The corresponding saturated β-lactam V showed an ultraviolet absorption at 248 mμ (ε 1300). *Anal.* Found: C, 81.25; H, 5.25, N, 6.60. The n.m.r. spectrum (in $CDCl_3$, chemical shifts in p.p.m. from tetramethylsilane) shows a broad multiplet at 7.0–7.5 δ (10 H) and a multiplet at 5.0 δ (1 H) which could be assigned to the aromatic hydrogens and the vinyl hydrogen, respectively.

Hydrogenation of VI over platinum catalyst proceeded with the uptake of one equivalent of hydrogen and yielded 1,4-diphenyl-2-azetidinone (V), m.p. 154–156°. An authentic sample of V was prepared as described by Gilman and Speeter,[8] m.p. 154–155.5° (lit.[8] 153–154°), undepressed upon admixture with the sample of V obtained by hydrogenation of VI and having an identical infrared spectrum (potassium bromide).

Acknowledgment.—We are indebted to the National Institutes of Health for financial support (AI-05286).

(8) H. Gilman and C. Speeter, *J. Am. Chem. Soc.*, **65**, 2255 (1943).

DEPARTMENT OF CHEMISTRY KENNETH R. HENERY-LOGAN
UNIVERSITY OF MARYLAND JOSEPH V. RODRICKS
COLLEGE PARK, MARYLAND

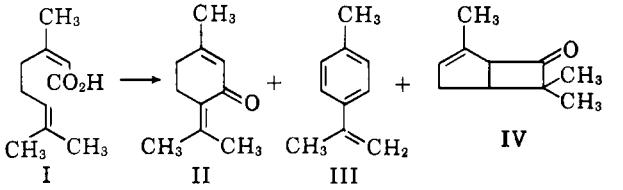
RECEIVED SEPTEMBER 9, 1963

The Cyclization of Geranic Acids. Preparation of a Cyclobutanone

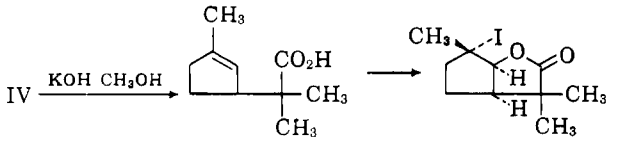
Sir:

In a series of papers describing the self-condensation products of unsaturated acids, Schinz[1] treated the geranic acids (I) with acetic anhydride and sodium acetate and obtained piperitenone (II). We have repeated this work using the mixture of geranic acids obtained by the silver oxide oxidation of citral[2,3] and find that the neutral fraction of the reaction product is composed of three compounds. By fractional distillation one of the three was separated and was shown to be II [b.p. 118–120° (2 mm.); dinitrophenylhydrazone, m.p. 184–185°].[4] The other two components were easily separated by g.l.c. The first of these was an aromatic hydrocarbon $C_{10}H_{12}$ (III); n.m.r. (all in $CDCl_3$; chemical shifts in p.p.m. from Me_4Si) 2.13 δ (3 H, multiplet), 2.33 δ (3 H, singlet), 5.04 δ (1 H, multiplet), 5.35 δ (1 H, multiplet), 7.15 and 7.33 δ (4 H in an A_2B_2 pattern); $\lambda_{max}^{CH_3OH}$ 247, 283, and 294 mμ (ε 12,500, 5100, 2000), which established the structure of III as 4-methyl-α-methylstyrene.[5]

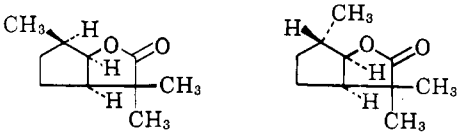
The third compound, $C_{10}H_{14}O$[6] (IV), b.p. 86–88° (20 mm.) ($\lambda_{max}^{CCl_4}$ 3.28, 5.62, 12.49 μ), was a cyclobutanone or a highly strained cyclopentanone; 2,4-dinitrophenylhydrazone, m.p. 120–122°. IV, with hydrogen and platinum catalyst formed a dihydro derivative V [b.p. 124–126° (150 mm.); $\lambda_{max}^{CCl_4}$ 5.62 μ; $\lambda_{max}^{CH_3OH}$ 309 mμ (ε 53); 2,4-dinitrophenylhydrazone, m.p. 103–104°] indicating a single double bond in a bicyclic ring system in IV. The ultraviolet spectrum of IV ($\lambda_{max}^{CH_3OH}$ 310 mμ (ε 260)) suggested that the double bond was located β,γ to the carbonyl group with some π-bond overlap.[7] The n.m.r. spectrum of IV [1.12 δ (3 H, singlet), 1.19 δ, (3 H, singlet), 1.75 δ (3 H, multiplet), 2.55 δ (3 H, broad multiplet), 4.03 δ (1 H, broad multiplet), 5.46 δ (1 H, multiplet)] indicated the presence of a dimethyl group next to the carbonyl, a third methyl group attached to a trisubstituted double bond, and a single hydrogen located on the carbon between the carbonyl and the double bond. The mass spectrum[8] of IV confirmed the molecular weight of the compound and also showed very intense peaks at *m/e* 80 and *m/e* 70, indicative of a methylcyclopentadiene and dimethyl ketene ions. On the basis of these data we propose that IV is 2,6,6-trimethyl[3.2.0]-bicyclo-2-heptene-7-one.



Refluxing methanolic potassium hydroxide converted IV to α-fencholenic acid (VI), m.p. 45–46°. The structure of VI was established by comparison of its infrared spectrum with that of an authentic sample of α-fencholenic acid prepared by the hydrolysis of fenchone oxime.[9] The position of the double bond of α-fencholenic acid was established by conversion to the iodolactone VII; m.p. 74–75°; $\lambda_{max}^{CCl_4}$ 5.61 μ; n.m.r. 2.20 δ (3 H, singlet), 5.10 δ (1 H, doublet, J = 5.0 c.p.s.).



Aqueous acid degradation of IV led to a mixture of 3-methyl-2-cyclohexenone,[10] 2,4-dinitrophenylhydrazone, m.p. 177–178°, and two isomeric lactones (VIII and IX) ($\lambda_{max}^{CCl_4}$ 5.63 μ) that were difficultly separable even by g.l.c. While the n.m.r. spectrum of VIII had a low field triplet (4.80 δ, J = 6 c.p.s.), in contrast the spectrum of IX showed a pair of doublets (4.48 δ, J = 6 and 2.5 c.p.s.). The mixture of γ-lactones VIII and IX could also be prepared from methyl α-fencholenate[11] by refluxing in benzene with *p*-toluenesulfonic acid monohydrate.



Refluxing IV in toluene with *p*-toluenesulfonic acid monohydrate caused a series of rearrangements to X (b.p. 68–71° (1 mm.); $\lambda_{max}^{CCl_4}$ 5.72 μ, $\lambda_{max}^{CH_3OH}$ 301 mμ (ε 323); 2,4-dinitrophenylhydrazone, m.p. 185–187°. n.m.r. 1.03 δ (3 H, singlet), 1.13 δ (3 H, singlet), 1.75 δ (1 H, doublet, J = 11 c.p.s.), 2.04 δ (1 H, doublet, J = 11 c.p.s.), 2.40 δ (3 H, multiplet), 3.13 δ (1 H, multiplet), 4.92 δ (1 H, multiplet), 5.16 δ (1 H, multiplet). Upon catalytic reduction X was converted only to a dihydro derivative XI [b.p. 100° (10 mm.); $\lambda_{max}^{CCl_4}$ 5.73 μ; 2,4-dinitrophenylhydrazone, m.p. 144–146°] so X must be bicyclic. $NaIO_4$ and $KMnO_4$ oxidation

(1) C. Balant, C. A. Vodoz, H. Kappeler, and H. Schinz, *Helv. Chim. Acta*, **34**, 722 (1951).

(2) K. Bernhauer and R. Forster, *J. Prakt. Chem.*, **147**, 199 (1936).

(3) G. A. Howard and R. Stevens, *J. Chem. Soc.*, 161 (1960).

(4) Y. R. Naves and G. Papazian, *Helv. Chim. Acta*, **25**, 1028 (1942).

(5) M. J. Murray and W. S. Galloway, *J. Am. Chem. Soc.*, **70**, 3867 (1948).

(6) Satisfactory elementary analyses were obtained for all new compounds reported herein.

(7) R. C. Cookson and N. S. Wariyar, *J. Chem. Soc.*, 2302 (1956).

(8) We are indebted to Professor K. Biemann for the mass spectrum of IV.

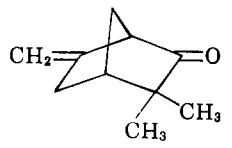
(9) G. B. Cockburn, *J. Chem. Soc.*, **75**, 501 (1899); O. Wallach, *Ann.*, **379**, 182 (1911).

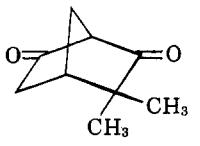
(10) L. I. Smith and J. F. Rouault, *J. Am. Chem. Soc.*, **65**, 631 (1943).

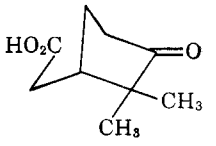
(11) Prepared by CH_2N_2 treatment of VI or by refluxing IV in methanolic hydrogen chloride.

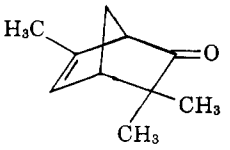
of X provided the β-diketone (XII); $\lambda_{max}^{CCl_4}$ 5.66, 5.74 μ; n.m.r. 3.22 δ (1 H, singlet), 1.26 δ (3 H, singlet), 1.03 δ (3 H, singlet) (the remaining protons appeared as a complicated series of multiple peaks from 2.1–3.0 δ indicating that the equivalent bridge protons has moved downfield as expected). Mild base treatment of XII provided the keto acid XIII; $\lambda_{max}^{CCl_4}$ 5.74 and 5.86 μ.

The acid rearrangement of IV also gave small amounts of the isomeric ketone XIV; $\lambda_{max}^{CCl_4}$ 3.27, 5.73 μ; $\lambda_{max}^{CH_3OH}$ 305 mμ (ε 282); n.m.r. 1.04 δ (3 H, singlet), 1.13 δ (3 H, singlet), 1.81 δ (3 H, doublet, J = 2.0 c.p.s.), 2.18 δ (2 H, narrow multiplet), 2.65 δ (1 H, triplet, J = 4.5 c.p.s.), 2.82 δ (1 H, doublet, J = 1.0 c.p.s.), and 6.15 δ (1 H, quartet, J = 2.0 c.p.s.). The structure of XIV was established by catalytic hydrogenation to XI.

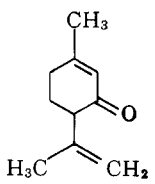

X

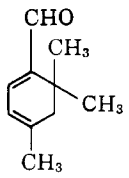

XII


XIII


XIV

Pyrolysis of IV at 340° provided isopiperitenone[12] (XV) (2,4-dinitrophenylhydrazone, m.p. 155–156°) and piperitenone (II) as the major products. A minor pyrolysis product was the aldehyde XVI ($\lambda_{max}^{CH_3OH}$ 310 mμ (ε 9800); $\lambda_{max}^{CCl_4}$ 3.69, 5.95 μ; semicarbazone, m.p. 211–213°). The structure of XVI was established by comparison with an authentic sample[13] prepared from 3-methyl crotonaldehyde. Pyrolysis of IV at higher temperatures led to piperitenone and *m*-xylene


XV


XVI

formed by the demethylation and decarbonylation of XVI.

Acknowledgment.—The author is indebted to Professor G. Büchi for many stimulating discussions.

(12) Y. R. Naves, *Bull. Soc. Chim. France*, 1881 (1961).

(13) F. G. Fischer and K. Löwenberg, *Ann.*, **494**, 263 (1932); E. A. Braude and E. A. Evans, *J. Chem. Soc.*, 3334 (1955).

MEDICAL RESEARCH LABORATORIES
CHAS. PFIZER & CO., INC. J. J. BEEREBOOM
GROTON, CONNECTICUT

RECEIVED SEPTEMBER 3, 1963

The Interaction of Urea and Acetamide with Polyglycine[1]

Sir:

We have measured the association of urea and acetamide with polyglycine in water and dioxane, by observing the mobility of the amides on polyglycine columns, a technique which permits rapid comparison of the interaction under a variety of conditions. If it is assumed that the binding of the amides is through peptide hydrogen bonds, then the association is a measure of hydrogen bond formation and strength. Several differing estimates of peptide hydrogen bond strength have been reported,[2-4] the most recent being that of Klotz and Franzen,[2] who found that in water the bond is very weak. The data presented here confirm this conclusion.

Polyglycine was prepared by polymerization of the N-carboxyanhydride in pyridine.[5] Thermostated columns (0.6 × 20 to 30 cm.) were operated under 5 lb. pressure, with a flow rate of no more than 2 ml./hr. Samples (0.1 ml.) were applied to the column, and the effluent fractions were analyzed for urea or acetamide by acid hydrolysis followed by ninhydrin determination of the ammonia liberated. The volume at which unretarded material emerged was determined using solutes which would not interact with polyglycine (*i.e.*, sodium chloride, acetic acid, or acetone, when water was the solvent, and azulene or acetic acid for dioxane).

Simple chromatographic theory shows $R_f = 1/(1 + K_d)$, where R_f is the mobility, and K_d is the distribution coefficient of the solute between the liquid and solid phases.[6] Table I presents values of K_d for chromatography of urea and acetamide on polyglycine, in water and dioxane, at several temperatures. Neither solute was measurably retarded in water, but acetamide was retarded in dioxane. The insolubility of urea in dioxane precluded measurement of its chromatographic behavior using this solvent. The distribution coefficient for acetamide in dioxane was at least 100 times that in water, in agreement with the data of Klotz and Franzen[2] for the dimerization of N-methylacetamide in these same solvents, *i.e.*, association constants 0.005 and 0.52, for water and dioxane, respectively, at 25°. An association constant for the formation of an acetamide–polyglycine complex can be calculated from the distribution coefficient by introducing the concentration of polymer peptide bonds, which was crudely approximated as the molar concentration of monomer in the column packing. The resulting values are shown in Table I. The agreement with the constants of Klotz and Franzen is remarkable, and almost certainly fortuitous. The probable unavailability of some peptide bonds of the solid polyglycine may have been compensated by more than one hydrogen bond formed per acetamide bound, or a more favorable entropy for binding to solid polyglycine, compared with the dimerization of two free molecules. It must be emphasized that the chromatographic

TABLE I
THE CHROMATOGRAPHY OF UREA AND ACETAMIDE ON POLYGLYCINE

Solute	Solvent	Temperature, °C.	Distribution coefficient	Monomer concn., M	Association constant
0.05 M urea or acetamide	H_2O	0 or 40	<0.035	5.2	<0.007
0.05 M acetamide	Dioxane	12	4.0	5.6	0.72
0.05 M acetamide	Dioxane	40	2.3	5.6	0.41

(1) This work was supported by Research Grant G-21030, from the National Science Foundation.

(2) I. M. Klotz and J. S. Franzen, *J. Am. Chem. Soc.*, **84**, 3461 (1962).

(3) J. A. Schellman, *Compt. rend. Trav. Lab. Carlsberg*, **29**, 223 (1955).

(4) S. J. Gill, J. Hutson, J. R. Clopton, and M. Downing, *J. Phys. Chem.*, **65**, 1432, (1961).

(5) Y. Go and H. Tani, *Bull. Chem. Soc. Japan*, **14**, 510 (1939).

(6) J. C. Giddings and R. A. Keller, in "Chromatography," E. Heftmann, Ed., Reinhold Publishing Corp., New York, N. Y., 1961.