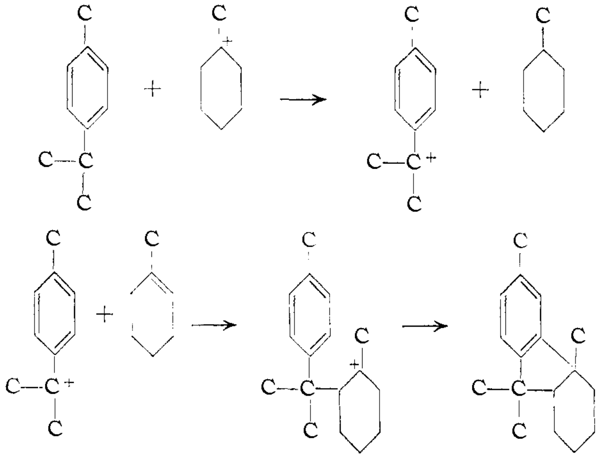

VII

Methylcyclohexane required by the mechanism was isolated in 48% yield; 1,3,3,6-tetramethyl-1-*p*-tolyl-indan[17] also was produced (expt. 19).

Additional studies of the alkylation of *p*-substituted benzenes will be reported in the future.

Experimental

Acknowledgment is due Dr. F. L. Voelz, Mr. F. L. Boys and Mr. R. Wertzler for interpretation of the infrared spectrograms and Mr. J. F. Kinder and F. L. Boys for the mass spectrometric analyses.

Alkylation Procedures.—Those previously described[5] were used (see Table I).

Identification.—The infrared absorption spectrogram of 1-methyl-1-phenylcyclohexane was identical to that previously reported.[2a] 1,4-Di-(1′-methylcyclohexyl)-benzene was prepared as described by Linsk.[2b]

In most instances the *t/s* ratio (ratio of tertiary to secondary cycloalkylation) was determined by dehydrogenating[18] the monoalkylate and examining the product by infrared and/or by mass spectrometry. For example, the monoalkylate of benzene was passed over a 0.5% platinum-on-alumina catalyst[19] or a 10% platinum-on-carbon[19] at 300–310° until the index of refraction remained fairly constant (usually 3 passes). The product was analyzed by comparison to infrared standards for compound I, biphenyl, 2-methylbiphenyl,[20] 3-methylbiphenyl[20] and 4-methylbiphenyl (synthesized[21] by diazotization of *p*-toluidine followed by condensation with benzene).

The *t/s* ratio for alkylates of benzene, toluene and *p*-xylene was estimated by noting the amount of biphenyls formed (from secondary alkylates) during dehydrogenation and noting the peak intensity of the parent mass of the tertiary alkylate surviving dehydrogenation (Table II).

The methylcyclohexyl derivative of *p*-cymene was assigned the indane structure VII on the basis of the following evidence:

MCH derivative of	n^{20}_{D}	d^{20}_{4}	C, %	H, %	Parent mass
o-Cymene[14]	1.5230	0.9318	88.86	11.19	..
o-Cymene[14]	1.5170	.9213	88.92	11.38	..
p-Cymene[13]	1.5305	.9581	89.40	10.68	..
p-Cymene (VII)	1.5301	.9564	89.11	10.64	228
Calcd. for true alkylate ($C_{17}H_{26}$)			88.62	11.37	230
Calcd. for indan ($C_{17}H_{24}$)			89.40	10.60	228

The higher refractive index and greater density bespeak a tricyclic structure, as do the carbon, hydrogen and parent mass values. However, the data in Table II (Expt. 19) do indicate the presence of about 10% of true alkylate, mass 230, as an impurity.

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[17] Formation of this indan is accompanied by production of methylcyclohexane.[13]

[18] V. N. Ipatieff and H. Pines, THIS JOURNAL, **58**, 1056 (1936).

[19] Baker & Company, Inc., Newark, N. J.

[20] We are grateful to Addison M. Rothrock, National Advisory Committee for Aeronautics, Washington, D. C., for making available to us these standards previously described by K. T. Serijan, I. A. Goodman and W. J. Yankauskas, National Advisory Committee Aeronautics Technical Note No. 2557 (1951).

[21] "Organic Reactions," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1945, p. 247.

HARVEY, ILL.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

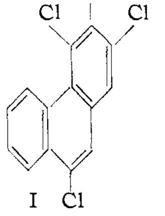
The Synthesis of 2,4,9-Trichloro-3-phenanthrol

BY CHARLES K. BRADSHER, FRANCES C. BROWN AND PRESTON H. LEAKE[1]

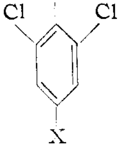
RECEIVED SEPTEMBER 21, 1956

In order to obtain further evidence concerning a compound believed to be 2,4,9-trichloro-3-phenanthrol (I), 2,4-dichloro-3-methoxyphenanthrene (X) was synthesized by the general method of Pschorr. The 2,5-dichlorohomoanisic acid (VI) required in the Pschorr synthesis was synthesized in 65% yield in a five-step reaction sequence starting with ethyl 3,5-dichloro-4-hydroxybenzoate. Cleavage of the ether linkage of X, and chlorination of the resulting phenanthrol XI, afforded I.

In connection with the study of the chlorination of 3-phenanthrol[2] we prepared a new trichlorophenanthrol which, on the basis of further reactions, was believed to be 2,4,9-trichloro-3-phenanthrol (I). Prior to the completion of that study, but after the location of one chlorine at position 9 had been definitely established, it had seemed desirable to undertake the synthesis of I by a method which would afford unequivocal evidence concerning the position of the chlorine atoms believed to be at positions 2 and 4. It seemed likely that this might be achieved by the synthesis of 2,4-dichloro-3-methoxyphenanthrene by the general method of Pschorr, followed by chlorination at the 9-position of the phenanthrene ring.



I



II, X = $COOCH_3$
III, X = CH_2OH
IV, X = CH_2Br
V, X = CH_2CN
VI, X = CH_2COOH

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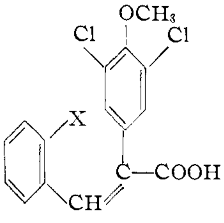
[1] Allied Chemical and Dye Corporation Fellow 1953–1954. Taken in part from the thesis submitted by P. H. Leake in partial fulfillment of the requirements for the degree of Doctor of Philosophy at Duke University, 1954. This work was supported in part by the Chemical Corps, Fort Detrick, Md., under contract with Duke University.

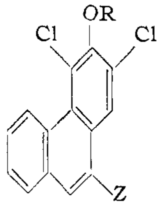
[2] C. K. Bradsher, F. C. Brown and P. H. Leake, THIS JOURNAL, **78**, 4400 (1956).

The new 3,5-dichlorohomoanisic acid (VI) required for the Pschorr synthesis was obtained by a series of reactions starting with ethyl 3,5-dichloro-4-hydroxybenzoate.[3] The hydroxy ester, in methanol solution, was methylated by the action of dimethyl sulfate and sodium methoxide, affording (by ester exchange) methyl 3,5-dichloroanisate II in 81% yield. Reduction of II by means of lithium aluminum hydride was effected in 96.5% yield, and the resulting carbinol III was converted to the bromide IV (99% yield). This was followed by the conversion of the bromide IV to the nitrile V (94.5%) which was hydrolyzed to the desired 2,5-dichlorohomoanisic acid (VI) (89% yield). The over-all yield for the five-step synthesis was 65%.

Condensation of VI with *o*-nitrobenzaldehyde yielded the arylcinnamic acid VII, which was reduced to the corresponding amine VIII. Amine VIII was cyclized to 2,4-dichloro-3-methoxyphenanthrene-10-carboxylic acid(IX). It was found that IX could best be decarboxylated by heating it in quinoline for only ten minutes.



VII, X = NO$_2$
VIII, X = NH$_2$



IX, R = CH$_3$, Z = COOH
X, R = CH$_3$, Z = H
XI, R = Z = H

It had been shown previously[2] that 4-chloro-3-methoxyphenanthrene, on chlorination with an equivalent quantity of sulfuryl chloride, yielded 4,9-dichloro-3-methoxyphenanthrene. It was somewhat surprising to find that the new 2,4-dichloro-3-methoxyphenanthrene (X), differing only in having a chlorine atom at the somewhat remote position 2, on chlorination afforded not the expected 2,4,9-trichloro-3-methoxyphenanthrene but an isomer of unknown structure. A possible explanation is that the methoxyl at position 3 is displaced from the plane of the ring by chlorine atoms at positions 2 and 4 and is therefore unable to exercise its usual activation at position 9.

When the ether X was heated with hydrobromic acid, a mixture of products was obtained, but when heated with pyridine hydrochloride, the ether afforded the desired 2,4-dichloro-3-phenanthrol (XI) in 18% yield. On chlorination, XI afforded the desired 2,4,9-trichloro-3-phenanthrol (I), identical with that obtained earlier[2] starting with 3-phenanthrol. This definitely confirmed the location of the chlorine atoms originally believed to be at positions 2 and 4.

Experimental[4]

Methyl 3,5-Dichloroanisate (II).—A solution containing 145 g. of ethyl 3,5-dichloro-4-hydroxybenzoate[3] in 300 ml. of methanol was stirred while 200 ml. of a methanol solution of sodium methoxide (prepared from 17.3 g. of sodium) was added cautiously. Next, 150 g. of dimethyl sulfate was added and the mixture refluxed for one hour. At the end of this period, enough solid sodium methoxide was added to make the solution basic. It was refluxed for another hour, then treated with more dimethyl sulfate, and refluxing continued. This alternate addition of reagents was repeated once more, then a large excess of dimethyl sulfate was added and refluxing continued for an additional ten hours. The cooled solution was poured into water and extracted with ether. The ethereal solution was washed with 10% sodium hydroxide solution and water, and then dried over sodium sulfate. Evaporation of the ether left 124 g. (81%) of a clear oil which soon crystallized, m.p. 75–77°. The analytical sample prepared by recrystallization from methanol consisted of small colorless needles, m.p. 76–77°.

Anal. Calcd. for $C_9H_8Cl_2O_3$: C, 45.98; H, 3.43. Found: C, 46.26; H, 3.65.

3,5-Dichloro-4-methoxybenzyl Alcohol (III).—In a flask protected from moisture, 18 g. of crushed lithium aluminum hydride was stirred with 600 ml. of anhydrous ether. To the resulting solution–suspension, a solution of 110 g. of methyl 3,5-dichloroanisate in 500 ml. of anhydrous ether was added at such a rate that gentle refluxing was maintained. When addition was complete, refluxing was continued for an additional 15 minutes, after which 500 ml. of cold 10% sulfuric acid was added. The ether layer was separated, washed with 10% sodium carbonate solution, and with water, dried, and concentrated. The residual oil was distilled, b.p. 149° (3–4 mm.), yield 87.5 g. (94%) of a white solid m.p. 45–46°. In another experiment 148 g. of II yielded 125.2 g. of the carbinol III (96.5%).

Anal. Calcd. for $C_8H_8Cl_2O_2$: C, 46.40; H, 3.89. Found: C, 46.67; H, 4.15.

3,5-Dichloro-4-methoxybenzyl Bromide (IV).—To a well-cooled solution of 3,5-dichloro-4-methoxybenzyl alcohol (III) in 500 ml. of anhydrous ether, 77 g. of phosphorus tribromide was added and the mixture allowed to stand in an ice-bath for 12 hours. At the end of this period, 20 ml. of methyl alcohol was added to destroy any unreacted phosphorus tribromide, and the ethereal solution washed with water, sodium bicarbonate solution and again with water. The solution was dried over sodium sulfate and evaporated. The residue consisted of 112 g. (99%) of a white crystalline solid, m.p. 61–63°, pure enough for further reactions. A sample recrystallized from ethanol was obtained as tiny colorless needles, m.p. 63–64°.

Anal. Calcd. for $C_8H_7BrCl_2O$: C, 35.59; H, 2.61. Found: C, 35.58; H, 2.68.

3,5-Dichloro-4-methoxybenzyl Cyanide (V).—To a boiling solution containing 112 g. of 3,5-dichloro-4-methoxybenzyl bromide (IV) in 400 ml. of 95% ethanol, 43 g. of potassium cyanide, dissolved in 60 ml. of water, was added in portions through the reflux condenser. An additional 40 ml. of water was used to effect the transfer. The mixture was refluxed for nine hours,[5] during which time it turned from yellow to red. It was poured into water and thrice extracted with ether. The extract was washed, dried, and concentrated, and the residue distilled, b.p. 163° (4–5 mm.), yield 83.3 g. (91%). The distillate solidified to a colorless solid, m.p. 62–63°. An analytical sample, m.p. 63–64°, was obtained by recrystallization from dilute ethanol.

Anal. Calcd. for $C_8H_7Cl_2NO$: C, 50.03; H, 3.42. Found: C, 50.30; H, 3.27.

One run which was allowed to reflux for 17 hours yielded a second fraction, b.p. 171–210° (4–5 mm.). Four recrystallizations from ethanol yielded clusters of colorless needles, m.p. 122–122.5°. This material can be hydrolyzed to 3,5-dichlorohomoanisic acid and has the composition expected for **3,5-dichlorohomoanisamide**.

Anal. Calcd. for $C_9H_9Cl_2NO_2$: C, 46.18; H, 3.88. Found: C, 46.54; H, 4.02.

3,5-Dichlorohomoanisic Acid (VI).—The hydrolysis of 3,5-dichloro-4-methoxybenzyl cyanide (128 g.) was carried out by refluxing it for several hours with 20% alcoholic potassium hydroxide. Worked up in the usual way, this afforded 115 g. of the acid VI, m.p. 131–133°. The analytical sample crystallized from dilute ethanol as elongated rectangular plates, m.p. 135–136°.

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(3) D. S. Tarbell, J. W. Wilson and P. E. Fanta, *Org. Syntheses*, **29**, 35 (1949).

(4) All analyses are by Micro-Tech Laboratories, Skokie, Ill. All melting points are corrected.

(5) In a subsequent experiment a 94.5% yield was obtained in only seven hours.

Anal. Calcd. for $C_9H_8Cl_2O_3$: C, 45.98; H, 3.45; Cl, 30.17. Found: C, 46.02, H, 3.57; Cl, 29.94.

o-Nitro-α-(3,5-dichloro-4-methoxyphenyl)-cinnamic Acid (VII).—The sodium salt of 3,5-dichlorohomoanisic acid was prepared by treating 21.1 g. of the acid with a solution of sodium methoxide formed by dissolving 2.1 g. of sodium in 50 ml. of methanol. The methanol was evaporated and the residue dried at 100° for 12 hours. The resulting salt, along with 14.9 g. of *o*-nitrobenzaldehyde and 46 g. of acetic anhydride, was stirred at 100° for 23 hours. At the end of this period 50 ml. of water was added to decompose the anhydride. The mixture was cooled and extracted with ether, and the ethereal solution was washed with water and then extracted with 5% sodium hydroxide solution. Acidification of the alkaline extract afforded a brown oil which solidified on standing and, on recrystallization from dilute alcohol, afforded 15.4 g. (45.5%) of a colorless product, m.p. 187–189°.

The analytical sample was obtained as very small colorless needles, m.p. 190–191°, by further recrystallization.

Anal. Calcd. for $C_{16}H_{11}Cl_2NO_5$: C, 52.19; H, 3.01. Found: C, 52.05; H, 2.90.

o-Amino-α-(3,5-dichloro-4-methoxyphenyl)-cinnamic Acid (VIII).—A solution containing 14.4 g. of *o*-nitro-α-(3,5-dichloro-4-methoxyphenyl)-cinnamic acid (VII) in 50 ml. of dilute ammonium hydroxide solution was added to a hot (93°) mixture containing 100 g. of ferrous sulfate dihydrate, 300 ml. of water and 250 ml. of concentrated ammonium hydroxide. After a 15-minute heating period the reaction mixture was filtered and the precipitate washed with hot water. Careful acidification of the filtrate afforded a yellow precipitate which was collected and air-dried. The yield was 10.15 g. (79%), m.p. 183–184°. The analytical sample crystallized from dilute ethanol as irregular yellow plates, m.p. 184.5–185°.

Anal. Calcd. for $C_{16}H_{13}Cl_2NO_3$: C, 56.82; H, 3.87. Found: C, 56.54; H, 4.09.

2,4-Dichloro-3-methoxyphenanthrene-10-carboxylic Acid (IX).—To 600 ml. of 25% sulfuric acid, maintained at a temperature below 5° and stirred vigorously, a solution containing 10.15 g. of *o*-amino-α-(3,5-dichloro-4-methoxyphenyl)-cinnamic acid, 1.26 g. of sodium hydroxide and 2.5 g. of sodium nitrite in 75 ml. of water was added dropwise. After addition was complete, stirring was continued for one hour at 4° and, after addition of 4 g. of copper bronze, for an additional 35 hours at room temperature. The mixture was heated to 80° for an additional two hours, then cooled and extracted with methylene chloride. Some solid material was removed by filtration and the methylene chloride layer dried and concentrated. The residue crystallized from acetic acid as needles, m.p. 269–271°, yield 4.8 g. (50%).

The solid removed from the methylene chloride by filtration was stirred with concentrated sodium hydroxide for two hours at steam-bath temperature. The resulting solution was filtered and acidified affording 1.55 g., m.p. 271–273°; total yield 6.3 g. (65%). The analytical sample was obtained as colorless needles, m.p. 273–274°.

Anal. Calcd. for $C_{16}H_{10}Cl_2O_3$: C, 59.83; H, 3.14; Cl, 22.08. Found: C, 59.78; H, 3.20; Cl, 22.60.

Hydrazide of 2,4-Dichloro-3-methoxyphenanthrene-10-carboxylic Acid.—Six-tenths gram of the ethyl ester (m.p. 92–93°) of the above acid IX was refluxed with 5 ml. of 100% hydrazine hydrate and 10 ml. of dry amyl alcohol until a quantity of solid had precipitated. The crude product (0.5 g., 85%) melted at 244–246°.

The analytical sample was obtained as colorless crystals from methyl alcohol, m.p. 248–249°.

Anal. Calcd. for $C_{16}H_{12}Cl_2N_2O_2$: C, 57.33; H, 3.61. Found: C, 57.48; H, 3.73.

2,4-Dichloro-3-methoxyphenanthrene (X).—A solution containing 5.5 g. of 2,4-dichloro-3-methoxyphenanthrene-10-carboxylic acid in 100 ml. of quinoline was heated with 2 g. of copper-bronze at 210 ± 5° for ten minutes. The reaction mixture was cooled and filtered and the filtrate diluted with 400 ml. of ether and again filtered. The ethereal solution was washed well with 10% hydrochloric acid, water, sodium hydroxide and again with water. The ethereal solution was dried and concentrated and the residue dissolved in 300 ml. of dry benzene and passed through a 25-cm. column of activated alumina. Elution was effected using an additional 300 ml. of benzene. The residue obtained by evaporation of the benzene was recrystallized from ethanol as needles, m.p. 102–103°, yield 1.82 g. On acidification of the sodium hydroxide extract, 0.9 g. of starting material was recovered; thus, the yield based on acid IX consumed is 61%.

Anal. Calcd. for $C_{15}H_{10}Cl_2O$: C, 65.00; H, 3.64. Found: C, 64.91; H, 3.94.

2,4,x-Trichloro-3-methoxyphenanthrene.—To 0.55 g. of 2,4-dichloro-3-methoxyphenanthrene dissolved in 7 ml. of acetic acid, 0.27 g. of sulfuryl chloride was added. After one hour at room temperature, the solvent was removed under vacuum. On crystallizing the residue from ethanol, 43 mg. of white solid was obtained. The filtrate was evaporated and the residue was taken up in 2 ml. of benzene which was then diluted with 100 ml. of 60–90° ligroin and the solution chromatographed on alumina. Elution was effected by addition of 100 ml. of ligroin followed by 100 ml. of benzene. Of the twelve 25-ml. fractions taken, fractions 4–9 afforded a crystalline residue upon evaporation and were crystallized from ethanol as long white fluffy needles, m.p. 145–149°, yield 187 mg. The combined yield of crude solid was 230 mg. (37%), m.p. 145–155°. The analytical sample melted at 161–161.5°.

Anal. Calcd. for $C_{15}H_9OCl_3$: C, 57.82; H, 2.91; Cl, 34.14. Found: C, 57.85; H. 2.99; Cl, 34.25.

2,4-Dichloro-3-phenanthrol (XI).—One gram of 2,4-dichloro-3-methoxyphenanthrene (X) and 3 g. of pyridine hydrochloride were heated for 11 hours at 200 ± 10°. The reaction mixture was cooled and dissolved by treatment with acetone, water and ether. The ethereal layer was washed well with dilute hydrochloric acid, then with water, and finally with 5% sodium hydroxide solution. When solid carbon dioxide was added to the alkaline solution, 0.4 g. of a tan precipitate was formed. This product crystallized as white micro needles from isoöctane m.p. 151–152°, yield 0.179 g. (18%).

Anal. Calcd. for $C_{14}H_8Cl_2O$: C, 63.90; H, 3.06; Cl, 26.95. Found: C, 63.72; H, 3.32; Cl, 26.97.

2,4,9-Trichloro-3-phenanthrol (I).—When 22 mg. of 2,4-dichloro-3-phenanthrol (XI) was dissolved in 0.5 ml. of acetic acid and allowed to react for 0.5 hour with 12 mg. of sulfuryl chloride, 13 mg. of product, m.p. 164–165°, crystallized from the reaction mixture. This product gave no mixed-melting point depression with a sample of 2,4,9-trichloro-3-phenanthrol,[2] m.p. 165.5–166°, obtained from 3-phenanthrol.

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