New Lithium Porphyrin Derivatives: Synthesis of $Li_2(P)(Et_2O)_2$ (P = TTP, TBPP) and Solution Structure of $Li_2(TTP)(Et_2O)_2$ by ^7Li and ^{15}N NMR

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The preparation of new lithium porphyrinates $Li_2(P)(ether)_2$ [P = dianion of tetra-*p*-tolylporphyrin (TTP), dianion of tetrakis(*p-tert*-butylphenyl)porphyrin (TBPP); ether = Et_2O, Bu_2O] is reported, employing a slight modification of the established literature procedure. The new derivatives are quite soluble in nonpolar solvents and possess a well-defined stoichiometry. Variable temperature ^1H, ^7Li, and ^{15}N NMR spectroscopy served to elucidate the solution structure of $Li_2(TTP)(Et_2O)_2$. The two lithium atoms are coordinated symmetrically to the four porphyrin nitrogens above and below the porphyrin plane and each binds to an additional diethyl ether oxygen. Base-free dilithium porphyrins were also prepared. In addition an improved synthesis of 3,4-diethylpyrrole, the precursor for preparation of octaethylporphyrin (H_2OEP), is reported.

Introduction

Recently we reported the synthesis and characterization of a variety of alkali metal porphyrin complexes $M_2(P)(solv)_n$ (M = Li, Na, K; P = OEP, TPP, TTP, TBPP, TMPP; solv = THF, py, DME).[1] These compounds have proven to be very useful as reagents for the synthesis of porphyrin derivatives of the early transition metals.[2] In an attempt to prepare transition metal porphyrin compounds employing Et_2O as solvent, we isolated the dilithium tetraarylporphyrin complex $Li_2TTP(Et_2O)_2$. In contrast to the previously reported alkali metal porphyrins this compound possesses a well-defined stoichiometry, it contains exactly two Et_2O molecules, and it is very soluble in nonpolar solvents. The solubility properties of $Li_2TTP(Et_2O)_2$ allows metalation reactions to be performed in Et_2O or hexanes at room temperature, therefore nicely complementing the dilithium porphyrin reagents reported earlier. Furthermore, the absence of strongly coordinating solvents such as THF or pyridine allows for improved synthesis of transition metal porphyrins. Herein we report the synthesis and the characterization of a variety of dilithium tetraarylporphyrinato dietherates as well as some base-free analogs.

Results and Discussion

The dilithium tetraarylporphyrinate etherates are prepared in ether employing the general reaction scheme reported earlier.[1] Due to the low boiling point of diethyl ether rather long reaction times are necessary. This problem can be circumvented by employing toluene containing several equivalents of diethyl ether or dibutyl ether as solvent (eq 1).

$$H_2(P) + 2LiN(SiMe_3)_2 \xrightarrow{\text{toluene/ether}} Li_2(P)(ether)_2 + 2HN(SiMe_3)_2 \quad (1)$$

$$P = TTP, TBPP; ether = Et_2O, Bu_2O$$

The color of the reaction mixture immediately took the blue-green color of the product upon addition of the solvent to the starting materials, and soon all solids were dissolved when heated at reflux. Multigram quantities of pure highly crystalline product are obtained directly from the reaction mixture after cooling to −40 °C. Interestingly the dilithium compounds crystallize with exactly 2 equiv of ether present and show no tendency to loose coordinated solvent even after prolonged exposure to vacuum. Furthermore, these derivatives show enhanced solubility in nonpolar solvents as compared to the previously isolated alkali metal porphyrins. $Li_2TTP(Et_2O)_2$ is very soluble in CH_2Cl_2 and toluene and moderately soluble in Et_2O and hexanes. The dibutyl ether analog is even quite soluble in hexanes. $Li_2TBPP(Et_2O)_2$ proved too soluble to isolate in good yields from diethyl ether or toluene, but appreciable amounts of the product can be crystallized from pentane. In an attempt to extend this chemistry to octaethylporphyrins we reacted H_2OEP with $LiN(SiMe_3)_2$ in toluene/Et_2O. We obtained a red, microcrystalline compound which was only slightly soluble in noncoordinating solvents. The ^1H NMR spectrum in acetone-d_6 showed it to be base-free Li_2-OEP, which was confirmed by elemental analysis. Judging from its solubility properties we believe this compound to be oligomeric in nature. Base-free Li_2TTP is generated by heating H_2TTP and 2 equiv of $LiN(SiMe_3)_2$ at reflux in toluene in the absence of any coordinating cosolvent. This methodology can easily be extended to sodium and potassium derivatives.

The ^1H NMR spectra of the dilithium derivatives provide valuable information about their solution structures (Figure 1). The ortho and meta protons of the aryl groups in $Li_2(TTP)(Et_2O)_2$ each display a doublet. Only one sharp high-field signal (fwhh = 7 Hz) at −11.5 ppm is encountered in the ^7Li NMR spectrum at room temperature (Figure 2), indicating equivalence of the two porphyrin faces.[3] The signals of the diethyl ether

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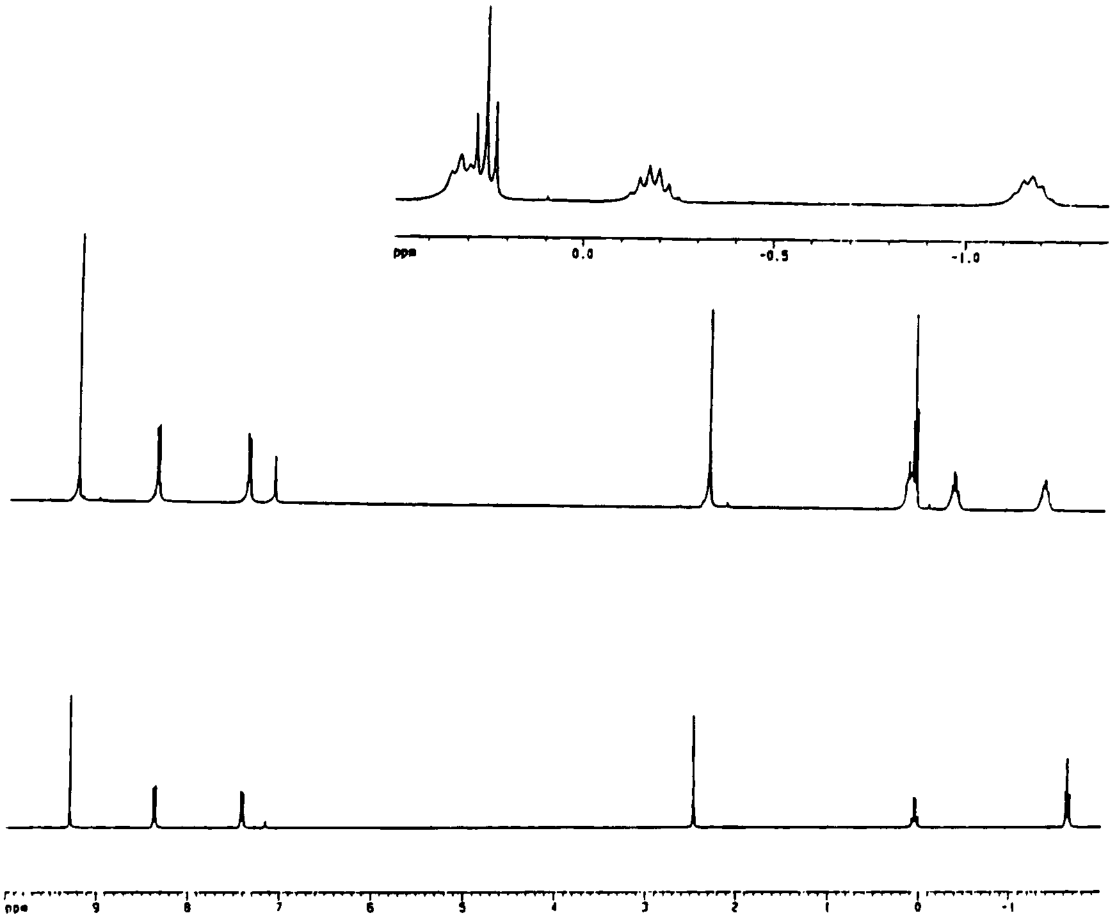

Figure 1. ^1H NMR of $Li_2(TTP)(Bu_2O)_2$ (top) and $Li_2(TTP)(Et_2O)_2$ (bottom) in C_6D_6.

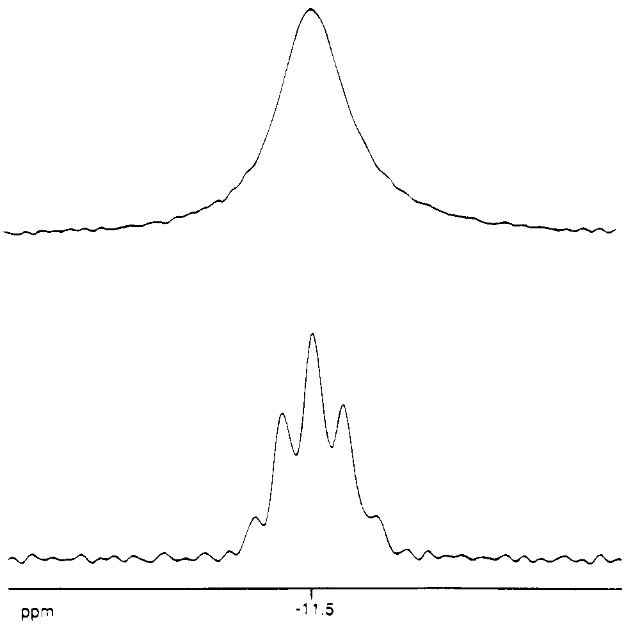

Figure 2. ^7Li NMR spectra of $Li_2(TTP)(Et_2O)_2$ at −96 °C (top) and ^{15}N-labeled $Li_2(TTP)(Et_2O)_2$ at −90 °C (bottom). The top spectrum is offset by 0.7 ppm and the signal appears at −10.8 ppm.

methylene and methyl protons are shifted considerably upfield, the former resonating at 0.06 and the latter at −1.63 ppm. In general, the anisotropy of the aromatic porphyrin macrocycle induces large upfield shifts of the proton signals of attendant ligands in metalloporphyrins. The large upfield shift of the ^{7}Li signal is likewise indicative of strong shielding by π-electron density.[4] Therefore the lithium atoms and ether molecules must be closely coordinated to the porphyrin ring, effectively excluding a solvent separated ion pair (as encountered for $[Li(THF)_4]^+[Li(OEP)]^-$) as a possible solution structure.[1] Surprisingly, the overall appearance of the ^1H and ^7Li NMR spectra are quite invariant over the temperature range −100 to +100 °C in C_7D_8, with only minor changes in the chemical shifts. These results point to a symmetrical solution structure with one ether molecule bound to each Li cation, the latter being coordinated to four nitrogen atoms on top and below the porphyrin plane as shown in **A**. We cannot exclude fluxional processes involving structures such as **B** or **C**, both of which have precedent in transition metal porphyrin chemistry.[5] However, we note that the ionic radius of lithium (0.76 Å)[6] is large enough to allow a solution structure as shown in **A** and that lithium is known to display high coordination numbers in the absence of overriding steric effects.[7] The crystal structure of 1,4,7,10-tetrakis(2-hydroxyethyl)-1,4,7,10-tetraazacyclododecane lithium chloride dihydrate provides precedent for the proposed structure **A**.[8] In this compound lithium is coordinated in a square pyramid with four nitrogen atoms in the basal plane and one ether oxygen in the apical position.

In order to gain more insight into the nature of the Li−N

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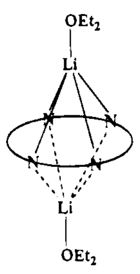
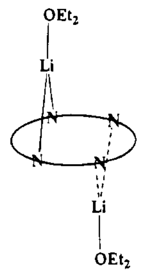


A



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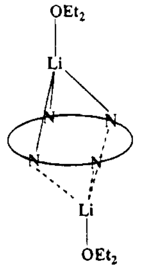

C

bond, the ^{7}Li and ^{15}N NMR spectra of [$^{15}N_4$]Li_2(TTP)(Et_2O)$_2$ (96% ^{15}N) were obtained over a range of temperatures. At −90 °C only one singlet at −159.0 ppm (fwhh = 22 Hz) is encountered in the ^{15}N NMR spectrum. The ^{7}Li NMR spectrum at this temperature, however, displays a 1:4:6:4:1 quintet at −11.5 ppm with a ^{7}Li—^{15}N coupling constant of 4.7 Hz (no coupling could be detected at room temperature). This is consistent with a symmetrical solution structure in which each lithium atom is coordinated to all four porphyrin nitrogen atoms as proposed above, although it does not exclude intramolecular exchange of the Li ions. Furthermore, the fact that ^{7}Li—^{15}N coupling is observed points to some covalent contribution to the Li—N bond.[9]

The Li_2(P)(ether)$_2$ compounds are valuable reagents for the preparation of early transition metal porphyrins. For example, employing Li_2(TTP)(DME)$_n$ or Li_2(TTP)(THF)$_n$ for the preparation of (TTP)$ZrCl_2$ proved unsatisfactory since the product was obtained only in low yield and low purity. The use of Li_2(TTP)(Et_2O)$_2$ as porphyrin transfer reagent however, allowed the high-yield preparation of the pure target molecule.[10]

Conclusions

Dilithium tetraarylporphyrinate dietherates have been prepared with properties complementing those of the previously isolated dilithium derivatives. In particular, their high solubility in nonpolar solvents and the absence of strongly coordinating solvents such as THF and pyridine, which might interfere with metalation reactions, establish these compounds as useful synthons. ^{7}Li NMR experiments conducted with fully ^{15}N labeled Li_2(TTP)(Et_2O)$_2$ proved a valuable tool for elucidating the solution structure.

Experimental Section

General Considerations. Inert atmosphere glovebox and Schlenk-line techniques were used throughout the preparative procedures.[11] NMR tube experiments were performed either in flame-sealed or Teflon-stoppered NMR tubes, unless stated otherwise. Diethyl ether, hexanes, benzene, pentane, and toluene were all predried over 4 Å molecular sieves and, with the exception of toluene, were all distilled from purple sodium/benzophenone under N_2. Toluene was distilled from sodium under N_2. Dibutyl ether was dried over 4 Å molecular sieves. All NMR solvents were dried as for their undeuterated counterparts, but were purified by vacuum transfer and additionally, were passed through alumina (activated at 350 °C under vacuum) in the glovebox. Acetone-d_6 was dried over activated molecular sieves and vacuum transferred prior to use. H_2OEP was prepared according to the literature.[12] The yield of intermediate 3,4-diethylpyrrole, however, was improved considerably by employing the barium-promoted copper chromite (Aldrich) catalyzed decarboxylation procedure reported by Whitlock et al.[13] [^{15}N]pyrrole was obtained from Cambridge Isotope Laboratories. H_2TTP and [$^{15}N_4$]H_2TTP were prepared according to Lindsey[14] and purified following the procedure of Smith.[15] Melting points were determined in sealed capillary tubes under nitrogen and are uncorrected. IR samples, unless stated otherwise, were either prepared as Nujol mulls between CsI or KBr plates or as KBr pressings in an airtight cell. UV/vis spectra were recorded in 0.2 cm quartz cells and are reported in the form: λ_{max} in nm (log ϵ). Elemental analyses were performed within the College of Chemistry, University of California, Berkeley, CA. ^{1}H, ^{7}Li, ^{13}C{^{1}H}and ^{15}N NMR spectra were recorded at ambient temperatures unless noted otherwise. Chemical shifts (δ) for ^{1}H NMR spectra are reported relative to residual protons in the deuterated solvents, for ^{13}C NMR spectra relative to carbons in the deuterated solvent, for ^{7}Li relative to external LiCl in D_2O, and for ^{15}N relative to external O_2NCH_3.

Li_2TTP(OEt_2)$_2$. H_2TTP (5.0 g, 7.45 mmol) and LiN($SiMe_3$)$_2$ (2.87 g, 17.14 mmol) were heated at reflux in Et_2O (350 mL) for 48 h to give a blue-green solution. The precipitate which formed during this time was collected by filtration after cooling the solution to room temperature. The filtrate was concentrated to 100 mL and cooled to −40 °C. Another batch of blue crystals was collected to afford 5.50 g (89%) of Li_2TTP(Et_2O)$_2$. Mp > 300 °C. ^{1}H NMR (C_6D_6): δ 9.28 (s, 8 H, pyrrole *H*), 8.36 (d, ^3J = 7.9 Hz, 8 H, Ph—*H*), 7.41 (d, ^3J = 7.9 Hz, 8 H, Ph—*H*), 2.45 (s, 12 H, Ph—CH_3), 0.06 (q, ^3J = 7.0 Hz, 8 H, CH_2), −1.63 (t, ^3J = 7.0 Hz, 12 H, CH_2CH_3). ^{7}Li NMR (C_7D_8): δ −11.5 (s, fwhh = 7 Hz), ^{13}C NMR (C_6D_6): δ 152.9, 142.6, 136.3, 135.3, 132.3, 127.3, 121.7, 62.4, 21.5, 11.5. ^{15}N NMR (C_7D_8): δ −159.0 (s, fwhh = 22 Hz). UV/vis (toluene): 436 (5.50), 574 (4.23), 614 (4.15). IR: 1519, 1497, 1326, 1196, 1172, 1067, 973, 797, 724, 522 cm^{-1}. Anal. Calcd for $C_{56}H_{56}N_4Li_2O_2$: C, 80.94; H, 6.79; N, 6.74. Found: C, 80.85; H, 6.70; N, 6.84.

Li_2TTP(Bu_2O)$_2$. H_2TTP (2.0 g, 3.21 mmol) and LiN($SiMe_3$)$_2$ (1.24 g, 7.39 mmol) were heated at reflux for 4 h in 40 mL of toluene containing 2 mL of Bu_2O. After the blue-green solution had cooled to room temperature, it was filtered and concentrated to 15 mL. Hexane (25 mL) was added and the solution slowly cooled to −40 °C. Blue crystals (2.04 g, 67%) were collected by filtration. Mp > 300 °C. ^{1}H NMR (C_6D_6): δ 9.27 (s, 8 H, pyrrole *H*), 8.40 (d, ^3J = 7.8 Hz, 8 H, Ph—*H*), 7.43 (*d*, ^3J = 7.8 Hz, 8 H, Ph—*H*), 2.47 (s, 12 H, Ph—CH_3), 0.32 (br, t, 12 H, CH_3), 0.26 (t, ^3J = 7.3 Hz, 8 H, OCH_2), −0.18 (br sext, 8 H, C$H_2$$CH_3$), −1.18 (br quin, 8 H, OCH_2CH_2). ^{13}C NMR (C_6D_6): δ 152.8, 142.6, 136.3, 135.3, 132.3, 127.3, 121.6, 67.8, 28.6, 21.5, 18.0, 13.5. UV/vis (toluene): 437 (5.62), 574 (4.28), 615 (4.17). Anal. Calcd for $C_{60}H_{64}N_4Li_2O_2$: C, 81.50; H, 7.69; N, 5.94; Found: 80.92; H, 7.51; N, 6.09.

Li_2TBPP(Et_2O)$_2$. H_2TBPP (0.250 g, 0.279 mmol) and LiN($SiMe_3$)$_2$ (0.103 g, 0.642 mmol) were stirred in 45 mL of pentane containing 3 mL of Et_2O for 24 h after which all of the starting materials were dissolved, giving a dark blue-green solution. This mixture was filtered and slowly cooled to −40 °C affording 0.187 g (67%) of blue crystals. Mp > 300 °C. ^{1}H NMR (C_6D_6: δ 9.21 (s, 8 H, pyrrole *H*), 8.42 (d, 8 H, Ph—*H*), 7.71 (d, 8 H, Ph—*H*), 1.51 (s, 36 H, ^{t}Bu—*H*), 0.55 (q, 8 H, OCH_2), −1.20 (t, 12 H, OCH_2CH_3). UV/vis (toluene): 436 (5.71), 574 (4.26), 615 (4.16). IR: 1523, 1326, 1266, 1197, 1108, 1065, 1025, 1002, 976, 851, 810, 796, 723, 584 cm^{-1}. Anal. Calcd for $C_{68}H_{80}N_4Li_2O_2$: C, 81.73; H, 8.07; N, 5.61; Found: C, 81.82; H, 7.90; N, 5.65.

Li_2TTP. H_2TTP (0.300 g, 0.447 mmol) and LiN($SiMe_3$)$_2$ (0.165 g, 0.984 mmol) were heated at reflux in 80 mL toluene for 1 h after which all of the starting materials were dissolved. The solution was then allowed to slowly cool to room temperature, filtered, and slowly cooled to −40 °C. Blue crystals (0.217 g, 71%) were collected by filtration. Mp > 300 °C. A ^{1}H NMR spectrum in acetone-d_6 shows it to be base-free Li_2TTP. Anal. Calcd for $C_{48}H_{36}N_4Li_2$: C, 84.45; H, 5.31; N, 8.21; Found: C, 84.03; H, 5.69; N, 8.86.

Li_2OEP. H_2OEP (1.00 g, 1.87 mmol) and LiN($SiMe_3$)$_2$ (0.72 g, 4.3 mmol) were heated at reflux in 80 mL of Et_2O for 6 h. Purple crystals

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(0.907 g, 89%) were collected after cooling to −40 °C. The compound is quite insoluble in non coordinating solvents. A ^{1}H NMR spectrum in acetone-d_6 shows it to be base-free Li_2OEP. Anal. Calcd for $C_{36}H_{44}N_4Li_2$: C, 79.10; H, 8.11; N, 10.25; Found: C, 78.96; H, 7.74; N, 10.37.

3,4-Diethylpyrrole. Crude ethyl 3,4-diethylpyrrole-2-carboxylate was obtained from 3-acetoxy-2-nitrohexane and ethyl isocyanoacetate as described in the literature. The crude ethyl 3,4-diethylpyrrole-2-carboxylate (140.5 g, 0.720 mol) was heated at reflux in 1.2 L of water containing NaOH (120 g, 3.00 mol) for 20 h. After cooling to room temperature, the solution was extracted with diethyl ether (3 × 100 mL). The combined diethyl ether fraction was cooled in ice water and 20 % aqueous HCl was slowly added until the pH was between 3 and 4. A bulky, slightly purple precipitate was collected by filtration and dried in air for 1 d. The crude 3,4-diethylpyrrole-2-carboxylic acid (about 90 g) was used directly in the next step.

A 500 mL three-necked round bottom flask equipped with a distillation apparatus, a thermometer and a solid-addition device (a Tygon tube connected to a 1000 mL flask containing the crude pyrrolecarboxylic acid) was charged with 1.0 g of barium-promoted copper chromite catalyst and 140 mL of quinoline. The temperature was raised to 190 °C and the pyrrole acid added in small portions. Each addition caused a vigorous reaction, effervescence, and a drop in temperature of about 10−20 °C. After the addition was complete, the reaction mixture was stirred for another 2 h and then the temperature was raised and the product and the solvent distilled at 222−236 °C. The liquid was added to 1.4 L of 5% aqueous HCl and extracted with diethyl ether (200 mL). The aqueous layer was then saturated with NaCl and extracted with diethyl ether (5 × 200 mL). The combined ether extracts were dried over $MgSO_4$ and the ether removed in vacuo. The product was distilled and the fraction boiling at 190−195 °C was collected affording 59.4 g (67%, lit.[12] 38.1−40%; this is the combined yield from three steps, relative to ethyl isocyanate) pure 3,4-diethylpyrrole.

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