Synthesis of Spiro Pyrazolone-Oxindole and Bicyclic Pyrazolone Derivatives via Solvent-Dependent Regioselective Aza-1,4/1,6-Michael and Intramolecular Cycloaddition under Catalyst-Free Conditions

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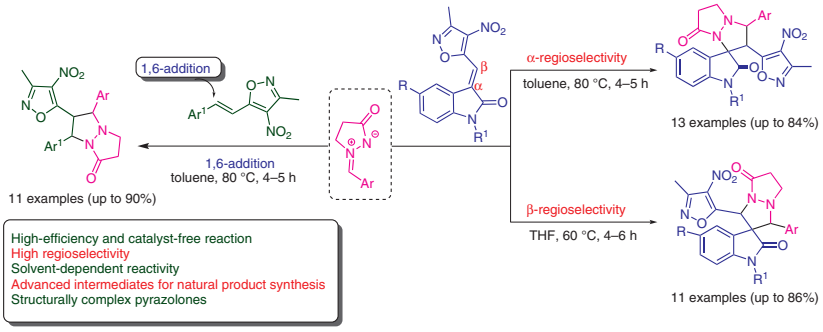

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Abstract A solvent-dependent, highly regioselective [3+2]-cycloaddition reaction of isoxazole-styrenes and azomethine imines under catalyst-free conditions is reported, furnishing a library of pyrazolone–spirooxindole hybrids. Good regioselectivity for the isomeric structures was achieved by the reaction of isoxazole-styrene and azomethine imine in different solvents and temperatures. The developed method was extended for the synthesis of tri-substituted dinitrogen-fused pyrazolones by using a 1,6-Michael addition reaction. Furthermore, the isoxazole moiety was converted into a carboxylic acid as a model study via ring opening.

Key words spirooxindole-pyrazolone hybrids, bicyclic pyrazolones, isoxazole-styrenes, switchable 1,3-dipolar cycloaddition, solvent-dependent reactivity, catalyst-free conditions

Spirooxindoles are structurally complex molecules with a quaternary carbon at C-3 of the indole nucleus, joined by multiply substituted five-membered pyrrolidine rings with defined stereocenters. The spirooxindole skeleton is present in many natural products such as spirotryptostatins, rhynchophyllines, horsfiline, and (+)-elacomines, and members of this class show a wide range of biological properties. Due to their structural complexity and biological prominence, these compounds have attracted the attention of synthetic chemists. As a result, many methods have been developed over the years for their synthesis. The [3+2]-cycloaddition and tandem (one-pot), multicomponent reactions of isatin or its derivatives in the presence of metal-based and organocatalysis are some of the common methods employed.[1a–c] In many cases, the synthesized compounds were tested for biological activity and, as a result, this moiety has become a promising scaffold in drug discovery.[1d]

Pyrazolones (pyrazole-5-ones) represent another useful scaffold commonly found in many biologically active molecules. Derivatives of pyrazolones such as morazone, phenazone, phenylbutazone (NSAIDs), tartrazine (anticancer) phenidone, and BW357U (anorectic) are sold as commercial drugs.[2] Acyl substituted pyrazolones can undergo isomerization (proton exchange) and keto–enol tautomerism. These features make them useful synthons in organic chemistry for electrophilic and nucleophilic addition reactions.[3] Reports on N,N′-fused bicyclic pyrazolones are rare. They have been reported as γ-lactam antibiotics, antibacterial agents,[4a,b] acetyl-CoA carboxylase (ACC) inhibitors,[4c] sarcoplasmic reticulum Ca^{+2}-ATPase inhibitors,[4d] and anticancer agents,[4e] and they have also been used as herbicides and pesticides (Figure 1).[5]

The development of a regioselective method to access these derivatives is highly desirable, particularly one that allows the generation of complex molecules with structural diversity.[6a] In this context, domino-cascade, cycloaddition and chelation controlled reactions have proven to be efficient in the presence of Lewis acids,[6b] organocatalysts,[6c,d] metal catalysts,[6e] and in various solvents.[6f,g]

Nitrones, *N*-imides and pyridinium ylides are useful intermediates for the synthesis of functionalized pyrrolidines, dihydrooxazoles, and isoxazoles via 1,3-dipolar cycloaddition reactions (Michael addition, followed by Mannich type cyclization).[7] In particular, azomethine imines (acyclic and

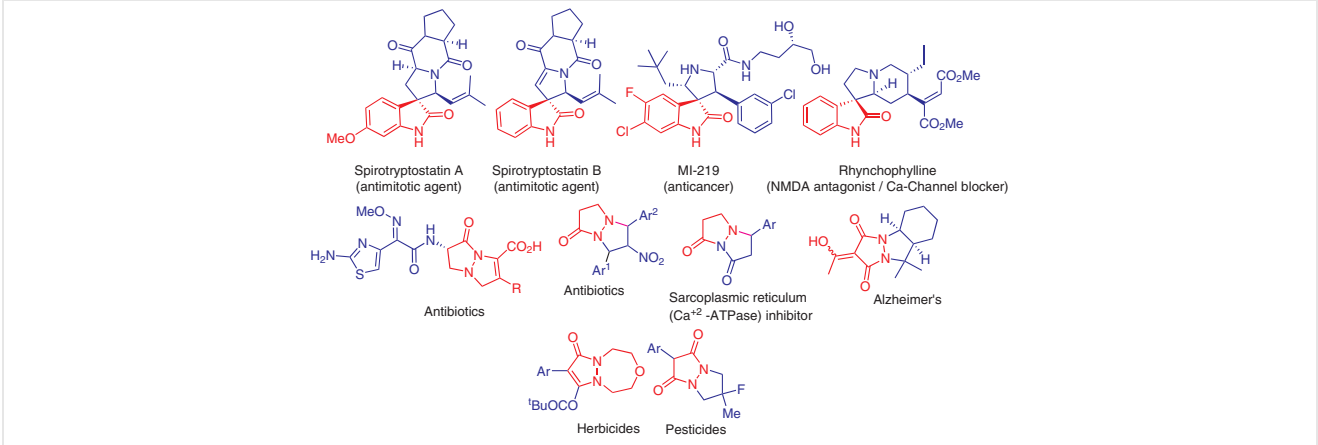
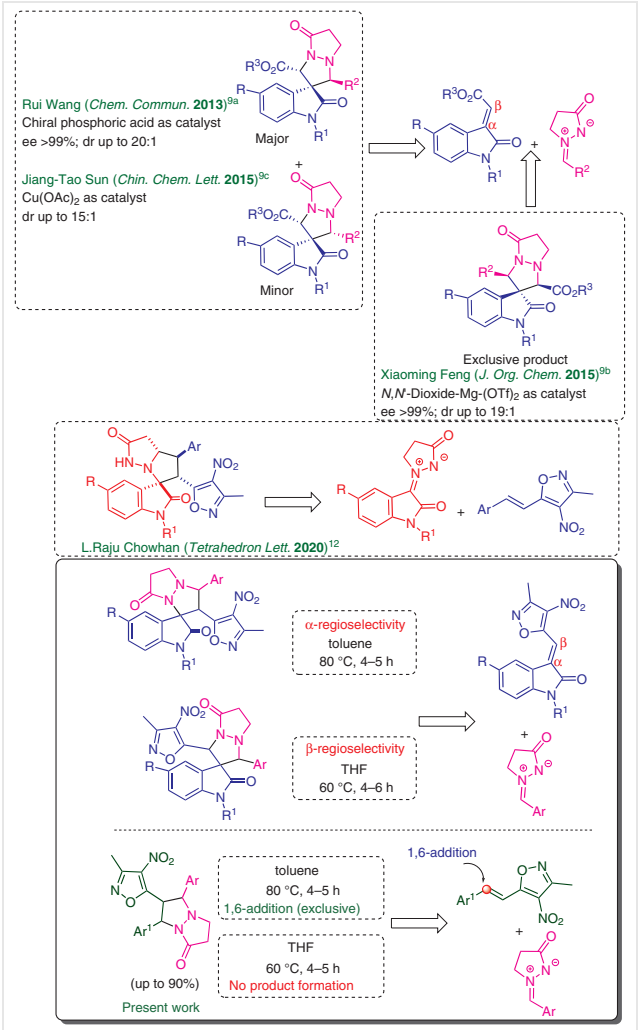


Figure 1 Representative biologically important spirooxindoles and pyrazolidinones

N,N′-cyclic) have been used as 1,3-dipoles for [3+2]-cycloaddition reactions[4a,8] to give complex spirooxindole derivatives. In this connection, spiro[pyrazolidin-3,3′-oxindoles] have been obtained by [3+2]-cycloaddition reaction (β-regioselective 1,4-aza Michael addition and intramolecular cyclization) of azomethine imines and methyleneindolinones in the presence of chiral bis-phosphoric acid,[9a] *N*,*N*′-dioxide–Mg(OTf)$_2$,[9b] or Cu(OAc)$_2$[9c] as catalysts with high enantioselectivity. In a similar approach, Yan and co-workers reported a catalyst-free method for generating spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazoles] using 3-phenacyliceneoxindoles.[9d]

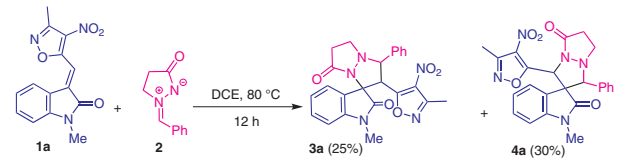
3-Methyl-4-nitro-5-isatylidenyl-isoxazole (**1**)[10a] represents an excellent precursor for our studies, having two reactive cites at the α- and β-positions to the unsaturated double bond, as shown in Scheme 1. This feature has been applied for use as a dipolarophile for the construction of functionalized 3,3-disubstituted oxindoles and spirocyclic oxindoles (via tandem Michael addition and aldol/Mannich reactions)[10b–f] to give the desired products in good yields with excellent regio- and/or stereoselectivity. In a similar study, Liu and co-workers synthesized isoxazole-dispirobisoxindole and bispirocyclic hexahydroxanthones via β-regioselective [3+2]-cycloaddition and domino Michael–Michael addition reactions using quinine and chiral thioureas as organocatalysts.[11] In a recent report, Chowhan and co-workers demonstrated an unusual C-N-C [3+2]-cycloaddition of 3-methyl-4-nitro-5-styrylisoxazole and isatin N,N′-cyclic azomethine imines with high diastereoselectivity.[12] All these methods have their own advantages in terms of regioselectivity, stereoselectivity and product yields. However, a switchable regioselective reaction has never been realized on 3-methyl-4-nitro-5-isatylidenyl-isoxazole (**1**). Considering the importance of spiro- and bicyclic pyrazolones, we herein report the first example of a solvent-dependent, regioselective-switchable reaction between N,N′-



Scheme 1 Reactivity profile of isoxazole-styrenes: reported methods and current strategy

cyclic azomethine imines and 3-methyl-4-nitro-5-isatylidenyl-isoxazoles leading to complex dinitrogen-fused bicyclic and spirocyclic oxindoles in good yields.

Towards the synthesis of functionalized spirooxindole derivatives, we utilized 3-methyl-4-nitro-5-isatylidenyl-isoxazole (**1a**) and azomethine imine (**2**) as model substrates in dichloromethane (DCM), both in the presence of organic bases (TEA and DABCO) and Lewis acids ($Zn(OTf)_3$, $AlCl_3$) at room temperature and heating (25–60 °C), but these conditions did not yield the expected products (Table 1; entries 1–5). The same reaction was then performed in 1,2-dichloroethane (DCE) at 80 °C for 12 h under catalyst-free conditions. To our satisfaction, the formation of products **3a** and **4a** was observed in 25 and 30% yield, respectively (Scheme 2 and Table 1, entry 6).

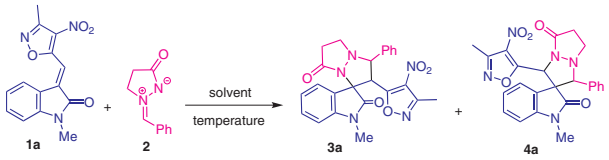


Scheme 2 Synthesis of dinitrogen-fused spirooxindoles

Encouraged by this result, the reaction was carried out in different solvents under catalyst-free conditions; the results are summarized in Table 1 (entries 7–26). It is important to note that the use of polar solvents (DMSO, DMF, MeCN, MeOH, EtOH and water) did not give the products even at elevated temperature. Even for the chlorinated solvents, the overall yield of products **3a** and **4a** could not be related to their boiling points and relative polarity [CH_2Cl_2 (no product), DCE (55%) and $CHCl_3$ (60%)]. At this point, the use of other common solvents such as toluene, xylene, ethyl acetate, diethyl ether and tetrahydrofuran (from non-polar to moderately polar) were examined at temperatures between 40 and 80 °C (without the catalyst). Surprisingly, the reaction in toluene and xylene at 80 °C gave **3a** in 84 and 70% yield, respectively, as major products, along with **4a** in 5–10% yield as the minor regioisomer (Table 1, entries 14 and 15). On the other hand, reaction in tetrahydrofuran at 60 °C, gave a contrasting outcome, with **4a** formed as the major product (75%) and **3a** as the minor product (15%) for 4 h (Table 1, entry 21). Both the isomers were characterized by ^1H and ^{13}C NMR spectroscopic and mass spectrometric analyses. The ^1H NMR spectrum of compound **3a** in $CDCl_3$ included two doublets at δ = 5.05 (d, *J* = 10.8 Hz) and 4.49 (d, *J* = 10.8 Hz) ppm, indicating that the phenyl and isoxazole ring protons are on adjacent carbons (Figure 1 in the Supporting Information); whereas for **4a** the two characteristic protons appeared as singlets at δ = 5.97 and 4.12 ppm due to the phenyl and isoxazole rings being separated. The observed HRMS mass ion of **3a** (*m*/*z* 460.1614 [M+1]) and of **4a** (*m*/*z* 460.1591 [M+1]) further confirmed the formation of the desired products.

At this juncture, we attempted to understand the solvent effect on the outcome of the reaction. Towards this, different combinations of toluene and tetrahydrofuran were studied (Table 1, entries 22–26). From these observations, we suggest that the polar chelating nature of the tetrahydrofuran helps to increase the electron density on the α-carbon of isoxazole-oxindole styrene, which facilitates attack of negatively charged nitrogen of the azomethine imine **2** to deliver product **4a** as the major isomer.

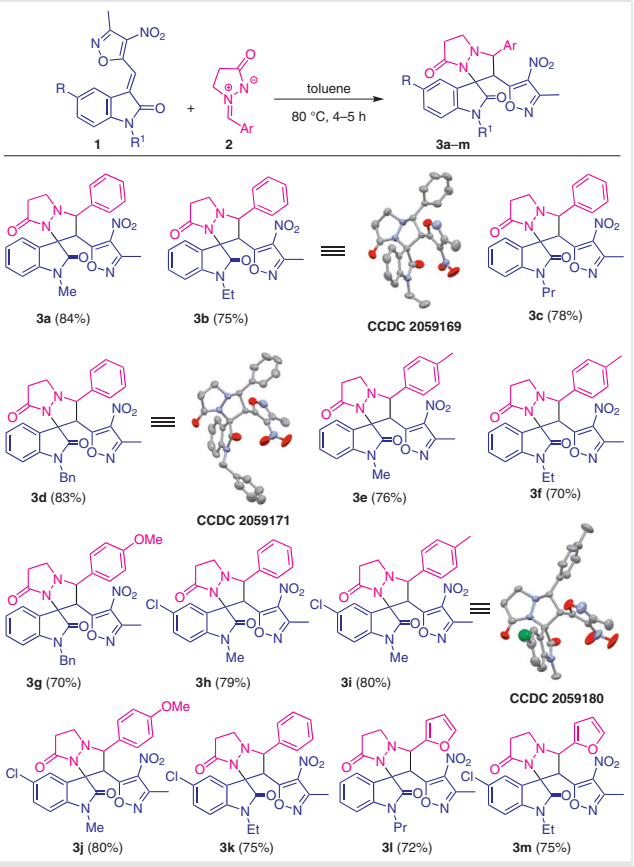
Table 1 Optimization of Reaction Conditions[a]



Entry	Solvent	Cat. (20 mol%)	Temp (°C)	Time (h)	Yield (%)[b]	
					3a	**4a**
1	CH_2Cl_2	TEA	rt	12	ND	ND
2	CH_2Cl_2	DABCO	rt	12	ND	ND
3	CH_2Cl_2	$Zn(OTf)_3$	rt	12	ND	ND
4	CH_2Cl_2	$AlCl_3$	rt	12	ND	ND
5	CH_2Cl_2	–	60	12	ND	ND
6	DCE	–	80	12	25	30
7	$CHCl_3$	–	60	12	15	45
8	DMSO	–	80	12	ND	ND
9	DMF	–	80	12	ND	ND
10	CH_3CN	–	80	12	ND	trace
11	MeOH	–	80	12	ND	ND
12	EtOH	–	80	12	ND	ND
13	H_2O	–	80	12	ND	ND
14	**toluene**	**–**	**80**	**4**	**84**	**10**
15	xylene	–	80	4	70	5
16	toluene	–	rt	24	trace	ND
17	EtOAc	–	80	12	ND	ND
18	Et_2O	–	40	4	ND	ND
19	THF	–	80	12	20	60
20	THF	–	rt	48	ND	60
21	**THF**	**–**	**60**	**4**	**15**	**75**
22	THF/Tol (1:1)	–	80	4	45	30
23	THF/Tol (1:2)	–	80	4	55	20
24	THF/Tol (1:3)	–	80	4	60	15
25	THF/Tol (2:1)	–	80	4	30	40
26	THF/Tol (3:1)	–	80	4	25	55

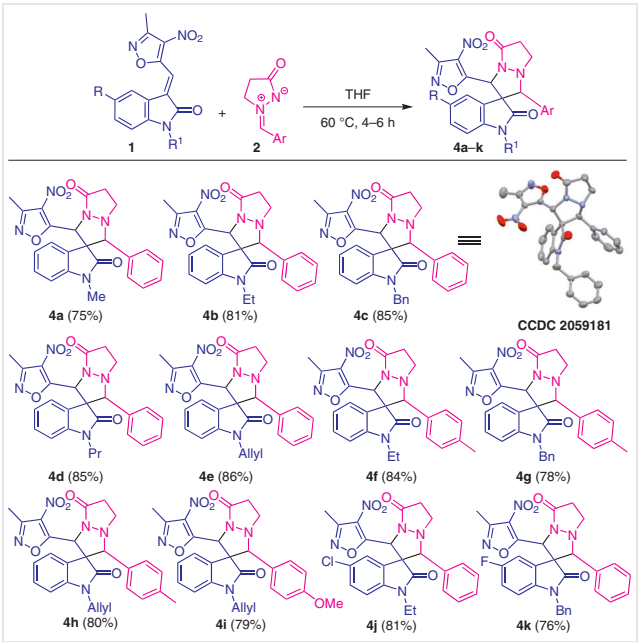
[a] All reactions were performed with **1a** (0.35 mmol) and **2** (0.35 mmol) in solvent (4 mL).
[b] Isolated yields.

After identifying the two optimal reaction conditions, we turned our attention towards the substrate scope of the reactions. Accordingly, variously substituted isatins (substitution on aromatic ring and nitrogen) and azomethine imines (aromatic and heteroaromatic) were reacted under the optimized conditions (both in toluene and THF) to afford the corresponding cycloaddition products **3a–m** (Scheme 3) and **4a–k** (Scheme 4) in good yields 70–86% in 4–6 h. All newly synthesized compounds were characterized using ^{1}H, ^{13}C NMR spectroscopy and mass spectrometry. Furthermore, single-crystal X-ray crystallographic data were obtained for compounds **3b**, **3d**, **3i** and **4c**, clearly indicating that the isoxazole and phenyl groups are adjacent to each other in products in Scheme 3; whereas in the products in Scheme 4, the rings were assigned opposite each other.

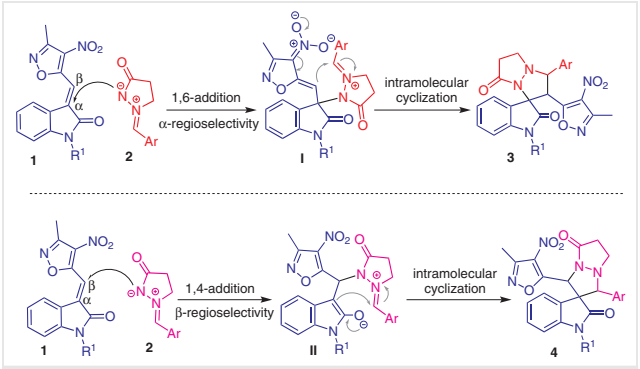


Scheme 3 Substrate scope for the synthesis of functionalized dinitrogen-fused spirooxindoles **3a–m**

Based on above results and on single-crystal data, a plausible mechanism can be proposed for the [3+2]-cycloaddition reaction (Scheme 5). Azomethine imine **2** reacts with 3-methyl-4-nitro-5-isatylidenyl-isoxazole **1** via aza-1,6 Michael addition (α-regioselectivity) to give adduct **I**. This adduct can undergo intramolecular cyclization to afford desired product **3**; in contrast, in THF the same reaction proceeds through aza-1,4 Michael addition (β-regioselectivity) followed by intramolecular cyclization to deliver product **4**.



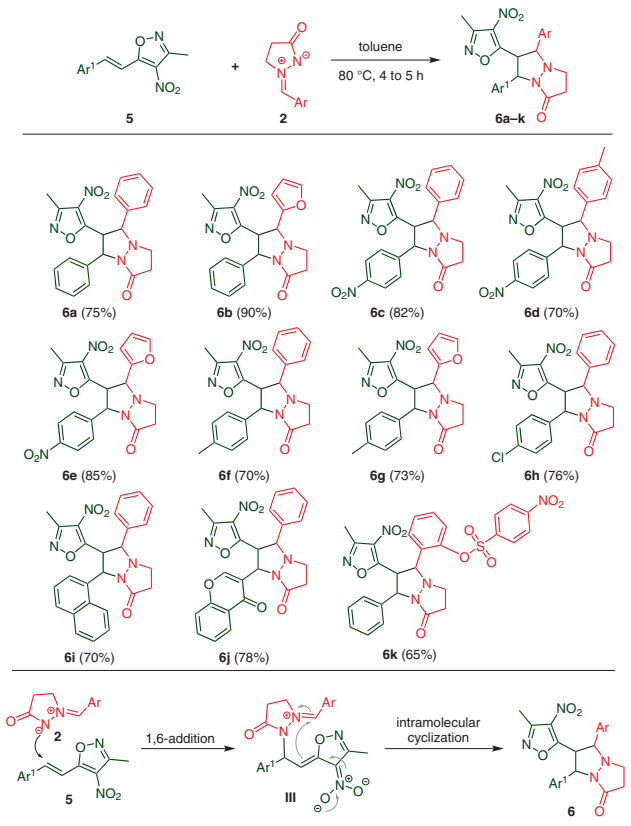
Scheme 4 Substrate scope for the synthesis of functionalized dinitrogen-fused spirooxindoles **4a–k**



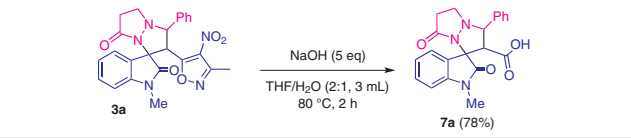
Scheme 5 Proposed mechanism for the two cycloaddition pathways

Considering the biological importance of spirooxindoles, isoxazoles and pyrazolones (Figure 1), we extended our strategy to the synthesis of diphenyltetrahydropyrazolo pyrazolones (dinitrogen-fused heterocycles). To achieve this, isoxazole-styrenes **5** were treated with azomethine imines **2** under the optimized reaction conditions (in toluene and THF). To our surprise, the reaction was successful only in toluene, delivering isoxazole-based dinitrogen-fused compounds **6a–k** in good yields of 65–90% in 4–5 hours (Scheme 6). Similar to the above mechanism, in this case the desired compounds **6** were also formed by the reaction of isoxazole styrene **5** with azomethine imine **2** to afford adduct **III** via aza-1,6-Michael addition followed by

intramolecular cyclization. The isoxazole moiety was also used as a masked ester to generate carboxylic acid via ring opening under basic-oxidative conditions.[13] Finally the cycloadducts **3a** and **6b** were converted into carboxylic acids **7a** and **8b** in 78 and 85% yield, respectively, by treatment with aq. NaOH (Scheme 7 and Scheme 8). The carboxylic acid **8b** was then further functionalized into ester **9b** and amide **10b** derivatives in 65 and 85% yield, respectively, under the standard conditions (Scheme 8).

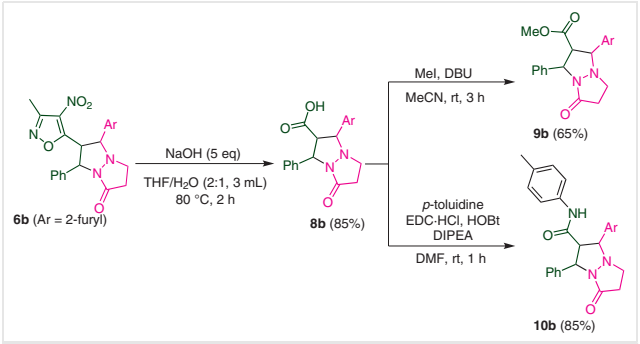


Scheme 6 Substrate scope for the synthesis of functionalized N,N'-fused bicyclic pyrazolones and possible mechanism for the reaction



Scheme 7 Synthesis of spirooxindole-pyrazolone carboxylic acid derivative **7a**

In summary, we have demonstrated a simple and catalyst-free [3+2]-cycloaddition reaction for the synthesis of dinitrogen-fused pyrazolone derivatives with moderate to good yields. The reaction proceeds via aza-1,4/1,6-Michael addition of azomethine imines onto a conjugated system followed by intramolecular cyclization. The generated dinitrogen-fused heterocyclic compounds **3a** and **6b** were converted into pyrazolone-based carboxylic acids by hydrolysis of the isoxazole ring. The carboxylic acid can be used as a starting point for the construction of hybrid molecules using esterification or amide bond formation, as shown in Scheme 8.



Scheme 8 Functionalization of pyrazolo pyrazolone **6b**

All the solvents and required chemicals were procured from SD-Fine, Sigma–Aldrich, and Spectrochem, and used without purification and distillation. ^{1}H and ^{13}C NMR spectra were recorded with Bruker Avance 400 or 500 MHz spectrometers using $CDCl_3$ or DMSO-d_6 as solvents and are reported in δ units (ppm). Mass spectra of all the compounds were record with an Agilent Technologies-6530 spectrometer.

[3+2] Cycloaddition Reaction; General Procedure

To a solution of isoxazole-styrene **1** or **5** (0.35 mmol, 1 equiv) in THF/toluene (4 mL) was added azomethine imine **2** (0.35 mmol, 1 equiv) and the contents were heated at reflux (Table 1) for 4–6 h. After completion of reaction (monitored by TLC) the mixture was cooled to r.t., solvent was evaporated, and the crude product was purified by silica gel column chromatography. Elution of the column with hexane/EtOAc (40–50%) gave the desired products **3**, **4**, and **6**.

Synthesis of Pyrazolopyrazole Carboxylic Acids; General Procedure

To a solution of cyclic adduct **3a** or **6b** (0.25 mmol, 1 equiv) in THF (2 mL) was added aq. NaOH [1.25 mmol, 5 equiv] and the resulting mixture was heated at reflux for 2 h. After completion of the reaction (monitored by TLC), the reaction was quenched with 2 M HCl at 0 °C. The mixture was extracted with EtOAc (3 × 10 mL), and the combined organic layers were dried using sodium sulfate, filtered, and evaporation of the solvent under reduced pressure gave the crude product, which was purified by silica gel column chromatography (hexane/EtOAc) to give the desired products **7a** or **8b** as white solids.

Synthesis of Methyl 1-(Furan-2-yl)-5-oxo-3-phenylhexahydropyrazolo[1,2-*a*]pyrazole-2-carboxylate (9b)

To a solution of carboxylic acid **8b** (0.32 mmol, 1 equiv) MeCN (3 mL) was added DBU (0.32 mmol, 1 equiv) and MeI (0.38 mmol, 1.2 equiv). The reaction mixture was stirred at r.t. for 3 h, then the crude product was purified over silica gel by column chromatography to afford the desired product **9b**.

Synthesis of 1-(Furan-2-yl)-5-oxo-3-phenyl-*N*-(*p*-tolyl)hexahydropyrazolo[1,2-*a*]pyrazole-2-carboxamide (10b)

To a solution of acid **8b** (0.32 mmol, 1 equiv) in DMF (3 mL) was added DIPEA (0.96 mmol, 3 equiv). The mixture was cooled to 0 °C and treated with EDC·HCl (0.64 mmol, 2 equiv), HOBt (0.64 mmol, 2 equiv) and the amine (0.38 mmol, 1.2 equiv). The reaction mixture was then stirred at r.t. for 1 h. After completion, the mixture was diluted with H_2O (15 mL) and extracted with EtOAc (15 mL). The organic layer was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The resulting material was purified by silica gel column chromatography to provide the final product **10b** as a white solid.

1-Methyl-2′-(3-Methyl-4-nitroisoxazol-5-yl)-3′-phenyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3a)

Yield: 134 mg (84%); yellow solid; mp 183–185 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (dd, *J* = 8.0, 1.6 Hz, 2 H), 7.34–7.27 (m, 3 H), 7.16 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.04 (dd, *J* = 7.2, 0.8 Hz, 1 H), 6.89–6.82 (m, 1 H), 6.69 (d, *J* = 8.0 Hz, 1 H), 5.05 (d, *J* = 10.8 Hz, 1 H), 4.49 (d, *J* = 10.8 Hz, 1 H), 3.55–3.48 (m, 1 H), 3.17 (s, 3 H), 2.99–2.80 (m, 2 H), 2.64–2.57 (m, 1 H), 2.20 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.89, 167.35, 163.10, 155.70, 144.12, 133.83, 131.04, 130.76, 129.43, 129.18, 128.19, 124.08, 122.73, 122.01, 108.98, 70.96, 64.18, 59.54, 51.09, 36.15, 26.95, 11.17.

MS (ESI): *m*/*z* calcd for $C_{24}H_{21}N_5O_5$: 459.1543; found: 460.1614 [M + 1].

1-Ethyl-2′-(3-Methyl-4-nitroisoxazol-5-yl)-3′-phenyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3b)

Yield: 120 mg (75%); white solid; mp 168–170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.0 Hz, 2 H), 7.27–7.14 (m, 4 H), 7.15 (d, *J* = 7.4 Hz, 1 H), 6.94 (t, *J* = 7.6 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 5.18 (d, *J* = 10.8 Hz, 1 H), 4.56 (d, *J* = 10.8 Hz, 1 H), 3.93–3.68 (m, 2 H), 3.58 (t, *J* = 8.0 Hz, 1 H), 2.97 (m 2 H), 2.73–2.62 (m, 1 H), 2.35 (s, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.03, 166.93, 163.18, 155.75, 142.05, 133.57, 131.12, 130.70, 129.51, 129.23, 128.12, 127.96, 124.85, 123.98, 109.97, 70.88, 63.94, 59.06, 51.09, 36.13, 35.74, 12.01, 11.23.

MS (ESI): *m*/*z* calcd for $C_{25}H_{23}N_5O_5$: 473.1699; found: 474.1714 [M + 1].

2′-(3-Methyl-4-nitroisoxazol-5-yl)-3′-phenyl-1-propyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3c)

Yield: 121 mg (78%); yellow solid; mp 168–170 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 6.5 Hz, 2 H), 7.39 (q, *J* = 6.4 Hz, 3 H), 7.24 (d, *J* = 7.8 Hz, 1 H), 7.15 (d, *J* = 7.5 Hz, 1 H), 6.93 (t, *J* = 7.5 Hz, 1 H), 6.79 (d, *J* = 7.8 Hz, 1 H), 5.19 (d, *J* = 10.7 Hz, 1 H), 4.59 (d, *J* = 10.7 Hz, 1 H), 3.82–3.55 (m, 3 H), 2.99 (dtd, *J* = 28.6, 13.1, 8.3 Hz, 2 H), 2.68 (dd, *J* = 15.1, 6.6 Hz, 1 H), 2.30 (s, 3 H), 1.74 (td, *J* = 14.1, 6.9 Hz, 2 H), 1.00 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 172.81, 167.41, 162.99, 155.71, 143.93, 133.92, 130.68, 129.40, 129.17, 128.16, 127.41, 124.31, 122.47, 122.18, 109.21, 71.00, 64.15, 59.18, 51.12, 42.49, 36.23, 20.42, 11.35, 11.22.

MS (ESI): *m*/*z* calcd for $C_{26}H_{25}N_5O_5$: 487.1856; found: 488.1971 [M + 1].

1-Benzyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-phenyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3d)

Yield: 123 mg (83%); white solid; mp 175–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62–7.56 (m, 2 H), 7.35–7.23 (m, 8 H), 7.09 (dd, *J* = 7.2, 0.8 Hz, 1 H), 7.03 (td, *J* = 8.0, 1.2 Hz, 1 H), 6.83 (td, *J* = 7.6, 0.8 Hz, 1 H), 6.48 (d, *J* = 8.0 Hz, 1 H), 5.23 (d, *J* = 16.0 Hz, 1 H), 5.17 (d, *J* = 10.8 Hz, 1 H), 4.59 (s, 1 H), 4.53 (d, *J* = 10.8 Hz, 1 H), 3.52 (t, *J* = 8.4 Hz, 1 H), 3.04–2.92 (m, 1 H), 2.91–2.82 (m, 1 H), 2.61 (dd, *J* = 16.8, 7.6 Hz, 1 H), 2.21 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.07, 167.30, 163.14, 155.72, 143.48, 134.71, 133.78, 131.09, 130.68, 129.46, 129.20, 128.86, 128.17, 127.57, 127.04, 124.19, 122.81, 122.17, 110.18, 70.93, 64.13, 59.33, 51.19, 44.66, 36.29, 11.23.

MS (ESI): *m*/*z* calcd for $C_{30}H_{25}N_5O_5$: 535.1856; found: 536.1940 [M + 1].

1-Methyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-(*p*-tolyl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3e)

Yield: 126 mg (76%); light-yellow solid; mp 189–191 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.56 (d, *J* = 8.0 Hz, 2 H), 7.27–7.19 (m, 3 H), 7.13 (d, *J* = 7.6 Hz, 1 H), 6.95 (t, *J* = 7.6 Hz, 1 H), 6.77 (d, *J* = 7.6 Hz, 1 H), 5.13 (d, *J* = 10.4 Hz, 1 H), 4.56 (d, *J* = 10.4 Hz, 1 H), 3.59 (t, *J* = 7.2 Hz, 1 H), 3.26 (s, 3 H), 3.09–2.87 (m, 2 H), 2.69 (dd, *J* = 14.4, 6.4 Hz, 1 H), 2.35 (s, 3 H), 2.29 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.91, 167.41, 163.09, 155.65, 144.10, 139.44, 131.07, 130.72, 130.67, 129.85, 128.08, 124.09, 122.71, 122.07, 108.95, 70.85, 64.16, 59.49, 51.06, 36.15, 26.94, 21.20, 11.17.

MS (ESI): *m*/*z* calcd for $C_{25}H_{23}N_5O_5$: 473.1699; found: 474.2758 [M + 1].

1-Ethyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-(*p*-tolyl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3f)

Yield: 114 mg (70%); white solid; mp 194–196 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.55 (d, *J* = 8.0 Hz, 2 H), 7.26–7.18 (m, 3 H), 7.15 (d, *J* = 7.2 Hz, 1 H), 6.94 (t, *J* = 7.6 Hz, 1 H), 6.80 (d, *J* = 8.0 Hz, 1 H), 5.18 (d, *J* = 10.8 Hz, 1 H), 4.56 (d, *J* = 10.8 Hz, 1 H), 3.93–3.68 (m, 2 H), 3.58 (t, *J* = 8.0 Hz, 1 H), 3.10–2.84 (m, 2 H), 2.73–2.62 (m, 1 H), 2.35 (s, 3 H), 2.30 (s, 3 H), 1.30 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.43, 167.42, 163.04, 155.70, 143.43, 133.90, 131.00, 130.72, 129.41, 129.18, 128.17, 124.37, 122.50, 122.27, 109.05, 71.00, 64.26, 59.13, 51.08, 36.19, 35.58, 12.08, 11.21.

MS (ESI): *m*/*z* calcd for $C_{26}H_{25}N_5O_5$: 487.1856; found: 488.1868 [M + 1].

1-Benzyl-3′-(4-methoxyphenyl)-2′-(3-methyl-4-nitroisoxazol-5-yl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3g)

Yield: 109 mg (70%); white solid; mp 175–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.51 (d, *J* = 8.6 Hz, 2 H), 7.25 (m, 5 H), 7.10 (d, *J* = 7.4 Hz, 1 H), 7.02 (t, *J* = 7.5 Hz, 1 H), 6.83 (t, *J* = 6.7 Hz, 3 H), 6.47 (d, *J* = 7.8 Hz, 1 H), 5.22 (d, *J* = 16.1 Hz, 1 H), 5.14 (d, *J* = 10.7 Hz, 1 H), 4.57 (d, *J* = 16.1 Hz, 1 H), 4.50 (d, *J* = 10.7 Hz, 1 H), 3.50 (t, *J* = 8.1 Hz, 1 H), 3.40 (s, 3 H), 3.02–2.81 (m, 2 H), 2.61 (dd, *J* = 15.4, 7.1 Hz, 1 H), 2.21 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.10, 167.39, 163.14, 160.45, 155.69, 143.43, 134.72, 131.13, 130.65, 129.37, 128.86, 127.57, 127.03, 125.34, 124.20, 122.81, 122.25, 114.58, 110.16, 70.58, 64.10, 59.24, 55.33, 51.16, 44.65, 36.27, 11.23.

MS (ESI): *m*/*z* calcd for $C_{31}H_{27}N_5O_6$: 565.1961; found: 566.2041 [M + 1].

5-Chloro-1-methyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-phenyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3h)

Yield: 122 mg (79%); white solid; mp 166–168 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 6.4 Hz, 2 H), 7.41–7.33 (m, 3 H), 7.23 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.10 (d, *J* = 1.6 Hz, 1 H), 6.69 (d, *J* = 8.0 Hz, 1 H), 5.11 (d, *J* = 10.8 Hz, 1 H), 4.55 (d, *J* = 10.8 Hz, 1 H), 3.58 (t, *J* = 7.6 Hz, 1 H), 3.23 (s, 3 H), 3.07–2.89 (m, 2 H), 2.73–2.65 (m, 1 H), 2.32 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.49, 166.88, 163.23, 155.75, 142.76, 133.50, 131.18, 130.72, 129.53, 129.24, 128.21, 128.15, 124.59, 123.70, 109.91, 70.86, 63.88, 59.46, 51.11, 36.11, 27.08, 11.20.

MS (ESI): *m*/*z* calcd for $C_{24}H_{20}ClN_5O_5$: 493.1153; found: 494.1235 [M + 1].

5-Chloro-1-methyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-(*p*-tolyl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3i)

Yield: 127 mg (80%); white solid; mp 223–225 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.54 (d, *J* = 8.0 Hz, 2 H), 7.25 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.21 (d, *J* = 8.0 Hz, 2 H), 7.12 (d, *J* = 2.0 Hz, 1 H), 6.71 (d, *J* = 8.4 Hz, 1 H), 5.11 (d, *J* = 10.8 Hz, 1 H), 4.54 (d, *J* = 10.8 Hz, 1 H), 3.62–3.56 (m, 1 H), 3.25 (s, 3 H), 3.08–2.88 (m, 2 H), 2.74–2.66 (m, 1 H), 2.35 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.03, 166.93, 163.18, 155.75, 142.05, 133.57, 131.12, 130.70, 129.51, 129.23, 128.12, 127.96, 124.85, 123.98, 109.97, 70.88, 63.94, 59.06, 51.09, 36.13, 35.74, 12.01, 11.23.

MS (ESI): *m*/*z* calcd for $C_{25}H_{22}ClN_5O_5$: 507.1309; found: 508.1412 [M + 1].

5-Chloro-3′-(4-methoxyphenyl)-1-methyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3j)

Yield: 131 mg (80%); light-yellow solid; mp 194–196 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 8.8 Hz, 2 H), 7.25 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.12 (d, *J* = 1.6 Hz, 1 H), 6.92 (d, *J* = 8.8 Hz, 2 H), 6.71 (d, *J* = 8.0 Hz, 1 H), 5.09 (d, *J* = 10.8 Hz, 1 H), 4.52 (d, *J* = 10.8 Hz, 1 H), 3.81 (s, 3 H), 3.63–3.54 (m, 1 H), 3.25 (s, 3 H), 3.08–2.87 (m, 2 H), 2.74–2.66 (m, 1 H), 2.34 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.50, 166.98, 163.20, 160.50, 155.70, 142.72, 131.22, 130.67, 129.35, 128.19, 125.06, 124.58, 123.78, 114.60, 109.86, 70.51, 63.84, 59.37, 55.33, 51.06, 36.08, 27.07, 11.20.

MS (ESI): *m*/*z* calcd for $C_{25}H_{22}ClN_5O_6$: 523.1259; found: 524.1379 [M + 1].

5-Chloro-1-ethyl-2′-(3-methyl-4-nitroisoxazol-5-yl)-3′-phenyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3k)

Yield: 114 mg (75%); light-yellow solid; mp 193–195 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.57 (dd, *J* = 7.6, 1.6 Hz, 2 H), 7.34–7.27 (m, 3 H), 7.15 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.04 (d, *J* = 2.0 Hz, 1 H), 6.64 (d, *J* = 8.4 Hz, 1 H), 5.09 (d, *J* = 10.4 Hz, 1 H), 4.48 (d, *J* = 10.4 Hz, 1 H), 3.81–3.70 (m, 1 H), 3.70–3.58 (m, 1 H), 3.53–3.46 (m, 1 H), 2.99–2.80 (m, 2 H), 2.64–2.56 (m, 1 H), 2.25 (s, 3 H), 1.20 (d, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.03, 166.93, 163.18, 155.75, 142.05, 133.57, 131.12, 130.70, 129.51, 129.23, 128.12, 127.96, 124.85, 123.98, 109.97, 70.88, 63.94, 59.06, 51.09, 36.13, 35.74, 12.01, 11.23.

MS (ESI): *m*/*z* calcd for $C_{25}H_{22}ClN_5O_5$: 507.1309; found: 508.1393 [M + 1].

3′-(Furan-2-yl)-2′-(3-methyl-4-nitroisoxazol-5-yl)-1-propyl-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3l)

Yield: 109 mg (72%); white solid; mp 180–183 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45 (d, *J* = 0.8 Hz, 1 H), 7.24 (t, *J* = 7.6 Hz, 1 H), 7.09 (d, *J* = 7.6 Hz, 1 H), 6.91 (t, *J* = 7.6 Hz, 1 H), 6.79 (d, *J* = 8.0 Hz, 1 H), 6.59 (s, 1 H), 6.39–6.35 (m, 1 H), 5.47 (d, *J* = 10.4 Hz, 1 H), 4.77 (d, *J* = 10.4 Hz, 1 H), 3.81–3.69 (m, 2 H), 3.68–3.60 (m, 1 H), 3.11–2.91 (m, 2 H), 2.72–2.61 (m, 1 H), 2.34 (s, 3 H), 1.82–1.70 (m, 2 H), 1.00 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.35, 167.17, 163.06, 155.69, 146.68, 143.99, 143.88, 130.76, 124.23, 122.44, 122.09, 110.73, 110.15, 109.21, 63.98, 63.89, 55.07, 51.43, 42.47, 36.00, 20.40, 11.32, 11.23.

MS (ESI): *m*/*z* calcd for $C_{24}H_{23}N_5O_6$: 477.1648; found: 478.1706 [M + 1].

5-Chloro-1-ethyl-3′-(furan-2-yl)-2′-(3-methyl-4-nitroisoxazol-5-yl)-5′,6′-dihydro-2′*H*-spiro[indoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2,7′(3′*H*)-dione (3m)

Yield: 111 mg (75%); white solid; mp 170–172 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 0.8 Hz, 1 H), 7.24 (dd, *J* = 8.4, 2.0 Hz, 1 H), 7.08 (d, *J* = 2.0 Hz, 1 H), 6.74 (d, *J* = 8.4 Hz, 1 H), 6.59 (s, 1 H), 6.41–6.36 (m, 1 H), 5.46 (d, *J* = 10.4 Hz, 1 H), 4.75 (d, *J* = 10.4 Hz, 1 H), 3.90–3.79 (m, 1 H), 3.79–3.65 (m, 2 H), 3.14–2.91 (m, 2 H), 2.69 (dd, *J* = 16.0, 6.8 Hz, 1 H), 2.39 (s, 3 H), 1.29 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.72, 166.81, 163.29, 155.75, 146.42, 144.00, 142.11, 131.03, 130.78, 127.95, 124.77, 123.90, 110.77, 110.40, 109.99, 63.84, 63.70, 54.95, 51.32, 35.90, 35.74, 12.00, 11.24

MS (ESI): *m*/*z* calcd for $C_{23}H_{20}ClN_5O_6$: 497.1102; found: 498.1188 [M + 1].

1-Methyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4a)

Yield: 120 mg (75%); white solid; mp 161–162 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22 (t, *J* = 7.6 Hz, 2 H), 7.14 (t, *J* = 7.6 Hz, 2 H), 6.99 (d, *J* = 7.6 Hz, 2 H), 6.89 (t, *J* = 7.6 Hz, 1 H), 6.57 (d, *J* = 8.0 Hz, 1 H), 6.47 (d, *J* = 31.2 Hz, 1 H), 5.97 (s, 1 H), 4.12 (s, 1 H), 3.69 (t, *J* = 8.4 Hz, 1 H), 3.36–3.15 (m, 2 H), 3.02–2.93 (m, 1 H), 2.84 (s, 3 H), 2.49 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.54, 167.82, 164.29, 156.16, 144.28, 130.35, 129.09, 128.30, 128.07, 127.59, 127.32, 123.01, 122.87, 122.48, 108.69, 77.28, 67.59, 54.07, 52.27, 36.63, 26.19, 11.31.

MS (ESI): *m*/*z* calcd for $C_{24}H_{21}N_5O_5$: 459.1543; found: 460.1591 [M + 1].

1-Ethyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4b)

Yield: 128 mg (81%); white solid; mp 156–158 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24 (t, *J* = 7.6 Hz, 2 H), 7.16 (t, *J* = 7.2 Hz, 2 H), 7.00 (d, *J* = 7.6 Hz, 2 H), 6.90 (t, *J* = 7.6 Hz, 1 H), 6.60 (d, *J* = 8.0 Hz, 1 H), 6.50 (d, *J* = 7.6 Hz, 1 H), 5.99 (s, 1 H), 4.15 (s, 1 H), 3.73 (t, *J* = 8.4 Hz, 1 H), 3.67–3.55 (m, 1 H), 3.34–3.19 (m, 2 H), 3.09–2.96 (m, 1 H), 2.92–2.82 (m, 1 H), 2.51 (s, 3 H), 0.68 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.07, 167.83, 164.22, 156.10, 143.43, 130.40, 130.27, 129.27, 129.02, 128.28, 127.34, 123.23, 123.13, 122.24, 108.73, 77.42, 67.46, 53.91, 52.20, 36.67, 34.53, 11.61, 11.31.

MS (ESI): *m*/*z* calcd for $C_{25}H_{23}N_5O_5$: 473.1699; found: 474.1714 [M + 1].

1-Benzyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4c)

Yield: 125 mg (85%); light-yellow solid; mp 160–162 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 7.2 Hz, 1 H), 7.22 (t, *J* = 7.6 Hz, 2 H), 7.19–7.14 (m, 1 H), 7.14–7.06 (m, 5 H), 6.87 (t, *J* = 7.6 Hz, 1 H), 6.55 (d, *J* = 7.6 Hz, 1 H), 6.44 (d, *J* = 7.2 Hz, 2 H), 6.37 (d, *J* = 8.0 Hz, 1 H), 6.06 (s, 1 H), 5.09 (d, *J* = 16.4 Hz, 1 H), 4.33 (d, *J* = 16.4 Hz, 1 H), 4.26 (s, 1 H), 3.76 (t, *J* = 8.4 Hz, 1 H), 3.35–3.22 (m, 1 H), 3.08–2.98 (m, 1 H), 2.89 (dd, *J* = 16.0, 7.6 Hz, 1 H), 2.51 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.75, 167.69, 164.29, 156.10, 143.84, 143.53, 134.55, 130.58, 130.33, 129.17, 128.71, 128.63, 127.70, 127.24, 126.29, 123.09, 122.81, 122.46, 110.03, 77.24, 67.54, 54.59, 52.29, 43.91, 36.66, 11.29.

MS (ESI): *m*/*z* calcd for $C_{30}H_{25}N_5O_5$: 535.1856; found: 536.1940 [M + 1].

3′-(3-Methyl-4-nitroisoxazol-5-yl)-1′-phenyl-1-propyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4d)

Yield: 132 mg (85%); yellow solid; mp 155–157 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–7.18 (m, 2 H), 7.14 (t, *J* = 7.6 Hz, 2 H), 7.00 (d, *J* = 7.2 Hz, 2 H), 6.86 (t, *J* = 7.6 Hz, 1 H), 6.58 (d, *J* = 8.0 Hz, 1 H), 6.48 (d, *J* = 7.6 Hz, 1 H), 5.96 (s, 1 H), 4.14 (s, 1 H), 3.70 (t, *J* = 8.4 Hz, 1 H), 3.55–3.46 (m, 1 H), 3.31–3.13 (m, 2 H), 3.03–2.92 (m, 1 H), 2.85 (m, 1 H), 2.49 (s, 3 H), 1.22–1.07 (m, 2 H), 0.58 (t, *J* = 7.6 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.40, 167.82, 164.23, 156.10, 144.06, 130.46, 130.26, 129.05, 128.34, 128.16, 127.41, 123.16, 122.96, 122.15, 108.93, 77.22, 67.37, 54.13, 52.28, 41.67, 36.65, 20.20, 11.31, 11.00.

MS (ESI): *m*/*z* calcd for $C_{26}H_{25}N_5O_5$: 487.1856; found: 488.1971 [M + 1].

1-Allyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4e)

Yield: 134 mg (86%); white solid; mp 162–164 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.27–7.12 (m, 4 H), 7.00 (d, *J* = 7.2 Hz, 2 H), 6.93–6.87 (m, 1 H), 6.53 (dd, *J* = 27.2, 7.6 Hz, 2 H), 5.97 (s, 1 H), 5.24–5.16 (m, 1 H), 4.83 (d, *J* = 10.4 Hz, 1 H), 4.32 (dd, *J* = 60.4, 17.6 Hz, 2 H), 4.16 (s, 1 H), 3.82 (dd, *J* = 16.4, 4.0 Hz, 1 H), 3.70 (t, *J* = 8.4 Hz, 1 H), 3.30–3.17 (m, 1 H), 3.07–2.82 (m, 2 H), 2.49 (s, 3 H).

MS (ESI): *m*/*z* calcd for $C_{26}H_{23}N_5O_5$: 485.1699; found: 486.1767 [M + 1].

1-Ethyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-(*p*-tolyl)-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4f)

Yield: 136 mg (84%); white solid; mp 203–205 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.06 (d, *J* = 7.6 Hz, 1 H), 7.01–6.89 (m, 3 H), 6.88 (d, *J* = 8.0 Hz, 2 H), 6.70 (t, *J* = 7.6 Hz, 1 H), 6.49 (d, *J* = 8.0 Hz, 1 H), 6.26 (s, 1 H), 4.35 (s, 1 H), 3.91–3.81 (m, 1 H), 3.79–3.69 (m, 1 H), 3.71–3.63 (m, 1 H), 3.26–3.16 (m, 1 H), 2.97–2.88 (m, 2 H), 2.35 (s, 3 H), 2.17 (s, 3 H), 1.20 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 174.50, 169.61, 160.76, 157.62, 155.55, 142.53, 138.26, 129.20, 128.74, 128.56, 127.28, 126.08, 124.30, 121.61, 108.23, 78.14, 66.01, 59.04, 45.91, 35.16, 30.34, 21.07, 12.15, 11.11.

MS (ESI): *m*/*z* calcd for $C_{26}H_{25}N_5O_5$: 487.1856; found: 488.1868 [M + 1].

1-Benzyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-(*p*-tolyl)-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4g)

Yield: 118 mg (78%); yellow solid; mp 166–168 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.15 (t, *J* = 7.2 Hz, 1 H), 7.09–7.04 (m, 3 H), 6.99 (q, *J* = 8.0 Hz, 4 H), 6.84 (t, *J* = 7.6 Hz, 1 H), 6.51 (d, *J* = 7.2 Hz, 1 H), 6.46 (d, *J* = 7.2 Hz, 2 H), 6.34 (d, *J* = 8.0 Hz, 1 H), 6.02 (s, 1 H), 5.12 (d, *J* = 16.0 Hz, 1 H), 4.30 (d, *J* = 16.0 Hz, 1 H), 4.19 (s, 1 H), 3.71 (t, *J* = 8.4 Hz, 1 H), 3.34–3.19 (m, 1 H), 3.05–2.93 (m, 1 H), 2.86 (m, 1 H), 2.48 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.85, 167.75, 164.28, 156.08, 143.54, 139.02, 134.63, 131.02, 130.25, 129.39, 128.47, 127.62, 127.47, 127.23, 126.42, 123.07, 122.91, 122.41, 109.99, 76.98, 67.49, 54.59, 52.25, 43.94, 36.65, 21.33, 11.29.

1-Allyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-(*p*-tolyl)-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4h)

Yield: 128 mg (80%); white solid; mp 151–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (t, *J* = 7.6 Hz, 1 H), 6.98 (d, *J* = 8.0 Hz, 2 H), 6.95–6.85 (m, 3 H), 6.57 (d, *J* = 8.0 Hz, 1 H), 6.49 (d, *J* = 7.6 Hz, 1 H), 6.00 (s, 1 H), 5.33–5.22 (m, 1 H), 4.85 (d, *J* = 10.4 Hz, 1 H), 4.42–4.27 (m, 2 H), 4.15 (s, 1 H), 3.85 (dd, *J* = 16.4, 5.2 Hz, 1 H), 3.71 (t, *J* = 8.8 Hz, 1 H), 3.32–3.19 (m, 1 H), 3.04–2.93 (m, 1 H), 2.86 (dd, *J* = 15.8, 8.0 Hz, 1 H), 2.51 (s, 3 H), 2.27 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.36, 167.82, 164.23, 156.09, 143.56, 139.07, 130.99, 130.30, 130.16, 129.12, 127.39, 127.28, 123.04, 122.88, 122.36, 116.63, 109.66, 77.27, 67.53, 54.13, 52.20, 42.19, 36.64, 21.03, 11.30.

MS (ESI): *m*/*z* calcd for $C_{27}H_{25}N_5O_5$: 499.1856; found: 500.1868 [M + 1].

1-Allyl-1′-(4-methoxyphenyl)-3′-(3-methyl-4-nitroisoxazol-5-yl)-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4i)

Yield: 130 mg (79%); white solid; mp 145–147 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (t, *J* = 7.6 Hz, 1 H), 6.98 (d, *J* = 8.8 Hz, 2 H), 6.89 (t, *J* = 7.6 Hz, 1 H), 6.70 (d, *J* = 8.8 Hz, 2 H), 6.59 (d, *J* = 8.0 Hz, 1 H), 6.48 (d, *J* = 7.6 Hz, 1 H), 6.01 (s, 1 H), 5.41–5.27 (m, 1 H), 4.91 (d, *J* = 10.4 Hz, 1 H), 4.50 (d, *J* = 17.2 Hz, 1 H), 4.34–4.25 (m, 1 H), 4.19 (s, 1 H), 3.97–3.85 (m, 1 H), 3.74 (s, 3 H), 3.70 (d, *J* = 8.4 Hz, 1 H), 3.30–3.18 (m, 1 H), 3.07–2.95 (m, 1 H), 2.88 (dd, *J* = 16.0, 7.6 Hz, 1 H), 2.51 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.42, 167.82, 164.23, 160.32, 156.10, 143.54, 130.98, 130.32, 130.16, 128.73, 123.01, 122.91, 122.37, 122.11, 116.81, 113.88, 109.68, 77.23, 67.49, 55.25, 54.13, 52.19, 42.22, 36.62, 11.31.

MS (ESI): *m*/*z* calcd for $C_{27}H_{25}N_5O_6$: 515.1805; found: 516.1817 [M + 1].

5-Chloro-1-ethyl-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4j)

Yield: 123 mg (81%); light-yellow solid; mp 164–166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.25 (d, *J* = 7.2 Hz, 1 H), 7.24–7.16 (m, 3 H), 7.05 (d, *J* = 7.2 Hz, 2 H), 6.53 (d, *J* = 8.4 Hz, 1 H), 6.41 (s, 1 H), 5.96 (s, 1 H), 4.10 (s, 1 H), 3.72 (t, *J* = 8.4 Hz, 1 H), 3.65–3.54 (m, 1 H), 3.30–3.21 (m, 2 H), 3.04–2.94 (m, 1 H), 2.92–2.83 (m, 1 H), 2.55 (s, 3 H), 0.66 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.63, 167.52, 164.25, 156.23, 141.98, 131.07, 130.22, 130.03, 129.26, 128.44, 127.51, 127.37, 124.82, 123.67, 109.59, 77.19, 67.55, 53.89, 52.16, 36.63, 34.71, 11.53, 11.15.

MS (ESI): *m*/*z* calcd for $C_{25}H_{22}ClN_5O_5$: 507.1309; found: 508.1324 [M + 1].

1-Benzyl-5-fluoro-3′-(3-methyl-4-nitroisoxazol-5-yl)-1′-phenyl-6′,7′-dihydro-1′*H*-spiro[indoline-3,2′-pyrazolo[1,2-*a*]pyrazole]-2,5′(3′*H*)-dione (4k)

Yield: 110 mg (76%); white solid; mp 159–161 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.32–7.27 (m, 1 H), 7.16 (t, *J* = 7.6 Hz, 2 H), 7.08–6.99 (m, 5 H), 6.74–6.68 (m, 1 H), 6.33 (d, *J* = 7.2 Hz, 2 H), 6.25–6.17 (m, 2 H), 5.96 (s, 1 H), 4.98 (d, *J* = 16.0 Hz, 1 H), 4.23 (d, *J* = 16.0 Hz, 1 H), 4.11 (s, 1 H), 3.66 (t, *J* = 8.4 Hz, 1 H), 3.25–3.13 (m, 1 H), 2.98–2.87 (m, 1 H), 2.84–2.74 (m, 1 H), 2.45 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 173.47, 167.32, 164.32, 159.76, 157.34, 156.19, 139.53, 134.18, 130.27, 129.37, 128.83, 128.72, 127.72, 127.40, 126.27, 116.94, 116.71, 111.27, 111.02, 77.16, 67.72, 54.44, 52.24, 44.05, 36.61, 11.25.

MS (ESI): *m*/*z* calcd for $C_{30}H_{24}FN_5O_5$: 553.1761; found: 554.1669 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-5,7-diphenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6a)

Yield: 131 mg (75%); white solid; mp 142–144 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (m, 4 H), 7.32–7.26 (m, 1 H), 7.14 (m, 3 H), 7.07–7.02 (m, 2 H), 5.53 (d, *J* = 4.0 Hz, 1 H), 4.88 (dd, *J* = 6.8, 4.8 Hz, 1 H), 4.51 (d, *J* = 6.8 Hz, 1 H), 3.32 (t, *J* = 10.4 Hz, 1 H), 3.05 (dd, *J* = 20.0, 10.0 Hz, 1 H), 2.72–2.58 (m, 2 H), 2.28 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.32, 155.89, 148.02, 144.92, 132.07, 130.65, 129.36, 128.98, 128.07, 127.80, 127.52, 124.53, 70.45, 57.03, 56.75, 49.65, 35.12, 10.59.

MS (ESI): *m*/*z* calcd for $C_{22}H_{20}N_4O_4$: 404.1485; found: 405.1558 [M + 1].

5-(Furan-2-yl)-6-(3-methyl-4-nitroisoxazol-5-yl)-7-phenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6b)

Yield: 154 mg (90%); yellow semi-solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.42 (d, *J* = 7.6 Hz, 2 H), 7.33 (s, 1 H), 7.29 (t, *J* = 7.6 Hz, 2 H), 7.23 (d, *J* = 7.2 Hz, 1 H), 6.25–6.20 (m, 2 H), 6.02 (d, *J* = 8.4 Hz, 1 H), 4.99 (d, *J* = 6.8 Hz, 1 H), 4.79–4.74 (m, 1 H), 3.55 (dd, *J* = 22.0, 10.0 Hz, 1 H), 3.12 (m, 1 H), 2.39 (s, 3 H), 1.78–1.61 (m, 2 H).

MS (ESI): *m*/*z* calcd for $C_{20}H_{18}N_4O_5$: 394.1277; found: 395.1369 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-7-(4-nitrophenyl)-5-phenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6c)

Yield: 133 mg (82%); white solid; mp 182–184 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.29 (d, *J* = 8.8 Hz, 2 H), 7.66 (d, *J* = 8.8 Hz, 2 H), 7.28 (m, 3 H), 7.12 (d, *J* = 7.6 Hz, 2 H), 5.76 (d, *J* = 4.0 Hz, 1 H), 4.97–4.90 (m, 1 H), 4.66 (d, *J* = 6.8 Hz, 1 H), 3.41 (t, *J* = 11.2 Hz, 1 H), 3.22 (dd, *J* = 20.0, 10.0 Hz, 1 H), 2.76–2.63 (m, 2 H), 2.38 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.90, 155.89, 148.02, 144.92, 132.07, 130.65, 129.36, 128.98, 128.07, 127.80, 127.52, 124.53, 70.45, 57.03, 56.75, 47.61, 35.12, 11.37.

MS (ESI): *m*/*z* calcd for $C_{22}H_{19}N_5O_6$: 449.1335; found: 450.1403 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-7-(4-nitrophenyl)-5-(*p*-tolyl)tetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6d)

Yield: 117 mg (70%); white solid; mp 179–181 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (d, *J* = 8.8 Hz, 2 H), 7.64 (d, *J* = 8.8 Hz, 2 H), 7.05 (d, *J* = 8.0 Hz, 2 H), 6.97 (d, *J* = 8.0 Hz, 2 H), 5.79 (d, *J* = 4.4 Hz, 1 H), 4.91–4.84 (m, 1 H), 4.66 (d, *J* = 6.8 Hz, 1 H), 3.33 (t, *J* = 10.4 Hz, 1 H), 3.23 (dd, *J* = 19.2, 9.6 Hz, 1 H), 2.61 (m, 2 H), 2.38 (s, 3 H), 2.28 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.97, 155.97, 147.99, 139.40, 130.66, 129.71, 128.97, 128.15, 127.45, 124.52, 124.42, 114.91, 70.15, 57.10, 56.64, 34.70, 29.71, 21.12, 11.43.

MS (ESI): *m*/*z* calcd for $C_{23}H_{21}N_5O_6$: 463.1492; found: 464.1566 [M + 1].

5-(Furan-2-yl)-6-(3-methyl-4-nitroisoxazol-5-yl)-7-(4-nitrophenyl)tetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6e)

Yield: 135 mg (85%); light-yellow solid; mp 175–177 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15 (d, *J* = 8.8 Hz, 2 H), 7.60 (d, *J* = 8.4 Hz, 2 H), 7.34 (s, 1 H), 6.25 (m, 2 H), 6.11 (d, *J* = 8.4 Hz, 1 H), 5.01 (d, *J* = 6.8 Hz, 1 H), 4.71–4.65 (m, 1 H), 3.59 (dd, *J* = 22.0, 9.6 Hz, 1 H), 3.20–3.10 (m, 1 H), 2.41 (s, 3 H), 2.38–2.32 (m, 1 H), 1.64 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.97, 155.97, 147.99, 139.40, 130.66, 129.71, 128.97, 128.15, 127.45, 124.52, 124.42, 114.91, 70.15, 57.10, 56.64, 29.71, 21.12, 11.43.

MS (ESI): *m*/*z* calcd for $C_{20}H_{17}N_5O_7$: 439.1128; found: 440.1188 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-5-phenyl-7-(*p*-tolyl)tetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6f)

Yield: 119 mg (70%); white solid; mp 164–166 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33 (d, *J* = 7.6 Hz, 2 H), 7.22 (m, 5 H), 7.14–7.09 (m, 2 H), 5.53 (d, *J* = 3.6 Hz, 1 H), 4.94 (dd, *J* = 7.2, 4.8 Hz, 1 H), 4.54 (d, *J* = 7.2 Hz, 1 H), 3.39 (t, *J* = 8.4 Hz, 1 H), 3.07 (dd, *J* = 20.4, 9.6 Hz, 1 H), 2.86–2.65 (m, 2 H), 2.36 (s, 3 H), 2.34 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.00, 154.53, 137.51, 133.66, 131.54, 129.50, 129.01, 128.89, 127.98, 127.68, 126.84, 125.32, 69.35, 56.76, 56.25, 34.97, 28.68, 20.15, 10.36.

MS (ESI): *m*/*z* calcd for $C_{23}H_{22}N_4O_4$: 418.1641; found: 419.1713 [M + 1].

5-(Furan-2-yl)-6-(3-methyl-4-nitroisoxazol-5-yl)-7-(*p*-tolyl)tetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6g)

Yield: 122 mg (73%); light-yellow semi-solid.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (d, *J* = 3.2 Hz, 2 H), 7.36 (s, 1 H), 7.16 (d, *J* = 8.0 Hz, 2 H), 6.31–6.28 (m, 1 H), 6.26 (d, *J* = 3.2 Hz, 1 H), 6.04 (d, *J* = 8.4 Hz, 1 H), 5.03 (d, *J* = 6.8 Hz, 1 H), 4.82 (dd, *J* = 8.0, 6.8 Hz, 1 H), 3.59 (dd, *J* = 22.0, 10.0 Hz, 1 H), 3.21–3.13 (m, 1 H), 2.47 (s, 1 H), 2.45 (s, 3 H), 2.44–2.38 (m, 1 H), 2.32 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 174.34, 168.90, 156.06, 147.18, 144.10, 138.08, 136.60, 130.71, 129.73, 126.15, 112.20, 111.19, 62.26, 57.54, 55.05, 31.45, 29.71, 21.13, 11.52.

MS (ESI): *m*/*z* calcd for $C_{21}H_{20}N_4O_5$: 408.1434; found: 409.1505 [M + 1].

7-(4-Chlorophenyl)-6-(3-methyl-4-nitroisoxazol-5-yl)-5-phenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6h)

Yield: 126 mg (76%); white solid; mp 148–150 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (s, 4 H), 7.22 (m, 3 H), 7.13–7.08 (m, 2 H), 5.57 (d, *J* = 4.0 Hz, 1 H), 4.91 (dd, *J* = 7.2, 4.8 Hz, 1 H), 4.56 (d, *J* = 7.2 Hz, 1 H), 3.39 (m, 1 H), 3.11 (q, *J* = 10.0 Hz, 1 H), 2.70 (m, 2 H), 2.35 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.50, 155.73, 136.21, 134.65, 132.13, 130.60, 129.48, 129.27, 128.90, 128.01, 127.90, 70.35, 57.37, 56.97, 35.40, 29.71, 11.38.

MS (ESI): *m*/*z* calcd for $C_{22}H_{19}ClN_4O_4$: 438.1095; found: 439.1161 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-7-(naphthalen-1-yl)-5-phenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6i)

Yield: 113 mg (70%); white solid; mp 151–153 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (t, *J* = 8.8 Hz, 2 H), 7.75 (d, *J* = 7.2 Hz, 1 H), 7.63 (d, *J* = 8.4 Hz, 1 H), 7.57 (t, *J* = 7.6 Hz, 1 H), 7.49 (t, *J* = 6.8 Hz, 1 H), 7.43 (t, *J* = 7.2 Hz, 1 H), 7.24–7.17 (m, 3 H), 7.09 (d, *J* = 6.8 Hz, 2 H), 6.24 (d, *J* = 2.8 Hz, 1 H), 4.96 (dd, *J* = 6.4, 3.6 Hz, 1 H), 4.47 (d, *J* = 6.8 Hz, 1 H), 3.52 (m, 1 H), 3.11 (m, 2 H), 2.86 (m, 1 H), 2.40 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.05, 165.10, 155.60, 134.33, 132.21, 132.17, 130.53, 129.99, 129.44, 129.32, 129.05, 128.62, 127.59, 127.06, 126.06, 125.32, 123.92, 121.71, 69.74, 56.61, 55.18, 36.85, 29.72, 11.47.

MS (ESI): *m*/*z* calcd for $C_{26}H_{22}N_4O_4$: 454.1641; found: 455.1701 [M + 1].

6-(3-Methyl-4-nitroisoxazol-5-yl)-7-(4-oxo-4*H*-chromen-3-yl)-5-phenyltetrahydropyrazolo[1,2-*a*]pyrazol-1(5*H*)-one (6j)

Yield: 123 mg (78%); white solid; mp 180–182 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, *J* = 8.0, 1.2 Hz, 1 H), 8.02 (s, 1 H), 7.68–7.62 (m, 1 H), 7.44 (d, *J* = 8.4 Hz, 1 H), 7.37 (t, *J* = 7.6 Hz, 1 H), 7.12 (m, 5 H), 5.24 (d, *J* = 3.2 Hz, 1 H), 5.14 (dd, *J* = 7.2, 3.6 Hz, 1 H), 4.63 (d, *J* = 7.2 Hz, 1 H), 3.43 (m, 1 H), 2.98–2.86 (m, 2 H), 2.73 (m, 1 H), 2.27 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 175.42, 169.82, 164.87, 155.34, 154.37, 153.22, 133.22, 131.71, 129.30, 127.78, 127.48, 126.45, 124.65, 122.75, 118.23, 117.24, 69.84, 52.71, 52.31, 48.24, 35.34, 10.37.

MS (ESI): *m*/*z* calcd for $C_{25}H_{20}N_4O_6$: 472.1383; found: 473.1453 [M + 1].

2-(2-(3-Methyl-4-nitroisoxazol-5-yl)-7-oxo-3-phenylhexahydropyrazolo[1,2-*a*]pyrazol-1-yl)phenyl 4-nitrobenzenesulfonate (6k)

Yield: 170 mg (65%); light-yellow solid; mp 159–161 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.41 (d, *J* = 8.8 Hz, 2 H), 8.16 (d, *J* = 8.8 Hz, 2 H), 7.46 (d, *J* = 4.0 Hz, 5 H), 7.32 (dd, *J* = 5.4, 1.9 Hz, 1 H), 7.29 (d, *J* = 1.6 Hz, 1 H), 7.24 (dd, *J* = 11.0, 4.0 Hz, 1 H), 7.06 (d, *J* = 8.0 Hz, 1 H), 5.48 (d, *J* = 2.4 Hz, 1 H), 5.01 (d, *J* = 6.4 Hz, 1 H), 4.99–4.95 (m, 1 H), 3.51 (t, *J* = 8.6 Hz, 1 H), 3.21 (dd, *J* = 20.2, 9.8 Hz, 1 H), 3.05–2.99 (m, 1 H), 2.82 (dd, *J* = 15.2, 8.0 Hz, 1 H), 2.39 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 169.29, 164.87, 155.50, 151.21, 147.30, 141.14, 137.22, 130.64, 130.36, 129.57, 129.35, 128.89, 128.59, 127.73, 126.46, 126.43, 124.71, 122.36, 63.57, 58.53, 55.60, 49.52, 36.41, 11.37.

MS (ESI): *m*/*z* calcd for $C_{28}H_{23}N_5O_9S$: 605.1216; found: 606.1297 [M + 1].

1-Methyl-2,7′-dioxo-3′-phenyl-3′,5′,6′,7′-tetrahydro-2′*H*-spiroindoline-3,1′-pyrazolo[1,2-*a*]pyrazole]-2′-carboxylic Acid (7a)

Yield: 64 mg (78%); cream solid; mp 217–219 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.56 (d, *J* = 7.2 Hz, 2 H), 7.45 (d, *J* = 7.2 Hz, 1 H), 7.37 (t, *J* = 7.2 Hz, 2 H), 7.32–7.27 (m, 2 H), 7.04–6.97 (m, 2 H), 4.27 (d, *J* = 11.2 Hz, 1 H), 3.68 (d, *J* = 10.8 Hz, 1 H), 3.15 (s, 3 H), 3.02–2.94 (m, 1 H), 2.80–2.71 (m, 1 H), 2.42–2.29 (m, 2 H).

MS (ESI): *m*/*z* calcd for $C_{21}H_{19}N_3O_4$: 377.1376; found: 378.1460 [M + 1].

1-(Furan-2-yl)-5-oxo-3-phenylhexahydropyrazolo[1,2-*a*]pyrazole-2-carboxylic Acid (8b)

Yield: 67 mg (85%); cream solid; mp 233–235 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 12.78 (s, 1 H), 7.71–7.70 (d, *J* = 8.0 Hz, 1 H), 7.43 (d, *J* = 7.2 Hz, 2 H), 7.38 (t, *J* = 7.2 Hz, 2 H), 7.30 (t, *J* = 6.8 Hz, 1 H), 6.53–6.52 (m, 1 H), 6.46 (d, *J* = 2.8 Hz, 1 H), 5.40 (d, *J* = 8.4 Hz, 1 H), 4.66 (d, *J* = 7.2 Hz, 1 H), 3.85 (t, *J* = 7.6 Hz, 1 H), 3.43 (dd, *J* = 22.4, 10.0 Hz, 1 H), 3.13–3.07 (m, 1 H), 2.27–2.20 (m, 1 H), 1.26–1.17 (m, 1 H).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 175.41, 170.67, 149.21, 144.03, 141.93, 129.03, 127.87, 126.62, 111.95, 111.49, 61.24, 59.15, 58.48, 42.70, 30.70.

MS (ESI): *m*/*z* calcd for $C_{17}H_{16}N_2O_4$: 312.1110; found: 313.1194 [M + 1].

Methyl 1-(Furan-2-yl)-5-oxo-3-phenylhexahydropyrazolo[1,2-*a*]pyrazole-2-carboxylate (9b)

Yield: 67 mg (65%); light-yellow liquid.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.69 (d, *J* = 1.2 Hz, 1 H), 7.44–7.42 (m, 2 H), 7.38 (t, *J* = 7.2 Hz, 2 H), 7.32–7.28 (m, 1 H), 6.53 (dd, *J* = 3.6, 2.0 Hz, 1 H), 6.46 (d, *J* = 3.2 Hz, 1 H), 5.43 (d, *J* = 8.0 Hz, 1 H), 4.70 (d, *J* = 7.2 Hz, 1 H), 3.99 (t, *J* = 8.0 Hz, 1 H), 3.45 (s, 3 H), 3.42–3.39 (m, 1 H), 3.15–3.09 (m, 1 H), 2.28–2.20 (m, 1 H), 1.25–1.17 (m, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 174.94, 169.37, 148.48, 143.70, 141.11, 128.61, 127.53, 126.22, 111.52, 111.01, 60.66, 58.20, 57.99, 52.16, 42.30, 30.20.

MS (ESI): *m*/*z* calcd for $C_{18}H_{18}N_2O_4$: 326.1267; found: 327.1350 [M + 1].

1-(Furan-2-yl)-5-oxo-3-phenyl-*N*-(*p*-tolyl)hexahydropyrazolo[1,2-*a*]pyrazole-2-carboxamide (10b)

Yield: 109 mg (85%); white solid; mp 222–224 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 9.88 (s, 1 H), 7.70 (d, *J* = 1.2 Hz, 1 H), 7.38 (d, *J* = 4.4 Hz, 4 H), 7.32–7.28 (m, 1 H), 7.24 (d, *J* = 8.4 Hz, 2 H), 7.04 (d, *J* = 8.4 Hz, 2 H), 6.46–6.45 (m, 1 H), 6.41 (d, *J* = 3.2 Hz, 1 H), 5.64 (d, *J* = 8.4 Hz, 1 H), 4.85 (d, *J* = 6.8 Hz, 1 H), 3.82 (t, *J* = 7.6 Hz, 1 H), 3.45 (dd, *J* = 22.0, 10.0 Hz, 1 H), 3.15–3.08 (m, 1 H), 2.35–2.20 (m, 1 H), 2.20 (s, 3 H), 1.45–1.33 (m, 1 H).

^{13}C NMR (125 MHz, DMSO-d_6): δ = 174.60, 165.32, 148.27, 143.99, 141.59, 135.96, 132.59, 129.04, 128.69, 127.38, 125.83, 119.59, 111.54, 111.12, 61.63, 60.77, 57.35, 42.53, 30.69, 20.40.

MS (ESI): *m*/*z* calcd for $C_{24}H_{23}N_3O_3$: 401.1739; found: 402.1829 [M + 1].

Conflict of Interest

The authors declare no conflict of interest.

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Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/a-1480-9837.

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