Note

Designing hydroxy-functionalized chiral salen ligand and its use in the synthesis of dioxadiazasilamacroheterocycles

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Received 9 March 2009; accepted (revised) 19 April 2010

Synthesis of dioxadiazasilamacroheterocycles is described. The key step involves the initial synthesis of symmetrical hydroxyl-functionalized chiral salen ligand, \(N,N'\)-bis(2-hydroxyacetophenonylidene)-1,2-diaminocyclohexane followed by sequential deprotonation with NaH to form dianion intermediate \(in\ situ\), which reacts with diorganodichlorosilanes to furnish desired heterocycles. The products have been characterized by satisfactory elemental analyses and spectral (IR, \(^1\)H, \(^13\)C, \(^29\)Si NMR and mass) studies.

Keywords: \(N,N'\)-bis(2-hydroxyacetophenonylidene)-1,2-diaminocyclohexane, dianion, diorganodichlorosilanes, dioxadiazasilacyclotridecines

Schiff bases are valuable synthons for the preparation of macroheterocycles\(^1,2\). To the best of our knowledge there are no reports on the synthesis of thirteen membered dioxadiazasilaheterocycles containing five heteroatoms (2N, 2O and Si). Our aim is to broaden the range of useful dioxadiazasilaheterocycles, which can provide an easy access to synthetic intermediates and therapeutic agents. With this background, the goal of the present article is to provide cyclization reactions of remote dianion via cyclosilylation. Heteroatom-based remote dianion has become increasingly popular strategic tool for the synthetic planning\(^3,4\). A remarkable feature of this reaction is the construction of oxygen-silicon bonds via a tandem process. In continuous to studies on the synthesis of new heterocyclic systems\(^5-8\), using efficient intermolecular cyclization reactions via dianion intermediate, herein we have developed a modular approach to a new class of structurally diverse dioxadiazasilacyclotridecines in good yields. The compounds may be used in chemical vapor deposition and deoxygenation reactions in organic transformations. Their derivatives may be of use in pharmaceutical chemistry.

Results and Discussion

The reaction of 1 equivalent of diaminocyclohexane with 2 equivalents of \(o\)-hydroxyacetophenone in ethanol under reflux for 36 hr according to the literature method\(^9\) afforded the corresponding symmetrical salen Schiff base ligand, \(N,N'\)-bis(2-hydroxyacetophenonylidene)-1,2-diaminocyclohexane 1 (Scheme I). The structure of ligand 1 was established from its spectral and analytical data. The introduction of diorganosilylene group is normally achieved by the reaction of diorganodichlorosilane with proper substrate in the presence of a base to prepare heterocyclic compounds containing silicon atom. The synthesis involves the initial formation of dianion 2 from sequential deprotonation of the phenolic OH group of ligand 1 by sodium hydride in dry toluene at \(-4^\circ\)C. The remote dianion 2 thus generated attacks to a variety of diorganodichlorosilanes leading to the formation of compounds 3-10 (Scheme II). We believe that such a protocol would provide one-pot access to target molecules possessing a high degree of complexity, which would otherwise require technically demanding multistep syntheses. TLC of all compounds confirmed their purity.

Formation of compound is suggested by the disappearance of absorption band and signal corresponding to the -OH group in both IR and \(^1\)H NMR spectra and appearance of new band in the region 845-721 cm\(^{-1}\) assignable to Si-O bond\(^10,11\). The azomethine C=N band, which appears at 1618 cm\(^{-1}\) in the IR spectrum of the ligand, is found almost at the same position in all the newly synthesized compounds exhibiting no lowering of \(\nu(C=N, \text{ref. 12})\) indicates non-coordination of C=N to the silicon atom showing tetracoordinated\(^13\) state, which is further supported by \(^29\)Si NMR chemical shifts.

![Scheme I](image-url)


$^1$H NMR spectra display a multiplet in the range $\delta$ 7.85-6.60 ppm for aromatic protons, a multiplet for two aliphatic C-H protons in the range $\delta$ 3.86-3.80 ppm, a multiplet in the range $\delta$ 1.97-1.40 ppm for eight aliphatic CH$_2$ protons and singlets of silicon methyl in the range $\delta$ 0.98-0.11 ppm. The signal attributable to the imine proton (HC=N) in the spectra of silaheterocycles is not accompanied by $^{29}$Si satellites, again indicating that the corresponding nitrogen atom is not involved in bonding with silicon. The alkyl groups attached to silicon display single resonance for chemically equivalent protons. In addition the $^{13}$C NMR spectra supported the assigned structures. The up-field shifts of the $^{29}$Si NMR signal of the compounds indicate the presence of tetracoordinate silicon in all the compounds. The newly synthesized dioxadiazasilamacroheterocycles gain rigidity due to the presence of two benzene and one cyclohexane ring in their skeleton. All the spectral data of newly synthesized compounds are mentioned in Table I.

**Experimental Section**

Chemicals were obtained from Sigma-Aldrich, Merck, Fluka and Lancaster, and are used as such without further purification. All solvents (AR or extra pure grade) used for spectroscopic and other physical studies were further purified by literature methods.$^{14}$ All operations were performed under nitrogen atmosphere using standard glass wares. IR spectra were recorded as KBr discs and in nujol mull on JASCO FT-IR-5300 spectrophotometer. Melting points were determined using a calibrated thermometer by Büchi B-540 melting point apparatus and are uncorrected. Elemental analyses were determined with a Vario-EL analyser. NMR ($^1$H, $^{13}$C and $^{29}$Si) spectra were recorded on a JEOL AL 300 FT-NMR spectrometer. All chemical shifts were reported in parts per million ($\delta$) relative to TMS as an internal standard in CDCl$_3$. Mass spectra were recorded at 70 eV ionizing voltage on a JEOL SX-102 (FAB). Chromatography columns were prepared from Merck silica gel 100-200 meshes.
Table I — IR and NMR (¹H, ¹³C and ²⁹Si) spectral data of compounds 3-10

<table>
<thead>
<tr>
<th>Compd No</th>
<th>IR (KBr, cm⁻¹)</th>
<th>¹H</th>
<th>¹³C</th>
<th>²⁹Si</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>7.40-6.68 (m, 8H, ArH), 3.86 (m, 2H, CH), 2.20 (s, 6H, CH₃), 1.90-1.40 (m, 8H, CH₂CH₂)</td>
<td>170.65, 163.48, 132.18, 128.22, 119.10, 118.30, 116.97, 62.82, 32.19, 24.02, 14.20, 1.00</td>
<td>-57.26</td>
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<tr>
<td>4</td>
<td>7.85-6.63 (m, 18H, ArH), 3.86 (m, 2H, CH), 2.20 (s, 6H, CH₃), 1.85-1.42 (m, 8H, CH₂CH₂)</td>
<td>170.65, 163.48, 132.20, 132.18, 128.22, 119.22, 119.10, 119.09, 118.30, 116.77, 116.97, 62.82, 32.19, 24.02, 14.20</td>
<td>-82.24</td>
<td></td>
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<tr>
<td>5</td>
<td>7.30-6.63 (m, 8H, ArH), 3.80 (m, 2H, CH), 2.20 (s, 6H, CH₃), 1.84-1.42 (m, 8H, CH₂CH₂), 0.88 (t, J = 6.0Hz, 6H, SiC₂H₅)</td>
<td>170.65, 163.48, 132.18, 128.22, 119.10, 118.30, 116.97, 62.82, 32.19, 24.02, 16.44, 14.20, 13.22</td>
<td>-53.46</td>
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<td>6</td>
<td>7.40-6.60 (m, 8H, ArH), 3.86 (m, 2H, CH), 2.40 (s, 6H, CH₃), 1.97-1.40 (m, 8H, CH₂CH₂), 1.39 (m, 2H, SiC₂H₅), 0.98 (t, J = 6.6Hz, 3H, SiCH₂CH₂CH₃), 0.59 (t, J = 6.8Hz, 2H, SiCH₂), 0.18 (s, 3H, SiCH₃)</td>
<td>171.08, 164.05, 132.52, 128.37, 118.95, 118.67, 116.99, 62.74, 32.29, 24.11, 18.27, 17.85, 14.31, 1.04, 0.96</td>
<td>-63.76</td>
<td></td>
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<tr>
<td>7</td>
<td>7.30-6.63 (m, 8H, ArH), 3.86 (m, 2H, CH), 2.40 (s, 6H, CH₃), 1.84-1.40 (m, 8H, CH₂CH₂), 0.89 (t, J = 6.0Hz, 3H, SiC₂H₅), 0.59 (q, J = 6.3Hz, 2H, SiCH₂), 0.28 (s, 3H, SiCH₃)</td>
<td>170.65, 163.48, 132.18, 128.22, 119.10, 118.30, 116.97, 62.82, 32.19, 24.02, 16.18, 14.20, 14.11, 1.00</td>
<td>-58.56</td>
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<tr>
<td>8</td>
<td>7.40-6.68 (m, 8H, ArH), 5.98 (m, 3H, SiCH=CH₂), 3.86 (m, 2H, CH), 2.40 (s, 6H, CH₃), 1.97-1.40 (m, 8H, CH₂CH₂), 0.38 (s, 3H, SiCH₃)</td>
<td>170.94, 163.80, 136.91, 132.46, 128.46, 119.32, 118.61, 117.96, 63.05, 32.45, 24.27, 14.46, 0.49</td>
<td>-51.26</td>
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<td>9</td>
<td>7.80-6.80 (m, 13H, ArH), 3.86 (m, 2H, CH), 2.48 (s, 6H, CH₃), 1.97-1.49 (m, 8H, CH₂CH₂), 0.48 (s, 3H, SiC₂H₅)</td>
<td>170.92, 163.87, 136.28, 133.31, 133.09, 132.37, 129.96, 129.51, 127.52, 118.87, 118.74, 118.20, 116.89, 62.62, 32.14, 29.54, 26.41, 23.97, 14.19, 0.89</td>
<td>-62.86</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>7.40-6.68 (m, 8H, ArH), 4.78 (s, 1H, SiH), 3.86 (m, 2H, CH), 2.20 (s, 6H, CH₃), 1.97-1.40 (m, 8H, CH₂CH₂), 0.80 (s, 3H, SiCH₃)</td>
<td>170.94, 163.80, 136.91, 132.46, 128.46, 119.32, 118.61, 117.96, 63.05, 32.45, 24.27, 14.46, 1.25</td>
<td>-64.26</td>
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</tr>
</tbody>
</table>

Synthesis of N,N'-bis(2-hydroxyacetophenonylede)-1,2-diaminocyclohexane 1

To a solution of 1,2-diaminocyclohexane (1.23 mmole, 140 mg) in absolute ethanol (1 mL) was added 2-hydroxyacetophenone (2.46 mmole, 334 mg). The resulting mixture was then refluxed at 78°C for 36 hr. After cooling to RT, water (5 mL) was added and the mixture was stirred for 30 min. The yellow precipitate formed was filtered, washed with water and DCM followed by recrystallization from absolute ethanol to give yellow needles 1 (Scheme II). Yield: 322 mg (70.5%); m.p. 144-45°C; IR (Nujol, cm⁻¹): 3060, 1618, ¹H NMR (300 MHz, CDCl₃): δ 16.34 (s, 2H, OH), 7.40-6.68 (m, 8H, ArH), 3.86 (dd, 2H, CH), 2.88 (s, 6H, CH₃), 1.92-1.97 (m, 4H, CH₂), 1.25-1.65 (m, 4H, CH₂), ¹³C NMR (75 MHz, CDCl₃): δ 170.65, 163.48, 132.18, 128.22, 119.10, 118.30, 116.97, 62.82, 32.19, 24.02, 14.20; FAB MS m/z: 351 [M+H⁺]; UV/vis (C₂H₅OH): 320, 270, 225 nm.

Synthesis of dioxadiazasilatetracyclocyclorides 3-10

Typical procedure: The typical procedure involves the dropwise addition of dry toluene solution (55 mL) of ligand (350 mg, 1 mmole) to a stirred suspension of NaH (48 mg, 2 mmoles) in dry toluene (5 mL) with constant stirring at −4°C for 6 hr in an inert atmosphere. Dichlorodimethylsilane (129 mg, 1 mmole) in dry toluene (5 mL) was added dropwise with constant stirring to the light yellowish solution of diamin in a solvent generated in situ. The reaction-mixture was stirred at RT for an additional 4 hr. Completion of the reaction was checked by TLC. The solvent was removed under reduced pressure with the help of rotary evaporator and the residue was subjected to column chromatography (diethyl ether) to give yellow solid 3. All other silaheterocycles 4-10 were synthesized analogously as mentioned above. The synthetic, physical and analytical data of the compounds are listed in Table II.
Conclusion

In conclusion, a quite simple procedure, low consumption of solvent, fast reaction rates, mild reaction condition and good yield of the reaction make this protocol an attractive and useful contribution to the preparation of a rare class of nitrogen, oxygen and silicon macroheterocycles.

Acknowledgements

This work was supported by a research grant from the Council of Scientific and Industrial Research (Grant 01(2260)/08/EMR-II) and Department of Science and Technology (Grant SR/S1/OC-66/2009), New Delhi.

References