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Water promoted C–C bond cleavage: facile synthesis of 3,3-bipyrrole derivatives from dienones and tosylmethyl isocyanide (TosMIC)†

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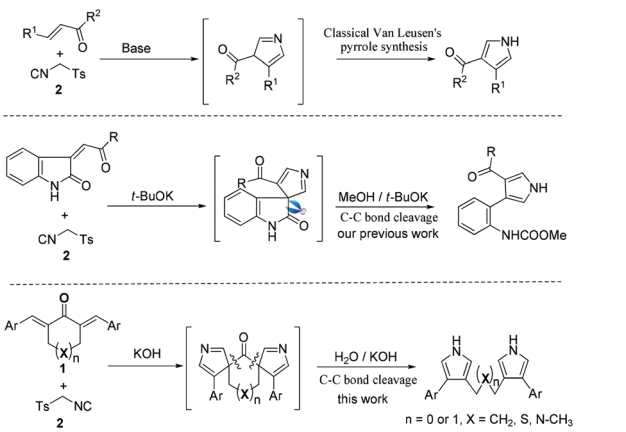
A simple and highly efficient synthetic strategy to access 3,3-bipyrrole derivatives by the reaction of dienone derivatives with TosMIC is reported. The reaction involves a van Leusen's pyrrole synthesis followed by an unusual C–C bond cleavage in the presence of water under mild conditions.

Pyrroles[1] represent an important class of five-membered ring heterocycles and useful synthons for alkaloids in natural product synthesis and medicinal chemistry, and this structural motif can be found in many natural products and bioactive molecules.[2] Pyrroles also play crucial roles not only in heterocyclic chemistry,[3] but also in materials chemistry.[4] Specifically, bipyrrolic structures are also widespread in nature[2d,5] and have been the focus of material science[6] and medicinal chemistry.[7] Particularly, 3,3-bipyrroles were building blocks for the synthesis of the antitumor agent CC-1065.[8] However, the efficient synthesis of 3,3-bipyrroles is quite limited, and it also suffers from a number of drawbacks such as lengthy steps, harsh reaction conditions and poor yields. Although much effort has been directed toward the synthesis and functionalization of 3,3-bipyrroles, relatively few reports in the literature are known for the preparation of 3,3-bipyrrole derivatives.[8,9] Therefore, using a simple and convenient synthetic approach toward 3,3-bipyrrole derivatives is compatible with the efficient process.

Tosylmethyl isocyanide (TosMIC) is a versatile and widely exploited reagent in organic synthesis.[10] van Leusen's pyrrole synthesis is a well known method to prepare the pyrrole moiety through the reaction of TosMIC with Michael acceptors. However, the synthesis of 3,3-bipyrroles through van Leusen's methodology has never been reported so far. More recently, we have reported an efficient route for the synthesis of pyrrole derivatives through a base-promoted reaction of 3-phenacylideneoxindole and TosMIC *via* C–C bond cleavage.[11] As a continuation of our studies related to isonitriles,[12] we reasoned that dienones could be applied in the reaction with TosMIC to form the pyrrole moiety as well. Herein, we demonstrate an efficient approach for the synthesis of 3,3-bipyrrole derivatives **3** by the non-classical van Leusen's reaction of dienone derivatives **1** with TosMIC **2** through a water-promoted C–C bond cleavage (Scheme 1).

Initially, model reaction of (2*E*,5*E*)-2,5-dibenzylidenecyclopentanone **1a** with TosMIC **2** was studied in the presence of *t*-BuOK in DMF. However, the expected 1,2-bis(4-phenyl-1*H*-pyrrol-3-yl)ethane **3a** was only obtained in 32% isolated yield (Table 1, entry 1). In our efforts to improve the yield of **3a**, different bases were screened subsequently (Table 1, entries 2–5). It was found that only a trace amount of product **3a** was observed when Cs_2CO_3 or DBU was used as the additive (Table 1, entries 4 and 5). Gratifyingly, the yield could be improved (34%) when KOH was employed as a base (Table 1, entry 3). We further explored the reaction in various solvents, and DMF was demonstrated to be a suitable solvent (see ESI†). A lower yield was obtained when the reaction was performed at 0 °C (10% yield, see ESI†). The yield of **3a** could be increased



Scheme 1 Classical van Leusen's pyrrole synthesis, our previous work and this work.

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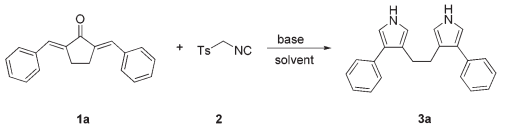
Table 1 Optimization of reaction conditions[a]



1a 2 3a

Entry	Base	Solvent	Temp (°C)	Yield[b] (%)
1	*t*-BuOK	DMF	25	32
2	NaOH	DMF	25	29
3	KOH	DMF	25	34
4	Cs_2CO_3	DMF	25	Trace
5	DBU	DMF	25	Trace
6	KOH	DMF	80	67
7	KOH	DMF	100	72
8	KOH	DMF	150	71
9	KOH	Dry DMF	100	58
10	KOH	Dry DMF + 40 μl H_2O	100	80
11	KOH	Dry DMF + 80 μl H_2O	100	86
12	KOH	Dry DMF + 100 μl H_2O	100	82

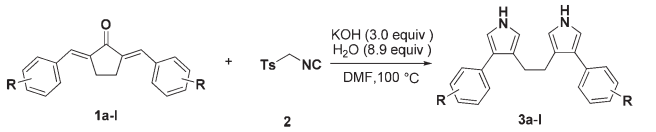
[a] The reactions were performed with **1a** (0.5 mmol, 1.0 eq.) and TosMIC **2** (1.2 mmol, 2.4 eq.) in the presence of a base. [b] Isolated yield.

to 72% by elevating the reaction temperature to 100 °C (Table 1, entry 7). However, increasing the temperature to 150 °C did not increase the yield of the desired product at all (Table 1, entry 8). To our surprise, the product could be afforded in 58% yield when dry DMF was used as the solvent (Table 1, entry 9). Undoubtedly, water was involved in the reaction and promoted the reaction. Thus, we explored the effects of the amount of water on this reaction (Table 1, entries 10–12). Gratifyingly, the reaction worked more efficiently when 80 μl (about 8.9 equiv.) water was added, delivering the corresponding product **3aa** in 86% yield (Table 1, entry 11).

We next explored the scope of this reaction involving (2*E*,5*E*)-2,5-dibenzylidenecyclopentanone **1** and TosMIC **2** under the optimized conditions (3.0 equiv. of KOH, dry DMF with 8.9 equiv. H_2O, 100 °C). The results are summarized in Table 2. In all cases, (2*E*,5*E*)-2,5-dibenzylidenecyclopentanone **1b–l** reacted with TosMIC **2** leading to the corresponding substituted 1,2-bis(4-phenyl-1*H*-pyrrol-3-yl)ethane **3bl** in good to excellent yields. For instance, **1c** and **1d** with methyl substituents in different positions were examined in the reaction, which afforded the corresponding products **3c** and **3d** in good yields, respectively. The sterically more hindered substrate **1b** furnished the desired product **3b** in 91% yield. We next examined the reaction of (2*E*,5*E*)-2,5-dibenzylidenecyclopentanone **1e–l** with varying substituents on the aromatic ring. To our delight, during the reaction process, the methoxy, fluoro, bromo, and nitro groups on the phenyl ring did not affect the final outcomes, affording the expected products in good yields.

Furthermore, a number of conformationally restricted dienones **1m–q**, some of them bearing pyridyl or furyl groups instead of the phenyl group, were also examined. As expected, both (2*E*,5*E*)-2,5-bis(pyridin-2-ylmethylene)cyclopentanone **1m** and (2*E*,5*E*)-2,5-bis(pyridin-3-ylmethylene)cyclopentanone **1n** can provide the products **3m** and **3n** in 80% and 81% yields,

Table 2 Substrate scope for the synthesis of 1,2-bis(4-phenyl-1*H*-pyrrol-3-yl)ethanes[a]



1a-l 2 3a-l

Entry	R^1	Product	Yield[b] (%)
1	H	**3a**	86
2	2-CH_3	**3b**	91
3	3-CH_3	**3c**	85
4	4-CH_3	**3d**	88
5	2-OCH_3	**3e**	91
6	3-OCH_3	**3f**	85
7	4-F	**3g**	88
8	3-Cl	**3h**	87
9	4-Cl	**3i**	85
10	4-Br	**3j**	86
11	3-NO_2	**3k**	84
12	4-NO_2	**3l**	88

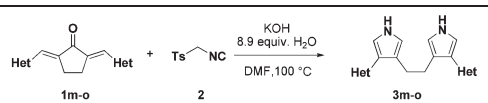
[a] The reactions were performed with **1** (0.5 mmol, 1.0 eq.) and **2** (1.2 mmol, 2.4 eq.) in the presence of KOH in DMF at 100 °C. [b] Isolated yield.

respectively. Similarly, the reaction of (2*E*,5*E*)-2,5-bis(furan-2-ylmethylene)cyclopentanone **1o** with TosMIC **2** worked equally well, leading to the corresponding product **3o** in 81% yield (Table 3).

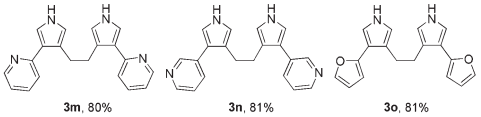
Subsequently, (2*E*,6*E*)-2,6-dibenzylidenecyclohexanone **1p** and (3*Z*,5*Z*)-3,5-dibenzylidenedihydro-2*H*-thiopyran-4(3*H*)-one **1q** were subjected to the reactions under the optimal reaction conditions. As anticipated, the desired products **3p** and **3q** were obtained in 84% and 83% yields (Scheme 2, eqn (1) and (2)), respectively. In addition, the reaction using (3*E*,5*E*)-3,5-dibenzylidene-1-methylpiperidin-4-one **1r** afforded not only the expected product **3r** in 71%, but also bis(4-phenyl-1*H*-pyrrol-3-yl)methanone **3s** in 10% yield through C–C bond cleavage in other positions (Scheme 2, eqn (3)).

To better understand the reaction mechanism, two control experiments were carried out (Scheme 3). When the reaction of **1a** with **2 was** performed in dry DMF in the presence of KOH at 0 °C, an unstable dual [3 + 2] cycloaddition product **4** could be formed (determined by crude NMR and LC-MS). In comparison, when 8.9 equiv. H_2O was added to the reaction system and the reaction temperature was increased to 100 °C,

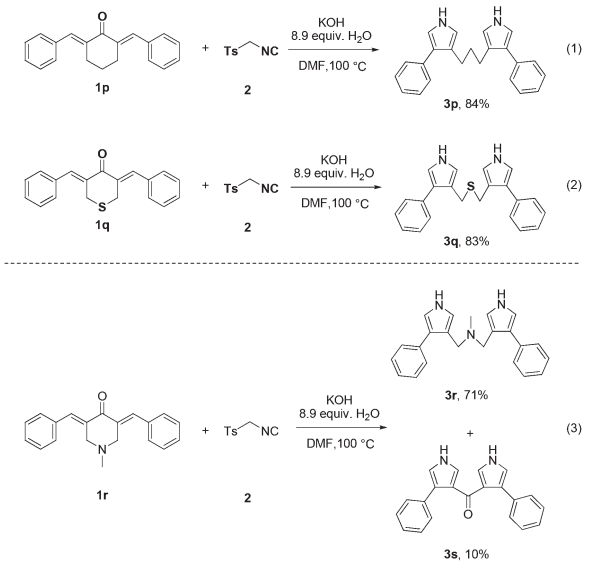
Table 3 Investigation of the scope of the reaction involving dienones **1m–q** and TosMIC **2**



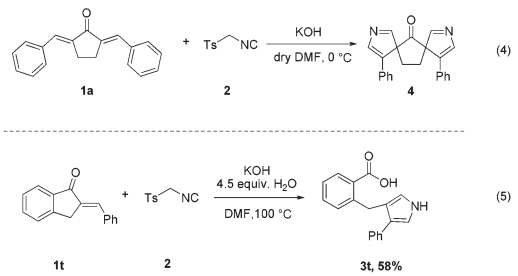
1m-o 2 3m-o



3m, 80% 3n, 81% 3o, 81%



Scheme 2 Investigation of the scope of the reaction of dienones **1p–r** and TosMIC **2**.

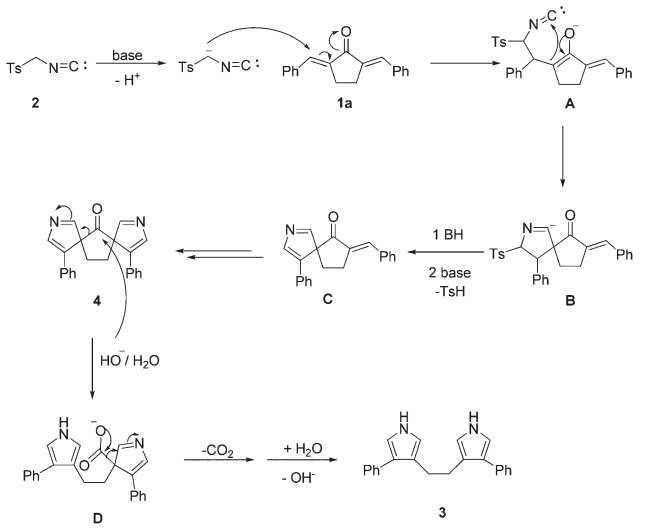


Scheme 3 Control experiments.

3a could also be obtained in good yield (Table 1, entry 11). Then, we tried the reaction of **1t** with **2** under similar conditions. Interestingly, 2-((4-phenyl-1*H*-pyrrol-3-yl)methyl)-benzoic acid **3t** was obtained in 58% yield (Scheme 3, eqn (5)). These results indicated that water is important for the C–C bond cleavage.

Based on van Leusen's pyrrole synthesis mechanism and the above results, we proposed a plausible mechanism for this reaction (Scheme 4). The 1,4-addition of **2** to **1a** in the presence of KOH gives the enolate intermediate **A**. A subsequent intramolecular cyclization occurs to produce a spirocyclic intermediate **B**. Then, the spirocyclic intermediate **C** could be formed after further detosylation of **B**. After an iterative process, the bispirocyclic **4** is generated. In the presence of water and KOH, one of the spiro rings is opened to give intermediate **D**, followed by decarboxylation and protonation to give the desired product **3**.

In conclusion, we have demonstrated a simple and highly efficient synthetic strategy to access 3,3-bipyrrole derivatives. The reaction involves a van Leusen's pyrrole synthesis followed by an unusual C–C bond cleavage in the presence of water under mild conditions. It is very interesting to trap the



Scheme 4 A possible mechanism for the formation of 3,3-bipyrroles **3**.

reaction intermediates as proposed in Scheme 4 to construct new stable spiro compounds as well as other useful heterocycles, which is currently ongoing in our laboratory.

Experimental

General

All reactions were carried out at ambient temperature in oven-dried glassware. All solvents were dried and distilled according to standard procedures. Column chromatography was generally performed on silica gel (300–400 mesh) and reactions were monitored by thin layer chromatography (TLC) using UV light to visualize the course of the reactions. Melting points were recorded on an electrothermal digital melting point apparatus and are uncorrected. IR spectra were recorded on an FT-IR spectrometer using KBr optics. NMR spectra were recorded at room temperature in d_6-DMSO at 300/400 Hz and 75/100 Hz with TMS as an internal reference. High resolution mass spectra (HRMS) were obtained on a TOF MS instrument with ESI source. X-ray diffraction data were recorded with graphite monochromatic Mo-Kα radiation.

General procedures for products 3a–3s

Dienones **1** (0.5 mmol), TosMIC **2** (1.2 mmol, 2.4 equiv.) and KOH (1.5 mmol, 3.0 equiv.) were suspended in 2 mL of dry DMF in an oven-dried flask. 80 μl H_2O was added to the mixture, which was stirred at 100 °C for 2 h. After cooling the mixture to ambient temperature, the reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under vacuum, the residue was purified by preparative silica gel column chromatography to give the corresponding products **3** as a white solid.

General procedures for product 3t

(*E*)-2-Benzylidene-2,3-dihydro-1*H*-inden-1-one **1t** (0.5 mmol), TosMIC **2** (0.6 mmol, 1.2 equiv.) and KOH (1.0 mmol, 2.0 equiv.) were suspended in 2 mL of dry DMF in an oven-dried flask. 40 μl H_2O was added to the mixture, which was stirred at 100 °C for 2 h. After cooling the mixture to ambient temperature, the reaction mixture was neutralized with 6 M HCl and extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under vacuum, the residue was purified by preparative silica gel column chromatography to give the corresponding products **3t** as a white solid.

General procedures for intermediate D

(2*E*,5*E*)-2,5-Dibenzylidenecyclopentanone **1a** (0.5 mmol), TosMIC **2** (1.2 mmol, 2.4 equiv.) and KOH (1.5 mmol, 3.0 equiv.) were suspended in 2 mL of dry DMF in an oven-dried flask. The reaction mixture was stirred at 0 °C for 3 h. The reaction mixture was quenched with H_2O (10 mL) and extracted with EtOAc (3 × 15 mL). The combined organic phase was washed with brine (15 mL) and dried over anhydrous Na_2SO_4. After filtration and evaporation of the solvents under vacuum, the residue was purified by preparative silica gel column chromatography to give the corresponding products **D** as a white solid.

1,2-Bis(4-phenyl-1*H*-pyrrol-3-yl)ethane (3a). Yield: 86%; white solid; melting point: 217.2–218.1 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.66 (s, 2H), 7.33 (d, J = 7.5 Hz, 4H), 7.28 (t, J = 7.5 Hz, 4H), 7.13 (t, J = 6.8 Hz, 2H), 6.86 (s, 2H), 6.63 (s, 2H), 2.77 (s, 4H); ^{13}C NMR (d_6-DMSO, 100 MHz): δ 137.7, 130.0, 129.0, 127.7, 125.4, 121.3, 117.1, 116.8, 28.1; MS: Anal. calcd for $C_{22}H_{20}N_2$: 312.1626. Found: 311.1547 (M − H^+); IR (KBr, cm^{-1}): ν 3363, 1603, 1532, 1432, 1076, 976, 845.

1,2-Bis(4-*o*-tolyl-1*H*-pyrrol-3-yl)ethane (3b). Yield: 91%; white solid; melting point: 101.1–102.4 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.51 (s, 2H), 7.17 (d, J = 6.9 Hz, 2H), 7.10 (dt, J = 14.3, 7.0 Hz, 4H), 6.98 (d, J = 6.9 Hz, 2H), 6.55 (s, 2H), 6.49 (s, 2H), 2.35 (s, 4H), 2.07 (s, 6H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 136.9, 136.6, 130.9, 130.0, 126.3, 125.5, 122.3, 122.0, 116.4, 115.3, 27.4, 20.6; MS: Anal. calcd for $C_{24}H_{24}N_2$: 340.1939. Found: 339.1879 (M − H^+); IR (KBr, cm^{-1}): ν 3372, 1604, 1525, 1479, 1597, 1061, 1302, 991, 893.

1,2-Bis(4-*m*-tolyl-1*H*-pyrrol-3-yl)ethane (3c). Yield: 85%; white solid; melting point: 76.8–77.4 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.64 (s, 2H), 7.14 (d, J = 9.3 Hz, 6H), 6.95 (d, J = 6.8 Hz, 2H), 6.84 (s, 2H), 6.61 (s, 2H), 2.76 (s, 4H), 2.27 (s, 6H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 137.6, 137.4, 128.6, 128.2, 125.9, 124.6, 123.0, 121.1, 116.7, 116.4, 27.8, 21.6; MS: Anal. calcd for $C_{24}H_{24}N_2$: 340.1939. Found: 339.1880 (M − H^+); IR (KBr, cm^{-1}): ν 3371, 1602, 1523, 1480, 1068, 900, 838.

1,2-Bis(4-*p*-tolyl-1*H*-pyrrol-3-yl)ethane (3d). Yield: 88%; white solid; melting point: 149.1–151.3 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.61 (s, 2H), 7.22 (d, J = 7.5 Hz, 4H), 7.09 (d, J = 7.5 Hz, 4H), 6.81 (s, 2H), 6.61 (s, 2H), 2.74 (s, 4H), 2.27 (s, 6H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 134.6, 134.1, 129.3, 127.4, 122.9, 121.0, 116.6, 116.2, 27.9, 21.1; MS: Anal. calcd for $C_{24}H_{24}N_2$: 340.1939. Found: 339.1867 (M − H^+); IR (KBr, cm^{-1}): ν 3353, 1530, 1497, 1112, 1075, 887, 794.

1,2-Bis(4-(2-methoxyphenyl)-1*H*-pyrrol-3-yl)ethane (3e). Yield: 91%; white solid; melting point: 77.9–80.1 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.99 (s, 2H), 7.68 (t, J = 7.6 Hz, 2H), 7.59 (d, J = 7.1 Hz, 2H), 7.45 (d, J = 8.1 Hz, 2H), 7.37 (t, J = 7.3 Hz, 2H), 7.16 (s, 2H), 6.99 (s, 2H), 4.14 (s, 6H), 2.99 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 157.0, 131.1, 127.2, 126.2, 122.9, 120.4, 119.3, 117.3, 115.1, 111.4, 55.3, 27.6; MS: Anal. calcd for $C_{24}H_{24}N_2O_2$: 372.1838. Found: 371.1769 (M − H^+); IR (KBr, cm^{-1}): ν 3380, 1726, 1580, 1458, 1178, 984.

1,2-Bis(4-(3-methoxyphenyl)-1*H*-pyrrol-3-yl)ethane (3f). Yield: 85%; white solid; melting point: 125.1–126.3 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.68 (s, 2H), 7.19 (t, J = 7.9 Hz, 2H), 6.90 (dd, J = 13.0, 6.7 Hz, 6H), 6.71 (d, J = 6.8 Hz, 2H), 6.63 (s, 2H), 3.71 (s, 6H), 2.78 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 159.7, 138.9, 129.7, 122.76, 121.1, 119.9, 116.8, 112.9, 110.7, 107.9, 55.2, 27.8; MS: Anal. calcd for $C_{24}H_{24}N_2O_2$: 372.1838. Found: 371.1765 (M − H^+); IR (KBr, cm^{-1}): ν 3370, 1596, 1460, 1247, 1016, 860.

1,2-Bis(4-(4-fluorophenyl)-1*H*-pyrrol-3-yl)ethane (3g). Yield: 88%; white solid; melting point: 161.4–162.8 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.68 (s, 2H), 7.32 (t, J = 8.7 Hz, 4H), 7.10 (t, J = 8.7 Hz, 4H), 6.84 (s, 2H), 6.63 (s, 2H), 2.72 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 160.6 (C–F, J = 240.0 Hz), 133.9 (C–C, J = 3.0 Hz), 129.2 (C–H, J = 7.5 Hz), 122.0, 120.9, 116.7 (C–H, J = 24.0 Hz), 115.5, 115.3, 27.7; MS: Anal. calcd for $C_{22}H_{18}N_2F_2$: 348.1438. Found: 347.1370 (M − H^+); IR (KBr, cm^{-1}): ν 3358, 1529, 1492, 1212, 1155, 1071, 878.

1,2-Bis(4-(3-chlorophenyl)-1*H*-pyrrol-3-yl)ethane (3h). Yield: 87%; white solid; melting point: 98.0–99.4 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.64 (d, J = 135.6 Hz, 2H), 7.36 (s, 2H), 7.29 (s, 4H), 7.18 (s, 2H), 6.98 (s, 2H), 6.65 (s, 2H), 2.76 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 139.7, 133.5, 130.5, 126.8, 125.8, 125.0, 121.4, 120.9, 117.3, 117.2, 27.7; MS: Anal. calcd for $C_{22}H_{18}N_2Cl_2$: 380.0847. Found: 379.0770 (M − H^+); IR (KBr, cm^{-1}): ν 3368, 1595, 1466, 1150, 1074, 976, 888.

1,2-Bis(4-(4-chlorophenyl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 85%; white solid; melting point: 118.2–119.3 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.75 (s, 2H), 7.34 (d, J = 8.8 Hz, 8H), 6.91 (s, 2H), 6.65 (s, 2H), 2.74 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 136.4, 129.8, 129.0, 128.7, 121.6, 120.9, 117.2, 116.9, 27.7; MS: Anal. calcd for $C_{22}H_{18}N_2Cl_2$: 380.0847. Found: 379.0768 (M − H^+); IR (KBr, cm^{-1}): ν 3351, 1522, 1461, 1067, 1007, 966, 824.

1,2-Bis(4-(4-bromophenyl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 86%; white solid; melting point: 158.4–159.8 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.76 (s, 2H), 7.45 (d, J = 8.2 Hz, 4H), 7.28 (d, J = 8.3 Hz, 4H), 6.91 (s, 2H), 6.65 (s, 2H), 2.74 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 136.8, 131.6, 129.4, 121.6, 120.9, 118.1, 117.2, 116.9, 27.7; MS: Anal. calcd for $C_{22}H_{18}N_2Br_2$: 467.9837. Found: 466.9745 (M − H^+); IR (KBr, cm^{-1}): ν 3360, 1523, 1475, 1399, 1123, 1074, 1003, 899.

1,2-Bis(4-(3-nitrophenyl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 84%; yellow solid; melting point: 222.5–223.3 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.93 (s, 2H), 8.09 (s, 2H), 7.94 (d, J = 7.8 Hz, 2H), 7.78 (d, J = 7.5 Hz, 2H), 7.53 (t, J = 7.9 Hz, 2H), 7.10 (s, 2H), 6.72 (s, 2H), 2.82 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 148.4, 139.1, 133.6, 130.1, 121.0, 120.8, 120.7, 119.8, 117.9, 117.7, 27.8; MS: Anal. calcd for $C_{22}H_{18}N_4O_4$: 402.1328. Found: 401.1244 (M − H$^+$); IR (KBr, cm^{-1}): ν 3390, 1531, 1341, 1143, 1084, 993, 875.

1,2-Bis(4-(4-nitrophenyl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 88%; yellow solid; melting point: 270.7–271.1 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 11.05 (s, 2H), 8.11 (d, J = 8.5 Hz, 4H), 7.61 (d, J = 8.5 Hz, 4H), 7.20 (s, 2H), 6.77 (s, 2H), 2.86 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 144.9, 144.5, 127.2, 124.2, 121.3, 120.9, 119.2, 118.4, 27.8; MS: Anal. calcd for $C_{22}H_{18}N_4O_4$: 402.1328. Found: 401.1260 (M − H$^+$); IR (KBr, cm^{-1}): ν 3390, 1590, 1495, 1324, 1107, 923, 852.

1,2-Bis(4-(pyridin-2-yl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 80%; white solid; melting point: 143.6–1449.5 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.81 (s, 2H), 8.44 (d, J = 3.6 Hz, 2H), 7.63 (t, J = 7.4 Hz, 2H), 7.51 (d, J = 7.9 Hz, 2H), 7.28 (s, 2H), 7.02 (t, J = 7.4 Hz, 2H), 6.67 (s, 2H), 3.02 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 156.5, 149.2, 136.5, 122.8, 122.5, 120.4, 119.8, 119.1, 117.4, 28.5; MS: Anal. calcd for $C_{20}H_{18}N_4$: 314.1531. Found: 313.1456 (M − H$^+$); IR (KBr, cm^{-1}): ν 3160, 1727, 1590, 1521, 1474, 1155, 1081, 982.

1,2-Bis(4-(pyridin-3-yl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 81%; white solid; melting point: 149.1–150.2 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.84 (s, 2H), 8.58 (s, 2H), 8.34 (d, J = 4.1 Hz, 2H), 7.69 (d, J = 7.7 Hz, 2H), 7.29 (t, J = 7.4 Hz, 2H), 7.00 (s, 2H), 6.69 (s, 2H), 2.77 (s, 4H); ^{13}C NMR (d_6-DMSO, 100 MHz): δ 148.2, 146.3, 134.3, 133.1, 123.9, 121.1, 119.3, 117.3, 117.2, 27.6; MS: Anal. calcd for $C_{20}H_{18}N_4$: 314.1531. Found: 313.1459 (M − H$^+$); IR (KBr, cm^{-1}): ν 3221, 1719, 1576, 1471, 1258, 1137, 1076, 986.

1,2-Bis(4-(furan-2-yl)-1*H*-pyrrol-3-yl)ethane (3a). Yield: 81%; white solid; melting point: 101.6–103.5 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.77 (s, 2H), 7.50 (s, 2H), 7.00 (s, 2H), 6.66 (s, 2H), 6.43 (s, 2H), 6.19 (s, 2H), 2.79 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 152.0, 140.1, 120.4, 116.8, 116.0, 113.8, 111.6, 102.6, 27.3; MS: Anal. calcd for $C_{18}H_{16}N_2O_2$: 292.1212. Found: 291.1137 (M − H$^+$); IR (KBr, cm^{-1}): ν 3378, 1617, 1444, 1156, 1078, 992, 879.

1,3-Bis(4-phenyl-1*H*-pyrrol-3-yl)propane (3a). Yield: 84%; white solid; melting point: 101.7–103.3 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.65 (s, 2H), 7.31–7.28 (m, 8H), 7.14 (d, J = 5.9 Hz, 2H), 6.86 (s, 2H), 6.57 (s, 2H), 2.58 (t, J = 7.0 Hz, 4H), 1.71 (t, J = 7.0 Hz, 2H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 137.5, 128.7, 127.4, 125.2, 122.86, 120.8, 116.9, 116.6, 31.9, 26.3; MS: Anal. calcd for $C_{23}H_{22}N_2$: 326.1783. Found: 325.1731 (M − H$^+$); IR (KBr, cm^{-1}): ν 3451, 3357, 1600, 1526, 1432, 1112, 1074, 981.

Bis((4-phenyl-1*H*-pyrrol-3-yl)methyl)sulfane (3qa). Yield: 83%; white solid; melting point: 99.2–99.8 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.82 (s, 1H), 7.46 (d, J = 7.8 Hz, 4H), 7.29 (t, J = 7.2 Hz, 4H), 7.15 (t, J = 7.1 Hz, 2H), 6.94 (s, 2H), 6.75 (s, 2H), 3.69 (s, 4H); ^{13}C NMR (d_6-DMSO, 100 MHz): δ 136.7, 128.8, 127.6, 125.5, 123.0, 119.2, 117.0, 116.5, 27.9; MS: Anal. calcd for $C_{22}H_{20}N_2S$: 344.1347. Found: 343.1260 (M − H$^+$); IR (KBr, cm^{-1}): ν 3352, 1737, 1630, 1556, 1321, 1032, 981.

***N*-Methyl-1-(4-phenyl-1*H*-pyrrol-3-yl)-*N*-((4-phenyl-1*H*-pyrrol-3-yl)methyl)methanamine (3a).** Yield: 71%; white solid; melting point: 86.3–86.8 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 10.77 (s, 2H), 7.60 (d, J = 7.2 Hz, 4H), 7.13 (t, J = 7.6 Hz, 4H), 7.02 (t, J = 7.6 Hz, 4H), 6.73 (s, 2H), 3.38 (s, 4H), 2.18 (s, 3H); ^{13}C NMR (d_6-DMSO, 100 MHz): δ 136.9, 128.5, 127.6, 125.0, 123.8, 120.4, 117.5, 116.7, 53.2, 42.2; MS: Anal. calcd for $C_{23}H_{23}N_3$: 341.1892. Found: 340.1808 (M − H$^+$); IR (KBr, cm^{-1}): ν 3341, 1756, 1595, 1460, 1295, 1128, 981.

Bis(4-phenyl-1*H*-pyrrol-3-yl)methanone (3a). Yield: 10%; white solid; melting point: 293.7–294.1 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 11.37 (s, 2H), 7.35 (d, J = 6.4 Hz, 4H), 7.24 (d, J = 19.5 Hz, 6H), 7.12 (d, J = 6.2 Hz, 2H), 6.99 (s, 2H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 196.4, 136.1, 128.5, 128.0, 127.0, 125.7, 125.4, 123.5, 119.4; MS: Anal. calcd for $C_{21}H_{16}N_2O$: 312.1263. Found: 311.1181 (M − H$^+$); IR (KBr, cm^{-1}): ν 3260, 1723, 1580, 1546, 1512, 1445, 1084, 848.

2-((4-Phenyl-1*H*-pyrrol-3-yl)methyl)benzoic acid (3a). Yield: 58%; white solid; melting point: 146.8–147.2 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ 12.77 (s, 1H), 10.73 (s, 1H), 7.78 (d, J = 7.7 Hz, 1H), 7.39 (t, J = 7.4 Hz, 1H), 7.33 (d, J = 7.5 Hz, 2H), 7.27 (t, J = 7.3 Hz, 3H), 7.17 (d, J = 7.6 Hz, 1H), 7.12 (t, J = 7.1 Hz, 1H), 6.96 (s, 1H), 6.27 (s, 1H), 4.27 (s, 2H); ^{13}C NMR (d_6-DMSO, 100 MHz): δ 169.5, 143.1, 137.2, 131.8, 131.1, 130.8, 130.3, 128.8, 127.3, 126.2, 125.4, 123.2, 119.41, 118.31, 117.0, 30.29; MS: Anal. calcd for $C_{18}H_{15}NO_2$: 277.1103. Found: 276.1022 (M − H$^+$); IR (KBr, cm^{-1}): ν 3060, 2959, 1720, 1532, 1362, 1243, 990.

Intermediate (D). White solid; melting point: 202.5–203.6 °C; ^{1}H NMR (400 MHz, d_6-DMSO): δ11.88 (s, 2H), 7.41–7.34 (m, 8H), 7.26 (t, J = 6.4 Hz, 2H), 7.18 (s, 2H), 2.92 (s, 4H); ^{13}C NMR (d_6-DMSO, 75 MHz): δ 171.8, 135.5, 130.4, 128.9, 128.8, 127.3, 126.3, 125.2, 122.8, 24.7; MS: Anal. calcd for $C_{14}H_{14}N_2O_3$: 322.0106. Found: 321.0035 (M − H$^+$); IR (KBr, cm^{-1}): ν 3061, 2860, 1732, 1586, 1461, 1398, 1265, 1160, 1082.

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