After addition of 100 ml. of benzene and 100 ml. of water, the reaction mixture was shaken thoroughly. After standing for 15 minutes, the yellow triphenylpyrylium salt (8.8 g.), m.p. 210–215°, was collected. The yield was 9% calculated on the basis that four moles of acetophenone was required to form one mole of pyrylium salt. After four recrystallizations from 95% ethanol, the salt melted at 232–234°, and after drying at 80° and 20 mm. for several hours it melted at 252–254°. Dovey and Robinson[4] report m.p. 225–226° for a hydrate which furnished analytical figures corresponding to $C_{23}H_{17}OBF_4\cdot 0.66H_2O$. The fluoborate was shaken with 3% sodium hydroxide solution and the ferrichloride was precipitated by addition of a saturated solution of ferric chloride in concentrated hydrochloric acid. After one recrystallization from acetone-benzene, the yellow needles melted at 273–275°; reported m.p. 277°.[17] For further identification, the crude pyrylium fluoborate was converted to 2,4,6-triphenylpyridine, m.p. 138–139°, according to Dilthey.[17]

The two layers of the filtrate from the pyrylium fluoborate were separated. The benzene layer was washed with five 100-ml. portions of 5% sodium bicarbonate solution. On acidification of the bicarbonate extracts 1.30 g. of benzoic acid, m.p. and mixture m.p.'s with an authentic sample 121–123°, was obtained. After washing with water, the residue, after removal of the benzene, was distilled under reduced pressure through a 20-cm. Vigreux column. The first fraction (30 g., b.p. 90–100° (20–25 mm.)) was unreacted acetophenone. The second fraction (0.45 g., b.p. 110–150° (0.4–0.5 mm.)) was discarded. The third fraction, b.p. 151–175° (0.4–0.5 mm.), weighed 30.1 g. The residue was 40.1 g. of a brown glassy solid from which, after trituration with a mixture of 60 ml. of hexane and 10 ml. of benzene, 6.0 g. of crude 1,3,5-triphenylbenzene, m.p. 165–172°, was isolated. After recrystallization from benzene-hexane, it melted at 174–176°; reported m.p. 172°.[18] Nitration of the substance gave 1-(*p*-nitrophenyl)-3,5-diphenylbenzene, m.p. 144–145°; reported m.p. 142–143°.[18]

The third fraction obtained above was carefully redistilled through a 20-cm. Vigreux column and separated into four fractions as presented in Table I. Each fraction was examined in the infrared and the spectra were compared with that of dypnone. The spectra of fractions I and II were similar to that of dypnone except that the peak at 3.35 m. showed much stronger absorption and two new peaks at 5.86 and 5.95 m. were present. The spectra of fractions III and IV were identical with that of dypnone. Fraction III gave a semicarbazone, m.p. and mixture m.p.'s with an authentic sample 150–152°, identical with the semicarbazone of dypnone.

TABLE I

Fraction	B.p., °C. at 0.3–0.5 mm.	$n^{25.5}_D$	Wt., g.
I	150–152	1.6060	1.99
II	152–154	1.6196	6.73
III	154–156	1.6245	5.90
IV	156–157	1.6278	13.45
Residue			2.09

Condensation of Dypnone in the Presence of Boron Trifluoride Etherate.—Dypnone (3.0 g., 0.00135 mole) was heated with 3.0 g. (0.00211 mole) of boron trifluoride etherate at 120–130° for ten minutes. After cooling, 10 ml. of benzene and 20 ml. of water were added to the mixture. The yellow precipitate (0.30 g., 11%) melted at 233–234° after recrystallization from 10 ml. of 95% ethanol. The mixture m.p. with authentic II was not depressed.

Reaction of Dypnone and Benzoyl Fluoride in the Presence of Boron Trifluoride Etherate.—Benzoyl fluoride was prepared by heating a mixture of benzoic anhydride (36.5 g., 0.162 mole) with 14 g. (0.245 mole) of potassium fluoride in a Woods metal-bath.[19] Distillation of the fluoride began at 190° bath temperature. The slightly pink fluoride (13.1 g., 65%) boiled at 150–154°.

To a cooled mixture of dypnone (8.38 g., 0.04 mole) and benzoyl fluoride (4.96 g., 0.04 mole) was added slowly 14.20 g. (0.10 mole) of boron trifluoride etherate. The mixture was allowed to stand overnight at room temperature. After working up as in the preceding case, 2.00 g. (12.6%) of II, m.p. 229–233°, was obtained.

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[17] W. Dilthey, *J. prakt. Chem.*, [2] **94**, 53 (1916).

[18] D. Vorlander, E. Fischer and H. Wille, *Ber.*, **62**, 2837 (1929).

[19] A. I. Mashentev, *J. Gen. Chem.* (*USSR*), **15**, 915 (1945).

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

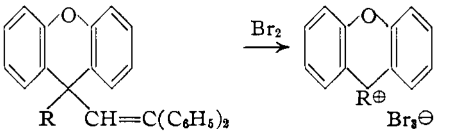
An Investigation of the Possibility of Benzopyrylium Salt Formation by Hydrocarbon Elimination from Chromens[1]

BY ROBERT C. ELDERFIELD AND TE PIAO KING[2]

RECEIVED DECEMBER 23, 1953

In order to investigate possibilities of facile carbon–carbon bond cleavage with formation of benzopyrylium salts, 2,4-diphenyl-4-methyl-1,4-chromene and 2,4-diphenyl-2-methyl-1,2-chromene have been synthesized. No carbon–carbon bond cleavage in either of these compounds was noted under a wide variety of conditions. Alkaline and acid hydrolysis of ethyl α-cyano-β-(*o*-anisyl)-β-(9-fluorenyl)-β-phenylpropionate has been studied.

In the preceding paper[3] evidence was presented to show that the formation of 2,4,6-triphenylpyrylium salts from acetophenone does not proceed by ejection of a methyl group from an intermediate pyran as had been suggested previously. Although such elimination of a hydrocarbon fragment does not occur in this particular instance, the possibility that, under favorable conditions, elimination of a methyl group from an oxygen heterocycle may occur as a result of the energy supplied by resonance stabilization of a resultant pyrylium salt remains.[4] One case of carbon–carbon bond cleavage with the formation of an oxonium salt has been reported. Ziegler[5] noted that when 9-(β,β-diphenylvinyl)-xanthene (I) or its 9-substituted analogs (Ia, Ib, Ic) were treated with bromine in ether at room temperature, xanthylium perbromide (II) or 9-substituted xanthylium perbromides (IIa, IIb, IIc) and 2,2-diphenyl-1,1,2-tribromoethane were formed.



I, R = H; Ib, R = C_6H_5
Ia, R = C_2H_5; Ic, R = α-$C_{10}H_7$

II, IIb,
IIa, IIc
+ $Br_2CHCBr(C_6H_5)_2$

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[1] The material here reported is taken from a dissertation presented by Te Piao King in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Michigan.

[2] Parke–Davis and Company Fellow 1952–1953.

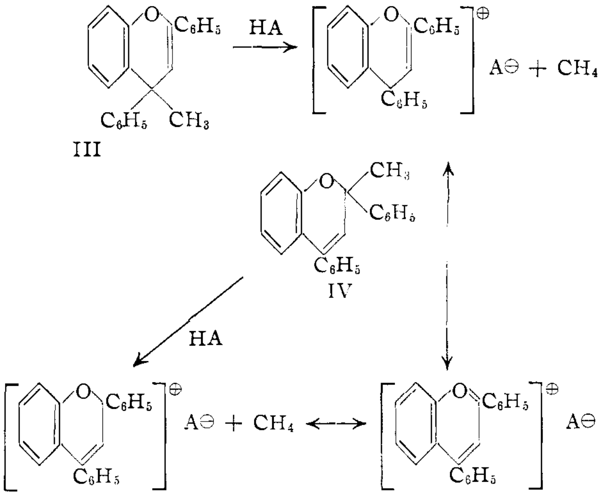
[3] R. C. Elderfield and T. P. King, THIS JOURNAL, **76**, 5437 (1954).

[4] For examples of such eliminations in other series, see ref. 3.

[5] K. Ziegler, *Ann.*, **434**, 34 (1923).

Further, when these 9,9-disubstituted xanthenes were boiled with hydriodic acid and red phosphorus in acetic acid, the corresponding monosubstituted xanthenes were formed probably by reduction of the xanthylium salts.

We wish to report a study of such reactions applied to selected members of the chromene group. 2,4-Diphenyl-4-methyl-1,4-chromene (III) and 2,4-diphenyl-2-methyl-1,2-chromene (IV) were chosen as model compounds. The choice was made on the basis of the expected lower energy of the transition state in the reaction leading to the formation of a benzopyrylium salt compared to the transition state in the reaction leading to a pyrylium salt. The projected elimination reaction can be formulated in an over-all sense as

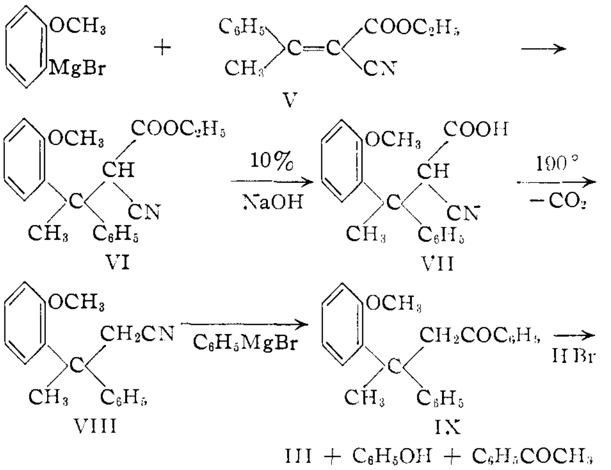


Inasmuch as III and IV represent hitherto unreported chromenes, it became necessary to develop suitable syntheses for them.

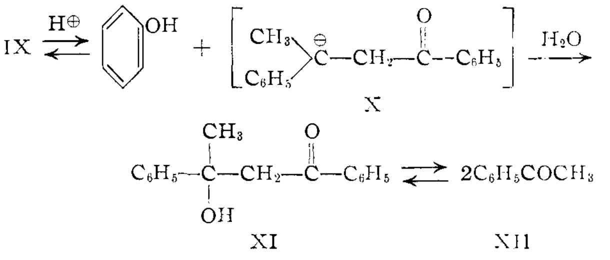
The literature on the condensation of α,β-unsaturated ketones with phenol is confusing. Dianin[6] reports the formation of 2-(p-hydroxyphenyl)-2,4,4-trimethylchroman from the condensation of phenol with mesityl oxide in the presence of hydrogen chloride. The chroman possesses the interesting property of decomposing to 2,4,4-trimethyl-1,4-chromene and phenol on distillation. Niederl[7] reports that the same condensation carried out with concentrated sulfuric acid as catalyst results in the formation of 2,4,4-trimethyl-2-chromanol. On the other hand, Smith and Prichard[8] obtained none of the condensation product from phenol and mesityl oxide reported by Niederl with either aluminum chloride or sulfuric acid as catalysts. Our results confirm those of Smith and Prichard insofar as the general reaction is concerned. The condensation of phenol and 1,3-diphenyl-2-butene-1-one (dypnone) with either aluminum chloride or sulfuric acid failed.

In view of the 1,4-addition of phenylmagnesium bromide to dypnone[9] in 44% yield, a similar reaction with o-methoxyphenylmagnesium bromide was attempted. Cyclization of the resulting product after cleavage of the ether should result in III. However, only intractable tars were obtained from the addition reaction.

Synthesis of III was finally achieved by the sequence



o-Methoxyphenylmagnesium bromide added to ethyl α-cyano-β-phenylcrotonate (V) to give ethyl β-(o-anisyl)-β-phenyl-α-cyanobutyrate (VI) in 38% yield.[10-12] Hydrolysis of VI with sodium hydroxide gave the corresponding acid VII in 89% yield which was decarboxylated by heating to give the nitrile VIII. Reaction of VIII with phenylmagnesium bromide gave β-(o-anisyl)-β-phenylbutyrophenone (IX) in 78% yield. When IX was refluxed with hydrobromic acid in glacial acetic acid, III resulted in 56% yield. In the ether cleavage reaction, small amounts of acetophenone and phenol were formed. The formation of these side-products can be accounted for by reactions IX–XII.



Reversal of a Friedel–Crafts alkylation[13] would lead to the carbonium ion X which can solvate to give the aldol XI. Reversal of the aldol condensation can then be expected to give two moles of acetophenone XII.

Definite proof of the structure assigned to III was provided by its degradation to 2-(o-hydroxyphenyl)-2-phenyl-1-propanol (XV) and synthesis of the latter.

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[6] A. Dianin, *J. Russ. Phys. Chem. Ges.*, **46**, 1310 (1914) (*Chem. Centr.*, **86**, I, 1063 (1915)).

[7] J. B. Niederl, THIS JOURNAL, **51**, 2426 (1929).

[8] L. I. Smith and W. W. Prichard, *ibid.*, **62**, 771 (1940); W. Baker, R. F. Curtis and J. F. W. McOmie, *J. Chem. Soc.*, 1774 (1952).

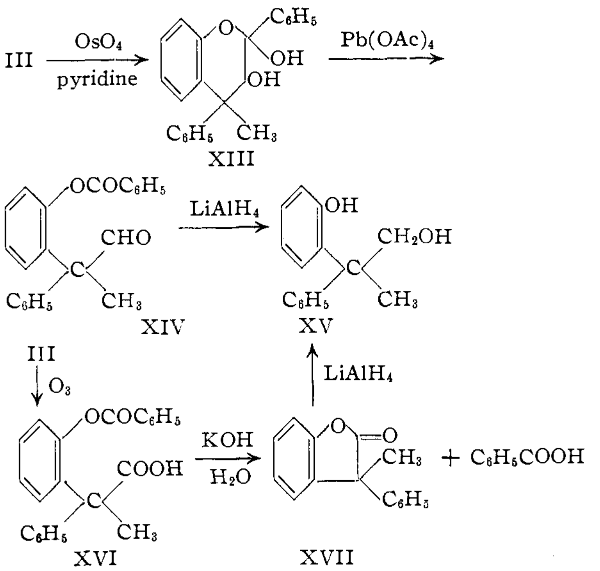
[9] E. P. Kohler, *Am. Chem. J.*, **31**, 642 (1904).

[10] W. H. Hook and R. Robinson, *J. Chem. Soc.*, 152 (1944).

[11] R. C. Fuson, H. L. Jackson and E. W. Grieshaber, *J. Org. Chem.*, **16**, 1529 (1951).

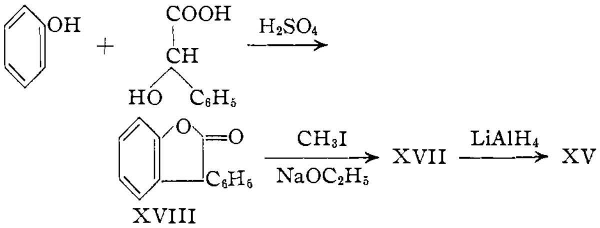
[12] E. J. Prout, E. P. Y. Huang and H. L. Young, Abstracts of papers presented at the American Chemical Society Meeting, Buffalo, N. Y., March 24–27, 1952, p. 58K.

[13] C. C. Price and J. M. Ciskowski, THIS JOURNAL, **60**, 2499 (1938).



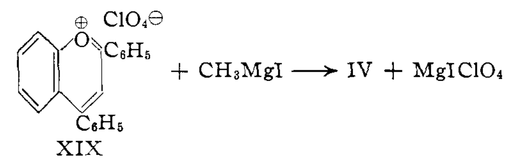
Oxidation of III with osmium tetroxide led to the glycol XIII which on further oxidation with lead tetraacetate gave an oil, presumably XIV. Reduction of XIV with lithium aluminum hydride gave XV. XV was also obtained by ozonolysis of III followed by oxidative decomposition of the ozonide to yield XVI. The oil XVII resulting from hydrolysis of XVI on reduction with lithium aluminum hydride gave XV.

XV was prepared by lithium aluminum hydride reduction of 3-methyl-3-phenyl-2-coumaranone (XVIII).[14]



III gave a dihydro derivative on catalytic hydrogenation and a monobromo derivative with bromine in carbon tetrachloride. In the latter compound, the bromine is probably in the 3-position since on ozonolysis of its solution in ethyl acetate, bromine was liberated. We interpret this as indicating that the bromine was not present on one of the phenyl groups.

IV was prepared by condensation of methylmagnesium iodide with 2,4-diphenylbenzopyrylium perchlorate (XIX). Reaction of XIX with phenylmagnesium bromide gives 2,2,4-triphenyl-1,2-chromene.[15]

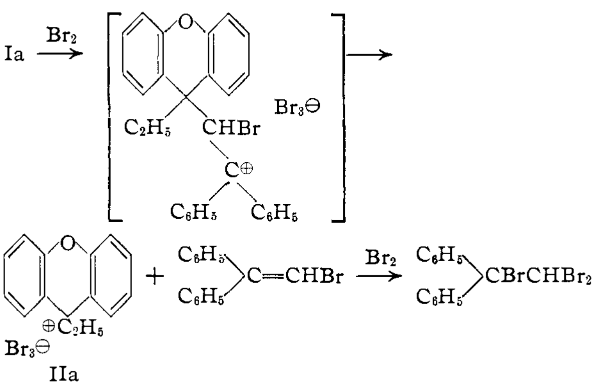


The structure assigned to IV is based on its method of synthesis and the fact that it is different from III, the structure of which has been demonstrated. IV gave a bromo derivative, the analytical figures for which agreed with those demanded by $C_{22}H_{17}BrO_2$. The substance was not investigated further.

III and IV were subjected to various conditions under which elimination of a methyl group could be expected. These included heating with concentrated hydrochloric acid and ferric chloride at 195°, refluxing with ferric chloride, acetic anhydride and acetic acid, and heating with boron trifluoride etherate at 155°. In no case was a benzopyrylium salt isolated.

In order to form a 2,4-diphenylbenzopyrylium salt by direct cleavage of III or IV, it is necessary for the methyl group to leave as an anion. Failure of the reaction to take place can be explained only on the basis that the reaction requires a high energy of activation because of the energy required to break the bond in question and the relatively low energy gain in the formation of the benzopyrylium salt. This energy may be lowered if the separated anion has considerable stability of its own by resonance, *e.g.*, the *p*-nitrobenzyl- or 9-fluorenyl-anions.

A reasonable explanation for the cleavage of I and its analogs (Ia, Ib, Ic) by bromine under extremely mild conditions to give xanthylium perbromides may be found in the postulate that the fragment split off leaves as a neutral molecule and that as a result, no separation of charges is involved. On this basis, the reaction proceeds first by an attack of a positive bromine ion at the α-position of the vinyl group. By a shift of the electron pair (located between the xanthene and vinyl groups) toward the vinyl group, xanthylium ion and β,β-diphenylvinyl bromide are formed. Addition of a second mole of bromine to the latter compound then gives 1,1,2-tribromo-2,2-diphenylethane, *e.g.*



In the light of these considerations, syntheses of 2,4-diphenyl-4-(9-fluorenyl)-1,4-chromene (XX) and of 2,4-diphenyl-4-(2,2-diphenylvinyl)-1,4-chromene (XXI) or their 2-substituted analogs were attempted. Although the projected syntheses were unsuccessful, the course of the reactions investigated is not without interest.

Synthesis of XX was investigated through the same series of reactions which led to III. Condensation of *o*-methoxybenzophenone with ethyl cyanoacetate in the presence of ammonium acetate[16] gave ethyl α-cyano-β-(*o*-anisyl)-cinnamate (XXI) in two

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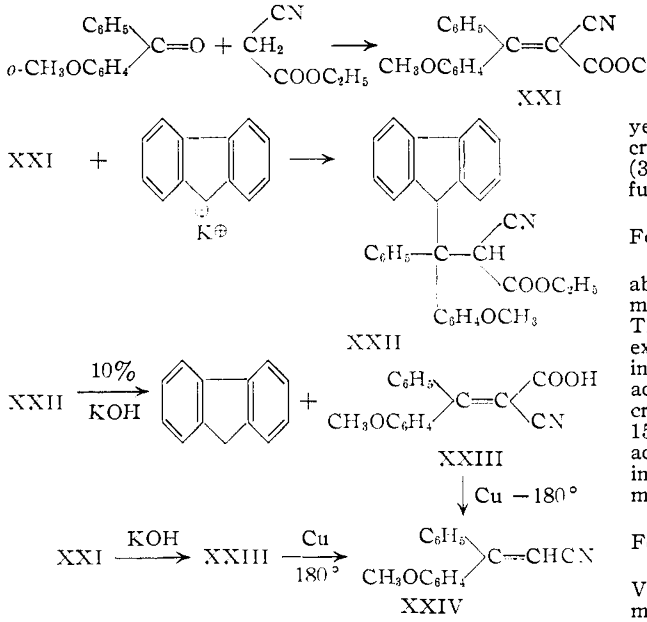
(14) A. Lowenbein and H. Simonis, *Ber.*, **57**, 2044 (1924).

(15) A. Lowenbein and B. Rosenbaum, *Ann.*, **448**, 227 (1926).

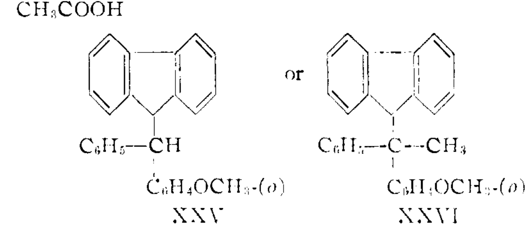
(16) A. C. Cope, C. M. Hofmann, C. Wyckoff and E. Hardenbergh, THIS JOURNAL, **63**, 3452 (1941).

isomeric forms, A, m.p. 103–105°, and B, m.p. 71–73°. Addition of 9-fluorenylpotassium to A gave a product to which is assigned the structure of ethyl α-cyano-β-(*o*-anisyl)-β-(9-fluorenyl)-β-phenylpropionate (XXII). This structure is based on elementary analysis, on the infrared spectrum which showed absorption peaks at 4.43 and 5.85 μ characteristic of nitrile and ester groups respectively, and on the products of hydrolysis of XXII.

When hydrolysis of the ester group of XXII with 10% ethanolic potassium hydroxide was attempted, complete reversal of the addition reaction resulted and from the reaction mixture, fluorene and α-cyano-β-(*o*-anisyl)-cinnamic acid (XXIII) were isolated. The structure of XXIII was demonstrated by decarboxylation in the presence of copper powder to give β-(*o*-anisyl)-cinnamonitrile (XXIV) which was in turn prepared by hydrolysis and decarboxylation of XXI.



A second attempt to hydrolyze the ester grouping in XXII with a phosphoric–acetic acid mixture gave a neutral compound which contained no nitrogen. Its infrared spectrum showed no peaks characteristic of nitrile or carboxyl groups. Analytical data corresponded to those demanded by *o*-anisylphenyl-9-fluorenylmethane (XXV) which would result by cleavage of the cyanoacetic acid fragment of XXII. Alternately, the analytical data agree, although less satisfactorily, with those demanded by 2-(*o*-anisyl)-2-(9-fluorenyl)-2-phenylethane (XXVI) which would arise by hydrolysis of both the ester and nitrile groups of XXII followed by bis-decarboxylation. This reaction is being investigated further.



Attempts to condense 2,4-diphenylbenzopyrylium perchlorate with 9-fluorenyllithium gave no definite product. From a similar condensation of β,β-diphenylvinylmagnesium bromide with 2,4-diphenylpyrylium perchlorate which was hoped would lead to XXI, 1,1,4,4-tetraphenyl-1,3-butadiene was the only product isolated. These reactions are also under further investigation.

Experimental[17,18]

Ethyl α-Cyano-β-(*o*-anisyl)-β-phenylbutyrate (VI).—To a solution of *o*-methoxyphenylmagnesium bromide prepared from *o*-bromoanisole (74.8 g., 0.4 mole) and magnesium (9.72 g., 0.4 mole) in 400 ml. of absolute ether cooled in an ice-bath, was added a solution of ethyl α-cyano-β-phenylcrotonate[16] (68.8 g., 0.32 mole) in 320 ml. of absolute ether with stirring over 30 minutes. The resultant viscous yellow mixture was refluxed for an additional hour. After cooling, the mixture was decomposed by addition of 400 ml. of ice-cold 5% sulfuric acid. The ether layer was separated, washed successively with water, 5% sodium bicarbonate solution, water and dried over calcium chloride. Vacuum distillation of the residue after removal of the ether gave 43.0 g. of light yellow viscous oil, b.p. 170–190° (0.5–1.0 mm.), which on crystallization from 32 ml. of 95% ethanol gave 37.8 g. (38%) of white crystalline material, m.p. 70–85°. Several further recrystallizations raised the m.p. to 94–96°.

Anal. Calcd. for $C_{20}H_{21}NO_3$: C, 74.3; H, 6.5; N, 4.3. Found: C, 74.4; H, 6.4; N, 4.0.

α-Cyano-β-(*o*-anisyl)-β-phenylbutyric Acid (VII).—The above crude ester (38.7 g., 0.12 mole) was refluxed with 130 ml. of 10% sodium hydroxide solution for one-half hour. The cooled solution was diluted with 300 ml. of water and extracted with two 150-ml. portions of ether. After warming to drive off dissolved ether, the alkaline solution was acidified with 10% hydrochloric acid with cooling. The crude acid (31.6 g., 89%) which separated melted at 150–155°. After three recrystallizations from 50% ethanol, the acid melted at 173–176° when the capillary was introduced into the bath at 170° and the rate of heating was 4° per minute.

Anal. Calcd. for $C_{18}H_{17}NO_3$: C, 73.0; H, 5.8; N, 4.6. Found: C, 73.2; H, 5.8; N, 4.7.

2-(*o*-Anisyl)-1-cyano-2-phenylpropane (VIII).—The acid VII (31.6 g., 0.107 mole) was heated at 180–190° for 20 minutes. After evolution of carbon dioxide ceased, the residue was distilled under reduced pressure yielding 23.0 g. of colorless distillate, b.p. 155–160° (0.5–0.7 mm.). The distillate was recrystallized from 50 ml. of 95% ethanol to give 21.9 g. of crystalline material, m.p. 95–97° (82%). After several further recrystallizations, the nitrile melted at 95.6–96.6°.

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.3; H, 6.8; N, 5.6. Found: C, 81.6; H, 6.4; N, 5.6.

β-(*o*-Anisyl)-β-phenylbutyrophenone (IX).—To a cooled solution of phenylmagnesium bromide prepared from 22.3 g. (0.142 mole) of bromobenzene and 3.45 g. (0.142 mole) of magnesium in 140 ml. of absolute ether was added a suspension of 11.9 g. (0.0472 mole) of powdered VIII in 100 ml. of ether. The mixture was refluxed for three hours under a nitrogen atmosphere. The cooled reaction mixture was carefully decomposed with 60 g. of ice. The imine was precipitated as its salt by dropwise addition of 170 ml. of 2% sulfuric acid. The collected precipitate was refluxed with 250 ml. of 4% sulfuric acid for one-half hour. The resultant brown gum was dissolved in a mixture of 250 ml. of ether and 75 ml. of ethyl acetate. The extract was washed with three 100-ml. portions of water and dried over anhydrous sodium sulfate. Removal of the solvent and recrystalliza-

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(17) All melting points are corrected and boiling points are uncorrected.

(18) Microanalyses by Mr. Goji Kodama of these laboratories, Clark Microanalytical Laboratories, Urbana, Ill., or Schwarzkopf Microanalytical Laboratories, Middle Village, N. Y.

tion of the residue from 40 ml. of 95% ethanol with carbon gave 12.2 g. (78%) of the ketone, m.p. 97–99°. Further recrystallization raised the m.p. to 99.5–100.5°.

Anal. Calcd. for $C_{23}H_{22}O_2$: C, 83.6; H, 6.7. Found: C, 83.6; H, 6.6.

The 2,4-dinitrophenylhydrazone melted at 206–208° after recrystallization from methanol–benzene.

Anal. Calcd. for $C_{29}H_{26}O_5N_4$: C, 68.2; H, 5.1; N, 11.0. Found: C, 68.5; H, 5.0; N, 11.0.

2,4-Diphenyl-4-methyl-1,4-chromene (III).—A solution of 16.0 g. (0.0486 mole) of IX in 400 ml. of glacial acetic acid which had been previously saturated with hydrogen bromide, was refluxed under a nitrogen atmosphere for 14 hours. After removal of about 340 ml. of acetic acid by distillation, the mixture was diluted with 300 ml. of water and extracted twice with a total of 500 ml. of ether. After successive washings of the ether extract with water, sodium carbonate solution and water and drying over sodium carbonate, the solvent was removed. The red oily residue was dissolved in 20 ml. of dry benzene and chromatographed in benzene over an alumina column (32 × 4.5 cm.). The first 300 ml. of effluate (fraction I) upon evaporation left 9.40 g. of red oil. The column was then washed with a 90–10 benzene–ethanol mixture. The intermediate 200 ml. of eluate was discarded. The third fraction collected (*ca.* 800 ml.) on evaporation left 3.50 g. of red oil.

The red oil from fraction I on vacuum distillation gave 8.68 g. of yellow oil, b.p. 170–200° (1–1.6 mm.). A solution of this in 80 ml. of 95% ethanol was seeded with seed accidentally obtained from acetic acid and allowed to crystallize at 48–50° yielding 7.3 g. (56% based on starting material reacted) of white crystals, m.p. 87–89°. Further recrystallization raised the m.p. to 88–89°.

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.5; H, 6.1. Found: C, 88.7; H, 6.3.

The red oil from the third fraction of the chromatogram gave 1.50 g. of starting IX when its solution in 10 ml. of 95% ethanol was allowed to stand. When the filtrate from this was treated with 1 g. of 2,4-dinitrophenylhydrazine in 20 ml. of ethanol, 6 ml. of water and 4 ml. of concentrated sulfuric acid, an immediate precipitate of the 2,4-dinitrophenylhydrazone of acetophenone formed; m.p. and mixed m.p. with a known sample, 242–244°.

The aqueous alkaline extract obtained prior to chromatographing was washed with ether, acidified and a solution of 0.5 g. of bromine and 1.5 g. of potassium bromide in 50 ml. of water was added. Tribromophenol (0.5 g.), m.p. 91–93° after recrystallization from 50% ethanol, precipitated. The m.p. of mixtures with known material was not depressed.

2,4-Diphenyl-4-methylchroman.—A solution of 0.335 g. of III in 20 ml. of glacial acetic acid was shaken with hydrogen and 0.05 g. of Adams platinum oxide catalyst at room temperature and atmospheric pressure. The calculated amount of hydrogen was taken up in three hours. The filtrate from the catalyst was diluted with water and extracted with ether. Removal of the ether from the washed and dried extract and recrystallization of the residue from 95% ethanol gave 0.214 g. (64%) of material, m.p. 114.5–116°.

Anal. Calcd. for $C_{22}H_{20}O$: C, 87.9; H, 6.7. Found: C, 87.7; H, 6.6.

Bromo Derivative of III.—A solution of 0.26 g. of bromine in 15 ml. of carbon tetrachloride was added dropwise to a solution of 0.45 g. of III in 15 ml. of carbon tetrachloride until the color of bromine persisted. Evaporation to dryness and recrystallization of the residue from methanol with carbon gave 0.35 g. of white needles, m.p. 111–113°.

Anal. Calcd. for $C_{22}H_{17}BrO$: C, 70.0; H, 4.5; Br, 21.2. Found: C, 70.1; H, 4.6; Br, 21.1.

Oxidation of III with Osmium Tetroxide—XIII.—A solution of 0.298 g. (0.001 mole) of III in 5 ml. of dry benzene was added to a solution of 0.254 g. (0.001 mole) of osmium tetroxide in 0.160 g. of redistilled pyridine and 5 ml. of dry benzene. After standing for a day at room temperature, the black precipitated osmate ester was collected and decomposed according to Criegee[19] by shaking its solution in 30 ml. of chloroform with 30 ml. of water containing 0.3 g. of potassium hydroxide and 3.0 g. of mannitol. After washing the chloroform solution with 1% hydrochloric acid and water, removal of the solvent and recrystallization of the residue from benzene–hexane (1:5) gave 0.193 g. of crystalline glycol, m.p. 168–170°.

Anal. Calcd. for $C_{22}H_{20}O_3$: C, 79.5; H, 6.1. Found: C, 79.4; H, 6.2.

2-(*o*-Hydroxyphenyl)-2-phenyl-1-propanol (XV). A. By Degradation of XIII.—To a solution of 0.2 g. of XIII in 20 ml. of dry benzene was added 0.240 g. of lead tetraacetate with slight warming. After standing overnight, the solution was washed with water and evaporated to dryness. A solution of the oily residue in 20 ml. of anhydrous ether was refluxed with 0.25 g. of lithium aluminum hydride for three hours. After destruction of excess reagent with ethyl acetate, 20 ml. of cold 10% hydrochloric acid was added. After washing the ether solution with water, it was extracted with two 15-ml. portions of 5% sodium hydroxide solution. The alkaline extract was acidified and extracted with ether. From the ether extract, a colorless oil was obtained. On standing in 1.5 ml. of benzene and 15 ml. of petroleum ether, this deposited 0.107 g. (77%) of XV as needles, m.p. 106–107°. The mixed m.p. with a sample prepared as described below showed no depression.

B. By Ozonization of III.—A solution of 0.3 g. (0.001 mole) of III in 15 ml. of ethyl acetate was ozonized at 0° for four minutes. After removal of the ethyl acetate, the residue was refluxed with 2 ml. of water for half an hour. To the resultant suspension of XVI was added 1 g. of potassium hydroxide and 8 ml. of ethanol and refluxing was continued for another half-hour. After dilution with water, the mixture was extracted with ether

The alkaline aqueous solution was acidified and extracted with ether. This ether extract was extracted with 5% sodium bicarbonate solution. From the bicarbonate extract on acidification, 99 mg. of benzoic acid, identified by conversion to benzanilide, was obtained.

The material (XVII) remaining in the ether after the bicarbonate extract was reduced with lithium aluminum hydride as in A above and gave 30 mg. of XV, m.p. 106–107°. This showed no depression in m.p. when mixed with material prepared as in A above or by the procedure described below.

3-Phenyl-2-coumaranone (XVIII).—The method used was a modification of that of Bistrzycki and Flatau.[20] A mixture of mandelic acid (23 g., 0.15 mole), phenol (22 g., 0.23 mole) and 60 ml. of 73% sulfuric acid was heated at 125–130° with stirring for half an hour. After cooling, it was diluted with 300 ml. of ice-water. The gummy precipitate was washed with water and taken into 100 ml. of benzene. After washing the benzene solution with 5% sodium carbonate solution, removal of the solvent and recrystallization from 95% ethanol gave 7.4 g. (23%) of XVIII, m.p. 110–113°.

2-(*o*-Hydroxyphenyl)-2-phenyl-1-propanol (XV).—3-Methyl-3-phenyl-2-coumaranone (XVII) (0.28 g.), prepared from XVIII,[14] was reduced with lithium aluminum hydride as in the above case. The yield of material, m.p. 106–107°, was 74%.

Anal. Calcd. for $C_{15}H_{16}O_2$: C, 78.9; H, 7.1. Found: C, 78.8; H, 7.0.

Salicylideneacetophenone.—The procedure was a modification of that of LeFevre.[21] To a solution of salicylaldehyde (50 g., 0.41 mole) and acetophenone (32 g., 0.27 mole) in 200 ml. of ethanol was added a solution of 40 g. of potassium hydroxide in 50 ml. of water. After standing overnight, the mixture was diluted with 600 ml. of water and acidified with 40 ml. of glacial acetic acid with cooling. The yellow precipitate was washed successively with ethanol and water and recrystallized from 100 ml. of 80% ethanol to yield 44 g. (74%) of material, m.p. 154–156° dec.

2,4-Diphenyl-2-methyl-1,2-chromene (IV).—Salicylideneacetophenone was converted to 2,4-diphenylbenzopyrylium perchlorate (XIX) according to Lowenbein.[22] To 1.80 g. (0.0047 mole) of XIX suspended in 30 ml. of absolute ether, a solution of 0.02 mole of methylmagnesium iodide in 30 ml. of absolute ether was added over five minutes. The salt dissolved and heat was evolved. After stirring for half an hour, the mixture was decomposed with 30 ml. of 5% hydrochloric acid. The ether solution was washed with dilute sodium bisulfite for removal of iodine. Removal of

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[19] R. Criegee, *Ann.*, **522**, 75 (1936); R. Criegee, B. Marchand and H. Wannowius, *ibid.*, **550**, 99 (1942).

[20] A. Bistrzycki and J. Flatau, *Ber.*, **30**, 124 (1897).

[21] R. J. W. LeFevre, *J. Chem. Soc.*, 2773 (1929).

[22] A. Lowenbein, *Ber.*, **57**, 1517 (1924).

the solvent after drying and distillation of the residue gave 1.3 g. of oil, b.p. 170–174° (0.2–0.4 mm.) which solidified on trituration with a small volume of ether. Recrystallization from 11 ml. of methanol gave 0.93 g. (67%) of needles, m.p. 66–68°.

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.5; H, 6.1. Found: C, 88.2; H, 6.1.

Bromination of 2,4-Diphenyl-2-methyl-1,2-chromene.—A solution of bromine (0.53 g., 0.003 mole) in 20 ml. of carbon tetrachloride was added gradually to a solution of 0.90 g. (0.003 mole) of IV in 20 ml. of carbon tetrachloride over 20 minutes. After washing the resultant solution with dilute sodium bisulfite solution and water, removal of the solvent left a residue which solidified on scratching. Recrystallization from methanol gave 0.95 g. (80%) of plates, m.p. 105–107°. The substance was not investigated further.

Anal. Calcd. for $C_{22}H_{17}BrO_2$: C, 67.2; H, 4.4; Br, 20.3. Found: C, 67.4; H, 4.5; Br, 20.5.

***o*-Methoxybenzophenone.**—To a solution of *o*-methoxyphenylmagnesium bromide prepared from 46.7 g. (0.25 mole) of *o*-bromoanisole and 6.1 g. (0.25 mole) of magnesium in 150 ml. of absolute ether, a solution of 25.7 g. (0.25 mole) of benzonitrile in 100 ml. of absolute ether was added dropwise during 20 minutes. After refluxing for one hour, the mixture was cooled and decomposed with 200 ml. of cold 10% hydrochloric acid. The aqueous layer was warmed on the steam-bath for one hour and the brown oil which separated was extracted with ether. After washing with water and drying over anhydrous magnesium sulfate, the residue, after removal of the ether, was distilled to give 38 g. of yellow oil, b.p. 136–139° (0.5–0.6 mm.). On standing in the refrigerator, the oil crystallized, m.p. 35–37°; reported m.p. 39°.[23] The yield was 72%.

Ethyl α-Cyano-β-(*o*-anisyl)-cinnamate (XXI).—The procedure was adapted from that of Cope, *et al.*,[16] for similar condensations. A mixture of *o*-methoxybenzophenone (43.0 g., 0.204 mole), ethyl cyanoacetate (7.7 g., 0.1 mole), acetic acid (19.2 g., 0.32 mole) and 180 ml. of benzene was refluxed for 17 hours in a flask equipped with a Soxhlet extractor, the thimble of which contained anhydrous sodium sulfate for the removal of water. The reaction mixture was washed with water and concentrated. Distillation of the residue gave 26.9 g. of yellow oil, b.p. 175–190° (0.35–0.4 mm.). A solution of the distillate in 20 ml. of 95% ethanol on standing, deposited 21 g. of a mixture of isomers, m.p. 62–90°. The mixture was separated into its components by fractional crystallization from ethanol. The less soluble higher melting isomer separated as a fluffy yellow solid and the lower melting isomer formed large clear plates. From 10.3 g. of crude high melting isomer, m.p. 90–100°, 7.8 g. of yellow needles (12.4%), m.p. 101–105°, was obtained on recrystallization from ether–petroleum ether. After two further recrystallizations, it melted at 103–105°.

Anal. Calcd. for $C_{19}H_{17}NO_3$: C, 74.3; H, 5.6; N, 4.6. Found: C, 74.2; H, 5.6; N, 4.5.

From the mixture, 5.3 g. of crude low melting isomer, m.p. 60–70°, was obtained. One recrystallization from 95% ethanol gave 4.3 g. (6.8%) of large plates, m.p. 71–73°.

Anal. Found: C, 74.2; H, 5.6; N, 4.6.

β-(*o*-Anisyl)-cinnamonitrile.—A solution of 8.6 g. of the above mixed isomers, m.p. 60–90°, in 20 ml. of 95% ethanol containing 3 g. of potassium hydroxide was refluxed for 45 minutes. After dilution with water and extraction with ether, the alkaline solution was acidified and extracted with ether. After washing and drying the ether extract, removal of the solvent left 7.7 g. of yellow oil which solidified, m.p. 150–154°, on trituration with petroleum ether.

When 1.5 g. of the above acid was heated with 0.3 g. of copper powder at 150–180° for ten minutes, and the residue was distilled under reduced pressure, 1.0 g. of yellowish oil, b.p. 145–150° (0.3 mm.), was obtained. After redistillation and trituration with ether, the substance solidified. Two recrystallizations from a mixture of 6 ml. of ether and 10 ml. of petroleum ether gave 0.82 g. of material, m.p. 77.5–79.5°. The infrared spectrum in carbon tetrachloride showed an absorption peak at 4.46 μ, characteristic of a nitrile group.

Anal. Calcd. for $C_{16}H_{13}NO$: C, 81.7; H, 5.6. Found: C, 81.6; H, 5.5.

Ethyl α-Cyano-β-(*o*-anisyl)-β-(9-fluorenyl)-β-phenylpropionate (XXII).—A suspension of 3.07 g. (0.01 mole) of XXI (high melting isomer) in 30 ml. of absolute ether was added to a solution of 9-fluorenylpotassium prepared from 0.43 g. of potassium in 30 ml. of liquid ammonia and 1.66 g. of fluorene in 30 ml. of absolute ether.[24] The cooling bath was removed and the ammonia was allowed to evaporate. After two hours, the mixture was refluxed for one hour and allowed to stand overnight. The mixture was saturated with solid carbon dioxide and decomposed with 40 ml. of water. After shaking with 40 ml. of benzene, the organic layer was separated, washed and dried. The residue after removal of the benzene was recrystallized from 150 ml. of 95% ethanol to give 2.0 g. (42%) of tan solid, m.p. 187–193°. Three further recrystallizations from ethanol gave white crystals, m.p. 194–196°. The infrared spectrum in chloroform showed peaks at 4.43 and 5.85 μ characteristic of a nitrile and ester group, respectively.

Anal. Calcd. for $C_{32}H_{27}NO_3$: C, 81.2; H, 5.7; N, 3.0. Found: C, 80.8; H, 5.8; N, 3.0.

Hydrolysis of XXII. A. With Alcoholic Potassium Hydroxide.—A solution of 0.40 g. of XXII and 1 g. of potassium hydroxide in 10 ml. of 95% ethanol was refluxed for ten minutes. After addition of 10 ml. of water, the mixture was refluxed for an additional 40 minutes. After cooling, the precipitate (0.15 g., m.p. 110–113°) was collected and recrystallized from ethanol, m.p. and mixture m.p. with fluorene, 113–115°. The filtrate was diluted with water, acidified and extracted with benzene. The benzene extract was extracted with 5% sodium bicarbonate solution. Acidification of the bicarbonate extract and extraction with ether gave a yellow oil (0.20 g.) which solidified on trituration with petroleum ether, m.p. 150–154°. Decarboxylation in the presence of copper powder and purification of the product by sublimation and recrystallization from ether–petroleum ether gave β-(*o*-anisyl)-cinnamonitrile identified by mixture m.p.'s with the material prepared as described above.

B. With Phosphoric–Acetic Acid Mixture.—A mixture of 1.0 g. of XXII, 8 ml. of 85% phosphoric acid and 16 ml. of glacial acetic acid was refluxed for 15 hours. After dilution with water, the mixture was extracted with ether. The residue, after removal of the solvent from the washed and dried extract, was recrystallized three times from 95% ethanol by solution in 50–60 ml. of solvent and concentration to about 10 ml. yielding 0.4 g. of crystalline material, m.p. 172–174°. Three further recrystallizations raised the m.p. to 175–177°. The infrared spectrum in chloroform did not show absorption peaks characteristic of nitrile or ester groups.

Anal. Calcd. for $C_{27}H_{21}O$ (XXV): C, 89.7; H, 5.9. Calcd. for $C_{28}H_{23}O$ (XXVI): C, 89.6; H, 6.2. Found: C, 89.9; H, 5.6.

1,1-**Diphenyl-2-bromoethylene.**—The procedure was a modification of that of Wittig and Kethur.[25] A solution of 50 g. (0.32 mole) of bromine in 50 ml. of glacial acetic acid was added dropwise over a period of 20 minutes to a solution of diphenylethylene (57 g., 0.32 mole) in 150 ml. of glacial acetic acid cooled in a water-bath. After the addition, the mixture was refluxed for an hour during which evolution of hydrogen bromide occurred. After distillation of about three-fourths of the solvent, the solution was diluted with water and extracted with ether. Removal of the solvent from the washed and dried extract gave a residue which on distillation gave 64 g. of clear oil, b.p. 115–122° (0.4–0.6 mm.). Recrystallization from methanol gave 52 g. (51%) of needles, m.p. 43–45°; reported m.p. 46–47.5.[25]

Condensation of 1,1-Diphenyl-2-vinylmagnesium Bromide with 2,4-Diphenylbenzopyrylium Perchlorate.—To 0.26 g. (0.011 mole) of magnesium turnings suspended in 10 ml. of boiling absolute ether was added dropwise, with stirring, a solution of 1,1-diphenyl-2-bromoethylene (2.58 g., 0.01 mole) in 10 ml. of absolute ether over 20 minutes. After refluxing for two hours, only about half the magnesium had reacted. The solution was cooled to room temperature and 1.70 g. (0.045 mole) of the benzopyrylium salt was added in portions. At each addition, refluxing occurred and the solution turned red. The solution was refluxed for 30 minutes and decomposed with ammonium chloride. Ex-

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[23] R. Stoermer and E. Friderici, *Ber.*, **41**, 325 (1908).

[24] R. S. Yost and C. R. Hauser, THIS JOURNAL, **69**, 2325 (1947).

[25] G. Wittig and R. Kethur, *Ber.*, **69**, 2085 (1936).

traction with benzene and removal of the solvent from the washed extract gave a residue which solidified on trituration with ether. The solid (0.55 g.) was recrystallized from ethyl acetate giving 0.50 g. of 1,1,4,4-tetraphenyl-1,3-butadiene, m.p. 192–193°; reported m.p. 192–193°[26] and 205–206°.[27]

Anal. Calcd. for $C_{28}H_{22}$: C, 93.8; H, 6.2. Found: C, 93.7; H, 6.1.

Evaporation of the ethereal filtrate from the above crystalline material gave a brown oil from which no pure compound could be isolated after distillation and chromatography on alumina.

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[26] J. Salkind and V. Teterin, *Ber.*, **62**, 1748 (1929).

[27] P. Lipp, *ibid.*, **56**, 567 (1923).

[CONTRIBUTION FROM THE WARNER–CHILCOTT RESEARCH LABORATORIES]

Aminoalkyl Esters of 1,2,3,10b-Tetrahydrofluoranthene-10b-carboxylic Acid

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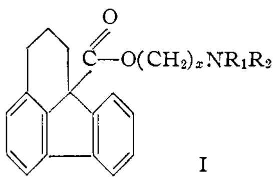
Several basic esters were prepared from tertiary aminoalkyl chlorides and 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid. The starting point for the preparations of the required acid was the parent hydrocarbon, fluoranthene. Fluoranthene was partially reduced with sodium amalgam to 1,2,3,10b-tetrahydrofluoranthene and the latter was then metalated in the 10b-position with sodamide. The intermediate sodio derivative was carboxylated to the acid. Most of the esters described were prepared by the Horenstein-Pahlicke condensation of the acid with a chloralkamine. These esters as hydrochlorides and methobromides were found to have significant antispasmodic activity. A brief description of the preliminary pharmacological data will be presented.

The present paper describes the synthesis of several alkamine esters of 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid (I).



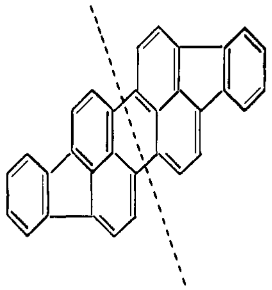
I

These esters in the form of their hydrochlorides and their quaternary salts were prepared in an effort to obtain more useful antispasmodics of the atropine type. The esters and their derivatives prepared in this present series are listed in Table I.

The acid moiety of the esters was prepared starting from the commercially available present hydrocarbon, fluoranthene.[1] This was reduced in almost quantitative yields with 10% sodium amalgam.[2] Other methods of reduction which have been reported are hydriodic acid and phosphorus at 180°,[3] powdered sodium in boiling decalin followed by alcohol to decompose the tetrasodio compound,[4] and catalytic reduction with Raney nickel[5] or palladized charcoal.[2]

The preparation of the desired acid from 1,2,3,10b-tetrahydrofluoranthene has been described by Kruber.[6] He used two methods of synthesis: (1) by fusion of 1,2,3,10b-tetrahydrofluoranthene with sodium followed by the addition of carbon dioxide to the resulting melt (10% yield), and (2) by treating 1,2,3,10b-tetrahydrofluoranthene with a solution of ethylmagnesium bromide and then treating the intermediate Grignard compound with carbon dioxide (10% yield). In our laboratories 1,2,3,10b-tetrahydrofluoranthene-10b-carboxylic acid was prepared by treating 1,2,3,10b-tetrahydrofluoranthene with sodamide using dry toluene as a solvent. The resulting sodio derivative was treated with carbon dioxide followed by acidification to yield the desired acid (69% yield). The carboxylation was also carried out *via* a transmetalation using butyllithium to form the intermediate lithium compound which then reacted readily with carbon dioxide to yield the acid (72% yield). The former method was more convenient to use, especially for larger runs.

When the reaction of 1,2,3,10b-tetrahydrofluoranthene and sodamide was carried out in toluene a small amount of red material was obtained which appeared to go through the subsequent treatment with carbon dioxide without change. These deep red crystals did not melt up to 360° and were insoluble in the usual organic solvents. It is probably a compound similar to periflanthene[7] (II). It can be seen that periflanthene is a result of fusion of two molecules of fluoranthene through the bonds indicated by the dissecting dotted line. It is formed in 0.5% yield on heating fluoranthene with sodamide in boiling xylene. The compound isolated in the sodamide–tetrahydrofluoranthene reaction had the solubility, melting point and color characteristics of periflanthene.



II

Esters of aminoalcohols are generally prepared

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[1] Reilly Tar and Chemical Co.

[2] J. von Braun and G. Manz, *Ber.*, **63**, 2608 (1930).

[3] G. Goldschmidt, *Monatsh.*, **1**, 221 (1880).

[4] E. A. Coulson, *Chemistry & Industry*, **60**, 699 (1944); O. Kruber, *Ber.*, **64**, 84 (1931).

[5] J. M. Beaton and S. H. Tucker, *J. Chem. Soc.*, 3870 (1952). This was reported after the work described in this paper was completed. It would seem to be the method of choice for this reduction (80% yield).

[6] O. Kruber, *Ber.*, **67**, 1000 (1934).

[7] J. von Braun and G. Manz, *ibid.*, **70**, 1603 (1937).