using liquid ammonia has been described in connection with the preparation of diacetoneamine.[12]

Alcohols, amines, ketones, aldehydes and cyanides were freed of any halogen-containing impurity by means of Raney nickel before they were submitted to reaction. In other respects these compounds were prepared and purified by the usual procedures.

Amines distilling over with solvents were recovered as the hydrochlorides and the amines regenerated with alkali and purified by fractional distillation. Amines were characterized by analysis and by the formation of solid derivatives. Neutral equivalents were determined upon all the amines reported.

Analytical data and physical properties of several amines and their derivatives not previously reported are given in Table II. References for certain other amines and their derivatives are given herewith: N-ethylpiperidine,[13] N-*n*-propylpiperidine,[13] N-*i*-propylpiperidine,[13] N-*n*-butylpiperidine,[14] N-*n*-hexylpiperidine,[15] N-cyclohexylpiperidine,[2] N-*n*-dodecylpiperidine,[16] N-cyclohexylphenethylamine,[17] N-*n*-dodecylphenethylamine,[18] α-phenethylamine,[19] benzhydrylamine,[20] 5-aminononane,[21] benzylamine,[22] *n*-heptylamine,[23] furfurylamine,[8] 2,5-di-Me-pyrrole, N-*n*-butyl-*n*-amylamine,[24] 2,2-di-Me-3-aminopentane,[25] 2,4-di-Me-3-aminopentane.[26]

(12) Martha E. Smith and Adkins, THIS JOURNAL, **60**, 408 (1938).
(13) Evans, *J. Chem. Soc.*, **71**, 524 (1897).
(14) Von Braun, *Ber.*, **40**, 3930 (1907).
(15) Von Braun and Buckman, *ibid.*, **64B**, 2610 (1931).
(16) Wojcik and Adkins, THIS JOURNAL, **56**, 2419 (1934).
(17) Wieland, Schopf and Hermsen, *Ann.*, **444**, 40 (1925).
(18) Wojcik and Adkins, THIS JOURNAL, **56**, 2424 (1934).

Summary

Favorable conditions for the reaction of eight representative alcohols with four different amines to give secondary and tertiary amines have been ascertained.

It has been found that representative aldehydes, dialkyl ketones and alkyl aryl ketones may be directly converted in good yields to primary amines by hydrogenating them over Raney nickel in an ammonia–methanol mixture.

The formation of secondary amines in the hydrogenation of cyanides over Raney nickel may be almost entirely prevented by carrying out the hydrogenation in the presence of sufficient ammonia.

(19) Tafel, *Ber.*, **19**, 1929 (1886).
(20) Heilbron, "Dictionary of Organic Compounds," Vol. I, Eyre and Spottiswoode, London, 1934, p. 49.
(21) Unpublished work by G. M. Whitman.
(22) Hoogewerff, *Rec. trav. chim.*, **5**, 253 (1886).
(23) Mulliken, "Identification of Pure Organic Compounds," Vol. II, John Wiley and Sons, New York, N. Y., 1916, p. 140.
(24) Ochiai and Tsuda, *J. Pharm. Soc. Japan*, **56**, 352 (1936).
(25) Markownikoff, *Ber.*, **32**, 1448 (1899).
(26) Mailhe, *Bull. soc. chim.*, **27**, 541 (1920).

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Conjugation of Amino Acids with Isocyanates of the Anthracene and 1,2-Benzanthracene Series[1]

BY LOUIS F. FIESER AND HUGH J. CREECH[2]

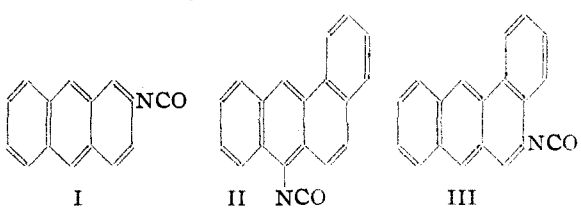
This communication describes results obtained in an extension of the program of research initiated by Franks and one of us[3,4,5] on the problem of conjugating carcinogenic hydrocarbons with proteins and investigating their possible immunizing action against hydrocarbon carcinogenesis. In the previous work the meso isocyanate derivatives of anthracene and 1,2,5,6-dibenzanthracene were prepared, characterized by reaction with simple amines and alcohols, and linked to various proteins by interaction in aqueous dioxane solution. The conjugated proteins were found to possess definite antigenic properties, varying with the nature of the prosthetic group, and experiments with preparations of 1,2,5,6-dibenzanthryl-9-carbamido-casein afforded some indications of an immunization against the action of dibenzanthracene. The material was also found to be mildly carcinogenic, and this property was discovered also in the conjugate from dibenzanthryl isocyanate and glycine.

As one step in the extension of this work we have prepared and characterized the isocyanates resulting from the interaction of phosgene with

(1) The investigations in this series were undertaken in coöperation with Dr. W. R. Franks of the Banting Institute and have been supported by a grant from the International Cancer Research Foundation.
(2) Research Fellow of the University of Toronto.
(3) Creech and Franks, *Am. J. Cancer*, **30**, 555 (1937).
(4) Creech and Franks, THIS JOURNAL, **60**, 127 (1938).
(5) Franks and Creech, *Am. J. Cancer*, **35**, 203 (1939).

β-anthramine, 10-amino-1,2-benzanthracene[6] and 3-amino-1,2-benzanthracene.[7] These starting materials were selected largely because of their availability. While it is desirable eventually to produce protein derivatives having affixed residues to which can be ascribed both carcinogenic and non-carcinogenic characteristics, the information at hand provides little basis for foretelling the biological properties of simple functional derivatives of even the much studied 1,2-benzanthracene. Since the potently carcinogenic 10-methyl-1,2-benzanthracene contrasts sharply with the inactive 3-isomer while the 10- and 3-methoxy compounds are both weakly carcinogenic[8] the relationship between corresponding isomeric carbamido derivatives is entirely problematical and seemed worthy of investigation.

In order to provide samples for biological assay, and as a prelude to preparation of the protein derivatives, the isocyanates I–III were converted into



I II III

the methyl and ethyl carbamates (ArNHCOOR), the substituted ureas ($ArNHCONH_2$), disubstituted ureas (ArNHCONHAr), and carbamido ethanol derivatives ($ArNHCONHCH_2CH_2OH$). The 10-substituted 1,2-benzanthracene derivatives contrasted sharply with the corresponding compounds in the other two series in tending to separate in a gelatinous condition. Crystalline samples were obtained only after tedious manipulation, whereas the derivatives from I and III and also from 1,2,5,6-dibenzanthryl-9-isocyanate crystallized readily. It may be noted that Badger and Cook[9] encountered similar difficulties with other 10-substituted 1,2-benzanthracenes.

The preparation of carbamido acids by linking the isocyanates to amino acids is of interest as a possible route to water-soluble carcinogens[3,10] and because of Boyland and Levi's[11] observation that certain polynuclear aromatic hydrocarbons fed to animals are excreted in part in conjugation with amino acids. Furthermore, the experiments of White and White[12] suggest a possible interaction of amino acids with carcinogenic hydrocarbons in the organism, and the striking discovery of Kögl and Erxleben[13] of the presence of amino acids of "unnatural" configuration in the hydrolyzates from tumor tissue gives impetus to the extensive study of the rôle of amino acids in respect to malignant growth. The reaction of the isocyanates I–III with glycine and with ε-aminocaproic acid was studied in aqueous dioxane solution in order to gain further experience with a procedure which could be employed for conjugating the compounds with proteins.[3,5] The condensations proceeded satisfactorily under very mild conditions, and pure reaction products were obtained in a crystalline condition in the experiments with β-anthryl- and 1,2-benzanthryl-3-isocyanate and also from the reaction of 1,2,5,6-dibenzanthryl-9-isocyanate with each of the above amino acids; the dibenzanthryl carbamido acetic acid previously assayed[3] had not been isolated in a pure state. A tendency to form gels was again encountered in the 10-substituted 1,2-benzanthracene series and the carbamido acetic and caproic acids were not obtained crystalline. Suitable processes of precipitation gave amorphous preparations of satisfactory analysis, and the ethyl ester of the former compound was isolated in a crystalline form. The glycine conjugates are sensitive substances and decompose below the melting point or when heated in organic solvents at temperatures above about 50–60°. The caproic acid derivatives are more easily purified and melt sharply without decomposition.

The present experiments provide some assurance that the method of conjugation in aqueous dioxane solution is suitable for application to proteins, and results to be reported later have borne out this expectation. In a trial of pyridine as the solvent it was found that 1,2-benzanthryl-10-isocyanate in the absence of any other reagent is polymerized rapidly by pyridine at room temperature to an amorphous, high-melting product (dimer?[14]).

Experimental Part[15]

β-Anthryl Isocyanate.—β-Aminoanthracene was prepared in 40% yield from commercial β-aminoanthra-

(6) Fieser and Hershberg, THIS JOURNAL, **60**, 1893 (1938).
(7) Fieser, Hershberg, Long and Newman, *ibid.*, **59**, 475 (1937).
(8) Summary: Fieser, *Am. J. Cancer*, **34**, 37 (1938).
(9) Badger and Cook, *J. Chem. Soc.*, 802 (1939).
(10) Bachmann and Cole, *J. Org. Chem.*, **4**, 60 (1939).
(11) Boyland and Levi, *Biochem. J.*, **30**, 1225 (1936).
(12) White and White, *Proc. Soc. Exptl. Biol. Med.*, **39**, 527 (1938).
(13) Kögl and Erxleben, *Z. physiol. Chem.*, **258**, 57 (1939).
(14) van Hoogstraten, *Rec. trav. chim.*, **51**, 414 (1932).
(15) Melting points below 275° are corrected; more reliable results often were obtained using an evacuated capillary. Microanalyses by Lyon Southworth

quinone by the method of von Braun and Bayer.[16] After several crystallizations from acetone, methanol, and benzene–ligroin, the amine was obtained as bright greenish-yellow plates, m. p. 243.5–244.5° (in vacuum: 245–245.5°).[17]

Gradual addition of excess phosgene (20 g.) in toluene to a solution of the purified amine (3 g.) in benzene produced a flocculent white precipitate of the amine hydrochloride which disappeared after refluxing for about one-half hour. The solution was evaporated at diminished pressure (100 mm.) in an atmosphere of nitrogen until it became opalescent, and it was then filtered and transferred to a vacuum desiccator. The isocyanate crystallized on further removal of the solvent and recrystallization from benzene and from carbon tetrachloride gave 2.4 g. (70%) of small, faintly yellow needles, m. p. 207.5–208°.

Anal. Calcd. for $C_{15}H_9ON$: N, 6.39; C, 82.17; H, 4.14. Found: N, 6.66 (Kjeldahl), 6.64 (Dumas); C, 81.98; H, 4.10.

In the preparation of the derivatives listed below the crude reaction products were obtained in very nearly quantitative yield.

Methyl β-anthrylcarbamate was prepared by refluxing a solution of the isocyanate (100 mg.) in methanol (10 cc.) for one-half hour. Crystallized from methanol–ligroin the substance formed lustrous, weakly yellow plates, m. p. 231–231.5°.

Anal. Calcd. for $C_{16}H_{13}O_2N$: N, 5.57. Found: N, 5.59.

The **ethyl carbamate**, obtained by refluxing the isocyanate (200 mg.) in chloroform (20 cc.) with absolute ethanol (10 cc.) for fifteen minutes, formed glistening light yellow plates from ethanol–ligroin, m. p. 216–216.5°.

Anal. Calcd. for $C_{17}H_{15}O_2N$: N, 5.28. Found: N, 5.31.

β-Anthrylcarbamidoethanol.—On adding a solution of 250 mg. of the isocyanate in 20 cc. of chloroform to 0.25 cc. of β-aminoethanol in 10 cc. of chloroform an amorphous greenish precipitate formed at once; after short warming to 40° it was cooled and the product collected and washed with 35 cc. of warm chloroform. Crystallization from 75 cc. of ethanol containing 3 cc. of dioxane gave slender, bright yellow needles. In an evacuated capillary the substance darkened at 310° and melted at about 350°.

Anal. Calcd. for $C_{17}H_{16}O_2N_2$: N, 9.99; C, 72.84; H, 5.75. Found: N, 9.82; C, 73.10; H, 5.76.

β-Anthryl Urea.—To 150 mg. of the isocyanate in 15 cc. of dioxane there was added 5 cc. of dioxane containing several drops of concentrated ammonium hydroxide. The greenish-yellow material which precipitated was crystallized from dioxane, forming small yellow plates (unmelted at 360°).

Anal. Calcd. for $C_{15}H_{12}ON_2$: N, 11.80. Found: N, 11.74.

N,N'-Di-β-anthryl Urea.—A mixture of benzene solutions of the isocyanate and β-anthramine was refluxed for twenty minutes and cooled. The yellowish-brown precipitate was washed, dried and purified by solution in dioxane and precipitation with benzene or by evaporation. Crystals were not obtained; the amorphous material was unmelted at 340° (Calcd.: N, 6.79; found: 6.02, 6.06).

β-Anthrylcarbamidoacetic Acid.—A solution of 75 mg. of glycine in 3 cc. of water was brought to *p*H 8.5 (colorimetric) by suitable addition of sodium hydroxide and added with stirring to 200 mg. of β-anthryl isocyanate in 25 cc. of dioxane. A greenish precipitate appeared at once, and after ten minutes a large volume of water was added, the mixture was warmed to 40°, alkali was added to bring the *p*H to 8.5, and the solution was filtered. Dilute hydrochloric acid was added to the opalescent filtrate to bring the *p*H to 3.0, and the greenish-white, flocculent precipitate, separated by centrifugation, was dissolved either in 500 cc. of water adjusted to *p*H 8.5 or in 1% sodium carbonate solution. Filtration through a No. 50 Whatman paper removed a trace of insoluble material. The conjugate was reprecipitated and washed with copious amounts of slightly acidified water. The process of solution and precipitation was repeated twice and the product dried in a vacuum desiccator. Further purification of the amorphous material was accomplished using water–dioxane–ethanol (5:1:2) and cooling very slowly. Eventually the substance was obtained as slender yellow needles. In an evacuated capillary the substance darkened at 250° and melted at about 310° with decomposition.

Anal. Calcd. for $C_{17}H_{14}O_3N_2$: N, 9.51; C, 69.38; H, 4.80. Found: N, 9.70; C, 68.99; H, 4.74.

ε-(β-Anthrylcarbamido)-caproic acid was prepared by conjugation of the isocyanate with ε-aminocaproic acid[18] by the above procedure and the material purified by repeated precipitation was crystallized from water–dioxane–alcohol (2:1:3) and obtained as short, dull yellow needles which darkened slightly at 260° and melted at 285–286° (vacuum).

Anal. Calcd. for $C_{21}H_{22}O_3N_2$: N, 7.98. Found: N, 8.07.

Nitration of 1,2-Benzanthracene.—A nearly colorless commercial sample of the hydrocarbon, m. p. 161–162.5° (Fraenkel and Landau), and a yellowish sample, m. p. 159–161.5° (Dominion Tar and Chemical Co.), were found unsatisfactory for the reaction, apparently because of the presence of significant quantities of chrysene. A supply of pure 1,2-benzanthracene was consequently synthesized according to Bachmann,[19,20] the hydrolysis of the intermediate naphthyl tolyl ketimine being conducted by the procedure of Fieser and Seligman.[21] Purification of the crude yellow pyrolysis product (m. p. 158.5–160°) by filtration of a benzene solution through an alumina tower removed some of the color and raised the m. p. (160–161°), but subsequent treatment with maleic anhydride[19] gave blue-fluorescent colorless plates, m. p. 160.5–161° in 30% over-all yield.

On nitrating 50 g. of the pure hydrocarbon in six lots

(16) von Braun and Bayer, *Ann.*, **472**, 116 (1929).

(17) The uncorrected m. p. is reported as 236–237°, or 238°: Liebermann and Bollert, *Ber.*, **15**, 226 (1882); Roemer, *ibid.*, **15**, 224 (1882).

(18) Eck, *Org. Syntheses*, **17**, 7 (1937).

(19) Bachmann, *J. Org. Chem.*, **1**, 349 (1936).

(20) See also Fieser and Hershberg, THIS JOURNAL, **59**, 2502 (1937).

(21) Fieser and Seligman, *ibid.*, **58**, 2486 (1936).

by the procedure of the literature[6,22] with some trial variations the yields were from 25 to 45% and the combined yield of pure 10-nitro-1,2-benzanthracene, m. p. 164–164.5°, was 20.2 g. (33%). No pure products were isolated from the mother liquors.

10-Amino-1,2-benzanthracene.—Since hydrogenation[6] of the nitro compound did not appear practical for preparative purposes, other methods were tried. Using phenylhydrazine for the reduction, the yield was only 20%, but satisfactory results were obtained with stannous chloride. In a typical run a solution of 6 g. of the pure nitro compound in 250 cc. of hot glacial acetic acid was treated with 50 g. of stannous chloride in 60 cc. of hot concentrated hydrochloric acid. After refluxing for one-half hour with mechanical stirring, 50 cc. of glacial acetic acid was added to bring about complete solution. On cooling the yellow tin double salt crystallized and was washed with acetic acid, dilute hydrochloric acid, alcohol and ether. The dried solid (7.8 g.) was decomposed by stirring with 175 cc. of 1 *N* ammonium hydroxide at 5° for one-half hour and at room temperature for one and one-half hours. The yellow solid was dried and crystallized twice from ether–petroleum ether, giving 4.1 g. (77%) of yellow needles of the amine, m. p. 175.5–176° (176–176.5° in an evacuated tube).

1,2-Benzanthryl-10-isocyanate.—On proceeding as above, 7.5 g. of the amine gave 6.5 g. (78%) of the isocyanate as slightly yellow diamond-shaped plates, m. p. 144–144.5°, after crystallization from benzene–toluene and benzene–ligroin.

Anal. Calcd. for $C_{19}H_{11}ON$: N, 5.20; C, 84.74; H, 4.12. Found: N, 5.25; C, 84.68; H, 4.10.

The purification of the carbamates described below presented considerable difficulty because of their marked tendency to separate in a gelatinous condition. A similar property was noted by Morgan and Pettet[23] in methyl and ethyl *p*-xenylcarbamates. The substances are very soluble in methanol, chloroform, ether, benzene and carbon tetrachloride and on evaporation nearly to dryness separate as amorphous powders; the addition of petroleum ether, in which the solublity is slight, invariably led to separation as a gel.

Methyl 1,2-Benzanthryl-10-carbamate.—The isocyanate was refluxed with methanol for fifteen minutes, the solution was evaporated to dryness, and the yellowish-white residue washed with methanol (m. p. 224–225°). On evaporation of a solution of the substance in ether the solid separating on the walls melted at 223–224.5° and that deposited on the bottom melted at 226–227°. Another preparation, after repeated precipitation as a gel from dioxane, methanol, or benzene by suitable addition of petroleum ether or ligroin, dried to a white powder, m. p. 226–227°. This eventually was crystallized from methanol as tiny white needles, m. p. 227–227.5°.

Anal. Calcd. for $C_{20}H_{15}O_2N$: N, 4.65. Found: N, 4.78.

The **ethyl carbamate** after similar tedious manipulation finally crystallized from absolute ethanol as rosets of small, colorless needles, m. p. 204–204.5°.

Anal. Calcd. for $C_{21}H_{17}O_2N$: N, 4.44. Found: N, 4.63.

1,2-Benzanthryl-10-carbamidoethanol also initially formed a gel but eventually was obtained from absolute ethanol–dioxane as slender white needles, m. p. 247–248° (in vacuum), with slight darkening at 240°.

Anal. Calcd. for $C_{21}H_{18}O_2N_2$: N, 8.47. Found: N, 8.37.

1,2-Benzanthryl-10-urea.—Slow cooling of a solution of the dried gelatinous reaction product in dioxane–ethyl acetate gave fine, colorless needles, m. p. (in vacuum) 334–336°, dec.

Anal. Calcd. for $C_{19}H_{14}ON_2$: N, 9.78. Found: N, 9.42.

N,N'-Di-(1,2-benzanthryl-10)-urea.—The dried powder from the flocculent brown precipitate resulting from the interaction of the 10-isocyanate and the 10-amine was repeatedly deposited from dioxane in an amorphous condition but failed to crystallize (unmelted at 330°).

Anal. Calcd. for $C_{37}H_{24}ON_2$: N, 5.47. Found: N, 5.38.

Polymerization of 1,2-Benzanthryl-10-isocyanate.—Since difficulties were encountered in attempts to prepare derivatives of aromatic isocyanates in pyridine solution, trial was made of the action of this solvent on pure 1,2-benzanthryl-10-isocyanate. The substance (100 mg.) dissolved at once at room temperature in purified anhydrous pyridine (5 cc.) to give a yellow solution, and in a few minutes the polymer began to separate. Collected and washed with ether, this was obtained as a slightly yellow powder, m. p. 305–307° (vacuum), very sparingly soluble in dioxane or benzene and only moderately soluble in pyridine. The absence of unpolymerized material was shown by the observation that boiling alcohol dissolved only a trace of material and left a residue of the same melting point.

Anal. Calcd. for $(C_{19}H_{11}ON)_x$: N, 5.20. Found: N, 5.57.

1,2-Benzanthryl-10-carbamidoacetic Acid.—The conjugate prepared from 0.5 g. of the isocyanate and 0.2 g. of glycine by the above procedure separated on acidification of the aqueous solution as a gel, which on drying afforded 0.6 g. of a light brown powder (calcd.: N, 8.13; found: 8.78). After two more precipitations, the dried material (N, 7.49) was washed with cold ether to an almost colorless powder (N, 8.16). The substance decomposed when heated in organic solvents. The addition of petroleum ether to solutions of the conjugate in cold acetone–dioxane or aqueous dioxane gave light brown amorphous precipitates which darkened at 230–240° and melted with decomposition in the region 270–275° (found for different samples: N, 7.68, 7.77). The substance was not obtained crystalline.

The **ethyl ester** was prepared by adding 0.13 g. of glycine ethyl ester in 5 cc. of benzene to 325 mg. of the isocyanate in 15 cc. of benzene at 35°. A gelatinous precipitate separated at once and after shaking for fifteen minutes this was collected, dried and washed with benzene. The yellowish solid (0.4 g.) was dissolved in pyridine at 50°; on cooling a granular product separated and was washed with ether (0.24 g., colorless; attempted concentration

(22) Barnett and Mathews, *Chem. News*, **130**, 339 (1925).
(23) Morgan and Pettet, *J. Chem. Soc.*, 1124 (1931).

of the filtrate led to decomposition). On slow cooling of a solution of this substance in ethanol–dioxane colorless microcrystals were obtained, m. p. 245–245.5°. Hydrolysis to the free acid was tried without success (decomposition).

Anal. Calcd. for $C_{23}H_{20}O_3N_2$: N, 7.52; C, 74.17; H, 5.41. Found: N, 7.67; C, 74.44; H, 5.34.

ε-(1,2-Benzanthryl-10-carbamido)-caproic acid was obtained initially as a flocculent precipitate. It formed a gel on the first two treatments with dioxane–ethanol–water and then was obtained as an amorphous precipitate giving when dried an almost colorless powder, m. p. 265–267°, with slight darkening at 200°.

Anal. Calcd. for $C_{25}H_{24}O_3N_2$: N, 7.00. Found: N, 7.06.

1,2,5,6-Dibenzanthryl-9-urea was prepared as above and obtained from dioxane in a colorless microcrystalline condition, m. p. 360–363°, dec. (vacuum).

Anal. Calcd. for $C_{23}H_{16}ON_2$: N, 8.33. Found: N, 8.19.

1,2,5,6-Dibenzanthryl-9-carbamidoacetic Acid.—This previously reported[8] substance has now been crystallized from dioxane–ethanol–water and obtained as slightly yellow needles darkening at 270° and melting at about 300° with decomposition.

Anal. Calcd. for $C_{25}H_{18}O_3N_2$: N, 7.10. Found: N, 6.64.

ε-(1,2,5,6-Dibenzanthryl-9-carbamido)-caproic acid crystallized from dioxane–ethanol–water as colorless plates which turned yellow at about 250°; m. p. about 305°.

Anal. Calcd. for $C_{29}H_{26}O_3N_2$: N, 6.21. Found: N, 6.07.

Attempted Formation of Ureas.—On refluxing a benzene solution of the 9-isocyanate and the 9-amine of 1,2,5,6-dibenzanthracene for two hours there was no evidence of reaction and both starting materials were isolated from the solution. The isocyanate reacted readily with aniline, however, giving an amorphous powder which was not obtained in a satisfactory condition. It was further found that the reaction proceeds readily with the corresponding *meso*-anthracene derivatives, giving **N,N'-di-(anthryl-9)-urea** (m. p. above 360°. Calcd.: N, 6.79. Found: N, 6.51). It therefore appears that the failure of the reaction between the two *meso*-dibenzanthracene derivatives is attributable to steric hindrance.[6,24]

1,2-Benzanthryl-3-isocyanate.—A supply of the 3-amine kindly synthesized by F. C. Novello by the previously described method[7] was recrystallized from ethanol and from benzene–ligroin, giving yellow needles, m. p. 211–212° (213.5–214° in an evacuated capillary). The isocyanate was prepared as usual (73% yield, pure) and obtained from benzene–ligroin as light yellow needles, m. p. 163–163.5°.

Anal. Calcd. for $C_{19}H_{11}ON$: N, 5.20; C, 84.74; H, 4.12. Found: N, 4.99; C, 84.83; H, 4.06.

Treated with pyridine at 25° the substance gave an amorphous, high melting polymer.

Methyl 1,2-benzanthryl-3-carbamate crystallized readily from methanol as slender white needles, m. p. 203.5–204°.

Anal. Calcd. for $C_{20}H_{15}O_2N$: N, 4.65; C, 79.71; H, 5.02. Found: N, 4.84; C, 79.57; H, 4.92.

The **ethyl carbamate** formed long, colorless needles from ethanol, m. p. 211.5–212° (Calcd.: N, 4.44. Found: N, 4.62).

1,2-Benzanthryl-3-carbamidoethanol at first separated from dioxane–ethanol in a flocculent condition but eventually formed colorless needles, m. p. 343–345° (vacuum).

Anal. Calcd. for $C_{21}H_{18}O_2N_2$: N, 8.47. Found: N, 8.50.

1,2-Benzanthryl-3-urea formed fine white needles, m. p. above 350°, from dioxane.

Anal. Calcd. for $C_{19}H_{14}ON_2$: N, 9.78. Found: N, 9.89.

The **N,N'-disubstituted urea** was obtained only as a light brown powder, m. p. above 350° (Calcd.: N, 5.47. Found: N, 5.31.).

1,2-Benzanthryl-3-carbamidoacetic acid separated from dioxane–ethanol–water as fragile, slightly yellow needles, m. p. about 310°, dec. (vacuum).

Anal. Calcd. for $C_{21}H_{16}O_3N_2$: N, 8.13. Found: N, 7.91.

ε-(1,2-Benzanthryl-3-carbamido)-caproic acid crystallized readily from dioxane–ethanol–water as glistening white needles, m. p. 295–297° (some darkening at 230°).

Anal. Calcd. for $C_{25}H_{24}O_3N_2$: N, 7.00; C, 74.97; H, 6.04. Found: N, 7.01; C, 74.84; H, 5.54.

Summary

β-Anthryl-, 1,2-benzanthryl-3- and 1,2-benzanthryl-10-isocyanate have been prepared and characterized by conversion to various carbamates and substituted ureas. The isocyanates were coupled with glycine and with ε-aminocaproic acid to give alkali-soluble substances some of which are being tested for carcinogenic activity. The method of conjugation in aqueous dioxane was found suitable for application to proteins.

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(24) Fieser and Hershberg, THIS JOURNAL, **60**, 2542 (1938).