2,3-Dihydroxy-6-methoxyquinoline (X, R = OCH_3).—To a stirred, refluxing solution of 1.0 g. (0.018 mole) of potassium hydroxide in 100 ml. of water was added dropwise over a ten-minute period, a solution of 5-methoxy-2-(N-chloracetylamino)-benzaldehyde (0.8 g., 0.0035 mole) in 20 ml. of hot *n*-propyl alcohol. The solution was refluxed and stirred for two hours and then concentrated to 30 ml. After treatment of the reaction mixture with charcoal followed by acidification with concentrated hydrochloric acid, a light tan solid separated which was filtered and washed with water; yield 0.5 g. (75%). One recrystallization from water with charcoal gave fine, white needles, m.p. 231–232°.

For analysis, the compound was recrystallized successively from aqueous 50% methanol and aqueous 20% methanol using charcoal each time, m.p. 228–230°.

Anal. Calcd. for $C_{10}H_9O_3N$: C, 62.82; H, 4.75; N, 7.32. Found: C, 62.64; H, 4.85; N, 7.45.

The compound gave an intense blue coloration with aqueous ferric chloride.

Acetylation of the crude quinoline (0.6 g.) with acetic anhydride (5 ml.) and pyridine (3 drops) at 90° for two hours gave, from aqueous 20% methanol, nearly white needles, m.p. 185–186°.

Anal. Calcd for $C_{12}H_{11}O_4N$: C, 61.80; H, 4.75; N, 6.00. Found: C, 61.82; H, 4.67; N, 5.95.

2,3,6-Trihydroxyquinoline (XI, R = OH).—Crude 2,3-dihydroxy-6-methoxyquinoline (0.5 g., 0.0026 mole) was refluxed with a mixture of 48% hydrobromic acid (4 ml.) and glacial acetic acid (4 ml.) for three hours. The reddish-brown solution was diluted with water (150 ml.) and refrigerated for three days. The tan crystals which separated were filtered and recrystallized from hot water using charcoal to give small, cream-colored needles (105 mg., 23%), m.p. 305–315°.

For analysis, the product was recrystallized twice from 30% aqueous methanol using charcoal each time, m.p. 318–319° dec.

Anal. Calcd. for $C_9H_7O_3N$: C, 61.01; H, 3.99; N, 7.91. Found: C, 60.67; H, 4.13; N, 8.14.

A mixed melting point with 2,3,6-trihydroxyquinoline prepared from 4-acetoxyhydrazobenzene showed no depression. Both specimens of 2,3,6-trihydroxyquinoline had identical infrared spectra (Nujol mull).

The acetyl derivative, prepared in the usual manner, melted at 228–229° and did not depress the m.p. of the acetyl derivative of 2,3,6-trihydroxyquinoline prepared from 4-acetoxyhydrazobenzene.

Anal. Calcd. for $C_{11}H_9O_4N$: N, 6.39. Found: N, 6.28.

2,3-Dihydroxyquinoline (VII, R = H). 2-(N-Chloracetamino)-benzaldehyde (X, R = H).—To a solution of 2-aminobenzaldehyde[13] (1.50 g., 0.0124 mole) in anhydrous ether (100 ml.) was added dropwise chloroacetic anhydride (2.5 g., 0.0146 mole) in anhydrous ether (75 ml.) and the reaction mixture allowed to stand at room temperature overnight. After removal of the solvent under reduced pressure, the resulting solid was recrystallized from 80% methanol to give 1.9 g. (78% of theory) of colorless needles, m.p. 105–106°.

Anal. Calcd. for $C_9H_8O_2NCl$: C, 54.70; H, 4.08; N, 7.09; Cl, 17.94. Found: C, 54.58; H, 4.25; N, 7.20; Cl, 17.94.

2,3-Dihydroxyquinoline (XI, R = H).—To a boiling solution of 2-(N-chloracetamino)-benzaldehyde (0.80 g., 4.05 mmoles) in methanol (20 ml.) and water (50 ml.) was added a solution of potassium hydroxide (1.0 g.) in 10 ml. of water in one portion. After refluxing for one hour, the methanol was distilled, the solution treated with charcoal and filtered. On acidification of the filtrate with concentrated hydrochloric acid, a white solid separated which after filtering and washing with 10 ml. of cold water weighed 0.60 g. (92%). The product was recrystallized successively from aqueous 10% methanol (190 ml.), methanol and finally water, using charcoal each time to give small, snow-white needles, m.p. 256–257° uncor. (recorded[3] m.p. 258°). A mixed m.p. with 2,3-dihydroxyquinoline prepared through hydrazobenzene[3] showed no depression. The infrared spectra (Nujol mull) of both samples were identical.

The acetyl derivative made in the usual way melted at 211–212° (recorded[3] m.p. 214°) and did not depress the melting point of the acetyl derivative of 2,3-dihydroxyquinoline made by Diels and Reese[3] *via* hydrazobenzene.

[13] E. Bamberger and E. Demuth, *Ber.*, **34**, 1329 (1901).

CAMAS, WASHINGTON

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Free Radical Substitution in 3,4-Benzpyrene[1]

BY WALTER CONWAY AND D. STANLEY TARBELL

RECEIVED NOVEMBER 10, 1955

Irradiation of 3,4-benzpyrene and thioglycolic acid with a mercury arc in quartz vessels gives a 43% yield of 5-benzpyrenylacetic acid, whose structure is proved by decarboxylation to 5-methylbenzpyrene. 5-Mercaptobenzpyrene appears to be formed also. 5-Benzpyrenylmercaptoacetic acid has been synthesized, and irradiation of its methyl ester decomposes it to yield some methyl 5-benzpyrenylacetate. Azoisobutyronitrile and benzpyrene yield a small amount of a monocyanopropyl product, and an appreciable amount of 1,2-bis-(cyanopropyl)-1,2-dihydrobenzpyrene. The significance of these results for the theoretical calculations of reactivity of benzpyrene is discussed. An improved paper chromatographic technique for benzpyrene and its derivatives is described. Numerous experiments show that benzpyrene is not rapidly attacked by RS radicals.

The study of the action of free radicals on aromatic nuclei is of considerable theoretical and practical interest. The impetus for the present study on free radical attack on the carcinogenic hydrocarbon 3,4-benzpyrene arose during an investigation[2] of the nature of the chemical combination between benzpyrene and skin protein.[3] A possible route for attachment of benzpyrene to cell constituents would involve a free radical attack on the hydrocarbon by a grouping present in tissue.[4] We have therefore investigated a number of systems expected to lead to free radical formation in the presence of benzpyrene, particularly systems in which sulfur radicals, RS·, would be formed.

Irradiation of hydrogen sulfide or a mercaptan by a mercury arc is known to yield RS radicals,[5] which can add to carbon–carbon double bonds. We have found, however, that irradiation of thioglycolic acid and benzpyrene (I) by a mercury arc in a

[1] This research was supported in part by the United States Air Force, through the Office of Scientific Research of the Air Research and Development Command, and in part by the Damon Runyon Memorial Fund for Cancer Research.

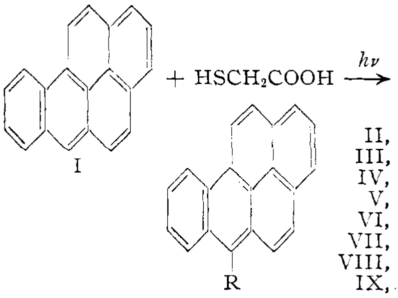
[2] D. S. Tarbell, E. G. Brooker, P. Seifert, A. Vanterpool, C. J. Claus and W. Conway, *Cancer Research*, **16**, 37 (1956).

[3] *Cf.* E. C. Miller, *ibid.*, **11**, 100 (1951).

[4] *Cf.* E. C. Kooyman and J. W. Heringa, *Nature*, **170**, 661 (1952).

[5] W. E. Vaughan and F. F. Rust, *J. Org. Chem.*, **7**, 472 (1942); J. I. Cunneen, *J. Chem. Soc.*, 36 (1947).

quartz vessel yields 5-benzpyrenylacetic acid (II) in 43% yield (based on unrecovered benzpyrene).



II, R = CH_2COOH
III, R = CH_2COOCH_3
IV, R = $CH_2COOC_2H_5$
V, R = CH_3
VI, R = SH
VII, R = SCH_3
VIII, R = SCH_2COOH
IX, R = SCH_2COOCH_3

The free acid II was characterized through the crystalline methyl and ethyl esters III and IV. The structure of the product was proved by saponification of the methyl ester, followed by decarboxylation with copper chromite in boiling quinoline to 5-methylbenzpyrene, which was shown to be identical with an authentic sample,[6] prepared by reduction of the 5-aldehyde[6] by the modified[7] Wolff–Kishner procedure. Irradiation of thioglycolic acid and benzpyrene thus does not yield products derived from SCH_2COOH radicals.

If the reaction proceeds by way of dissociation of thioglycolic acid into CH_2COOH and SH radicals, followed by attack of these on benzpyrene, a mercaptobenzpyrene should also be present in the mixture. Attempts were made to identify 5-mercaptobenzpyrene by conversion to methyl 5-benzpyrenylmercaptoacetate (IX), a sample of which was synthesized for comparison. Treatment of the reaction mixture with chloroacetic acid, followed by methylation with diazomethane and chromatography on paper[8] showed a spot which had the same R_f value as a known sample of IX; the crystalline product could not be isolated, however.

Irradiation of a known sample of IX, in hexane, by the mercury arc, caused its decomposition. The photolysis was followed by paper chromatography, and it was found that the spot corresponding to IX disappeared, and a spot with the same R_f value as methyl benzpyrenylacetate (III) appeared, in addition to two other spots, of R_f 0.07 and 0.97, respectively.

Irradiation of benzpyrene and dimethyl dithiodiglycolate in quartz vessels gives methyl 5-benzpyrenylacetate in 57% yield (based on unrecovered benzpyrene). Examination of the reaction mixture using paper chromatography indicated that a small amount of methyl 5-benzpyrenylmercaptoacetate was present but the crystalline material could not be isolated.

Irradiation of benzpyrene and thioglycolic acid in Pyrex vessels gave no substitution product, the benzpyrene being recovered. This indicates that the reaction is a free radical reaction induced photochemically.

Irradiation of benzpyrene and *n*-hexyl mercaptan with the mercury arc in a quartz vessel gave a 96% recovery of benzpyrene. Paper chromatography of the reaction mixture gave a second spot, in addition to the one due to benzpyrene, but no product could be isolated. Thioglycolic acid thus behaves quite differently from a saturated mercaptan.[9]

Treatment of benzpyrene with ethyl thioglycolate, ferrous ion and peroxide (Fenton reagent) gave no evidence of substitution. Benzpyrene did not react appreciably with thioglycolic acid or with thiolacetic acid in the presence of oxygen.[10]

The action of cyanopropyl radicals, generated by refluxing azoisobutyronitrile in benzene, on benzpyrene gave two products. One was a monocyanopropyl-benzpyrene, perhaps the 5-substituted compound, formed in small yield and the other was a bis-cyanopropyldihydrobenzpyrene, obtained in appreciable amount. This substance was obtained in two different crystalline forms, of m.p. 209.5–210° and m.p. 222–224°; the two were shown to be identical by analysis and seeding experiments, and they showed identical infrared and ultraviolet spectra. The ultraviolet spectrum (Fig. 1) shows that the compound is a 1,2-dihydrobenzpyrene, because its spectrum is very similar to that of 9-methyl-1,2-benzanthracene,[11,12] but is distinctly different from the spectrum of other possible dihydrobenzpyrenes.

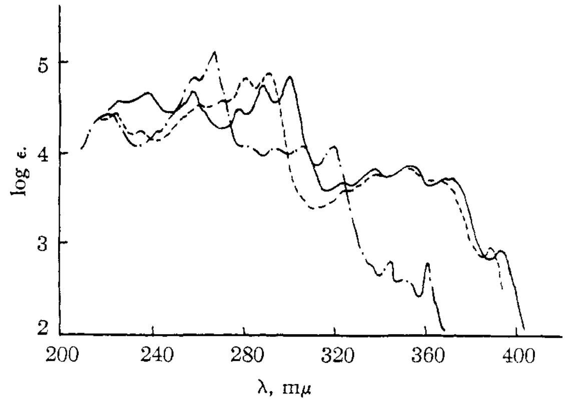
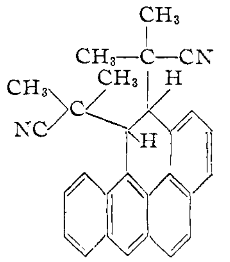


Fig. 1.—— · ——, chrysene[12]; - - - - - - - -, 9-methyl-1,2-benzanthracene[12]; ————, 1,2-dihydro-1,2-bis-(cyanopropyl)-benzpyrene.

Structure X is therefore indicated for the com-



X

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[6] L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **60**, 2542 (1938).

[7] Huang-Minlon, *ibid.*, **68**, 2487 (1946).

[8] D. S. Tarbell, E. G. Brooker, A. Vanterpool, W. Conway, C. F. Claus and T. J. Hall, *ibid.*, **77**, 767 (1955); for improvements in this procedure, see Experimental below.

[9] (a) R. A. Gregg, D. M. Alderman and F. R. Mayo, *ibid.*, **70**, 3740 (1948), and (b) C. Walling, *ibid.*, **70**, 2561 (1948), have shown that ethyl thioglycolate is much more effective as a chain transfer agent than are saturated mercaptans.

[10] G. Calcutt, *Brit. J. Cancer*, **3**, 306 (1949), observed changes in fluorescence spectra on incubation of benzpyrene with various mercapto compounds.

[11] R. N. Jones, THIS JOURNAL, **62**, 148 (1940).

[12] R. A. Friedel and M. Orchin, "Ultraviolet Spectra of Aromatic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1951, curves 447, 508.

pound.[13] Dehydrogenation experiments on X using palladium–charcoal at 315°, and sulfur at 215° yielded benzpyrene; chloranil in boiling xylene yielded a mixture of benzpyrene and starting material.[14]

Discussion

Lead tetraacetate[6] and benzoyl peroxide[15] attack benzpyrene at the 5-position, forming the 5-acyloxy product, although it is not certain that these reactions involve free radical intermediates. It is concluded from studies of the inhibitory effects of polycyclic hydrocarbons on the addition of trichloromethyl radicals to olefins[16] that benzpyrene is extremely susceptible to free radical attack, being about 10^5 times as reactive as benzene toward radicals, and the most reactive of all the hydrocarbons examined.[16] The products formed by the radical attack on benzpyrene were not isolated,[16] and hence the position of free radical substitution was not known.

There can be no question that, in the present work, the formation of 5-benzpyrenylacetic acid actually involves a free radical attack on the benzpyrene nucleus. The fact that substitution occurs in the 5-position agrees with the results of quantum mechanical calculations of the free valence number for the various positions in the benzpyrene nucleus.[16,17]

The fact that methyl 5-benzpyrenylmercaptoacetate (IX) was converted in part to methyl benzpyrenylacetate (III) by irradiation indicates that IX *may* be an intermediate in the formation of III; in any case, III must be the result of a photochemical dissociation of a carbon–sulfur bond, either at the thioglycolate stage (path 1) or in the conversion of IX to III.

Irradiation of thioglycolate might result in dissociation according to (1) or (2). The photochemical addition of hydrogen sulfide and mercaptans to olefins[5] must involve the radicals produced according to (2).

$$\mathrm{HSCH_2COOH} \xrightarrow{h\nu} \begin{cases} \mathrm{HS\cdot + \cdot CH_2COOH} & (1) \\ \mathrm{H\cdot + \cdot SCH_2COOH} & (2) \end{cases}$$

Pauling gives a value of 87.5 kcal. for the strength of the H–S bond, compared with 54.5 kcal. for the C–S bond and 63.8 kcal. for the S–S bond.[18] Franklin and Lumpkin, using the electron impact method, obtained a value of 73.4 kcal. for the C–S bond, and 86.8 kcal. for the S–H bond in ethyl mercaptan,[19] while in allyl mercaptan the C–S bond strength was found to be 54.3 kcal. The S–S bond strength in dimethyl disulfide was found to be 73.2 kcal. The C–S bond strength should be weakened in thioglycolic acid, due to resonance stabilization of the $\mathrm{CH_2CO_2H}$ radical. Therefore, path 1 should be favored energetically. It is also possible that there is some photosensitizing effect of the benzpyrene on the dissociation.[20]

The products obtained by irradiating ethyl mercaptan with a mercury arc[21] have been attributed to formation of hydrogen atoms and RS radicals, but the evidence is inconclusive, and dissociation to ethyl radicals (analogous to route 1) may also be involved.[22]

It is not surprising in the present work that the dihydrobenzpyrene, which is formed by addition of two cyanopropyl radicals to benzpyrene, is the 1,2-dihydro compound rather than the 6,7-dihydro compound, since the bond indexes for the two bonds do not differ by very much. The bond index of the 6,7-bond is 0.784 while that for the 1,2-bond is 0.754.[23] The resonance energies of the aromatic systems remaining in the dihydrobenzpyrenes, after addition to either the 1,2- or 6,7-bond in benzpyrene, are also comparable. The resonance energy for chrysene is 7.19β while that for 1,2-benzanthracene is 7.10β.[24]

The failure to get substitution in benzpyrene by sulfur radicals from thioacetic acid and by various systems using Fenton reagent indicates that sulfur radicals do not attack benzpyrene with great facility.[25] The much greater reactivity of benzpyrene toward free radicals in general, compared to benzanthracene, pyrene and chrysene, which has been noted earlier[15,16] is confirmed in the present work.

Experimental[26]

Paper Chromatography.—It was found that the procedure for paper chromatography previously described[8] could be greatly improved by drying the paper for 1 hr. at 120° and storing it in a desiccator over calcium chloride before saturating it with N,N-dimethylformamide. The atmosphere in the developing chamber should also be kept dry by placing open containers containing calcium chloride in the chamber. When this treatment is used, the time required for development of the chromatogram does not vary with relative humidity, and development requires 3–4 hr.; better separation is obtained for substances with close R_f values, and the R_f values are more reproducible. Average R_f values are as follows: methyl 5-benzpyrenylacetate 0.31,

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[13] It is possible that the cyanopropyl groups are at positions other than 1 and 2, and that there has been a hydrogen shift to give the 1,2-dihydro compound, which the spectrum indicates. However, the product was isolated directly from the reaction mixture, and the 1,2-position for the cyanopropyl groups seems most probable.

[14] A. F. Bickel and E. C. Kooyman, *Rec. trav. chim.*, **71**, 1137 (1952), showed that cyanopropyl radicals added to anthracene to give a mixture of 9,10-bis-cyanopropyl-9,10-dihydroanthracenes, which were converted to anthracene, with loss of the cyanopropyl groups, by pyrolysis at 200–250°.

[15] I. M. Roitt and W. A. Waters, *J. Chem. Soc.*, 2695 (1952).

[16] E. C. Kooyman and E. Farenhorst, *Trans. Faraday Soc.*, **49**, 58 (1953); *cf.* J. R. Dunn, W. A. Waters and I. M. Roitt, *J. Chem. Soc.*, 580 (1954).

[17] C. A. Coulson, *J. chim. phys.*, **45**, 243 (1948); K. Fukui, T. Yonezawa, C. Nagata and H. Shingu, *J. Chem. Phys.*, **22**, 1433 (1954); K. Fukui, T. Yonezawa and H. Shingu, *ibid.*, **20**, 722 (1952); M. Levy and M. Szwarc, THIS JOURNAL, **77**, 1949 (1955).

[18] L. Pauling, "The Nature of the Chemical Bond," 2nd Ed., Cornell Univ. Press, Ithaca, N. Y., 1945, p. 53.

[19] J. L. Franklin and H. E. Lumpkin, THIS JOURNAL, **74**, 1023 (1952).

[20] E. J. Bowen, *Discussions Faraday Soc.*, **14**, 143, 146 (1953).

[21] M. Meissner and H. W. Thompson, *Trans. Faraday Soc.*, **34**, 1238 (1938).

[22] *Cf.* W. A. Noyes, Jr., and P. A. Leighton, "The Photochemistry of Gases," Reinhold Publ. Corp., New York, N. Y., 1941, p. 409.

[23] B. Pullman and J. Bandet, *Compt. rend.*, **237**, 986 (1953).

[24] J. P. Greenstein and A. Haddow, "Advances in Cancer Research," Vol. I, Academic Press, Inc., New York, N. Y., 1953, p. 32.

[25] B. M. Mikhailov and A. N. Blokhina, *Doklady Akad. Nauk. U.S.S.R.*, **80**, 373 (1951); *C. A.*, **46**, 5025 (1952)) report the addition of thiolacetic acid to the 9,10-positions of anthracene in presence of oxygen.

[26] Melting points are corrected; microanalyses by Annette Smith and Microtech Laboratories. Ultraviolet spectra were determined in alcohol, using a Beckman or Cary spectrophotometer. Fluorescence spectra were measured using equipment and procedures described in detail elsewhere.[2] We are indebted to Carl Whiteman, Carol St. Clair and Carolyn McCamey for assistance with the spectral work.

methyl 5-benzpyrenylmercaptoacetate 0.41, benzpyrene 0.82.

3,4-Benzpyrene.—3,4-Benzpyrene was prepared in 16–25% yield from pyrene by the method described in the literature,[27,28] with the exception that the intermediate 4'-keto-1',2',3',4'-tetrahydrobenzpyrene was reduced to the tetrahydroalcohol in 82% yield, using lithium aluminum hydride. It was also found that 4'-keto-1',2',3',4'-tetrahydrobenzpyrene was more easily purified by chromatography on a fivefold amount of alumina, using benzene for elution, than by crystallization.[29]

Reaction of Thioglycolic Acid with Benzpyrene under the Mercury Arc. A. 5-Benzpyrenylacetic Acid (II).—Benzpyrene (1.0 g.) was dissolved in 20 ml. of redistilled thioglycolic acid (b.p. 95–99° (10 mm.)) by heating to 90°. The solution was contained in a quartz tube, under a nitrogen atmosphere; the tube was surrounded by a Hanovia C2055 quartz mercury arc. The irradiation lasted 10 hr., and the solution was kept at 90–95° by the heat evolved by the discharge tube. Water (50 ml.) was then added and the mixture allowed to stand overnight. The yellow precipitate which formed was collected and dried *in vacuo;* it weighed 1.08 g. Extraction with two 25-ml. portions of boiling benzene left 0.23 g. of yellow insoluble 5-benzpyrenylacetic acid, which decomposed slowly above 205°. The benzene solution was extracted with three 50-ml. portions of 2% potassium hydroxide. Acidification of this extract yielded 0.016 g. of yellow powder, which decomposed slowly above 170°.

The benzene layer was washed with water and dried; 0.57 g. of benzpyrene (m.p. 170–173°, identified by a mixed m.p.) was obtained.

5-Benzpyrenylacetic Acid Methyl Ester (III).—The crude acid (250 mg.), obtained as above, was suspended in ether and treated with an excess of diazomethane in ether at 0°, the ether was removed on the steam-bath under a stream of nitrogen, the residue was taken up in benzene and was chromatographed on 40 g. of Florisil. The eluate of the yellow fluorescent band yielded 150 mg. of yellow crystals, m.p. *ca.* 155°. Recrystallization from methyl ethyl ketone gave 99 mg. of yellow crystals, m.p. 165–166°.

Anal. Calcd. for $C_{23}H_{16}O_2$: C, 85.16; H, 4.97. Found: C, 85.47; H, 5.10.

The ethyl ester IV was obtained by esterification of the acid (100 mg.) by refluxing with 10 ml. of absolute ethanol and 0.5 ml. of concd. sulfuric acid for 3.5 hr. The solution was cooled, diluted with 20 ml. of water, neutralized with bicarbonate and extracted with three 20-ml. portions of benzene. This solution was concentrated, diluted with two volumes of petroleum ether and chromatographed on 10 g. of Florisil. The yellow, fluorescent band was eluted with 1:1 benzene–petroleum ether, which yielded 70 mg. of crude ethyl ester. Three crystallizations from absolute ethanol gave 43 mg. of light brown crystals, m.p. 121–122°.

Anal. Calcd. for $C_{24}H_{18}O_2$: C, 85.18; H, 5.36. Found: C, 85.28; H, 5.33.

Saponification of Methyl 5-Benzpyrenylacetate.—The ester (75 mg.) was heated under reflux with 5 ml. of 1 *N* potassium hydroxide in methanol for 2.5 hr. in a nitrogen atmosphere. About half of the methanol was evaporated under a stream of nitrogen, and 7 ml. of water was added. The solution was filtered hot and a small amount of sodium chloride dissolved in the hot solution. The solution was allowed to stand at 0° overnight and the crystalline acid salt was separated by filtration. The salt was dissolved in about 20 ml. of hot water. The solution was filtered hot, cooled and acidified with dilute hydrochloric acid. The precipitated acid was separated by centrifugation, washed several times with water and dried *in vacuo*. A dull green powder (62 mg.), m.p. 248–252° (*in vacuo*) with decomposition, was obtained.

Anal. Calcd. for $C_{22}H_{14}O_2$: C, 85.14; H, 4.55. Found: C, 85.57; H, 4.67.

Decarboxylation of 5-Benzpyrenylacetic Acid to 5-Methylbenzpyrene.—The acid (33 mg., m.p. 234–237°), obtained by saponification of the methyl ester, was heated with 5 mg. of copper chromite at 220–230° in 1.5 ml. of quinoline, under nitrogen, for 3 hr. The solution was cooled and poured into 10 ml. of 10% hydrochloric acid; the acid solution was extracted with two 25-ml. portions of benzene. The benzene solution was extracted with 25 ml. each of 10% hydrochloric acid, saturated bicarbonate solution, and 2% potassium hydroxide. This treatment did not remove any of the brown color. The benzene solution was evaporated to a few ml. and was chromatographed on 6 g. of alumina. The blue fluorescent band was eluted with benzene, yielding 16 mg. of yellow crystals, which was converted to the picrate, 16 mg. of brown needles, m.p. 193–200°. The picrate was decomposed by dissolving it in chloroform and passing the solution over 3 g. of alumina. The recovered hydrocarbon (10 mg. of yellow crystals) was recrystallized from benzene–hexane, and 6.6 mg. of yellow plates, m.p. 214–216°, was obtained. The mixed m.p. with an authentic sample of 5-methylbenzpyrene was undepressed; furthermore, the ultraviolet, infrared and fluorescence spectra of both samples were identical, as were the R_f values obtained on paper chromatography.[8]

Irradiation of Benzpyrene and *n*-Hexyl Mercaptan.—Benzpyrene (1.0 g.) dissolved in 20 ml. of *n*-hexyl mercaptan was irradiated for 10 hr., under nitrogen, as described above for thioglycolic acid. By crystallization, precipitation with picric acid and chromatography on alumina, 0.96 g. of benzpyrene was recovered. The solution remaining after removal of most of the benzpyrene as the picrate showed two spots on paper chromatography of R_f values 0.81 and 0.89. The spot with R_f 0.81 was benzpyrene, as shown by a control spot of benzpyrene on the same paper. The second material indicated by the paper chromatogram was not isolated from the reaction mixture.

5-Benzpyrenyl Methyl Sulfide (VII).—5-(Chlorodithio)-benzpyrene was prepared in 91% yield from benzpyrene and sulfur monochloride[30]; 0.5 g. of this compound was suspended in 50 ml. of dry benzene and 10 ml. of 1 *M* lithium aluminum hydride in ether was added dropwise. The solution was heated to 50° for 1 hr., cooled and was extracted with three 25-ml. portions of 3% potassium hydroxide containing a small amount of sodium hydrosulfite. The extract was filtered; 19 ml. was treated with 0.5 ml. of purified dimethyl sulfate and the solution was heated on the steam-bath for 15 min. All operations were carried out in an atmosphere of nitrogen as far as possible. The yellow powder (70 mg.) which was obtained on cooling melted, after two crystallizations from glacial acetic acid, at 169–170.5°, and weighed 43 mg.; it appeared to decompose when chromatography on Florisil was attempted.

Anal. Calcd. for $C_{21}H_{14}S$: C, 84.54; H, 4.73. Found: C, 84.41; H, 4.92.

5-Benzpyrenyl benzyl sulfide was prepared from 19 ml. of the above alkaline extract and 0.5 ml. of benzyl chloride. The product melted at 168–171°, after crystallization from glacial acetic acid; the reported[30] m.p. is 170.2–172.2°.

Methyl 5-Benzpyrenylmercaptoacetate (IX).—5-Chlorodithiobenzpyrene (1.34 g.) was reduced with lithium aluminum hydride as above. The benzene layer was extracted with 80 ml. of 3% potassium hydroxide (in three portions) containing a small amount of sodium hydrosulfite. The extract was filtered, half of it was treated with 0.25 g. of chloroacetic acid, and the solution was warmed on the steam-bath under nitrogen for 1 hr. The potassium salt of 5-benzpyrenylmercaptoacetic acid which precipitated was collected by centrifugation, washed with water, suspended in water, and the suspension was acidified with acetic acid. The solid acid was collected, washed with water and, after drying *in vacuo*, weighed 0.47 g., representing 69% yield from benzpyrene.

The crude acid was suspended in ether and was treated with an excess of ethereal diazomethane at 0°. After standing for 2 hr., the ether was removed on the steam-bath under a stream of nitrogen, the residue was taken up in benzene, and was chromatographed on 50 g. of Florisil. The yellow-green fluorescent band was eluted with benzene, giving 0.36 g. (52% yield from benzpyrene) of yellow-orange crystals, melting at 98–103°. Recrystallization of 100 mg. of this material from benzene–hexane, followed by two crystallizations from methyl ethyl ketone, yielded 39 mg. of yellow needles, m.p. 120–121.5°.

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[27] (a) A. Winterstein, H. Vetter and K. Schon, *Ber.*, **68**, 1079 (1935); (b) W. E. Bachmann, M. Carmack and S. R. Safir, THIS JOURNAL, **63**, 1682 (1941).

[28] L. F. Fieser and F. C. Novello, *ibid.*, **62**, 1858 (1940).

[29] We are indebted to Dr. Paul Seifert for this observation.

[30] J. L. Wood and L. F. Fieser, *ibid.*, **62**, 2674 (1940).

Anal. Calcd. for $C_{23}H_{16}O_2S$: C, 77.51; H, 4.53; S, 8.98. Found: C, 77.26; H, 4.70; S, 8.75.

Photochemical Decomposition of Methyl 5-Benzpyrenylmercaptoacetate (IX).—This compound (25 mg.) was dissolved in 10 ml. of boiling hexane under nitrogen in a quartz tube and was irradiated with the mercury arc for 8 hr. At intervals, a few drops were removed and chromatographed on paper, with results shown below.

Time irradiated, hr.	R_f values on paper chromatography[a]			
0			0.36	
0.5		0.28	.37	0.96
1	0.08	.27	.36	.99
2.5	.08	.28		.98
6	.07	.29		.96
8	.07	.30		.96

[a] R_f values of knowns: benzpyrene (0.73–0.80); methyl 5-benzpyrenylmercaptoacetate (*IX, 0.37–0.39); methyl* 5-benzpyrenylacetate (III, 0.26–0.29).

Reaction of Thiolacetic Acid with Benzpyrene in Presence of Oxygen.—Benzpyrene (0.50 g.) was dissolved in 10 cc. of thiolacetic acid (Eastman Kodak Co., redistilled, b.p. 86–93°) and the solution was stirred in an oxygen atmosphere for 6 days. About 52 ml. of oxygen had been absorbed or had leaked out. No further oxygen was absorbed when the solution was irradiated by the ultraviolet light from an alpine burner for 1 hr. Water (200 ml.) was added, the yellow gummy precipitate was collected and dissolved in toluene; the solution was boiled until anhydrous and was cooled and diluted with 2 vol. of petroleum ether. The solution was chromatographed on 30 g. of alumina. The benzene–petroleum ether eluate of the yellow-green fluorescent band yielded 0.41 g. of benzpyrene, m.p. 160–170°, raised to 176–180° by washing with hexane.

9-Mercaptoanthracene.—9-Chlorodithioanthracene was prepared in 87% yield by the method of Friedlander and Simon.[31]

9-Chlorodithioanthracene (4 g.) was suspended in 50 ml. of dry benzene and 40 ml. of 1 *M* lithium aluminum hydride in ether was added dropwise with stirring. When the addition was complete the solution was cooled and excess hydride was decomposed with ethyl acetate. The complex was then decomposed with cold 10% sulfuric acid. The organic layer was extracted with three 30-ml. portions of 3% potassium hydroxide containing a small amount of sodium hydrosulfite. The alkaline extract was acidified with acetic acid and the yellow precipitate was separated by centrifugation, washed with dilute hydrochloric acid and water and dried *in vacuo;* yield 2.5 g. of yellow powder, m.p. 83–88°. Recrystallization from hexane raised the melting point to 86–90°. Four further recrystallizations raised the melting point to 87–91°. On recrystallization from dioxane-water the substance apparently underwent oxidation since the product melted *ca.* 205°.

Reduction of 4 g. of chlorodithioanthracene by Friedlander's method using 14 g. of sodium sulfide in 50 ml. of methanol and working up the reaction mixture as described in the literature gave 2.0 g. (66%) of mercaptan, m.p. 85–91°. Friedlander reports a m.p. of 90–91° for 9-mercaptoanthracene.

9-Methylmercaptoanthracene.—Mercaptoanthracene (0.5 g.) was dissolved in 15 ml. of warm 20% sodium hydroxide containing a small amount of sodium hydrosulfite. Dimethyl sulfate (0.5 ml.) was added and the solution was warmed on the steam-bath for 1 hour. The solution was cooled and the crude product separated by filtration. A quantitative yield of material, m.p. *ca.* 55°, was obtained. After three recrystallizations from hexane the material formed yellow transparent crystals, m.p. 65–66°. Friedlander[20] reports the m.p. of 9-methylmercaptoanthracene to be 153°.

Anal. Calcd. for $C_{15}H_{12}S$: C, 80.33; H, 5.39. Found: C, 80.69; H, 5.52.

9-Benzylmercaptoanthracene.—Mercaptoanthracene (0.5 g.) was dissolved in 15 ml. of warm 20% sodium hydroxide containing a small amount of sodium hydrosulfite. One ml. of benzyl chloride was added and the solution was warmed on the steam-bath for 0.5 hr. The oily crystals which separated on cooling were collected by filtration and washed with ethanol; yield 0.55 g. (93%), m.p. 95–100°. After three recrystallizations from absolute ethanol yellow needles were obtained, m.p. 99–100°.

Anal. Calcd. for $C_{20}H_{14}S$: C, *83.90; H,* 4.93. *Found:* C, 83.81; H, 5.30.

Reaction of Cyanopropyl Radicals with Benzpyrene; Formation of X-Cyanopropylbenzpyrene and 1,2-Dihydro-1,2-bis-(cyanopropyl)-benzpyrene (X).—Benzpyrene (1.00 g., 0.004 mole) and 3.24 g. (0.02 mole) of azoisobutyronitrile[32] were refluxed in 25 ml. of benzene under nitrogen for 8 hr. Most of the solvent was removed on the steam-bath under a stream of nitrogen, and the remainder was removed at low pressure. Most of the tetramethylsuccinonitrile was removed by distillation at 150° (0.08 mm.) and the remaining yellow residue was distilled in a short path still under high vacuum. The fraction (1.23 g.) obtained at block temperatures of 220–290° (5×10^{-3} mm.) was dissolved in 1:1 petroleum ether–benzene and was chromatographed on 150 g. of Florisil. Elution with one-to-one petroleum ether–benzene, evaporation of the solvent, and recrystallization from benzene–hexane gave 0.36 g. of benzpyrene. The column was further eluted with one-to-one petroleum ether–benzene, and recrystallization of the material obtained from this fraction, from benzene–absolute ethanol, gave 100 mg. of yellow plates, m.p. 160–195°. Fifty mg. of this material was dissolved in 10 ml. of benzene and chromatographed on 50 g. of silica gel. The center section of the main band was eluted with benzene and the solvent was removed under reduced pressure. The residue was recrystallized from benzene and from benzene–hexane as 11.3 mg. of yellow plates, m.p. 204–206°.

Anal. Calcd. for $C_{24}H_{17}N$: C, 90.25; H, 5.37. Found: C, 90.14; H, 5.13.

The analysis indicates a monocyanopropylbenzpyrene, as does the ultraviolet spectrum; the latter shows maxima, in mμ (log ϵ) at: 256 (4.59), 266 (4.66), 276 (4.37), 288 (4.63), 300 (4.75), 333 (3.63), 350 (4.03), 3.69 (4.33), 387 (4.38), 392 (4.33). The fluorescence spectrum taken in benzene (0, 8 γ/ml.), shows peaks at 4083, 4181, 4316 and 4554 Å.

The picrate obtained from 10 mg. of the crude product was obtained, after one crystallization from benzene, as red-brown needles, m.p. *ca.* 170°, which could not be purified further by crystallization.

Further elution with petroleum ether–benzene and pure benzene gave only oils, which, by paper chromatography, were shown to contain the above cyanopropylbenzpyrene and benzpyrene, as well as substances having R_f 0.65 and 0.08.

Elution with chloroform-benzene and recrystallization of the residues from benzene-absolute ethanol gave two batches of white crystals, 99 mg., m.p. 208–222°, and 56 mg., m.p. 212–222°. These were combined and recrystallized from benzene–absolute ethanol, giving 73 mg. of white crystals, m.p. 209.5–210°. This solid, when melted, allowed to solidify and recrystallized from benzene, melted at 222–224°. The higher melting form was converted to the lower melting form by crystallization from absolute ethanol. The two forms showed the same ultraviolet and fluorescence spectra, and the same R_f values; the infrared spectra, taken on Nujol mulls, showed minor differences; ultraviolet spectrum: 225 (4.58), 238 (4.68), 258 (4.69), 278 (450), 289 (4.78), 301 (4.87), 324 (3.68), 339 (3.84), 355 (3.89), 370 (3.73). The fluorescence spectrum in benzene (0.6 γ/ml.) showed peaks at 3978, 4030, 4216, 4480 and 4740 Å.

Anal. Calcd. for $C_{28}H_{24}N_2$ (X): C, 86.56; H, 6.23; mol. wt., 388. Found (210° form): C, 86.55; *H*, 6.29. Found (224° form): C, 86.58; H, 6.41; mol. wt. (Rast), 334.

In another run, the dihydro-bis-(cyanopropyl)-benzpyrene was isolated from the reaction mixture without employing the short path distillation. Benzpyrene (1.0 g.)

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[31] P. Friedlander and A. Simon, *Ber.*, **55**, 3972 (1922).

[32] *Some was Eastman Kodak material and some was prepared by* Thiele's method (J. Thiele and K. Heuser, *Ann.*, **290**, 22, 30 (1896); A. F. Bickel and W. A. Waters, *Rec. trav. chim.*, **69**, 1492 (1950)). Both samples melted at 99–101°.

and azoisobutyronitrile (3.24 g.) were refluxed in 30 ml. of benzene for 8 hr. under nitrogen. The benzene and tetramethylsuccinonitrile were removed by steam distillation. The yellow residue was dissolved in benzene, dried, and the solvent was removed by heating on the steam-bath for 1 hr. *in vacuo*. The yellow glass which resulted (1.82 g.) did not form a crystalline picrate. Seeding of 187 mg. of this material in benzene–absolute ethanol with a crystal of dihydro-bis-(cyanopropyl)-benzpyrene (X, m.p. 222–224°) yielded 10 mg. of white crystals, m.p. 220–224°.

Dehydrogenation of the yellow glass with sulfur at 215° and with 10% palladium-charcoal at 315° yielded benzpyrene as the sole identifiable product. Dehydrogenation with chloranil in boiling xylene for 47 hr. yielded an impure sample of X.

Dehydrogenation of Dihydro-bis-(cyanopropyl)-benzpyrene (X).—The bis-compound X (29 mg., m.p. 208–220°) was mixed with 4 mg. of 10% palladium-charcoal and heated under nitrogen at 315° for 1 hr. in a sublimation apparatus. The sublimate was rinsed into the apparatus with benzene, the benzene was removed on the steam-bath, and the material was heated at 315° for 1 hr. more. The mixture was dissolved in benzene, filtered and was concentrated on the steam-bath under nitrogen. The residue could not be recrystallized from benzene–hexane; it was therefore sublimed at 140–165° (0.1 mm.), and the yellow sublimate (9.2 mg.) was recrystallized from benzene–hexane. The yellow crystals obtained (4.5 mg.) melted at 176–178° and gave no depression on mixed m.p. with authentic benzpyrene.

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[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

The Nef Reaction on 9,10-Dihydro-(11-nitroethano)-anthracenes. A New Route to 9,10-Dihydro-(11-ketoethano)-anthracenes[1]

BY WAYLAND E. NOLAND, M. SCOTT BAKER AND HOWARD I. FREEMAN

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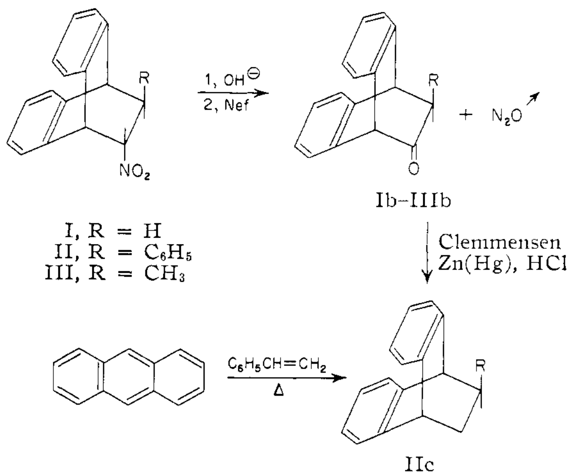
The application of the Nef reaction to the salts of the three most readily available secondary nitro 9,10-dihydro-9,10-ethanoanthracenes is reported. Two of the ketones corresponded in physical properties to samples previously prepared by other methods; the third was previously unknown. It was converted by Clemmensen reduction to a hydrocarbon, 9,10-dihydro-9,10-(11-phenylethano)-anthracene, which was synthesized independently by the Diels–Alder reaction of anthracene with styrene, thus establishing that no rearrangement had taken place during the formation of the ketone.

The preparation of 9,10-dihydro-9,10-(11-nitroethano)-anthracenes by the Diels–Alder reaction of anthracene with nitroölefins has been previously described.[2] Salts of the three secondary nitro adducts (I–III) obtained in the best yields have been found to undergo the Nef reaction,[3] yielding the corresponding ketones Ib–IIIb



I, R = H
II, R = C_6H_5
III, R = CH_3

Ib–IIIb

IIc

The Nef reaction on the potassium salt of I gave the corresponding ketone Ib in 87% crude yield. This, and its oxime, were identical with the corresponding compounds prepared by Wawzonek and Hallum[4] through a series of reactions from anthracene and methyl acrylate or vinyl acetate. The ketone IIb was isolated in 56% crude yield as the 2,4-dinitrophenylhydrazone and in 26% yield in free form, along with a large amount of an amorphous product. The ketone IIIb was obtained in 17% yield, along with nitrogen-containing products. The infrared spectrum and melting point of IIIb corresponded to those of the sample obtained by Vaughan and Milton[5] from the action of 48% hydrobromic acid on 9,10-dihydro-9,10-(11-hydroxy-*cis*-11,12-dicarboxyanhydro-12-methylethano)-anthracene. The lower yields of IIb and IIIb relative to Ib, and the presence of nitrogen-containing products in the former cases, suggest that neighboring methyl or phenyl groups may sterically hinder the Nef reaction on carbon and cause reaction on nitrogen to be relatively more favored.

The best yields of ketones were obtained in the present work by gradually adding acid to cold methanolic alkaline solutions of the nitro compounds, using ether to keep the organic reactants in solution. Gradual addition of acid permits the reaction to pass through a wide range of acidities, including whichever is most favorable to the Nef reaction. Reversal of the method by adding an alkaline solution of the nitro compound to acid generally gave lower yields of ketone; high initial acidity did not seem to favor the Nef reaction. Gradual addition of a methanolic alkaline solution of III to cold hydrochloric acid and ether gave only an 11% yield of the ketone IIIb, a higher yield of a

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(1) From the M.S. theses of Howard I. Freeman (on training assignment from the U. S. Air Force Institute of Technology), December 1953, and M. Scott Baker, June 1955, and from work by the senior author, 1953–1955. Paper presented before the Organic Division at the 128th National Meeting of the American Chemical Society, Minneapolis, Minn., Sept. 16, 1955.

(2) (a) W. E. Noland, H. I. Freeman and M. S. Baker, THIS JOURNAL, **78**, 188 (1956); (b) K. Klager, *J. Org. Chem.*, **20**, 650 (1955).

(3) W. E. Noland, *Chem. Revs.*, **55**, 137 (1955).

(4) S. Wawzonek and J. V. Hallum, *J. Org. Chem.*, **18**, 288 (1953).

(5) W. R. Vaughan and K. M. Milton, THIS JOURNAL, **74**, 5623 (1952).