(14)	119.6 (5)
C(4)–C(5)–C(8)	109.0 (4)	C(13)–C(14)–C(14)	119.6 (5)
C(8)–C(5)–C(6)	102.0 (4)	C(14)–C(14)–C(10)	121.2 (5)
	Exterior Angles, Deg		
C(1)–C(2)–O	122.2 (4)	C(10)–C(3)–N	108.0 (3)
C(3)–C(2)–O	119.7 (4)	C(2)–C(3)–N	105.4 (3)
C(2)–C(3)–C(10)	110.3 (3)	C(3)–N–C(9)	115.9 (3)
C(4)–C(3)–C(10)	115.3 (3)	C(3)–C(10)–C(15)	122.7 (4)
C(4)–C(3)–N	108.5 (3)	C(3)–C(10)–C(11)	118.7 (4

[a] Standard deviations derived from the variance-covariance matrix are given in parentheses for least significant figures.

rearrangements of **20** and **21** to give a third component in each of their respective equilibria may be attributed to severe steric hindrance encountered by the migrating phenyl from the two-carbon bridge in the highly strained transition states. That the amino ketone rearrangement is indeed very sensitive to steric factors has been implicated previously by showing the inability of an *o*-toluoyl group to migrate in a similar situation.[1] Phenyl migration was also not observed in amino ketone rearrangements involving other strained ring systems.[16] The fact that no further rearrangement was observed in the case of **10** and **15** may also be attributed to the same steric factors.

X-Ray Structure. This structure represents the first determination of the molecular parameters of an isolated bicyclo[3.2.1]octanone system. The structures of a number of natural product derivatives, structurally similar to bicyclo[3.2.1]octanone, have been reported.[17–22] The bond lengths, angles, and deviations from planarity of these compounds provide a good basis set for comparison with the current structure. The average nonphenyl C–C bond length is 1.530 Å, with a range of 1.498–1.554 Å. The shortest bond, C(1)–C(2), is consistent with the expected effect of the sp^2 hybridization at C(2); that C(2)–C(3) (d = 1.544 Å) is not similarly influenced may be attributed to the tendency toward bond lengthening with increasing substitution, as is the case at C(3). This tendency is also indicated by the relatively long C(3)–C(4) bond (d = 1.552 Å). A Q test on the phenyl bond lengths showed that the C(12)–C(13) bond (d = 1.360 Å) was significantly shorter than the remaining bonds (d = 1.393 Å). This deviation is presumably attributable to some ambiguity in the position of C(13), a fact which is reflected by the relatively high thermal parameters associated with this atom. No librational corrections have been applied to the bond lengths. The N–H···Cl distance of 3.105 Å and angle of 175.8° is within the expected range for N–Cl hydrogen bonds.

A least-squares plane was fitted to the chair-like, six-membered ring, C(1), C(2), C(3), C(4), C(5), C(8), and indicated that atoms C(1), C(2), C(4), and C(5) are coplanar (<0.002 Å deviation), C(3) is displaced by −0.64 Å, and C(8) by +0.73 Å. The natural products[17–22] had bridging-atom displacements ranging from 0.79 to 0.90 Å with an average of 0.85 Å. The value found in the current study, however, is in agreement with that expected for an ideal cyclohexane ring. The C(5), C(8), C(1) bridging angle of 101.1° agrees well with the average bridging angle of 102° for the other structures. An interesting trend is noticeable when the bridging angles and bridging-atom displacements of the natural products are compared as in Table IV. The inverse relation between bridging angle and out-of-plane displacement of the central atom is evident; indeed, angle broadening coupled with decreased displacement is expected. Fitting the current structure into this pattern we would expect either a bridging angle of 113° or a C(8) displacement of ~0.88 Å. The effect of the sp^2 hybridization at C(2) is apparently sufficient to counterbalance the perturbation introduced by the addition of the C(6)–C(7) bridge to the basic six-membered ring. The excessive displacements observed in the natural product structures may well be the result of substantial substitution on the ring, rather than a reflection of the true geometry of the bicyclo[3.2.1]octane system. Similarly, an attempt was made to describe the five-membered subunit, C(1), C(5), C(6), C(7), C(8), in terms of a least-squares plane through C(1), C(5), C(6), C(7). These atoms, however, evinced significant deviations from coplanarity. The average interior angle of 103.8° is comparable to the 103° reported for

Table IV. Bridging Angles and Bridging Atom Displacements

Compd	Angle, deg	Displacement, Å
Acetyl(bromoacetyl)dihydro(enmein)[18]	99	0.90
Methyl bromogibberellate[21]	101	0.88
16α-Methyl 15β-bromoacetate enmein[17]	102	0.87
Methyl gibberellate di-*p*-bromobenzoate[22]	102	0.86
Trichlorodermol *p*-bromobenzoate[20]	103	0.82
Verrucarin A *p*-iodobenzenesulfonate[19]	105	0.79

(16) R. M. Weier, Ph.D. Dissertation, Wayne State University, 1967, p 43.
(17) P. Coggon and G. A. Sim, *J. Chem. Soc. B*, 413 (1969).
(18) M. Natsume and Y. Iitaka, *Acta Crystallogr.*, 20, 197 (1966).
(19) A. T. McPhail and G. A. Sim, *J. Chem. Soc. C*, 1394 (1966).
(20) S. Abrahamsson and B. Nilsson, *Acta Chem. Scand.*, 20, 1044 (1966).
(21) F. McCapra, A. T. McPhail, A. I. Scott, G. A. Sim, and D. W. Young, *J. Chem. Soc. C*, 1577 (1966).
(22) J. A. Hartsuck and W. N. Lipscomb, *J. Amer. Chem. Soc.*, 85, 3414 (1963).

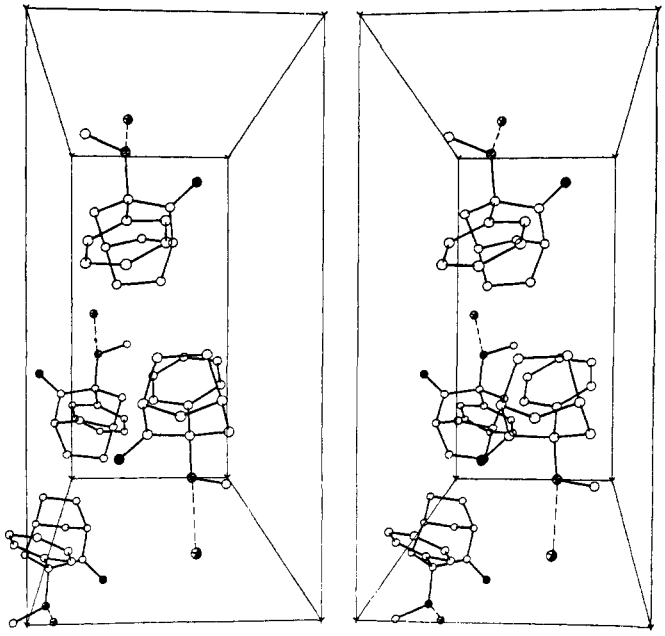


Figure 2. A stereoscopic packing diagram viewed down the c axis with $a \rightarrow$ and $b \uparrow$. The chloride ions are represented as half-shaded circles, oxygens are fully shaded, and nitrogens are striped. The N–H···Cl hydrogen bonds are indicated by dashed lines.

ring D of 16α-methyl 15β-bromoacetate enmein.[17] Torsion angles for the five-membered ring are given in Table V. Comparison of this data with that tabulated

Table V. Torsion Angles for Five-Membered Subunit in One Epimer[a]

$\theta_{1,8} = 44.6\ (4)°$	$\theta_{5,6} = 32.3\ (4)°$
$\theta_{5,8} = -47.6\ (4)°$	$\theta_{6,7} = -4.6\ (5)°$
$\theta_{1,7} = -24.4\ (5)°$	

[a] Standard deviations are given in parentheses for least significant figures.

by Brutcher and Leopold[23] for ring D of the steroids suggests a distorted α-envelope conformation. The corresponding rings of the six natural products mentioned here are intermediate between half-chair and envelope forms, but show a tendency toward the former.[17]

A stereoscopic packing diagram is shown in Figure 2. None of the intermolecular contacts are unusual. The shortest interaction is 3.38 Å between the chloride of one asymmetric unit and H(6) of the symmetry related inverted molecule.

Experimental Section[24]

endo-2-Hydroxy-*exo*-2-(α-*N*-methylimino)benzylbicyclo[2.2.1]heptane (1). A mixture of 2.83 g (0.01 mol) of *exo*-2-bromo-*endo*-2-benzoylbicyclo[2.2.1]heptane[8] (5) and 20 ml of anhydrous CH_3NH_2 was stirred at −78° for 1 hr and at room temperature for 2 hr. The excess CH_3NH_2 was evaporated and the residue extracted with ether. The ether was removed and the product recrystallized from hexane to give 1.60 g (72%) of 1, mp 67–67.5°, ir (KBr) 1650 cm^{-1} (C=N).

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.68; H, 8.65; N, 5.95.

A small portion of 1 was converted to the HCl salt, mp 166–167°, $pK_a = 5.44$.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 67.80; H, 7.52; N, 5.44.

A solution of 650 mg (0.0028 mol) of 1 in 10 ml of 1.5 *M* HCl was allowed to stand at room temperature for 6 hr. The cloudy mixture was extracted with ether and dried (Na_2SO_4), and the ether was expelled. The residue was recrystallized from hexane to give 480 mg (90%) of *endo*-2-hydroxy-*exo*-2-benzoylbicyclo[2.2.1]heptane[8] (6), mp 57–58°.

exo-2-Hydroxy-*endo*-2-(α-*N*-methylimino)benzylbicyclo[2.2.1]heptane (2). A mixture of 510 mg (0.0024 mol) of hydroxy ketone 8, 4.0 g of K_2CO_3, and 15 ml of anhydrous CH_3NH_2 was heated in a sealed tube at 110° for 3 days. The product was extracted with ether, the solvents were removed, and the residue was recrystallized from hexane to give 402 mg (74%) of 2, mp 116–117°, ir (KBr) 1648 cm^{-1} (C=N). Another crystalline form of 2, mp 71–72°, was also isolated occasionally from the same reaction, but the two samples were shown to be identical by mixture melting point (116–117°) and superimposable ir spectra.

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.32; H, 8.28; N, 6.19.

A small portion of 2 was converted to the HCl salt, mp 208–210°.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.68; H, 7.57; N, 5.27; Cl, 13.34. Found: C, 67.53; H, 7.82; N, 5.22; Cl, 13.40.

Hydrolysis of 100 mg (0.00043 mol) of 2 with 5 ml of 1.5 *M* HCl at room temperature for 5 hr gave 70 mg (75%) of hydroxy ketone[8] 8, mp 71–72°.

exo-2-Benzoyl-*endo*-2-*N*-methylaminobicyclo[2.2.1]heptane (3). A suspension of $LiNHCH_3$ in ether was prepared by adding 10 ml of a 1.6 *M* solution of BuLi in hexane to an excess of CH_3NH_2 in ether followed by evaporation of the solvents and stirring with 50 ml of fresh ether. A solution of 3.68 g (0.013 mol) of bromo ketone 5 in 25 ml of ether was added and the mixture was stirred at 25° for 8 hr. The mixture was extracted with 30 ml of 3 *M* HCl, and the aqueous layer was neutralized with $NaHCO_3$. The basic materials were reextracted with ether, dried (K_2CO_3), and evaporated to dryness. The residue (320 mg) was separated by preparative tlc (ether–hexane–benzene–methanol = 10:10:10:1 system) to yield 71 mg of pure amino ketone 3: ir (CCl_4) 1670 (C=O), 3300 cm^{-1} (NH). It was converted to the HCl salt, mp 231–233° dec.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27; Cl, 13.34. Found: C, 67.88; H, 7.73; N, 5.07; Cl, 13.46.

The neutrals from this reaction showed the presence of unreacted bromo ketone 5, hydroxy ketone 6, and 2-benzoylbicyclo[2.2.1]-heptane by tlc. The low yield of the amino ketone 3 may be explained by the formation of the neutral side products.

A portion of the HCl salt of 3 (46 mg) was reduced with $NaBH_4$ in MeOH. The resulting amino alcohol (34 mg) was dissolved in 3 ml of MeOH and cleaved with 90 mg of $NaIO_4$ in 5 ml of water at 25° for 4 hr. The mixture was steam distilled into a solution of 2,4-dinitrophenylhydrazine. The 2,4-dinitrophenylhydrazones were separated by preparative tlc to give 34 mg (78%) of norcamphor 2,4-dinitrophenylhydrazone, mp 127–129°, and 21 mg (53%) of benzaldehyde 2,4-dinitrophenylhydrazone, mp 237–239°.

endo-2-Benzoyl-*exo*-2-*N*-methylaminobicyclo[2.2.1]heptane (4). A mixture of 2.998 g (13 mmol) of 3′-methoxy-3′-phenylspiro-[norbornane-*endo*-1′-*O*-2,2′-oxirane][8] (7) and 6 ml of CH_3NH_2 was heated in a sealed tube at 140° for 72 hr. The CH_3NH_2 was evaporated and the residue was dissolved in ether and extracted with 3 *N* HCl. The aqueous layer was basified with NaOH, reextracted with ether, and dried (K_2CO_3), and the solvent was removed. The residue was recrystallized from hexane to give 2.24 g (75%) of 4, mp 53–54°; ir (CCl_4) 1680 cm^{-1} (C=O).

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.27; H, 8.35; N, 6.32.

A small portion was converted to the HCl salt, mp 260–262° dec, $pK_a = 6.30$.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 68.05; H, 7.84; N, 5.43.

Reduction of 218 mg (0.92 mmol) of 4 with $NaBH_4$ followed by cleavage with $NaIO_4$ as described under 3 gave 60% of norcamphor

(23) F. V. Brutcher, Jr., and E. J. Leopold, *J. Amer. Chem. Soc.*, 88, 3156 (1966).

(24) All melting points were taken on a Thomas–Hoover melting point apparatus and are uncorrected. Thin layer chromatography was performed using Silica Gel H from Brinkman Instruments on 5 × 20 cm plates. Gas chromatographic analyses were performed on a F & M Model 810 instrument with a flame ionization detector using a 4-ft 3% ethylene glycol succinate column. Infrared spectra were recorded with a Perkin-Elmer 237B grating spectrophotometer. Nuclear magnetic resonance spectra were obtained using a Varian A-60 spectrometer. The pK_a's were determined in 50% aqueous methanol. Elemental analyses were provided by Midwest Microlab, Inc., Indianapolis, Ind.

and 67% of benzaldehyde, both isolated as their 2,4-dinitrophenylhydrazones.

exo-**2-*N*-Methylamino-*endo*-2-phenyl-3-bicyclo[3.2.1]octanone (10).** A solution of 310 mg (1.35 mmol) of **1** in 10 ml of freshly distilled *o*-dichlorobenzene was heated at 185° in a metal bath under a N_2 atmosphere. The reaction was followed by gc (4-ft 3% ethylene glycol succinate column), and after 3 hr all the starting material had disappeared. The reaction mixture contained two compounds in a ratio 96:4 as shown by gc. Most of the solvent was removed under vacuum; the residue was dissolved in ether and extracted with 3 *M* HCl. The aqueous layer was neutralized with $NaHCO_3$, reextracted with ether, dried (K_2CO_3), and evaporated to dryness. The residue was converted to the HCl salt and recrystallized from methanol–ether to give 263 mg (75%) of **10** as its hydrochloride, mp 262–264° dec, ir (KBr) 1708 cm^{-1} (C=O), pK_a = 7.68.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 67.99; H, 7.70; N, 5.27.

The minor product was not characterized but its gc retention time was different from all other amino ketones and hydroxyimines discussed in this article.

endo-**2-*N*-Methylamino-*exo*-2-phenyl-*exo*-3-hydroxybicyclo[3.2.1]-octane (11) and *endo*-2-*N*-Methylamino-*exo*-2-phenyl-*endo*-3-hydroxybicyclo[3.2.1]octane (12).** A solution of 3.64 g (16 mmol) of **10** in 16 ml of MeOH was reduced by adding 2.0 g of $NaBH_4$ in small portions while the mixture was stirred magnetically. After the reaction was complete as shown by tlc, most of the MeOH was removed *in vacuo* and the remainder was diluted with water. The product was extracted with ether and dried (K_2CO_3), and the solvent was evaporated to dryness. The residue (3.6 g) was fractionally crystallized from hexane to give 440 mg (12%) of the cis amino alcohol, **12**, mp 91–93°, nmr ($CDCl_3$) 262 Hz (broad s, 1, C-3 H).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.61; H, 9.17; N, 5.78.

Fractional crystallization of the mother liquor provided 1.174 g (32.3%) of pure trans amino alcohol **11**, mp 160–161°, nmr ($CDCl_3$), 248 Hz [t, J = 9 Hz, 1, C-3 H].

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.60; H, 9.13; N, 5.88.

Conversion of Trans Amino Alcohol 11 to Cis Amino Alcohol 12. A solution of 404 mg (1.75 mmol) of **11** in 10 ml of triethylamine and 2 ml of pyridine was acetylated with 5 ml of acetic anhydride at 0° for 4 hr. The product after the usual work-up was recrystallized from hexane to yield 300 mg (63%) of the *N*-acetyl derivative of **11**, mp 102–103°.

Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.47; N, 5.12. Found: C, 74.83; H, 8.30; N, 5.16.

A mixture of 189 mg (0.7 mmol) of the *N*-acetate and 5 ml of thionyl chloride was heated at 50° for 14 hr and then stirred at room temperature for 15 hr. The solution was poured into ice, basified with NaOH, and extracted with ether, and the ether was removed. The residue (188 mg) was hydrolyzed with 6 *M* HCl on a steam bath for 12 hr. The solution was cooled, basified with NaOH, extracted with ether, and dried (K_2CO_3) and the solvent removed to give 48 mg of the product which on recrystallization from hexane yielded 24 mg of **12**, mp 91–92°, identical in all respects with an authentic sample.

2-(3-Benzoylcyclopentyl)acetaldehyde (14). A solution of 244 mg (1.06 mmol) of **11** in 20 ml of MeOH was treated with 850 mg of $NaIO_4$ in 80 ml of water at room temperature for 14 hr. Most of the MeOH was removed *in vacuo* and the solution was extracted with ether. The ether solution was extracted with 1.5 *M* HCl to remove any unreacted **11**, washed with water, dried (K_2CO_3), and evaporated to give 198 mg (86%) of **14** as a liquid: ir (neat) 1675 and 1725 (C=O), 2725 cm^{-1} (aldehyde); nmr ($CDCl_3$) δ 9.6 (t, J = 1.3 Hz, 1, aldehyde H). Aldehyde **14** was further characterized as follows. It was oxidized with basic Ag_2O to 2-(3-benzoylcyclopentyl)acetic acid as a liquid which on treatment with an alcoholic solution of 2,4-dinitrophenylhydrazine in the presence of HCl gave crystalline **14a**, mp 83–85°.

Anal. Calcd for $C_{22}H_{24}N_4O_6$: C, 59.99; H, 5.49; N, 12.73. Found: C, 59.74; H, 5.63; N, 12.58.

Keto aldehyde **14** was also obtained in 90% overall yield from hydroxy ketone[8] **13** by reduction with $NaBH_4$ followed by cleavage with $NaIO_4$. The two samples of **14** had identical ir and nmr spectra and a mixture melting point of the crystalline derivatives **14a** was not depressed.

endo-**3-Phenyl-*exo*-3-*N*-methylamino-2-bicyclo[3.2.1]octanone (15).** A solution of 307 mg (1.35 mmol) of **2** in 10 ml of freshly distilled *o*-dichlorobenzene was heated at 185° in a metal bath under a N_2 atmosphere. The reaction was followed by gc and was found to be complete after 14 hr yielding a single product, **15**. The solvent was removed *in vacuo* and the residue was dissolved in ether and treated with HCl in 2-propanol to yield 295 mg (86%) of **15** as its HCl salt, mp 272–273° dec, ir (KBr) 1708 cm^{-1} (C=O), pK_a = 7.69.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 67.51; H, 7.44; N, 5.28.

endo-**2-Hydroxy-*exo*-3-*N*-methylamino-*endo*-3-phenylbicyclo-[3.2.1]octane (16).** A solution of 1.29 g (5.24 mmol) of **15** in 75 ml of MeOH was treated with 2.0 g of $NaBH_4$ at room temperature for 2 days. The solution was diluted with 30 ml of water and most of the MeOH was removed *in vacuo*. The product was extracted with $CHCl_3$ and dried (K_2CO_3), and the solvent was evaporated to dryness. The residue was recrystallized from MeOH to give 1.074 g (89%) of **16**, mp 182–183; ir (KBr) 3300 cm^{-1} (NH, OH); nmr ($CDCl_3$) 242 Hz (broad d, J = 2.5 Hz, 1, C-2 H).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.85; H, 8.93; N, 6.09.

exo-**2-Hydroxy-*exo*-3-*N*-methylamino-*endo*-3-phenylbicyclo-[3.2.1]octane (19).** A solution of 414 mg (1.8 mmol) of **16** in 15 ml of triethylamine and 15 ml of pyridine was acylated with 2.5 ml of acetic anhydride at 0° for 4 hr. The crude neutral product (387 mg) was recrystallized from hexane to give 150 mg (31%) of the *N*-acetate of **16**: mp 133–134°; ir (KBr) 1625 (amide), 3275 cm^{-1} (OH).

Anal. Calcd for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.47; N, 5.12. Found: C, 74.64; H, 8.27; N, 5.05.

The cis amino alcohol **19** was obtained from the *N*-acetate of **16** essentially by the same method used for the conversion of **11** to **12**. Compound **19** had mp 138–139°, ir (KBr) 3300 cm^{-1} (OH, NH), nmr ($CDCl_3$) 268 Hz (broad d, J = 3 Hz, 1, C-2 H).

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.87; H, 9.44; N, 6.35.

3-Benzoylmethylcyclopentanecarboxaldehyde (18). A solution of 171 mg (0.70 mmol) of **16** in 20 ml of MeOH was treated with 350 mg of $NaIO_4$ in 20 ml of water at 24° for 3 days. After most of the MeOH was removed *in vacuo*, the solution was extracted with ether, and the ether solution was washed with 1.5 *M* HCl followed by water, dried (K_2CO_3), and evaporated to dryness to give 101 mg (67%) of **18** as a liquid: ir (neat) 1675, 1715 (C=O), 2725 cm^{-1} (aldehyde); nmr ($CDCl_3$) δ 9.6 (d, J = 2 Hz, 1, aldehyde H). A portion of this material was converted to its mono-2,4-dinitrophenylhydrazone, mp 128–132°.

Anal. Calcd for $C_{20}H_{20}N_4O_5$: C, 60.60; H, 5.08; N, 14.13. Found: C, 60.31; H, 5.29; N, 14.35.

Keto aldehyde **18** was also obtained in 70% overall yield from hydroxy ketone[8] **17** by reduction with $NaBH_4$ followed by cleavage with $NaIO_4$. The two samples of **18** had identical ir and nmr spectra, and a mixture melting point determination of the 2,4-dinitrophenylhydrazones confirmed their identity.

exo-**2-Phenyl-*endo*-2-hydroxy-3-*N*-methylimino[3.2.1]octane (20).**

(a) From Hydroxy Ketone 13. A mixture of 2.137 g (9.9 mmol) of **13**[8] and 10 ml of CH_3NH_2 was heated in a sealed tube at 130° for 56 hr. The CH_3NH_2 was evaporated off and the residue was recrystallized from hexane to give 1.98 g (87%) of **20**, mp 67–68°, ir (KBr) 1646 (C=N), nmr (CCl_4) δ 3.3 (s, 3, $=NCH_3$).

Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.38; H, 8.29; N, 6.33.

A small portion of **20** was converted to the HCl salt, mp 218–219°, ir (KBr) 1690 cm^{-1} (C=N), pK_a = 7.18.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 67.97; H, 7.85; N, 5.43.

(b) By the Rearrangement of 3. A solution of 36 mg (0.158 mmol) of **3** in 1 ml of *o*-dichlorobenzene was heated at 152° for 21 hr under a N_2 atmosphere. An examination by gc indicated that the mixture contained 98% of **20** and 2% of **3**. The solvent was removed *in vacuo* and the residue was dissolved in ether and treated with HCl in 2-propanol to give 24 mg (57%) of **20** as the HCl salt, mp 216–218°, identical in all respects with a sample previously prepared.

Reduction of 723 mg (3.16 mmol) of **20** with $NaBH_4$ in MeOH gave 715 mg (98%) of a liquid amino alcohol: HCl salt, mp 261–262°. *Anal.* Calcd for $C_{15}H_{22}ClNO$: C, 67.53; H, 8.28; N, 5.23. Found: C, 67.23; H, 8.31; N, 5.33. A solution of 171 mg (0.79 mmol) of this amino alcohol in 20 ml of MeOH was cleaved with 350 mg of $NaIO_4$ in 20 ml of water at 24° for 3 days to give 101 mg (60%) of **14**, identical in all respects with an authentic sample including the crystalline derivative **14a**.

Thermal Rearrangement of 20. A solution of 57 mg (0.25 mmol) of **20** in 1 ml of *o*-dichlorobenzene was heated at 185° under a

N_2 atmosphere. The rearrangement was followed by gc. In 12 hr 1–2% of **3** was formed. As heating the mixture for 3 more days did not increase the amount of **3**, the reaction was stopped and 35 mg (53%) of **20** was recovered as the HCl salt.

Attempted rearrangements of the HCl salt of **20** in *o*-dichlorobenzene both at 180 and at 225° were also unsuccessful.

Reaction of Methylamine with Epoxy Ether 9. A solution of 300 mg (1.3 mmol) of 3′-methoxy-3′-phenylspiro[norbornane-*exo*-1′-*O*-2,2′-oxirane][10] (**9**) in 3 ml of MeOH and 2 ml of CH_3NH_2 was heated in a sealed tube at 100° for 2 days. An ir spectrum of the crude product obtained after evaporation of the solvents was identical with that of **9**. Also 285 mg (95%) of **9**, mp 86–88°, was reisolated by recrystallization of this material from hexane.

A mixture of 230 mg (100 mmol) of **9** and 5 ml of CH_3NH_2 was heated in a sealed tube at 150° for 6 days. Separation of the product with 3 *M* HCl gave 144 mg of a basic mixture which by preparative tlc gave 69 mg (30%) of pure hydroxyimine **20**, mp 65–66°. A spot corresponding to amino ketone **3** was also detected in the reaction mixture by tlc.

Attempted Rearrangement of Amino Ketone 4. A solution of 105 mg (0.46 mmol) of **4** in 2 ml of *o*-dichlorobenzene was heated at 185° for 4 days. Analysis of the mixture by gc and tlc indicated no change except slight decomposition. Dilution with ether followed by addition of HCl in 2-propanol gave 83 mg (68%) of the HCl salt of **4**, mp 260–262° dec, identical with an authentic sample.

Thermal Rearrangement of Hydroxyimine 21. A solution of 101 mg (0.44 mmol) of *exo*-3-hydroxy-*endo*-3-phenyl-2-*N*-methyliminobicyclo[3.2.1]hexane[8] (**21**) in 2 ml of *o*-dichlorobenzene was heated at 185° under a N_2 atmosphere. The reaction was followed by tlc. After 1.5 hr a spot corresponding to **4** appeared. In about 4 hr, **4** became the major product, and after 67 hr only a trace of **21** remained in the mixture. Isolation of the product gave 84 mg (72%) of **4** as its HCl salt, mp 259–261° dec, identical with an authentic sample. Rearrangement of the HCl salt of **21** also provided the same results.

X-Ray Experimental. A single crystal of the hydrochloride salt of 3-*N*-methylamino-3-phenyl-2-bicyclo[3.2.1]octanone (**15**) was examined with Cu Kα radiation in both Weissenberg and precession geometries. Final intensity data were collected on a Picker card-controlled diffractometer utilizing Mo Kα radiation (λ 0.71069 Å) filtered with 0.05-mm Zr foil.[25] A θ–2θ, moving crystal–moving counter scan technique with a takeoff angle of 1.7° was employed. Asymmetric scans from 2θ (Kα_1) − 0.50° to 2θ (Kα_2) + 0.75° were made at a rate of 1.00°/min with stationary background counts of 10-sec duration at both ends of the scan. Data were collected in the $\pm hkl$ quadrant to a 2θ of 43°. Four standard reflections, inserted after every 100 reflections, showed no significant intensity variations in the course of the data collection. The raw data were corrected for background, Lorentz, and polarization effects. Of the 1706 independent data, 1359 were found to have net intensities greater than 2.5 standard deviations and were used in the structure determination. The $\sigma(I)$'s were calculated from the formula

$$\sigma(I) = \left[\left(\frac{I\sigma(S)}{S}\right)^2 + \left(\frac{I\sigma(A)}{A}\right)^2 + S^2A^2(P + \sigma^2(B)) + (0.03I)^2\right]^{1/2}$$

where I is the net intensity, P the gross intensity, S the scale factor, $\sigma(S)$ its standard deviation, A the appropriate attenuator factor, $\sigma(A)$ its standard deviation, and $\sigma^2(B)$ defined as

$$\sigma^2(B) = 9(B1 + B2)[(\Delta 2\theta)^2 + (1.25 + 10^{-5})(B1 + B2)]$$

with $B1$ and $B2$ the stationary background counts. No absorption corrections were made.

The observed structure factor amplitudes (F^2's) were converted to normalized structure factors (E's) by removing the angular dependence of the reflections. The E's were subsequently used in Long's program for phase determination based on the Σ_2 relationship.[26] A total of 256 E's with magnitudes greater than 1.3 were used. An E map derived from the most self-consistent set of phases contained all 18 nonhydrogen atoms in the asymmetric unit as the highest peaks. Full-matrix least-squares refinement[27] with anisotropic thermal parameters yielded a residual index, $R = \Sigma_i|\Delta F_i|/\Sigma_i|F_i^o|$ of 0.090 and a weighted residual index, $wR = [\Sigma_i w_i(\Delta F_i)^2/\Sigma_i w_i(F_i^o)^2]^{1/2}$, of 0.124, where $w_i = 1/\sigma^2(F_i)$. A Fourier difference map indicated positions for all 20 hydrogen atoms. Further refinement of the nonhydrogen parameters converged to an R = 0.054 (wR = 0.075) with an error of fit of 3.297.[28] A final difference map contained three negative peaks, all ≈0.35 e/Å^3, in the vicinity of the chloride ion.

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(25) Local versions of the following programs were used in the course of this investigation: PICK-2, J. Ibers, "A Diffractometer Setting and Cell Constant Parameter Refinement Program for the Picker-4-Circle Automatic Diffractometer," Northwestern University (based on W. C. Hamilton's MODE 1); DACOR, D. L. Smith, "A Crystallographic Data Reduction Program," Eastman Kodak; FORDAP, A. Zalkin, "A Crystallographic Fourier and Data Reduction Program," Lawrence Radiation Laboratory; ORFLS, W. R. Busing, K. O. Martin, and H. A. Levy, "A Fortran Crystallographic Function and Error Program," ORNL-TM-306, 1964; ORTEP, C. K. Johnson, "A Fortran Thermal Ellipsoid Plot Program for Crystal Structure Illustrations," ORNL-3794, 1965; PLANES, D. L. Smith's program for fitting a group of atoms with a least-squares plane.

(26) R. E. Long, "A Program for Reiterative Application of Sayre's Equation," Ph.D. Dissertation (Part III), University of California, Los Angeles, 1965.

(27) Atomic scattering factors were taken from "International Tables for X-Ray Crystallography," Vol. III, Kynoch Press, Birmingham, England, 1968, p 201.

(28) A table of observed and calculated structure factors will appear following these pages in the microfilm edition of this volume of the journal. Single copies may be obtained from the Business Operations Office, Books and Journals Division, American Chemical Society, 1155 Sixteenth St., N.W., Washington, D. C. 20036, by referring to code number JACS-73-1978. Remit check or money order for $3.00 for photocopy or $2.00 for microfiche.