Supramolecular Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713649759

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Jonathan L. Sessler[a]; Bobbi L. Rubin[a]; Salvatore Camiolo; Won-Seob Cho[a]; G. Dan Pantos[a]; Vincent M. Lynch[a]
[a] Department of Chemistry and Biochemistry, 1 University Station - A5300, The University of Texas at Austin, Austin, Texas, USA

To cite this Article Sessler, Jonathan L. , Rubin, Bobbi L. , Camiolo, Salvatore , Cho, Won-Seob , Pantos, G. Dan and Lynch, Vincent M.(2006) 'Diamidopyrazoles: A New Class of Anion Receptors', Supramolecular Chemistry, 18: 2, 103 — 109
To link to this Article: DOI: 10.1080/10610270500445523
URL: http://dx.doi.org/10.1080/10610270500445523

Supramolecular Chemistry, April 2006 Vol. 18 (2), pp. 103–109

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Diamidopyrazoles: A New Class of Anion Receptors

JONATHAN L. SESSLER[a,*], BOBBI L. RUBIN[a], SALVATORE CAMIOLO[b], WON-SEOB CHO[a], G. DAN PANTOS[a] and VINCENT M. LYNCH[a]

[a]*Department of Chemistry and Biochemistry, 1 University Station - A5300, The University of Texas at Austin, Austin, Texas, 78712-0165, USA;*
[b]*Present address: S.V. Monte Oro 45, 07100 Sassari (SS), Italy*

Received (in Southampton, UK) 30 October 2005; Accepted 11 November 2005

The synthesis of a series of 3,5-diamidopyrazoles is reported. The anion binding properties of these systems were examined *via* ^{1}H NMR, UV/Vis and ITC titration techniques. Target compound 2a acts as a selective receptor for phosphate and sulfate anions in DMSO, whereas N-methylated 2b and the unmethylated species 4d show no appreciable binding affinity. Insights into the binding events occurring in solution came from the solid state structures of compounds 2a and 4a, 4b, and 4d, which were deduced from single crystal X-ray diffraction analyses.

Keywords: Pyrazole; Anion receptor; Dihydrogen phosphate; Hydrogen sulfate; Methyl orange

INTRODUCTION

Inspired in part by the ubiquity of anions in nature, anion binding has attracted considerable attention within the broader field of molecular recognition chemistry. In fact, many research groups have devoted considerable effort to the design and study of artificial anion receptors [1–4]. To date, an impressive number of heterocyclic anion receptors have been reported in the literature. These include systems that run the gamut from simple linear monomeric pyrroles to open chain polypyrroles, as well as cyclic pyrrolic structures [5–7]. Among the most versatile of these systems are the simple 2,5-diamidopyrroles reported by Gale and co-workers [8–11], which were found to interact strongly with benzoate and dihydrogen phosphate anions. On the basis of this work and prior studies involving cyclic systems, e.g., calixpyrroles, sapphyrins, and others systems [7], the utility of pyrrole as a neutral anion-binding motif has become well established. However, less attention has been devoted to the study of systems containing other neutral heterocyclic subunits, especially those containing more than a single heteroatom, such as imidazoles, biimidazoles, and pyrazoles. Among the work in this area that has been carried out to date, that of Allen *et al*. [12] is noteworthy; these researchers described a series of biimidazole-based anion receptors that exhibit strong affinities for dihydrogen phosphate and chloride anions. Separate from this, Kim and Yoon [13–15] have reported on a series of imidazolium-based receptors, including an imidazolium tripodal species that binds chloride and dihydrogen phosphate anions well. Although these latter receptor systems are not neutral, they are of particular interest because the putative host-guest complex is the result of carbon-hydrogen interactions as opposed to nitrogen-hydrogen interactions. Taken in concert, this work with imizadole-based systems has prompted us to explore whether pyrazole could be exploited as a useful "building block" for the construction of anion receptors. In accord with such thinking we report here the synthesis of 2,5-diamido functionalized pyrazoles, **2a**, **2b**, **4a**, **4b**, and **4c**, and show that the first of these acts as an effective receptor for phosphate and sulfate anions in DMSO.

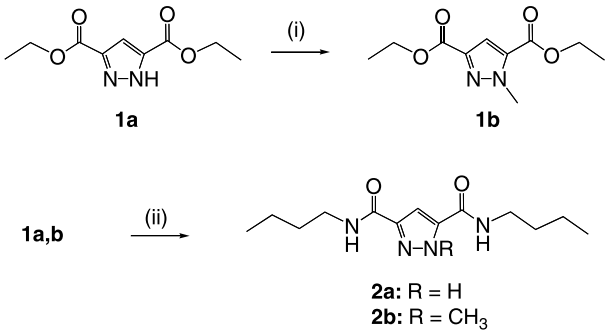
RESULTS AND DISCUSSION

Synthesis

Two different strategies were pursued for the synthesis of targets **2a**,**b** and **4a**–**c**. Scheme 1 depicts the first of these as applied to the synthesis of

*Corresponding author. E-mail: sessler@mail.utexas.edu

ISSN 1061-0278 print/ISSN 1029-0478 online © 2006 Taylor & Francis
DOI: 10.1080/10610270500445523

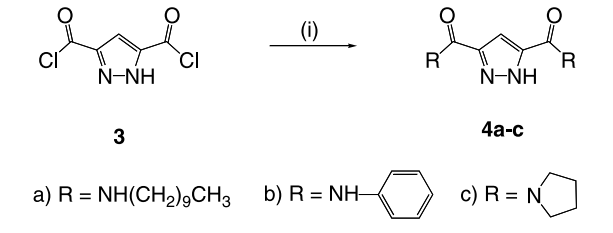


SCHEME 1 Preparation of pyrazoles **2a** and **2b**. *Reagents:* (i) CH_3I, Na_2CO_3, acetone, reflux; (ii) NaCN, butylamine, CH_3OH, reflux.

pyrazoles **2a**,**b**. As shown, these targets were obtained from the reaction of **1a** and **1b** (obtained from **1a** *via* methylation according to a literature procedure [16]) with butylamine using sodium cyanide as a catalyst. Although target **2a** has been previously reported as a component in an inorganic complex [17], details of its synthesis were unavailable and are thus included in this report. Both compounds (**2a**,**b**) were fully characterized using standard spectroscopic methods.

Scheme 2 depicts the synthesis of targets **4a**–**c**. Here, acid chloride **3** was prepared according to the literature [18] and then directly converted to the desired diamidopyrazoles by treatment with the appropriate amine (**a**–**c**) in methylene chloride in the presence of a pyridine-functionalized polymer, added to quench the hydrochloric acid formed in the reaction. Due to the poor solubility of the pyrazole targets, the use of a pyridine-bound polymer, as opposed to the use of neat pyridine, was found to be helpful. In particular, it simplified the work-up by allowing the resulting pyridinium hydrochloride salt to be removed by filtration, as opposed to organic-aqueous washings (which proved difficult with these products).

Structural proof for compound **2a** was obtained from a single crystal X-ray diffraction analysis. Two molecular conformations are seen in the unit lattice (Fig. 1). The two distinct molecules form a hydrogen-bonded dimer. There are two NH···N hydrogen bonds that involve the amide NH proton of one molecule linked to the imine-like pyrazole nitrogen



SCHEME 2 Preparation of pyrazoles **4a**–**4c**. *Reagents*: (i) RH, CH_2Cl_2, 2,6–di–*tert*–butylpyridine, polymer-bound 200–400 mesh, cross-linked with 1% divinylbenzene.

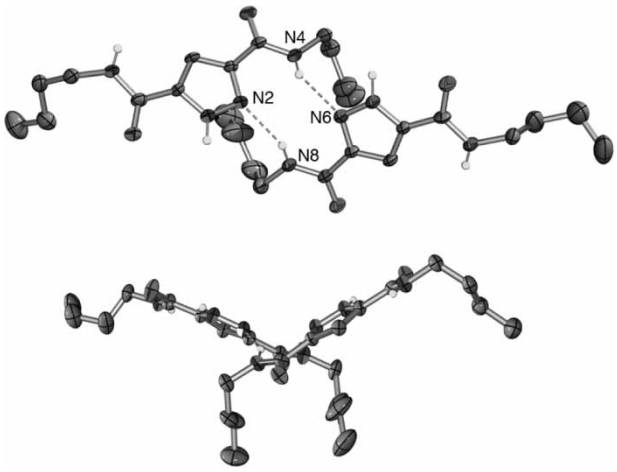


FIGURE 1 Top and side ORTEP-POVray rendered views of the dimer of **2a** seen in the solid state as determined from an X-ray diffraction analysis. The thermal ellipsoids are drawn to 50%. Most hydrogen atoms have been removed for clarity.

atom of another molecule (N4H···N6, 3.00 Å, 155°; N8H···N2, 2.96 Å, 149°).

Diffraction grade crystals of pyrazole **2b** were grown by slow evaporation from methylene chloride (Fig. 2). Single crystal X-ray analysis of **2b** revealed that it forms dimers in the solid state as the result of hydrogen bonding interactions involving the carboxyl oxygen atom of one molecule and the amidic NH proton and pyrazole CH of another molecule. The geometries of these interactions are: N9H···O15, 2.89 Å, 163° and C4H···O15, 3.29 Å, 152°.

Diffraction grade crystals of pyrazole **4b** were obtained by slow evaporation from methanol (Fig. 3). Single crystal X-ray analysis of **4b** revealed that it forms dimers in the solid state as the result of hydrogen bonding interactions involving the imine nitrogen of one pyrazole with the carboxyl oxygen of another pyrazole (N2H···O7, 2.75 Å, 145°). π–Stacking of the benzene rings also likely contributes to

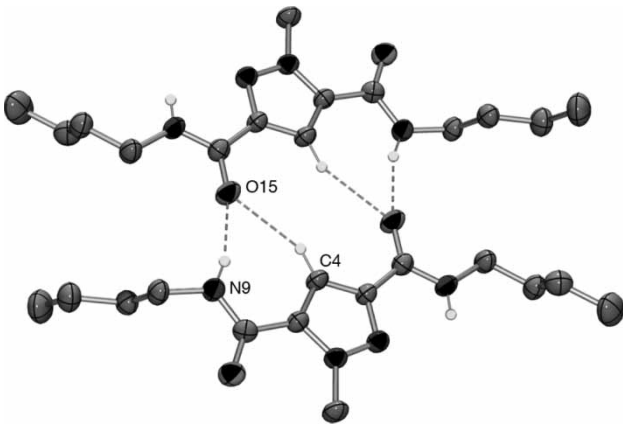


FIGURE 2 An ORTEP-POVray rendered view of the dimer of **2b** seen in the solid state as determined from single crystals grown from methylene chloride. The thermal ellipsoids are scaled to the 50%. Most hydrogen atoms have been removed for clarity.

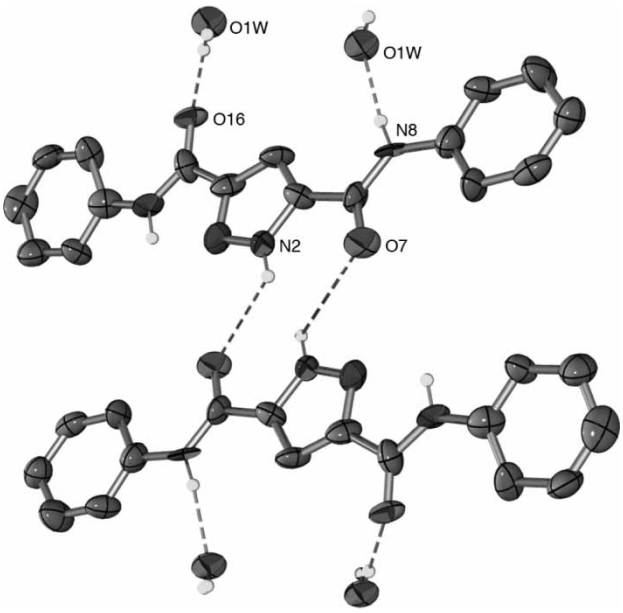


FIGURE 3 An ORTEP-POVray rendered view of the dimer of **4b** seen in the solid state as determined from single crystals grown from methanol. The thermal ellipsoids are scaled to the 50%. Most hydrogen atoms have been removed for clarity.

dimerization. Two water molecules are hydrogen bound to the exterior of this dimer, forming in this way a three-dimensional array. The geometries of these interactions are: O1WH···O16, 2.82 Å, 179° and N8H···O1W, 2.88 Å, 168°.

Diffraction grade crystals of pyrazole **4c** were obtained by slow evaporation from acetonitrile (Fig. 4). In this case, the observed hydrogen bonding network involves the amide carboxyl oxygen and the pyrazole NH proton (N2H···O2, 2.75 Å, 153°).

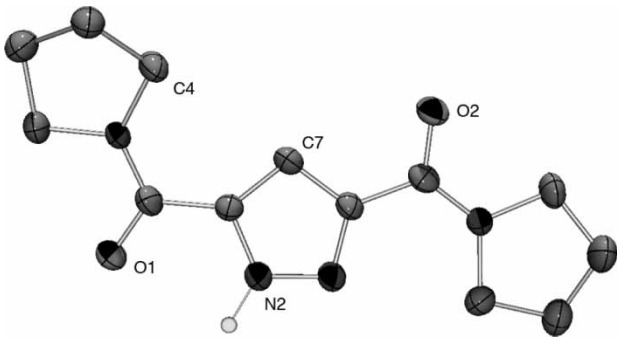


FIGURE 4 An ORTEP-POVray rendered view of solid state structure of **4c** as determined from an X-ray diffraction analysis of single crystals grown from acetonitrile. The thermal ellipsoids are scaled to the 50%. Most hydrogen atoms have been removed for clarity.

Anion Binding Studies

With the targets readily available in substantial quantities, anion binding experiments were carried out in an effort to determine whether this group of molecules has potential in the area of anion recognition. For these studies, dimethyl sulfoxide was selected as the solvent of choice for reasons of solubility. The anions were studied in the form of their respective tetrabutylammonium salts. Initial studies of anion binding, involving targets **2a**,**b** and **4a–c**, were made using ^{1}H NMR spectroscopy (DMSO-d_6; host concentration ca. 5 mM). On the basis of these analyses, it was concluded that the pyrazoles-diamide receptors **2a**,**b** and **4a**,**b** interact with dihydrogenphosphate, and in the case of **2a** additionally with chloride and hydrogen sulfate, as inferred from the change in the chemical shift of the amide NH peak seen upon addition of the anion. Unfortunately, at the concentrations needed for these studies, systems **2a**,**b** and **4a–c** proved to be highly aggregated (as determined from dilution experiments). Thus, the ^{1}H NMR spectroscopic studies, although of qualitative interest, could not be used to assess the putative the host-guest interactions quantitatively.

In an effort to obtain more quantitative information, the host-guest binding events were monitored in DMSO using isothermal titration calorimetry (ITC). This method was chosen because it requires lower concentrations of both the host and guest as compared to NMR spectroscopy-based techniques. It was hoped, therefore, that the problems with host aggregation could be avoided. Consistent with what was inferred from the ^{1}H NMR spectroscopic studies, only pyrazole **2a** was found to interact with anions in DMSO, giving rise to association constants (K_a) with dihydrogenphosphate and hydrogen sulfate of 5.76×10^5 and $2.94 \times 10^5\ M^{-1}$, respectively (Table I), assuming a 1:1 binding stoichiometry. Other anions tested, including benzoate, perchlorate, cyanide, bromide, dihydrogen phosphate, and hydrogen sulfate, failed to give rise to heat pulses consistent with binding.

Although ITC provides an excellent means of assessing the strength of binding interactions, it does not, unfortunately, provide an unambiguous definition of the host:guest binding stoichiometry [19]. Therefore, efforts were made to confirm the presumed 1:1 interaction using UV-Vis spectroscopic titrations. Unfortunately, none of the pyrazole

TABLE I Summary of ITC anion recognition studies involving pyrazole **2a**[a]

Anion	$C_6H_5CO_2^-$	ClO_4^-	$H_2PO_4^-$	HSO_4^-	CN^-	Br^-
2a	N.D.	N.D.	5.76×10^5	2.94×10^5	N.D.	N.D.

[a] N.D. indicates no evidence of binding observed. Association constants are in units of M^{-1}. All experiments were performed in DMSO at 30°C using the tetrabutylammonium salts of the anion in question.

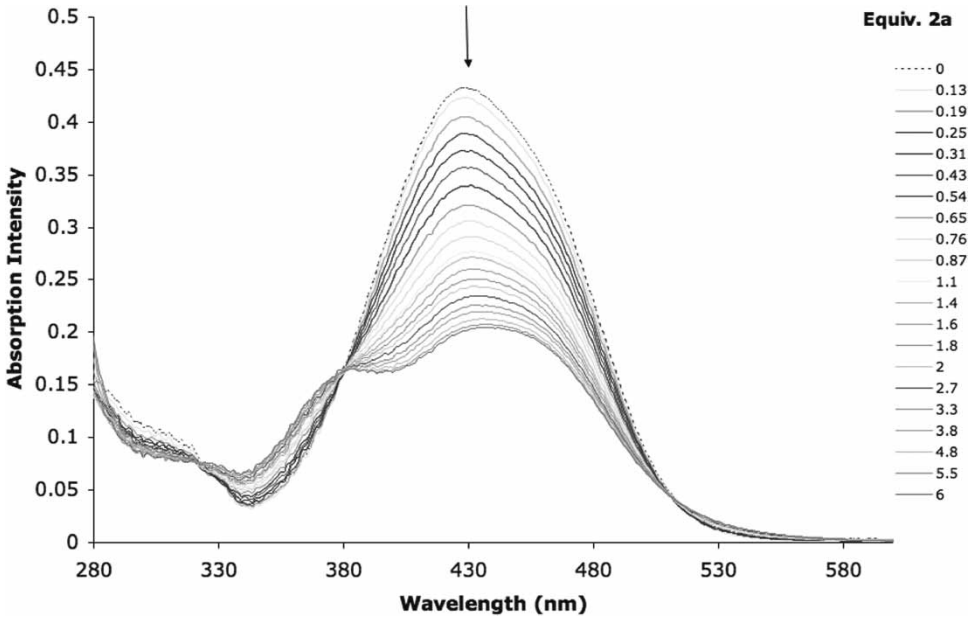


FIGURE 5 UV-Vis absorption spectral changes observed when a DMSO solution of methyl orange (sodium salt; 21.0 μM) is titrated with a stock solution of **2a** in DMSO.

diamide systems prepared in the context of this study displayed absorption bands in 220–1100 nm UV-Vis spectral region. Direct titration method involving the addition of an anionic guest to the pyrazole host could thus not be employed. Furthermore, no suitable dye could be found that would allow use of the so-called indicator displacement assay (IDA) used by Anslyn and others [20,21]. It thus proved necessary to develop an alternative means of monitoring the pyrazole:guest interaction. This, we proposed, could be done by basically "reversing" the host and guest by adding the colorless receptor **2a** to a solution of a colored anionic analyte. To the extent that a color change was engendered upon binding, it would allow the anion-receptor interactions to be probed.

After considerable experimentation, it was found that methyl orange could be used as the requisite UV-Vis active "reversed host". In fact, as illustrated in Fig. 5, the addition of receptor **2a** to a DMSO solution of methyl orange, a functionalized sulfonate anion studied in the form of its sodium salt, caused a decrease in the absorbance intensity of this well known indicating dye. This decrease in absorbance intensity is seen throughout the course of the addition, with saturation behavior being seen after ca. 3 equiv had been added. Linear least squares analysis of the data gave an association constant, K_a, of $4.9 \pm 0.5 \times 10^4\,M^{-1}$. Moreover, Job plot analysis revealed a 1:1 interaction between pyrazole **2a** and methyl orange.

In order to determine whether the observed reduction in methyl orange spectral intensity was predominantly due to hydrogen bonding-based anion binding, as proposed, or π-stacking, as the most likely alternative interaction mode, additional titrations involving **2a** and methyl orange were performed in DMSO solutions containing 5%, 10%, and 20% water (v/v), respectively. As the water percentage was increased, the calculated binding constant was found to decrease markedly and when the water concentration was 20% water, no appreciable change in the methyl orange absorbance was observed. Since π-stacking effects are likely to be enhanced, not reduced, in polar environments, these results are consistent with the appealing notion that the host-guest binding event interaction is largely a result of hydrogen bonding.

CONCLUSION

The first example of a potentially large series of anion receptors, the 3,5-diamidopyrazoles, is reported. These systems, specifically pyrazoles **2a,b** and **4a–d**, are readily synthesized in two steps from commercially available materials. Moreover, a convenient method for amide formation, involving the use of a pyridine-bound resin, was introduced that allows for simplified work-up and purification procedures in the case of less-than-optimally-soluble targets. Among the new pyrazole derivatives prepared, only **2a** was found to show an affinity for anions, displaying good specificity for dihydrogenphosphate and hydrogen sulfate in DMSO, as determined from ITC measurements. In addition to the ITC titration methods, the host-guest recognition process was studied using a "reversed" UV-Vis titration that entailed observing the quenching of the methyl orange absorbance induced by the addition of

receptor **2a**. These latter experiments served to confirm the 1:1 host:guest stoichiometry inferred from the ITC measurements and provided an indication that this receptor also binds substituted sulfonate anions (e.g., methyl orange) in addition to the simpler tetrahedral anions, dihydrogenphosphate and hydrogen sulfate. That these latter are bound in preference over other small anions such as halides is rationalized in terms of the nature of these smaller species not being able to avail themselves of the potentially cooperative interactions provided by both amide hydrogen atoms and the pyrazole nitrogen atoms of the receptor. Unlike dihydrogen phosphate and hydrogen sulfate, which contain both hydrogen-bonding donor and acceptor sites and which can potentially interact with both the hydrogen-bonding donor and acceptor sites of the receptor, halide anions (and a number of the other "test" anions) can only act as hydrogen bond acceptors.

Currently, we are exploring the use of methyl orange and other anionic dyes as a colored "hosts" for the study of host:guest interactions in the case of receptors that are inherently non-colored. To the extent this proves true, this method could emerge as a useful alternative to the IDA approach [20,21] to which it bears some degree of analogy. In preliminary work, we have found that octafluorocalix[4]pyrrole, a colorless compound known for its anion binding abilities [22], also acts to reduce the absorbance intensity when added to DMSO solutions of methyl orange sodium salt. Efforts are now underway to quantify these effects and to correlate the findings with independent measurements involving other techniques.

EXPERIMENTAL

Measurements and Materials

All chemicals were purchased from Aldrich and used without further purification with the following exceptions: Methanol was dried by passage through two columns of molecular sieves. Methylene chloride was dried by distillation under argon over calcium hydride. Thionyl chloride was purified by distillation from 10% (w/w) triphenylphosphite. All reactions requiring anhydrous conditions were performed using rigorously dried solvents and in glassware that had been flame-dried under argon. Proton NMR spectra were recorded on a Unity Plus Varian 300 MHz NMR spectrometer. Mass spectra were obtained using a Finnigan VG analytical ZAB2-E Spectrometer.

General Procedure for 2,5-Diamidopyrazole 2

Sodium cyanide (0.0449 mmol, 0.10 equiv.) was added to a solution of butylamine (44.2 mmol, 10 equiv.) and methyl ester **1** (0.442 mmol) dissolved in 10 mL dry methanol under argon. The reaction was heated at reflux for 2 days, removed from the heat source, allowed to cool, and subsequently concentrated *in vacuo* to give the crude product.

N^3, N^5-Dibutyl-1H-pyrazole-3,5-dicarboxamide (2a)

Sodium cyanide (0.24 mmol) was added to a solution of butylamine (240 mmol) and ester **1a** (2.4 mmol) dissolved in 20 mL of dry methanol under argon. The reaction was heated at reflux for 2 days using an oil bath. It was then removed from the heat source, allowed to cool, and concentrated *in vacuo* to give an off-white solid. Trituration with ethyl acetate gave **2a** in 94% yield as a white solid. m.p. = 202–205°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ) 0.88 (t, $J = 7.2$ Hz, 6H), 1.30 (comp, 4H), 1.46 (comp, 4H), 3.19 (q, $J = 7.2$ Hz, 4H), 6.88 (s, 1H), 7.91 (t, $J = 5.6$ Hz, 2H). ^{13}C NMR (100 MHz) δ 13.99, 19.91, 32.02, 38.02, 104.35, 146.87, 164.18. HR-MS (CI^+) *m/z* ($M + H^+$) calcd. for $C_{13}H_{22}N_4O_2$: 267.1821, found: 267.1830.

N^3, N^5-Dibutyl-1-methyl-1H-pyrazole-3,5-dicarboxamide (2b)

Using the same procedure, sodium cyanide (0.0449 mmol) was added to a solution of butylamine (44.2 mmol) and methyl ester **1b** (0.442 mmol) in 10 mL dry methanol under argon. The reaction was heated at reflux for 2 days in an oil bath. It was then removed from the heat source, allowed to cool, and concentrated *in vacuo* to give an off-white solid. Column chromatography over silica gel was performed by eluting initially with methylene chloride and slowly increasing the polarity to 5% methanol in methylene chloride. Fractions with Rf ~0.2 by TLC (silica gel; 95% methylene chloride 5% methanol) were combined, concentrated *in vacuo*, and dried under vacuum to yield product **2b** as a white solid in 92% yield. m.p. = 114–116°C. ^{1}H NMR (400 MHz, CD_3OD, δ) 0.972 (t, $J = 9.6$ Hz, 6H), 1.42 (m, $J = 2.0$ Hz, 4H), 1.60 (q, $J = 9.6$ Hz, 4H), 3.339 (q, $J = 10.0$ Hz, 4H), 4.15 (s, 3H), 7.14 (s, 1H). ^{13}C NMR (100 MHz) δ 14.11, 21.10, 32.50, 39.93, 40.24, 108.27, 138.67, 145.69, 161.35, 163.77. HR-MS (CI^+) *m/z* ($M + H^+$) calcd. for $C_{14}H_{25}N_4O_2$: 281.1977, found: 281.1978. Anal. Calcd. for $C_{14}H_{24}N_4O_2$: C, 59.98; H, 8.63; N, 19.98; O, 11.41. Found: C, 60.35; H, 8.94; N, 19.70; O, 11.23.

General Procedure for 2,5-Diamidopyrazole 4

Compound **3** (2.6 mmol), prepared *in situ*, was dissolved in 50 mL of dry methylene chloride under argon to give a white suspension. 2,6-Di-*tert*-butylpyridine resin (5% mmol) and amine (5.7 mmol, 2.2 equiv.) were added to the reaction and the mixture was stirred under argon at room temperature until no **3** remained, as judged by TLC analysis (95% CH_2Cl_2, 5% CH_3OH).

The reaction mixture was filtered through celite, washed with excess methanol and concentrated *in vacuo* to give the crude product. The material was purified by chromatography on a silica gel column.

N^3, N^5-Didecyl-1H-pyrazole-3,5-dicarboxamide (4a)

Addition of 129 mg (5% mmol) of 2,6-di-*tert*-butylpyridine resin and 900 mg (5.7 mmol) of decylamine to a solution of 502 mg (2.6 mmol) of compound **3** in 50 mL dry methylene chloride, after 12 hrs, gave an off-white solid. Column chromatography was performed eluting initially with methylene chloride and slowly increasing to 2% methanol in methylene chloride. Fractions with Rf ~ 0.4 on TLC (95% CH_2Cl_2, 5% CH_3OH) were combined, concentrated *in vacuo*, and dried to give a white solid in 11.2% yield. m.p. = 135–158°C. ^{1}H NMR (400 MHz, CD_3OD, δ) 0.84 (m, 6H), 1.24 (s, 18H), 1.57 (m, 6H), 2.73 (t, J = 8.0 Hz, 8H), 3.12 (q, J = 6.5 Hz, 4H), 7.120 (s, 1H), 7.89 (br, 1H), 8.33 (br, 1H). ^{13}C NMR (125 MHz, DMSO-d_6, δ) 13.92, 22.04, 25.77, 26.36, 26.98, 28.48, 28.64, 28.70, 28.79, 28.84, 28.91, 28.94, 29.02, 31.24, 38.46, 38.77, 105.00. HR-MS (CI^+) m/z ($M + H^+$) calcd. for $C_{25}H_{47}N_4O_2$: 435.3699, found: 435.3695.

N^3, N^5-Diphenyl-1H-pyrazole-3,5-dicarboxamide (4b)

Using the same procedure, addition of 25.8 mg (5% mmol) of 2,6-di-*tert*-butylpyridine resin and 106 mg (1.14 mmol) of decylaniline to a solution of 100 mg (0.518 mmol) of compound **3** 10 mL dry methylene chloride, after 2 days, gave an off-white solid. Column chromatography was performed eluting initially with methylene chloride and slowly increasing the polarity to 3% methanol in methylene chloride. Fractions with Rf ~ 0.3 on TLC (95% CH_2Cl_2, 5% CH_3OH) were combined, concentrated *in vacuo*, and dried to give a white solid in 57%. m.p. = 273–280°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ) 7.10 (t, J = 1.8 Hz, 2H), 7.35 (t, J = 7.6 Hz, 4H), 7.67 (s, 1H), 7.80 (d, J = 8.0 Hz, 4H), 10.28 (s, 2H). ^{13}C NMR (125 MHz, DMSO-d_6, δ) 106.73, 120.31, 123.70, 128.62, 138.49. HR-MS (CI^+) m/z ($M + H^+$) calcd. for $C_{17}H_{14}N_4O_2$: 307.1195, found: 307.1191.

N^3, N^5-Dipyrrolyl-1H-pyrazole-3,5-dicarboxamide (4c)

Using the same procedure, addition of 25.8 mg (5% mmol) of 2,6-di-*tert*-butylpyridine resin and 80 mg (1.14 mmol) of pyrrolidine to a solution of 100 mg (0.518 mmol) of compound **3** 10 mL dry methylene chloride, after 2 days, gave an off-white solid. Column chromatography was performed over silica gel eluting initially with methylene chloride and slowly increasing the polarity of the eluent to 3% methanol in methylene chloride. Fractions with Rf ~ 0.3 on TLC (95% CH_2Cl_2, 5% CH_3OH) were combined, concentrated *in vacuo* and dried to give a white solid in 57%. m.p. = 196–200°C. ^{1}H NMR (400 MHz, DMSO-d_6, δ) 1.82 (br, 4H), 1.90 (br, 4H), 3.47 (t, J = 6.4 Hz, 4H), 3.68 (br, 2H), 3.81 (br, 2H), 6.99 (d, J = 1.6 Hz, 1H). ^{13}C NMR (100 MHz) (500 MHz, DMSO-d_6, δ) 23.38, 26.00, 45.68, 46.53, 47.59, 48.29, 108.22, 136.78, 148.20, 157.68, 160.69. HR-MS (CI^+) m/z ($M + H^+$) calcd. for $C_{13}H_{19}N_4O_2$: 263.1508, found: 263.1517.

TABLE II Crystallographic and structure refinement data for compounds **2a**, **2b**, **4b**, and **4c**

Compound	**2a**	**2b**	**4b**	**4c**
Empirical formula	$C_{13}H_{22}N_4O_2$	$C_{14}H_{24}N_4O_2$	$C_{17}H_{16}N_4O_3$	$C_{13}H_{18}N_4O_2$
Formula weight	266.35	280.37	324.34	262.31
Temperature (K)	153(2)	153(2)	153(2)	153(2)
Crystal system	Monoclinic	Triclinic	Triclinic	Orthorhombic
Space Group	P21/c	P–1	P–1	Pbca
a (Å)	20.7327(9)	4.8959(3)	4.554(1)	7.799(5)
b (Å)	9.0253(5)	10.6111(6)	12.421(2)	12.284(5)
c (Å)	16.9704(13)	15.9522(10)	28.252(5)	27.001(5)
α (°)	90.0	103.883(2)	78.100(6)	90.00
β (°)	109.001(3)	96.697(2)	86.730(6)	90.00
γ (°)	90.0	99.552(2)	81.530(8)	90.00
V (Å^3)	3002.5(3)	782.70(8)	1546.1(5)	2587(2)
Z	8	2	4	8
D_c (g cm^{-3})	1.178	1.190	1.393	1.347
μ (mm^{-1})	0.082	0.082	0.099	0.094
F(000)	1152	304	680	1120
CCDC ref. number	286270	286269	286272	286271
No. of collected reflections	8400	5273	3420	16859
θ-range (°)	2.94 to 27.6	3.75 to 27.50	3.04 to 22.50	3.18 to 27.38
No. of unique reflections	5225	3439	3420	2899
No. of refined parameters	368	190	434	245
Final R indices R (= $\Sigma\|\Delta F\|/\Sigma\|F_o\|$)	0.0752	0.0585	0.120	0.058
No. of values used [$I > 2\sigma(I)$]	2451	1536	1204	1170
ωR on F^2	0.142	0.136	0.248	0.094
Goodness of fit on F^2	1.060	0.975	1.305	1.061

X-ray Crystallography

Crystals suitable for single crystal X-ray analysis were obtained by slow evaporation of solutions of compounds **2a**, **2b**, **4b**, and **4c** in appropriate solvents.

The intensity data of compounds **2a**, **2b**, **4b**, and **4c** were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073 Å). The data were collected at 153 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table II. Other details of the structures may be obtained from the Cambridge Crystallographic Data Centre, citing reference numbers 286270, 286269, 286272, and 286271 for compounds **2a**, **2b**, **4b**, and **4c**, respectively. Data reduction was performed using DENZO-SMN [23]. The structure was solved by direct methods using SIR97 [24] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97 [25]. The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992) [26].

Acknowledgements

This project was supported by the National Science Foundation Integrative Graduate Education and Research Traineeship Program (grant no. DGE 9870653) and the National Science Foundation (grant no. CHE 0515670 to J.L.S.).

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