

Daniel L. Comins* and Nathan B. Mantlo

Department of Chemistry and Biochemistry,
Utah State University, Logan, Utah 84322

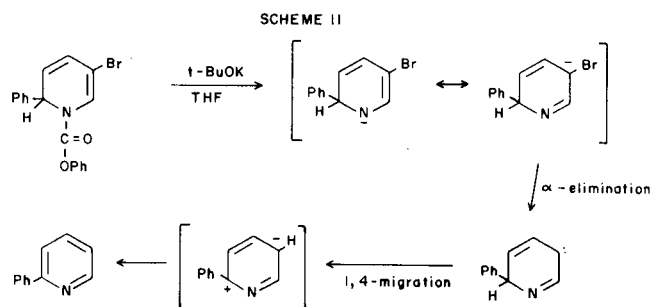
Received December 23, 1982

The addition of aryl Grignard reagents to the 1-phenoxy-carbonyl salt of 3-bromopyridine affords 2-aryl-5-bromo-1-phenoxy-carbonyl-1,2-dihydropyridines and 4-aryl-3-bromo-1-phenoxy-carbonyl-1,4-dihydropyridines. The crude dihydropyridines were aromatized with *o*-chloranil in refluxing toluene to give 4- and 6-aryl-3-bromopyridines. The regioselectivity of this two-step process, 6- vs. 4-substitution, was examined and found to be dependent upon the structure of the Grignard reagent. Unhindered aryl Grignard reagents, *e.g.*, phenyl and 2-naphthyl, gave mainly 6-aryl-3-bromopyridines (49-52%) along with 9% of the 4-substituted isomer and less than 4% of the 2-aryl-3-bromopyridine. Hindered aryl Grignard reagents, *e.g.*, *o*-tolyl and 1-naphthyl, are less regioselective. When a catalytic amount of cuprous iodide is present during the Grignard reaction, nearly exclusive 1,4-addition results. The crude 4-aryl-3-bromo-1,4-dihydropyridines were aromatized with *p*-chloranil to provide 4-aryl-3-bromopyridines in good yield and high isomeric purity. The sequential use of the cuprous iodide-catalyzed Grignard reaction and the "normal" Grignard reaction provided a regioselective synthesis of 3-bromo-6-(*p*-methoxyphenyl)-4-phenylpyridine from 3-bromopyridine.

J. Heterocyclic Chem., **20**, 1239 (1983).

Although some 3-bromopyridines can be prepared by direct bromination of the pyridine nucleus, the reaction is of limited scope due to the lack of regioselectivity, polybromination of the pyridine ring, and possible bromination of substituents [1]. Most arylbromopyridines cannot be prepared by direct bromination of arylpyridines, since the aryl substituent is generally more reactive toward bromination than the electron-deficient pyridine ring. The arylation of commercially available 3-bromopyridine by reaction with an aryl Grignard or lithium reagent would be an attractive route, however metal halogen exchange predominates over addition to the azomethine bond of the pyridine nucleus [2]. Giam and Stout reported obtaining 3-bromo-6-phenylpyridine from the reaction of 1-lithio-2-phenyl-1,2-dihydropyridine with bromine [3a]. This method may be useful for the synthesis of other 6-aryl-3-bromopyridines, however, it appears that the yields may be low [3].

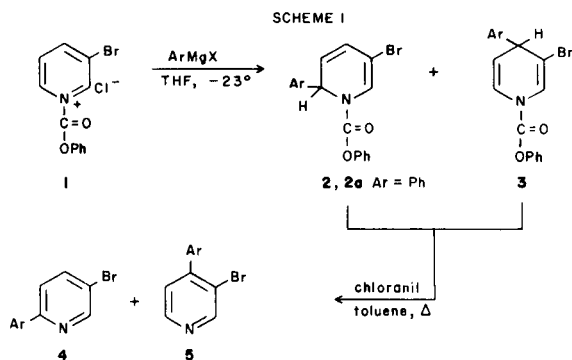
Recently, we examined in detail the synthesis of substituted pyridines *via* the addition of Grignard reagents to the 1-acylpyridinium salts of pyridine, 2-picoline, and 3-picoline. The intermediate 1-acyldihydropyridines were

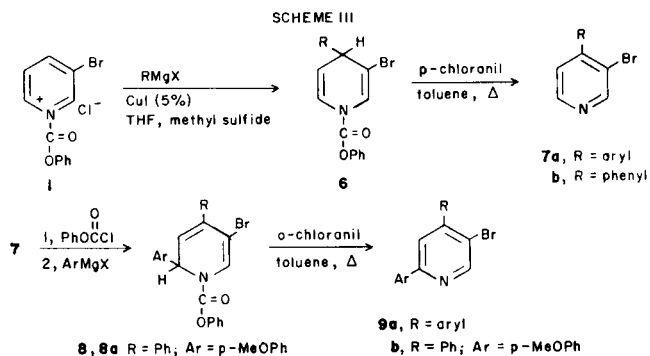


aromatized with hot sulfur to provide substituted pyridines in good yield [4]. The 1-acylpyridinium salts are so reactive toward Grignard reagents that addition to the pyridine ring will occur in the presence of other reactive functional groups (*e.g.*, esters [4] and ketones [5]). We anticipated that addition of a Grignard reagent to the azomethine bond of an 1-acylpyridinium salt would be faster than the metal-halogen exchange reaction of a bromine substituent. We have investigated this reaction and now report a regioselective synthesis of 6- (or 4-)aryl-3-bromopyridines by the reaction of aryl Grignard reagents with the 1-phenoxy-carbonyl salt of 3-bromopyridine (Scheme I).

Results and Discussion.

Initially, the reaction of phenylmagnesium chloride with various acyl salts of 3-bromopyridine was studied. When pivaloyl chloride was used as the acyl chloride, *t*-butyl phenyl ketone was isolated (90%). This result was probably due to a lack of *in situ* salt formation [6]. The use of ethyl chloroformate provided the desired product (56%), however phenyl chloroformate was the acyl chloride of choice allowing for the preparation of 5-bromo-1-phenoxy-carbonyl-2-phenyl-1,2-dihydropyridine (**2a**) in high yield (85%). The reaction was regioselective giving less than 10% (by nmr) of the isomeric 1,4-dihydropyridine **3**, Ar = Ph.





Several attempts were made to aromatize dihydropyridine **2a**. Hot sulfur, which is effective in aromatizing other 1-acyldihydropyridines [4,7], gave only intractable tar. Oxygen has been used to aromatize 1-ethoxycarbonyl-4-phenyl-1,4-dihydropyridine to 4-phenylpyridine [8]. In con-

trast, dihydropyridine **2a** was stable to an oxygen atmosphere for twelve hours while being irradiated with a 100-W bulb. The phenoxycarbonyl substituent of **2** stabilizes the dihydropyridine structure toward oxidation [9]. In an attempt to remove the 1-acyl group, dihydropyridine **2a** was treated with potassium *t*-butoxide (2.2 equivalents) in THF. Interestingly, the only pyridine isolated from this reaction was 2-phenylpyridine (55%) presumably arising *via* a carbene mechanism as shown in Scheme II.

Aromatization utilizing *o*-chloranil [10] as the dehydrogenating agent proved to be a practical route. The crude dihydropyridine **2a** and 1.1 equivalents of *o*-chloranil in refluxing toluene for six hours gave 3-bromo-6-phenylpyridine in an overall yield of 52% for the two-step sequence (Scheme I). This result prompted us to use other aryl Grignard reagents and study the scope of this synthesis with regard to regioselectivity and yield. The results of this study are given in Table I.

Table I
Synthesis of 6-Aryl-3-bromopyridines **4**

Entry [a]	ArMgX	Product [b]	Overall Yield, % 4 (5)	Mp, °C 4 [e]	¹ H NMR (deuteriochloroform) δ 4 (α-H) [f]
a	C ₆ H ₅ MgCl	3-bromo-6-phenylpyridine	52 (9) [c]	74-75 (lit [1b] 71-72.5)	8.84
b	<i>p</i> -ClC ₆ H ₄ MgBr	3-bromo-6-(<i>p</i> -chlorophenyl)pyridine	48 (5) [d]	109-110	8.84
c	<i>p</i> -CH ₃ OC ₆ H ₄ MgBr	3-bromo-6-(<i>p</i> -methoxyphenyl)pyridine	48 (11)	136.136.5	8.84
d	<i>o</i> -CH ₃ C ₆ H ₄ MgBr	3-bromo-6-(<i>o</i> -tolyl)pyridine	28 (20)	140-141 (picrate)	8.86
e	1-C ₁₀ H ₇ MgBr	3-bromo-6-(1-naphthyl)pyridine	29 (24)	68-68.5	8.96
f	2-C ₁₀ H ₇ MgBr	3-bromo-6-(2-naphthyl)pyridine	49 (9) [c]	132.5-133.5	8.92

[a] The reactions were performed on a 3-mmol scale and the products were isolated by preparative layer chromatography (silica gel) unless indicated. [b] The products from entries b-f are new compounds and their structures are consistent with all spectral and elemental analyses. [c] The yield of the minor isomer was determined by gc. [d] The yield of the minor isomer was determined by ¹H nmr analysis of the crude product mixture. [e] The melting points are for products **4** recrystallized from hexanes. [f] All the ¹H nmr signals were broad singlets exhibiting a shoulder due to *meta* coupling (*J* = 2 Hz).

Table II
Synthesis of 4-Aryl-3-bromopyridines **5**

Entry [a]	ArMgX (5 mole % CuI)	Product [b]	Overall Yield, % 5	Mp, °C [d]	¹ H NMR (deuteriochloroform) δ protons at C2, C6 [f]
a	C ₆ H ₅ MgCl	3-bromo-4-phenylpyridine	66 [c]	49-50	8.86 (s), 8.57 (d)
b	<i>p</i> -CH ₃ OC ₆ H ₄ MgBr	3-bromo-4-(<i>p</i> -methoxyphenyl)pyridine	57	77.5-78.5	8.92 (s), 8.61 (d)
c	<i>o</i> -CH ₃ C ₆ H ₄ MgBr	3-bromo-4-(<i>o</i> -tolyl)pyridine	62	49-50	8.93 (s), 8.66 (d)
d	1-C ₁₀ H ₇ MgBr	3-bromo-4-(1-naphthyl)pyridine	64	112.5-113.5 [e]	9.02 (s), 8.69 (d)
e	2-C ₁₀ H ₇ MgBr	3-bromo-4-(2-naphthyl)pyridine	63	70.5-71.5	8.96 (s), 8.69 (d)

[a] The reactions were performed on a 3-mmol scale and the products were isolated by preparative layer chromatography (silica gel) unless indicated. [b] All products are new compounds and their structures are consistent with all spectral and elemental analyses. [c] The reaction was performed on a 0.1-mol scale and the product was purified by recrystallization from hexanes. [d] The melting points are for compounds **5** recrystallized from hexanes unless indicated. [e] Recrystallized from ethanol. [f] All the ¹H nmr signals for the protons at the 6 position of the pyridine rings were doublets, *J* = 5 Hz.

Aromatization of the crude dihydropyridines (**2** and **3**) derived from unhindered aryl Grignard reagents (entries a,b,c,f of Table I) gave mainly 6-aryl-3-bromopyridines (48-52%) and small amounts of the isomeric 4-aryl-3-bromopyridines (5-11%). Minute amounts of 2-aryl-3-bromopyridines were also formed in some cases, but not isolated. The crude aromatized product from the reaction of phenylmagnesium chloride and the 1-phenoxy carbonyl salt of 3-bromopyridine contained 3-bromo-2-phenylpyridine [**11**] (3.6%) by gc analysis. Reactions of hindered aryl Grignard reagents were less regioselective, giving approximately equal amounts of 6- and 4-substitution (entries d,e). The 6- and 4-aryl-3-bromopyridines were easily separated and isolated by chromatography (silica gel).

Synthesis of 4-Aryl-3-bromopyridines.

We recently reported that a catalytic amount (5 mole %) of cuprous iodide has a major effect on the regioselectivity of the Grignard reaction with 1-acylpyridinium salts, causing nearly exclusive attack at the 4-position of the pyridine ring. Subsequent aromatization of the crude 1,4-dihydropyridines provides 4-substituted pyridines in good yield [4]. We have studied the effect of cuprous iodide (5 mole %) on the reaction of aryl Grignard reagents with the 1-phenoxy carbonyl-3-bromopyridinium salt **1** and the results are given in Table II.

The Grignard reagent was added dropwise to a solution of 3-bromopyridine, cuprous iodide (5%), and phenyl chloroformate in THF-methyl sulfide (3 equivalents) at -20° to give 1,4-dihydropyridines **3** (see Scheme I). The reaction is regiospecific, forming only trace amounts of the isomeric 1,2-dihydropyridines **2**. Aromatization of the crude 1,4-dihydropyridines (**3**) with *p*-chloranil in refluxing toluene gave 4-aryl-3-bromopyridines (**5**) in good yield. This two-step procedure is convenient and amenable to large scale preparation of 4-aryl-3-bromopyridines.

Synthesis of 3-Bromo-4,6-diaryl Pyridines.

The sequential use of the above discussed cuprous iodide-catalyzed Grignard reaction and the "normal" Grignard reaction could lead to 3-bromo-4,6-diaryl pyridines **9** as shown in Scheme III. To demonstrate this potential, 3-bromo-4-phenylpyridine (**7b**) was prepared from dihydropyridine **6** (R = Ph), treated with phenyl chloroformate and *p*-methoxyphenylmagnesium bromide to give the 5-bromo-2,4-diaryl-1,2-dihydropyridine **8a**. Aromatization with *o*-chloranil gave 3-bromo-4,6-diarylpyridine **9b** (50% from **7b**). Thus, **9b** was prepared by the diarylation of 3-bromopyridine using two aryl Grignard reagents in sequential regiospecific nucleophilic aromatic substitution reactions.

EXPERIMENTAL

Reactions involving organometallic reagents were performed in oven-dried glassware under a nitrogen atmosphere. Tetrahydrofuran (THF)

was dried by distillation from sodium benzophenone ketyl prior to use. Toluene was dried over 3 Å molecular sieves. Cuprous iodide (CuI), ultrapure, was obtained from Alfa Products. Other solvents and reagents from commercial sources were generally used without further purification.

Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are uncorrected. The ^1H nmr spectra were recorded on a Varian EM-360 spectrometer. Gas-liquid chromatography (gc) was performed with a Hewlett-Packard 5830A gas chromatograph equipped with a 30 m \times 0.25 mm FSOT column packed with OV-101.

5-Bromo-1-phenoxy carbonyl-2-phenyl-1,2-dihydropyridine (**2a**). General Procedure.

A solution of 3-bromopyridine (0.35 ml, 3.6 mmoles) in 6 ml of dry THF under nitrogen was cooled to -20° (dry ice/carbon tetrachloride). Phenyl chloroformate (0.39 ml, 3.0 mmoles) was added dropwise and the mixture was stirred at -20° for 15 minutes. A solution of phenylmagnesium chloride (3.0 mmoles) in 1.5 ml of THF was added dropwise. The mixture was stirred at -20° for 15 minutes followed by the addition of aqueous 20% ammonium chloride solution (20 ml). Ether (50 ml) was added and the organic layer was washed with 20-ml portions of 10%

aqueous hydrochloric acid (2 \times), water, and brine. After drying (magnesium sulfate), the solution was filtered and evaporated to yield 1.0 g of the crude product **2a** as a viscous oil. Purification by preparative layer chromatography (silica gel, 20% acetone-hexanes) gave 910 mg (85%) of **2a** as a clear viscous oil which crystallized on standing. The product was recrystallized from hexanes to give an analytical sample of **2a** as white needles, mp 112-112.5 $^{\circ}$; nmr (carbon tetrachloride): δ 6.80-7.72 (m, 12H), 5.42-6.28 (m, 2H); ir (potassium bromide): 1730, 1590, 1203 cm^{-1} .

Anal. Calcd. for $\text{C}_{18}\text{H}_{14}\text{BrNO}_2$: C, 60.69; H, 3.96; N, 3.93. Found: C, 60.48; H, 3.98; N, 3.91.

Reaction of Dihydropyridine **2a** with Potassium *t*-Butoxide in THF.

A solution of potassium *t*-butoxide (665 mg, 5.93 mmoles) in 8 ml of dry THF under nitrogen was cooled in an ice bath. Dihydropyridine **2a** (purified) (960 mg, 2.69 mmoles) in 2 ml of THF was added *via* a double tipped needle and the mixture was stirred at room temperature for 2 hours. Water (20 ml) and ether (50 ml) were added and the organic layer was washed with 1 *N* aqueous sodium hydroxide (20 ml) and brine. After drying (potassium carbonate), the solution was filtered and evaporated to yield 535 mg of a brown oil. Purification by preparative layer chromatography (silica gel, 10% acetone-hexanes) gave 20 mg of *t*-butyl phenyl carbonate and 230 mg (55%) of 2-phenylpyridine as a clear oil, picrate, mp 175-176 $^{\circ}$ (lit [12] mp 176-177 $^{\circ}$); the nmr spectrum was identical with the spectrum of authentic material.

3-Bromo-6-phenylpyridine by Aromatization of Dihydropyridine **2a**. General Procedure.

To a solution of crude dihydropyridine **2a** (3 mmoles) in dry toluene (20 ml) was added 811 mg (3.3 mmoles) of *o*-chloranil. The mixture was heated under reflux under nitrogen for 6 hours and cooled to room temperature. Ether (50 ml) and 25 ml of 1 *N* aqueous sodium hydroxide were added and after stirring for 15 minutes the mixture was filtered through celite. The organic layer was washed with 20-ml portions of water and brine. After drying (potassium carbonate), the solution was filtered and concentrated to yield 990 mg of a tan oil. Purification by preparative layer chromatography (silica gel, dichloromethane/hexanes) gave 370 mg (52%) of 3-bromo-6-phenylpyridine as a white solid. The product was recrystallized from hexanes to give an analytical sample of **2a**: mp 74-75 $^{\circ}$ (lit [16,3] 71-72.5 $^{\circ}$); nmr (deuteriochloroform): δ 8.86 (broad s, 1H), 7.30-8.22 (m, 7H).

Anal. Calcd. for $\text{C}_{11}\text{H}_8\text{BrN}$: C, 56.44; H, 3.44; N, 5.98. Found: C, 56.39; H, 3.53; N, 5.84.

3-Bromo-4(*o*-tolyl)pyridine. General Procedure for the Synthesis of 4-Aryl-3-bromopyridines.

A solution of 3-bromopyridine (0.35 ml, 3.6 mmoles), 30 mg of cuprous iodide, and 0.66 ml of methyl sulfide in 6 ml of dry THF was cooled to -20° (dry ice/carbon tetrachloride). Phenyl chloroformate (0.39 ml, 3.0

mmoles) was added dropwise and the mixture was stirred at -20° for 10 minutes. A solution of *o*-tolylmagnesium bromide (3.0 mmoles) in 3.0 ml of THF was added dropwise. The mixture was stirred at -20° for 15 minutes followed by the addition of 20% aqueous ammonium chloride solution (20 ml). Ether (50 ml) was added and the organic layer was washed with 20-ml portions of 20% aqueous ammonium chloride/ammonium hydroxide (50:50), water, 10% hydrochloric acid (2 \times), water and brine. The mixture was dried (magnesium sulfate), filtered, and concentrated to yield 1.1 g of a viscous yellow oil. The crude oil and 885 mg (3.6 mmoles) of *p*-chloranil in 20 ml of dry toluene was heated at reflux under nitrogen for 6 hours and then cooled to room temperature. Ether (50 ml) and 25 ml of 1*N* aqueous sodium hydroxide were added and after stirring for 15 minutes the mixture was filtered through celite. The organic layer was washed with 20-ml portions of water and brine. After drying (potassium carbonate), the solution was filtered and concentrated to yield 920 mg of a tan oil. Purification by preparative layer chromatography (silica gel, dichloromethane) gave 460 mg (62%) of 3-bromo-4(*o*-tolyl)pyridine as an oil which crystallized on standing. The product was recrystallized from hexanes to give an analytical sample, mp 49-50 $^{\circ}$; nmr (deuteriochloroform): δ 8.92 (s, 1H), 8.66 (d, 1H), 6.95-7.60 (m, 5H), 2.13 (s, 3H).

Anal. Calcd. for $C_{12}H_{10}BrN$: C, 58.09; H, 4.06; N, 5.64. Found: C, 58.07; H, 4.29; N, 5.75.

3-Bromo-4-phenylpyridine (0.1 mole scale).

In a 1-*l* three-necked flask equipped with an overhead stirrer were placed 3-bromopyridine (10.6 ml, 0.11 mole), cuprous iodide (952 mg, 5 mmoles), methyl sulfide (22 ml, 0.3 mole), and 250 ml of THF under nitrogen. The solution was cooled to -20° and 12.9 ml (0.1 mole) of phenyl chloroformate was added *via* syringe with stirring. After 5 minutes, phenylmagnesium chloride (0.1 mole) in 50 ml of THF was added dropwise over 10 minutes. The mixture was stirred for 15 minutes at -20° and then at room temperature for another 15 minutes followed by the addition of aqueous 20% ammonium chloride solution (75 ml). Ether (200 ml) was added and the organic layer was washed with 50-ml portions of 20% ammonium chloride/ammonium hydroxide (50:50), (2 \times), water, 10% aqueous hydrochloric acid, water and brine. After drying (magnesium sulfate), the solution was filtered and concentrated to yield 25.6 g of crude 5-bromo-1-phenoxy carbonyl-4-phenyl-1,4-dihydropyridine as a light yellow oil. To the crude dihydropyridine in 250 ml of dry toluene was added 29.5 g (0.12 mole) of *p*-chloranil. The mixture was heated at reflux for 10 hours under nitrogen and cooled to room temperature. An aqueous solution of 1*N* sodium hydroxide (100 ml) was added, stirred 15

minutes, and then the mixture was filtered through celite. The dark organic layer was washed with 2 \times 50-ml portions of 1*N* sodium hydroxide and water, then extracted with 4 \times 50-ml of 10% hydrochloric acid. The combined acid extracts were concentrated (roto-vap) to approximately 75 ml, cooled, made basic with 20% sodium hydroxide, and extracted with methylene chloride (3 \times 75 ml). The combined organic layer was washed with brine, dried (potassium carbonate/Norite), filtered through a Florisil pad, and concentrated to yield 18.27 g of a red oil. Bulb-to-bulb distillation (105-140 $^{\circ}$ /0.3 mm) gave 15.8 g (68%) of a white solid. Recrystallization from cold hexanes provided 15.5 g (66%) of 3-bromo-4-phenylpyridine as white crystals: mp 49-50 $^{\circ}$; nmr (deuteriochloroform): δ 8.86 (s, 1H), 8.57 (d, 1H), 7.44 (s, 5H), 7.21 (d, 1H).

Anal. Calcd. for $C_{11}H_8BrN$: C, 56.44; H, 3.44; N, 5.98. Found: C, 56.17; H, 3.57; N, 5.82.

3-Bromo-6(*p*-methoxyphenyl)-4-phenylpyridine (9b).

Using the procedure for the preparation of **2a**, 843 mg (3.6 mmoles) of 3-bromo-4-phenylpyridine, 0.39 ml (3.0 mmoles) of phenyl chloroformate, and 3.0 mmoles of *p*-methoxyphenylmagnesium bromide in 6 ml of THF gave 1.4 g of the crude dihydropyridine **8a** as a yellow oil. Treatment of crude **8a** with *o*-chloranil (3 mmoles) in refluxing toluene (12 hours) gave, after preparative layer chromatography (silica gel), 20% hexanes/dichloromethane, 505 mg (50%) of **9b** as an oil which crystallized on standing. The product was recrystallized from hexane to give an analytical sample of **9b** as white crystals, mp 105-106 $^{\circ}$; nmr (carbon tetrachloride):

δ 8.84 (s, 1H), 8.01 (d, 2H), 7.61 (s, 1H), 7.50 (s, 5H), 6.90 (d, 2H), 3.81 (s, 3H).

Anal. Calcd. for $C_{16}H_{14}BrNO$: C, 63.55; H, 4.15; N, 4.12. Found: C, 63.39; H, 4.27; N, 4.10.

The nmr spectral data and elemental analyses for the 6- and 4-aryl-3-bromopyridines from Tables I and II are reported in this section.

3-Bromo-6(*p*-chlorophenyl)pyridine.

This compound had mp 109-110 $^{\circ}$; nmr (deuteriochloroform): δ 8.84 (bs, 1H), 7.70-8.20 (m, 3H), 7.32-7.68 (m, 3H).

Anal. Calcd. for $C_{11}H_7BrClN$: C, 49.20; H, 2.63; N, 5.22. Found: C, 49.09; H, 2.79; N, 5.15.

3-Bromo-6(*p*-methoxyphenyl)pyridine.

This compound had mp 136-136.5 $^{\circ}$; nmr (deuteriochloroform): δ 8.84 (bs, 1H), 7.46-8.20 (m, 4H), 7.03 (d, 2H, $J = 9$ Hz), 3.89 (s, 3H).

Anal. Calcd. for $C_{12}H_{10}BrNO$: C, 54.59; H, 3.79; N, 5.30. Found: C, 54.63; H, 3.93; N, 5.38.

3-Bromo-6(*o*-tolyl)pyridine.

The picrate of this compound had mp 140-141 $^{\circ}$; nmr (deuteriochloroform): δ 8.86 (bs, 1H), 7.90 (d of d, 1H, $J = 2, 8$ Hz), 7.21-7.55 (m, 5H), 2.36 (s, 3H).

Anal. Calcd. for $C_{12}H_{10}BrN$: C, 58.09; H, 4.06; N, 5.64. Found: C, 57.83; H, 3.89; N, 5.70.

3-Bromo-6(1-naphthyl)pyridine.

This compound had mp 68-68.5 $^{\circ}$; nmr (deuteriochloroform): δ 8.96 (bs, 1H), 7.75-8.34 (m, 4H), 7.32-7.75 (m, 5H).

Anal. Calcd. for $C_{15}H_{10}BrN$: C, 63.40; H, 3.55; N, 4.93. Found: C, 63.26; H, 3.62; N, 4.88.

3-Bromo-6(2-naphthyl)pyridine.

This compound had mp 132.5-133.5 $^{\circ}$; nmr (deuteriochloroform): δ 8.92 (bs, 1H), 8.56 (bs, 1H), 7.80-8.32 (m, 6H), 7.45-7.80 (m, 2H).

Anal. Calcd. for $C_{15}H_{10}BrN$: C, 63.40; H, 3.55; N, 4.93. Found: C, 63.28; H, 3.64; N, 4.91.

3-Bromo-4(*p*-methoxyphenyl)pyridine.

This compound had mp 77.5-78.5 $^{\circ}$; nmr (deuteriochloroform): δ 8.92 (s, 1H), 8.61 (d, 1H, $J = 5$ Hz), 6.85-7.66 (m, 5H), 3.93 (s, 3H).

Anal. Calcd. for $C_{12}H_{10}BrNO$: C, 54.59; H, 3.79; N, 5.30. Found: C, 54.60; H, 3.94; N, 5.37.

3-Bromo-4(1-naphthyl)pyridine.

This compound had mp 112.5-113.5 $^{\circ}$; nmr (deuteriochloroform): δ 9.02 (s, 1H), 8.69 (d, 1H, $J = 5$ Hz), 7.80-8.22 (m, 2H), 7.25-7.78 (m, 6H).

Anal. Calcd. for $C_{15}H_{10}BrN$: C, 63.40; H, 3.55; N, 4.93. Found: C, 63.43; H, 3.65; N, 4.94.

3-Bromo-4(2-naphthyl)pyridine.

This compound had mp 70.5-71.5 $^{\circ}$; nmr (deuteriochloroform): δ 8.96 (s, 1H), 8.68 (d, 1H, $J = 5$ Hz), 7.72-8.20 (m, 4H), 7.30-7.72 (m, 4H).

Anal. Calcd. for $C_{15}H_{10}BrN$: C, 63.40; H, 3.55; N, 4.93. Found: C, 63.20; H, 3.77; N, 5.00.

Acknowledgement.

We wish to express appreciation to the National Institute of General Medical Sciences of the NIH for partial support of this project from Grant GM 30255. Financial assistance by a Utah State University Faculty Research Grant (Mineral Lease) Project No. FAC-SC-13 is also acknowledged.

REFERENCES AND NOTES

[1a] H. E. Mertel, "Pyridine and Its Derivatives", Vol 14, Part 2, E. Klingsberg, ed, Interscience, New York, NY, 1961, p 299; [b] M. M.

Boudakian, "Pyridine and Its Derivatives", Vol 14 supplement, Part 2, R. A. Abramovitch, ed, Wiley Interscience, New York, NY, 1974, p. 407; [c] L. van der Does and H. J. den Hertog, *Rec. Trav. Chim.*, **84**, 951 (1965); [d] L. van der Does, A. van Veldhuizen and H. J. den Hertog, *ibid.*, **93**, 61 (1974).

[2a] H. Gilman and S. M. Spatz, *J. Org. Chem.*, **16**, 1485 (1951); [b] H. H. Paradies and M. Gorbng, *Angew. Chem.*, **81**, 293 (1969); [c] H. L. Yale, "Pyridine and Its Derivatives", Vol 14 supplement, Part 2, R. A. Abramovitch, ed, Wiley Interscience, New York, NY, 1974, p. 489; [d] R. A. Abramovitch, K. S. Ahmed and C. S. Giam, *Can. J. Chem.*, **41**, 1752 (1963).

[3a] C. S. Giam and J. L. Stout, *Chem. Commun.*, 478 (1970). No yield was given for 3-bromo-6-phenylpyridine; [b] C. S. Giam, E. E. Knaus, R. A. Lockhart and I. G. Keener, *Can. J. Chem.*, **53**, 2305 (1975); [c] E. E. Knaus, T. A. Ondrus and C. S. Giam, *J. Heterocyclic Chem.*, **13**, 789 (1976).

[4] D. L. Comins and A. H. Abdullah, *J. Org. Chem.*, **47**, 4315 (1982).

[5] R. E. Lyle, J. L. Marshall and D. L. Comins, *Tetrahedron Letters*,

1015 (1976).

[6] The addition of pivaloyl chloride to phenylmagnesium chloride and pyridine in THF gives a good yield of 1,2- and 1,4-dihydropyridines; reference 4.

[7] R. E. Lyle and D. L. Comins, *J. Org. Chem.*, **41**, 3250 (1976).

[8] K-y. Akiba, Y. Iseki and M. Wada, *Tetrahedron Letters*, 429 (1982).

[9] F. W. Fowler, *J. Org. Chem.*, **37**, 1321 (1972).

[10] Chloranil has been used to aromatize dihydropyridines. [a] R. C. Fuson and J. J. Miller, *J. Am. Chem. Soc.*, **79**, 3477 (1957); [b] Y. Omote, T. Komatsu, R. Kobayashi and N. Sugiyama, *Tetrahedron Letters*, 93 (1972); [c] R. Dommissie, H. Desseyne and F. Alderweireldt, *Spectrochim. Acta*, **29**, 107 (1973).

[11] R. A. Abramovitch, K. S. Ahmed and C. S. Giam, *Can. J. Chem.*, **41**, 1752 (1963).

[12] J. W. Haworth, I. M. Heilbron and D. H. Hey, *J. Chem. Soc.*, 349 (1940).