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NICKEL–PHOSPHINE COMPLEX-CATALYZED GRIGNARD COUPLING—II[1]

GRIGNARD COUPLING OF HETEROCYCLIC COMPOUNDS[2]

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Abstract—A general, versatile method for alkylation and arylation of haloheterocyclic compounds is reported. In the presence of a catalytic quantity of [$NiCl_2$(dppp)], where dppp stands for $Ph_2P(CH_2)_3PPh_2$, bromothiophenes, halopyridines, haloquinoline, and haloisoquinolines reacted with alkyl and aryl Grignard reagents at room temperature or at ether refluxing temperature to give the cross-coupling products. The coupling reaction has been applied to the synthesis of isoquinoline alkaloids. Reactivities of 2-thienyl and 2-pyridyl Grignard reagents have also been examined.

While there have been a number of methods for introducing organic groups into heterocycles,[3] only a limited number of reactions have so far been developed for the substitution reaction of halogenated heterocycles. Such processes include the Ullmann reaction,[4] coupling with organolithium,[5] organocuprates,[6] and Wittig reagents,[3] and palladium catalyzed alkenylation[7] and alkynylation.[8] The Ullmann reaction occurs only with reactive halides, requires drastic conditions, and usually gives symmetrical biaryls. Coupling with organolithium and organocuprate reagents seems not to be of general applicability. The recently developed coupling reaction of heteroaryl halides with Wittig reagents may be widely useful, but this reaction is also applicable only to reactive halides.

It has now been established that nickel–phosphine complexes are extremely effective catalysts for the cross-coupling between Grignard reagents and C(sp^2)-halides.[1,9] This paper describes the cross-coupling reaction of heterocyclic halides with various kinds of Grignard reagents in the presence of nickel–phosphine complexes as catalysts. Reactions of heteroaryl Grignard reagents are also mentioned.

RESULTS AND DISCUSSION

In almost all cases, [$NiCl_2$(dppp)], (dppp = $Ph_2P(CH_2)_3PPh_2$), was used as catalyst, because the complex has been found to be one of the most effective catalysts for the Grignard coupling.[1] The catalyst concentration was in the range of 1–0.1 mol% of organic halides. Reactions were carried out in the usual manner, i.e. a Grignard solution was added to a mixture of organic halide, catalyst and solvent. Stirring at room temperature or under reflux for a given period of time followed by hydrolysis gave a coupling product, which was purified by distillation, recrystallization, or preparative GLC. Table 1 summarizes the results of coupling reactions of bromothiophenes, halopyridines, haloquinolines, and haloisoquinolines. Physical constants, ^{1}H NMR spectral and analytical data for coupling products are listed in the Experimental section.

The characteristic features of the present procedures are summarized as follows. (1) The coupling reaction requires only a catalytic amount of nickel–phosphine complex, proceeds under mild conditions, and usually gives the coupling product in high yield. (2) The organic group is introduced onto the carbon atom to which the halogen has been attached, giving an isomerically pure coupling product. (3) The reaction is applicable to five- and six-membered nitrogen or sulfur containing heterocyclic compounds. (4) Both of the heterocyclic chlorides and bromides exhibit sufficient reactivities. Additional comments will be made in individual cases.

Bromothiophenes

Coupling reactions of 2-bromo-, 3-bromo-, 2,5-dibromo-, and 3,4-dibromo-thiophenes were examined. These four bromothiophenes coupled with trimethylsilylmethyl, benzyl, phenyl, and 2-thienyl Grignard reagents to give cross-coupling products in high yields. With a simple alkyl (such as *n*-butyl) Grignard reagent, 3-bromo- and 3,4-dibromo-thiophene gave the coupling

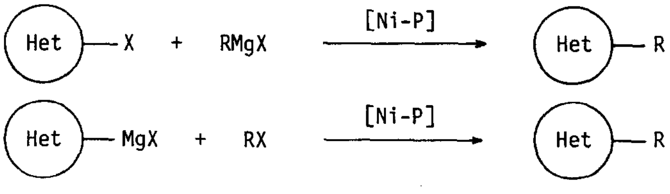

Table 1. Coupling reactions of heterocyclic halides with Grignard reagents[a]

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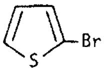
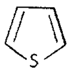
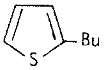
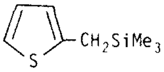
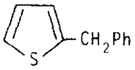
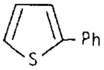
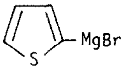
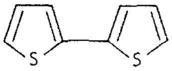
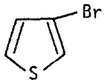
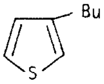
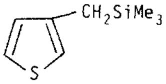
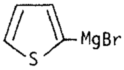
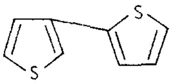
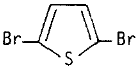
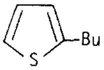
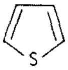
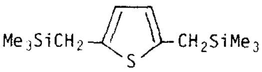
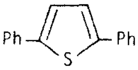
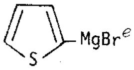
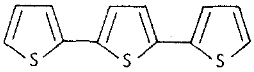
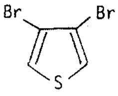
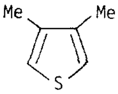
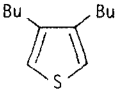
	BuMgBr	r.t., 2		92
				8
	Me_3SiCH_2MgCl	rfx., 6		67[d]
	$PhCH_2MgCl$	rfx., 16		100
	PhMgBr	rfx., 2		98
		rfx., 3		90[d]
	BuMgBr	r.t., 2		78
	Me_3SiCH_2MgCl	rfx., 5		43
		rfx., 20		100
	BuMgBr	r.t., 22		17
				81
	Me_3SiCH_2MgCl	rfx., 45		34
	PhMgBr	rfx., 1		94
		60°, 15		80
	MeMgBr	rfx., 20		95
	BuMgBr	rfx., 16		100

Table 1. (*Contd*)

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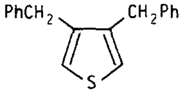
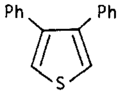
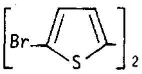
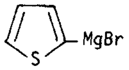
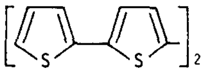
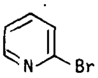
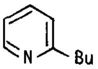
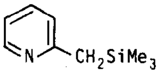
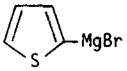
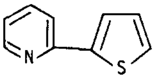
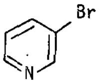
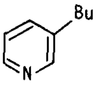
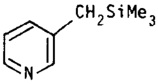
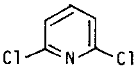
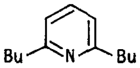
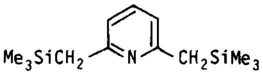
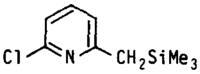
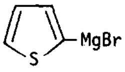
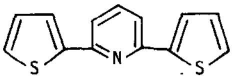
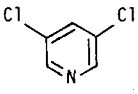
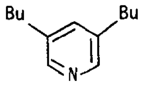
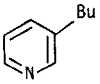
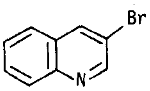
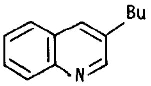
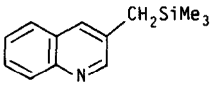
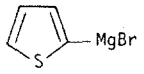
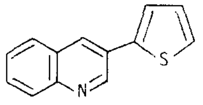
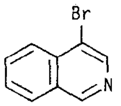
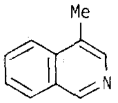
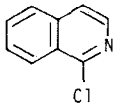
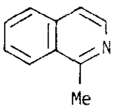
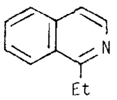
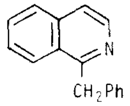
	PhCH$_2$MgCl	rfx., 20		95
	PhMgBr	rfx., 16		70
		rfx., 3		64[d]
	BuMgBr	r.t., 2.5		71[d]
	Me$_3$SiCH$_2$MgCl	rfx., 3		72
		rfx., 20		78
	BuMgBr	r.t., 2.5		47
	Me$_3$SiCH$_2$MgCl	rfx., 3		35
	BuMgBr	rfx., 6		63
	Me$_3$SiCH$_2$MgCl	rfx., 20		69
				11[d]
		rfx., 21		11
	BuMgBr	rfx., 20		42
				9
	BuMgBr	r.t., 3		57
	Me$_3$SiCH$_2$MgCl	rfx., 3		44

Table 1. (*Contd*)

Halide	Grignard reagent	Conditions[b] (°C, h)	Product(s)	Yield (%)[c]
		rfx., 20		49
	MeMgI	rfx., 20		73
	MeMgBr MeMgBr[f]	rfx., 4 r.t., 18		67 61
	EtMgBr	rfx., 8		55
	$PhCH_2MgCl$	r.t., 21		74
1	2	r.t., 20	3	66[d]
1	4	r.t., 20	5	92[d]
6	4	r.t., 20	7	66[d]

[a] Reactions were carried out on 5 - 20 mmol scales in the presence of $[NiCl_2(dppp)]$ as a catalyst (0.5 - 1 mol%) in ether, unless otherwise stated. About 1.2 equiv of the Grignard reagent was used. [b] R.t. = room temperature; rfx. = reflux.

[c] Yields are determined by GLC, unless otherwise stated. [d] Isolated yield.

[e] In a mixture of ether and THF. [f] $[NiCl_2(PPh_3)_2]$ was used as a catalyst.

product in high yield, but 2-bromo- and 2,5-dibromothiophene formed thiophene as a major or sole product instead of the coupling product; 2,5-dibutyl-thiophene was not formed at all. The predominant formation of thiophene from 2-bromo- and 2,5-dibromo-thiophene may be attributable to a rapid metal–halogen exchange reaction between these halides with reactive alkyl Grignard reagents.[10] With more stabilized Grignard reagents described above, the coupling reaction proceeded faster than the metal–halogen exchange.

In view of the ready accessibility of isomerically pure bromothiophenes, the present reaction provides a much more convenient method for the preparation of alkyl- and aryl-thiophenes in comparison with the conventional acylation-reduction, lithiation–alkylation, or thiophene ring construction.[11] The present method also provides the most convenient and efficient route to polythienyls. For example, terthienyl, a color constituent of the "Lemon" variety of the common marigold (*Tagetes erecta* L.)[12] has been obtained in 80% yield, which should be compared with 4% yield by the Ulmann reaction of iodothiophene.[13]

Halopyridines

Reactions with Grignard reagents are generally exothermic and the color of the reaction mixture sometimes changes from red to greenish. 2-bromo- and 2,6-dichloropyridine seem to be more reactive than 3-bromo- and 3,5-dichloropyridine. Yields of thienylpyridines are not very high, but these types of compound have so far been prepared in rather low yields.[14] One-step synthesis of [*n*](2,6)pyridinophanes by the coupling of 2,6-dichloropyridine with di-Grignard reagents has already been reported elsewhere.[15]

Haloquinolines

3-bromoquinoline readily reacts with alkyl and thienyl Grignard reagents. Since the Wittig procedure cannot be applied to the 3-haloquinolines,[3] the present procedure provides a convenient route to 3-alkylquinolines. The reactivity of the halide appeared to be somewhat higher than that of 3-bromopyridine.

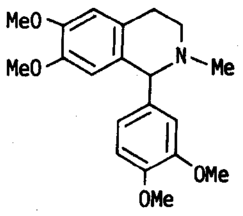
Haloisoquinolines

Alkylation of 1-chloro- and 4-bromo-isoquinoline proceeds smoothly. $[NiCl_2(dppp)]$ and $[NiCl_2(PPh_3)_2]$ showed a comparable catalytic activity for methylation of 1-chloro-isoquinoline.

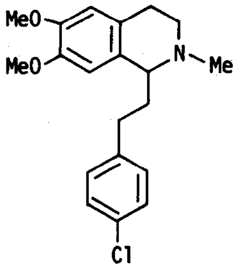
Since the present method provides a new efficient procedure for the introduction of an organic group into the isoquinoline nucleus, we have applied this coupling reaction to the synthesis of some substituted isoquinolines which are precursors for the preparation of isoquinoline alkaloids of pharmaceutical interest.[16] The results are illustrated in Scheme 1. Thus, 1-chloro-6,7-dimethoxyisoquinoline **1** was treated with 3,4-dimethoxyphenylmagnesium bromide **2** in the presence of $[NiCl_2(dppp)]$ as a catalyst to give 1 - (3,4 - dimethoxyphenyl) - 6,7 - dimethoxyisoquinoline **3** in 66% yield. This compound is a precursor for cryptostyline II.[17] Similarly, the same chloride **1** coupled with 2 - (4 - chloro - phenyl)ethylmagnesium bromide **4** to give the corresponding coupling product **5** which is a possible precursor for the synthetic phenethylisoquinoline, methopholine.[18] It should be noted here that the *para*-chlorine atom in the Grignard reagent was kept intact under the reaction conditions employed. 1 - chloro - 6,7 - (methylenedioxy)isoquinoline **6** also coupled with 3,4-(methylenedioxy)phenylmagnesium bromide **4** to form the corresponding coupling product **7** in 66% yield.

Heteroaryl Grignard reagents

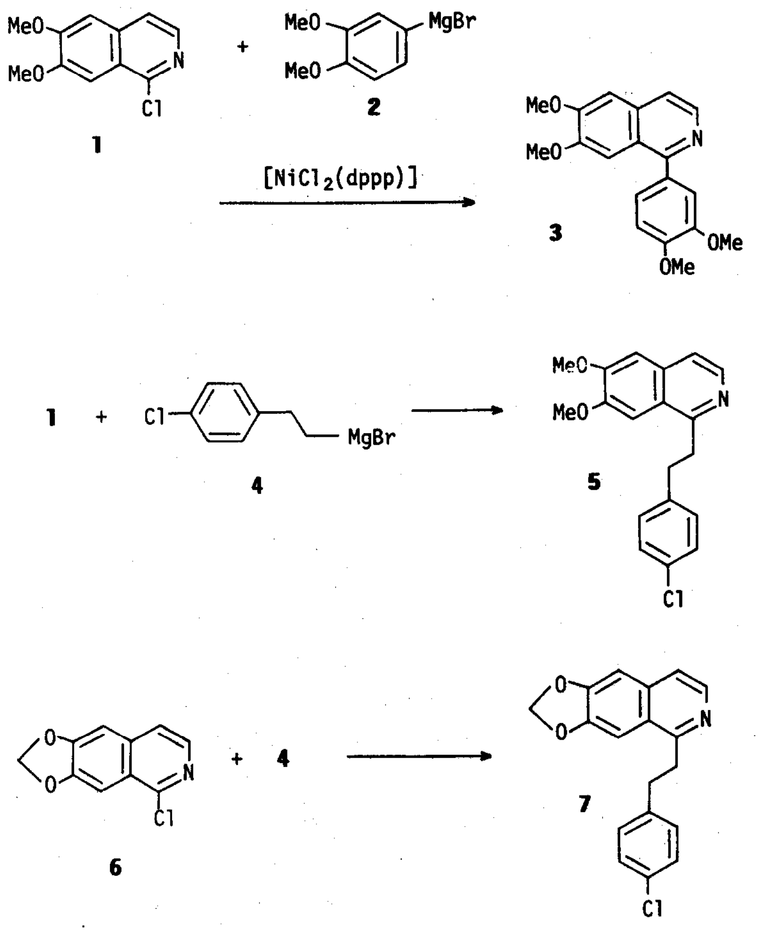
Besides its reaction with hererocyclic halides listed in Table 1, the 2-thienyl Grignard reagent reacts with vinyl chloride, bromobenzene, chlorobenzene, and 1-bromonaphthalene (1-NpBr), as shown below. Yields were determined by GLC. The low yield with chlorobenzene may be consistent with the argument that the thienyl Grignard reagent, like a vinyl Grignard reagent discussed in the previous paper,[1] might interact, probably through



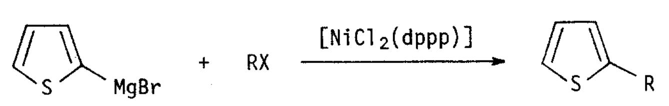
Cryptostyline II



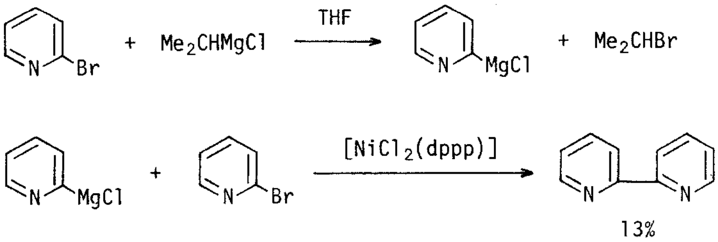
Methopholine



Scheme 1.



RX =			
	CH_2=CHCl	(r.t., 2.5 hr)	100%
	PhCl	(reflux, 44 hr)	17%
	PhBr	(reflux, 20 hr)	56%
	1-NpBr	(reflux, 20 hr)	76%



the sulfur atom, with a catalytically active nickel species strongly enough to prevent the coordination of less reactive chlorobenzene.

The 2-pyridyl Grignard reagent, derived from the Grignard exchange reaction between 2-bromopyridine and isopropyl Grignard reagent in THF,[10,19] failed to react with chloro- and bromo-benzene, possibly for the same reason as above. Even the reaction with 2-bromopyridine, one of the most reactive halides, gave bipyridyl only in a poor yield (13%).

SUMMARY

We have presented a convenient and versatile method for the introduction of organic groups into heterocyclic compounds such as thiophene, pyridine, quinoline and isoquinoline. In the course of our investigation, several papers have appeared dealing with similar nickel-catalyzed Grignard coupling reactions of halopyridines,[20] -quinolines,[21] -pyrimidines,[22] and -pyridazines.[23] In light of these observations and the ready accessibility of halogenated heterocycles, the nickel-catalyzed Grignard coupling reaction may prove to be of great and general use.[24]

EXPERIMENTAL

General. ^1H NMR spectra were determined with a Varian EM360 or A-60A spectrometer in CCl_4, unless otherwise stated. For several compounds indicated below, a JEOL JNM-MH-100 (100 MHz) spectrometer was used. Chemical shifts are recorded in δ ppm down field from Me_4Si. GLC analyses and preparative purification were performed on a Shimadzu GC-4B gas chromatograph, equipped with a 3-m column packed with 30% Silicone DC 550 on Celite 545.

Materials. The following halides were prepared as reported, the references being given after the compounds; 2-bromo-,[25] 3-bromo-,[25] 2,5-dibromo-[26] and 3,4-dibromo-thiophenes,[27] 1,8-dibromodithienyl,[28] 2-bromo-[29] and 3-bromo-pyridine,[30] 3-bromoquinoline,[31] 1-chloro-[32] and 4-bromo-isoquinoline.[33] Conversion of catechol to the methylenedioxy derivative[34] and bromination of 1,2-dimethoxy- and 1,2-methylenedioxy-benzene[35] were carried out by the reported procedures. 2-(4-chlorophenyl) ethyl bromide was prepared by the reaction of 4-chlorophenylmagnesium bromide with ethylene oxide and subsequent treatment of the resulting alcohol with PBr_3. Commercially available 2,6- and 3,5-dichloropyridine and other chemicals were used without further purification. References for the preparation of nickel–phosphine complexes have been compiled in our previous paper.[1] 1 - chloro - 6,7 - dimethoxyisoquinoline **1**, m.p. 140–142° (hexane) (lit.[36] m.p. 155–160°), was prepared by the following known procedures from 3,4-dimethoxy-benzaldehyde: The Perkin reaction[37] gave dimethoxycinnamic acid (60% yield), the modified Curtius reaction[38] gave the corresponding acyl azide $(MeO)_2C_6H_3CH{=}CHCON_3$, m.p. 105° (EtOH) (57% yield), thermolysis in toluene[39] yielded the cyanate $(MeO)_2C_6H_3CH{=}CHNCO$, subsequent thermal cyclization in diphenyl ether[39] afforded 6,7-dimethoxyisoquinolone, and finally treatment with $POCl_3$[39] gave **1**. 1 - chloro - 6,7 - (methylenedioxy)isoquinoline **6** was prepared similarly (m.p. 185–186°).

Coupling reactions. Since a general procedure of the cross-coupling reactions has previously been presented,[1,40] a few representative examples are described here. Liquid products were isolated by distillation and/or preparative GLC.

2-(*Trimethylsilylmethyl*)*thiophene.* To a mixture of 2-bromothiophene (8.2 g; 50 mmol), $[NiCl_2(dppp)]$ (0.15 g; 0.3 mmol), and dry ether (100 ml) was added a soln of (trimethylsilylmethyl)magnesium chloride in ether (70 mmol; 1 M soln) at 0°. The mixture was refluxed for 6 h. After usual work-up, distillation gave 5.68 g (67% yield) of 2-(trimethylsilylmethyl)thiophene: b.p. 72°/13 Torr. NMR (100 MHz): 0.04 (s, 9H), 2.26 (s, 2H), 6.48–6.55 (m, 1H), 6.7–6.95 (m, 2H). (Calc. for $C_8H_{14}SSi$: C, 56.41; H, 8.28%. Found: C, 56.53; H, 8.50).

1 - (*3,4 - dimethoxyphenyl*) - *6,7 - dimethoxyisoquinoline* **3**. To a mixture of **1** (1.23 g; 5.5 mmol), $[NiCl_2(dppp)]$ (40 mg; 0.073 mmol), and anhydrous THF (6 ml) was added dropwise a THF soln of 3,4-dimethoxyphenylmagnesium bromide (6.6 mmol) at 0° under N_2 atmosphere. The resulting blackish homogeneous mixture was stirred at room temp for 22 h, hydrolysed, made alkaline by adding 10% NaOH soln, and then extracted with benzene and ether. The organic layer was dried and evaporated to give crystalline crude product, 1.18 g (66% yield, m.p. 153–155° (lit.[41] m.p. 154°). Recrystallization from benzene afforded 0.60 g (33%) of pure product as colourless prisms; m.p. 155–157°. NMR: 3.88 (s, 3H), 3.95 (s, 3H), 3.98 (s, 3H), 4.03 (s, 3H), 6.92–7.5 (m, 6H), 8.47 (d, $J = 6$ Hz, 1H). (Calc. for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89%. Found: C, 69.84; H, 6.07.)

Other products were characterized as follows.

2-*butylthiophene.* n_D^{20} 1.4952 (lit.[42] 1.49635). NMR (100 MHz): 0.95 (t, $J = 7$ Hz, 3H), 1.2–1.85 (m, 4H), 2.80 (t, $J = 7$ Hz, 2H), 6.6–6.85 (m, 2H), 6.98 (br. d, $J = 5$ Hz, 1H). (Calc. for $C_8H_{12}S$: C, 68.51; H, 8.62%. Found: C, 68.35; H, 8.88.)

2-*benzylthiophene*. n_D^{20} 1.5915. NMR: 4.12 (s, 2H), 6.7–6.95 (m, 2H), 7.0–7.15 (m, 1H), 7.23 (s, 5H).

2-*phenylthiophene*. m.p. 34–35° (lit.[43] m.p. 37°). NMR 6.8–7.7 (m).

2-(1-*naphthyl*)*thiophene*. NMR: 6.95–7.60 (m, 7H), 7.65–7.90 (m, 2H), 8.05–8.35 (m, 1H). (Calc. for $C_{14}H_{10}S$: C, 79.96; H, 4.79%. Found: C, 80.08; H, 4.76.)

2-*vinylthiophene*. NMR: 5.16 (br. d, $J = 11$ Hz, 1H), 5.40 (br. d, $J = 14$ Hz, 1H), 6.46–7.13 (m, 4H, involving an upper field doublet of a quartet at 6.60, $J = 11$ Hz). (Calc. for C_6H_6S: C, 65.41; H, 5.49%. Found: C, 73.61; H, 5.28.)

3-*butylthiophene*. n_D^{20} 1.5041 (lit.[44] n_D^{20} 1.5114). NMR: 0.94 (t, $J = 6.5$ Hz, 3H), 1.15–2.0 (m, 4H), 2.62 (t, $J = 6.5$ Hz, 2H), 6.75–7.0 (br. d, 2H), 7.0–7.3 (m, 1H). (Calc. for $C_8H_{12}S$: C, 68.51; H, 8.62%. Found: C, 68.59; H, 8.57.)

3-(*trimethylsilylmethyl*)*thiophene*. NMR (100 MHz): 0.00 (s, 9H), 2.07 (s, 2H), 6.55–6.75 (m, 2H), 7.07–7.18 (m, 1H). (Calc. for $C_8H_{14}SSi$: C, 56.41; H, 8.28%. Found: C, 56.54; H, 8.35.)

2,5-*bis*(*trimethylsilylmethyl*)*thiophene*. NMR: 0.03 (s, 18H), 2.13 (s, 4H), 6.22 (s, 2H). (Calc. for $C_{12}H_{24}SSi_2$: C, 56.18; H, 9.43%. Found: C, 56.26; H, 9.36.)

2,5-*diphenylthiophene*. m.p. 153–154° (hexane) (lit.[45] m.p. 152–153°). NMR: 7.26 (s, 2H), 7.26–7.75 (m, 10H).

3,4-*dimethylthiophene*. n_D^{25} 1.5191 (lit.[26] n_D^{25} 1.5187). NMR: 2.15 (s, 6H), 6.75 (s, 2H).

3,4-*dibutylthiophene*. n_D^{20} 1.5000. NMR: 0.94 (t, $J = 6$ Hz, 6H), 1.15–1.8 (m, 8H), 2.52 (t, $J = 6$ Hz, 4H), 6.86 (s, 2H). (Calc. for $C_{12}H_{20}S$: C, 73.41; H, 10.27%. Found: C, 73.61; H, 10.45.)

3,4-*dibenzylthiophene*. m.p. 55–56° (ethanol). NMR: 3.85 (s, 4H), 6.89 (s, 2H), 7.05–7.4 (m, 10H). (Calc. for $C_{18}H_{16}S$: C, 81.77; H, 6.10%. Found: C, 81.76; H, 6.25.)

3,4-*diphenylthiophene*. m.p. 112–113° (hexane) (lit.[46] m.p. 114°). NMR: 7.24 (s, 10H), 7.33 (s, 2H).

2,2′-*dithienyl*. b.p. 144°/25 torr; m.p. 33° (lit.[47] m.p. 33°).

2,3′-*dithienyl*. m.p. 60–61° (contaminated by a trace amount of 2,2′-dithienyl) (lit.[44] m.p. 68–68.5°). NMR: 6.8–7.4 (m). (Calc. for $C_8H_6S_2$: C, 57.80; H, 3.63%. Found: C, 58.16; H, 3.55).

2,2′:5′,2″-*terthienyl*. m.p. 88–89° (ligroin) (lit.[48] m.p. 94–95°). NMR: 6.85–7.25 (m).

2,2′:5′,2″:5″,2‴-*quarterthienyl*. m.p. 211–213° (ligroin) (lit.[48] m.p. 210–211°).

2-*butylpyridine*. b.p. 84–86°/15 torr. NMR (100 MHz): 0.92 (t, $J = 6.5$ Hz, 3H), 1.2–1.9 (m, 4H), 2.75 (t, $J = 6.5$ Hz, 2H), 6.9–7.15 (m, 2H), 7.35–7.6 (m, 1H), 8.4–8.5 (m, 1H). (Calc. for $C_9H_{13}N$: C, 79.94; H, 9.69%. Found: C, 79.30; H, 9.76.)

2-(*trimethylsilylmethyl*)*pyridine*. n_D^{20} 1.4873 (lit.[49] n_D^{25} 1.4866). NMR: 0.02 (s, 9H), 2.26 (s, 2H), 6.7–7.0 (m, 2H), 7.2–7.6 (m, 1H), 8.25–8.5 (m, 1H). (Calc. for $C_9H_{15}NSi$: C, 65.39; H, 9.15%. Found: C, 65.36; H, 9.30.)

3-*butylpyridine*. n_D^{25} 1.4905 (lit.[50] n_D^{25} 1.4917). NMR: 0.93 (t, $J = 6.5$ Hz, 3H), 1.1–1.9 (m, 4H), 2.60 (t, $J = 6.5$ Hz, 2H), 7.0–7.55 (m, 2H), 8.37 (br. s, 2H). (Calc. for $C_9H_{13}N$: C, 79.94; H, 9.69%. Found: C, 79.27; H, 9.91.)

3-(*trimethylsilylmethyl*)*pyridine*. n_D^{25} 1.4967. NMR (100 MHz, $CDCl_3$): 0.02 (s, 9H), 2.08 (s, 2H), 7.05–7.43 (m, 2H), 8.2–8.45 (br., 2H). (Calc. for $C_9H_{15}NSi$: C, 65.39; H, 9.15%. Found: C, 65.61; H, 9.44.)

2,6-*dibutylpyridine*. NMR (100 MHz): 0.95 (t, $J = 6.5$ Hz, 6H), 1.2–1.9 (m, 8H), 2.70 (t, $J = 6.5$ Hz, 4H), 6.80 (d, $J = 8$ Hz, 2H), 7.36 (t, $J = 8$ Hz, 1H). (Calc. for $C_{13}H_{21}N$: C, 81.61; H, 11.06%. Found: C, 81.82; H, 11.28.)

2,6-*bis*(*trimethylsilylmethyl*)*pyridine*. m.p. 40–41°. NMR: 0.02 (s, 18H), 2.21 (s, 4H), 6.52 (d, $J = 7$ Hz, 2H), 7.21 (t, $J = 7$ Hz, 1H). (Calc. for $C_{13}H_{25}NSi$: C, 62.08; H, 10.02%. Found: C, 62.33; H, 9.96.). The by-products were tentatively characterized as follows. 2 - methyl - 6 - (trimethylsilylmethyl)pyridine: NMR: 0.02 (s, 9H), 2.20 (s, 2H), 2.40 (s, 3H), 6.5–6.8 (m, 2H), 7.1–7.4 (m, 1H). 2 - chloro - 6 - (trimethylsilylmethyl)pyridine: NMR: 0.01 (s, 9H), 2.23 (s, 2H), 6.6–7.0 (m, 2H), 7.2–7.5 (m, 1H).

3,5-*dibutylpyridine*. NMR: 0.95 (t, $J = 6.5$ Hz, 6H), 1.1–1.9 (m, 8H), 2.56 (t, $J = 6.5$ Hz, 4H), 7.1–7.25 (m, 1H), 8.17 (s, 2H). (Calc. for $C_{13}H_{21}N$: C, 81.61; H, 11.06%. Found: C, 81.72; H, 11.06.)

2-(2-*thienyl*)*pyridine*. m.p. 63–64° (lit.[51] m.p. 64°). NMR: 7.0–7.8 (m, 6H), 8.5–8.7 (m, 1H). (Calc. for C_9H_7NS: C, 67.05; H, 4.38%. Found: C, 66.98; H, 4.31.)

2,6-*bis*(2-*thienyl*)*pyridine*. m.p. 78–79° (lit.[51] m.p. 79°). NMR (100 MHz): 6.95–7.1 (m, 2H), 7.25–7.65 (m, 7H). (Calc. for $C_{13}H_9NS_2$: C, 64.17; H, 3.73%. Found: C, 63.90; H, 3.56.)

3-*butylquinoline*. NMR: 0.95 (t, $J = 6.5$ Hz, 3H), 1.1–1.9 (m, 4H), 2.75 (t, $J = 6.5$ Hz, 2H), 7.1–7.9 (m, 2H), 7.9–8.2 (m, 1H), 8.6–8.8 (m, 1H). (Calc. for $C_{13}H_{15}N$: C, 84.23; H, 8.16%. Found: C, 83.63; H, 8.30.)

3-(2-*thienyl*)*quinoline*. NMR (100 MHz): 5.75–5.9 (m, 1H), 6.0–6.55 (m, 5H), 6.7–6.9 (m, 2H), 7.83 (d, $J = 3$ Hz, 1H). (Calc. for $C_{13}H_9NS$: C, 73.90; H, 4.29%. Found: C, 74.37; H, 5.04.)

4-*methylisoquinoline*. NMR: 2.54 (s, 3H), 7.18–7.55 (m, 2H), 7.55–7.72 (m, 2H), 8.05 (br. s, 1H), 8.75 (br. s, 1H). (Calc. for $C_{10}H_9N$: C, 83.88; H, 6.34%. Found: C, 84.17; H, 6.35.)

1-*methylisoquinoline*. NMR: 2.85 (s, 3H), 7.23–8.08 (m, 5H), 8.28 (d, $J = 6$ Hz, 1H). (Calc. for $C_{10}H_9N$: C, 83.88; H, 6.34%. Found: C, 84.08; H, 6.51.)

1-*ethylisoquinoline*. NMR: 1.43 (t, $J = 7.5$ Hz, 3H), 3.25 (q, $J = 7.5$ Hz, 2H), 7.28–8.2 (m, 5H), 8.35 (d, $J = 6$ Hz, 1H). (Calc. for $C_{11}H_{11}N$: C, 84.04; H, 7.05%. Found: C, 84.06; H, 7.22.)

1-*benzylisoquinoline*. m.p. 56° ($CHCl_3$/petroleum ether) (lit.[52] m.p. 51–52°). NMR: 4.60 (s, 2H), 7.0–7.8 (m, 9H), 8.12 (br. d, $J = 6$ Hz, 1H), 8.48 (d, $J = 6$ Hz, 1H). (Calc. for $C_{16}H_{13}N$: C, 87.64; H, 5.98%. Found: C. 87.60; H, 5.73.)

1 - [2 - (4 - *chlorophenyl*)*ethyl*] - 6,7 - *dimethoxyisoquinoline*. m.p. 104–106° (hexane) (lit.[53] m.p. 100–102°). NMR: 3.0–3.65 (m, 4H), 3.99 (s, 3H), 4.03 (s, 3H), 7.05 (s, 1H), 7.22 (s, 5H), 7.38 (d, $J = 6$ Hz, 1H), 8.35 (d, $J = 6$ Hz, 1H). Calc. for $C_{19}H_{18}ClNO_2$: C, 69.62; H, 5.53%. Found: C, 69.72; H, 5.70.)

1 - [2 - (4 - *chlorophenyl*)*ethyl*] - 6,7 - *methylenedioxyisoquinoline*. m.p. 143–145° (benzene/hexane). NMR: 3.04–3.6 (m, 4H), 6.12 (s, 2H), 7.12 (s, 1H), 7.29 (s, 4H), 7.4–7.45 (deformed d, 2H), 8.41 (d, $J = 6$ Hz, 1h). (Calc. for $C_{18}H_{14}ClNO_2$: C, 69.35; H, 4.53%. Found: C, 69.45; H, 4.57.)

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