

Synthesis of 2,4,8-Trisubstituted 1,7-Naphthyridines by the Reaction of 4-(1-Aryl-2-methoxyethenyl)-3-isocyanopyridines with Excess Organolithiums

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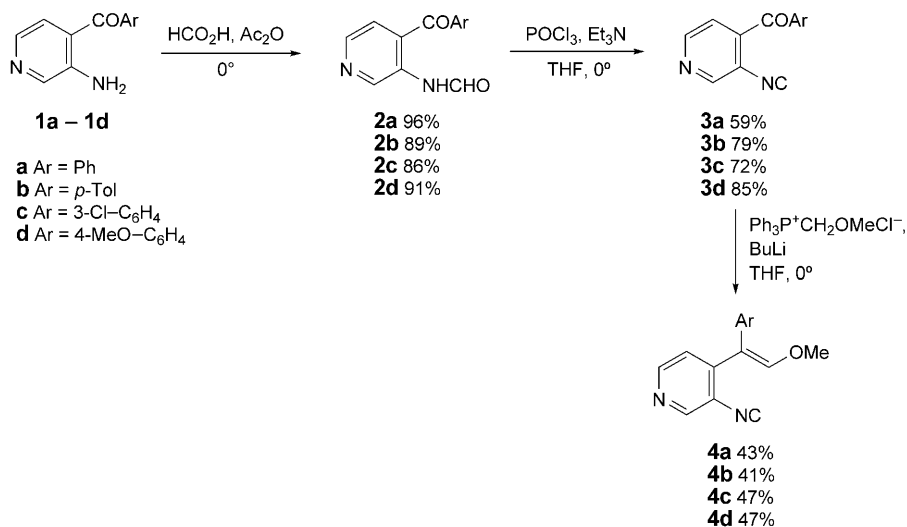
A convenient method for the synthesis of 2,4,8-trisubstituted 1,7-naphthyridines **6** by the reaction of (*E*)-4-(1-aryl-2-methoxyethenyl)-3-isocyanopyridines **4**, which could be easily prepared from commercially available 3-aminopyridine *via* arylation of lithium (4-lithiopyridin-3-yl)pivalamide with *N*-methoxy-*N*-methylbenzamides, with excess organolithiums has been developed.

Introduction. – In previous papers, we reported an efficient synthesis of 2,4-disubstituted quinolines by the reaction of 1-(1-aryl-2-methoxyethenyl)-2-isocyanobenzenes with various organolithiums [1]. We anticipated that the use of 4-(1-aryl-2-methoxyethenyl)-3-isocyanopyridines **4** in place of 1-(1-aryl-2-methoxyethenyl)-2-isocyanobenzenes would give 2,4-disubstituted 1,7-naphthyridines. In this article, we report the results of our study on reactions of **4** with organolithiums. We found that 2,4-disubstituted naphthyridines could not be prepared satisfactorily, but that 2,4,8-trisubstituted naphthyridines **6** were obtained instead in reasonable yields by reacting **4** with excess organolithiums. 1,7-Naphthyridine derivatives have attracted considerable attention, mainly because some of these derivatives exhibit significant biological activities [2]. Although several efficient methods for the preparation of this class of heterocycles have been reported [3]¹⁾, to date, there are no examples of the synthesis of 2,4,8-trisubstituted derivatives in the literature.

Results and Discussion. – 3-Aminopyridin-4-yl aryl ketones **1**, which could be easily prepared from commercially available 3-aminopyridine using the reaction of lithium (4-lithiopyridin-3-yl)pivalamide [4] with *N*-methoxy-*N*-methylbenzamides as described in the *Exper. Part*, were converted to (*E*)-4-(1-aryl-2-methoxyethenyl)-3-isocyanopyridines **4** *via* the route illustrated in *Scheme 1*. The first step was *N*-formylation of amino ketones **1** with HCOOH in the presence of Ac₂O at 0° to form *N*-(4-arylpiperidin-3-yl)formamides **2**. Dehydration of these formamides to form the corresponding isocyano derivatives **3** was accomplished on treatment with POCl₃ in THF in the presence of Et₃N as a base at 0°. These isocyano ketones were allowed to

¹⁾ See also pertinent references cited in [2].

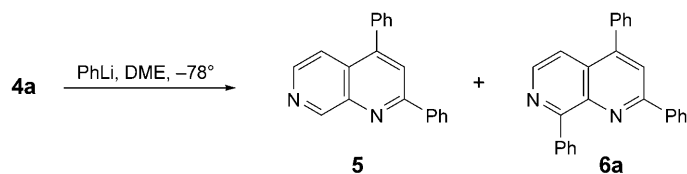
Scheme 1



react with (methoxymethyl)triphenylphosphonium chloride in THF at 0° to give **4**; in each case, the (*E*)-isomer was obtained exclusively.

First, the reaction of (*E*)-3-isocyano-4-(2-methoxy-1-phenylethenyl)pyridine (**4a**) with PhLi was examined. Thus, **4a** was treated with an equimolar amount of PhLi in 1,2-dimethoxyethane (DME) at –78° for 3 h, as shown in Scheme 2. After the usual aqueous workup, only a trace amount of 2,4-diphenylnaphthyridine (**5**) was obtained, and the starting material **4a** was recovered almost quantitatively (Table 1, Entry 1). An

Scheme 2

Table 1. Results of Reactions of **4a** with PhLi in DME at –78°

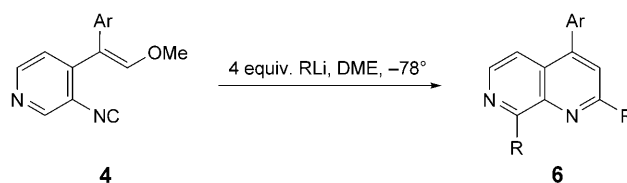
Entry	PhLi [equiv.]	Yield of 5 [%] ^{a)}	Yield of 6a [%] ^{a)}
1	1	trace	0
2	2	14	4
3	3	7	25
4	4	0	47

^{a)} Yields of isolated products.

extended reaction time and/or a higher reaction temperature (0°) led to similar results. Interestingly, use of 2 mol-equiv. of PhLi under similar conditions resulted in the formation of 2,4,8-triphenyl-1,7-naphthyridine (**6a**) in 4% yield along with 14% of **5a** (Entry 2). We assumed that the formation of **6a** was due to the preference of the addition of the second molecule of PhLi to C(8) of **5a**. For this reason, we focused our efforts on obtaining **6a** as the sole product in a reasonable yield. Compound **4a** was allowed to react with 3 mol-equiv. of PhLi to give **6a** in 25% yield along with 7% of **5a** (Entry 3). Subsequently, we found that treatment of **4a** with 4 mol-equiv. of PhLi gave **6a** in 47% yield after column chromatography on silica gel (Entry 4); no trace of **5a** was detected.

To examine the generality of the present procedure, we conducted reactions using four (*E*)-4-(1-aryl-2-methoxyethenyl)-3-isocyanopyridines **4** including **4a** and six organolithiums including PhLi under the conditions given in Table 1, Entry 4, as shown in Scheme 3, and obtained ten 2,4,8-disubstituted 1,7-naphthyridines including **6a**. The results are summarized in Table 2, which indicates that yields of the desired products, 2,4,8-trisubstituted 1,7-naphthyridines **6**, are generally modest. When alkylolithiums, such as BuLi and MeLi (Entries 2 and 7, resp.), were used, the yields of the corresponding products **6b** and **6g** are significantly lower than those with aryllithiums. It should be noted that there is no significant difference in yields between substrates **4** with an α -aryl substituent containing electron-donating or electron-withdrawing groups.

Scheme 3

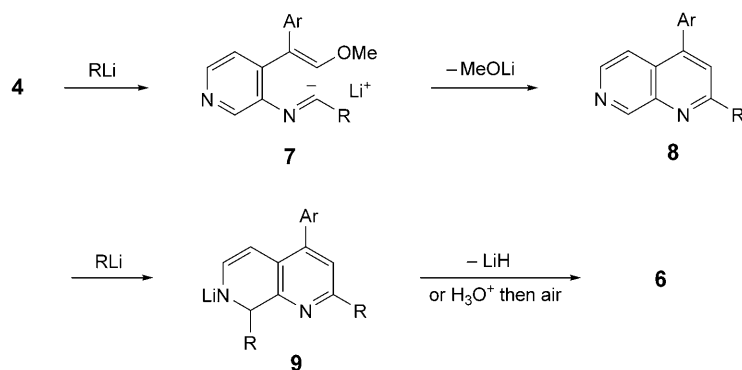
Table 2. Preparation of 1,7-Naphthyridines **6**

Entry	4	R in RLi	Ar	6	Yield ^a) [%]
1	4a	Ph	Ph	6a	47
2	4a	Bu	Ph	6b	25
3	4b	Ph	<i>p</i> -Tol	6c	45
4	4b	4-Cl-C ₆ H ₄	<i>p</i> -Tol	6d	43
5	4b	4-MeO-C ₆ H ₄	<i>p</i> -Tol	6e	47
6	4c	Ph	3-Cl-C ₆ H ₄	6f	48
7	4c	Me	3-Cl-C ₆ H ₄	6g	25
8	4c	<i>p</i> -Tol	3-Cl-C ₆ H ₄	6h	47
9	4d	Ph	4-MeO-C ₆ H ₄	6i	43
10	4d	4-Cl-C ₆ H ₄	4-MeO-C ₆ H ₄	6j	46

^a) Yields of isolated products.

A possible mechanism for the formation of 1,7-naphthyridines **6** from **4** and organolithiums starts with the addition of 1 equiv. of organolithium compound to the isocyano C-atom of **4**, which generates the imidoyl anion intermediates **7** (Scheme 4). Then, the 1,7-naphthyridine skeleton **8** is formed by the intramolecular attack of this anion to the C(α)-atom of the methoxyethenyl moiety with loss of MeOLi. Subsequently, **8** is attacked by a second equiv. of the organolithium compound at C(8) to form the intermediate **9**, from which elimination of LiH gives rise to **6**. Alternatively, formation of **6** may be accomplished by dehydrogenation of 7,8-dihydro-1,7-naphthyridines, formed by protonation of **9**, during workup and/or isolation procedures.

Scheme 4



In conclusion, we have demonstrated that 2,4,8-trisubstituted 1,7-naphthyridines could be prepared by the reaction of (*E*)-4-(1-aryl-2-methoxyethenyl)-3-isocyanopyridines with excess amounts of organolithiums. Although the yields of the products are not so high, in view of the ready availability of the starting materials as well as the ease of operations, the present procedure offers a convenient synthetic method for this class of heterocycles. Studies toward the synthesis of related heterocycles utilizing 3-isocyanopyridin-4-yl ketones are currently under way in our laboratory.

Experimental Part

General. All of the org. solvents used in this study were dried over appropriate drying agents and distilled prior to use. TLC: Merck silica gel 60 PF_{254} . Column chromatography (CC): Wako Gel C-200E. M.p.: Laboratory Devices MEL-TEMP II melting-point apparatus; uncorrected. IR Spectra: Shimadzu FT-IR-8300 spectrophotometer. ^1H -NMR Spectra: in CDCl_3 with TMS as an internal reference, with a JEOL ECP500 FT NMR spectrometer, at 500 MHz. ^{13}C -NMR Spectra: measured in CDCl_3 with TMS as an internal reference with a JEOL ECP500 FT NMR spectrometer, at 125 MHz. LR- and HR-MS (EI, 70 eV): JEOL JMS AX505 HA spectrometer.

(3-Aminopyridin-4-yl)(phenyl)methanone (**1a**) and (3-aminopyridin-4-yl)(4-methoxyphenyl)methanone (**1d**) were prepared according to the method described in [4]. All other chemicals used in this study were commercially available.

N-(4-Aroylpyridin-3-yl)-2,2-dimethylpropanamides. These compounds were prepared by a successive treatment of 2,2-dimethyl-*N*-(pyridin-3-yl)propanamide [4] with 2 mol-equiv. of BuLi and *N*-methoxy-*N*-methylbenzamides under the conditions reported previously for the reaction of 2,2-dimethyl-*N*-lithio-*N*-(4-lithiopyridin-3-yl)propanamide with benzaldehyde [4].

2,2-Dimethyl-*N*-[4-(4-methylbenzoyl)pyridin-3-yl]propanamide. Yield: 68%. Pale-yellow solid. M.p. 151–153° (hexane/CH₂Cl₂). IR (KBr): 3318, 1678. ¹H-NMR: 1.34 (s, 9 H); 2.47 (s, 3 H); 7.33 (d, *J* = 7.8, 2 H); 7.37 (d, *J* = 4.1, 1 H); 7.67 (d, *J* = 7.8, 2 H); 8.45 (d, *J* = 4.1, 1 H); 9.90 (s, 1 H); 10.35 (br. s, 1 H). Anal. calc. for C₁₈H₂₀N₂O₂ (296.37): C 72.95, H 6.80, N 9.45; found: C 72.72, H 7.02, N 9.43.

N-[4-(3-Chlorobenzoyl)pyridin-3-yl]-2,2-dimethylpropanamide. Yield: 75%. Pale-yellow solid. M.p. 119–120° (hexane/Et₂O). IR (KBr): 3400, 1674. ¹H-NMR: 1.35 (s, 9 H); 7.35 (d, *J* = 4.6, 1 H); 7.48 (t, *J* = 7.8, 1 H); 7.61 (d, *J* = 7.8, 1 H); 7.63 (d, *J* = 7.8, 1 H); 7.76 (s, 1 H); 8.48 (d, *J* = 4.6, 1 H); 9.92 (s, 1 H); 10.34 (br. s, 1 H). Anal. calc. for C₁₇H₁₇ClN₂O₂ (316.79): C 64.46, H 5.41, N 8.84; found: C 64.36, H 5.58, N 8.78.

(3-Aminopyridin-4-yl)(aryl)methanones **1**. These compounds were prepared by acid hydrolysis under the conditions reported previously for the conversion of *N*-(4-benzoylpyridin-3-yl)-2,2-dimethylpropanamide into (3-aminopyridin-4-yl)(phenyl)methanone [4].

(3-Aminopyridin-4-yl)(4-methylphenyl)methanone (**1b**). Yield: 81%. Pale-yellow solid. M.p. 115–117° (hexane/CH₂Cl₂). IR (KBr): 3435, 3327, 1651, 1613. ¹H-NMR: 2.45 (s, 3 H); 5.72 (br. s, 2 H); 7.24 (d, *J* = 5.5, 1 H); 7.29 (d, *J* = 7.8, 2 H); 7.62 (d, *J* = 7.8, 2 H); 7.95 (d, *J* = 5.5, 1 H); 8.28 (s, 1 H). Anal. calc. for C₁₃H₁₂N₂O (212.25): C 73.56, H 5.70, N 13.20; found: C 73.51, H 5.94, N 13.10.

(3-Aminopyridin-4-yl)(3-chlorophenyl)methanone (**1c**). Yield: 81%. Yellow solid. M.p. 165–167° (hexane/THF). IR (KBr): 3445, 3306, 1634, 1607. ¹H-NMR: 3.89 (br. s, 2 H); 7.20 (d, *J* = 5.0, 1 H); 7.44 (t, *J* = 7.8, 1 H); 7.54 (dd, *J* = 7.8, 1.8, 1 H); 7.56 (dd, *J* = 7.8, 1.8, 1 H); 7.67 (t, *J* = 1.8, 1 H); 7.95 (d, *J* = 5.0, 1 H); 8.30 (s, 1 H). Anal. calc. for C₁₂H₉ClN₂O (232.67): C 61.95, H 3.90, N 12.04; found: C 61.94, H 3.94, N 11.82.

N-(4-Aroylpyridin-3-yl)formamides **2**. These compounds were prepared by treating **1** with HCO₂H/Ac₂O under the previously reported conditions [5].

N-(4-Benzoylpyridin-3-yl)formamide (**2a**). Pale-yellow, viscous oil. *R*_f (THF/hexane 1:1) 0.35. IR (neat): 3308, 1699, 1668. ¹H-NMR: 7.39 (d, *J* = 5.0, 1 H); 7.54 (dd, *J* = 7.8, 7.3, 2 H); 7.68 (tt, *J* = 7.3, 1.4, 1 H); 7.77 (d, *J* = 7.8, 2 H); 8.48 (s, 1 H); 8.53 (d, *J* = 5.0, 1 H); 9.90 (br. s, 1 H); 9.91 (s, 1 H). Anal. calc. for C₁₃H₁₀N₂O₂ (226.23): C 69.02, H 4.46, N 12.38; found: C 68.97, H 4.50, N 12.27.

N-[4-(4-Methylbenzoyl)pyridin-3-yl]formamide (**2b**). Pale-yellow, viscous oil. *R*_f (AcOEt/hexane 1:2) 0.35. IR (neat): 3308, 1697, 1661, 1605. ¹H-NMR: 2.47 (s, 3 H); 7.33 (d, *J* = 7.8, 2 H); 7.38 (d, *J* = 5.0, 1 H); 7.69 (d, *J* = 7.8, 2 H); 8.46 (s, 1 H); 8.52 (d, *J* = 5.0, 1 H); 9.79 (br. s, 1 H); 9.88 (s, 1 H). Anal. calc. for C₁₄H₁₂N₂O₂ (240.26): C 69.99, H 5.03, N 11.66; found: C 69.72, H 5.23, N 11.47.

N-[4-(3-Chlorobenzoyl)pyridin-3-yl]formamide (**2c**). Beige solid. M.p. 115–117° (hexane/THF). IR (KBr): 3277, 1699, 1670. ¹H-NMR: 7.37 (d, *J* = 4.6, 1 H); 7.48 (t, *J* = 7.8, 1 H); 7.62 (d, *J* = 7.8, 1 H); 7.65 (dd, *J* = 7.8, 1.4, 1 H); 7.77 (t, *J* = 1.4, 1 H); 8.48 (s, 1 H); 8.55 (d, *J* = 4.6, 1 H); 9.84 (br. s, 1 H); 9.90 (s, 1 H). Anal. calc. for C₁₃H₉ClN₂O₂ (260.68): C 59.90, H 3.48, N 10.75; found: C 59.82, H 3.72, N 10.73.

N-[4-(4-Methoxybenzoyl)pyridin-3-yl]formamide (**2d**). Beige solid. M.p. 140–143° (hexane/CH₂Cl₂). IR (KBr): 3349, 1701, 1640. ¹H-NMR: 3.92 (s, 3 H); 7.00 (d, *J* = 8.7, 2 H); 7.39 (d, *J* = 5.0, 1 H); 7.80 (d, *J* = 8.7, 2 H); 8.44 (s, 1 H); 8.53 (d, *J* = 5.0, 1 H); 9.62 (br. s, 1 H); 9.84 (br. s, 1 H). Anal. calc. for C₁₄H₁₂N₂O₃ (256.26): C 65.62, H 4.72, N 10.93; found: C 65.52, H 4.72, N 10.70.

(Aryl)(3-isocyanopyridin-4-yl)methanones **3**. These compounds were prepared by dehydration of **2** with POCl₃/Et₃N under the conditions reported in [6].

(3-Isocyanopyridin-4-yl)(phenyl)methanone (**3a**). Yellow solid. M.p. 72–75° (dec.; hexane). IR (KBr): 2124, 1672. ¹H-NMR: 7.43 (dd, *J* = 5.0, 0.9, 1 H); 7.54 (dd, *J* = 8.2, 7.3, 2 H); 7.69 (tt, *J* = 7.3, 1.4, 1 H); 7.81 (dd, *J* = 8.2, 1.4, 2 H); 8.78 (d, *J* = 5.0, 1 H); 8.83 (s, 1 H). Anal. calc. for C₁₃H₈N₂O (208.22): C 74.99, H 3.87, N 13.45; found: C 75.01, H 4.05, N 13.21.

(3-Isocyanopyridin-4-yl)(4-methylphenyl)methanone (**3b**). Pale-yellow solid. M.p. 72–73° (dec.; hexane/CH₂Cl₂). IR (KBr): 2126, 1669, 1604. ¹H-NMR: 2.46 (s, 3 H); 7.33 (d, *J* = 8.2, 2 H); 7.41 (d, *J* = 5.0, 1 H); 7.70 (d, *J* = 8.2, 2 H); 8.77 (d, *J* = 5.0, 1 H); 8.81 (s, 1 H). Anal. calc. for C₁₄H₁₀N₂O (222.24): C 75.66, H 4.54, N 12.60; found: C 75.40, H 4.61, N 12.39.

(3-Chlorophenyl)(3-isocyanopyridin-4-yl)methanone (**3c**). Brown solid. M.p. 74–76° (dec.; pentane). IR (KBr): 2133, 1668. ¹H-NMR: 7.42 (*d*, *J* = 5.0, 1 H); 7.49 (*t*, *J* = 7.8, 1 H); 7.65–7.68 (*m*, 2 H); 7.80 (*t*, *J* = 1.8, 1 H); 8.81 (*d*, *J* = 5.0, 1 H); 8.85 (*s*, 1 H). Anal. calc. for C₁₃H₇ClN₂O (242.66): C 64.34, H 2.91, N 11.54; found: C 64.17, H 2.98, N 11.51.

(3-Isocyanopyridin-4-yl)(4-methoxyphenyl)methanone (**3d**). Brown solid. M.p. 50–52° (pentane). IR (KBr): 2124, 1661. ¹H-NMR: 3.91 (*s*, 3 H); 6.99 (*d*, *J* = 8.7, 2 H); 7.40 (*d*, *J* = 5.0, 1 H); 7.78 (*d*, *J* = 8.7, 2 H); 8.76 (*d*, *J* = 5.0, 1 H); 8.80 (*s*, 1 H). Anal. calc. for C₁₄H₁₀N₂O₂ (238.24): C 70.58, H 4.23, N 11.76; found: C 70.40, H 4.39, N 11.68.

4-[(E)-1-Aryl-2-methoxyethenyl]-3-isocyanopyridines **4**. These compounds were prepared by reacting **3** with (methoxymethyl)(triphenyl)phosphonium chloride under the conditions reported for the conversion of (2-isocyanophenyl)(phenyl)methanone to 1-isocyano-2-(2-methoxy-1-phenylethenyl)-benzene [**1b**].

3-Isocyano-4-[(E)-2-methoxy-1-phenylethenyl]pyridine (**4a**). Pale-yellow oil. *R*_f (THF/hexane 1:5) 0.28. IR (neat): 2124, 1645, 1634. ¹H-NMR: 3.86 (*s*, 3 H); 6.73 (*s*, 1 H); 7.10 (*dd*, *J* = 8.2, 1.4, 2 H); 7.20 (*d*, *J* = 5.0, 1 H); 7.26 (*tt*, *J* = 7.3, 1.4, 1 H); 7.30 (*dd*, *J* = 8.2, 7.3, 2 H); 8.54 (*d*, *J* = 5.0, 1 H); 8.69 (*s*, 1 H). HR-MS: 236.0937 (C₁₅H₁₂N₂O⁺; calc. 236.0950).

3-Isocyano-4-[(E)-2-methoxy-1-(4-methylphenyl)ethenyl]pyridine (**4b**). Yellow oil. *R*_f (THF/hexane 1:5) 0.28. IR (neat): 2126, 1636. ¹H-NMR: 2.33 (*s*, 3 H); 3.84 (*s*, 3 H); 6.69 (*s*, 1 H); 6.99 (*d*, *J* = 7.8, 2 H); 7.11 (*d*, *J* = 7.8, 2 H); 7.19 (*d*, *J* = 5.0, 1 H); 8.53 (*d*, *J* = 5.0, 1 H); 8.68 (*s*, 1 H). HR-MS: 250.1086 (C₁₆H₁₄N₂O⁺; calc. 250.1106).

4-[(E)-1-(3-Chlorophenyl)-2-methoxyethenyl]-3-isocyanopyridine (**4c**). Yellow oil. *R*_f (THF/hexane 1:5) 0.29. IR (neat): 2123, 1636. ¹H-NMR: 3.87 (*s*, 3 H); 6.77 (*s*, 1 H); 6.94–6.98 (*m*, 1 H); 7.08–7.09 (*m*, 1 H); 7.19 (*d*, *J* = 5.0, 1 H); 7.22–7.24 (*m*, 2 H); 8.22 (*d*, *J* = 5.0, 1 H); 8.71 (*s*, 1 H). HR-MS: 270.0553 (C₁₅H₁₁ClN₂O⁺; calc. 270.0560).

3-Isocyano-4-[(E)-2-methoxy-1-(4-methoxyphenyl)ethenyl]pyridine (**4d**). Colorless needles. M.p. 111° (hexane/Et₂O). IR (KBr): 2126, 1636. ¹H-NMR: 3.80 (*s*, 3 H); 3.84 (*s*, 3 H); 6.63 (*s*, 1 H); 6.84 (*d*, *J* = 9.2, 2 H); 7.02 (*d*, *J* = 9.2, 2 H); 7.18 (*d*, *J* = 5.0, 1 H); 8.52 (*d*, *J* = 5.0, 1 H); 8.68 (*s*, 1 H). Anal. calc. for C₁₆H₁₄N₂O₂ (266.29): C 72.16, H 5.30, N 10.52; found: C 72.07, H 5.37, N 10.26.

2,4,8-Triphenyl-1,7-naphthyridine (**6a**) (Representative Procedure). To a stirred soln. of **4a** (0.14 g, 0.59 mmol) in 1,2-dimethoxyethane (DME; 3 ml) at –78° was added PhLi (1.08M in cyclohexane/Et₂O; 2.4 mmol); the mixture was stirred for 3 h at the same temp. before addition of sat. aq. NH₄Cl (10 ml). The warmed mixture was extracted with Et₂O (3 × 10 ml), and the combined extracts were washed with brine and dried (anh. Na₂SO₄). Evaporation of the solvent gave a residue, which was purified by CC (silica gel; THF/hexane 1:10) to give **6a** (0.10 g, 47%). Pale-yellow needles. M.p. 150–153° (hexane/CH₂Cl₂). IR (KBr): 1593. ¹H-NMR: 7.45–7.60 (*m*, 11 H); 7.70 (*d*, *J* = 5.5, 1 H); 8.07 (*s*, 1 H); 8.21 (*dd*, *J* = 8.2, 1.4, 2 H); 8.26 (*dd*, *J* = 8.2, 1.4, 2 H); 8.64 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 117.31; 121.55; 127.48; 127.66; 128.71; 128.83; 128.85; 128.88; 129.46; 129.86; 129.92; 131.59; 137.35; 138.65; 138.94; 141.72; 142.97; 148.49; 156.73; 160.51. MS: 358 (100, *M*⁺). Anal. calc. for C₂₆H₁₈N₂ (358.44): C 87.12, H 5.06, N 7.82; found: C 87.22, H 5.14, N 7.66.

2,4-Diphenyl-1,7-naphthyridine (**5**). This compound was obtained by using less than 4 mol-equiv. of PhLi. Pale-yellow solid. M.p. 123–125° (hexane/Et₂O). IR (KBr): 1593. ¹H-NMR: 7.50–7.61 (*m*, 8 H); 7.75 (*dd*, *J* = 5.5, 0.9, 1 H); 8.03 (*s*, 1 H); 8.23 (*dd*, *J* = 7.8, 1.4, 2 H); 8.57 (*d*, *J* = 5.5, 1 H); 9.63 (*d*, *J* = 0.9, 1 H). ¹³C-NMR: 117.77; 122.65; 127.59; 128.87; 128.91; 128.98 (2 C); 129.39; 129.98; 136.78; 138.74; 143.63; 148.83; 148.16; 154.74; 158.44. MS: 282 (100, *M*⁺). Anal. calc. for C₂₀H₁₄N₂ (282.34): C 85.08, H 5.00, N 9.92; found: C 84.95, H 5.16, N 9.72.

2,8-Dibutyl-4-phenyl-1,7-naphthyridine (**6b**). Pale-yellow oil. *R*_f (THF/hexane 1:10) 0.42. IR (neat): 1597. ¹H-NMR: 0.99 (*t*, *J* = 7.3, 3 H); 1.00 (*t*, *J* = 7.3, 3 H); 1.43–1.55 (*m*, 4 H); 1.86–1.93 (*m*, 4 H); 3.03 (*t*, *J* = 7.3, 2 H); 3.56 (*t*, *J* = 7.8, 2 H); 7.38 (*s*, 1 H); 7.47–7.54 (*m*, 6 H); 8.39 (*d*, *J* = 6.0, 1 H). ¹³C-NMR: 13.98; 14.07; 22.43; 22.98; 31.19; 31.88; 33.84; 38.69; 116.11; 124.82; 128.55; 128.66 (2 C); 129.41; 137.36; 141.92; 141.95; 147.34; 162.47; 165.17. MS: 318 (100, *M*⁺). Anal. calc. for C₂₂H₂₆N₂ (318.46): C 82.97, H 8.23, N 8.80; found: C 82.88, H 8.35, N 8.77.

4-(4-Methylphenyl)-2,8-diphenyl-1,7-naphthyridine (**6c**). Pale-yellow solid. M.p. 144–146° (hexane/Et₂O). IR (KBr): 1591. ¹H-NMR: 2.50 (*s*, 3 H); 7.39 (*d*, *J* = 8.2, 2 H); 7.44–7.52 (*m*, 6 H); 7.57 (*t*, *J* = 7.3,

2 H); 7.72 (*d*, *J* = 5.5, 1 H); 8.04 (*s*, 1 H); 8.20 (*d*, *J* = 7.3, 2 H); 8.26 (*d*, *J* = 7.3, 2 H); 8.63 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 21.32; 117.41; 121.49; 127.48; 127.65; 128.68; 128.88; 129.39; 129.54; 129.82; 130.05; 131.60; 134.44; 138.74; 138.91; 138.99; 141.77; 142.89; 148.55; 156.73; 160.51. MS: 372 (100, *M*⁺). Anal. calc. for C₂₇H₂₀N₂ (372.46): C 87.07, H 5.41, N 7.52; found: C 87.05, H 5.52, N 7.32.

2,8-Bis(4-chlorophenyl)-4-(4-methylphenyl)-1,7-naphthyridine (6d). Pale-yellow crystals. M.p. 195–197° (hexane/Et₂O). IR (KBr): 1593. ¹H-NMR: 2.51 (*s*, 3 H); 7.40 (*d*, *J* = 7.8, 2 H); 7.47 (*d*, *J* = 7.8, 2 H); 7.49 (*d*, *J* = 8.7, 2 H); 7.54 (*d*, *J* = 8.7, 2 H); 7.74 (*d*, *J* = 6.0, 1 H); 8.01 (*s*, 1 H); 8.12 (*d*, *J* = 8.7, 2 H); 8.20 (*d*, *J* = 8.7, 2 H); 8.63 (*d*, *J* = 6.0, 1 H). ¹³C-NMR: 21.34; 117.76; 121.27; 127.90; 128.69; 129.19; 129.35; 129.62; 130.13; 132.86; 134.12; 135.00; 136.24; 137.03; 137.32; 139.15; 141.57; 143.06; 148.97; 155.67; 159.15. MS: 440 (100, *M*⁺). Anal. calc. for C₂₇H₁₈Cl₂N₂ (441.35): C 73.48, H 4.11, N 6.35; found: C 73.30, H 4.10, N 6.22.

2,8-Bis(4-methoxyphenyl)-4-(4-methylphenyl)-1,7-naphthyridine (6e). Pale-yellow solid. M.p. 102–104° (hexane/Et₂O). IR (KBr): 1603. ¹H-NMR: 2.49 (*s*, 3 H); 3.88 (*s*, 3 H); 3.94 (*s*, 3 H); 7.02 (*d*, *J* = 8.7, 2 H); 7.10 (*d*, *J* = 8.7, 2 H); 7.38 (*d*, *J* = 7.8, 2 H); 7.47 (*d*, *J* = 7.8, 2 H); 7.63 (*d*, *J* = 6.0, 1 H); 7.97 (*s*, 1 H); 8.17 (*d*, *J* = 8.7, 2 H); 8.28 (*d*, *J* = 8.7, 2 H); 8.56 (*d*, *J* = 6.0, 1 H). ¹³C-NMR: 21.31; 55.36; 55.38; 113.13; 114.27; 116.83; 120.95; 128.89; 129.38; 129.49; 129.78; 131.51; 131.75; 133.06; 134.65; 138.77; 141.74; 142.52; 148.32; 156.16; 159.63; 160.22; 161.14. MS: 432 (100, *M*⁺). Anal. calc. for C₂₉H₂₄N₂O₂ (432.51): C 80.53, H 5.59, N 6.48; found: C 80.39, H 5.50, N 6.40.

4-(3-Chlorophenyl)-2,8-diphenyl-1,7-naphthyridine (6f). Pale-yellow solid. M.p. 148–150° (hexane/Et₂O). IR (KBr): 1601, 1589. ¹H-NMR: 7.46–7.59 (*m*, 10 H); 7.65 (*d*, *J* = 5.5, 1 H); 8.05 (*s*, 1 H); 8.21 (*dd*, *J* = 8.2, 1.4, 2 H); 8.25 (*dd*, *J* = 8.2, 1.4, 2 H); 8.67 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 116.87; 121.51; 127.47; 127.66; 127.68; 128.80; 128.93; 129.00; 129.44; 129.54; 129.99; 130.11; 131.59; 134.89; 138.40; 138.77; 139.05; 141.63; 143.21; 146.92; 156.73; 160.59. MS: 392 (100, *M*⁺). Anal. calc. for C₂₆H₁₇ClN₂ (392.88): C 79.48, H 4.36, N 7.13; found: C 79.48, H 4.57, N 7.08.

4-(3-Chlorophenyl)-2,8-dimethyl-1,7-naphthyridine (6g). Pale-yellow solid. M.p. 124–126° (hexane/Et₂O). IR (KBr): 1605, 1591. ¹H-NMR: 2.82 (*s*, 3 H); 3.11 (*s*, 3 H); 7.36 (*d*, *J* = 6.0, 1 H); 7.39 (*s*, 1 H); 7.45–7.50 (*m*, 4 H); 8.39 (*d*, *J* = 6.0, 1 H). ¹³C-NMR: 21.36; 25.62; 115.89; 125.36; 127.52; 127.59; 128.81; 129.38; 129.97; 134.76; 138.85; 142.17; 142.36; 145.96; 158.91; 161.54. MS: 268 (100, *M*⁺). Anal. calc. for C₁₆H₁₃ClN₂ (268.74): C 71.51, H 4.88, N 10.42; found: C 71.41, H 5.02, N 10.21.

4-(3-Chlorophenyl)-2,8-bis(4-methylphenyl)-1,7-naphthyridine (6h). Pale-yellow crystals. M.p. 124–126° (hexane/Et₂O). IR (KBr): 1611, 1587. ¹H-NMR: 2.43 (*s*, 3 H); 2.49 (*s*, 3 H); 7.33 (*d*, *J* = 8.2, 2 H); 7.38 (*d*, *J* = 8.2, 2 H); 7.45–7.47 (*m*, 1 H); 7.52–7.53 (*m*, 2 H); 7.58 (*t*, *J* = 0.9, 1 H); 7.59 (*d*, *J* = 5.5, 1 H); 8.00 (*s*, 1 H); 8.11 (*d*, *J* = 8.2, 2 H); 8.18 (*d*, *J* = 8.2, 2 H); 8.63 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 21.35; 21.43; 116.57; 121.31; 126.49; 127.40; 127.68; 128.45; 128.92; 129.45; 129.67; 130.07; 131.58; 134.86; 135.78; 135.96; 138.72; 139.23; 140.19; 141.69; 143.01; 146.74; 156.63; 160.38. MS: 420 (100, *M*⁺). Anal. calc. for C₂₈H₂₁ClN₂ (420.93): C 79.89, H 5.03, N 6.66; found: C 79.62, H 5.11, N 6.42.

4-(4-Methoxyphenyl)-2,8-diphenyl-1,7-naphthyridine (6i). Pale-yellow solid. M.p. 157–160° (CHCl₃). IR (KBr): 1608, 1593. ¹H-NMR: 3.94 (*s*, 3 H); 7.12 (*d*, *J* = 8.7, 2 H); 7.46–7.59 (*m*, 8 H); 7.75 (*d*, *J* = 5.5, 1 H); 8.04 (*s*, 1 H); 8.21 (*d*, *J* = 8.2, 1.4, 2 H); 8.26 (*d*, *J* = 8.2, 1.4, 2 H); 8.64 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 55.44; 114.32; 117.40; 121.41; 127.47; 127.64; 128.67; 128.87; 129.60; 129.80; 130.11; 130.77; 131.58; 138.74; 138.99; 141.81; 142.85; 148.19; 156.71; 160.21; 160.49. MS: 388 (100, *M*⁺). Anal. calc. for C₂₇H₂₀N₂O (388.46): C 83.48, H 5.19, N 7.21; found: C 83.39, H 5.21, N 6.93.

2,8-Bis(4-chlorophenyl)-4-(4-methoxyphenyl)-1,7-naphthyridine (6j). Pale-yellow solid. M.p. 255–257° (hexane/AcOEt). IR (KBr): 1611, 1595. ¹H-NMR: 3.94 (*s*, 3 H); 7.17 (*d*, *J* = 8.7, 2 H); 7.48–7.55 (*m*, 6 H); 7.75 (*d*, *J* = 5.5, 1 H); 7.99 (*s*, 1 H); 8.12 (*d*, *J* = 8.7, 2 H); 8.20 (*d*, *J* = 8.7, 2 H); 8.63 (*d*, *J* = 5.5, 1 H). ¹³C-NMR: 55.50; 114.44; 117.76; 121.23; 127.90; 128.71; 129.20; 129.32; 130.24; 130.77; 132.87; 135.01; 136.24; 137.08; 137.34; 141.66; 143.04; 148.65; 155.71; 159.20; 160.39. MS: 456 (100, *M*⁺). Anal. calc. for C₂₇H₁₈Cl₂N₂O (457.35): C 70.91, H 3.97, N 6.13; found: C 70.85, H 4.03, N 6.36.

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