Ring Expansions. I. Diazomethane and Tiffeneau–Demjanov Ring Expansions of Norcamphor and Deyhydronorcamphor[1]

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Received November 22, 1972

The ring expansion of norcamphor (**1**) with diazomethane in methanol leads to a complex mixture of homologous ketones. When **1** was allowed to react with less than a stoichiometric amount of diazomethane, bicyclo[3.2.1]-octan-2-one (**3**) and bicyclo[3.2.1]octan-3-one (**4**) were formed in the ratio of 70:30. Ring expansion of *exo*-2-aminomethylbicyclo[2.2.1]heptan-*endo*-2-ol (**12**) gave ketones **3** and **4** in the ratio of 62:38 while ring expansion of *endo*-2-aminomethylbicyclo[2.2.1]heptan-*exo*-2-ol (**15**) yielded **3** and **4** in the ratio of 91:9. Comparison of these results indicates a predominance of exo attack of diazomethane on **1**. Similarly, the reaction of less than a stoichiometric amount of diazomethane in methanol with dehydronorcamphor (**2**) yielded bicyclo[2.1.1]oct-6-en-2-one (**7**) and bicyclo[3.2.1]oct-6-en-3-one (**8**) in the ratio of 53:47. Ring expansion of *exo*-2-aminomethylbicyclo[2.2.1]hept-5-en-*endo*-2-ol (**18**) yielded ketones **7** and **8** in the ratio of 50:50. Ring expansion of *endo*-2-aminomethylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (**21**) afforded **7** and **8** in the ratio of 77:23. Predominant exo attack of diazomethane on **2** is indicated by these results. Competition experiments indicated that **2** was two times as reactive as **1** toward diazomethane in methanol. The migratory aptitudes for the compounds examined in this study are compared to other *exo*- and *endo*-2-norbornylcarbinyl systems.

Cyclic ketones can be transformed into their higher homologs by reaction with diazoalkanes[2] and by the Tiffeneau–Demjanov[3] rearrangement of amino alcohols derived from the cyclic ketone. If the diazoalkane ring expansion is carried out in an alcoholic solvent[4] the intermediates in both types of ring expansion reactions is a β-hydroxy diazonium ion.

The extensive investigations of Gutsche[5] on the ring expansion of unsymmetrical cyclic ketones by the diazoalkane method have elucidated the importance of electronic and steric factors in governing the migratory aptitude of the ring carbon atoms. Steric factors also play an important role in determining the stereochemistry of attack of the diazoalkane as well as the amount of epoxide formation accompanying ring expansion.[6]

The stereochemistry of attack of diazomethane on *trans*-2-decalone[7] and 5*A*-3-oxo steroids[8] has been determined. Comparison of the ratio of isomeric ketone products obtained in these systems, when ring expanded with diazomethane, to the ratio obtained from the epimeric amino alcohols indicated predominant equatorial attack of diazomethane. The stereochemistry of attack and the migratory aptitudes in the diazoethane ring expansion of 4-alkylcyclohexanones[9] and methylcyclopropanones[10] have been examined. The product ratios obtained in these studies were explained in terms of steric approach control and conformational interactions in the intermediates.

Only recently has the diazomethane ring expansion of bridged bicyclic ketones been investigated. The reaction of norcamphor with diazomethane was first reported by Sauers.[11] In a more extensive study Pietra[12] determined the relative reactivities of a series of bicyclo[*n*.2.1]alkanones toward diazomethane as well as the migratory aptitudes for norcamphor and bicyclo[3.2.1]octan-2-one. The migratory aptitudes in the ring expansion of bicyclo[2.1.1]hexan-2-one and its monomethylated derivatives have also been reported.[13] The effect of unsaturation on the stereochemistry of attack and the product ratios obtained in the reaction of diazomethane with 7-ketonorbornene and 7-ketonorborane has been examined by Bly.[14] In order to assess the importance of stereochemistry in determining the migratory aptitudes in the ring expansion of bridged bicyclic ketones we have studied the Tiffeneau–Demjanov ring expansion of the epimeric β-amino alcohols of norcamphor (**1**) and dehydronorcamphor (**2**). The ketonic product ratios obtained in these ring expansions are compared with the product ratios obtained in the diazomethane ring enlargement of **1** and **2**.

Experimental Section[15]

Preparation of *exo*-2-Aminomethylbicyclo[2.2.1]heptan-*endo*-2-ol (12).—A 300-ml pressure reaction vessel (Autoclave Engineers, Inc.) was flushed with nitrogen and cooled externally by a Dry Ice–acetone bath. The vessel was charged with 3.0 g (25 mmol) of epoxide 11[16] in 10 ml of anhydrous ether and 4.8 g (0.12 mol) of sodium amide[17] in 65 ml of liquid ammonia. The apparatus was sealed and allowed to warm to room temperature.

(1) This work was supported in part by a grant from the donors of the Petroleum Research Fund, administered by the American Chemical Society, and a Marquette University Committee on Research Grant.

(2) (a) C. D. Gutsche, *Org. React.*, **8**, 364 (1954); (b) C. D. Gutsche and D. Redmore, "Carbocyclic Ring Expansion Reactions," Academic Press, New York, N. Y., 1968.

(3) P. A. S. Smith and D. R. Baier, *Org. React.*, **11**, 157 (1960).

(4) J. N. Bradley, G. W. Cowell, and A. Ledwith, *J. Chem. Soc.*, 4334 (1964).

(5) (a) C. D. Gutsche, *J. Amer. Chem. Soc.*, **71**, 3513 (1949); (b) C. D. Gutsche and H. H. Peter, *ibid.*, **77**, 5971 (1955).

(6) C. D. Gutsche, H. F. Strohmayer, and J. M. Chang, *J. Org. Chem.*, **23**, 1 (1958).

(7) R. G. Carlson and N. J. Behn, *J. Org. Chem.*, **33**, 2069 (1968).

(8) J. B. Jones and P. Price, *J. Chem. Soc. D*, 1478 (1969).

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

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

(11) R. R. Sauers and R. J. Tucker, *J. Org. Chem.*, **28**, 876 (1963).

(12) G. Fachinetti, F. Pietra, and A. Marsili, *Tetrahedron Lett.*, 393 (1971).

(13) T. Gibson, *J. Org. Chem.*, **37**, 700 (1972).

(14) R. S. Bly, F. B. Culp, and R. K. Bly, *J. Org. Chem.*, **35**, 2235 (1970).

(15) All boiling and melting points are uncorrected. The infrared spectra were recorded on a Beckman IR-12 spectrophotometer and a Perkin-Elmer spectrophotometer. The nuclear magnetic resonance spectra were recorded on a Varian A-60A nmr spectrometer. Quantitative gas–liquid phase chromatographic analyses were obtained using an F & M Model 700 gas chromatograph equipped with a Leeds and Northrup Speedomax H nonintegrating recorder, and preparative separations were performed on an F & M Model 770 automatic preparative gas chromatograph; both instruments were equipped with thermal conductivity detectors. Microanalyses were performed by Chemalytics, Inc., Tempe, Ariz. Mass spectra were run on a Hitachi RMU-6A spectrometer at Purdue University, Lafayette, Ind.

(16) R. S. Bly, C. M. DuBose, Jr., and G. B. Konizer, *J. Org. Chem.*, **33**, 2188 (1968).

(17) C. R. Hauser, J. T. Adams, and R. Levine, "Organic Syntheses," Collect. Vol. III, Wiley, New York, N. Y., 1955, p 291.

After 24 hr,[18] the apparatus was recooled in a Dry Ice–acetone bath and opened, and the ammonia was allowed to evaporate upon warming to room temperature. The resulting slurry was quenched with a saturated ammonium chloride solution and extracted with five 150-ml portions of ether. The combined ether extract was dried ($MgSO_4$) and concentrated. The residue was flash vacuum distilled in a short-path distillation apparatus to yield 2.77 g of crude amino alcohol, bp 104° (0.05 mm). The crude product was vacuum sublimed (50–60°, 0.02 mm) three successive times to yield 1.5 g (44%) of amino alcohol, mp 108.5–111° dec. The amino alcohol was extremely hygroscopic and was therefore characterized through its hydrochloride and benzamide derivatives.

A hydrochloride was prepared using the method of Parham:[19] mp 259–260° dec; ir (Nujol) 3493, 1623, 1600, 1212, 1023, 1000, 1163, 795, and 708 cm^{-1}; nmr (CF_3CO_2H) δ 1.27–2.33 (unresolved pattern, 9 protons), 2.44 (broad s, 2, bridgehead protons), 3.47 (q, 2, J = 6 Hz, $CH_2NH_3^+$), 7.0 (broad, 3, NH_3^+).

Anal. Calcd for $C_8H_{16}ONCl$: C, 54.08; H, 9.01; N, 7.88; Cl, 19.97. Found: C, 54.11; H, 8.82; N, 7.47; Cl, 19.82.

A benzamide derivative was prepared in the usual manner,[20] mp 150–151°.

Anal. Calcd for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.80; N, 5.36. Found: C, 73.13; H, 7.68; N, 5.71.

Preparation of *endo*-2-Aminomethylbicyclo[2.2.1]heptan-*exo*-2-ol (15).—A 3.31-g (26.7 mmol) sample of epoxide **17**[16] in 10 ml of anhydrous ether was allowed to react with a freshly prepared solution of 5.2 g (0.134 mol) of sodium amide in 65 ml of liquid ammonia in the manner described in the synthesis of **12**. The crude product was vacuum sublimed (50–60°, 0.01 mm) and desiccated over phosphorus pentoxide to yield 2.32 g (62%) of amino alcohol: mp 60–130°; ir (Nujol) 3315, 3280, 2950, 1640, and 1375 cm^{-1}. The amino alcohol was extremely hygroscopic and therefore was characterized as its benzamide derivative:[20] mp 132–132.5°; nmr ($CDCl_3$) δ 7.6 (m, 5, phenyl), 6.9 (broad s, 1, NH), 3.6 (d, J = 5.5 Hz, 2, CH_2N), 3.13 (s, 1, OH), 2.4–0.85 (unresolved pattern, 10 protons).

Anal Calcd for $C_{15}H_{19}O_2N$: C, 73.44; H, 7.80; N, 5.36. Found: C, 73.57; H, 7.77; N, 5.68.

Preparation of *exo*-2-Aminomethylbicyclo[2.2.1]hept-5-ene-*endo*-2-ol (18).—A 3.0-g (25 mmol) sample of epoxide **14**[16] in 10 ml of anhydrous ether was allowed to react with a solution of 4.8 g (0.12 mol) of sodium amide in 65 ml of liquid ammonia as described previously. After normal work-up the crude product was flash vacuum distilled in a short-path distillation apparatus, bp 60–105° (0.02 mm), to yield 2.74 g of crude product. Vacuum sublimation (50–60°, 0.01 mm) and vacuum desiccation (20 mm) over phosphorus pentoxide afforded 2.45 g (72%) of **18**: mp 108–109° dec; ir (Nujol) 3360 (s, OH), 3280, 3300 (broad doublet, primary NH_2), 1215, and 1050 cm^{-1} (CN); nmr (CCl_4) δ 6.25 (ABX multiplet, 2, CH=CH), 2.8 (broad s, 4, bridgeheads and CH_2N), 2.00 (broad s, 3, OH and NH_2), 0.85–1.85 (unresolved pattern, 4 protons). A benzamide derivative was prepared in the usual manner,[20] mp 152–153°.

Anal. Calcd for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.04; N, 5.78. Found: C, 73.77; H, 6.85; N, 5.95.

Preparation of *endo*-2-Aminomethylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (21).—A 3.0-g (25 mmol) sample of epoxide **20**[16] in 10 ml of anhydrous ether was allowed to react with 4.8 g (0.123 mol) of sodium amide in 65 ml of liquid ammonia as described previously. Work-up and flash vacuum distillation in a short-path distillation apparatus yielded 3.8 g, bp 80–101° (0.02 mm), of crude product. Vacuum sublimation (50–60°, 0.01 mm) and vacuum desiccation (20 mm) over phosphorus pentoxide yielded 2.8 g (82%) of **21**: mp 72–74° dec; ir (Nujol) 3345, 1380, 1180, 1130, 1075, 810, and 710 cm^{-1}; nmr ($CDCl_3$) δ 6.1 (ABX multiplet, 2, CH=CH), 2.85 (broad, m, 1, bridgehead proton), 2.6 (broad s, 3, CH_2N and OH), 2.1–1.0 (unresolved pattern, 7 protons). A benzamide derivative was prepared in the usual manner,[20] mp 107–107.5°.

Anal. Calcd for $C_{15}H_{17}O_2N$: C, 74.04; H, 7.04; N, 5.78. Found: C, 73.69; H, 6.98; N, 5.88.

Ring Expansion of Amino Alcohol 12. A.—A 500-mg (3.55 mmol) sample of **12** dissolved in 5 ml of water containing 266 mg (4.43 mmol) of acetic acid was stirred magnetically and cooled in an ice–water bath. To this, a solution of 310 mg (4.4 mmol) of sodium nitrite in 5 ml of water was added dropwise over a period of 15 min. The mixture was stirred for an additional 1 hr at ice-bath temperature, heated at reflux for another 1 hr, and then allowed to cool to room temperature. The solution was neutralized with sodium bicarbonate solution and extracted with five 100-ml portions of ether, and the combined ether extracts were dried ($MgSO_4$) and concentrated. The crude product was vacuum sublimed (50–60°, 20 mm) yielding 207 mg (47%) of a mixture which was shown by glpc analysis[21] to consist of two components which were collected individually and identified as follows. The first component (retention time 5.5 min, relative abundance 37.7%) was identical in all respects (ir, nmr, and retention time) with an authentic sample of bicyclo[3.2.1]octan-3-one (**4**), mp 139–140° (lit.[22] mp 139°). The second component (retention time 6.8 min, relative abundance 62.3%) was identical in all respects (ir, nmr, and retention time) with an authentic sample of bicyclo[3.2.1]octan-2-one (**3**), mp 120–122° (lit.[23] mp 121–123.5°).

B.—A 266-mg (1.5 mmol) sample of **12** HCl dissolved in 10 ml of water containing 112 mg (1.87 mmol) of acetic acid was stirred magnetically and cooled in an ice–water bath. To this, a solution of 129 mg (1.87 mmol) of sodium nitrite was added dropwise over a period of 15 min. The mixture was stirred for an additional 1 hr at ice-bath temperature, heated at reflux for 1 hr, and then allowed to cool to room temperature. Normal work-up afforded 160 mg (86%) of a mixture which was shown by glpc analysis[21] to consist of 61.3% ketone **3** and 38.7% ketone **4**, by their glpc retention times and spectral properties.

Ring Expansion of Amino Alcohol 15.—A 500-mg (3.55 mmol) sample of **15** was ring expanded according to procedure A used for **12**. Work-up and sublimation (50–60°, 20 mm) afforded 230 mg (53.5%) of a mixture which by glpc analysis was shown to consist of 9% ketone **4** and 91% ketone **3**, by their glpc retention times and spectral properties.

Ring Expansion of Amino Alcohol 18.—A 1.2-g (8.64 mmol) sample of amino alcohol **18** was ring expanded according to the procedure outlined above for amino alcohol **12**. Normal work-up and sublimation (50–60°, 20 mm) yielded 490 mg (46%) of a mixture which was shown by glpc analysis[21] to consist of two components which were collected individually and identified as follows. The first component (retention time 9 min, relative abundance 50%) was identified as bicyclo[3.2.1]oct-6-en-2-one (**7**): mp 74–75.5°; nmr (CCl_4) δ 6.05 (ABX multiplet, 2, CH=CH), 3.05–1.6 (unresolved pattern, 8 protons); ir (CCl_4) 1725, 1455–1425, and 720 cm^{-1}; mass spectrum (70 eV) m/e 122. The second component (retention time 9.8 min, relative abundance 50%) was identical in all respects (ir, nmr, and retention time) with an authentic sample of bicyclo[3.2.1]oct-6-en-3-one[24] (**8**), mp 98–99.5° (lit.[24] mp 99–100.5°).

Ring Expansion of Amino Alcohol 21.—A 1.2-g (8.64 mmol) sample of amino alcohol **21** was ring expanded according to the procedure outline above for amino alcohol **12**. Normal work-up and sublimation (50–60°, 20 mm) yielded 510 mg (49%) of a mixture which was shown gy glpc[21] analysis to consist of 77.3% ketone **7** and 22.7% ketone **8**.

A part of the mixture from this experiment was combined with a sample of the ketone mixture obtained from the ring expansion of **18**. The mixture (600 mg, 4.9 mmol) was hydrogenated in 25 ml of absolute ethanol at 50 psi (Parr hydrogenation apparatus) using 6.7 mg of 5% palladium on charcoal as catalyst. After the hydrogen uptake had ceased, the solution was filtered and concentrated and the residue was sublimed (50–60°, 20 mm) to give 494 mg (81%) of a mixture which was shown by glpc analysis[21] to contain ketones **3** and **4**, by their glpc retention times and spectral properties. Thus, the assigned structures for the unsaturated ketones obtained in the ring expansion of amino alcohols **18** and **21** were further confirmed.

Reaction Products of Bicyclo Ketones with Diazomethane. A. Norcamphor (1).—To a solution of 500 mg (4.55 mmol) of nor-

(18) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, **87**, 1353 (1965).

(19) W. E. Parham and L. J. Czuba, *J. Amer. Chem. Soc.*, **90**, 4030 (1968).

(20) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1935, p 260.

(21) A 13 ft × 0.25 in. aluminum column packed with 20% diethylene glycol succinate (DEGS) on 45–60 mesh Chromosorb W-AW was employed at a temperature of 170° and a helium flow rate of 110 ml/min.

(22) C. W. Fefford and B. Waegell, *Tetrahedron Lett.*, 1981 (1963).

(23) K. Alder and W. E. Windemuth, *Chem. Ber.*, **71**, 2404 (1938).

(24) N. A. LeBel and R. N. Liesmer, *J. Amer. Chem. Soc.*, **87**, 4301 (1965).

camphor (1) in 5 ml of 3% methanolic potassium carbonate solution was added dropwise 500 mg (3.8 mmol) of nitrosomethylurethane.[25] After an induction period, the reaction started, as evidenced by a rise in temperature. The solution was cooled to maintain the temperature between 20 and 25°. After the addition was complete, the solution was stirred for an additional 30 min, filtered, and concentrated by distillation. The residue was analyzed by glpc.[21] The reaction was repeated under the above conditions except that the amount of nitrosomethylurethane used was varied. Each run was analyzed by glpc.[21]

In another experiment 2.04 g (18.6 mmol) of 1 in 10 ml of methanol was allowed to react as described above with 8.05 g (61 mmol) of nitrosomethylurethane in the presence of anhydrous sodium carbonate. The concentrated residue was shown by glpc analysis[26] to consist of eight components which were collected individually and identified as follows. The first component (retention time 5.3 min, relative abundance 4.2%) was identical in all respects (ir, nmr, and retention time) with norcamphor (1). The second component (retention time 7.5 min, relative abundance 24.8%) and the third component (retention time 8.8 min, relative abundance 1.4%) were collected together and assigned structures 4 and 3, respectively, by their glpc retention times and spectral properties. The fourth component (retention time 11.6 min, relative abundance 20.5%) was assigned structure 5: ir (CCl_4) 1700 cm^{-1} (C=O, seven-membered cyclic ketone[27]); mass spectrum (70 eV) *m/e* 138; mp 80–83.5° (lit.[28] mp 95–96°). The fifth component (retention time 14.2 min, relative abundance 25.6%) was assigned structure 6: ir (CCl_4) 1700 cm^{-1} (C=O, seven-membered cyclic ketone[27]); mass spectrum (70 eV) *m/e* 138; mp 102–108° (lit.[28] mp 122–123°); semicarbazone mp 191–192° (lit.[28] mp 193–195°). The sixth component (retention time 18 min, relative abundance 3.4%) and the seventh component (retention time 18 min, relative abundance 3.4%) were collected together and are believed to be bicyclo[5.2.1]decan-3-one and bicyclo[5.2.1]decan-4-one, respectively: ir (CCl_4) 1695 cm^{-1} (C=O, eight-membered cyclic ketone[27]); mass spectrum (70 eV) *m/e* 152; mp 60–62°. The eighth component (relative abundance 1.5%) was not identified.

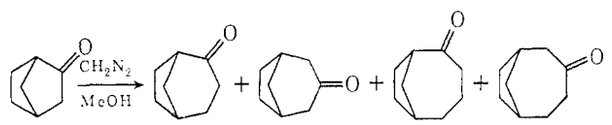
B. Dehydronorcamphor (2) (500 mg, 4.63 mmol) was ring expanded exactly as described for 1 (part A), and the reaction was repeated with varying amounts of nitrosomethylurethane. Each run was analyzed by glpc.[26]

In a separate experiment, 2.0 g (18.4 mmol) of 2 in 5 ml of methanol was allowed to react as described above (part A) with 8.0 g (61 mmol) of nitrosomethylurethane in the presence of anhydrous sodium carbonate. The concentrated residue was shown by glpc analysis[26] to consist of eight components which were collected individually and identified as follows. The first component (retention time 4.3 min, relative abundance 6.1%) was identical in all respects with dehydronorcamphor (2). The second component (retention time 6.6 min, relative abundance 4.9%) and the third component (retention time 7 min, relative abundance 34.8%) were collected together and assigned structures 7 and 8, respectively, by their glpc retention times and spectral properties. The fourth component (retention time 9.3 min, relative abundance 28.3%) and the fifth component (retention time 10 min, relative abundance 9%) were collected together and identified as 10 and 9, respectively. The structural assignments were made by converting the mixture of olefinic ketones into their known[28] saturated analogs 6 and 5 by catalytic hydrogenation. The sixth, seventh, and eighth components, formed in the ratio of 13.6:5.5:2.5, were shown to exhibit carbonyl absorption in the ir but were not further characterized.

Competition Reaction of 1 and 2 with Diazomethane.—To a solution of 200 mg (1.85 mmol) of 2 and 200 mg (1.82 mmol) of 1 in 5 ml of methanol containing anhydrous sodium carbonate was added 0.2 g (1.5 mmol) of nitrosomethylurethane as described previously. The solution was analyzed by glpc.[7] The mixture was found to contain 41.9% 6, 47.5% 1, and ring-expanded products. The relative reactivity of ketones 1 and 2 is therefore approximately 1:2.2.[29]

Results

Norcamphor (1) and dehydrononorcamphor (2) were allowed to react with varying amounts of diazomethane, generated from nitrosomethylurethane, in methanol at 25°. The reaction mixtures were analyzed by gas–liquid partition chromatography (glpc). The reactions resulted in mixtures of ring-expanded bicyclic ketones, the exact amount of each depending upon the molar amount of diazomethane used. The results are summarized in eq 1 and 2 and listed in Tables I and II.



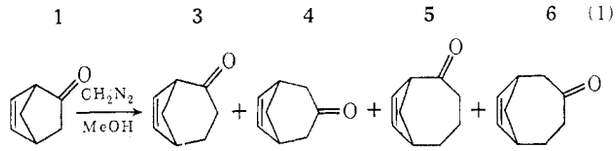


TABLE I

REACTION OF NORCAMPHOR (1) WITH DIAZOMETHANE[a]

Mole ratio of 1:urethane	Unreacted 1, %	Product, % 3	4	5	6	Higher ketones
1:0.41	80.3	8.8	6.0	3.1	2.1	
1:0.82	59.6	10.6	12.8	10.1	7.1	
1:1.64	38.6	9.5	18.6	19.2	11.3	3.2
1:2.46	21.6	9.1	23.0	20.6	14.2	11.4
1:3.28	19.6	3.9	26.5	21.3	17.4	12.0

[a] See Experimental Section for exact reaction conditions.

TABLE II

REACTION OF DIAZOMETHANE WITH DEHYDRONORCAMPHOR (2)[a]

Mole ratio of 2:urethane	Unreacted 2, %	Product, % 7	8	9	10	Higher ketones
1:0.41	83.0	5.8	8.1	1.8	1.9	
1:0.82	63.7	9.0	16.5	4.6	6.2	
1:1.64	36.5	7.1	28.4	9.9	14.6	3.8
1:2.46	29.8	5.6	34.6	7.0	16.2	6.9
1:3.28	10.2	5.1	42.0	6.4	23.2	13.0

[a] See Experimental Section for exact reaction conditions.

The structures of ketones 3, 4, and 8 were established by comparison of their retention times and spectral properties with those of the authentic compounds.[22–24] The structures of 5 and 6 were established by spectral comparison and melting points of collected samples with those reported by Hartmann.[28] Finally, the structures of 7, 9, and 10 were assigned by conversion of these olefinic ketones by catalytic hydrogenation to 3, 5, and 6, respectively.

The relative reactivity of 1 and 2 toward diazomethane was estimated by allowing an equimolar mixture of the two to react with a less than stoichiometric amount of diazomethane. The composition of the reaction mixture was determined by glpc analysis.

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

(26) Same column as in ref 21 used at 180° and a helium flow rate of 120 ml/min.

(27) R. T. Conley, "Infrared Spectroscopy," Allyn and Bacon, Boston, Mass., 1966, p 141.

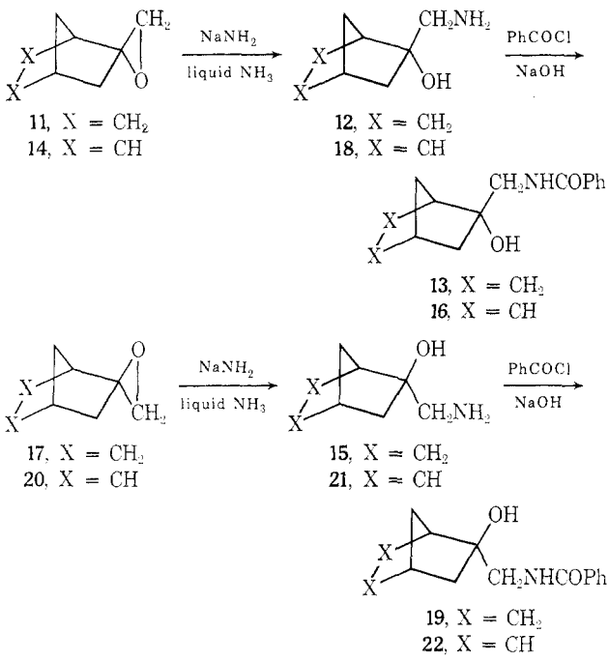
(28) M. Hartmann, *Justus Liebigs Ann. Chem.*, **724**, 102 (1969).

(29) T. S. Lee in "Technique in Organic Chemistry," Vol. VIII, S. L. Friess and A. Weissberger, Ed., Interscience, New York, N. Y., 1953, p 100.

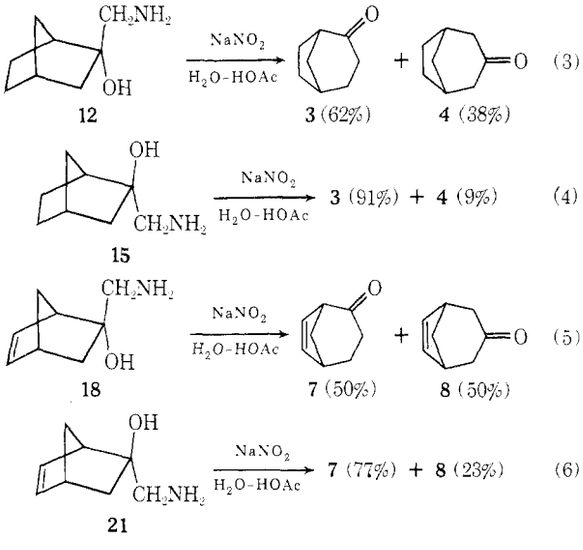
From these data it was calculated[29] that **2** was about two times as reactive as **1**.

The amino alcohols **12**, **18**, **15**, and **21** were prepared from the known epoxides **11**, **14**, **17**, and **20**[16] as outlined in Scheme I and characterized as their

SCHEME I



benzamide derivatives. The amino alcohols were ring expanded by the Tiffeneau–Demjanov method and the ketonic mixtures obtained were analyzed by glpc. The relative percentages of the ketones obtained in each case are summarized in eq 3–6. No epoxides

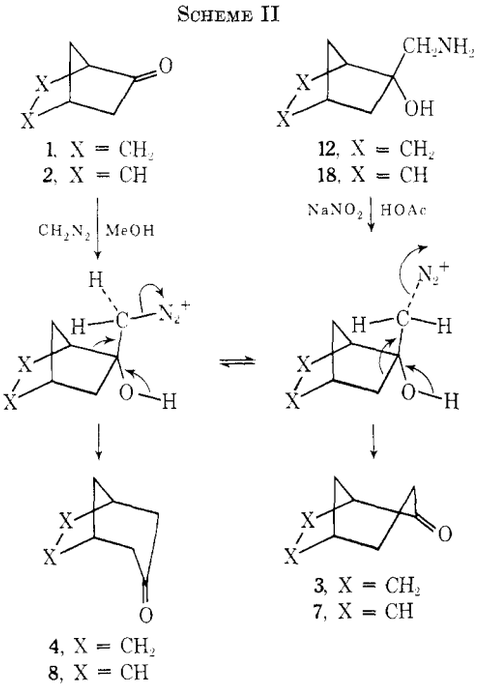


were detected as products in any of the amino alcohol or diazomethane ring-expansion reactions.[30] The yields of sublimed products obtained in the amino alcohol ring expansions studied were between 46 and 54%; no other volatile products were detected by glpc analysis. The hydrochloride of amino alcohol **12** was also ring expanded under identical reaction conditions, yielding **3** and **4** in the ratio of 61:39 in 86% yield. Thus, although the yield of ketonic products obtained increased, the ratio of products obtained remained constant. We therefore believe, despite the relatively low yields obtained in the amino alcohol ring expansions, that the ratio of ketones obtained in each case is an accurate measure of the relative migratory aptitudes of the methine and methylene carbons in these derivatives.

Discussion

Ring Expansion of Norcamphor.—The reaction of norcamphor (**1**) with nucleophiles such as Grignard reagents, metal hydrides, and mixed hydrides[31] yields predominantly (>90%) the product of exo attack, an endo alcohol. The neutral nucleophiles dimethyloxosulfonium methylide and dimethylsulfonium methylide also attack **1** on its exo face to yield an endo epoxide.[16] One would therefore predict that the neutral nucleophile diazomethane would also react with **1** in an exo fashion. As shown in Scheme II, the intermediate

SCHEME II



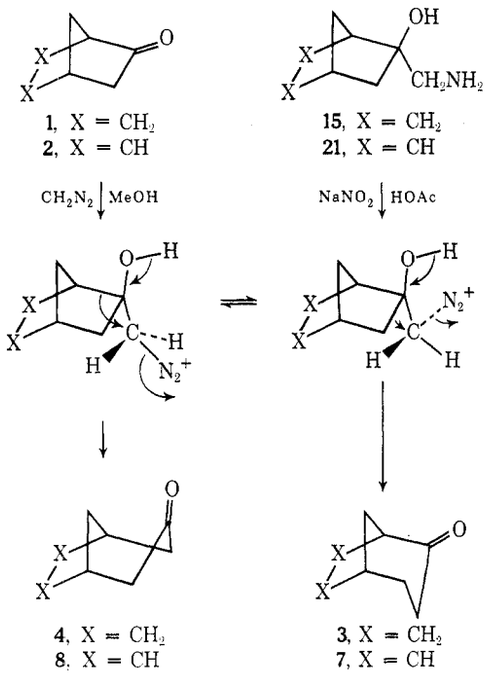
diazonium ion produced by exo attack of diazomethane on **1** can also be formed from the treatment of **12** with nitrous acid. The ratio of ketones **3** and **4** formed in the deamination of **12** should serve as the expected ratio of products that would be formed in the exo attack of diazomethane on **1**. Similarly, the product ratio obtained in the deamination of amino alcohol **15** should serve as the expected product ratio for endo attack of diazomethane on **1** (Scheme III). Comparison of the deamination results for **12** and **15** (eq 2 and 3) with the initial product ratio (70:30)[32] of ketones **3** and **4** formed when **1** was allowed to react with a less than stoichiometric amount of diazomethane indicates a predominance of exo attack (75%) of diazomethane on **1**.

(30) Authentic samples of the most probably epoxide[11] products were shown to be stable to the glpc analysis conditions and could have been detected if present in amounts greater than 1%.

(31) See Table I, ref 16.

(32) Estimated from the data in Table I.

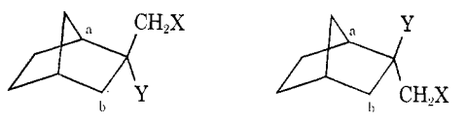
SCHEME III



The ring expansion product ratios from amino alcohols **12** and **15** allow a comparison of the migratory aptitudes of the methine and methylene carbons in these systems with those observed in other 2-norbornylcarbinyl systems. The pertinent data are summarized in Table III. As can be seen from the data, b

TABLE III

MIGRATORY APTITUDES IN THE REARRANGEMENT OF *exo*- AND *endo*-2-NORBORNYLCARBINYL SYSTEMS



I II

		X	Y	a migration, %	b migration, %
I		OBs[a]	H	7	93
		NH_2[b]	H	18	82
	12	NH_2[c]	OH	38	62
II		OBs[c]	H	0 (1)[a]	~100 (70)
		NH_2[d]	H	<1	~100
	15	NH_2[c]	OH	9	91

[a] Data taken from ref 11. [b] Taken from ref 33b. [c] This work. [d] J. A. Berson and P. Reynolds-Warnhoff, *J. Amer. Chem. Soc.*, **86**, 595 (1964).

or methylene migration is favored over a or methine migration in both the *exo*- and *endo*-2-norbornylcarbinyl systems. The preference for methylene migration in the exo systems, which is unexpected from electronic considerations and an unfavoral boat-like transition state, has been considered previously.[33] Sauers and Beisler[33] proposed that torsional nonbonded interactions between the substituents on C-2 and C-3 are relieved in the methylene migration transition state and that such strain relief is not rendered in the methine migration transition state. We would like to propose an alternative explanation based on the principle of least motion.[34] Methylene migration can proceed by a rotation around the C-3–C-4 bond which involves the motion of relatively few atoms in the molecule. However, methine migration requires the motion of the bridgehead carbon and thus most of the other atoms in the rigid bicyclic system. Thus, least motion favors methylene migration.

The selectivity of methylene over methine migration is reduced in going from the solvolytic brosylate system to the amine deamination. This is generally found to be the case,[35,36] because of the compressed energy scale in the energetically favorable loss of molecular nitrogen in the deamination. We see from the data for amino alcohol **12** that the selectivity is further reduced in deamination of an amino alcohol. Thus, the facile loss of nitrogen is further enhanced by the fact that a hydroxy carbonium ion, rather than a secondary carbonium ion, is produced as an intermediate.

In the *endo*-2-norbornylcarbinyl systems methylene migration predominates to even a greater extent. In the endo system the factors which favored methylene migration in the exo series are further reinforced by a conformationally favorable chairlike transition state. The trends in selectivity are maintained and are slightly enhanced.

Ring Expansion of Dehydronorcamphor.—The reaction of dehydronorcamphor (**2**) with a wide variety of nucleophiles occurs predominantly from the exo side with one notable exception.[16] The neutral nucleophile dimethyloxosulfonium methylide attacks **2** preferentially from its endo side to produce a 29:71 mixture of epoxides **14** and **20**, respectively.[16] Bly attributed this selectivity to an electronic stabilization of the endo attack transition state through an interaction of the double bond in **2** with the developing zwitterion.[16] Bly attempted to test the generality of this behavior of neutral nucleophiles toward **2** by studying the reaction of **2** with diazomethane in 10% methanolic ether.[37] In this solvent system, however, the diazomethane reacted exclusively with the double bond of **2** to produce ketopyrazolines.

Our results for the reaction of **2** with diazomethane in pure methanol indicate that in the more polar solvent the diazomethane reacts exclusively with the carbonyl double bond, resulting in ring expansion. As shown in Scheme II, the diazonium ion produced by exo attack of diazomethane on **2** can also be formed from the diazotization of amino alcohol **18**. The ratio of ketones formed in the deamination of **18** should therefore serve as the expected ratio of products that would result from an exo attack of diazomethane on **2**. Applying a similar argument, a model system for the endo attack of diazomethane on **2** is the deamination of amino alcohol **21**. This is shown in Scheme III. Comparison of the deamination results for **18** and **21** (eq 5 and 6) with the initial product ratio (53:47)[38]

(33) (a) R. R. Sauers and J. A. Beisler, *J. Org. Chem.*, **29**, 210 (1964); (b) J. A. Berson and D. Willner, *J. Amer. Chem. Soc.*, **86**, 609 (1964).

(34) (a) J. Hine, *J. Org. Chem.*, **31**, 1236 (1966); (b) J. Hine, *J. Amer. Chem. Soc.*, **88**, 5525 (1966); (c) S. I. Miller, *Advan. Phys. Org. Chem.*, **6**, 185 (1968); (d) O. S. Tee, *J. Amer. Chem. Soc.*, **91**, 7144 (1969).

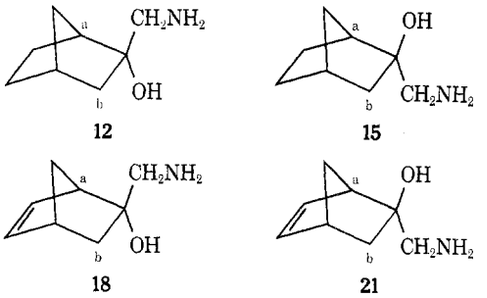
(35) E. H. White, "The Chemistry of the Amino Group," S. Patai, Ed., Wiley, New York, N. Y., 1968, Chapter 8.

(36) J. A. Berson, J. W. Foley, J. M. McKenna, H. Junge, D. S. Donald, R. T. Luibrand, N. G. Kundu, W. J. Libby, M. S. Poonian, J. J. Gajewski, and J. B. E. Allen, *J. Amer. Chem. Soc.*, **93**, 1299 (1971).

(37) R. S. Bly, F. B. Culp, Jr., and R. K. Bly, *J. Org. Chem.*, **35**, 2235 (1970).

(38) Estimated from the data in Table II.

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

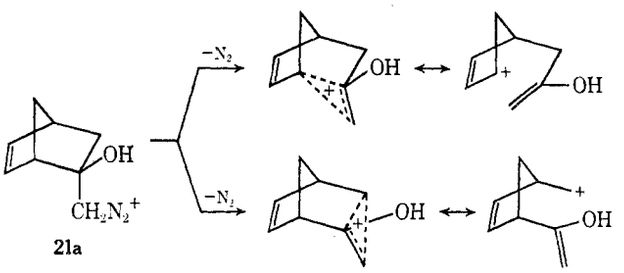


Compd	a migration, %	b migration, %
12	38	62
18	50	50
15	9	91
21	23	77

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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Received November 22, 1972

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).