

Syntheses and Characterizations of New Cyano-substituted Pyrazoles

Arielle Pompilius, Kelechi Akwataghibe, Everett Shelly
Department of Chemistry
Jacksonville University
2800 University Blvd. North
Jacksonville, Florida 32211 USA

Faculty Advisor: Dr. Ningfeng Zhao

Abstract

Polypyrazolylborates are popular ligands used in the inorganic community, largely due to the relative ease with which one can synthesize pyrazole rings with different substituents, giving rise to ligands with varying steric and electronic properties. Most of the studies involving scorpionate ligands have concentrated on those with alkyl or aryl substituents shown to be able to turn the electronic and reactivity properties of the metal complexes. Reported here are the new substituted cyano-pyrazoles, including their syntheses and structural characterizations. The new compounds indicate a promising future in synthesizing new polypyrazolylborate ligands.

Keywords: cyano-substituted pyrazoles, polypyrazolylborates, inorganic chemistry

1. Introduction

Polypyrazolylborates, commonly known as scorpionates, are a popular class of ligands characterized by pyrazole rings bonded through one of the nitrogen atoms to a boron “apex.” The boron atom can have between two and four pyrazolyl substituents, affording three basic forms of scorpionates: dihydrobis(pyrazolyl)borates (Bp), hydrotris(pyrazolyl)borates (Tp), and tetrakis(pyrazolyl)borates (pzTp) (Figure 1)¹. Seminal author Trofimenko, who identified the first class of polypyrazolylborates in the 1960s, dubbed them “scorpionates” due to their coordination behavior.² For example, in a Tp complex, the available nitrogen atoms from two of the ligand’s pyrazolyl rings form the scorpion’s claws, capturing a central metal atom, while the other nitrogen from the third pyrazolyl ring may come over the top of the boron atom to “sting” the metal like the tail of a scorpion.

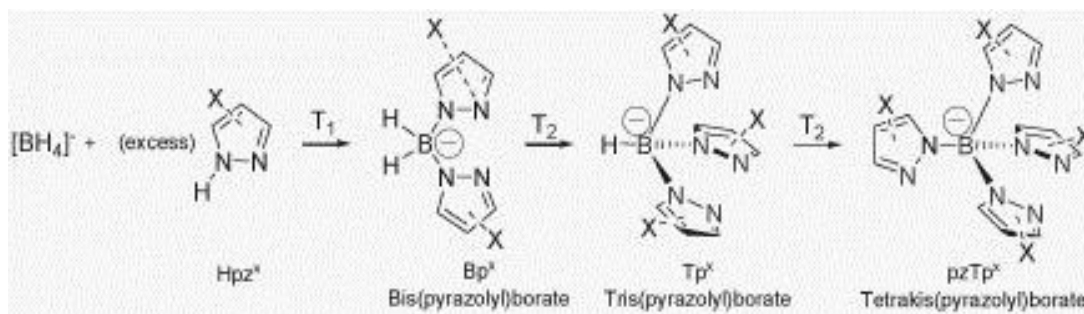
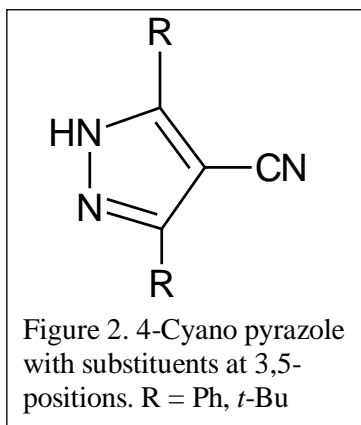


Figure 1: Naming conventions for degree of pyrazole substitution on boron atom. Hpz^X indicates a pyrazolyl group where X represents an unspecified substituent. Bp^X , Tp^X , and $pzTp^X$ indicate that the boron has been substituted with two, three, and four pyrazolyl groups, respectively.¹

Scorpionates provide versatility: varying the type and position of the substituents on the ligand leads to the “steric and electronic effects” of the complex and provides a greater degree of control over the property and reactivity of the coordinated metal atom.³⁻⁵ These properties have potential applications in areas from pharmaceutical development to bioinorganic mimesis.⁶ A “second generation” of scorpionates emerged around 1986 after the work of Han and Parkin,⁷ featuring ligands with more steric substituents on the pyrazole ring. These second generation of ligands provided better “steric coordination control,” and encouraged further study. The “third generation” of scorpionates, first given the designation by Reger *et.al.*, indicated the “ligands that are specifically functionalized at the noncoordinating back position,” which referred to the substituted position distal from the metal core.⁸ Further studies of the third generation of scorpionates examined the electron-withdrawing properties of trifluoromethyl-substituted and cyano-substituted ligands, affecting metal complex electronic properties dramatically^{9,10}. The cyanoscorpionates such as dihydrobis(4-cyanopyrazolyl)borate became a compound of interest because in addition to acting as a bidentate chelating ligand, it also maintained the capacity for additional coordination through the CN groups.¹¹ Continued studies of cyanoscorpionates have focused on further exploring the electron-withdrawing characteristics of the CN groups as well as their potential in constructing coordination polymers.¹²

This research is built on prior examinations of the cyano-substituted scorpionates. Cyanoscorpionates fall under the “third generation” scorpionates,⁸ showing that the cyano group as a strong electron-withdrawing character also had the capability to coordinate a second metal center.^{11, 12} Thus, metal complexes of cyanoscorpionate ligands can potentially be linked together through coordination of another metal ion to the cyano groups of the complexes, with a fully conjugated pathway connecting the pyrazole- and cyano coordinated metals.¹² Extension of this motif can potentially result in a coordination polymer in which the intermetallic communication might be expected to yield materials demonstrating useful bulk properties such as magnetism and conductivity. In particular, this study focuses on the syntheses and structural characterizations of new 4-cyano pyrazoles with symmetrical bulky substituents, such as the phenyl and *tert*-butyl groups, at the 3,5- positions of the pyrazole ring (Figure 2), and corresponding scorpionate ligands. Metal complexes of the ligands will also be compared to analogous structures to investigate the steric and electron-withdrawing effects of the substituents. Finally, the exploration of magnetic and electronic properties, as well as the reactivity, of the compounds will be examined. Reported here is the first stage of the study, involving the syntheses and characterizations of the substituted pyrazoles.



2. Experimental

Unless otherwise stated, all solvents and reagents were used as received from Alfa Aesar and Fisher Scientific without further purification. Toluene was dried over sodium/benzophenone. A BUCHI SWITZERLAND Rotavapor RII was used to remove solvents from solutions under reduced pressure. Glassware were soaked in a KOH/isopropanol/water bath, rinsed with de-ionized water, and dried over night at 80°C. FT-IR spectra were recorded on a PerkinElmer Spectrum100 FTIR spectrometer. ¹H NMR spectra were measured on a Eft-90 NMR spectrometer from Anasazi Instrument in CDCl₃ solution with TMS as internal standard. X-ray crystallographic data were obtained from the

University of California, San Diego Crystallography Laboratory, where the crystals were sent and analyzed using a Bruker Kappa APEX-II CCD diffractometer equipped with Mo K α radiation ($\lambda = 0.71073 \text{ \AA}$).

Figure 3 below shows the overall synthesis route to the scorpionate ligands. The synthesis of 4-cyano-3,5-bisphenyl pyrazole has been reported.¹³ The procedure was modified in this work to recrystallize of the final product. 0.69 g (17.24 mmol, 60% dispersion in mineral oil) of sodium hydride was added to 100 mL dry toluene. To this solution was added 2.50 g of benzoylacetonitrile (17.24 mmol), resulting in the immediate appearance of bubbles. The mixture was stirred for 18 hours before benzoyl chloride (2.43 g, 17.24 mmol) was added. The reaction mixture was stirred overnight followed by three extractions using 100 mL of 0.2 M NaOH solution each time. The aqueous layers were combined and acidified with HCl/H₂O (50/50) solution to pH~1. A white precipitate appeared immediately and was extracted with three portions of 100 mL of ethyl acetate. Removal of the solvent under reduced pressure yielded 2.55 g (10.24 mmol, yield 59.40%) of crude product, which was recrystallized from ethanol to give 2-cyano-1,3-diphenyl-1,3-propanedione (1.38 g, 5.54 mmol, 32.15%), compound 1 in Figure 3. Infrared spectroscopy showed a signal at 2216 cm⁻¹ for the C \equiv N stretch. The ¹H NMR (chloroform-d) showed chemical shifts at 7.59 ppm (m, 6H) and 8.12 ppm (m, 4H). This diketone compound (1.38 g, 5.54 mmol) was then reacted with hydrazine monohydrate (0.28 g, 5.54 mmol) in 100 mL of methanol and stirred overnight. The solvent was removed under reduced pressure to yield the crude product of 4-cyano-3,5-bisphenyl pyrazole as a pale yellow solid, compound 2 in Figure 3, which was recrystallized from ethanol (1.01 g, 4.65 mmol, 27.00%). Infrared spectroscopy showed characteristic peaks at 3177 cm⁻¹ and 2227 cm⁻¹ for N-H and C \equiv N stretches respectively. The ¹H NMR (chloroform-d) showed chemical shifts at 8.06 ppm (d, 4H), 7.64 ppm (t, 4H), and 7.54 ppm (t, 2H). X-ray crystal structures were yet to be determined.

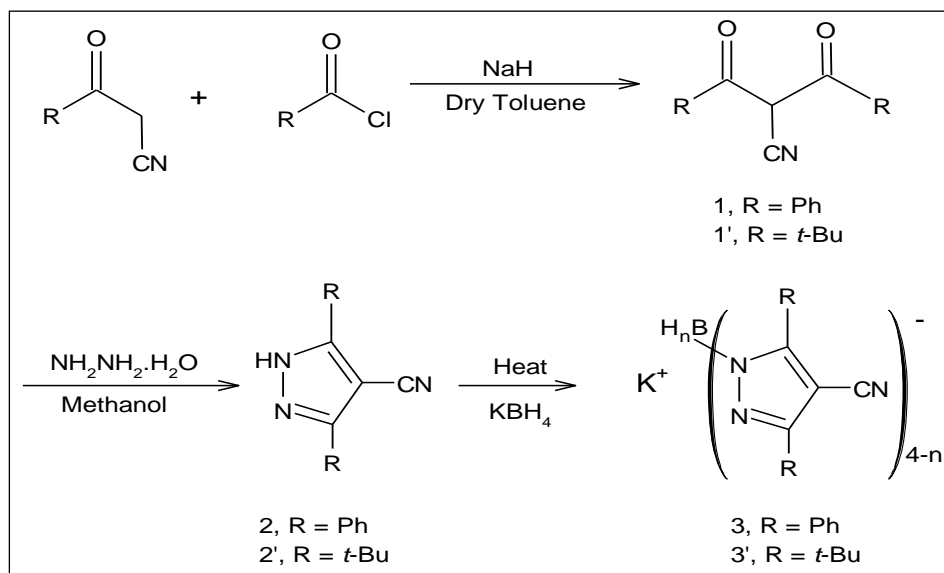


Figure 3. Synthesis route of the scorpionate ligands.

Similar procedure was applied to synthesize 4-cyano-3,5-bis(*tert*-butyl) pyrazole, using trimethylacetylacetonitrile and trimethylacetyl chloride. The crude yield for 4-cyano-2,2,6,6-tetramethyl-3,5-heptanedione, compound 1' in Figure 3, was 2.15 g (10.29 mmol, 59.67%). It was recrystallized from ethanol to give 1.07 g of the crystals (5.12 mmol, 29.70%). Infrared spectroscopy showed peak at 2212 cm⁻¹ for the C \equiv N stretch. The ¹H NMR (chloroform-d) showed chemical shifts at 1.41 ppm (s, 18H). This diketone crystal was then reacted with hydrazine monohydrate to produce the crude product of 4-cyano-3,5-bis(*tert*-butyl) pyrazole as a white solid (0.93 g, 4.54 mmol, 26.31%), compound 2' in Figure 3. The X-ray quality crystals were isolated from recrystallization in ethanol at room temperature (0.66 g, 3.22 mmol, 18.67%). Infrared spectroscopy showed characteristic peaks at 3232 cm⁻¹ and 2223 cm⁻¹ for N-H and C \equiv N stretches respectively. The ¹H NMR (chloroform-d) showed chemical shift at 1.45 ppm (s, 18H). X-ray crystal structures of 4-cyano-2,2,6,6-tetramethyl-3,5-heptanedione (compound 1') and 4-cyano-3,5-bis(*tert*-butyl) pyrazole (compound 2')¹⁴ are shown in Figure 4 and Figure 5, with crystallographic data in Table 1.

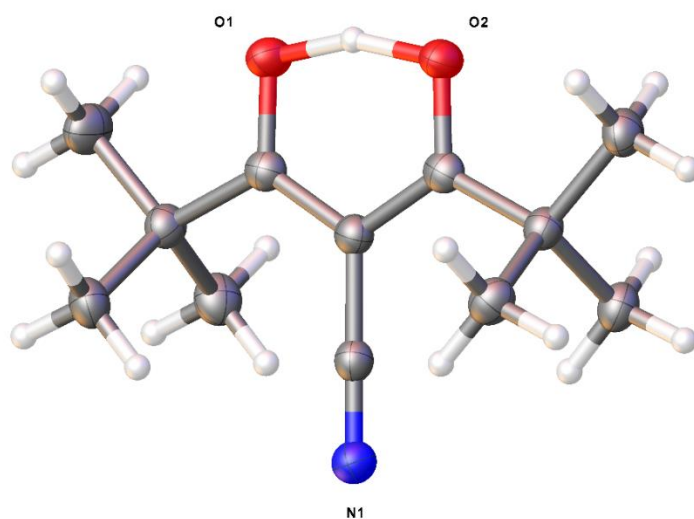


Figure 4. X-ray crystal structures of 4-cyano-2,2,6,6-tetramethyl-3,5-heptanedione. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms are shown at arbitrary radii.

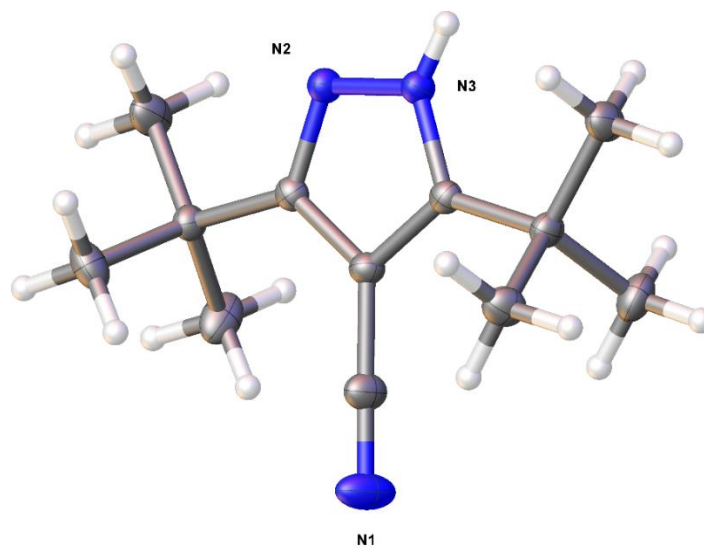


Figure 5. X-ray crystal structures of 4-cyano-3,5-bis(*tert*-butyl)pyrazole. Displacement ellipsoids are drawn at the 50% probability level. Hydrogen atoms are shown at arbitrary radii.

Table 1. X-ray Crystallography Data

Compound	4-cyano-2,2,6,6-tetramethyl-3,5-heptanedione	4-cyano-3,5-bis(<i>tert</i> -butyl) pyrazole
Molecular formula	C ₁₂ H ₁₉ NO ₂	C ₁₂ H ₁₉ N ₃
Formula weight	209.28	205.30
Temperature (K)	100.0	100.0
Crystal system	Monoclinic	Monoclinic
Space group	<i>P2₁/c</i>	<i>P2₁/c</i>
a (Å)	9.9604(3)	10.5993(3)
b (Å)	20.3890(8)	9.7641(3)
c (Å)	5.9851(2)	12.4435(4)
α (°)	90	90
β (°)	91.278(3)	109.0650(10)
γ (°)	90	90
Volume (Å ³)	1215.17(7)	1217.17(6)
Z	4	4
Density _{calc.} (g cm ⁻³)	1.144	1.120
F(000)	456	448
Absorption coefficient (mm ⁻¹)	0.616	0.529
Crystal size (mm ³)	0.179 x 0.122 x 0.063	0.153 x 0.097 x 0.088
Crystal color, shape	Colorless, Block	Colorless, Block
θ range (°) data collection	4.337 to 68.276	4.413 to 68.242
Index ranges	-11<=h<=12 -21<=k<=24 -7<=l<=7	-10<=h<=12 -11<=k<=11 -14<=l<=13
Total reflections collected	12269	11126
Independent reflections (<i>R_{int}</i>)	2202 (0.0489)	2183 (0.0395)
Data / restraints / parameters	2202 / 0 / 146	2183 / 0 / 150
Goodness-of-fit on F ²	1.078	1.054
Final R indices [<i>I</i> >2σ(<i>I</i>)]	<i>R</i> ₁ = 0.0417 <i>wR</i> ₂ = 0.1041	<i>R</i> ₁ = 0.0366 <i>wR</i> ₂ = 0.0942
R indices (all data)	<i>R</i> ₁ = 0.0539, <i>wR</i> ₂ = 0.1099	<i>R</i> ₁ = 0.0386 <i>wR</i> ₂ = 0.0958
Max, min Δρ (e.Å ⁻³)	0.202, -0.175	0.208, -0.195

3. Results and Discussion

Both 4-cyano-3,5-bisphenyl pyrazole and 4-cyano-3,5-bis(*tert*-butyl) pyrazole have been prepared, serving as precursors for the preparation of scorpionate ligands and corresponding metal complexes. The synthetic routes are relatively straightforward with acceptable yields. The structures of 4-cyano-2,2,6,6-tetramethyl-3,5-heptanedione and 4-cyano-3,5-bis(*tert*-butyl) pyrazole are also determined by X-ray crystallography. In the structure of the substituted pyrazole, the H atom is shown to be disordered across the two N atoms of the pyrazole ring.¹⁴ Future work will involve structural characterization of the 4-cyano-3,5-bisphenyl pyrazole, and further syntheses and characterizations of the scorpionate ligands and corresponding metal complexes.

4. Acknowledgements

The authors thank Dr. Curtis Moore, Director of X-ray Crystallography Facility at University of California, San Diego, for providing the single-crystal X-ray diffraction data, and the Department of Chemistry at Jacksonville University for supporting the research.

5. References

1. Pettinari, C. Scorpionates: Pinch and Sting...the Metal. *La Chimica e l'Industria*. 2004, 86(10), 94-100.
2. Trofimenko S (1966) *J Am Chem Soc* 88: 1842.
3. Oliver J, Hutchinson B, Milligan W (1980) *Inorg Chem* 19: 165.
4. Long GJ, Hutchinson BB (1987) *Inorg Chem* 26: 608.
5. Eichhorn D, Armstrong W (1990) *Inorg Chem* 29: 3607.
6. Trofimenko S (1999) *Scorpionates: The Coordination Chemistry of Polypyrazolylborate Ligands*. Imperial College Press, London.
7. Calabrese J, Trofimenko S, Thompson J (1986) *J Chem Soc, Chem Commun* 1122.
8. Reger, D.L.; Gardinier, J.R.; Gemmill, W.R.; Smith, M.D.; Shahin, A.M.; Long, G.J.; Rebbouh, L.; Grandjean, F. Formation of Third Generation Poly(pyrazolyl)borate Ligands from Alkyne Coupling Reactions of $\text{Fe}[(p\text{-IC}_6\text{H}_4)\text{B}(3\text{-Rpz})_3]_2$ (R = H, Me; pz = Pyrazolyl): Pathways toward Controlling an Iron(II) Electronic Spin-State Crossover. *J. Am. Chem. Soc.* **2005** 127 (7), 2303-2316
9. Dias H, Lu H, Ratcliff R, Simon G (1995) *Inorg Chem* 34: 1975.
10. Rheingold A, Incarvito C, Trofimenko S (2000) *Inorg Chem* 39: 5569.
11. Siemer C, Goswami N, Kahol P, Van Stipdonk M, Eichhorn D (2001) *Inorg Chem* 40: 4081.
12. Zhao N, Van Stipdonk M, Bauer C, Campana C, Eichhorn D (2007) *Inorg Chem* 46: 8662.
13. Som B, (2013) M.S. Thesis, East Tennessee State University.
14. Zhao N, Akwataghibe K, Pompilius A, Shelly E (2016) *IUCr Data* 1: x160673.