The cake was washed with diethyl ether and dried under vacuum at room temperature. The product (the cesium salt of perfluoropropionic acid) was a white crystalline solid: yield 175 g. This salt (174.5 g) was added slowly to 96% sulfuric acid (180 g) at 0–5°. The slurry was allowed to stand overnight at room temperature, separating into two layers. The upper layer (62 cc in volume, 93 g) was separated and distilled at 50° (112–113 mm) to yield 88.5 g (0.42 mole). It was identified by infrared spectrum[3] as pentafluoropropionic acid. The F^{19} resonance spectrum comprised a triplet at +7.27 ppm and a quartet at +46.14 ppm with relative areas of 3 and 2. The proton resonance showed only a singlet at +11.58 ppm. These spectra support the infrared characterization of the product as pentafluoropropionic acid. The same product was prepared, using potassium fluoride and acetonitrile in a steel bomb. The TFE and CO_2 were added cold and the bomb was heated to 150° with shaking for 10 hr. The excess KF was filtered off. The solvent was stripped off at 50° under reduced pressure, and the resulting cake was acidified cold (0–5°) with 96% sulfuric acid. The product was distilled off under reduced pressure and obtained in a yield of 75% of theory based on TFE charged.

B. The Condensation of Chlorotrifluoroethylene with Carbon Dioxide.—Cesium fluoride (15 g, 0.1 mole) was slurried in diethylene glycol dimethyl ether (diglyme) and TFE and CO_2 were added in the absence of air as in A but at a temperature of 50°. The completed charge was drowned in diethyl ether (500 g), chilled, and filtered. The cake, washed with ether and dried, weighed 19.5 g. Acidification of a small portion of this material with cold 96% sulfuric acid yielded a clear liquid identified by nmr spectrum as $CF_3CClFCOOH$. On the basis of previous observations, the two possible structures were I, $CF_3CClFCOOH$, and II, ClF_2CF_2COOH. The F^{19} resonance spectrum consisted of two multiplets, a doublet and a quartet with an area ratio of 3 to 1. This was sufficient to resolve the question in favor of structure I.

C. Preparation of Perfluoroisobutyric Acid by Condensation of Hexafluoropropene with Carbon Dioxide.—Although TFE was condensed with CO_2 at 100° to yield a stable salt, in the case of hexafluoropropene (HFP), it was necessary to drop the reaction temperature to 70° to avoid reversal of the reaction. Otherwise, the procedure was similar to that employed in the condensation of TFE with CO_2.

Cesium fluoride (90 g, 0.59 mole) was slurried in triethylene glycol dimethyl ether (triglyme) (180 g), and hexafluoropropene (118 g, 0.79 mole) and carbon dioxide (26 g, 0.59 mole) were added together at 70° and 20–25-psig pressure. A liquid fluorocarbon layer of 21 g (dimers and trimers of HFP) was separated off. The triglyme layer was filtered and drowned in benzene, and the cesium salt of perfluoroisobutyric acid (132 g) was separated and dried. Acidification yielded the free acid (72 g, 0.33 mole). The structure was confirmed by an infrared spectrum which matched an earlier result[3] and by nmr spectra. The F^{19} spectrum showed a doublet at +1.63 ppm and a septet at +107.8 ppm with relative areas of 6 and 1. The proton resonance showed a singlet at 11.76 ppm. These results were consistent with the assigned structure.

D. Attempted Condensation of Perfluoroisobutylene with Carbon Dioxide.—Perfluoroisobutylene (PFIB) added readily to cesium fluoride in dry diglyme at room temperature to form a complex soluble in the diglyme, presumably perfluoro-*t*-butylcesium. Acidification by addition of dry HCl to a portion of the charge yielded a small quantity of a product which was removed under vacuum, trapped at liquid nitrogen temperature, and characterized by nmr spectra. The F^{19} resonance spectrum was a doublet at −11.7 ppm and the proton resonance spectrum was a group of ten peaks at +3.13 ppm, indicating that the product was 2H-hexafluoro-2-(trifluoromethyl)propane, $(CF_3)_2CH$.

Carbon dioxide was added to the unacidified remainder of the charge at −25 to −30° in approximately stoichiometric quantity. The charge was then acidified with sulfuric acid (85%). A heavy precipitate was formed and it was necessary to thin the charge by addition of CCl_2FCClF_2. The charge was filtered and the cake (cesium sulfate) was washed with CCl_2FCClF_2. The filtrate was then washed repeatedly with 25% sulfuric acid to remove as much of the diglyme as possible. The major portion of the CCl_2FCClF_2 was distilled off quickly and the balance of the charge was fractionated to obtain the product. Instead of perfluoropivalic acid, the product was found to be 2H-trifluoro-2-(trifluoromethyl)propionic acid, $(CF_3)_2CHCOOH$, which might be considered a hydrolysate of PFIB. The product was characterized by direct comparison with a sample of this structure which has been disclosed previously.[4] Its F^{19} resonance spectrum consists of a doublet at −13.65 ppm. The proton resonance spectrum comprised a septet at +4.03 ppm and a singlet at +11.60.

In an attempt to avoid the hydrolytic action of aqueous sulfuric acid, the run was repeated using dry HCl for the acidification. In this case, the product was again not perfluoropivalic acid but, instead, a perfluoro olefin identical with the product obtained by the cesium fluoride–diglyme dimerization of PFIB.[5] It was believed to be a mixture of two dimers of PFIB, heptafluoro-2,4,4-tris(trifluoromethyl)-1-pentene, $(CF_3)_3CCF_2C(CF_3)=CF_2$, and heptafluoro-2,4,4-tris(trifluoromethyl)-2-pentene, $(CF_3)_3CCF=C(CF_3)_2$. Although PFIB forms a stable complex with cesium fluoride in diglyme, the CO_2 adduct is apparently not a stable carboxylic acid salt.

Attempts to add carbon dioxide to long-chain perfluoro α-olefins were unsuccessful owing to a tendency for the cesium fluoride–diglyme system to catalyze a shift of the double bond toward the center of the chain. This shift was apparently much more rapid than the addition of CO_2 and no carboxylic acid was isolated.

(3) J. H. Simons, *Fluorine Chem.*, **2**, 491 (1954).

(4) I. L. Kunyants, L. S. German, and B. L. Dyatkin, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1931 (1956).

(5) D. P. Graham, *J. Org. Chem.* **31**, 955 (1966).

Amino-N-cyanocarboxamides. I. *m*- and *p*-N,N-Dimethylamino-N-cyanobenzamide[1,2]

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Amino-N-cyanocarboxamides present a new, interesting, and possibly useful field of investigation. None of these compounds has been reported despite the fact that their amphoteric properties make them analogs (and potential antimetabolites) of the amino acids.

Since N-cyanocarboxamides are known to be stronger acids than carboxylic acids,[3] it seemed probable that some aromatic amino-N-cyanocarboxamides would exist as inner salts. We chose to investigate this possibility by preparing *m*- and *p*-N,N-dimethylamino-N-cyanobenzamide and comparing their second dissociation constants and infrared spectra with those of the corresponding carboxylic acids.

The two compounds were synthesized from their acid chlorides by allowing them to react with sodium hydrogen cyanamide in dimethylformamide. The melting points and analysis of these and several other N-cyanobenzamides are listed in Table I.

Their infrared spectra, and the spectra of the related acids as mineral oil mulls (Figure 1) clearly show that the *para* isomer **1** exists in the solid state as the uncharged species, but that the *meta* isomer **2** exists as the inner salt. This is in contrast to the analogous

(1) This work was supported by Grant GM 11408 from the National Institutes of Health.

(2) Presented at the Southeast-Southwest Regional Meeting of the American Chemical Society, Memphis, Tenn., Dec 1965.

(3) R. Bader, *Z. Physik. Chem.*, **6**, 304 (1890).

TABLE I

MELTING POINTS AND ANALYSIS OF N-CYANOBENZAMIDES

Substituent	Mp, °C Obsd	Mp, °C Lit.	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
H	141.5–142.0	140[a]	...	...	...	...	...	...
p-CH_3	155–156	155–156[b]	...	...	...	...	...	...
p-NO_2	158–159	...	50.27	2.64	21.98	50.35	2.85	21.76
m-NO_2	151–152	...	50.27	2.64	21.98	49.94	2.56	21.71
p-Cl[c]	165–166	...	53.20	2.79	15.51[c]	53.22	2.66	15.02[c]
p-$N(CH_3)_2$	147–148	...	63.48	5.86	22.21	63.34	5.85	21.87
m-$N(CH_3)_2$	156–157	...	63.48	5.86	22.21	63.37	6.06	21.94

[a] J. C. Ambelang and T. B. Johnson, *J. Am. Chem. Soc.*, **61**, 632 (1939). [b] G. Ponzio, *Gazz. Chim. Ital.*, **62**, 415 (1932); *Chem. Abstr.*, **26**, 5563 (1932). [c] *Anal.* Calcd. for $C_8H_5ClN_2O$: Cl, 19.63. Found: Cl, 19.57

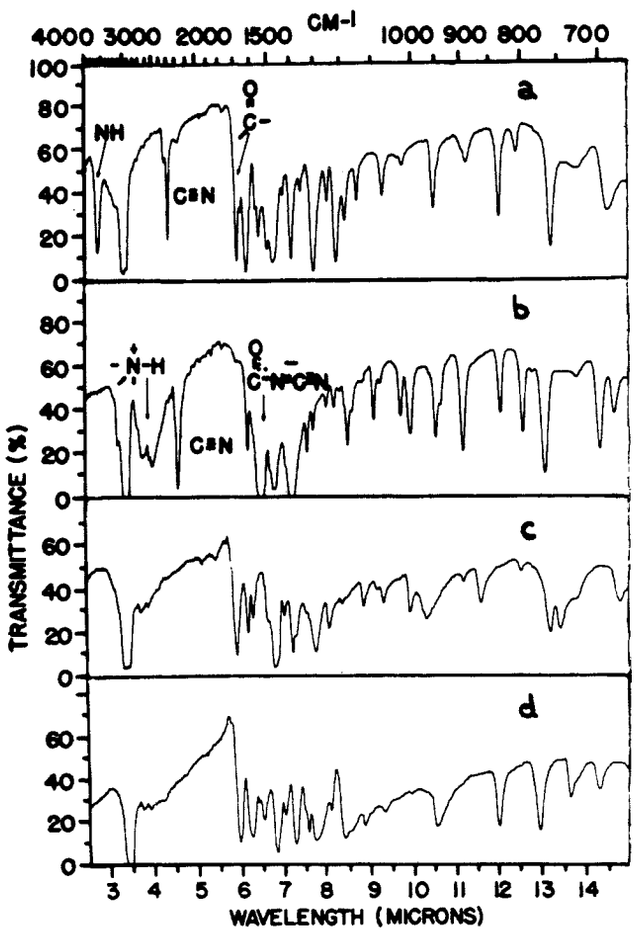
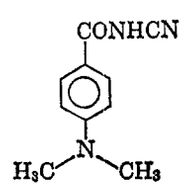


Figure 1.—Infrared spectra of *p*- (1) (a) and *m*-N,N-dimethylamino-N-cyanobenzamide (2) (b) and the corresponding carboxylic acids, *m*- (c) and *p*-N,N-dimethylaminobenzoic acid (d).

carboxylic acids, both of which appear uncharged in the solid state.



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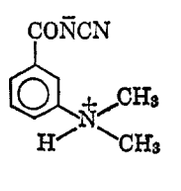

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Information regarding the structure of 1 and 2 in solution was desired. This was obtained from their second dissociation constants by two observations. First, a comparison of the pK values in water and 50 wt % methanol[4] of benzoic acid and N-cyanobenzamide with the pK_2 value of 2 (Table II) revealed that ionization of 2 was increased in the mixed solvent, whereas the ionization of benzoic acid and N-cyanobenzamide was decreased. This is a characteristic property of inner salts[5] and is consistent with the ionization of the charged substituted ammonium ion rather than an uncharged N-cyanocarboxamide group.[6a]

TABLE II

pK VALUES[a] OF N-CYANOBENZAMIDES AND RELATED BENZOIC ACIDS

Substituent	p_sK[b]	$p_{H_2O}K$
	N-Cyanobenzamides	
H	3.10	2.71 (*2.8*)[c]
p-CH_3	3.27	*d*
p-NO_2	2.12	*d*
m-NO_2	2.12	*d*
p-Cl	2.73	*d*
m-$N(CH_3)_2$	4.18[e]	4.78
p-$N(CH_3)_2$	4.12[e]	*d*
	Benzoic Acids	
H	5.33	4.20 (4.198 ± 0.012)[f]
m-$N(CH_3)_2$	5.55[e]	5.12[e] (*5.10*)[e,g]
p-$N(CH_3)_2$	6.15[e]	*d* (*5.02*)[e,h]

[a] Thermodynamic values on molal scale. Values in parentheses are from the literature; those in italicized type are not thermodynamic values. [b] Solvent 50 wt % methanol–water. [c] Reference 3. [d] Insoluble in water. [e] pK_2 values. [f] Reference 6b, p 421. [g] A. C. Cumming, *Proc. Roy. Soc.* (London), **A78**, 103 (1906). [h] J. Johnston, *ibid.*, **A78**, 82 (1906).

The second observation was made from a Hammett plot of the p_sK_2 values of 1 and 2 and the p_sK values of several nonamphoteric N-cyanobenzamides (Figure 2). It was immediately apparent that the second dissociation constant of 2 did not fit the Hammett

(4) M. Paabo, R. A. Robinson, and R. G. Bates, *J. Am. Chem. Soc.*, **87**, 415 (1965).

(5) A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," John Wiley and Sons, Inc., New York, N. Y., 1962, p 117.

(6) (a) Although it appears from Table II and Figure 1 that *m*-N,N-dimethylaminobenzoic acid is uncharged in aqueous solution as well as in the solid state, it can be shown by Ebert's equation [L. Ebert, *Z. Physik. Chem.*, **121**, 385 (1926)] that in water about 73% of the compound exists as the inner salt. Thus, the experimentally determined aqueous dissociation constant does not represent the correct value for the ionization of the carboxylic acid. (b) See D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 424 (1958), for the application of Ebert's equation to *m*-aminobenzoic acid.

equation for the ionization of N-cyanobenzamides. A reasonable explanation of this result is that the p_sK_2 of **2** actually depicts the ionization of the charged substituted ammonium ion of the inner salt. A Hammett plot of this reaction would, of course, have a different slope and in the case of **2**, the unknown σ value for the *m*-N-cyanoamide anion would have to be used.

Experimental Section[7]

Nonamphoteric N-Cyanobenzamides.—These were all prepared from the acid chlorides and 2 equiv of sodium hydrogen cyanamide (prepared from cyanamide and either 1 or 2 *N* sodium hydroxide) at room temperature. The sodium salts of the *m*-nitro-, *p*-nitro-, and *p*-chloro-N-cyanobenzamides precipitated during the reaction period and were separated by filtration. The salts were dissolved in water and acidified with ice-cold hydrochloric acid. The reaction mixture itself was acidified in the cases of N-cyanobenzamide and *p*-methyl-N-cyanobenzamide. The crude products were recrystallized from aqueous acetone; yields were all about 50%.

***m*-N,N-Dimethylamino-N-cyanobenzamide, Inner Salt.**—To 300 ml of dry dimethylformamide in a three-neck flask equipped with stirrer, condenser and drying tube, nitrogen inlet, and thermometer was added 16.8 g (0.40 mole) of cyanamide. The apparatus was flushed with dry nitrogen and cooled to 5–10° and 19.2 g (0.4 mole) of 50% sodium hydride–mineral oil dispersion[8] was added from a flask attached to the reaction vessel with Gooch tubing. The temperature was kept at 15–35° by means of an ice bath. When the reaction was complete, 22.0 g (0.10 mole) of *m*-N,N-dimethylaminobenzoyl chloride hydrochloride[9] (mp 138–140°, lit.[9] mp 135–136°) was added. The temperature was kept at 20–25° during the addition. The mixture was allowed to stir for 0.5 hr then was added under nitrogen to 2–3 l. of anhydrous ether. The precipitate was collected by filtration through a medium-porosity sintered-glass funnel, washed with anhydrous ether, and dried in a desiccator over concentrated sulfuric acid. The mixture of salts (30 g) was dissolved in 70 ml of water and filtered (Darco), and the filtrate was adjusted to pH 4.2 with concentrated hydrochloric acid. The pale yellow solid was collected, washed with distilled water, and dried at room temperature under vacuum. The yield was 7.0 g (37%), mp 156–157°, unchanged after recrystallization from acetonitrile.

***p*-N,N-Dimethylamino-N-cyanobenzamide.**—In the apparatus described above, the reaction was carried out using 12.6 g (0.30 mole) of cyanamide, 300 ml of dimethylformamide, 20.7 g (0.43 mole) of sodium hydride–mineral oil dispersion, and 18.4 g (0.10 mole) of *p*-N,N-dimethylaminobenzoyl chloride[10a] (mp 135–136°, lit.[10b] mp 135–136°). After the mixture of salts was precipitated with anhydrous ether, it was dissolved in 250 ml of water (Darco), filtered, and then acidified to pH 3.5 with concentrated hydrochloric acid. The yellow-orange product was extracted with 150 ml of 5% sodium bicarbonate (Darco) and reprecipitated with acid as before. The crude product was washed with distilled water and dried at room temperature. The weight in several runs varied from 7 to 14 g (37–74%), mp 137–138°. Although an infrared spectrum of this product showed it to be essentially pure, it was yellow and did not give satisfactory analytical data. A colorless, analytically pure product was obtained by recrystallization from acetone followed by recrystallization in small quantities from toluene (1 g/500 ml) which was not heated above 65°. The melting point was then 147–148°.

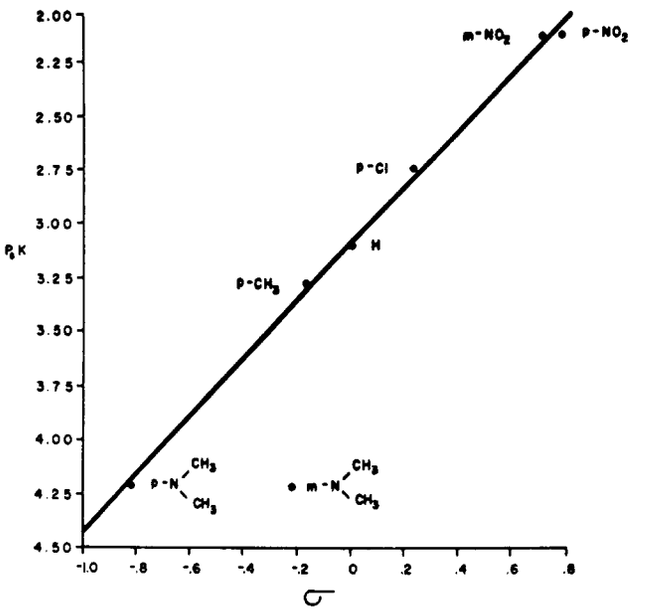

Figure 2.—Hammett plot of the p_sK values of *meta*- and *para*-substituted N-cyanobenzamides in 50 wt % methanol.

Dissociation Constants.—All pK values were determined with a Model 4 Radiometer pH meter equipped with a Type GK 2021C combination calomel–glass electrode. The p_sK values in 50 wt % methanol were measured in solutions containing 200 g of solvent, 2.00 mmoles of the N-cyanobenzamide, 1.00 mmole of sodium chloride, and 0.500 mmole of sodium carbonate. All N-cyanobenzamides and substituted benzoic acids were either analytical samples or were more than 99% pure by titration. The meter was calibrated using the pH*(S) values of phosphate, acetate, and succinate buffers in 50 wt % methanol (ionic strength 0.01) reported by Bates and co-workers.[4] The temperature was kept at 25 ± 0.3. Determinations were run in duplicate or triplicate and the spread of pH readings was never greater than 0.02 pH unit (the standard deviation was 0.008). The pH data were converted to molal thermodynamic (p_sK) values by the Debye–Hückel relationship

$$p_sK = \text{pH} + \log \frac{[\text{HA}] - (\text{H}^+)}{[\text{A}^-] + (\text{H}^+)} + \frac{AZ^+Z^-I^{1/2}}{1 + Ba_iI^{1/2}}$$

using the constants (A, B, and a_i equal to 0.8015, 0.3708×10^8, and 4.3×10^{-8}, respectively) reported by Bates.[11]

The last expression in the equation is approximately equal to +0.07 at 0.01 ionic strength.

The pK values in water were determined with the meter adjusted to aqueous phthalate and borax buffers. Solutions of the compounds were prepared as before except that 200 g of distilled water was used instead of the mixed solvent. Thermodynamic constants were obtained from the equation[12]

$$pK = \text{pH} + \log \frac{[\text{HA}] - (\text{H}^+)}{[\text{A}^-] + (\text{H}^+)} + 0.5I^{1/2}$$

Hammett Plot.—The best straight line was prepared by the method of least squares: $\rho = 1.32$; correlation coefficient, 1.00; standard deviation from straight lines, 0.045. σ values were taken from Hine.[13]

Acknowledgment.—We wish to acknowledge the capable technical assistance of Mrs. Ruth Balcom.

(7) Melting points were determined in capillaries which were introduced into a calibrated electrically heated block at about 5° below the anticipated melting point and then heated at a rate of 2–3°/min. All of the N-cyanobenzamides decomposed slowly on heating. Infrared spectra were determined with a Perkin-Elmer 137-B spectrophotometer. Analyses were by Clark Microanalytical Laboratory, Urbana, Ill.

(8) Metal Hydrides Co., Beverly, Mass.

(9) This was prepared in the usual manner from thionyl chloride, the acid, and benzene solvent. Yields of acid chloride hydrochloride by this method were better than when the method of G. Bramanti, G. DiPaco, and C. S. Tauro [*Boll. Chim. Farm.*, **99**, 517 (1960); *Chem. Abstr.*, **5**, 9333 (1961)] was used.

(10) (a) Prepared the same way as the *meta* isomer. (b) A. I. Kiprianov and U. A. Shrubovich, *Zh. Obsch. Khim.*, **26**, 2891 (1956); *Chem. Abstr.*, **51**, 8072 (1957).

(11) M. Paabo, R. A. Robinson, and R. G. Bates, *J. Chem. Eng. Data*, **9**, 374 (1964).

(12) Reference 5, p 60.

(13) J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 97.