Anal. Calcd for $C_{12}H_{18}O$: C, 80.84; H, 10.18. Found: C, 80.64; H, 10.11. (c) A fraction at 33 min had carbonyl absorption at 5.91 μ (cis 6–4 fusion) and a methyl singlet at δ 1.31. It was the minor compound, and was identical with the product of equilibrium of **11**. It is assigned the cis–syn–cis structure **12**. *Anal.* Calcd for $C_{12}H_{18}O$: C, 80.84; H, 10.18. Found: C, 80.97; H, 10.20.

Equilibration of 11.—The photoadduct **11** (30 mg) was dissolved in 30 ml of ether, basic alumina was (2.0 g) added, and the solution was stirred for 3.5 hr. After filtration and evaporation of the ether, the infrared showed a band at 5.91 μ and the nmr had a methyl singlet at δ 1.30, characteristic of isomer **12** (see below). Analysis on a 10 ft × 0.125 in. 12% QF-1 at 194° showed the disappearance of a peak of retention time 10.5 min and the appearance of a peak at 8.3 min corresponding to **12**.

Photolyses with 2-Phenyl-2-cyclohexenone.—Irradiation of 2-phenyl-2-cyclohexenone (1.779 g, 0.0103 mol) and cyclopentene (16.87 g, 0.248 mol) for 45 hr in *tert*-butyl alcohol (380 ml) and methanol (20 ml) gave less than 5% cross-addition products as indicated by vpc and recovery of starting enone.

Photoaddition of 3-Phenyl-2-cyclohexenone and Cyclopentene.—Irradiation of 3-phenyl-2-cyclohexenone (1.663 g, 0.0097 mol) and cyclopentene (11.06 g, 0.163 mol) in *tert*-butyl alcohol (375 ml) and methanol (20 ml) for 7 hr resulted in reaction of 97% of 3-phenyl-2-cyclohexenone, determined by vpc analysis on 3 ft × 0.125 in. of 10% FFAP at 245°. The vpc analysis showed that two products were formed having retention times of 7.4 (**13**) and 12.3 min (**14**), in the ratio 90:7 as measured from vpc peak areas. After removing the solvent by distillation, the residue (1.873 g) was chromatographed on a 3 × 28 cm column of silica gel slurry packed in benzene, and 200-ml fractions were collected. Fractions 1–5 were eluted with benzene, 6–10 with 0.5% ethyl acetate–benzene, 11–20 with 1%, 21–25 with 2%, 26 and 27 with 4%, 28 with 8%, and 29–30 with 15% ethyl acetate–benzene. Fractions 14–16 contained the major photoadduct **13** (959 mg). This gave colorless prisms, mp 59.5–61°, from aqueous ethanol. *Anal.* Calcd for $C_{17}H_{20}O$: C, 84.95; H, 8.93 Found: C, 84.99; H, 8.30. The compound had infrared absorption at 5.91 μ and was stable to base, strongly suggesting cis fusion of the cyclohexanone ring. It is assigned the cis–syn–cis structure **13**.

Fractions 29–30 contained the photodimer of 3-phenyl-2-cyclohexanone (500 mg), which had mp 199–200° from ether–light petroleum (lit.[15c] mp 204–205°).

Registry No.—**3**, 34404-88-1; **3** thiosemicarbazone, 34404-89-2; **4**, 34404-90-5; **6**, 34404-91-6; **6** *p*-bromophenylurethane, 34404-92-7; **7**, 34404-93-8; **8**, 34404-94-9; **9**, 34404-95-0; **10**, 34404-96-1; **11**, 34404-97-2; **12**, 34404-98-3; **13**, 34404-99-4; cyclopentene, 142-29-0; 4,4-dimethyl-2-cyclohexenone, 1073-13-8; 3-methyl-2-cyclohexenone, 1193-18-6; 2-phenyl-2-cyclohexenone, 4556-09-6; 3-phenyl-2-cyclohexenone, 10345-87-6.

Acknowledgments.—The authors thank Mr. Roderick Miller for assistance with the preparative work and Romulo Faggiani for help with the X-ray analysis. Financial support from the National Research Council of Canada is gratefully acknowledged.

Stereochemistry and Mechanism of Thermal and Base-Catalyzed Rearrangements of α-Hydroxy Ketones

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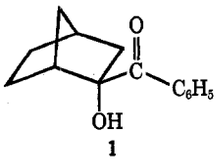
A pair of diastereomeric α-hydroxy ketones, *exo*-2-benzoyl-*endo*-2-hydroxybicyclo[2.2.1]heptane (**1**) and *endo*-2-benzoyl-*exo*-2-hydroxybicyclo[2.2.1]heptane (**2**), were prepared starting from 2-benzoylbicyclo[2.2.1]heptane (**3**). Rearrangement of these hydroxy ketones under pyrolytic conditions yielded products predicted by a cyclic concerted mechanism, **1** giving exclusively *endo*-2-hydroxy-*exo*-2-phenyl-3-bicyclo[3.2.1]octanone (**8**) and **2** yielding an equilibrium mixture of *exo*-3-hydroxy-*endo*-3-phenyl-2-bicyclo[3.2.1]octanone (**9**) and *exo*-2-hydroxy-*endo*-2-phenyl-3-bicyclo[3.2.1]octanone (**10**). On the other hand, treatment of hydroxy ketone **1** with sodium hydroxide in a water–dioxane system yielded **10** while compound **2** rearranged to give **8** under more severe alkaline conditions. The proof of structure for all the rearrangement products is presented and mechanisms are discussed for the transformations.

The rearrangements of 17-hydroxy-20-keto steroids have been studied extensively as a method for D-homoannulation.[2] Outside the steroidal field, the only investigation in this area appears to be that of Elphimoff-Felkin and coworkers, who extended this reaction for the preparation of a few cyclic acyloins.[3] The present work was undertaken to investigate the stereochemistry of this rearrangement in simpler systems where diastereomeric hydroxy ketones (**1** and **2**) could be prepared. The norbornane ring system was chosen, as it has the additional advantage of undergoing carbon skeletal rearrangements with great facility.



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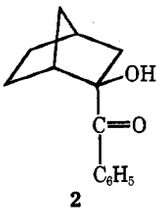


2

Results

Hydroxy ketone **1** was prepared by a series of reactions starting from the known 2-benzoylbicyclo[2.2.1]-heptane[4] (**3**). Treatment of **3** with bromine in CCl_4 at room temperature yielded a single crystalline bromo ketone, *exo*-2-bromo-*endo*-2-benzoylbicyclo[2.2.1]heptane (**4**). That the bromine and benzoyl groups were attached to the same carbon in **4** was indicated by the nmr spectrum, which showed no downfield protons characteristic of hydrogen on a carbon bearing a bromine or a benzoyl group. The exo configuration of

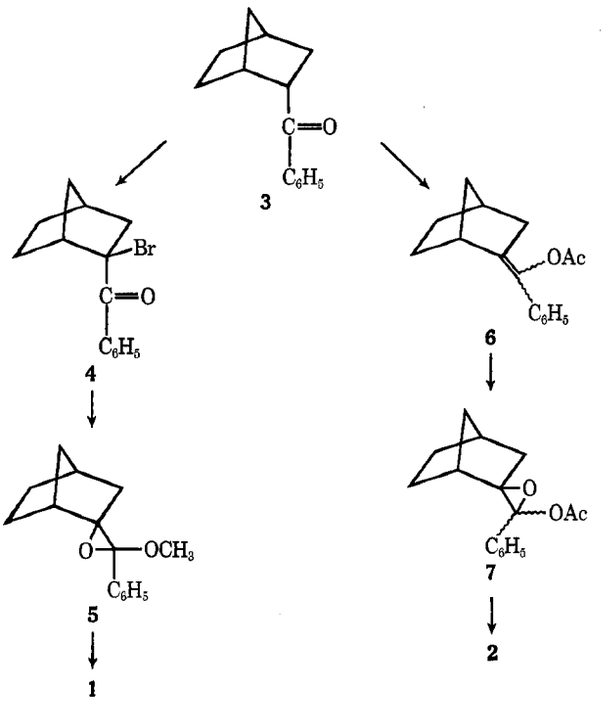
(1) Taken in part from the Ph.D. Dissertation of T. A. Treat, Wayne State University, 1969; Ethyl Corporation Fellow, 1968–1969.

(2) For a review, see N. L. Wendler in "Molecular Rearrangements," Part II, P. de Mayo, Ed., Interscience, New York, N. Y., 1964, p 1114.

(3) I. Elphimoff-Felkin, G. LeNy, and B. Tschoubar, *Bull. Soc. Chim. Fr.*, 522, 581 (1958).

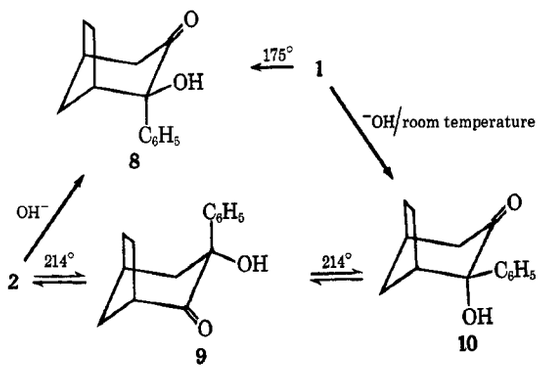
(4) N. K. Kochetkov and A. Y. Khorlin, *Zh. Obshch. Khim.*, **27**, 3182 (1957); *Chem. Abstr.*, **52**, 8984*g* (1958).

bromine was expected on the basis that bromine would attack the enol of **4** from the less hindered side.[5] Bromo ketone **4** was converted to a crystalline epoxy ether, **5**, by the general method involving the use of sodium methoxide on an α-bromo ketone.[6] Hydroxy ketone **1** was prepared by the acid hydrolysis of epoxy ether **5**. As the formation and hydrolysis of epoxy ethers are known to be stereospecific[7] and to yield hydroxy ketones with inversion at the α position, endo configuration for the hydroxyl group in the product was expected. That the hydroxy ketone **1** was indeed 2-hydroxy-2-benzoylnorbornane was shown by its reduction to a mixture of two vicinal diols with sodium borohydride followed by the cleavage of the mixture with sodium periodate to give benzaldehyde and norcamphor, which were isolated and characterized as their 2,4-dinitrophenylhydrazones.



As the epimer of bromo ketone **4** was not available, the synthesis of hydroxy ketone **2** was accomplished by a different route. The most successful approach was through the enol acetate **6**, which was prepared[8] as a diastereomeric mixture by the action of hot acetic anhydride on ketone **3** in the presence of *p*-toluenesulfonic acid as a catalyst. The enol acetate **6** was easily epoxidized on treatment with pure *m*-chloroperbenzoic acid at $-20°$ to give the epoxy acetate **7**. Assignment of the exo configuration for the epoxide ring is based on the known stereospecificity of peracid attack on the double bond from the less hindered side,[9] in this case from the exo side.[5] The epoxy acetate **7** was thermally unstable and was found to rearrange to the corresponding acetoxy ketone under a variety of gas phase chromatographic conditions.[10] Although **7** could be hydrolyzed to **2** under acidic and basic conditions, the best results were obtained when methylamine was used for this reaction. The crystalline hydroxy ketone **2** thus prepared was different from **1**, but had the same gross structure as shown by its reduction with sodium borohydride followed by cleavage with sodium metaperiodate to benzaldehyde and norcamphor, which were isolated and characterized as their 2,4-dinitrophenylhydrazones.

Rearrangements.—Hydroxy ketones **1** and **2** behaved very differently under rearrangement conditions. Compound **1** was converted completely to **8** when pyrolyzed neat at 175° for 2 hr. Rearrangement of **2** involved a more complex equilibrium and it required 14 hr at 214° for **2** to reach its lowest concentration, 7%. At this point, the major component in the reaction mixture was **9** (65%) and the remainder (28%) was another hydroxy ketone, **10**. However, on prolonged heating, **10**, which is perhaps the thermodynamic product, began to increase and was the major product (60%) after about 50 hr. The fact that **10** was produced more rapidly when pure **9** was rearranged under the same conditions and that the reaction mixture eventually reached the same equilibrium concentrations indicates that most, if not all, of **10** was formed from **9** by phenyl migration. However, a part of **10** being formed from **2** by C-1 migration cannot completely be ruled out.



Hydroxy ketones **1** and **2** were also rearranged under basic conditions. Thus **1** was converted to **10** in over 90% yield when rearranged in the presence of sodium hydroxide in a water–dioxane solution at room temperature for 24 hr. A small amount of hydroxy ketone **8** was also formed in this reaction. Compound **2** rearranged extremely slowly under the same conditions and, when **2** was treated with sodium hydroxide in a water–dioxane solution at 62° for 6 days, only 10% of **8** was formed. Periodic examination of the reaction mixture by gas chromatography showed that no detectable amount of hydroxy ketone **10** was generated in this reaction. The absence of the formation of **10** indicated that it is not an intermediate in the base-catalyzed conversion of **2** to **8**. Further, the formation of hydroxy ketone **1** can also be ruled out in this reaction because, if **1** were formed, it would have been converted to **10** under the same conditions. Rearrangement of **2** to **8** in 75% yield was accomplished by heating a water–dioxane solution of **2** under reflux for 8 hr in the presence of sodium hydroxide. The mother liquor from this reac-

(5) Electrophiles are known to attack similar olefins from the exo (less hindered) side. *Cf.* H. Kwart and T. Takeshita, *J. Org. Chem.*, **28**, 670 (1963); H. C. Brown and W. J. Hammer, *J. Amer. Chem. Soc.*, **89**, 1524 (1967).

(6) See, for example, C. L. Stevens and E. Farkas, *J. Amer. Chem. Soc.*, **74**, 618 (1952).

(7) H. Patel and G. Hite, *J. Org. Chem.*, **30**, 4337 (1965).

(8) H. O. House and H. W. Thomson, *ibid.*, **26**, 3729 (1961).

(9) H. O. House, "Modern Synthetic Reactions," W. A. Benjamin, New York, N. Y., 1965, p 114.

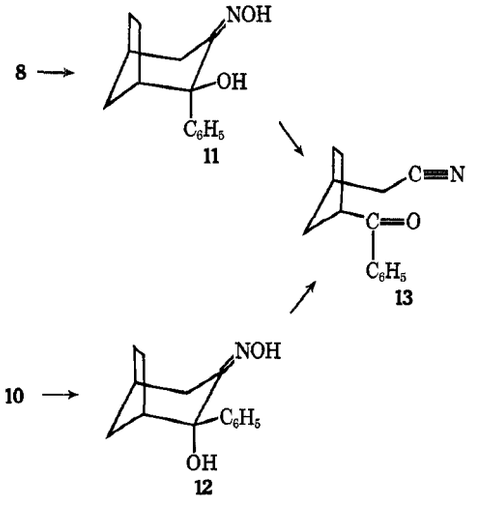
(10) Epoxy acetates, in general, rearrange to acetoxy ketones easily. See, for example, ref 9, p 121.

tion did not show the presence of **10** but contained only **2** and **8** in the ratio 2:3 as indicated by gas chromatography.

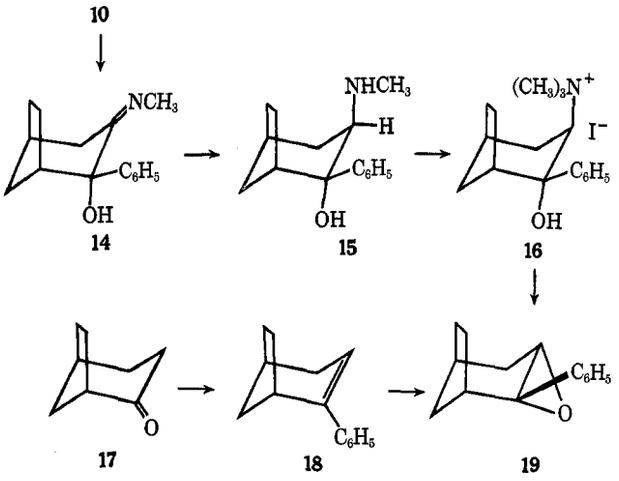
Slow conversion of **10** to **8** was also observed under basic conditions. Thus treatment of **10** with sodium hydroxide in a water–dioxane solution at 62° for 6 days produced a mixture containing 8% of **8** and 92% of **10** as shown by gas chromatography. Although an infrared spectrum of the reaction mixture did not reveal the presence of **1** (as a carbonyl conjugated to a phenyl group), the formation of **1** in small quantities as an intermediate in this transformation cannot be ruled out. Hydroxy ketone **8**, which is apparently the thermodynamic product in base-catalyzed rearrangements, was also the major product when **1** was treated with sodium hydroxide in boiling ethanol. It may be noted here that no evidence was obtained for the interconversion of hydroxy ketones **1** and **2** under any rearrangement conditions. Also treatment of **8** with sodium hydroxide in a water–dioxane solution at 62° for 6 days did not produce any other hydroxy ketone, **1**, **2**, **9**, or **10**.

The structures of hydroxy ketones **8**, **9**, and **10** were established by a combination of degradative, synthetic, and spectral data. Compounds **8** and **10** were shown to be α-hydroxy 3 ketones by their incorporation of three deuterium atoms on treatment with deuterium oxide in the presence of sodium deuteroxide. Only 3-keto compounds in this series are enolizable and therefore capable of deuterium exchange at the α carbon. This uptake of deuterium was easily observed by a comparison of the nmr spectra of the compounds before and after deuterations.

Hydroxy ketones **8** and **10** were shown to differ only in their configuration at C-2 by conversion to a common keto nitrile, **13**. Each hydroxy ketone was converted to its oxime (**11** and **12**), which underwent a second-order Beckmann rearrangement when treated with *p*-toluenesulfonyl chloride and base.[11] The resulting keto nitriles **13** were identical in all respects, including their crystalline semicarbazones.



The exo configuration of the C-2 hydroxyl of **10** was established by its conversion to epoxide **19**. Hydroxy ketone **10**, when heated with methylamine, gave hydroxy imine **14**, which was reduced with sodium borohydride to yield a crystalline amino alcohol,[12] **15**. Compound **15** was methylated under Clark–Eshweiler reaction conditions[13] and converted to the quaternary ammonium iodide **16**. Treatment of **16** with freshly prepared wet silver oxide in methanol at 25° yielded the



crystalline epoxide **19**. The structure of **19** was established by synthesizing it from 2-bicyclo[3.2.1]octanone[14] (**17**) by an unequivocal route. Ketone **17** was converted to olefin **18** by addition of phenyllithium followed by dehydration of the resultant alcohol. Epoxidation of **18** with *m*-chloroperbenzoic acid yielded **19** in 80% yield. The exo epoxide is expected in this reaction, as the peracid is known to attack similar olefins from the less hindered side.[9,15]

As the structure of **10** has now been assigned as *exo*-2-hydroxy-*endo*-2-phenyl-2-bicyclo[3.2.1]octanone, the structure of **8** must be *endo*-2-hydroxy-*exo*-2-phenyl-3-bicyclo[3.2.1]octanone, because it was established earlier that the two compounds are C-2 epimers. Further evidence to this effect was obtained by a comparison of their infrared spectra. Hydroxy ketone **10** exhibited both a sharp (free OH) absorption at 3583 cm^{-1} and a broad (H-bonded OH) absorption at 3455 cm^{-1}, the relative intensity of the latter decreasing on dilution with carbon tetrachloride. This was indicative that the H bonding in **10** was intermolecular.[16] On the other hand, **8** exhibited only a broad OH absorption (intramolecular H bonding) that remained unchanged on dilution with carbon tetrachloride. This is in agreement with the fact that the hydroxyl group in **10** is held far away from the carbonyl preventing intramolecular H bonding, whereas the two groups in **8** are thrust close together, a perfect setting for a strong intramolecular H bonding.

In order to establish the structure of hydroxy ketone **9**, it was converted to the Schiff base **20** by treating it with methylamine. The hydroxy imine **20** was reduced with sodium borohydride to a crystalline amino alcohol,[12] **21**. Conversion of **21** to the quaternary am-

(11) For abnormal Beckman rearrangements of this type, see R. K. Hill, *J. Org. Chem.*, **27**, 29 (1962).

(12) Trans configuration is expected for this amino alcohol on the basis of previous findings in cyclohexane ring systems. See C. L. Stevens, H. T. Hanson, and K. G. Taylor, *J. Amer. Chem. Soc.*, **88**, 2769 (1966).

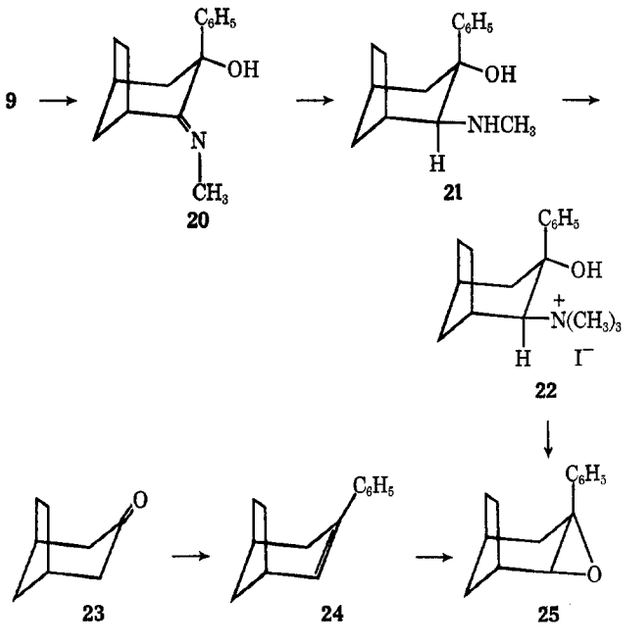
(13) R. N. Icke and B. B. Wisegarver, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 723.

(14) Available from Aldrich Chemical Co., Milwaukee, Wis.

(15) R. R. Saners, H. M. Howard, and H. Feilich [*Tetrahedron*, **21**, 983 (1965)] obtained 95% of exo epoxide by the reaction of peracetic acid on 2-bicyclo[3.2.1]octene.

(16) J. R. Dyer, "Applications of Absorption Spectroscopy of Organic Compounds," Prentice-Hall, Englewood Cliffs, N. J., 1965, p 40.

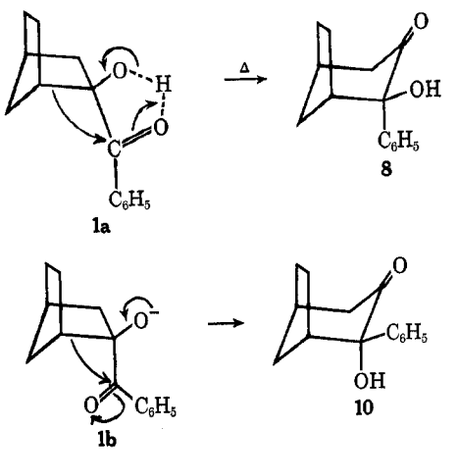
monium iodide **22** followed by treatment with silver oxide yielded a quaternary ammonium hydroxide which on heating under vacuum gave a crystalline epoxide, **25**. This epoxide was also prepared by a different route as follows. Treatment of 3-bicyclo[3.2.1]octanone[17]



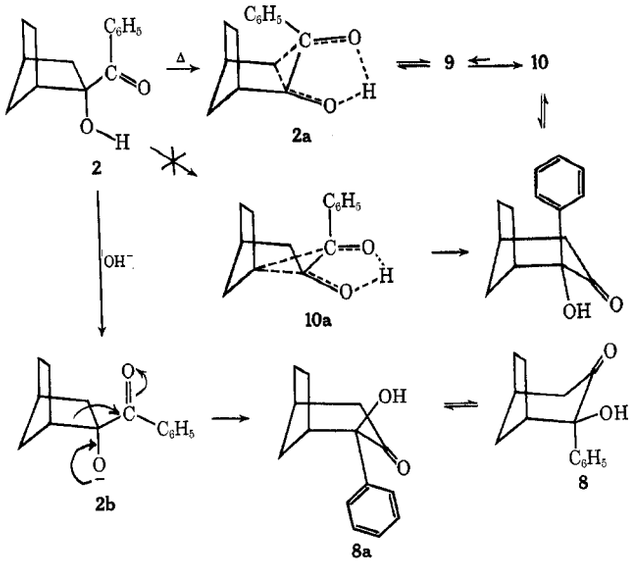
(**23**) with phenyllithium followed by dehydration gave olefin **24**. Reaction of **24** with *m*-chloroperbenzoic acid gave compound **25**. This indicates that the epoxide in **25** and hence the hydroxyl group in **9** have exo configuration.[15]

Discussion

The thermal rearrangements of **1** and **2** are stereospecific and yield products predicted by a cyclic concerted mechanism. The configuration of the hydroxyl group is reversed when the rearrangement condition is switched from pyrolysis to base catalysis. Turner has explained similar findings in steroids on the basis of reagent control of carbonyl orientation in the transition state.[18] Thus in the thermal rearrangement, the carbonyl and hydroxyl groups are cisoid (**1a**) due to H bonding and the transfer of hydrogen and alkyl migration take place in a concerted fashion. On the other hand, alkali produces a negative charge on the hydroxyl oxygen and the charge–dipole repulsion causes the hydroxyl and carbonyl to be transoid in the active species **1b**, so that the rearrangement product has an inverted hydroxyl group. Because the carbonyl group is not held rigidly in the trans configuration, a small amount of **8** can be expected and was, in fact, detected in the base-catalyzed rearrangement of **1**.[19] In all the cases, at least part of the driving force for the rearrangement is derived from the strain relief realized in going from the [2.2.1] system to a [3.2.1] system.



In the thermal rearrangement of **1** and in the base-catalyzed rearrangement of both **1** and **2**, it is the 1,2 bond that migrates. In fact, electronic considerations should lead one to predict that the 1,2 bond should migrate in all the cases, since the more substituted carbon should be more effective in stabilizing the charge deficiency created at the carbonyl center. An immediate rationale for the migration of the 3,2 bond in the thermal rearrangement of **2** would be that this rearrangement is conformationally controlled and that the transition state which resembles a bridged chair (**2a**) leads to the product.[20] However, this argument fails to explain the fact that it is the 1,2 bond that migrates in the base-catalyzed rearrangement of **2**. If the answer was indeed conformational control, the migrating group should be C-3 in this rearrangement as well. In other words, the product (**8**) in the base-catalyzed rearrangement of **2** is formed through a bridged cyclohexane boat transition state (**2b**). However, a close examination of the boat conformation (**8a**) of **8** and the transition state (**2b**) leading to it reveals that the nonbonded interaction between the bulky phenyl group and the 2-carbon bridgehead is at a minimum in these structures. In the thermal rearrangement of **2**, this nonbonded interaction would be very high if C-1 was to migrate and the transition state would resemble a bridged cyclohexane boat (**10a**). It is probably to pre-



(17) Prepared according to a briefly outlined procedure in L. F. Fieser and M. Fieser, "Reagents in Organic Synthesis," Wiley, New York, N. Y., 1967, p 758.

(18) R. B. Turner, *J. Amer. Chem. Soc.*, **75**, 3484 (1953).

(19) *Cf.* D. K. Fukushima, S. Dobriner, M. S. Haffler, T. H. Kritchevsky, F. Herling, and G. Roberts, *J. Amer. Chem. Soc.*, **77**, 6585 (1955).

(20) N. L. Wendler, D. Taub, and R. Firestone [*Experientia*, **15**, 237 (1959)] first advanced a similar argument for explaining rearrangements in steroidal acyloins, but later came to the conclusion that conformational argument is less definitive and the rearrangement is more diverse in character. See N. L. Wendler, D. Taub, and R. W. Walker, *Tetrahedron*, **11**, 163 (1960), and also ref 1, p 1121.

vent this energetically unfavorable transition state that the less substituted C-3 migrates to form **9** under very strenuous conditions. The small amount of **10** obtained in this reaction is probably formed from **9** by phenyl migration. In conclusion, then, the more substituted C-1 migrates in all rearrangements where the steric interactions are not prohibitive. In the thermal rearrangement of **2**, the interaction between the phenyl and hydrogens of the 2-carbon bridgehead is so severe that C-3 migrates in preference to C-1.

This view is in agreement with the fact that, as expected for a higher energy process, the thermal rearrangement of **2** requires a higher temperature compared to the thermal rearrangement of **1**.

Experimental Section

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 × 15 cm plates. Gas chromatographic analyses were performed on an F & M Model 810 instrument with a flame ionization detector. Preparative gc was accomplished on an F & M Model 775 preparative gas chromatograph using a 0.75 in. × 8 ft, 4% ethylene glycol succinate column. Infrared spectra were obtained with a Perkin-Elmer 237B grating spectrophotometer. Nuclear magnetic resonance spectra were obtained using a Varian A-60 spectrometer. All pK_a's were obtained in 50% methanol. Elemental analyses were performed by Midwest Microlab, Inc., Indianapolis, Ind.

***exo*-2-Bromo-*endo*-2-benzoylbicyclo[2.2.1]heptane (4).**—A solution of 4.0 g (0.025 mol) of bromine in 10 ml of CCl_4 was added dropwise to a stirred solution of 5.0 g (0.025 mol) of 2-benzoylbicyclo[2.2.1]heptane[4] (**3**). After the addition was complete, the solvent was removed and the residue was crystallized from hexane to yield 6.10 g (90%) of **4**, mp 21–21.5°, ir (neat) 1670 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{15}BrO$: C, 60.23; H, 5.37; Br, 28.66. Found: C, 60.46; H, 5.50; Br, 28.38.

3′-Methoxy-3′-phenylspiro[norbornane-*endo*-1′-*O*-2,2′-oxirane] (5).—Fresh sodium (0.52 g, 0.0226 g-atom) was weighed under toluene and added to 30 ml of dry methanol. After the reaction of the sodium with methanol was complete and the solution had cooled to room temperature, bromo ketone **4** (3.72 g, 0.0133 mol) was added. The homogeneous solution was stirred at room temperature for 2 hr and then heated to reflux for 5 min. The solution was cooled and poured into a separatory funnel containing 150 ml of petroleum ether (bp 30–60°) and 100 g of ice. The separatory funnel was shaken until the ice melted, and the petroleum ether layer was separated and dried with anhydrous K_2CO_3. Removal of the petroleum ether gave a crystalline solid which was recrystallized from hexane to yield 2.7 g (88%) of **5**, mp 45–47°, ir (KBr) 1060 and 1080 cm^{-1}, no C=O or OH. A sample was recrystallized from hexane for analysis, mp 52.5–53.5°.

Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.26; H, 7.83. Found: C, 78.54; H, 7.64.

***exo*-2-Benzoyl-*endo*-2-hydroxybicyclo[2.2.1]heptane (1).**—Epoxy ether **5** (0.698 g, 0.003 mol) was dissolved in a mixture of 20 ml of methanol and 1 ml of water. One drop of concentrated HCl was added and the solution was allowed to stand at room temperature for 12 hr. Most of the methanol was removed and the product was extracted with ether after dilution with water. The ether solution was dried (Na_2SO_4) and evaporated to dryness and the residue was recrystallized from hexane to give 0.490 g (71%) of **1**, mp 59–60°, ir (CCl_4) 1685 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.78; H, 7.34.

The structure of **1** was established as follows. The hydroxy ketone **1** (0.509 g, 0.0024 mol) was dissolved in methanol, and $NaBH_4$ (250 mg) was added in portions over a 6-hr period. The solution was allowed to stir at room temperature for 24 hr. The methanol was removed *in vacuo*, water was added, and the product was extracted with ether. Removal of ether yielded 0.499 g (96%) of a mixture of diols, mp 137–148°. The mixture (122 mg, 0.00065 mol) was cleaved with $NaIO_4$ (140 mg, 0.00065 mol) by refluxing in 10 ml of water for 3 hr. The reaction mixture was then distilled into a solution containing 2 equiv of 2,4-dinitrophenylhydrazine in ethanol. The mixture of 2,4-dinitrophenylhydrazones was filtered and separated by preparative tlc (ether–hexane, 1:1 system) to give 74 mg (68%) of norcamphor 2,4-DNP, mp 127–128°, and 61 mg (58%) of benzaldehyde 2,4-DNP, mp 237–239°. The identities of the DNPs were established by mixture melting point determinations with authentic samples.

2-Benzoylbicyclo[2.2.1]heptane Enol Acetate (6).—A mixture of 10.0 g (0.05 mol) of **3**, 100 ml of acetic anhydride, and 1.0 g *p*-toluenesulfonic acid was heated at 140° for 2 days, during which time 50 ml of a mixture of acetic acid and acetic anhydride was distilled off. Potassium acetate (1.0 g) was added to the cooled reaction mixture and the mixture was poured into 200 ml of water. The product was extracted with hexane and dried (Na_2SO_4) and the solvent was removed. The residue was distilled at 115–121° (0.5 mm) to give 10.9 g of **6**, ir (neat) 1750 cm^{-1} (C=O). Glc of this material showed that it was a mixture of two diastereomeric enol acetates and 9% starting ketone. An analytical sample was obtained by preparative glc.

Anal. Calcd for $C_{16}H_{18}O_2$: C, 78.90; H, 7.49. Found: C, 79.05; H, 7.43.

***endo*-2-Benzoyl-*exo*-2-hydroxybicyclo[2.2.1]heptane (2).**—The impure enol acetate mixture, **6** (8.60 g, 0.0355 mol), was dissolved in 30 ml of chloroform and cooled to −5° in an ice–salt bath. *m*-Chloroperbenzoic acid (6.30 g, 0.0356 mol), which had been purified by washing with a phosphate buffer solution, was dissolved in 130 ml of chloroform and added dropwise to a stirred solution of the enol acetates. Addition was conducted at such a rate that the temperature did not exceed 0°. After addition was complete, the solution was placed in a freezer at −20° for 60 hr. The *m*-chlorobenzoic acid which had precipitated by this time was filtered from the chloroform solution and the filtrate was stirred with saturated bicarbonate solution for 2 hr at 0°. The chloroform layer was separated and dried (K_2CO_3), and the $CHCl_3$ was removed *in vacuo* to yield epoxy ester **7** as an oil (8.90 g, 98%), 90% pure by gc. This impure compound **7** (7.87 g, 0.0305 mol) was cleaved with methylamine in a sealed tube at 25° for 8 hr. After the reaction was complete, the methylamine was removed, and the residue was dissolved in ether, washed with water, dried (K_2CO_3), and evaporated to dryness. The product was crystallized from hexane to give 6.20 g (74%) of **2**, mp 73.5–74.5°, ir (CCl_4) 1675 cm^{-1} (C=O). A mixture melting point with hydroxy ketone **1** was depressed to 45–51°.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.68; H, 7.40.

Hydroxy ketone **2** (82 mg) was reduced with $NaBH_4$ in methanol to yield 70 mg (85%) of *exo*-2-hydroxy-*endo*-2-(α-hydroxybenzyl)bicyclo[2.2.1]heptane, mp 136.5–137.5°. *Anal.* Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.93; H, 8.34. This diol (105 mg, 0.00048 mol) was oxidized with 273 mg (0.00128 mol) of $NaIO_4$ in water and the products were isolated as their 2,4-dinitrophenylhydrazones as previously described. The yield of norcamphor 2,4-DNP was 88 mg (84%), mp 127–129°, and that of benzaldehyde 2,4-DNP was 80 mg (74%), mp 236–239°.

***endo*-2-Hydroxy-*exo*-2-phenyl-3-bicyclo[3.2.1]octanone (8). Thermal Rearrangement of 1.**—Hydroxy ketone **1** (3.02 g, 0.014 mol) was heated neat at 175° under a N_2 atmosphere. The rearrangement was followed by ir and was found to be complete after 2 hr. The product was crystallized from hexane to give 2.20 g (73%) of **8**, mp 58–59°, ir (CCl_4) 1712 (C=O), 3475 cm^{-1} (OH). Gc analysis of the mother liquor using a 4 ft, 3% diglycerol on Chromosorb W column which cleanly separated hydroxy ketones **2**, **8**, **9**, and **10** at 150° showed the presence of only **8** and no other hydroxy ketone.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.63; H, 7.47.

Treatment of **8** with D_2O in the presence of NaOD in dioxane provided evidence that three deuterium atoms were incorporated, as shown by nmr.

Thermal Rearrangement of *endo*-2-Benzoyl-*exo*-2-hydroxybicyclo[2.2.1]heptane (2).—A solution of 31 mg of **2** in 2 ml of tridecane was heated at 214° under a N_2 atmosphere. The rearrangement was followed by gc using a 4 ft 3% diglycerol column at 150°. After 14 hr, **2** reached its lowest concentration (7%), hydroxy ketone **9** was at its maximum (65%) and the remainder

was hydroxy ketone **10** (28%). On prolonged heating **10** increased and at 50 hr reached its maximum value (60%).

exo-**3-Hydroxy-*endo*-3-phenyl-2-bicyclo[3.2.1]octanone (9).**—A solution of 2.0 g (0.0092 mol) of hydroxy ketone **2** was heated at 225° in 30 ml of tridecane for 17 hr. The tridecane was removed *in vacuo* and the hydroxy ketones **9** and **10** were separated by preparative tlc (ether–hexane–benzene–MeOH, 10:10:10:1). The yield of **9** was 0.905 g (45%), ir (CCl_4) 1712 cm^{-1} (C=O).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.68; H, 7.57.

Thermal Rearrangement of *exo*-3-Hydroxy-*endo*-3-phenyl-2-bicyclo[3.2.1]octanone (9).—A solution of 31 mg of **9** in 2 ml of tridecane was heated at 214° under a N_2 atmosphere. The rearrangement was followed by gc. Hydroxy ketone **10** began building up immediately. Equilibrium was reached after 25 hr. The equilibrium mixture consisted of 60% of **10**, 7% of **2**, and 23% of **9**.

exo-**2-Hydroxy-*endo*-2-phenyl-3-bicyclo[3.2.1]octanone (10). Base-Catalyzed Rearrangement of 1.**—Hydroxy ketone **1** (5.20 g, 0.024 mol) was dissolved in 310 ml of freshly distilled dioxane and 2.8 g of NaOH in 170 ml of water was added. The homogeneous solution was stirred at room temperature for 30 hr. The dioxane was removed *in vacuo*, the product was extracted with ether, washed with water, and dried (K_2CO_3) and the solvent was removed to give 4.90 g (94%) of **10**.[21] Recrystallization from hexane yielded 4.31 g (83%) of **10**, mp 100–101°, ir (CCl_4) 1712 (C=O), 3585 and 3455 cm^{-1} (OH).

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.78; H, 7.41. Found: C, 77.78; H, 7.52.

Deuterium exchange with D_2O in the presence of NaOD showed that three deuterium atoms were incorporated in the molecule, as shown by nmr.

Base-Catalyzed Rearrangement of *endo*-2-Benzoyl-*exo*-2-hydroxybicyclo[2.2.1]heptane (2).—A solution of 2.0 g (0.0092 mol) of **2** in 75 ml of dioxane was mixed with 1.0 g of NaOH in 50 ml of water and the homogeneous solution was stirred at room temperature for 5 hr. As the ir spectrum indicated no reaction, the solution was heated under reflux. In about 8 hr, 90% of the starting material had disappeared and no more reaction was observed in another 2 hr. Most of the dioxane was removed *in vacuo* and the product was extracted with ether, washed with water, dried (K_2CO_3), and removed from the solvent. The residue was crystallized from hexane to give 1.53 g (75%) of **8**, mp 56–57°. Analysis of the mother liquor by gc showed that it consisted of hydroxy ketones **2** and **8** in the ratio 2:3.

A solution of 101 mg of **2** in 5 ml of dioxane was treated with a solution of 30 mg of NaOH in 2 ml of water at 62°. The slow rearrangement was followed by gc. After 6 days, the mixture showed 10% of **8** and 90% of **2**. No other hydroxy ketone was detected.

Base-Catalyzed Rearrangement of 10 to 8.—A solution of 101 mg of **10** in 5 ml of dioxane was treated with a solution of 30 mg of NaOH in 2 ml of H_2O at 62° and the rearrangement was followed by gc. After 6 days the mixture contained 92% of **10** and 8% of **8**. The solvents were evaporated and the residue was extracted with ether. An ir spectrum (CCl_4) did not show any peak at 1675 cm^{-1}, indicating that **1** was not present in any significant amount.

Base-Catalyzed Rearrangement of 1 in Boiling Ethanol.—A solution of 3.4 g (0.016 mol) of **1** in 50 ml of 95% EtOH was refluxed with 2.5 ml of a saturated solution of NaOH in EtOH for 2 days. The alcohol was removed *in vacuo*, the residue was extracted with ether, and the ether solution was decolorized by passing through a short column of fluorisil. The solution was evaporated to dryness and the residue was crystallized from hexane to give 1.0 g (30%) of **8**, mp 58–59°. The low yield in this reaction is probably due to base cleavage of the hydroxy ketones. The mother liquor contained **8** and **10** as shown by gc, and an ir spectrum (CCl_4) did not show any absorption at 1675 cm^{-1}.

Attempted Rearrangement of 8 under Base Catalysis.—A solution of 102 mg of **8** in 5 ml of dioxane was treated with 30 mg of NaOH in 2 ml of water at 62° and the reaction was followed by gc. No new product was formed for 6 days. Work-up of the mixture provided 81 mg (80%) of **8**, mp 57–58° after recrystallization from hexane.

endo-**2-Hydroxy-*exo*-2-phenyl-3-bicyclo[3.2.1]octanone Oxime (11).**—A mixture of 1.015 g (0.0047 mol) of **8**, 1.0 g of hydroxylamine hydrochloride, 10 ml of absolute ethanol, and 10 ml of pyridine was heated on a steam bath for 3 hr. The solvents were removed *in vacuo*, the product was dissolved in ether, washed with 1.5 *N* HCl followed by water, and dried (K_2CO_3), and the solvent was evaporated. The residue was evaporatively distilled to give 0.752 g (69.3%) of **11**, which crystallized on standing, mp 82–88°.

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 73.00; H, 7.40; N, 5.93.

exo-**2-Hydroxy-*endo*-2-phenyl-3-bicyclo[3.2.1]octanone Oxime (12).**—Hydroxy ketone **10** (1.465 g, 0.0067 mol) was mixed with 1.53 g of hydroxylamine hydrochloride, 10 ml of pyridine, and 10 ml of ethanol and heated on a steam bath for 3 hr. After removal of the solvents the residue was dissolved in ether, washed with dilute HCl, dried (K_2CO_3), and evaporated to dryness. The oily residue was crystallized from acetonitrile to give 0.79 g (50.5%) of **12**, mp 163–165°.

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.50; H, 7.49; N, 6.24.

3-Cyanomethylcyclopentyl Phenyl Ketone (13).—Oxime **11** (438 mg, 0.0019 mol) was shaken vigorously with 800 mg of *p*-toluenesulfonyl chloride and 400 mg of sodium hydroxide in 40 ml of water for 2 hr. The product was extracted with ether, dried (K_2CO_3), removed from the solvent, and evaporatively distilled to give 299 mg (73.8%) of **13** as a colorless oil, ir (neat) 1678 (C=O) and 2250 cm^{-1} (C≡N).

Anal. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57. Found: C, 78.77; H, 7.03; N, 6.50.

A small portion of **13** was converted to its semicarbazone, mp 122–124°.

Anal. Calcd for $C_{15}H_{18}N_4O$: C, 66.65; H, 6.71; N, 20.03. Found: C, 66.90; H, 6.80; N, 20.67.

Oxime **12** (204 mg, 0.00089 mol) was also converted to 151 mg (80%) of ketonitrile **13** under the above conditions. The ir spectra of the two samples of **13** were superimposable and their semicarbazones were identical in all respects.

exo-**2-Hydroxy-*endo*-2-phenyl-3-bicyclo[3.2.1]octanone-*N*-methylimine (14).**—A mixture of 414 mg (0.0019 mol) of hydroxy ketone **10**, 15 ml of anhydrous methylamine, and 3.0 g of K_2CO_3 was heated in a sealed tube at 110° for 45 hr. Filtration followed by evaporation of excess methylamine from the reaction mixture yielded 420 mg (95%) of **14** as an oil, ir (neat) 1645 (C=N), 3400 cm^{-1} (OH). It was converted to a crystalline HCl salt, mp 160–162°, ir (KBr) 1680 cm^{-1} (C=N), pK_a 6.68.

Anal. Calcd for $C_{13}H_{20}ClNO$: C, 67.78; H, 7.57; N, 5.27. Found: C, 67.85; H, 7.53; N, 5.51.

exo-**2-Hydroxy-*endo*-2-phenyl-*endo*-3-*N*-methylaminobicyclo[3.2.1]octane (15).**—A solution of 420 mg (0.0018 mol) of **14** in 40 ml of methanol was reduced with 500 mg of $NaBH_4$ over an 18-hr period. Water was added and the mixture was heated at 60° for 30 min. Most of the methanol was removed *in vacuo*, and the product was extracted with ether and dried (K_2CO_3) and the ether removed. The residue was recrystallized from hexane to yield 306 mg (73%) of **15**, mp 78–79°.

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: 77.84; H, 9.23; N, 6.23.

A small portion of **15** was converted to the HCl salt, mp 228–230°, pK_a 8.37.

Anal. Calcd for $C_{15}H_{22}ClNO$: C, 67.27; H, 8.28; N, 5.23. Found: C, 67.15; H, 8.36; N, 5.34.

exo-**2-Hydroxy-*endo*-2-phenyl-*endo*-3-*N*,*N*,*N*-trimethylammoniumbicyclo[3.2.1]octane Iodide (16).**—A mixture of 221 mg (0.001 mol) of **15**, 220 mg of a 40% solution of formaldehyde, and 230 mg of a 90% solution of formic acid was heated on a steam bath for 12 hr. The excess formaldehyde and formic acid were removed and the product was extracted with ether after treatment with $NaHCO_3$ solution. The ether solution was dried (K_2CO_3) and the solvent was removed to give 199 mg of the dimethylamino alcohol, which was refluxed with 2 ml of methyl iodide in 5 ml of acetonitrile for 1 hr. After removal of the solvent *in vacuo*, the residue was crystallized from ethanol–ether to yield 236 mg (74%) of **16**, mp 215–216°.

Anal. Calcd for $C_{17}H_{26}INO$: C, 52.72; H, 6.77; N, 3.62. Found: C, 52.97; H, 6.63; N, 3.86.

endo-**2-Phenyl-2-bicyclo[3.2.1]octene Oxide (19). A. From Quaternary Salt 16.**—A solution of 150 mg (0.000388 mol) of **16** in 5 ml of MeOH was treated with 44 mg (0.0002 mol) of freshly prepared NaOH-free silver oxide at room temperature for 12 hr. The AgI was filtered off and the methanol was evap-

(21) The mother liquor showed the presence of **8** by gc and did not show the presence of **1** or **2** by an ir spectrum.

orated to dryness to give 47 mg (61%) of epoxide **19**, mp 59.5–60.5°.

Anal. Calcd for $C_{14}H_{16}O$: 83.96; H, 8.05. Found C, 83.95; H, 8.06.

B. From 2-Phenyl-2-bicyclo[3.2.1]octene (18).—A solution of phenyllithium (10 ml, 0.02 mol) was added with stirring to an ethereal solution of 1.192 g (0.0096 mol) of 2-bicyclo[3.2.1]-octanone[14] (**17**) at −78° under a nitrogen atmosphere. After stirring for 1 hr, the mixture was warmed to room temperature, water was added, and the product was extracted with ether. After removal of the solvent, the residue was evaporatively distilled to give 1.260 g (65%) of 2-hydroxy-2-phenylbicyclo[3.2.1]-octane, which was dehydrated by azeotroping with toluene in the presence of *p*-toluenesulfonic acid to yield 860 mg (74.8%) of 2-phenyl-2-bicyclo[3.2.1]octene (**18**).

A solution of 860 mg of **18** in 50 ml of $CHCl_3$ was epoxidized using 850 mg of *m*-chloroperbenzoic acid. After refluxing for 14 hr the mixture was cooled and filtered, and the filtrate was washed with $NaHCO_3$ solution and dried (K_2CO_3). Removal of chloroform yielded 850 mg of an oil, 500 mg of which was purified by preparative tlc to give 140 mg of the epoxide **19**, mp 60–61°, identical in all respects with the epoxide obtained from **16**.

***exo*-3-Hydroxy-*endo*-3-phenyl-2-bicyclo[3.2.1]octanone-*N*-methylimine (20).**—A mixture of 625 mg (0.00287 mol) of hydroxy ketone **9** and 10 ml of methylamine was heated at 110° in a sealed tube for 4 days. The excess methylamine was removed to give 650 mg (98%) of **20** as an oil, ir 3300 (OH) and 1660 cm^{-1} (C=N). This material was converted to its HCl salt, 605 mg (85%), mp 259–260° dec, ir (KBr) 1675 cm^{-1} (C=N), pK_a 7.70.

Anal. Calcd for $C_{15}H_{20}ClNO$: C, 67.78; H, 7.57; Cl, 13.34; N, 5.27. Found: C, 68.05; H, 7.74; Cl, 13.57; N, 5.33.

***endo*-2-*N*-Methylamino-*exo*-3-hydroxy-*endo*-3-phenylbicyclo-[3.2.1]octane (21).**—A solution of 605 mg (0.00227 mol) of the HCl salt of **20** in 50 ml of anhydrous methanol was reduced with 1.0 g of $NaBH_4$ for 12 hr. Water (20 ml) was added to the reaction mixture, most of the methanol was removed *in vacuo*, and the amino alcohol was extracted with 1 *N* HCl. The acid solution was basified with NaOH, extracted with ether, dried (K_2CO_3) and removed from the solvent. The residue was recrystallized from hexane to give 500 mg (95%) of **21**, mp 106–107°.

Anal. Calcd for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 77.97; H, 8.99; N, 6.06.

***endo*-2-*N*,*N*,*N*-Trimethylammonium-*exo*-3-hydroxy-*endo*-3-phenylbicyclo[3.2.1]octane Iodide (22).**—The conversion of 403 mg (0.00174 mol) of amino alcohol **21** to the quaternary salt **22** was accomplished under the same conditions as for the synthesis of **16**. The yield of **22** was 540 mg (80%), mp 190–191°.

Anal. Calcd for $C_{17}H_{26}INO$: C, 52.72; H, 6.77; I, 32.51; N, 3.62. Found: C, 52.47; H, 6.87; I, 32.77; N, 3.46.

***endo*-3-Phenyl-2-bicyclo[3.2.1]octene Oxide (25). A. From Compound 22.**—A solution of 104 mg (0.00029 mol) of **22** in 5 ml of methanol was treated with 100 mg of freshly prepared wet silver oxide at room temperature for 5 hr. The precipitated AgI was removed by filtration and the filtrate was evaporated to dryness. The resultant quaternary hydroxide was sublimed at 60° (0.1 mm) to yield 44 mg (83%) of **25**, mp 28–29°.

Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.70; H, 8.04.

B. From 3-Phenyl-2-bicyclo[3.2.1]octene (24).—3-Phenyl-2-bicyclo[3.2.1]octene (**24**) was prepared from 3-bicyclo[3.2.1]-octanone[17] (**23**) using essentially the same conditions for the synthesis of 2-phenyl-2-bicyclo[3.2.1]octene (**18**). A solution of 0.78 g (0.0042 mol) of **24** in 25 ml of $CHCl_3$ was refluxed with 0.90 g (0.0052 mol) of *m*-chloroperbenzoic acid for 90 min. The mixture was allowed to stand at room temperature for 12 hr and then cooled at −20° for 2 hr. The precipitated *m*-chlorobenzoic acid was removed by filtration and the filtrate was washed with $NaHCO_3$ solution. After drying (K_2CO_3), the $CHCl_3$ was removed to yield 655 mg (89%) of **25** as an oil which could be crystallized from hexane, mp 27–28°. The epoxide **25** obtained by both the routes were identical in all respects.

Registry No.—**1**, 34546-64-0; **2**, 34546-65-1; **4**, 34546-66-2; **5**, 34546-67-3; **6**, 34546-68-4; **8**, 34546-69-5; **9**, 34546-70-8; **10**, 34546-71-9; **11**, 34546-72-0; **12**, 34546-73-1; **13**, 34546-74-2; **13** semicarbazone, 34546-75-3; **14**, 34546-76-4; **15**, 34546-77-5; **15** HCl, 34546-78-6; **16**, 34546-79-7; **19**, 34546-80-0; **20** HCl, 34546-81-1; **21**, 34546-82-2; **22**, 34546-83-3; **25**, 34546-84-4.

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