[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE VIRGINIA POLYTECHNIC INSTITUTE]

The Synthesis of the Six Isomeric 9-Dimethylphenyl-1,2-benzanthracenes[1,2]

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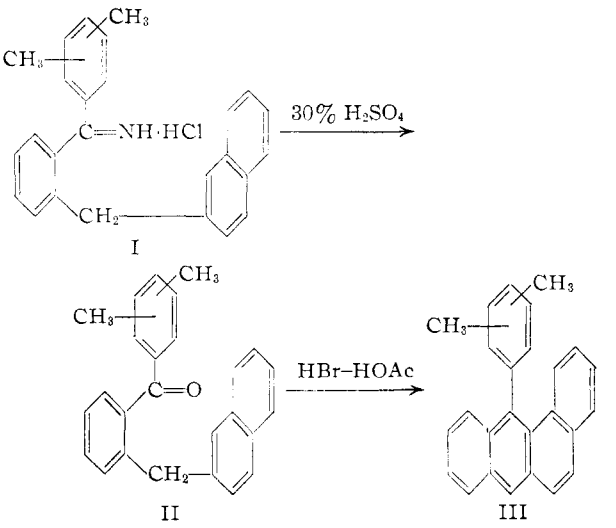
Using a previously described method, the synthesis of one new ketimine hydrochloride, six new ketones and six new hydrocarbons has been accomplished. Bradsher's aromatic cyclodehydration reaction[3] has been extended to the 9-dimethylphenyl-1,2-benzanthracene system.

Previous publications have shown the usefulness of Bradsher's aromatic cyclodehydration reaction in the synthesis of certain aryl-1,2-benzanthracenes.[4,5,6] We felt that the further extension of this reaction to the synthesis of the six isomeric 9-dimethylphenyl-1,2-benzanthracenes would be interesting for several reasons. First, these hydrocarbons might be carcinogenic. Second, all these hydrocarbons, with the exception of the 2,6-isomer, should be capable of undergoing dehydrogenation to give the respective 1,2,3,4-dibenzopyrenes[7] which would be difficult to prepare by other means. Finally, these hydrocarbons are of interest from still another point of view. The molecular models indicate and the evidence presented in this work proves quite conclusively that the substituted phenyl ring in the 9-position is not coplanar with the benzanthracene part of the molecule. If the model of a dimethylphenyl derivative[8] is examined, the possibility of the existence of two enantiomorphic forms becomes obvious, acknowledging restricted rotation about the 9–1′ pivot bond. Although similar cases concerning biphenyl derivatives are known,[9] only a few of them seem as illustrative. Although we did not attempt the separation of these antipodes in the present work, the fact that they will be made relatively easily obtainable appears to be of importance.

The reaction between 2-(2-cyanobenzyl)-naphthalene[6] and the appropriate Grignard reagent led to the ketimine hydrochlorides (I). The ease of hydrolysis of the ketimines varies greatly with the structure of the compound. The unsubstituted ketimine salt can be partially hydrolyzed with boiling water; the 2,6-dimethyl compound was successfully hydrolyzed only by heating it with 40% sulfuric acid at 180°. The susceptibility to partial hydrolysis seems to be specially developed in some of the unsymmetrical dimethyl compounds. Consequently, the preparation of an analytical sample was made so difficult that although all six ketimine hydrochlorides were isolated as such, only the 2,6-dimethyl compound was successfully analyzed.



The ketimine hydrochlorides were hydrolyzed to their corresponding ketones II in good yield by heating them with 30% sulfuric acid in the presence of a layer of toluene. The ketones form colorless crystals or very viscous oils of generally lower melting or boiling points than those in the 1-naphthyl series.[5]

The hydrocarbons III were prepared by heating the ketones with a mixture of hydrobromic and acetic acids in a sealed tube at about 180°. The cyclizations in the 2-naphthyl series are confronted with problems which do not exist in the 1-naphthyl series.[5] While cyclization occurs predominantly into the α-position, as is to be expected, some cyclization seems to occur into the β-position. It is also possible that at the high temperatures employed in preparing the hydrocarbons, a cyclodehydrogenation occurred after the initial cyclodehydration thereby yielding some 1,2,3,4-dibenzopyrenes. The yields of the hydrocarbons III were generally somewhat lower than those in the 1-naphthyl series, and there was always present a small amount (1–5%) of a deeply yellow material which could be separated only after many recrystallizations, repeated chromatography, or by Cook's method using maleic anhydride.[10] This yellow fraction which accompanied every cyclization possessed a strong yellowish-green fluorescence which disappeared after irradiation with strong ultraviolet light, and formed an addition compound with maleic anhydride. Both of these phenomena can be observed with unsubstituted tetracene, the first being presumably due to the formation of photooxides[11] and the second to the easy formation of a

(1) Presented before the Section of Organic Chemistry at the Seventh Southeastern Regional Meeting of the American Chemical Society, Columbia, South Carolina, November, 1955.

(2) This paper has been abstracted from the Doctorate thesis presented to the Virginia Polytechnic Institute by Alexej Bořkovec in 1955.

(3) C. K. Bradsher, THIS JOURNAL, **62**, 486 (1940).

(4) F. A. Vingiello, A. Bořkovec and J. Shulman, *ibid.*, **77**, 2320 (1955).

(5) F. A. Vingiello and A. Bořkovec, *ibid.*, **77**, 3413 (1955).

(6) F. A. Vingiello and A. Bořkovec, *ibid.*, **77**, 4823 (1955).

(7) E. Clar, "Aromatische Kohlenwasserstoffe Polycyclische System, Zweite Auflage," Springer-Verlag, Berlin, 1952, p. 340.

(8) The 2′,6′- and 3′,5′- isomers would not be expected to have enantiomorphs.

(9) E. Clar and D. G. Stewart, *J. Chem. Soc.*, 4738 (1952).

(10) J. W. Cook, *ibid.*, 3273 (1931).

(11) C. Dufraisse and R. Horclois, *Bull. soc. chim.*, **3**, 1880 (1936).

colorless adduct.[12] The benzanthracenes (III) are colorless, possess a blue fluorescence and do not add maleic anhydride under the same conditions. It was attempted several times to isolate the yellow by-product in crystalline form, but without success. Several other unidentified by-products were found.

The ultraviolet spectra of the hydrocarbons III were taken and the maxima are recorded in Table II. These spectra imply that the 9-phenyl group is not coplanar with the 1,2-benzanthracene group.[13]

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Experimental[14,15]

2-(2-Naphthylmethyl)-2′,6′-dimethyldiphenylketimine Hydrochloride (I, 2′,6′-Dimethyl).—A Grignard reagent was prepared from 63 g. (0.27 mole) of 2,6-dimethyliodobenzene and 6.6 g. (0.27 mole) of magnesium in 300 ml. of dry ether. After all the metal had reacted, the ether was replaced with a solution of 36.5 g. (0.15 mole) of 2-(2-naphthylmethyl)-benzonitrile[6] in 300 ml. of dry toluene and the solution was heated under reflux overnight. The mixture was then decomposed with 30 ml. of 20% ammonium chloride solution. The yellow precipitate which formed was separated and boiled for two hours with 20% hydrochloric acid. The undissolved yellow ketimine salt was separated and recrystallized from a mixture of dioxane and petroleum ether (1:5); m.p. 200° dec. An additional amount of ketimine salt was obtained from the toluene solution by precipitation with concd. hydrochloric acid. The combined ketimine salts were decomposed with boiling 20% sodium hydroxide solution, the free imine extracted with benzene, and the hydrochloride precipitated with concd. hydrochloric acid; yield 49 g. (85%). An analytical sample was prepared from the crude ketimine hydrochloride by recrystallization from a mixture of ethanol and acetone (1:10). It formed small lemon-yellow prisms, m.p. 192° dec.[16]

Anal. Calcd for $C_{26}H_{24}NCl$: C, 80.91; H, 6.26. Found: C, 80.81; H, 6.24.

2-(2-Naphthylmethyl)-2′,6′-dimethylbenzophenone (II, 2′,6′-Dimethyl).—A suspension of 10 g. of the above ketimine hydrochloride in 50 ml. of 40% sulfuric acid was sealed in a Carius tube and heated in a Carius furnace at 180° for eight hours. The tube was then cooled to about 5°, opened, the brown solid separated, washed with water and recrystallized from acetic acid giving brown prisms, m.p. 84–87°, yield 6.6 g. (73%). Several recrystallizations from ethanol gave colorless prisms, m.p. 86.5–87°.

Anal. Calcd. for $C_{26}H_{22}O$: C, 89.10; H, 6.33. Found: C, 89.33; H, 6.38.

2-(2-Naphthylmethyl)-2′,5′-dimethylbenzophenone (II, 2′,5′-Dimethyl).—A Grignard reagent was prepared from 5.6 g. (0.24 mole) of magnesium, 43 g. (0.23 mole) of 2,5-dimethylbromobenzene and 250 ml. of dry ether. The ether was replaced with a solution of 37 g. (0.15 mole) of 2-(2-naphthylmethyl)-benzonitrile in 250 ml. of dry toluene, and the mixture was heated under reflux for five hours. The mixture was decomposed with 20% ammonium chloride solution, the toluene layer separated, and the ketimine salt precipitated with concd. hydrochloric acid. The crystals were separated, mixed with 200 ml. of 30% sulfuric acid and 100 ml. of toluene, and heated under reflux for seven hours. The toluene layer was separated, the solvent removed, and the resulting oil distilled *in vacuo*. A fraction distilling at 242° (1.2 mm.) was collected and again distilled under reduced pressure. The ketone was recovered as a yellow viscous oil, b.p. 236–238° (1.0 mm.), yield 44 g. (84%).

Anal. Calcd. for $C_{26}H_{22}O$: C, 89.10; H, 6.33. Found: C, 89.05; H, 6.54.

The remaining ketones were prepared in a similar way.

TABLE I

ISOMERIC NEW KETONES II

Me groups at	Yield, %	B.p., °C.	Mm.	Analyses,[c] %, found Carbon	Hydrogen
2,3	77	240–243	1.0	88.92	6.31
2,4	53	235	1.0	89.29	6.11
2,5	84	236–238	1.0	89.05	6.54
2,6	73	[a]		89.33	6.38
3,4	80	238	1.0	89.01	6.41
3,5	82	[b]		88.74	6.20

[a] M.p. 86.5–87°, crystallized from ethanol. [b] M.p. 124.5–125° crystallized from ethanol. [c] Calcd. for $C_{26}H_{22}O$: C, 89.10; H, 6.33.

9-(3′,5′-Dimethylphenyl)-1,2-benzanthracene (III, 3′,5′-Dimethyl).—A mixture of 2.0 g. of the corresponding ketone, 20 ml. of acetic acid and 10 ml. of 48% hydrobromic acid was sealed in a Carius tube and heated in a Carius furnace at 180° for four hours. The tube was cooled, opened and the contents extracted with benzene and chromatographed[17] on alumina. The first fraction, eluted with pe-

TABLE II

ISOMERIC NEW HYDROCARBONS[a] III

Me groups at	Yield, %	M.p., °C.	Analyses, %, found[e] Carbon	Hydrogen
2,3	34	152–153	93.94	6.14
2,4	75	58–64[b]	93.61	6.30
2,5	34	64–69[b]	93.46	6.28
2,6	6[c]	123.5	94.00	6.25
3,4	65	120–120.5[d]	93.72	6.08
3,5	79	230	93.69	6.07

[a] The ultraviolet spectra of the hydrocarbons were determined with a Beckman spectrophotometer (model DU, 1-cm. silica cell) at a concn. of 10 mg./l. using 95% EtOH as the solvent. The curves for all six hydrocarbons are practically identical. The wave length maxima for III where the methyl groups are at the 3′- and 4′-positions are: λ 226 mμ, λ 259 mμ, λ 269 mμ, λ 279 mμ, λ 290 mμ, λ 337 mμ, λ 351 mμ, λ 362 mμ. [b] These formed colorless glassy solids which resisted all attempts at crystallization. The values given are for melting ranges of small particles scraped from these solids. [c] This value is given only to complete the table. The hydrocarbon could not be prepared as were its isomers but was successfully made by a new method currently being investigated. [d] Two polymorphic forms grew from ethanolic solution: first, colorless crystals, m.p. 142–143°; second, colorless crystals, m.p. 120–120.5°. The higher melting form was less soluble in ethanol, acetone and ether and was preferentially formed from very concentrated, warm solutions. Both forms yielded red solutions with concd. H_2SO_4 which turned greenish-brown after long standing. A composite sample of the polymorphs was taken for analysis. [e] Calcd. for $C_{26}H_{20}$: C, 93.94; H, 6.06.

(12) E. Clar, *Ber.*, **65**, 518 (1932).

(13) R. N. Jones, THIS JOURNAL, **67**, 2127 (1945).

(14) All melting points are corrected.

(15) All the analyses were carried out by the Micro-Tech Laboratories, Skokie, Ill.

(16) The hydroiodides seem to be in general less soluble, and their formation may sometimes lead to appreciable losses. For example, in the preparation of the 2,6-dimethyl compound, 2,6-dimethyliodobenzene was used as a starting material. During the decomposition of the mixture resulting from the reaction between the Grignard reagent and the nitrile, the ketimine hydroiodide precipitated together with the magnesium salts and had to be recovered by quite a lengthy procedure.

(17) For this and other chromatographic separations a glass column (60 × 1 cm.) wet-packed (purified petroleum ether, 50–90°) with Fisher alumina for chromatographic analysis (80–200 mesh) was used. The hydrocarbon mixture was applied to the column in the minimum quantity of benzene and usually eluted with petroleum ether. If the ultraviolet lamp used to follow the development of the chromatogram was allowed to irradiate the column for protracted periods, some fractions seemed to be noticeably changed. Best results were obtained when the lamp was used sparingly and direct illumination by even visible light was minimized as far as practicable. Repeated chromatography was necessary in some instances.

troleum ether, yielded 1.5 g. (79%) of colorless crystals, m.p. 230°. The second fraction, eluted with a mixture of benzene and petroleum ether (1:4), gave 0.10 g. of unidentified yellow material. The third fraction, eluted with benzene, gave 0.25 g. of an unidentified, deeply red material.

Anal. Calcd. for $C_{26}H_{20}$: C, 93.94; H, 6.06. Found: C, 93.69; H, 6.07.

The other hydrocarbons were prepared in a similar way.

BLACKSBURG, VIRGINIA

[CONTRIBUTION FROM THE UNITED STATES DEPARTMENT OF AGRICULTURE, AGRICULTURAL RESEARCH SERVICE, ENTOMOLOGY RESEARCH BRANCH]

The Synthesis of *dl*-Sesamin and *dl*-Asarinin[1]

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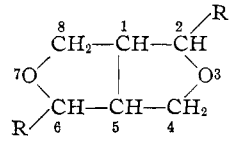
dl-Sesamin—2,6-bis-(3,4-methylenedioxyphenyl)-*cis*-3,7-dioxabicyclo[3.3.0]octane—and its diastereoisomer, *dl*-asarinin, have been synthesized. Separate reductions of the oily and crystalline forms of the diethyl ester of 2,3-bis-(3,4-methylenedioxybenzoyl)-succinate (X) with lithium aluminum hydride gave different tetrahydroxy compounds XIa, XIb. Compound XIa, from the reduction of the oily form of X upon heating with ethanolic hydrochloric acid, lost two molecules of water to give *dl*-sesamin. *dl*-Sesamin has been epimerized in part to *dl*-asarinin. The tetrahydroxy compound XIb, from the reduction of the crystalline form of X upon heating with ethanolic hydrochloric acid, lost only one molecule of water to give as the main product a tetrahydrofuran compound XII. The stereochemistry of the synthesis is discussed and an explanation for the course of the synthesis is presented. Stereochemical considerations indicate that a third racemic isomer of *dl*-sesamin and *dl*-asarinin should be possible.

Although the chemical structure of sesamin and asarinin shown in formula I was proved in 1939 by Bruchhausen and Gerhard,[2] a synthesis of these compounds has not been reported. This paper describes the synthesis of the racemic forms of these compounds.



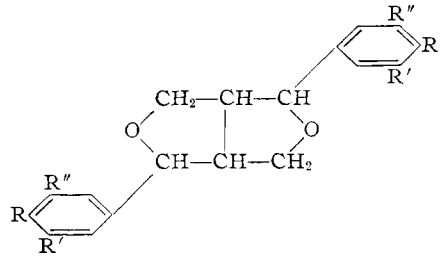
I, R = 3,4-methylenedioxyphenyl

The known optically active stereoisomers having the sesamin formula (I) are *d*- and *l*-sesamin (rotations +68° and −68°), isosesamin and asarinin (rotations +122° and −122°). *d*-Sesamin is a constituent of the unsaponifiable fraction of sesame oil. Each of the other isomers has been found naturally.[3-6]

Sesamin, asarinin and isosesamin became important when they were found[7,8] to increase markedly the insecticidal potency of pyrethrins without themselves being insecticidal. Haller, *et al.*,[7] demonstrated that the 3,4-methylenedioxyphenyl group was essential for sesamin's synergistic activity with pyrethrins. This discovery led to the commercial development of such excellent synergists as piperonyl butoxide,[9] sulfoxide,[10] *n*-propyl isomer,[11] and piperonyl cyclonene.[9]

Treatment of *d*-sesamin with ethanolic hydrochloric acid results in an equilibrium mixture of it and its diastereoisomer isosesamin.[3,4] Similar treatment of asarinin gives an equilibrium mixture of it and *l*-sesamin. These changes result from the reversible epimerization of the groups on carbon atoms 2 and 6.

Paralleling the structural studies on sesamin and its isomers were the investigations on pinoresinol (IIa) and eudesmin (IIb). The relationship of these compounds to asarinin and sesamin was established by the conversion of asarinin and *d*-sesamin to eudesmin and pinoresinol dimethyl ether,[12] the epimeric forms of which are also known.[13]



IIa, R = OH, R′ = OCH_3, R″ = H for pinoresinol
IIb, R = R′ = OCH_3, R″ = H for eudesmin and pinoresinol dimethyl ether
IIc, R = OH, R′ = R″ = OCH_3 for syringaresinol

Each of the aforementioned compounds contains a 3,7-dioxabicyclo[3.3.0]octane nucleus with 3,4-substituted aryl groups in the 2- and 6-positions. Further confirmation of the correctness of this structure was supplied by Erdtman and Gripenberg[14] and Beroza,[15] who isolated the *di*-γ-lactone of α,β-bis-(hydroxymethyl)-succinic acid (III) as an oxidation product from pinoresinol and from *d*-sesamin and asarinin. Because dilactone III was optically active, they concluded that the hydrogen atoms at positions 1 and 5 must be in the *cis* configuration. A *trans* configuration would give a symmetrical molecule which could not exhibit optical activity.

(1) Presented at the 128th Meeting of the American Chemical Society, Minneapolis, Minn., September 15, 1955.
(2) F. von Bruchhausen and H. Gerhard, *Ber.*, **72**, 830 (1939).
(3) T. Kaku, N. Kutani and J. Takahashi, *J. Pharm. Soc. Japan*, **56**, 80 (1936).
(4) Huang-Minlon, *Ber.*, **70**, 951 (1937).
(5) T. Kaku and H. Ri, *J. Pharm. Soc. Japan*, **57**, 184 (1937).
(6) J. B. Davenport and M. D. Sutherland, *Australian J. Chem.*, **7**, 384 (1954).
(7) H. L. Haller, F. B. La Forge and W. N. Sullivan, *J. Econ. Entomol.*, **35**, 247 (1942).
(8) C. Eagleson, U. S. Patent 2,202,145 (May 28, 1940).
(9) H. Wachs, *Science*, **105**, 530 (1947).
(10) M. E. Synerholm, A. Hartzell and V. Cullmann, *Contrib. Boyce Thompson Inst.*, **15**, 35 (1947).
(11) M. E. Synerholm and A. Hartzell, *ibid.*, **14**, 79 (1945).
(12) T. Kaku and H. Ri, *J. Pharm. Soc. Japan*, **57**, 1015 (1937).
(13) T. Kaku and H. Ri, *Keizyo J. Med.*, **9**, 5 (1938).
(14) H. Erdtman and J. Gripenberg, *Acta Chem. Scand.*, **1**, 71 (1947).
(15) M. Beroza, THIS JOURNAL, **77**, 3332 (1955).