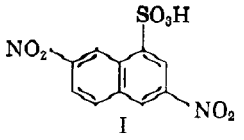
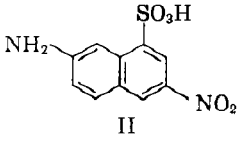


I

being produced.

Reduction of I furnished the corresponding diaminosulfonic acid, isolated as the monohydrochloride salt. This substance was also prepared by reduction of 7-amino-3-nitronaphthalene-1-sulfonic acid (II), obtained as described by Blangey.[4]



II

The infrared spectra of the two diaminosulfonic acids obtained by reduction were the same, thus providing further proof of structure.

Attempts to sulfonate 6-nitro-2-naphthylamine under several reaction conditions failed, dark tars being formed.

EXPERIMENTAL

The yields are not given as each product or its precursor was contaminated unavoidably by sodium chloride.

3,7-Dinitronaphthalene-1-sulfonic acid, sodium salt. 2,6-Dinitronaphthalene (0.2 g.) was treated with 5.2 ml. of 30% oleum at room temperature, and left sealed with occasional shaking for 7 hr. The mixture was then poured on ice, the solution filtered and the filtrate saturated with sodium chloride. The crystalline deposit of sodium salt was filtered and washed twice with brine, yield, 0.22 g. For spectral tests, the light yellow salt was redissolved in water and resalted with sodium chloride to eliminate any sodium sulfate.

Sulfonation of the dinitronaphthalene with 100% sulfuric acid did not occur during 3 days in the cold.

Other salts. The aqueous acid is readily salted out by potassium chloride giving a product resembling the sodium salt, but the ammonium salt is formed with more difficulty.

A cobaltammine salt is formed as a pink crystalline deposit from solutions of chloropentaminocobaltic chloride and the sodium salt. The complex ammine salts of copper, nickel and zinc are produced from ammoniacal solutions of the respective ions as heavy crystalline precipitates.

3,7-Dinitronaphthalene-1-sulfonyl chloride. A mixture of 0.9 g. of the sodium salt and 3.5 g. of phosphorus pentachloride was ground together and 0.1 ml. of phosphorus oxychloride added. After heating in a bath at 120–125° for 2.5 hr., the product was cooled, hydrolyzed by ice, and the solids filtered off and washed. The filtered acetone solution was diluted slowly with ice water to obtain a crystalline product free of inorganic impurities. It was recrystallized from aqueous acetone at 0–10°, and then from chloroform-hexane, yielding light yellow crystals, m.p. 126–127.5°.

Anal. Calcd. for $C_{10}H_5N_2SO_6Cl$: S, 10.1. Found: S, 10.2.

Conversion of the sulfonyl chloride to 1,3,7-trichloronaphthalene. The sulfonyl chloride was mixed with five times its weight of phosphorus pentachloride and heated to 175–180° for 2 hr. It was then cooled, hydrolyzed, and the semisolid material steam distilled for several hours. The solid product in the distillate was filtered, washed, and dried and the infrared spectrum taken and compared with that of authentic 1,3,7-trichloronaphthalene. These were found to be the same.

3,7-Diaminonaphthalene 1-sulfonic acid monohydrochloride (from the dinitrosulfonic acid I). The sodium salt of I was dissolved in hot 1*N* hydrochloric acid and three times its weight of stannous chloride added. The solution was boiled for 1 hr. with concentration to one-third of the original volume. On cooling, a paste of crystalline product formed, which was filtered and washed with 9*N* hydrochloric acid. After recrystallization from 9*N* hydrochloric acid, it formed a white crystalline powder.

From 7-amino-3-nitronaphthalene-1-sulfonic acid (II). The starting material (II) was prepared and separated from its isomers as Blangey describes.[4] It was reduced by stannous chloride as outlined above for the dinitro acid. The sparingly soluble nitroamino acid slowly dissolved as the reduction proceeded and the diamino acid hydrochloride was isolated as before.

Anal. Calcd. for $C_{10}H_{11}N_2SO_3Cl$: Cl, 12.9. Found: Cl, 13.1. The infrared spectra of the two samples were identical.

Acknowledgment. The author is indebted to W. Morgan Padgett II, Dietrich Heinritz, and Mrs. Dobbie Roisen for consultations, spectral measurements and analytical determinations, and to Dr. J. Hyman for encouragement during this work. Thanks are also due to H. P. C. Lee for technical assistance.

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The Synthesis of Some Pyridylpyridazines and -pyrimidines[1]

WALTER A. BUTTE AND FRANCIS H. CASE

A previous report from this laboratory[2] described the preparation of 2,4,6-tris(2′-pyridyl)-*s*-triazine (I). The arrangement of nitrogen atoms in this molecule resembles that in 2,6-bis(2′-pyridyl)-pyridine (II) and other workers[3] have demonstrated that like the latter it forms stable coordination compounds with transition metal ions. This analogy can be extended to ring systems containing two nitrogens. Goodwin and Lions[4] have prepared the structurally related 2,3,5,6-tetrakis(2′-pyridyl)pyridine (III) and studied its chelate salts. This paper describes the synthesis of pyrimidines and pyridazines which are similarly substituted with 2-pyridyl groupings on the carbons adjacent to the nitrogen atoms.

The condensation of amidines with β-ketonic esters, which is perhaps the most general route to substituted pyrimidines, was adapted to the preparation of pyridyl-substituted pyrimidines.

(1) This work was supported by a grant (G 2162) from the National Science Foundation.
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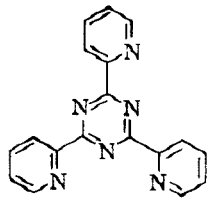
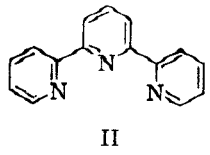
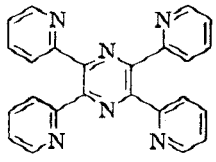


I

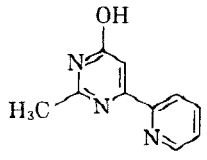


II

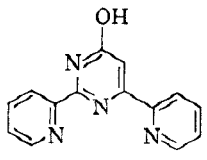


III

Thus, ethyl picolinoylacetate was condensed with acetamidine and with picolinamidine to provide 2 - methyl - 4 - (2′ - pyridyl) - (IV) and 2,4 - bis-(2′-pyridyl)-6-hydroxypyrimidine (V), respectively.

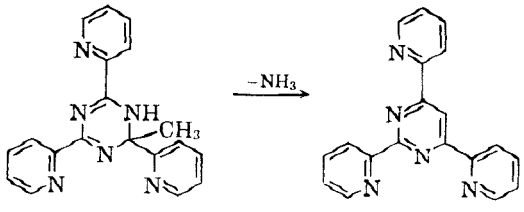


IV



V

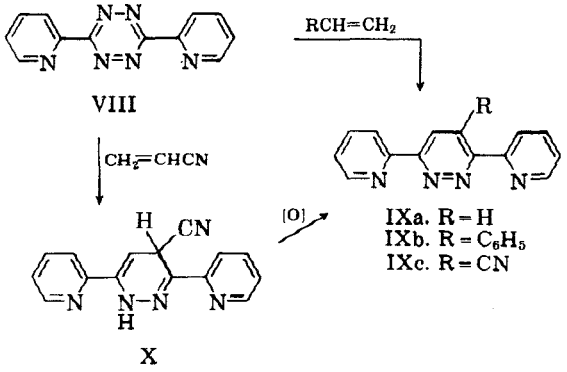
An interesting rearrangement has been reported by Anker and Cook[5] in which alkyldihydrotriazines evolve ammonia at elevated temperatures and are converted to pyrimidines. In this laboratory an analogous rearrangement was carried out leading to the formation of 2,4,6-tris(2′-pyridyl)-pyrimidine (VII). This required the preparation of 2,4,6-tris(2′-pyridyl)-2-methyl-1,2-dihydrotriazine (VI). This intermediate, together with a small amount of I, resulted from the reaction of methyl lithium with 2-cyanopyridine. Upon heating, VI lost ammonia and was smoothly transformed to VII.



VI VII

The reaction of 1,2,4,5-tetrazines bearing strongly electrophilic substituents with unsaturated compounds has been shown[6] to produce pyridazines. In this laboratory this reaction was successfully applied to the preparation of some 2,6-bis(2′-pyridyl)pyridazines. The starting material, 2,6-bis(2′-pyridyl)-1,2,4,5-tetrazine (VIII), was prepared by us by the action of hydrazine on 2-cyanopyridine followed by oxidation with nitric acid. Before the results had been published, the preparation of this intermediate was reported by Dallacker[7] from the reaction of 2-cyanopyridine hydrochloride with hydrazine in the presence of Raney nickel followed by oxidation.

The electron withdrawing power of the pyridyl groupings was sufficiently great to make the 3- and 6-carbon atoms of VIII readily susceptible to attack by nucleophilic unsaturates. Thus, VIII reacted with acetylene and phenylacetylene providing 3,6-bis(2′-pyridyl)pyridazine (IXa) and its 4-phenyl derivative (IXb), respectively. With acrylonitrile, VIII formed a dihydro derivative (X) which was oxidized to 3,6-bis(2′-pyridyl)-4-cyanopyridazine (IXc).



VIII

IXa. R = H
IXb. R = C_6H_5
IXc. R = CN

X

The pyridylpyrimidines and pyridylpyridazines described here, as well as the pyridyltetrazine (VIII), formed intensely colored chelates when added to aqueous-alcoholic ferrous ammonium sulfate. A more detailed report on the chelating properties of these compounds will be published later.

EXPERIMENTAL

2-Methyl-4-(2′-pyridyl)-6-hydroxypyrimidine (IV). Sufficient ethanol was added to 1.93 g. of ethyl picolinoylacetate,[8] 0.94 g. of acetamidine hydrochloride and 10 ml. of 4% aqueous sodium hydroxide to produce a homogeneous mixture. The solution was left standing for 48 hr. and was then concentrated to one half of the original volume. Upon cooling, a copious precipitate of felt-like needles separated which were recrystallized from absolute alcohol giving 1.2 g. (64%) of colorless needles, m.p. 268–269°.

Anal. Calcd. for $C_{10}H_9N_3O$: C, 64.16; H, 4.85. Found: C, 63.67; H, 4.82.

2,4-Bis(2′-pyridyl)-6-hydroxypyrimidine (V). An ice-cold solution of 6 g. of 2-cyanopyridine and 3 ml. of ethanol in 50 ml. of chloroform was saturated with dry hydrogen chloride. After standing overnight, the solid imino ether hydrochloride had separated. The mixture was shaken with cold, concentrated alkali. The solvent was recovered by distillation and the residual oil was dissolved in 40 ml. of 75% ethanol containing 3 g. of ammonium chloride. After heating for 3 hr. at incipient reflux, the cooled solution was diluted with 50 ml. of acetone. The insoluble material was

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removed by filtration, the acetone was recovered and 3.9 g. of ethyl picolinoylacetate was added. After 48 hr., the solution was concentrated to 30 ml., cooled, and filtered. A crystalline solid was obtained which was recrystallized from dilute ethanol providing 0.4 g. (8% based on ethyl picolinoylacetate) of colorless needles, m.p. 222.5–223.0°.

Anal. Calcd. for $C_{14}H_{10}N_4O$: C, 67.18; H, 4.03. Found: C, 67.25; H, 4.37.

2-Methyl-2,4,6-tris(2'-pyridyl)-1,2-dihydro-s-triazine (VI). A solution of 3.1 ml. of methyl iodide in 10 ml. of ether was added dropwise to a suspension of 1.1 g. of lithium metal in 10 ml. of anhydrous ether. The resulting solution was siphoned through a tube containing a glasswool plug into 20 g. of 2-cyanopyridine. Cooling was necessary in order to control the rapid exothermic reaction which ensued. Excess chopped ice was added and the insoluble material was removed by filtration to give 0.4 g. of a colorless solid, m.p. 243–244°, undepressed by admixture with an authentic sample of tris(2'-pyridyl)-s-triazine trihydrate (I).[6]

The aqueous portion of the filtrate was extracted with 60 ml. of ether. The combined ethereal solutions were dried over potassium sulfate and concentrated to 30 ml. Upon standing, a crystalline, yellow solid separated which was recrystallized from petroleum ether (b.p. 90–100°) yielding 3.7 g. of pale yellow solid, m.p. 163.0–163.5°.

Anal. Calcd. for $C_{19}H_{16}N_6$: C, 69.49; H, 4.91. Found: C, 69.97; H, 5.10.

2,4,6-Tris(2'-pyridyl)pyrimidine (VII). When 1.0 g. of VI was heated to 300°, ammonia was rapidly evolved. The resulting residue was recrystallized from methanol to give 0.71 g. (76%) of colorless needles, m.p. 255.5–256.5°.

Anal. Calcd. for $C_{19}H_{13}N_5$: C, 73.30; H, 4.21. Found: C, 73.75; H, 4.31.

3,6-Bis(2'-pyridyl)-1,2,4,5-tetrazine (VIII) was prepared by a modification of the procedure subsequently reported by Dallacker.[7] A solution of 10.4 g. (0.1 mole) of 2-cyanopyridine and 13.4 g. (0.4 mole) of 95% hydrazine in 50 ml. of absolute ethanol was refluxed gently for 6 hr. The resulting orange precipitate was removed and recrystallized from ethanol providing 9.1 g. (76%) of the dihydro base, large yellow needles, m.p. 193–194° (lit.,[7] m.p. 194.2°).

The dihydro base obtained above was dissolved in 50 ml. of glacial acetic acid, and 8.0 ml. of concentrated nitric acid was added dropwise with cooling. Excess chopped ice was added and the mixture was made distinctly alkaline by the addition of sodium bicarbonate. The crystalline precipitate was separated and washed with ethanol to give 5.5 g. (64%) of VIII, a deep red solid, m.p. 222° dec. (lit.,[7] m.p. 224.5°).

3,6-Bis(2'-pyridyl)pyridazine (IXa). Acetylene was slowly bubbled through refluxing dimethylformamide containing 1.0 g. of finely divided VIII. The disappearance of the red color indicated the completion of the reaction. The solvent was recovered by distillation and the solid residue was recrystallized from absolute ethanol producing 0.79 g. (84%) of colorless needles, m.p. 179–180°.

Anal. Calcd. for $C_{14}H_{10}N_4$: C, 71.78; H, 4.30. Found: C, 71.80; H, 4.35.

3,6-Bis(2'-pyridyl)-4-phenylpyridazine (IXb). One gram of VIII was added to a solution of 0.50 g. of phenylacetylene in 25 ml. of toluene. The resulting mixture was refluxed overnight. After this time the red color of the tetrazine had disappeared. The solid residue which remained after recovery of the solvent was recrystallized from ethanol to give 0.90 g. (68%) of colorless needles, m.p. 177.5–178.5°.

Anal. Calcd. for $C_{20}H_{14}N_4$: C, 77.40; H, 4.55. Found: C, 77.24; H, 4.66.

3,6-Bis(2'-pyridyl)-4-cyano-1,4-dihydropyridazine (X). A procedure identical with that just outlined above was used except that acrylonitrile was used in place of phenylacetylene. From 1.6 g. of VIII and 1.1 g. of acrylonitrile was obtained 1.2 g. (68%) of yellow needles, m.p. 137–138°.

Anal. Calcd. for $C_{15}H_{11}N_5$: C, 68.95; H, 4.24. Found: C, 68.81; H, 4.29.

3,6-Bis(2'-pyridyl)-4-cyanopyridazine (IXc). A solution of 0.18 g. of potassium dichromate in 1.5 ml. of water was added to 0.42 g. of X in 7.5 ml. of glacial acetic acid. The mixture was refluxed gently for 1 hr. and then was neutralized with concentrated aqueous ammonia. The resulting precipitate was recrystallized from ethanol, providing 0.21 g. (54%) of pale yellow needles, m.p. 206–207°.

Anal. Calcd. for $C_{15}H_9N_5$: C, 69.49; H, 3.50. Found: C, 69.80; H, 3.44.

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On the Generality of the Hammett Equation

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Hine has shown that a check of the general applicability of the Hammett equation is the constancy of the σ-difference ratio

$$\frac{\sigma_{p-x_1} - \sigma_{p-x_2}}{\sigma_{m-x_1} - \sigma_{m-x_2}}$$

where the σ's are substituent constants for x_1 and x_2 groups in the *meta* or *para* position.[2] Using the σ-constants for $-NO_2$, $-OCH_3$, $-F$, and $-CH_3$ groups as examples it was concluded that with the presently known σ-values "the unmodified Hammet equation could not possibly fit the equilibrium constants of *m*- and *p*-substituted benzene derivatives in general." This conclusion applies to direct substitution on the aromatic ring. It has generally been assumed that the Hammett equation may be applicable to many, if not all, equilibria involving only side-chain reactions although practically all of the equilibria which are known[3] to follow the Hammett equation are simply ionization equilibria. Hine's criterion provides a means to test the generality of the Hammett equation as applied to side chains.

In order to apply Hine's criterion to equilibria involving only side chain reactions it is necessary in computing the σ-difference ratio to use only σ-constants for substituents having the same atom attached to the aromatic ring. As the σ-difference ratio represents the slope of the line joining two points in a plot of σ_p vs. σ_m, plots were made for all of the values obtained from the dissociation constants of benzoic acids where data were available for at least two points.[4,5] Fig. 1 shows the results.

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(4) Sigma constants from D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 23, 420 (1958).