

Department of Chemistry, University of Oregon

## Synthesis of 6,13-Diazadibenz[a,h]anthracene (I)

L. H. Klemm and Annekäte Weisert (2)

6,13-Diazadibenz[a,h]anthracene (XIa) was synthesized in 15% overall yield for four steps beginning with 2,5-diphenyl-1,4-benzoquinone. Miscellaneous reactions which led to side products are also described.

In continuation of our studies on syntheses of aza-cyclic analogs of carcinogenic polynuclear aromatic hydrocarbons wherein a nitrogen atom replaces one of the CH-moieties of the K-region (3), we have now prepared the new compounds 6,13-diazadibenz[a,h]anthracene (XIa) and its 5,12-dimethyl derivative (XIb). The general plan envisaged (*cf.* Scheme I) was first replacement of the oxygen atoms in the commercially available 2,5-diphenyl-1,4-benzoquinone (I) by nitrogen functions, and then cyclizations to form the two pyridinoid rings present in XI. Both oxime formation and the Leuckart reaction (4) were explored as means of introducing a nitrogen function into I. Refluxing I with hydroxylammonium chloride in ethanol did allow the isolation of either a monoxime or a dioxime in very high yield, but these results were attained only by use of large excesses of reagent. I, thus, reacts analogously to 2,5-dimethyl- and 2,5-dichlorobenzoquinones, but with apparent decreased facility (5). On the other hand, use of hydroxylamine in pyridine and absolute ethanol (6) gave a different, unidentified product; while hydroxylamine in alcoholic potassium hydroxide effected reduction (presumably *via* the intermediate II) to the aminophenol V (5). The N-formyl derivative of V also was obtained under slightly acidic Leuckart conditions. Refluxing I with formamide for 4 hours (conditions identical to those reported (7) to convert anthraquinone to 9,10-diformamidoanthracene in excellent yield) produced the parent hydrocarbon *p*-terphenyl.

Difficulty was encountered in reducing the dioxime III to the diamine VII, obtained pure in only very low yield. Rather than to isolate the pure diamine itself, it was found to be better to acylate the impure, unstable reduction mixture directly, either to the diformyl derivative VIII or to the diacetyl derivative X. Although X cyclized readily to XIb by means of hot polyphosphoric acid, VIII was merely deformed under the same conditions. Fortification with phosphorus pentoxide of the polyphosphoric acid used brought about some limited cyclization of VIII (as evidenced by the isolation of IX) but deformylation remained the principal reaction and none of the desired XIa was found. Badger and Sasse (8) have noted similarly that polyphosphoric acid serves to deformylate 2,2'-diformamidobiphenyl. Facile cyclization of VIII to the parent aromatic nitrogen heterocycle XIa (in 15% overall yield from

I) was, nonetheless, achieved by means of a melt of sodium chloride-aluminum chloride. When these latter conditions were used with X, however, there resulted a mixture from which we were unable to isolate any pure substance.

In Table I are presented data on the ultraviolet absorption spectral maxima for XIa, XIb, and dibenz[a,h]anthracene (DBA). The very close similarities between the positions and intensities of the absorption maxima for ethanolic solutions of XIa and DBA imply that identical  $\pi$ -electronic systems are present in both compounds and, hence, serve to confirm the structural assignment of the former substance (9). On acidification of the solvent the spectrum of XIa loses some fine structure and shows small shifts in wavelength and/or intensity of other maxima. The dimethyl derivative XIb (in ethanol) has a spectrum which closely resembles that of its parent molecule, but with less fine structure, small bathochromic shifts at shorter wavelengths, and small hypsochromic shifts in the range 360-390  $m\mu$ .

### EXPERIMENTAL (10)

#### 2,5-Diphenyl-1,4-benzoquinone Dioxime (III).

A suspension of 75 g. (0.29 mole) of 2,5-diphenyl-1,4-benzoquinone (13) (Aldrich Chemical Co., Milwaukee) and 375 g. (5.4 moles) of reagent grade hydroxylammonium chloride in 4 l. of 95% ethanol was stirred and refluxed for 4 days. The resultant precipitate, collected by filtration of the hot solution, was washed several times with 300-ml. portions of hot ethanol, dried, and recrystallized once from dimethylformamide, yield 71.8 g. (85%), m.p. 261-263°. An analytical sample, obtained as yellow needles, m.p. 263-264° (dec.), resulted from further recrystallization.

*Anal.* Calcd. for  $C_{18}H_{14}N_2O_2$ : C, 74.47; H, 4.86; N, 9.65. Found: C, 74.55; H, 4.75; N, 10.02.

#### 2,5-Diphenyl-1,4-benzoquinone Monoxime (II).

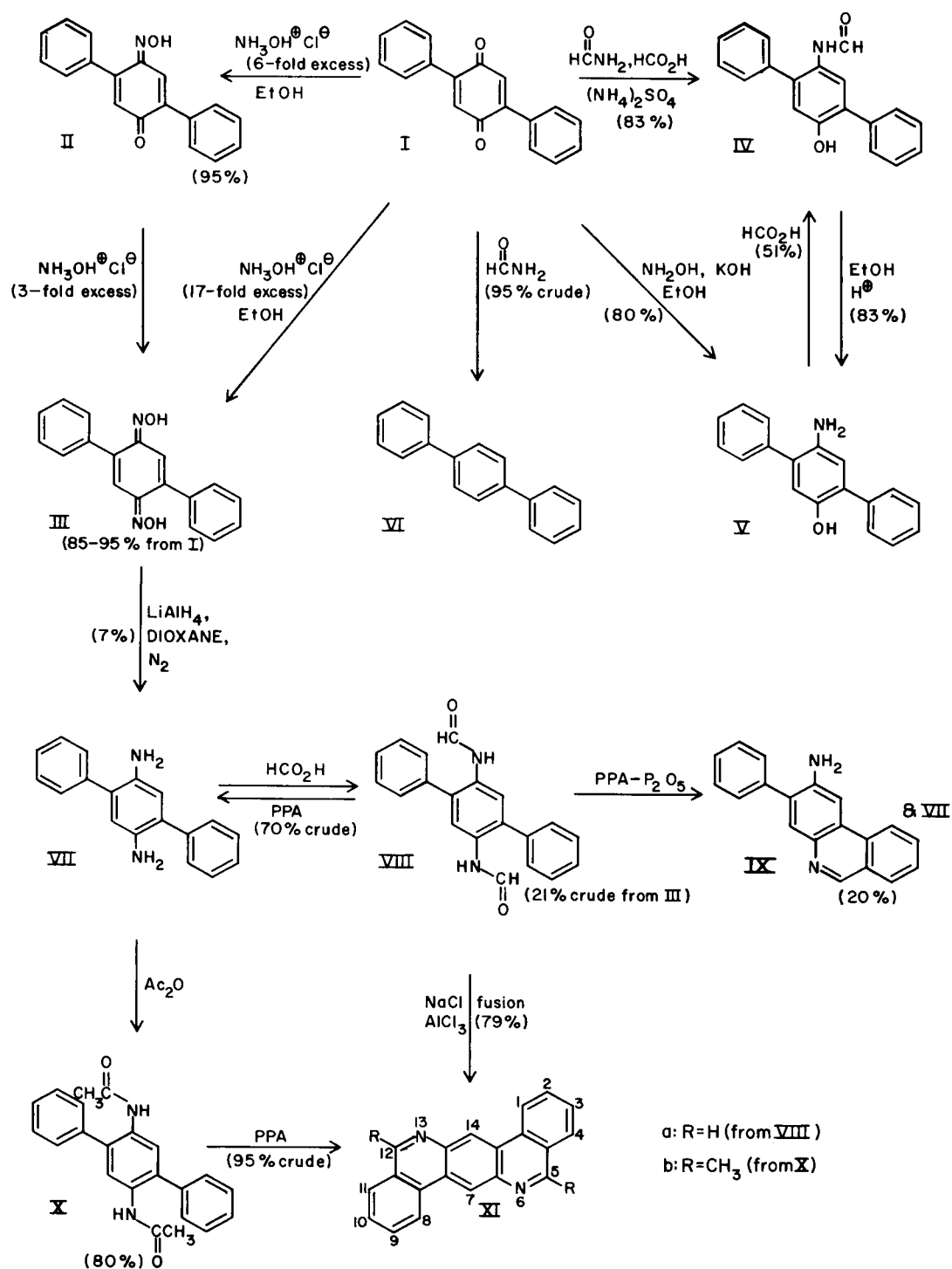
A suspension of 5 g. (0.019 mole) of I and 10 g. (0.14 mole) of hydroxylammonium chloride in 300 ml. of 65% ethanol (aqueous) was refluxed for 12 hours. The precipitate was washed with water, yield 5 g. (95%) of crude product, m.p. 232-235°, obtained as yellow-green crystals, m.p. 242-243° (dec.) on recrystallization from dimethylformamide.

*Anal.* Calcd. for  $C_{18}H_{13}NO_2$ : C, 78.53; H, 4.76; N, 5.09. Found: C, 77.78; H, 4.97; N, 5.53, 5.44.

Further treatment of II by the aforementioned method (but with only a threefold excess of hydroxylammonium chloride) gave III.

#### 2,5-Diphenyl-4-formamidophenol (IV). (a) From I.

A stirred mixture of 5.2 g. (0.02 mole) of 2,5-diphenyl-1,4-benzoquinone, 9 g. (0.2 mole) of formamide, 0.1 g. of ammonium sulfate, and 0.2 ml. of anhydrous formic acid was maintained at 150-160° for



SCHEME I

TABLE I

Ultraviolet Absorption Maxima for 6,13-Diazadibenz[a,h]anthracene and Related Compounds (a)

Compound	Solvent	$\lambda$ max		$\lambda$ max		$\lambda$ max		$\lambda$ max		$\log \epsilon$	
		$m\mu$	$\log \epsilon$	$m\mu$	$\log \epsilon$	$m\mu$	$\log \epsilon$	$m\mu$	$\log \epsilon$		
XIa	EtOH (b)	218	4.66	228	4.45	282	4.86	287	4.95	293	4.94
	(c)	318	4.18	332	4.15	347	4.11	369	3.81	387	3.83
XIb	EtOH (b)	221	4.55	231	4.40					291	4.83
	(c)			333	3.99	348	3.97	366	3.82	384	3.83
Dibenz[a, h]- anthracene	EtOH (b)	222	4.76	230	4.43	278	4.65	288	4.95	298	5.20
	(c)	317	4.32	332	4.20	348	4.15	371	3.3 (d)	390	3.3 (d)
XIa	EtOH-HCl (b)	218	4.48							293	4.80
	(e) (c)	323	4.00			352 (f)	4.14	368	4.18		
XIb	EtOH-HCl (b)	224	4.45			282	4.71			293	4.81
	(e) (c)					347	3.97	363	3.94	384	3.89

(a) Data for corresponding maxima (as adjudged from observations on the total spectral curves) are placed in the same column. (b) Spectral features below 310  $m\mu$ . (c) Spectral features above 310  $m\mu$ . (d) Approximate values for  $\log \epsilon$ . (e) Solvent, 0.01 M hydrochloric acid in 95% ethanol. (f) A shoulder, not a true maximum.

6 hours. Meanwhile, an additional quantity of 0.2 ml. of formic acid was added if a test with wet litmus paper showed that the reaction mixture was basic. The mixture was poured into 100 ml. of ice-water. The dark, denser liquid phase crystallized when it was separated and stirred with fresh water, yield 4.8 g. (83%) of brown powder, m.p. 89-97°. Recrystallization from benzene gave colorless crystals, m.p. 214-215°; infrared absorption bands at 2.99, 3.05, and 6.01  $\mu$ .  
*Anal.* Calcd. for  $C_{19}H_{15}NO_2$ : C, 78.87; H, 5.23; N, 4.84. Found: C, 79.06; H, 5.40; N, 4.57.

(b) From V.

A solution of 483 mg. of 2,5-diphenyl-4-aminophenol (*vide infra*) in 10 ml. of anhydrous formic acid was refluxed for 8 hours. The residue from evaporation of the solvent *in vacuo* was recrystallized once from benzene, yield 272 mg. (51%) of IV, m.p. 208-210°, raised to 213-214.5° on further recrystallization, identical with product from (a) as based on mixture melting point and infrared spectrum.

2,5-Diphenyl-4-aminophenol (V). (a) From I.

To a cold (0°), stirred suspension of 2 g. (7.7 mmoles) of 2,5-diphenyl-1,4-benzoquinone and 5 g. (72 mmoles) of hydroxylammonium chloride in 100 ml. of ethanol was added a solution of 4 g. of potassium hydroxide in 100 ml. of ethanol. The mixture was refluxed for 12 hours, cooled, filtered, and poured into 500 ml. of water. The brown precipitate (yield 1.61 g., 80%, m.p. 220-225°) was recrystallized once from ethyl acetate and four times from benzene to give flesh-colored crystals, m.p. 230-231°; infrared absorption bands at 2.81 and 2.99  $\mu$ ;  $\lambda$  max (EtOH) at 240  $m\mu$  ( $\log \epsilon$  4.68), 333 (3.88);  $\lambda$  max (EtOH-HCl) at 259 (4.57), 301 (4.28).

*Anal.* Calcd. for  $C_{18}H_{15}NO$ : C, 82.73; H, 5.79; N, 5.36. Found: C, 82.41; H, 5.78; N, 5.35.

V gave a blue color test with ferric chloride solution (11) and formed (by addition of hydrogen chloride to an ethereal solution of V) a difficultly soluble hydrochloride.

(b) From IV.

A solution of 52 mg. of 2,5-diphenyl-4-formamidophenol (formed directly from I) in 5 ml. of ethanol and 1 ml. of concentrated hydrochloric acid was refluxed for 30 minutes, cooled, made faintly alkaline with saturated aqueous sodium bicarbonate solution, and extracted exhaustively with ether. Removal of the solvent from the dried (sodium

sulfate) ethereal solution left 39 mg. (83%) of V, m.p. 225.5-226.5°, raised (on recrystallization) to 228.5-230°, undepressed on admixture with product from (a). Its infrared spectrum was identical with that of product from (a).

Conversion of I to *p*-Terphenyl (VI).

A solution of 5 g. of 2,5-diphenyl-1,4-benzoquinone in 100 ml. of formamide was refluxed for 4 hours, and then poured into 300 ml. of water. The brown, amorphous precipitate (4.2 g., 95%, m.p. 162-180°) was twice sublimed at 200° and 0.1 mm. to give pure *p*-terphenyl, identified by direct comparison (melting point, mixture melting point, and infrared spectrum) with an authentic sample.

2,5-Diphenyl-1,4-diaminobenzene (VII).

To a stirred suspension of 6.9 g. (0.024 mole) of 2,5-diphenyl-1,4-benzoquinone dioxime in 800 ml. of purified dioxane (12) was added (in an atmosphere of nitrogen) in three equal portions a total of 5 g. (0.132 mole) of lithium aluminum hydride. After the addition of each portion the mixture (kept in the inert atmosphere) was heated to boiling, refluxed 6-8 hours, and allowed to cool to room temperature. Thereafter, were added dropwise over a period of 2 hours and in succession 5 ml. of water, 5 ml. of 20% aqueous sodium hydroxide solution, and 5 ml. of water. The precipitate was collected by filtration and extracted with dioxane. Combined organic solutions were evaporated to leave 4.7 g. of dark brown liquid which was dissolved in 500 ml. of ether. The ethereal solution was extracted five times with 200-ml. portions of 2 N hydrochloric acid. The aqueous extract was basified with sodium hydroxide and extracted exhaustively with ether. Evaporation of the ether left 1.9 g. of liquid which crystallized on stirring with ethanol, yield 0.46 g. (7.4%) of brown product, m.p. 205-207.5°, obtained (after three recrystallizations from ethanol) as yellow-brown prisms, m.p. 214-215.5°;  $\lambda$  max (EtOH) at 235  $m\mu$  ( $\log \epsilon$  4.66), 338 (3.65);  $\lambda$  max (EtOH-HCl) at 238 (4.68), 318 (3.90); n.m.r. absorptions ( $CDCl_3$ ) at  $\delta = 3.3$  (4 amino protons), 6.62 (2 aromatic protons on central ring), and 7.4 p.p.m. (10 protons on phenyl groups).

*Anal.* Calcd. for  $C_{18}H_{15}N_2$ : C, 83.04; H, 6.20; N, 10.76. Found: C, 82.84; H, 6.07; N, 10.95.

In cases where the product was to be converted to VIII reduction of I was conducted in ether solution (rather than in dioxane) and the crude, liquid VII which resulted from evaporation of the solvent was formylated directly, as indicated in the next paragraph.

## 2,5-Diphenyl-1,4-diformamidobenzene (VIII).

A mixture of 5.2 g. of the preceding crude diamine VII and 50 ml. of anhydrous formic acid was refluxed for 5 hours and then allowed to cool. The resultant, dark precipitate (3 g., m.p. 157-169°) was recrystallized first from ethanol (with charcoal decolorization) and subsequently from dimethylformamide-ethanol and ethyl acetate. There resulted nearly colorless crystals, m.p. 264-265°; infrared absorption bands at 3.08 and 6.06  $\mu$ .

*Anal.* Calcd. for  $C_{20}H_{18}N_2O_2$ : C, 75.93; H, 5.10; N, 8.86. Found: C, 75.81; H, 5.15; N, 8.93.

## 2,5-Diphenyl-1,4-diacetamidobenzene (X).

The colorless precipitate which resulted from admixture of 413 mg. of 2,5-diphenyl-1,4-diaminobenzene (m.p. 208-210°) and 2 ml. of acetic anhydride was collected by filtration and washed with ethanol, yield 435 mg. (80%) of bright yellow X, m.p. 300-304°, converted to colorless platelets, m.p. 312-313° after successive recrystallizations from benzene, glacial acetic acid, and ethanol; infrared absorption bands at 3.10 and 6.01  $\mu$ ;  $\lambda$  max (EtOH) at 245  $m\mu$  ( $\log \epsilon$  4.52).

*Anal.* Calcd. for  $C_{22}H_{20}N_2O_2$ : C, 76.72; H, 5.85; N, 8.13. Found: C, 76.41; H, 5.97; N, 7.87.

## Cyclization Studies on VIII. (a) Formation of 6,13-Diazadibenz[a,h]-anthracene (XIa).

A mixture of 5.5 g. of 2,5-diphenyl-1,4-diformamidobenzene, 10 g. of sodium chloride, and 100 g. of anhydrous aluminum chloride was heated at 285° for 4 hours. The cooled reaction mixture was added, portionwise, to a mixture of ice and water. The dark green precipitate was collected by filtration, washed free of acid using water and 10% ammonium hydroxide, dried *in vacuo*, and extracted with hot benzene (ca. 1.1 l.). From the filtered, bright yellow, strongly fluorescent solution was obtained 3.85 g. (79%) of light yellow crystals, m.p. 277.5-279.5°, converted to prisms, m.p. 280-281°, on further recrystallization.

*Anal.* Calcd. for  $C_{26}H_{12}N_2$ : C, 85.69; H, 4.32; N, 9.99. Found: C, 85.36; H, 4.40; N, 9.78.

## (b) Use of Polyphosphoric Acid.

A well-stirred mixture of 1.1 g. of VIII and 30 g. of polyphosphoric acid was heated at 185° for 3 hours. The reaction mixture was cooled to 80° and poured into ice and water. The mixture was basified with ammonium hydroxide and filtered. The collected precipitate (0.63 g., m.p. 185-190°) was recrystallized from ethanol and identified as the diamine VII (m.p. 213.5-214.5°, no depression on admixture with an authentic sample).

## (c) Use of Polyphosphoric Acid--Phosphorus Pentoxide.

To a clear solution of 1.8 g. of phosphorus pentoxide in 28 g. of polyphosphoric acid was added (at 145°) 515 mg. of VIII. The mixture was stirred vigorously at this temperature for 1.5 hours and then processed as in part (b). There resulted 395 mg. of precipitate, from which was obtained 58 mg. of pure diamine VII on recrystallization.

The mother liquor was evaporated to dryness and the residue was recrystallized from cyclohexane to give 83 mg. (20%) of crystals of 3-amino-2-phenylphenanthridine, m.p. 145-148°, converted to yellow-tan prisms, m.p. 151-153° (with sintering) on further recrystallization;

infrared absorption bands at 3.01 and 3.14  $\mu$ ;  $\lambda$  max (EtOH) at 253  $m\mu$  ( $\log \epsilon$  4.58), 336 sh (3.89), 347 (3.93), 368 (3.92);  $\lambda$  max (EtOH-HCl) at 261 (4.59) and 324 (3.81).

*Anal.* Calcd. for  $C_{19}H_{14}N_2$ : C, 84.42; H, 5.22; N, 10.36. Found: C, 84.10; H, 5.38; N, 10.29.

## 5,12-Dimethyl-6,13-diazadibenz[a,h]anthracene (XIb).

As in the preceding cyclization procedure (b), 0.93 g. of 2,5-diphenyl-1,4-diacetamidobenzene (X) was heated with 30 g. of polyphosphoric acid for 5 hours. Processing of the reaction mixture gave 0.79 g. (95%) of brown powder, m.p. > 330°, difficultly soluble in most common solvents. Recrystallizations from dimethylformamide and from dioxane gave yellow needles, m.p. > 330° (with darkening and decomposition starting at 280°).

*Anal.* Calcd. for  $C_{22}H_{18}N_2$ : N, 9.09. Found: N, 8.95.

An attempt to effect cyclization of X by means of sodium chloride-aluminum chloride (preceding method a) gave a mixture which could not be purified.

## REFERENCES

- (1) This investigation was supported by research grant no. CA-5969 from the National Cancer Institute, U. S. Public Health Service.
- (2) Research Associate, 1962-1964.
- (3) L. H. Klemm and A. Weisert, *J. Heterocyclic Chem.*, **2**, 15 (1965).
- (4) M. L. Moore in "Organic Reactions" Vol. V., R. Adams *et al.*, Eds., John Wiley and Sons, Inc., New York, N. Y., 1949, pp. 301-330.
- (5) W. J. Hickinbottom, "Reactions of Organic Compounds," 3rd Ed., John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 281-288.
- (6) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 4th Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, pp. 254-255.
- (7) B. Schiedt, *J. prakt. Chem.*, **157**, 203 (1941).
- (8) G. M. Badger and W. F. Sasse, *J. Chem. Soc.*, **4** (1957).
- (9) H. H. Jaffé and M. Orchin, "Theory and Applications of Ultraviolet Spectroscopy," John Wiley and Sons, Inc., New York, N. Y., 1962, pp. 361-373.
- (10) Microanalyses were determined by Micro-Tech Labs., Skokie, Illinois. Ultraviolet spectra were obtained by means of a Cary model 11 spectrophotometer; infrared spectra, by means of a Beckman IR-5 spectrophotometer using nujol mulls; and n.m.r. spectra, by means of a Varian Associates A-60 instrument using tetramethylsilane as internal reference. Melting points below 260° are corrected; above 260° they are uncorrected.
- (11) Ref. 6, pp. 112-113.
- (12) See footnote 17, ref. 3.
- (13) Starting material I was recrystallized from ethyl acetate before use, m.p. 208-210°. Use of I directly as purchased gave a black solution from which no III could be isolated.

Received February 26, 1965

Eugene, Oregon 97403