troleum (b.p. 60–80°); they can be readily crystallized from benzene or toluene.

Action of Nitric Acid on: (A) 1,3-Diphenyl-1,3-dihydroxyindane-2-one Oxime (IXa).—A mixture of 0.5 g. of IXa, 10 ml. of concentrated nitric acid (d. 1.42) and 20 ml. of water was refluxed for two hours. A light-yellow oil was formed which, after cooling, solidified to yield 0.31 g. of material. This was crystallized from benzene–light petroleum (b.p. 50–60°) to give colorless crystals, m.p. 147°, which were identified as *o*-dibenzoylbenzene (m.p. and mixed m.p. with an authentic sample).

(B) **Triketoindane-2-oxime (VIII).**—One-half gram of VIII was treated with nitric acid as described above for IXa. The reaction mixture was allowed to evaporate on a steam-bath and the solid residue was washed with ether (30 ml.); the ether-insoluble fraction was crystallized from water and identified as phthalic acid (0.14 g.) by its m.p., mixed m.p. and the phthalein reaction. On evaporation, the ether washings gave an oil which solidified on treatment with cold light petroleum (b.p. 50–60°); the solid was crystallized from a mixture of benzene and ether to yield 0.24 g. of colorless crystals, m.p. 143–4°, which were identified as phthalonic acid[21] (m.p. and mixed m.p.).

(C) **Triketohydrindane Hydrate (Ninhydrin).**—One gram of the trione was refluxed with nitric acid as described above. The reaction mixture gave, on evaporation, a solid residue (0.34 g.) which proved to be phthalic acid (m.p. and mixed m.p.).

Action of Hydroiodic Acid on IXa.—A solution of 1 g. of IXa in a mixture of 15 ml. of hydroiodic acid (d. 1.7) and 30 ml. of glacial acetic acid, was refluxed for three hours. The cooled reaction mixture was poured onto ice; the solid that separated was filtered off, washed with water, and crystallized from acetic acid to yield 0.51 g. of colorless crystals, m.p. 169°. The compound was identified as 1,3-diphenylindane-2-one (m.p. and mixed m.p. with an authentic sample[14]).

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[21] J. Tcherniac, *J. Chem. Soc.*, **109**, 1236 (1916).

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[CONTRIBUTION FROM THE LILLY RESEARCH LABORATORIES, ELI LILLY AND CO.]

The Willgerodt Reaction Applied to α- and γ-Alkylpyridines

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It is known that the chemical reactivities of α- and γ-alkylpyridines closely resemble those exhibited by alkyl ketones. It was of interest, therefore, to investigate the possibility that such alkylated pyridines could participate in the Willgerodt reaction. Further, the successful conversion of α- and γ-alkylpyridines to thioamides would involve only oxidative steps; the absence of easily reducible functional groups precludes the occurrence of the Willgerodt reaction by the route of King and McMillan.[1]

The reaction of γ-picoline with sulfur has been thoroughly investigated by Thayer and Corson[2]; the products so obtained are 1,2-di-(4-pyridyl)-ethane, 1,2-di-(4-pyridyl)-ethylene, 1,2,3-tri-(4-pyridyl)-propane, 1,2,3,4-tetra-(4-pyridyl)-thiophene and hydrogen sulfide. The yield of the thiophene derivative is markedly enhanced by the addition of alkali to the reaction mixture.

Recently, Emmert and Groll[3] have discovered that the reaction of α-picoline with sulfur does not give products corresponding to those obtained from γ-picoline; instead a compound $C_{36}H_{24}N_6S_2$ was isolated and its structure elucidated. Further, they[4] report that the reaction of α-picoline, sulfur and either nitrobenzene or aniline gives thiopicolinanilide and 2-(2-pyridyl)-benzothiazole. This final observation prompts the disclosure of the results of an investigation underway in our laboratories.

We have found that thioamides are produced by the reaction of either α- or γ-picoline with sulfur in the presence of an amine. When morpholine was the amine utilized, γ-picoline produced thioisonicotinoyl morpholine in 40% yield while α-picoline produced thiopicolinoyl morpholine in 22% yield. In each case an unidentified sublimate appeared in the condenser. Because of this complication, a further study was made using the picolines, sulfur and aniline. α-Picoline proved to be the most reactive producing the desired thioanilide[4] in 63% yield after twelve hours of heating in an oil-bath maintained at 160°. To obtain a comparable yield with γ-picoline, the oil-bath temperature was increased to 180° and the reaction time prolonged to 24 hours. However, the product isolated proved to be 2-(4-pyridyl)-benzothiazole; this may be regarded as being derived from the expected thioisonicotinanilide by further oxidation with sulfur and ring closure. The supposition that the methyl group must be in an activated position for reaction to take place is supported both by the observation that β-picoline survived attack to the extent of 79% after 24 hours and by the fact that no thionicotinanilide, or related product, could be isolated from the reaction mixture.

The success of the reaction with α- and γ-picolines encouraged us to investigate the reaction with the higher homologs, 4-ethyl- and 4-propylpyridines. The reaction of morpholine with 4-ethylpyridine and sulfur produced the anticipated thiomorpholide; the reaction of aniline with 4-propylpyridine and sulfur produced a benzothiazole derivative in analogy with the reaction of γ-picoline with the same reagents. Although these observations are highly encouraging from the standpoint of expanding the usefulness of the Willgerodt procedure to include compounds containing activated alkyl substituents, it is realized that the products may have arisen *via* the olefin route[5] involving initial dehydrogenation to 4-vinylpyridine and 1-(4-pyridyl)-propene-1, respectively.

The exact limits of the usefulness of this extension of the Willgerodt reaction cannot now be defined. The results of our experiments suggest that the alkyl group must be highly activated in order to

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[1] J. A. King and F. H. McMillan, THIS JOURNAL, **68**, 632 (1946).

[2] H. I. Thayer and B. B. Corson, *ibid.*, **70**, 2330 (1948).

[3] B. Emmert and M. Groll, *Chem. Ber.*, **86**, 205 (1953).

[4] B. Emmert and M. Groll, *ibid.*, **86**, 208 (1953).

[5] M. Carmack and D. F. DeTar, U. S. Patent 2,495,567 (January 24, 1950).

obtain a reasonable yield of thioamide under the Kindler[6] conditions. However, Naylor[7] has recently demonstrated that toluene can be converted to benzamide by the action of sulfur and aqueous ammonia at pressures in the neighborhood of 1500 lb./sq. in. and at a temperature of about 270°. Under similar conditions, cumene gives both α-methyl phenylacetamide and phenylacetamide. Naylor's yields, although low, clearly indicate that the Willgerodt reaction is more general than previously believed; further, it indicates that our understanding of the mechanism of the Willgerodt reaction remains inadequate.

Experimental[8]

Thioisonicotinoyl Morpholine.—A suspension of 96.2 g. (3.0 g. atom) of sulfur in a mixture of 93.1 g. (1.0 mole) of γ-picoline and 130.7 g. (1.5 mole) of morpholine was heated at 170°, under an 80-cm. condenser, for 12 hours. Hydrogen sulfide was evolved and a sublimate appeared in the condenser. (On this scale, a water cooled condenser became plugged with sublimate and an explosion resulted.) The cooled reaction mixture was diluted with 500 ml. of absolute alcohol. The small black needles that separated on cooling were collected by filtration and the product was recrystallized from 2 l. of absolute alcohol (Norite); yield 66.2 g. Concentration of the mother liquors and the repeated extraction of the resultant black tar with *n*-hexane (Skellysolve B) produced an additional 20.5 g. of less pure material. Recrystallization of the combined crops from *n*-hexane (the thiomorpholide was divided into several portions; the filtrate obtained after the recrystallization of the first portion was used as the solvent for the second portion, and so on) produced 83.1 g. (40%) of thioisonicotinoyl morpholine, m.p. 141–147°. The analytical sample, obtained by a further recrystallization from *n*-hexane and two recrystallizations from absolute ethanol, melted at 149–151°.

Anal. Calcd. for $C_{10}H_{12}N_2OS$: C, 57.67; H, 5.81; N, 13.45; S, 15.39. Found: C, 57.51; H, 6.10; N, 13.16; S, 15.24.

Thiopicolinoyl Morpholine.—A suspension of 96.2 g. (3.0 g. atom) of sulfur, 93.1 g. (1.0 mole) of α-picoline and 130.7 g. (1.5 moles) of morpholine was heated at 150°, under an 80-cm. condenser, for 14 hours. Hydrogen sulfide was evolved and a white sublimate appeared in the condenser. The cooled reaction mixture was diluted with 1.5 l. of benzene and 3 l. of boiling *n*-hexane. After the separation of tar, the supernatant liquid was cooled to give blunt yellow needles; wt. 13.3 g.; m.p. 103–105°. The preceding tars and mother liquors were combined and concentrated to dryness *in vacuo*. The residue gave an additional 33.4 g. of product by repeated extraction with boiling *n*-hexane. The combined yield of 46.7 g. corresponds to 22% of theoretical. The analytical sample, prepared by recrystallization from 500 parts of *n*-hexane, formed yellow platelets; m.p. 104–106°.

Anal. Calcd. for $C_{10}H_{12}N_2OS$: N, 13.45; S, 15.39. Found: N, 13.61; S, 15.23.

Thiopicolinanilide.[4]—A suspension of 96.2 g. (3.0 g. atom) of sulfur, 93.1 g. (1.0 mole) of α-picoline and 139.7 g. (1.5 mole) of aniline was heated in an oil-bath, maintained at 160°, for 12 hours. Unreacted α-picoline and aniline were removed by distillation *in vacuo*. (Redistillation of this mixture produced 22.4 g. (25% recovery) of α-picoline, and 65.8 g. (47% recovery) of aniline.) A total of 19.0 g. (19.7% recovery) of sulfur was obtained, in two crops, by solution of the residue remaining in the still pot in 1500 ml. of boiling absolute ethanol and cooling. Distillation of the ethanol soluble material produced 149.5 g. of thiopicolinanilide, b.p. 188–198° (3–4 mm.). Recrystallization of the distillate from *n*-hexane–benzene produced 134.1 g. (63%) of material melting at 44–47°. Three recrystallizations from *n*-hexane raised the melting point to 50–51°; the reported melting point[4] is 51–52°.

2-(4-Pyridyl)-benzothiazole.—A suspension of 96.2 g. (3.0 g. atom) of sulfur, 93.1 g. (1.0 mole) of γ-picoline and 139.7 g. (1.5 moles) of aniline was heated under reflux, in an oil-bath maintained at 180°, for 24 hours. The unreacted γ-picoline and aniline, separated from the reaction mixture by distillation *in vacuo*, was redistilled to yield 24.8 g. (26.5% recovery) of γ-picoline and 47.6 g. (24% recovery) of aniline. Continuing the vacuum distillation produced 137.0 g. of crude 2-(4-pyridyl)-benzothiazole, b.p. 198–210° (6–7 mm.). The distillate, on recrystallization from absolute ethanol, gave 114.1 g. (53%) of lemon yellow needles, m.p. 126–130°. The analytical sample, prepared by two recrystallizations from *n*-hexane, melted at 131.5–133°.

Anal. Calcd. for $C_{12}H_8N_2S$: C, 67.89; H, 3.80; N, 13.20; S, 15.10. Found: C, 68.18, 68.15; H, 3.68, 4.06; N, 13.55, 12.67; S, 14.82, 15.07.

The benzothiazole structure is supported by the infrared spectra, determined in chloroform. Typical NH stretching bands in the 2.9–3.0 μ region are absent; the major bands present in the 6–9 μ region are similar to the bands of 2-phenylbenzothiazole and pyridine.

Reaction of β-Picoline, Sulfur and Aniline.—A suspension of 96.2 g. (3.0 g. atom) of sulfur; 93.1 g. (1.0 mole) of β-picoline and 139.7 g. (1.5 mole) of aniline was heated under vigorous reflux, using an oil-bath maintained at 200°, for 24 hours. Dilution of the reaction mixture with an equal volume of absolute ethanol caused 33.9 g. (35% recovery) of sulfur to separate. Distillation of the ethanol-soluble material produced 73.5 g. (79% recovery) of β-picoline, and 77.5 g. (55% recovery) of aniline. Due to excessive decomposition, it was not possible to continue the distillation *in vacuo*, attempts to isolate crystalline material from the 105.5 g. of tarry residue by extraction with either alcohol or *n*-hexane were not successful.

4-Pyridylthioacetmorpholide.—A suspension of 9.6 g. (0.3 g. atom) of sulfur in 10.7 g. (0.1 mole) of 4-ethylpyridine,[9] and 13.1 g. of morpholine was heated under reflux for eight hours in an oil-bath maintained at 160°. The cooled reaction mixture crystallized on standing for two days. The product was dissolved in the minimum quantity of boiling absolute alcohol; the black rosettes that separated on cooling were collected by suction filtration; yield 7.7 g. The mother liquors were concentrated to dryness and the residue was extracted with 2 l. of boiling *n*-hexane in small portions. Concentration of the extracts and recrystallization of the residue from absolute ethanol produced an additional 5.6 g. of material. The combined crops were recrystallized from *n*-hexane to give 11.1 g. (50%) of light yellow needles, m.p. 97–99°. Repeated recrystallization from benzene, *n*-hexane raised the melting point to 102–103.5°. A mixed melting point with an authentic sample, m.p. 102–104°, prepared from 4-acetylpyridine by the method of Malan and Dean,[10] was 102–104°.

2-(β-4-Pyridylethyl)-benzothiazole.—4-*n*-Propylpyridine was prepared by the method of Tschitschibabin[11]; b.p. 184–187° (740 mm.), $n^{25}D$ 1.4932. A solution formed from 9.6 g. (0.3 g. atom) of sulfur, 12.1 g. (0.1 mole) of 4-*n*-propylpyridine and 14.0 g. (0.15 mole) of aniline was heated, in an oil-bath maintained at 180°, for 24 hours. After the removal of unreacted γ-propylpyridine and aniline by distillation *in vacuo*, a fraction, b.p. 187–196° (2 mm.) was collected. Upon recrystallization from *n*-hexane, the yellow granules so obtained melted at 74–77°; wt. 5.4 g. (22.5%). The analytical sample, purified by four recrystallizations from *n*-hexane, melted at 81.5–83°.

Anal. Calcd. for $C_{14}H_{12}N_2S$: C, 69.97; H, 5.03; N, 11.66; S, 13.34. Found: C, 69.75, 70.03; H, 4.91, 5.25; N, 11.60, 11.48; S, 12.99, 13.23.

The benzothiazole structure is supported by the infrared spectra, determined in chloroform, showing the absence of typical NH stretching bands in the 2.9–3.0 μ region and by the general similarity of the bands in the 6–9 μ region to the major bands of 2-methylbenzothiazole and pyridine.

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(6) K. Kindler and T. Li, *Ber.*, **74B**, 321 (1941).

(7) M. A. Naylor, U. S. Patent 2,610,980 (September 16, 1952).

(8) All melting points and boiling points are uncorrected. The author is indebted to Mr. W. L. Brown, H. L. Hunter, W. J. Schenck and G. M. Maciak for microanalytical data and to Dr. H. E. Boaz for infrared spectra and interpretation.

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(11) A. E. Tschitschibabin, *Bull. soc. chim. France*, [5] **3**, 1607 (1936).