

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BOSTON COLLEGE]

Facile Hydrolysis of the Trifluoromethyl Group in the Presence of Base. Some Trifluoromethylated Indoles

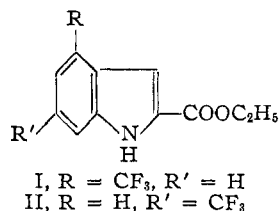
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Fischer ring closure of ethyl pyruvate *m*-trifluoromethylphenylhydrazone by zinc chloride in glacial acetic acid yielded a mixture of ethyl 4-trifluoromethyl-2-indolecarboxylate and ethyl 6-trifluoromethyl-2-indolecarboxylate. The unexpected conversion of the trifluoromethyl group of both isomers to a carboxyl function on treatment with aqueous sodium hydroxide afforded known indolecarboxylic acids thereby establishing the structure of each isomer. An interpretation based on resonance is offered of this surprising susceptibility of the trifluoromethyl group to hydrolytic attack in the presence of base. Examination of the infrared spectra of a number of esters of indole has revealed that in addition to the normal N-H stretching band there is present a second band at somewhat lower frequency which appears to be characteristic of this group of compounds. This band is attributed to intermolecular hydrogen bonding.

The refractory nature of the trifluoromethyl group has been known for a long time.² Normally, a CF₃- group that is located on an aromatic or heterocyclic nucleus can be hydrolyzed to a carboxyl function only by the action of strong mineral acids at elevated temperatures.³ However, in 1947, Jones⁴ discovered that a trifluoromethyl group which is situated *ortho* or *para* to a hydroxyl substituent is extremely sensitive to hydrolytic attack by aqueous alkali. This observation has been confirmed by other investigators.⁵ Roberts and co-workers⁶ have ascribed the facile loss of fluoride ion from *o*- and *p*-trifluoromethylphenol, but not *m*-trifluoromethylphenol, in aqueous base⁴ to an interaction of the two substituents which was expressed by "no-bond" resonance.

Recently, we had occasion to prepare ethyl 4-trifluoromethyl-2-indolecarboxylate (I) and ethyl 6-trifluoromethyl-2-indolecarboxylate (II) for use as intermediates in the synthesis of compounds with potential activity as plant hormones. In the



course of attempting to determine the saponification equivalent of these isomeric esters it was found that substantially more than one equivalent of base was consumed. Further investigation revealed that the trifluoromethyl group had been hydrolyzed extensively to a carboxyl function. The hydrolysis of the CF₃- group of I and II under these circumstances was completely surprising

(1) Abstracted in part from the M.S. theses of Stephen A. Leone, William F. Sullivan and O. Francis Bennett.

(2) F. Swarts, *Bull. sci. acad. roy. Belg.*, **6**, 389 (1920); **8**, 343 (1922).

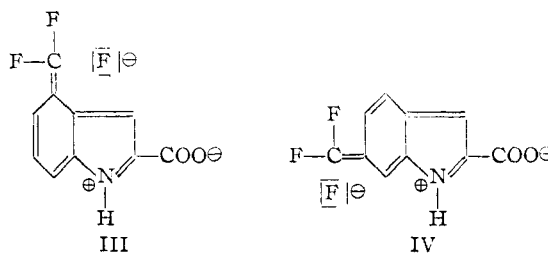
(3) (a) H. Gilman and D. Blume, *THIS JOURNAL*, **65**, 2467 (1943); (b) G. M. Le Fave, *ibid.*, **71**, 4148 (1949); (c) P. M. Maginnity and C. A. Gaulin, *ibid.*, **73**, 3579 (1951); (d) M. Hauptschein, E. A. Nodiff and A. J. Saggiomo, *ibid.*, **76**, 1051 (1954).

(4) R. G. Jones, *ibid.*, **69**, 2346 (1947).

(5) R. Belcher, M. Stacey, A. Sykes and J. C. Tatlow, *J. Chem. Soc.*, 3846 (1954). The basic hydrolysis and alcoholysis of trifluoromethyl groups in acyclic compounds are reviewed by M. W. Buxton, M. Stacey and J. C. Tatlow, *ibid.*, 366 (1954). See also R. Mechoulam, S. Cohen and A. Kaluszyn, *J. Org. Chem.*, **21**, 801 (1956).

(6) J. D. Roberts, R. L. Webb and E. A. McElhill, *THIS JOURNAL*, **72**, 408 (1950).

since these substituents occupy positions in the phenylene moiety which are *meta* to the electron-donating heteroatom. Indeed, treatment of *m*-aminobenzotrifluoride with potassium hydroxide in aqueous methanol under considerably more vigorous conditions afforded no evidence of the formation of *m*-aminobenzoic acid; the starting amine was recovered in 90% yield. On the other hand, benzotrifluorides which carry amino groups on the *o*- and *p*-positions are reported to lose fluoride ion under relatively mild conditions.^{3a,4} On the basis of these observations, it is reasonable to conclude that the pyrrole ring of I and II permits an electronic interaction involving the trifluoromethyl group and the nitrogen atom, a situation which is impossible in *m*-aminobenzotrifluoride. This interaction would account for the loosening of the C-F bonds and may be represented by resonance structures III and IV.



Thus, resonance structures III and IV indicate that CF₃- groups at the 4- and 6-positions of an indole nucleus are activated by the nitrogen atom just as are the CF₃- groups of *o*- and *p*-aminobenzotrifluoride.^{6,7}

The preparation of the isomeric ethyl 4- and 6-trifluoromethyl-2-indolecarboxylates (I and II) followed, in general, well-known procedures. The diazonium chloride from *m*-aminobenzotrifluoride was reduced by stannous chloride in concentrated hydrochloric acid to *m*-trifluoromethylphenylhydrazine (V). Reaction of V with pyruvic acid afforded pyruvic acid *m*-trifluoromethylphenylhydrazone (VI), which was smoothly esterified by ethanolic hydrogen chloride to ethyl pyruvate *m*-trifluoromethylphenylhydrazone (VII). The overall yield of VII, based on the starting amine, was 80%.

We were unable to cyclize VII to I and II satis-

(7) Alternatively, I and II may be considered as cyclic vinylogs derived from *o*- and *p*-aminobenzotrifluoride, respectively.

factorily by employing the usual procedures; the yields of indoles never exceeded 3%.⁸ Eventually, it was found that treatment of the hydrazone ester with very large amounts of zinc chloride⁹ in glacial acetic acid at reflux temperature effected the desired ring closure in satisfactory yield (40–50% of mixture of crude indole esters).¹⁰ The mixture of I (preponderant, low-melting isomer) and II was resolved by fractional crystallization from aqueous ethanol. Saponification of the indole esters I and II to the corresponding acids, 4-trifluoromethyl-2-indolecarboxylic acid (VIII) and 6-trifluoromethyl-2-indolecarboxylic acid (IX), was accomplished in over 60% yield by heating the esters at just below the reflux temperature with aqueous methanolic potassium hydroxide until solution was effected. Partial hydrolysis of the trifluoromethyl groups occurred when the reaction mixture was boiled for as little as five minutes. Heating of either the indole esters I and II or the derived acids VII and IX with 10 *N* sodium hydroxide at 80–90° for 4 hr. gave on acidification the corresponding diacids 2,4-indolecarboxylic acid (X) and 2,6-indolecarboxylic acid (XI). Reaction of X and XI with either diazoethane or ethanolic hydrogen chloride afforded the respective diethyl esters, diethyl 2,4-indolecarboxylate (XII) and diethyl 2,6-indolecarboxylate (XIII). XII and XIII were found to be identical with authentic¹¹ specimens by comparison of melting points and infrared spectra, thereby establishing the structures of I and II.

Our efforts to effect a satisfactory decarboxylation of VIII to 4-trifluoromethylindole were unsuccessful. When VIII or its silver or ammonium salt was pyrolyzed in the presence or absence of solvents only tars and starting compound were isolated. Heating of VIII in the usual high-boiling basic solvents with or without copper powder present likewise failed to yield isolable amounts of the desired product, although a positive pine-splinter test¹² was obtained in several instances. No at-

tempt was made to decarboxylate 6-trifluoromethyl-2-indolecarboxylic acid (IX) since only small amounts of this acid were available.

The infrared absorption spectra of the substituted ethyl 2-indolecarboxylates described in this paper proved interesting. All of the indole esters in carbon tetrachloride (non-bonding solvent) showed two prominent bands in the region of the N–H stretching vibrations, one in the range 3460–3430 cm^{-1} attributable to the NH group of the indole nucleus,¹³ and the other in the 3350–3300 cm^{-1} region. The low-frequency band was broader and considerably stronger in concentrated solution than the band at higher frequency. Dilution of the solution caused the low-frequency band to become markedly weaker than the high-frequency band. Solutions of the indole esters in chloroform (bonding solvent) exhibited the same two bands, but the low-frequency band was always the weaker of the two and practically disappeared on dilution. These observations indicate that the low-frequency band at 3350–3300 cm^{-1} is due to hydrogen bonding. Since this band might arise from hydrogen-bonded cyclic dimers (in which case the rings would contain ten members), it was decided to examine other esters of indole which might be expected to be less prone to yield cyclic dimers. Accordingly, methyl 4-chloro-2-indolecarboxylate,¹⁴ methyl 4-indolecarboxylate,¹⁴ dimethyl 2,3-indolecarboxylate¹⁵ and ethyl 3-indoleacetate¹⁶ were prepared and their infrared absorption spectra determined in solutions of carbon tetrachloride and chloroform. All of these compounds exhibited the same type of spectrum in the NH stretching region as described above in the case of the esters of the 2-indolecarboxylic acids. This observation indicates that the low-frequency band, which appears to be characteristic of esters of indole, may actually be due to intermolecular (chain-like) hydrogen bonding involving the hydrogen of the NH groups and the oxygen of the carbonyl groups. However, hydrogen-bonded cyclic dimers in the case of the esters of the 2-indolecarboxylic acids are still not precluded since the available evidence is inconclusive. The spectra of the acids corresponding to the esters described in this paper could not be examined in solution but were measured in potassium bromide. They showed only one band in the NH stretching region. In potassium bromide the spectra of the esters showed two bands in this region, but their frequencies were somewhat lower than those obtained with the solutions.

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Experimental¹⁷

m-Trifluoromethylphenylhydrazine (V).—To 52 ml. (65.0 g., 0.40 mole) of freshly redistilled *m*-aminobenzotri-

Taylor, *J. Chem. Soc.*, 3399 (1954), and H. Plieninger, *Ber.*, **88**, 370 (1955).

(13) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 214–217.

(14) F. C. Uhle, *This Journal*, **71**, 761 (1949).

(15) O. Diels and J. Reese, *Ann.*, **511**, 168 (1934).

(16) R. W. Jackson, *J. Biol. Chem.*, **88**, 659 (1930).

(17) Melting points are corrected and boiling points are uncorrected.

(8) The ring closure was attempted with ethanolic hydrogen chloride, boron trifluoride, polyphosphoric acid, zinc chloride in dimethylformamide, zinc chloride in *cymene*, concentrated sulfuric acid, trifluoroacetic acid and by fusion with zinc chloride.

(9) Contrary to reports that only catalytic amounts of zinc chloride are necessary for the Fischer indole synthesis; cf. W. C. Sumpter and F. M. Miller, "Heterocyclic Compounds with Indole and Carbazole Systems," Interscience Publishers, Inc., New York, N. Y., 1954, p. 4.

(10) In view of the large number of phenylhydrazones of ethyl pyruvate which have been successfully transformed to derivatives of ethyl indolecarboxylate (cf., for example, W. Robson, *J. Biol. Chem.*, **62**, 495 (1924); V. Prelog and Z. Vejdělek, *Helv. Chim. Acta*, **31**, 1178 (1948); R. B. Van Order and H. G. Lindwall, *Chem. Rev.*, **30**, 69 (1942)) by methods which failed when applied to VII, it may be inferred that the resistance shown by VII is due to the strongly meta-directing CF_3 group, which deactivates the benzene nucleus at precisely those positions where bond formation occurs. A similar resistance to Fischer ring closure was observed with ethyl pyruvate *m*-carbethoxyphenylhydrazone (*vide infra*).

(11) W. O. Kermack, *J. Chem. Soc.*, **125**, 2287 (1924); A. Roder, *Ann.*, **236**, 164 (1886).

(12) The positive pine-splinter test indicates that decarboxylation has occurred to some extent. All the indoles described in this paper carry a substituent on the 2-position; they gave negative pine-splinter tests; cf. T. W. J. Taylor and W. Baker in N. V. Sidgwick, "The Organic Chemistry of Nitrogen," Oxford University Press, London, 1942, p. 500. The extreme variation in the susceptibility to decarboxylation of substituted 2-indolecarboxylic acids has been pointed out by F. C. Uhle, C. G. Vernick and G. L. Schmir, *This Journal*, **77**, 3334 (1955). Compare J. A. Barltrop and D. A. H.

fluoride, cooled in a salt-ice-bath, was added slowly and with stirring 250 ml. of chilled, concentrated hydrochloric acid. When the temperature of the white, pasty hydrochloride had dropped to 0°, a precooled solution of 27.6 g. (0.40 mole) of sodium nitrite in 125 ml. of water was added from a separatory funnel whose tip was immersed beneath the surface of the suspension. The addition of the nitrite required 75 minutes and the temperature of the reaction mixture was not allowed to exceed 3°. To the stirred and cooled diazonium solution was added dropwise over a 3-hour period a chilled solution of 200.0 g. (0.89 mole) of stannous chloride dihydrate in 200 ml. of concentrated hydrochloric acid. The temperature of the reaction mixture was maintained at 0–5° during the addition. Upon completion of the addition the reaction mixture was stirred at 0° for an additional hour. The cream-colored solid was collected by filtration, pressed as dry as possible and then shaken, without delay, with 700 ml. of 25% sodium hydroxide. The yellow mixture, after standing overnight at room temperature, was extracted with three 300-ml. portions of benzene. The benzene extracts were combined, filtered and dried over pellets of potassium hydroxide (20–30 g.) overnight. The solvent was removed at diminished pressure and the residue distilled to yield 45.8 g. (65%) of V as a light yellow oil, b.p. 80–83° (9 mm.), d_{20}^{20} 1.348, n_D^{20} 1.5052; MR calcd. 38.2, MR found 38.4.

Anal. Calcd. for $C_7H_7N_2F_3$: N, 15.90. Found: N, 15.7.

Pyruvic Acid *m*-Trifluoromethylphenylhydrazone (VI).—To a solution of 36.2 g. (0.205 mole) of *m*-trifluoromethylphenylhydrazine in 325 ml. of 10% acetic acid was added dropwise with stirring a solution of 27.2 g. (21.5 ml., 0.31 mole) of redistilled pyruvic acid in 65 ml. of water. The suspension, after being kept in the cold for several hours, was filtered and the solid was washed with water. The crude hydrazone acid was purified by dissolving it in dilute potassium carbonate, treating the solution with charcoal, filtering and precipitating the hydrazone by addition of dilute hydrochloric acid. The yield of VI, sufficiently pure for use in preparing the corresponding ethyl ester, was 41.9 g. (83%), m.p. 181.8–183.6°, with vigorous frothing. The analytical sample was obtained as almost white, glistening crystals from 80% ethanol, m.p. 193–194°, with evolution of gas.

Anal. Calcd. for $C_{10}H_9O_2N_2F_3$: N, 11.38; neut. equiv., 146.2. Found: N, 11.26; neut. equiv., 245.8.

VI could be prepared more conveniently and in better yield by slowly adding 36.8 g. (0.42 mole) of pyruvic acid directly to the stirred benzene extract of V (reduced *in vacuo* to a volume of about 300 ml.). The product was worked up in the manner described above; yield 80 g. (83%, based on *m*-aminobenzotrifluoride).

Ethyl Pyruvate *m*-Trifluoromethylphenylhydrazone (VII).—A gently refluxing solution of pyruvic acid *m*-trifluoromethylphenylhydrazone (80.0 g., 0.325 mole) in 550 ml. of commercial absolute ethanol was treated under anhydrous conditions with a stream of hydrogen chloride (2–3 bubbles of gas per second) for 3 hr. The light yellow solution was cooled to room temperature and was then poured slowly onto cracked ice with vigorous stirring. Refrigeration of the mixture overnight yielded 88 g. (98%) of VII as white needles, after being washed on the funnel successively with water, dilute potassium carbonate and water. The air-dried product had m.p. 82–86°. The ester (85 g.) was recrystallized from 250 ml. of 60% ethanol in 10-g. portions (Norite); the mother liquor obtained from the recrystallization of the first 10-g. batch was saved and was used in the subsequent recrystallizations. In this way, 77 g. of the ester was obtained, m.p. 97–100°, of suitable purity for use in the ring closure reaction. The analytical sample, obtained from ethanol as silky, felted needles, melted at 108.6–109.6°.

Anal. Calcd. for $C_{12}H_{13}O_2N_2F_3$: N, 10.21. Found: N, 10.10.

Treatment of VII with boiling aqueous sodium hydroxide, followed by acidification, regenerated the acid VI in 90% yield; the trifluoromethyl group remained intact.

Infrared measurements were made using a Baird double beam recording spectrophotometer equipped with a sodium chloride prism. Elemental analyses were performed by Dr. Carol K. Fitz, Needham Heights, Massachusetts, and by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y.

Fischer Ring Closure of Ethyl Pyruvate *m*-Trifluoromethylphenylhydrazone (VII) with Zinc Chloride in Glacial Acetic Acid. A. Ethyl 6-Trifluoromethyl-2-indolecarboxylate (II).—Ethyl pyruvate *m*-trifluoromethylphenylhydrazone (11.0 g., 0.040 mole) was intimately mixed with 115 g. (0.85 mole) of freshly fused, finely powdered zinc chloride. This mixture was stirred at room temperature for 5 minutes with 135 ml. of glacial acetic acid to which 5 ml. of acetic anhydride had been added. During the course of stirring, all of the ester and most of the zinc chloride dissolved. The stirred mixture was then heated under reflux for 20 minutes and the resulting light red solution was poured, after being cooled to room temperature, onto a mixture of chopped ice and water. Refrigeration of the mixture overnight yielded 8.0 g. of yellow powder, which was dissolved in 50 ml. of hot 95% ethanol. The warm solution was treated with charcoal, filtered, the filtrate diluted with 12 ml. of water and the solution was refrigerated for 1 hr. The light yellow precipitate was collected and air-dried, 830 mg., m.p. 138–150° (uncor.). The solid was dissolved in the minimum amount of ethanol at room temperature, the solution treated with charcoal, and the filtrate was diluted with water until the cloudiness just disappeared on heating. Cooling of the solution in the refrigerator for several hours gave II as white needles, 600 mg. (5.8%), m.p. 163–164°.

Anal. Calcd. for $C_{12}H_{10}O_2NF_3$: C, 56.03; H, 3.92; N, 5.44. Found: C, 56.1; H, 4.0; N, 5.4.

B. Ethyl 4-Trifluoromethyl-2-indolecarboxylate (I).—Refrigeration overnight of the aqueous ethanolic mother liquor from which crude II, m.p. 138–150° (uncor.), was obtained, gave 3.0 g. of light yellow crystals, m.p. 100–120°. The crystals were dissolved in the minimum amount of cold 95% ethanol, the solution was treated with charcoal and the filtrate diluted with water until the cloudiness just disappeared on heating. The solution, after being refrigerated 1 to 2 hr., yielded long, white needles of I, 1.0 g. (9.7%), m.p. 148–149°.

Anal. Calcd. for $C_{12}H_{10}O_2NF_3$: C, 56.03; H, 3.92; N, 5.44. Found: C, 55.9; H, 4.1; N, 5.55.

Further cooling of the mother liquor from which pure I had separated yielded 1.8 g. (17.5%) of small white needles, m.p. 120–121°, which could not be resolved by additional recrystallizations. This sharply melting material was shown by means of its infrared spectrum and elemental analyses to be a mixture of I and II. In addition, a mixture prepared from equal parts of I and II melted at 120.6–121.8°.

6-Trifluoromethyl-2-indolecarboxylic Acid (IX).—Ethyl 6-trifluoromethyl-2-indolecarboxylate (400 mg., 1.56 mmoles) was warmed at just below the reflux temperature with a mixture prepared from 5 ml. of 1:1 aqueous methanol and 5 ml. of 10% aqueous potassium hydroxide. When complete solution was achieved (usually no longer than 5 minutes from the start of heating) 10 ml. of water was added and the solution was cooled and acidified with dilute hydrochloric acid. Cooling of the solution overnight in the refrigerator gave white needles which were recrystallized with the air of charcoal from dilute ethanol. The yields of IX, m.p. 165–165.8°, were over 60% in the several runs which were made. The analytical sample was obtained by sublimation, m.p. unchanged.

Anal. Calcd. for $C_{10}H_8O_2NF_3$: C, 52.29; H, 2.63. Found: C, 52.4; H, 2.7.

The starting ester II was obtained from the action of ethereal diazoethane on IX, m.p. 163–164°.

4-Trifluoromethyl-2-indolecarboxylic Acid (VIII).—Saponification of 200 mg. (0.78 mmole) of I by the procedure used above with the 6-isomer yielded 150 mg. (85%) of the acid, m.p. 219.4–220.4°.

Anal. Calcd. for $C_{10}H_8O_2NF_3$: C, 52.29; H, 2.63; F, 24.87. Found: C, 52.5; H, 2.7; F, 24.70.

Treatment of VIII with ethereal diazoethane or ethanolic hydrogen chloride, according to the usual procedures, regenerated the corresponding ethyl ester I, m.p. 148.6–149.4° (from aqueous ethanol), no depression on admixture.

Larger amounts of VIII could be obtained expeditiously, but at the expense of the 6-trifluoromethyl isomer, by directly saponifying the crude mixture obtained from the ring closure of VII. In this way, there was obtained from 13.4 g. of ethyl pyruvate *m*-trifluoromethylphenylhydrazone 2.46 g. (22%) of 4-trifluoromethyl-2-indolecarboxylic acid, m.p. 218–219°, on recrystallization from benzene.

2,6-Indoledicarboxylic Acid (XI).—Ethyl 6-trifluoromethyl-2-indolecarboxylate (100 mg., 0.39 mmole) or an equimolar amount of the corresponding acid IX was warmed in a polyethylene test-tube with 10 ml. of 10 *N* sodium hydroxide by means of an oil-bath at 80–90°. The light yellow solution was diluted with 20 ml. of water and acidified with dilute hydrochloric acid. Cooling of the mixture yielded a brown powder which, after recrystallization from glacial acetic acid, was recovered as tan crystals which remained unmelted at 330°. This observation is in accord with that reported by Kermack¹¹ for his preparation of the dicarboxylic acid.

The hydrolysis may be carried out by boiling the reactants in a glass vessel for 10 minutes, but considerable etching occurs and as a result the product is difficult to purify.

2,4-Indoledicarboxylic Acid (X).—The hydrolysis of I or its corresponding acid VIII to X was carried out by the same procedure used with the 6-trifluoromethyl isomers. X was obtained in yields as high as 94% as colorless crystals from glacial acetic acid, m.p. 299–300° with darkening at 283°; calcd. neut. equiv. 102.6, found 102.1.

Diethyl 2,6-Indoledicarboxylate (XIII).—Into a solution of 110 mg. (0.536 mmole) of 2,6-indoledicarboxylic acid in 10 ml. of absolute ethanol at 70° was bubbled hydrogen chloride (2 bubbles per second) for 1 hr. The reaction mixture was cooled and poured onto cracked ice. The flocculent precipitate was collected and washed on the funnel with dilute potassium carbonate and water. Crystallization of the air-dried product successively from benzene-petroleum ether and aqueous ethanol gave 90 mg. (65%) of XIII as long, felted needles, m.p. 131–132°, which was found to be identical by means of m.p. and mixed m.p., as well as by comparison of the infrared spectrum, to an authentic sample of the diester prepared by the procedure of Kermack.¹¹

Anal. Calcd. for C₁₄H₁₈O₄N: C, 64.35; H, 5.79. Found: C, 64.34; H, 5.90.

The esterification of XI to XIII was effected in almost quantitative yield when ethereal diazoethane was used.

Diethyl 2,4-Indoledicarboxylate (XII).—The conversion of 2,4-indoledicarboxylic acid to the corresponding diethyl ester XII was carried out with ethanolic hydrogen chloride and with ethereal diazoethane by the procedures described

above for the 2,6-isomer; white needles, m.p. 143.4–144.2°, from aqueous ethanol.

Anal. Calcd. for C₁₄H₁₈O₄N: C, 64.35; H, 5.79. Found: C, 64.1; H, 5.7.

This compound was identical in m.p. with (no depression on admixture) and had the same infrared spectrum as an authentic specimen prepared from ethyl pyruvate *m*-carbethoxyphenylhydrazone by a modification of the method of Roder.¹¹ The fusion of the hydrazone with zinc chloride following the Roder procedure gave 1% of XII. The yields of XII were raised to 8% when the Fischer ring closure reaction was carried out in zinc chloride-acetic acid by the procedure used above for the preparation of I and II.

Treatment of *m*-Aminobenzotrifluoride with Boiling Aqueous Methanolic Potassium Hydroxide.—*m*-Aminobenzotrifluoride, 3.0 g., b.p. 189–190°, *n*²⁰_D 1.4811, was heated under reflux for 10.5 hr. with 15 ml. of a solution prepared from 20 g. of potassium hydroxide, 80 ml. of methanol and 40 ml. of water. The reaction mixture was protected by a soda-lime tube during the period of reflux. The amber solution was then cooled, diluted with 10 ml. of water and extracted with three 50-ml. portions of ether. The combined ethereal extract was washed with 15 ml. of water, which was added to the aqueous phase. The aqueous extract was concentrated to a volume of 12 ml., acidified with 1:1 hydrochloric acid and extracted three times with 50-ml. portions of ether. Evaporation of the ether yielded 20 mg. of tan needles which were obtained as a colorless solid by sublimation at 80° and 0.1 mm. Lack of material prevented its being identified and, although the substance was acidic to moist litmus, its m.p. of 189–190° ruled out *m*-aminobenzoic acid. The m.p. of an authentic sample of *m*-aminobenzoic acid, determined simultaneously with that of the unknown product, was 174–175°.

Removal of the ether from the extraction of the reaction mixture followed by distillation of the residue gave 2.7 g. (90%) of *m*-aminobenzotrifluoride, b.p. 189–191°, *n*²⁰_D 1.4802.

Repetition of the experiment under the same conditions, but with the time of reflux reduced to 2 hr., resulted in a 90% recovery of the amine; none of the acidic solid was observed.

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Spectrophotometric Relationships between Furoxanes and Nitroso Compounds¹

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Furoxanes, *ψ*- and normal nitroso aromatic compounds gave closely related infrared absorption patterns, 2–25 μ . Absorption in the ultraviolet at 255–285 $m\mu$ for furoxanes, at 265–310 $m\mu$ (two bands) for normal aromatic nitroso compounds and at 350–410 $m\mu$ for *ψ*-dinitrosoaromatic compounds was observed.

Furoxanes, *ψ*-dinitrosoaromatic compounds and normal nitroso compounds are closely related in certain chemical and physical properties. Significant differences between furoxanes and *ψ*-dinitrosoaromatic compounds have been described.² Characteristic properties in the absorption of light for certain members of the individual series have been recorded previously, but apparently their similarities and differences in this respect have not been discussed.

Seven absorption regions in the infrared between 1800 and 800 cm^{-1} characteristic of furoxanes were

recently reported.³ These included 1625–1600 cm^{-1} for the C=N bond; 1475–1410 cm^{-1} (doublet) for the O-N→O group; 1360–1300 cm^{-1} for the N-O bond; 1190–1150, 1030–1000 and 890–840 cm^{-1} for the furoxane ring; and 950–900 cm^{-1} (usually a doublet) for diarylfuroxanes, their carbonyl derivatives and diarylfuroxanes. Bands characteristic of monomeric and dimeric aromatic nitroso compounds were found at *ca.* 1540–1500 (monomer) and 1500–1480 (dimer) cm^{-1} (C=C str. conjugated with the nitroso group), *ca.* 1380–1340 (monomer) and 1270–1260 (dimer) cm^{-1} (N=O str.), *ca.* 850–810 (monomer) and 855 (dimer) cm^{-1} (N=O bend).⁴ The data recorded

(1) Financial support of this work by the Office of Ordnance Research, U. S. Army, under Contract Nos. DA-01-009-ORD-331 and DA-01-009-ORD-428 is gratefully acknowledged.

(2) J. H. Boyer, R. F. Reinisch, M. J. Danzig, G. A. Stoner and P. Sahar, *THIS JOURNAL*, **77**, 5688 (1955).

(3) N. E. Boyer, G. M. Czerniak, H. S. Gutowsky and H. R. Snyder, *ibid.*, **77**, 4238 (1955).

(4) K. Nakamoto and R. E. Rundt, *ibid.*, **78**, 1113 (1956).