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Synthesis and Reactivity of *Aza*-Dipyrrin Alkali Metal Salts

Roberto M. Diaz-Rodriguez,[a] Katherine N. Robertson[b] and Alison Thompson*[a]

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We report the lithium, sodium and potassium salts of *aza*-dipyrrins and detail their use as anionic *aza*-dipyrrinato ligand sources in complexation. Of the three types of alkali salts studied, those of lithium are found to be most useful as synthetic precursors. For example, they selectively afford heteroleptic *aza*-dipyrrinato zinc complexes which can be further modified via ligand exchange.

BODIPYs, dipyrrinato ligands complexed with boron, have been extensively used in applications[1-3] that exploit their photophysical properties. Furthermore, as the dipyrrinato ligand coordinates through two nitrogen atoms, chelation offers potential as a "spectator ligand" within organometallic complexes to adjust the reactivity of the metal center.[4]

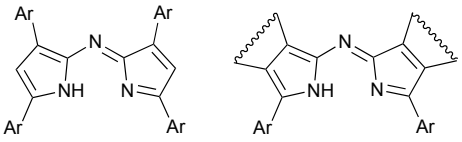
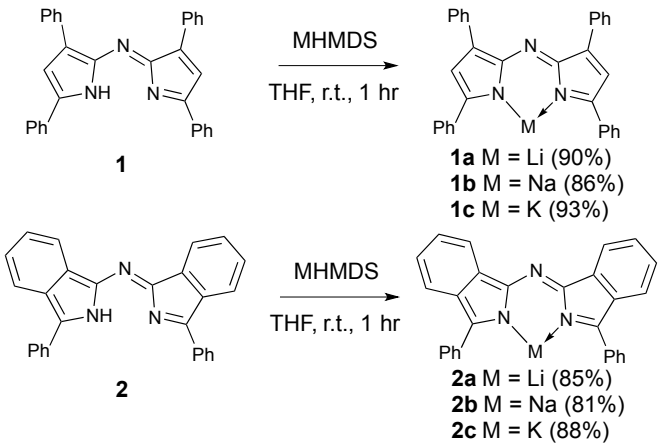


Figure 1-aza-Dipyrrins – tetra-aryl (left) and fused-ring (right) frameworks.

Replacement of the bridging methine moiety in dipyrrins with an imine-type nitrogen atom decreases the HOMO-LUMO energy gap and red-shifts the absorption maximum by ca. 100 nm.[5, 6] *aza*-BODIPYs are especially attractive for their far red and near infrared absorption/emission profiles. Improved penetration of red light reduces tissue damage[7] and renders photosensitisation practical.[8-10] However, *aza*-dipyrrins are understudied relative to dipyrrins. Almost all known *aza*-dipyrrins conform to one of two topologies:[11] a β-free tetra-aryl markush, and a fused-ring markush (Figure 1).

Homo- and heteroleptic *aza*-dipyrrinato metal complexes are known, including those of Co, Zn, Cu, Ni, Pd, Au, Hg, Re, Ir and Rh.[11] Some have potential in photovoltaics[5] and others have luminescent properties, [12, 13] but their utility in areas such as catalysis or biomedicine has yet to be comprehensively explored. Current methods by which to complex the *aza*-dipyrrinato ligand involve reactions of the neutral *aza*-dipyrrin, rather than the anionic form. The reported conditions for complexation involve extended reaction times, excesses of either metal precursor or ligand, or heat, or some combination thereof.[14-17] Although there is precedent for the use of *tert*-butoxide bases to promote *aza*-dipyrrin complexation reactions,[7, 18-20] there are no reports involving the anionic [21, 22] *aza*-dipyrrinato unit as a ligand source. Herein we report the synthesis and reactivity of lithium, sodium and potassium salts of the two representative *aza*-dipyrrin frameworks (Scheme 1).

Solutions of tetraphenyl-substituted and benzannulated *aza*-dipyrrins **1** and **2**, respectively, in tetrahydrofuran were treated with a stoichiometric amount of a tetrahydrofuran solution of lithium hexamethyldisilazide (HMDS) to generate the first *aza*-dipyrrinato lithium salts **1a** and **2a** (Scheme 1). Conversion to the lithium salt was quantitative in both cases (≥95%) according to analysis using NMR spectroscopy. Trituration of the crude product material with pentane,



Scheme 1- Alkali metal salts of aza-dipyrrins **1** and **2**. Parentheses signify isolated yields.

[a] *R. M. Diaz-Rodriguez, Prof. Dr. A. Thompson*
Department of Chemistry, Dalhousie University, PO BOX 15000
Halifax, Nova Scotia B3H 4R2 (Canada)
E-mail: Alison.Thompson@dal.ca
[b] *Dr. K. N. Robertson*
Department of Chemistry , Saint Mary's University
Halifax, Nova Scotia B3H 3C3 (Canada)

† Footnotes relating to the title and/or authors should appear here.
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followed by removal of the residual hexamethyldisilazane in vacuo, gave the desired lithium salts **1a** and **2a** in high isolated yields (Scheme 1). The salts could be generated in situ and carried forward into other transformations with no ill effects (vide infra). Lithium diisopropylamide (as a commercially available solution in tetrahydrofuran/ethylbenzene/heptane) was found to be an effective alternative, with the added benefit of generating an easier-to-remove amine by-product compared to when LiHMDS was used. *n*-Butyllithium was also investigated as an alternative lithium source. However, rapid consumption of the starting *aza*-dipyrrin **1** returned an intractable mixture. In contrast, *n*-butyllithium reacts cleanly with dipyrrins.[21, 22]

The crystal structure of **1a**[23] (Figure 2) shows a triclinic unit cell with four similar and complete molecules in the asymmetric unit. Each comprises a pseudotetrahedral lithium centre chelated by the *aza*-dipyrrinato ligand and stabilised by two molecules of tetrahydrofuran. The stabilising effect was significant, given that solutions of **1a** in solvents other than tetrahydrofuran tended towards rapid decomposition. The lithium atom is accommodated in plane with the dipyrrin core. The N-Li bond lengths in **1a** are longer than those found in lithium diisopropylamide,[24] suggesting a high degree of lability of this bond and thus considerable reactivity of the nitrogen centre.

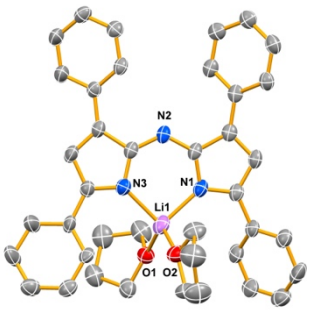


Figure 2-ORTEP diagram (50%, H atoms omitted) of **1a**.

The sodium salts **1b** and **2b** were synthesised using NaHMDS (Scheme 1). Similarly, the tetraphenyl-substituted *aza*-dipyrrinato potassium salt **1c** was synthesised from KHMDS. The full characterisation of the five alkali complexes **1a-c** and **2a-b** revealed expected resonance, integral and splitting characteristics across ^{1}H and ^{13}C NMR analyses. Incorporation of Li and Na were confirmed via ^{7}Li and ^{23}Na NMR resonances.

The reaction of the benzannulated *aza*-dipyrrin **2** with KHMDS also occurred quantitatively. Although the reaction progression seemed consistent with that for the other salts, the isolated potassium salt **2c** differed in NMR spectroscopic characteristics from those of the lithium and sodium salts **2a** and **2b,** as well as the related potassium salt **1c**. The ^{1}H NMR spectrum of **2c** shows a pattern of broad peaks that were poorly resolved despite changes in acquisition parameters such as relaxation delay. The ^{13}C NMR spectrum of the material contains 24 signals comprised of two sets of 12 with comparable intensity, whereas a single *aza*-dipyrrin or complex with a single *aza*-dipyrrinato ligand of this type should reveal only 12 signals due to symmetry. This lack of symmetry suggests that **2c** may exist as an oligomeric or cluster structure. While the other isolated salts are homogeneous powders, solid **2c** reproducibly comprises both a fine green powder and shiny purple plates. It is thus also plausible that the two different forms may be representative of restricted rotamers, causing doubling of the NMR resonances observed in solution. All attempts to grow quality crystals of **2c**, as well as those of **1b-c** and **2a-b**, returned amorphous residue or resulted in demetallation. For comparison, sodium and potassium salts of dipyrrins appear more stable than these *aza*-dipyrrinato counterparts.[21, 22]

The colour difference between solutions of the *aza*-dipyrrins **1** and **2** (indigo and blue, respectively) and their lithium salts **1a** and **2a** (sapphire blue and turquoise/teal, respectively) is substantial for both ligands, and offers a convenient qualitative indicator of reaction progress. Table 1 lists the photophysical properties of the *aza*-dipyrrins and their salts. The absorbance curves of **1**-**1c** are presented in Figure 3, and the curves for **2**-**2c** are included in the Supporting Information. Alkali *aza*-dipyrrinato salt formation is accompanied by a bathochromic shift in absorption maximum, which decreases with increasing cation size. Furthermore, the absorbance profile narrows upon salt formation, although the narrowing (full width at half maximum (FWHM) of the curve) is less dramatic with increasing cation size. Overall, the visual differences between the *aza*-dipyrrin ligand precursors and their *aza*-dipyrrinato salts are progressively less noticeable as the cation size increases.

Table 1. *aza*-Dipyrrins and their *aza*-dipyrrinato alkali salts in THF.

Entry	Compound	λ_{abs} (nm)	ε (log E)	FWHM [a]
1	**1**	597	4.71	79
2	**1a**	619	4.72	69
3	**1b**	608	4.62	72
4	**1c**	604	4.76	78
5	**2**	649	4.64	83
6	**2a**	660	4.96	50
7	**2b**	650	4.92	53
8	**2c**	652	4.86	62

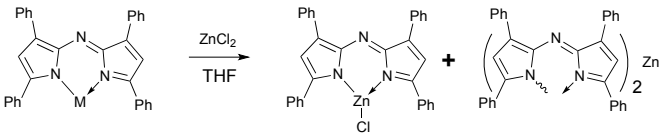
[a] Full Width at Half Maximum, in nm.

The *aza*-dipyrrinato alkali metal salts decompose to *aza*-dipyrrins upon prolonged exposure to air, or the introduction of non-anhydrous solvents or otherwise acidic conditions. This instability is likely due to the high degree of ionic character of the nitrogen-metal bond in these salts, imparting strong Lewis basicity to the *aza*-dipyrrinato anion. This property allows the salts to act as convenient sources of the monoanionic *aza*-dipyrrinato ligand. To investigate the synthetic utility of the *aza*-dipyrrinato alkali salts, **1a**, **1b** and **1c** were synthesised *in situ* from **1**, and then reacted with 0.5 and 1 eq. zinc(II) chloride. The results are summarised in Scheme 2.

Treatment of *aza*-dipyrrinatolithium salt **1a** with 1 eq. zinc(II) chloride gave quantitative conversion (^{1}H NMR analysis) to the unreported heteroleptic *aza*-dipyrrinatozinc(II) chloride complex **3a**. Treatment of *aza*-dipyrrin **1** with $ZnCl_2$ returns only the known homoleptic bis(*aza*-dipyrrinato)zinc(II) complex **5**,[12] and so the lithium salt offers unprecedented reactivity. Treatment of the lithium salt with 0.5 eq. zinc(II) chloride instead gave quantitative conversion to homoleptic **5**, highlighting the stoichiometric effects that control the reaction

in concert with the source of the ligand. The sodium and potassium salts **1b** and **1c** quantitatively generated **5** regardless of the amount of zinc(II) chloride added. All the complexation reactions involving the anionic ligand source proceeded rapidly: complete conversion was observed within one hour at room temperature as opposed to the many hours or days[14, 17] reported for similar reactions from the *aza*-dipyrrin.

Similar reactivity is observed for benzannulated lithium salt **2a**; i.e. treatment with stoichiometric zinc(II) chloride quantitatively returns the previously unreported heteroleptic aza-dipyrrinatozinc(II) chloride complex **4a**, while treatment with 0.5 eq. zinc(II) chloride quantitatively gives the corresponding, known homoleptic complex **6**.[14] Cognisant of the unusual NMR spectroscopic signature of **2c**, this salt was treated with 0.5 eq. zinc(II) chloride to investigate its reactivity and to confirm constitution. The corresponding homoleptic complex **6** was furnished quantitatively in high isolated yield within one hour. This confirms that the species generated from the reaction of **2** with KHMDS retains the expected reactivity of an *aza*-dipyrrinato alkali metal salt and supports the notion that the unexpected NMR characteristics of **2c** can likely be attributed to the presence of isomeric or cluster forms.



	3a	5
1a M = Li + 0.5 eq. $ZnCl_2$	≤5%	≥95%
1a M = Li + 1 eq. $ZnCl_2$	95% (84%)	≤5%
1b M = Na + 0.5 eq. $ZnCl_2$	≤5%	95%
1b M = Na + 1 eq. $ZnCl_2$	≤5%	95%
1c M = K + 0.5 eq. $ZnCl_2$	≤5%	95%
1c M = K + 1 eq. $ZnCl_2$	≤5%	95%

Scheme 2-Reactivity of alkali salts **1a – 1c** towards complexation with zinc(II) chloride. Conversions are given; parentheses signify isolated yields.

Homoleptic bis(*aza*-dipyrrinato) metal complexes tend to be air- and moisture-stable.[12, 17, 19] The heteroleptic complexes **3a** and **4a**, despite the labile chloro ligand, are not as sensitive to atmospheric conditions as their precursory alkali metal salts and may be handled in air with care. Photophysical data for these compounds are presented in Table 2 and plotted in Figure 3.

Table 2. Heteroleptic *aza*-dipyrrinatozinc(II) complexes in THF.

Entry	Compound	λ_{abs} (nm)	ε (log E)	FWHM [a]
1	**3a**	620	4.41	47
2	**4a**	664	4.92	45
3	**3b**	618	n. d.	46
4	**4b**	665	n. d.	44

[a] Full Width at Half Maximum, in nm.

Figure 3. UV/Vis absorbance curves for heteroleptic zinc chloride complexes **3a** and **4a** in THF. Absorbance curves for the corresponding *F-aza*-BODIPYs in toluene are included for comparison.

The absorbance curves closely resemble those of the parent *aza*-BODIPYs. Indeed, complexation of the *aza*-dipyrrin ligand precursor with BF_2 results in a narrowing of the absorbance profile,[25] reflecting the rigidification of structure and increase in molecular symmetry. The observed resemblance suggests a similar rigidification and symmetrisation occurs upon formation of heteroleptic **3a** and **4a**: however, neither is fluorescent.

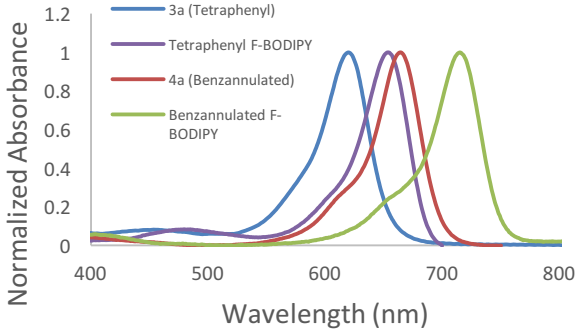


Figure 3-UV/Vis absorbance curves for **1** and its alkali metal salts in THF

The crystal structure[26] of **3a** shows a triclinic unit cell containing four molecules in two slightly, but unremarkably, different conformations (Figure 4). A pseudotetrahedral zinc centre is bound to a chloro ligand and chelated by the *aza*-dipyrrinato unit and one molecule of tetrahydrofuran. The chelation of zinc completes a distorted, planar six-membered ring at the center of the molecule, which is highly typical of dipyrrinato complexes.[3] This geometry is indeed reminiscent to that of *F*-aza-BODIPYs,[25] which helps rationalise the similar absorbance curve. The N-Zn-N bite angle of **3a** is relatively acute at 96.44(12)°, in contrast to the wider bite angles (e.g. 105°) usually seen in BODIPYs.[25] Bond lengths are universally typical: the ca. 2 Å long N-Zn bonds are in line with various other dipyrrinato metal complexes,[14, 17, 27] and the ca. 2.2 Å Zn-Cl bond is longer than zinc (II) chloride alone and agrees with other zinc chloride complexes bearing a variety of ligands.[28-30]

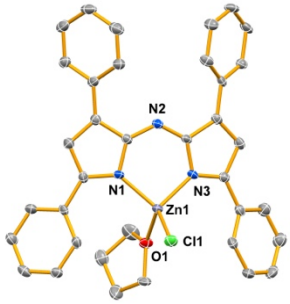
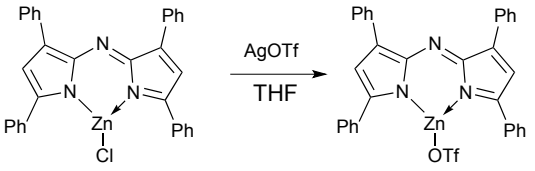


Figure 4-ORTEP diagram (50%, H atoms omitted) of **3a**.

These complexes, though indefinitely stable under nitrogen in the solid state, generate the corresponding homoleptic bis(*aza*-dipyrrinato) complexes if solvated for extended periods of time. For example, the slow evaporation of a solution of **4a** in tetrahydrofuran yielded X-ray quality crystals of **6**; a crystal structure can be found in the Supporting Information. Although a crystal structure of this compound exists in prior literature,[14] our structure differs due to it being unsolvated.

The weak zinc-chlorine bond and lability of the chloro ligand in **3a** and **4a** suggests feasible ligand exchange, thus making them useful synthons for *aza*-dipyrrinato transition metal complexes. Both compounds were treated with stoichiometric

silver triflate to exchange the chloro ligand for triflate (Scheme 3). A white precipitate (silver chloride) was observed in both cases. Quantitative conversion to new species was confirmed by ^{1}H NMR spectroscopy, accompanied by a ^{19}F resonance distinct from the reagent silver triflate (AgOTf, ^{19}F δ = -77.5 ppm in 80:3 tetrahydrofuran/D_2O). The ^{19}F resonances for both products appear at essentially identical chemical shifts (-79.4 ppm) despite the differences in *aza*-dipyrrinato ligand, suggesting that the choice of ligand has little effect on the chemical environment of the triflate. No colour changes were observed upon triflation of **3a** or **4a**. The zinc(II) triflate complexes **3b** and **4b** proved very unstable, quickly dimerising to the homoleptic complexes **5** or **6** in solution and de-complexing in the instrument during any attempt at mass spectrometry. The rapid dimerisation also precluded growth of X-ray quality crystals.



3a **3b**

Scheme 3-Triflation of heteroleptic zinc(II) chloride complex 3a. The same method was used for triflation of benzannulated heteroleptic zinc(II) chloride complex 4a.

In summary, six alkali metal salts featuring *aza*-dipyrrinato ligands were synthesised and characterised. The lithium salts selectively generated heteroleptic products in complexation reactions with zinc(II) chloride. The corresponding sodium and potassium salts greatly increase the rate of complexation reactions. This work represents the first investigation into the synthesis, properties and reactivity of *aza*-dipyrrinato alkali metal salts, with promising implications for their use as precursors to chemically complex transition metal constructs containing the *aza*-dipyrrin ligand framework.

Acknowledgements

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Conflicts of interest

The authors declare no conflict of interest.

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