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

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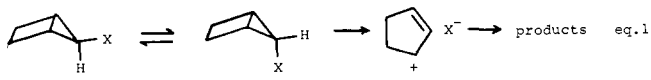
Abstract: A synthetic route has been devised to provide access to a number of 5-substituted bicyclo[2.1.0]pentanes, including those bearing π-acceptor substituents (i.e., *exo*- and *endo*-5-cyanobicyclo[2.1.0]pentane and *exo*- and *endo*-5-carbomethoxybicyclo[2.1.0]pentane). The thermochemically induced 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).

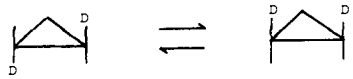


1 **2**

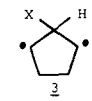
a, X = OH
b, X = $OCH_2C_6H_5$
c, X = OPNB
d, X = OTs

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



3

a representation of the transition state in the bicyclopentane isomerizations; however, it was found recently[6] 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.**

Hoffmann[11] and Günther[12] proposed a theoretical rationale to account for the effect of substituents on equilibria involving substituted cyclopropyl systems. Using a treatment

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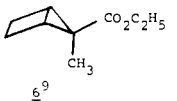
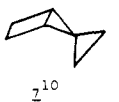
4[8] E_a = 38.9 kcal/mole

5[9] E_a = 34-36 kcal/mole



6[9] E_a = 37-38 kcal/mole



7[10] E_a = 29 kcal/mole

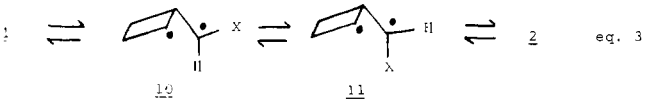
based on Walsh orbitals, these workers suggested that electron-supplying π-donor substituents (e.g., OR, NR_2) should weaken the cyclopropyl bond (antibonding interaction) remote from the substituent by a resonance effect involving electron supply into ψ_4 (cf. **8**). In contrast, substituents capable of

8 9

electron withdrawal by resonance (e.g., CO_2Me, CN) should strengthen the same bond by diminishing an antibonding interaction in ψ_3 (cf. **9**). Indeed, it has been suggested that π-acceptors may induce larger effects than π-donor substituents.[13b] These concepts were able to correlate much of what was then known regarding cycloheptatriene-norcaradiene equilibria,[14] including ground-state effects on related systems.[15] Since this hypothesis achieved such apparent success in treating thermodynamic effects, it was of considerable interest to learn whether the kinetic effects noted in our bicyclopentyl systems could be treated similarly. Toward this end, we devised a synthetic approach capable of introducing π-acceptor substituents to complement our earlier synthetic efforts designed to introduce oxygen (π donor) substituents at C-5. Moreover, we sought to determine whether the bicyclopentane isomerizations might proceed other than by involvement of the C_1-C_4 bond.

Central Bond Involvement

The large apparent effect of π-donor (i.e., OR) substitution at C-5 in lowering the activation barrier for *exo-* ⇄ *endo*-bicyclo[2.1.0]pentane isomerization might be explained if one of the external bonds (i.e., C_1-C_5 or C_4-C_5) was involved in the process of stereomutation to afford an intermediate resembling **10** (or **11**).[16] Alternatively, the stereomutation at C-5

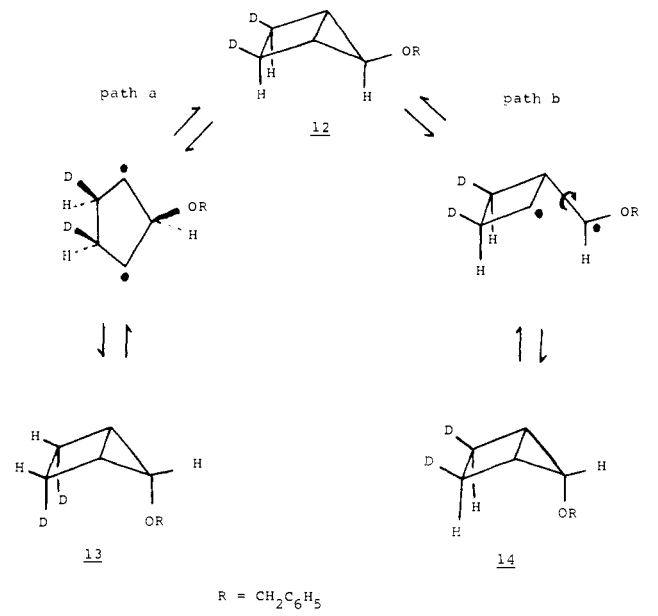


10 11 eq. 3

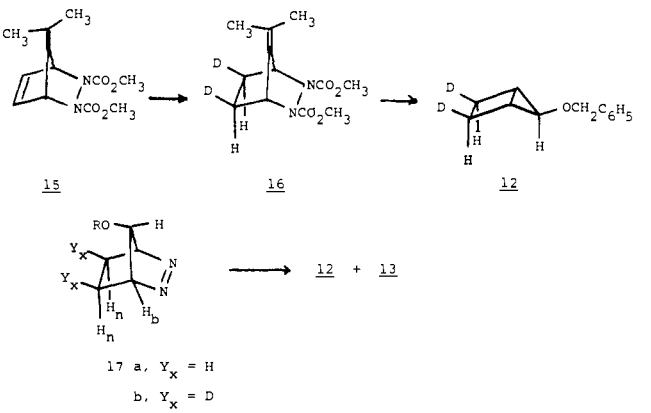
might be attributed to a concerted single rotation mechanism without definable intermediates.[4a] A process resembling that depicted in eq 3 is tempting in that it appears to rationalize the large substituent effect noted since the oxygen function (e.g., X = OPNB) is directly bound to a radical-bearing carbon. In order to distinguish between external and internal (C_1-C_4) bond involvement in the stereomutation process, we sought to prepare *exo,exo*-2,3-dideuterio-*exo*-5-benzyloxybicyclo-[2.1.0]pentane (**12**). Thermal isomerization of **12** (Scheme I) would afford endo,endo-dideuterio endo ether **13** as a result of internal bond involvement and exo,exo-dideuterio endo ether **14** from external bond involvement.

We prepared **12** by the selective catalytic addition of deuterium gas to **15** to afford **16,** followed by conversion of the latter into **12** by our previously outlined route.[1,17] The final step in this transformation involves the photolytic decomposition of azocycloalkane **17b** into a mixture of **12** and **13**. The diprotio

Scheme I. External (Path b) and Internal (Path a) Cyclopropyl Bond Cleavage



isomer **17a** displays absorptions at δ 0.96 (H_n, dd, J = 10, 4 Hz) and 1.86 ppm (H_x, bd, J = 10 Hz). In both the norbornene system[18] and in the closely related 2,3-diazabicyclo[2.2.1]-hept-2-ene[19] the endo protons appear substantially upfield of their exo counterparts. The δ 0.96 ppm signal simplifies to a broadened singlet in the dideuterated analogue, whereas the pattern at δ 1.86 ppm is no longer exhibited by **17b.** This in-



dicates that the deuteriums were introduced in the exo configuration as anticipated.[19] This indication is supported by the singlet nature at the δ 0.96 ppm signal, indicating a lack of coupling to the bridgehead protons, demanded by the unfavorable dihedral angle relationship between H_n and H_b.[18]

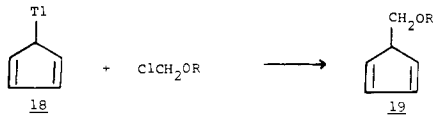
A pure sample of exo benzyl ether **12** could be separated from the photolysis mixture.[1] The endo protons at C_2 and C_3 appear as a broad singlet at δ 1.26 ppm. Deuteration has removed the multiplet, assigned to the corresponding exo protons, at δ 1.90-2.18 ppm in **1b.** These assignments are consistent with the assignments on bicyclo[2.1.0]pentane itself.[19] That the δ 1.75 ppm signal, due to the bridgehead hydrogens, is a singlet suggests a configuration with exo deuteriums because exo hydrogens at C_2 and C_3 should result[26] in observable coupling ($J \sim 4$ Hz) to the bridgehead hydrogens. On the other hand, from published reports,[26] the coupling between the endo hydrogens and the bridgehead hydrogens is expected to be small. The singlets belonging to **13** were readily identified from the photolysis mixture by subtracting the absorptions belonging to **12** (cf. Experimental Section).

When **12** was heated at 95 °C in benzene-d_6, an NMR examination clearly showed a conversion of **12** into **13**. The ap-

pearance of the NMR spectrum, after 86 h, is identical in every respect, except for integration, with that of the 3:1 mixture of **12** and **13** obtained in the photodecomposition of **17b**. We see no sign of the singlet at δ 1.70 ppm expected for the endo protons (i.e., at C_2 and C_3) of **14** (Scheme I).[20] Thus, the stereomutation must largely, or entirely, proceed via path a (Scheme I). The observed involvement of the internal bond rules out a direct, radical stabilizing influence (i.e., as in **10**) of the 5-substituent as being responsible for the facile exo-endo interconversion.[21] Moreover, the alternative concerted single rotation pathway (vide supra) is simultaneously rendered untenable. This finding suggests that the resonance effect of π donors to destabilize the ground state of cyclopropanes, and thereby facilitate stereomutation, must be considered carefully.[11,12] We chose to test the predictions of this theory with regard to π-acceptor substituents.

Bicyclopentane Synthesis

Our previous entry into the bicyclopentanes is unable to make provision for the requisite π-acceptor substituents (e.g., CO_2Me, CN). We therefore devised a route, still based in azoalkane chemistry, which would provide access to the desired compounds. Treatment of thallous cyclopentadienide with chloromethyl methyl ether can be arranged to produce dienyl ether **19a,** which can be trapped at −75 °C with 4-phenyl-



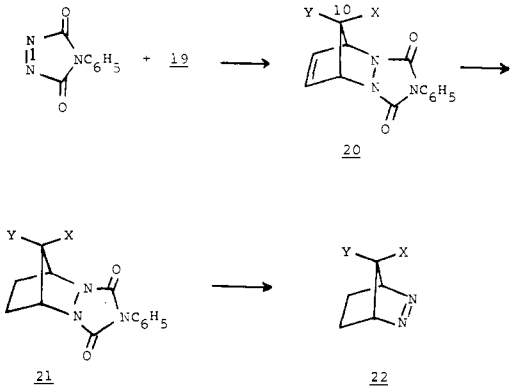
18 19

a, R = CH_3
b, R = $CH_2C_6H_5$

1,2,4-triazoline-3,5-dione[23,24] to afford a mixture of adducts, **20a** and **20b,** in quantitative yield (Scheme II). The NMR spectrum of this mixture displays two vinylic absorptions at δ 6.64 and 6.48 ppm and a pair of triplets at δ 3.58 and 3.28 ppm, attributable to the ether methylene protons (J = 6 Hz). This data, and the corresponding integration results, indicates the product to be a mixture of anti and syn epimers, **20a** and **20b,** in a 3:1 ratio, respectively. On the basis of earlier reports[22,24] that the Diels-Alder trapping of 5-substituted cyclopentadienes gives an exclusively anti orientation of substituents at C-10, we assign the anti stereochemistry[25] to the major product (i.e., **20a**). The isomeric mixture could be separated by careful fractional crystallization from a hexane-methylene chloride solvent mixture.

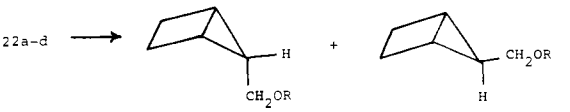
Both Diels-Alder adducts could be separately reduced to their corresponding dihydro adduct **21a** and **21b,** respectively.

Scheme II



a, X = H, Y = CH_2OCH_3
b, X = CH_2OCH_3, Y = H
c, X = H, Y = $CH_2OCH_2C_6H_5$
d, X = $CH_2OCH_2C_6H_5$, Y = H

Hydrolysis and oxidation produced the corresponding syn and anti azoalkanes (**22b** and **22a,** respectively).[27] The azo compound **22a** was subjected to photolysis using a low-pressure mercury lamp. The epimeric bicyclopentanes (**23a** and **24a**),



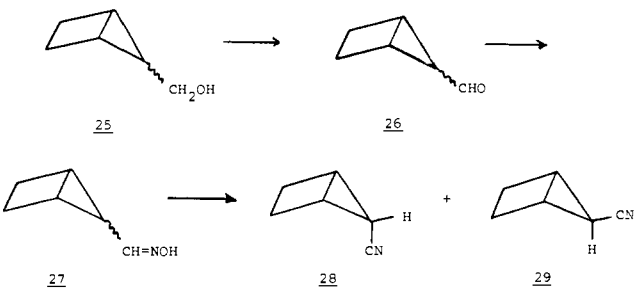
23 24

a, R = CH_3
b, R = $CH_2C_6H_5$

obtained in a combined yield of 82%, were separated by preparative gas chromatography. The ratio of the endo and exo epimers, obtained from the photolysis of azo compound **22a,** was shown to be 35:65, respectively, by NMR analysis of the photolysate. The endo epimer **23a** reveals a quintet at δ 1.12 ppm (J = 7 Hz) for its C-5 proton, while the corresponding exo epimer exhibits a triplet at δ 1.30 ppm (J = 7 Hz) for the same proton. This conforms to expectation since $J_{cis} > J_{trans}$ for vicinal coupling in cyclopropanes.[1,26] Indeed, we anticipated, on the basis of our earlier work,[1] not to detect coupling of the C-5 proton to the bridgehead hydrogens in **24a.** These assignments were further supported by double irradiation of the doublet at δ 3.66 ppm ($-OCH_2-$) in the NMR spectrum of **23a** and noting a collapse of the quintet at δ 1.12 ppm into a triplet (J = 7 Hz). A similar double irradiation of the doublet at δ 3.14 ppm ($-OCH_2-$) of **24a** collapses the triplet to a broadened singlet.

Since it was our intention to cleave the ether function as a means of generating π-acceptor substitution at C-5, we repeated the synthetic sequence (Scheme II) starting from chloromethyl benzyl ether. Alkylation of thallous cyclopentadienide with chloromethyl benzyl ether at −20 °C for 10 h was followed by the addition, at −78 °C, of 4-phenyl-1,2,4-triazoline-3,5-dione to give a 95:5 isomeric mixture of Diels-Alder adducts, **20c** and **20d,** respectively. Hydrogenation of this mixture was followed by the separation of the dihydro-adducts, **21c** and **21d,** on silica gel. The imide grouping was hydrolyzed, and the resulting hydrazine oxidized, to give azo ether **22c** (from **21c**) and **22d** (from **21d**). Photolysis of **22c** in benzene gave a 58:42 mixture of epimeric bicyclopentanes, **23b** and **24b,** while the same bicyclopentanes were obtained in a 39:61 ratio starting from **22d.** The stereochemical assignments were made in a manner analogous to that used for the methyl ethers (vide supra). We cleaved the benzyl ether mixture with sodium or lithium in liquid ammonia[1] to give a 58:42 ratio of epimeric alcohols, **25,** in 92% yield. These alcohols have been prepared independently by totally different approaches.[28]

The mixture of epimeric alcohols (**25**) was converted into the corresponding aldehydes **26** by oxidation with a chromium



25 26 27 28 29

trioxide-pyridine complex.[29] The epimeric mixture of aldehydes showed carbonyl absorption (IR) at 5.85 μ and a pair of doublets in the NMR spectrum at δ 8.90 and 9.90 ppm (CHO). The aldehyes were converted into the corresponding oximes, **27,** and thence into the 5-cyanobicyclo[2.1.0]pentanes, **28** and **29,** by dehydration with 1,1-carbonyldiimidazole in methylene chloride at ambient temperature. The overall yield

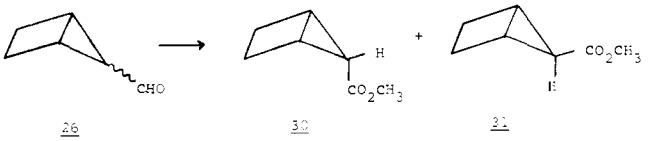
Table I. Kinetic and Equilibrium for the Epimerization of *endo*-5-Cyanobicyclo[2.1.0]pentane (**28**) in Benzene-d_6

temp, °C	k_{obsd}, s^{-1} [a]	K [b]	k_f, s^{-1} [c]	k_r, s^{-1} [d]
214.3 ± 0.2	5.617 ± 10^{-4}	0.423	1.67×10^{-4}	3.95×10^{-4}
204.7 ± 0.2	2.309×10^{-4}	0.396	6.55×10^{-5}	1.65×10^{-4}
195.0 ± 0.2	8.884×10^{-5}	0.412	2.58×10^{-5}	6.27×10^{-5}
184.4 ± 0.2	3.182×10^{-5}	0.393	8.98×10^{-5}	2.28×10^{-5}

[a] Observed rate constant = $k_f + k_r$. [b] Calculated equilibrium constant, $K = (A_{0,e} - a_{\infty,c})/(A_{\infty,c})$. [c] Rate constant of forward reaction, endo → exo. [d] Rate constant of reverse reaction, exo → endo.

from the alcohols, **25,** was 33%. The epimeric cyano compounds were separated by preparative gas chromatography. The major component isolated was the endo epimer **28,** exhibiting a one-proton triplet (NMR, C_6D_6) at δ 1.02 ppm (J = 5 Hz) for the C-5 exo proton. The minor component, exo isomer **29,** displays its endo C-5 proton at δ 0.94 ppm.

Treatment of the mixture of aldehydes **26** with silver oxide afforded a mixture of epimeric carboxylic acids, from which the corresponding mixture of methyl esters (**30** and **31**) could



26 30 31

be prepared, using diazomethane, in 44% overall yield from the alcohols (**25**). Chromatography of the ester mixture on silica gel gave the pure components, **30** and **31,** in a 1.4:1 ratio. The more rapidly eluting component was assigned the endo configuration on the basis of its NMR spectrum, which revealed a triplet at δ 1.68 ppm, characteristic of an exo proton at C-5. The second component displayed a singlet at δ 1.80 ppm associated with the corresponding endo proton at C-5.

Thermochemical Studies

With the availability of bicyclopentanes substituted with π acceptors at C-5, we were equipped to contrast the effect such substituents had on the stereomutation process with the effects noted for π-donor substituents. Thermolytic studies for *endo*-5-cyanobicyclo[2.1.0]pentane (**28**) were carried out in benzene-d_6. The ratio of endo and exo isomers was determined by GLC analysis. It was found that no olefin was formed over a 40-h period at 220 °C. The endo/exo composition at the end of this period was 2.22:1.00, only slightly different from the 2.17:1.00 ratio 13 h earlier, indicating a close approach of this system to equilibrium. That there is no observable olefin production under these conditions indicates that the activation barrier to olefin formation is considerably higher, relative to isomerization, than in the 5-benzyloxy,[1,30] 5-trimethylsilyl,[31] and 5-methoxymethyl[32] analogues.

The kinetic measurements were carried out by GLC analysis, integrating the peak areas against an internal standard of *n*-butylbenzene. The rate measurements were made at 184.4, 195.5, 204.7, and 214.3 °C. The rate constants, k_{obsd}, for the disappearance of endo-cyano compound **28** were calculated by using the FOK FORTRAN IV computer program of Ritchie.[33] Thus program utilizes the first-order rate equation

$$A_i = \Delta A e^{-k_{obsd} t_i} + A_\infty$$

where A_i is the concentration at time t_i, ΔA is the difference between the initial concentration, A_0, and the final concentration, A_∞, and k_{obsd} is the pseudo-first-order rate constant (i.e., observed rate constant). The latter is calculated by minimization of the quantity

$$\sum_i [A_i - A_\infty - (\Delta A) \exp(-k_{obsd} t_i)]^2$$

Table II. Activation Parameters for the Epimerization of 5-Substituted Bicyclo[2.1.0]pentanes

reaction	E_a, [a] kcal/mol	ln A [b]	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
28 → **29**	43.2 ± 0.5	35.89 ± 0.50	42.3 ± 0.9	9.98 ± 1.01
29 → **28**	42.4 ± 0.4	35.94 ± 0.42	41.5 ± 0.8	10.06 ± 0.82
30 → **31**	36.6 ± 1.1	31.61 ± 1.22	35.7 ± 1.5	1.44 ± 2.42
31 → **30**	39.4 ± 1.4	32.59 ± 1.57	38.5 ± 1.8	3.37 ± 3.11

[a] Errors were evaluated from the standard deviation of the slope of the Arrhenius plots. [b] Errors were evaluated from the standard deviation of the intercept of the Arrhenius plots.

Table III. Kinetic and Equilibrium Data for the Epimerization of *endo*-5-Carbomethoxybicyclo[2.1.0]pentane (**30**) in Bromobenzene-d_5

temp, °C	k_{obsd}, s^{-1} [b]	K [b]	k_f, s^{-1} [c]	k_r, s^{-1} [d]
180.2 ± 0.2	1.316×10^{-4}	8.617	1.18×10^{-4}	1.37×10^{-5}
165.3 ± 0.2	3.527×10^{-5}	9.381	3.19×10^{-5}	3.40×10^{-6}
150.2 ± 0.2	7.249×10^{-6}	10.753	6.63×10^{-6}	6.07×10^{-7}

[a] Observed rate constant = $k_f + k_r$. [b] Calculated equilibrium constant, $K = (A_{0,e} - A_{\infty,c})/(A_{\infty,c})$. [c] Rate constant of forward reaction, endo → exo. [d] Rate constant of reverse reaction, exo → endo.

with respect to k_{obsd}, ΔA, and A_∞ (cf. Experimental Section). From the calculated final concentration,[33] $A_{\infty,c}$, and the experimentally determined initial concentration, $A_{0,e}$, the equilibrium constant, $K = (A_{0,e} - A_{\infty,c})/A_{\infty,c}$, for the interconversion of endo and exo isomers was obtained. Using the observed rate constant, k_{obsd}, and the equilibrium constant, K, the rate constant of the forward (endo → exo), k_f, and that of the reverse reaction, k_r, can be calculated. The pertinent results are summarized in Table I. Excellent linear Eyring plots were obtained for cyano compounds **28** and **29,** respectively. From these plots, the activation parameters ($\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$, E_a, and ln A) were determined (cf. Table II).

The thermolysis of pure *endo*-5-carbomethoxybicyclo[2.1.0]pentane (**30**) in benzene-d_6 was monitored by NMR spectroscopy. No olefin production was noted under the conditions utilized. The kinetic determinations on the interconversions of exo and endo isomers were carried out at 150.2, 165.3, and 180.2 °C and were monitored by integration (NMR) of the methyl ester signal relative to an internal standard (*n*-butylbenzene). The rate and equilibrium constants were determined as noted above (Table III).

The equilibrium data for some substituted bicyclo[2.1.0]-pentanes are summarized in Table IV. Of the systems listed, only the 5-cyano- and 5-benzyloxybicyclo[2.1.0]pentanes provide an equilibrium mixture enriched with the endo epimer. We suggest that in these two cases the steric involvement of the 5 substituent with the endo protons of the ethano bridge is minimized.[9] Another important steric interaction involves the nearly eclipsing involvement of the 5 substituent with the bridgehead protons at C_1 and C_4. A substantial contribution

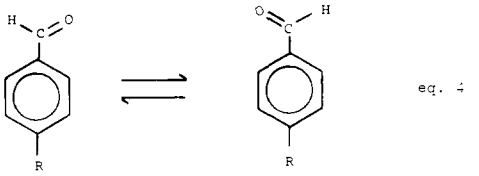
Table IV. Equilibrium Data for Substituted Bicyclo[2.1.0]-pentanes

Reaction	temp, °C	K	ΔG, kcal/mol	ref
28 → 29	214.3	0.423	0.833	this work
	204.7	0.396	0.879	this work
	195.0	0.412	0.825	this work
	184.4	0.393	0.849	this work
30 ⇄ 31	180.2	8.617	−1.940	this work
	165.3	9.381	−1.950	this work
	150.2	10.753	−1.997	this work
23b ⇄ 24b	155.0	4.052	−1.190	this work
2b ⇄ 1b	95.0	0.075	1.891	1
I[a] ⇄ II[b]	220.0	0.172	1.724	45
	198.9	0.166	1.684	45
	135.0	0.148	1.549	45
III[c] ⇄ IV[d]	242.8	1.754	−0.576	8
	203.3	1.667	−0.484	8
V[e] ⇄ VI[f]	150.1	0.225	1.254	9
	159.6	0.233	1.235	9
VII[g] ⇄ VIII[h]	139.9	0.355	0.863	9
	150.1	0.403	0.764	9
	159.6	0.431	0.724	9

[a] *endo*-2-Methoxybicyclo[2.1.0]pentane. [b] *exo*-2-Methoxybicyclo[2.1.0]pentane. [c] *endo*-2-Methylbicyclo[2.1.0]pentane. [d] *exo*-2-Methylbicyclo[2.1.0]pentane. [e] *exo*-5-Methyl-*endo*-5-carboethoxybicyclo[2.1.0]pentane. [f] *exo*-5-methyl-*exo*-5-carboethoxybicyclo[2.1.0]pentane. [g] 1-Methyl-*exo*-5-methyl-*endo*-5-carboethoxybicyclo[2.1.0]pentane. [h] 1-Methyl-*endo*-5-methyl-*exo*-5-carboethoxybicyclo[2.1.0]pentane.

from these interactions would encourage the substituent to adopt an endo orientation. A balance of these factors appears to favor an endo orientation only for small (i.e., A value of 0.9 kcal/mol for ethoxyl and 0.2 kcal/mol for cyano)[34] or linear groupings, and an exo preference for the rest.

The activation parameters for the epimerization of the 5-cyano- and 5-carbomethoxybicyclo[2.1.0]pentanes are included in Table II. A comparison of the rates and activation parameters for *exo*-5-substituted bicyclo[2.1.0]pentanes is provided by Table V. A perusal of Table V reveals that the difference in $\Delta H^{\ddagger}$ between π-acceptor (e.g., cyano) and π-donor substituents (e.g., *p*-nitrobenzoate) is very large ($\Delta\Delta H^{\ddagger} \sim 13$ kcal/mol). This is indeed an enormous substituent effect to be associated with a nonionic process, and to act at a site (i.e., the C_1–C_4 bond) remote from the center of substitution (i.e., C_5). By contrast, Anet and Ahmad[35] reported a considerably smaller effect ($\Delta\Delta G^{\ddagger} \sim 3$ kcal/mol) on the free energies of activation for a process involving resonance-induced restricted rotation about the aldehydo group of para-substituted benzaldehydes (eq 4). It can be seen (Table V) that the cyano grouping has an enthalpy of activation ($\Delta H^{\ddagger}$) for isomerization approximately 4 kcal/mol higher than that of 2-methylbicyclopentane,[8] while the corresponding value for the *p*-nitrobenzoate is about 9 kcal/mol lower. Surprisingly,

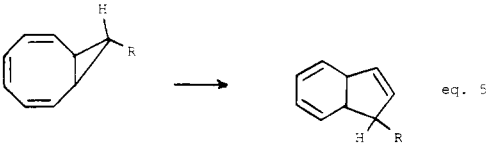


eq. 4

the carbomethoxy group, which is a good π acceptor, appears to have little effect on the activation barrier. Since the data of Chesick[8] were obtained in the gas phase, the above comparisons are based on the assumption that such results can be extrapolated into the condensed phase. An extended Hückel MO treatment[13] has suggested that π-donor substituents should have an attenuated effect in comparison with their π-acceptor counterparts; however, our results, while in qualitative agreement with the theoretical predictions, suggest that the primary kinetic effects are to be associated with the π-donor substituents.[36]

Although external bond cleavage has not been tested experimentally for the 5-cyano- or 5-carbomethoxybicyclo-[2.1.0]pentanes, this possibility appears remote since this mode of involvement has been excluded for the 5-benzyloxy compound (vide supra), which is the most reactive of the systems studied. Moreover, a stereochemical test has excluded central bond cleavage from consideration in the stereomutation of the 5-acetyl-5-methylbicyclo[2.1.0]pentanes.[21] Involvement of the internal bond (C_1–C_4) has the potential for a much greater strain energy release as noted above.

The effects of π-donor and π-acceptor substituents have been studied in the thermal rearrangement of 9-substituted *cis*-bicyclo[6.1.0]nona-2,4,6-trienes (eq 5),[37] which are sug-



eq. 5

gested to undergo rearrangement via bicyclopentyl intermediates.[37e] It is worthy of note that the mechanism of this rearrangement remains somewhat uncertain.[37a,c] Thus, while the substituent effects on this rearrangement conform to theoretical expectation,[37a,e] the present work constitutes the first unambiguous kinetic study of substituent effects on bicyclopentyl stereomutation.

The hypothesis of Hoffmann and Günther deals principally with a ground-state effect.[11,12] Recently, the X-ray structure of tosylate **1d** was determined and the C_1–C_4 bond was found to have a "normal" length of 1.525 Å;[38] however, it is not clear to what extent this substituent effect would be reflected in an elongated bond, especially for π-donor substituents.[13]

We have attempted to correlate the activation parameters of the 5-substituted bicyclo[2.1.0]pentanes with a variety of substituent constants, including the charge density at the C_1 position of monosubstituted benzenes[39] and ^{13}C chemical shifts

Table V. Comparison of Rates and Activation Parameters for the Epimerization of *exo*-5-Substituted Bicyclo[2.1.0]pentanes

X	$10^7 k^{150\,°C}$, s^{-1}	$\Delta G^{\ddagger}$ (150 °C), kcal/mol	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	ref
-CN	5.01	37.2 ± 1.1	41.5 ± 0.8	10.1 ± 0.8	this work
$-CO_2CH_3$	6.24	37.1 ± 3.1	38.5 ± 1.8	3.4 ± 3.1	this work
-H[a]	8.56	36.8	37.7 ± 0.8	2.2	8
exo-CO_2Et-5-CH_3[b]	131.00	34.6 ± 4.4	35.8 ± 2.2	2.9 ± 5.2	9
exo-$COCH_3$-5-CH_3[b]	59.39	35.2 ± 1.7	33.9 ± 0.9	−3.0 ± 2.0	22
-OTs	1790.00	32.2	30.0	−5.2	3
-OPNB	52 900.00	29.5	28.6	−2.1	1

[a] This reaction was run in gas phase and involved 2-methylbicyclo[2.1.0]pentane. [b] This is a 5,5-disubstituted compound (cf. **6**).

(NMR) at C_1, C_{ortho}, C_{meta}, and C_{para} of monosubstituted benzenes,[40] at C_α of monosubstituted ethylenes,[41] and at C_1 of monosubstituted *n*-pentanes.[42] We could find no ideal correlations. Indeed, correlation was especially poor for the Hammett-type σ values,[43] σ_I and σ_R. We believe that this implies that neither the inductive nor the resonance effect plays an individually dominant role in the stereomutation process. One of the better correlations involved the comparison of our activation data ($\Delta H^\ddagger$) with the ^{13}C NMR chemical shift data at the ortho, but not the para or meta, position of monosubstituted benzenes (correlation coefficient = 0.986), suggesting a combination of resonance and inductive, or field, effects in the isomerization process. It is possible that electronegative substituents (e.g., $OCH_2C_6H_5$) play dual roles in facilitating the stereomutation process. In addition to the π-donor effect noted above, such groups might eliminate a symmetry-imposed barrier to ring opening,[44] since this barrier in bicyclo[2.1.0]-pentane can be associated with a destabilizing hyperconjugative interaction involving the C-5 methylene with C_1 and C_4 of the incipient biradical intermediate (or transition state). Moreover, it has been suggested that electronegative substituents might, in fact, stabilize the symmetric state of the biradical species by a hyperconjugative interaction.[37e] In this connection we note that **1c**, bearing the more electronegative and less electron-releasing *p*-nitrobenzoate group, appears to undergo stereomutation approximately ten times faster than **1b** under the same conditions.

In summary, our results are qualitatively in agreement with the prediction that π-donor substituents, but not π acceptors, should facilitate the stereomutation of 5-substituted bicyclopentanes; however, we believe that other effects involving the electronegativity of the attached substituent are also important.

Experimental Section

All melting points are uncorrected. A Mel-Temp capillary tube apparatus was used to determine melting points. Infrared spectra were recorded on a Perkin-Elmer Model 727 spectrophotometer and calibrated using the 6.245-μ band of polystyrene. All infrared data are reported in microns (w, m, s, and vs indicate intensity of bands as weak, medium, strong, and very strong, respectively). Nuclear magnetic resonance spectra were recorded on either a Varian A-60, Varian T-60, or JEOL MH-100 spectrometer. Tetramethylsilane (Me_4Si) was used as an internal standard. The positions of peaks are reported in parts per million downfield relative to Me_4Si. The notations s, d, t, q, m, dd, and cm indicate 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 integrated value is shown in parentheses. Ultraviolet spectra were recorded on a Cary 14 spectrophotometer. Values are reported in nanometers. Mass spectra were recorded on a Hitachi Perkin-Elmer RMU-6E spectrometer. The ionization voltage was 70 V with a current of 80 μA. Gas-liquid phase chromatographic analyses were performed with a Hewlett-Packard Model 5750 gas chromatograph with a helium flow of 25 mL/min. Preparative work was performed on an Aerograph A-90-P instrument with a helium flow of 60 mL/min. Microanalyses were performed at Scandinavian Microanalytical Laboratory, Herlev, Denmark, Instranal Microanalytical Laboratory, Rensselaer, N.Y., and Atlantic Microlab, Inc., Atlanta, Ga.

***exo,exo*-5,6-Dideuterio-7-isopropylidene-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptane (17b).** The Diels–Alder adduct[1] derived from 6,6-dimethylfulvene and dimethyl azodicarboxylate (60.0 g, 0.238 mol) was dissolved in 525 mL of ethyl acetate. After 6.0 g of 5% Pd/C in 10 mL of solvent had been conditioned for 0.5 with 99.5% deuterium gas in a Joshel atmospheric hydrogenation apparatus, the solution was added to the apparatus and the equivalent of 5.33 L of D_2 (0.239 mol) (corrected for the vapor pressure of the solvent, temperature, and atmospheric pressure) was added. The identical process was repeated. The hydrogenation flask was kept at room temperature by means of a water bath, and vigorous magnetic stirring was used. Total reaction time was approximately 1 h. Removal of the catalyst by filtration on a Celite pad under vacuum, followed by removal of the solvent in vacuo, gave 115 g of a glass (95%). Washing of the solid, which gradually crystallized, with ether gave a compound with mp 88.0–89.0 °C. The mass spectrum showed the parent *m/e* 276 and analysis of the M − 1 peak and the M − 2 peak indicated 70% deuterium incorporation. The mass spectrum of the deuterium used indicated that it was equal to or better than the specification of 99.5% D. **17b:** IR (KBr) 4.60 (w), 5.7–5.9 (s), 10.4 (m), 13.0 μ (s); NMR ($CDCl_3$) δ 1.80 and 1.87 (s and bs, respectively, 8 H), 3.73 (s, 6 H), 4.78 ppm (bs, 2 H).

***exo,exo*-5,6-Dideuterio-2,3-dicarbomethoxy-*anti*-2,3-diazabicyclo[2.2.1]heptan-7-ol.** The title compound was prepared by the method previously described[1] in 91% yield. The product was a glass which is purifiable only by column chromatography. Dideuterio compound: IR (film) 3.0 (m), 4.6 (w), 5.7–5.9 (s), 13.2 μ (s); NMR ($CDCl_3$) δ 1.68 (bs, 2 H), 3.78 (s, 6 H), 4.12 (bs, 1 H), 4.22 (bs, 2 H), 4.54 ppm (vbs, 1 H, removable by shaking with D_2O). Irradiation of the sample at δ 1.68 ppm after shaking with D_2O resulted in the δ 4.12 ppm signal collapsing to a triplet of J = 2 Hz and the δ 4.22 ppm signal collapsing to a bd, J = 2 Hz.

***exo,exo*-Dideuterio-*anti*-7-benzyloxy-2,3-dicarbomethoxy-2,3-diazabicyclo[2.2.1]heptane.** This compound was prepared in a manner analogous to that used for the fully protonated compound:[1] IR (film) 4.60 μ (w); NMR (CCl_4) δ 1.70 (bs, 2 H), 3.65 (s, 6 H), 3.83 (bs, 1 H), 4.25 (bs, 2 H), 4.45 ppm (s, 2 H).

***exo,exo*-5,6-Dideuterio-*anti*-7-benzyloxy-2,3-diazabicyclo-[2.2.1]hept-2-ene (17b).** This deuterated analogue was prepared in a manner analogous to that used for the fully protonated compound: IR (film) 4.55 (w), 6.8 (m), 6.9 (s), 7.4 (s), 14.4 μ (s); NMR (CCl_4) δ 0.80 (bs, 2 H), 3.16 (bs, 1 H), 4.20 (s, 2 H), 4.60 ppm (d, J = 2 Hz, 2 H). Irradiation at 0.80 ppm leads to a triplet of J = 2 Hz at 3.16 ppm.

***exo,exo*-2,3-Dideuterio-*exo*-5-benzyloxybicyclo[2.1.0]pentane (12) and *endo,endo*-2,3-Dideuterio-*endo*-5-benzyloxybicyclo[2.1.0]pentane (13).** Spectral data for the deuterium analogues **12** and **13**, which were prepared in a manner identical with that used for the fully protonated isomers:[1] IR (film) 4.53 μ (m); NMR (C_6D_6) δ 1.26 (s, 2 H, $C_{2,3}$ endo H of exo), 1.56 (m, 2 H, $C_{1,4}$ H of endo), 1.75 (s, 2 H, $C_{1,4}$ H of exo), 1.99 (m, 2 H, $C_{2,3}$ exo H of endo), 3.29 (t, J = 5 Hz, 1 H, C_5 H of endo), 3.40 (s, 1 H, C_5H of exo), 4.48 (s, 2 H, benzyl H of exo), 4.54 (s, 2 H, benzyl H of endo), 7.28 ppm (m, 5 H, aromatic H of exo and endo). The above data was obtained from a 76:24 mixture (endo isomer predominates). Spin decoupling of this sample at 1.56 ppm resulted in the collapse of the 3.29-ppm triplet to a singlet. Irradiation at 1.99 ppm collapses the 1.56-ppm multiplet to a doublet of J = 5 Hz. Irradiation at 3.29 ppm sharpens the 1.99-ppm multiplet slightly, and the 1.56-ppm multiplet, which is sharpened tremendously, approaches a doublet.

***exo,exo*-2,3-Dideuterio-*exo*-5-benzyloxybicyclo[2.1.0]pentane (12).** The mixture of deuterated *exo*- and *endo*-5-benzyloxybicyclo[2.1.0]pentanes obtained from the photolysis reaction was treated with alumina, according to our previously described method.[1] It was found that activity grade I alumina obtained from Fisher Scientific Co. worked well. Completion of the separation was carried out in the manner as before.[1] The yield was 14% from the starting mixture, bp 62 °C (0.04 mmHg) (lit.[1] bp 62 °C (0.04 mmHg)). Deuterium compound: IR (film) 4.53 μ (m); NMR (C_6D_6) δ 1.26 (bs, 2 H), 1.75 (bs, 2 H), 3.40 (s, 1 H), 4.48 (s, 2 H), 7.28 ppm (m, 5 H). Double irradiation at 1.75 ppm gives essentially no change in the NMR spectrum.

NMR Thermolysis of *exo,exo*-2,3-Dideuterio-*exo*-5-benzyloxybicyclo[2.1.0]pentane (12) in Benzene-d_6. A sample which was 0.92 M in **12** was made by dissolving the compound in an appropriate solvent. The sample was sealed into an NMR tube and the spectrum recorded. The sample was placed into a constant-temperature bath at 95.0 ± 0.2 °C. The tube was withdrawn from the bath at various times and cooled with cold water, and its NMR spectrum was recorded. As time progressed, new peaks appeared at δ 1.56 (m), 1.99 (m), 3.29 (t, J = 5 Hz), and a singlet at 4.54 ppm. These absorbances correspond exactly to those of the 76:24 mixture of **13** and **12** previously described. Integration of the δ 3.29 triplet of **13** and the δ 3.40 singlet of **12** allowed us to calculate an accurate ratio (±5%) of these two epimers. At 86 h and 19 min 3-benzyloxycyclopentene-d_2 appeared to the extent of 7% of the reaction mixture. This compound was identified by the olefin absorption of δ 5.84 ppm and the benzyl absorption of δ 4.40 ppm which was identical with that of an authentic sample.

Thallous Cyclopentadienide (18). The title compound was prepared by the method of Cotton[46] in 91% yield, mp 120 °C (blackening in air) (lit.[46] mp 60 °C (blackening in air)).

4-Phenyl-1,2,4-triazoline-3,5-dione. The title compound was prepared by the method of Plummer[47] in 85% yield, mp 170–180 °C dec (lit.[47] mp 170–180 °C dec).

***anti*- and *syn*-10-Methoxymethyl-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (20a and 20b).** The title compounds were prepared by adapting methodology described by Corey[22] and Breslow.[24] To a stirred suspension of 5.38 g (20 mmol) of freshly prepared thallous cyclopentadienide in 8 mL of anhydrous ether was added dropwise 2.42 g (30 mmol) of chloromethyl methyl ether at −20 °C under nitrogen atmosphere. After 8 h, the reaction mixture was cooled down to −40 °C and there was added 20 mL of anhydrous ether. The insoluble thallous chloride was quickly filtered and washed with ether. The filtrate was cooled in a dry ice–acetone bath and there was added dropwise a solution of 3.68 g (21 mmol) of 4-phenyl-1,2,4-triazoline-3,5-dione in 150 mL of methylene chloride until a light pink solution was obtained. The reaction mixture was then gradually warmed to room temperature and the excess dione was decomposed by addition of a few drops of diethylamine. Removal of solvent at reduced pressure gave 5.90 g (20 mmol) of white solid (quantitative). The NMR spectrum of this crude product indicated a 3:1 isomeric mixture. This isomeric mixture was separated by repeated fractional recrystallizations from methylene chloride–hexane. The major component crystallized in the earlier crops to give a total of 4.02 g (14 mmol, 70%) of white crystals. The mother liquor contained the minor component which was recrystallized from hexane and ether to give 0.625 g (2.2 mmol, 11%) of white crystals. The major component was assigned as the anti isomer **20a:** mp 155–156 °C; IR (CH_2Cl_2) 3.45 (w), 5.62 (s), 5.81 (vs), 6.25 (w), 7.15 (s), 8.85 (s), and 9.80 μ (m); NMR ($CDCl_3$) δ 2.54 (t, 1, J = 6 Hz) 3.44 (s, 3), 3.58 (d, 2, J = 6 Hz), 5.08 (m, 2), 6.64 (m, 2), and 7.58 ppm (m, 5); UV max (CH_3CN) 230 nm (ϵ 6577); mass spectrum *m/e* (rel intensity) 45 (100), 77 (77), 79 (87), 110 (88) and 119 (30).

Anal. ($C_{15}H_{15}N_3O_3$) C, H, N.

The minor component was assigned as the syn isomer **20b:** mp 129–130 °C; IR (CH_2Cl_2) 3.42 (w), 5.65 (m), 5.83 (s), 6.24 (w), 6.67 (m), 7.20 (m), 8.85 (m), and 9.09 μ (m); NMR ($CDCl_3$) δ 3.10 (t, 1, J = 6 Hz), 3.32 (s, 3), 5.08 (m, 2), 6.48 (m, 2), and 7.52 ppm (m, 5); UV max (CH_3CN) 229 nm (ϵ 3220); mass spectrum *m/e* (rel intensity) 45 (100), 77 (82), 110 (65), and 119 (40).

Anal. ($C_{15}H_{15}N_3O_3$) C, H, N.

***anti*- and *syn*-10-Methoxymethyl-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (21a and 21b).** A mixture of 2.10 g (7.4 mmol) of anti adduct **20a,** 150 mL of ethyl acetate, and 37 mg of 5% palladium on powdered charcoal was shaken on a Parr hydrogenator at 40 psi hydrogen pressure for 1 h. Filtration, removal of solvent in vacuo, and recrystallization from ethyl ether gave 2.10 g (7.3 mmol, 98%) of **21a** as white crystals: mp 115–116 °C; IR (CH_2Cl_2) 3.5 (w), 5.68 (s), 5.90 (vs), 6.24 (w), 7.20 (s), and 9.06 μ (s); NMR ($CDCl_3$) δ 1.94 (s, 4), 2.50 (t, 1, J = 7 Hz), 3.36 (s, 3), 3.56 (d, 2, J = 7 Hz), 4.56 (s, 2), and 7.52 ppm (m, 5); UV max (CH_3CN) 229 nm (ϵ 8304); mass spectrum *m/e* (rel intensity) 287 (M^+, 75) and 288 (M + 1, 15).

Anal. ($C_{15}H_{17}N_3O_3$) C, H, N.

In a similar manner, the syn isomer **21b** was prepared quantitatively: mp 114–115 °C; IR (CH_2Cl_2) 3.42 (w), 5.65 (m), 5.88 (s), 6.24 (w), 7.20 (s), and 9.09 μ (m); NMR ($CDCl_3$) δ 1.92 (bs, 4), 2.56 (t, 1, J = 7 Hz), 3.34 (s, 3), 3.35 (d, 2, J = 7 Hz), 4.46 (bs, 2), and 7.48–7.92 ppm (m, 5); UV max (CH_3CN) 229 nm (ϵ 8950); mass spectrum *m/e* (rel intensity) (M^+, 30) and 288 (M + 1, 8).

Anal. ($C_{15}H_{17}N_3O_3$) C, H, N.

***anti*- and *syn*-7-Methoxymethyl-2,3-diazabicyclo[2.2.1]hept-2-ene (22a and 22b).** The title compound was prepared by utilizing methodology modification described by Paquette[48] and Snyder.[27b] Under an oxygen-free argon atmosphere, 10.5 g (36.6 mmol) of hydrogenated adduct **21a** was dissolved in 86 mL of hot ethylene glycol (ca. 100 °C) and a solution of 29.4 g of potassium hydroxide in 86 mL of distilled water was added all at once. The resulting mixture was heated to gentle reflux with magnetic stirring for 2 h. The reaction mixture was then cooled down to room temperature, diluted with 300 mL of distilled water, and extracted ten times with 50-mL portions of methylene chloride. The combined methylene chloride extracts, along with an equal volume of methanol and 370 mg of 5% palladium on powdered charcoal, were treated with a stream of oxygen. The oxidation reaction was monitored by a cupric chloride test. A few drops of reaction mixture was shaken with 0.5 mL of a 3% aqueous cupric chloride solution. A decolorization in the blue aqueous layer, or the formation of brick-red solution in organic layer, indicates the presence of unreacted hydrazo compound. The oxidation reaction was completed in 2 h. The reaction mixture was then dried over magnesium sulfate and filtered and the solvent was removed in vacuo. Vacuum distillation of the crude product at 89 °C (3.8 mm) gave 4.20 g (30.0 mmol, 82%) of **22a** as a watery liquid: IR (neat) 3.40 (m), 3.50 (m), 8.30 (m), 9.01 (s), and 11.4 μ (w); NMR ($CDCl_3$) δ 0.96 (dd, 2, J = 12, 5 Hz), 1.60 (m, 2), 1.87 (t, 1, J = 8 Hz), 2.90 (d, 2, J = 8 Hz), 3.20 (s, 3), and 5.23 ppm (m, 2); UV max (CH_3CN) 343 nm (ϵ 112.5).

Anal. ($C_7H_{12}N_2O$) C, H, N.

The syn isomer **22b** was prepared in a similar manner in 76% yield: bp 85 °C (4.5 mm); IR (neat) 3.40 (m), 8.30 (m), 9.01 (s), and 11.4 μ (w); NMR ($CDCl_3$) δ 0.96 (dd, 2, J = 12, 5 Hz), 1.60 (m, 2), 1.87 (t, 1, J = 8 Hz), 3.25 (d, 2, J = 8 Hz), 3.29 (s, 3), and 4.97 ppm (m, 2); UV max (CH_3CN) 343 nm (ϵ 104.1).

Anal. ($C_7H_{12}N_2O$) C, H, N.

Photolysis of *anti*-7-Methoxymethyl-2,3-diazabicyclo[2.2.1]-hept-2-ene (22a). A solution of 2.98 g (21.3 mmol) of the azo methyl ether **22a** in 700 mL of purified pentane was irradiated using 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 343 nm. The reaction was completed in 5 h. The pentane was removed in vacuo and the residue was vacuum distilled to give 1.99 g (17.8 mmol, 82%) of a clear, colorless liquid, bp 58 °C (10 mm). The NMR spectrum of this liquid indicated a 35:65 isomeric mixture which was separated by gas chromatography on a 4-ft, 15% Carbowax 20M on Chromosorb W column at 70 °C. The minor component, retention time 8.6 min, exhibited the following spectral data: IR (film) 3.45 (m), 3.55 (m), and 9.30 μ (s); NMR ($CDCl_3$) δ 1.30 (t, 1, J = 7 Hz), 1.40–1.60 (m, 4), 2.00–2.24 (m, 2), 3.14 (d, 2, J = 7 Hz), and 3.34 ppm (s, 3). This component was identified as the *exo*-5-methoxymethylbicyclo[2.1.0]pentane (**24a**).

Anal. ($C_7H_{12}O$) C, H.

The major component, retention time 10.6 min, was identified as the endo isomer **23a** as follows: IR (film) 3.42 (m), 3.55 (m), and 9.30 μ (s); NMR ($CDCl_3$) δ 1.12 (quintet, 1, J = 5 Hz), 1.44 (d, 2, J = 7 Hz), 1.60–1.94 (m, 2), 2.00–2.32 (m, 2), 3.42 (s, 3), and 3.66 (d, 2, J = 7 Hz).

Anal. ($C_7H_{12}O$) C, H.

The structural assignments were confirmed by NMR spin decoupling results. Double irradiation of the doublet at 3.14 ppm collapses the triplet at 1.30 ppm to a singlet, while a similar irradiation of the doublet at 3.66 ppm collapses the quintet at 1.12 ppm to a triplet (J = 7 Hz).

Chloromethyl Benzyl Ether. The title compound was prepared by the method of Mamedov[49] in 68% yield. As observed by the original worker, an attempt to distill this compound caused decomposition of the product. Since the crude product obtained was suitable for the subsequent alkylation reaction, further purification was not attempted.

***anti*- and *syn*-10-Benzyloxymethyl-4-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (20c and 20d).** To a stirred mixture of 3.04 g (11.3 mmol) of freshly sublimed thallous cyclopentadienide in 20 mL of anhydrous ether was added, under nitrogen at ca. −10 °C, 2.62 g of 90% pure chloromethyl benzyl ether. After 4.5 h, the reaction mixture was cooled down to −75 °C and quickly filtered to remove the insoluble thallous chloride. This white solid was washed thoroughly with anhydrous ether. The washings were combined with the previous ether filtrate. To the combined ether solution, at −75 °C, was added dropwise a solution of 1.98 g (11.3 mmol) of 4-phenyl-2,3,4-triazoline-1,5-dione in 50 mL of methylene chloride. Persistence of a pink color is an indication of the reaction end point. The resulting mixture was gradually warmed up to room temperature and the excess dione was decomposed by a few drops of diethylamine. Removal of solvent in vacuo gave a white solid. NMR analysis of this crude product indicated a 95:5 isomeric mixture. This crude product was repeatedly recrystallized from methylene chloride–hexane. The major component crystallized in the earlier crops. After three cycles of recrystallizations, the mother liquor, now enriched with the minor component, was concentrated and delivered to an alumina (neutral) column. This column was eluted with methylene chloride to separate the two isomers. The overall yields are 3.42 g (9.5 mmol, 84%) of the

major component and 0.10 g (0.28 mmol, 2.5%) of the minor component. The major component was identified as the anti isomer **20c** based on the following physical and spectral data: mp 154–155 °C; IR (CH_2Cl_2) 3.50 (w), 5.62 (s), 5.80 (vs), 6.24 (w), 7.10 (vs), and 8.80 μ (s); NMR ($CDCl_3$) δ 2.52 (t, 3, J = 6 Hz), 3.61 (d, 2, J = 6 Hz), 4.56 (s, 2), 5.02 (m, 2) 6.52 (m, 2), and 7.45 ppm (m, 10); UV max (CH_3CN) 230 (ϵ 7058) and 248 nm (ϵ 3809); mass spectrum *m/e* (rel intensity) 77 (78), 79 (85), 80 (88), 91 (100), 119 (20), and 186 (7).

Anal. ($C_{21}H_{19}N_3O_3$) C, H, N.

The minor component was identified as the syn isomer **20d** as follows: mp 104.5–105.5 °C; IR (CH_2Cl_2) 3.50 (w), 5.67 (s), 5.84 (vs), 6.24 (w), 7.20 (vs), and 8.90 μ (s); NMR ($CDCl_3$) δ 3.06 (t, 1, J = 8 Hz), 3.32 (d, 2, J = 8 Hz), 4.46 (s, 2), 5.02 (m, 2), 6.38 (m, 2), and 7.45 ppm (m, 10); UV max (CH_3CN) 230 (ϵ 6896) and 252 nm (ϵ 4498); mass spectrum *m/e* (rel intensity) 77 (70), 79 (84), 80 (81), 91 (100), 119 (16), and 186 (17).

Anal. ($C_{21}H_{19}N_3O_3$) C, H, N.

***anti*- and *syn*-10-Benzyloxymethyl-5-phenyl-2,4,6-triazatricyclo[5.2.1.0^{2,6}]decane-3,5-dione (21c and 21d).** A mixture of 4.06 g (11.2 mmol) of adduct **20c**, 250 mL of ethyl acetate, and 0.146 g of 5% palladium on powdered charcoal was shaken on a Parr hydrogenator at 15 psi hydrogen pressure for 0.5 h. Filtration, removal of solvent, and recrystallization from hexane–methylene chloride afforded 3.76 g (10.3 mmol, 92%) of white crystals: mp 149–150 °C; IR (CH_2Cl_2) 3.50 (w), 5.66 (s), 5.86 (vs), 6.24 (w), 6.68 (m), and 7.16 μ (s); NMR ($CDCl_3$) δ 1.90 (s, 4), 2.50 (t, 1, J = 6 Hz), 3.58 (d, 2, J = 6 Hz), 4.52 (bs, 4), 7.30 (m, 5), and 7.42 ppm (m, 5); UV max (CH_3CN) 229 nm (ϵ 9778); mass spectrum *m/e* (rel intensity) 363 (M^+, 4).

Anal. ($C_{21}H_{21}N_3O_3$) C, H, N.

The syn isomer **21d** was prepared in a similar manner in 81% yield: mp 112.5–113.5 °C; IR (CH_2Cl_2) 3.48 (w), 5.56 (m), 5.58 (s), 6.25 (w), 7.15 (s), 9.35 (m), and 11.83 μ (w); NMR ($CDCl_3$) δ 1.88 (m, 4), 2.58 (t, 1, J = 7 Hz), 3.42 (d, 2, J = 7 Hz), 4.52 (s, 2), 4.56 (m, 2), 7.36 (m, 5), and 7.48 ppm (m, 5); UV max (CH_3CN) 229 nm (ϵ 9389); mass spectrum *m/e* (rel intensity) 363 (M^+, 5).

Anal. ($C_{21}H_{21}N_3O_3$) C, H, N.

***anti*-7-Benzyloxymethyl-2,3-diazabicyclo[2.2.1]hept-2-ene (22c).** Under an oxygen-free argon atmosphere, 11.8 g (32.5 mmol) of hydrogenated adduct **21c** was dissolved in 84 mL of hot ethylene glycol (ca. 100 °C) and a solution of 27.5 g of potassium hydroxide in 84 mL of water was added all at once. The resulting mixture was heated to gentle reflux with stirring for 11 h. The reaction mixture was cooled to room temperature, diluted with 150 mL of water, and extracted ten times with 80-mL portions of methylene chloride. To the combined methylene chloride extracts were added 325 mg of 5% palladium on powdered charcoal and 400 mL of methanol. A stream of oxygen was bubbled through this stirred mixture. The oxidation reaction was monitored by a cupric chloride test. A few drops of reaction mixture was shaken with 0.5 mL of a 3% aqueous cupric chloride solution. A decolorization in the blue aqueous layer or the formation of brick-red solution in organic layer indicates the presence of unreacted hydrazo compound. The oxidation reaction was completed in 2 h. The reaction mixture was then dried over magnesium sulfate. Filtration, removal of solvent, and vacuum distillation at 120 °C (0.03 mm) gave 6.78 g (31.3 mmol, 96% yield) of watery liquid which solidified at room temperature. Recrystallization from pentane gave **22c** as white crystals: mp 45.5–46.5 °C; IR (film) 3.52 (m), 6.70 (w), 6.90 (m), 8.45 (m), 9.10 (s), 13.7 (s), and 14.5 μ (s); NMR ($CDCl_3$) δ 0.90 (dd, 2, J = 4, 12 Hz), 1.58 (m, 2), 1.88 (t, 1, J = 7.5 Hz), 3.00 (d, J = 7.5 Hz), 4.38 (s, 2), 5.12 (bs, 2), and 7.32 ppm (bs, 5); UV max (CH_3CN) 344 nm (ϵ 87.8); mass spectrum *m/e* (rel intensity) 65 (43), 66 (31), 67 (90), 79 (34), and 91 (100).

Anal. ($C_{13}H_{16}N_2O$) C, H, N.

The syn isomer **22d** was prepared in a similar manner in 77% yield: bp 84 °C (4.5 mm); IR (neat) 3.50 (w), 6.67 (m), 7.81 (m), 9.18 (s), 13.5 (s), and 14.5 μ (s); NMR ($CDCl_3$) δ 0.94 (dd, 2, J = 4, 12 Hz), 1.54 (m, 2), 1.86 (t, 1, J = 7 Hz), 4.50 (s, 2), 5.02 (bs, 2), and 7.40 ppm (s, 5); UV max (CH_3CN) 344 nm (ϵ 98.7).

Anal. ($C_{13}H_{16}N_2O$) C, H, N.

Photolysis of *anti*- and *syn*-7-Benzyloxymethyl-2,3-diazabicyclo[2.2.1]hept-2-ene (22c and 22d). A solution of 6.69 g (30.9 mmol) of the azo compound **22c** in 700 mL of purified benzene 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 of the azo absorption at 344 nm. The reaction was completed in 6.5 h. The solvent was removed in vacuo and the residue distilled under vacuum to afford 5.58 g (29.6 mmol, 96%) of a clear, colorless liquid: bp 86 °C (0.17 mm); IR (film) 3.29 (m), 3.50 (s), 6.85 (m), 7.36 (w), 9.17 (s), 13.70 (s), and 14.49 μ (s); NMR ($CDCl_3$) δ 1.00–2.20 (m, 7), 3.18 (d, J = 7 Hz, exo CH_2O–), 3.70 (d, J = 7 Hz, endo CH_2O–), 4.46 (s, exo OCH_2Ph) 4.56 (s, endo OCH_2Ph), and 7.24 ppm (m, 5); mass spectrum *m/e* (rel intensity) 188 (M^+, 3). The NMR spectrum of this photolysate indicates a 58:42 mixture of *endo*- and *exo*-5-benzyloxybicyclo[2.1.0]pentane (**23b** and **24b**), respectively.

Anal. ($C_{13}H_{16}O$) C, H.

In a similar manner, azo compound **22d** was photolyzed to give a 39:61 mixture of *endo*- and *exo*-5-benzyloxymethylbicyclo[2.1.0]-pentane.

***endo*- and *exo*-5-Hydroxymethylbicyclo[2.1.0]pentane (25).** To a solution of 5.53 g (29.4 mmol) of benzyl ethers **23b** and **24b** (a 42.58 mixture of exo and endo isomers) in 60 mL of anhydrous ether and 250 mL of anhydrous liquid ammonia at −78 °C under an argon atmosphere were added several pieces of freshly cut sodium metal until a blue solution was obtained. After stirring for an additional 20 min, the reaction mixture was quenched by adding anhydrous ammonium chloride until the deep blue color disappeared. The ammonia was evaporated by gradually warming up to room temperature, and the white solid residue was triturated with 200 mL of anhydrous ether. Filtration and removal of solvent gave an oily liquid which was vacuum distilled to give 2.57 g (26.2 mmol, 92%) of a watery liquid: bp 88–92 °C (9.5 mm); IR (film) 3.01 (s), 3.29 (m), 3.41 (s, 7.03 (m), 9.90 (s), 11.34 (m), and 12.82 μ (m); NMR ($CDCl_3$) δ 3.82 (d, endo CH_2O–, J = 7 Hz), 3.32 (d, exo CH_2O–, J = 7 Hz), 2.82 (bs, -OH), and three sets of complex multiplets centered at δ 1.28, 1.72, and 2.14 ppm integrating for seven protons. The NMR spectrum of this product indicated a 42:58 mixture of *exo*- and *endo*-5-hydroxymethylbicyclo[2.1.0]pentane.

Anal. ($C_6H_{10}O$) C, H.

***endo*- and *exo*-Bicyclo[2.1.0]pentane-5-carboxyaldehyde (26).** The following procedure is adapted from that of Radcliffe and Rodehorst.[29] Anhydrous chromium trioxide (3.3 g, 33 mmol) was added to a mechanically stirred solution of 5.2 g (66 mmol) of dry pyridine in 83 mL of methylene chloride (freshly purified by passing through a neutral alumina column under an argon atmosphere). The deep burgundy solution was stirred for 15 min at room temperature. At the end of this period, a solution of 0.54 g (5.5 mmol) of a mixture of the isomeric alcohols **25**, dissolved in a small volume of methylene chloride, was added in one portion to the burgundy solution. A tarry, black deposit separated immediately. After stirring for an additional 15 min at room temperature, the solution was decanted from the residue, which was washed with 140 mL of methylene chloride. The combined methylene chloride solutions were washed with three 70-mL portions of 5% aqueous sodium hydroxide solution, 70 mL of 5% aqueous hydrochloric acid, 70 mL of 5% sodium bicarbonate solution, and 70 mL of saturated aqueous sodium chloride solution, and then dried over anhydrous magnesium sulfate. Filtration and evaporation of solvent through a 1.5-ft Vigreux column gave a watery liquid: IR (film) 3.41 (w), 3.51 (w), 3.70 (w), and 5.85 μ (s); NMR ($CDCl_3$) δ 1.03–2.75 (m, 7), 8.90 (d, exo CHO, J = 6 Hz), 9.90 (d, endo CHO, J = 6 Hz). This crude aldehyde was used immediately and without further purification.

Oximes of Aldehydes (26). To a solution containing the crude aldehydes (**26**) were added 25 mL of 95% ethanol and 5 mL of water. At this point, 0.424 g (6.1 mmol) of hydroxylamine hydrochloride and 0.354 g (8.8 mmol) of sodium hydroxide were introduced. The resulting mixture was stirred and heated to reflux for 12 h. The solvent was removed in vacuo and the residue was taken up in 100 mL of methylene chloride. The methylene chloride solution was washed four times with 25-mL portions of water, dried over magnesium sulfate, filtered, and concentrated to ca. 25 mL. This crude aldoxime solution was used immediately in the succeeding dehydration reaction without further purification. Recrystallization of the crude product from hexane gave a white, crystalline solid: mp 137–140 °C; IR (KBr) 3.25 (vs and broad), 3.51 (vs and broad), 6.06 (m), 6.90 (s), 7.46 (s), and 10.64 μ (s); NMR ($CDCl_3$) δ 1.52–2.48 (three sets of multiplets) and 2.56 (d, J = 8 Hz) integrated for seven protons, 6.12 and 7.12 (d, 2, J = 8 Hz), and 8.20 ppm (bs, 1, exchangeable).

Anal. ($C_6H_9N_2O$) C, H, N.

***endo*- and *exo*-5-Cyanobicyclo[2.1.0]pentane (28 and 29).** The title compound was prepared by utilizing methodology developed by Foley

and Dalton.[50] To the dried, stirred solution of aldoximes in methylene chloride (vide supra) was added 0.966 g (6.15 mmol) of carbonyldiimidazole under inert atmosphere. Initially, vigorous carbon dioxide evolution was observed. The reaction mixture was stirred overnight. An additional 25 mL of methylene chloride was added to the reaction mixture which was then washed four times with 20-mL portions of salt water, dried over magnesium sulfate, filtered, concentrated, and vacuum distilled at 88 °C (9.5 mm) to give 0.168 g (1.8 mmol, 33% yield based on the starting alcohols **25**) of a watery liquid. Gas chromatographic analysis of this liquid using a 15% Carbowax on Chromosorb W column at 150 °C revealed three peaks with retention times 4.1, 4.9, and 6.0 min and a relative peak area ratio of 1:11:18, respectively. Ignoring the first minor component, the last two major components were separated and collected by preparative gas chromatographic methods. The second component displayed the following spectral characteristics: IR (neat) 3.42 (s), 4.50 (s), 7.90 (s), and 13.0 μ (s); NMR (benzene-d_6) δ 0.94 (s, 1), 1.00 (m, 2), and 1.74 ppm (m, 4); mass spectrum *m/e* (rel intensity) 65 (25), 66 (100), 67 (15), 92 (15), and 93 (M^+, 5). This second component was identified as *exo*-5-cyanobicyclo[2.1.0]pentane (**29**).

Anal. (C_6H_7N) C, H.

The major component showed the following spectral properties: IR (film) 3.42 (s), 4.50 (s), 7.90 (s), and 13.0 μ (s); NMR (benzene-d_6) δ 1.02 (t, 1, J = 5 Hz) and 1.30–2.18 ppm (m, 6); mass spectrum *m/e* (rel intensity) 65 (22), 66 (100), 67 (15), and 93 (M^+, 4). The latter was identified as *endo*-5-cyanobicyclo[2.1.0]pentane (**28**).

Anal. (C_6H_7N) C, H.

***endo*- and *exo*-Bicyclo[2.1.0]pentane-5-carboxylic Acid.** To a solution of crude aldehydes **26**, obtained from 0.560 g (5.75 mmol) of isomeric alcohols **25** by Collins oxidation as described previously, in 30 mL of absolute ethanol was added a solution of 2.25 g (13.2 mmol) of silver nitrate in 5 mL of water. To this vigorously stirred mixture was then added dropwise a solution of 1.7 g (30 mmol) of potassium hydroxide in 30 mL of water. Addition was completed in 1 h, and the resulting mixture was stirred for an additional 3 h. The gray mixture was filtered and the silver salts were washed with 65 mL of water. To the filtrate combined with an additional 50 mL of methylene chloride, cooled in an ice bath, was added 3 N hydrochloric acid dropwise with stirring until the aqueous layer was acidic (ca. pH 4). The aqueous layer was separated and extracted five times with 50-mL portions of methylene chloride. The methylene chloride extracts were combined, dried over magnesium sulfate, filtered, and concentrated to give crude acid **26** as a pale yellow solid. This crude carboxylic acid was esterified subsequently without further purification.

Vacuum distillation of the crude acid at 70 °C (0.05 mm) gave a clear liquid which solidified on standing at room temperature. Further recrystallization of this distilled acid from hexane–methylene chloride and sublimation at 40 °C (0.01 mm) gave a white, crystalline solid: mp 43–45 °C IR (film) 3.40 (m), 3.88 (w), 5.92 (s), 6.95 (s), and 10.87 μ (m); NMR ($CDCl_3$) δ 1.23–2.80 (cm, 7) and 12.06 ppm (bs, 1, exchangeable); mass spectrum *m/e* (rel intensity) 65 (15), 66 (15), 67 (100), and 112 (M^+, 1).

Anal. ($C_6H_8O_2$) C, H.

***endo*- and *exo*-5-Carbomethoxybicyclo[2.1.0]pentane (30 and 31).** To an ice-cold, magnetically stirred solution of carboxylic acid (vide supra) obtained from 3.18 g (32.4 mmol) of isomeric alcohols **25** in 250 mL of anhydrous ether was added dropwise a solution of diazomethane in anhydrous ether prepared by a method of Arndt.[51] Addition was continued until a persistent pale yellow color was observed. After an additional 10 min of stirring, the excess diazomethane was decomposed by slow addition of glacial acetic acid. The resulting mixture was washed three times with 30-mL portions of saturated sodium bicarbonate and 30 mL of water, dried over magnesium sulfate, filtered, concentrated in vacuo, and distilled at reduced pressure to give 1.77 g (14.0 mmol, 44% yield based on alcohol) of a watery liquid, bp 34–36 °C (0.8 mm). The NMR spectrum indicated a 1.4:1 isomeric mixture of *endo*- and *exo*-5-carbomethoxybicyclo[2.1.0]-pentane (**30** and **31**). This mixture was separated on an activated silica gel column by elution with pure pentane and 10% ether in pentane. The faster moving component was identified as *endo*-5-carbomethyoxybicyclo[2.1.0]pentane (**30**): IR (film) 3.40 (m), 5.80 (s), 6.95 (s), 7.25 (m) 8.51 (s), and 13.2 μ (w); NMR ($CDCl_3$) δ 1.68 (t, 1, J = 7 Hz), 1.82–2.40 (m, 6), and 3.72 ppm (s, 3); mass spectrum *m/e* (rel intensity) 65 (22), 66 (30), 67 (100), 95 (16), and 126 (M^+, 2).

Anal. ($C_7H_{10}O$) C, H.

The second component was identified as *exo*-5-carbomethoxybicyclo[2.1.0]pentane (**31**): IR (film) 3.40 (m), 5.80 (s), 6.95 (s), 7.25 (m), 8.54 (s), and 13.2 μ; NMR ($CDCl_3$) δ 1.40–1.67 (m, 2), 1.80 (s, 1), 1.87–2.40 (m, 4), and 3.65 ppm (s, 3); mass spectrum *m/e* (rel intensity) (25), 66 (32), 67 (100), 95 (22), and 126 (M^+, 2).

Anal. ($C_7H_{10}O_2$) C, H.

Thermolysis of *exo*-5-Cyanobicyclo[2.1.0]pentane (29) in Benzene-d_6. A solution of 67 mg of pure *exo*-5-cyanobicyclo[2.1.0]pentane (**29**) in 0.2 mL of benzene-d_6 was sealed in a Pyrex Carius tube (EDTA washed) under an argon atmosphere and heated in a constant-temperature bath at 220.0 ± 0.2 °C. At the end of each time interval the tube was removed from the oil bath and cooled to room temperature. The reaction was analyzed by NMR and GLC. Every spectrum was carefully examined in the region of olefinic absorption. The ratio of the endo and exo isomers at each time interval was determined by using a gas chromatographic peak integrator (Perkin-Elmer Printing Integrator, Model 194**B**).

Kinetic Measurements of the Epimerization of *endo*-5-Cyanobicyclo[2.1.0]pentane in Benzene (28). A. Purification. The title compound was purified by preparative gas chromatography and short-path distillation (Kugelrohr apparatus). Reagent grade benzene was distilled over sodium wire. Butylbenzene was distilled once at 75 °C (15 mm).

B. Reaction Vessels. A number of 4 × 120 mm pyrex tubes were washed with soap water, distilled water, 10% aqueous disodium ethylenediaminetetraacetate solution, distilled water, and acetone sequentially and then dried in an oven at 120 °C for at least 5 h before use.

C. Preparation of Samples. A stock solution of 30 μL of pure *endo*-5-cycanobicyclo[2.1.0]pentane (**28**) and 5 μL of distilled butylbenzene in 1 mL of dry benzene was prepared under an argon atmosphere. A 30-μL aliquot of this solution was placed in each of a series of 4 × 120 mm cleaned, dry Pyrex tubes. These tubes were degassed to 0.05 mm in four freeze-thaw cycles, then sealed.

D. The Reaction. A series of sealed sample tubes (at least ten per run) were placed in a constant-temperature silicon oil bath maintained to ±0.2 °C. Individual tubes were removed and cooled in an ice bath at appropriate intervals. The reaction was followed until an equilibrium was reached. A control run for the equilibrium constant determination was carried out by heating at least three samples of pure *exo*-5-cyanobicyclo[2.1.0]pentane (**29**) in benzene at the same temperature. The reaction was run at 214.3, 204.7, 195.0, and 184.4 °C.

E. Sample Analysis. Samples were analyzed by gas chromatography using an 8 ft × 1/8 in., 15% Carbowax 20M on 80–100 mesh Chromosorb W column at 120 °C. The retention times, relative to the benzene peak, for butylbenzene and the exo and endo isomers were 5, 10.3, and 12.8 min, respectively. The peak area was determined by a Perkin-Elmer Model 194B printing integrator. At least three analyses were done for each sample.

F. Treatment of Data. The initial concentration, $A_{0,e}$, was taken from the ratio of the endo isomer (ENDO) and butylbenzene (**BB**) at time zero. The concentration at different times, A_t, was measured by the ratio of ENDO/BB at time t. The estimated final concentration, $A_{\infty,e}$, was determined from the ratio of ENDO/BB in the equilibrium mixture. The equilibrium point was determined when the ratio of ENDO/EXO in the thermolysis of endo isomer became equal to that obtained in the thermolysis of exo isomer at the same temperature. The observed rate constants, k_{obsd}, were calculated using the FOK FORTRAN IV computer programs of Ritchie[33] by feeding in A_t, t, and an established final concentration. The observed rate constants along with the calculated initial concentration, $A_{0,e}$, the final concentrations, $A_{\infty,c}$, and the best fit exponential curves were output. The equilibrium constant, K, was obtained from the measured initial concentration and the calculated final concentration according to the equation $K = (A_{0,e} - A_{\infty,c})/A_{\infty,c}$. Using the calculated equilibrium constant and the observed rate constant, the rate constants of the forward reaction, k_f, and the reverse reaction, k_r, were calculated. The activation parameters were obtained from a linear least-squares treatment of the corresponding Eyring plot and Arrhenius plots.

Thermolysis of *endo*-5-Carbomethoxybicyclo[2.1.0]pentane (30) in Bromobenzene-d_5. A solution of 20 mg of pure endo ester **30** in 0.2 mL of bromobenzene-d_5 was sealed in a thick-walled NMR tube under vacuum (0.05 mm) and then heated in a constant-temperature bath maintained at 200.0 ± 0.2 °C. The reaction was followed by NMR for 19 h. At the end of each appropriate time interval the sample

was removed, cooled to room temperature, and analyzed by NMR. The ratio of endo and exo isomer was determined by integrating the corresponding carbomethoxy proton absorptions. The olefinic absorption region was also examined carefully for the possible formation of isomeric olefin. After 19 h of thermolysis at 200 °C, a 7.8:1 mixture of exo and endo esters was obtained. There was no detectable olefinic compound produced.

Kinetic Measurements of the Epimerization of *endo*-5-Carbomethoxybicyclo[2.1.0]pentane (30). A. Purification. The title compound was purified by silica gel column chromatography followed by vacuum distillation (Kugelrohr apparatus). Reagent grade bromobenzene-d_5 was used without further purification. Reagent grade *n*-butylbenzene was distilled once at 75 °C (15 mm).

B. Reaction Vessels. A number of thick-walled NMR tubes (type 504 pp, Wilmad Glass) were washed with soap and water, distilled water, 10% aqueous disodium ethylenediaminetetraacetate solution, distilled water, and acetone sequentially, and then dried in an oven at 120 °C for at least 5 h before use.

C. Preparation of Samples. A stock solution of 900 mg of pure endo ester **30** and 0.3 mL of distilled butylbenzene in 5 mL of bromobenzene-d_5 was prepared under argon. A 0.2-mL aliquot of this solution was placed in each of a series of cleaned, dried NMR tubes. These tubes were degassed to 0.05 mm in four freeze-thaw cycles and then sealed.

D. The Reaction. A series of sealed sample tubes (at least ten per run) were placed in a constant-temperature silicon oil bath maintained to ±0.2 °C. Individual tubes were removed and cooled in a dry ice-acetone bath. The reaction was followed for at least 5 half-lives and was run at 180.2, 165.3, and 150.2 °C.

E. Sample Analysis. Samples were analyzed by 100-MHz NMR using a JEOL-MH-100 spectrometer. The integrations of the carbomethoxyl proton absorptions, corresponding to the endo and exo isomers, were measured against that of the aromatic signal absorption of the internal standard.

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