APPLIED ORGANOMETALLIC CHEMISTRY
Appl. Organometal. Chem. 2004; **18**: 359–362
Main Group Metal Compounds
Published online in Wiley InterScience (www.interscience.wiley.com). DOI:10.1002/aoc.659

Regioselective synthesis of symmetrical pyridyl selenium compounds by bromine–magnesium exchange of bromopyridines using isopropyl magnesium chloride: X-ray crystal structure of 2,2′,5,5′-tetrabromo-3,3′-dipyridyldiselenide

K. K. Bhasin* and Veena Arora

Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh, 160 014, India

Received 30 January 2004; Revised 28 February 2004; Accepted 2 April 2004

2,2′-Dipyridyl-3,3′-dipyridyl,5,5′-dipyridyl-diselenides have been synthesized by a convenient method employing non-cryogenic conditions. Various bromopyridines (2-Bromopyridine, 2,5-dibromopyridines and 2,3,5-Tribromopyridines) undergo selective monobromine–magnesium exchange to yield the corresponding pyridyl magnesium chlorides at room temperature upon treatment with ^{i}PrMgCl. The resulting pyridyl magnesium chloride is quenched with elemental selenium, which upon further oxidation affords the above diselenides in good yields. The compounds prepared using this methodology have been characterized by elemental analysis, IR, NMR (^{1}H, ^{13}C, ^{77}Se) and mass spectral analysis. The molecular structure of 2,2′,5,5′-Tetrabromo-3,3′-dipyridyldiselenide has been established by single-crystal X-ray diffraction analysis. It exists as a dimeric form due to the non-bonding interactions between the selenium of one pyridine moiety and the hydrogen of the other.

KEYWORDS: chalcogens; selenium; diselenides; pyridine; bromopyridine; magnesium exchange

INTRODUCTION

Research on alkyl, aryl and mixed alkylaryl selenides is fast developing and is of immense interest to organic chemists[1,2] and biochemists.[3,4] In contrast, the corresponding pyridyl selenium chemistry, in spite of the greater utility in organic chemistry[5,6] and biochemistry,[7,8] is largely underdeveloped. This is primarily due the non-availability of a convenient synthesis. Amongst the known methods, the two most common routes involve either the reaction of alkali metal diselenide[9–12] with 2-bromopyridine at elevated temperatures, or by the aerial oxidation of lithium-2-pyridylselenoate (obtained by the lithium–bromine exchange of 2-bromopyridine with *n*-BuLi[13]) under cryogenic conditions. In our studies on the chemistry of pyridylselenium compounds,[14–17] efforts were made to synthesize these compounds on the molar scale in non-cryogenic conditions.

In this paper we report a methodology of practical and scalable synthesis of various symmetrical 2,2′-dipyridyl-, 3,3′-dipyridyl- and 5,5′-dipyridyl-diselenides under remarkably mild reaction conditions. This methodology involves bromine–magnesium exchange of bromopyridine using isopropylmagnesium chloride (^{i}PrMgCl). To the best of our knowledge, there is no report in the literature for the preparation of these 3-pyridyl- and 5-pyridyl-selenium compounds.

EXPERIMENTAL

All experiments were carried out in a dry, oxygen-free nitrogen atmosphere. IR spectra were recorded between KBr pellets on a Perkin–Elmer Model 1430 ratio recording spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ using tetramethylsilane as an internal standard and ^{77}Se with dimethylselenide as an external

*Correspondence to: K. K. Bhasin, Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh, 160 014, India.
Contract/grant sponsor: CSIR, UGC.

reference on a Jeol 300 MHz spectrometer. The mass spectra were obtained on a VG-705 11-250J mass spectrometer. Carbon, hydrogen and nitrogen were estimated microanalytically on a Perkin–Elmer 2400 CHN elemental analyzer. Bromopyridines were prepared from the corresponding 2-aminopyridines by literature methods.[18,19]

General method for the preparation of symmetrical dipyridyl diselenides

Bromopyridine (20 mmol) was added dropwise to a vigorously stirred solution of ^{i}PrMgCl (20 mmol) in tetrahydrafuran (THF). After 2 h of continuous stirring at room temperature, elemental selenium (20 mmol) was added after cooling in an ice bath. When all the selenium was dissolved, the reaction was quenched with acidified water. The mixture was extracted with diethyl ether (4 × 100 ml) and the organic layer was dried over anhydrous sodium sulfate. The diethyl ether was evaporated and the residue thus obtained was purified by column chromatography using silica gel and hexane–ethylacetate as eluent (5 : 1) to yield pure diselenides. Using this methodology, we prepared the following compounds (with details of the data obtained from spectroscopic analysis).

*2,2′-Dipyridyldiselenide (**1**)*

Yield 2.8 g (80%), m.p. 48–50 °C. ^{1}H NMR: δ, 7.07 (q, 2H, 5.5, 1.7 Hz), 7.53 (m, 2H, 1.9, 5.9, 1.7, 5.9, 2.0 Hz), 7.77 (d, 2H, 8.0 Hz), 8.43 (d, 2H, 5.5 Hz). ^{13}C NMR: δ, 121.1, 123.4, 137.3, 149.4, 154.2. ^{77}Se NMR: δ, 449. IR (KBr, cm^{-1}): 3060, 2960, 2920, 1565, 1552, 1444, 1105, 1076, 1031, 983, 748, 660. Anal. Found : C, 37.93; H, 2.13; N, 8.45. Calc. for $C_{10}H_8N_2Se_2$: C, 38.22; H, 2.54; N, 8.91%.

*3,3′-Dimethyl-2,2′dipyridyldiselenide (**2**)*

Yield 2.6 g (78%), m.p. 142–144 °C. ^{1}H NMR: δ, 2.42 (s, 2H), 7.03 (q, 2H, 5.0, 2.5, 4.8 Hz), 7.34 (d, 2H, 7.4 Hz), 8.3 (d, 2H, 5.1 Hz). ^{13}C-NMR: δ, 20.5, 121.7, 133.5, 136.6, 147.7, 153.0. ^{77}Se NMR: δ, 437. IR (KBr, cm^{-1}): 3030, 2960, 2920, 1664, 1570, 1543, 1460, 1277, 1060, 785, 635, 575, 470. MS (EI): 344 $[M(^{80}Se)]^+$ (19.6); 263 $[M - SeH]^+$ (24.4); 183 $[M - Se_2H]^+$ (100); 92 $[M - CH_3PySe_2]^+$ (62.2). Anal. Found : C, 41.45; H, 3.62; N, 8.34. Calc. for $C_{12}H_{12}N_2Se_2$: C, 41.86; H, 3.48; N, 8.13.

*4,4′- Dimethyl-2,2′-dipyridyldiselenide (**3**)*

Yield 2.2 g (65%), m.p. 96–98 °C. ^{1}H NMR: δ, 2.20 (s, 6H), 6.89 (d, 2H, 4.1 Hz), 7.62 (s, 2H), 8.31 (d, 2H, 4.9 Hz). ^{13}C NMR: δ, 21.0, 123.4, 123.9, 148.8, 149.0, 154.0. IR (KBr, cm^{-1}): 3060, 2960, 2920, 1580, 1540, 1460, 1270, 1120, 1080, 840, 700, 500. MS (EI): 344 $[M(^{80}Se)]^+$ (36); 263 $[M - SeH]^+$ (10.1); 183 $[M - Se_2H]^+$ (100); 92 $[M - CH_3PySe_2]^+$ (63). Anal. Found : C, 41.72; H, 3.92; N, 8.22. Calc. for $C_{12}H_{12}N_2Se_2$: C, 41.86; H, 3.48; N, 8.13.

*5,5′-Dimethyl-2,2′-dipyridyldiselenide (**4**)*

Yield 2.58 g (75%), m.p. 75–77 °C. ^{1}H NMR: δ, 2.27 (s, 2H), 7.35 (d, 2H, 8.1 Hz), 7.68 (d, 2H, 8.1 Hz), 8.27 (s, 2H). ^{13}C NMR: δ, 17.8, 123.3, 130.7, 136.1, 149.8, 150.7. IR (KBr, cm^{-1}): 3030, 2983, 2914, 1579, 1559, 1446, 1219, 1081, 822, 723, 592, 479. MS (EI): 344 $[M(^{80}Se)]^+$ (36); 263 $[M - SeH]^+$ (10.1); 183 $[M - Se_2H]^+$ (100); 92 $[M - CH_3PySe_2]^+$ (60.5). Anal. Found : C, 41.12; H, 3.35; N, 8.32. Calc. for $C_{12}H_{12}N_2Se_2$: C, 41.86; H, 3.48; N, 8.13%.

*6,6′-Dimethyl-2,2′-dipyridyldiselenide (**5**)*

Yield 2.58 g (75%), m.p. 62–64 °C. ^{1}H NMR: δ, 2.52 (s, 2H), 6.92 (d, 2H, 7.6 Hz), 7.43 (t, 2H, 7.7 Hz), 7.61 (d, 2H, 7.8 Hz). ^{13}C NMR: δ, 24.2, 120.5, 136.0, 137.5, 153.6, 158.5. IR (KBr, cm^{-1}): 3060, 2960, 2920, 1580, 1540, 1430, 1120, 1020, 840, 780, 660, 540. MS (EI): 344 $[M(^{80}Se)]^+$ (27); 263 $[M - SeH]^+$ (43.3); 183 $[M - Se_2H]^+$ (83); 92 $[M - CH_3PySe_2]^+$ (100). Anal. Found : C, 41.08; H, 3.28; N, 8.42. Calc. for $C_{12}H_{12}N_2Se_2$: C, 41.86; H, 3.48; N, 8.13%.

*2,2′-Dibromo-5,5′-dipyridyldiselenide (**6**)*

Yield 3.0 g (65%), m.p. 125–127 °C. ^{1}H NMR: δ, 8.47 (d, 2H, 2.0 Hz), 7.68 (q, 2H, 2.0, 8.0 Hz), 7.407 (d, 2H, 8.0 Hz). ^{13}C NMR: δ, 121.66, 128.93, 142.6, 143.6, 152.86. ^{77}Se NMR: δ, 456. MS (EI): 474 $[M(^{80}Se)]^+$ (8.3); 386 $[(PyBr)_2Se]^+$ (100); 237 $[BrPySeH]^+$ (20.3). Anal. Found : C, 25.06; H, 1.23; N, 5.88. Calc. for $C_{10}H_6Br_2N_2Se_2$: C, 25.316; H, 1.265; N, 5.907%.

*2,2′-Dibromo-4,4′-dimethyl-5,5′-dipyridyldiselenide (**7**)*

Yield 3.24 g (65%), m.p. 56–58 °C. ^{1}H NMR: δ, 8.623 (s, 2H), 7.31 (s, 2H,), 2.633 (s, 6H). ^{13}C NMR: δ, 22.52, 121.637, 125.362, 148.05, 150.74, 152.905. Anal. Found : C, 28.50; H, 2.28; N, 5.42. Calc. for $C_{12}H_{12}Br_2N_2Se_2$; C, 28.57; H, 2.38; N, 5.556%.

*2,2′-Dibromo-3,3′-dimethyl-5,5′-dipyridyldiselenide (**8**)*

Yield 3.0 g (60%), m.p. 110–112 °C. ^{1}H NMR: δ, 2.466 (s, 2H), 7.47 (d, 2H, 2.0 Hz), 8.38 (d, 2H, 2.0 Hz). ^{13}C NMR: δ, 24.27, 120.194, 137.205, 138.862, 140.428, 149.607. Anal. Found : C, 28.51; H, 2.33; N, 5.53. Calc. for $C_{12}H_{12}Br_2N_2Se_2$: C, 28.57; H, 2.38; N, 5.556%.

*2,2′5,5′-Tetrabromo-3,3′-dipyridyldiselenide (**9**)*

Yield 3.8 g (60%), m.p. 96–98 °C. ^{1}H NMR: δ, 8.403 (d, 2H, 2 Hz), 8.22 (d, 2H, 2 Hz). ^{13}C NMR: δ, 121.6, 131.4, 139.1, 140.4, 149.5. ^{77}Se NMR: δ, 425. MS (EI): 632 $[M(^{80}Se)]^+$ (100); 316 $[Br_2PySeH]^+$ (69.1); 235 $[BrPySeH)^+$ (98.7). Anal. Found : C, 18.77; H, 0.60; N, 4.41. Calc. for $C_{10}H_4Br_4N_2Se_2$: C, 18.98; H, 0.63; N, 4.43%.

*6,6′-Dimethyl-2,2′5,5′-tetrabromo-3,3′-dipyridyldiselenide (**10**)*

Yield 3.6 g (55%), m.p. 85–88 °C. ^{1}H NMR: δ, 2.58 (s, 6H), 7.48 (s, 2H). ^{13}C NMR: δ, 22.7, 120.1, 136.3, 138.8, 142.3, 150.3. Anal. Found : C, 21.58; H, 1.28; N, 4.42. Calc. for $C_{12}H_8Br_4N_2Se_2$: C, 21.81; H, 1.21; N, 4.24%.

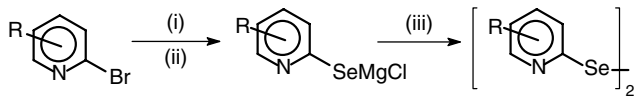
RESULTS AND DISCUSSION

Meunier and co-workers[20] carried out the bromine–magnesium exchange of 2-bromopyridine with ^{i}PrMgCl in THF to obtain pyridyl magnesium chloride; later, Queguiner and co-workers[21] reported the trapping of this reagent with different electrophiles. No attempts have been made to study the utility of this exchange toward the synthesis of pyridyl selenium compounds.

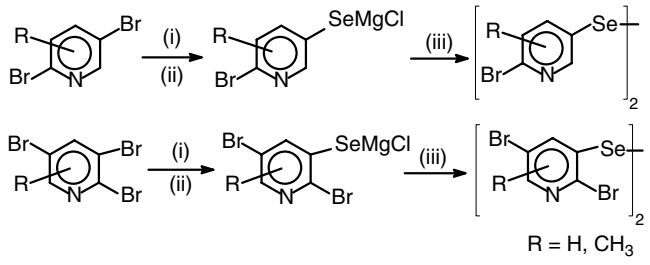
Using this methodology, we found that elemental selenium adds smoothly to pyridyl magnesium chloride generated by the reaction of bromopyridine with ^{i}PrMgCl, which upon aerial oxidation gives dipyridyldiselenide with good yields, as shown in Scheme 1.

This methodology was also further extended toward the selective synthesis of various symmetrical 3,3′-dipyridyl- and 5,5′-dipyridyl-diselenides. It was found that, when isopropylmagnesium chloride reacts with 2,5-dibromopyridine, the bromine–magnesium exchange takes place at C-5 of the pyridine ring, which is attributed to the fact that electrophilic attack at C-5 is more favorable than at C-2. Also, the bromine–magnesium exchange in the case of 2,3,5-tribromopyridine occurs at C-3, due to the ortho-activation effect of the bromine present on C-2. The successive bromine–magnesium exchange did not occur even after the addition of twice the amount of isopropylmagnesium chloride, as shown in Scheme 2.

It is important to note that the use of equimolar amounts of various bromopyridines and ^{i}PrMgCl resulted in poor yield. However, a slight excess of ^{i}PrMgCl increases the yield considerably. The conditions throughout the reaction were maintained extremely dry, as even traces of moisture can hinder the insertion of selenium into the pyridylmagnesium halide generated *in situ*.



Scheme 1. Reagents and conditions: (i) ^{i}PrMgCl, THF, r.t., 2 h; (ii) Se, 15 min; (iii) H_2O, O_2.



Scheme 2. Reagents and conditions: (i) ^{i}PrMgCl, THF, r.t., 2 h; (ii) Se, 15 min; (iii) H_2O, O_2.

As a part of our study, we also compared the efficiency of the reaction by employing different Grignard reagents, such like ^{i}PrMgCl, ethylmagnesium bromide and *n*-butylmagnesium chloride. The results are given for 3,3′-dimethyl-2,2′-dipyridyldiselenide in Table 1. These results shows that the more sterically hindered Grignard reagent results in the better yield.

Solid-state structure features

In order to understand the structural details, a single-crystal X-ray diffraction study was carried out. A perspective view of the structure of 2,2′, 5,5′-tetrabromo-3,3′-dipyridyldiselenide (along with the atom numbering scheme used) is given in Fig. 1, and selected bond lengths, bond angles and torsion angles are given in Table 2.

Each pyridine ring is substituted by selenium at C-3 and by bromine at C-2 and C-5, with Br–C bond lengths of 1.897(8) Å and 1.885(8) Å respectively. The average C–Se and Se–Se bond lengths, 1.917(8) Å and 2.3135(17) Å respectively, are similar to those found in 2,2′-dipyridyldiselenide,[22] i.e. 1.913(10) Å and 2.299(2) Å respectively, and fall within the ranges of 1.91–1.97 Å and 2.28–2.33 Å respectively found in most organic diselenides.[23] The torsion angles Se(1)–Se(1)$^{\#}$–C(2)–C(3) and Se(1)–Se(1)$^{\#}$–C(2)–C(1), −7.4° and 171.4° respectively, are responsible for the reduced

Table 1. Comparison of the effect of different Grignard reagents on the efficiency of the reaction

Grignard reagent	Compound	Solvent	Yield (%)
EtMgBr	3,3′-Dimethyl-2,2′-dipyridyl-diselenide	THF	10
^{i}PrMgCl	3,3′-Dimethyl-2,2′-dipyridyl-diselenide	THF	80
n-BuMgCl	3,3′-Dimethyl-2,2′-dipyridyl-diselenide	THF	60

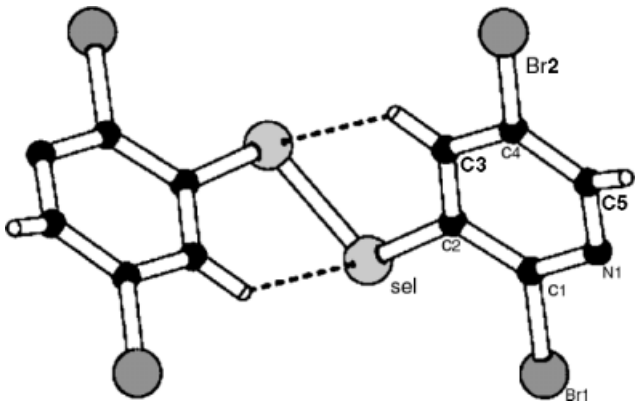


Figure 1. Molecular structure showing the intramolecular non-bonding interactions between hydrogen and selenium.

Table 2. Bond lengths (Å), bond angles (°) and torsion angles for 2,2′, 5,5′-tetrabromo-3,3′-dipyridyldiselenide.[a]

Se1–Se1[i]	2.3135(17)
Se1–C2	1.917(8)
Br1–C1	1.897(8)
Br2–C4	1.885(8)
C2–Se1–Se1[i]	101.9(2)
Se1–C2–C1	118.0(6)
Se1–C2–C3	125.7(6)
N(1)–C(1)–C(2)–Se(1)	−177.2(6)
Br(1)–C(1)–C(2)–Se(1)	3.2(8)
Se(1)[#1]–Se(1)–C(2)–C(3)	−7.4(7)
Se(1)[#1]–Se(1)–C(2)–C(1)	171.4(5)
C(1)–C(2)–C(3)–C(4)	0.4(11)
Se(1)–C(2)–C(3)–C(4)	179.3(6)

[a] Symmetry operation i: $1-x, y, 1.5-z$.
[b] Symmetry transformations used to generate equivalent atoms: [#1] $-x+1, y, -z+1.5$

interatomic repulsive interaction between the lone pair of electron on the selenium atoms.

The interesting feature of this structure is the non-bonding interactions between the selenium of one pyridine ring and the hydrogen of the other pyridine ring, as shown in Fig. 1.

Crystal structure determination

A rectangular-shaped crystal of size $0.15 \times 0.15 \times 0.30\ mm^3$ was mounted in a Lindemann glass capillary at 293 K on an Enraf-Nonius CAD-4 diffractometer and the structure determined using graphite monochromated Mo Kα radiation. Crystal data for $C_5H_2Br_2NSe$: $M = 630$, monoclinic space group $C2/c$, $a = 12.1430(14)$, $b = 9.1030(7)$, $c = 14.274(1)$ Å, $\beta = 113.295(8)°$, $V = 1449.2(2)\ A^3$, $Z = 8$, $D_x = 2.886\ Mg\ m^{-3}$, $\mu = 16.113\ mm^{-1}$, $\theta_{max} = 24.9°$, $R = 0.043$ (971 data with $I \geq 2\sigma(I)$) and $wR = 0.114$ (all 1113 data), $\rho_{max} = 1.10\ e^-\ Å^{-3}$. Data solution and refinement were performed using SHELXS-97 and SHELXL-97.[24] CCDC deposition number: 222022.

Acknowledgements

We would like to thank CSIR, UGC for funding this study; Professor Mathur, at the X-ray diffraction facility, IIT Mumbai, for providing information on crystal structure.

REFERENCES

1. Klayman DL, Gunther WHH. *Organic Selenium Compounds: Their Chemistry and Biology*. Wiley–Interscience: New York, 1973.
2. Patai S, Rappoport Z (eds). *The Chemistry of Organic Selenium and Tellurium Compounds*, vol. 1. Wiley–Interscience: New York, 1986.
3. Mugesh G, Singh HB. *Chem. Soc. Rev.* 2000; **29**: 347.
4. Mugesh G, du Mont W-W, Sies H. *Chem. Rev.* 2000; **101**: 2125.
5. Barton DHR, Crich D. *Tetrahedron* 1985; **41**: 4347.
6. Toshimitsu A, Hayashi G, Terao K. *J. Chem. Soc. Perkin Trans. 1* 1988; 2113.
7. Inglot AD, Zielinska J, Piasecki E, Syper L, Mlochowski J. *Experimentia* 1990; **46**: 308.
8. Pan B-C, Chen Z-H, Piras G, Dutschman GE, Rowe EC. *J. Heterocycl. Chem.* 1994; **31**: 177.
9. Toshimitsu A, Owada H, Terao K, Uemura S, Okano M. *J. Org. Chem.* 1984; **49**: 3796.
10. Cheng Y, Emge TJ, Brennan JG. *Inorg.Chem.* 1994; **33**: 3711.
11. Kienitz CO, Thone C, Jones PG. *Inorg. Chem.* 1996; **35**: 3990.
12. Khasnis DV, Buretea M, Emge TJ, Brennan JG. *J. Chem. Soc. Dalton Trans.* 1995; **2**: 45.
13. Bhasin KK. Bhandal BS, Singh J, Singh KN, Singh P. *Synth. Commun.* 2002; **9**: 1319.
14. Bhasin KK, Bhandal BS, Singh J, Singh KN. *Phosphorus Sulphur Silicon* 2002; **177**: 597.
15. Bhasin KK, Jain VK, Kumar H, Sharma S, Mehta SK, Singh J. *Synth. Commun.* 2003; **33**: 977.
16. Bhasin KK, Venugopalan P, Singh J. *Phosphorus Sulphur Silicon* 2002; **177**: 2579.
17. Bhasin KK, Singh J. *J. Organometal. Chem.* 2002; **658**: 71.
18. Craig LC. *J. Am. Chem. Soc.* 1934; **56**: 231.
19. Canebano V, Rodriguez JF, Santos M, Tejedor MAD, Carrene MC, Gonzalez C, Ruano JLG. *Synthesis* 2001; **10**: 2175.
20. Martin GJ, Mechin B, Leroux Y, Paulmier C, Meunier JC. *J. Organometal. Chem* 1974; **67**: 327.
21. Trecourt F, Breton G, Veronique B, Mongin F, Marsais F, Queguiner G. *Tetrahedron Lett.* 1999; **40**: 4339.
22. Romero J, Duran ML, Garcia-Vazquez A, Castineiras A, Sousa A, Christiaens L, Zubieta J. *Inorg. Chim. Acta* 1997; **307**: 255.
23. Back TG, Codding PW. *Can. J. Chem.* 1983; **61**: 2749.
24. Sheldrick GM. SHELXL-97 and SHELXL-97. University of Göttingen, Germany.

