tained. An analytical sample was prepared by recrystallization from cyclohexane, m.p. 179.5–180°.

Anal. Calcd. for $C_{12}H_{22}N_2O$: C, 68.52; H, 10.56; N, 13.31. Found: C, 68.35; H, 10.46; N, 13.10.

The infrared spectrum ($CHCl_3$) showed bands at 3290 (N–H), 1678 (C=O), and 1665 cm.$^{-1}$.

N-Aminocamphidine Hydrochloride (4c).—N′-Acetyl-N-aminocamphidine (2.5 g., 0.012 mole) was dissolved in concentrated hydrochloric acid (10 ml.) and water (25 ml.) and heated on the steam bath for 5 hr. The solution was evaporated to dryness on a rotary evaporator (steam bath) and N-aminocamphidine hydrochloride (2.3 g., 95%) was obtained, m.p. 218–220°. An analytical sample was prepared by recrystallization from ethyl acetate containing a small amount of methanol, m.p. 220–221°.

Anal. Calcd. for $C_{10}H_{21}ClN_2$: C, 58.64; H, 10.35; N, 13.67. Found: C, 58.70; H, 10.39; N, 13.53.

N′-*p*-Toluenesulfonyl-N-aminocamphidine (4d).—The tosyl hydrazide was prepared by the method of Carpino.[3a] N-Aminocamphidine hydrochloride (2.3 g., 11.8 mmoles) was dissolved in dimethylformamide (50 ml.) and triethylamine (3.3 ml., 23.6 mmoles) was added. A white precipitate appeared immediately. *p*-Toluenesulfonyl chloride (2.5 g., 13.1 mmoles) was added in small portions to the stirred mixture at 0°. After the addition was complete, it was stirred for an additional 15 min. at 0° and then quenched in water (250 ml.). The oil which was formed crystallized on overnight standing. The *p*-toluenesulfonhydrazide, m.p. 102.8–103.5°, was recrystallized from methanol–water and a total yield of 2.6 g. (68%) was obtained by repeated concentration of the mother liquors.

Anal. Calcd. for $C_{17}H_{26}N_2O_2S$: C, 63.32; H, 8.12; N, 8.68. Found: C, 63.27; H, 8.26; N, 8.57.

Oxidation of N-Aminocamphidine with Mercuric Oxide.—N-Aminocamphidine·HCl (204 mg., 1.0 mmole) was dissolved in 95% ethanol (13 ml.) and stirred at reflux under a nitrogen atmosphere. Sodium methoxide in methanol (3.3 ml. of a 0.304 *M* solution) was added to form the free base. Then yellow mercuric oxide (460 mg., 2.1 mmoles) was added in one portion. The mixture was stirred and refluxed for 0.5 hr. and filtered hot through Celite. The filtrate was warmed to the boiling point and water was added until a permanent cloudiness appeared. The tetrazene **5** was obtained (100 mg., 62%), m.p. 224–225°, and was recrystallized from ethanol, λ_{max} (ethanol) 287 mμ (log ε 4.10).

Anal. Calcd. for $C_{20}H_{36}N_4$: C, 72.24; H, 10.91; N, 16.84. Found: C, 72.08; H, 11.04; N, 16.79.

Pyrolysis of the Sodium Salt of N′-*p*-Toluenesulfonyl-N-aminocamphidine.—N′-*p*-Toluenesulfonyl-N-aminocamphidine (625 mg., 2 mmoles) was dissolved in methanolic sodium methoxide (3.85 ml. of a 0.65 *M* solution) and the resulting solution was concentrated to dryness *in vacuo* and on the steam bath. The solid sodium salt was transferred to a glass tube, sealed, and heated to 220–230° in an oil bath. A sublimate (50–60 mg.) appeared during the course of 1 hr. The residue was then cooled, dissolved in water, and acidified, and *p*-toluenesulfinic acid (melting point, mixture melting point, and infrared spectrum) was isolated. The sublimate, m.p. 167–200°, had a strong absorption at 1650 cm.$^{-1}$. Hydrogenation of this material in acetic acid (4 ml.) with PtO_2 (40 mg.) took up 1.25 equiv. of hydrogen based on an equimolar mixture of camphidine and the corresponding imine. The catalyst was filtered off and the acetic acid was evaporated *in vacuo*. The resultant oil was converted to the *p*-nitrobenzenesulfonamide (70 mg., 63%), m.p. 143–144°.

Pyrolysis of the Sodium Salt of N′-*p*-Toluenesulfonyl-N-aminocamphidine in Tetraglyme.—N′-*p*-Toluenesulfonyl-N-aminocamphidine (625 mg., 2 mmoles) was dissolved in methanolic sodium methoxide (2.9 ml. of a 0.74 *M* solution), and the resulting solution was concentrated to dryness on the steam bath and *in vacuo*. The dry sodium salt was dissolved in tetraglyme (25 ml., dried by passing through a column of chromatographic grade alumina). The solution was heated in an oil bath at 200° and after a few minutes a white precipitate appeared. After a total heating time of 15 min., the mixture was quenched in 60 ml. of ice water. The aqueous solution was extracted with ether and the resultant ethereal solution was washed with water and saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. Concentration to dryness afforded the tetrazene **5** (120 mg. 37%), m.p. 223–224°. In a similar experiment the white material which had formed during the pyrolysis was filtered, dissolved in water, and acidified. It proved to be *p*-toluenesulfinic acid (melting point, mixture melting point, and infrared spectrum). The filtrate (tetraglyme solution) was subjected to gas–liquid chromatography (silicone rubber column, oven temperature 145°, and helium flow rate of 60 cc./min.) and camphane was detected by comparing retention times of an observed peak with an authentic sample. Control experiments revealed that no other component of the system had a similar retention time. The filtrate was also subjected to thin layer chromatography on silica gel with a $CaSO_4$ binder and again camphane was detected. The estimated amount (g.l.c.) was about 0.5% and the isolation of this amount was not attempted.

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The Photodehydrogenation of Levopimaric Acid in the Presence of Sulfur

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The photosensitized oxidation of the pine gum resin acids has been described.[2] In an attempt to replace oxygen with sulfur in this reaction, we found that levopimaric acid in ethanol in the presence of sulfur, visible light, and air gave off hydrogen sulfide, exhibited a total loss of conjugated dienic unsaturation, and yielded dehydroabietic acid on work-up of the mixture. No sensitizing dye was used in the reaction. In the absence of sulfur, visible light, or air, no reaction was observed. None of the other pine gum resin acids, namely palustric, neoabietic, abietic, pimaric, isopimaric, and dehydroabietic acids reacted to any extent under the same conditions. In the reaction of levopimaric acid in ethanol, the sulfur in dispersion or in solution may act as a sensitizer for the visible light.

The photochemical reaction was then attempted in carbon disulfide in which all reactants, including sulfur, were soluble. It was observed that isomerization of levopimaric to abietic acid took place. Neither sulfur nor air was found necessary. No reaction took place in the dark. It was noted that the isomerization proceeded to completion when the light was turned off in the middle of a run. It would thus appear that irradiation in carbon disulfide results in the formation of an acidic[3] (or possibly basic[4]) substance which catalyzes the isomerization of levopimaric acid to abietic acid.[3,4]

Experimental

Reaction of Levopimaric Acid with Sulfur, Light, and Air in 95% Ethanol.—To a solution of 8.16 g. of levopimaric acid ($[\alpha]_D$ −273°) in 2700 ml. of 95% ethanol was added 8.64 g. of flowers of sulfur. The dispersion was charged to a 2700-ml. reactor[2] equipped with an internal 40-w. daylight fluorescent lamp bulb and four external 15-w. fluorescent lamps. Aeration and irradia-

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article is not copyrighted.

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tion were carried out simultaneously. A large amount of hydrogen sulfide was liberated. The rotation fell and leveled off at $[\alpha]D+18°$ after 19 hr. The solution was filtered and stripped under reduced pressure. The crude residue exhibited no characteristic absorption from 220–320 mμ. A portion of the crude solid was esterified with diazomethane and gas chromatographed on Versamide-900 at 240°. A single peak was observed of emergence time identical with that of an authentic sample of methyl dehydroabietiate. The cyclohexylamine salt of the crude residue was prepared in acetone and recrystallized from 95% ethanol; yield 4.88 g. The filtrate was concentrated to give a black, noncrystallizable oil. The salt was regenerated using dilute phosphoric acid and ether.[2] The crude acid was chromatographed on 92 g. of silicic acid and eluted with benzene. The eluate was crystallized from 95% ethanol to give 0.69 g. of dehydroabietic acid, $[\alpha]D$ +61.8° (*c* 0.6, 95% ethanol), λ_{max} 268 mμ (α 2.21) and 276 (α 2.34), infrared spectrum essentially identical with an authentic sample. A second crop of 0.32 g. was obtained, λ_{max} 268 mμ (α 2.51) and 276 (α 2.60), for a total of 1.01 g. or 13% over-all yield. The remainder of the material from the column could not be crystallized.

Blank Runs in 95% Ethanol.—A series of runs was made in 100-ml. Pyrex reactors,[2] 0.01 *M* in resin acid, and 0.01 *M* in sulfur, and followed by means of the change in rotation and/or ultraviolet spectrum for 7 hr. A 15-w. daylight fluorescent bulb was used as a light source. No reaction occurred in the case of levopimaric acid under nitrogen, on aeration in the dark, or on aeration in the absence of sulfur. In the presence of air, light, and sulfur, the reaction with levopimaric acid was over in less than 12 hr. No reaction occurred in the presence of air, light, and sulfur when levopimaric acid was replaced with palustric, neoabietic, abietic, dehydroabietic, pimaric, or isopimaric acids.

Isomerization of Levopimaric Acid in Carbon Disulfide.—A 0.011 *M* solution of levopimaric acid in carbon disulfide was charged to a 100-ml. Pyrex reactor[2] open to the air and irradiated with a 15-w. daylight fluorescent lamp. The original rotation of −200° fell to −116° after 8 hr. At this point the light was turned off and the reactor was stored in the dark. After an additional 16 hr. the rotation was +20° (abietic acid exhibits $[\alpha]^{25}D$ +20° in carbon disulfide), and the ultraviolet spectrum showed a single major peak at λ_{max} 241 mμ (α 69). The product was esterified with diazomethane and analyzed *via* g.l.c. The yield of abietic acid was 83%. The reaction proceeded more slowly under nitrogen. The presence of dissolved sulfur did not affect the reaction. No reaction occurred in the dark over the same period of time.

3′-Iodopteroylglutamic Acid (Iodofolic Acid)

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Several chloro and bromo derivatives of pteroylglutamic acid have been described in the literature.[2] The iodo derivatives, except 3′-iodo-4-amino-4-deoxypteroylglutamic acid (3′-iodoaminopterin),[3] are not as well studied. Iodination of 1 mole of pteroylglutamic acid with 2 moles of iodine monochloride in hydrochloric acid yielded a substance which, on the basis of nitrogen and iodine analyses alone, seemed to be the 3′-iodopteroylglutamic acid.[2b] However, this substance, prepared by identical procedure, was claimed by the same authors as the 3′,5′-diiodo derivative in patent literature.[2c,d] In either case structural proof was lacking.

We repeated this reaction. In addition, we prepared a magnesium salt of the iodinated compound. Both displayed correct analyses of all elements for monoiodopteroylglutamic acid and the magnesium salt, respectively. Moreover, oxidation of the iodinated product with potassium permanganate in dilute alkali degraded it to two fragments, separately identified as 2-amino-4-hydroxy-6-pteridinecarboxylic acid[4] and 3-iodo-4-aminobenzoylglutamic acid,[3] thus definitely establishing the structure of the iodo compound as 3′-iodopteroylglutamic acid.

The iodination of pteroylglutamic acid with iodine monochloride was also carried out in dimethylformamide. In this case, iodination was accompanied by cleavage of pteroylglutamic acid into 3,5-diiodo-4-aminobenzoylglutamic acid[2] and 2-amino-4-hydroxy-6-pteridinecarboxaldehyde,[5] similar to the case with aminopterin.[3]

Experimental[6]

3′-Iodopteroylglutamic Acid.—The published procedure[2] was faithfully followed. For the preparation of the magnesium salt, the free iodinated acid (100 mg.) was dissolved in a minimal amount of a saturated solution of sodium bicarbonate and mixed with 100 mg. of anhydrous magnesium sulfate powder. To the thick paste was added 5 ml. of water, and the mixture was centrifuged. The precipitate was washed with 5 ml. of water and recrystallized from 50 ml. of boiling water. The yellow magnesium salt was collected and washed with water and alcohol. The yield was 100 mg.

Anal. Calcd. for $C_{19}H_{16}IMgN_7O_6$: C, 38.70; H, 2.74; I, 21.52; Mg, 4.13; N, 16.63. Found: C, 38.69; H, 2.83; I, 20.76; Mg, 3.99; N, 16.90.

Reconversion of the magnesium salt into the free acid was easily achieved by dissolving the former (100 mg.) in 2 ml. of concentrated hydrochloric acid and diluting with 20 ml. of water. The precipitate was collected by filtration and washed with water and methanol. It weighed 40 mg.

Anal. Calcd. for $C_{19}H_{18}IN_7O_6$: C, 40.23; H, 3.20; I, 22.37; N, 17.28. Found: C, 40.03; H, 3.18; I, 22.22; N, 17.06.

The ultraviolet absorption spectra of 3′-iodopteroylglutamic acid bear close resemblance to those of 3′-iodoaminopterin,[3] differing by the absence in 3′-iodopteroylglutamic acid of an absorption maximum at 336 mμ in dilute acid. The characteristics are: in 0.1 *N* sodium hydroxide, λ_{max} 223 mμ (log ε 4.77), 255 (4.48), 282 (4.38), and 366 (4.12); in 0.1 *N* hydrochloric acid, λ_{max} 223 mμ (log ε 4.48) and 301 mμ (log ε 4.28).

Oxidative Degradation of 3′-Iodopteroylglutamic Acid.—The procedure was exactly the same as for the oxidation of 3′-iodoaminopterin.[3] From 100 mg. of the iodo compound were obtained 25 mg. of a substituted pteridine and 15 mg. of a nonpteridine moiety.

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(6) Melting points were determined on a Fisher-Johns apparatus. Ultraviolet absorption spectra were recorded with a Cary spectrophotometer, Model 14. All analyses were performed by Dr. William C. Alford and staff of the National Institute of Arthritis and Metabolic Diseases, to whom we express our gratitude.