ence of **1,3-diphenyloxindole**[1] was detected by thin layer chromatography (silica gel G and aluminum oxide G in four different solvent systems: 97% benzene–3% ether, 99% benzene–1% ethyl acetate, 99% benzene–1% dioxane, and 99% benzene–1% methanol).

However, two other products,[1] which are derivable from the α-lactam I, namely 1-keto-2,3-diphenylisoindole and 3,3-diphenyloxindole, could not be found.

Acknowledgment.—I. L. gratefully acknowledges financial support from Public Health Predoctoral Fellowship GPM-11,445-C2. We are indebted to Professor K. Biemann and Dr. W. Richter for the mass spectra.

The Synthesis of Naphtho[2,1-*a*]perylene and Dibenzo[*ae*]perylene[1,2]

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Received May 14, 1963

Many papers attest to the fact that a causal relationship very likely exists between air pollution and respiratory diseases including lung cancer.[6] A relationship between polynuclear aromatic hydrocarbons found in certain polluted air and lung cancer is also suggested.[7] Continuing our work in this area,[8] we were concerned with the dehydrogenation of 7-(1-naphthyl)benz[*a*]anthracene (I). This compound, on catalytic intramolecular dehydrogenation, might lead to dibenzo[*ae*]perylene (II) and/or naphtho[2,1-*a*]perylene (III). When I was dehydrogenated with aluminum chloride and stannic chloride, only one perylene derivative was found. In order to establish the structure of the product, which was either II or III, we undertook an unequivocal synthesis of naphtho[2,1-*a*]perylene (III).

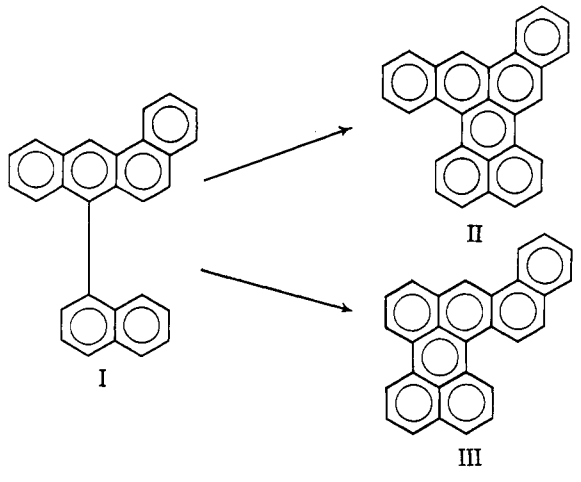
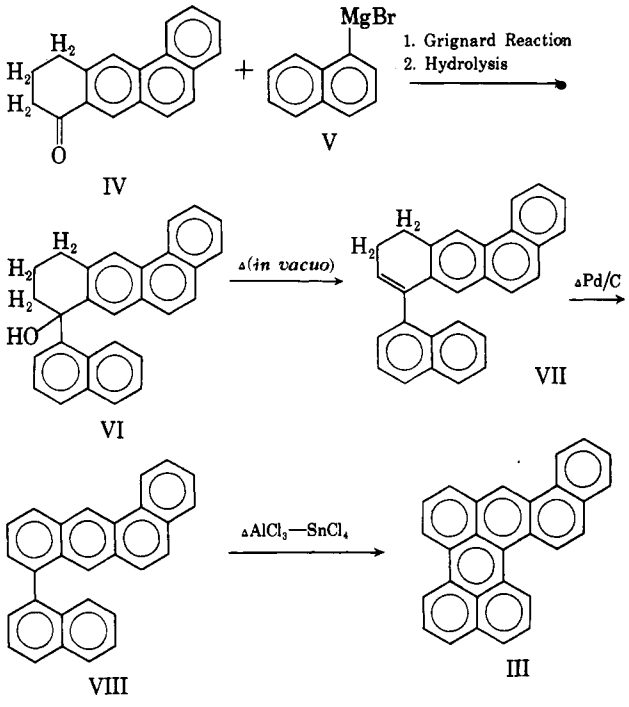


CHART I



On the basis of similar experiments,[9] it seemed that if we could prepare 8-(1-naphthyl)benz[*a*]anthracene (VIII), an unequivocal dehydrogenation to III might be achieved. The reactions shown in Chart I were undertaken to this end. A four-step reaction sequence was used to prepare 8-keto-8,9,10,11-tetrahydrobenz[*a*]anthracene (IV).[10] The action of 1-naphthylmagnesium bromide on this ketone followed by hydrolysis afforded a mixture of 8-(1-naphthyl)-8-hydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene (VI) in a 22% yield and the dehydrated product, 8-(1-naphthyl)-10,11-dihydrobenz[*a*]anthracene (VII) in 13% yield. Satisfactory analytical data could not be obtained on the carbinol VI due to its easy dehydration on crystallization. The carbinol was converted quantitatively to the dehydration product 8-(1-naphthyl)-10,11-dihydrobenz[*a*]anthracene (VII) when it was heated *in vacuo*. VII on dehydrogenation with a palladium-on-charcoal catalyst in boiling *p*-cymene gave 8-(1-naphthyl)benz[*a*]anthracene (VIII) in 83% yield.

Many known dehydrogenation agents and reaction procedures[8] were used in an attempt to convert VIII to naphtho[2,1-*a*]perylene (III); heating with sulfur, with selenium, with palladium on carbon; vapor phase dehydrogenation at 430° on asbestos; fusion with sodium chloride and aluminum chloride[11]; pyrolysis at 700°; aluminum chloride in boiling benzene[8];

(1) The nomenclature used in this paper is that presented in the "Definitive Rules for Nomenclature of Organic Chemistry," *J. Am. Chem. Soc.*, **82**, 5545 (1960).

(2) Presented before the Division of Organic Chemistry at the Combined Southeastern-Southwestern Regional Meeting of the American Chemical Society, New Orleans, La., December, 1961.

(3) Chemistry Department, Villanova University, Villanova, Pa.

(4) This paper has been taken from the Doctorate thesis of Walter W. Zajac, Jr., and the Masters thesis of Louis G. Mahone presented to the Virginia Polytechnic Institute in 1959 and 1961, respectively.

(5) This investigation was supported by a research grant (AP-88) from the Division of Air Pollution, Bureau of State Services, Public Health Service.

(6) M. Katz, *Occupational Health Rev.*, **14**, 3 (1962); M. O. Amdur, *New Engl. J. Med.*, **266**, 555 (1962); W. McDermott, *Sci. Am.*, **205**, 49 (1961); M. R. Purvis, S. Miller, and R. Ehrlich, *J. Infect. Diseases*, **109**, 238 (1961); *Japan. Heart J.*, **2**, 180 (1961); J. Cuthbert, *Public Health* (London), **74**, 123 (1960); E. Gorham, *Med. Officer* (London), **101**, 178 (1959).

(7) E. L. Wynder, F. R. Lemon, and I. J. Bross, *Cancer*, **12**, 1016 (1959); P. Stocks, *Brit. J. Cancer*, **14**, 397 (1960); L. Kreyberg, *ibid.*, **13**, 618 (1959); H. L. Falk, P. Kotin, and A. Miller, *Intern. J. Air Pollution*, **2**, 201 (1960).

(8) F. A. Vingiello and W. W. Zajac, Jr., *J. Org. Chem.*, **26**, 2228 (1961).

(9) See, for example, M. Orchin and R. Friedel, *J. Am. Chem. Soc.*, **68**, 573 (1946); P. G. Copeland, R. E. Dean, and D. McNeil, *J. Chem. Soc.*, 1689 (1960); E. Clar and M. Zander, *ibid.*, 1861 (1958).

(10) J. Cook, *ibid.*, 1592 (1933).

(11) A. Zincke and E. Ziegler, *Ber.*, **74**, 115 (1951).

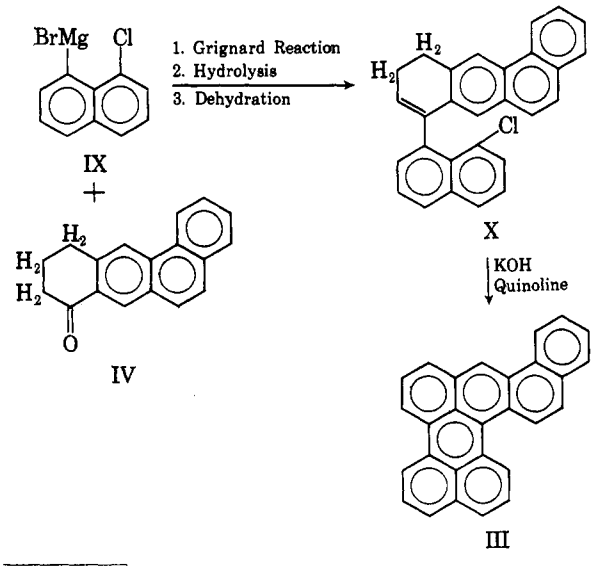
and aluminum bromide in boiling benzene—all failed to yield any of the desired product III. Finally, cyclodehydrogenation of VIII with stannic chloride and aluminum chloride in boiling benzene for five minutes gave a 40% yield of naphtho[2,1-*a*]perylene. A comparison of the ultraviolet and infrared spectra with known benzoperylenes and dibenzoperylenes revealed a similarity in type. A 2,4,7-trinitrofluorenone adduct (TNF) was formed and this gave a satisfactory analysis for a 1:1 adduct.

A comparison of the properties of the naphtho[2,1-*a*]perylene (III) with the product obtained by the dehydrogenation of 7-(1-naphthyl)benz[*a*]anthracene revealed many strong differences and therefore we believe this latter compound is dibenzo[*ae*]perylene (II). It is interesting to note that both calculated localization energies[12] and frontier electron densities[13] for benz[*a*]anthracene suggest that position 8 is more susceptible than position 6 to electrophilic attack. Since I gives II and not III, it may be that under the conditions of the experiment the attack on the benz[*a*]anthracene moiety is not electrophilic in nature; indeed, the mechanism may not be ionic.

In view of the modest yield achieved in the conversion of VIII to III, and because such a powerful catalyst as stannic chloride and aluminum chloride had to be used, another route to III was sought. Clar[14] has effected the cyclodehydrochlorination of 1-chloro-9,10-di-1-naphthylanthracene to 7-(1-naphthyl)benz[*a*]perylene with potassium hydroxide and quinoline. It occurred to us that we might pattern an experiment after Clar's[14] and prepare III using a milder catalyst than the stannic chloride–aluminum chloride mixture. With this idea in mind, we prepared 8-[1-(8-chloronaphthyl)]-10,11-dihydrobenz[*a*]anthracene (X) as shown in Chart II. 1-Bromo-8-chloronaphthalene was prepared from naphthalene in four steps according to the method of Fieser and Seligman.[15] The Grignard reagent IX was prepared and allowed to react with the ketone IV to give, after dehydration, 8-[1-(8-chloronaphthyl)]-10,11-dihydrobenz[*a*]anthracene (X). No attempt was made to isolate the carbinol which is presumably an intermediate in the preparation of X because of the known instability of a similar compound VI. The action of potassium hydroxide and quinoline upon compound X gave a 36% yield of naphtho[2,1-*a*]perylene (III). On treatment with palladium on carbon, X gave a 52% yield of VIII and a 2% yield of III. Naphtho[2,1-*a*]perylene formed a 1:1 adduct with TNF.

A III sample, submitted for carcinogenicity testing,[16] revealed the compound to be a potent carcinogen.

CHART II



(12) M. J. S. Dewar, *J. Am. Chem. Soc.*, **74**, 3357 (1952).

(13) K. Fukui, T. Yonezawa, C. Nagata, and H. Shinyu, *J. Chem. Phys.*, **22**, 1433 (1954).

(14) E. Clar, W. Kelly, D. Stewart, and J. Wright, *J. Chem. Soc.*, 2652 (1956).

(15) L. F. Fieser and A. Seligman, *J. Am. Chem. Soc.*, **61**, 136 (1939).

Experimental[17-19]

8-(1-Naphthyl)-8-hydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene (VI) with Partial Dehydration.—A Grignard reagent was prepared in ether from 2.74 g. (0.113 g.-atom) of magnesium and 23.4 g. (0.113 mole) of 1-bromonaphthalene. The ether was distilled while 200 ml. of anhydrous benzene was added slowly. The Grignard reagent was then cooled and 20.5 g. (0.0833 mole) of 8-keto-8,9,10,11-tetrahydrobenz[*a*]anthracene[10] was added in four portions during a period of 10 min. The clear solution which resulted was stirred at room temperature for 21 hr. The solution was cooled and decomposed with cold 20% ammonium chloride solution. The organic layer was separated and concentrated until *ca.* 50 ml. of solution remained. Treatment with hot ethanol followed by cooling gave 6.7 g. (22%) of the carbinol VI, m.p. 215–223°. The filtrate was concentrated, to remove the benzene, and *ca.* 500 ml. of ethanol was added. The solid was recrystallized from 10% benzene–ethanol and gave 3.8 g. (13%) of the dehydrated carbinol, 8-(1-naphthyl)-10,11-dihydrobenz[*a*]anthracene, m.p. 257–258°.

8-(1-Naphthyl)-10,11-dihydrobenz[*a*]anthracene (VII).—A sample of 1.00 g. of 8-(1-naphthyl)-8-hydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene was heated for 12 hr. in a drying pistol at 180° (1.0 mm.). There was obtained 0.95 g. (100%) of 8-(1-naphthyl)-10,11-dihydrobenz[*a*]anthracene (VII), m.p. 257–258°. Recrystallization of this sample from a benzene–ethanol mixture gave colorless plates, m.p. 260–261°.

Anal. Calcd. for $C_{28}H_{20}$: C, 94.34; H, 5.66. Found: C, 94.28; H, 5.62.

8-(1-Naphthyl)benz[*a*]anthracene (VIII).—A mixture of 1.12 g. (0.00314 mole) of 8-(1-naphthyl)-10,11-dihydrobenz[*a*]anthracene, 0.88 g. of 10% palladium on charcoal, and 115 ml. of *p*-cymene was heated under reflux for 12 hr. The hot mixture was filtered and the solution evaporated under reduced pressure. The solid obtained was recrystallized from a benzene–ethanol mixture. There was obtained 0.92 g. (83%) of 8-(1-naphthyl)-benz[*a*]anthracene, m.p. 241–242°.

Anal. Calcd. for $C_{28}H_{18}$: C, 94.87; H, 5.13. Found: C, 94.84; H, 5.47.

Naphtho[2,1-*a*]perylene (III).[20]—A mixture of 0.50 g. of stannic chloride, 0.60 g. of anhydrous aluminum chloride, and 50 ml. of anhydrous benzene was heated on a steam bath. To this was added 0.50 g. (0.0014 mole) of 8-(1-naphthyl)benz[*a*]anthracene in 25 ml. of hot benzene. The mixture was heated under reflux for 5 min., then cooled to room temperature and decomposed with 100 ml. of dilute hydrochloric acid. The organic layer was separated, washed with water, dried over anhydrous calcium sulfate, and concentrated to *ca.* 5 ml. Treatment with 100 ml. of ethanol gave 0.20 g. (40%) of III, m.p. 201–203°. The material was recrystallized from 10% benzene–ethanol giving red needles, m.p. 203–204°.

(16) Private communication from Dr. Paul Kotin, Chief, Carcinogenesis Studies Branch, National Cancer Institute, National Institutes of Health, Bethesda, Md. Compound II was not prepared in sufficient quantities for carcinogenicity testing. An adequate amount is now being prepared and will be tested.

(17) Unless otherwise indicated all melting points were taken on a Fisher-Johns melting point block and are corrected.

(18) (a) All the analyses were carried out by Geller Laboratories, Bardonia, N. Y., except those which were performed by (b) Galbraith Laboratories, Knoxville, Tenn.

(19) All procedures involving naphtho[2,1-*a*]perylene, dibenzo[*ae*]perylene, and their derivatives were carried out with a minimum of exposure to light.

(20) This experiment was performed by Mr. Jose Yanez.

Anal. Calcd. for $C_{28}H_{16}$: C, 95.42; H, 4.59. Found[18b]: C, 95.24; H, 4.72.

The compound dissolved in concentrated sulfuric acid giving a green color which turned blue on prolonged standing.

8-[1-(8-Chloronaphthyl)]-10,11-dihydrobenz[*a*]anthracene (X).—A Grignard reagent was prepared in ether from 9.0 g. (0.037 mole) of 1-bromo-8-chloronaphthalene[15] and 0.95 g. (0.039 g.-atom) of magnesium. The reaction mixture was stirred and heated under reflux for 24 hr. Anhydrous benzene was added as needed to keep the Grignard reagent from crystallizing too much. The ether was distilled and benzene was added to bring the volume to *ca.* 100 ml. In one portion, 9.1 g. (0.037 mole) of 8-keto-8,9,10,11-tetrahydrobenz[*a*]anthracene was added and the solution was heated under reflux for 24 hr. The solution was cooled, decomposed with cold 20% ammonium chloride solution, and extracted with ether. The organic layer was separated, washed with water, dried over anhydrous calcium sulfate, and concentrated to *ca.* 20 ml. The oil was crystallized using acetone, giving 3.5 g. of solid, m.p. 219–220°. The solid was vacuum sublimed at 210° (0.6 mm.) and then recrystallized from 20% benzene–ethanol giving 3.4 g. (23%) of X as colorless needles, m.p. 222–223°. Recrystallization from 1:1 benzene–petroleum ether (30–60°) gave colorless needles, m.p. 225–226°.

Anal. Calcd. for $C_{28}H_{19}Cl$: C, 86.03; H, 4.90; Cl, 9.07. Found: C, 85.63; H, 4.89; Cl, 8.95.

Cyclization of 8-[1-(8-Chloronaphthyl)]-10,11-dihydrobenz[*a*]anthracene (X). A. *Via* Potassium Hydroxide and Quinoline.—A mixture of 0.50 g. (0.0013 mole) of X, 10.0 g. of potassium hydroxide, and 15 ml. of quinoline was heated under reflux for 30 min. The mixture was cooled, decomposed with cold dilute hydrochloric acid, and extracted with ether. The organic layer was filtered. The filtrate was washed with dilute hydrochloric acid, then water, and finally dried over anhydrous calcium sulfate. The solid, crude naphtho[2,1-*a*]perylene was dissolved in benzene and combined with the ether extract. This solution was then concentrated to *ca.* 5 ml. and chromatographed[21] on alumina[22] using petroleum ether[23] as the eluant. A blue fluorescent[24] band appeared, followed by a red band with a green-yellow fluorescence.[24] Concentration and recrystallization of the first band, after elution, gave 0.06 g. of starting material. The red band was eluted, concentrated, and crystallized. The yield was 0.17 g. (36%) of naphtho[2,1-*a*]perylene, m.p. 201.5–203.5°.

B. *Via* Palladium on Charcoal.—A mixture of 0.50 g. (0.0012 mole) of X and 0.10 g. of 10% palladium on charcoal was heated at 310° for 15 min. and then at 350° for 1 hr. The mixture was worked up and chromatographed as described under A. There was obtained 0.26 g. (52%) of compound VIII and 0.11 g. (2%) of III, m.p. 202–203°.

TNF Adduct of Naphtho[2,1-*a*]perylene (III).—A solution of 0.12 g. (0.00034 mole) of naphtho[2,1-*a*]perylene in 40 ml. of hot 10% benzene–ethanol was added to a hot solution of 0.10 g. of 2,4,7-trinitrofluorenone in 40 ml. of 10% benzene–ethanol. On cooling, a black precipitate appeared, 0.10 g. (47%), which on recrystallization from 10% benzene–ethanol gave fine black needles, m.p. 222–223°.

Anal. Calcd. for $C_{41}H_{23}O_6N_3$: C, 73.76; H, 3.17; N, 6.29. Found: C, 73.52; H, 3.44; N, 6.30.

Dibenzo[*ae*]perylene (II).—A mixture of 0.50 g. of 7-(1-naphthyl)benz[*a*]anthracene[25] and 0.5 g. of powdered anhydrous aluminum chloride and 0.5 g. of fuming stannic chloride in 50 ml. of dry benzene was heated in a steam bath for 30 min. The deep red solution was allowed to cool to room temperature and was then decomposed with 100 ml. of 10% hydrochloric acid. The green fluorescent organic layer was separated and the aqueous layer was extracted twice with 50-ml. portions of benzene. The combined benzene extracts were washed with water and dried over anhydrous magnesium sulfate. The solvent was distilled until only *ca.* 10 ml. remained. This solution was chromatographed.[19,21] Two bands appeared on the column, a colorless blue fluorescent band and a red-orange band. The first band was eluted with petroleum ether[23] and discarded. The second band was removed with benzene and the resultant solution concentrated to give red crystals of dibenzo[*ae*]perylene (II), 0.24 g. (48%), m.p. 183–186°.

An analytical sample was prepared by recrystallization of the hydrocarbon from benzene, m.p. 188–189°.

Anal. Calcd. for $C_{28}H_{16}$: C, 95.42; H, 4.28. Found[18b]: C, 95.72; H, 4.37.

The hydrocarbon dissolved in concentrated sulfuric acid giving a Prussian blue color which changed to brown on standing.

TNF Adduct of Dibenzo[*ae*]perylene.[26]—A hot saturated solution of 0.12 g. of dibenzo[*ae*]perylene in benzene was mixed with a hot saturated solution of 0.4 g. of 2,4,7-trinitrofluorenone in ethanol. A brown solid formed immediately, 0.21 g. (quantitative). Four recrystallizations from benzene gave a brown, granular solid, m.p. 253–254°.

Anal. Calcd. for $C_{41}H_{21}N_3O_7$: C, 73.75; H, 3.17; N, 6.30. Found[18b]: C, 73.51; H, 3.61; N, 6.19.

(21) The column used throughout this investigation was 18 × 370 mm.

(22) Fisher's adsorption alumina, 80–200 mesh.

(23) The petroleum ether used as an eluent had a 30–60° boiling point range.

(24) Fluorescent under ultraviolet radiation with a Blak-ray ultraviolet long wave lamp (3660 Å.) as the source.

(25) F. A. Vingiello, A. Borkovec, and W. W. Zajac, Jr., *J. Am. Chem. Soc.*, **80**, 1714 (1958).

(26) This experiment was performed by Mr. Leo Ojakaar.

α-Hydroxy Acid Amides. A Convenient Synthesis

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Received June 24, 1963

Using a procedure patterned after the one described for the preparation of α-amino acid amides,[1] a variety of cyanohydrins have been converted in reasonable yield to the corresponding α-hydroxy acid amides. This reaction probably proceeds similarly[1]; an intermediate imido ester salt is formed which, upon heating, eliminates alkyl chloride to produce the desired amide. With the possible exception of a recently reported preparation of α-hydroxyphenylacetamide[2] this report apparently is the first record of an application of the Pinner amide synthesis[3] to the synthesis of α-hydroxy acid amides.

$$\mathrm{RCHCN} + \mathrm{R'OH} + \mathrm{HCl} \longrightarrow \underset{\mathrm{OH}}{\mathrm{RCHCN}}$$

$$\mathrm{RCHCOR'} \longrightarrow \mathrm{RCHCNH_2} + \mathrm{R'Cl}$$
(NH·HCl on the first; O on the second; OH on both)

The best yields of amides were generally obtained by allowing the cyanohydrin to react with isopropyl alcohol saturated with hydrogen chloride. Evaporation of the solvent followed by pyrolysis of the imido ester salt and subsequent distillation produced the hydroxy amide in yields as high as 80%. Alternatively, the synthesis was performed in an inert solvent such as xylene, employing a slight excess over equivalent quantities of an alcohol. After a suitable reaction time with hydrogen chloride, the reaction mixture was heated under reflux to decompose the imido ester salt and the product recovered by a filtration of the cooled mixture. The combined versatility of these two procedures was sufficient to allow the preparation of the various α-hydroxy amides tabulated in Table I.

(1) H. E. Johnson and D. G. Crosby, *J. Org. Chem.*, **27**, 798 (1962).

(2) R. Roger and D. G. Neilson, *Chem. Rev.*, **61**, 179 (1961), ref. 329.

(3) Refer to S. M. McElvain and B. E. Tate, *J. Am. Chem. Soc.*, **73**, 2233 (1951), for pertinent references.