Synthesis, Structure, and DFT Analysis of the THF Solvate of 2-Picolyllithium: A 2-Picolyllithium Solvate with Significant Carbanionic Character

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Dedicated to Professor Dr. Manfred Scheer in Celebration of his 65th Birthday

Abstract. Previous studies of different solvates of 2-methylpyridyllithium (2-picolyllithium) have uncovered electronic structures corresponding to aza-allyl and enamido resonance forms of the metallated pyridine-based compounds. Here, we report the synthesis and characterization of [2-CH$_2$Li(THF)$_2$C$_5$H$_4$N], a new THF solvate. X-ray crystallographic studies reveal a dimeric arrangement featuring a non-planar eight-membered [NCCLi]$_2$ ring, in which the primary cation-anion interaction is between the central Li atom and the C atom of the deprotonated methyl group [length, 2.285(2) Å], suggesting a new carbanionic resonance structure for this 2-picolyllithium series. The significant carbanionic character of [2-CH$_2$Li(THF)$_2$C$_5$H$_4$N] was confirmed by gas-phase DFT calculations [B3LYP/6-311+G(d)] with the calculated electron density interrogated by means of quantum theory of atoms in molecules (QTAIM) and natural bond orbital (NBO) analyses. For comparison these computational analyses were also performed on the literature structures of [2-CH$_2$Li(2-Picoline)C$_5$H$_4$N] and [2-CH$_2$Li(PMDETA)C$_5$H$_4$N]. In a reactivity study, [2-CH$_2$Li(THF)$_2$C$_5$H$_4$N] was found to undergo nucleophilic addition to pyridine to generate dipyridylmethane in a good yield.

Introduction

General interest in metallated pyridine compounds stems from their vast utility as intermediates in synthetic chemistry, a topic that has spawned several excellent review articles.[1] Evidence of the importance of functionalizing the pyridine scaffold stems from the impressive statistic that it is the second most frequently encountered nitrogen-based heterocycle in pharmaceuticals (behind its saturated derivative piperidine) with over 60 % of these pyridines exhibiting C2 substitution.[2] Pyridines possessing alkyl substituents at the 2-position are particularly important ligands in asymmetric catalysis.[3] These compounds can trace their Celtic routes back to 19th Century Glasgow where *Anderson* first obtained picoline from the distillation of coal tar in 1846[4] and *Sir William Ramsay* refined a successful early synthetic procedure in the 1870's.[5] Inorganic groups can also be grafted onto the 2-position following a metallation-metathesis process as recently illustrated through the synthesis of 2-borylmethylpyridines, such as C$_5$H$_4$N-CH$_2$-B(C$_6$F$_5$)$_2$.[6] Therefore, metallated derivatives of 2-alkylpyr-

idines are of special interest. Metallation was carried out by MeLi or PhLi in the original syntheses in the 1930's,[7] but the base employed in the metallation process is often now *n*-butyllithium.

Formally, lithiation of the alkyl substituent at the 2-position of the parent 2-alkylpyridine should generate a Li–C bond. However, in the case of 2-methylpyridine (2-picoline), the simplest 2-alkylpyridine, the interaction between the lithium (or other alkali metal) cation and the anionic pyridyl moiety can be more complex in reality, having a distinct electronic signature in a variety of structural motifs depending on the alkali metal and the nature of any Lewis basic ligands (L) that may be additionally supporting the metal (Figure 1).

This complexity has been subject to a vast number of multinuclear NMR studies[8] and has further piqued the interest of Group 1 specialists for over 30 years since *Raston* published the first X-ray crystal structure determination of a substituted picolyllithium complex in the form of [{2-(Me$_3$Si)$_2$C(Li)C$_5$H$_4$N}$_2$].[9] A comprehensive analysis of the electronic distribution in the aromatic pyridyl anion was carried out by *Stalke* using a combination of charge density studies and X-ray crystallographic studies of the representative solvates, [2-CH$_2$Li(Et$_2$O)C$_5$H$_4$N] (**1**) and [2-CH$_2$Li(2-Picoline)C$_5$H$_4$N] (**2**), both of which aggregate into dimers (see Figure 2 for structure of **2**).[10]

These prior reports prompted us to synthesize and characterize a series of 2-picolyl alkali metal complexes of lithium, sodium and potassium.[11] Interestingly, the engagement of the pyridyl anion with the lithium cation in both of *Stalke's* dimers **1** and **2** were interpreted predominantly as aza-allyl resonance structures comprising Li–N and Li–C interactions. On the
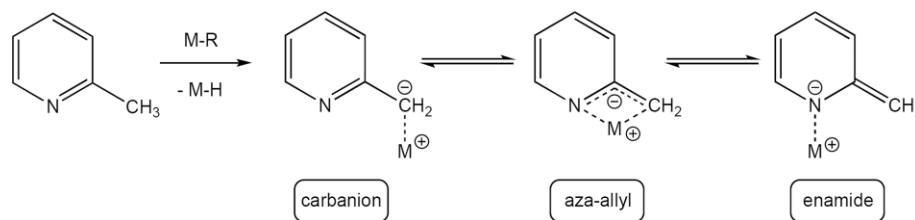
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Figure 1. Deprotonation of 2-picoline and the tautomeric forms available to be adopted between the resulting anion and a metal.

other hand, in our report the structure of [2-CH$_2$Li(PMDETA)C$_5$H$_4$N] (**3**) (PMDETA = N,N,N',N'',N''-pentamethyldiethylenetriamine, [(Me$_2$NCH$_2$CH$_2$)$_2$NMe]), a monomeric 2-picolyllithium solvate, revealed an enamido electronic arrangement comprising essentially a single Li–N interaction, as shown in Figure 2. This form was explicitly recognized by *Kaiser* who noted that "lateral metallations of these heterocycles are facilitated by delocalization of negative charge predominantly to the ring N atom".[8g] Thus, two of the three extreme resonance structures of the 2-picolyl anion (Figure 1) had been experimentally confirmed, leaving only the carbanionic resonance structure yet to be identified. Here, in this paper, we fill this missing gap in this resonance series by reporting the synthesis and crystallographic characterization of dimeric [2-CH$_2$Li(THF)$_2$C$_5$H$_4$N] (**4**) and for completeness present our findings of a comparative theoretical study of **2**, **3**, and **4**, employing *Bader's* QTAIM (quantum theory of atoms in molecules)[12] as well as Natural Bond Order (NBO) calculations.
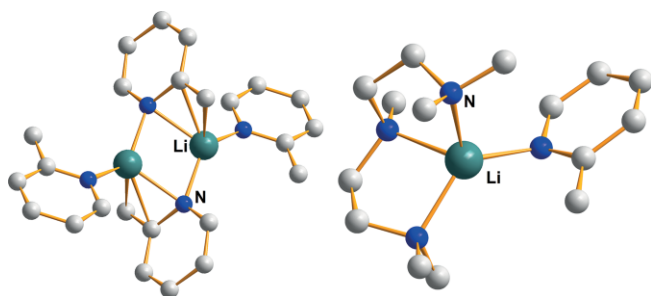
Figure 2. Molecular structures of aza-allylic tautomer [2-CH$_2$Li(2-Picoline)C$_5$H$_4$N]$_2$ (**2**) (left)[10] and enamido tautomer [2-CH$_2$Li(PMDETA)C$_5$H$_4$N] (**3**) (right).[11]

Results and Discussion

Synthesis and Characterization of Carbanionic Picolyllithium

The deprotonation of 2-picoline at the lateral methyl position was achieved in a facile manner through the addition of a *n*BuLi solution in hexane to a THF solution of the substituted pyridyl substrate. A very small crop of dark, sticky crystals resulted upon cooling which were amenable to a single crystal diffraction study that determined the molecular structure to be a cyclo-dimer (**4**, Figure 3). The yield was subsequently improved by repeating the reaction in less polar hexane solution, in the presence of two molar equivalents of THF to match the

stoichiometry of the structure (vide infra). Note it was vital to add the THF prior to the *n*BuLi induced deprotonation otherwise a competing nucleophilic addition occurred resulting in the competitive formation of some 1-lithio-2-*n*-butyl-6-methyl-1,2-dihydropyridine.[13]
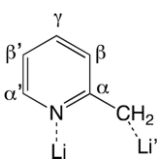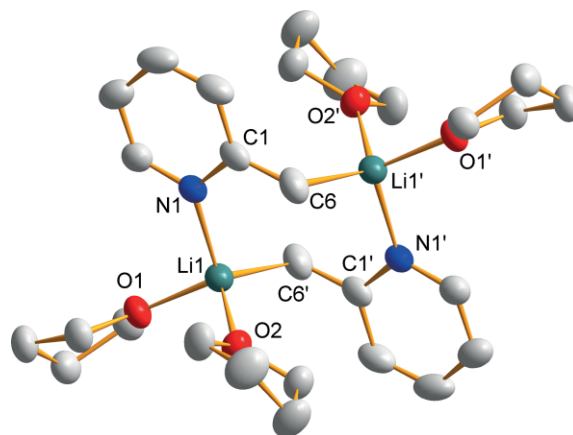
Figure 3. Molecular structure of [2-CH$_2$Li(THF)$_2$C$_5$H$_4$N]$_2$ (**4**) with ellipsoids displayed at 50% probability and all hydrogen atoms and minor disordered component of one THF molecule omitted for clarity. Symmetry operation to generate equivalent atoms denoted with a ': 1-x. 2 –*y*, 1 –*z*. Selected bond parameters /Å,°: Li1–N1, 2.023(2); N1–C1, 1.390(2); C1–C6, 1.382(2); C6–Li1', 2.285(2); Li1–O1, 1.989(2); Li1–O2, 1.979(2); Li1–N1–C1, 121.7(1); N1–C1–C6, 120.4(1); C1–C6–Li1', 107.3(1); N1–Li1–C6', 110.8(1); N1–Li1–O1, 106.5(1); N1–Li1–O2, 110.2(1); C6'–Li1–O1, 105.4(1); C6'–Li1–O2, 118.9(1); O1–Li1–O2, 103.9(1).

The key feature of centrosymmetric **4** is a non-planar eight-membered [NCCLi]$_2$ ring similar to that seen in the TMEDA-solvated structure of lutidyllithium,[14] with two molecules of THF solvating each lithium cation giving it overall a distorted tetrahedral arrangement. An analysis of the bond parameters suggests that the picolyl anion in **4** is carbanionic, thus completing the set of structural isomers for 2-picolyllithium in light of *Stalke's* aza-allyl structures[10] and our own enamido structure.[11] Table 1 contains the key bond lengths of complex **4** alongside those of the aza-allyl (**2**) and enamido (**3**) structures and the protonated 2-picoline which acts as a neutral donor in the aza-allyl structure, for comparison.

Compared to 2-picoline itself, there is some deformation of the aromatic structure with a more pronounced definition of alternating longer and shorter bonds, although such distortion from aromaticity is not nearly as extreme as in the enamido conformation **3** [e.g., the C$_\gamma$–C$_\beta$–C$_\alpha$ unit is 1.356(2)/1.439(2) Å in **4** and 1.326(6)/1.457(5) Å in **3**]. However, looking at the

Table 1. Selected bond lengths /Å and angles /° for the picolyl unit of complex **4** alongside the 2-picoline-solvated aza-allyl and PMDETA-solvated enamido forms **2** and **3**. The solvating ligand of 2-picoline in complex **2** is also included for completeness.

	2 (aza-allyl)	3 (enamido)	4 (carbanion)	2-Picoline
N–C$_{\alpha'}$	1.358(1)	1.358(6)	1.344(2)	1.342(1)
C$_{\alpha'}$–C$_{\beta'}$	1.372(1)	1.364(6)	1.367(2)	1.389(1)
C$_{\beta'}$–C$_\gamma$	1.423(1)	1.421(6)	1.404(2)	1.391(1)
C$_\gamma$–C$_\beta$	1.361(1)	1.326(6)	1.356(2)	1.390(1)
C$_\beta$–C$_\alpha$	1.448(1)	1.457(5)	1.439(2)	1.395(1)
C$_\alpha$–N	1.394(1)	1.387(4)	1.390(2)	1.347(1)
C$_\alpha$–CH$_2$	1.382(1)	1.356(6)	1.382(2)	1.498(1) [a]
Li–N	2.021(1)	2.007(8)	2.023(2)	2.018(1)
Li–CH$_2$	2.328(1)	2.980(7)	3.201(3)	–
Li'–CH$_2$	2.328(1)	–	2.285(2)	–
Li'–N	2.136(1)	–	3.603(2)	–
Ring–Li	0.206(1)	1.126(6)	0.210(2)	0.247(1)

a) CH$_2$–Li=CH$_3$.

position of the lithium cations and their relationship with the picolyl anions further supports the carbanionic character of **4**. The Li–N bond length in **4** at 2.023(2) Å is only marginally longer than that in complex **3** [2.007(8) Å], however what is more revealing is the position of the Li–N bond which is almost in the same plane as the ring (Figure 4, top right). Specifically, the C$_\gamma$–N–Li angle is 173.24(8)° showing only a modest deviation from the pyridyl ring plane and strongly supporting the interpretation of the ring nitrogen as being sp^2 hybridized and forming a dative bond to lithium via its lone pair, whereas the corresponding angle in enamido structure **3** is 145.9(2)° suggesting a sp^3 hybridized anionic nitrogen atom.[15] The lithium cation is displaced by just over 0.2 Å from the plane of the six-membered ring, very close to the value seen for the neutral picoline donor in the aza-allyl structure **2** [0.247(1) Å] and vastly different from the enamido structure whose corresponding deviation is 1.126(6) Å (Figure 4, top middle).
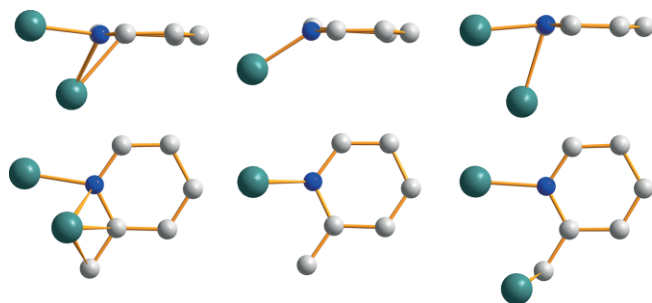
Figure 4. Side-on (top) and top-down (bottom) view of interactions between lithium cations and picolyllithium anion demonstrating aza-allyl form (**2**, left), enamido form (**3**, center) and carbanionic form (**4**, right) of picolyl anion.

This evidence suggests that the Li1–N1 interaction is the secondary oligomerizing interaction in **4** and that the primary cation-anion interaction is between Li1 and C6' [2.285(2) Å]. That this is a carbanion and not an aza-allyl type structure is clear from comparing the top-down views in Figure 4 which clearly show the lithium cation in **4** to be removed from the NCC unit unlike in the aza-allyl structure. The C–C–Li bond angle of 107.3(1)° is close to tetrahedral supporting a sp^3 hybridized carbanion and this is further supported by the location and refinement of the two hydrogen atoms which demonstrates further the pyramidalization of the carbon center. The CH$_2$–Li bond length of 2.285(2) Å in **4** is shorter than the corresponding length in lutidyllithium [2.351(1) Å][14] and is within the range of reported RCH$_2$–Li(L)$_3$ complexes, that is four-coordinate CH$_2$ carbanions bound to a tri-solvated lithium cation. For example, the CH$_2$–Li distance in PhCH$_2$Li(L)$_3$ ranges from 2.152–2.210 Å [(L)$_3$ = PMDETA,[16] Me$_3$TACN,[17] THF/TMEDA[18]], whereas a TMEDA solvated phosphinimine substituted benzyl complex shows a corresponding distance of 2.300(10) Å.[19]

Complex **4** was also probed in solution by multinuclear NMR spectroscopy in weakly coordinating C$_6$D$_6$ in an attempt to limit any influence on the coordination and aggregation of the molecule. The resulting data can be seen in Table 2 alongside the corresponding data for the diethyl ether, 2-picoline and PMDETA solvated picolyllithium complexes **1**–**3**.

The ^{1}H NMR spectrum of complex **4** suggests the carbanionic nature of the ligand is maintained in C$_6$D$_6$ solution. Specifically, the CH$_2$ group is represented by a single resonance at δ = 3.17 ppm suggesting its two hydrogen atoms are equivalent. This is in contrast to the ether-solvated aza-allyl and enamido complexes **1** and **3** which show this resonance split into two, suggesting inequivalence and thus more sp^2-type hybridization at the carbon. The ^{13}C chemical shift of the β' resonance is believed to be indicative of the degree of charge delocalization/aromaticity in these anions, with a more shielded resonance indicating greater charge delocalization into the ring form the deprotonated alkyl arm.[8e,8f] The value for complex **4** (δ =100.1 ppm) is less shielded than aza-allylic **1** or enamido **3** and would support the suggestion that this is

Table 2. Selected NMR spectroscopic data of complex **4** in C_6D_6 alongside comparable data for PMDETA-solvated enamido **3** and Et$_2$O- and 2-picoline-solvated aza-allyl structures **1** and **2**. The 2-picoline solvating molecule in **2** is also included for comparison.

	1		**2**		**3**		**4**		2-Picoline	
α'	6.76	148.7	7.52	148.4	7.08	148.3	7.40	148.4	8.55	149.7
β'	4.67	95.8	5.47	100.2	5.41	95.2	5.43	100.1	6.52	120.9
γ	5.92	131.0	6.52	132.9	6.61	131.3	6.51	132.9	6.83	136.5
β	5.53	115.9	6.31	117.5	6.36	115.7	6.24	117.0	6.42	123.5
α	–	163.7	–	162.8	–	162.5	–	163.9	–	158.9
CH$_2$	2.55, 2.41	58.5	3.39	57.8	3.44, 2.79	60.6	3.17	56.2	2.43 a)	24.0* a)
Li	0.35		Not reported		0.79		0.47		–	

a) CH$_2$–Li = CH$_3$.

the least delocalized (that is the most CH$_2$ carbanionic) structure.

We previously speculated that the vastly different values for the ^{1}H resonances of the ether solvate **1** with respect to the other complexes were due to the nature of the donor atom (that is *O*-donor vs. *N*-donor). The ^{1}H NMR spectroscopic data for (*O*-donor) complex **4**, which are very similar to the (*N*-donor) picoline solvated complex **2** would suggest that this is not the case. It is perhaps more likely that the picoline-solvated aza-allyl complex alters its structure and is in fact more carbanionic in benzene solution. This is further supported by the similarity in the ^{13}C chemical shift of the β′ resonance in **2** and **4** (100.2 and 100.1 ppm, respectively) although with only a limited number of examples this is by no means definite.

Computational Analysis

In order to further substantiate the experimental assignment of a 2-picolyl carbanion in **4**, gas-phase DFT calculations (B3LYP/6-311+G(d)) were performed on **4** and the resulting electron density interrogated by means of quantum theory of atoms in molecules (QTAIM) and natural bond orbital (NBO) analyses. The results are analyzed and compared with respect to those for **2** and **3**. The optimized geometries of all complexes are in excellent agreement with their experimental counterparts (see Figure 5 and Supporting Information for bond metric data), closely reproducing key bond parameters.

The QTAIM topological analysis of **4** reveals distinct bond paths between each lithium atom and the nitrogen from one picolyl unit, and the exocyclic carbon atom from the other picolyl fragment (i.e. Li1–N1, Li1–C6', Li1'–N1' and Li1'–C6, figure 5, right). When considered together with the bond paths for the C1–C6 and C1'–C6' bonds, these bond paths trace the eight-membered [NCCLi]$_2$ ring motif, which is also confirmed by the presence of a ring critical point (RCP) at its approximate geometric center. Bond paths to two oxygen atoms of THF complete the coordination sphere around each Li center. The observed molecular graph can be reconciled with carbanionic resonance character in **4**. As such the results of the topological analysis for **4** are distinctly different from **2** and **3**: in the former, bond paths between Li and N1 as well as Li and the carbon center C6 (Figure S5, Supporting Information) imply Li coordination to an aza-allyl system, whereas in the latter a single bond path between Li and N1 (Figure S8, Supporting Information) suggests interaction of Li with an enamido conformation in **3**. The properties associated with the Li–N, Li–O, and Li–C BCPs in **4** are consistent with closed-shell ionic interactions [electron density, $\rho(r)$ = 0.018–0.028 a.u.; Laplacian, $\nabla^2\rho(r)$ = 0.084–0.020 a.u., and total energy density, $H(r)$ = 0.002–0.008 a.u.], according to the criteria proposed by *Kraka* and *Cremer*.[20] As anticipated, the properties of the C1–C6 and its symmetry-related BCP [$\rho(r)$ = 0.300 a.u.; Laplacian, $\nabla^2\rho(r)$ = –0.797 a.u., $H(r)$ = –0.304 a.u.] are indicative of strong covalent character. The calculated ellipticity profiles along all C–C bond paths closely resemble those calculated for **2** (Figure S7, Supporting Information), revealing the highest $\varepsilon(r)$ values for the C1–C6 bond and diagnostic of significant double bond character. Ellipticities along the C2–C3 and C4–C5 ring bond path signal notable double bond character, while C1–C2 and C3–C4 bonds display appreciably lower π-bonding character [their $\varepsilon(r)$ values are approximately halved in size compared to C2–C3/C4–C5]. Hence, by this criterion, the enamido form makes a non-negligible contribution to the description of the 2-picolyl resonance structures in **4**.

The experimental characterization of **4** was further substantiated by NBO calculations (Figure 5, left). These calculations yield the carbanionic resonance form as the natural Lewis structure, and place NBO charges of similar magnitude on N1 (–0.68 e) and the THF oxygen centers (–0.65 e). Considerably more negative charge is located on C6 (–0.80 e). Charge polarization of the carbon centers flanking N1 is observed (C1 +0.18 e, C5 +0.06 e), as has been reported for the 2-picolyl anion in **2**.[10] The sum of NBO charges concentrated on each 2-picolyl anion yields a total of –0.92 e, which is counterbalanced by the charges on Li (+0.86 e) and the THF moieties (+0.03 e). A distinctly more pronounced charge gradient towards C6 is observed for compound **4** (N1: –0.68 e, C6: –0.80 e, |Δ| = 0.12 e), whilst charges on these centers are more evenly distributed in **2** (N1: –0.78 e, C6 –0.70e, |Δ| = 0.08) and **3** (N1: –0.74 e, C6: –0.66 e, |Δ| = 0.08 e) with the charge gradient towards N1 in each case. This charge accumulation upon deprotonation is also evident when compared to the protonated 2-picoline donor in **2**, which serves as a convenient reference point. The charge increase in **4** relative to picoline (N2: –0.56 e; CH$_3$: +0.06 e) is largest on the methylene group (Δ$_{CH2}$ = –0.49 e) but much smaller on nitrogen (Δ$_N$ = –0.12). In contrast, the charge increases more evenly in **2** (Δ$_N$ = –0.22 e and Δ$_{CH2}$ = –0.37 e) and **3** (Δ$_N$ = –0.18 e and Δ$_{CH2}$ = –0.38 e). The above observation is consistent with significant degree of carbanionic character of the CH$_2$ unit in **4**.
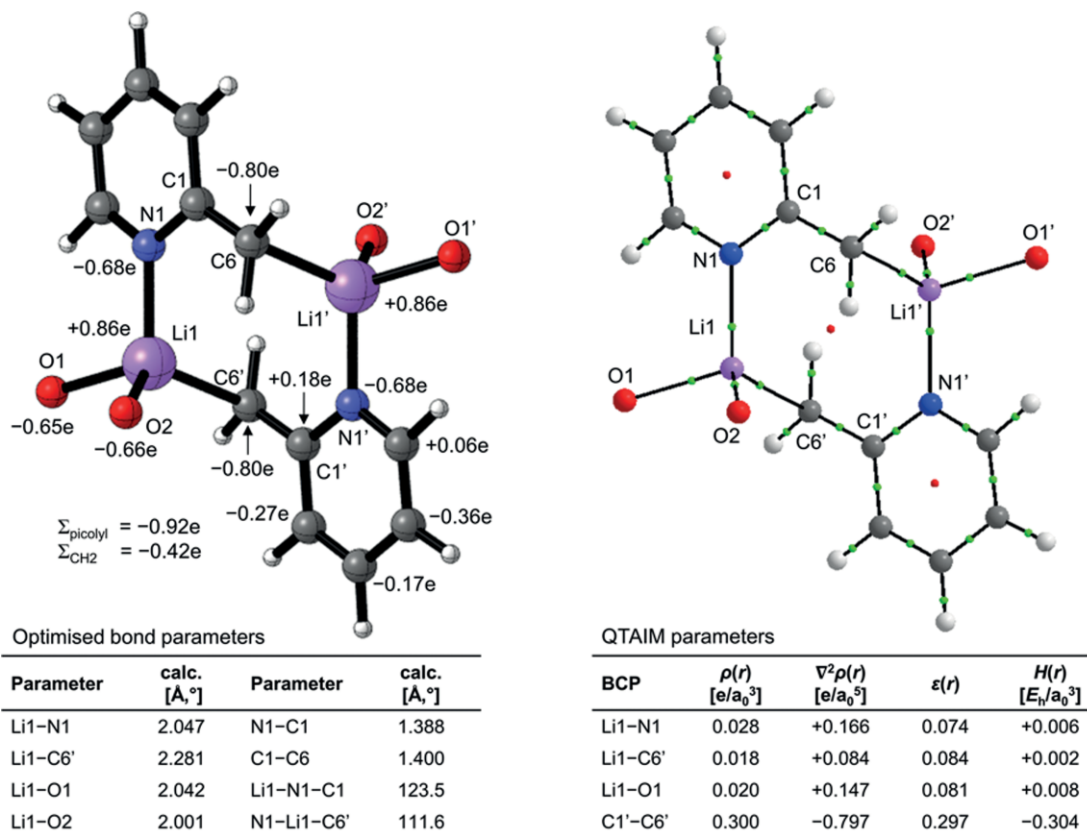
Figure 5. Optimized geometry (left, B3LYP/6-311+G(d)) of compound **4** along with NPA charges. QTAIM molecular graph (right) showing bond critical points (BCP) in green, ring critical points (RCP) in red and bond paths as black lines. Selected bond paths and critical points as well as carbon and hydrogen atoms of THF units have been cloaked for simplicity. Tables summarize key bond parameters and calculated QTAIM parameters for selected BCPs [$\rho(r)$ = electron density, $\nabla^2\rho(r)$ = Laplacian of electron density; $\varepsilon(r)$ ellipticity and $H(r)$ = local energy density].

Reactivity Studies

Larionov et al. have recently reported a synthetic protocol for the synthesis of methylene bridged *N*-heterobiaryls (that is, diquinolylmethanes) by nucleophilic addition of quinaldylmagnesium chloride to quinoline, where a 1-metallo-2-quinaldyl-1,2-dihydroquinoline was presumably the intermediate.[21] However, it is explicitly noted that this protocol only proceeded with fused ring systems (quinolines and isoquinolines) and not with simple picolylmagnesium chlorides to yield dipyridylmethanes. However, lithiated picolines can add to pyridine to yield dipyridylmethanes (presumably also via a 1,2-dihydropyridine intermediate).[22] Given our long-standing interest in the synthesis of 1,2-dihydropyridine species (the putative intermediate in this process)[13d,23] and with a complex containing a 2-picolyl anion with significant carbanionic character now to hand, we tested this as a nucleophile for the addition to pyridine as depicted in Scheme 1, postulating that this carbanionic resonance form would be more nucleophilic and thus give enhanced yields.

Complex **4** was prepared in situ in THF/hexane solution through *n*BuLi induced deprotonation of 2-picoline. An equimolar amount of pyridine was added and this was heated overnight at 50 °C. All attempts to isolate and characterize this intermediate dihydropyridine complex proved unsuccessful.
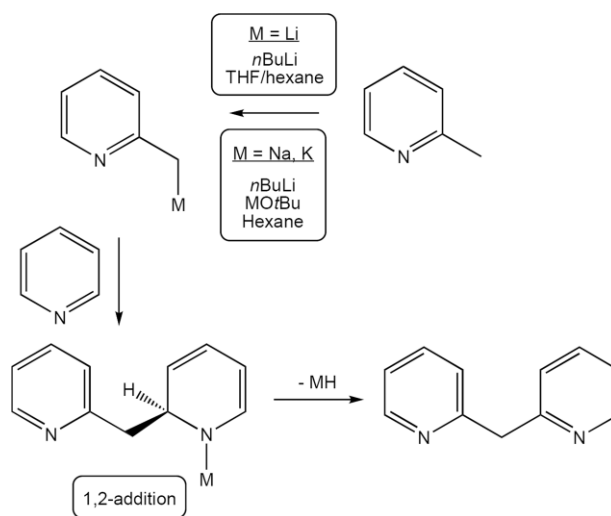
Scheme 1. Synthetic protocol to prepare di-2-pyridylmethane by nucleophilic addition of the 2-picolyl alkali-metal complex to pyridine, M = Li, Na or K.

However, upon work-up and distillation, di-2-pyridylmethane was obtained as a pure oil in a 68 % yield. This yield is lower than that published previously for the synthesis of di-2-pyridylmethane by salt-metathesis of picolyllithium with 2-fluoro-

pyridine[24] but is higher than that obtained by addition of 2-picolyllithium to pyridine in ether, xylene, pyridine, toluene or glyme and is achieved at a lower temperature. Furthermore, this methodology precludes the utilization of more expensive fluorinated pyridine acceptor molecules in favor of inexpensive non-fluorinated pyridine.

To test whether there was an alkali-metal effect on the synthesis of di-2-pyridylmethane, 2-picolylsodium, and 2-picolylpotassium were prepared by the Lochmann-Schlosser superbase deprotonation of 2-picoline in hexane, as dark orange precipitates in high yield. These were subsequently reacted with pyridine and worked up as per Scheme 1, with the resulting yield of di-2-pyridylmethane being much lower than previously observed with 2-picolyllithium. This is perhaps unsurprising as we have previously observed no clean reaction in the nucleophilic addition of *n*-butylsodium to pyridine to yield dihydropyridylsodium complexes, with the preferred route being synthesis of the lithium derivative followed by lithium/sodium exchange.[25] This pattern follows the general trend that lithium intermediates are more kinetically stable than their heavier congeners.[26]

Conclusions

In essence the QTAIM analysis shows that in all three modeled compounds the enamido resonance form plays an important role. The charge distribution from NBO analysis gives more insight into other relevant resonance forms, and it can be argued that in [2-CH₂Li(THF)₂C₅H₄N] the largest portion of the negative charge resides on C6, the deprotonated carbon atom of the methyl group. Taken together with the bond path analysis this implies significant carbanionic character in the picolyl unit and thus this study has located the "missing" tautomeric (carbanionic) form of 2-picolyllithium in the solid-state, complementing the already characterized aza-allyl and enamido forms, which completes the full set of crystallographically-characterized tautomers of the simplest alkyl-substituted pyridine anion.

By using this carbanionic picolyllithium resonance form, nucleophilic addition to pyridine could be performed to yield di-2-pyridylmethane in good yield. This methodology provides an advantage over the currently utilized salt metathesis between picolyllithium and 2-fluoropyridine as it removes the necessity of using expensive fluorinated starting materials. Furthermore, this approach of using the carbanionic resonance form has the potential to provide access to a wider range of substituted di-pyridylmethanes by simple modification of the acceptor pyridine molecule without having to rely on the availability of a 2-fluorinated derivative, which is particularly desirable given the potential utility of these compounds, for example as flexible ligands in coordination chemistry.[27] Research into exploiting THF to enhance the carbanionic nature and hence nucleophilicity of picolyl-based anions to synthesize non-symmetric dipyridylmethanes is currently underway in our laboratory.

Experimental Section

General Experimental: All reactions and manipulations were conducted in a protective argon atmosphere using either standard Schlenk techniques or an MBraun glove box fitted with an in-built gas purification and recirculation unit. Solvents were dried by heating to reflux over sodium benzophenone ketyl and then distilled under nitrogen prior to use. *n*BuLi was obtained from commercial sources and used as received. Pyridine and 2-picoline were distilled prior to use and stored over 4 Å molecular sieves. ^{1}H, ^{7}Li and ^{13}C NMR spectra were recorded on a Bruker AV400 MHz spectrometer operating at 400.03, 155.47 and 100.58 MHz, respectively.

X-ray Diffraction: Crystallographic data for **4** were collected on an Oxford Diffraction instrument using Mo-K_α radiation (λ = 0.71073 Å) at 163 K. Structures were solved using OLEX2, while refinement was carried out on F^2 against all independent reflections by the full-matrix least-squares method by the Gauss-Newton algorithm using OLEX2.[28] All non-hydrogen atoms were refined using anisotropic displacement parameters. Selected crystallographic details and refinement details: empirical formula, $C_{28}H_{44}Li_2N_2O_4$; mol mass, 486.53; crystal system, orthorhombic; space group, *Pbca*; *a*(Å), 16.962(2); *b*(Å), 9.5921(11); *c*(Å), 17.516(2); α(°), 90; β(°), 90; γ(°), 90; *V*(Å^3), 2849.9(6); measured reflections, 22364; unique reflections, 3429; R_{int}, 0.0370; observed reflections [$I > 2\sigma(I)$], 2547; GooF, 1.031; *R* [on *F*, obs reflns only], 0.0420; *wR* [on *F*^{2}, all data], 0.1172; largest diff. peak and hole (e·Å^{-3}), 0.210/–0.146.

Crystallographic data (excluding structure factors) for the structure in this paper have been deposited with the Cambridge Crystallographic Data Centre, CCDC, 12 Union Road, Cambridge CB21EZ, UK. Copies of the data can be obtained free of charge on quoting the depository number CCDC-1970267 (Fax: +44-1223-336-033; E-Mail: deposit@ccdc.cam.ac.uk, http://www.ccdc.cam.ac.uk).

Computational Methods: All electronic structure calculations presented in this paper were carried out using the Gaussian 09 (Revision E.01) program suite at the DFT level of theory.[29] Geometries of all 2-picolyllithium species were fully optimized without imposing symmetry constraints, employing the B3LYP hybrid functional.[30] The 6-311+G(d) basis set was used on all atoms (Li, C, N, O and H).[31] Optimized minima were confirmed by the absence of imaginary eigenvalues in their Hessian matrix. The topology of the electron density was analyzed using QTAIM (quantum theory of atoms in molecules), as implemented in the AIMALL package.[32] Bond ellipticity profiles were generated with the help of the Multiwfn (version 3.6) program.[33] The NBO (version 6.0) package was utilized to perform Natural Bond Orbital analyses (NPA, NRT).[34]

Synthesis of [2-CH₂Li(THF)₂C₅H₄N]₂ (4): *n*BuLi (5 mL, 1.6 M in hexanes, 8 mmol) was slowly added to a hexane solution containing 2-picoline (0.79 mL, 8 mmol) and THF (1.30 mL, 16 mmol) at room temperature, immediately turning from colorless to yellow. Cooling of the solution resulted in the formation of a crop of dark crystals suitable for x-ray diffraction. Yield 0.737 g (38%). **^{1}H NMR** (400.03 MHz, C₆D₆, 300 K): δ = 7.40 (d, 1 H, $^3J_{H,H}$ = 5.01 Hz, H5), 6.51 (dt, 1 H, H3), 6.24 (d, 1 H, $^3J_{H,H}$ = 8.97 Hz, H2), 5.43 (m, 1 H, $^3J_{H,H}$ = 5.80 Hz, H4), 3.59 (s, 8 H, OCH₂ THF), 3.17 (s, 2 H, CH₂), 1.33 ppm (s, 8 H, CH₂ THF). **^{13}C NMR** (100.47 MHz, C₆D₆, 300 K): δ = 163.9 (C1), 148.4 (C5), 132.9 (C3), 117.0 (C2), 100.1 (C4), 68.4 (OCH₂ THF), 56.2 (CH₂), 25.5 ppm (CH₂ THF). **^{7}Li NMR** (155.46 MHz, C₆D₆, 300 K): δ = 0.47 ppm. Satisfactory elementary analyses could not be obtained as the sticky crystals seemed to lose some THF under vacuum

while retaining some low volatility 2-picoline coating. See Supporting Information for spectra.

Synthesis of Di-2-pyridylmethane: Complex **4** was prepared in THF on a 32 mmol scale as described above. Pyridine (2.59 mL, 32 mmol) was added and this solution was heated at 50 °C for 16 h. The cooled solution was quenched with ice water and extracted with DCM (3 × 50 mL). The product was dried with magnesium sulfate, filtered, and the solvent removed in vacuo. Vacuum distillation gave a fraction with boiling point of 128 °C and a ^{1}H NMR spectrum identical to that already published (see Supporting Information) as the final product (Yield 1.845g, 68%).[24]

Supporting Information (see footnote on the first page of this article): NMR spectra, computational data and X-ray crystallographic data

Acknowledgements

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