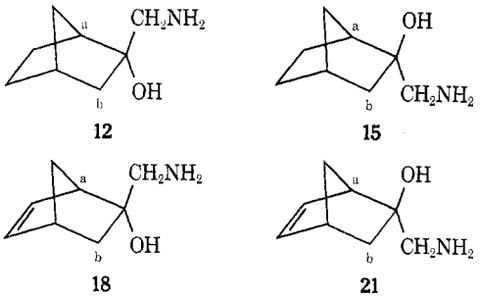
TABLE IV
MIGRATORY APTITUDES IN THE DEAMINATION OF *exo*- AND *endo*-2-NORBORNENYLCARBINYL AND *exo*- AND *endo*-2-NORBORNYLCARBINYL SYSTEMS

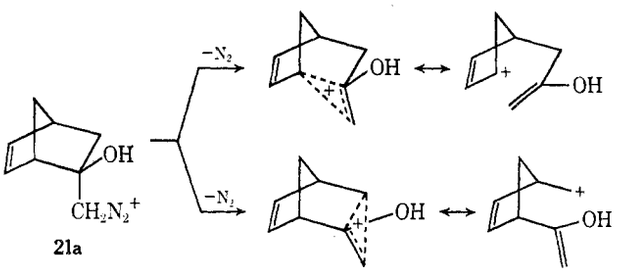


Compd	a migration, %	b migration, %
12	38	62
18	50	50
15	9	91
21	23	77

of ketones **7** and **8** formed in the reaction of **2** with a less than equivalent amount of diazomethane indicates a predominance of exo attack (86%) of diazomethane on **2**. The increase in exo attack of diazomethane on **2** as compared to **1** may be attributed to a greater steric repulsion on the endo face of **2** toward the attack of diazomethane as compared to **1**. Definitely, there is not a favorable interaction between the diazomethane and the double bond in **2** as in the attack of dimethyloxosulfonium methylide on **2**.

A quantitative comparison of methine *vs.* methylene migratory aptitudes observed in the deamination of **18** and **21** with other 2-norbornenyl carbinyl systems cannot be made because, although other systems have been studied,[39] the multiple rearrangements involved led to product mixtures which did not reflect kinetic product control. We can, however, compare the results for the amino alcohols ring expanded in this study. The results are summarized in Table IV. It is seen that the amount of methine migration increases in going from the norbornylcarbinyl to the norborenylcarbinyl system in both the exo and endo carbinyl substrates. Thus, although rearrangement did not occur, the double bond did have the effect of promoting methine migration.

If we look at the transition state for methine migration in **21** we see that one resonance form of this



carbon-bridged species would be stabilized by the double bond, whereas methylene migration would not gain such a stabilizing influence. This could then account for the increased methine migration observed. This represents the first time that such an effect has been observed in a norbornenylcarbinyl system which is uncomplicated by rearrangements.

Registry No.—**1**, 497-38-1; **2**, 694-98-4; **7**, 34956-68-8; **11**, 16282-11-4; **12**, 41915-37-1; **12** hydrochloride, 40344-79-4; **12** benzamide derivative, 41915-39-3; **14**, 16282-09-0; **15**, 41915-41-7; **15** benzamide derivative, 41915-42-8; **17**, 16282-10-3; **18**, 41915-44-0; **18** benzamide derivative, 41915-45-1; **20**, 16282-08-9; **21**, 41915-47-3; **21** benzamide derivative, 41915-48-4; diazomethane, 334-88-3.

(39) R. R. Sauers, R. A. Parent, and H. M. How, *Tetrahedron*, **21**, 2907 (1965).

Notes

Ring Expansions. II. Diazoethane Ring Expansion of Norcamphor

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The reaction of diazoethane with methyl-substituted cyclopropanones has been studied by Turro.[1] The mechanisms of these reactions were discussed in terms of the stereoelectronics of the ring expansions and the role of conformational equilibria on the product distributions. It was concluded that conformational restrictions play an important role in the diazoethane ring expansions and that, owing to the exothermicity of the reactions, a synchronous addition–rearrangement mechanism may be operative. Thus, the product ratios could be explained on the bases of the energy content of the transition states favored by steric approach considerations. Marshall and Partridge[2] had earlier studied the ring expansion of 4-alkylcyclohexanones with diazoethane. Steric approach control of the diazoethane and conformational interactions in the intermediates were the important factors controlling the product distributions found in their work also.

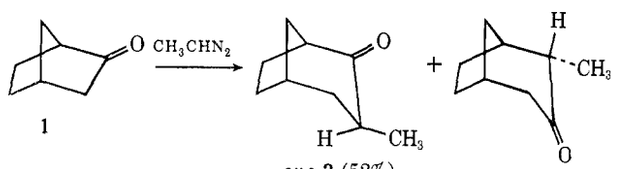
We would like to report our results on the diazoethane ring expansion of norcamphor (**1**). The product ratios obtained can be explained in terms of steric approach control of the diazoethane on the exo face of norcam-

(1) N. J. Turro and R. B. Gagosian, *J. Amer. Chem. Soc.*, **92**, 2036 (1970).

(2) J. A. Marshall and J. J. Partridge, *J. Org. Chem.*, **33**, 4090 (1968).

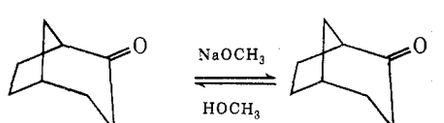
phor, the migratory aptitude of the methine and methylene carbons in the product-forming intermediates, and conformation equilibria in the intermediates.

The ring expansion of norcamphor (1) was carried out in methanol by generation *in situ* of diazoethane from *N*-ethyl-*N*-nitrosourethane.[3] The reaction of 1 with a fourfold excess of diazoethane yielded two ring-expansion products in 59% yield. The two ketones were isolated by preparative glpc. One ketone was identified as *exo*-3-methylbicyclo[3.2.1]octan-2-one (*exo*-2) by comparison of its spectral properties and the melting point of its 2,4-dinitrophenylhydrazone derivative with those reported by Sisti.[4] The other ketone was identified as *endo*-2-methylbicyclo[3.2.1]octan-3-one (*endo*-3) by comparison of its spectral properties with those of a sample prepared by the methylation of bicyclo[3.2.1]-octan-3-one (see Experimental Section). The reaction of 1 with less than 1 equiv of diazoethane yields *exo*-2 and *endo*-3 in the ratio of 1.1:1, as shown below.



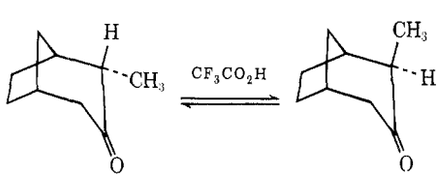
1 *exo*-2 (52%) *endo*-3 (48%)

The exo and endo isomers of 3-methylbicyclo[3.2.1]-octan-2-one (2) were also prepared by methylation of bicyclo[3.2.1]octan-2-one with tritylsodium and methyl iodide in dioxane. The two isomers were separated by preparative glpc and independently isomerized to a thermodynamic mixture with 3% sodium methoxide in methanol. The results are shown below.



exo-2 (70%) *endo*-2 (30%)

In a similar manner bicyclo[3.2.1]octan-3-one was methylated and a mixture of the exo and endo isomers, which could not be separated by glpc, was collected by preparative glpc and the mixture was equilibrated by heating with trifluoroacetic acid. The isomer ratio was determined by nmr integration of the doublet methyl absorptions. The following mixture was obtained.



endo-3 (67%) *exo*-3 (33%)

Thus, the methyl ketones obtained in the ring expansion of 1 with diazoethane are the thermodynamically more stable isomers.

These results for the ring expansion of 1 with diazoethane indicate that methylene and methine migration occur to an almost equal extent. The similar reaction of diazomethane with 1 results in a 70:30 ratio of methylene to methine migration.[5] This reaction was found to occur with preferential exo attack (75%) of diazomethane on 1.[5]

The rate-limiting step in the diazoalkane ring expansion is the addition of the diazoalkane to the ketone,[6] and therefore the steric approach of the diazoethane on 1 as well as steric interactions in the rotameric forms of the product-determining intermediates should control which carbon–carbon bond migrates. Thus, Scheme I outlines a reasonable reaction pathway for reaction of diazoethane with 1. Only exo attack intermediates are considered on the assumption that endo attack of diazoethane would be sterically less accessible than endo attack of diazomethane on 1, which occurred to the extent of 25%.

Exo attack of diazoethane with the methyl group "out" would lead to rotameric intermediates A and B, of which A would be sterically most favored. Ring expansion from A affords *endo*-3, which is one of the observed products. Expansion of B gives *exo*-2, the other observed ring-enlarged product. The ring-enlarged products which would result from the methyl "in" intermediates C and D are not observed. Thus, steric approach control strongly favors initial formation of intermediate A. Although methylene migration was favored in the ring expansion of 1 with diazomethane, the ring expansion of 1 with diazoethane led to equal amounts of methylene and methine carbon migration. This is reasonable if ring expansion occurs by the back-side displacement of nitrogen by the migrating carbon atom,[7] for conformer B, which allows methylene migration, should be sterically less favorable than A owing to the position of the methyl group opposed to the C-7 methylene. These results therefore are explainable in terms of a ring-expansion mechanism in which the diazoalkane approaches the ketone in the sterically most favorable fashion leading to a β-hydroxy diazonium ion as an intermediate. This intermediate is then partitioned to products through its various rotameric forms, most probably with a trans relationship between the migrating carbon and the expelled nitrogen molecule. If a synchronous mechanism were operative, with structures A–D of Scheme I representing transition states, one would have expected some *endo*-2 as a product because structure D should be sterically more favorable than B and this would balance, at least in part, the small energy difference (0.5 kcal) between the *exo*-2 and *endo*-2 products.

Experimental Section[8]

Ring Expansion of Norcamphor (1).—To a solution of 2.0 g (18.2 mmol) of 1 in 10 ml of 3% methanolic K_2CO_3 was added 8.7

(3) W. W. Hartmann and R. Phillips, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 464.

(4) A. J. Sisti, *J. Org. Chem.*, **35**, 2670 (1970).

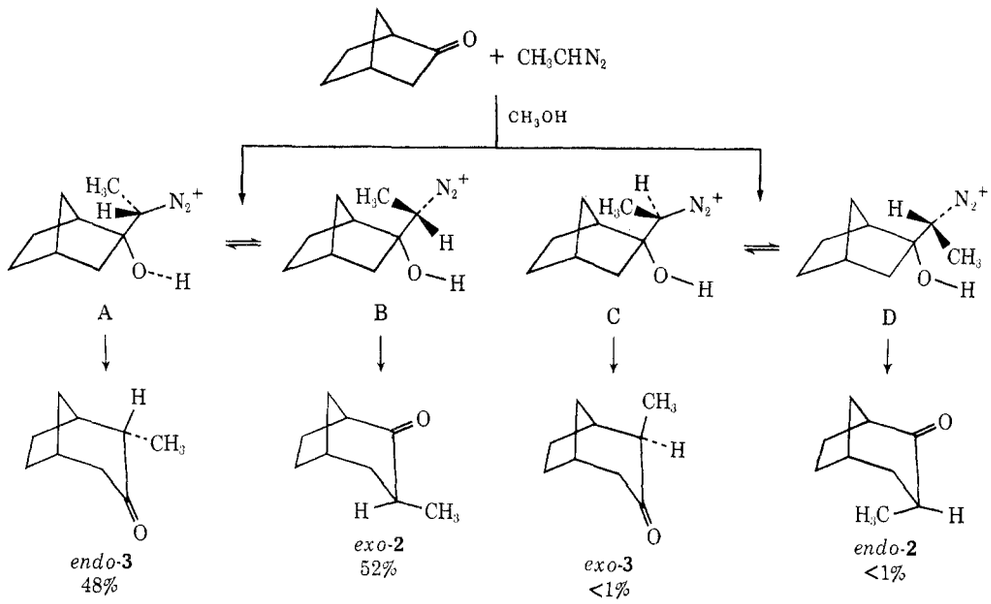
(5) M. A. McKinney and P. P. Patel, *J. Org. Chem.*, **38**, 4059 (1973).

(6) J. N. Bradley, C. W. Cowell, and H. Ledwith, *J. Chem. Soc.*, 4334 (1964).

(7) C. D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reaction," Academic Press, New York, N. Y., 1968.

(8) All melting points and boiling points are uncorrected. Nuclear magnetic resonance spectra were obtained on a Varian A-60A spectrometer, using TMS as the internal standard and CCl_4 as the solvent. Infrared spectra were recorded on a Beckman IR-12 spectrometer. Mass spectra were obtained using a CEC 21-104 mass spectrometer. Gas chromatographic analyses were performed on an F & M Model 700 gas chromatograph equipped with a thermal conductivity detector and a Disc integrator. Microanalysis was performed by Chemalytics, Inc., Tempe, Ariz.

SCHEME I



g (59.6 mmol) of *N*-ethyl-*N*-nitrosourethane[3] at such a rate so as to maintain the temperature of the reaction mixture between 20 and 25°. The reaction solution was concentrated and analyzed by glpc.[9] The chromatogram indicated three components, which were collected individually and identified as follows.

Fraction 1 (40%, retention time 6.4 min) was identified as unreacted **1**.

Fraction 2 (33%, retention time 9.6 min) had nmr δ 0.93 (d, J = 7 Hz, 3, CH_3), 1.1–2.8 (m, 11 hydrogens); ir (neat) 1715 cm^{-1} (C=O); mass spectrum (70 eV) m/e 138. A semicarbazone derivative was prepared in the usual manner,[10] mp 203–204° dec from ethanol–water.

Anal. Calcd for $C_{10}H_{17}N_3O$: C, 61.51; H, 8.77; N, 21.53. Found: C, 61.61, H, 8.80; N, 21.56.

This compound was assigned the structure *endo*-2-methylbicyclo[3.2.1]octan-3-one (*endo*-**3**) by comparison of its nmr spectrum with that of the thermodynamically most stable product obtained from the methylation of bicyclo[3.2.1]octan-3-one (see below).

Fraction 3 (25%, retention time 10.4 min) was identified as *exo*-3-methylbicyclo[3.2.1]octan-2-one (*exo*-**2**): nmr δ 0.94 (d, J = 6 Hz, CH_3), 2.4 (b s, 1 bridgehead H, C-5), 2.7 (b s, 1 bridgehead H, C-1); ir (CCl_4) 1713 cm^{-1}; 2,4-DNP derivative mp 146–147° (lit.[4] mp 144–145.5°).

In another experiment a solution of 0.5 g of **1** in 5 ml of 3% methanolic K_2CO_3 was allowed to react with 0.27 g (1.86 mmol) of *N*-ethyl-*N*-nitrosourethane as described above. The solution was concentrated and glpc analysis[9] showed that *exo*-**2** and *endo*-**3** were formed in the ratio 1.1:1 in 1–2% yield.

***exo*- and *endo*-3-Methylbicyclo[3.2.1]octan-2-one (2).**—To a solution of 2.0 g (16 mmol) of bicyclo[3.2.1]octan-2-one in 6 ml of dry dioxane was added a solution of 0.15*M* tritylsodium[11] in ether under a nitrogen atmosphere. The addition was continued until a deep red color persisted, the mixture was stirred for 5 min, and then 11.5 g (80.6 mmol) of freshly distilled methyl iodide was added as rapidly as possible. The reaction mixture was stirred overnight, diluted with water, and extracted with five 100-ml portions of petroleum ether, and the extracts were combined and dried (Na_2SO_4). The solution was concentrated and short-path distillation gave 0.55 g (25%, corrected for 30% unreacted starting material), bp 68–71° (2.25 mm), of methylated product. The ketones were separated by preparative glpc[12] and identified as follows.

The first fraction (21%, retention time 6.3 min) was identified as *endo*-3-methylbicyclo[3.2.1]octan-2-one (*endo*-**2**): nmr δ 1.09 (d, J = 5 Hz, CH_3), 1.67–2.17 (m, 9 hydrogens), 2.47 (b s, 1, bridgehead, C-5), 2.72 (b s, 1 bridgehead, C-1); ir (CCl_4) 1713 cm^{-1} (C=O).

Fraction 2 (49%, retention time 7 min) was identified as *exo*-3-methylbicyclo[3.2.1]octan-2-one (*exo*-**2**): nmr δ 0.94 (d, J = 6 Hz, CH_3), 1.23–2.25 (m, 9 hydrogens), 2.4 (b s, 1, bridgehead, C-5), 2.7 (b s, 1, bridgehead, C-1); ir (CCl_4) 1713 cm^{-1} (C=O); 2,4-DNP derivative mp 146–147° (lit.[4] mp 144–145.5°). This component was identical in all respects with one of the products of the diazoethane ring expansion of **1**.

Fraction 3 (25%, retention time 8 min) was identical in all respects with unreacted bicyclo[3.2.1]octan-2-one.

Isomerization of *exo*-2 and *endo*-2.—A 200-mg sample of *endo*-**2** was dissolved in 2 ml of 3% sodium methoxide in methanol and the solution was heated under reflux in a nitrogen atmosphere for 24 hr. The solution was cooled and diluted with 15 ml of ice–water, extracted with a pentane–methylene chloride mixture, washed to neutrality with water, dried (Na_2SO_4), and concentrated using a 10-in. Vigreux column. The residue was analyzed by glpc[12] and shown to consist of a 31:69 mixture of *endo*-**2** and *exo*-**3**, respectively.

In another experiment a 200-mg sample of *exo*-**2** was isomerized in a similar manner and glpc[12] analysis after work-up showed a 30:70 mixture of *endo*-**2** and *exo*-**3**, respectively.

***exo*- and *endo*-2-Methylbicyclo[3.2.1]octan-3-one (3).**—A 1.2-g sample of bicyclo[3.2.1]octan-3-one was methylated as described previously for bicyclo[3.2.1]octan-2-one. Work-up of the reaction mixture gave 1.04 g of product, bp 59–61° (1 mm). The product mixture was analyzed by glpc[13] and shown to consist of three components.

Fraction 1 (14%, retention time 4.5 min)[14] was identical in all respects with bicyclo[3.2.1]octan-2-one.

Fraction 2 (61%, retention time 6 min) was shown by nmr analysis (integration of doublet methyl absorptions) to be a 24:76 mixture of *exo*-**3** and *endo*-**3**, respectively: nmr δ 0.95 (d, J = 6.5 Hz, endo CH_3), 1.12 (d, J = 7 Hz, exo CH_3), 1.4–2.7 (m, 11 hydrogens; ir (neat) 1718 cm^{-1} (C=O); mass spectrum (70 eV) m/e 138. The major component of this mixture had a doublet methyl absorption in the nmr which matched the abforption obtained for one of the ring-expansion products obtained from **1** and diazoethane.

Fraction 3 (25%, retention time 7.7 min) was not fully characterized, but nmr, ir, and mass spectral analysis showed it to be a mixture of dimethylbicyclo[3.2.1]octan-3-ones.

(9) A 13 ft × 0.25 in. aluminum column packed with 20% diethylene glycol succinate (DEGS) on 60–80 mesh Chromosorb W was used at 140° with a 120 ml/min He flow rate.

(10) D. J. Pasto and C. R. Johnson, "Organic Structure Determination," Prentice-Hall, Englewood Cliffs, N. J., 1969, p 390.

(11) W. B. Renfrow, Jr., and C. R. Hauser, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 607.

(12) Same column as in ref 9 at 175° and a 70-ml/min He flow rate.

(13) A 6 ft × 0.25 in. aluminum column packed with 20% SE-30 on 60–80 mesh Chromosorb W was used at 160° with a 50-ml/min He flow rate.

(14) All attempts to resolve this mixture on other glpc columns were unsuccessful.

Isomerization of *exo*-3 and *endo*-3.[15]—A 50-mg sample of fraction 3 from above was heated to 110° in trifluoroacetic acid for 60 hr under nitrogen, diluted with water, neutralized with solid $NaHCO_3$, extracted with ether, dried (Na_2SO_4), and concentrated. Nmr analysis showed a 33:67 mixture of *exo*-3 and *endo*-3 respectively.

Registry No.—1, 497-38-1; *exo*-2, 41828-85-7; *endo*-2, 41828-86-8; *endo*-3, 41828-87-9; *endo*-3 semicarbazone, 41828-88-0; *exo*-3, 41828-89-1; *N*-ethyl-*N*-nitrosourethane, 614-95-9; bicyclo[3.2.1]octan-2-one, 5019-82-9; methyl iodide, 74-88-4; bicyclo-[3.2.1]octan-3-one, 5019-82-9.

(15) Attempted isomerization with sodium methoxide in methanol led to a complex reaction mixture, apparently owing to aldol condensations.

Preparation of 4-Phenyl Medium- and Large-Sized Ring Ketones

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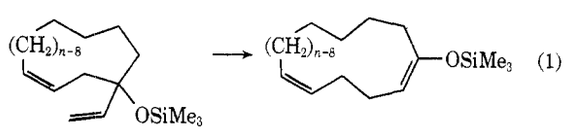
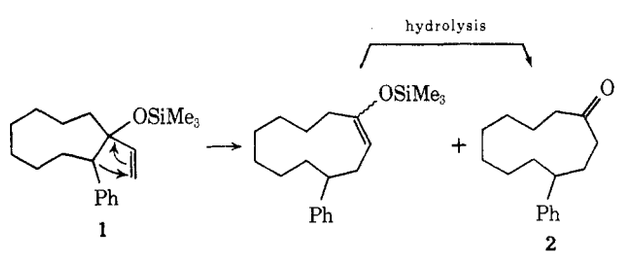
Previous studies in these laboratories[1] have described the siloxy-Cope rearrangement as a ring expansion for medium-sized rings (*e.g.*, eq 1). The present



(1)

n = 8, 9, 10

work shows that 2-phenyl-1-trimethylsiloxy-1-vinylcyclononane (**1**) undergoes a related rearrangement



cis and trans

which represents a general ring expansion route to 4-phenyl medium- and large-sized ring ketones. Other synthetic approaches to such compounds are quite limited.[2]

Cyclooctanone was converted by a previously described procedure[3] to 2-phenylcyclononanone. The reaction of this ketone with vinylmagnesium bromide gave only very low conversion and that with vinylmagnesium chloride gave serious side reactions. However, the reaction with vinyllithium gave a 60% conversion to the vinyl alcohol. The incomplete reaction presumably arises because enolate anion formation competes with the desired reaction. The conversion can be increased by allowing the crude mixture to react again (*ca.* 75% conversion). Alternatively, the unreacted ketone can be readily removed by chromatography and recycled. Trimethylsilylation of the alcohol gives complete conversion to **1**.

Heating **1** in sealed ampoules in the 210–280° temperature range gave enol ethers corresponding to a [1,3] sigmatropic shift and also the corresponding ketone **2**. Hydrolysis of the mixture gave **2** in 80% overall yield from **1**.

The structure of **2** was assigned from the nmr spectrum and from decoupling experiments carried out on samples in which the chemical shifts had been separated with Eu(fod)$_3$. Thus sufficient shift reagent was added so that the α-proton multiplet moved to δ 5.0, the benzylic proton (a broad triplet) to δ 4.5, and three of the β protons to δ 3.9.[4] Decoupling established that the benzylic proton was coupled to the β protons, which were in turn coupled to the α protons, thus establishing the position of the phenyl on the ring.

Kinetic measurements were made (Table I); however, the data were somewhat erratic and gave activation parameters that are unreasonable for a simple process (E_a = 25.4 and log A = 5.5). Presumably a major part of the reaction involves some sort of surface catalysis or radical chain process. This process apparently causes formation of ketone during the pyrolysis, which is not normal for this type of reaction. Major amounts of ketone were formed with this system even when the ampoules were carefully dried.

TABLE I

AMPOULE PYROLYSIS OF 2-PHENYL-1-TRIMETHYLSILOXY-1-VINYLCYCLONONANE (**1**)

Temp, °C	Time, hr	% **2**[a,b]	% nonvolatile[b]
213	11.75	42	
	24	58	
225	6	44	
	12	63	
260	6	30	
	12	66	
	18	74	
280	6	59	12
	12	74	17
310	0.67	58	41
330	0.67	52	48

[a] Measured after hydrolysis of the pyrolysis mixture. [b] Yield and nonvolatile were determined by gc using an internal standard.

Although the reaction is not kinetically well behaved, it is high yield and clean in the sense that it leads to a single product after hydrolysis. The success of the reaction depends on the balance between the change in ring strain and the favorable energy change associated with formation of the enol (*ca.* 4.5 kcal/mol[5]). By analogy with the related systems shown in eq 1, the reaction should be feasible for rings larger than eight membered.

(1) (a) R. W. Thies, *Chem. Commun.*, 237 (1971); (b) R. W. Thies, *J. Amer. Chem. Soc.*, **94**, 7074 (1972); (c) R. W. Thies, M. T. Wills, A. W. Chin, L. E. Schick, and E. S. Walton, *ibid.*, **59**, 5281 (1973); (d) R. W. Thies and J. E. Billigmeier, 161st National Meeting of the American Chemical Society, Los Angeles, Calif, March 28–April 12, 1971, Abstract 162.

(2) For syntheses of 4-phenylcyclooctanone see A. C. Cope and R. B. Kinnel, *J. Amer. Chem. Soc.*, **88**, 752 (1966); A. C. Cope and R. B. Kinnel, *ibid.*, **89**, 5995 (1967); A. C. Cope, M. A. McKervey, and N. M. Weinshenker, *ibid.*, **89**, 2932 (1967).

(3) A. J. Sisti, *J. Org. Chem.*, **33**, 453 (1968). For an alternative method, see E. Müller and R. Heischkeil, *Tetrahedron Lett.*, 1032 (1962).

(4) The remainder of the spectra consists of the phenyl protons at δ 7.2 and 7.6, a two-proton multiplet containing the remaining β proton at δ 3.2, and a large multiplet at δ 2.9–1.8.

(5) S. J. Rhoads and E. E. Waali, *J. Org. Chem.*, **35**, 3358 (1970).