m.p. 139° (reported[4] m.p. for *p*-chlorophenyl biguanide 139–140°, mixed melting point showed no depression).

*Action of dilute HCl on diethyl chelidamate.*Four-grams of the pyridone was suspended in 20 ml. of water and treated with 0.5 ml. of concentrated HCl; after standing for an hour the solid was collected and washed with water; m.p., 80–81°; yield, 3.8 g. (Reported[5] m.p. for diethyl chelidamate, 81°.) The product shows no depression in melting point when mixed with an authentic sample. Hence the pyridone was not hydrolyzed to the corresponding pyrone.

Action of dilute HCl on chelidamic acid. The chelidamic acid was treated with HCl using the same conditions as in the previous experiment. The product was identified as unchanged chelidamic acid.

Action of dilute HCl on 2,6-dimethyl-4-pyridone. Five grams of the pyridone was dissolved in 30 ml. of water and treated with three drops of concentrated HCl. On evaporation of the water a residue was obtained which was crystallized from water with m.p., 224–225°. This substance also gave a hydrochloride salt, m.p. 246–247°. (Reported[6] m.p. for the pyridone is 225° and for the HCl salt 247°.) It may be concluded that no hydrolysis took place.

Action of dilute HCl on 4-pyridone. Using the same procedure as the previous one, 4-pyridone and HCl gave only unchanged pyridone as the product. The product gave a hydrochloride, m.p. 138–139°. (Reported[7] m.p. 139°.)

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Synthesis and Rate of Acetolysis of 1-Bicyclo[2.2.1]heptylmethyl Tosylate

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The mechanism and driving force of the Wagner-Meerwein rearrangement has been investigated by Winstein *et al.*[1] and it has been concluded that the acetolysis of neopentyl type halides proceeds with minimal solvent participation and neighboring group effects. Furthermore, the relief of steric strain *via* formation of an intermediate carbonium ion appears to have no accelerating effect on the reaction.

Acetolysis of 1-bicycloheptylmethyl[2] tosylate also may involve a minimum amount of solvent participation, and formation of an intermediate carbonium ion should not have any different steric effect on the rate than in the case of neopentyl tosylate. Should the migrating group not participate in the rate determining step of the rearrangement, it would be expected that the rates of acetolysis of neopentyl tosylate and bicycloheptylmethyl tosylate would be nearly the same. However, should the migrating group participate in the rate controlling step, essentially through a nucleophilic displacement, it might be predicted that the acetolysis of bicycloheptylmethyl tosylate would be faster than that of neopentyl tosylate, for participation by the former would involve rearrangement to a bicyclo [2.2.2]octyl radical, with relief of some steric strain, and concomitant increase in driving force.

The preparation of 1-bicycloheptylmethyl derivatives has not been reported. However, methods have been described which lead to their synthesis, *via* bridgehead substituted bicycloheptanes. Many attempts to prepare bridgehead substituted bicycloheptanes have failed. Thus, *trans*-halogenation of bicycloheptane with *t*-butyl chloride and aluminum chloride gave only *exo*-2-chloro-bicycloheptane,[3] and the peroxide-directed chlorination of bicycloheptane gave the same product.[4] On the other hand, vapor phase nitration of bicycloheptane gave 1-nitrobicycloheptane,[5] and 1-chlorobicycloheptane has been reported,[6] although its method of preparation and physical properties were not described.

The Wagner-Meerwein rearrangement of 2-chlorobicycloheptane gives only the mirror image of the starting material, but rearrangement of 2,2-dichlorobicycloheptane should give 1,2-dichlorobicycloheptane. This reaction has been carried out in the camphane series by Houben and Pfankuch.[7] The 2-chloro substituent can be selectively removed either by catalytic hydrogenation in the presence of base,[8] or by means of a trans-halogenation reaction.[9] The dichloride can be obtained from 2-ketobicycloheptane using phosphorus pentachloride.[10] The ketone can be prepared by the method of Alder and Rickert.[11] Thus, 1-chlorobicycloheptane synthesized *via* the ketone, 2,2-dichloride and 1,2-dichloride, was converted to 1-carboxybicycloheptane *via* the lithium salt of bicycloheptane, the acid reduced to 1-hydroxymethylbicycloheptane, and the latter converted to its tosyl derivative.

The rate of acetolysis of the tosylate was determined in anhydrous acetic acid at 99.7°, using the method described by Winstein, Grunwald and

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Ingraham.[12] The first-order rate constant was found to be 11.69 ± 0.29 × 10^{-6} sec.$^{-1}$, compared with the value of 1.66 ± 0.09 × 10^{-6} sec.$^{-1}$ observed for neopentyl tosylate at 99.58°.[1] These results suggest that anchimeric assistance may occur in the former solvolysis reaction. If the solvolysis of neopentyl derivatives involves no anchimeric assistance,[1,13] and if the carbonium ions derived from neopentyl tosylate and bicycloheptylmethyl tosylate have the same solvation energy, it would be possible to relate the increase in rate of the bicyclic derivative over the neopentyl derivative to relief of steric strain. However, at the present, there is no definite evidence that this is possible, particularly since the possibility of differing steric effects on the solvation of the ion first produced cannot be excluded.

EXPERIMENTAL[14,15]

endo-2-Hydroxybicycloheptane. A total of 604 g. (9.15 moles) of freshly distilled cyclopentadiene and 906 g. (9.55 moles) of technical vinyl acetate was sealed in 20 Pyrex tubes and heated at 185° for 10–15 hr. The contents of the tubes were aspirated for 20 hr., and the residue distilled *in vacuo* to give 568 g. (40%) of crude endo-2-acetoxybicycloheptane, b.p. 88.5–103°/33 mm., lit.,[13] 82–83°/17 mm. The crude product was hydrogenated in a low-pressure apparatus using Adam's catalyst in methanol solution. The catalyst was removed by filtration, and the filtrate concentrated until the crude *endo*-2-acetoxybicycloheptane was dissolved in *ca.* 1250 ml. of methyl alcohol. To this solution was added 200 g. (3.58 moles) of potassium hydroxide and the mixture held at reflux for 4 hr. The reaction mixture was cooled, diluted with 2200 ml. of water, extracted with 3 1200-ml. portions of 30–60° petroleum ether, the ethereal extracts combined and dried over sodium sulfate. The petroleum ether solution was passed through a column packed with 3000 g. of alumina. Three fractions were collected and the infrared spectra taken of each. Fractions one and two contained essentially no bicyclic alcohol, while fraction three did. The column was eluted with 4 l. of dry ethanol, and the eluate combined with the third fraction above. The solvents were removed *in vacuo* to give an oily residue, which, after recrystallization from hexane, gave 253 g. (25% based on cyclopentadiene) of product, m.p. 151–151.5°, lit.,[13] 152–153°.

2-Ketobicycloheptane. To an ice-cooled 5-l. round-bottomed flask, fitted with a stirrer, were added 1500 ml. of water, 74 ml. (1.39 mole). of 96% sulfuric acid, 99.5 g. (0.338 mole) potassium dichromate, and 600 ml. of glacial acetic acid. To the ice cold solution was added 115 g. (1.025 moles) *endo*-2-hydroxybicycloheptane and the solution stirred for 6 hr. The ice bath was allowed to melt, and the solution to stand overnight. A cold solution of 500 g. of technical sodium hydroxide in 800 ml. of water was then added, keeping the temperature of the reaction mixture between 0–10°. The resulting slurry was steam distilled and 1500 ml. of distillate collected. The distillate was saturated with sodium chloride, extracted with 3 500-ml. portions of ether, the ethereal extracts combined and dried over calcium sulfate. The solution was then filtered and the ether removed by distillation. The residue was distilled *in vacuo* to give 85.4 g. (76%) of 2-ketobicycloheptane, b.p. 89–94°/60 mm.; 2,4-dinitrophenylhydrazone, m.p. 131.5–132.0°, lit.,[16] 131.5–132.5°.

2,2-Dichlorobicycloheptane. To a 500-ml. round-bottomed flask protected by a calcium chloride drying tube and containing 29 ml. of phosphorus trichloride cooled to 0° in an ice-salt bath was added 45.1 g. (0.41 mole) of 2-ketobicycloheptane. After the ketone had dissolved, 96.7 g. (0.463 mole) of phosphorus pentachloride was added portionwise over a period of one hour with vigorous shaking and cooling. The solution was allowed to stand overnight, then poured onto 500 g. of ice and the hydrolysis allowed to proceed, keeping the temperature below 0° at all times. After 30 min. the reaction was allowed to come to room temperature. There were two phases. The mixture was extracted with 4 250-ml. portions of pentane, the pentane extract washed with 2 300-ml. portions of water and then dried over magnesium sulfate. The pentane was removed by distillation and the residue distilled *in vacuo* to give 1 g. of forerun, 47.8 g. (64%) of dichloride, b.p. 65.0–68.1°/12.0–12.4 mm., and *ca.* 5 g. of residue. The product solidified to a low-melting solid.

Anal. Calcd. for $C_7H_{10}Cl_2$: C, 50.9; H, 6.1. Found: C, 51.0; H, 6.3.

1-Chlorobicycloheptane. Aluminum chloride, 16.9 g. (0.127 mole), was added in four portions over a period of five hours to a solution of 43.9 g. (0.266 mole) of the dichloride dissolved in 700 ml. of pentane previously dried over aluminum chloride. Hydrogen chloride was slowly evolved and a red brown sludge formed. After six hours the walls of the flask were covered with sludge. The mixture stood for 43 additional hours before the clear pentane solution was decanted from the oil and the oil washed with 100 ml. of dry hexane. The combined hexane and pentane solution was washed with 4 300-ml. portions of water and then dried over magnesium sulfate. The solvent was removed and residue distilled *in vacuo* to give 1.1 g. of forerun, 14.9 g. (43%) of 1-chlorobicycloheptane, and 5.6 g. of residue. The product b.p. 70–72°/54 mm., $n_{\rm D}^{25.7}$ 1.4722 solidified at 0° and gave a slight test with an alcoholic silver nitrate solution at room temperature. This positive test may have been due to the presence of small amounts of either *exo*-2-chlorobicycloheptane or 1-chloro-*exo*-2-chlorobicycloheptane, or both. The infrared spectrum showed no absorption of *exo*- or *endo*-2-chlorobicycloheptane[17] and no absorption in the 12.5 μ region characteristic of nortricyclene derivatives.[18] A redistilled sample, b.p. 70–71°/54 mm., $n_{\rm D}^{25.7}$ 1.4722, gave no halide test.

Anal. Calcd. for $C_7H_{11}Cl$: C, 64.4; H, 8.5; Cl, 27.2. Found: C, 64.1; H, 8.5; Cl, 27.3.

1-Carboxybicycloheptane. Lithium wire, 2.4 g. (0.345 mole), was placed under 20 ml. of mineral oil in a 200-ml. round-bottomed three-necked flask equipped with a stirrer, separatory funnel, condenser with drying tube attached and a Y-inlet for carbon dioxide and nitrogen. The equipment was flamed, then purged with dry nitrogen for 30 min., before the lithium and oil were added. The vigorously stirred oil was heated to boiling with a bare flame and the suspension of lithium so obtained allowed to cool. The mineral oil was removed under nitrogen and the lithium sand washed with 3 20-ml. portions of dry cyclohexane. A glass-sealed magnetic stirring bar was introduced and the flask sealed. One half of a solution of 10.0 g. (0.0767 mole) of 1-chlorobicycloheptane in 40 ml. of dry cyclohexane was added to the lithium sand and the suspension, while being stirred, was heated to 90°. An exothermic reaction soon started, and was main-

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(15) Microanalyses by Dr. A. Elek.

(16) W. C. Wildman and C. H. Hemminger, *J. Org. Chem.*, **17**, 1641 (1952).

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(18) J. D. Roberts, E. R. Trumbull, Jr., W. Bennett, and R. Armstrong, *J. Am. Chem. Soc.*, **72**, 3116 (1950).

tained by the addition of the other half of the solution of the halide. The suspension was heated for one hour at reflux under a positive nitrogen pressure, then cooled, and 65 ml. of dry pentane added. Carbon dioxide, dried by passage through concentrated sulfuric acid, was passed over the vigorously stirred suspension for two hours. The excess lithium was removed by the addition of 20 ml. of absolute ethanol, followed by 60 ml. of water. Following the addition of 50 ml. of ether, the aqueous phase was acidified with concd. hydrochloric acid. The phases were separated, and the aqueous phase, after saturation with salt, was extracted with 3 100-ml. portions of ether. The combined ethereal extracts were extracted with 3 100-ml. portions of aqueous sodium carbonate, the sodium carbonate phase acidified with $12N$ hydrochloric acid, saturated with salt, and extracted with 3 100-ml. portions of ether. The ethereal extracts were dried and the solvent removed by distillation through a 12-inch column. The product was sublimed at 10 mm. and 80° to give 5.48 g. (51%) of 1-carboxybicycloheptane, m.p. 113.8-115.5°.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.5; H, 8.6. Found: C, 68.5; H, 8.5.

The reported melting points for *exo-* and *endo-*2-carboxybicycloheptane are 48°[19] and 65°,[20] respectively. The acid has an odor similar to that of butyric acid.

1-Hydroxymethylbicycloheptane. The above acid, 2.19 g. (0.0156 mole), was reduced in 130 ml. of ether with 3.0 g. (0.0790 mole) lithium aluminum hydride. The excess hydride was destroyed by addition of water and the contents of the flask poured into 100 ml. of 10% aqueous sulfuric acid. The phases were separated, and the aqueous phase extracted with 2 25-ml. portions of ether. The combined ethereal extracts were washed with water, saturated aqueous sodium bicarbonate and water and dried over magnesium sulfate. The solvent was removed by distillation through a 12-inch Vigreux column to yield an oily residue. The residue was sublimed at 6 mm. and 65° to give 1.76 g. (91%) of product, m.p. 59.0-60.2°, soft waxy needles.

Anal. Calcd. for $C_8H_{14}O$: C, 76.1; H, 11.2. Found: C, 75.9; H, 11.3.

1-Bicycloheptylmethyl tosylate. To an ice cold solution of 0.70 g. (5.56 mole) of the above alcohol dissolved in 6 ml. of dry pyridine was added 1.06 g. (5.56 mole) of tosyl chloride. The solution was allowed to stand overnight at 4° and then added to 12 ml. of ice cold $6N$ hydrochloric acid. An oil formed and began to crystallize whereupon the mixture was stirred with 25 ml. of carbon tetrachloride until all of the solid had dissolved. The phases were separated and the aqueous phase extracted with 15 ml. of carbon tetrachloride. The organic phases were combined and dried. The solvent removed by evaporation and the residue was recrystallized from 6 ml. of hexane to give 1.33 g. (86%) of tosyl derivative, m.p. 78.9-80.0°.

Anal. Calcd. for $C_{15}H_{20}O_3S$: C, 64.3; H, 7.2. Found: C, 64.2: H, 7.2.

Rate of acetolysis of 1-bicycloheptylmethyl tosylate. The acetolysis was conducted in anhydrous acetic acid, according to the method of Winstein, Grunwald, and Ingraham.[12] Anhydrous acetic acid was prepared by adding sufficient acetic anhydride to react with the water present in glacial acetic acid as determined by its freezing point, allowing the mixture to reflux for 3 hr. and then distilling. The distillate was made approximately 0.5% in acetic anhydride, held at reflux for 3 hr., cooled, and then stored in sealed containers.

Approximately $0.05N$ perchloric acid in acetic acid was prepared by dilution of a $9N$ aqueous solution with the anhydrous acid. This solution was standardized against potassium acid phthalate to a brom phenol blue end point.[21] Approximately $0.10N$ sodium acetate in acetic acid was prepared by the addition of anhydrous sodium carbonate to the anhydrous acid and was standardized against the perchloric acid solution. The acetic anhydride in the anhydrous acid was determined to be 0.50% by the method of Kilpi,[22] *i.e.*, the addition of anthranilic acid to the anhydrous acid and titration with perchloric acid. In all titrations, 8 drops of 1% brom phenol blue indicator in the anhydrous acid were used per 5 ml. of solution.

The acetolysis was conducted as follows: 6-ml. aliquots of a $0.03547M$ solution of the tosyl derivative in the anhydrous acid were placed in ampoules, the ampoules sealed, placed in an oil bath at 99.66 ± 0.02°, single ampoules removed at selected time intervals, immediately cooled, opened, 5.00-ml. aliquots removed, and titrated with the sodium acetate solution. The time was computed from the time of opening the ampoules. The aliquots were titrated with the aid of a syringe buret,[23] previously calibrated by titration of the perchloric acid solution with the sodium acetate solution. The first order rate constants were calculated from the expression $kt = \ln(a/a - x)$. The hydrolysis was followed to 64%. The results are summarized in Table I.

TABLE I

RATE OF ACETOLYSIS OF 1-BICYCLOHEPTYLMETHYL TOSYLATE[a]

Time, Sec.	Base,[b] Ml.	$(a - x)$ (M)	$k \times 10^6$ Sec.$^{-1}$
0[c]	0.1933	0.03147	...
9549	0.3529	0.02816	11.63
21860	0.5435	0.02472	11.97
34676	0.7000	0.02098	11.70
44576	0.8213	0.01847	11.95
74040	1.0938	0.01283	12.13
86384	1.1129	0.01243	10.76
95565	1.2147	0.01033	11.66[d]

[a] In an hydrous acetic acid containing 0.50% acetic anhydride at 99.66 ± 0.02°. [b] $0.1035N$ sodium acetate per 5.00-ml. aliquot. [c] $a_0 = 0.03547\ M$. [d] $k_{\text{mean}} = 11.69 \pm 0.29 \times 10^{-6}$ sec.$^{-1}$

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[20] K. Alder and G. Stein, *Ann.*, **514**, 197 (1934).

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Reaction of Bis(chloromethyl) Ether with Methanol and with Ethanol[1,2]

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Bis(methoxymethyl) ether (I) was first prepared by Descudé[4] in 1904 by reaction of bis(chloro-

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