Articles

Solution-Phase Parallel Synthesis of a Library of Δ^2-Pyrazolines

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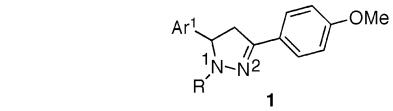
A parallel synthesis of a library (80 members) of 2-pyrazolines in solution phase is described. The 2-pyrazoline core was accessed through the [3 + 2] cycloaddition of nitrilimines with enoyl oxazolidinones. The cycloaddition provided two regioisomers, the major product being the C regioisomer. The oxazolidinone moiety was further reduced to the primary alcohol, producing another library of 5-hydroxymethyl-2-pyrazolines. The Lipinski profiles and calculated ADME properties of the compounds are also reported.

Introduction

The solution-phase parallel synthesis of primary or focused libraries is an established practice in medicinal chemistry.[1] The solution-phase approach avoids the need to reoptimize the chemistry to the solid phase prior to library generation. Δ^2-Pyrazolines[2] (2-pyrazolines or 4,5-dihydropyrazoles, Figure 1) are an important class of heterocyclic small molecules[3] that have shown potential bioactivity in numerous screening tests.[4] For example, pyrazolines **1** have demonstrated moderate to good MIC_{90} values against *Helicobacter pylori*.[5] The optimized pyrazoline **2** showed nanomolar inhibition (IC_{50} = 26 nM) against kinesin spindle protein; inhibitors of this protein constitute a novel approach to cancer treatment.[6] Pyrazoline **3** displayed 70% inhibitory activity against neuronal nitric oxide synthase and was inactive against kynurenine 3-hydroxylase.[7] Such selective inhibition is indicative of potential neuroprotective properties. Compounds containing the pyrazoline core have also been examined for antidepressant activity through screening against monoamine oxidases,[8] treatment of obesity as cannabinoid-1 antagonists,[9] antiviral activity against the West Nile virus,[10] and multidrug resistance modulators in tumor cells.[11]

Most of these studies were limited to structures lacking substitution at N1 and C4; additionally, only a few modifications at C5 have been reported. Such constraints have been predominantly due to the similarity of existing synthetic strategies to the dihydropyrazole framework; namely, the cyclocondensation of acrylates or chalcones with hydrazines.[2] Carreira and co-workers have developed a different strategy, the dipolar cycloaddition of $TMSCHN_2$ to enoates generating



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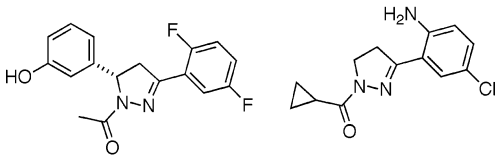
R	Ar^1	MIC_{90} (μg/mL)
4-ClC_6H_4–	2-OHC_6H_4–	64
$CH_3C(O)$–	4-OHC_6H_4–	8



2 **3**

Figure 1. Δ^2-Pyrazolines as biologically active compounds.

2-pyrazolines lacking substitution at N1 and C3.[12] It must be noted that these approaches are advantageous when specific modification at N1 is desired.

Recently, one of us reported the enantioselective [3 + 2] dipolar cycloaddition of nitrilimines to α,β-unsaturated enoates **4** under chiral Lewis acid catalysis for the construction of 2-pyrazolines **8** with high yields and high enantioselectivities (Scheme 1).[13] The *E* geometry of the dipolarophile is translated to trans stereochemistry at the C4 and C5 positions of 2-pyrazolines **8.** This study suggested that the method could rapidly supply a diverse set of 2-pyrazolines. Specifically, the development of this methodology to parallel synthesis would clearly provide access to tetrasubstituted pyrazolines and allow for their primary high-throughput biological screening.[14] Additionally, there is only one report of a solution-phase parallel synthesis of 2-pyrazolines, and the authors utilized the cyclocondensation approach.[15]

Hence, it was pertinent to evaluate the accessibility of tetrasubstituted 2-pyrazolines through solution-phase parallel synthesis employing the nitrilimine cycloaddition. At the

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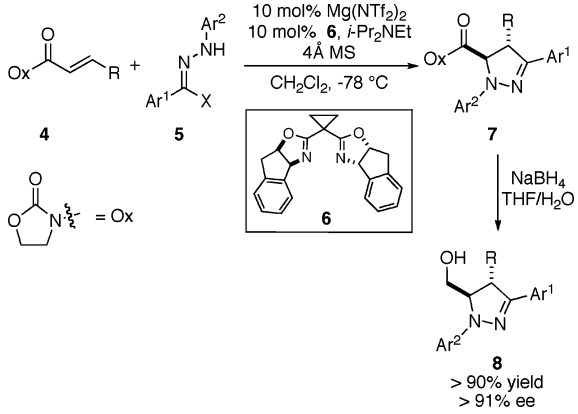
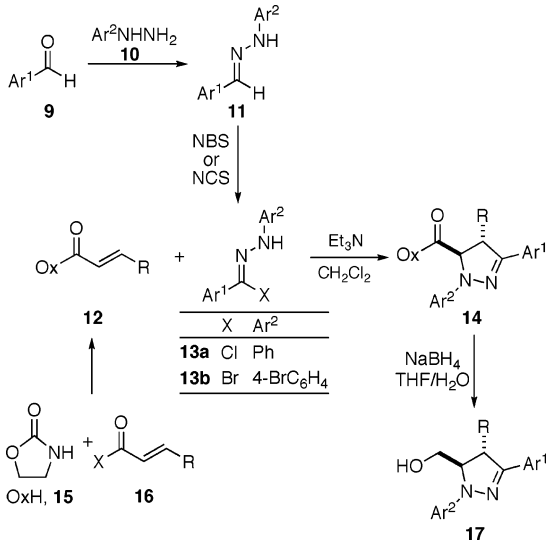
Scheme 1. Enantioselective Nitrilimine Cycloaddition



Scheme 2. Library Design for 2-Pyrazolines



outset, the preparation of racemic compounds was targeted to avoid influencing the biological screening process toward either enantiomer. The demonstration of this methodology in parallel synthesis is documented here through the synthesis of 80 compounds containing the 2-pyrazoline moiety.

Results and Discussion

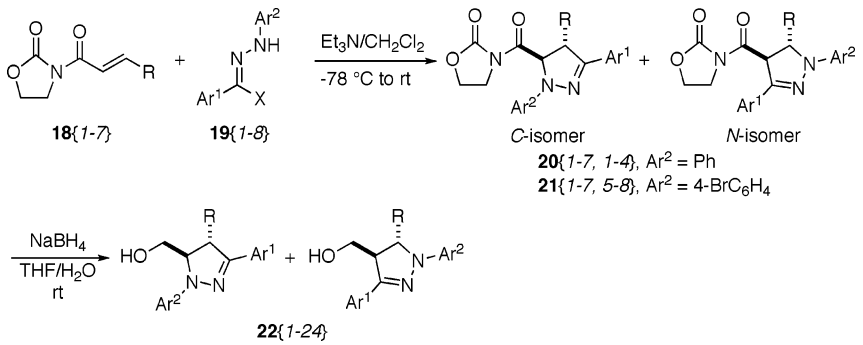
The strategy for library production is shown in Scheme 2. The libraries were designed to contain both alkyl and aryl substituents at the β-carbon of the alkenoyl oxazolidinones **12** and varying aryl groups on the hydrazonyl halides **13**, providing two diversity elements. In addition, a third diversification opportunity presents itself in the preparation of the hydrazonyl halides using *N*-chlorosuccinimide or *N*-bromosuccinimide.[16] Thus, chlorination provided hydrazonyl chloride **13a**, whereas bromination with NBS provides **13b**, containing bromine at the para position of the electron-rich aromatic ring. The libraries with structure **14** could then be reduced to library **17**, the hydroxyl group of which could be further diversified.

The initial cycloaddition experiments were carried out in the absence of the chiral ligand to obtain the racemic cycloadducts (Scheme 3). In addition to the expected product (**20** C-isomer), the regioisomeric cycloadduct (**20** N-isomer) was also obtained.[17] This unexpected result further diversifies the number of library members in this endeavor.[18] Such N regioisomers were not observed in the enantioselective reactions, leading to the speculation that regiocontrol is provided by complexation to the chiral Lewis acid. Attempts to control the regioselectivity through activation with main-group, transition metal, or lanthanide Lewis acids [$Mg(ClO_4)_2$, $Mg(NTf_2)_2$, $TiCl_4$, $SnCl_4$, or $Yb(OTf)_3$] or by altering the amine base provided products with decreased regioselection. Additionally, the regioisomers were inseparable through either normal or reversed-phase HPLC. However, an increase in the regioisomeric ratio could be obtained through a decrease in temperature to −78 °C.

With these preliminary results, we proceeded to the library synthesis as described in Scheme 3. The dipolarophiles and dipole precursors were chosen to demonstrate the scope of the methodology (Figure 2). Both alkyl and aryl (with both electron-donating and electron-withdrawing substituents) groups at the β-carbon of **18** were chosen. Similar considerations were applied in the choice of hydrazonyl halides. The dipolarophiles **18**{*1*−*7*} were prepared using literature procedures starting from either the commercial alkenoyl acid chlorides or alkenoic acids. The hydrazone precursors to the dipoles were obtained through a simple condensation of the aldehydes and phenyl hydrazine using magnesium sulfate or 10 mol % magnesium perchlorate.[19] These hydrazones were then converted to the hydrazonyl chlorides **19**{*1*−*4*} by treatment with *N*-chlorosuccinimide and Me_2S and to hydrazonyl bromides **19**{*5*−*8*} with *N*-bromosuccinimide and Me_2S.[16]

The dipolar cycloaddition between **18**{*1*−*7*} and **19**{*1*−*8*} to provide 56 compounds was carried out in two runs with either an Innovasyn SynthArray-24 reactor or a 6 × 4 Bohdan MiniBlock XT. The MiniBlock reaction system was cooled to −78 °C prior to the addition of Et_3N. The 56 library

Scheme 3. Synthetic Route to 2-Pyrazoline Libraries



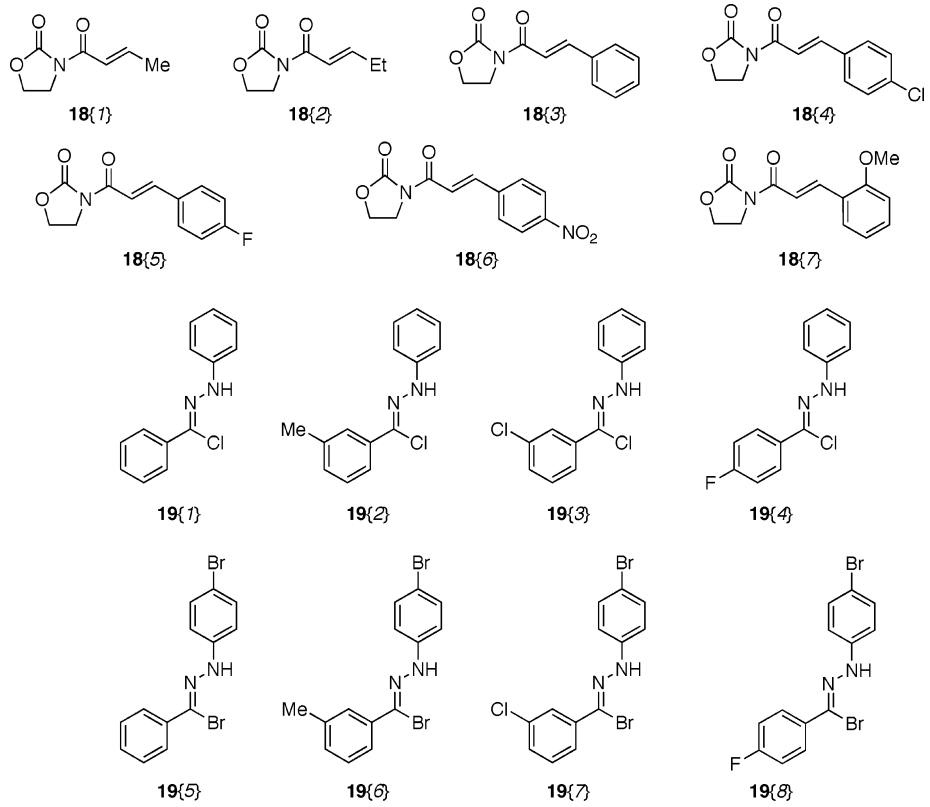
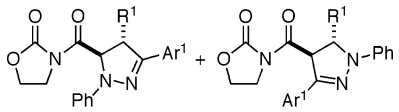


Figure 2. Library components **18**{*1*−*7*} and **19**{*1*−*8*}.

Table 1. Library Data for Compounds **20**{*1*−*28*} from **18**{*1*−*7*} and **19**{*1*−*4*}[a]



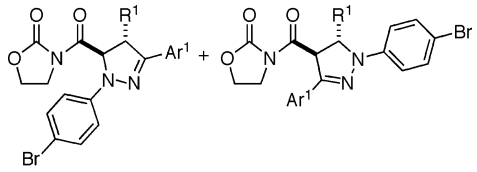
compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]	compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]
20{*1*}	Me	Ph	46	100	100	>30:1	**20**{*15*}	Me	3-ClC_6H_4	85	97	100	23:1
20{*2*}	Et	Ph	56	100	98	30:1	**20**{*16*}	Et	3-ClC_6H_4	37	99	100	34:1
20{*3*}	Ph	Ph	49	100	100	6.2:1	**20**{*17*}	Ph	3-ClC_6H_4	32	99	100	8.4:1
20{*4*}	4-FC_6H_4	Ph	46	100	100	4.8:1	**20**{*18*}	4-FC_6H_4	3-ClC_6H_4	31	100	100	6.2:1
20{*5*}	4-ClC_6H_4	Ph	59	99	100	5.2:1	**20**{*19*}	4-ClC_6H_4	3-ClC_6H_4	36	100	100	8.0:1
20{*6*}	4-$NO_2C_6H_4$	Ph	47	96	100	2.9:1	**20**{*20*}	4-$NO_2C_6H_4$	3-ClC_6H_4	42	100	100	4.3:1
20{*7*}	2-$OMeC_6H_4$	Ph	51	100	92	5.6:1	**20**{*21*}	2-$OMeC_6H_4$	3-ClC_6H_4	46	100	97	9.1:1
20{*8*}	Me	3-MeC_6H_4	73	98	100	27:1	**20**{*22*}	Me	4-FC_6H_4	76	98	100	22:1
20{*9*}	Et	3-MeC_6H_4	44	100	100	32:1	**20**{*23*}	Et	4-FC_6H_4	52	100	100	32:1
20{*10*}	Ph	3-MeC_6H_4	51	99	100	5.5:1	**20**{*24*}	Ph	4-FC_6H_4	53	99	100	8.5:1
20{*11*}	4-FC_6H_4	3-MeC_6H_4	48	100	100	4.4:1	**20**{*25*}	4-FC_6H_4	4-FC_6H_4	51	100	100	6.5:1
20{*12*}	4-ClC_6H_4	3-MeC_6H_4	44	100	100	4.6:1	**20**{*26*}	4-ClC_6H_4	4-FC_6H_4	60	99	100	7.1:1
20{*13*}	4-$NO_2C_6H_4$	3-MeC_6H_4	47	99	100	2.6:1	**20**{*27*}	4-$NO_2C_6H_4$	4-FC_6H_4	69	100	100	3.7:1
20{*14*}	2-$OMeC_6H_4$	3-MeC_6H_4	48	100	93	5.7:1	**20**{*28*}	2-$OMeC_6H_4$	4-FC_6H_4	61	100	96	5.8:1

[a] See Supporting Information for experimental details. [b] Isolated yields after purification on LC. [c] UV purity determined at 215 nm after LC purification. [d] ELSD purity after LC purification. [e] Estimated from ^{1}H NMR.

members were easily purified by filtration through a SPE cartridge containing silica gel. These crude products were analyzed by LC/MS, followed by purification by preparative LC with UV trigger to provide **20**{*1*−*28*} and **21**{*1*−*28*} as mixtures of the C and N regioisomers. The regioisomeric ratios were determined from the purified products before cataloging them for biological screening. The isolated yields, purities determined by UV (215 nm), MS (ELSD), and C:N regioisomeric ratios are collected for these 56 samples (Tables 1 and 2). For the dipolarophiles containing alkyl substituents at the β-carbon, the C regioisomer was predominantly observed. In comparison to **18**{*3*}, electron-withdrawing groups on the aryl ring decreased the regioselectivity. However, **18**{*7*} containing the electron-donating 2-OMe group provided a higher ratio of C regioisomer. In general, the reactions with hydrazonyl chlorides provided slightly better regioselectivities as compared to the hydrazonyl bromides.

The next library, **22**, containing the primary alcohol at C5, was obtained from a subset of library **20** through a reduction

Table 2. Library Data for Compounds **21**{*1*−*28*} from **18**{*1*−*7*} and **19**{*5*−*8*}[a]

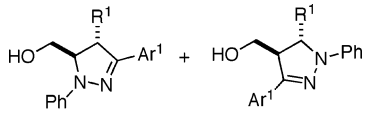


21{*1-28*}

compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]	compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]
21{*1*}	Me	Ph	58	100	97	>30:1	**21**{*15*}	Me	3-ClC_6H_4	94	98	100	>30:1
21{*2*}	Et	Ph	57	100	100	30:1	**21**{*16*}	Et	3-ClC_6H_4	31	100	100	30:1
21{*3*}	Ph	Ph	51	92	94	5:1	**21**{*17*}	Ph	3-ClC_6H_4	32	100	100	4.6:1
21{*4*}	4-FC_6H_4	Ph	31	86	91	3.6:1	**21**{*18*}	4-FC_6H_4	3-ClC_6H_4	53	100	100	4.4:1
21{*5*}	4-ClC_6H_4	Ph	38	96	99	4.5:1	**21**{*19*}	4-ClC_6H_4	3-ClC_6H_4	54	100	100	4.3:1
21{*6*}	4-$NO_2C_6H_4$	Ph	49	100	83	3.0:1	**21**{*20*}	4-$NO_2C_6H_4$	3-ClC_6H_4	61	100	100	3.3:1
21{*7*}	2-$OMeC_6H_4$	Ph	44	99	98	5.4:1	**21**{*21*}	2-$OMeC_6H_4$	3-ClC_6H_4	39	100	100	12.1:1
21{*8*}	Me	3-MeC_6H_4	37	96	100	>30:1	**21**{*22*}	Me	4-FC_6H_4	72	99	100	>30:1
21{*9*}	Et	3-MeC_6H_4	21	97	100	30:1	**21**{*23*}	Et	4-FC_6H_4	57	100	100	30:1
21{*10*}	Ph	3-MeC_6H_4	46	96	91	4.8:1	**21**{*24*}	Ph	4-FC_6H_4	53	86	96	6.5:1
21{*11*}	4-FC_6H_4	3-MeC_6H_4	36	92	85	3.3:1	**21**{*25*}	4-FC_6H_4	4-FC_6H_4	52	86	93	4.8:1
21{*12*}	4-ClC_6H_4	3-MeC_6H_4	49	97	92	3.9:1	**21**{*26*}	4-ClC_6H_4	4-FC_6H_4	47	94	99	5.2:1
21{*13*}	4-$NO_2C_6H_4$	3-MeC_6H_4	59	100	71	2.5:1	**21**{*27*}	4-$NO_2C_6H_4$	4-FC_6H_4	53	99	100	4.3:1
21{*14*}	2-$OMeC_6H_4$	3-MeC_6H_4	49	100	99	6.6:1	**21**{*28*}	2-$OMeC_6H_4$	4-FC_6H_4	15	100	100	3.9:1

[a] See Supporting Information for experimental details. [b] Isolated yields after purification on LC. [c] UV purity determined at 215 nm after LC purification. [d] ELSD purity after LC purification. [e] Estimated from ^1H NMR.

Table 3. Library Data for Compounds **22**{*1*−*24*} from 18{*1*−*5,7*} and 19{*1*−*4*}[a]



22{*1-24*}

compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]	compd	R^1	Ar^1	yield (%)[b]	purity (%)[c]	purity (%)[d]	C:N ratio[e]
22{*1*}	Me	Ph	35	99	100	30:1	**22**{*13*}	Me	3-ClC_6H_4	27	99	100	30:1
22{*2*}	Et	Ph	21	99	100	30:1	**22**{*14*}	Et	3-ClC_6H_4	27	100	100	30:1
22{*3*}	Ph	Ph	55	98	100	6.2:1	**22**{*15*}	Ph	3-ClC_6H_4	48	100	100	8.0:1
22{*4*}	4-FC_6H_4	Ph	72	100	100	5.1:1	**22**{*16*}	4-FC_6H_4	3-ClC_6H_4	50	98	100	6.0:1
22{*5*}	4-ClC_6H_4	Ph	49	98	100	5.0:1	**22**{*17*}	4-ClC_6H_4	3-ClC_6H_4	59	100	100	6.3:1
22{*6*}	2-$OMeC_6H_4$	Ph	77	93	100	6.7:1	**22**{*18*}	2-$OMeC_6H_4$	3-ClC_6H_4	54	96	100	10.1:1
22{*7*}	Me	3-MeC_6H_4	32	93	99	30:1	**22**{*19*}	Me	4-FC_6H_4	80	99	100	30:1
22{*8*}	Et	3-MeC_6H_4	24	99	100	30:1	**22**{*20*}	Et	4-FC_6H_4	48	96	100	30:1
22{*9*}	Ph	3-MeC_6H_4	72	99	100	5.5:1	**22**{*21*}	Ph	4-FC_6H_4	40	98	100	8.4:1
22{*10*}	4-FC_6H_4	3-MeC_6H_4	59	99	100	4.1:1	**22**{*22*}	4-FC_6H_4	4-FC_6H_4	30	99	100	7.0:1
22{*11*}	4-ClC_6H_4	3-MeC_6H_4	71	99	100	4.4:1	**22**{*23*}	4-ClC_6H_4	4-FC_6H_4	56	100	100	7.5:1
22{*12*}	2-$OMeC_6H_4$	3-MeC_6H_4	54	97	100	5.5:1	**22**{*24*}	2-$OMeC_6H_4$	4-FC_6H_4	44	100	100	8.6:1

[a] See Supporting Information for experimental details. [b] Isolated yields after purification on LC. [c] UV purity determined at 215 nm after LC purification. [d] ELSD purity after LC purification. [e] Estimated from ^1H NMR.

of the oxazolidinone group using $NaBH_4$ as shown in Scheme 3. This parallel synthesis was also performed in a 6 × 4 Bohdan MiniBlock XT, followed by parallel purification using an aqueous workup to remove inorganic salts. The aqueous workup was performed using Alltech phase-separator columns containing hydrophobic frits followed by drying through polypropylene tubes containing $MgSO_4$. The crude products were analyzed by LC/MS and subjected to purification by preparative LC with UV-triggered separation. The isolated yields, purities (UV at 215 nm and ELSD), and C:N ratios of the compounds over two steps are presented in Table 3. In general, the C:N ratios in this library were slightly higher than the previous libraries due to enrichment obtained through the fraction trigger during preparative HPLC purification.

The compounds prepared in these parallel syntheses were evaluated in silico for their drug-like properties on the basis of the Lipinski's "rule of five."[20] Molecular weight, clogP, number of hydrogen bond donors, and acceptors were calculated using SYBYL[21] and are presented in Figure 3. Overall, 24% of the library had two violations, 66% of the library had one violation, and 10% of the library had zero violations. Many of the compounds in the collection had high clogP values (<5 is normal), which would be addressed in future libraries directed toward orally active agents. In addition, standard absorption−distribution−metabolism−

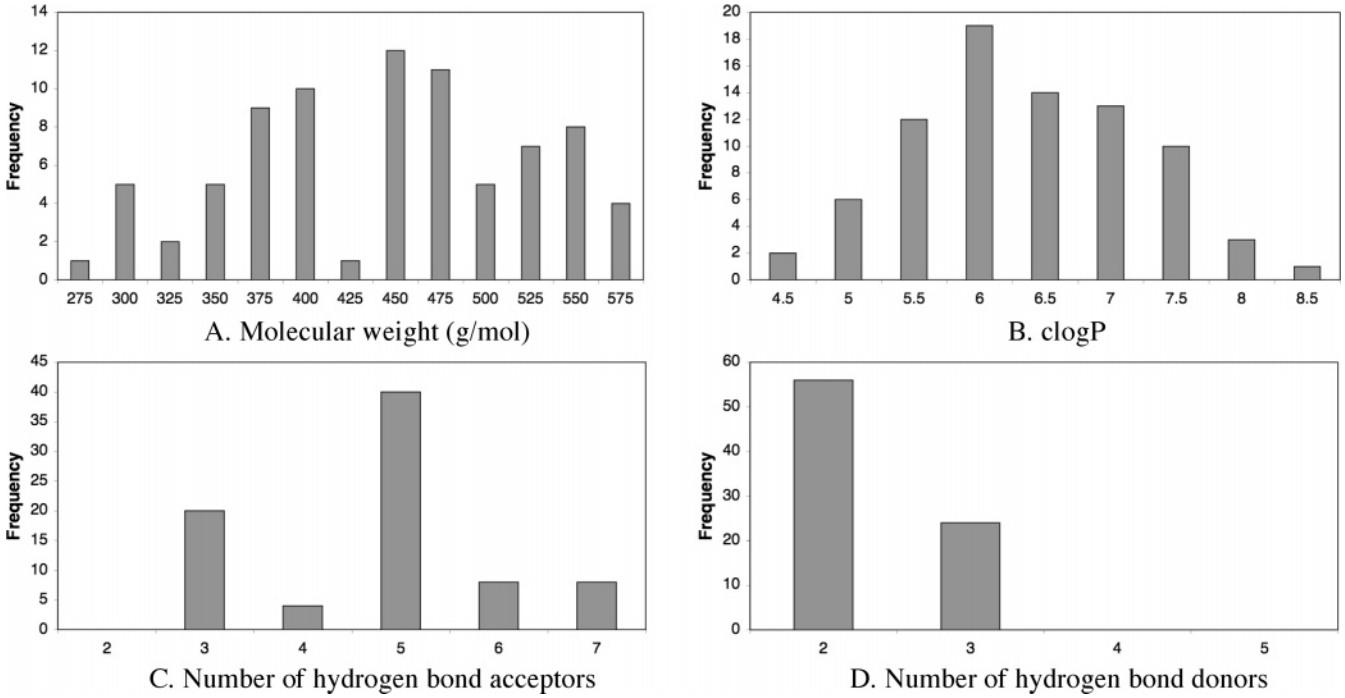


Figure 3. Analysis of Lipinski rule parameters.

excretion (ADME) properties were calculated using the VolSurf[22] program and are presented in the Supporting Information. Chemical diversity analysis relative to the PubChem collection (as performed via DiverseSolutions[23]) suggests that the present collection occupies regions of PubChem space that already have substantial populations. However, the library members do not directly duplicate compounds in PubChem and will, thus, be a unique addition to the database and compound collection.

In summary, the efficient parallel synthesis of a library of eighty tetrasubstituted 2-pyrazolines containing either oxazolidinone or hydroxymethyl groups at C5 have been described. Further diversification of the current library compounds will be explored. The compounds will be evaluated in high-throughput screens and modified accordingly.

Experimental Section

General. All chemicals were used as purchased from commercial suppliers. Methylene chloride and THF were dried by being passed through two packed columns of neutral alumina using the PurSolv solvent purification system (Innovative Technology, Inc.) prior to use. Reactions with air-sensitive materials were carried out with oven-dried glassware under a stream of dry argon using standard syringe techniques. The parallel syntheses were performed either on a SynthArray-24 reactor obtained from InnovaSyn or a MiniBlock XT synthesizer obtained from Mettler-Toledo AutoChem. The phase-separator columns were obtained from AllTech, and PrepSep silica gel SPE cartridges were obtained from Fisher Scientific. Automated weighing was performed using the Bohdan Balance Automator (Mettler-Toledo AutoChem). Parallel evaporation was performed on the GeneVac EZ-2 plus evaporator system. Flash chromatography was performed using EM Science silica gel 60 (230−400 mesh) or RediSep silica gel cartridges on an Isco CombiFlash companion. Library enumeration was carried out using Synthematix software (Symyx Technologies, Inc.). *C* log *P* calculations were performed with SYBYL 6.9.2. Melting points were determined using the Thomas Hoover capillary melting-point apparatus (Uni-Melt).

^{1}H NMR spectra were recorded on a Bruker-500 DRX (500 MHz) or a Bruker Avance 400 (400 MHz) spectrometer. Chemical shifts are reported in parts per million (ppm) downfield from TMS (0 ppm). Data are reported as follows: chemical shift, multiplicity (app = apparent, s = singlet, d = doublet, t = triplet, q = quartet, dd = doublets of doublets, m = multiplet, br = broad), coupling constants, and integration. ^{13}C NMR spectra were recorded on a Bruker-500 DRX (125 MHz) or a Bruker Avance 400 (100 MHz) spectrometer using broadband proton decoupling. Chemical shifts are reported in parts per million (ppm) downfield from TMS, using the middle resonance of $CDCl_3$ (77.2 ppm) as an internal standard. IR spectra were recorded on a Shimadzu FTIR-8400S spectrophotometer.

HPLC analyses were carried out using a Xterra MS C-18 column (5 μm, 4.6 × 150 mm) and gradient elution (10% CH_3CN/water to 100% CH_3CN) on a Waters mass-directed fractionation instrument using a Waters 2767 sample manager, Waters 2525 HPLC pump, a 2487 dual λ absorbance detector, and Waters/MicroMass ZQ (quadrupole) MS ELSD detector (Sedex 85) connected to a PC with a MassLynx workstation. Purification was carried out using an Xterra MS C-18 column (5 μm, 10 × 150 mm), a gradient elution (40% CH_3CN/water to 100% CH_3CN) with a UV fraction trigger. High-resolution mass spectra (HRMS) [ESI+] were obtained using Waters/MicroMass LCT Premier (TOF instrument).

General Procedure for Libraries 20{*1*−*28*} and 21{*1*−*28*}. Stock solutions of four hydrazonyl bromides, **19**, and six enoyl oxazolidinones, **18**, were prepared initially. To a

SynthArray-24 (InnovaSyn) reactor block fitted with 24 (13 × 100 mm) screw-top reaction vials or a 6 × 4 position Bohdan MiniBlock fitted with 24 (17 × 110 mm) reaction vials, under an atmosphere of argon, was added **18**{*1*−*6*} (0.5 mL, 0.1 mmol) at the appropriate positions, followed by **19**{*1*−*4*} for library **20** or **19**{*5*−*8*} for library **21** (1.0 mL, 0.15 mmol). The 24 reaction vials were cooled to −78 °C using a dry ice/acetone bath, and after 20 min, triethylamine (20.9 μL, 0.15 mmol) was added. The reactions were allowed to warm overnight to room temperature. Three hundred milligrams of silica gel were added to the reaction mixtures using the MiniBlock resin dispenser (calibrated for silica gel), followed by parallel evaporation, to dryness, in the GeneVac EZ-2 plus evaporator. The dried silica gel containing the reaction mixtures was then transferred individually to 24 PrepSep silica gel columns (500 mg) wetted with 2 mL of hexanes. The PrepSep columns containing the crude products were then washed sequentially with hexanes (20 mL), 1:1 hexanes/ether (5 mL), and EtOAc (10 mL). The EtOAc fractions were evaporated, in parallel, to dryness in a GeneVac EZ-2 plus evaporator. The products were submitted for LC/MS analyses followed by preparative LC to obtain the pure products.

3-(4′-Methyl-1,3-diphenyl-4,5-dihydropyrazole-5-carbonyl)oxazolidin-2-one 20{***1***}**.** Yield: 46%. Purity: 100%. ^{1}H NMR (400 MHz, $CDCl_3$, major isomer reported): δ 1.53 (d, J = 7.0 Hz, 3H), 3.62 (qd, J = 2.0, 7.0 Hz, 1H), 3.91−4.05 (m, 2H), 4.47−4.51 (m, 2H), 5.75 (d, J = 2.0 Hz, 1H), 6.85−6.89 (m, 1H), 7.10 (dd, J = 1.2, 8.4 Hz, 2H), 7.28−7.42 (m, 5H), 7.77 (dd, J = 1.2, 8.4, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, major isomer reported): δ 18.2, 42.7, 46.4, 63.2, 68.3, 113.0, 119.7, 126.2, 128.8, 128.9, 129.5, 131.5, 144.5, 151.4, 154.2, 169.3. HRMS Exact mass calcd for $C_{20}H_{20}N_3O_3$ [M + H]$^+$: 350.1505. Found: 350.1506.

3-(4′-(4″-Chlorophenyl)-1′,3′-diphenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***5***}**.** Yield: 59%. Purity: 99%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 3.98−4.04 (br m, 2H), 4.41−4.48 (br m, 2H), 4.57 (d, J = 2.1 Hz, 1H), 5.94 (d, J = 2.2 Hz, 1H), 6.88 (t, J = 7.4 Hz, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.17−7.37 (m, 9H), 7.63 (dd, J = 1.4, 8.0 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 42.8, 43.2, 56.5, 58.0, 62.5, 63.2, 69.4, 113.4, 113.8, 116.6, 120.0, 120.2, 126.0, 126.4, 128.1, 128.7, 129.0, 129.1, 129.2, 129.4, 129.5, 129.6, 131.3, 131.9, 134.0, 134.2, 136.4, 137.6, 143.5, 144.2, 149.5, 153.6, 153.9, 168.5, 169.9. HRMS Exact mass calcd for $C_{25}H_{21}ClN_3O_3$ [M + H]$^+$: 446.1271. Found: 446.1268.

3-(4′-Ethyl-1′-phenyl-3′-*m*-tolyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***9***}**.** Yield: 44%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 0.93 (t, J = 7.5 Hz, 3H), 1.83−2.10 (m, 2H), 2.41 (s, 3H), 3.70 (ddd, J = 2.0, 2.5, 7.7 Hz, 1H), 3.93−4.06 (m, 2H), 4.48−4.57 (m, 2H), 5.95 (d, J = 2.4 Hz, 1H), 6.86 (t, J = 7.4 Hz, 1H), 7.10 (d, J = 7.8 Hz, 2H), 7.16 (d, J = 7.5 Hz, 1H), 7.27−7.32 (m, 3H), 7.53 (d, J = 7.8 Hz, 1H), 7.65 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 9.6, 21.7, 24.7, 42.8, 52.4, 63.1, 65.3, 112.9, 119.5, 123.5, 126.9, 128.6, 129.5, 129.7, 131.8, 138.4, 144.1, 149.7, 154.1, 170.3. HRMS Exact mass calcd for $C_{22}H_{24}N_3O_3$ [M + H]$^+$: 378.1818. Found: 378.1839.

3-(4′-(4″-Nitrophenyl)-1′-phenyl-3′-*m*-tolyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***13***}**.** Yield: 47%. Purity: 99%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 2.31 (s, 3H), 3.97−4.14 (m, 2H), 4.43−4.57 (m, 2H), 4.69 (d, J = 1.9 Hz, 1H), 5.93 (d, J = 2.1 Hz, 1H), 6.91 (t, J = 7.4 Hz, 1H), 7.01−7.32 (m, 10H), 7.49 (d, J = 8.8 Hz, 2H), 7.55 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 21.6, 21.7, 42.8, 43.2, 56.4, 57.8, 62.6, 63.3, 68.9, 69.3, 113.5, 113.7, 120.3, 120.6, 123.2, 123.5, 124.5, 124.6, 126.7, 126.9, 127.9, 128.7, 129.0, 129.2, 129.4, 129.6, 130.2, 130.3, 130.9, 131.5, 138.6, 138.8, 143.3, 144.0, 145.0, 145.1, 146.2, 147.8, 147.9, 149.1, 153.8, 154.0, 167.9, 169.3. HRMS Exact mass calcd for $C_{26}H_{23}N_4O_5$ [M + H]$^+$: 471.1668. Found: 471.1664.

3-(3′-(3″-Chlorophenyl)-1′,4′-diphenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***17***}**.** Yield: 32%. Purity: 99%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 3.99−4.11 (m, 2H), 4.46−4.57 (m, 2H), 4.59 (d, J = 2.3 Hz, 1H), 6.06 (d, J = 2.3 Hz, 1H), 6.92 (t, J = 7.4 Hz, 1H), 7.16 (d, J = 7.8 Hz, 2H), 7.19−7.23 (m, 2H), 7.27−7.36 (m, 7H), 7.48 (dt, J = 1.8, 6.8 Hz, 1H), 7.74 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 42.8, 43.2, 57.1, 57.9, 62.5, 63.1, 69.6, 70.4, 113.5, 113.9, 120.1, 120.4, 124.0, 124.5, 125.9, 126.3, 126.5, 128.0, 128.4, 128.5, 128.6, 128.8, 129.2, 129.3, 129.4, 129.6, 129.9, 133.5, 134.0, 134.1, 134.6, 135.0, 137.5, 138.8, 143.0, 143.4, 144.0, 148.5, 153.6, 153.7, 168.8, 170.1. HRMS Exact mass calcd for $C_{25}H_{21}ClN_3O_3$ [M + H]$^+$: 446.1271. Found: 446.1288.

3-(3′-(3″-Chlorophenyl)-4′-(2″-methoxyphenyl)-1′-phenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***21***}**.** Yield: 46%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 3.92 (s, 3H), 4.02−4.06 (m, 2H), 4.43−4.49 (m, 2H), 5.14 (d, J = 3.5 Hz, 1H), 6.13 (d, J = 3.5 Hz, 1H), 6.81 (t, J = 7.2 Hz, 1H), 6.87 (t, J = 7.4 Hz, 1H), 6.93 (d, J = 8.0 Hz, 1H), 6.99 (dd, J = 1.6, 7.6 Hz, 1H), 7.07−7.31 (m, 7H), 7.45−7.50 (m, 1H), 7.73 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 42.9, 43.3, 49.6, 55.4, 55.8, 56.7, 62.3, 62.9, 65.8, 68.3, 110.8, 111.0, 113.2, 113.8, 119.9, 120.1, 121.3, 121.7, 123.9, 124.4, 126.0, 126.3, 126.5, 126.9, 127.3, 128.0, 128.5, 128.7, 129.2, 129.4, 129.5, 129.6, 129.8, 130.2, 133.6, 134.0, 134.5, 135.0, 143.5, 143.8, 143.9, 148.2, 153.3, 153.4, 155.9, 156.0, 170.1, 171.4. HRMS Exact mass calcd for $C_{26}H_{23}ClN_3O_4$ [M + H]$^+$: 476.1377. Found: 476.1356.

3-(3′,4′-bis(4″-Fluorophenyl)-1′-phenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 20{***25***}**.** Yield: 51%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 3.95−4.10 (m, 2H), 4.38−4.52 (m, 2H), 4.55 (d, J = 2.1 Hz, 1H), 5.94 (d, J = 2.2 Hz, 1H), 6.87 (t, J = 7.3 Hz, 1H), 6.93−7.30 (m, 10H), 7.58−7.67 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 42.8, 43.2, 56.5, 58.3, 62.5, 63.2, 69.5, 69.6, 113.3, 113.8, 115.8 (d, J = 21.9 Hz), 116.1 (d, J = 22.1 Hz), 116.2 (d, J = 21.8 Hz), 116.3 (d, J = 22.1 Hz), 120.0, 120.3, 127.69, 127.72 127.8 (d, J = 8.2 Hz), 128.2 (d, J = 8.2 Hz), 128.3 (d, J = 8.3 Hz), 129.2, 129.6, 129.8 (d, J = 8.2 Hz), 133.3 (d, J = 3.1 Hz), 134.8 (d, J = 3.0 Hz), 143.5, 143.6, 144.2, 148.9,

153.6, 153.8, 162.6 (d, J = 249.8 Hz), 163.1 (d, J = 246.7 Hz), 168.7, 169.9. HRMS Exact mass calcd for $C_{25}H_{20}F_2N_3O_4$ $[M + H]^+$: 448.1473. Found: 448.1459.

3-(1′-(4″-Bromophenyl)-4′-ethyl-3′-phenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*2*}. Yield: 57%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 0.92 (t, J = 7.5 Hz, 3H), 1.83−2.11 (m, 2H), 3.71 (ddd, J = 2.4, 4.3, 5.6 Hz, 1H), 3.95−4.08 (m, 2H), 4.49−4.57 (m, 2H), 5.91 (d, J = 2.4 Hz, 1H), 6.96−6.99 (m, 2H), 7.34−7.42 (m, 5H), 7.75−7.77 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 9.6, 24.6, 42.8, 52.6, 63.1, 65.4, 111.6, 114.5, 126.4, 128.8, 129.1, 131.6, 132.3, 143.2, 150.3, 154.0, 169.7. HRMS Exact mass calcd for $C_{21}H_{21}BrN_3O_3$ $[M + H]^+$: 442.0766. Found: 442.0754.

3-(1′-(4″-Bromophenyl)-4′-(4″-nitrophenyl)-3′-phenyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*6*}. Yield: 49%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 4.02−4.16 (m, 2H), 4.49−4.62 (m, 2H), 4.74 (d, J = 2.1 Hz, 1H), 5.93 (d, J = 2.1 Hz, 1H), 7.02−7.05 (m, 2H), 7.27−7.32 (m, 4H), 7.36−7.53 (m, 3H), 7.62−7.65 (m, 2H), 8.17−8.21 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 42.8, 43.2, 56.6, 57.9, 62.6, 63.4, 68.9, 69.4, 112.6, 112.7, 115.2, 115.3, 124.5, 124.7, 126.1, 126.4, 127.8, 128.9, 129.1, 129.2, 129.6, 129.7, 130.6, 131.2, 132.2, 132.4, 142.2, 143.2, 144.7, 145.5, 145.6, 147.8, 148.0, 149.7, 153.7, 154.0, 167.6, 169.1. HRMS Exact mass calcd for $C_{25}H_{20}BrN_4O_5$ $[M + H]^+$: 535.0617. Found: 535.0626.

3-(1′-(4″-Bromophenyl)-4′-phenyl-3′-*m*-tolyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*10*}. Yield: 46%. Purity: 96%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 2.33 (s, 3H), 4.00−4.14 (m, 2H), 4.44−4.58 (m, 2H), 4.63 (d, J = 2.2 Hz, 1H), 5.98 (d, J = 2.2 Hz, 1H), 7.02−7.05 (m, 2H), 7.08 (d, J = 7.6 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H), 7.25−7.40 (m, 6H), 7.41−7.63 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 21.6, 21.7, 42.8, 43.2, 57.5, 58.3, 62.4, 63.2, 69.4, 70.1, 111.8, 112.0, 115.0, 115.4, 123.3, 123.8, 126.5, 126.8, 127.1, 128.0, 128.3, 128.5, 128.6, 128.9, 129.3, 129.4, 130.0, 130.2, 131.2, 131.6, 131.9, 132.3, 137.7, 138.3, 138.6, 138.7, 142.8, 143.6, 145.5, 150.8, 153.5, 153.7, 168.7, 170.2. HRMS Exact mass calcd for $C_{26}H_{23}BrN_3O_3$ $[M + H]^+$: 504.0923. Found: 504.0931.

3-(1′-(4″-Bromophenyl)-4′-(2″-methoxyphenyl)-3′-*m*-tolyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*14*}. Yield: 49%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 2.33 (s, 3H), 3.94 (s, 3H), 4.07−4.10 (m, 2H), 4.49−4.56 (m, 2H), 5.20 (d, J = 3.3 Hz, 1H), 6.09 (d, J = 3.3 Hz, 1H), 6.83 (td, J = 0.8, 7.6 Hz, 1H), 6.95 (d, J = 7.9 Hz, 1H), 7.01−7.04 (m, 3H), 7.08 (d, J = 7.4 Hz, 1H), 7.15 (t, J = 7.7 Hz, 1H), 7.23−7.31 (m, 2H), 7.36−7.40 (m, 2H), 7.64 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 21.6, 43.0, 50.2, 55.8, 62.9, 68.1, 110.9, 111.8, 114.8, 121.6, 123.8, 127.0, 127.1, 128.0, 128.5, 129.4, 129.8, 131.4, 132.3, 138.2, 143.4, 150.4, 153.3, 155.9, 170.2. HRMS Exact mass calcd for $C_{27}H_{25}BrN_3O_4$ $[M + H]^+$: 534.1028. Found: 534.1024.

3-(1′-(4″-Bromophenyl)-3′-(3″-chlorophenyl-4′-(4″-fluorophenyl)-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*18*}. Yield: 53%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 4.02−4.16 (m, 2H), 4.52−4.61 (m, 2H), 4.59 (d, J = 2.2 Hz, 1H), 5.95 (d, J = 2.2 Hz, 1H), 7.01−7.08 (m, 4H), 7.20−7.34 (m, 4H), 7.39−7.42 (m, 2H), 7.45 (dt, J = 1.5, 7.4 Hz, 1H), 7.70 (d, J = 1.7 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 42.8, 56.4, 63.3, 69.7, 112.8, 115.2, 116.4 (d, J = 21.8 Hz), 124.5, 126.4, 129.1, 129.7 (d, J = 8.3 Hz), 130.0, 132.4, 132.9 (d, J = 3.4 Hz), 133.0, 134.8, 143.2, 149.1, 153.8, 162.8 (d, J = 247.2 Hz), 168.2. HRMS Exact mass calcd for $C_{25}H_{19}BrClFN_3O_3$ $[M + H]^+$: 542.0282. Found: 542.0270.

3-(1′-(4″-Bromophenyl)-3′-(4′-fluorophenyl)-4′-methyl-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*22*}. Yield: 72%. Purity: 99%. ^{1}H NMR (400 MHz, $CDCl_3$, major isomer reported): δ 1.51 (d, J = 7.5 Hz, 3H), 3.61 (q, J = 7.0 Hz, 1H), 3.92−4.06 (m, 2H), 4.48−4.54 (m, 2H), 5.70 (s, 1H), 6.96 (d, J = 7.9 Hz, 2H), 7.07−7.11 (m, 2H), 7.37 (d, J = 7.8 Hz, 2H), 7.72−7.75 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$, major isomer reported): δ 18.0, 42.6, 46.7, 63.2, 68.3, 111.7, 114.6, 115.9 (d, J = 21.9 Hz), 127.4 (d, J = 3.3 Hz), 128.1 (d, J = 8.2 Hz), 132.2, 143.7, 151.2, 154.1, 163.3, (d, J = 249.6 Hz), 169.0. HRMS Exact mass calcd for $C_{26}H_{23}BrN_3O_3$ $[M + H]^+$: 446.0516. Found: 446.0496.

3-(1′-(4″-Bromophenyl)-4′-(4″-chlorophenyl)-3′-(4″-fluorophenyl)-4′,5′-dihydropyrazole-5′-carbonyl)oxazolidin-2-one 21{*26*}. Yield: 47%. Purity: 94%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 4.02−4.16 (m, 2H), 4.50−4.61 (m, 2H), 4.58 (d, J = 2.1 Hz, 1H), 5.93 (d, J = 2.1 Hz, 1H), 6.97−7.02 (m, 3H), 7.20−7.32 (m, 5H), 7.38−7.41 (m, 2H), 7.61−7.65 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 42.8, 56.8, 63.3, 69.5, 112.4, 115.1, 115.4, 115.9 (d, J = 22.0 Hz), 128.0, 128.3 (d, J = 8.2 Hz), 129.4, 129.6, 132.4, 134.4, 135.8, 143.4, 149.3, 153.8, 163.3, (d, J = 250.1 Hz), 168.2. HRMS Exact mass calcd for $C_{26}H_{23}BrN_3O_3$ $[M + H]^+$: 542.0282. Found: 542.0280.

General Procedure for Library 22{*1*−*24*}. A library of **20**{*1*−*24*} was obtained as described above, and the crude products were redissolved in THF (2.5 mL). An aqueous $NaBH_4$ (22.7 mg in 0.5 mL, 0.6 mmol) solution, prepared immediately prior to addition, was added to this collection of solutions. The reaction mixtures were stirred for 4 h, quenched with 2 N HCl (3.5 mL), and extracted with DCM (3 × 1 mL). The organic layers were separated using an AllTech hydrophobic frit, washed with brine (1 mL), and filtered through fritted polypropylene (Mettler) tubes containing ∼1 g of 1:1 magnesium sulfate and silica gel. The filtrates were concentrated in parallel using the GeneVac EZ-2 plus evaporator and submitted for LC-MS analyses, followed by preparative LC, to obtain the pure products.

(1′,3′,4′-Triphenyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*3*}. Yield: 55%. Purity: 98%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 1.65 (br s, 1H), 3.81−4.01 (m, 2H), 4.28 (q, J = 4.2 Hz, 1H), 4.69 (d, J = 4.2 Hz, 1H), 6.88 (t, J = 7.3 Hz, 1H), 7.19−7.32 (m, 12H), 7.67

(dd, J = 1.3, 8.2 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 55.0, 62.2, 71.6, 113.7, 119.8, 126.1, 127.6, 127.7, 128.6, 128.7, 129.4, 129.45, 129.53, 132.1, 141.0, 144.7, 150.5. HRMS Exact mass calcd for $C_{22}H_{21}N_2O$ $[M + H]^+$: 329.1654. Found: 329.1625.

(4′-Methyl-1′-phenyl-3′-*m*-tolyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*7*}. Yield: 32%. Purity: 93%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 1.32 (d, J = 7.2 Hz 3H), 1.65 (br s, 1H), 2.39 (s, 3H), 3.63 (qd, J = 3.2, 7.0 Hz 1H), 3.75−3.80 (m, 2H), 4.08 (d, J = 3.5 Hz, 1H), 6.85 (t, J = 7.2 Hz, 1H), 7.15 (d, J = 7.5 Hz, 1H), 7.21 (d, J = 8.0 Hz, 1H), 7.26−7.31 (m, 4H), 7.54 (d, J = 7.7 Hz, 1H), 7.62 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 19.1, 21.7, 43.1, 62.0, 69.4, 113.4, 119.4, 123.6, 127.0, 128.7, 129.5, 129.7, 131.9, 138.5, 145.0, 153.5. HRMS Exact mass calcd for $C_{18}H_{21}N_2O$ $[M + H]^+$: 281.1654. Found: 281.1630.

(4′-(4″-Chlorophenyl)-1′-phenyl-3′-*m*-tolyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*11*}. Yield: 71%. Purity: 99%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 1.66 (br s, 1H), 2.31 (s, 3H), 3.85−3.91 (m, 2H), 4.23 (app q, J = 4.1 Hz, 1H), 4.66 (d, J = 4.0 Hz, 1H), 6.88 (tt, J = 1.0, 7.3 Hz, 1H), 7.05−7.36 (m, 11H), 7.56 (s, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 21.65, 21.67, 54.2, 59.0, 62.0, 62.5, 66.8, 71.3, 113.2, 113.4, 113.5, 113.6, 113.9, 119.4, 119.9, 123.3, 126.7, 127.1, 127.4, 128.6, 128.9, 129.0, 129.3, 129.5, 129.56, 129.59, 129.7, 131.7, 132.0, 133.4, 133.5, 138.3, 138.7, 139.5, 140.0, 143.9, 144.5, 146.2, 150.2. HRMS Exact mass calcd for $C_{18}H_{21}N_2O$ $[M + H]^+$: 377.1421. Found: 377.1400.

(3′-(3″-Chlorophenyl)-1′,4′-diphenyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*15*}. Yield: 48%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 1.64 (br s, 1H), 3.86−3.97 (m, 2H), 4.31 (ddd, J = 3.6, 4.2, 5.0 Hz, 1H), 4.66 (d, J = 4.2 Hz, 1H), 6.90 (tt, J = 1.0, 7.3 Hz, 1H), 7.13−7.35 (m, 12H), 7.67 (dt, J = 1.7, 7.1 Hz, 1H), 7.75 (d, J = 1.9 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 54.7, 58.7, 62.1, 62.5, 67.7, 71.6, 113.4, 113.7, 119.6, 120.1, 124.0, 124.7, 125.8, 125.9, 126.4, 127.6, 127.8, 127.9, 128.5, 129.2, 129.3, 129.4, 129.56, 129.59, 129.8, 130.2, 134.0, 134.2, 134.6, 135.0, 140.6, 141.1, 143.7, 144.3, 144.5, 149.0. HRMS Exact mass calcd for $C_{22}H_{20}ClN_2O$ $[M + H]^+$: 363.1264. Found: 363.1240.

(4′-Ethyl-3′-(4″-fluorophenyl)-1′-phenyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*20*}. Yield: 48%. Purity: 96%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 0.91 (t, J = 7.5 Hz, 3H), 1.55−1.79 (br m, 3H), 3.51 (dt, J = 3.3, 8.3 Hz, 1H), 3.73−3.86 (m, 2H), 4.18 (dt, J = 3.6, 5.1 Hz, 1H), 6.85 (t, J = 7.3 Hz, 1H), 7.06−7.31 (m, 6H), 7.73−7.76 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, major isomer reported): δ 10.5, 24.7, 49.8, 62.5, 66.4, 113.0, 115.7 (d, J = 21.8 Hz), 119.2, 128.0 (d, J = 8.1 Hz), 128.3 (d, J = 3.3 Hz), 129.3, 144.6, 150.8, 163.0, (d, J = 248.9 Hz). HRMS Exact mass calcd for $C_{18}H_{20}FN_2O$ $[M + H]^+$: 299.1560. Found: 299.1532.

(3′-(4″-Fluorophenyl)-4′-(2″-methoxyphenyl)-1′-phenyl-4′,5′-dihydropyrazol-5′-yl)methanol 22{*24*}. Yield: 44%. Purity: 100%. ^{1}H NMR (500 MHz, $CDCl_3$, major isomer reported): δ 1.92 (br s, 1H), 3.81−3.99 (m, 2H), 3.89 (s, 3H), 4.23 (app q, J = 4.6 Hz, 1H), 6.78−7.07 (m, 5H), 7.18−7.30 (m, 6H), 7.62−7.66 (m, 2H). ^{13}C NMR (125 MHz, $CDCl_3$, both isomers reported): δ 48.4, 55.8, 55.9, 58.5, 62.5, 63.0, 63.5, 71.3, 110.9, 111.0, 113.0, 113.5, 115.7 (d, J = 21.9 Hz), 116.0 (d, J = 21.8 Hz), 119.1, 119.7, 121.6, 126.8, 127.9 (d, J = 8.2 Hz), 128.3 (d, J = 8.3 Hz), 128.4, (d, J = 3.4 Hz), 128.5 (d, J = 3.0 Hz), 128.85, 128.90, 128.95, 129.2, 129.4, 129.5, 143.8, 144.9, 145.6, 149.4, 155.8, 156.1, 163.3, (d, J = 249.0 Hz). HRMS Exact mass calcd for $C_{23}H_{22}FN_2O_2$ $[M + H]^+$: 377.1665. Found: 377.1638.

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Supporting Information Available. Characterization data for new compounds, LC traces, ^{1}H and ^{13}C NMR for library members, and ADME property table. This material is available free of charge via the Internet at http://pubs.acs.org.

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