cipitated solids. The almost colorless acid solution was extracted with chloroform; and the chloroform was extracted with 5% potassium hydroxide solution. When this alkaline solution was acidified and allowed to stand two days at room temperature and then two days in the refrigerator, a white solid formed. This was collected, washed with cold ethanol, and dried in the air. The 2-benzoyl-4,5-dimethoxybenzoic acid so obtained (37% yield) melted before as well as after crystallization from alcohol at 193–194° (reported 199–200°).[29]

A convenient derivative for the 2-benzoyl-4,5-dimethoxybenzoic acid was a phthalazone, which was prepared by boiling a solution of 0.4 g. of the acid in 6 ml. of ethanol with approximately 0.02 g. of phenylhydrazine for two hours. The reaction mixture, after standing overnight at room temperature, deposited white crystals, which were collected, washed with cold ethanol and air-dried. 2,4-Diphenyl-6,7-dimethoxyphthalazone, after crystallization from ethanol, melted at 198–198.5° (reported 212°).[29]

Anal. Calcd. for $C_{22}H_{18}N_2O_3$: C, 73.73; H, 5.06. Found: C, 73.52; H, 5.10.

2-Phenylacetylstyrene (VIIb) from 1-Benzyl-3,4-dihydroisoquinoline (VIIa).—The dihydroisoquinoline was formed by cyclizing N-(phenylethyl)-phenylacetamide with phosphorus pentoxide in boiling xylene.[11] Passing dry hydrogen chloride in a benzene solution of the crude undistilled product furnished an oily hydrochloride, which became semisolid on standing overnight. Benzene was removed by decantation and by warming the residue on the steam-bath *in vacuo*. The hydrochloride of 1-benzyl-3,4-dihydroisoquinoline, m.p. 227–228°, was obtained in 31% yield after several crystallizations from isopropanol–ligroin and from methanol–ether. Exposure of the crude dihydroisoquinoline to high temperatures on attempted distillation led to a mixture containing 1-benzylisoquinoline.[30]

The ring opening experiment was carried out under nitrogen with 4 g. (0.016 mole) of 1-benzyl-3,4-dihydroisoquinoline hydrochloride, 12.6 ml. (0.133 mole) of dimethyl sulfate, and 156 ml. of 10% aqueous sodium hydroxide. Distillation of the crude product through a 7-cm. Vigreux column gave 1.89 g. (55%) of pale yellow 2-phenylacetylstyrene (VIIb), b.p. 162–164° (2.5 mm.), $n^{25}D$ 1.6180. The yield was lower than it should have been, since some of the product was accidentally lost. The 2,4-dinitrophenylhydrazone, recrystallized from alcohol, melted at 137–137.5°.

Anal. Calcd. for $C_{22}H_{18}O_4N_4$: C, 65.66; H, 4.5. Found: C, 65.2; H, 4.7.

o-Propenylbenzophenone (VIIIb) from 1-Phenyl-3-methyl-3,4-dihydroisoquinoline (VIIIa).—The dihydroisoquinoline hydrochloride[10,11] (0.35 g., 0.0013 mole) was treated in the usual way with 1.03 ml. of dimethyl sulfate, and 13 ml. of 20% sodium hydroxide solution. The solvent-free, dry product VIIIb (0.26 g.) failed to crystallize after standing four months in the refrigerator. The 2,4-dinitrophenylhydrazone melted at 165–167°.

Anal. Calcd. for $C_{22}H_{18}O_4N_4$: C, 65.7; H, 4.5. Found: C, 65.5; H, 4.6.

2-Benzoyl-4,5-dimethoxycinnamic Acid from Methyl 1-Phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline-3-carboxylate (IXa).—A solution of 20 g. of α-benzamido-3,4-dimethoxycinnamic acid,[31] m.p. 206–207°, in 250 ml. of alcohol containing 8 g. of 10% palladium-on-carbon was stirred in an atmosphere of hydrogen until absorption of hydrogen stopped. α-Benzamido-3,4-dimethoxyhydrocinnamic acid, m.p. 179.5–181°, after crystallization from alcohol and from alcohol–water, was obtained in 94% yield. The methyl ester of the hydrocinnamic acid was formed according to the general procedure of Galat[32] in 97% yield. Two grams of the methyl ester, m.p. 103–104°,[28,33] was boiled with 6 ml. of phosphorus oxychloride for 1.25 hr.[33] The reaction mixture was quenched on ice and made basic. The precipitated product, after washing with water and drying, weighed 1.17 g. and melted at 119–120°. Recrystallization from methanol, after treatment with decolorizing carbon, furnished methyl 1-phenyl-6,7-dimethoxy-3,4-dihydroisoquinoline-3-carboxylate,[28,33] m.p. 119.5–121°.

The ring-opening was run with 0.33 g. (0.001 mole) of the dihydroisoquinoline IXa, 1.04 ml. of dimethyl sulfate and 13 ml. of 20% sodium hydroxide solution. Acidification of the reaction mixture precipitated a pale-yellow solid, which was collected, washed with cold water and dried. This crude product (0.27 g.) was treated with decolorizing carbon in methanol, and then crystallized twice from the same solvent. 2-Benzoyl-4,5-dimethoxycinnamic acid (0.13 g.), m.p. 227–228° dec., was obtained in 41% yield. Further crystallizations did not change the melting point.

Anal. Calcd. for $C_{18}H_{16}O_5$: C, 69.2; H, 5.2. Found: C, 69.0; H, 5.2.

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(29) A. Oliverio, *Gazz. chim. ital.*, **64**, 139 (1934); *C. A.*, **28**, 4727 (1934).

(30) *Cf.* C. I. Brodrick and W. F. Short, *J. Chem. Soc.*, 2587 (1949).

(31) K. S. Narang, J. N. Ray and T. D. Sachdeva, *J. Indian Chem. Soc.*, **13**, 260 (1936); also *cf.* V. Deulofeu and G. Mendivelzua, *Z. physiol. Chem.*, **219**, 233 (1933).

(32) A. Galat, THIS JOURNAL, **73**, 3654 (1951).

(33) M. Hartmann and H. Kagi, U. S. Patent 1,437,802 (1922); *C. A.*, **17**, 854 (1923).

[CONTRIBUTION FROM PITTSBURGH CONSOLIDATION COAL CO., RESEARCH AND DEVELOPMENT DIVISION]

Synthesis of *p*-Hydroxybenzylpyrene and Homologs[1]

BY R. J. SHOZDA, E. A. DEPP, C. M. STEVENS AND M. B. NEUWORTH

RECEIVED OCTOBER 11, 1955

Direct condensation of a series of 1-pyrenealkanoic acids $Py(CH_2)_nCOOH$, where $n = 0, 1, 3$, with 2,6-xylenol using BF_3 catalyst produced the corresponding 4-substituted phenolic ketones in good yield. Catalytic hydrogenolysis with copper chromite to the substituted methylene, ethane and butane compounds is described. These compounds are models for bituminous coal, the aliphatic portion representing probable weak linkages.

In connection with a study on the structure of coal being conducted in this Laboratory, it was of interest to synthesize model compounds in which the tetracyclic hydrocarbon, pyrene, is linked to a phenolic nucleus by an aliphatic chain containing 1, 2 and 4 carbon atoms, respectively.

The synthetic procedure involves condensation of pyrenealkanoic acids (I) with 2,6-xylenol to the corresponding ketone (II) using anhydrous BF_3 as a condensing agent as shown

Condensation with 2,6-xylenol should result in a single condensation product in the 4-position of the phenol moiety. The ketones were reduced to the hydrocarbon analogs III by catalytic hydrogenolysis with copper chromite catalyst.

Since the three pyrene derivatives were new compounds, the conditions for the ketone synthesis and reduction were tested on a lower molecular weight acid, 1-naphthaleneacetic acid. BF_3 was bubbled continuously into 1-naphthaleneacetic acid dissolved in a 3–5 fold molar excess of 2,6-xylenol for 5 hours at 70°. The naphthalene-substituted ketone

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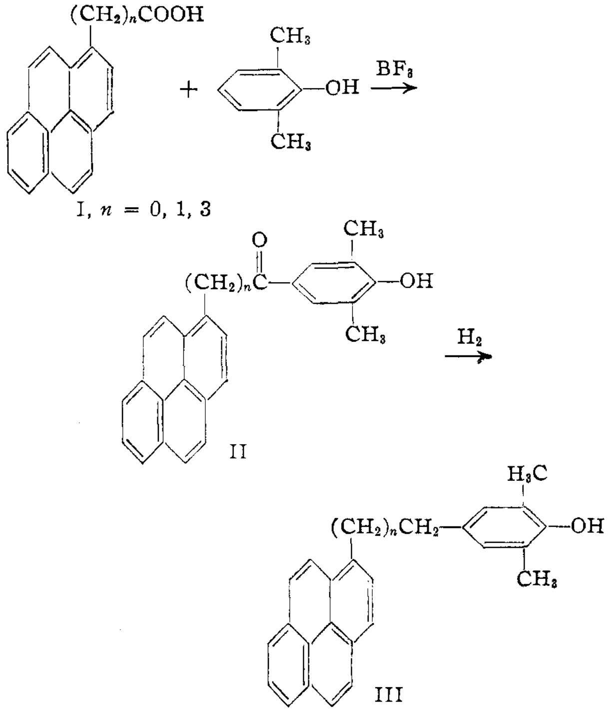
[1] Presented in part at the American Chemical Society Meeting, Division of Gas and Fuel Chemistry at Cincinnati, Ohio, April 5, 1955.



was produced in 80% yield. This ketone was reduced using copper chromite catalyst and hydrogen by the procedure of Nightingale and Radford.[1a] The naphthalene-substituted ethane was recovered in 89% yield.

The synthetic procedure was then applied to three pyrenealkanoic acids, 1-pyrenecarboxylic acid, 1-pyreneacetic acid and γ-1-pyrenebutyric acid, producing the desired pyrene derivatives in satisfactory yield.

The pyrolysis of these pyrene derivatives is being investigated. The results will be described in a separate communication.

Experimental

Starting Materials.—2,6-Xylenol was purchased from Reilly Tar and Chemical Co., Indianapolis, Ind. This phenol was further purified by precision distillation, a heart cut being retained with a minimum purity of 95% as determined by infrared analysis.

1-Naphthaleneacetic acid was purchased from F. O. Cockerville, Greenwood, Virginia, m.p. 131.2–132.2°,[2] and used without further purification.

1-Pyrenecarboxylic acid was prepared by hypochlorite oxidation of 1-acetylpyrene[3] using the procedure of Newman and Holmes.[4] The reaction was started by heating to 100°, reaction being maintained at 90°. A 97% yield of crude 1-pyrenecarboxylic acid was obtained, m.p. 268–269°; pure 1-pyrenecarboxylic acid is reported to melt at 274°.[5] The crude acid was used without further purification.

1-Pyreneacetic acid was prepared by direct reaction of pyrene with chloroacetic acid. A mixture[5a,6] of 910 g. (4.5 moles) of pyrene (Reilly Tar and Chemical Co.), m.p. 145–150°, 141 g. of chloroacetic acid (1.5 moles), 8 g. of potassium bromide and 6 g. of anhydrous ferric chloride was charged to a 2-liter Parr stirred autoclave. The air in the bomb was displaced by nitrogen. The mixture was heated to 240° during 2 hours and held at this temperature for 30 minutes. The autoclave was cooled to 210° and the hydrogen chloride vented. Longer reaction time results in a significant loss in yield. The contents of the bomb were dissolved in 1500 ml. of benzene. The benzene extract was filtered. The filtrate was extracted six times with 500-ml. portions of 10% KOH solution. The alkaline extract was washed with 1000 ml. of benzene. The washed alkaline extract was acidified with concd. hydrochloric acid. After cooling, the crude pyreneacetic acid was filtered and washed free of mineral acid with distilled water followed by vacuum drying at 110°. The yield of crude pyreneacetic acid was 138 g. (35% based on chloroacetic acid).

The crude pyreneacetic acid was dissolved in 2500 ml. of methanol and 4 ml. of concd. sulfuric acid added as an esterification catalyst. The mixture was refluxed for 7 hours. About 2000 ml. of methanol was distilled over by atmospheric distillation. The residue was dissolved in 1000 ml. of benzene, the benzene solution was freed of acid by washing with water and sodium bicarbonate solution and was dried by azeotropic distillation. The dried benzene solution was freed of benzene by distillation to a pot temperature of 120°. The residue was fractionated in a Vigreux column. A heart cut was retained, b.p. 232–245° (1 mm.), weighing 87.8 g. (m.p. 83.0–84.5°). An analytical sample of the methyl ester was prepared by recrystallization from hexane as ivory plates, m.p. 90–91.5°. A mixed melting point with an authentic sample of methyl ester prepared from 1-pyreneacetic acid, *via* the Willgerodt–Kindler reaction on 1-acetylpyrene, was undepressed.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.19; H, 5.14. Found: C, 82.93; H, 5.34.

The methyl ester was hydrolyzed using methanolic potassium hydroxide and the hydrolyzate was acidified with concd. hydrochloric acid. The white precipitate was filtered and washed free of chloride ion with distilled water. The wet product was dried in a vacuum oven at 100°. The yield of purified acid was 80 g. (20% based on chloroacetic acid), a white powder, m.p. 214–219° (vac.).

Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.05; H, 4.65. Found: C, 82.64; H, 4.91.

1-Pyrenebutyric acid, γ-(1-Pyrene)-butyric acid, Eastman Kodak Co. White Label, m.p. 186–188°, was used without further purification. This compound has been reported to melt at 185–186°.[7]

I. Synthesis of 1-[β-(4-Hydroxy-3,5-dimethylphenyl)-ethyl]-naphthalene. A. Ketone Synthesis—Anhydrous BF_3 was bubbled through a mixture of 100 g. of 1-naphthaleneacetic acid dissolved in 300 g. of 2,6-xylenol.[8] The temperature was maintained at 75–80° for 4 hours. At the end of this time, the molten reaction mixture was poured into 1 liter of cold water, the water layer was decanted, washing repeated three times, and an aqueous solution of Na_2CO_3 added. The organic layer solidified and was freed of sodium carbonate solution by filtration. The solid was dissolved in benzene and dried azeotropically. The benzene was distilled at atmospheric pressure. The residue was freed of the bulk of unreacted 2,6-xylenol by distillation in a Claisen flask at a pressure of 2–5 mm. The last traces of 2,6-xylenol were removed by repeated leaching of the solid ketone with anhydrous methanol. The crude ketone was recrystallized from ethanol–acetone to yield 124.5 g. (80%) of purified ketone, a white solid, m.p. 191–192°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.76; H, 6.21. Found: C, 82.37; H, 6.58.

B. Ethane Synthesis.—The ketone (72.5 g.) was mixed with 4 g. of copper chromite and 100 ml. of absolute methanol in a 300-ml. Aminco rocking autoclave. Hydrogenation was carried out at 125° for 4 hours, cold hydrogen pressure 2000 p.s.i. The cooled reaction mixture was filtered to remove catalyst. The methanol was removed by atmospheric distillation. The residual yellow oil crystal-

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(1a) D. Nightingale and H. D. Radford, *J. Org. Chem.*, **14**, 1089 (1949).

(2) All melting points corrected.

(3) W. E. Bachmann and M. Carmack, THIS JOURNAL, **63**, 2494 (1941).

(4) M. S. Newman and H. L. Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., p. 428.

(5) H. Vollmann, *et al.*, *Ann.*, **531**, 1 (1937).

(5a) Vollman[5] reported a 9.8% yield by refluxing this mixture in *o*-dichlorobenzene at 180–190° for 100 hours.

(6) G. Ogata and J. Ishiguro, THIS JOURNAL, **72**, 4302 (1950), used ferric oxide and KBr as catalysts in the synthesis of naphthaleneacetic acid from naphthalene and chloroacetic acid.

(7) J. W. Cook and C. L. Hewitt, *J. Chem. Soc.*, 1098 (1933).

(8) K. Kindler, *et al.*, *Arch. Pharm.*, **287**, 210 (1954), describe a similar procedure for condensation of lower molecular weight carboxylic acids.

lized. Recrystallization from hexane produced 42 g. of a white solid, m.p. 76–77.5°. In addition, 24 g. of hexane-insoluble matter was recovered. This proved to be unreacted ketone. Rehydrogenation and workup resulted in the recovery of 19.7 g. of additional product bringing the yield to 90%. An analytical sample produced by recrystallization from hexane melted at 77.5–78.5°. The phenolic nature of this material was indicated from its solubility in hot 10% sodium hydroxide.

Anal. Calcd. for $C_{20}H_{20}O$: C, 86.95; H, 7.25; mol. wt., 276. Found: C, 86.96; H, 7.03; mol. wt. (ebullioscopic in benzene), 275, 283.

II. **Synthesis of 1-(4-Hydroxy-3,5-dimethylbenzyl)-pyrene.**—The ketone was synthesized as previously described by BF_3-catalyzed condensation of 1-pyrenecarboxylic acid and 2,6-xylenol. A 20-g. batch of acid produced 23.7 g. (83%) of crude ketone, m.p. 245–246°. An analytical sample was prepared by recrystallization from toluene, producing yellow-orange prisms, m.p. 246–247°.

Anal. Calcd. for $C_{25}H_{18}O_2$: C, 85.59; H, 5.18. Found: C, 85.79; H, 5.55.

The ketone reduction procedure was modified due to the very low solubility of the pyrene ketones in methanol. A mixture of 25 g. of ketone, 7 g. of copper chromite and 100 g. of phenol, as a solvent, was hydrogenated (cold pressure 2000 p.s.i.) at 140° for 4 hours. The contents of the bomb were dissolved in a minimum of hot benzene and the benzene solution was filtered to remove catalyst. The filtrate was distilled at atmospheric pressure to remove benzene. The residue was distilled at 50 mm. to remove the bulk of the phenol. The last traces of phenol were removed by repeated leaching of the solid ketone with methanol followed by aqueous methanol. The yield of crude product was 17.0 g. (70% yield), m.p. 124–126°. An analytical sample was prepared by recrystallizing twice from absolute methanol producing white needles, m.p. 130–131°.

Anal. Calcd. for $C_{25}H_{20}O$: C, 89.26; H, 5.99. Found: C, 89.06; H, 6.88.

An analytical sample of the acetate ester prepared by reaction with acetic anhydride and pyridine melted at 117.7–118.7°.

Anal. Calcd. for $C_{27}H_{22}O_2$: C, 85.68; H, 5.86. Found: C, 85.58; H, 6.55.

III. **Synthesis of 1-[β-(4-Hydroxy-3,5-dimethylphenyl)-ethyl]-pyrene.**—The ketone was synthesized by BF_3-catalyzed condensation of 1-pyreneacetic acid and 2,6-xylenol. A 39-g. batch of acid produced 49 g. of crude ketone (90% yield), m.p. 234–236.5°. An analytical sample was obtained by recrystallization from xylene yielding white crystals, m.p. 235–238°.

Anal. Calcd. for $C_{26}H_{20}O_2$: C, 85.70; H, 5.53. Found: C, 85.66; H, 5.77.

The ketone (20 g.) was reduced using the procedure described in section II. The yield of crude substituted ethane was 16.4 g. (90%), m.p. 130–140°. An analytical sample was prepared by recrystallizing twice from absolute methanol yielding colorless plates (weak blue-green fluorescence) m.p. 153.5–154.4°. This compound was hygroscopic.

Anal. Calcd. for $C_{26}H_{22}O$: C, 89.15; H, 6.33. Found: C, 88.89; H, 6.49.

An acetate ester was synthesized using acetic anhydride and pyridine. An analytical sample produced by recrystallization from ethanol was recovered as cream-colored plates, m.p. 152.3–153.3°; mixed melting point with the ethane model was depressed to 139.5–144.5°.

Anal. Calcd. for $C_{28}H_{24}O_2$: C, 85.68; H, 6.16. Found: C, 85.44; H, 6.35.

IV. **Synthesis of 1-[γ-(4-Hydroxy-3,5-dimethylphenyl)-butyl]-pyrene.**—The ketone was synthesized by BF_3-catalyzed condensation of γ-1-pyrenebutyric acid and 2,6-xylenol. A 76.9-g. batch of acid produced 100 g. of crude ketone (100% yield), m.p. 152–160°. An analytical sample was prepared by recrystallization from toluene, yielding fine yellow needles, m.p. 168–169°.

Anal. Calcd. for $C_{28}H_{24}O_2$: C, 85.68; H, 6.16. Found: C, 85.77; H, 6.24.

The crude ketone was reduced using the procedure described under II. A 25-g. batch of ketone produced 24.1 g. of crude substituted butane, m.p. 94–97° (100% yield). An analytical sample resulted from recrystallizing twice from methanol, yielding colorless prisms, m.p. 101.6–103.6°.

Anal. Calcd. for $C_{28}H_{26}O$: C, 88.84; H, 6.93. Found: C, 88.82; H, 7.11.

Spectra of the Pyrene Derivatives.—All the pyrene derivatives showed a characteristic OH absorption band at 2.9–3.0 μ in the infrared and the absence of any appreciable carbonyl absorption. The ultraviolet spectra of the compounds were determined in $CHCl_3$ on a Beckman model DU spectrophotometer. Each compound showed a typical pyrene spectrum. This would indicate that there has been little hydrogenation of the pyrene nucleus during hydrogenolysis of the carbonyl group.

Acknowledgment.—We wish to thank Emmy Lee McWilliams and R. J. Laufer for development of the synthesis conditions for production of 1-pyreneacetic acid and actual preparation of the material used in this investigation.

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[CONTRIBUTION FROM THE MCARDLE MEMORIAL LABORATORY, MEDICAL SCHOOL, UNIVERSITY OF WISCONSIN, AND THE DEPARTMENTO DE QUIMICA DA FACULDADE DE FILOSOFIA, CIENCIAS E LETRAS, UNIVERSIDADE DE SÃO PAULO, SÃO PAULO, BRASIL]

On the Addition of Protons to Derivatives of 4-Aminoazobenzene[1]

BY G. CILENTO, E. C. MILLER AND J. A. MILLER

RECEIVED JUNE 11, 1955

The absorption spectra of 4-aminoazobenzene and a variety of its derivatives in acid–alcohol solution have been investigated. Study of the spectra indicates that two absorbing species are present: one in which the proton is added to the amino group and the other in which the proton is on the azo nitrogen farthest from the amino group. The influence of methyl and fluoro substituents upon the proportions of the tautomeric forms is considered.

Introduction

As a part of our studies on the relationship between structure and hepatocarcinogenic activity in the series of aminoazo dyes related to 4-dimethylaminoazobenzene, we have studied the absorption spectra of ethanolic and acid–ethanolic solutions of about thirty derivatives of 4-aminoazobenzene. This is a continuation of earlier work in which the spectra of the C-monomethyl derivatives of 4-dimethylaminoazobenzene were examined.[2]

These compounds are yellow in non-acidic media, but exhibit an intense red color on the addition

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(1) This investigation was supported by research grant C355 from the National Cancer Institute, U. S. Public Health Service, Institutional Grant 71 of the American Cancer Society and the Alexander and Margaret Stewart Trust Fund.

(2) J. A. Miller, R. W. Sapp and E. C. Miller, THIS JOURNAL, **70**, 3458 (1948).