toacetate and 4-nitrophenylhydrazine were refluxed together in equimolecular quantities in glacial acetic acid as solvent. The pyrazolone (II) was also obtained when the condensation of ethyl acetoacetate and 4-nitrophenylhydrazine was carried out in the presence of concentrated hydrochloric acid with or without the addition of ethanol.

The samples of II obtained in these several procedures were identified by comparison with an authentic sample prepared by the nitration of 1-phenyl-3-methylpyrazolone-5 as described in German Patent 61794.[2]

Experimental

Ethyl Acetoacetate 4-Nitrophenylhydrazone (I).—A mixture of 15.3 g. (0.1 mole) of 4-nitrophenylhydrazine and 13.0 g. (0.1 mole) of ethyl acetoacetate with or without the addition of a small quantity of ethanol as solvent was heated under reflux on the steam-bath for several hours. The orange colored crystalline product which separated on cooling was purified by crystallization from 95% ethanol; m. p. 118°.

Anal. Calcd. for $C_{12}H_{15}N_3O_4$: N, 15.84. Found: N, 15.85, 15.76.

1-(4′-Nitrophenyl)-3-methylpyrazolone-5 (II). A.—A sample of ethyl acetoacetate 4-nitrophenylhydrazone (5 g.) was treated with sufficient glacial acetic acid to dissolve it and the resulting solution heated under reflux at steam-bath temperature for five hours. The yellow crystalline product which separated on cooling was purified by crystallization from 95% ethanol from which it separated as light yellow crystals; m. p. 218°. Heating the hydrazone (I) for fifteen minutes at steam-bath temperature with concentrated hydrochloric acid brought about the same transformation.

B.—A mixture of 7.65 g. (0.05 mole) of 4-nitrophenylhydrazine, 6.5 g. (0.05 mole) of ethyl acetoacetate and 25 g. of glacial acetic acid was heated under reflux at steam-bath temperature for five hours. The product which separated on cooling was crystallized from 95% ethanol from which it separated as light yellow crystals; m. p. 218°. The pyrazolone (II) was also obtained when a mixture of ethyl acetoacetate (0.05 mole) and 4-nitrophenylhydrazine (0.05 mole) was heated in the presence of 2 ml. of concentrated hydrochloric acid either with or without the addition of ethanol.

C.—The compound was prepared from 1-phenyl-3-methylpyrazolone-5 by nitration according to the procedure given in German Patent 61794[2]; light yellow crystals; m. p. 218°.

The identity of the samples prepared by procedures A, B and C was established by melting point methods. The melting points reported herein are uncorrected.

Anal. Calcd. for $C_{10}H_9N_3O_3$: N, 19.17. Found: N, 18.74, 18.80.

(2) *Friedländer*, **3**, 926.

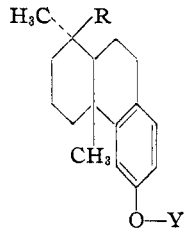
DEPARTMENT OF CHEMISTRY
WESTERN KENTUCKY STATE COLLEGE
BOWLING GREEN, KENTUCKY

RECEIVED JANUARY 10, 1948

Studies on Resin Acids. III. A Direct Reduction of Podocarpic Acid[1]

BY HAROLD H. ZEISS, CHESTER E. SLIMOWICZ AND VARSENIG Z. PASTERNAK

The constitution of the naturally occurring podocarpic acid (I) has suggested this resin acid as an unusually attractive starting material for the preparation of compounds having structural and perhaps physiological similarity to estradiol. One such compound is the hitherto unknown podocarpinol (II), the preparation of which is described in one step from podocarpic acid in this paper.



I, R = COOH; Y = H
II, R = CH_2OH; Y = H
III, R = COOCH; Y = CH_3
IV, R = COCl; Y = CH_3
V, R = CH_2OH; Y = CH_3

The direct reduction of the carboxylic acid group of the resin acids is usually attended by more or less difficulty, depending upon the configuration of these groups at the C_1 position. The *trans* acids,[2] represented by abietic acid, are less hindered and therefore more easily reduced than the *cis* acids,[2] represented by agathic and podocarpic acids, which are quite resistant to reaction owing to the extremely large effect of steric hindrance. While methyl abietate responds readily to a forced Bouveault–Blanc reduction, the methyl ester of isonoragathic acid is converted to isonoragathenol in very poor yield.[3] Alternately Campbell and Todd[4] have used an indirect method for reducing the O-methyl derivative of podocarpic acid to O-methylpodocarpinol *via* the acid chloride and the aldehyde.

It has been found that lithium aluminum hydride,[5] a compound recently discovered by Schlesinger and co-workers[6] and developed by Nystrom and Brown,[7] converts podocarpic acid directly to podocarpinol in satisfactory yield (56%). Under the same experimental conditions the methyl ester (III) and the acid chloride (IV) of O-methylpodocarpic acid also react with lithium aluminum hydride to give, after hydrolysis of the metal complex, O-methylpodocarpinol (V). The identity of podocarpinol is established by methylation to the known O-methylpodocarpinol.

Although the rate of reaction of lithium aluminum hydride with podocarpic acid is slow, it appears that the reduction of hindered acids with this reagent is not unreasonably limited by steric effects.

Experimental

Podocarpinol (II).—A solution of 8 g. of lithium aluminum hydride in 300 ml. of dry ether was placed in a one-liter flask equipped with dropping funnel, reflux condenser and mercury seal stirrer. All outlets were provided with calcium chloride tubes to exclude moisture during the reaction. To this solution was added dropwise with stirring 7 g. of podocarpic acid (m. p. 194–196°) dissolved in 150 ml. of ether. The mixture was then

(1) Paper II: Zeiss, THIS JOURNAL, **70**, 858 (1948).

(2) Zeiss, *Chem. Rev.*, **42**, 163 (1948).

(3) Ruzicka and Jacobs, *Rev. trav. chim.*, **57**, 509 (1938).

(4) Campbell and Todd, THIS JOURNAL, **64**, 928 (1942).

(5) Metal Hydrides, Inc., Beverly, Mass.

(6) Finholt, Bond and Schlesinger, THIS JOURNAL, **69**, 1199 (1947).

(7) Nystrom and Brown, *ibid.*, **69**, 1197; **69**, 2548 (1947).

allowed to stand for four days with occasional warming. Ice was next introduced to decompose excess hydride reagent and the reaction complex then hydrolyzed with dilute sulfuric acid. The ether layer was removed and the aqueous layer extracted with fresh ether. The combined ether extracts were then washed with water and extracted with dilute sodium carbonate solution to remove unreacted podocarpic acid. After drying over anhydrous potassium carbonate the ether solution was concentrated and hexane added. On cooling transparent cubes of podocarpinol crystallized out of solution; m. p. 177–178.5°. Recrystallization from ether gave 3.7 g. (56%) of pure material; m. p. 178–179°.

Anal.[8] Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.09; H, 9.08.

In an earlier run in which the total reaction time was two hours a yield of 4.6% of podocarpinol was obtained.

Methylation of podocarpinol with dimethyl sulfate in the usual manner gave O-methylpodocarpinol (m. p. 90–91°), first prepared by Campbell and Todd.[4] A mixed m. p. with the O-methylpodocarpinol prepared as described below showed no depression.

O-Methylpodocarpinol (V). (*a*) **From O-Methylpodocarpoyl Chloride** (IV).—Reaction between 33 g. of O-methylpodocarpoyl chloride (m. p. 61°) in 1 liter of ether and 10 g. of lithium aluminum hydride in 800 ml. of ether was carried out over a period of four days. The mixture was worked up in the same manner as described above (m. p. 91°) from which 28 g. (92%) of pure O-methylpodocarpinol was obtained after one crystallization from ether–hexane.

(*b*) **From Methyl O-Methylpodocarpate** (III).—Lithium aluminum hydride (8 g.) in 400 ml. of ether was treated with 15 g. of methyl O-methylpodocarpate m. p. 158–159° in 300 ml. of ether as above. From this experiment there was obtained 12.7 g. (93%) of O-methylpodocarpinol; m. p. 91°.

(8) Analysis by Dr. Carl Tiedcke Microlaboratories, New York.

RIDBO LABORATORIES, INC.
PATERSON 3, NEW JERSEY RECEIVED JANUARY 12, 1948

NEW COMPOUNDS

α-Nitrostilbene Analogs

The *alpha*-nitrostilbenes are physiologically active. Also compounds of the *alpha*, *beta*-diphenylethylamine type obtained by further reduction have been reported to have a selective effect in damaging sarcoma cells.[3]

Accordingly we have prepared nitro compounds of this type and submitted them to the National Cancer Institute for testing.

1-α-Thienyl-2-phenyl-2-nitroethylene was prepared by mixing 9.0 g. phenylnitromethane, 8.1 g. 2-thiophenealdehyde[4] and 3 ml. of a 10% solution of methylamine in methanol, warming gently, then shaking for three hours at room temperature. The bright yellow crystals which separated weighed 4.9 g. After triple recrystallization from absolute ethanol the product melted at 123° cor.

Anal. Calcd. for $C_{12}H_9O_2SN$: C, 62.34; H, 3.90; N, 6.06. Found: C, 62.45; H, 3.76; N, 6.06.

(1) Present address: Medical School, University of Tennessee, Memphis, Tennessee.

(2) Present address: Plough, Inc., Memphis, Tennessee.

(3) Shear, *et al.*, *Approaches to Tumor Chemotherapy*, American Association for the Advancement of Science, Washington, D. C. (1947), page 236 ff.; also Hartwell and Kornberg, THIS JOURNAL, **67**, 1607 (1946).

(4) Purchased from Arapahoe Chemicals, Inc., Boulder, Colo.

1-α-Furyl-2-*o*-chlorophenyl-2-nitroethylene was prepared by mixing 7.82 g. of *o*-chlorophenylnitromethane, 4.36 g. of freshly distilled furfural, and 5.16 cc. of a 16% solution of methylamine in methanol. The crystals which separated on standing three days weighed 3.96 g. The product was dissolved in absolute ethanol and the solution decolorized with activated carbon. After recrystallization from absolute ethanol the melting point was 101.1° cor.

Anal. Calcd. for $C_{12}H_8NO_3Cl$: C, 57.72; H, 3.21; N, 5.61. Found: C, 57.92; H, 3.12; N, 5.53.

1-*m*-Nitrophenyl-2-phenyl-2-nitroethylene was prepared by mixing 3 ml. of phenylnitromethane, 3.0 g. of *m*-nitrobenzaldehyde,[5] 0.5 ml. of 10% methylamine and 6 ml. of methanol. After standing four days the solution was diluted with 25 ml. of petroleum ether and chilled in Dry Ice. The yield of crystals was only 0.4 g. (7.5%). After recrystallization from absolute ethanol the melting point was 112.0° cor.

Anal. Calcd. for $C_{14}H_{10}N_2O_2$: C, 62.22; H, 3.70; N, 10.37. Found: C, 62.60; H, 3.75; N, 10.12.

1-*p*-Nitrophenyl-2-phenyl-2-nitroethylene, reported by Baker and Wilson[6] as melting at 155°, was prepared by us and found to melt at 157.5° cor., after repeated recrystallization.

Acknowledgment.—We wish to acknowledge our indebtedness to Dr. M. J. Shear and Dr. Jonathan L. Hartwell of the National Cancer Institute for suggestions and encouragement, to Mr. Charles A. Kinser and Mrs. Margaret M. Ledyard of the National Institute of Health for carrying out the microanalyses recorded above, and to the National Cancer Institute for financial assistance.

(5) Purchased from Eastman Kodak Company, Rochester, N. Y.

(6) Baker and Wilson, *J. Chem. Soc.*, 842–848 (1927).

CHEMISTRY DEPARTMENT
CARSON-NEWMAN COLLEGE
JEFFERSON CITY, TENNESSEE
CARL T. BAHNER,
HARRY E. DICKSON[1]
LYDIA MOORE[2]

RECEIVED FEBRUARY 24, 1948

3-Chloro-6-methoxy-8-nitroquinoline

To a stirred mixture of 300 ml. of concentrated hydrochloric acid, 50.4 g. of 3-nitro-4-aminoanisole and 85.2 g. of arsenic acid, at 100°, there was added 30.0 g. of α-chloroacrolein during one hour. After an additional hour at 100°, the mixture was poured on ice. A solid which separated was filtered off and recrystallized from acetone; yield 16 g., m. p. 151–153°. Recrystallization from methanol raised the m. p. to 159.5–160°.

Anal. Calcd. for $C_{10}H_7ClN_2O_3$: C, 50.31; H, 2.94; Cl, 14.88; N, 11.74. Found: C, 50.68; H, 2.84; Cl, 15.06; N, 11.75.

The original aqueous filtrate gave no product on neutralization.

THE DIVISION OF MEDICINAL CHEMISTRY
THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
NEW BRUNSWICK, N. J.
HARRY L. YALE

RECEIVED JANUARY 23, 1948

New Compounds as Insect Repellents

The compounds listed in Table I were prepared as part of a project to discover new insect repellents.[1]

2,2-Diethyl-1,3-Propanediol.—A solution of 43 g. of potassium hydroxide in 400 ml. of 95% ethanol was added to an ice-cooled, well-stirred mixture of 167 g. of 38% formaldehyde solution and 100 g. of 2-ethylbutyraldehyde (Eastman Kodak Co.) at such a rate that the tem-

(1) This work was performed under Contract NDCrc 136 between Harvard University and the Office of Scientific Research and Development, with Paul D. Bartlett as official investigator.