[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Intramolecular Condensation of 2-Biphenylylglyoxal

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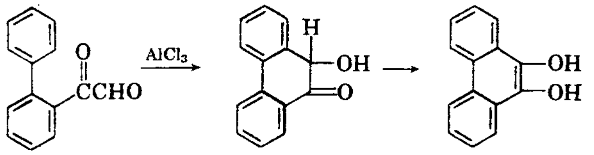
2-Biphenylylglyoxal, prepared by oxidation of the corresponding methyl ketone with selenium dioxide in ethanol, has been found to undergo cyclization. The product, however, was not the benzoin or its expected enol form, 9,10-dihydroxyphenanthrene, but instead phenanthrenequinone. Not only did the cyclization take place with aluminum chloride, but the quinone was also formed in the preparation of the glyoxal if dioxane was used as solvent. Presumably an intermediate produced by the reaction of the ketone with selenious acid may have been responsible for the ring closure. The reaction with aluminum chloride even in the presence of anisole appeared to be entirely intramolecular.

The synthesis of benzoins by intermolecular condensation of aromatic compounds with arylglyoxals in the Friedel and Crafts manner[2] might also occur intramolecularly with suitably constituted arylglyoxals. Since the most favorable cases would be expected to be those involving the formation of six-membered rings, attention has been directed to the behavior of *o*-arylphenylglyoxals. The simplest of these, 2-biphenylylglyoxal, when treated with aluminum chloride in anisole as solvent, gave phenanthrenequinone in a yield of 40%. The production of the enol form of the corresponding benzoin, 9,10-dihydroxyphenanthrene, would have been predicted.

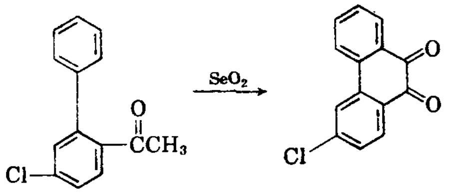


Formation of the quinone directly from an intermediate in the reaction rather than by air oxidation of the dihydroxy compound would require that a hydride ion as well as a proton be lost before hydrolysis but after ring closure of the glyoxal-aluminum chloride complex had occurred.

The starting material, 2-acetylbiphenyl, was prepared by the procedure of Campaigne and Reid[3] as well as that of Huber, Renoll, Rossow, and Mowry.[4] The ketone gave a negative iodoform test. Oxidation of 2-acetylbiphenyl with selenium dioxide in dioxane did not give usable amounts of the expected glyoxal. Instead phenanthrenequinone was obtained in yields varying from 2.4 to 15%. In an experiment in which the yield of quinone was only 2.4% two other products were found after the reaction mixture had been heated. 2-Biphenylylglyoxal was isolated in 5.7% yield as a distillate; di-9-phenanthryl ether was obtained in 4.6% yield from the residue.

The formation of the ether suggests that ring closure occurs with an intermediate (formed from 2-acetylbiphenyl and selenious acid) prior to the usual rearrangement steps[5] leading to the glyoxal. In very dilute solution the oxidation apparently did give the expected glyoxal; alkaline treatment of the reaction mixture produced an α-hydroxy acid which was assigned the structure of 2-biphenylylglycolic acid. The yield based on the methyl ketone was 19%.

5-Chloro-2-acetylbiphenyl exhibited this same unusual behavior. 3-Chlorophenanthrenequinone (0.4% yield) was isolated.



The preparation of 2-biphenylylglyoxal was achieved (27% yield) by oxidation of 2-acetylbiphenyl with selenium dioxide in absolute ethanol under a nitrogen atmosphere. The product, a high-boiling oil, was characterized by its infrared spectrum and its conversion to 2-biphenylylglycolic acid.

EXPERIMENTAL[6]

Oxidation of 2-acetylbiphenyl[3,4] with selenium dioxide in dioxane. The procedure used was patterned after that employed in the preparation of phenylglyoxal by Riley and Gray,[7] as modified by Arnold and Fuson.[2] To a warm solu-

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[1] National Science Foundation Predoctoral Fellow, 1957-60.

[2] R. T. Arnold and R. C. Fuson, *J. Am. Chem. Soc.*, **58**, 1295 (1936).

[3] E. Campaigne and W. B. Reid, Jr., *J. Am. Chem. Soc.*, **68**, 1663 (1946).

[4] W. F. Huber, M. Renoll, A. G. Rossow, and D. T. Mowry, *J. Am. Chem. Soc.*, **68**, 1109 (1946).

(5) E. J. Corey and J. P. Schaefer, *J. Am. Chem. Soc.*, **82**, 918 (1960).

(6) All melting points are corrected; all boiling points are uncorrected. Refractive indices were determined with white light. The infrared spectra were determined on a Perkin-Elmer model 21 recording infrared spectrophotometer by Mr. Paul E. McMahon, Mrs. Mary Verkade, Miss Charlene Leubke, Mr. D. H. Johnson, Mr. William Dalton, and Mr. Daniel Vittum. The microanalyses were performed by Mr. Josef Nemeth, Miss Claire Higham, Mrs. A. S. Bay, Miss Jane Liu, and Mrs. Frederick Ju.

(7) H. A. Riley and A. R. Gray, *Org. Syntheses*, Coll. Vol. II, 509 (1943).

tion of 2.58 g. (0.020 mole) of selenious acid, 14 ml. of peroxide-free dioxane, and 0.40 ml. of water was added 3.92 g. (0.020 mole) of the pure ketone (m.p. 57.0–58.0°) in one lot. The reaction mixture was heated under reflux and under nitrogen for 4.5 hr., and the precipitated selenium metal was removed by pouring the mixture through a plug of glass wool.

The product, isolated by conventional methods, was a red oil; it was chromatographed over acid-washed alumina with benzene and ether as eluents. The solvents in the eluted fractions were removed in a nitrogen atmosphere, and the residues were stored under nitrogen. The fractions eluted by 3:1 and 1:1 ratios of benzene and ether as well as by pure ether contained 0.86 g. of a yellow solid melting at 199–204°. One recrystallization from benzene and ethanol gave phenanthrenequinone, melting at 207.5–209.0°; yield, 0.63 g. (15%). A mixture of this material and an authentic sample of phenanthrenequinone (m.p., 208.2–208.9°) prepared by oxidation of phenanthrene[8] melted at 207.5–209.0°. The infrared spectra of the two samples are identical. The quinone could also be isolated before chromatography by crystallization of the reaction mixture from benzene, but the yields were lower (2.4–6.4%).

In one experiment which was not carried out in a nitrogen atmosphere, impure phenanthrenequinone was crystallized directly from benzene-ethanol. After one recrystallization from ethanol the quinone melted at 189–202°, yield 50 mg. (1.2%). Removal of the solvent from the filtrate in a nitrogen atmosphere left an oil which was distilled at diminished pressure. The residue was treated with 20 ml. of hot ethanol. The insoluble material was dissolved in 20 ml. of benzene, the solution was treated with decolorizing carbon, and 3.0 ml. of ethanol was added. A powdery solid (0.17 g., m.p. 203–204°) was obtained. Two more recrystallizations from benzene-ethanol gave 0.13 g. of colorless needles, m.p. 202–203°. The analytical sample melted at 202.5–203.0°.

Anal. Calcd. for $C_{28}H_{18}O$: C, 90.78; H, 4.90. Found: C, 90.62; H, 5.03.

On the basis of its melting point, solubility, and composition this compound was assigned the structure of di-9-phenanthryl ether (m.p. 200–202°,[9] 209°,[10] 210°[11]). The infrared spectrum is in agreement with this assignment. The yield (0.17 g.) was 4.6% of the theoretical amount. The picrate, prepared in benzene, melted at 186.5–188.0°.

Anal. Calcd. for $C_{28}H_{18}O \cdot C_6H_3N_3O_7$: C, 68.11; H, 3.53; N, 7.01. Found: C, 68.10; H, 3.88; N, 7.00.

The combustion data confirmed the identity of this substance as the monopicrate of di-9-phenanthryl ether. Previous workers had isolated the dipicrate (m.p. 148°[10,11]).

At a higher dilution the reaction gave different products. To a warm solution of 400 ml. of peroxide-free dioxane, 1.94 g. (0.015 mole) of selenious acid, and 0.1 ml. (0.005 mole) of water was added in one lot 2.94 g. (0.015 mole) of 2-acetylbiphenyl. The entire procedure was carried out in a nitrogen atmosphere. The reaction mixture was heated under reflux for 24 hr.; any remaining selenious acid was then neutralized by the addition of 0.84 g. (0.01 mole) of sodium bicarbonate. The product obtained in this way did not give a crystalline glyoxal hydrate or a sodium bisulfite adduct. A mixture of 1 g. of the product, 4 g. of potassium hydroxide, 5 ml. of water, and 10 ml. of ethanol, was heated at the reflux temperature for 1 hr. and neutralized with dilute hydrochloric acid. The product, isolated by conventional procedures, was an orange sirup; when triturated with a mixture of ether, petroleum ether, and carbon disulfide it gave a solid, gummy material which was recrystallized from benzene. 2-Biphenylylglycolic acid was obtained as a colorless powder, m.p. 113–115°, yield 0.17 g. (19%, based on 2-acetylbiphenyl). The analytical sample melted at 114.0–114.5°.

Anal. Calcd. for $C_{14}H_{12}O_3$: C, 73.67; H, 5.30. Found: C, 73.46; H, 5.38.

The infrared spectrum of the acid in a Nujol–hexachlorobutadiene mull has bands attributable to an alcoholic hydroxyl group (3600 cm.$^{-1}$), an acid hydroxyl group (3480 cm.$^{-1}$ and a broad band in the region 3300–2500 cm.$^{-1}$), a nonconjugated acid carbonyl group (1740 cm.$^{-1}$), a monosubstituted aromatic ring (705 cm.$^{-1}$), and the presence of both mono- and 1,2-disubstituted aromatic rings (755 and 780 cm.$^{-1}$). A mixture of this material and the acid (m.p. 113–115°), obtained later by alkali-catalyzed rearrangement of 2-biphenylylglyoxal, melted at 113–114°.

5-Chloro-2-iodobiphenyl. 2-Aminobiphenyl was acetylated by the method of Sako.[12] The 2-acetamidobiphenyl was chlorinated by the method of Bell and Gibson.[13] Two recrystallizations of the 5-chloro-2-acetamidobiphenyl from cyclohexane-benzene gave colorless crystals, m.p. 114–118°, yield 84.7 g. (79%). A solution of 137.5 g. (0.562 mole) of slightly impure 5-chloro-2-acetamidobiphenyl, 1800 ml. of absolute ethanol, and 180 ml. of concd. hydrochloric acid was heated under reflux for 3 hr.; the solvent was then allowed to distill. To the crude hydrochloride salt was added 250 ml. of water and 250 ml. of concd. hydrochloric acid. The suspension was cooled with stirring to −5°, and 550 g. of crushed ice was added. The amine salt was then diazotized with a chilled solution of 40.0 g. (0.58 mole) of sodium nitrite in 250 ml. of water. After the diazonium suspension had been stirred at 5° for 15 min., a chilled solution of 275 g. (1.65 mole) of potassium iodide in 430 ml. of water was added over a period of 1.5 hr. This mixture was stirred at 10° for 2 hr. and then heated with shaking on a steam bath until the gas evolution had ceased and the temperature of the mixture had reached 80°. Toluene extraction and removal of the solvent gave crude 5-chloro-2-iodobiphenyl as a black oil, which distilled at reduced pressure through a 12-in. wrapped Vigreux column and Claisen head at 125–155° (0.4–0.6 mm.), $n_D^{25°}$ 1.663, yield, 117.6 g. (67%). When allowed to stand for a long time in the cold the oil solidified. Several recrystallizations from absolute ethanol gave colorless crystals, m.p., 41.0–42.0°.

Anal. Calcd. for $C_{12}H_8ClI$: C, 45.82; H, 2.56. Found: C, 45.68; H, 2.58.

The infrared spectrum of 5-chloro-2-iodobiphenyl has bands which may be assigned to aromatic hydrogen (3060 cm.$^{-1}$), to a monosubstituted aromatic ring (695 cm.$^{-1}$), and to a 1,2,4-trisubstituted aromatic ring (805 and 870 cm.$^{-1}$).

5-Chloro-2-biphenylcarboxylic acid. A Grignard reagent was prepared in ether solution from 3.78 g. (0.012 mole) of 5-chloro-2-iodobiphenyl and an excess of freshly ground magnesium. Entrainment with methyl iodide was necessary to start the reaction when it was carried out on this scale. The reagent was injected into a slurry of finely ground Dry Ice in ether. The 5-chloro-2-biphenylcarboxylic acid, a colorless solid (from aqueous ethanol), melted at 152.5–154.0° (lit.[13,14] m.p. 152°). The infrared spectrum of this acid has absorption peaks which may be assigned to an aromatic carboxylic acid (1695 cm.$^{-1}$ and a broad band in the region 3200–2500 cm.$^{-1}$), a mono-substituted aromatic ring (695 cm.$^{-1}$), and a 1,2,4-trisubstituted aromatic ring (835 and 885 cm.$^{-1}$).

1-(5-Chloro-2-biphenylyl)ethanol. A Grignard reagent, prepared in ether solution from 62.81 g. (0.20 mole) of 5-chloro-2-iodobiphenyl and 6.08 g. (0.25 g.-atom) of freshly ground

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[8] R. Wendland and J. LaLonde, *Org. Syntheses*, **34**, 76 (1954).

[9] R. F. Schultz, E. D. Schultz, and J. Cochran, *J. Am. Chem. Soc.*, **62**, 2902 (1940).

[10] F. R. Japp and J. Knox, *J. Chem. Soc.*, **87**, 681 (1905).

[11] F. R. Japp and A. Findlay, *J. Chem. Soc.*, **71**, 1115 (1897).

[12] S. Sako, *Bull. Chem. Soc. Japan*, **9**, 55 (1934).

[13] F. Bell and J. A. Gibson, *J. Chem. Soc.*, 3560 (1955).

[14] I. M. Heilbron, D. H. Hey, and R. Wilkinson, *J. Chem. Soc.*, 113 (1938).

magnesium, was allowed to condense with acetaldehyde. The product after recrystallization from warm petroleum ether weighed 27.1 g. (58% yield) and melted at 85–91°. An analytical sample of colorless needles of 1-(5-chloro-2-biphenylyl)-ethanol, obtained after several more recrystallizations from petroleum ether or from a mixture of petroleum ether and benzene, melted at 96.5–97.0°.

Anal. Calcd. for $C_{14}H_{13}OCl$: C, 72.26; H, 5.63. Found: C, 72.04; H, 5.62.

The infrared spectrum of the alcohol has absorption peaks attributable to a monosubstituted aromatic ring (695 cm.$^{-1}$), a 1,2,4-trisubstituted aromatic ring (820 and 880 cm.$^{-1}$), two types of aliphatic hydrogen (2900 and 2950 cm.$^{-1}$), aromatic hydrogen (3060 cm.$^{-1}$), and a hydroxyl group (3590 cm.$^{-1}$ merged with a broad band in the region 3500–3200 cm.$^{-1}$).

The *p*-nitrobenzoate of 1-(5-chloro-2-biphenylyl)ethanol after several recrystallizations from absolute ethanol melted at 105.5–106.5°.

Anal. Calcd. for $C_{21}H_{16}O_4NCl$: C, 66.06; H, 4.23; N, 3.67. Found: C, 66.00; H, 4.15; N, 3.58.

The compound exploded during combustion.

5-Chloro-2-acetylbiphenyl. This ketone was prepared by a procedure similar to that used in the preparation of 2-acetylbiphenyl from 1-(2-biphenylyl)-ethanol. To a sulfuric acid–acetic acid solution of potassium dichromate at 50° was added with stirring 12.9 g. of slightly impure 1-(5-chloro-2-biphenylyl)-ethanol. The reaction mixture was stirred at 45–55° for a period of 2 hr. and was then worked up in the usual way. The product was dissolved in methanol, and the solution was cooled at −78° with prolonged scratching. After 20 min. a colorless solid separated, yield 7.55 g. (59%), m.p. 40–45°. After three more recrystallizations from aqueous methanol the 5-chloro-2-acetylbiphenyl melted at 44.0–45.0°. The infrared spectrum has absorption peaks attributable to a monosubstituted aromatic ring (695 cm.$^{-1}$), to a 1,2,4-trisubstituted aromatic ring (815 and 880 cm.$^{-1}$), to a methyl group next to a carbonyl group (1350 cm.$^{-1}$), to an aromatic ketone (1685 cm.$^{-1}$), and to aromatic hydrogen (3060 cm.$^{-1}$).

Anal. Calcd. for $C_{14}H_{11}OCl$: C, 72.88; H, 4.81. Found: C, 72.69; H, 4.74.

Oxidation of 5-chloro-2-acetylbiphenyl with selenium dioxide in dioxane. To a warm solution of 2.45 g. (0.019 mole) of selenious acid, 15.0 ml. of peroxide-free dioxane, and 0.2 ml. (0.011 mole) of water was added 4.4 g. (0.019 mole) of impure 5-chloro-2-acetylbiphenyl in one lot. The reaction mixture was heated at the reflux temperature for 4.5 hr. Chromatography of the oily product over acid-washed alumina gave 0.13 g. of a yellow solid which melted in the range 250–260°. When this solid was recrystallized from a solution of benzene and ethanol, orange needles of 3-chlorophenanthrenequinone were obtained, m.p. 243–247° [lit., m.p. 253° (corr., 261°),[15] 256.5–257° (corr., 264.5–265°),[16] 253–254°[17]], yield 18.1 mg. (0.40%).

The infrared spectrum of this material in a Nujol mull is nearly identical with that of authentic phenanthrenequinone. It possesses bands attributable to a 1,2,4-trisubstituted aromatic ring (805 and 890 cm.$^{-1}$).

The fractions eluted by 1:1 and 1:5 ratios of benzene and ether contained 0.59 g. (12.7% yield) of yellow, waxy material whose infrared spectrum possesses two carbonyl bands (1680 cm.$^{-1}$ and 1725 cm.$^{-1}$), a sharp peak attributable to an aldenyde (2820 cm.$^{-1}$), and bands assignable to a monosubstituted aromatic ring (695 cm.$^{-1}$) and to a 1,2,4-trisubstituted aromatic ring (820 and 880 cm.$^{-1}$). The spectrum was later shown to be similar to that of 2-biphenylylglyoxal with the exception of the region 700–900 cm.$^{-1}$ This material may be 5-chloro-2-biphenylylglyoxal.

2-Biphenylylglyoxal. To a boiling solution of 5.16 g. (0.040 mole) of selenious acid in 25 ml. of absolute ethanol was added 7.85 g. (0.040 mole) of 2-acetylbiphenyl in one lot. The reaction mixture was heated at the reflux temperature with stirring for 12 hr. and was then allowed to stand at room temperature for an additional 12 hr. The entire operation was carried out in a nitrogen atmosphere. The precipitated selenium metal was collected on a filter, and the solvent was distilled from the filtrates; 10.0 ml. of toluene was added to the residue and then distilled. This process was repeated twice, and the residual red oil was distilled *in vacuo.* 2-Biphenylylglyoxal was obtained as a yellow oil distilling at 135–137° (0.6 mm.), $n_D^{25°}$ 1.6128, yield 2.24 g. (27%). The infrared spectrum has absorption peaks which may be assigned to a nonconjugated aldehyde (1715 cm.$^{-1}$), an aromatic ketone (1680 cm.$^{-1}$), the carbon-hydrogen bond in an aldehyde (2805 cm.$^{-1}$), aromatic hydrogen (3060 cm.$^{-1}$), a monosubstituted aromatic ring (695 cm.$^{-1}$), and the presence of both mono- and 1,2-disubstituted aromatic rings (740 and 770 cm.$^{-1}$).

2-Biphenylylglycolic acid. A solution of 4.0 g. of potassium hydroxide, 15 ml. of ethanol, 5 ml. of water, and 0.60 g. (0.0028 mole) of 2-biphenylylglyoxal was heated at the reflux temperature for 1 hr. The colorless 2-biphenylylglycolic acid melted at 111–115°, yield, 0.49 g. (75%). After one recrystallization from benzene it melted at 113.0–115.0°.

Treatment of 2-biphenylylglyoxal with aluminum chloride. This procedure was patterned after that used in the synthesis of benzoins by Arnold and Fuson.[2] To an ice-cold suspension of 1.00 g. (0.0075 mole) of anhydrous aluminum chloride and 15 ml. of anisole was added slowly with stirring a solution of 0.50 g. (0.0024 mole) of 2-biphenylylglyoxal in 10 ml. of anhydrous carbon disulfide over a 30-min. period. Stirring at 0° was continued for 3 hr., the entire procedure being carried out in a nitrogen atmosphere. The complex was decomposed by ice chips followed by a small amount of dilute hydrochloric acid. Benzene was added to dissolve the dark-colored solid that precipitated. The benzene layer was washed with water containing a little hydrochloric acid and then with water. The excess anisole was removed by adding water to the benzene solution and steam-distilling the mixture until the distillate was clear. The aqueous mixture left in the distilling flask was extracted with benzene. Removal of the solvent gave an orange solid which was recrystallized from hot benzene. Orange crystals of phenanthrenequinone were obtained, m.p. 205–208°. A mixture of this material and authentic phenanthrenequinone,[8] m.p. 208.0–209.0°, melted at 207–209°. A second crop of crystals, m.p. 204–207°, was obtained by addition of absolute ethanol to the recrystallization filtrate. The total yield of phenanthrenequinone was 0.20 g. (40%). The infrared spectrum of the sample melting at 205–208° was identical to that of authentic phenanthrenequinone.

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(16) P. Nylen, *Ber.*, **53**, 158 (1920).

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