TABLE II

THERMAL ISOMERIZATION OF METHYL NEOABIETATE AT 200°

Time, hr.	$[\alpha]_D$, 2% EtOH	α at 252 mμ
0	+148°	81.0
1	+144	80.5
2	+145	80.2
5	+146	80.0
16	+145	79.8
72	+144	79.8
168	+133	71.5

moval of the last traces of ether under vacuum, neoabietenol crystallized. The yield was quantitative. After two recrystallizations from ethanol–water the melting point was constant at 98–99.5° and the specific extinction coefficient at 251–252 mμ was 88.3.

Anal. Calcd. for $C_{20}H_{32}O$: C, 83.27; H, 11.18. Found: C, 83.56, 83.30; H, 11.10, 11.16.

The specific rotation of a 1% solution of neoabietenol in various organic solvents was: ethanol, +184.6°; methanol, +179.0°; benzene +200.6°; acetone, +197.7°; ether, +189.2°; chloroform, +187.0°; acetonitrile, +182.0°; heptane, +200.1°; isoöctane, +199.1°; cyclohexane, +204.0°.

TABLE III

THERMAL ISOMERIZATION OF NEOABIETENOL AT 200°

Time, hr.	$[\alpha]_D$ 2% EtOH	α at 252 mμ
0	+184.6°	88.3
8	+161.4	81.1
16	+149.5	77.8
72	+146.8	75.3
168	+142.5	74.0

Thermal Isomerization of Neoabietenol at 200°.—One-gram samples of neoabietenol were sealed in evacuated tubes as described above and heated at 200° for various lengths of time. The rate of isomerization was measured by the change in the specific rotation and the specific extinction coefficient at 252 mμ (Table III).

OLUSTEE, FLORIDA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES, MEDICAL CORPS, ISRAEL DEFENCE FORCES]

The Cyclization Reaction of Di-(*p*-halogenophenyl)-trifluoromethylcarbinols

BY SASSON COHEN

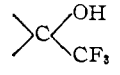
RECEIVED OCTOBER 18, 1956

Solutions of di-(*p*-halogenophenyl)-trifluoromethylcarbinols in concentrated sulfuric acid yield 3-halogeno-6-hydroxy-9-trifluoromethylfluorenes upon dilution with water, and the corresponding 6-methoxy compounds upon dilution with methanol. The trifluoromethyl group in the latter substances undergoes alkaline methanolysis to yield methyl 3-halogeno-6-methoxyfluorene-9-carboxylates, which are further degraded, by oxidation, to 3-halogeno-6-methoxyfluorenones. In the case of 3-chloro-6-methoxyfluorenone, the identity of the product has been proved by an unambiguous synthesis.

In a study of the chemical and biochemical behavior of the recently described di-(*p*-halogenophenyl)-trifluoromethylcarbinols (I),[1-5] it has been observed that the color of their halochromic solutions in concentrated sulfuric acid changes within a few minutes from intensely purple (λ_{max} 570–580 mμ) to orange (λ_{max} 495 mμ); in more concentrated solutions, this change is accompanied by the liberation of gas which, in the case of the fluoro compound (I, X = F), was identified as hydrogen fluoride. The reaction is specific for the *p*-halogen compounds, as di-(*p*-methoxyphenyl)-trifluoromethylcarbinol gives a fairly stable halochromic solution in concentrated sulfuric acid (λ_{max} 580 mμ); the color fades only very slowly, and the solution becomes colorless.

This behavior of the di-(*p*-halogenophenyl)-trifluoromethylcarbinols (I) seemed to deserve a more detailed study. Its results will be discussed for the case of the difluoro compound $C_{14}H_9F_5O$ (I, X = F). When the orange solution in concentrated sulfuric acid was diluted with water, a phenolic compound $C_{14}H_8F_4O$ was obtained, while dilution with methanol led to its methyl ether. Treatment with a mixture of acetic and hydrobromic acids led to substance $C_{14}H_8F_4O$, in which the presence of a hydroxyl group was indicated by the preparation of a crystalline acetyl derivative.

That the original CF_3 grouping was still present in the molecule could be demonstrated by the treatment of the compound $C_{15}H_{10}F_4O$ with dilute methanolic alkali: the methyl ester $C_{16}H_{13}FO_3$ of a carboxylic acid was formed, the CF_3 group being replaced by a carbomethoxy group. The ease with which the reaction took place proved, in view of previous results for this type of compounds,[5] that the substance $C_{15}H_{10}F_4O$ no longer contained the system



which is extremely resistant to hydrolysis, but rather the grouping

$$>CH\cdot CF_3$$

which hydrolyzes easily. Oxidation of the methyl ester $C_{16}H_{13}FO_3$ with alkaline hydrogen peroxide gave a *yellow* ketone $C_{14}H_9FO_2$, which had the spectral properties of a fluorenone derivative (Fig. 1). Also the ultraviolet absorption spectra of the previously mentioned substances (see, *e.g.*, Fig. 2) pointed to the presence of a fluorene system. The yellow ketone $C_{14}H_9FO_2$ must, therefore, be a fluoro-methoxy-fluorenone. Its formula is that of 3-fluoro-6-methoxyfluorenone (V, X = F).

The same series of reactions has been carried out with di-(*p*-chlorophenyl)-trifluoromethylcarbinol

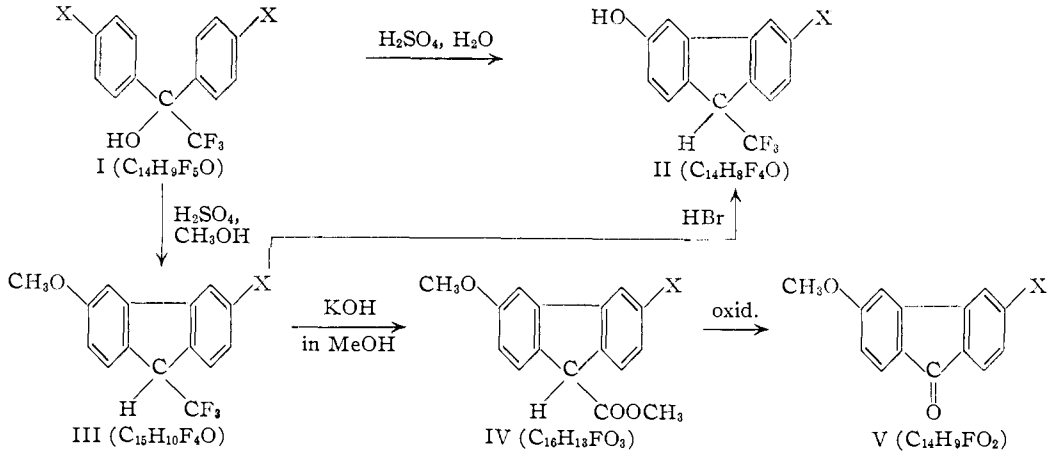
(1) E. D. Bergmann, A. S. Tahori, A. Kaluszyner and S. Reuter, *Nature*, **176**, 266 (1955).

(2) A. Kaluszyner, S. Reuter and E. D. Bergmann, THIS JOURNAL, **77**, 4146 (1955).

(3) A. S. Tahori, *J. Econom. Entomol.*, **48**, 638 (1955).

(4) S. Reuter, S. Cohen, R. Mechoulam, A. Kaluszyner and A. S. Tahori, *Rivista di Parassitol.*, **17**, 125 (1956).

(5) R. Mechoulam, S. Cohen and A. Kaluszyner, *J. Org. Chem.*, **21**, 801 (1956).



(I, X = Cl), which has been degraded to 3-chloro-6-methoxyfluorenone (V, X = Cl). In this case, the identity of the degradation product has been proved by an unambiguous synthesis (*vide infra*).

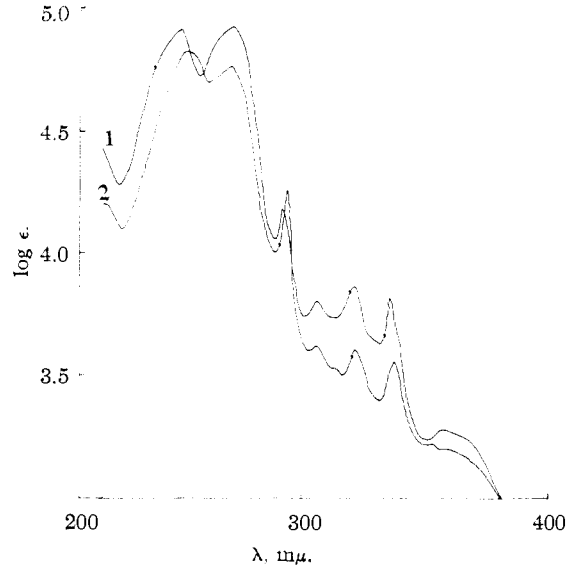
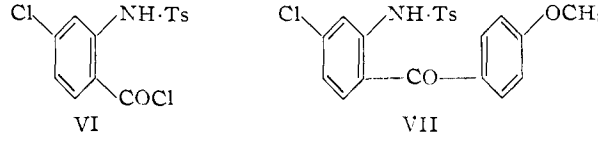


Fig. 1.—Ultraviolet spectrum of 3-methoxyfluorenone (curve 1) and 3-fluoro-6-methoxyfluorenone (V, X = F) (curve 2) in isoöctane.

The yield in the case of I, X = Cl, was lower than for the fluoro compound; in the case of the bromo compound (I, X = Br) it was so low that no further experiments have been carried out with the product. The dimethoxy compound (I, X = OCH_3) was recovered unchanged from its solution in concentrated sulfuric acid, and from the parent substance (I, X = H), a compound of m.p. 168–169° was obtained, which behaves unlike the products derived from the *p*-halogenated carbinols and has so far not been investigated.

The reactions described here can be rationalized by the scheme shown above.

For the synthesis of V, X = Cl, the following scheme, based on Ullmann's synthesis of 3-methoxyfluorenone,[6] was realized easily: The chloride VI of N-tosyl-4-chloroanthranilic acid was condensed with anisole in the presence of aluminum chloride and the resulting 4-chloro-4′-methoxy-2-tosyl-aminobenzophenone (VII) deacylated and subjected to diazotization. Upon heating, the diazonium salt gave 3-chloro-6-methoxyfluorenone (V, X = Cl).



In order to explain the formation of II and III from the di-(*p*-halogenophenyl)-trifluoromethylcarbinols (I), one must consider the carbonium ion VIII which is formed in the halochromic solutions of I in concentrated sulfuric acid. This can be written in the form IX, in which the halogen X is replaced by the $-OSO_3H$ group (X). X, in the form of the resonance structure XI, is isomerized by the attack of the carbonium ion on the second ring to give XII. Addition of water or methanol then yields II or III, respectively. The contribution of structure IX to the actual state of the carbonium ion is enhanced by the pronounced inductive effect of the trifluoromethyl group[7] and supported by the mesomeric effect of the halogen,

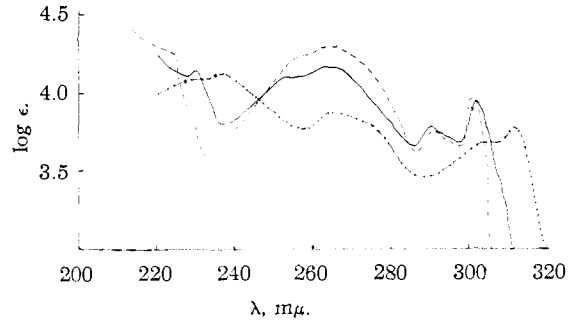
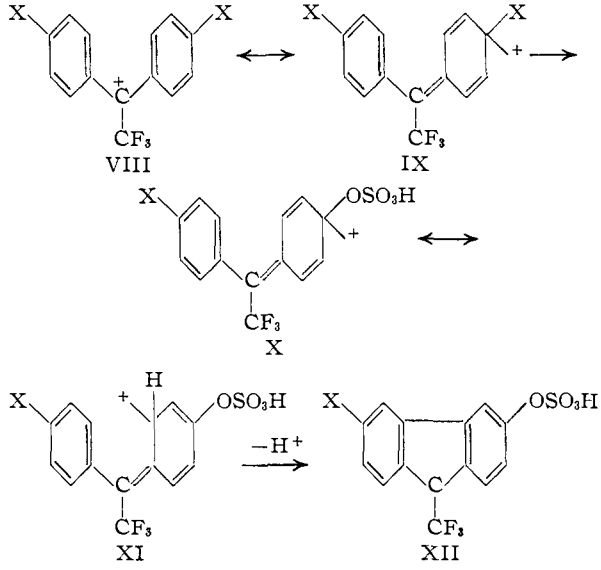


Fig. 2.—Ultraviolet spectrum of fluorene (— — — — —), 3-fluoro-6-methoxy-9-trifluoromethylfluorene (III, X = F) (|—|—|—|—|) and 3-fluoro-6-acetoxy-9-trifluoromethylfluorene (————) in ethanol.

(6) F. Ullmann and H. Bleier, *Ber.*, **35**, 4273 (1907); *cf.* L. Chardonnens and A. Wurmli, *Helv. Chim. Acta*, **29**, 922 (1946).

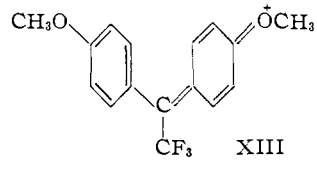
(7) It is interesting to compare with the observations recorded here, the behavior of di-(*p*-chlorophenyl)-methylcarbinol toward concentrated sulfuric acid; see M. S. Newman and N. C. Deno, THIS JOURNAL, **73**, 3645 (1951).

which is largest for the fluorine atom.[8] This may explain that the yields of II and III decrease in the order F > Cl > Br. It has often been noted that the system $CF_3C{=}C$ is surprisingly stable.[9-11]



VIII IX X XI XII

The inability of the methoxy compound (I, X = OCH_3) to undergo similar reactions is best explained by the consideration that the main contributing resonance form of its carbonium ion will be XIII.[12]



XIII

The only similar reaction of a diarylcarbinol derivative known so far is the conversion of benzilic acid to fluorene-9-carboxylic acid[13]; the former acid is indeed similar to I, as far as its electronic structure is concerned. Otherwise, only triarylcarbinols have been known to undergo cyclodehydration processes leading to fluorene derivatives, and generally only when at least one of the aryl groups was a naphthyl or phenanthryl radical.[14-17]

Acknowledgments.—The author wishes to express his thanks to Professor Ernst D. Bergmann for valuable advice and kind interest in this study, to Mr. Samuel Guttman for the spectrophotometric data, and to the Minnesota Mining & Manufacturing Co., Minneapolis, Minn., for a supply of trifluoroacetic acid.

(8) R. N. Haszeldine and A. G. Sharpe, "Fluorine and its Compounds," Methuen & Co., London, 1951.

(9) A. L. Henne and S. Kaye, THIS JOURNAL, **72**, 3369 (1950).

(10) K. N. Campbell, V. D. Knobloch and B. K. Campbell, *ibid.*, **72**, 4380 (1950).

(11) A. L. Henne, M. A. Smook and P. L. Pelley, *ibid.*, **72**, 4756 (1950).

(12) For the stabilization of carbonium ions by methoxyl groups, see L. A. Wiles, *Chem. Revs.*, **56**, 373 (1956), and A. G. Davies and J. Kenyon, *Quart. Revs.*, **9**, 203 (1955).

(13) D. Vorlaender, *Ber.*, **44**, 2467 (1911).

(14) C. S. Schoepfle, THIS JOURNAL, **44**, 192 (1922).

(15) R. G. Clarkson and M. Gomberg, *ibid.*, **52**, 2881 (1930).

(16) E. Berliner, *ibid.*, **64**, 2894 (1942).

(17) F. Bergmann and S. Israelashwili, *ibid.*, **68**, 1 (1946).

Experimental

The diaryl-trifluoromethylcarbinols used in this study have been prepared according to Kaluszyner, Reuter and Bergmann.[1,2] The carbon-hydrogen determinations have been carried out by the method of Bodenheimer and Goldstein,[18] the fluorine determinations by the method of Eger and Yarden.[19]

3-Fluoro-6-hydroxy-9-trifluoromethylfluorene (II, X = F).—Di-(*p*-fluorophenyl)-trifluoromethylcarbinol (5 g.) was shaken with concentrated sulfuric acid (50 ml.) in a glass-stoppered flask for six hours. Occasionally, the flask was opened to release the liberated hydrofluoric acid.[20] The orange colored reaction product was then poured slowly and with stirring on crushed ice, and extracted twice with ether. The combined ether extracts were dried over anhydrous sodium sulfate, decolorized with charcoal and concentrated, and the residue was recrystallized from a benzene–cyclohexane mixture. Thus, white silky needles of m.p. 184° were obtained; yield 3.1 g. (67%).

Anal. Calcd. for $C_{14}H_8F_4O$: C, 62.7; H, 3.0; F, 28.3. Found: C, 62.9; H, 3.0; F, 28.1.

3-Fluoro-6-methoxy-9-trifluoromethylfluorene (III, X = F).—The product obtained from di-(*p*-fluorophenyl)-trifluoromethylcarbinol (5 g.) and concentrated sulfuric acid (50 ml.) was added, dropwise and with stirring, to methanol (150 ml.), kept at 0–5°. Crushed ice (200 g.) was then added and the suspension filtered. The crystals obtained were washed with water and recrystallized from methanol as colorless prisms, m.p. 91–92°, yield 3.2 g. (66%).

Anal. Calcd. for $C_{15}H_{10}F_4O$: C, 63.8; H, 3.5; F, 26.9. Found: C, 63.3; H, 3.7; F, 26.7.

3-Chloro-6-hydroxy-9-trifluoromethylfluorene (II, X = Cl).—Di-(*p*-chlorophenyl)-trifluoromethylcarbinol (5 g.) was treated as above. Upon repeated recrystallizations from a benzene–cyclohexane mixture, the product was obtained as white silky needles, m.p. 191–192°, yield 1.2 g. (27%).

Anal. Calcd. for $C_{14}H_8ClF_3O$: C, 59.1; H, 2.8; Cl, 12.5; F, 20.3. Found: C, 59.5; H, 3.0; Cl, 12.3; F, 19.8.

3-Chloro-6-methoxy-9-trifluoromethylfluorene (III, X = Cl).—From di-(*p*-chlorophenyl)-trifluoromethylcarbinol (5 g.), one obtained by successive treatment with sulfuric acid and methanol, and upon recrystallization from methanol, 1.2 g. (24%) of colorless prisms, m.p. 95–96°.

Anal. Calcd. for $C_{15}H_{10}ClF_3O$: C, 60.3; H, 3.4; Cl, 11.8; F, 19.1. Found: C, 60.5; H, 3.6; Cl, 11.6; F, 18.7.

Demethylation of 3-Fluoro-6-methoxy-9-trifluoromethylfluorene (III, X = F).—The compound (0.3 g.) was refluxed for three hours with a mixture of acetic acid (5 ml.) and 48% hydrobromic acid (5 ml.). Water (2 ml.) was added to the warm solution, from which, upon cooling, separated 0.2 g. (72%) of 3-fluoro-6-hydroxy-9-trifluoromethylfluorene (II, X = F), identified by melting point and mixed melting point.

3-Fluoro-6-acetoxy-9-trifluoromethylfluorene.—The compound (II, X = F) (0.2 g.) was dissolved in anhydrous pyridine (3 ml.) and a few drops of acetyl chloride was added. The mixture was left to stand at room temperature for 30 minutes; then water (3 ml.) was added. Upon standing, 3-fluoro-6-acetoxy-9-trifluoromethylfluorene crystallized as small cubes, which, after recrystallization from methanol, melted at 125–126°, yield 0.18 g. (78%).

Anal. Calcd. for $C_{16}H_{10}F_4O_2$: C, 61.9; H, 3.2: F, 24.5; acetyl, 13.9. Found: C, 62.4; H, 3.5; F, 25.0; acetyl, 13.6.

Methyl 3-fluoro-6-methoxyfluorene-9-carboxylate (IV, X = F).—3-Fluoro-6-methoxy-9-trifluoromethylfluorene (III, X = F, 1.2 g.) was refluxed with 1 *N* methanolic potassium hydroxide (25 ml.) for one hour. The solution was cooled, and 1 *N* hydrochloric acid (30 ml.) added. Upon extraction with ether, evaporation of the solvent and re-

(18) W. Bodenheimer and M. Goldstein, *Bull. Res. Council Israel*, **3**, 53 (1953).

(19) Ch. Eger and A. Yarden, *Anal. Chem.*, **28**, 512 (1956).

(20) This was identified according to J. H. Simons and E. O. Ramler, THIS JOURNAL, **65**, 389 (1943).

crystallization from methanol (IV, X = F) was obtained as thin colorless prisms, m.p. 107–108°, yield 0.8 g. (70%).

Anal. Calcd. for $C_{16}H_{13}FO_3$: C, 70.6; H, 4.8; F, 7.0. Found: C, 70.5; H, 4.8; F, 6.8.

Methyl 3-chloro-6-methoxyfluorene-9-carboxylate (IV, X = Cl), was obtained analogously from 3-chloro-6-methoxy-9-trifluoromethylfluorene (III, X = Cl, 1.2 g.). It formed thin colorless prisms of m.p. 129–130°, yield 0.92 g. (79%).

Anal. Calcd. for $C_{16}H_{13}ClO_3$: C, 66.6; H, 4.5. Found: C, 65.9; H, 4.8.

3-Fluoro-6-methoxyfluorenone (V, X = F).—A well-stirred suspension of methyl 3-fluoro-6-methoxyfluorene-9-carboxylate (IV, X = F, 0.4 g.) in 5 *N* sodium hydroxide solution (5 ml.) was heated on a boiling water-bath. To this was added, drop by drop, 30% hydrogen peroxide (2 ml.). When the reaction had subsided, water (10 ml.) was added and the mixture extracted with ether. By evaporation of the solvent and recrystallization of the residue from a benzene–petroleum ether mixture, there were obtained bright yellow prisms, which dissolve in concentrated sulfuric acid with a deep purple color; m.p. 152–153°, yield 0.1 g. (30%).

Anal. Calcd. for $C_{14}H_9FO_2$: C, 73.7; H, 4.0. Found: C, 74.0; H, 3.8.

3-Chloro-6-methoxyfluorenone (V, X = Cl).—Methyl 3-chloro-6-methoxyfluorene-9-carboxylate (IV, X = Cl, 0.5 g.), when treated as above, gave 0.12 g. (28%) of bright yellow prisms, giving the same color reaction with concentrated sulfuric acid as the fluorine analog, m.p. 181–182°.

Anal. Calcd. for $C_{14}H_9ClO_2$: C, 68.7; H, 3.7. Found: C, 68.6; H, 3.8.

The oxime formed small yellowish prisms, which, after recrystallization from alcohol, melted at 229–230° dec., yield 66%.

Anal. Calcd. for $C_{14}H_{10}ClNO_2$: C, 64.7; H, 3.9. Found: C, 65,0; H, 4.0.

Synthesis of 3-Chloro-6-methoxyfluorenone (V, X = Cl).—(a) To a hot solution of pure[21] 4-chloroanthranilic acid[22] (9 g.) in 20% sodium carbonate solution (45 ml.), there was added, in small portions, *p*-toluenesulfonyl chloride (9 g.). Decolorizing charcoal was then added and the mixture held at 70–80° for 10 minutes, filtered while still hot and, after cooling, acidified with excess hydrochloric acid. The precipitated N-*p*-toluenesulfonyl-4-chloroanthranilic acid was filtered off and recrystallized successively from 70% ethanol and benzene; m.p. 223–225°, yield 8.5 g. (50%).

Anal. Calcd. for $C_{14}H_{12}ClNO_4S$: C, 51.6; H, 3.7. Found: C, 50.6; H, 4.0.

(b) The foregoing compound (7.5 g.) was refluxed with phosphorus pentachloride (5.5 g.) in carbon disulfide (150 ml.) for 45 minutes. The solution was cooled in ice-water, and anisole (8 g.) and finely powdered aluminum chloride (6 g.) added. The reaction mixture was then refluxed for 2 hours, with occasional shaking, decomposed with a mixture of ice and excess hydrochloric acid, and extracted with ether. By removal of the solvent and recrystallization of the crude product from methanol, **4-chloro-4′-methoxy-2-*p*-tosylaminobenzophenone** (VII) was obtained as long colorless needles, m.p. 107–108°, yield 5.4 g. (56%).

Anal. Calcd. for $C_{21}H_{18}ClNO_4S$: C, 60.7; H, 4.4. Found: C, 61.0; H, 4.3.

(c) The ketone VII (5 g.) was heated with a mixture of acetic acid (10 ml.) and concentrated sulfuric acid (10 ml.) on a water-bath for 30 minutes. Water (20 ml.) was added and the reaction mixture, which crystallized partly, cooled to 0–5° and diazotized by the slow addition of a solution of sodium nitrite (0.8 g. in 15 ml. of water). The reaction mixture was then heated on a boiling water-bath for 45 minutes, cooled and extracted with ether. The ether extracts were washed with 10% sodium hydroxide solution, dried over anhydrous sodium sulfate and evaporated to dryness. The residue was recrystallized from a mixture of benzene and petroleum ether, and gave bright yellow crystals of 3-chloro-6-methoxyfluorenone (V, X = Cl), melting at 181–182°. A mixture with the product described above showed no depression of the melting point; yield 1.2 g. (41%).

TEL-AVIV, ISRAEL

(21) M.p. 232–234°; the purity is very important, as otherwise difficulties are encountered in the purification of the reaction products.

(22) E. B. Hunn, THIS JOURNAL, **45**, 1024 (1923).

[CONTRIBUTION FROM AVERY LABORATORY, UNIVERSITY OF NEBRASKA]

Synthesis of 3-Amino- and 3-Nitro-2-arylquinolines[1]

BY HENRY E. BAUMGARTEN AND JOHN L. SAYLOR

RECEIVED JULY 16, 1956

Condensation of *o*-aminobenzaldehyde with ω-nitroacetophenone gave 3-nitro-2-phenylquinoline, while condensation of *p*-chloro-, *p*-methyl- and *p*-methoxy-ω-nitroacetophenone and of *o*,ω-dinitroacetophenone with *o*-aminobenzaldehyde yielded 3-nitro-2-(*p*-chlorophenyl)-quinoline, 3-nitro-2-(*p*-tolyl)-quinoline, 3-nitro-2-(*p*-anisyl)-quinoline and 3-nitro-2-(*o*-nitrophenyl)-quinoline, respectively. All but the last-named 3-nitro-2-arylquinoline were reduced with iron and acetic acid to the corresponding 3-amino-2-arylquinolines.

For other studies being carried out in this Laboratory a ready source of variously substituted 3-amino- and 3-nitro-2-phenylquinolines was required. This communication describes a reaction sequence that we found to be convenient for the preparation of 3-amino-2-phenylquinoline (VIIa) and 3-nitro-2-phenylquinoline (VIa) and a number of their derivatives.

The various methods available for the preparation of 3-nitroquinolines have been reviewed.[2] Of these methods, the one involving the condensation of methazonic acid (II, R_2 = H, Y = N − OH) with *o*-amino carbonyl compounds[2–4] appeared to be the most promising for the purpose at hand. This reaction can be regarded as a specific application of the general sequence illustrated in I → III. According to this sequence, the condensation of *o*-aminobenzaldehyde (IV) with ω-nitroacetophenones (V) should lead to the desired 3-nitro-2-arylquinolines (VI).

The required ω-nitroacetophenones were prepared by the base-catalyzed condensation of an aromatic aldehyde with nitromethane followed by oxidation of the intermediate α-aryl-β-nitroeth-

(1) This work was supported in part by grant G-1090 of the National Science Foundation.

(2) K. Schofield and R. S. Theobald, *J. Chem. Soc.*, 395 (1950).

(3) K. Schofield and R. S. Theobald, *ibid.*, 2992 (1951).

(4) D. W. Ockenden and K. Schofield, *ibid.*, 1915, 3914 (1953).