DOI: 10.1002/ejoc.201101592

Complex-Induced Proximity Effect in the Regioselective Lithiation of Pyridine Derivatives

Jaspreet S. Dhau,*[a] Amritpal Singh,[a] Yoganjaneyulu Kasetti,[b] and P. V. Bharatam*[b]

Keywords: Nitrogen heterocycles / Lithiation / Lithium / Regioselectivity / Density functional calculations

The regioselective ring lithiation of BF_3-complexed 3-picoline (**1a**), 3,4-lutidine (**1b**), and 3,5-lutidine (**1c**) was studied. The dilithiation of **1a**, **1b**, and **1c** was also investigated to experimentally explore the relative preference of the sites on the substituted pyridine ring for lithiation. The role of the complex-induced proximity effect (CIPE) for inducing lithiation in these moieties was investigated using both experimental and computational studies.

Introduction

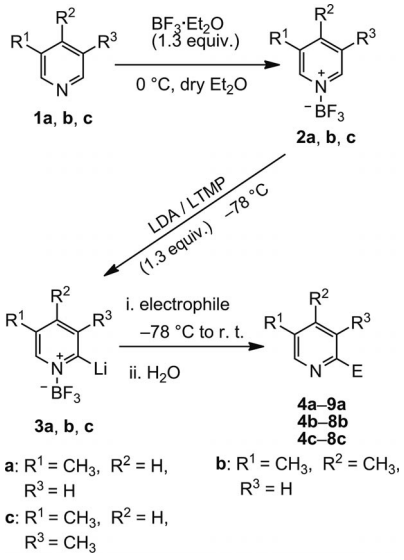
The lithiation of substituted and unsubstituted pyridine rings has attracted the attention of chemists worldwide, as it is a convenient route to many functional group manipulations leading to molecules that are of material[1] and biological interest.[2] The direct lithiation of picolines and lutidines invariably leads to the functionalization of the acidic methyl group(s), showing no preference for the ring protons.[3] One of the methods for preferential ring lithiation in these derivatives involves the reaction of lithiating reagents with halopyridines and halopicolines under cryogenic[4] and noncryogenic conditions.[5] The direct ring lithiation of picolines and lutidines has only been achieved with the aid of complexing reagents. For example, the α-lithiation of substituted pyridines by using 3–8 equiv. of BuLi–LDMAE (lithium dimethylethanolamine) complex (6–16 equiv. BuLi) has been reported.[6] A large excess amount of base was used in these reactions which necessitated the exorbitant consumption of the electrophiles and a tedious purification procedure. This drawback limits the scope of these reactions, particularly for large-scale synthesis. The complexation of boron trifluoride with pyridine,[7] 4-picoline,[8] and 4-(*N*,*N*-dimethylamino)pyridine[9] was also explored for abstracting the α-proton with lithium tetramethylpiperidide (LTMP). All of the BF_3-aided lithiations were studied on pyridyl substrates possessing two equivalent α-protons, whereas there are no reports of studies on substrates with two nonequivalent α-protons. Herein, the regioselective ring lithiation of 3-picoline (**1a**), 3,4-lutidine (**1b**), and 3,5-lutidine (**1c**) aided by complexation with BF_3 is presented. The origin of the regioselectivity in the BF_3-controlled lithiation of pyridine has not been studied in detail. Up until now, the electrostatic effect was considered the only factor responsible for the observed regioselectivity.[3c] The role of the complex-induced proximity effect (CIPE), which is the ability of the heteroatom (N, O, F, etc.) to coordinate with the metal (lithium) to bring about the directed deprotonation of the substrate, has not been explored as a possible contributor to the regioselectivity achieved in these reactions. In this paper, we report experimental and computational studies on the role of CIPE in directing lithiation at various sites of 3-methyl-substituted pyridyl derivatives.

Results and Discussion

Compound **1a** has two nonequivalent α-protons, whose acidity is likely to increase when **1a** is complexed with $BF_3{\cdot}Et_2O$. The primary objective of this reaction was to determine which of the two α-protons would undergo lithiation with LDA (lithium diisopropylamide). Treatment of **1a** with $BF_3{\cdot}Et_2O$ in dry ether at 0 °C gave adduct **2a** (Scheme 1). This adduct upon reaction with LDA at –78 °C gave a dark orange solution containing the carbanion. Addition of an electrophile followed by hydrolysis afforded products **4a**–**9a** (see Table 1), indicating exclusive lithiation at C-6. No product arising from C-2 lithiation was detected in these reactions. Under similar conditions, **1b** also gave monosubstituted products **4b**–**8b**, corresponding to lithiation at C-6 (see Table 1). The lithiation of BF_3-complexed 3,5-lutidine (**2c**) yielded a carbanion corresponding to the selective lithiation of one of the two α-protons. When quenched with an electrophile, this anion exclusively afforded the C-2 lithiated products **4c**–**8c** in excellent yields. The results obtained from the lithiation of **1c** followed by reaction with elemental selenium as the electrophile were

[a] Department of Chemistry, Punjabi University,
Patiala 147002, India
Fax: +91-175-2286682
E-mail: jassiv02@yahoo.co.in
[b] Department of Medicinal Chemistry, National Institute of Pharmaceutical Education and Research (NIPER), Sector-67, S. A. S.,
Nagar 160062, Punjab, India

reported in an earlier communication of ours.[10] When benzophenone was used as the electrophile, we only obtained the dimer of **1c**.



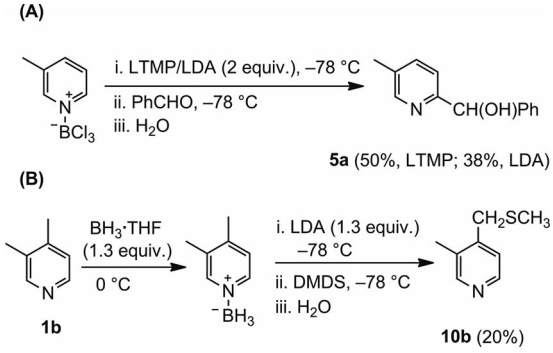
Scheme 1. Lithiation of 3-picoline (**1a**), 3,4-lutidine (**1b**), and 3,5-lutidine (**1c**) aided by complexation with BF_3.

Table 1. Reaction involving monolithiation of **1a**, **1b**, and **1c**.

Entry	*R[a]	Base [1.3 equiv.]	Electrophile [1.3 equiv.]	E	Product	Yield [%]
1	**1a**	LDA	I_2	I	**4a**	78
2	**1a**	LDA	PhCHO	CH(OH)Ph	**5a**	67
3	**1a**	LTMP	PhCHO	CH(OH)Ph	**5a**	71
4	**1a**	LDA	$(CH_3S)_2$	SCH_3	**6a**	69
5	**1a**	LDA	(i) Se (ii) CH_3I	$SeCH_3$	**7a**	62
6	**1a**	LDA	Ph_2CO	Ph_2COH	**8a**	59
7	**1a**	LDA	Br_2	Br	**9a**	68
8	**1b**	LDA	I_2	I	**4b**	63
9	**1b**	LDA	PhCHO	CH(OH)Ph	**5b**	57
10	**1b**	LDA	$(CH_3S)_2$	SCH_3	**6b**	72
11	**1b**	LDA	(i) Se (ii) CH_3I	$SeCH_3$	**7b**	67
12	**1b**	LDA	Ph_2CO	Ph_2COH	**8b**	64
13	**1c**	LDA	I_2	I	**4c**	86
14	**1c**	LDA	PhCHO	CH(OH)Ph	**5c**	70
15	**1c**	LDA	$(CH_3S)_2$	SCH_3	**6c**	74
16	**1c**	LDA	(i) Se (ii) CH_3I	$SeCH_3$	**7c**	70[10]
17	**1c**	LDA	Br_2	Br	**8c**	80

[a] *R = reactant.

Next, we investigated the lithiation of 3-picoline aided by complexation with BCl_3. Treatment of the 3-picoline–BCl_3 adduct generated in situ with 1.3 equiv. of LDA followed by reaction with various electrophiles did not result in any ring or side-chain lithiation. Instead, the stable picoline–BCl_3 adduct was isolated in good yield. Identical results were achieved by replacing LDA with LTMP (2 equiv.). However, when the isolated 3-picoline–BCl_3 adduct was treated with LTMP (2 equiv.) followed by reaction with benzaldehyde, (5-methylpyridin-2-yl)phenyl methanol (**5a**) was isolated in 50% yield (Scheme 2, A). The major difference between this reaction and the one where the picoline–BCl_3 adduct is generated in situ is that the isolated adduct forms a clear solution with diethyl ether at all temperatures (room temperature to –78 °C) instead of suspension as in the former reaction. When LDA (2 equiv.) was used in place of LTMP, we obtained **5a** in 38% yield.

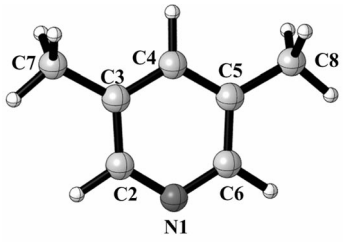


Scheme 2. Lithiation of 3-picoline (**1a**), 3,4-lutidine (**1b**), and 3,5-lutidine (**1c**) aided by complexation with: i) BCl_3 and (ii) BH_3.

To compare the roles of the CIPE and the electrostatic effect in the above reactions, we examined the lithiation of **1a**, **1b**, and **1c** with LDA/LTMP through the complexation with BH_3 instead of BF_3 or BCl_3. The lithiation of the in situ generated 3-picoline– and 3,5-lutidine–BH_3 adducts with LDA or LTMP did not result in any ring or side-chain lithiation. However, when the in situ generated 3,4-lutidine–BH_3 adduct was treated with 1.3 equiv. of LTMP and dimethyl disulfide, 3-methyl-4-[(methylsulfanyl)methyl]pyridine (**10b**) was isolated in low yield (20%), corresponding to lithiation at the methyl carbon at C-4 (Scheme 2, B). No product resulting from ring lithiation was noticed in this reaction. In addition, we attempted the lithiation of a pyridine–BH_3 adduct with LDA, and no product resulting from ring lithiation was noticed. In consideration of these results, it appears that the interaction of lithium with a halogen atom is essential for achieving the ring lithiation in the pyridine moieties.

The mechanism of the aforementioned lithiation process was then studied by performing quantum chemical analysis on neutral **1a** and **1c** along with their boron trifluoride adducts. As a representative example, the numbering scheme for **1c** is shown in Figure 1. 3-Picoline, in principle, can undergo ionization (deprotonation) at five different sites, in other words, at α-carbons (C-2 and C-6), C-4, C-5, and C-7 (methyl carbon). Computational analysis indicates that the most favorable site for deprotonation is C-7 (see Table 2). This is supported by a reported observation on uncomplexed 3-picoline.[3a,3b] In the case of BF_3-complexed 3-picoline (**2a**), C-7 is also the preferred site for deprotonation (Table 2), which is contrary to experimental observation. This implies that the information with respect to the ionization energies of the pyridine derivatives does not provide any clues regarding the product formation. This prompted us to study the relative stabilities of the lithiated species of **1a**, **2a**, **1c**, and **2c** under explicit solvent conditions. The results indicate that the species with lithiation at

the methyl carbon (**1a-L**) is the most stable species (Table 3, Column 2), again confirming the experimental observation. However, when the relative stabilities of **2a** were compared, it became clear that C-6 is the most preferred site for lithiation (Table 3, Column 3). This indicates that there is a switch in the observed preferences of the sites for lithiation of 3-picoline before and after complexation with BF_3. Strong coordination between the lithium (on the α-carbon) and the fluoride of BF_3, leading to the formation of a five-membered chelating ring (Figure 2), is the major contributor to the seesaw change in the lithiation site preference. This type of coordinating effect in lithiation processes is commonly known as the complex-induced proximity effect (CIPE), recently reported by Kessar et al. in the BF_3-controlled lithiation of aniline with *s*BuLi.[11] In addition, the data in Table 3 reveals that lithiation at C-6 gave a more stable species than the one obtained by lithiation at C-2, which further substantiates the aforementioned experimental results for **1a** (Scheme 1). In the light of the small contribution from the inductive effect, the steric factor at C-2, from the adjacent methyl group, appears to play a critical role in determining the site of lithiation.



1c

Figure 1. 3D structure of **1c** (with the numbering scheme presented in the article).

Table 2. Deprotonation energy studies on 3-picoline (**1a**), 3,5-lutidine (**1c**), and their coordinated complexes with BF_3, **2a** and **2c**, respectively.

Site of deprotonation	DPE[a] of **1a** [kcal/mol]	DPE of **2a** [kcal/mol]	DPE of **1c** [kcal/mol]	DPE of **2c** [kcal/mol]
C-2	355.34	334.69	355.91	335.46
C-4	349.19	336.42	350.03	337.18
C-5	350.00	336.99	–	–
C-6	355.10	334.54	–	–
C-7	339.40	326.38	340.01	326.87

[a] DPE = deprotonation energy.

3,5-Lutidine (**1c**) has three possible deprotonation sites, that is to say, C-2, C-4, and C-7. The deprotonation energy studies on **1c** as well as on its BF_3 adduct (**2c**) show that the methyl carbon is the most favorable site for deprotonation (Table 2, Columns 4 and 5). However, the stabilities of the lithiated complexes of **1c** and **2c** indicate that there is a change in the preference for the site of lithiation (Table 3, columns 4 and 5). Also in this case, the intramolecular chelation of lithium (on the α-carbon) with the fluoride of BF_3 is responsible for increasing the stability of **3c** in comparison to the other BF_3-complexed lithiated species (Figure 2).

Table 3. Relative energy stabilities of lithiated molecules of 3-picoline (**1a-L**), 3,5-lutidine (**1c-L**), and their coordinated complexes with BF_3, **2a** and **2c**, respectively.

Site of lithiation	Relative stability of **1a-L** [kcal/mol]	Relative stability of **2a** [kcal/mol]	Relative stability of **1c-L** [kcal/mol]	Relative stability of **2c** [kcal/mol]
C-2	3.90	0.46	3.93	0.00
C-4	3.35	10.78	3.87	11.19
C-5	3.06	10.04	–	–
C-6	2.77	0.00	–	–
C-7	0.00	8.92	0.00	8.89

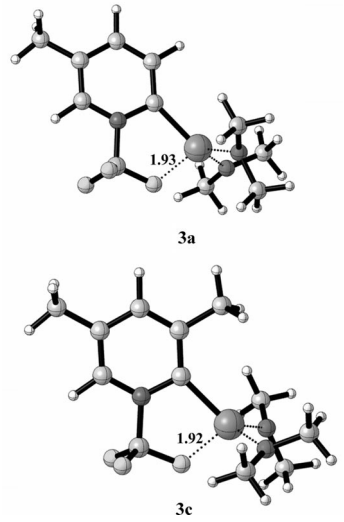
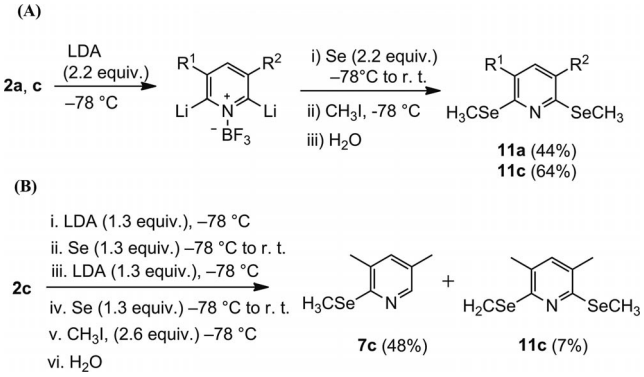


Figure 2. 3D structures of **3a** and **3c** (showing the Li···F contacts). The important interatomic distances leading to CIPE are given in Å units.

As a conclusion to the theoretical studies, the complexation of BF_3 with 3-picoline and 3,5-lutidine decreases the deprotonation energy of the ring protons to a greater extent than compared to the methyl protons, however, this decrease is not enough to promote lithiation at the ring protons. It is the CIPE which renders the α-carbons more prone to attack by the lithiating reagents in comparison to the methyl carbons.

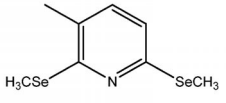
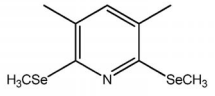
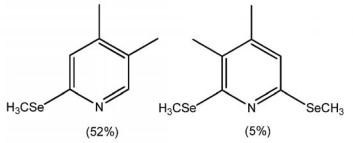
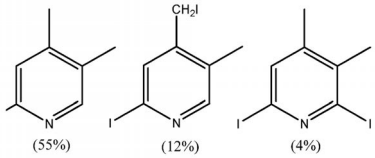
To further substantiate the theoretical findings, we attempted the dilithiation of **2a** with 2.2 equiv. of LDA. Insertion of elemental selenium (2.2 equiv.) to the dicarbanion-like species followed by reaction with iodomethane (2.2 equiv.) gave 3-methyl-2,6-bis (methylselenenyl)pyridine (**11a**) in a moderate yield. The result for **1a** (Scheme 3, A, Table 4) along with our earlier reported result for the dilithiation of **1c** giving 3,5-dimethyl-2,6-bis(methylselenenyl)-pyridine (**11c**)[10] suggests that effective deprotonation occurs at the two α-positions with no sign of side-chain metallation. To check whether the preceding reaction segues through an intermediate dianion formation or proceeds through the intermediate formation of a monocarbanion followed by electrophlic quenching and then a second deprotonation and electrophilic quenching sequence, we carried out the dimetallation reaction in two steps. The first

step involved the quenching in situ of carbanion **3c** with elemental selenium. The second step involved the treatment of the resulting selenolate anion with LDA (1.3 equiv.) at –78 °C. The ensuing species was again quenched with elemental selenium (1.3 equiv.) and iodomethane (2.6 equiv.). Upon purification of the crude product, **7c** was obtained as the major product (48%), whereas **11c** was only obtained in 7% yield (Scheme 3B). This is contrary to our earlier observation for the single-step dilithiation reaction (Scheme 3A), where **11c** was the main product (64%). In this case, **7c** was never isolated, but noticed only as a very minute quantity in the GC–MS chromatogram. The reversal of the yields for the two products through the two different routes suggests that the single-step dilithiation reaction segues through the intermediate formation of the dicarbanion.

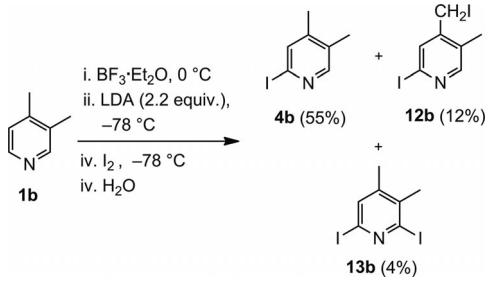


Scheme 3. (A) Dilithiation of **2a** and **2c** in a single-step reaction and (B) dilithiation of **2c** in a two-step reaction.

Table 4. Multilithiation of **1a**, **1b**, and **1c**.

	R	Base 2.2 equiv.	E 2.2 equiv.	Products	Yield (%)
1	**1a**	LDA	i. Se ii. CH_3I		44
2	**1c**	LDA	i. Se ii. CH_3I		64[10]
3	**1b**	LDA	i. Se ii. CH_3I	 (52%) (5%)	
4	**1b**	LDA	I_2	 (55%) (12%) (4%)	

Interestingly, the dilithiation of **1b** behaved differently from that of **1a** and **1c**. In case of selenium and iodomethane as the electrophiles, 2-(selenomethyl)-4,5-lutidine (**7b**), corresponding to monolithiation at C-6, was the major product. The dilithiated product 3,4-dimethyl-2,6-bis-(methylselenenyl)pyridine (**11b**) was isolated in a very minute quantity (Table 4, Column 3). When iodine was used as the electrophile, monolithiated product 2-iodo-4,5-lutidine (**4b**, 55%) was formed in a major quantity. However, two different disubstituted products (i.e., **12b** and **13b**) were isolated as well, one corresponding to a second lithiation at C-8 (i.e., **12b**) in 12% yield and the other from a second lithiation at C-2 (i.e., **13b**) in 4% yield (Scheme 4, Table 4). This implies that after complexation with BF_3, C-8 is more prone to lithiation than C-2. Therefore, it appears that the CIPE, which plays a detrimental role in directing the first lithiation at C-6, does not exert the same effect at C-2 in **1b**.



Scheme 4. Dilithiation of 3,4-lutidine with iodine as the electrophile.

On the basis of the experimental findings, the order of preference of the sites for BF_3-aided lithiation of **1a**, **1b**, and **1c** is: (i) C-6 > C-2 > C-7 (methyl carbon) for **1a**; (ii) C-6 > C-8 (methyl carbon) > C-2 > C-7 (methyl carbon) for **1b**; and (iii) C-6 = C-2 > C-7 = C-8 (methyl carbon) for **1c**.

Conclusions

In conclusion, we have: (i) demonstrated the regioselective ring lithiation of 3-picoline, 3,4-lutidine, and 3,5-lutidine and (ii) established the relative preference of each of the positions on the picoline and lutidine ring for lithiation. The greater role of the complex-induced proximity effect in comparison to the electrostatic effect for determining the regioselective lithiation of **1a**, **1b**, and **1c** has also been established. The present methodology offers advantages over those previously reported, as it negates the use of an excess amount of base in affecting the selective ring lithiation and dilithiation of picolines and lutidines along with the benefit of completing the reaction in a single step.

Experimental Section

General Comments: All the apparatus was flame dried, and all the solvents were dried and distilled before use. BuLi was prepared in the lab by the reaction of BuBr with lithium metal in dry hexane. ^1H NMR and ^{13}C NMR spectroscopic data were recorded with a

400 MHz spectrometer in $CDCl_3$ using TMS as an internal standard.

GC–MS Conditions: The GC–MS analyses were carried out with a GC–Mass Spectrometer. A capillary column used for the GC was Rtx-1MS (30 m × 0.25 mm, inner diameter 0.25 μm). The mass spectrometry conditions used had the electron ionization source set at 70 eV, the MS source temperature at 200 °C, and the solvent cut time was 3.5 min.

Methodology for Theoretical Studies: Ab initio density functional theory (DFT) studies were carried out using the Gaussian 03 software package.[12] The quantum chemical study was carried out to understand the role of BF_3 as a promoter and the BF_3-assisted (through the coordination bonds) lithiation process in the pyridine derivatives. The B3LYP (Becke3, Lee, Yang, Parr) method with the 6-31+G(d,p) basis set was employed for geometry optimizations, transition-state searches, and frequency calculations throughout this study,[13,14] and a scaling factor of 0.9806 was used for the zero-point energy (ZPE) corrections. The explicit solvent effect was studied using two units of the model solvent dimethyl ether, and the complexes were optimized under the implicit solvent conditions using the conductor-like polarizable continuum model (CPCM) with diethyl ether as the solvent (RMIN = 0.5, OFAC = 0.8; ε = 4.24).[15] All the reported transition states in the present study have only one imaginary frequency.

General Procedure 1. Monolithiation of 3-Picoline, 3,4-Lutidine, and 3,5-Lutidine: 3-Picoline, 3,4-lutidine, or 3,5-lutidine (9.0 mmol) was added to a three-necked 100-mL round-bottom flask (RBF) containing dry diethyl ether (30 mL) under an inert atmosphere. Boron trifluoride–diethyl ether (BF_3·Et_2O; Spectrochem, Mumbai, India, 45–50%; 1.38 g, 1.23 mL, 9.9 mmol) was added to the reaction mixture at 0 °C. The resulting curdy white suspension was stirred for 10 min. In another three-necked 100-mL RBF, *n*BuLi (1.3 N solution, 7.6 mL, 9.9 mmol) was added slowly to a solution of diisopropylamine (0.99 g, 1.4 mL, 9.9 mmol) or tetramethylpiperidine (1.35 g, 1.6 mL, 9.9 mmol) in diethyl ether (20 mL) at –10 °C to form LDA or LTMP, respectively. The temperature of the RBF containing the BF_3-complexed picoline/lutidine was lowered to –78 °C and LDA/LTMP was added slowly by cannula. The color of the suspension changed from white to orange brown in about 10 min. The orange brown solution (i.e., **3a**, **3b**, or **3c**) was stirred for 15 min at –78 °C.

2-Iodo-5-methylpyridine (4a):[6a] Iodine (2.51 g, 9.9 mmol) was added to the solution containing **3a** at –78 °C. The temperature was slowly raised to room temperature. The reaction mixture was hydrolyzed, and the resulting mixture was extracted with diethyl ether. The organic layer was washed with sodium thiosulfate, water, and a brine solution. The organic layer was then dried with anhydrous sodium sulfate. The solvent was removed, and the crude residue was purified by column chromatography using 60–120 mesh silica gel with hexane/ethyl acetate (5:1) as the eluent to yield **4a** (1.54 g, 78%); m.p. 52–54 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20–8.21 (d, J = 2.2 Hz, 1 H, Ar), 7.58–7.60 (d, J = 8.0 Hz, 1 H, Ar), 7.14–7.16 (dd, J = 2.4, 8.1 Hz, 1 H, Ar) 2.27 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 151.2, 138.6, 134.2, 132.9, 114.0, 17.8 ppm. MS (EI): *m*/*z* (%) = 219 (38) $[M]^{+\cdot}$, 127 (6), 92 (100). C_6H_6IN (219.02): calcd. C 32.90, H 2.76, N 6.39; found C 32.63, H 2.68, N 6.22.

(5-Methylpyridin-2-yl)phenylmethanol (5a): Yield: 1.12 g (67%, with LDA), (71% with LTMP); m.p. 174–176 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35 (s, 1 H, Ar), 7.23–7.41 (m, 6 H, Ar), 7.02–7.04 (d, J = 8.0 Hz, 1 H, Ar), 5.71 (s, 1 H, CH), 5.34 (s, 1 H, OH) 2.29 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 158.2, 148.0, 143.4, 137.5, 131.95, 128.5, 127.7, 127.0, 120.8, 74.8, 18.1 ppm. MS (EI): *m*/*z* (%) = 199 (77) $[M]^{+\cdot}$, 182 (5), 122 (60), 93 (100), 77 (60). $C_{13}H_{13}NO$ (199.25): calcd. C 78.36, H 6.58, N 7.03; found C 78.43, H 6.60, N 7.01.

5-Methyl-2-(methylsulfanyl)pyridine (6a):[6a] Yellow viscous oil (0.86 g, 69%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.18 (s, 1 H, Ar), 7.20–7.22 (d, J = 8.0 Hz, 1 H, Ar) 6.97–6.99 (d, J = 8.1 Hz, 1 H, Ar), 2.45 (s, 3 H, SCH_3), 2.16 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 156.5, 149.6, 136.8, 128.5, 120.9, 17.8, 13.4 ppm. MS (EI): *m*/*z* (%) = 139 (100) $[M]^{+\cdot}$, 124 (4), 106 (25), 93 (73), 79 (11).

5-Methyl-2-(methylselenenyl)pyridine (7a):[16] Elemental selenium (0.78 g, 9.9 mmol) was added to the solution containing **3a** at –78 °C. The temperature was slowly raised until all of the selenium dissolved. The reddish brown solution was again cooled to –78 °C, and iodomethane (1.40 g, 0.6 mL, 9.9 mmol) was added. The reaction mixture was slowly warmed to the room temperature and hydrolyzed, and the workup above was followed to yield a viscous oil (1.0 g, 62%). ^{1}H NMR: (400 MHz, $CDCl_3$): δ = 8.15 (s, 1 H, Ar), 7.13–7.15 (d, J = 8.0 Hz, 1 H, Ar), 6.99–7.01 (d, J = 8.1 Hz, 1 H, Ar), 2.35 (s, 3 H, $SeCH_3$), 2.10 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 151.6, 149.8, 136.5, 129.0, 123.6, 17.6, 5.2 ppm. MS (EI): *m*/*z* (%) = 187 (19) $[M]^{+\cdot}$, 172 (1), 117 (3), 107 (100), 92 (25), 77 (7).

(5-Methylpyridin-2-yl)diphenylmethanol (8a): Light brown viscous liquid (1.46 g, 59%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.37 (s, 1 H, Ar), 7.40–7.42 (d, J = 7.7 Hz, 2 H, Ar), 7.26–7.28 (d, J = 7.2 Hz, 1 H, Ar), 7.16–7.24 (m, 9 H, Ar and OH), 7.11–7.12 (d, J = 7.9 Hz, 1 H, Ar), 2.26 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 150.2, 147.9, 146.3, 136.6, 128.5, 127.9, 126.5, 123.2, 122.3, 86.1, 18.5 ppm. MS (EI): *m*/*z* (%) = 275 (100) $[M]^{+\cdot}$, 257 (13), 198 (60), 183 (10), 105 (90), 92 (95), 77 (99). $C_{19}H_{17}NO$ (275.35): calcd. C 82.88, H 6.22, N 5.08; found C 82.63, H 6.49, N 5.35.

2-Bromo-5-methylpyridine (9a):[4d] Yield: 1.05 g (68%); m.p. 50–52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (s, 1 H, Ar), 7.35 (s, 2 H, Ar), 2.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 150.4, 139.1, 138.6, 132.2, 127.5, 17.6 ppm. MS (EI): *m*/*z* (%) = 171 (25) $[M]^{+\cdot}$, 92 (100).

4,5-Dimethyl-2-iodopyridine (4b): Yield: 1.32 g (63%); m.p. 60–62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06 (s, 1 H, Ar), 7.48 (s, 1 H, Ar), 2.23 (s, 3 H, CH_3), 2.19 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 150.6, 148.1, 135.0, 132.1, 115.0, 18.7, 15.9 ppm. MS (EI): *m*/*z* (%) = 233 (32) $[M]^{+\cdot}$, 106 (100), 127 (7), 77 (65). C_7H_8IN (233.05): calcd. C 36.08, H 3.46, N 6.01; found C 36.19, H 3.26, N 5.74.

(4,5-Dimethylpyridin-2-yl)phenylmethanol (5b): Yield: 1.1 g (57%); m.p. 81–82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (s, 1 H, Ar), 7.15–7.30 (m, 5 H, Ar), 6.83 (s, 1 H, Ar), 5.61 (s, 1 H, CH), 4.70 (s, 1 H, OH), 2.14 (s, 3 H, CH_3), 2.10 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 157.5, 146.7, 145.7, 142.6, 130.0, 127.4, 126.5, 125.9, 120.8, 73.6, 18.3, 15.0 ppm. MS (EI): *m*/*z* (%) = 213 (100) $[M]^{+\cdot}$, 194 (15), 136 (93), 106 (66), 77 (50). $C_{14}H_{15}NO$ (213.28): calcd. C 78.84, H 7.09, N 6.57; found C 78.64, H 6.92, N 6.69.

4,5-Dimethyl-2-(methylsulfanyl)pyridine (6b):[6e] Yellow viscous oil (1.0 g, 72%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1 H, Ar), 6.87 (s, 1 H, Ar), 2.45 (s, 3 H, SCH_3), 2.11 (s, 3 H, CH_3), 2.08 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 155.7, 148.3, 144.9, 127.0, 120.9, 18.1, 14.8, 12.3 ppm. MS (EI): *m*/*z* (%) = 153 (100) $[M]^{+\cdot}$, 138 (3), 121 (4), 106 (38), 91 (4), 77 (21). $C_8H_{11}NS$

(153.24): calcd. C 62.7, H 7.23, N 9.14; found C 62.59, H 7.30, N 9.18.

4,5-Dimethyl-2-(methylselenenyl)pyridine (7b): Viscous oil (1.2 g, 67%). ^{1}H NMR: (400 MHz, $CDCl_3$): δ = 8.14 (s, 1 H, Ar), 7.05 (s, 1 H, Ar), 2.38 (s, 3 H, $SeCH_3$), 2.16 (s, 3 H, CH_3), 2.11 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 152.0, 149.2, 146.9, 129.3, 125.4, 19.2, 15.9, 5.8 ppm. MS (EI): *m*/*z* (%) = 201 (35) $[M]^{+\cdot}$, 186 (1), 121 (100), 106 (27), 91 (7), 77 (24). $C_8H_{11}NSe$ (200.14): calcd. C 48.02, H 5.54, N 7.00; found C 47.94, H 5.63, N 7.13.

(4,5-Dimethylpyridin-2-yl)diphenylmethanol (8b): Yield: 1.76 g (64%); m.p. 208–210 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.21 (s, 1 H, Ar), 7.31–7.33 (d, *J* = 7.9 Hz, 2 H, Ar), 7.13–7.26 (m, 9 H, Ar and OH), 6.99 (s, 1 H, Ar), 2.19 (s, 3 H, CH_3), 2.16 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 149.3, 146.7, 146.2, 132.4, 128.0, 127.8, 127.1, 126.2, 124.7, 80.5, 19.2, 16.4 ppm. MS (EI): *m*/*z* (%) = 289 (93) $[M]^{+\cdot}$, 271 (13), 254 (3), 212 (69), 194 (2), 184 (13), 167 (11), 152 (4), 134 (17), 134 (17), 106 (100), 92 (4), 77 (97). $C_{20}H_{19}NO$ (289.38): calcd. C 83.01, H 6.61, N 4.84; found C 83.13, H 6.54, N 4.68.

3,5-Dimethyl-2-iodopyridine (4c):[6b] Yield: 1.8 g (86%); m.p. 51–53 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.0 (s, 1 H, Ar), 7.26 (s, 1 H, Ar), 2.34 (s, 3 H, CH_3), 2.24 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 148.2, 138.4, 137.8, 132.8, 121.4, 25.9, 17.5 ppm. MS (EI): *m*/*z* (%) = 233 (48) $[M]^{+\cdot}$, 106 (100), 77 (72), 76 (4). C_7H_8IN (233.05): calcd. C 36.08, H 3.46, N 6.01; found C 35.83, H 3.42, N 5.77.

(3,5-Dimethylpyridin-2-yl)phenylmethanol (5c): Yield: 1.34 g (70%); m.p. 61–62 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.19 (s, 1 H, Ar), 7.20–7.11 (m, 6 H, Ar), 5.86 (s, 1 H, OH), 5.61 (s, 1 H, CH), 2.21 (s, 3 H, CH_3), 1.94 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 155.1, 145.1, 142.6, 139.4, 134.5, 129.7, 128.5, 127.6, 126.9, 72.4, 17.9, 17.7 ppm. MS (EI): *m*/*z* (%) = 213 (79) $[M]^{+\cdot}$, 194 (28), 136 (90), 107 (100), 77 (76). $C_{14}H_{15}NO$ (213.28): calcd. C 78.84, H 7.09, N 6.57; found C 78.58, H 7.13, N 6.83.

3,5-Dimethyl-2-(methylsulfanyl)pyridine (6c):[10] Viscous oil (1.0 g, 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.03 (s, 1 H, Ar), 7.07 (s, 1 H, Ar), 2.55 (s, 3 H), 2.15 (s, 3 H), 2.12 (s, 3 H) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 155.0, 146.4, 137.5, 130.3, 128.2, 18.3, 17.6, 13.0 ppm. MS (EI): *m*/*z* (%) = 153 (82) $[M]^{+\cdot}$, 138 (16), 120 (100), 106 (40), 92 (26), 77 (38).

3,5-Dimethyl-2-(methylselenenyl)pyridine (7c):[10] Viscous oil (1.26 g, 70%). ^{1}H NMR: (400 MHz, $CDCl_3$): δ = 8.05 (s, 1 H, Ar), 7.05 (s, 1 H, Ar), 2.36 (s, 3 H, $SeCH_3$), 2.11 (s, 6 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 152.0, 147.3, 137.0, 132.5, 129.0, 19.3, 17.6, 5.2 ppm. MS (EI): *m*/*z* (%) = 201 (100) $[M]^{+\cdot}$, 186 (64), 121 (99), 106 (75), 92 (25), 77 (61).

2-Bromo-3,5-dimethylpyridine (8c):[6b] Liquid (1.32 g, 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.09 (s, 1 H, Ar), 7.42 (s, 2 H, Ar), 2.35 (s, 3 H, CH_3), 2.28 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 147.0, 140.3, 140.2, 134.7, 133.1, 20.7 ppm. MS (EI): *m*/*z* (%) = 185 (35) $[M]^{+\cdot}$, 106 (100), 91 (3), 79 (91).

3-Picoline–BCl_3 Adduct: 3-Picoline (0.84 g, 9.0 mmol) was added to a three-necked 100-mL RBF containing dry diethyl ether (30 mL) under an inert atmosphere. Boron trichloride (1.0 M in hexane, 9.9 mL, 9.9 mmol) was added to the reaction mixture at 0 °C. The resulting dark curdy white suspension was stirred for 10 min. The solvent was removed on a rotary evaporator, and the white solid was used without purification for future reactions. M.p. 101–102 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.12–9.16 (br. d and s, *J* = 6.8 Hz, 2 H, Ar), 8.10–8.12 (d, *J* = 7.8 Hz, 1 H, Ar), 7.73–7.76 (dd, *J* = 6.7, 7.1 Hz, 1 H, Ar), 2.59 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 144.5, 142.1, 137.1, 125.6, 18.9 ppm. $C_6H_7BCl_3N$ (210.30): calcd. C 34.26, H 3.35, N 6.66; found C 34.14, H 3.19, N 6.55.

Lithiation of 3-Picoline–BCl_3 Adduct: The 3-picoline–BCl_3 adduct (0.35 g, 1.63 mmol) obtained from the above reaction was added to a three-necked 100-mL RBF containing dry diethyl ether (30 mL) under an inert atmosphere. The resulting clear solution was cooled to –78 °C, and LTMP/LDA (3.26 mmol), prepared as above, was added slowly by cannula. Initially, the solution turned from yellow to brown in color. This solution was stirred for 30 min at this temperature. Benzaldehyde (0.35 g, 0.33 mL, 3.26 mmol) was added dropwise, and after the complete addition, the reaction mixture was slowly warmed to room temperature, and the workup was followed as in the case of BF_3. Compound **5a** was isolated in 50% yield (0.162 g) in the case of LTMP and 38% yield (0.12 g) in the case of LDA.

Procedure for the Lithiation of 3,4-Lutidine Aided by BH_3-Complexation: 3,4-Lutidine (0.642 g, 0.673 mL, 6.0 mmol) was added to a three-necked 100-mL RBF containing dry diethyl ether (30 mL) under an inert atmosphere. Borane (BH_3) in diethyl ether (1.0 M solution, 6.6 mL, 6.6 mmol) was added to the reaction mixture at 0 °C. The resulting curdy white suspension was cooled to –78 °C, and LDA (6.6 mmol), as prepared above, was added slowly by cannula. The color of the suspension changed from white to yellowish orange in about 10 min. The yellowish orange solution was stirred for 20–25 min at –78 °C. Dimethyl disulfide (0.621 g, 0.594 mL, 6.6 mmol) was added dropwise, and after the complete addition, the reaction mixture was slowly warmed to room temperature with the same workup as above. The crude product was purified by column chromatography using 60–120 mesh silica gel and hexane/ethyl acetate as the eluent.

3-Methyl-4-[(methylsulfanyl)methyl]pyridine (10b):[6e] Light brownish yellow oil (0.18 g, 20%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1 H, Ar), 8.29 (s, 1 H, Ar), 7.02–7.03 (d, *J* = 4.9 Hz, 1 H, Ar), 3.54 (s, 2 H, CH_2), 2.27 (s, 3 H, CH_3), 1.94 (s, 3 H, SCH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 151.0, 147.3, 144.8, 131.9, 123.9, 35.0, 15.8, 15.1 ppm. MS (EI): *m*/*z* (%) = 153 (69) $[M]^{+\cdot}$, 138 (1), 106 (34), 105 (100), 91 (4), 77 (29).

General Procedure 2. Dilithiation of 3-Picoline, 3,4-Lutidine, and 3,5-Lutidine: LDA (26.4 mmol) was added slowly to the BF_3-complexed 3-picoline, 3,4-lutidine, or 3,5-lutidine (12 mmol) by cannula. The color of suspension changed from white to orange brown in about 10 min. The orange brown solution was stirred for 15 min at –78 °C.

3-Methyl-2,6-bis(methylselenenyl)pyridine (11a): Elemental selenium (2.08 g, 26.4 mmol) was added to the solution containing dilithiated BF_3-complexed **1a** at –78 °C. The temperature was raised slowly until complete dissolution of the selenium took place. The blackish brown solution was again cooled to –78 °C, and iodomethane (3.74 g, 1.64 mL, 26.4 mmol) was added. The reaction mixture was slowly warmed to the room temperature, hydrolyzed, and purified to yield a yellow viscous oil (1.1 g, 44%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94–6.95 (d, *J* = 7.6 Hz, 1 H, Ar), 6.86–6.88 (d, *J* = 7.7 Hz, 1 H, Ar), 2.40 (s, 3 H, $SeCH_3$), 2.38 (s, 3 H, $SeCH_3$), 2.08 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 155.6, 151.3, 136.0, 129.2, 120.3, 18.7, 5.58, 5.51 ppm. MS (EI): *m*/*z* (%) = 281 (47) $[M]^{+\cdot}$ for ^{80}Se, 266 (8), 200 (100), 186 (26), 106 (47), 91 (67), 77 (14). $C_8H_{11}NSe_2$ (279.10): calcd. C 34.40, H 3.95, N 5.01; found C 34.15, H 3.94, N 4.87.

3,4-Dimethyl-2,6-bis(methylselenenyl)pyridine (11b): Yield: 0.13 g (5%); m.p. 72–75 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.87 (s, 1 H, Ar), 2.46 (s, 6 H, $SeCH_3$), 2.18 (s 3 H, CH_3), 2.13 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 155.1, 150.7, 144.7, 128.0, 122.2, 19.5, 15.2, 6.1, 5.4 ppm. MS (EI): *m*/*z* (%) = 295 (40) $[M]^{+\cdot}$ for ^{80}Se, 280 (8), 214 (100), 200 (20), 185 (4), 120 (23), 105 (24), 90 (8), 77 (35). $C_9H_{13}NSe_2$ (293.13): calcd. C 36.89, H 4.47, N 4.78; found C 37.05, H 4.32, N 4.91.

3,5-Dimethyl-2,6-bis(methylselenenyl)pyridine (11c):[16] Yield: 2.6 g (64%); m.p. 79–80 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.94 (s, 1 H, Ar), 2.50 (s, 6 H, $SeCH_3$), 2.16 (s, 6 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 151.3, 136.9, 128.6, 18.4, 5.4 ppm. MS (EI): *m*/*z* (%) = 295 (35) $[M]^{+\cdot}$ for ^{80}Se, 280 (7), 214 (100), 200 (23), 185 (8), 120 (36), 105 (30), 90 (8), 77 (81).

2-Iodo-4-(iodomethyl)-5-methylpyridine (12b): Yield: 0.38 g (12%); m.p. 98–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (s, 1 H, Ar), 7.60 (s, 1 H, Ar), 4.19 (s, 2 H, CH_2), 2.23 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 153.9, 149.8, 135.5, 132.9, 116.6, 16.9, 0.0 ppm. MS (EI): *m*/*z* (%) = 359 (4) $[M]^{+\cdot}$, 358 (86), 232 (100), 191 (5), 127 (12), 105 (63), 90 (2), 78 (38), 77 (27). $C_7H_7I_2N$ (358.95): calcd. C 23.42, H 1.96, N 3.90; found C 23.48, H 1.90, N 3.86.

2,6-Diodo-3,4-dimethylpyridine (13b): Yield: 0.12 g (4%); m.p. 74–78 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.43 (s, 1 H, Ar), 2.31 (s, 3 H, CH_3), 2.26 (s, 3 H, CH_3) ppm. ^{13}C NMR (400 MHz, $CDCl_3$): δ = 146.8, 136.4, 134.4, 123.3, 111.4, 21.7, 19.7 ppm. MS (EI): *m*/*z* (%) = 359 (39) $[M]^{+\cdot}$, 232 (100), 127 (11), 105 (65), 77 (21). $C_7H_7I_2N$ (358.95): calcd. C 23.42, H 1.96, N 3.90; found C 23.85, H 1.99, N 3.94.

Acknowledgments

We are thankful to the Council of Scientific and Industrial Research (CSIR), New Delhi, for financial support. Additional support from SAP by the University Grants Commission (UGC), New Delhi, is also acknowledged. We are also thankful to Mr. Avtar Singh, CIL, Punjab University, Chandigarh, for the NMR spectra.

[1] a) R. Ziessel, *Synthesis* **1999**, 1839–1865; b) Y. Uchida, N. Echikawa, S. Oae, *Heteroat. Chem.* **1994**, *5*, 409–413.
[2] a) T. Sammakia, E. L. Stangeland, M. C. Whitcomb, *Org. Lett.* **2002**, *4*, 2385–2388; b) E. De Vos, E. L. Esmans, F. C. Alderweireldt, *J. Heterocycl. Chem.* **1993**, *30*, 1245–1252.
[3] a) W. R. F. Goundry, J. E. Baldwin, V. Lee, *Tetrahedron* **2003**, *59*, 1719–1729; b) Y. Ma, S. Breslin, I. Keresztes, E. Lobkovsky, D. B. Collum, *J. Org. Chem.* **2008**, *73*, 9610–9618; c) D. A. Evans, V. J. Cee, T. E. Smith, K. J. Santiago, *Org. Lett.* **1999**, *1*, 87–90; d) M. L. Davis, B. J. Wakefield, J. A. Wardell, *Tetrahedron* **1992**, *48*, 939–52.
[4] a) B. J. Wakefield in *The Chemistry of Organolithium Compounds*, Pergamon Press, Oxford, **1974**; b) L. Engman, M. P. Cava, *Organometallics* **1982**, *1*, 470–473; c) M. Schlosser, M. Florence, *Chem. Soc. Rev.* **2007**, *36*, 1161–1172; d) K. K. Bhasin, P. Venugopalan, J. Singh, *Phosphorus, Sulfur Silicon Relat. Elem.* **2002**, *177*, 2579–2587.
[5] a) A. Doudouh, P. C. Gros, Y. Fort, C. Woltermann, *Tetrahedron* **2006**, *62*, 6166–6171; b) P. Gros, F. Elaachbouni, *Chem. Commun.* **2008**, 4813–4815.
[6] a) J. Mathieu, P. Gros, Y. Fort, *Chem. Commun.* **2000**, 951–952; b) P. Gros, C. Viney, Y. Fort, *Synlett* **2002**, 628–630; c) P. Gros, Y. Fort, *Eur. J. Org. Chem.* **2009**, 4199–4209; d) H. K. Khartabil, P. Gros, Y. Fort, M. F. Ruiz-Lopez, *J. Am. Chem. Soc.* **2010**, *132*, 2410–2416; e) T. Kaminski, P. Gros, Y. Fort, *Eur. J. Org. Chem.* **2003**, 3855–3860.
[7] S. V. Kessar, P. Singh, K. N. Singh, M. Dutt, *J. Chem. Soc., Chem. Commun.* **1991**, 570–571.
[8] S. V. Kessar, P. Singh, *Chem. Rev.* **1997**, *97*, 721–737.
[9] E. Vedejs, X. Chen, *J. Am. Chem. Soc.* **1996**, *118*, 1809–1810.
[10] J. S. Dhau, A. Singh, R. Dhir, *J. Organomet. Chem.* **2011**, *696*, 2008–2013.
[11] S. V. Kessar, P. Singh, K. N. Singh, P. V. Bharatam, A. K. Sharma, S. Lata, A. Kaur, *Angew. Chem.* **2008**, *120*, 4781; *Angew. Chem. Int. Ed.* **2008**, *47*, 4703–4706.
[12] M. J. Frisch, G. W. Trucks, H. B. Schlegel, G. E. Scuseria, M. A. Robb, J. R. Cheeseman, J. A. Montgomery, T. Vreven Jr, K. N. Kudin, J. C. Burant, J. M. Millam, S. S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G. A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, L. X. M. Klene, J. E. Knox, H. P. Hratchian, J. B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R. E. Stratmann, O. Yazyev, A. J. Austin, R. Cammi, C. Pomelli, J. W. Ochterski, P. Y. Ayala, K. Morokuma, G. A. Voth, P. Salvador, J. J. Dannenberg, V. G. Zakrzewski, S. Dapprich, A. D. Daniels, M. C. Strain, O. Farkas, D. K. Malick, A. D. Rabuck, K. Raghavachari, J. B. Foresman, J. V. Ortiz, Q. Cui, A. G. Baboul, S. Clifford, J. Cioslowski, B. B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. L. Martin, D. J. Fox, T. Keith, M. A. Al-Laham, C. Y. Peng, A. Nanayakkara, M. Challacombe, P. M. W. Gill, B. Johnson, W. Chen, M. W. Wong, C. Gonzalez, J. A. Pople, *Gaussian 03*, rev. E.01, Gaussian, Inc., Pittsburgh, PA, **2003**.
[13] R. G. Parr, W. Yang, *Density Functional Theory of Atoms and Molecules*, Oxford University Press, New York, **1989**.
[14] L. J. Bartolotti, K. Fluchick, in: *Reviews in Computational Chemistry* (Eds.: K. B. Lipkowitz, D. B. Boyd), VCH Publishers, New York, **1996**, vol. 7, pp. 187–216.
[15] V. Barone, M. Cossi, *J. Phys. Chem. A* **1998**, *102*, 1995–2001.
[16] K. K. Bhasin, J. Singh, *J. Organomet. Chem.* **2002**, *658*, 71–76.

Received: November 1, 2011
Published Online: February 3, 2012

