collected, redissolved in 70 ml. of boiling water, and precipitated by the addition of concentrated hydrochloric acid to *p*H 1.5; yield 420 mg.; white microcrystalline solid. This was 2-amino-1-methyl-4-oxo-1,4-dihydropteridine-7-carboxylic acid (XVI). R_f 0.17 [isopropyl alcohol–1*N* NH_4OH (7:3)] (abs.); ultraviolet absorption spectra at pH 7.0, λ_{max} 245 mμ (ε 14,600), 337 mμ (ε 10,200); 0.1*N* HCl, λ_{max} 238 mμ (ε 12,800), 329 mμ (ε 9,500).

Anal. Calcd. for $C_8H_7N_5O_3$ (221): C, 43.4; H, 3.2; N, 31.6. Found: C, 43.2; H, 3.3; N, 31.2.

2-Methylamino-4-hydroxpteridine-7-carboxylic acid (XVII). A solution of 150 mg. (0.62 mmole) of 2-amino-3-methyl-4-oxo-3,4-dihydropteridine-7-carboxylic acid (XV) in 15 ml. of 0.5*N* sodium hydroxide was heated 25 min. on the steam bath, treated with Norit, filtered, and acidified to *p*H 1.5 with 0.7 ml. of concentrated hydrochloric acid. This was cooled and the crystalline product was collected; yield 120 mg. (80%). This was purified by solution in 50 ml. of hot water containing 1.6 ml. of pyridine followed by acidification with 2 ml. of concentrated hydrochloric acid; yield of product 80 mg. (53%); R_f 0.58 (3% NH_4Cl) (blue); ultraviolet absorption spectra in 0.1*N* NaOH, λ_{max} 265 mμ (ε 19,000), 380 mμ (ε 6,900); pH 7.0, λ_{max} 248 mμ (ε 12,200), 274 mμ (ε 12,500), 358 mμ (ε 6,400); 0.1 *N* HCl, λ_{max} 241 mμ (ε 13,500), 332 mμ (ε 6,900).

Anal. Calcd. for $C_8H_7N_5O_3$ (221): C, 43.4; H, 3.2; N, 31.7. Found: C, 43.2; H, 3.4; N, 31.7.

Acknowledgment. Thanks are due to Mr. William Fulmor and his group for all of the spectral data and to Mr. Louis Brancone and staff for the elemental analyses and the pK_a determinations.

PEARL RIVER, N. Y.

[CONTRIBUTION FROM THE NAVAL STORES LABORATORY, OLUSTEE, FLORIDA][1]

The Chemistry of Pinolic Acid. I. Rearrangement by Acid-Catalyzed Acylation[2]

J. D. PARK,[3] R. L. SETTINE,[3] B. A. PARKIN, JR., AND G. W. HEDRICK

Received September 25, 1961

cis-dl-Pinolic acid has previously been reported to yield *dl*-2,2-dimethyl-3-(1-acetoxyethyl)cyclobutaneacetic acid by normal acylating procedures. It has been found that in acetylation of the acid in the presence of *p*-toluenesulfonic acid, 40 grams per mole of pinolic acid, rearrangement occurs producing *dl*-2,2,4-trimethyl-3-acetoxycyclopentaneacetic acid and a delta lactone of 2,2,4-trimethyl-3-hydroxycyclopentaneacetic acid. Pyrolysis of the acetate gave *dl*-2,2,4-trimethyl-3-cyclopenteneacetic acid. Elucidation of the structure of these materials was achieved by chemical evidence and comparison of nuclear magnetic resonance spectra of the 2,2,4-trimethyl and 2,2,3-trimethyl unsaturated acids.

Pinolic acid, 2,2-dimethyl-3-(1-hydroxyethyl)-cyclobutaneacetic acid (I), is an easily obtainable acid derived from turpentine. Tiemann and Kerschbaum[4] were first to prepare *cis-dl*-pinolic acid and observed that upon distillation, an unsaturated acid was formed which these authors named pinocampholenic acid. They later believed this to be α-campholenic acid, 2,2,3-trimethyl-3-cyclopenteneacetic acid (II) formed by molecular rearrangement.

A number of other workers[5–8] have reported the product from either the acid catalyzed or thermal rearrangement of pinolic acid to be the same as that obtained by Tiemann and Kerschbaum.

With the availability of vapor phase chromatography and spectrographic equipment, which were not used by earlier workers, except for infrared spectroscopy used by Kergomard, a study was undertaken in this laboratory to investigate the chemistry of pinolic acid. This paper is primarily concerned with the rearrangement of pinolic acid under the conditions for acid catalyzed acetylation. A second paper will describe results obtained on reinvestigation of earlier reports on the rearrangement of pinolic acid. A third paper will deal with the mechanism of the rearrangement.

During the course of studies on acylation of pinolic acid to produce 2,2-dimethyl-3-(1-acetoxyethyl)cyclobutaneacetic acid (III) using *p*-toluenesulfonic acid as a catalyst[9] it was observed that, under certain conditions of acetylation, an abnormal acetate was formed. This material, has been identified as 2,2,4-trimethyl-3-acetoxycyclopentaneacetic acid (V). Characterization of the acetate was accomplished by saponification, pyrolysis, degradative oxidation, and infrared and NMR spectral analyses.

The two most likely structures for an acetate produced by rearrangement from pinolic acid, explainable by a simple mechanistic scheme, are 2,2,3-trimethyl-4-acetoxycyclopentaneacetic acid (IV), formed by migration of the gem dimethyl group, and 2,2,4-trimethyl-3-acetoxycyclopentane-

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

(2) Presented at the 140th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 3–8, 1961. Work done at the Naval Stores Laboratory.

(3) Dept. of Chemistry, University of Colorado, Boulder, Colo.

(4) F. Tiemann and M. Kerschbaum, *Ber.*, **33**, 2661 (1900).

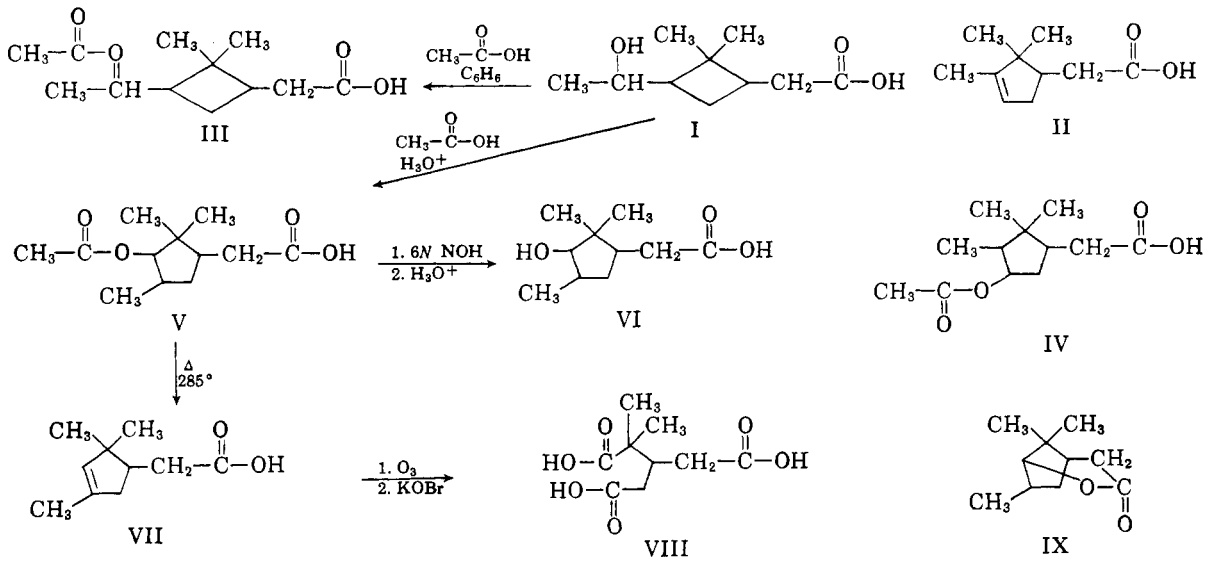
(5) L. Ruzicka and H. Trebler, *Helv. Chim. Acta*, **3**, 756 (1920).

(6) Le-Van-Thoi, *Ann. chim.*, **10**, 35 (1955).

(7) A. Kergomard, *Bull. soc. chim. France*, 1161 (1957).

(8) M. Harrispe and D. Mea, *Bull. soc. chim. France*, 1562 (1960).

(9) B. A. Parkin, Jr., and G. W. Hedrick, *J. Org. Chem.*, **25**, 1417 (1960).



acetic acid (V), formed by migration of the methylene group.

The saponification of the acetate yielded a hydroxy acid VI, isomeric with pinolic acid, which resisted oxidation by permanganate and aluminum isopropoxide in acetone. This would be expected in the case of 2,2,4-trimethyl-3-hydroxycyclopentaneacetic acid (VI), as the steric effects of the methyl groups would retard the attack by a bulky reagent.

Pyrolysis of the acetate V yielded an unsaturated acid VII. This acid was indicated to be homogeneous by vapor phase chromatography of its methyl ester. Degradative oxidation of this unsaturated acid, by the procedure of King and Farber,[10] yielded isocamphoronic acid (VIII),[11] 2,2-dimethyl-3-carboxymethylpentanedioic acid.

The formation of isocamphoronic acid, although it established the basic cyclopentene structure of this acid, however, did not differentiate between 2,2,4-trimethyl-3-cyclopenteneacetic acid (VII) and 2,2,3-trimethyl-3-cyclopenteneacetic acid (II). The difference was demonstrated by infrared, vapor phase chromatography, and NMR spectral analysis. The infrared spectrum of the two acids differed considerably in the region of the double bond absorption. The known α-campholenic acid, prepared from camphor oxime,[12] absorbed in the olefin region at 12.60 μ while that of 2,2,4-trimethyl-3-cyclopenteneacetic acid was at 12.16 μ.

In addition the infrared spectrum of this material compared with known 2,2,4-trimethyl-3-cyclopenteneacetic acid (VII), obtained from α-pinene epoxide by the method of King and Farber,[10] showed the two to be identical.

(10) L. C. King and H. Farber, *J. Org. Chem.*, **26**, 326 (1961).

(11) W. H. Perkin, Jr., *J. Chem. Soc.* (London), **81**, 246 (1902).

(12) F. Tiemann and F. W. Semmler, *Ber.*, **29**, 529 (1896); F. Tiemann, *Ber.*, **29**, 3006 (1896).

Vapor phase chromatography of the corresponding methyl esters showed different retention times (Table I) and a mixture of the two esters was separable.

TABLE I

GAS CHROMATOGRAPHIC DATA[a] AND PHYSICAL CONSTANTS OF ESTERS

Compound	Retention Time	B.P./ Mm.	n_D^{20}
Methyl-2,2,4-trimethyl-3-cyclopentene acetate	2-1/2 min.	88–89/10	1.4512
Methyl-2,2,3-trimethyl-3-cyclopentene acetate	3 min.		
Methyl-2,2,4-trimethyl-3-hydroxycyclopentane acetate	13-1/2 min.	95–96/0.2	1.4657
Methyl-2,2,4-trimethyl-3-acetoxycyclopentane acetate	10 min.	97–98/0.2	1.4508
Methyl-2,2-dimethyl-3-(1-hydroxyethyl)cyclobutane acetate	11 min.	82–83/0.05	1.4595
Methyl-2,2-dimethyl-3-(1-acetoxyethyl)cyclobutane acetate	10 min.	85–86/ 0.02	1.4456

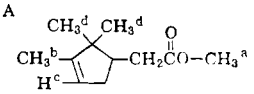
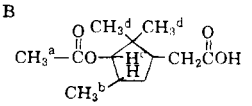
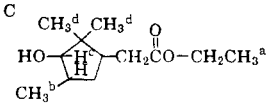
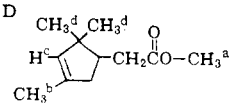
[a] F and M Model 500 Gas Chromatograph, Craig Succinate on Chromasorb 100 column, 225°, Helium 50 ml./min.

The choice between acetates IV and V was made by means of the NMR spectra. The methine proton H^c, B, (Table II), compound V, is split into a doublet by spin-spin coupling with one proton adjacent to it. This is in accordance with the assigning of structure B (Table II), rather than structure IV, in which the methine hydrogen would be expected to show splitting by three adjacent protons.

Finally, the NMR spectra of the methyl esters of the two unsaturated acids were compared. These showed conclusively that the structures although similar were not identical. In D (Table II), the methyl ester of XII, the *gem*-dimethyl

TABLE II

PROTON NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA[a]

Compound	Principal NMR Assignments T[b]			
	H^a	H^b	H^c	H^d
A 	6.33(3)	8.35, 8.41(3) $J^c = 4.0$	4.87(1)	9.17(3) 8.94(3)
B 	7.84(3)	9.02, 8.90(3) J = 7.8	5.36, 5.49(1) J = 7.9	9.23(3) 9.04(3)
C 	8.55, 8.68, 8.81(3) J = 7.70	8.81, 8.94(2) J = 6.74	?	9.34(3) 9.00(3)
D 	6.35(3)	8.40(3)	4.95(1)	9.18(3) J = 5.61 8.96(3) J = 2.69

[a] Proton NMR spectra were obtained in deuterochloroform solution at 60 mc. (spinning). [b] Hydrogen superscript letters refer to lettering shown in structural formulas. Tau values (T) are given in p.p.m. relative to tetramethyl silane (10.00). Values in parentheses are relative peak areas. [c] Splitting constants (J) are given in cycles sec.$^{-1}$

protons H^d were partially split by the vinyl proton H^c due presumably to the rigidity of the cyclopentene ring system. The vinyl proton H^c, although split slightly by interaction with neighboring methyl protons, was considerably different than H^c A (Table II), in which the methyl ester of X, was split symmetrically by the adjacent methylene protons. Other absorption values are tabulated in Table II.

Thus from both physical and chemical data it was concluded that acid VII is 2,2,4-trimethyl-3-cyclopenteneacetic acid.

An investigation of the acid fraction formed during the acylation reaction was conducted by means of vapor phase chromatography and infrared spectral analyses of the methyl esters prepared with diazomethane. Under the conditions used for this reaction all acid material was found to be rearranged and to consist of V, VI, and VII. No indication of cyclobutane derivatives was found.

The study of the nonacidic materials (neutrals) formed along with the acids as a result of molecular rearrangement in the acylation reaction has not been extensive. It is believed important to mention, however, that one of the major components of the neutral material is the Δ-lactone of 2,2,4-trimethyl-3-hydrocyclopentaneacetic acid, IX.

EXPERIMENTAL

cis-dl-Pinolic acid. The pinolic acid used was prepared by the method of Parkin and Hedrick.[9] The hydrogenation was terminated when the pinonic acid content had dropped below 3%. The analysis of the mixture was carried out by means of the ultraviolet absorption peak of the pinonic acid keto group at 280 mμ. The procedure follows.

A small sample of the solution was withdrawn from the hydrogenation bomb. The solution was acidified, the mixture extracted with ether, dried over anhydrous sodium sulfate, and the ether evaporated on a Rotovac. The crystalline residue was broken up and 1.00 g. was weighed into a 10-ml. volumetric flask. The sample was made up to 10 ml. with 95% ethanol. The optical density at 280 mμ was determined by means of Beckman DU spectrophotometer. The optical density was converted directly to per cent pinonic acid by means of a standard curve which was prepared as follows. The optical density of solutions of recrystallized pinonic acid in the range of 1 to 5 mg./ml. was measured at 280 mμ.

The optical density of pinolic acid solutions in the range of 95 to 100 mg./ml. was found to be between 0.18 and 0.3. Because of this the optical density values for the pinonic acid solutions above were increased by 0.2 and these adjusted values plotted against concentration of pinonic acid in mg./ml. The straight line curve then passed through the point 0.2 on the optical density axis at zero concentration and 1.62 optical density at 5 mg./ml. Under the conditions of analysis (*i.e.*, 100 mg. of acid per ml.) the concentration scale becomes % pinonic acid contained in the sample.

2,2,4-Trimethyl-3-acetoxycyclopentaneacetic acid (VII). To a well stirred, refluxing, dry solution of 186 g. (1.0 mole) of *cis-dl*-pinolic acid (m.p. 104–105°) in 300 ml. of benzene was added a dry solution of 40 g. (0.23 mole) of *p*-toluenesulfonic acid and 240 g. (4.0 mole) of glacial acetic acid in 200 ml. of benzene. The solution was refluxed until no more water was evolved.

The resultant solution was cooled, washed with 200 ml. of water, and the solvent removed under reduced pressure until the pot temperature reached 100°. The residue was taken up in *n*-heptane, 300 ml., treated with activated charcoal, and filtered. On cooling, there was obtained 105 g. (0.46 mole), 46% of 2,2,4-trimethyl-3-acetoxycyclopentaneacetic acid, m.p. 99–100°. Recrystallization from methanol water mixture gave needles, m.p. 103–104°.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.13; H, 8.83; neut. equiv., 228.17. Found: C, 63.16; H, 8.90; neut. equiv., 228.0.

Infrared spectral and vapor phase chromatographic analyses of the corresponding methyl ester showed this compound to be relatively free of contamination by hydroxyl containing materials or unrearranged acetate.

The infrared spectrum of the ester had the following major absorption bands: 5.80, 6.90, 7.00, 9.70, 10.15, 11.00, and 11.35 μ. This differed considerably from the normal acetate.

The acid portion of a reaction mixture from another experiment was separated by extraction with saturated sodium bicarbonate solution. Acidification and esterification of the acidic materials, 125 g., 55%, with diazomethane yielded an ester mixture. Separation of the mixture by vapor phase chromatography yielded three components: 2,2,4-trimethyl-3-acetoxycyclopentaneacetic acid (V), 2,2,4-trimethyl-3-cyclopenteneacetic acid (VII), and 2,2,4-trimethyl-3-hydroxycyclopentaneacetic acid (VI). Vapor phase chromatographic analysis of the nonacidic portion, 102 g., 45%, formed in the reaction showed it to consist of four materials. Separation of one of the principle components, saponification and isolation of the corresponding acid yielded crystals, m.p. 124–125°. A mixed m.p. with acid VI gave no depression. This component was undoubtedly the Δ lactone IX. From the chromatographic analysis this product represented 60% (estimated) of the nonacidic materials. The combined yield of materials having the 2,2,4-trimethylcyclopentyl structure, acetate and lactone, was, therefore, about 80%.

Methyl ester of V. The acid V, 12 g., in 100 cc. of ether was treated with excess diazomethane in ether. Isolation and distillation yielded a colorless oil, b.p. 97–98°/.2 mm., n_D^{20} 1.4508.

Anal. Calcd. for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.40; H, 9.25.

2,2,4-Trimethyl-3-cyclopenteneacetic acid (V). 2,2,4-Trimethyl-3-acetoxycyclopentaneacetic acid, 63 g. (0.28 mole) was pyrolyzed by distillation through a 6-inch column packed with protruded metal at atmospheric pressure and under a nitrogen atmosphere. After all the acetic acid was removed, a colorless liquid distilled, 42 g., b.p. 255°. Extraction of the acidic materials with sodium bicarbonate followed by acidification of the aqueous layer yielded upon re-extraction the acid VII, 25 g., 53%, b.p. 138°/9 mm., n_D^{20} 1.4683.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.43; H, 9.52; neut. equiv., 168.14. Found: C, 71.18; H, 9.60; neut. equiv., 169.0.

The methyl ester of this acid was prepared with diazomethane as above, b.p. 88–89°/10 mm.; n_D^{20} 1.4512.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.43; H, 9.89. Found: C, 72.09; H, 10.02.

Oxidative degradation to isocamphoronic acid (VIII). A solution of 10 g. (0.06 mole) of 2,2,4-trimethyl-3-cyclopentene-1-acetic acid (VII) in 100 cc. of methanol was ozonized following the procedure of King and Farber.[10] There was obtained 7.1 g., 54%, of isocamphoronic acid, m.p. 165–166°.

Calcd. for $C_9H_{14}O_6$: n.e. 72.70. Found: 73.14.

2,2,4-Trimethyl-3-hydroxycyclopentaneacetic acid (VI). The hydroxy acid VI was prepared by saponification of acetate V. For this solution of 40 g. (0.175 mole) of V in 100 ml. of 6*N* sodium hydroxide was refluxed for 3 hr. The product, 2,2,4-trimethyl-3-hydroxycyclopentaneacetic acid, crystallized when the hydrolysis mixture was made acid and cooled. A yield amounting to 31.2 g., 100%, was obtained, m.p. crude 123–124°. Recrystallization from water gave needles, m.p. 125–126°.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74; neut. equiv., 186.15. Found: C, 64.37; H, 9.58; neut. equiv., 186.0.

Infrared spectral analysis and vapor phase chromatographic analyses of the corresponding methyl ester showed this material to be pure. Methyl ester, b.p. 95–96°/0.2 mm., n_D^{20} 1.4657.

Anal. Calcd. for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. Found: C, 65.66; H, 10.03. Ethyl ester, b.p. 103–104°/.2 mm., n_D^{20} 1.4593.

Anal. Calcd. for $C_{12}H_{21}O_4$: C, 67.25; H, 10.35. Found: C, 67.25; H, 10.26.

The NMR spectrum of the ethyl ester C, Table II, is consistent with the assigned structure except that definite assignments have not yet been made for the H^c and OH protons.

Acknowledgment. We wish to thank Dr. Werner Herz and Mr. Gerald Caple, Florida State University, Tallahassee, Fla., for carrying out the NMR analyses and Mr. L. E. Brown, Southern Utilization Research and Development Division, New Orleans, La., for elemental analyses.

OLUSTEE, FLA.