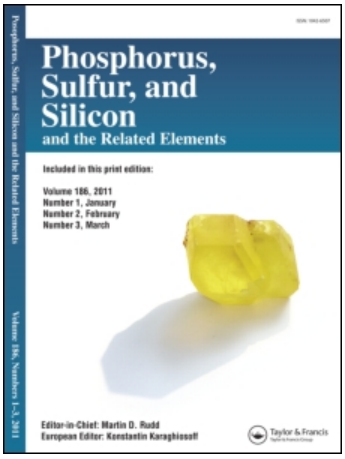

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Synthesis of Unsymmetrical Pyridyl Aryl Selenides by the Reductive Cleavage of Se–Se Bond

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An efficient protocol for the synthesis of novel hitherto unknown substituted and unsubstituted phenyl pyridyl selenides from dipyridyl/diphenyl diselenides and phenyl/pyridyl halides in the presence of copper catalysed system, $Cu_2O/Mg/bpy$ is being presented. All the synthesized selenides are either light yellow coloured liquids or low melting solids. All the newly synthesized compounds have been thoroughly characterized by elemental analysis employing various spectroscopic techniques viz., infrared, multinuclear NMR (^1H, ^{13}C, ^{77}Se) and mass spectrometry (in representative cases).

Keywords Copper; phenyl; pyridyl; reductive cleavage; selenide

INTRODUCTION

Chemistry of alkyl, aryl, and mixed alkyl aryl selenides has developed rapidly for the last two decades and find extensive applications in organic synthesis,[1] organic superconductors,[2] MOCVD,[3] and biochemistry.[4] It is curious to note that the analogous chemistry of pyridyl derivatives has remained neglected over the years probably due to non-availability of a convenient and efficient synthesis.

Recently, the chemistry of pyridyl derivatives has attracted the attention of the scientific community due to their unique properties, which

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endear them to new and exciting applications in organic synthesis and biochemistry.[5] In recognition of its importance, renewed efforts have evolved for the convenient methodologies of their synthesis.

Literature is swamped with several synthetic procedures for the preparation of alkyl, aryl and mixed alkyl aryl selenides. All these methods employ a reducing agent to reduce elemental selenium-to-selenium dianion (Se^{2-} and Se_2^{2-}) *viz.* $NaBH_4$,[6] $LiAlH_4$,[7] $R_4N^+BH_4^-$,[8] $LiEt_3BH$, [9] $HOCH_2SO_2Na$,[10] Na/NH_3,[11] and so on, followed by quenching with alkyl/aryl halides. Another versatile approach towards the synthesis of unsymmetrical organoselenium compounds involve the formation of intermediate selenolates RSe^- generated *insitu* by reductive cleavage of Se-Se bond in diorganyl diselenides. Reductive cleavage of Se-Se bond can be realized with a galaxy of reducing agents such as $N_2H_4.H_2O$,[12] $R_4N^+BH_4^-$,[8] $NaBH_4$,[13] $LiEt_3BH$, [9] and so on. In recent times, some metals like indium,[14] lanthanum,[15]samarium,[16]and their salts[17] have also been reported to cleave Se–Se bond.

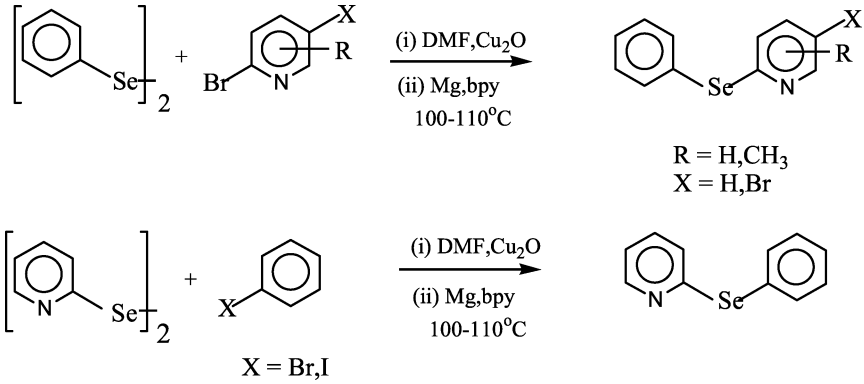
Catalytic procedures are considered more applicable, however, as many functional groups cannot withstand harsh reaction conditions. Various complexes such as $Pd(PPh_3)_4$,[18] $(bpy)_2NiBr_2$,[19] and $RhCl(PPh_3)_3$[20] have been successfully exploited to prepare unsymmetrical selenides. A number of selenides have been prepared by the direct nickel (II)[21] and copper (II)[22]-catalyzed coupling of a diselenide with aryl iodides.. In this paper, we wish to report a mild, convenient, and economical method for the synthesis of pyridyl phenyl selenides using eco-friendly reagents.

RESULTS AND DISCUSSION

Mautner et al.[23] synthesized 2,2′-dipyridyl diselenide by reacting 2-bromo pyridine with toxic hydrogen selenide. Later, many research groupsmodified this procedure by developing safe and convenient methods for their preparation by reducing elemental selenium with sodium borohydride in different solvents.[24] Researchers used different methodologies, in the subsequent years, explored variations of the published procedures to improve the yield of 2,2′-dipyridyl diselenide. Bhasin et al.[25]have developed and optimized the conditions for the preparation of stable substituted dipyridyl diselenides by the bromine exchange of 2-bromo methyl substituted pyridine using *n*-butyl lithium in THF at -78°C that avoids the use of toxic gases coupled with better yields.

In pursuance of our work on the synthesis of dipyridyl diselenides, we report herein a convenient, operationally simple, and facile synthetic route for the synthesis of hitherto unknown substituted and unsubstituted pyridyl phenyl selenides. The method involves the reductive

cleavage of dipyridyl/diphenyl diselenides in DMF at 110°–120°C using the catalyzed system Cu_2O/Mg/bpy. The intermediate selenolate anion generated in situ by the slow addition of dipyridyl/diphenyl diselenides to the heterogenous system was followed by quenching with different electrophiles as depicted in Scheme 1.



SCHEME 1 Synthesis of unsymmetric phenyl pyridyl selenides.

All the reactions were carried out in the presence of oxygen free nitrogen. The mixed pyridyl selenides thus prepared are all stable compounds and can be purified by column chromatography. All the synthesized phenyl pyridyl selenides are light yellow coloured liquids or low melting solids. The compounds dissolve readily in organic solvents and have a shelf life of several months without any sign of decomposition even at room temperature under nitrogen atmosphere.

EXPERIMENTAL

All the manipulations were carried under a dry and deoxygenated nitrogen atmosphere to prevent the oxidation of oxygen sensitive selenium intermediates. Elemental selenium (Himedia) was stored in a desiccator prior to use. Diphenyl[26] and dipyridyl[27] diselenides were prepared by literature methods. DMF was distilled using K_2CO_3 and stored on molecular sieves. Bromobenzene (Aldrich) and other chemicals were of analytical grade and used without further purification. 2-Bromopyridine and 2,5-dibromopyridine were preparedfrom the corresponding 2-aminopyridines [28](Aldrich). ^1H, ^{13}C, and ^{77}Se NMR spectra were recorded on a Jeol AL 300 MHz spectrometer in $CDCl_3$, using Me_4Si as an internal standard for ^1H and ^{13}C NMR. Me_2Se was used as an external reference for ^{77}Se NMR; Infrared spectra were obtained between KBr plates on a Perkin-Elmer model 1430 spectrophotometer. C, H, and N analysis was performed on a

Perkin-Elmer 2400 CHN analyzer. Mass spectra were obtained on a VG 7070H mass spectrometer. Separation and purification of compounds were done by column chromatography performed on activated silica gel using hexane as eluant.

General Procedure for the Synthesis of Unsymmetrical Selenides

In a 50 ml flame dried three necked round bottom flask (200 mg) activated magnesium, (28 mg) cuprous oxide, (62 mg) 2,2′-bipyridyl were taken in 15 ml dried DMF. Diphenyl diselenide (0.62 g, 2 mmol) was added to the above mixture followed by quenching with substituted 2-bromopyridines (4 mmol). The mixture was stirred at 110^{o}C for 15–20 h. The colour of the reaction mixture changed from red to dark brown within 20–25 min. Stirring and refluxing was continued until the completion of the reaction, which is monitored by TLC. After evaporation of the solvent, the residue obtained was dissolved in dichloromethane. Ionic impurities were removed by washing the organic extract repeatedly with distilled water. The combined organic fractions were dried over anhydrous sodium sulphate and the solvent was evaporated on rota-evaporator. The product thus obtained was purified over silica column using hexane as eluant. Using this methodology, a number of compounds were prepared which were characterized through elemental analysis and various spectroscopic techniques.

Unsymmetrical Pyridyl Phenyl Selenides

2-Pyridyl phenyl selenide, ($C_5H_4NSeC_6H_5$), [1].. Yellow viscous liquid; Yield: 60 %; ^{1}H NMR ($CDCl_3$/TMS): δ 8.29–8.31 (d, 1H, 3.6Hz), 7.56–7.63 (m, 2H), 7.26–7.33 (m, 4H), 6.85–6.9 (m, 2H); ^{13}C NMR ($CDCl_3$/TMS): δ 158.7, 149.53, 136.12, 129.12, 128.79, 127.66, 123.8, 119.99; ^{77}Se NMR: δ 469.859; I.R. (KBr, cm^{-1}): 3408.3,2984.1, 2924.9, 1951.3, 1734.8, 1569.7, 1476.3, 1302.4, 1275.5, 1147.6, 1042.7, 985.3, 840.2, 477.7, 461.3; MS (EI, %): 234 (85), 232 (70), 154 (30), 78(80); Anal. Calcd. : C, 56.17; H, 3.82; N, 5.95%; Found; C, 56.50; H, 3.53; N, 5.72%.

3-Methyl-2-pyridyl phenyl selenide, ($CH_3C_5H_3NSeC_6H_5$), [2].. Yellow viscous liquid; Yield: 70%; ^{1}H NMR ($CDCl_3$/TMS): δ 8.09(s, 1H), 7.50–7.55(m, 2H), 7.17–7.34(m, 4H), 6.84–6.88(q, 1H), 2.26(s, 3H); ^{13}C NMR ($CDCl_3$/TMS): δ 156.3, 147.2, 136.4, 136.3, 135.5, 133.2, 128.9, 128.7, 128.0, 127.8, 120.6, 20.0; I.R. (KBr, cm^{-1}): 3049.6, 2924.2, 2361.3, 1569.5, 1440.2, 1389.3, 1193.4, 1124.8, 1066.1, 1022.1, 987.6, 786.9, 736.8, 689.1, 661.5, 469.7; Anal. Calcd. : C, 57.83; H, 4.41; N, 5.62 %; Found; C, 57.69; H, 4.34; N, 5.54 %.

4-Methyl-2-pyridyl phenyl selenide, ($CH_3C_5H_3NSeC_6H_5$), [3].. Yellow viscous liquid; Yield: 70%; ^{1}H NMR ($CDCl_3$/TMS): δ 7.99–8.08(d, 1H, 26.1Hz), 7.44–7.54(m, 2H), 7.07–7.23(m, 3H), 6.61–6.65(m, 2H), 2.0(s, 3H); ^{13}C NMR ($CDCl_3$/TMS): δ 157.8, 149.0, 146.9, 135.6, 128.8, 128.1, 127.6, 124.2, 121.1, 20.4; ^{77}Se NMR: δ 467.05; I.R. (KBr, cm^{-1}): 3435.3, 3054.6, 2920.7, 2358.7, 1584.2, 1454.4, 1375.8, 1277.4, 1267.9, 1116.2, 1077.8, 1022.6, 819.6, 741.7, 692.3, 520.3, 471.5; Anal. Calcd. : C, 57.83; H, 4.41; N, 5.62 %; Found; C, 57.53; H, 4.91; N, 5.82 %.

5-Methyl-2-pyridyl phenyl selenide, $CH_3C_5H_3NSeC_6H_5$. Yellow viscous liquid ; Yield: 70%; ^{1}H NMR ($CDCl_3$/TMS): δ 8.15(s,1H), 7.52–7.61(m,2 H), 7.17–7.27(m,3H), 7.05–7.09(m, 1H), 6.80–6.84(m,1H), 2.13(s,3 H); ^{13}C NMR ($CDCl_3$/TMS): δ 154.24, 149.80, 136.96, 135.39, 130.41, 129.54, 128.17, 127.9, 18.89; ^{77}Se NMR: δ 464.11; I.R.(KBr , cm^{-1}): 2921.2, 1724.4, 1584.2, 1555.9, 1364.6, 1274.6, 1223.2, 1072.7, 1022.8, 999.9, 816.4, 640, 474.6; Anal. Calcd. : C, 57.83; H, 4.41; N, 5.62%; Found; C, 57.62; H, 4.57; N, 5.75%.

6-Methyl-2-pyridyl phenyl selenide, $CH_3C_5H_3NSeC_6H_5$.:. Yellow viscous liquid ; Yield: 70%; ^{1}H NMR ($CDCl_3$/TMS): δ 7.56 (s,2H),7.23–7.25(d,3H,6Hz),7.10–7.15(t,1H),6.61–6.73(dd,2H),2.39(s,3H); ^{13}C NMR ($CDCl_3$/TMS) : δ 158.5, 158.1, 136.4, 136.0, 129.40, 128.5, 127.9, 120.8, 120.7, 119.8, 119.5, 24.07; I.R.(KBr , cm^{-1}): 3053.8, 2923.1, 2852.3, 1577.2, 1476.0, 1388.6, 1327.1, 1302.5, 1248.9, 1161.2, 1086.7, 1065.7, 1021.8, 999.1, 842.6, 774.1, 740.4, 61.6, 663.8, 546.9, 474.5;Anal. Calcd.: C, 57.83; H, 4.41; N, 5.62 %; Found; C, 57.91; H, 4.34; N, 5.56 %.

5-Bromo-2-pyridyl phenyl selenide, $BrC_5H_3NSeC_6H_5$:. Yellow low melting solid; Yield: 70%; ^{1}H NMR ($CDCl_3$/TMS): δ 8.45–8.47(d,1H,2.1 Hz), 7.59–7.68(d,1H,1.5 Hz),7.38–7.56 (m,5H) , 6.83–6.86(d,1H,4.8 Hz); ^{13}C NMR ($CDCl_3$/TMS) : δ 157.3, 150.6, 139.8, 136.2, 129.8 ,129.0,127.4,124.4,117.4; ^{77}Se NMR : δ 473.09; I.R.(KBr , cm^{-1}): 3055.3, 2923.2, 1550.3, 1476.2, 1347.6, 1310.3, 1270.5,1211.7, 1179.3, 1071.7, 1020, 958.3, 918.2, 767.8, 670.0, 622.9, 591.3, 499.0, 476.0; MS (EI, %) 311(100), 234(30), 157(45), 77(80); Anal. Calcd. : C, 42.03; H, 2.54; N, 4.45%; Found; C, 41.89; H, 2.96; N, 4.78%

In summary, most of these synthetic protocols in the literature suffer from one or the other disadvantages viz., lengthy synthetic steps, harsh reaction conditions, expensive reducing agents, contamination of desired products with impurities, non-reproducible results and sensitive to aerial oxidation. The present paper takes into account these constraints in developing a mild, more convenient, commercially viable, and efficient reaction for the synthesis of desired phenyl pyridyl selenides under neutral conditions.

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