method described in procedure (a). Methyl-labeled phenyl acetate was prepared from $C^{13}H_3I$ in the same way.

Persulfuric Acid Oxidation of Cholestenone.—Cholestenone (8.8 g.) in 350 ml. of glacial acetic acid was treated with a solution of 26.4 g. of potassium persulfate and 29.0 g. of 96% sulfuric acid as described by Salamon.[11] The mixture was diluted with 530 ml. of acetic acid and allowed to stand at room temperature for one week with frequent shaking.

The sulfuric acid was neutralized by the addition of 50% potassium hydroxide, the salts were removed by filtration, and the filtrate concentrated to small volume. The crude oxidation product was then separated into acidic and neutral fractions by alkaline extraction from ether.

Crystallization of the neutral material from dilute acetone gave 2.25 g. of a product, m. p. 114–116°, that did not depress the melting point of a sample of lactone IVb. The acidic fraction was esterified with diazomethane and chromatographed on alumina. The early eluates furnished 450 mg. of crystalline material melting at 119–123°, which on repeated crystallization from ether gave a pure substance, m. p. 124.5–125.5°, identical in all respects with dihydro Diels ester.[23] Alkaline hydrolysis of the dimethyl ester afforded the free acid, m. p. 252–253°, identical with dihydro Diels acid (VII).

Summary

Two methods have been devised for the introduction of isotopic carbon in ring A of steroids. The best procedure involves condensation of an unsaturated ring A lactone with phenyl acetate and has been applied to syntheses of cholestenone-3-C^{14}, testosterone-3-C^{14}, testosterone-4-C^{14} and testosterone-4-C^{13}.

(23) Windaus, *Ber.*, **52**, 170 (1919).

CAMBRIDGE 38, MASS. RECEIVED OCTOBER 24, 1949

[COMMUNICATION NO. 1295 FROM THE KODAK RESEARCH LABORATORIES]

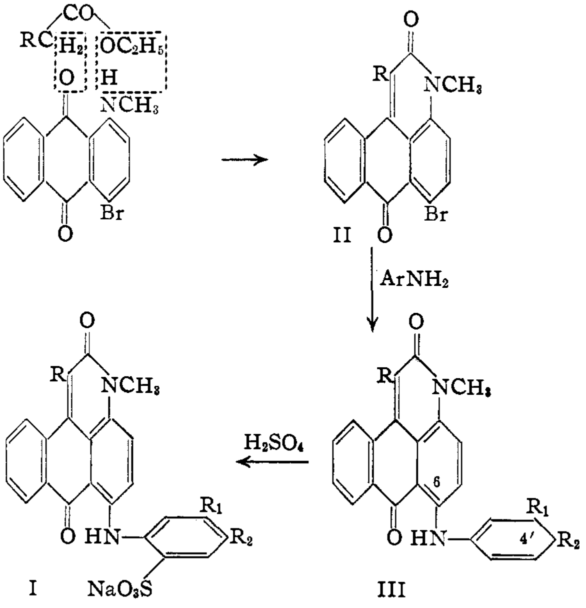
3-Azabenzanthrone Dyes[1]

BY C. F. H. ALLEN,* JEAN V. CRAWFORD,[3] R. H. SPRAGUE, ELEANOR R. WEBSTER[4] AND C. V. WILSON

The longest-known representative of dyes containing the 3-azabenzanthrone nucleus is Alizarin Rubinol R (I, R, R_1 = H, R_2 = CH_3),[5,6] but there are four other Alizarin Rubinols[6]; the entire series is characterized by the absence of a substituent in position 1 (R = H). Two other commercial dyes, belonging to the Brilliant Alizarin Light Red Class, have a substituent group in this position. In order to learn the effect of a variety of substituent groups at several positions in the molecule on light absorption in the visible portion of the spectrum, a considerable number of dyes has been prepared.

Most of these dyes have arylamino groups in the 6-position, with different substituents in position 1. The reactions used in their preparation are largely found in the patent literature.[7–13]

Substances of the general formula II, in which R = C_2H_5OOC, CH_3CO and C_6H_5CO, were prepared by treating 4-bromo-1-methylaminoanthraquinone with ethyl malonate,[7] with ethyl acetoacetate[7,14] and with ethyl benzoylacetate,[7] respectively; while substance II, R = C_6H_5, was formed by cyclization of 4-bromo-1-phenylacetylaminoanthraquinone. Substance II, R = CN, was formed by the action of potassium cyanide on 4-bromo-1-(N-chloroacetyl-N-methylamino)-anthraquinone; in the patent literature an alternative procedure, which starts with ethyl cyanoacetate, is given.[13]



The bromoazabenzanthrone (II) was then condensed with the appropriate aromatic amine[8,13] to give the "dye base" (III), which was sulfonated[9,13] to form the dye, I. Care was taken to use carefully purified intermediates throughout; most of the dye bases (III) were not sulfonated until they had been recrystallized enough

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* Harvard University Ph.D. 1924.

(1) The modern aza nomenclature has been adopted on account of its marked superiority over the older naming systems. In the previous paper[2] the substances were called "Anthrapyridones."

(2) Allen and Wilson, *J. Org. Chem.*, **6**, 594 (1945).

(3) Present address: University of Illinois, Urbana, Illinois.

(4) Present address: Radcliffe College, Cambridge, Massachusetts.

(5) "Colour Index," 1st Edition (1924), No. 1091.

(6) Fierz-David, "Künstliche Organische Farbstoffe," Verlag von Julius Springer, Berlin, 1926, p. 624.

(7) German Patent 578,995; *Frdl.*, **19**, 1964 (1934).

(8) German Patent 580,283; *ibid.*, **19**, 1969 (1934).

(9) German Patent 581,161; *ibid.*, **20**, 1335 (1935).

(10) German Patent 633,308; *C. A.*, **30**, 7870 (1936).

(11) German Patent 658,114; *ibid.*, **32**, 4798 (1938).

(12) French Patent 837,591; *Chem. Zentr.*, **110**, Part 2, 531 (1939).

(13) German Patents 655,650, 655,651; *ibid.*, **109**, Part 1, 3700 (1938).

(14) U. S. Patent 1,891,317; *C. A.*, **27**, 1892 (1933).

TABLE I

1-CARBETHOXY-3-METHYL-6-ANILINO DYE BASES

Substituents	Max. absorption of dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4'-Methyl	542	$C_{27}H_{22}N_2O_4$	202–204	74.0	73.8	5.0	5.2	6.4	6.5
4'-Ethyl	540	$C_{28}H_{24}N_2O_4$	174–176	74.3	74.0	5.4	5.4	6.2	6.3
4'-Isopropyl	543	$C_{29}H_{26}N_2O_4$	195–197					6.0	6.2
4'-*s*-Amyl	546	$C_{31}H_{30}N_2O_4$	148–150	75.3	75.2	6.4	6.1	5.7	5.4
4'-*t*-Amyl	542	$C_{31}H_{30}N_2O_4$	198–200					5.7	5.7
2',4'-Dimethyl	548	$C_{28}H_{24}N_2O_4$	199–201	74.3	74.5	5.4	5.3	6.2	6.1
4'-Methoxy	546	$C_{27}H_{22}N_2O_5$	183–184.5					6.2	6.5
3'-Trifluoromethyl	525	$C_{27}H_{19}F_3N_2O_4$	....	65.9	65.6	3.9	3.9	5.7	5.9
3'-Chloro	520	$C_{26}H_{19}ClN_2O_4$	....					Cl, 7.6	7.5
4'-Chloro	532	$C_{26}H_{19}ClN_2O_4$	215–217					Cl, 7.6	7.8
4'-Bromo	532	$C_{26}H_{19}BrN_2O_4$	....					Br, 15.9	15.7
4,4'-Dimethyl	545	$C_{28}H_{24}N_2O_4$	190–192	74.3	74.4	5.3	5.1	6.2	6.4
6-(β-Hydroxyethylamino)	521, 551	$C_{22}H_{20}N_2O_5$	240–242	67.3	67.4	5.1	5.1	7.1	7.0

TABLE II

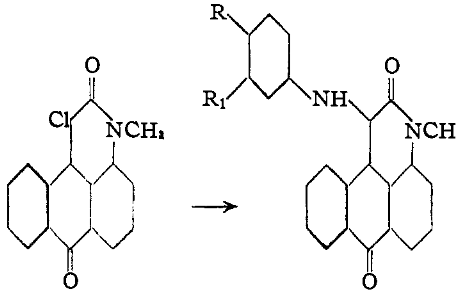
1-CYANO-3-METHYL-6-ANILINO DYE BASES

Substituents	Max. absorption of dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4'-Methyl	580	$C_{25}H_{17}N_3O_2$	>300 ind.					10.7	10.9
4'-Ethyl	584	$C_{26}H_{19}N_3O_2$	310–314	77.0	77.0	4.7	4.9	10.4	10.7
4'-*s*-Amyl	590	$C_{29}H_{25}N_3O_2$	Ind.					9.4	9.6
4'-*t*-Amyl	590	$C_{29}H_{25}N_3O_2$	Ind.					9.4	9.4
2',4'-Dimethyl	587	$C_{26}H_{19}N_3O_2$	343–350	77.0	77.1	4.7	4.9	10.4	10.6
4'-Methoxy	588	$C_{25}H_{17}N_3O_3$	>350	73.7	73.8	4.2	4.5	10.3	10.5
3'-Chloro	564	$C_{24}H_{14}ClN_3O_2$	332–334					Cl, 8.6	8.5
4'-Chloro	554	$C_{24}H_{14}ClN_3O_2$	368–372					10.2	10.0
4'-Cyano	570	$C_{25}H_{14}N_4O_2$	>360					13.9	13.8
4'-Acetyl	568	$C_{26}H_{17}N_3O_3$	>360					9.8	9.8

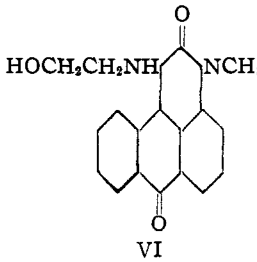
times to give acceptable values upon analysis. Sulfonation was carried out at 20–60°, using 100% sulfuric acid; these conditions were favorable for the introduction of one sulfonic acid group and avoided the undesirable over-sulfonation or ring closure. That the sulfonation does not effect hydrolysis of the carbethoxy group is confirmed by the fact that the product obtained from the dye I (R = C_2H_5OOC–, R_1 = H, R_2 = Cl) on treatment with nitric acid is identical with the product obtained by condensing II (R = C_2H_5-OOC–) with 4-chloro-2-nitroaniline as previously described for II (R = H).[2]

1 - Arylamino - 2 - keto - 3 - methyl - 3 - azabenzanthrones (IV) were obtained by treating 1-chloro-2-keto-3-methyl-3-azabenzanthrone (V) with an aromatic amine, the dyes being formed by a subsequent sulfonation. The one aliphatic derivative prepared was of the type VI, and was made using ethanolamine.

The location of the substituent groups, the maximum absorption of the dyes in aqueous solution, and analyses of the dye bases are listed in Tables I–VI. In some cases the absorption maxima of the dye bases in dioxane are included for comparison. The dyes of the 1-arylamino series (IV) are all somewhat fluorescent, and are not particularly fast to light; the fluorescent property is particularly noticeable in the ethanolamine derivative (VI).



V IV



VI

Experimental

Many of the intermediate products have been described in the patent literature. However, to facilitate repetition,

TABLE III

1-PHENYL-3-METHYL-6-ANILINO DYE BASES

Substituents	Max. absorption of dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4′-Methyl	535	$C_{30}H_{22}N_2O_2$	248–250	81.5	81.6	5.0	5.0		
4′-*s*-Amyl	536	$C_{34}H_{30}N_2O_2$	232–234					5.6	5.5
4′-*t*-Amyl	536	$C_{34}H_{30}N_2O_2$	281–282					5.6	5.7
2′,4′-Dimethyl	546	$C_{31}H_{24}N_2O_2$	199–200					6.1	6.1
4′-Methoxy	538	$C_{30}H_{22}N_2O_3$	245–246					6.1	6.1
4′-Chloro	525	$C_{29}H_{19}N_2O_2Cl$	283					Cl, 7.6	7.7

TABLE IV

1-BENZOYL-3-METHYL-6-ANILINO DYE BASES

Substituents	Max. absorption of dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4′-Methyl	544	$C_{31}H_{22}N_2O_3$	276–277	79.1	78.7	4.7	5.0	6.0	6.0
4′-Chloro	538	$C_{30}H_{19}ClN_2O_3$	302–304					5.7	6.0
4′-Methoxy	545	$C_{31}H_{22}N_2O_4$	255–257					5.8	5.5

TABLE V

1-ACETYL-3-METHYL-6-ANILINO DYE BASES

Substituents	Max. absorption of dyes Bases	Dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4′-Methyl	548	547	$C_{26}H_{20}N_2O_3$	210–212	76.4	76.8	4.9	5.2	6.9	6.8
3′-Methyl	546	540	$C_{26}H_{20}N_2O_3$	186–188	76.4	76.2	4.9	5.0	6.9	6.7
4′-Methoxy	541	543	$C_{26}H_{20}N_2O_4$	145–148	73.6	73.5	4.8	4.5	6.6	7.0
4′-*t*-Amyl	540	534	$C_{30}H_{28}N_2O_3$	270–272	77.6	78.2	6.1	5.9	6.0	6.1
4′-Chloro	534		$C_{25}H_{17}ClN_2O_3$	243–245	70.0	69.5	4.0	3.5	6.5	7.1

TABLE VI

1-ANILINO-3-METHYL DYE BASES

Substituents	Max. absorption of dyes	Empirical formula	M. p., °C.	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found
4′-Methyl[a]	463	$C_{24}H_{18}N_2O_2$	239–240	78.7	78.5	4.9	5.2	7.7	8.1
3′-Methyl	456	$C_{24}H_{18}N_2O_2$	244–245	78.7	78.7	4.9	4.9	7.7	7.5
4′-Chloro	455		238–239						
3′-Chloro	450	$C_{23}H_{15}ClN_2O_2$	252–253	71.5	71.3	3.9	3.6	7.2	7.2
2′,5′-Dichloro	440	$C_{23}H_{14}Cl_2N_2O_2$	194–195	65.5		3.3		6.6	6.6
3′-Trifluoromethyl	447	$C_{24}H_{15}F_3N_2O_2$	244–245	68.6	68.5	3.6	3.6	6.7	6.4
4′-Methoxy	467		189–190						
1-(β-Hydroxyethylamino)	440	$C_{19}H_{16}N_2O_3$	204–206	71.2	70.8	5.0	5.0	8.7	8.6

[a] A dye containing *p*-toluidino groups in both the 1- and 6-positions has been reported previously.[2] Its absorption maximum is at 535 mμ.

a type procedure with essential details is given for each operation.

A. **6-Bromo-1-carbethoxy-2-keto-3-methyl-3-azabenzanthrone** (II, R = $-COOC_2H_5$).—A mixture of 29.5 g. of 4-bromo-1-methylaminoanthraquinone, 60 g. of ethyl malonate[15] and 0.1 g. of sodium acetate was heated with stirring for four hours at 185–195°. The reaction was carried out in such a way that the alcohol and ethyl acetate formed in the reaction distilled out of the mixture. The reaction product was cooled to about 100° and diluted with 60 ml. of alcohol. The solid that formed was collected on a filter and washed with alcohol. The yield of yellow product melting at 183–185° was 21 g. (60%).

B. **1-Benzoyl-6-bromo-2-keto-3-methyl-3-azabenzanthrone** (II, R = $-COC_6H_5$).—A mixture of 60 g. of ethyl benzoylacetate, 30 g. of 4-bromo-1-methylaminoanthraquinone and 2 g. of sodium acetate was heated with stirring at 190–195° for one and one-half hours. During this time any alcohol or ethyl acetate formed was allowed to distil. The contents of the reaction flask were transferred to a beaker and diluted with an equal volume of methanol. The solid obtained was collected on a filter, washed thoroughly with methanol and dried. The yield of product melting at 272–275° was 32.5 g. Recrystallization, which is not necessary for the subsequent step, raises the melting point to 276–277°.

C. **1-Acetyl-6-bromo-2-keto-3-methyl-3-azabenzanthrone** (II, R = $-COCH_3$) is obtained by the procedure used for the benzoyl derivative from 200 ml. of ethyl acetoacetate, 50 g. of 4-bromo-1-methylaminoanthraquinone, heated for six hours at 160–180°; the yield was 34 g.; m. p. 235–237°.

D. **6-Bromo-2-keto-3-methyl-1-phenyl-3-azabenzanthrone** (II, R = $-C_6H_5$).—To a mixture of 158 g. of 4-bromo-1-methylaminoanthraquinone and 1200 ml. of

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(15) It is essential that the ethyl malonate be free from acid, otherwise the sodium acetate which acts as a catalyst will be destroyed. If necessary the ethyl malonate can be shaken with sodium acetate prior to use.

toluene was added 140 ml. of phenylacetyl chloride. The mixture was refluxed for two hours and then filtered. The filtrate was concentrated to one-fourth its original volume and chilled. The solid that separated was collected on a filter and washed with ether. The yield was 155 g. (71%). The crude 4-bromo-1-methylamino-N-phenylacetylanthraquinone melted at 167–168° (lit. 170–171°) and is sufficiently pure for the next step. The yield was 88% with one-fifth these amounts.

Ring Closure.—To a solution of 152 g. of the anthraquinone derivative in 1000 ml. of ethylene glycol monoethyl ether at 120–130° was added 15 g. of potassium hydroxide in 23 ml. of water over one-half hour with stirring. There was an immediate formation of a solid and a marked darkening in color. The mixture was cooled to 20° and filtered. The resulting orange colored solid was washed with ethylene glycol monoethyl ether and finally with ether. The yield was 142 g. (97%); m. p. 325–328°. It can be purified by recrystallization from cellosolve and melts at 332–334°, but it can be used successfully without this recrystallization.

E. **6-Bromo-1-cyano-2-keto-3-methyl-3-azabenzanthrone** (II, R = –CN).—A mixture of 59 g. (0.15 mole) of 4-bromo-1-chloroacetylmethylaminoanthraquinone[2] and 590 ml. of β-hydroxyethyl acetate was stirred and heated to about 180° in a 2-l. flask until solution was complete. While stirring was continued, the solution was cooled to about 120°, and a solution of 32 g. (0.5 mole) of potassium cyanide in 60 ml. of water was added all at once. The suspension of orange-yellow solid which appeared immediately was stirred and heated at 120–130° for one hour, and was allowed to cool slowly. After chilling in an ice-bath, the orange-yellow 6-bromo-1-cyano-3-methyl-3-azabenzanthrone was filtered and washed thoroughly with methanol, water, methanol and ether. The yield of crude material melting at 328–330° was 44.5 g. (81%). A small sample crystallized from dioxane melted at 345–347°, but larger samples are more conveniently crystallized from 1,2,4-trichlorobenzene. The recovery on crystallization is only about 60%; the crude material can be used directly in most cases.

F. **1-Chloro-2-keto-3-methyl-3-azabenzanthrone** was obtained following the published directions.[15a]

G. **The dye bases** were all obtained by the same general procedure, illustrated by the preparation of **1-carbethoxy-6-(4′-chloroanilino)-2-keto-3-methyl-3-azabenzanthrone.**—A mixture of 3 g. of 6-bromo-1-carbethoxy-2-keto-3-methyl-3-azabenzanthrone, 3 g. of *p*-chloroaniline, 1.1 g. of sodium acetate, and a trace of copper acetate was heated in a long test-tube in an oil-bath for five hours at 160–175° with stirring. The mixture was cooled somewhat and then treated with methanol. The dye which separated was collected on a filter and washed successively with warm water, warm dilute hydrochloric acid, water and methanol. The crude yield was 3.4 g. It was recrystallized from benzene or nitropropane, from which it separated in violet crystals that showed a greenish "oberflasche." The yields varied considerably often being quite low. The analytical figures and melting points (which are often indefinite) are given in the tables.

p-Aminobenzotrifluoride could not be condensed with the 6-bromoazabenzanthrone at 160°; the solution became red indicating some dye formation, but most of the trifluoride appeared to polymerize, probably with loss of hydrogen fluoride. The formation of polymer was brought about by heat; it appeared to be accelerated by copper acetate, but hindered by potassium acetate. The amine itself appeared to be essentially unchanged after two years. A decomposition of *o*- and *p*-trifluoromethylphenols in the presence of a basic reagent has been reported recently as well as polymerization and loss of hydrogen fluoride from *p*-aminobenzotrifluoride at 200°.[16,17]

The 6-(β-hydroxyethylamino)-derivative was made using an excess of ethanolamine as solvent and at 100° for two and one-half hours. It dyes acetate bright pink; the dyed material fluoresces orange and has a poor light stability.

The 1-(β-hydroxyethylamino)-derivative required only one hour at 100° for its preparation. It dyed acetate greenish-yellow.

H. **Sulfonation.**—The dye bases were all sulfonated by the same general procedure. One part of the dye in 5–6 parts of monohydrate (100% sulfuric acid) was stirred at room temperature until a sample dissolved in water and shaken with benzene imparted little or no color to the benzene layer. In most cases the sulfonation was carried out overnight but in a few instances, notably with the 1-cyano and 1-benzoyl derivatives, it was found necessary to heat for a short time on the steam-bath to complete the sulfonation. The dyes were generally isolated by pouring the sulfonation mixture on ice, collecting the precipitated free acid on a filter, dissolving the free acid in dilute ammonia, evaporating to dryness (steam-bath) and extracting the dye from its mixture with ammonium sulfate with methanol, finally recovering the dye by removal of the methanol. If the free acid failed to precipitate when the sulfonation mixture was poured on ice, the solution was made basic with ammonia and evaporated to dryness. The dye was then isolated by extraction with methanol as before. The absorption curves of the dyes are given in the tables.

An analysis of the finished dye I (R = C_2H_5OOC, R_1 = H, R_2 = Cl) is given, to show that the ethoxy group is not removed during the sulfonation. This dye crystallizes from acetic acid with a molecule of solvent, but this is lost on recrystallization from dilute alcohol.

Anal. Calcd. for $C_{26}H_{18}ClN_2NaO_9S \cdot C_2H_4O_2$: C, 54.0; H, 3.5; S, 5.2. Found: C, 53.8; H, 3.6; S, 5.0. Calcd. for $C_{26}H_{18}ClN_2NaO_9S$: C, 55.6; H, 3.2; S, 5.7; N, 5.0; Na, 4.1; C_2H_5O, 8.0. Found: C, 55.0; H, 3.1; S, 5.1; N, 4.9; Na, 4.5; C_2H_5O, 7.9.

I. **1-Carbethoxy-3-methyl-6-(4′-chloro-2′-nitro)-3-azabenzanthrone.**—This substance was prepared from II (R = C_2H_5OOC) and 4-chloro-2-nitroaniline in the manner previously described[2] for the synthesis of 3-methyl-6-(4′-methyl-2′-nitro)-3-azabenzanthrone. It was proved to be the same as the product obtained from I (R = C_2H_5OOC, R_1 = H, R_2 = Cl) by treatment with dilute nitric acid,[2] by analytical results, behavior on heating a mixture of the two compounds and the identity of the absorption curves.

Summary

A large number of variously substituted 3-azabenzanthrone dyes have been made, and their absorptions recorded.

No 1-arylamino derivatives have been reported previously; they are not particularly fast to light.

ROCHESTER 4, NEW YORK RECEIVED OCTOBER 18, 1949

[15a] Dupont, *Bull. soc. chim. Belg.*, **52**, 7 (1943); *C. A.*, **38**, 5215 (1944).

[16] Jones, THIS JOURNAL, **69**, 2347 (1947).

[17] *p*-Nitrobenzotrifluoride, *p*-aminobenzotrifluoride and the acetyl derivative of the latter were prepared by Mr. E. C. Armstrong and Miss Eleanor R. Webster[4] of these laboratories. As the procedures used and properties of the substances were essentially the same as those independently reported,[16] they will not be duplicated here.