and 50 ml. of acetic acid was stirred at room temperature for 4 hours and then refluxed for 1.5 hours. The reaction mixture yielded 0.00056 mole of *p*-iodobenzoic acid and 0.00142 mole of *p,p'*-diiodobenzophenone.

Reaction of I with NBS.—A mixture of 2.0 g. of I, 3.6 g. of NBS, 0.2 g. of benzoyl peroxide and 100 ml. of carbon tetrachloride was refluxed for 2 hours. The mixture was filtered and the filtrate concentrated to dryness. The residue was dissolved in 25 ml. of pyridine and the solution was refluxed for 1 hour, poured into water and filtered. The resulting solid was crystallized from benzene to give 1.8 g. of compound, m.p. 150–151°, believed to be 1,1-di-(*p*-iodophenyl)-2-bromomethylene.

Anal. Calcd. for $C_{14}H_9I_2Br$: C, 32.91; H, 1.78; Br, 15.64; I, 49.67. Found: C, 33.28; H, 1.88; Br, 15.28; I, 49.70.

The ultraviolet spectrum of the above compound in 95% ethanol shows a maximum at 255 mμ (ε 31,000) and shoulders at 235 (ε 18,000) and 270 mμ (ε 24,000). This spectrum compares favorably with that determined for 1,1-di-(*p*-iodophenyl)-ethylene in 95% ethanol which exhibits a maximum at 255 mμ (ε 31,000) and a shoulder at 233 mμ (ε 17,000). The oxidation of 1.8 g. of the above compound with 7.5 g. of chromic acid and 75 ml. of acetic acid gave 0.23 g. of *p*-iodobenzoic acid and 0.23 g. of *p,p'*-diiodobenzophenone.

Reaction of 1,1-Di-(*p*-anisyl)-ethane with NBS.—A mixture of 2.0 g. of the compound, 4.0 g. of NBS and 0.2 g. of benzoyl peroxide was refluxed in 100 ml. of carbon tetrachloride for 1 hour. Hydrogen bromide was evolved during the reaction. The mixture was filtered and the filtrate was concentrated to dryness. The residue was heated with 25 ml. of pyridine for 2 hours and the mixture worked up in the usual way to give 1.8 g. of a compound, m.p. 94–95°.

Anal. Calcd. for $C_{16}H_{14}O_2Br_2$: C, 48.30; H, 3.54; Br, 40.2. Found: C, 48.36; H, 3.55; Br, 40.0.

The oxidation of 1.0 g. of the above compound with 2.0 g. of chromic acid gave 0.026 g. of an unidentified acid, m.p. 172–176°, which depressed the m.p. of *p*-anisic acid, and 0.14 g. of *p,p'*-dimethoxybenzophenone.

Reaction of 1,2-Di-(*p*-anisyl)-ethane with NBS.—A mixture of 0.2 g. of the compound, 0.6 g. of NBS and 0.05 g. of benzoyl peroxide was refluxed in 50 ml. of carbon tetrachloride for 1.5 hours. Hydrogen bromide was evolved during the reaction. The reaction mixture was worked up in the usual way to give traces of an unidentified solid, m.p. 198–201°, which depressed the m.p. of *p,p'*-dimethoxystilbene and which gave a positive test for bromine (sodium fusion).

PITTSBURGH, PENNA.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUQUESNE UNIVERSITY]

Hydrazones of Nitrophenyl and Pyridyl Aldehydes and Ketones. New Preparation of *o*-Nitrobenzophenones and Differences in Behavior of *o*-Nitrobenzophenone and *o*-Nitrophenyl Mesityl Ketone[1]

BY H. HARRY SZMANT AND CHARLES M. HARMUTH

RECEIVED MAY 24, 1958

The preparation of a series of hydrazones of nitrobenzaldehydes, nitrobenzophenones, pyridine carboxaldehydes and pyridyl phenyl ketones is described. A new method of preparation of *o*-nitrobenzophenones was developed. Complex replacement reactions of *o*-nitrobenzophenones are discussed in terms of conformational differences.

The continuation of the study of the Wolff–Kishner reaction[2] required a series of hydrazones of the isomeric nitrobenzaldehydes, nitrobenzophenones, pyridine carboxaldehydes and pyridyl phenyl ketones. The preparation of the aldehydes and ketones required for this purpose did not offer any difficulties except in the case of *o*-nitrobenzophenone (I).

Our attempts to prepare I by the Friedel–Crafts reaction of *o*-nitrobenzoyl chloride and benzene gave black, resinous materials in agreement with the experiences of previous investigators.[3] Because of the failure of the Friedel–Crafts reaction involving *o*-nitrobenzoyl chloride, it has been customary to prepare I by the oxidation of *o*-nitrodiphenylmethane[4,5] and by the ferric chloride-catalyzed reaction of *o*-nitrobenzoyl chloride and benzene.[3] Since the latter reaction gives only a yield of 17% of I, and the former involves several steps, it was decided to apply the acylation procedure discovered recently in this Laboratory[6,7] to the synthesis of I.

The mixture of *o*-nitrobenzoic acid, trifluoroacetic anhydride and benzene failed to give I. This result is not unexpected for two reasons. Firstly, it is known[8] that this acylation procedure is only applicable to electron-rich systems. Secondly, the use of an acid containing an electron-withdrawing substituent would be expected to inhibit the dissociation of the mixed anhydride to give the acylonium ion necessary for the reaction. The use of additional catalysis by means of boron trifluoride[6,7] proved to be successful for the preparation of I and the related *o*-nitrophenyl anisyl and mesityl ketones. While the yield of I under the optimum conditions encountered so far is not better than that obtained by the ferric chloride-catalyzed acylation,[3] our procedure is nevertheless advantageous because of its simplicity and the recovery of unreacted *o*-nitrobenzoic acid. The yields of *o*-nitrophenyl anisyl and mesityl ketones by our procedure were 25 and 75%, respectively, and this represents a great improvement over the previously reported[3] yields of 1.5 and 7%, respectively.

Numerous experiments using *o*-nitrobenzoic acid, trifluoroacetic anhydride, boron trifluoride and either benzene, anisole or mesitylene, proved that the reaction conditions were of utmost importance. Addition of the aromatic substrate to the red solution of the complex formed between the mixed anhydride and boron trifluoride gave immediate

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(1) From Ph.D. thesis of C.M.H., 1956. Present address of H.H.S. where inquiries should be addressed: Universidad de Oriente, Santiago de Cuba, Cuba.

(2) H. H. Szmant, *et al.*, THIS JOURNAL, **74**, 2724 (1952).

(3) M. Boetius and H. Romisch, *Ber.*, **69**, 1924 (1936).

(4) R. Geigy and W. Koenigs, *ibid.*, **18**, 2403 (1885).

(5) P. A. Smith, THIS JOURNAL, **76**, 431 (1954).

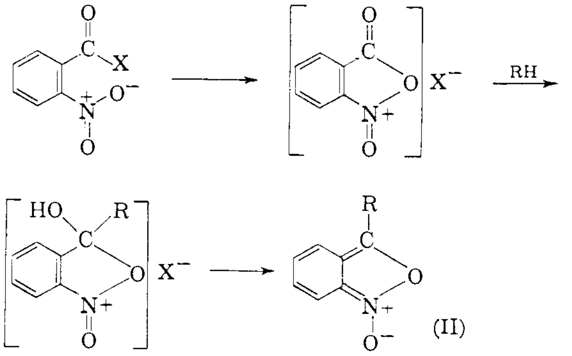
(6) H. H. Szmant and D. Irwin, *ibid.*, **78**, 4386 (1956).

(7) H. H. Szmant and G. Suld, *ibid.*, **78**, 3400 (1956).

(8) J. M. Tedder, *Chem. Revs.*, **53**, 787 (1955).

darkening of the mixture and within a few minutes, in the absence of external cooling, there took place an extremely exothermic reaction. When the reaction was allowed to proceed and the mixture was poured on ice there was obtained a black, unidentified resinous material. On the other hand, if the reaction was stopped a few seconds after the addition of the aromatic substrate (before heat evolution was noticed), then the desired ketone and unreacted acid were isolated and the resinous material was not formed. When the complex of the mixed anhydride and boron trifluoride was added dropwise to the aromatic substrate with stirring and cooling, then the formation of resinous material was also avoided but the yield of desired ketone was not thereby improved. Using the last mentioned procedure during the preparation of I there was also isolated a white solid (II) melting 187-188° and of empirical formula $C_{13}H_9O_2N$. The reduction of II with iron and acetic acid gave *o*-aminobenzophenone. With this fact in mind it was suspected that II has the structure of the hitherto unknown 3-phenylanthranil-1-oxide. To ascertain this possibility II was subjected to the Tanasescu reaction[9,10] and the expected acridone was indeed obtained.

The origin of II during the preparation of I is of interest. It was demonstrated that I is not the precursor of II since I could be recovered when subjected to reaction conditions simulating those which gave II. It is suggested that the formation of II results from the sequence of changes.



X = CF_3CO_2—;
R = C_6H_5

Regardless of the details of the reaction mechanism, it is obvious that the formation of II depends on the approach of the oxygen atom of the nitro group to the neighboring electron-deficient center at the carbonyl function. This type of reaction is probably also responsible for the formation of complex products during the conventional Friedel-Crafts reaction of *o*-nitrobenzoyl chloride.[11] The nucleophilic character of the oxygen atom of the nitro group is not widely recognized except under protonating conditions but nevertheless seems to be responsible for the following reactions: formation of 3-arylanthranils from *o*-nitrobenzaldehyde and aniline,[12] phenols,[13] or chlorobenzene in the presence of zinc chloride[9,10]; formation of 3-(4′-pyridyl)-anthranil from 4-(*o*-nitrobenzoyl)-pyridine in the presence of stannous chloride and hydrochloric acid[14]; formation of benzofuroxans by elimination of nitrogen from *o*-nitrophenyl azides[15,16] or by the oxidation of *o*-nitroaniline[17]; reaction of diazomethane with two moles of *o*-nitrobenzaldehyde to give methylene-bis-benz-isoxazolone[18]; photochemical rearrangements[19] of *o*-nitrobenzalanilines, *o*-nitrobenzaldehydes and derivatives of *o*-nitrobenzyl alcohol; and the recently discovered rearrangement of *o*-nitrophenylacetic acid.[20]

The hydrazones of *m*- and *p*-nitrobenzaldehydes were easily obtained by merely adding 85% hydrazine hydrate to a hot alcoholic solution of the corresponding aldehydes.[21] The preparation of the hydrazone of *o*-nitrobenzaldehyde required slow addition of hydrazine to a cold alcoholic solution of the aldehyde and careful cooling in order to prevent a violent evolution of nitrogen with formation of *o*-nitrotoluene.[22]

The preparation and isolation of the hydrazones of the pyridine carboxaldehydes was difficult since these hydrazones were easily converted to azines. The hydrazones were best isolated by fractionation at 1-2 mm. and purified by high vacuum distillation (10^{-6} mm.). Since exposure to air converted the hydrazones to azines they were stored in vacuum-sealed vials as viscous, glassy liquids.

The ketone hydrazones were prepared by refluxing the ketone, 85% hydrazine hydrate and 95% ethanol over calcium oxide in a Soxhlet apparatus.[23] The hydrazones which refused to crystallize were treated with concentrated sulfuric acid[24] which presumably removes traces of hydrazine as well as isomerizes the mixture of geometrical isomers to the more stable isomer.

A number of attempts to prepare the hydrazone of I were unsuccessful even when temperatures of 200° were employed. The reaction products were oily materials, and since most of the original ketone could always be recovered, it is concluded that hydrazone formation in the case of I is either extremely sluggish or non-existent. This conclusion is supported by the extremely slow Schmidt reaction of I[5,25] and our inability to force the formation of the 2,4-dinitrophenylhydrazone. In view of these results with I it was very surprising

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[9] I. Tanasescu and M. Susciu, *Bull. soc. chim.* (*France*), [5] **4**, 245 (1937).

[10] F. Bradbury and W. Linell, *J. Chem. Soc.*, 377 (1942).

[11] Boetius and Romisch (ref. 3) isolated an unidentified material which contained 53.42% C, 2.52% H, 8.85% N and 13.47% Cl.

[12] I. Tanasescu and A. Silberg, *Bull. soc. chim.* (*France*), **51**, 1357 (1932).

[13] J. C. Simpson and O. Stephenson, *J. Chem. Soc.*, 303 (1942).

[14] A. J. Nunn and K. Schofield, *ibid.*, 583 (1952).

[15] J. H. Boyer and F. C. Carter, *Chem. Revs.*, **52**, 34 (1954).

[16] R. J. Gaughran, J. R. Picard and V. R. Kaufman, THIS JOURNAL, **76**, 2233 (1954).

[17] A. G. Green and F. M. Rose, *J. Chem. Soc.*, **101**, 2452 (1912).

[18] F. Arndt and W. Portals, *Ber.*, **60**, 446 (1927).

[19] W. Ried and M. Wilk, *Ann.*, **590**, 91, 111 (1954).

[20] G. N. Walker, THIS JOURNAL, **77**, 6698 (1955).

[21] T. Curtius and A. Lublin, *Ber.*, **33**, 2461 (1900).

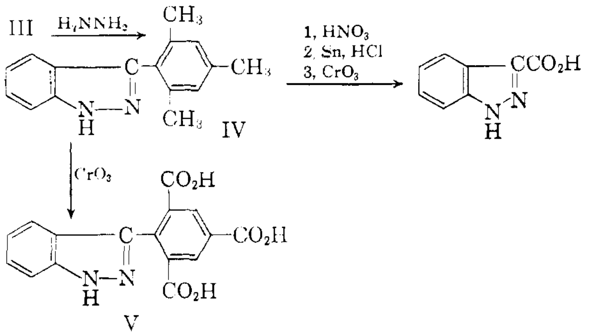
[22] A. Jaenisch, *ibid.*, **56**, 2448 (1923).

[23] H. H. Szmant and C. McGinnis, THIS JOURNAL, **72**, 2890 (1950). This procedure unlike that described in "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., p. 352, does not require the use of anhydrous hydrazine and absolute ethanol.

[24] D. E. Pearson, K. N. Carter and C. M. Greer, *ibid.*, **75**, 5905 (1953).

[25] G. M. Badger, R. T. Howard and A. Simons, *J. Chem. Soc.*, 2849 (1952).

to observe that *o*-nitrophenyl mesityl ketone (III), a compound more sterically hindered than I, reacted with hydrazine under relatively mild conditions to give excellent yields of a white solid (IV). The analytical results indicated that IV was not the expected hydrazone, and since the material resisted acetylation the possibility of an amino compound was also discarded. Oxidation of IV with chromic acid gave an acid (V) of neutralization equivalent of 106. The latter information and analysis agreed with the assumption that V has the structure of 2-(3′-indazolyl)-benzene-1,3,5-tricarboxylic acid. In order to prove the presence of the indazolyl nucleus in IV the material was degraded to the known indazole-3-carboxylic acid. This was done by nitration of IV, reduction of the resulting nitro compound by means of tin and hydrochloric acid, and finally by oxidation of the amino compound with authentic indazole-3-carboxylic acid prepared from isatin,[26] and its ultraviolet spectrum agreed with the spectra of 3-substituted indazoles.[27] The formation of IV from III and hydrazine involves a displacement of the nitro group followed by a cyclization reaction at the carbonyl group, or *vice versa*, or a simultaneous reaction of hydrazine at both reactive centers of III. The formation of IV and the proof of its structure are summarized as



Considering the remarkable difference in the behavior of I and III toward hydrazine, and keeping in mind the refusal of I to react with hydrazine and 2,4-dinitrophenylhydrazine as well as the fact that phenyl mesityl ketone is even less reactive[5] toward hydrazoic acid than I, it is suggested that the reaction of III with hydrazine is initiated at the nitro group. While replacement reactions of nitro groups are well known,[28,29] there is no reason *a priori* why I and III should not enter into such reactions with equal ease. Since this is not the case it is obvious that the nitro group in III is more labile because of special circumstances related to the presence of methyl groups on the neighboring benzene ring.

It is well known[30] that the interference between *ortho* hydrogen atoms in benzophenone does not permit both phenyl groups to be coplanar with the carbonyl function at the same time. In a substituted benzophenone such as I we recognize three possible rotational conformations (I-A,B,C in Fig. 1). Conformation I-A is most probable since it permits maximum conjugation between the carbonyl function and the more electron-donating of the two aryl groups. Conformation I-B is unfavorable because of the repulsion between oxygen atoms, and conformation I-C is unfavorable because of interference between the nitro group and the neighboring phenyl ring. Examination of I-A reveals that while the carbonyl group is sterically hindered, the nitro group is not subject to steric compression.[29] Replacement of phenyl by mesityl results in analogous conformations of III, but we note that the conformation which corresponds to that of I-A is also unfavorable since the *ortho* methyl groups interfere with the nitrophenyl group. Thus it results that the most probable conformation of III is one in which *neither* aryl group is coplanar with the carbonyl function. This conformation still does not explain the susceptibility of the nitro group in III to replacement reactions, and thus it is suggested that a hydrogen bond between the spatially near nitro and methyl groups may be responsible for the difference in the chemical properties of I and III. Such interaction is similar to that suggested by Koch in *o*-nitrotoluene[31] and it would be expected to destroy in part the aromatic character of the nitro group by causing it to rotate from the coplanar arrangement with respect to the benzene ring. Hydrogen bond formation involving nitro groups is known[32] to facilitate reduction of the latter, and similarly loss of aromatic character of the nitro group in III should facilitate nucleophilic substitution by hydrazine. In view of the facile reaction of III with hydrazine there was also carried out a reaction with 2,4-dinitrophenylhydrazine and, unlike I, the nitro mesityl ketone did react.[33]

In view of the postulated conformational differences between I and III it is of interest to examine the ultraviolet spectra of these and related compounds to determine if the spectra corroborate the suggested conformations.

The benzoyl chromophore has a characteristic intense absorption band at approximately 250 mμ (ε 10,000 - 20,000)[34] encountered in the spectra of benzaldehyde, acetophenone and benzophenone. The spectrum of benzophenone also possesses an intense band in the 200-210 mμ region attributed to the absorption of the phenyl group which cannot be coplanar with the remaining benzoyl chromophore.[30]

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(26) P. Schad, *Ber.*, **26**, 216 (1893).

(27) V. Rousseau and H. G. Lindwall, This Journal, **72**, 3047 (1950).

(28) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 284 (1951).

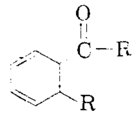
(29) M. S. Newman, ed., "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 186.

(30) R. N. Jones, This Journal, **67**, 2127 (1945).

(31) H. P. Koch, *J. Chem. Soc.*, 387 (1949).

(32) M. J. Astle, *et al.*, This Journal, **65**, 35, 2395, 2399 (1943).

(33) The structure of the reaction product is still uncertain. Its analytical results (45.6% C, 4.1% H, 22.7% N) correspond closely to the composition $C_{19}H_{14}O_9N_8$ (45.7% C, 2.83% H, 22.5% N). A substance of that composition could arise by nucleophilic displacement of the nitro group by 2,4-dinitrophenylhydrazine and an acid-catalyzed cleavage of the mesityl group with simultaneous formation of a 2,4-dinitrophenylhydrazide of structure (a)



(a) R = 2,4-$(O_2N)_2C_6H_3NHNH$–

(34) L. Doub and J. M. Vandenbelt, This Journal, **69**, 2714 (1947).

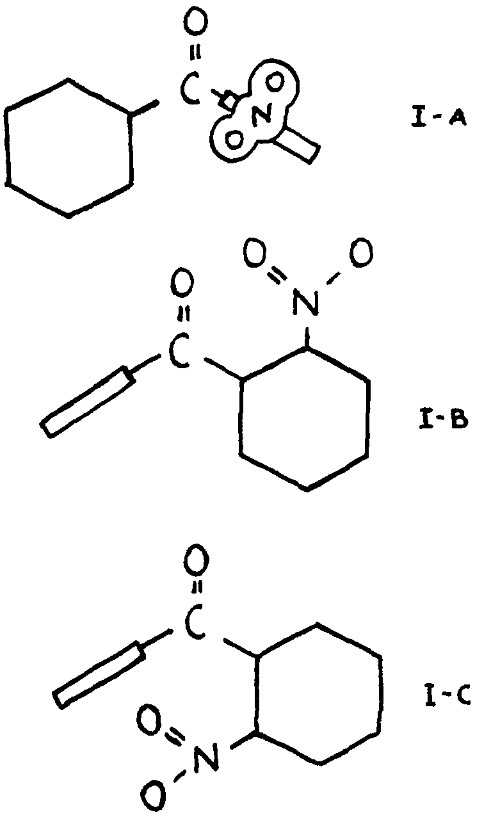


Fig. 1.—Conformations of *o*-nitrobenzophenone.

The absorption of the mesitoyl chromophore is apparent in the spectrum of mesitaldehyde,[35] but it is absent in 2,4,6-trimethylacetophenone[36,37] (and 2,3,5,6-tetramethylacetophenone[38] or 2,3,4,5,6-pentamethylacetophenone[39]) since the mesityl group cannot be coplanar with the carbonyl group. The intense but hypsochromically displaced maxima[37] of mesityl phenyl and dimesityl ketones indicate that in both compounds the predominant chromophore is the mesitoyl group and that the latter is not quite coplanar because of the repulsions between the methyl groups and the adjoining aromatic ring.[40] The *o*-nitrobenzoyl chromophore produces a medium strong band at 252-256 mμ as shown by the spectra[41] of *o*-nitrobenzaldehyde and *o*-nitroacetophenone.

With the above information in mind we can examine the ultraviolet spectra of I and III (Fig. 2). The intense maximum of I can be attributed to the contributions of the benzoyl and nitrophenyl chromophores and is in excellent agreement with the suggested conformation I-A. The spectrum of III reveals the absence of the coplanar or slightly twisted mesitoyl group absorption, and the rapidly rising absorption as one approaches lower wave lengths indicates the presence of isolated mesityl chromophore similar to that noticed in the spectrum of sterically hindered acetophenones. The greater intensity of the absorption at lower wave lengths in the case of III suggests that the nitroaryl group also contributes to the absorption although the shoulder at 252 mμ is probably due to small contributions made by the *o*-nitrobenzoyl chromophore more coplanar than in I-A because of the above-mentioned hydrogen bond interaction. Thus it is felt that the spectra of I and III support the suggested conformational differences deduced from the chemical behavior of these two ketones.

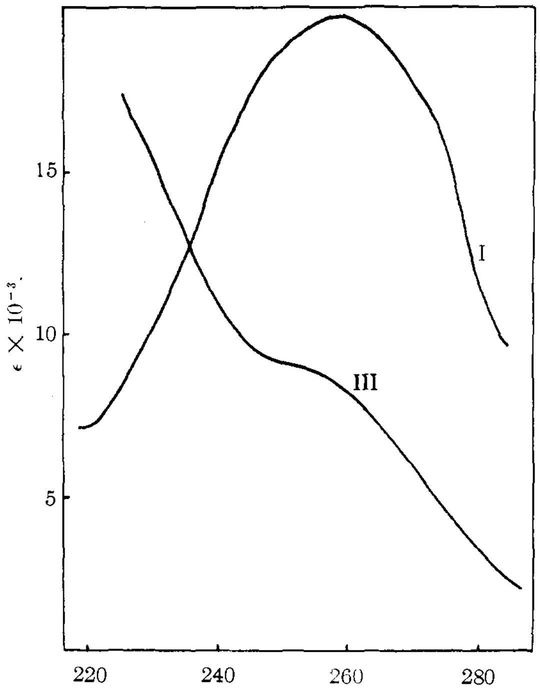


Fig. 2.—Ultraviolet spectra of I and III.

Experimental[42]

***o*-Nitrobenzophenone.**—A mixture of 8 g. of *o*-nitrobenzoic acid and 16 g. of trifluoroacetic anhydride was stirred until homogeneous and then the solution was saturated with boron trifluoride. The resulting solution was added to 5.8 g. of dry benzene and after 2–3 minutes the mixture was poured on crushed ice. The mixture was filtered and the solid was extracted with dil. alkali. Acidification of the alkaline extract gave unreacted *o*-nitrobenzoic acid. The original filtrate upon standing overnight deposited a tan solid which after several crystallizations from ethanol gave 1.4 g. (12%) of *o*-nitrobenzophenone, m.p. 103–104°, identical with product prepared by described procedures.[3–5]

Addition of the mixture of *o*-nitrobenzoic acid, trifluoroacetic anhydride and boron trifluoride, prepared as described above, to a large excess of dry benzene over a period of 1 hour, and allowing the resulting solution to stand in the cold for 15 hours gave 1–2 g. of solid, m.p. 181°. Crystallization of this solid from benzene gave a product of constant m.p. 187–188° (II).

Anal. Calcd. for $C_{13}H_9O_2N$: C, 73.9; H, 4.2; N, 6.6. Found: C, 73.6; H, 4.0; N, 6.6.

Reduction of II.—To a solution of 2 g. of II in 40 ml. of acetic acid there was added 1 g. of iron filings and the mixture was heated on a water-bath for 1 hour. An additional amount of 2 g. of iron filings was then added and the mixture

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[35] N. J. Leonard and E. R. Blout, This Journal, **72**, 484 (1950). Because of the electron-releasing effect of the methyl groups there is a 15 mμ bathochromic displacement of the 250 mμ band.

[36] L. H. Schwartzman and B. B. Corson, *ibid.*, **76**, 782 (1954).

[37] M. T. O'Shaughnessy and W. H. Rodebush, *ibid.*, **62**, 2906 (1940).

[38] W. F. Forbes and W. A. Mueller, *Can. J. Chem.*, **35**, 488 (1957).

[39] W. F. Forbes and W. A. Mueller, This Journal, **79**, 6495 (1957).

[40] Reference 29, p. 487.

[41] E. A. Walker and J. R. Young, *J. Chem. Soc.*, 2041 (1957).

[42] All melting points are uncorrected. Microanalyses by Drs. Strauss and Weiler, Oxford, England, and Elek Micro Analytical Laboratories, Los Angeles, Calif.

was heated for 2 hours and then diluted with 20 cc. of water. The mixture was filtered to remove inorganic matter and the filtrate was diluted to precipitate approximately 1 g. of *o*-aminobenzophenone, m.p. 105–106°, identical with an authentic sample.[43]

Tanasescu Reaction[10] of II.—To a solution of 2 g. of II in cold sulfuric acid there was added 5 g. of sodium nitrite with stirring and external cooling. Noticeable heat evolution occurred and the mixture acquired a deep blue color. The reaction mixture was kept below 40° for 30 minutes and then was poured on crushed ice. The tan precipitate was filtered and crystallized from benzene to give crystals, m.p. 350–352°, which did not depress the m.p. of authentic acridone.

***o*-Nitrophenyl Mesityl Ketone (III).**—A mixture of 8 g. of *o*-nitrobenzoic acid and 16 g. of trifluoroacetic anhydride was stirred until homogeneous and then boron trifluoride was introduced over 30 minutes. The resulting orange colored solution was added dropwise to 9 g. of cold mesitylene and after two hours the mixture was poured on crushed ice. The mixture was filtered and the solid was dissolved in benzene. The benzene solution was extracted with dilute alkali, dried and concentrated to give 10 g. of desired ketone which was crystallized from ethanol to give m.p. 145–146°.

Anal. Calcd. for $C_{16}H_{15}O_3N$: C, 71.5; H, 5.6; N, 5.2. Found: C, 71.4; H, 5.5; N, 5.1.

The aqueous extract upon acidification gave 1.5 g. of unreacted *o*-nitrobenzoic acid.

***o*-Nitrophenyl *p*-Anisyl Ketone.**—The mixture of *o*-nitrobenzoic acid, trifluoroacetic anhydride and boron trifluoride was prepared as described above and mixed with 8.1 g. of cold anisole. The reaction mixture darkened and was immediately poured on crushed ice. The dark precipitate was crystallized from ethanol to give 3 g. of the desired ketone, m.p. 105°, identical with material prepared by previously described procedure.[3]

2-, 3- and 4-Benzoylpyridine Hydrazone.—A mixture of 25 g. of the respective benzoylpyridine, 8.2 g. of anhydrous hydrazine (or its equivalent of 85% hydrazine hydrate) and 150 cc. of 95% ethanol was refluxed over 20 g. of calcium oxide in a Soxhlet apparatus over a period of 24 hours. The reaction mixture was filtered while hot in order to remove traces of calcium oxide and the filtrate was concentrated and cooled in a Dry Ice chest. The hydrazones precipitated in excellent yields (86–91%) and were crystallized from 95% ethanol to constant m.p.: *o*-isomer, 105–106°; *m*-isomer, 130–131°; *p*-isomer, 125–126°.

Anal. Calcd. for $C_{12}H_{11}N_3$: C, 73.02; H, 5.62; N, 21.30. Found (*o*-isomer): C, 73.23; H, 5.77; N, 21.70. Found (*m*-isomer):- C, 73.16; H, 5.60; N, 21.52. Found (*p*-isomer): C, 72.77; H, 5.64; N, 21.60.

***m*- and *p*-Nitrobenzophenone Hydrazone.**—Using the above-mentioned procedure the desired hydrazones were obtained in lower yields (30–60%) because of formation of by-products such as amino ketones and azines, and because of difficulty in crystallizing the reaction products. When the oily product refused to crystallize it was treated with 2 cc. of cold sulfuric acid, the precipitate of hydrazine sulfate was removed by filtration, and the filtrate was poured on crushed ice. Crystallization of the crude products from 95% ethanol gave the desired hydrazones, m.p. 82–83° and 67–69° for the *p*- and *m*-isomer, respectively.

Anal. Calcd. for $C_{13}H_{11}N_3O_2$: C, 64.73; H, 4.60. Found (*p*-isomer): C, 64.55; H, 4.50. Found (*m*-isomer): C, 64.62; H, 4.61.

2-, 3- and 4-Pyridinecarboxaldehyde Hydrazone.—The respective aldehyde, 21.4 g., was added dropwise to 20 g. of 85% hydrazine hydrate with efficient cooling. The reaction mixture was concentrated on a steam-bath using a water aspirator and the residuous, viscous, red liquid was fractionated at 1-2 mm. The fractions b.p. 105–107°, 103-105° and 130–134° for the 2-, 3- and 4-isomers, respectively, were distilled at 10^{-7} mm. and stored in sealed glass vials.

Anal. Calcd. for $C_6H_7N_3$: C, 59.4; H, 5.7; N, 34.6. Found (2-isomer): C, 59.4; H, 5.9; N, 35.0. Found (3-isomer): C, 59.2; H, 5.8; N, 35.0. Found (4-isomer): C, 59.6; H, 5.5; N, 34.3.

2-, 3- and 4-Pyridinecarboxaldehyde Azines.—Anhydrous hydrazine, 0.5 g., was added to 2.2 g. of the respective aldehyde and the reaction mixture was allowed to stand until it reached room temperature. The precipitated solid was filtered and crystallized from 95% ethanol to give m.p. 148–149°, 146–147° and 177–178°[44] for the 2-, 3- and 4-isomer, respectively.

Anal. Calcd. for $C_{12}H_{10}N_4$: C, 67.8; H, 4.7; N, 26.3. Found (2-isomer): C, 67.9; H, 4.7; N, 26.0. Found (3-isomer): C, 67.8; H, 4.7; N, 26.4.

Preparation of IV.—A mixture of 4.0 g. of III, 0.9 g. of anhydrous hydrazine and 100 cc. of 95% ethanol was refluxed over 20 g. of calcium oxide in a Soxhlet apparatus over a period of 20 hours. The reaction mixture was filtered while hot, the filtrate was concentrated and upon cooling gave some unreacted ketone. Further concentration of the filtrate yielded 2 g. of white solid which was crystallized from 95% ethanol to constant m.p. 162–163°.

Anal. Calcd. for $C_{16}H_{16}N_2$: C, 81.3; H, 6.7; N, 11.8. Found: C, 81.6; H, 6.8; N, 11.5.

Oxidation of IV.—A mixture of 2 g. of IV and an excess of chromic acid was refluxed in 100 cc. of acetic acid for six hours. The reaction mixture was poured on ice and the precipitate, 1.5 g., was filtered and crystallized from ethanol, m.p. 236–238° dec.

Anal. Calcd. for $C_{16}H_{10}O_6N_2$: C, 58.8; H, 3.1; N, 8.5; neut. equiv., 108.7. Found: C, 58.6; H, 3.2; N, 8.4; neut. equiv., 106.1.

Degradation of IV to Indazole-3-carboxylic Acid.—Eight ml. of concd. nitric acid was added dropwise to a solution of 2 g. of IV in 8 ml. of concd. sulfuric acid and the temperature was maintained at 40° for 15 minutes after completion of the addition. The reaction mixture was poured on ice and a light colored precipitate, m.p. 213°, was isolated. The nitration product, 1.1 g., and 3 g. of granulated tin was mixed with 20 cc. of dil. hydrochloric acid and 5 ml. of ethanol. The reaction mixture was refluxed for 30 minutes, cooled and treated with 40% sodium hydroxide. The mixture was filtered and the filtrate was extracted with ether. The ethereal solution was dried and concentrated to give a white solid, 0.5 g., which was dissolved in acetic acid and refluxed in the presence of an excess of chromic acid. The oxidation mixture was poured on ice and the resulting solid was crystallized from ethanol to constant m.p. 254–256°. This solid did not depress the m.p. of authentic indazole-3-carboxylic acid.[26]

Reaction of III with 2,4-Dinitrophenylhydrazine.—A hot, alcoholic solution of the ketone was added to 2,4-dinitrophenylhydrazine dissolved in ethanol and concd. sulfuric acid. After cooling, the solution was filtered to remove unreacted ketone, and the filtrate was concentrated to give an orange solid which was crystallized from ethanol to constant m.p. 125–126°.

Anal. Found: C, 45.6; H, 4.1; N, 22.7.

2,4-Dinitrophenylhydrazide of *o*-Nitrobenzoic Acid.—A solution of freshly prepared *o*-nitrobenzoyl chloride in toluene was added to an alcoholic solution of 2,4-dinitrophenylhydrazine. The resulting yellow solid was filtered and crystallized from 95% ethanol to constant m.p. 239–240°.

Anal. Calcd. for $C_{13}H_9O_7N_5$: C, 44.9; H, 2.6; N, 20.17. Found: C, 44.7; H, 2.9; N, 20.30.

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