

Synthesis and Reactivity of *exo*- and *endo*-Bicyclo[2.1.0]pentan-5-ol and Their Derivatives

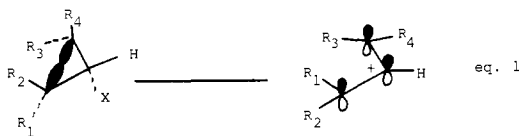
Joseph J. Tufariello,* Arthur C. Bayer, and Joseph J. Spadaro, Jr.

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214. Received August 25, 1978

Abstract: A rational synthesis of 5-substituted bicyclo[2.1.0]pentanes was developed from the Diels–Alder adduct of 6,6-dimethylfulvene and dimethyl azodicarboxylate. Kinetic investigations indicate enormous reactivity for derivatives of *endo*-bicyclo[2.1.0]pentan-5-ol, and a mechanism for solvolysis of the *exo*-*p*-nitrobenzoate, which proceeds via the corresponding *endo* isomer, is outlined.

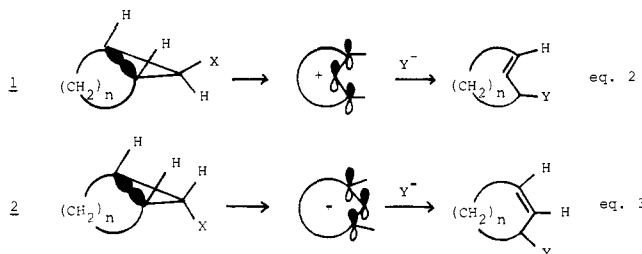
Introduction

Through the use of orbital symmetry methods and extended Hückel calculations, Woodward and Hoffmann predicted¹ that cyclopropyl derivatives would undergo solvolysis with the bond opposite the leaving group undergoing scission in a disrotatory manner to afford an alkyl cation. It was further suggested^{1b,2} that the substituents *trans* to the leaving group prefer an outward disrotation. The consequences of these predictions for cationic cyclopropyl ring openings are indicated in eq 1. The



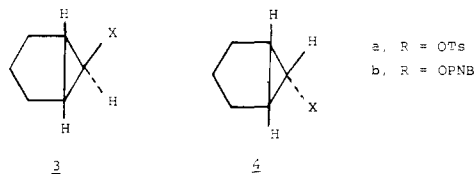
overall disrotatory process may be viewed as a backside displacement of the leaving group by the distant cyclopropyl carbon-carbon bond. The calculations and predictions of Woodward and Hoffmann and DePuy on simple cyclopropyl systems have found support in other theoretical³ and experimental⁴⁻⁷ work.

Application of the concepts outlined above to *exo*- and *endo*-($n + 3$)-substituted bicyclo[n .1.0]alkyl systems, where n is small (i.e., 2, 3, or 4), suggests that the appropriately substituted *endo* epimers should be more active toward conditions of solvolysis than their *exo* counterparts. Thus, an ionic disrotatory opening of **1** results in the formation of a *trans,trans* allylic cation (eq 2). The epimeric *cis*-fused *endo* system (eq 3) would be expected to undergo concerted ionization to a *cis,cis* allylic cation. Nucleophilic capture of the cation affords

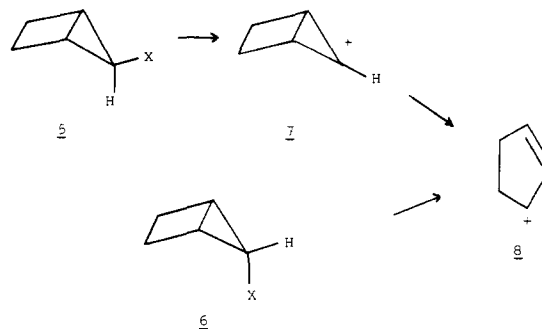


a *trans* cycloalkene from the *exo* substrate and a *cis* cycloalkene from the *endo* substrate. Clearly, when n is small, the strain incorporated at the transition state should retard solvolysis by a concerted mechanism for the *exo* substrate (eq 2), while a relief of ground-state strain and a configurationally favorable transition state should enhance the reactivity of its *endo* counterpart. Several studies have focused on systems of the type **1** and **2**. It was found⁸ that *endo*-7-chlorobicyclo[4.1.0]heptane undergoes acetolysis (125 °C) more than 175 times faster than its *exo* epimer. That the schemes illustrated

in eq 2 and 3 are capable of predicting product composition is indicated by the observation that only *trans*-3-cyclooctenol was produced by hydrolysis of *exo*-8-bromobicyclo[5.1.0]octane.⁹ The *p*-toluenesulfonate of *exo*-bicyclo[3.1.0]hexane-6-ol (**3a**) was shown to undergo acetolysis more slowly (i.e., rate factor 3×10^{-4}) than cyclopropyl *p*-toluenesulfonate, while its *endo* epimer^{4a} proved to be more reactive (i.e., rate factor 2.2×10^4).^{4b,6}

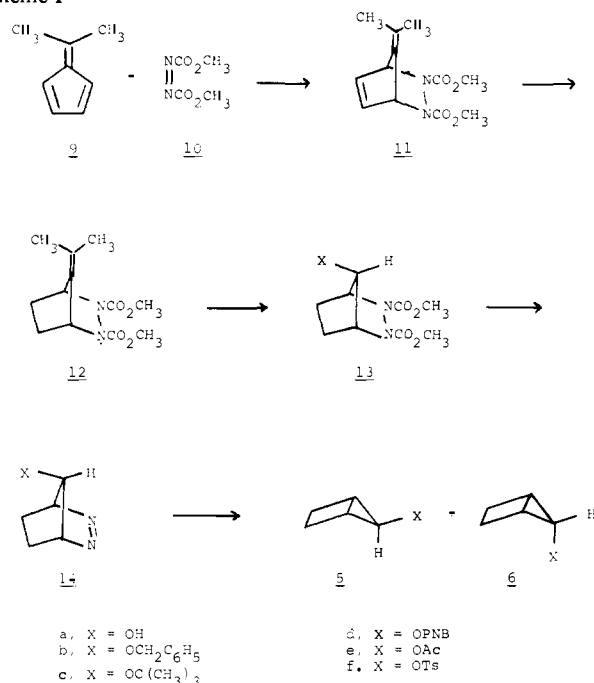


The 5-substituted bicyclopentyl system embodies features which would be expected to result in enormous *endo*/*exo* rate ratios. Indeed, after a consideration of various electronic and structural factors, it has been suggested¹⁰ that *exo* tosylate **5f** might undergo acetolysis more slowly than cyclopropyl tosylate by a factor of 10^5 . This expected rate retardation was attributed to the inability, for energetic reasons, of **5f** to undergo



concerted, disrotatory ring opening to give the allylic cation **8**. In fact, it is reasonable to suggest that a capturable cyclopropyl cation might be expected to be involved in the solvolysis of **5f** as has been implicated in the acetolysis of the triflate of *exo*-bicyclo[3.1.0]hexan-6-ol. The product composition in the latter case includes 50% of configurationally retained acetate.^{4b} It was also suggested¹⁰ that the *endo* tosylate **6f** might prove to be more reactive than cyclopropyl tosylate by a factor of 10^{15} ; thus, the estimated rate difference between the two epimers is a factor of 10^{20} ! The high reactivity expected for the *endo* tosylate can be attributed to an orbital symmetry allowed opening to the relatively unstrained *cis,cis* cation **8**, and to the large release in ground-state strain energy expected at the solvolysis transition state. Heat of hydrogenation studies¹¹ state that approximately 48 kcal/mol of strain energy is released when the C₁-C₄ bond of bicyclopentane is cleaved.¹² Indeed,

Scheme I



studies on 2-substituted bicyclo[2.1.0]pentyl systems indicate unusually high reactivity for the *endo* epimer.¹³ This finding is substantiated by the high reactivity found for other bicyclo[2.1.0]pentyl derivatives where the central bond is cleaved.¹³⁻¹⁵

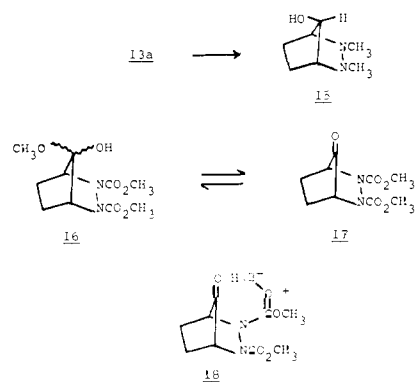
Synthesis

The theoretical interest associated with, and the reactivity differences expected for, *exo*- and *endo*-5-substituted bicyclo[2.1.0]pentanes (vide supra) made the goal of their synthesis an attractive challenge.^{16,17} We chose to approach the bicyclo[2.1.0]pentyl system through the use of diazacycloalkanes.^{16a} Thus, confronting the sequence outlined in Scheme 1, we prepared the Diels-Alder adduct **11** (78% yield) from 6,5-dimethylfulvene (**9**) and dimethyl azodicarboxylate (**10**). Selective reduction of the endocyclic double bond produced the dihydro adduct **12** in 94% yield.^{18,19}

Ozonolysis of **12** in methanol at -78°C , followed by reduction with sodium borohydride, results in the exclusive formation of *anti*-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptan-7-ol (**13a**) in 91% yield. The stereochemical assignment rests largely on the absence of intramolecular hydrogen bonding as determined by an examination of the first overtone region for hydroxyl stretching (i.e., $\sim 1.4\ \mu$).²⁰ This spectral technique has been used²¹ to determine the stereochemistry of the epimeric 2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptan-5-ols. The *exo* epimer displayed only a single absorption at $1.414\ \mu$ which was assigned to free hydroxyl stretching. Under identical conditions, the *endo* isomer exhibited two bands, at 1.410 and $1.456\ \mu$, the latter of which was assigned to the intramolecular hydrogen bonding. At a concentration of $10^{-3}\ \text{M}$ (CCl₄), **13a** showed only a single sharp band ($1.411\ \mu$) assigned to free hydroxyl stretching. Alcohol **13a** was converted into its *N,N'*-dimethyl derivative (70% yield) by reduction with lithium aluminum hydride. Again, at a concentration of $10^{-3}\ \text{M}$ in carbon disulfide, the dimethyl derivative **15** displays only a single absorption at $1.415\ \mu$, attributable to free hydroxyl. Moreover, the hydroxyl proton signal in the NMR spectrum of **15** shifts upfield from $\delta\ 5.35$ to 2.67 ppm as the concentration is varied from 2.0 to $0.125\ \text{M}$ in deuteriochloroform. This observation is consistent with the assigned stereochemistry but not for a strongly hydrogen bonded *syn* epimer.^{23,24}

The *anti* stereochemistry of **13a** requires special comment.

It appears likely that the reductive ozonolysis must at some stage proceed to the reactive ketone **17**,²⁵ presumably via hemiacetal **16**. Indeed, the **16** \rightleftharpoons **17** equilibrium might be facilitated by the borohydride present. Any tendency of borane



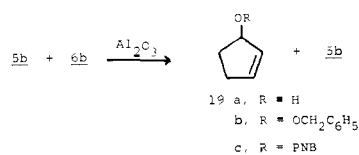
to complex with the carbamate carbonyl could deliver hydride to the keto grouping from the *syn* face of **17** (cf. **18**) to give *anti* alcohol **13a**. In fact, an independent investigation of the borohydride-induced reduction of **17** has been reported²⁵ to give **13a**. Moreover, complexation of the carbamate carbonyl with bromine has been proposed to rationalize *syn* bromination in closely related systems,²⁶ a finding in contradiction with expectation based on steric effects alone.²⁶

It was found necessary to block the alcohol function in **13a** prior to hydrolysis. Thus, **13a** was converted to the benzyl ether **13b** (98%) by treatment with benzyl bromide and sodium hydride, and to the *tert*-butyl ether **13c** (59%) by acid-catalyzed addition of isobutylene. Hydrolysis of the carbamate groupings in **13b** and **13c**, followed by oxidation of the resultant hydrazines, gave azo compounds **14b** and **14c**, respectively.

Photolysis of **14b** in hexane (Pyrex filter) gave a mixture of *exo*- and *endo*-5-benzyloxybicyclo[2.1.0]pentanes (**5b** and **6b**) in a 1:3 ratio, respectively. The stereochemical assignments rest on the reported²⁷ values of vicinal coupling constants in cyclopropanes and bicyclo[*n*.1.0]alkanes. The value of $J_{\text{cis}} > J_{\text{trans}}$ in these systems. The 5 proton of *endo* isomer **6b** appears as a triplet ($J = 5\ \text{Hz}$) at $\delta\ 3.28\ \text{ppm}$ (CDCl₃) as expected. In contrast, the 5 proton in the *exo* isomer **5b** appears as a singlet ($\delta\ 3.37\ \text{ppm}$, CDCl₃), indicating that this proton occupies a *trans* orientation with respect to the bridgehead protons. Catalytic hydrogenation of the *endo/exo* mixture over palladium on carbon affords an 89% yield of cyclopentanol.

It is interesting to note that the photolytic product composition reveals a net retention of configuration and does not appear to reflect the presence of a "recoil effect" noted^{28,29} in similar systems. We wished to test this effect under thermal conditions; however, attempted thermolysis of **14b** for 2.5 h at 158°C resulted in its recovery without change. At higher temperatures, decomposition was apparent.

The separation of the 75:25 mixture of isomers proved problematic. Chromatography of this mixture on alumina afforded a mixture of 3-benzyloxycyclopentene and the unchanged *exo* isomer (**5b**). Apparently, the *endo* isomer is



completely isomerized to the 3-benzyloxycyclopentene under these conditions. This isomerization could also be effected by trifluoroacetic acid. Ozonization of the mixture of **19b** and **5b** in pentane at -78°C led to the formation of an insoluble, amorphous ozonide of the olefin. The pentane solution was

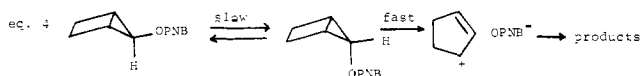
decanted from most of the ozonide and poured through an alumina column to give pure *exo* isomer.

Cleavage of the benzyl ether function of **5b** with sodium in liquid ammonia at $-78\text{ }^\circ\text{C}$ gave the desired alcohol **5a** from which the corresponding *p*-nitrobenzoate **5d** was prepared.²⁸ Attempts to derivatize the *endo* alcohol were largely unsuccessful owing to the reactivity of the system. For example, when a small drop of trifluoroacetic acid was added to an NMR sample containing the *endo* alcohol, it was spectacularly and completely converted into 3-cyclopentenol in less than 15 s. The only derivative of the *endo* alcohol **6a** that we were able to prepare was the corresponding acetate **6e**, isolated by directly treating the alkoxide obtained from the sodium in liquid ammonia benzyl ether cleavage reaction with acetyl chloride. The bicyclic acetates were identified by the expected paramagnetic shift³⁰ associated with the 5 hydrogen, in comparison with the starting alcohols, in the NMR spectrum of *endo* (0.78 ppm) and *exo* (0.65 ppm) derivatives. The remarkable reactivity of the *endo* acetate **5e** is illustrated by its rapid and complete isomerization into 3-acetoxycyclopentene when warmed to $60\text{ }^\circ\text{C}$ in CCl_4 solution. The *exo* acetate remains completely unchanged under these conditions.

Reactivity

The solvolytic behavior of *exo-p*-nitrobenzoate **5d** was examined and its behavior contrasted with similar systems (cf. Table I). One striking feature which emerges from the tabulated data relates to the relative independence of the solvolysis reaction of *p*-nitrobenzoate **5d** to solvent polarity. Thus, whereas *anti*-bicyclo[2.2.1]hept-2-en-7-ol *p*-nitrobenzoate experiences a 19-fold rate enhancement in going from 80% to 60% aqueous acetone, the rate of **5d** is virtually unaffected over the same solvent range. This finding is corroborated by an independent study¹⁷ on the *p*-toluenesulfonate **5f** (cf. Table I). Most dramatically, the rate constant for the isomerization of **5d** to 3-cyclopentenyl *p*-nitrobenzoate in bromobenzene- d_5 (NMR) is comparable to the corresponding solvolytic data. A second startling observation is that the rate of solvolysis of *p*-toluenesulfonate **5f** exceeds that of the corresponding *p*-nitrobenzoate **5d** ($75\text{ }^\circ\text{C}$, 80% aqueous acetone) by a factor of less than 6. Reported data suggests that this rate ratio would be expected to be approximately 10^{10} .

Since it was expected that **3b** would offer a good model for the solvolytic behavior of **5d**, as both might be expected to proceed through the intermediacy of cyclopropyl cations (vide supra), we were impressed to learn that acetolysis of *exo*-OPNB **5d** would exceed that of **3b** by a rate factor of approximately 10^{18} (Table I; consider acetolysis data of **5d** and **3b** at $25\text{ }^\circ\text{C}$). These results demand that **5d** and **3b** undergo solvolysis by unrelated mechanistic pathways, and strongly suggest that the rate-limiting step in the solvolysis of **5d** does not involve charge separation. These conclusions are embodied in a proposed mechanistic scheme (eq 4) also supported by Professors Schleyer and Schollkopf and their co-workers.¹⁷



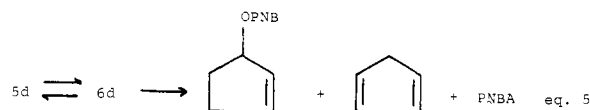
Initially, we could not rule out the direct formation of *p*-nitrobenzoate **19c** as the result of thermally allowed $[\sigma_{2a} + \sigma_{2s}]$ rearrangement. This process has been suggested^{31a} in bicyclopentene isomerization, although the original suggestion has generated controversy.^{31b} Several pieces of evidence suggest that the concerted process to afford **19c** is not operating in our system. First, the product compositions obtained after the solvolysis of **5d** and **19c** under the same conditions differ. The bicyclopentane **5d** gives $38 \pm 2\%$ cyclopentadiene and $62 \pm 2\%$ 3-cyclopentenol, while **19c** gives 8% cyclopentadiene and 92% 3-cyclopentenol in 80% aqueous acetone at $95\text{ }^\circ\text{C}$ (cf. Table

Table I. Solvolytic and Thermolytic Reactivity of $(n+3)$ -Substituted Bicyclo[*n*.1.0]pentanes^a

compd	solvent	temp, $^\circ\text{C}$	k , s^{-1}
5d	80% aq acetone	75.4	$(3.14 \pm 0.16) \times 10^{-6}$
5d	80% aq acetone	95.0	$(29.8 \pm 1.4) \times 10^{-6}$
5d	80% aq acetone	25.0	2.6×10^{-9} ^b
5d ^{g,h}	80% aq acetone	95.8	$(37.0 \pm 2) \times 10^{-6}$
5d	60% aq acetone	95.0	$(32.5 \pm 1.4) \times 10^{-6}$
5d	bromobenzene- d_5	75.5	$(3.3 \pm 0.2) \times 10^{-6}$ ^e
5d	80% aq acetone	135	1.6×10^{-3} ^b
5b	bromobenzene- d_5	135	160×10^{-6} ^{e,f}
19c	80% aq acetone	74.6	$(69.9 \pm 1.1) \times 10^{-6}$
19c ^{g,i}	80% aq acetone	75.5	$(83.0 \pm 4) \times 10^{-6}$
19c ^{g,j}	80% aq acetone	95.8	
3b	acetic acid	25.0	$\sim 10^{-27}$ ^d
5d	acetic acid	25.0	$\sim 3 \times 10^{-9}$ ^c
5f	80% aq acetone	75.0	1.81×10^{-5} ^j

^a Determined titrimetrically unless otherwise noted. ^b Extrapolated from kinetic data at 75.4 and $95\text{ }^\circ\text{C}$. ^c Since no significant change in rate is observed with change in solvent polarity, this rate constant is estimated from the datum in 80% aqueous acetone at $25\text{ }^\circ\text{C}$. ^d Estimated by assuming a OTs/OPNB rate ratio of 10^{10} (cf. ref 45 and 34) and a OTf/OTs rate ratio of 10^5 (cf. ref 4b). ^e Determined by NMR investigation. ^f Instantaneous rate constant determined over ca. 1 half-life. ^g Data were determined with 2,6-lutidine present to neutralize acid. ^h Product consists of 38% cyclopentadiene and 62% 3-cyclopentenol. ⁱ Product consists of 12% cyclopentadiene and 88% 3-cyclopentenol. ^j Product consists of 8% cyclopentadiene and 92% 3-cyclopentenol.

1, footnote g). If the same intermediate were involved in both reactions, the product compositions would be expected to be identical.³² Secondly, when **5d** was heated in bromobenzene- d_5 (Table I), cyclopentadiene was produced along with the expected **19c**; however, **19c** proved to be stable to the thermal conditions employed (i.e., no cyclopentadiene was formed by heating **19c** under the conditions employed). Thus, the cyclopentadiene may be the product of an ionic process even in bromobenzene. Thirdly, we have demonstrated (Table I) that **5b** isomerizes to **19c** (bromobenzene- d_5 , $135\text{ }^\circ\text{C}$) at a rate which approximates the rate of solvolysis of **5d** in 80% aqueous acetone ($135\text{ }^\circ\text{C}$), evidence consistent with the proposal that the rate-limiting step in the solvolysis of **5d** is its conversion to **6d**. Thus, we believe that product formation occurs as indicated in eq 5, probably via a process involving ionization of **6d**.



Studies based on the corresponding *p*-toluenesulfonate have prompted similar conclusions.¹⁷

It is interesting to estimate, however approximately, the reactivity ratio k_{6d}/k_{5d} . If one makes the preposterous assumption, in order to set lower limits on the desired ratio, that benzyl oxide and acetate are equivalent in leaving-group ability, then, with knowledge of the rate constant for isomerization of **5d** ($1.1 \times 10^{-6}\text{ s}^{-1}$ in 87% aqueous acetone at $95\text{ }^\circ\text{C}$) to **19b**, and the known reactivity ratios $k_{\text{OPNB}}/k_{\text{OAc}}$ (**51**)³³ and $k_{\text{OTs}}/k_{\text{OPNB}}$ (10^{10}),³⁴ it is possible to calculate that the rate constant for hydrolysis (87% aqueous acetone, $95\text{ }^\circ\text{C}$) should be approximately $6 \times 10^5\text{ s}^{-1}$. Since the Y values for 87% aqueous acetone and glacial acetic acid are similar, one can set a lower limit on the rate constant for the acetolysis of **5f** (at $100\text{ }^\circ\text{C}$) at $6 \times 10^5\text{ s}^{-1}$. The rate constant for acetolysis of cyclopropyl tosylate at $100\text{ }^\circ\text{C}$ is $4.16 \times 10^{-8}\text{ s}^{-1}$.³⁵ Thus, the lower limit for the difference in rate, ca. 10^{13} , may be contrasted with the predicted value¹⁰ of 10^{15} . Taking the increased leaving ability of acetate, in comparison with benzyl

oxide, into account would undoubtedly make 15 powers of ten a conservative estimate of the $k_{5t}/k_{\text{cyclopropyl tosylate}}$ rate ratio.

On the basis of the solvolytic data presented in Table I, and the assumed mechanistic scheme (eq 4), it is possible to calculate an activation energy ($E_a = 29.2$ kcal/mol) for the **5d** \rightarrow **6d** interconversion. This value is substantially lower than that ($E_a = 38.9$ kcal/mol) reported¹⁵ for the 2-methylbicyclo[2.1.0]pentane isomerization, and compels³⁶ an examination of the influence of 5 substituents on the bicyclopentane isomerization barrier.

Experimental Section

All melting and boiling points are uncorrected. A Mel-Temp capillary tube apparatus was used to determine melting points. Infrared spectra were recorded on a Beckman IR-5A spectrophotometer and calibrated using the 6.238- μ band of polystyrene. All infrared absorptions are reported in microns; w, m, and s indicate the intensity of absorptions as weak, medium, and strong.

Nuclear magnetic resonance (NMR) spectra were recorded on a Varian A-60, Varian HA-60, or a JEOL MH-100 spectrometer using tetramethylsilane (Me_4Si) as an internal standard. The positions of absorbances are reported in δ (parts per million downfield relative to Me_4Si). Notations s, d, t, q, m, dd, and cm designate singlet, doublet, triplet, quartet, multiplet, doublet of doublets, and complex multiplet, respectively. A b in front of these letters indicates broad, and vb, very broad. The integration number is also shown in parentheses.

Ultraviolet spectra were recorded on a Perkin-Elmer 202 spectrophotometer, and values are reported in nanometers.

Mass spectra were recorded on a Hitachi-Perkin-Elmer RMU 6 mass spectrometer. The ionizing voltage was 70 V with a current of 80 μA .

Gas-liquid phase chromatographic analyses (GLC) were performed with a Perkin-Elmer Model 800 gas chromatograph with a nitrogen flow of 25 mL/min. Preparative work was performed on an Aerograph A-90-P instrument with a helium flow rate of 60 mL/min.

Elemental analyses were performed at Scandinavian Microanalytical Laboratory, Box 25, DK 2730 Herlev, Denmark, or by Drs. Weiler and Strauss, Microanalytical Laboratory, Oxford, England.

6,6-Dimethylfulvene (9). The title compound was prepared by the method of Wilder and Winston³⁷ in 56% yield; bp 55.0–56.5 °C (11 mm Hg) (lit.³⁷ bp 54–57 °C (12 mm)); NMR (CCl_4) δ 2.03 (s, 6 H), 6.32 ppm (s, 4 H).

Methyl Azodicarboxylate (10). The title compound was prepared by the method of Kauer³⁸ in 70% yield; bp 81.5–83.0 °C (3.9 mm Hg) (lit.³⁸ bp 90–91 °C (15 mm Hg)); IR (film) 5.60 μ (s).

7-Isopropylidene-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]hept-2-ene (11). A solution of 30.8 g (0.291 mol) of dimethylfulvene in 145 mL of anhydrous ether was cooled in an ice bath. To this solution was added a solution of 42.5 g (0.291 mol) of methyl azodicarboxylate in 145 mL of anhydrous ether. The reactants were mixed thoroughly and allowed to stand. The homogeneous solution was then allowed to gradually warm to room temperature and to stand for 24 h. The product was collected via suction filtration and washed with cold hexane until colorless to afford 63.0 g (0.250 mol, 86%) of white crystals; mp 93.5–94.5 °C; IR (Nujol) 5.80 (s), 7.68 (s), 8.31 μ (s); NMR (CDCl_3) δ 1.65 (s, 6), 3.73 (s, 6), 6.38 (bs, 2), 6.72 ppm (t, 2, $J = 2$ Hz).

Hydrogenation of 7-Isopropylidene-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]hept-2-ene (11). A mixture of 50.0 g (0.198 mol) of adduct **11**, 200 mL of ethyl acetate, and 2.5 g of 5% palladium on barium sulfate was stirred in a Brown² hydrogenator³⁹ until 1 equiv of hydrogen had been absorbed. The mixture was then filtered, the solvent removed under reduced pressure, and the residue distilled to afford 45.9 g (0.182 mol, 92%) of 7-isopropylidene-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptane (**12**) as a viscous liquid; bp 126–129 °C (0.12 mmHg); IR (film) 5.70–5.90 (s), 8.31 μ (s); NMR (CCl_4) δ 1.75 (bs, s, 10) 3.68 (s, 6), 4.70 ppm (bs, 2).

This material crystallized after long storage and after recrystallization from hexane had mp 87.5–89 °C.

Anal. ($\text{C}_{12}\text{H}_{18}\text{N}_2\text{O}_4$) C, H, N.

2,3-Dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptan-7-ol (13a). Ozone, 1.6 mmol/min, generated from a Welbach Model T-816 laboratory ozonizer, was passed through a solution of 5.25 g (0.020

mol) of dihydro-**12** in 60 mL of methanol for 12 min at -68 °C. The solution was then added dropwise with ice cooling and magnetic stirring to 90 mL of a 1 M solution of sodium borohydride in methanol. The rate of addition was such that a temperature of 0–5 °C was maintained throughout. After the addition was complete, the solution was allowed to warm to room temperature and to stir overnight. The solution was then carefully made acidic with 6 N hydrochloric acid, and the solvent removed under reduced pressure. The residue was dissolved in water and the aqueous solution saturated with salt and extracted with ether. The ether extracts were washed with saturated brine solution and dried over magnesium sulfate. Removal of the solvent afforded a colorless, glasslike material which was redissolved in benzene and refluxed with a Dean-Stark water separator to remove the final traces of moisture. The benzene was removed in vacuo and the residue chromatographed on silica gel. Elution with 50:50 chloroform-ether afforded 3.22 g (0.014 mol), 70% of theoretical, of **13a**: IR (film) 2.90 (m), 5.70–5.90 μ (s); NMR (CDCl_3) δ 1.60–2.10 (cp, 4), 3.78 (s, 6), 4.12 (bs, 1), 4.25 ppm (bs, 2).

The alcohol was converted into its acetate derivative in 66% yield via treatment with sodium acetate-acetic anhydride; bp 157–160 °C (0.025 mmHg); IR (film) 5.68–5.88 (s), 6.90 (s), 8.08 (s), 13.00 μ (m); NMR (CDCl_3) δ 1.90 (s, 4), 2.10 (s, 3), 3.82 (s, 6), 4.52 (bs, 2), 4.85 ppm (t, 1, $J = 2$ Hz).

Anal. ($\text{C}_{11}\text{H}_{16}\text{N}_2\text{O}_6$) C, H, N.

2,3-Dimethyl-2,3-diazabicyclo[2.2.1]heptan-7-ol (15). Alcohol **13a** was converted into its N,N' -dimethyl derivative via reduction with lithium aluminum hydride according to the method of Allred.²¹ After recrystallization from carbon tetrachloride, the yield of the N,N' -dimethyl derivative **15** was 2.40 g (0.017 mol, 70%); mp (sealed capillary) 79–81.5 °C; IR (CHCl_3) 3.1 (s), 6.90 (m), 7.10 (m), 8.85 μ (s); NMR (CDCl_3) δ 1.82 (s, 4) 2.47 (s, 6), 3.05 (bs, 2), 3.99 (bs, 1), 4.62 ppm (t, 1, $J = 2$ Hz).

Anal. ($\text{C}_7\text{H}_{14}\text{N}_2\text{O}$) C, H, N.

The dimethyl alcohol **15** was converted into its methiodide derivative via treatment with methyl iodide in 85% yield. Recrystallization from ethanol-ether afforded an analytical sample, mp 157–159 °C dec.

Anal. ($\text{C}_8\text{H}_{17}\text{N}_2\text{OI}$) C, H, N, I.

anti-7-Benzyloxy-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptane (13b). The precursor alcohol **13a** (78.0 g, 0.339 mol) was dissolved in 590 mL of benzene and to this solution was added 81.0 g (0.474 mol) of freshly distilled benzyl bromide. Small portions (0.5 g) of NaH (11.5 g, 0.415 mol) was added to this solution. After addition was complete and evolution of hydrogen had slowed (1.3 h), the solution was heated just below reflux for 4 h. When hydrogen evolution had again subsided, the solution was refluxed for 2 h. The flask was cooled, the excess NaH quenched with absolute EtOH, 100 mL of H_2O added, and the resultant mixture filtered to remove the precipitated salt. The mixture was then saturated with potassium carbonate. The benzene layer was separated, dried over magnesium sulfate, and filtered to remove drying agent, and the solvent was removed in vacuo. Prolonged heating of the resultant viscous dark liquid at 70 °C (0.1 mmHg) removed residual benzyl bromide. A crude yield of 105 g (98%) was obtained; IR (film) 5.68 (s), 5.82 (s), 7.45 (s), 8.55 μ (s); NMR (CCl_4) δ 1.82 (bs, 4), 3.68 (s, 6), 3.83 (bs, 1), 4.25 (bs, 2), 4.52 (s, 2), 7.25 ppm (s, 5).

7-Benzyloxy-2,3-diazabicyclo[2.2.1]hept-2-ene (14b). The following procedure is adapted from that of Gassman and Mansfield.⁴¹ A slow stream of nitrogen was bubbled through 100 mL of ethylene glycol for 20 min before 9.52 g (0.168 mol) of potassium hydroxide was added in four portions. The ethylene glycol solution was heated to 125 °C and the benzyl ether **13b** (12.2 g, 0.037 mol) was added rapidly. After the addition, the temperature of the reaction was maintained at 125–130 °C for 1 h. After being cooled, the mixture was cautiously added to 50 g each of ice and water and 30 mL of 12 N hydrochloric acid. The mixture was then warmed to about 40 °C and neutralized with 5 N ammonium hydroxide solution.

The mixture was divided in half and the following reactions carried out on each portion.

The solution was stirred slowly and ca. 1.5 mL of 2 N cupric chloride solution was added. The pH was adjusted to 5–6 by the addition of 5 N ammonium hydroxide solution.

The precipitate was carefully washed with 25 mL of 20% ammonium chloride solution, two 20-mL portions of 95% ethanol, and two 15-mL portions of cold water. The product was slurried with 50 mL of water and treated dropwise with an ice-cold solution of 3.2 g of sodium hydroxide in 10 mL of water. The resulting yellow-orange

suspension was continually extracted with hexane for 48 h. The hexane extracts were dried over magnesium sulfate, the solvent removed in vacuo, and the product distilled affording 5.0 g (0.024 mol), 66% of theoretical, of a water white liquid: bp 100–102 °C (0.05 mmHg); $\lambda_{\text{max}}^{\text{hexane}}$ 350 nm (ϵ 140); IR (film) 6.65 (w), 8.80 (s), 13.45 (s), 14.30 μ (s); NMR (CCl₄) δ 0.86 (m, 2), 1.83 (m, s), 3.22 (s, 1), 4.28 (s, 2), 4.68 (m, 2), 7.2 ppm (s, 5).

Anal. (C₁₂H₁₄N₂O) C, H, N.

7-*tert*-Butoxy-2,3-diazabicyclo[2.2.1]hept-2-ene (14c). A mixture of 13.0 g (0.056 mol) of alcohol **13a**, 250 mL of isobutylene, 4 mL of concentrated sulfuric acid, and 125 mL of methylene chloride was shaken on a mechanical shaker for 12 h.⁴² The excess isobutylene was then blown off under a stream of nitrogen, and the reaction mixture carefully added to an ice-cooled saturated sodium bicarbonate solution. The layers were separated and the organic layer was washed with saturated brine and dried over magnesium sulfate. The methylene chloride was removed under pressure and the residue hydrolyzed and oxidized as described for the 7-benzyl ether **13b**. The residue from the hydrolysis-oxidation was sublimed at 45 °C (0.07 mmHg) to afford 5.54 g (0.033 mol), 59% of theoretical, of *tert*-butyl ether **14**: mp (sealed capillary) 95.5–98.5 °C; $\lambda_{\text{max}}^{\text{hexane}}$ 395 nm (ϵ 141); IR (film) 6.65 (w), 7.16 (w), 7.31 (m), 8.81 μ (s); NMR (CCl₄) δ 0.91 (m, 2), 1.18 (s, 6), 1.19 (m, 2), 3.48 (bs, 1), 4.77 ppm (m, 2).

Anal. (C₉H₁₆N₂O) C, H, N.

***endo*- and *exo*-5-Benzyloxybicyclo[2.1.0]pentane (6b and 5b).** A solution of 4.70 g (0.023 mol) of the azo benzyl ether **14b** in 700 mL of hexane was photolyzed with an internally water-cooled mercury arc lamp (Hanovia, 450 W) with a Pyrex filter. The progress of the reaction was monitored by the decrease in the azo absorption at 350 nm. After 6 h the reaction had progressed to 90% completion. The hexane was then removed in vacuo and the residue distilled to afford 3.0 g (0.019 mol, 83%) of a clear, colorless liquid: bp 60–61 °C (0.05 mmHg); IR (film) 3.24 (m), 3.35 (m), 8.42 (s), 9.51 (s), 13.62 (s), 14.36 μ (s). The NMR spectrum of the photoproduct is actually a superimposition of the NMR spectra of *endo*- and *exo*-5-benzyloxybicyclo[2.1.0]pentane (**6b** and **5b**). Examination of the relative areas of the benzylic proton absorptions at 4.50 and 4.45 ppm reveals that the ratio of the *endo* isomer to the *exo* isomer is 75:25. The 5 proton in the *endo* isomer appears at 3.28 ppm as a triplet ($J = 5$ Hz), while the proton in the *exo* isomer appears as a singlet at δ 3.37 ppm.

Treatment of the 75:25 mixture of *endo*:-*exo*-5-benzyloxybicyclo[2.1.0]pentane with a few small drops of trifluoroacetic acid caused the *endo* isomer to rearrange to 3-benzyloxycyclopentene within 5 min. Under the same condition the *exo* isomer is relatively inert. After 33 h the *exo* isomer has been converted into a compound believed to result from the addition of trifluoroacetic acid across the internal cyclopropyl bond.

Hydrogenolysis of *endo*- and *exo*-5-Benzyloxybicyclo[2.1.0]pentane (6b and 5b). A mixture of *endo*- and *exo*-5-benzyloxybicyclo[2.1.0]pentane (75:25), 205 mg (1.1 mmol), 50 mL of pentane, and 100 mg of 10% palladium on charcoal was shaken on a Parr hydrogenator under 3 atm of hydrogen for 5 h. After filtration and concentration of the solution, GLC analysis of a 12-ft Carbowax column revealed the presence of cyclopentanol in 89% yield.

***exo*-5-Benzyloxybicyclo[2.1.0]pentane (5b).** The separation of the *exo* benzyl ether **5b** from its *endo* isomer was accomplished by the following sequence. An alumina column (Woelm neutral, activity grade I, 30 g, containing 0.60% water by weight) was prepared as a slurry in carbon tetrachloride. The *endo*-*exo* mixture of bicyclic benzyl ethers (2.00 g) was placed on the column and eluted with carbon tetrachloride. As the mixture moved down the column mild warming was noted. Elution with 200 mL of carbon tetrachloride afforded 1.42 g of a mixture of 3-benzyloxycyclopentene (ca. 55%) and the bicyclic benzyl ethers. This mixture was dissolved in 100 mL of purified pentane and cooled in a dry ice-acetone bath. Ozone-enriched oxygen (1.6 mmol/min) was passed through the solution until it was saturated. The amorphous ozonide was removed by rapid filtration. The filtrate was then passed through an alumina column (neutral, activity grade III), 10 g, and the eluant concentrated under reduced pressure. The residue was evaporatively distilled to afford 560 mg of a water white liquid, bp 62 °C (0.04 mmHg). Examination of the NMR spectrum of the distillate revealed the presence of a 56:44 mixture of *exo*- and *endo*-5-benzyloxybicyclo[2.1.0]pentane (**5b** and **6b**). The 56:44 mixture was treated exactly as above using 10 g of alumina, activity grade I, containing 0.60% water by weight. Ozonolysis, chromatography, and distillation afforded 265 mg of *exo*-5-benzyloxybicyclo[2.1.0]pentane (**5b**): bp 62 °C (0.04 mmHg); IR (film) 3.22 (w),

3.35 (m), 8.70 (s), 13.62 (s), 14.35 μ (s); NMR (CCl₄) δ 1.20–1.40 (m, 2), 1.68 (m, 2), 1.90–2.18 (m, 2), 3.37 (s, 1), 4.45 (s, 2), 7.22 ppm (s, 5).

exo-5-Benzyloxybicyclo[2.1.0]pentane (**5b**) was cleanly isomerized to 3-benzyloxycyclopentene upon attempted GLC through a 2-ft silicone gum rubber column (Chromosorb W) at 135 °C.

Hydrogenation of *exo*-5-Benzyloxybicyclo[2.1.0]pentane (5b). A mixture of 200 mg of *exo*-5-benzyloxybicyclo[2.1.0]pentane (**5b**), 35 mL of pentane, and 100 mg of 10% palladium on charcoal was shaken with hydrogen on a Parr hydrogenator. After filtration and concentration of the solution, GLC analysis on a 1.5-ft FFAP column revealed the presence of 75% of the theoretical amount of cyclopentanol.

***endo*- and *exo*-Bicyclo[2.1.0]pentan-5-ol (6a and 5a).** Under an argon atmosphere, 1.74 g (0.01 mol) of a 75:25 mixture of the bicyclic benzyl ethers **6b** and **5b** in 30 mL of ether was added to approximately 250 mL of liquid ammonia. Small pieces of clean sodium metal were added until a deep blue color remained for 15 min. The reaction mixture was quenched by the careful addition of 1.10 g (0.02 mol) of anhydrous ammonium chloride. After the ammonia was evaporated, the residue was triturated well with pentane. The pentane was removed very carefully under reduced pressure and the residue evaporatively distilled to afford 510 mg (6 mmol, 60%) of a mixture of the bicyclic alcohols **6a** and **5a** (60%). The receiver flasks were cooled in dry ice because of the volatility of the bicyclic alcohols: bp 65–70 °C (5 mmHg); IR (film) 3.00 (s), 3.25 (m), 8.45 (s), 12.50 μ (m); NMR (CCl₄) δ 1.20–2.30 (cp, 6), 3.63 (cp, 1, $J = 5$ Hz), 5.30 ppm (s, 1).

Addition of D₂O gave the same NMR spectrum except for the absence of the peak at δ 5.30 ppm. The absorption at δ 3.63 ppm is actually a superimposition of the singlet for the 5 proton in the *exo* alcohol and the triplet ($J = 5$ Hz) for the 5 proton in the *endo* alcohol.

Following the same procedure for the pure *exo* benzyl ether, one obtained a 73% yield of the corresponding *exo* alcohol: NMR (CCl₄) δ 1.20–2.30 (cp, 6 H), 3.63 (s, 1 H), 5.30 ppm (s, 1 H, removable upon shaking with D₂O).

***exo*-Bicyclo[2.1.0]pentan-5-ol *p*-Nitrobenzoate (5d).** The alcohol (0.275 g, 3.27×10^{-3} mol) as calculated to be present by an NMR spectrum of the mixture of products obtained from the cleavage of the benzyloxy protecting group, 0.25 mL of dry pyridine, and 10 mL of CCl₄ were mixed together and cooled in a ice-salt bath. Recrystallized *p*-nitrobenzoyl chloride (0.573 g, 3.09×10^{-3} mol) was added to the solution. The mixture was then filtered to remove the pyridinium hydrochloride, and the solvent removed in vacuo. The product was washed with cold pentane and recrystallized from hexane. In this manner, the product with mp 91.8–92.4 °C was obtained in 61% yield (0.4419 g): IR (KBr) 3.1 (w), 3.40 (w), 5.81 (s), 6.22 (m), 6.53 (s), 7.96 (s), 8.87 μ (s); NMR (CDCl₃) δ 1.60 (bd, $J = 6$ Hz, 2 H), 1.90 (m, 2 H), 2.23 (m, 2 H), 4.47 (s, 1 H), 8.21 ppm (d, $J = 2$ Hz, 4 H).

Anal. (C₁₂H₁₁NO₄) C, H, N.

***endo*- and *exo*-5-Acetoxybicyclo[2.1.0]pentane (6e and 5e).** The preparation of derivatives of the bicyclic alcohols directly from the bicyclic benzyl ethers was carried out as follows. The mixture of the bicyclic benzyl ethers in ether was dissolved in liquid ammonia. Under a nitrogen atmosphere small pieces of clean sodium were added slowly until the deep-blue color remained for 15 min. Excess sodium was discharged by the addition of enough of the bicyclic benzyl ethers to yield a colorless mixture. After the ammonia was evaporated, the salts were suspended in pentane and cooled in a dry ice-acetone bath. The appropriate acylating agent was added slowly, and the mixture allowed to stir at –78 °C for 1 h. The salts were then filtered off and the pentane removed under reduced pressure to yield the crude derivative.

Treatment of a 75:25 mixture of *endo*- and *exo*-5-benzyloxybicyclo[2.1.0]pentane (**6b** and **6a**) as described above, followed by acylation with acetyl chloride, afforded a 75:25 mixture of the *endo* and *exo* bicyclic acetates, free of any of the olefin isomer. The 5 proton in the *endo* isomer appeared as the characteristic triplet at δ 4.37 ppm ($J = 5$ Hz) in the NMR spectrum of the mixture, while the 5 proton in the *exo* isomer appeared as the characteristic singlet at δ 4.22 ppm.

endo-5-Acetoxybicyclo[2.1.0]pentane (**6e**) was remarkably reactive. Warming a carbon tetrachloride solution of the mixture of the bicyclic acetates resulted in the clean and complete conversion of the *endo* acetate into 3-acetoxycyclopentene within 15 min! Under the same conditions the *exo* acetate is unaffected.

3-Cyclopentenol. 3-Cyclopentenol was prepared by the method of Alder and Flock in 66% yield⁴³ by the addition of hydrogen chloride to cyclopentadiene to form 3-chlorocyclopentene followed by alkaline hydrolysis: bp 63–65 °C (13 mmHg) (lit.⁴³ 52 °C (12 mmHg)), IR (film) 2.95 (s), 3.22 (w), 9.55 μ (s).

3-Benzyloxycyclopentene (19b). Under a nitrogen atmosphere, 8.4 g (0.10 mol) of 3-cyclopentenol in 100 mL of dry benzene was added dropwise with vigorous stirring to sodium hydride, 3.1 g (0.11 mol, 85% active hydride), in 100 mL of dry benzene. When the addition was complete, the mixture was heated to reflux for 1 h. The reaction mixture was then cooled to room temperature and 11.3 g (0.09 mol) of benzyl chloride in 25 mL of dry benzene was added dropwise. The reaction mixture was then refluxed for 10 h. The excess hydride was destroyed by the careful addition of an ethanol-ether mixture. The benzene layer was then washed with saturated brine and dried over magnesium sulfate. The benzene was removed in vacuo and the product distilled yielding 11.0 g (0.07 mol, 70%) of a water-white liquid: bp 56.5–57 °C (0.5 mm); IR (film) 3.25 (m), 6.18 (w), 9.35 (s), 14.41 μ (s); NMR (CCl₄) δ 1.63–2.58 (cp, 4), 4.40 (s, 2), 4.31–4.72 (cp, 1), 5.86 (s, 2), 7.22 ppm (cp, 5).

3-Cyclopentenyl *p*-Nitrobenzoate (19c). A solution of 420 mg (5.0 mmol) of 3-cyclopentenol in 4 mL of dry pyridine was cooled in an ice-salt bath. *p*-Nitrobenzoyl chloride (1.02 g, 5.5 mmol) was added portionwise. The mixture was then stirred for 0.5 h. After the addition of ice, the chloride dissolved and then the crude *p*-nitrobenzoate precipitated. The precipitate was collected, washed well with water, and dried in a vacuum desiccator over calcium chloride. Recrystallization from hexane afforded 930 mg (4 mmol, 85%) of white leaves: mp 76–78 °C; IR (CHCl₃) 5.81 (s), 6.19 (m), 7.82 (s), 8.92 μ (s); NMR (CDCl₃) δ 1.75–2.67 (cp, 4), 5.83–6.30 (cp, 3), 8.20 ppm (s, 4).

Titrimetric Kinetics. Titrant. Sodium methoxide, in anhydrous methanol, approximately 0.01 M, was used as the titrant in all cases. It was prepared by dissolving the calculated amount of sodium metal in dry, distilled, reagent grade methanol. Standardization was performed by titration against a known solution of primary potassium acid phthalate to a phenolphthalein end point.

Acetone. Reagent grade acetone was dried according to the procedure of Smith.⁴⁴ The acetone obtained was distilled from a small amount of powdered molecular sieves (type 4A) immediately before use and then degassed with argon.

Aqueous Acetone. The aqueous acetone solutions (in volume percent) were prepared by mixing aliquots of freshly dried acetone (measured via syringe) with the appropriate amount of ion-resin exchanged distilled water which had been boiled and cooled while an argon stream was passed through it.

Sealed-Tube Technique. Pyrex Carius tubes (13 × 7 × 300 mm) were scrubbed with an Alconox solution, rinsed with cold water a number of times, and then rinsed with distilled water ten times and dried in an oven at 120 °C. The same procedure was used for all glassware needed in the measurements except for the buret and the 1-mL constant-dropping pipet. The buret and the pipet were both cleaned with chromic acid and then continuously rinsed with water and finally rinsed at least ten times with distilled water. The buret was conditioned with the sodium methoxide solution and the pipet was dried in an oven at 120 °C. The Carius tubes were flushed with argon and a 3-mL portion of the sample was added under an argon umbrella. The tube was corked and cooled in a salt-ice bath and sealed with an oxygen torch.

The tubes were immersed, all at once, into a constant-temperature bath (± 0.1 °C), 10 min was allowed for equilibration of the tubes, and then the *t*₀ tube was withdrawn.

Titration was accomplished by transferring a 1.00-mL aliquot into a 10-mL Erlenmeyer flask. Bromothymol blue indicator (3 drops, 1% by weight in 50% ethanol) was added and the sample was titrated with sodium methoxide to the green end point.

NMR Kinetics and Product Studies of *exo*-Bicyclo[2.1.0]pentan-5-yl *p*-Nitrobenzoate (5d) in 80% Acetone-*d*₆-D₂O at 95.8 \pm 0.2 °C. A 0.128 M solution of the title ester was made by addition of 0.1496 g of the ester to a 5.00-mL volumetric flask of 80% acetone-*d*₆-20% D₂O by volume. A portion of this sample was put into a NMR tube which had been degassed with argon. The tube was sealed and the rate measured at 95.8 \pm 0.2 °C. The rate constant was (3.7 \pm 0.2)10⁻⁵ s⁻¹. When another sample was made with a 0.360 M concentration of 2,6-lutidine present, the identical rate constant and error were obtained. The rate and product composition were obtained by NMR analysis.

NMR Kinetics and Product Studies of 3-Cyclopentenol *p*-Nitrobenzoate (19c) in 80% Acetone-*d*₆-D₂O at 75.5 \pm 0.2 and 95.8 \pm 0.2 °C. The data obtained in this series are the result of using the identical method outlined above. The proton of the starting material which is allylic to the double bond and geminal to the *p*-nitrobenzoate functionality absorbs 0.84 ppm upfield from the 2,6-lutidine doublet. Apparently because the concentration of cyclopentadiene product is low, no dimer of it is observed.

NMR Thermolysis at 135 °C of *exo*-5-Benzyloxycyclopentane (5b) in Bromobenzene. A sample of 5b, 30% by volume, was sealed into an NMR tube under argon. The spectrum was recorded. Absorptions appeared between 1.0 and 2.0 (cm, *exo* and *endo* H₂ and H₃ protons and H₁ and H₄ protons), at 3.20 (s, *endo* H₅), and at 4.25 ppm (s, benzyloxy protons). The aromatic region was submerged under the bromobenzene. After the sample was heated for 1.50 h in a constant-temperature bath absorptions at 3.12 (t, *J* = 5 Hz) and 4.30 ppm (s) appeared, which are assigned to the *endo* epimer 6b. Absorptions at 4.26 (shoulder) and 5.79 ppm (bs) also appeared to a smaller extent. These absorptions are reasonably assigned to 3-benzyloxycyclopentene (19b). The ratio of 5b:6b:19b is found to be 9.0:8.0:2.8 by integrating the 3.20 s, the 3.12 t, and the 5.79 ppm bs (correcting for 2 H), respectively.

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Synthesis and Stereomutation of 5-Substituted Bicyclo[2.1.0]pentanes

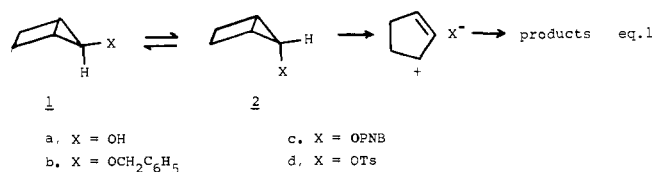
Joseph J. Tufariello,* Jun Hsin Chang, and Arthur C. Bayer

Contribution from the Department of Chemistry, State University of New York at Buffalo, Buffalo, New York 14214. Received August 25, 1978

Abstract: A synthetic route has been devised to provide access to a number of 5-substituted bicyclo[2.1.0]pentanes, including those bearing π -acceptor substituents (i.e., *exo*- and *endo*-5-cyanobicyclo[2.1.0]pentane and *exo*- and *endo*-5-carbomethoxybicyclo[2.1.0]pentane). The thermochemically induced stereomutation of these isomeric compounds was studied, and their activation parameters were contrasted with those of bicyclopentanes bearing π -donor (e.g., OPNB) substituents. The findings are consistent with substituent effects involving a resonance interaction that influences the stability of the ground-state molecules, and/or an effect acting at the transition state (or biradical state) which involves the electronegativity of the attached substituent.

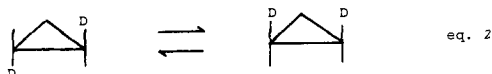
Introduction

It has been suggested^{1–3} that suitably 5-substituted (e.g., OPNB, OTS) bicyclo[2.1.0]pentyl derivatives undergo solvolysis according to the following mechanistic scheme (eq 1).



This suggestion is consistent with the observation that the solvolysis of **1c**^{1,2} and **1d**³ is independent of solvent polarity, and that the rate constants for the solvolysis of these compounds are virtually independent of the nature of the leaving group since the rate-limiting step involves bicyclopentane isomerization (i.e., **1c** → **2c** and **1d** → **2d**), and not ionization.

The thermal isomerization of cyclopropanes has attracted considerable attention^{4,5} (e.g., eq 2) with processes involving



diradicals, single methylene rotation, double methylene rotation, and even triple methylene rotation being considered.⁴ Our

work does not permit us to comment with regard to whether the diradical **3** plays the role of an intermediate or is merely



a representation of the transition state in the bicyclopentane isomerizations; however, it was found recently⁶ that the photolysis of 2,3-diazabicyclo[2.2.1]hept-2-ene at 1 K produced the triplet ground state of diradical **3** ($\Delta E_{ST} < 2$ kcal/mol). These workers suggest a potential surface bearing no minimum with singlet character, a finding in accord with theoretical calculations on trimethylene.⁷

What is most remarkable about the **1c** ⇌ **2c** stereomutation is the magnitude of the activation barrier, $E_a = 29.2$ kcal/mol, calculated from our solvolytic data.¹ In contrast, most simple bicyclopentanes (e.g., **4**, **5**, and **6**) exhibit isomerization barriers 5–10 kcal/mol higher than those noted for **1c**^{1,2} and **1d**.³ Only in the case of **7**, where the spiro system can reasonably be expected to lower the observed barrier, does *exo*-*endo* isomerization become as energetically favorable. This raises the question of the nature of the substituent effect that is apparently operating at the 5 position in **1**.

Hoffmann¹¹ and Günther¹² proposed a theoretical rationale to account for the effect of substituents on equilibria involving substituted cyclopropyl systems. Using a treatment