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The scope of the nucleophilic displacement of aromatic halogens on 1,4-benzodiazepine precursors by the anions of pyrroles, pyrazoles and imidazoles was studied both with and without electron-withdrawing substitutents on the heterocyclic nucleophiles. Some of the products proved to be useful intermediates for the synthesis of novel fused 1,4-benzodiazepines.

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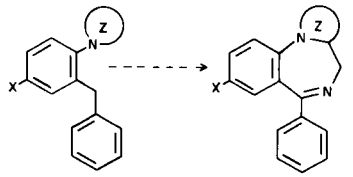
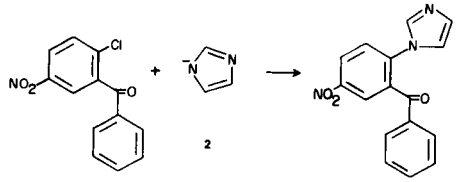
Introduction

As part of a program to prepare novel 1,4-benzodiazepines with a ring fused at the 1-2 positions, an approach based upon the preparation of intermediates of type "A" was initiated, where X could be halogen, nitro, etc., and Z was a heteroaromatic ring.

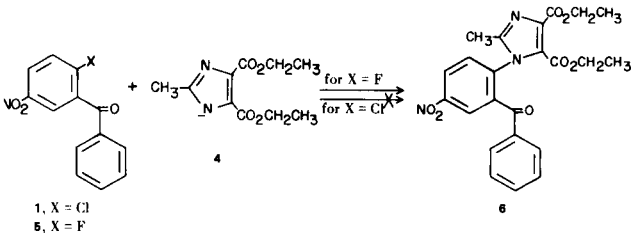


"A"

Our first approach to intermediates of type "A" was the synthesis of **3** which was obtained by the displacement of chlorine from **1** by the anion of imidazole (**2**).



Attempts to functionalize the imidazole ring of **3** were unsuccessful, therefore, the preparation of intermediates of type "A" was undertaken in which the hetero-ring was already functionalized. The dicarbethoxy imidazole **4** (2) was synthesized for use in the nucleophilic substitution reaction. Although the chloro compound **1** was recovered unchanged after heating at 100° with **4**, fluorine in compound **5** was readily displaced to give the benzophenone **6**.



1, X = Cl
5, X = F

The observed differences in the reactivity of chloro versus fluoroketones prompted an investigation of the nucleophilic displacement of aromatic halogens by heterocyclic compounds containing nitrogen.

The displacement of fluorine in both 4-nitrofluorobenzene and 2,4-dinitrofluorobenzene by imidazole has been previously reported (3,4). To our knowledge only one example of the use of a 2-halo-5-nitrobenzophenone as a substrate (5) and no examples of the use of heterocycles bearing carboxylic ester groups (*e.g.* **4**) as the nucleophiles have been described.

Results and Discussion

Our findings on the nucleophilic aromatic substitution of halogens by nitrogen-heterocycles are completely in accord with the known principles of aromatic S_nAr reactions (6). For example, fluorine is more reactive towards displacement than chlorine and heterocycles without electron withdrawing groups are the better nucleophiles. Nevertheless, some interesting observations of the many reactions studied can be summarized as follows (in all cases, the nitro group was *para* to the halogen and the benzoyl group was *ortho*.)

1) The anions of simple heterocyclics (imidazole, 2-methylimidazole and pyrrole) will displace chlorine from an aromatic ring only if a nitro group is present for activation. A benzoyl group is not sufficiently activating for the nucleophilic substitution of chlorine to occur.

2) The above heterocycles will displace fluorine from an aromatic ring if a benzoyl group and/or a nitro group is present.

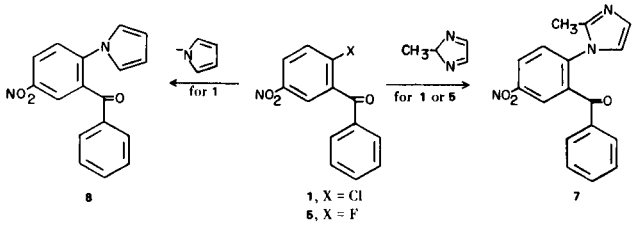
3) The anions of heterocyclic carboxylic esters will not displace chlorine from an aromatic ring even if both a nitro and a benzoyl group are present for activation.

4) The anions of heterocyclic esters will displace fluorine only if the fluorine is activated by a nitro group. These conclusions are based on the results of the following experiments:

A. Use of Imidazole, 2-Methylimidazole, 3,5-Diacetoxymethylpyrazole, and Pyrrole as nucleophiles.

The chlorobenzophenone, **1**, led to the products, **3**, **7**, and **8**, when reacted with the sodium salts of imidazole, 2-methylimidazole and pyrrole, respectively. The benzophenone **5** also yielded **7** when treated with the anion of 2-methylimidazole. Under the same conditions, the weakly activated 2,5-dichlorobenzophenone (9) did not react with 2-methylimidazole anion. However, it was

found that the benzoyl group was sufficiently activating if the halogen was fluorine, as exemplified by the formation of **10** from 2-fluorobenzophenone and sodium imidazole. Both **1** and **5** yielded the product **11** (7) when reacted with the anion of 3,5-diacetoxymethylpyrazole.



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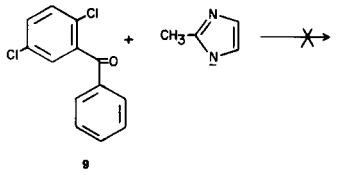

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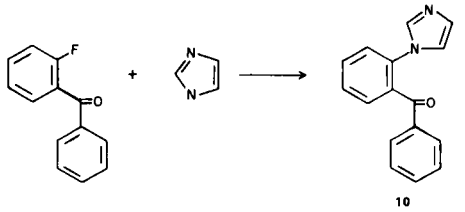

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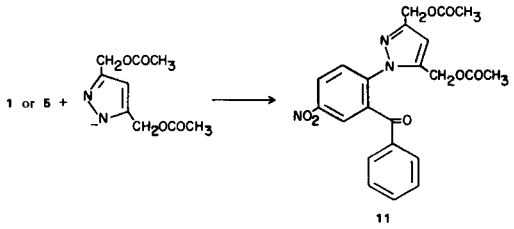

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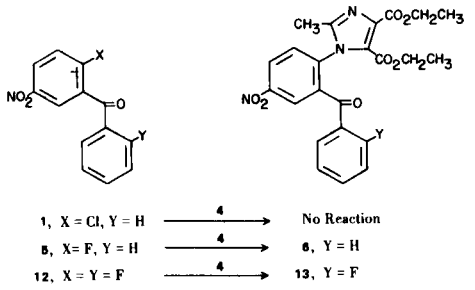
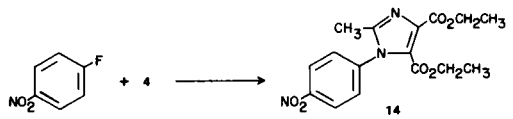
B. 2-Methyl-4,5-imidazoledicarboxylic acid, diethyl ester **4** as a nucleophile.

As discussed in the introduction, the chlorine in compound **1** could not be displaced by **4**, although the fluorine in **5** was readily displaced by **4** to give **6**. The difluorobenophenone **12** yielded the product **13**, resulting from displacement of only the doubly-activated fluorine. In line with this result, the fluorine in 2-fluorobenzophenone could not be displaced by **4**. However, a nitro group was found to be sufficiently activating as shown by the formation of **14** from 4-nitrofluorobenzene and **4**.





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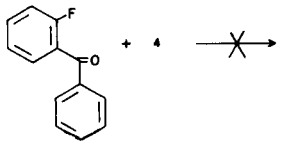
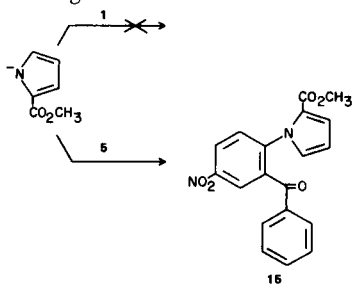


C. Pyrrole-2-carboxylic acid, methyl ester as a nucleophile.

As expected from the previous results, the chloro compound **1** was unreactive towards the anion of pyrrole-2-carboxylic acid, methyl ester, while the fluorine in **5** was readily displaced to give **15**.



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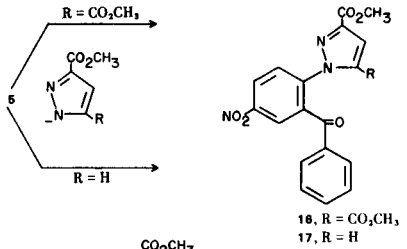
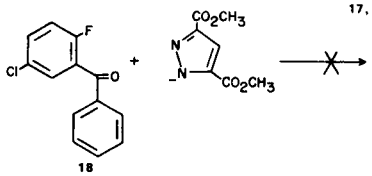
D. Pyrazole-3,5-dicarboxylic acid, dimethyl ester (**8**) and Pyrazole-3(5)-carboxylic acid, methyl ester (**9**) as nucleophiles.

The fluoronitrobenzophenone **5** yielded the pyrazolobenzophenones **16** and **17** when treated with the sodium salts of pyrazole-3,5-dicarboxylic acid, dimethyl ester and pyrazole-3(5)carboxylic acid, methyl ester, respectively. However, no product was obtained from the reaction of 2-fluoro-5-chlorobenzophenone **18** with the pyrazole-diester, again indicating that the *ortho*-benzoyl group is not sufficiently activating towards heterocycles substituted with electron withdrawing groups.





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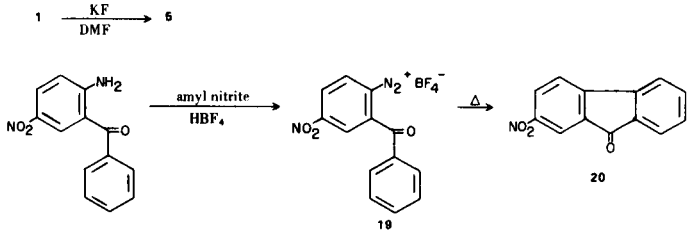
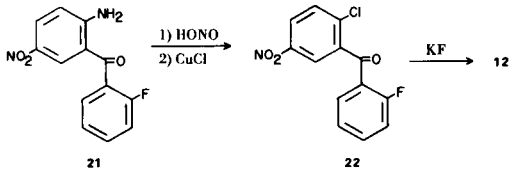
The imidazobenzophenone **6** and the pyrazolobenzophenones **11** and **16** proved to be useful intermediates for the construction of the 1,4-benzodiazepine ring system, as reported in the following papers (7,10).

Synthesis of Starting Materials

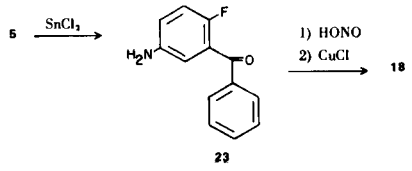
2-Methylimidazole-4,5-dicarboxylic acid, diethyl ester (**2**), pyrazole-3,5-dicarboxylic acid dimethyl ester (**8**) and 3(5)pyrazole carboxylic acid, methyl ester (**9**) were prepared by known literature procedures. The preparation of 3,5-diacetoxymethylpyrazole is described in reference (7). The benzophenone, **5**, was prepared by refluxing **1** with potassium fluoride in dimethylformamide. Attempts to prepare **5** by a Schiemann reaction gave as the main product the known fluorenone **20** (11).



The difluorobenzophenone **12** was prepared from 2-amino-5-nitro-2′-fluorobenzophenone (**21**) by conversion to the 2-chlorocompound **22** *via* a Sandmeyer reaction followed by displacement of chlorine by potassium fluoride in dimethylformamide as solvent.



2-Fluoro-5-chlorobenzophenone (**18**) was prepared by reduction of **5** with stannous chloride to give the amino compound **23** followed by a Sandmeyer reaction to convert the amino group to a chloro substituent.



EXPERIMENTAL

Melting points were determined with a Thomas-Hoover capillary apparatus and are corrected. The ir spectra were recorded on a Digilab FTS14 or a Perkin-Elmer 621 spectrometer, mass spectra on a Varian MAT CH5 or a CEC-21-110 spectrometer, and nmr spectra on a Jeolco C-60H, a Varian XL-100 or HA-100 instrument, using tetramethylsilane as a internal standard. Silica gel 60 (Merck, 60-230 mesh) was used for chromatography and either anhydrous sodium sulfate or magnesium sulfate was used for drying organic solutions.

1-(2-Benzoyl-4-nitrophenyl)imidazole (**3**).

To a solution of 1.35 g. (20 mmoles) of imidazole (**2**) in 20 ml. of dimethylformamide stirred at 0° under argon, was added 960 mg. of sodium hydride (20 mmoles, 50% suspension in mineral oil). After the evolution of hydrogen had ceased, a solution of 5.22 g. (20 mmoles) of 5-chloro-2-nitrobenzophenone (**1**), in 10 ml. of dimethylformamide was added dropwise. After warming to room temperature, the mixture was heated at 55° for 1.75 hours, cooled and poured into ice-water. The aqueous mixture was extracted with ethyl acetate. The organics were combined and extracted with 2*N* hydrochloric acid. The acidic phase was made basic with cold 40% sodium hydroxide and extracted with ethyl acetate. The organics were dried and concentrated to give 3.3 g. (56%) of product suitable for further reactions. The analytical sample was prepared by recrystallization from 2-propanol, pale yellow needles, m.p. 135-136°; ir (chloroform): 1665 cm^{-1} (C=O).

Anal. Calcd. for $C_{16}H_{11}N_3O_3$: C, 65.53; H, 3.78; N, 14.33. Found: C, 65.42; H, 3.69; N, 14.64.

2-Fluoro-5-nitrobenzophenone (**5**).

A mixture of 162 g. (0.62 mole) of 2-chloro-5-nitrobenzophenone (**1**), 169 g. (2.9 moles) of anhydrous potassium fluoride and 1.3 l. of dimethylformamide was stirred and refluxed overnight. After cooling, the mixture was poured over ice and extracted with ether. The organics were combined, washed well with dilute brine, dried and concentrated. The residue was filtered through silica gel using ether-hexane (1-1) as eluent. After removing the solvents, the residue was recrystallized from ethanol to give 124 g. of product (82%) m.p. 45-47°; mass spectrum: m/e 245 (M^+).

Anal. Calcd. for $C_{13}H_8FNO_3$: C, 63.68; H, 3.29; N, 5.71; F, 7.75. Found: C, 63.65; H, 3.14; N, 5.52; F, 7.68.

1-(2-Benzoyl-4-nitrophenyl)-2-methyl-4,5-imidazoledicarboxylic Acid, Diethyl Ester (**6**).

This compound was prepared from **4** and **5** in a manner analogous to that described for the preparation of **3**, except that a temperature of 75° was used. The yield was 63%. The analytical sample was obtained as off-white needles by recrystallization from ethanol-water, m.p. 151.5-153°; ir (chloroform): 1680 (C=O), 1710 cm^{-1} (CO_2Et); nmr (deuteriochloroform): δ 1.12 (3H, t, CH_3), 1.34 (3H, t, CH_3), 2.28 (3H, s, CH_3), 4.06 (2H, doublet of q, CH_2), 4.32 (2H, q, CH_2), 7.30-7.75 (6H, m, C_6H_5 and C_6H) and 8.35-8.54 (2H, m, C_6H_2).

Anal. Calcd. for $C_{23}H_{21}N_3O_7$: C, 61.20; H, 4.69; N, 9.31. Found: C, 61.33; H, 4.75; N, 9.19.

1-(2-Benzoyl-4-nitrophenyl)-2-methylimidazole (**7**).

This compound was prepared from either **1** or **5** (45-55% yield) and 2-methylimidazole in the same manner as that described for the preparation of **3**. The analytical sample was prepared by recrystallization from ethanol and obtained as pale yellow needles, m.p. 162-164°; ir (chloroform): 1675 cm^{-1} (C=O); nmr (deuteriochloroform): δ 2.25 (3H, s, CH_3), 6.80 (2H, s, CH=CH), 7.30-7.65 (6H, m, C_6H_5 and C_6H), and 8.47 (2H, m, C_6H_2).

Anal. Calcd. for $C_{17}H_{13}N_3O_3$: C, 66.44; H, 4.25; N, 13.67. Found: C, 66.53; H, 4.09; N, 13.88.

1-(2-Benzoyl-4-nitrophenyl)pyrrole (**8**).

To a slurry of 96 mg. (2 mmoles) of a 50% dispersion of sodium hydride in mineral oil in 10 ml. of dry dimethylformamide, which had been cooled to 3° under argon, was added *via* syringe 1 ml. of a solution of 1.40 ml. of pyrrole in 8.60 ml. of dry dimethylformamide. When the evolution of hydrogen had ceased, the reaction was warmed to room temperature and stirred 20 minutes. A solution of 490 mg. (2 mmoles) of **1** in 2 ml. of dry dimethylformamide was added to the reaction *via* syringe and rinsed in with 1 ml. of dimethylformamide. After stirring 15 minutes, the

reaction was heated to 55° for 3.5 hours, cooled, poured over ice-water and made basic with 3*N* sodium hydroxide. The mixture was extracted three times with ethyl acetate, and the combined extracts were washed with brine, dried, then washed twice with 3*N* hydrochloric acid, redried and concentrated to a brown oil. The crude product was chromatographed on silica gel using hexane with gradually increasing amounts of ethyl acetate (0-5%) as eluent to give 255 mg. (44%) of the desired product **8**. Recrystallization from ethyl acetate/hexane gave the analytical sample as pale yellow needles, m.p. 110-111°; ir (potassium bromide): 1670 cm^{-1} (C=O); nmr (deuteriochloroform): δ 6.06 (2H, t, C_4NH_2), 6.72 (2H, t, C_4NH_2), 7.10-7.40 (6H, m, C_6H_5 and C_6H_1), 8.33 (2H, m, C_6H_2).

Anal. Calcd. for $C_{17}H_{12}N_2O_3$: C, 69.86; H, 4.14; N, 9.58. Found: C, 70.05; H, 3.94; N, 9.66.

1-(2-Benzoylphenyl)imidazole (**10**).

To a slurry of 960 mg. (20 mmoles) of 50% sodium hydride in mineral oil in 25 ml. of dimethylformamide stirred at 0° under argon, was added dropwise 1.35 g. (20 mmoles) of imidazole in 15 ml. of dimethylformamide. After the evolution of hydrogen had ceased, the reaction mixture was warmed to room temperature and a solution of 4.0 g. (20 mmoles) of 2-fluorobenzophenone in 10 ml. of dimethylformamide was added dropwise. The mixture was heated at 100° for 2.5 hours followed by heating at 130° for 2 hours. After cooling, the mixture was poured into ice-water and extracted with ethyl acetate. The organics were combined and extracted with 3*N* hydrochloric acid. The acidic washes were made basic with 40% sodium hydroxide and extracted with ethyl acetate. After washing with brine, the organics were dried and concentrated. The residue was chromatographed on silica gel using ethyl acetate as an eluent to give 0.9 g. (18%) of **10**. The analytical sample was prepared by recrystallization from benzene-hexane and obtained as yellow prisms, m.p. 130-132°; ir (chloroform): 1670 cm^{-1} (C=O).

Anal. Calcd. for $C_{16}H_{12}N_2O$: C, 77.40; H, 4.87; N, 11.28. Found: C, 77.70; H, 4.93; N, 11.10.

2-Fluoro-5-nitro-2'-fluorobenzophenone (**12**).

A mixture of 1.4 g. (5 mmoles) of **22**, 1.47 g. (25 mmoles) of anhydrous potassium fluoride, and 20 ml. of dimethylformamide was stirred and refluxed overnight. The mixture was cooled, poured into ice-water and extracted well with ether. The organics were combined, washed well with dilute brine, dried, concentrated and the residue chromatographed on silica gel using benzene as the eluent. The crude product was recrystallized from ethanol-water to give 0.5 g. (38%) of **12** as off-white needles, m.p. 70-72°. The analytical sample was prepared by recrystallization from the same solvent mixture, m.p. 73-74.5°.

Anal. Calcd. for $C_{13}H_7F_2NO_3$: C, 59.33; H, 2.68; N, 5.32; F, 14.49. Found: C, 59.20; H, 2.43; N, 5.19; F, 14.59.

1-[2-(2-Fluorobenzoyl)-4-nitrophenyl]-2-methyl-4,5-imidazoledicarboxylic Acid, Diethyl Ester (**13**).

This compound was prepared *via* the procedure given for the preparation of **3**. The crude product was chromatographed on silica gel using benzene-ethyl acetate (3:1) as eluent. The product was obtained in 54% yield. The analytical sample was prepared by recrystallization from ethanol-water and obtained as yellow prisms; m.p. 121-122°; ir: (chloroform) 1680 (C=O) and 1715 cm^{-1} (CO_2Et); nmr (deuteriochloroform): δ 1.19 (3H, t, CH_3), 1.38 (3H, t, CH_3), 2.26 (3H, s, CH_3), 4.16 (2H, q, CH_2), 4.37 (2H, q, CH_2), 6.95-7.70 (5H, m, C_6H_4 and C_6H), 8.46-8.61 (2H, m, C_6H_2).

Anal. Calcd. for $C_{23}H_{20}FN_3O_7$: C, 58.85; H, 4.29; N, 8.95. Found: C, 58.87; H, 4.25; N, 8.99.

2-Methyl-1-(4-nitrophenyl)-4,5-imidazoledicarboxylic Acid, Diethyl Ester (**14**).

To a solution of 4.52 g. (20 mmoles) of **4** in 50 ml. of dimethylformamide, stirred at 0° under argon, was added 960 mg. (20 mmoles) of sodium hydride (50% suspension in mineral oil). After the evolution of hydrogen had ceased, 2.82 g. (20 mmoles) of 4-nitrofluorobenzene in a few ml. of dimethylformamide was added. The mixture was heated at 95° overnight, cooled, poured into ice-water and extracted with ethyl acetate. The organics were washed well with dilute brine, dried, concentrated and the residue recrystallized from ethanol to give 4.6 g. (66%) of **14**, m.p., 149-151°. The analytical sample was obtained as off-white plates from ethanol, m.p. 150-151.5°; ir (chloroform): 1735 cm^{-1} (C=O); nmr (deuteriochloroform): δ 1.18 (3H, t, CH_3), 1.42 (3H, t, CH_3), 2.29 (3H, s, CH_3), 4.18 (2H, q, CH_2), 4.43 (2H, q, CH_2), 7.48 (2H, d, C_6H_2), and 8.37 (2H, d, C_6H_2).

Anal. Calcd. for $C_{16}H_{17}N_3O_6$: C, 55.33; H, 4.93; N, 12.10. Found: C, 55.55; H, 4.90; N, 12.09.

1-(2-Benzoyl-4-nitrophenyl)pyrrole-2-carboxylic Acid, Methyl Ester (**15**).

To a suspension of 2.26 g. (47 mmoles) of 50% sodium hydride in mineral oil in 25 ml. of dimethylformamide, cooled to 5° and under argon, was added 5.9 g. (47 mmoles) of pyrrole-2-carboxylic acid, methyl ester in portions. After the evolution of hydrogen had ceased, the reaction was warmed to room temperature, and a solution of 10.3 g. (47 mmoles) of **5** in 50 ml. of dimethylformamide was added dropwise. After heating at 65° for 1.5 hours, the mixture was cooled, poured into ice-water and extracted with ethyl acetate. The extracts were dried, concentrated and the residue chromatographed on silica gel using a mixture of ether and ethyl acetate as the eluent. The product was recrystallized from ether/hexane to give 8.2 g. (56%) of **15**. The analytical sample was obtained as off-white needles by recrystallization from ether/hexane, m.p. 115.5-117°; ir (potassium bromide): 1700 cm^{-1} (C=O ester), 1640 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.63 (3H, s, CH_3), 6.07 (1H, t, C=CH), 6.78 (2H, d, 2X C=CH), 7.08-7.80 (6H, m, C_6H_5 and C_6H), 8.35 (2H, m, C_6H_2).

Anal. Calcd. for $C_{19}H_{14}N_2O_5$: C, 65.14; H, 4.03; N, 8.00. Found: C, 65.17; H, 3.98; N, 8.04.

1-(2-Benzoyl-4-nitrophenyl)-3,5-pyrazoledicarboxylic Acid Dimethyl Ester (**16**).

To a slurry of 5.3 g. (110 mmoles) of 50% sodium hydride in mineral oil in 425 ml. of dimethylformamide, stirred at 3° under argon, was added portionwise over a 20-minute time period, 20.26 g. (110 mmoles) of pyrazole-3,5-dicarboxylic acid, dimethyl ester, maintaining a temperature of 5-8°. When the vigorous hydrogen evolution had stopped, the ice bath was removed and the reaction allowed to warm to room temperature while stirring for 20 minutes. A solution of 24.5 g. (100 mmoles) of **5** in 100 ml. of dimethylformamide was added dropwise over 40 minutes and when addition was complete, the reaction was heated at 65° for 1.5 hours. After cooling, the mixture was poured over a mixture of ice and brine and extracted well with a 1:1 ethyl acetate-ether mixture. The combined extracts were washed with brine, dried and concentrated. The crude mixture was chromatographed on silica gel using as an eluent benzene mixed with 0-100% ethyl acetate. The residue remaining after the solvents were evaporated was recrystallized from ethyl acetate/hexane to give 26.9 g. (66%) of **16**. The analytical sample was prepared by an additional recrystallization from ethyl acetate/hexane and was obtained as off-white needles, m.p. 150-152°; ir (potassium bromide): 1730, 1745

(CO_2CH_3), 1650 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.81 (3H, s, CH_3), 3.95 (3H, s, CH_3), 7.25-7.90 (7H, m, C_6H_5, C_6H_1 and C=CH) and 8.50 (2H, m, C_6H_2).

Anal. Calcd. for $C_{20}H_{15}N_3O_7$: C, 58.68; H, 3.69; N, 10.26. Found: C, 58.98, 58.94; H, 3.67, 3.84; N, 10.21, 10.37.

1-(2-Benzoyl-4-nitrophenyl-3-pyrazolecarboxylic Acid, Methyl Ester (**17**).

To a solution of 2.6 g. (21 mmoles) of pyrazole-3(5)carboxylic acid, methyl ester in 100 ml. of dimethylformamide, stirred at 5° under argon, was added 1.0 g. (21 mmoles) of 50% sodium hydride in mineral oil. After the evolution of hydrogen had ceased, 4.9 g. (20 mmoles) of **5** was added. The ice-bath was removed and the solution heated at 70° for three hours. After cooling, the reaction mixture was poured over ice and brine and filtered. The crude solid was recrystallized from methanol to give 3.3 g. (47%) of **17**, m.p. 173.5-175°. The analytical sample was obtained as colorless needles by recrystallization from methanol: m.p. 174.5-176°; ir (chloroform): 1730 (CO_2CH_3) and 1685 cm^{-1} (C=O); nmr (deuteriochloroform): δ 3.83 (3H, s, OCH_3), 6.73 (1H, d, C=CH), 7.20-8.43 (9H, complex m, aromatic protons); mass spectrum: m/e 351 (M^+).

Anal. Calcd. for $C_{18}H_{13}N_3O_5$: C, 61.54; H, 3.73; N, 11.96. Found: C, 61.43; H, 3.89; N, 12.09.

5-Chloro-2-fluorobenzophenone (**18**).

To a solution of 3.25 g. (12.5 mmoles) of **23** (as the hydrochloride) in 20 ml. of glacial acetic acid and 20 ml. of 3*N* hydrochloric acid, stirred at 3°, was added dropwise, so as to maintain a temperature of 3-6°, a solution of 970 mg. (14 mmoles) of sodium nitrite in 9 ml. of water. When the addition was complete, the reaction was stirred at 3° for one hour. A freshly prepared solution of cuprous chloride in concentrated hydrochloric acid (3) was mixed with an equal volume of water and cooled to 3°. The cold diazotized solution was slowly poured into the cuprous chloride with vigorous stirring, in several portions to allow the foaming to subside (the diazotized compound must be kept cold at all times). When addition was complete, the mixture was stirred and allowed to slowly warm to room temperature over 1 hour, then heated on the steambath to an internal temperature of 95°. After cooling to room temperature, the mixture was made basic with ammonium hydroxide and extracted three times with dichloromethane. The combined extracts were washed with water, dried, and concentrated. The residue was chromatographed on silica gel using benzene as the eluent. After removing the solvent, the residue was crystallized from hexane to give 2.1 g. (72%) of product **18**. The analytical sample was prepared by recrystallization from hexane and was obtained as colorless needles, m.p. 70-72°; ir (potassium bromide): 1655 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_8ClFO$: C, 66.54; H, 3.44; Cl, 15.11. Found: C, 66.61; H, 3.48; Cl, 15.00.

2-Benzoyl-4-nitrobenzenediazonium Tetrafluoroborate (**19**).

To a solution fo 2-amino-5-nitrobenzophenone (2.42 g., 10 mmoles) in 20 ml. of tetrahydrofuran and 20 ml. of ethanol, cooled in an ice-bath, was added 3.7 ml. of 48% fluoboric acid. A solution of 1.34 ml. (20 mmoles) of *iso*-amyl nitrite in 3 ml. of ethanol was then added dropwise, followed by the addition of 1.7 ml. of 48% fluoboric acid. After stirring for 0.5 hours at 4-5°, the resulting precipitate was collected by filtration, washed with ethanol and ether, to give 1.5 g. (44%) of **19**. An analytical sample was prepared by recrystallization of **19** from ethanol, m.p. 160° dec., ir (potassium bromide): 2300 (N_2), and 1675 cm^{-1} (C=O).

Anal. Calcd. for $C_{13}H_8N_3O_3 \cdot BF_4$: C, 45.79; H, 2.36; N, 12.32. Found: C, 45.87; H, 2.26; N, 12.50.

3-Nitrofluorenone (**20**).

A small sample of the diazonium salt **19** was heated in a round-bottomed flask to 140°, at which temperature evolution of gases occurred. After heating briefly to 180°, the flask was cooled and ethyl acetate was added to dissolve the solids.

The ethyl acetate was washed with brine, dried and concentrated. The residue was dissolved in dichloromethane and filtered through silica gel. The dichloromethane was removed *in vacuo* and the residue recrystallized from ethanol to give **20** as yellow needles, m.p. 218-220°; ir (potassium bromide): 1715 cm^{-1} (C=O); mass spectrum: m/e 325 (M^+), 195 (M^+-NO), and 179 (M^+-NO_2).

Anal. Calcd. for $C_{13}H_7NO_3$: C, 69.33; H, 3.13; N, 6.22. Found: C, 69.28; H, 3.07; N, 6.02.

2-Chloro-5-nitro-2'-fluorobenzophenone (**22**).

To a solution of 13 g. (50 mmoles) of 2-amino-5-nitro-2'-fluorobenzophenone **21** in 100 ml. of tetrahydrofuran and 100 ml. of ethanol at 0° was added dropwise 27 ml. of aqueous 47% fluoboric acid. To this solution was added dropwise 5.85 g. (50 mmoles) of *iso*-amyl nitrite dissolved in 15 ml. of ethanol. The mixture was stirred at 0° for 1.5 hours and the resulting precipitate was collected by filtration and washed with cold ethanol and then cold ether to give 8 g. of the crude diazonium fluoroborate which was used without further purification. To a suspension of 3.45 g. (10 mmoles) of the above diazonium salt in 30 ml. of 6*N* hydrochloric acid, stirred in an ice-bath, was added a solution of 1.98 g. (20 mmoles) of cuprous chloride in 30 ml. of 6*N* hydrochloric acid. After stirring for 5 minutes, the mixture was heated on a steambath for 15 minutes, cooled, diluted with cold water, made basic with concentrated ammonium hydroxide, and extracted with ethyl acetate. The organics were combined, washed with brine, dried and concentrated *in vacuo*. The residue was filtered through a small amount of silica gel using dichloromethane as eluent to give 2.1 g. (75%) of **22**. The analytical sample was obtained as off-white needles from methanol, m.p. 119-120°.

Anal. Calcd. for $C_{13}H_7ClFNO_3$: C, 55.83; H, 2.52; N, 5.01; Cl, 12.68; F, 6.79. Found: C, 56.03; H, 2.64; N, 5.28; Cl, 12.64; F, 6.59.

2-Fluoro-5-aminobenzophenone Hydrochloride (**23**).

A solution of 13.5 g. (60 mmoles) of stannous chloride dihydrate in 25 ml. of 6*N* hydrochloric acid and 80 ml. acetic acid was added to a warm solution of 4.90 g. (20 mmoles) of **5** in 75 ml. of acetic acid. The reaction was allowed to cool to room temperature and after stirring for 68 hours, was poured over ice, made basic with 40% sodium hydroxide and extracted four times with dichloromethane. The combined extracts were then washed with water, dried and concentrated *in vacuo* to a gummy yellow residue which did not cyrstallize. The residue was chromatographed on silica gel using benzene with 0-15% ethyl acetate as the eluent. After removing the solvent, the residue was taken up in ether and converted to the hydrochloride salt. Recrystallization from ethyl acetate/ether gave 4.3 g. (85%) of **23**. A small amount was recrystallized twice from the same solvent system to give an analytical sample as colorless plates, m.p. 201-205° dec.; ir (potassium bromide): 1660 cm^{-1} (C=O); nmr (deuteriochloroform + dimethylsulfoxide-d_6): δ 7.10-7.92 (8H, m, C_6H_5 and C_6H_3), 10.51 (3H, bs, NH_3^+).

Anal. Calcd. for $C_{13}H_{10}FNO \cdot HCl$: C, 62.04; H, 4.41; N, 5.57. Found: C, 62.28; H, 4.37; N, 5.71.

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