86163-66-8; **32**, 5464-07-3; **33**, 1734-00-5; **34a**, 5959-52-4; **34b**, 21597-54-6; **35**, 29753-32-0; **36**, 86163-67-9; **37**, 29005-25-2; **40**, 91-59-8; **41**, 35051-46-8; **42**, 85601-43-0; **43**, 85601-44-1; **43** (disulfide), 109151-47-5; **44**, 109181-89-7; **46a**, 109151-49-7; **46b**, 109151-48-6; **47**, 109151-50-0; **48**, 109151-51-1; **49**, 109151-52-2; **50**, 109151-53-3; DCC, 538-75-0; *p*-nitroso-*N*,*N*-dimethylaniline, 138-89-6; chloroacetic acid, 79-11-8; 3-carboxy-2-naphthalenemercaptoacetic acid, 64289-70-9; naphtho[2,3-*b*]thiophen-3-one (5,6-benzothioindoxyl), 4735-10-8; 2-[*p*-(dimethylamino)-phenyl]iminonaphtho[2,3-*b*]thiophen-3-one, 109151-55-5.

Alkylation of Heteroaryl Halides by 2:1 Grignard Reagent/Cu(I) Mixtures. Synthesis of Alkylated Octahydrodibenzo[*b*,*j*][1,10]phenanthrolines

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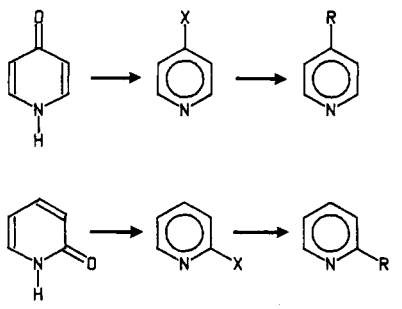
Treatment of 2-bromopyridine, 3-bromopyridine, 2-chloroquinoline, and 5,8-dichloro-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*][1,10]phenanthroline (**2**) with a fourfold excess of 2:1 Grignard reagent/Cu(I) salt mixtures gives alkylated products in 50–85% yield. Thus prepared are 2-methylpyridine, 2-*tert*-butylpyridine, 3-*tert*-butylpyridine, 2-methylquinoline, 2-ethylquinoline, 2-*tert*-butylquinoline, and the dimethyl- and di-*tert*-butylphenanthrolines **3a** and **3b**. Full experimental details are provided for the two phenanthrolines, which are prepared in four steps from *o*-phenylenediamine and ethyl 1-oxocyclohexane-2-carboxylate in 25–30% overall yield.

The preparation of C-alkylated pyridine derivatives is a frequently encountered problem in synthesis of heterocyclic natural products, pharmaceuticals, and ligands. Whereas reduced 2-alkyl- and 4-alkylpyridines are available from pyridinium species,[1] the most general method for alkylation of heterocyclic halides is reaction with Wittig reagents.[2] Since annelated pyridones (e.g. quinolones) are obtained by various condensations[3] and are readily converted into halopyridines, the alkylation of heterocyclic halides completes an effective synthetic strategy (Scheme I). Numerous methods have been applied to the direct coupling of heteroaryl halides with alkylorganometallic reagents,[4] but these procedures are not entirely general. For example, nickel and palladium catalysts often lead to elimination of secondary and tertiary Grignard reagents, accompanied by reduction of the aryl halide.[4b,c] We report here a more widely applicable method for Grignard alkylation of 2-halo, 3-halo, and 4-halo heterocycles, providing examples from the pyridine, quinoline, and 1,10-phenanthroline series.

Results

Our requirement for 5,8-dialkyl-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*][1,10]phenanthrolines as synthetic intermediates and potentially useful ligands led to the strategy outlined in Scheme II. Facile entry to the dibenzo[*b*,*j*][1,10]phenanthroline ring system is provided by Conrad–Limpach condensation of *o*-phenylenediamine with ethyl 1-oxocyclohexane-2-carboxylate, as described by Ege and Freund.[5] We have found that both steps are sensitive to reaction conditions, so complete details have been included in the Experimental Section. In particular, the neat condensation of *o*-phenylenediamine with ethyl 1-oxocyclohexane-2-carboxylate must be prolonged for weeks, if not months, to permit complete reaction. The crude intermediate is then heated at 220–230 °C in diphenyl ether, while the evolved ethanol is rapidly removed in a stream of nitrogen. This procedure affords the insoluble 1,10-phenanthroline-5,8-dione **1** in 48% overall yield. If the initial condensation step is conducted in refluxing benzene or methylene chloride then **1** does not crystallize from diphenyl ether after pyrolysis of the crude intermediate.

Scheme I



Direct treatment of diketone **1** with methyllithium, butyllithium, and Grignard reagents failed to produce significant quantities of the desired 5,8-dialkyl-1,10-phenanthrolines **3**. This necessitated a two-step alkylation procedure via a dihalide, as shown for the general case in Scheme I. We found that dichlorophenanthroline **2** could be prepared in high yield by heating **1** in phosphorus oxychloride (Scheme II). Hence, further efforts focused on

† Undergraduate research student, 1983–1985.

(1) (a) Schultz, A. G. *J. Org. Chem.* **1986**, *51*, 838–841. (b) Comins, D. L.; Mantlo, N. B. *J. Org. Chem.* **1985**, *51*, 4410–4411. Comins, D. L.; Abdullah, A. H.; Mantlo, N. B. *Tetrahedron Lett.* **1984**, *25*, 4867–4870. Comins, D. L.; Abdullah, A. H. *J. Org. Chem.* **1982**, *47*, 4315–4319. (c) Yamaguchi, R.; Nakazono, Y.; Kawanisi, M. *Tetrahedron Lett.* **1983**, *24*, 1801–1804. (d) Akiba, K.; Iseki, Y.; Wada, M. *Tetrahedron Lett.* **1982**, *23*, 3935–3936. (e) Review on dihydropyridines: Stout, D. M.; Meyers, A. I. *Chem. Rev.* **1982**, *82*, 223–243.

(2) Taylor, E. C.; Martin, S. F. *J. Am. Chem. Soc.* **1974**, *96*, 8095–8102.

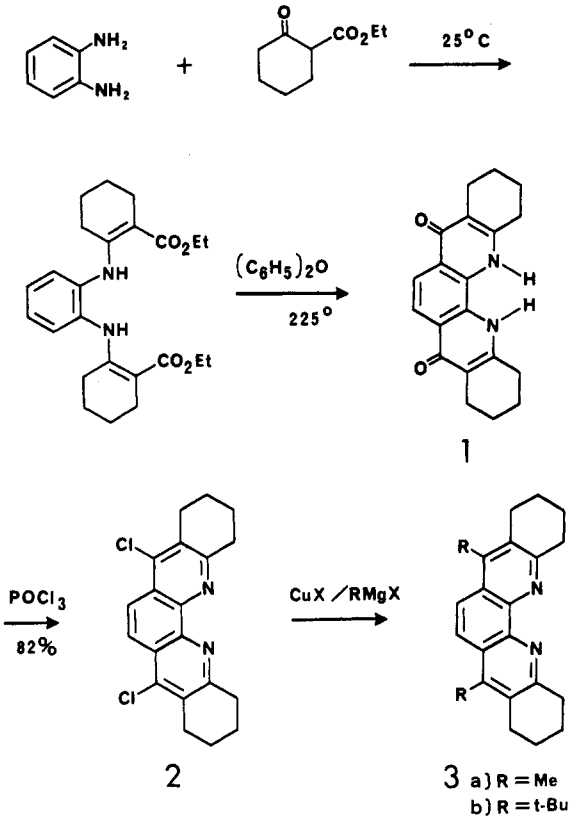
(3) Jones, G. in *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon: New York, 1984; Vol. 2, Chapter 2.08. Jones, G. In *Quinolines*; Jones, G., Ed.; Wiley: New York, 1977; Part 1, Chapter 2.

(4) (a) Negishi, E; Luo, F.-T.; Frisbee, R.; Matsushita, H. *Heterocycles* **1982**, *18*, 117–122. (b) Pridgen, L. N. *J. Heterocycl. Chem.* **1980**, *17*, 1289–1291. (c) Pridgen, L. N. *J. Heterocycl. Chem.* **1975**, *12*, 443–444. (d) Thorsett, E. D.; Stermitz, F. R. *J. Heterocycl. Chem.* **1973**, *10*, 243–244.

(5) Ege, G.; Freund, C. *Tetrahedron Lett.* **1978**, *39*, 3677–3680.

0022-3263/87/1952-3847$01.50/0

Scheme II



the alkylation of this readily available intermediate using transition-metal-catalyzed coupling of Grignard reagents. Thorsett and Stermitz[4d] and Pridgen[4b,c] have reported the use of nickel(II)–phosphine complexes as catalysts in Grignard alkylation of haloquinolines and halopyridines, respectively. We have not obtained dimethylphenanthroline **3a** by treatment of **2** with methylmagnesium bromide in the presence of catalytic quantities of dichlorobis(triphenylphosphine)nickel(II) or dichloro[1,2-bis(diphenylphosphino)ethane]nickel(II) (Ni(dppe)Cl_2), according to the literature procedures.[4b,c,6]

The sensitivity of catalytic aryl and heteroaryl coupling reactions to ligand structure[4,6] suggested that exchange between phosphine and phenanthroline ligands might account for the low reactivity of dichlorophenanthroline **2**. To test this hypothesis we treated **2** with a large excess of methylmagnesium bromide and 1.2 molar equiv of Ni(dppe)Cl_2 in THF and obtained **3a** in 40% yield. In an effort to improve the economy of this reaction we then employed 1.2 molar equiv of nickel(II) chloride and only 0.1 molar equiv of Ni(dppe)Cl_2 catalyst, leading to a 44% yield of **3a**. A further improvement was obtained (47%) when the Ni(dppe)Cl_2 was omitted entirely and replaced with 1 molar equiv of cuprous bromide! It was then discovered that nickel(II) could also be omitted when a large excess of cuprous bromide is employed. Thus, dichloride **2** was treated with a fourfold excess of methylmagnesium bromide/cuprous bromide (2:1) to yield 75% of 5,8-dimethyl-1,10-phenanthroline **3a**.

This successful alkylation of a dichlorophenanthroline with a large excess of a 2:1 mixture of methyl Grignard and copper(I) bromide led to an examination of the generality of this new procedure. We were particularly interested to

(6) Kumada, M.; Yokota, K.; Konishi, M.; Hayashi, T. *Chem. Lett.* **1980**, 767–768. Hayashi, T.; Konishi, M.; Kumada, M. *Tetrahedron Lett.* **1979**, *21*, 1871–1874.

Scheme III

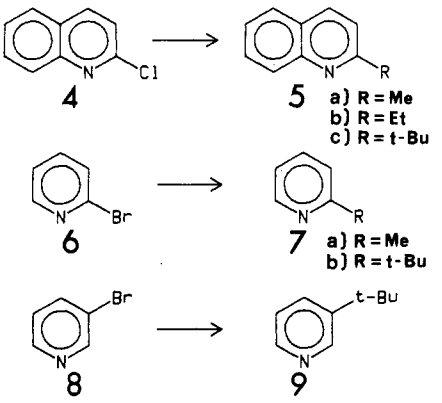


Table I. Alkylation of Heteroaryl Halides by Grignard Reagents in the Presence of Copper(I) Salts[a]

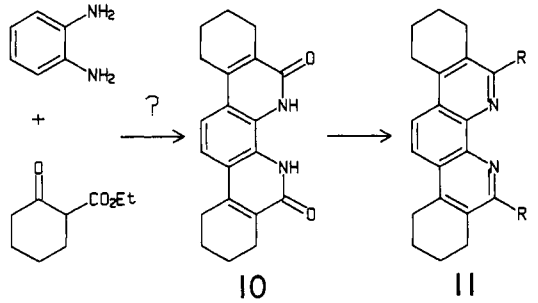
substr	reagent	Cu(I) salt	product	yield, %[b]
2	CH_3MgBr	Cu_2Br_2	**3a**	75
2	*t*-BuMgCl	Cu_2Br_2	**3b**	35
2	*t*-BuMgCl	Cu_2Cl_2	**3b**	20
2	*t*-BuMgCl	CuCN	**3b**	65
4	CH_3MgBr	Cu_2Br_2	**5a**	85
4	CH_3MgBr	CuCN	**5a**	75
4	EtMgBr	CuCN	**5b**	50
4	*t*-BuMgCl	Cu_2Br_2	**5c**	30 (47)
4	*t*-BuMgCl	CuCN	**5c**	67 (73)
6	CH_3MgBr	Cu_2Br_2	**7a**	(82)
6	*t*-BuMgCl	CuCN	**7b**	65
8	*t*-BuMgCl	CuCN	**9**	52

[a] All reactions were conducted in THF at −78 °C to room temperature, by employing a fourfold excess of a 2:1 mixture of Grignard reagent and Cu(I) salt. [b] Yields are for isolated products, except those given in parentheses, which were determined by GC analysis (see Experimental Section).

determine whether other Grignard reagents, other copper salts, and other substrates, such as haloquinolines and pyridines (Scheme III), could be employed. The more pertinent results of this survey are summarized in Table I. Importantly, *tert*-butylmagnesium chloride also alkylates dichlorophenanthroline **2**, although the yield of di-*tert*-butylphenanthroline **3b** is about half that of the methylation product (**3a**). Replacement of cuprous bromide with cuprous chloride led to a further drop in yield, whereas cuprous cyanide afforded the di-*tert*-butylphenanthroline in 65%, which is much closer to the methylation yield. The alkylation of 2-chloroquinoline, 2-bromopyridine, and 3-bromopyridine by 2:1 mixtures of Grignard reagents and copper(I) salts also proceeded in useful yields, as indicated in Table I. Comparing counterion effects in the case of 2-chloroquinoline (**4**), cuprous bromide gave a slightly higher yield of the methylation product, quinaldine (**5a**), whereas cuprous cyanide gave a far better yield of 2-*tert*-butylquinoline (**5c**). Also obtained were 2-ethylquinoline (**5b**) from 2-chloroquinoline, as well as 2-picoline (**7a**) and 2-*tert*-butylpyridine (**7b**) from 2-bromopyridine (**6**) and 3-picoline (**9**) from 3-bromopyridine. In some of these cases we found that alkylation yields dropped considerably when only a twofold excess of the 2:1 reagent mixture was used. Moreover, treatment of dichlorophenanthroline **2** with lithium cuprates, such as Me_2CuLi or Me_3CuLi_2,[7] or copper-free Grignard reagents gave no significant quantities of the dialkylphenanthrolines **3** under similar conditions. Tetrakis(triphenylphosphine)palladium(0) also failed to catalyze

(7) Clive, D. L. J.; Farina, V.; Beaulieu, P. L. *J. Org. Chem.* **1982**, *47*, 2572–2582.

Scheme IV



the reaction of **2** with *tert*-butylmagnesium chloride in the presence of $NiCl_2$ and $ZnCl_2$.[4a]

We have assumed that the structure of phenanthrolinedione **1** is correct as drawn, as reported,[5] and as predicted by the regioselectivity conventionally exhibited by the Conrad-Limpach reaction. On the other hand, the Knorr quinoline synthesis, involving initial condensation of an aromatic amine with a β-keto ester at elevated temperature, affords 2-hydroxyquinolines via an amide intermediate.[8] In view of this dichotomy and the variable regioselectivity of the Friedlander synthesis,[9] we searched for independent verification of the proposed structure. In the Knorr condensation product (**10**) the carbonyl groups would be located at positions 2 and 9 of the 1,10-phenanthroline ring (Scheme IV). Structure **10** and the corresponding dichloro- and dialkyl-1,10-phenanthrolines **11** would be spectroscopically similar to **1–3**. Some indication may be gained from analyzing the effect of substituent branching on ring carbon chemical shifts in ^{13}C NMR spectra. Alternatively, the effectiveness of 1,10-phenanthroline as a binding site for lanthanide shift reagents suggested a lanthanide-induced shift (LIS) study,[10] since this would probe the distance between the alkyl groups and the binding site of **3**. A series of ^1H NMR spectra were recorded at 80 MHz as aliquots of $Eu(fod)_3$ were added to a $CDCl_3$ solution of **3b** (0.1–0.2 M). The LIS slopes ($\Delta\delta$/equivalent) of selected proton resonances are approximately as follows (in ppm/equiv; note, positive values indicate downfield shifts): *tert*-butyl (δ_o 1.75) +0.8; CH_2,H1,H12 (δ_o 3.32) +12; Ar H, H6,H7 (δ_o 8.08) −3.

Discussion

The lanthanide-induced shift (LIS) study[10] of di-*tert*-butylphenanthroline **3b** corroborates the proposed structure, hence those of **3a**, **2**, and **1**, as well. The four methylene protons closest to the lanthanide binding site exhibit the largest LIS values of any protons in the molecule. The distant *tert*-butyl protons show small LIS values, whereas in **11** their LIS values would be very large. The *upfield* shift of H6 and H7 on the phenanthroline ring is in accord with LIS observations of 1,10-phenanthroline.[10a] Comparison of the ^{13}C NMR data for **3a** and **3b** also supports the indicated structures. Replacement of a methyl substituent by a *tert*-butyl group in pyridine causes a 10–13 ppm downfield shift of the attached carbon atom.[11] The 2,9-position carbon resonances of the phenanthroline ring, readily identified by their low-field positions,[12] are virtually unaffected by the substituent change (δ 158.3 in **3a** vs. 159.2 in **3b**), whereas the 4,7-positions experience the expected downfield shift (δ 141.1 in **3a** vs. 152.0 in **3b**).

The sequence of Conrad–Limpach, chlorination, and alkylation reactions makes phenanthrolines **3a** and **3b** readily available. Although the initial condensation step is slow, a pentacyclic bidentate ligand is constructed in four steps from commercial precursors in 25–30% overall yield. The flexible choice of substituent in the last step is beneficial to our general aim of tailoring the properties of metal ion receptors.[13] For example, the di-*tert*-butyl derivative **3b** is far more soluble than the dimethyl analogue (**3a**) in chloroform and other organic solvents. The poor solubility of phenanthrolinedione **1** may itself bar direct alkylation to afford **3**. Potent nucleophiles, such as alkyllithium reagents, probably deprotonate **1** and alkylation would result in polyanionic intermediates which would be even less soluble in organic solvents.

The failure of catalytic conditions in Grignard alkylation of dichlorophenanthroline **2** and the requirement of a large excess of 2:1 Grignard/Cu(I) mixtures in various reactions reported in Table I suggest the importance of substrate coordination. In the former case, the observed reaction in the presence of 1.2 molar equiv of Ni(II) (0.6 equiv on a stoichiometric basis) suggests that replacement of chloride or phosphine ligands by a phenanthroline may deactivate the catalyst. On the other hand, coordination of the heteroaryl halide to a transition metal may actually activate this substrate, as suggested by the substantial improvement in yield for Grignard/Cu(I) reactions when large excesses are used. Finally, the generality of these reactions shows that a phenanthroline/Cu(I) copper complex plays no catalytic role in alkylation of **2**.

Our discovery that a large excess of 2:1 Grignard reagent/Cu(I) salt effectively alkylates heterocyclic chlorides and bromides is in sharp contrast with usual substitution methods involving organocopper reagents (RCu) or lithium dialkylcuprates and relatively reactive halides, such as aryl iodides.[14] Although the coupling of halopyridines with stabilized carbanions is well-known,[15] the replacement of chlorine or bromine in pyridine heterocycles by simple alkyl groups is uncommon. Our new method is complementary to nickel(II)-catalyzed methods reported by Thorsett and Stermitz[4d] and by Pridgen[4b,c] and to the Wittig reagent method of Taylor and Martin.[2] In particular, this copper(I) method gives reasonable yields of ethyl and *tert*-butyl products, whereas Grignard reagents often suffer β-hydride elimination with nickel(II) phosphine catalysts, affording reduced or negligible yields of primary and tertiary alkylation products.[4b,c] The method of Taylor and Martin is comparable for quinaldine (82%) and su-

(8) For Knorr and Conrad–Limpach condensations of ethyl 1-oxocyclohexanecarboxylates with arylamines, see: Bajaj, H. S.; Desai, R. D.; Saharia, G. S. *J. Indian Chem. Soc.* **1975**, *52*, 962–965. Blount, B. K.; Perkin, W. H.; Plant, S. G. P. *J. Chem. Soc.* **1929**, 1975–1987.

(9) Thummel, R. P.; Jahng, Y. *J. Org. Chem.* **1985**, *50*, 2407–2412. Thummel, R. P.; Kohli, D. K. *J. Org. Chem.* **1977**, *42*, 2742–2747. Curran, A. C. W. *J. Chem. Soc., Perkin Trans. 1* **1976**, 975–977.

(10) (a) Sinha, S. P.; Green, R. D. *Spectrosc. Lett.* **1971**, *4*, 399–402. (b) Sohar, P. *Nuclear Magnetic Resonance Spectroscopy*; CRC: Boca Raton, FL, 1983; Vol 2, pp 115–133.

(11) A comparison of ^{13}C NMR effects in substituted pyridines is given in: Wedinger, R.; Hogeveen, H.; le Noble, W. J. *J. Org. Chem.* **1984**, *49*, 1338–1341.

(12) 1,10-Phenanthroline: ($CDCl_3$) δ 150.2 (C2, C9), 135.9 (C4, C7). 4,7-Dimethyl-1,10-phenanthroline: ($CDCl_3$) δ 149.8 (C2, C9), 144.0 (C4, C7). *The Sadtler Standard Spectra*; Sadtler Research Laboratories: Philadelphia, PA, 1979. 2,9-Dimethyl-1,10-phenanthroline: (CD_3OD) δ 159.9 (C2, C9), 137.6 (C4, C7) [this work].

(13) Bell, T. W.; Firestone, A. *J. Am. Chem. Soc.* **1986**, *108*, 8109–8111. Bell, T. W.; Firestone, A.; Guzzo, F.; Hu, L.-Y. *J. Inclusion Phenom.* **1987**, *5*, 149–152. Bell, T. W.; Guzzo, F. *J. Chem. Soc., Chem. Commun.* **1986**, 769–771. Bell, T. W.; Firestone, A. *J. Org. Chem.* **1986**, *51*, 764–765. Bell, T. W.; Guzzo, F. *J. Am. Chem. Soc.* **1984**, *106*, 6111–6112.

(14) Posner, G. H. *Org. React. (N.Y.)* 1974, *22*, Chapter 2.

(15) For example, 2-bromopyridine: Taguchi, T.; Kitigawa, O.; Morikawa, T.; Nishikawa, T.; Uehara, H.; Endo, H.; Kobayashi, Y. *Tetrahedron Lett.* **1986**, *27*, 6103–6106. Carpita, A.; Lessi, A.; Rossi, R. *Synthesis* **1984**, 571–572. Lewis, T. R.; Archer, S. *J. Am. Chem. Soc.* **1951**, *73*, 2109–2113.

perior in the case of 2-ethylquinoline (75%). Moreover, the need for a large excess of Grignard reagent is a distinct disadvantage of our method. On the other hand, the relative simplicity and ease of execution may make this Grignard/copper(I) combination the method of choice in many cases.

Experimental Section

General. All commercially obtained solvents and reagents were used without purification, except that tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl. Column chromatography employed Woelm neutral alumina (activity grade II) and thin-layer chromatography (TLC) plates were Machery-Nagel 0.2-mm alumina-coated plastic sheets. Gas-liquid chromatography (GC) was performed by using 1.5% OV-17 at 50–200 °C with yields determined by electronic integration relative to benzyl bromide as internal standard. Melting points were determined on a Thomas-Hoover apparatus and are uncorrected. Mass spectrometry gave molecular ions (M^+) as indicated and was conducted at 70 eV. NMR spectra were recorded at the indicated frequencies for samples dissolved in $CDCl_3$ and chemical shifts were measured relative to solvent resonances as follows: ^1H NMR $\delta(CHCl_3)$ = 7.25; ^{13}C NMR, $\delta(CDCl_3)$ = 77.0.

1,2,3,4,9,10,11,12,13,14-Decahydrodibenzo[*b*,*j*][1,10]-phenanthroline-5,8-dione (1). A mixture of 32.4 g (0.3 mol) of *o*-phenylenediamine and 107 g (0.65 mol) of ethyl 1-oxo-2-cyclohexanecarboxylate (containing 32% of the methyl ester) was placed in a large crystallizing dish and stored at reduced pressure (25–30 mm) over P_2O_5 for 2–3 months. Of the resulting crystalline intermediate, 5.0 g (13.2 mmol) was transferred into a flask equipped with a thermometer, nitrogen inlet, and a magnetic stirrer. Diphenyl ether (50 mL) was added, and the resulting solution was heated at 228–230 °C for 0.5 h under vigorous stirring while N_2 was bubbled into the reaction mixture (80–90 mL/min). After the reaction mixture was cooled to room temperature, the precipitated product was collected by vacuum filtration and washed with petroleum ether (3 × 50 mL) and ethanol (2 × 25 mL). Drying in vacuo afforded 2.04 g (48%) of **1** as a tan solid, mp 392–401 °C (lit.[5] mp 400–403 °C). Increasing the scale of the second step in this preparation causes yield reduction (e.g., to 35% for double scale).

5,8-Dichloro-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*]-[1,10]phenanthroline (2). A mixture of 4.58 g (23.3 mmol) of diketone **1** and 30 mL of phosphorus oxychloride was stirred under N_2 at 80 °C for 7 h. The cooled reaction mixture was poured into 120 g of crushed ice and then neutralized by *carefully* adding 50 g of Na_2CO_3 in small portions with vigorous stirring. The resulting mixture was extracted with chloroform (3 × 150 mL). The combined extracts were washed with water, dried (Na_2SO_4), and evaporated in vacuo. The beige residue was recrystallized from $CCl_4/CHCl_3$ (9:1) with hot filtration, yielding 4.2 g (82%) of dichlorophenanthroline **2** as a white solid, mp 324–328 °C dec, which was homogeneous by TLC: M^+ m/z 356 (100%); ^1H NMR (300 MHz) δ 1.97 (m, CH_2, H2, H3, H10, H11, 8 H), 3.06 (m, CH_2, H4, H9, 4H), 3.36 (m, CH_2, H1, H12, 4 H), 8.20 (s, CH, 2 H); ^{13}C NMR (75.5 MHz) δ 22.7, 22.7, 27.6, 34.8, 122.3, 125.2, 130.8, 141.9, 144.5, 160.2; IR (KBr) 2915 (s), 2860 (m), 1460 (s), 1420 (s), 1375 (m), 1225 (m), cm^{-1}. Anal. Calcd for $C_{20}H_{18}N_2Cl_2$: C, 67.16; H, 5.04; N, 7.83; Cl, 19.87. Found: C, 66.96; H, 5.11; N, 7.67, Cl, 20.01.

5,8-Dimethyl-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*]-[1,10]phenanthroline (3a). A mixture of 8.0 g (56 mmol) of anhydrous CuBr, 250 mL of anhydrous THF, and 40 mL of ethereal methylmagnesium bromide (2.9 M) was stirred under N_2 at −78 °C for 20 min. Dichlorophenanthroline **2** (2.5 g, 7.0 mmol) was added, and the reaction mixture was stirred for 2–3 h at −78 °C and then overnight at room temperature. The reaction mixture was quenched by dropwise addition of saturated aqueous NH_4OH and then extracted with $CHCl_3$ (3 × 75 mL). The combined extracts were stirred for 20 min with 50 mL of ethylenediamine, and then 250 mL of water was added cautiously. The aqueous layer was extracted with $CHCl_3$ (3 × 75 mL), and the combined $CHCl_3$ solutions were dried ($MgSO_4$) and evaporated in vacuo. Column chromatography of the residue (EtOAc/CH_3OH, 4:1) gave 75% of spectroscopically pure product as a white solid: mp 220 °C dec; M^+ m/z calcd for $C_{22}H_{24}N_2$ 316.1956, found, 316.1930 (100%); ^1H NMR (300 MHz) δ 1.95 (m, CH_2, H2, H3, H10, H11, 8 H), 2.60 (s, CH_3, 6 H), 2.92 (m, CH_2, H4, H9, 4 H), 3.34 (m, CH_2, H1, H12, 4 H), 7.90 (s, CH, 2 H); ^{13}C NMR (75.5 MHz) δ 13.9, 22.8, 23.3, 27.1, 35.0, 120.9, 125.7, 129.9, 141.1, 143.5, 158.3; IR (KBr) 2940 (s), 2870 (m), 1490 (s), 1440 (m), 1387 (m), cm^{-1}.

5,8-Di-*tert*-butyl-1,2,3,4,9,10,11,12-octahydrodibenzo[*b*,*j*][1,10]phenanthroline (3b). This reaction was conducted exactly as in the case of **3a**, except that CuCN (2.14 g, 24 mmol) and 2 M ethereal *tert*-butylmagnesium chloride were used, and the product was chromatographed by using CH_2Cl_2/hexanes as eluent (65% yield). A microanalysis sample was prepared by recrystallization from CH_2Cl_2/hexanes and drying in vacuo at 80 °C; mp 188–189 °C dec; M^+ m/z calcd for $C_{28}H_{36}N_2$ 400.2878, found 400.2877 (100%); ^1H NMR (300 MHz) δ 1.75 (s, CH_3, 18 H), 1.74, 1.95 (m, CH_2, H2, H3, H10, H11, 8 H), 3.12 (m, CH_2, H4, H9, 4 H), 3.32 (m, CH_2, H1, H12, 4 H), 8.08 (s, CH, 2 H); ^{13}C NMR (75.5 MHz) δ 21.4, 22.8, 30.3, 33.8, 33.9, 38.8, 121.5, 124.9, 132.1, 144.8, 152.0, 159.2; IR (neat) 2950 (s), 2870 (m), 1460 (m), 1355 (m) cm^{-1}. Anal. Calcd for $C_{28}H_{36}N_2$: C, 83.95; H, 9.06; N, 6.99. Found: C, 83.80; H, 9.08; N, 6.76%.

Alkylation of 2-Chloroquinoline (4), 2-Bromopyridine (6), and 3-Bromopyridine (8). These reactions were conducted as described for **3a** by using 8.0 mmol of Cu(I) salt, 16 mmol of Grignard reagent (e.g., 1.6 M ethylmagnesium bromide in ether), and 2.0 mmol of 2-chloroquinoline, 2-bromopyridine, or 3-bromopyridine. The reaction mixture was quenched by addition of saturated aqueous NH_4OH, the pH was adjusted to 10 by using 1 M aqueous NaOH, and the resulting solution was extracted with ether. The combined ether extracts were dried ($MgSO_4$), and then an aliquot of benzyl bromide was added to determine GC yields against this standard. Isolated yields were determined after purification of products by column chromatography. Products were identified by comparison with the literature data and commercial samples as follows: quinaldine (**5a**), ^1H NMR[16,17] and IR spectra, GC retention time, and TLC R_f value identical with those of a commercial sample; 2-ethylquinoline (**5b**), ^1H NMR spectrum consistent with the literature data,[16,17] picrate mp 148 °C (lit.[17] mp 148 °C); 2-*tert*-butylquinoline (**5c**), ^1H NMR spectrum consistent with the literature data,[16,17] M^+ m/z 185 (100%), picrate mp 170–171 °C (lit.[17] mp 171–172.5 °C); 2-picoline (**7a**), ^1H NMR and IR spectra, GC retention time, and TLC R_f value identical with those of a commercial sample; 2-*tert*-butylpyridine (**7b**), IR spectrum consistent with the literature data,[18] ^1H NMR (80 MHz) δ 1.35 (s, CH_3, 9 H), 8.5 (m, H6, 1 H), 6.9–7.7 (m, H3, H4, H5, 3 H), M^+ m/z 135 (100%); 3-*tert*-butylpyridine (**9**), ^1H NMR spectrum[11] and IR spectrum[18] consistent with the literature data.

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Registry No. **1**, 70071-65-7; **2**, 109152-25-2; **3a**, 20168-40-5; **3b**, 109152-26-3; **4**, 612-62-4; **5a**, 91-63-4; **5b**, 1613-34-9; **5c**, 22493-94-3; **6**, 109-04-6; **7a**, 109-06-8; **7b**, 5944-41-2; **8**, 626-55-1; **9**, 38031-78-6; MeMgBr, 75-16-1; *t*-BuMgCl, 677-22-5; EtMgBr, 925-90-6; Cu_2Br_2, 7787-70-4; Cu_2Cl_2, 7758-89-6; CuCN, 544-92-3; $2\text{-}H_2NC_6H_4NH_2$, 95-54-5; ethyl 1-oxo-2-cyclohexanecarboxylate, 1655-07-8; methyl 1-oxo-2-cyclohexanecarboxylate, 41302-34-5; *N*,*N*′-bis(ethyl cyclohex-1-en-2-yl-carbvoxylate)-1,2-benzenediamine, 70071-61-3.

(16) Peake, D. A.; Oyler, A. R.; Heikkila, K. E.; Liukkonen, R. J.; Engroff, E. C.; Carlson, R. M. *Synth. Commun.* **1983**, *13*, 21–26.
(17) Noyori, R.; Kato, M.; Kawanisi, M.; Nozaki, H. *Tetrahedron* **1969**, *25*, 1125–1136.
(18) *The Sadtler Standard Spectra*; Sadtler Research Laboratories: Philadelphia, PA, 1980.