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Magnetic Metal–Organic Framework $CoFe_2O_4$@SiO_2@IRMOF-3 as an Efficient Catalyst for One-Pot Synthesis of Functionalized Dihydro-2-oxopyrroles

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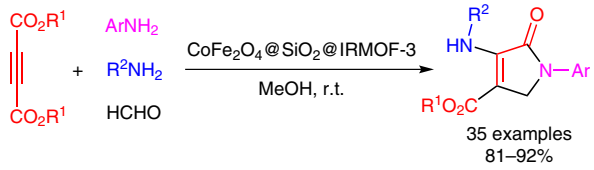

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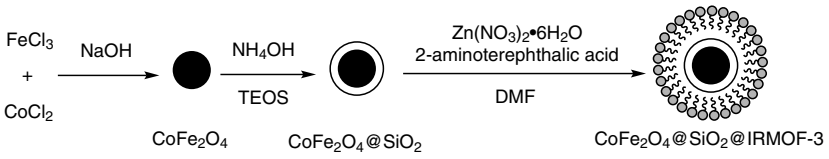
Abstract A magnetic metal–organic framework-based catalyst $CoFe_2O_4$@SiO_2@IRMOF-3 was prepared and identified as an efficient catalyst for the synthesis of a variety of functionalized dihydro-2-oxopyrroles by a one-pot, four-component reaction of a dialkyl acetylenedicarboxylate, an aryl amine, formaldehyde, and optionally a second amine or diamine at room temperature. The catalyst was magnetically separated and recovered without significant loss of its catalytic efficiency, even after eight reaction cycles.

Key words magnetic separation, metal–organic framework, nanostructures, multicomponent reactions, dihydropyrroles, cobalt catalysis

Dihydro-2-oxopyrroles are an important class of heterocycles that constitute the structural cores of many natural products, synthetic bioactive compounds, and functional materials. They exhibit a range of biological and pharmacological activities, and have been recognized as quorum-sensing inhibitors,[1] signal-regulating kinase 1 (ASK1) inhibitors,[2] DRAK2 inhibitors,[3] caspase-3 inhibitors,[4] potential cytotoxic agents,[5] or antibiofilm agents.[6] Consequently, the high demand for dihydro-2-oxopyrroles has stimulated rigorous research into the development of efficient methods for the construction of this skeleton. Among the numerous methods that provide access to dihydro-2-oxopyrroles, the one-pot, four-component reaction of amines, dialkyl acetylenedicarboxylates, and formaldehyde is among the most important strategies for the construction of highly substituted dihydro-2-oxopyrroles. A careful survey of the literature revealed that this conversion is promoted by such catalysts as $Cu(OAc)_2{\cdot}H_2O$,[7] $InCl_3$,[8] maltose,[9] sucrose,[10] xylose,[11] nanoparticulate $TiCl_4/SiO_2$,[12] Bu_4NHSO_4,[13] TsOH,[14] $ZrCl_4$,[15] UiO-66-SO_3H metal–organic framework,[16] BF_3/nanoparticulate sawdust,[17] trityl chloride,[18] or molecular iodine.[19] Despite the effectiveness of these catalysts, some of the associated methods have drawbacks such as narrow substrate scope, poor product yield, long reaction time, tedious purification protocols, or the use of expensive or nonrecyclable catalysts. Therefore, the development of more efficient catalytic systems for the construction of these heterocyclic compounds under environmentally benign conditions is still an attractive option.

Metal–organic frameworks (MOFs) constructed from metal ions or metallic clusters and multidirectional organic linkers have attracted considerable attention as an emerging class of potentially useful porous crystalline materials for several reasons: their large specific surface areas; tunable pore distributions; abundant aromatic ligands; outstanding thermal, mechanical, and solvent stabilities; high acid–base catalytic activities; and ease of functionalization and design.[20] By virtue of these special properties, MOFs have unquestionable potential for practical applications in a wide range of fields, such as gas adsorption/storage,[21] separations,[22] chemical sensors,[23] thin-film devices,[24] photoluminescence,[25] drug carriers,[26] or biomedical imaging.[27] Although the use of MOFs as heterogeneous catalysts in organic synthesis is still in its infancy, there has been significant growth in relevant research work.[28] Recently, MOFs based on Cu, Fe, Co, Zr, or Al have been shown to be effective and reusable heterogeneous catalysts for several reactions such as oxidation,[29] coupling,[30] condensation,[31] epoxidation,[32] cycloaddition,[33] hydroxylation,[34] cyclization,[35] acetalization,[36] ring-opening,[37] cyanosilylation,[38] Friedel–Crafts reactions,[39] or Friedländer reactions,[40] as well as multicomponent reactions.[41] Unfortunately, it is difficult to ensure complete separation and recycling of MOF-based heterogeneous catalysts from the reaction solutions. However, if MOFs are combined with magnetic components, the resulting magnetic MOFs will show magnetic susceptibility, which permits separation of the catalyst from the reaction medium simply by applying an external magnet after the



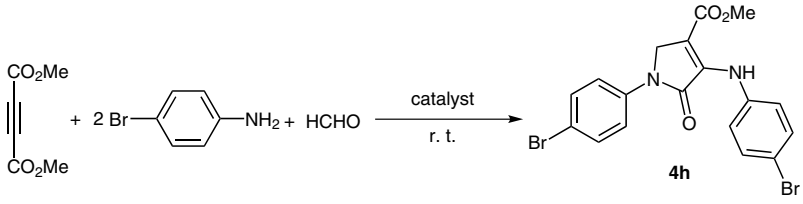
Scheme 1 Synthesis of $CoFe_2O_4$@SiO_2@IRMOF-3

reaction;[42] the catalyst can then be regenerated and reused without filtration or centrifugation operations, and without loss of catalytic activity. Nevertheless, there are few examples of syntheses or applications of magnetic MOFs.[43]

By taking account of the above reports, and as a part of our ongoing research into the design of magnetic nanocatalysts[44] and the development of environmentally friendly approaches for the construction of heterocyclic molecules,[45] we prepared a highly active and easily recyclable MOF-based porous magnetic core–shell material ($CoFe_2O_4$@SiO_2@IRMOF-3) by a simple approach, and we used it as an efficient catalyst for the synthesis of functionalized dihydro-2-oxopyrroles in a one-pot, four-component reaction of a dialkyl acetylenedicarboxylate, an aryl amine, formaldehyde, and optionally a second amine at room temperature.

Magnetic nanocomposite particles $CoFe_2O_4$@SiO_2@IRMOF-3, containing the basic isoreticular MOF IRMOF-3, were prepared in a three-step procedure (Scheme 1) by using $CoFe_2O_4$ as a magnetic core, Zn^{2+} ion as a connector, and 2-aminoterephthalic acid (H_2NH_2BDC) as a linker.[46] First, $CoFe_2O_4$ particles were synthesized by chemical co-precipitation from $FeCl_3$ and $CoCl_2$. Secondly, the $CoFe_2O_4$ particles were modified with a layer of SiO_2 by stirring them in suspension in an aqueous alkaline solution of tetraethyl orthosilicate (TEOS). Finally, IRMOF-3 MOFs were deposited on

Table 1 Optimization of the Conditions for the Synthesis of **4h**[a]



Entry	Catalyst	Solvent	Time (h)	Yield[b] (%)
1	–	MeOH	10 h	trace
2	$CoFe_2O_4$	MeOH	3 h	36
3	$CoFe_2O_4$@SiO_2	MeOH	3 h	33
4	$CoFe_2O_4$@SiO_2@IRMOF-3	MeOH	3 h	92
5	$CoFe_2O_4$@SiO_2@IRMOF-3	EtOH	3 h	85
6	$CoFe_2O_4$@SiO_2@IRMOF-3	H_2O	3 h	45
7	$CoFe_2O_4$@SiO_2@IRMOF-3	CH_2Cl_2	3 h	75
8	$CoFe_2O_4$@SiO_2@IRMOF-3	MeCN	3 h	72
9	$CoFe_2O_4$@SiO_2@IRMOF-3	THF	3 h	52
10	$CoFe_2O_4$@SiO_2@IRMOF-3	DMF	3 h	59
11	$CoFe_2O_4$@SiO_2@IRMOF-3	toluene	3 h	66
12	$CoFe_2O_4$@SiO_2@IRMOF-3	PEG 400	3 h	77
13	$CoFe_2O_4$@SiO_2@IRMOF-3	ChCl–glycerine	3 h	63
14	$CoFe_2O_4$@SiO_2@IRMOF-3 (10 mg)	MeOH	3 h	82
15	$CoFe_2O_4$@SiO_2@IRMOF-3 (15 mg)	MeOH	3 h	86
16	$CoFe_2O_4$@SiO_2@IRMOF-3 (30 mg)	MeOH	3 h	92
17[c]	$CoFe_2O_4$@SiO_2@IRMOF-3	MeOH	3 h	93

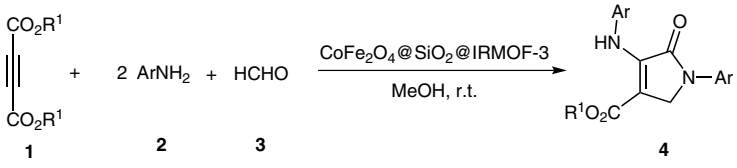
[a] Experimental conditions: DMAD (1 mmol), 4-bromoaniline (1 mmol), HCHO (1.5 mmol), solvent (3 ml), catalyst (20 mg unless otherwise stated), r.t.
[b] Isolated yield.
[c] The reaction was carried out on a 10 mmol scale.

the $CoFe_2O_4$@SiO_2 microspheres by dispersing the microspheres in a solution of zinc(II) nitrate hexahydrate and H_2NH_2BDC in DMF, and heating the mixture at 100 °C in a Teflon-lined steel autoclave. The morphology, structure, and composition of the thus-prepared $CoFe_2O_4$@SiO_2@IRMOF-3 nanocomposites were investigated by various techniques.

The activity of the prepared catalyst was probed in the model reaction of dimethyl acetylenedicarboxylate (DMAD; 1 mmol), 4-bromoaniline (2 mmol), and formaldehyde (1.5 mmol). Almost no target product was detected when the reaction mixture was stirred for ten hours in MeOH at room temperature in the absence of a catalyst (Table 1, entry 1). The reaction proceeded well in the presence of $CoFe_2O_4$@SiO_2@IRMOF-3, affording pyrrolidinone **4h** as the sole product in 92% yield (Table 1, entry 4). In contrast, magnetic $CoFe_2O_4$ also catalyzed the reaction, but its efficiency was much lower than that of $CoFe_2O_4$@SiO_2@IRMOF-3 (entries 2 and 3). Next, we examined the effect of the solvent. Among the various solvents screened, MeOH was found to be the solvent of choice. The use of EtOH decreased the yield of **4h** (entry 5). An inferior result was also observed when the model reaction was performed in H_2O (entry 6). The use of CH_2Cl_2, MeCN, THF, DMF, toluene, poly(ethylene glycol) (PEG 400) and choline chloride (ChCl)–glycerine gave the desired product in 52–77% yield (entries 7–13). Next, the catalyst loading was optimized, and 20 mg of catalyst was found to give the maximum product yield (entry 3). Increasing the amount of catalyst did not improve the results (entries 14–16), whereas decreasing the amount of catalyst resulted in a lower yield of product **4h**. Note that the efficiency of the reaction was unaffected by scaling up; for example, the model reaction of DMAD (10 mmol), 4-bromoaniline (20 mmol), and formaldehyde (15 mmol) gave the pure product **4h** in 93% yield (entry 17).

Next, we examined the substrate scope and limitations of this domino four-component reaction under the optimized conditions.[47] Representative results are given in Table 2. Generally, most anilines bearing electron-rich, electron-neutral, or electron-deficient substituents reacted successfully with DMAD and formaldehyde to give the corresponding highly substituted dihydropyrrol-2-one derivatives in good to excellent yields (entries 2–5). The position of the substituents on the phenyl ring had some effect on yield of the product. An *ortho*-substituted aniline gave a lower yield of the product compared with the corresponding *meta*- or *para*-substituted anilines, possibly due to steric hindrance (entries 6–8). However, almost none of the desired product was formed when an aniline with a strongly electron-deficient 4-trifluoromethyl substituent was used as a substrate (not shown). Unfortunately, 2-aminopyridine was also incompatible with reaction conditions (not

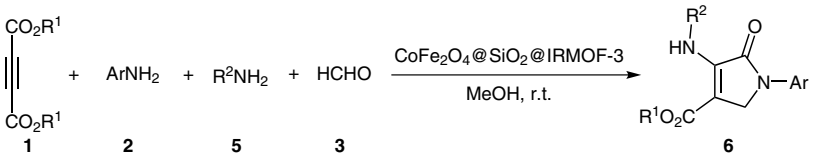
Table 2 Synthesis of Pyrrolidinones from Various Aromatic Amines



1 2 3 4

Entry	R^1	$ArNH_2$	Product	Time (h)	Yield (%)	Mp (°C)	
						Found	Lit.
1	Me	Ph	**4a**	3	90	154–155	154–155[8]
2	Me	4-$MeOC_6H_4$	**4b**	3	88	175–177	176–178[9]
3	Me	4-Tol	**4c**	3	89	175–176	177–179[8]
4	Me	4-FC_6H_4	**4d**	3	92	165–166	163–165[8]
5	Me	4-ClC_6H_4	**4e**	3	93	173–174	170–172[9]
6	Me	2-BrC_6H_4	**4f**	5	82	165–166	–
7	Me	3-BrC_6H_4	**4g**	4	88	143–144	–
8	Me	4-BrC_6H_4	**4h**	3	91	165–167	165–167[9]
9	Et	Ph	**4i**	3	92	139–140	136–138[8]
10	Et	4-$MeOC_6H_4$	**4j**	3	87	153–154	152–154[8]
11	Et	4-Tol	**4k**	3	88	129–130	128–130[8]
12	Et	4-FC_6H_4	**4l**	3	91	172–173	170–172[9]
13	Et	4-ClC_6H_4	**4m**	3	93	166–167	167–170[8]
14	Et	4-BrC_6H_4	**4n**	3	90	166–167	167–169[8]

Table 3 Synthesis of Polysubstituted Dihydropyrrol-2-ones from Two Different Amines



1 2 5 3 6

Entry	R^1	Ar	R^2	Product	Time (h)	Yield (%)[a]	Mp (°C) Found	Lit.
1	Me	4-$MeOC_6H_4$	Ph	**6a**	3.0	81	120–121	–
2	Me	4-MeC_6H_4	Ph	**6b**	3.0	83	153–154	154–156[7]
3	Me	4-ClC_6H_4	Ph	**6c**	3.0	89	149–150	–
4	Me	4-BrC_6H_4	Ph	**6d**	3.0	88	152–153	–
5	Me	4-$O_2NC_6H_4$	Ph	**6e**	3.0	85	146–147	–
6	Me	Ph	Bn	**6f**	2.0	85	137–139	140–141[7]
7	Me	4-$MeOC_6H_4$	Bn	**6g**	3.0	83	128–129	129–130[19]
8	Me	4-BrC_6H_4	Bn	**6h**	2.0	88	119–120	119–121[8]
9	Me	Ph	Cy	**6i**	1.5	90	96–97	96–97[19]
10	Me	4-$MeOC_6H_4$	Cy	**6j**	1.5	88	127–128	128–129[19]
11	Me	4-ClC_6H_4	Cy	**6k**	1.5	92	123–124	120–122[14]
12	Me	4-BrC_6H_4	Cy	**6l**	1.5	91	124–125	124–126[9]
13	Me	4-BrC_6H_4	*c*-Pent	**6m**	1.5	89	90–92	–
14	Me	4-BrC_6H_4	Bu	**6n**	1.0	90	107–108	108–110[9]
15	Me	4-BrC_6H_4	$Me(CH_2)_5NH_2$	**6o**	1.0	81	59–60	–
16	Et	4-$O_2NC_6H_4$	Cy	**6p**	1.5	86	143–144	–

[a] Isolated yield.

shown), probably due to inactivation of the catalyst by coordination. When the corresponding reactions of DEAD were evaluated, similar results were obtained, as expected (entries 9–14).

Encouraged by these results, we examined the multicomponent reaction with two different amines to further explore the scope of the protocol. The reactions of various anilines with DMAD, formaldehyde, and aniline, benzylamine, cyclohexylamine, butylamine, or hexylamine under the optimized conditions proceeded smoothly to give the corresponding dihydropyrrol-2-one derivatives **6a–p** in good to high yields (Table 3, entries 1–16).[48]

Finally, we extended the scope of the method to include the synthesis of substituted bisdihydropyrrol-2-ones. The four-component (pseudo-seven-component) reaction of propane-1,3-diamine (1 equiv), DMAD (2 equiv), various aromatic amines (2 equiv), and formaldehyde (2 equiv) was conducted under the optimized conditions. As expected, the desired bis-*N*-aryl-3-aminodihydropyrrol-2-one-4-carboxylates **8** were generated in high yields (Table 4).[48] The structures of the products were confirmed by FTIR, ^1H NMR, and ^{13}C NMR spectroscopy and mass spectrometry.

The recovery and reuse of the catalyst is an important economic benefit and an ecological requirement. Therefore, the reusability of $CoFe_2O_4$@SiO_2@IRMOF-3 was investigated in the model reaction of DMAD, 4-bromoaniline, and formaldehyde. After completion of the reaction, the catalyst was simply and efficiently recovered from the reaction mixture by using an external magnet, then washed with EtOAc,

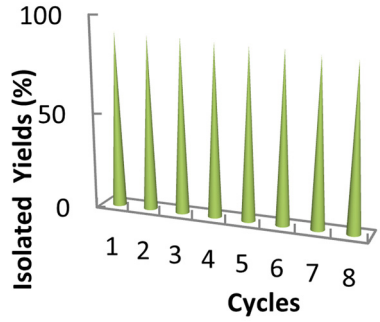
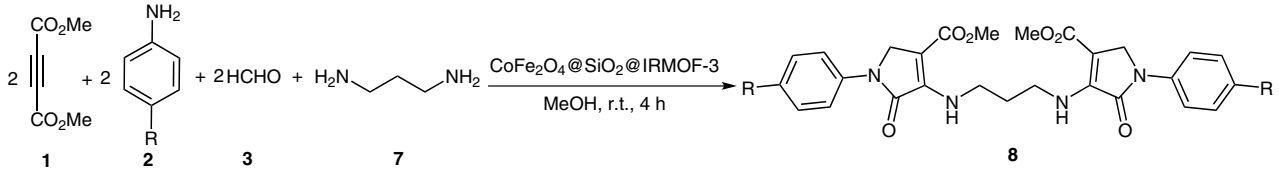


Figure 1 Reusability of the $CoFe_2O_4$@SiO_2@IRMOF-3

Table 4 Synthesis of Substituted Bisdihydropyrrol-2-ones



1 2 3 7 8

Entry	R	Product	Yield (%)[a]	Mp (°C)
1	H	**8a**	89	104–105
2	4-MeO	**8b**	91	135–136
3	4-Me	**8c**	90	109–110
4	4-Cl	**8d**	88	163–164
5	4-Br	**8e**	87	168–170

[a] Isolated yield.

dried under vacuum to remove residual solvent, and reused. The catalyst could be recycled seven times without significant loss of its activity (Figure 1).

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588924.

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(46) **Magnetic $CoFe_2O_4$@SiO_2@IRMOF-3 Nanoparticles**

$CoFe_2O_4$ magnetic nanoparticles (NPs) were synthesized by chemical co-precipitation from $FeCl_3{\cdot}6H_2O$ and $CoCl_2{\cdot}6H_2O$. The surface of the $CoFe_2O_4$ NPs was coated with a layer of SiO_2 by adding distilled H_2O (80 mL) to the purified $CoFe_2O_4$ NPs (1 g), heating for 1 h at 40 °C, adding concd aq NH_3 (1.5 mL), stirring at 40 °C for 30 min, adding TEOS (1.0 mL), and stirring continuously for 24 h. The mixture was then cooled to r.t. and the silica-coated NPs were collected by using a permanent magnet, washed three times with distilled H_2O and EtOH, and dried at 60 °C under vacuum for 6 h.

A versatile step-by-step assembly strategy was used to fabricate the porous $CoFe_2O_4$@SiO_2@IRMOF-3 core–shell nanoparticles. Briefly, the $CoFe_2O_4$@SiO_2 NPs (0.5 g) were dispersed in a solution of $Zn(NO_3)_2$ (1.7 g) and H_2NH_2BDC (0.4 g) in dry DMF (50 mL), and the mixture was stirred at r.t. for 20 min. The solution was then transferred to a Teflon-lined steel autoclave, which was sealed and kept at 100 °C for 20 h. The resulting brown solid was collected with a permanent magnet, washed with EtOH, and dried under vacuum at 60 °C for 6 h.

(47) **Pyrrolidinones 4a–h; General Procedure**

A mixture of the dialkyl acetylenedicarboxylate **1** (1 mmol), aromatic amine **2** (2 mmol), 37% aq HCHO (**3**, 5 mmol), and $CoFe_2O_4$@SiO_2@IRMOF-3 (0.02 g) in MeOH (3 mL) was stirred at r.t. for the appropriate time (Table 2). When the reaction was complete (TLC), the catalyst was separated by using a bar magnet, and the product was collected by filtration and washed with EtOH.

Methyl 1-(2-Bromophenyl)-4-[(2-bromophenyl)amino]-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate (4f)

White solid; yield: 482 mg (82%); mp 165–166 °C. IR (KBr): 3330, 1686, 1635, 1446, 1298, 825 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.80 (s, 3 H), 4.48 (s, 2 H), 7.03 (t, *J* = 7.5 Hz, 1 H), 7.18 (t, *J* = 7.0 Hz, 1 H), 7.33–7.36 (m, 5 H), 7.49–7.51 (m, 1 H), 8.40 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 49.7, 51.5, 106.7, 124.3, 125.1, 126.4, 126.5, 127.8, 129.2, 129.6, 129.7, 130.6, 132.4, 135.0, 135.4, 142.6, 164.1, 165.0. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{14}Br_2N_2O_3$: 464.9449; found: 464.9455.

(48) **Pyrrolidinones 6a–p and Bipyrrolidinones 8a–e; General Procedure**

A mixture of the aromatic amine **3** (1 mmol for product **6**; 2 mmol for product **8**) and dialkyl acetylenedicarboxylate (1 mmol for product **6**; 2 mmol for product **8**) in MeOH (3 mL) was stirred at r.t. for 20 min. Amine **5** (1 mmol) or propane-1,3-diamine (**7**, 1 mmol), 37% aq HCHO (1.5 mmol for product **6**; 3.0 mmol for product **8**), and $CoFe_2O_4$@SiO_2@IRMOF-3 (0.02 g) were added successively, and the mixture was stirred at r.t. for the appropriate time (Tables 3 and 4). When the reaction was complete (TLC), the catalyst was separated with a bar magnet, and the product was collected by filtration and washed with EtOH.

Methyl 1-(4-Methoxyphenyl)-5-oxo-4-(phenylamino)-2,5-dihydro-1*H*-pyrrole-3-carboxylate (6a)

White solid; yield: 273 mg (81%); mp 120–121 °C. IR (KBr): 3279, 1711, 1688, 1510, 1201, 823 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 3.74 (s, 3 H), 3.80 (s, 3 H), 4.49 (s, 2 H), 6.84–6.86 (m, 1 H), 6.91 (d, *J* = 9.0 Hz, 2 H), 7.09 (d, *J* = 8.5 Hz, 1 H), 7.13–7.15 (m, 1 H), 7.28–7.32 (m, 2 H), 7.64–7.67 (m, 2 H), 8.02 (s, 1 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 48.7, 51.3, 55.5, 100.8, 113.6, 114.3, 119.3, 121.1, 122.8, 124.6, 125.1, 128.3, 157.1, 163.5, 165.1. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{19}N_2O_4$: 339.1345; found: 339.1353.

Methyl 1-(4-Bromophenyl)-4-(cyclopentylamino)-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate (6m)

White solid; yield: 336 mg (89%); mp 90–92 °C. IR (KBr): 3335, 1713, 1683, 1259, 844 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.45–1.50 (m, 2 H), 1.60–1.65 (m, 3 H), 1.71–1.75 (m, 2 H), 2.02–2.07 (m, 2 H), 3.78 (s, 3 H), 4.37 (s, 2 H), 5.03 (s, 1 H), 7.49-7.51 (m, 2 H), 7.67–7.69 (m, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 23.7, 34.8, 47.8, 50.9, 54.1, 95.9, 117.7, 120.5, 128.8, 132.0, 137.9, 164.4, 165.5. HRMS (ESI): *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{20}BrN_2O_3$: 379.0657; found: 379.0661.

Dimethyl 4,4'-[Propane-1,3-diylbis(azanediyl)]bis(5-oxo-1-phenyl-2,5-dihydro-1*H*-pyrrole-3-carboxylate) (8a)

White solid; yield: 445 mg (89%); mp 104–105 °C. IR (KBr): 3314, 2950, 1706, 1686, 1499, 1259, 762 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): δ = 1.92–1.97 (m, 2 H), 3.78 (s, 6 H), 3.97–4.01 (m, 4 H), 4.39 (s, 4 H), 7.10 (t, *J* = 7.5 Hz, 2 H), 7.37 (t, *J* = 8.0 Hz, 4 H),

7.74 (d, J = 8.0 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.2, 40.3, 48.0, 51.0, 118.2, 119.4, 125.0, 129.1, 129.3, 138.8, 164.5, 165.5. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{27}H_{29}N_4O_6$: 505.2087; found: 505.2093.

Dimethyl 4,4'-[Propane-1,3-diylbis(azanediyl)]bis[5-oxo-1-(*p*-tolyl)-2,5-dihydro-1*H*-pyrrole-3-carboxylate] (8c)

White solid; yield: 479 mg (90%); mp 135–136 °C. IR (KBr): 3401, 2951, 1659, 1636, 1455, 1258, 820 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.93–1.95 (m, 2 H), 2.34 (s, 6 H), 3.77 (s, 6 H), 3.97–4.01 (m, 4 H), 4.36 (s, 4 H), 7.17 (d, J = 8.5 Hz, 4 H), 7.60 (d, J = 8.5 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.9, 29.7, 40.0, 47.4, 51.0, 119.4, 129.6, 129.7, 132.4, 134.7, 136.3, 161.9, 164.3. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{29}H_{33}N_4O_6$: 533.2400; found: 533.2406.

4,4'-[Propane-1,3-diylbis(azanediyl)]bis[1-(4-bromophenyl)-5-oxo-2,5-dihydro-1*H*-pyrrole-3-carboxylate] (8e)

Yellow solid; yield: 574 mg (87%); mp 168–170 °C. IR (KBr): 3324, 2941, 1703, 1687, 1645, 1430, 1290, 1200, 759 cm^{-1}. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.87–1.90 (m, 2 H), 3.73 (s, 6 H), 3.93-3.95 (m, 4 H), 4.28 (s, 4 H), 7.40–7.45 (m, 4 H), 7.59 (d, J = 9.0 Hz, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 33.0, 40.1, 47.8, 51.1, 117.7, 119.3, 119.6, 120.5, 132.0, 137.8, 164.5, 165.5. HRMS (ESI): m/z [M + H]$^+$ calcd for $C_{27}H_{27}Br_2N_4O_6$: 661.0297; found: 661.0292.