methylhydroxylamine (7.02 g.) were heated in a nitrogen atmosphere at 130° for two and one-half hours. The resulting yellow oil was seeded with triphenylcarbinol and filtered after partial crystallization had occurred. Recrystallization of the solid from a mixture of benzene and petroleum ether yielded 0.93 g. (14%) of triphenylcarbinol. The residue obtained from the mother liquors from this crystallization and the original filtrate from which triphenylcarbinol had been separated was crystallized from ethanol and yielded 3.59 g. (39%) of a condensation product, m. p. 112.5–115°. Recrystallization from ethanol raised the m. p. to a constant value of 119.5–120.5°. Stieglitz and Leech[18] report m. p. 114°. The ultraviolet absorption spectrum of this compound (Fig. 4) indicates that it is O-triphenylmethylbenzaldoxime (XIV).

*Anal.* Calcd. for $C_{26}H_{21}NO$: C, 85.92; H, 5.83; N, 3.85. Found: C, 85.93; H, 5.87; N, 4.14.

Evidence confirming the structure of XIV was obtained by reduction. A 2-g. sample of XIV was dissolved in 100 ml. of hot glacial acetic acid and reduced by addition of 1.44 g. of zinc dust, with stirring. The mixture was stirred for forty-five minutes at 100° and then concentrated under reduced pressure to a volume of 30 ml. One hundred milliliters of 1 *N* hydrochloric acid and benzene were added, and the benzene layer was separated. The benzene solution was concentrated and diluted with petroleum ether, yielding 0.99 g. (69%) of triphenylcarbinol. The aqueous phase was concentrated under reduced pressure to a volume of 15 ml. and made strongly basic with concentrated sodium hydroxide solution. The alkaline solution was extracted with four 25-ml. portions of benzene, and the benzene extracts were concentrated and treated with 5.5 millimoles of picric acid in benzene. Benzylamine picrate was obtained in a yield of 0.99 g., m. p. 191–193° (dec.) (53.6%) and after recrystallization from ethanol was identified by m. p. (197–199° dec.) and mixed m. p. with a known sample.

**Oxidation of N-Benzhydrylhydroxylamine.**—In an attempt to reduce N-benzhydrylhydroxylamine with zinc and sodium hydroxide, the product isolated was an oxidation product, benzophenone oxime. The following similar experiment in which the zinc was omitted showed that the compound is easily oxidized by air in alkaline solution. N-Benzhydrylhydroxylamine (0.50 g.) was stirred with a solution of 0.50 g. of sodium hydroxide in 20 ml. of 95% ethanol for three hours at room temperature. The solution was poured into 100 ml. of water and extracted with three 25-ml. portions of ether. The extracts were concentrated, and the residual oil was crystallized from a mixture of benzene and petroleum ether. Benzophenone oxime was obtained in a yield of 0.47 g. (95%) and identified by its m. p. (142.5–143.5°) and mixed m. p. with an authentic sample.

**Absorption Spectra.**—The ultraviolet absorption spectra shown in Figs. 1 and 4 were determined with a Beckman model DU quartz spectrophotometer. The methylcyclohexane used as a solvent was purified by redistillation (b. p. 100–101°) and passed through a column of activated silica gel. The same solvent and instrument were used in determining the concentration of VIII in mixtures of VIII and IX from the optical density at 310 mμ in kinetic runs.

## Summary

Benzophenone N-benzhydryloxime (VIII) has been found to rearrange quantitatively to benzophenone O-benzhydryloxime (IX) on heating at temperatures of 160 to 200°. The rate of the rearrangement in diethylcarbitol solution was determined by an analytical method depending upon differences in the ultraviolet absorption spectra of VIII and IX, and was found to follow first-order kinetics. This information indicates that the mechanism of rearrangement involves an intramolecular process, probably occurring through a transitory three-membered cyclic intermediate in which the benzhydryl group becomes attached to oxygen as it is detached from nitrogen.

Benzophenone N-benzyloxime (III) did not rearrange to benzophenone O-benzyloxime (IV) on heating, but decomposed into products which can be explained by initial thermal decomposition of III into benzaldehyde and benzhydrylideneimine. Attempts to prepare benzophenone N-triphenylmethoxime (X) and N-triphenylmethylbenzaldoxime led to benzophenone O-triphenylmethyloxime (XI) and O-triphenylmethylbenzaldoxime (XIV), respectively, instead, indicating that the triphenylmethyl group rearranged from nitrogen to oxygen under the conditions of the reactions employed with the object of preparing the N-substituted compounds.

CAMBRIDGE, MASSACHUSETTS RECEIVED APRIL 6, 1950

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MIAMI UNIVERSITY, AND THE CHEMISTRY DIVISION OF THE OAK RIDGE NATIONAL LABORATORY]

# Some Compounds of Interest in Cancer Chemotherapy[1]

BY JOHN G. BURR, JR.,[2a] WILLIAM F. HOLTON[2b] AND CARL N. WEBB[2c]

The inhibition of tumor growth, under special conditions, by hydrocarbon carcinogens[3] requires further investigation in view of the current interest in the chemotherapy of cancer. Effective use of this inhibitory power depends upon the preparation of hydrocarbon derivatives which possess enhanced ability to inhibit tumor growth and no carcinogenicity.

One possibility considered was a modification of the terminal ring of several polynuclear hydrocarbons to contain what was at the time thought to be the hydroxymethylene ketone structure of ring C of colchicine, one of the most effective agents against animal tumors. Recent work[4]

(1) The portion of this work which was done at the Oak Ridge National Laboratory was performed under Contract Number W-7405, eng 26 for the Atomic Energy Project at Oak Ridge National Laboratory.

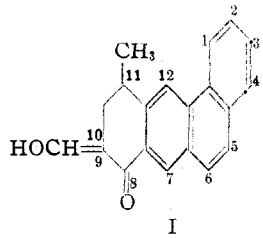
(2) (a) Chemistry Division, Oak Ridge National Laboratory, Oak Ridge, Tennessee; (b) Research Department, Bauer & Black, Chicago, Ill.; (c) Department of Chemistry, Miami University, Oxford, Ohio.

(3) Haddow and Robinson, *Proc. Roy. Soc.* (*London*), **B127**, 277 (1939).

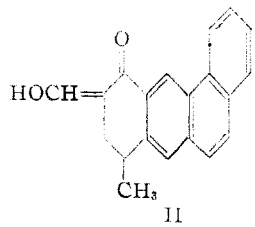
(4) (a) Dewar, *Nature*, **155**, 141, 479 (1945); (b) Tarbell, *et al.*, THIS JOURNAL, **71**, 244 (1949); **72**, 240–244 (1950); (c) Santavy, *Collection Czechoslovak. Chem. Commun.*, **14**, 145 (1949).

strongly (although not conclusively) indicates instead a tropolone system for the colchicine ring C.

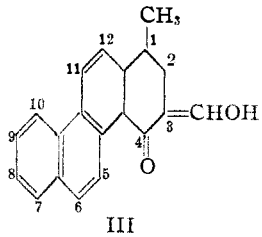
The compounds which were prepared to investigate this hypothesis are illustrated in formulas I–IV. Since these compounds retain possibility as chemotherapeutic agents, their synthesis, which offers points of interest, is here reported. In addition, the known compounds



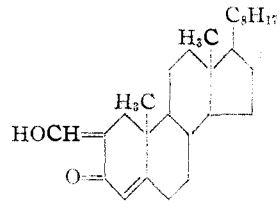

I




II




III




IV

1 - keto - 2 - hydroxymethylene - 1,2,3,4 - tetrahydronaphthalene, and 1-keto-2-hydroxymethylene-1,2,3,4-tetrahydrophenanthrene were prepared in order to obtain a more nearly complete homologous series of compounds.

The preparation of the cholestenone derivative (IV) was accomplished by treatment of cholestenone in benzene solution with ethyl formate in the presence of sodium hydride,[5] followed by evaporative distillation of the product. The substance forms yellow cubic prisms, from hexane, melting at 112–113°. In the condensation of ethyl formate with these ketones, sodium hydride was as effective as sodium methoxide[6] and was more convenient.

The ketone, whose hydroxymethylene derivative is represented in I, was prepared by the method of Riegel and Burr,[7] except that in the Stobbe condensation of 3-acetylphenanthrene with diethyl succinate, sodium hydride was employed in place of potassium *t*-butoxide.[8] There resulted a slight improvement in yield of the half-ester. The hydroxymethylene derivative of this ketone crystallized from ethanol as the enol ethyl ether. The free enol was obtained by crystallization of this ethyl ether from ethanol containing a drop of hydrochloric acid. Crystallization of the enol from methanol gave the corresponding methyl ether; however, treatment of the enol with higher alcohols resulted only in recovery of the enol. None of the other hydroxymethylene compounds prepared in this series have displayed such ease of ether formation and hydrolysis, although Johnson, *et al.*, report[9] that 2-hydroxymethylene-1-keto-7-methoxy-1,2,3,4-tetrahydrophenanthrene exhibited a similar behavior.

The ketones, whose derivatives are represented in II and III, were prepared by a similar series of reactions from 2-acetylphenanthrene. In this series of reactions a crystalline Stobbe half-ester and a crystalline arylvaleric acid were obtained. The cyclization of γ-(2-phenanthryl)-valeric acid with stannic chloride in benzene is reported[10,11] to give the hydrochrysene ketone in 72% yield. In our hands the cyclization of this acid has led to a mixture of ketones in 72.5% yield. This mixture consisted of almost equal amounts of the hydrochrysene and the hydrobenzanthracene ketones. These were identified by reduction and dehydrogenation to the corresponding known 1-methylchrysene, and 8-methylbenzanthracene, which were further characterized by their ultraviolet absorption spectra.

Both the hydrochrysene ketone and the hydrobenzanthracene ketone condensed easily with ethyl formate to give alkali-soluble hydroxymethylene derivatives, but only that (II) from the hydrobenzanthracene ketone could be obtained crystalline, and then in poor yield.

2-Hydroxymethylene-α-tetralone was prepared by the method of Johnson, Anderson and Shelberg.[6] 1-Keto-2-hydroxymethylene-1,2,3,4-tetrahydrophenanthrene was prepared by the same method and had the known[12] physical constants.

**Acknowledgment.**—That portion of the work which was accomplished at Miami University was supported by a grant-in aid from the U. S. Public Health Service, which the authors gratefully acknowledge.

Samples of several of these compounds have been submitted to the National Cancer Institute for testing of their effect upon animal tumors.

## Experimental[13]

**2-(Hydroxymethylene)-cholesten-4-one-3 (IV).**—A solution of 3.0 g. of cholestenone[14] in 25 ml. of dry benzene was added to a suspension of about 0.5 g. of sodium hydride in a mixture of 15 ml. of benzene and 3 ml. of ethyl formate. The reaction, which began immediately, was

(5) The sodium hydride was supplied by the Electrochemical Department of E. I. du Pont de Nemours and Co.

(6) Johnson, Anderson and Shelberg, THIS JOURNAL, **66**, 218 (1944).

(7) Riegel and Burr, *ibid.*, **70**, 1070 (1948).

(8) Daub and Johnson, *ibid.*, **70**, 418 (1948); **72**, 501 (1950).

(9) Johnson, Peterson and Gutsche, *ibid.*, **69**, 2942 (1947).

(10) Bachmann and Struve, *J. Org. Chem.*, **5**, 416 (1940).

(11) The cyclization direction of γ-(2-phenanthryl)-butyric acids has been shown (Adams, "Organic Reactions," John Wiley and Sons, New York, N. Y., 1944, Vol. 2, p. 176)) to be quite sensitive to both the type of the reagent and the type of the solvent employed. In general, Friedel-Crafts conditions lead to a mixture of ketones with the hydrochrysene ketone predominating; while the use of hydrogen fluoride appears to lead entirely to the hydrobenzanthracene ketone.

(12) Meyer and Reichstein, *Pharm. Acta Helv.*, **19**, 128 (1944).

(13) All melting points were taken on a Fisher–Johns block and are uncorrected. Microanalyses were by P. Z. Westerdahl, Chemistry Division, Oak Ridge National Laboratory.

(14) Prepared by Clinton H. Parsons, Jr., using the method of Schoenheimer, *J. Biol. Chem.*, **110**, 462 (1935). An oxidation of eight hours was necessary to obtain a 70% yield.

allowed to continue overnight at room temperature before the deep red semi-solid mass was hydrolyzed with dilute sulfuric acid. Since the enol formed water-insoluble sodium, potassium, and ammonium salts, and the neutral products of the reaction were negligible in amount, the reaction solution was hydrolyzed and the whole reaction product was evaporatively distilled. The distillate was a yellow oil, which slowly crystallized, weighing 2.40 g. It crystallized slowly from dilute alcohol as a pale yellow cottony mass, and more quickly from hexane as yellow cubic prisms, melting at 112–113°. The solid gave a deep brown color with alcoholic ferric chloride, and alcoholic cupric chloride precipitated a blue solid which redissolved in excess reagent.

*Anal.* Calcd. for $C_{28}H_{44}O_2$: C, 81.5; H, 1.08. Found: C, 81.8; H, 10.7.

**8-Keto-9-hydroxymethylene-11-methyl-8,9,10,11-tetrahydrobenz[a]anthracene (I).**—This was prepared from 5.0 g. of the ketone, 4 ml. of ethyl formate, about 1 g. of sodium hydride, and 50 ml. of benzene. The dark-green reaction solution was hydrolyzed, and the acidic reaction product was crystallized twice from ethanol (Nuchar) to give 3.6 g. of pale yellow cottony needles, melting at 148–149°. This substance did not dissolve in 10% sodium hydroxide nor did it color alcoholic ferric chloride, and thus is presumably the enol ethyl ether.

*Anal.* Calcd. for $C_{22}H_{20}O_2$: C, 83.5; H, 6.4. Found: C, 83.6; H, 6.6.

Crystallization of this substance from ethanol containing a few drops of hydrochloric acid gave a tan solid which after two more similar crystallizations melted at 138–139°. A mixture of this with the above ether melted at 110–130°. This second substance was soluble in alkali and gave a deep green color with alcoholic ferric chloride. It is presumably the free enol.

*Anal.* Calcd. for $C_{20}H_{16}O_2$: C, 83.3; H, 5.6. Found: C, 83.3; H, 5.3.

Crystallization of this enol from ethanol again led to the above enol ethyl ether. Crystallization of the enol from methanol gave the enol methyl ether, yellow crystals melting at 145–146°.

*Anal.* Calcd. for $C_{21}H_{18}O_2$: C, 83.4; H, 6.0. Found: C, 83.5; H, 6.28.

**Stobbe Half-ester from 2-Acetylphenanthrene.**—To a solution of 2.01 g. of potassium in 28.5 ml. of anhydrous *t*-butyl alcohol was added 8.73 g. (0.04 mole) of 2-acetylphenanthrene and 14.0 (0.08 mole) of diethyl succinate. The mixture was refluxed for eight hours, hydrolyzed with 3 *N* hydrochloric acid, and the *t*-butyl alcohol distilled off. The residual product was extracted with 5% sodium bicarbonate. This solution upon acidification deposited a red oil. Crystallization of the oil from benzene gave 2.34 g. of crystalline half-ester, melting at 157–158°, and 4.44 g. of a red glassy half-ester. Since 1.55 g. of unreacted 2-acetylphenanthrene was recovered, the net yield of half-ester was 60%. The crystalline half-ester possessed a neutralization equivalent of 342 (calcd. for $C_{22}H_{20}O_4$, 348).

*Anal.* Calcd. for $C_{22}H_{20}O_4$: C, 75.8; H, 5.8. Found: C, 75.7; H, 5.7.

Both the crystalline half-ester and the gummy half-ester were suitable for use in the following step of the synthesis. This Stobbe condensation, like the one with 3-acetylphenanthrene, was promoted by both sodium hydride and potassium *t*-butoxide. Although use of sodium hydride gave slightly better total yields (72%) of crude half-ester, the non-crystalline fraction of the product gave a much poorer conversion to lactone than did the corresponding fraction of the product from the butoxide condensation.

**γ-(2-Phenanthryl)-valerolactone.**—A mixture of 3.30 g. (0.0095 mole) of the crystalline Stobbe half-ester with 6.5 ml. of 48% hydrobromic acid, 2.2 ml. of water, and 9.6 ml. of glacial acetic acid was heated under reflux for 7 hours. The cooled reaction mixture was diluted with a large volume of water; the precipitated solid was dissolved in benzene and extracted with bicarbonate solution. The neutral substance recovered from the benzene was crystallized from benzene to give 1.76 g. (68%) of white solid melting at 132–133°.

*Anal.* Calcd. for $C_{19}H_{18}O_2$: C, 82.6; H, 5.8. Found: C, 83.0; H, 6.1.

**γ-(2-Phenanthryl)-valeric Acid.**—A 4.22 g. portion of the above lactone was refluxed with 57 ml. of glacial acetic acid, 3.59 g. of red phosphorus, 1.18 g. of iodine and 1.3 ml. of water for twelve hours. The hot solution was filtered and poured into a large excess of water containing some bisulfite. The precipitated product was dissolved in benzene, from which it was extracted with sodium carbonate solution. Acidification of this solution yielded a product in 73% yield, which melted at 123–128°. One crystallization from ethanol raised the melting point to 135–136° (lit.[10] 136.5–137.5°). A mixture of this with the lactone showed a depressed melting point. A neutralization equivalent of 272 (calcd. for $C_{19}H_{18}O_2$, 278) was found.

**8-Methyl-11-keto-8,9,10,11-tetrahydrobenz(a)anthracene and 1-Methyl-4-keto-1,2,3,4-tetrahydrochrysene.**—To a solution of 5.53 g. (0.0199 mole) of the substituted valeric acid in 100 ml. of benzene was added 5.5 g. of phosphorus pentachloride in portions. After standing at room temperature for twenty minutes, the solution was chilled with an ice-bath, and to it was added, in a slow stream with constant stirring, a solution of 6.5 ml. of stannic chloride in 25 ml. of benzene. A finely divided red complex settled out. After twenty minutes of standing in the ice-bath, the mixture was hydrolyzed with ice and hydrochloric acid. The benzene solution was washed with acid, bicarbonate solution and water, and the solvent was removed. The residue was a pale yellow gum (3.76 g., 72.5% yield). This material deposited from hexane solution as a mixture of massive prisms and needles. These were separated mechanically, and the separated fractions each crystallized several times from hexane to give 1.52 g. of prisms which melted at 95–96° (lit.[10] for the hydrochrysene ketone; 98.5–99.5°), 1.93 g. of needles which melted at 113–114° and 0.15 g. of a yellow gum.

*Anal.* Calcd. for $C_{19}H_{16}O$: C, 87.7; H, 6.2. Found: needles: C, 87.4; H, 6.4; prisms: C, 88.3; H, 6.7.

Samples (0.5 g.) of each of these ketones were subjected to Clemmensen reduction (Martin modification),[15] and the resulting dark gums were dehydrogenated at 320° with a palladium-on-charcoal catalyst. The dehydrogenated products in benzene solution were passed through alumina columns, and then the recovered substance sublimed *in vacuo*. The crystalline sublimates were crystallized from alcohol.

The needle-form ketone gave 8-methylbenz[a]anthracene as yellow prisms melting at 153–154° (lit.[16] 157.5–158.5°). This hydrocarbon had absorption peaks in alcohol (wave lengths in mμ, absorption as log $E_M$) at: 261 (4.47), 269 (4.66), 278 (4.85), 289 (4.91), 315 (3.70), 328 (3.80).

The prism-form ketone gave 1-methylchrysene as colorless leaflets melting at 253–254° (lit.[10] 253–254°). This hydrocarbon had absorption peaks in alcohol (wave lengths in mμ, absorption as log $E_M$) at: 260 (4.88), 270 (5.09), 285 (4.10), 298 (4.07), 310 (4.16), 324 (4.14). These are in good agreement with the recorded spectra.[17]

**8-Methyl-10-hydroxymethylene-11-keto-8,9,10,11-tetrahydrobenz[a]anthracene (II).**—A solution of 0.5 g. of the hydrobenzanthracene ketone and 0.5 g. ethyl formate in 20 ml. of dry benzene was treated with 0.5 g. of sodium hydride as above. The product was 0.44 g. (79%) of a dark, alkali-soluble solid. Repeated crystallization of this from dilute acetone gave a small amount of yellow plates which melted at 93–93.5°. The solid gave a deep

(15) Martin, THIS JOURNAL, **58**, 1438 (1936).

(16) (a) Cook, *J. Chem. Soc.*, 1592 (1933); (b) Fieser and Hershberg, THIS JOURNAL, **58**, 2376 (1936); (c) Bachman, *ibid.*, **60**, 624 (1938); (d) Fieser and Johnson, *ibid.*, **61**, 1647 (1939).

(17) Brode and Patterson, THIS JOURNAL, **63**, 3253 (1941).

color with alcoholic ferric chloride. The bulk of the product could not be crystallized.

*Anal.* Calcd. for $C_{20}H_{16}O_2$: C, 83.3; H, 5.6. Found: C, 83.5; H, 5.3.

## Summary

The α-hydroxymethylene derivatives of cholestenone, 8-keto-11-methyl-8,9,10,11-tetrahydrobenz[a]anthracene, α-tetralone, and 8-methyl-11-keto-8,9,10,11-tetrahydrobenz[a]anthracene and 1-keto-1,2,3,4-tetrahydrophenanthrene have been prepared for testing as agents in the chemotherapy of cancer.

The hydroxymethylene derivative of 8-keto-11-methyl 8,9,10,11-tetrahydrobenz[a]anthracene has shown an interesting lability of ether formation and cleavage.

OAK RIDGE, TENNESSEE RECEIVED APRIL 3, 1950

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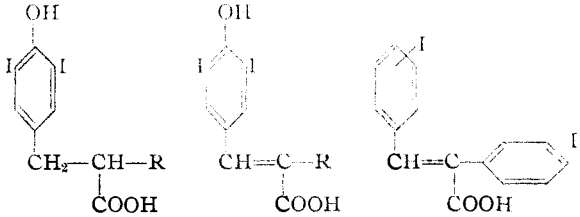
[CONTRIBUTION FROM THE CHEMICAL RESEARCH DIVISION OF SCHERING CORPORATION]

# X-Ray Diagnostics. IV. Cholecystographic Agents

BY DOMENICK PAPA, HILDA BREIGER, ERWIN SCHWENK AND VIRGINIA PETERSON

In continuation of studies[1] on the correlation of structure and cholecystographic property of organic iodine compounds, we have prepared for pharmacological evaluation a limited number of compounds of four different types. In none of these four groups of compounds do the structures depart radically from the known clinically efficacious cholecystographic medium, α-phenyl-β-(3,5-diiodo-4-hydroxyphenyl)-propionic acid[2] (I).

The first two types of iodinated compounds are of general formulas II and III[1e] wherein Z is either sulfur or oxygen. The structural similarity of these two types of compounds to I is apparent from an inspection of the formulas, II being identical to I except for the presence of a hetero atom, whereas III differs from I in having both a hetero atom and a double bond in the aliphatic portion of the molecule.



I, R = $C_6H_5$–
II, R = $C_6H_5Z$–
III, R = $C_6H_5Z$–
IV, R = $C_6H_5$; $CH_2C_6H_5$–
V, R = alkyl group

The third group of compounds are of general formula IV, wherein R is phenyl, benzyl and the corresponding *p*-iodo derivatives. These substances embrace the basic Priodax structure, but are unsaturated aliphatic acid derivatives. In the latter respect, substances of type IV are structurally related to the recently described[1c] 3,5-diiodo-4-hydroxyphenylalkenoic acid (V) and the diiodo-diarylacrylic acids[1a] (VI).

Several additional compounds of general formula IV were synthesized in which the radiopaque element is bromine, chlorine or a combination of either of these elements and iodine. Although iodine is recognized as the radiopaque element of choice, bromo and chloro compounds have been used clinically with success as contrast agents. In addition, the chemical and patent literature is replete with reports of bromo and chloro compounds which have been proposed or studied as contrast agents. It was also of interest to compare the solubility of these compounds with the corresponding iodo compounds in view of the apparent correlation of this physical property and cholecystographic properties.[1b]

The diiodo compounds of formula II were secured from the known substituted propionic acids[3] by iodination with potassium triiodide in alkaline solution. The compounds of formulas III, IV and IX were prepared by the conventional Perkin reaction of the anhydrous alkali metal salt of the appropriately substituted acetic acids and benzaldehydes. The condensation of the free acid with the substituted benzaldehyde in the presence of an equimolecular amount of anhydrous triethylamine or potassium acetate[4] was used in the synthesis of α-phenoxy-3,5-diiodo-4-hydroxycinnamic acid and X. The yield in these instances was not comparable to those obtained using the anhydrous alkali metal salts of the acids.

The fourth type of compound to be investigated differs from types I–V in that the hydroxyl group has been replaced by an amino group.[5] Two propionic acids, VII and VIII, an acrylic acid, IX, and a substance, X, having both a hydroxyl and an amino group were prepared.

The intermediates, α-phenyl-β-(*p*-aminophenyl)-propionic acid (XI) and α-(*p*-aminophenyl)-β-

(1) (a) Schwenk and Papa, U. S. Patent 2,436,270, Feb. 17, 1948; (b) Papa, *Arch. Biochem.*, **23**, 163 (1949); (c) Papa, Schwenk, Breiger and Peterson, THIS JOURNAL, **72**, 2619 (1950); (d) Papa, Schwenk and Klingsberg, *ibid.*, **72**, 2623 (1950); (e) Papa and Schwenk, U. S. Patent 2,503,296, April 11, 1950.

(2) See references in 1c.

(3) Papa and Schwenk, THIS JOURNAL, **69**, 3022 (1947).

(4) Papa, Breiger and Peterson, *J. Org. Chem.*, **14**, 363 (1949) (see references 6 and 7 in this paper).

(5) (a) While this work was in progress, the diiodoamino acid VII was reported by Barnett, Robinson and Wilson, *J. Chem. Soc.*, 203 (1947); (b) diiodoamino acids VII and VIII have been reported recently by Lewis, Pratt, Homiller, Tullar and Archer, THIS JOURNAL, **71**, 3749 (1949).