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PAPER

Phosphine-mediated cascade reaction of azides with MBH-acetates of acetylenic aldehydes to substituted pyrroles: a facile access to *N*-fused pyrrolo-heterocycles†

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One-pot synthesis of substituted pyrroles by a cascade reaction of azides with Morita–Baylis–Hillman acetates of acetylenic aldehydes is described and the reaction is efficiently mediated by triphenyl phosphine at room temperature. Sodium azide is successfully used to provide *N*-unsubstituted pyrroles, while alkyl azides afforded the corresponding *N*-alkylated pyrroles through a sequence of allylic substitution/azide reduction/cycloisomerization reactions. The obtained products have provided a new entry to indolizino indoles, pyrrolo isoquinolines and 8-oxo-5,6,7,8-tetrahydroindolizine.

Introduction

Pyrrole is one of the important heterocyclic motifs present in number of bio-active natural products as well as pharmaceuticals and has attracted lot of interest for its synthesis.[1] Traditional methods such as Hantzsch,[2] Knorr[3] and Paal–Knorr[4] synthesis rely on precursors which often need multi-step reactions and some times harsh conditions.[5] Recently, a range of new approaches have been developed.[6–8] Among these, cycloisomerization of alkynyl- and allenyl-compounds are prominent and the majority of them involve metal-catalyzed reactions.[8] Therefore, it remains a challenge to have an efficient method for the synthesis of substituted pyrroles under metal-free conditions from easily accessible starting materials. Recently, we have reported a mild and metal-free access to 1,2,4-tri- as well as 1,2,4,5-tetra-substituted pyrroles *via* a one-pot reaction of Morita–Baylis–Hillman (MBH)-acetates of acetylenic aldehydes with amines and sulphonamides.[9]

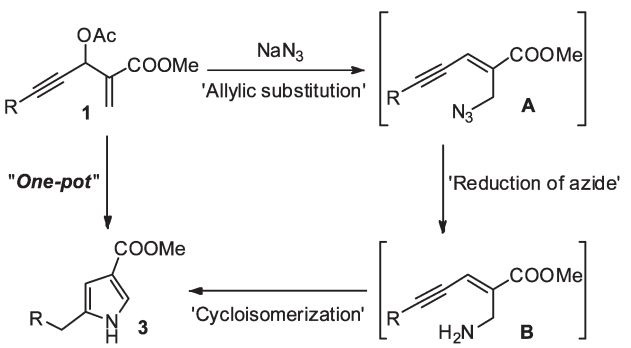
However, the direct formation of *N*-unsubstituted pyrroles was the limitation of the method and to overcome this, we became interested in exploring the possibility of using azide as a N-atom transfer agent. Azides have drawn much attention for use as potential N-atom precursors for the construction of C–N bonds due to their ease of accessibility and because they produce environmentally benign N_2 gas as a by-product.[10] Further, the products obtained from Morita–Baylis–Hillman (MBH) reaction and their acetate derivatives have already been established as handy substrates for heterocyclic compounds.[11] It is worth mentioning that the majority of the Morita–Baylis–Hillman adducts studied were derived either from aromatic aldehydes or aliphatic aldehydes and the MBH-chemistry of acetylenic aldehydes is much less investigated.[12]

Herein, we wish to report the reaction of azides with MBH-acetates of acetylenic aldehydes affording substituted pyrroles under mild reaction conditions.

We hypothesized that sodium azide would participate in allylic substitution with MBH-acetate (**1**) to obtain allylic azide **A**, which would be reduced to amine **B** and subsequently would undergo cycloisomerization to afford the desired pyrrole (**3**, Scheme 1) in a one-pot operation. Further, we anticipated that Ph_3P in THF–H_2O (Staudinger reaction conditions) would be the reagent system of choice.

Results and discussion

To verify the aforementioned hypothesis, MBH-acetate **1a** was treated with sodium azide in presence of triphenyl phosphine in



Scheme 1 Proposed route for the synthesis of *N*-unsubstituted pyrroles.

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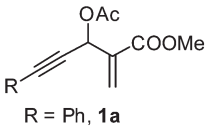
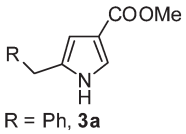
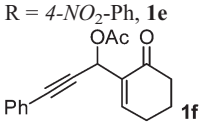
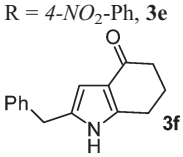
†Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra of all the new compounds. See DOI: 10.1039/c2ob25272d

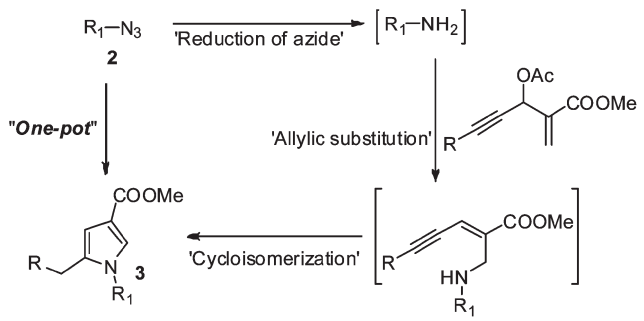
Table 1 Synthesis of *N*-unsubstituted pyrroles[a]

Entry	MBH-Acetate (**1**)	Time (h)	Pyrrole (**3**)[b]	Yield[c] (%)
1	 R = Ph, **1a**	18	 R = Ph, **3a**	91
2	R = 2-Thiophenyl, **1b**	20	R = 2-Thiophenyl, **3b**	95
3	R = nPropyl, **1c**	22	R = n-Propyl, **3c**	79
4	R = *4-MeO*-Ph, **1d**	08	R = *4-MeO*-Ph, **3d**	72
5	R = *4-NO*$_2$-Ph, **1e**	06	R = *4-NO*$_2$-Ph, **3e**	63
6	 **1f**	16	 **3f**	65

[a] *Reaction conditions*: MBH-acetate (1 mmol), NaN_3 (1.2 mmol), Ph_3P (1.25 mmol), THF–H_2O (8 : 2, 5 mL), rt. [b] All the products were characterized by ^1H, ^{13}C NMR, IR and MS spectra. [c] Isolated yield.

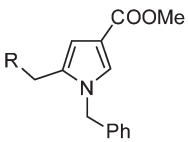
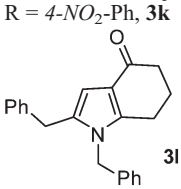
THF–H_2O as a solvent system. To our delight, the reaction proceeded efficiently to completion in 18 h at room temperature furnishing the pyrrole **3a** in 91% yield (entry 1, Table 1).[13] With this success, the scope of the reaction was studied using a set of MBH-acetates **1b** to **1e** as presented in Table 1. MBH-Acetates derived from various substituted acetylenic aldehydes (**1b–1e**) were reacted with sodium azide to provide the corresponding *N*-unsubstituted pyrroles **3b–3e** in good yields. The reactions demonstrate the tolerance of aliphatic (entry 3) and aromatic groups with electron-donating (entry 4) as well as electron-withdrawing groups (entry 5) on the alkyne functionality. In addition, the reaction of MBH-acetate **1f**, obtained from cyclohexenone, with NaN_3 also gave the desired 2-benzyl-6,7-dihydro-1*H*-indol-4(5*H*)-one (**3f**) in 65% yield (entry 6).

Next, we focused our attention on finding out the reactivity of alkyl azide with MBH-acetate (**1**) to provide the corresponding *N*-alkyl pyrrole under similar reaction conditions *via* the reduction of azide to amine/allylic substitution/cycloisomerization sequence (Scheme 2). Thus, MBH-acetate **1a** was treated with benzyl azide (**2b**) under Ph_3P in THF–H_2O at room temperature. Interestingly, as expected, the domino process ensued well in 10 h to furnish 2,4-disubstituted *N*-benzyl pyrrole **3g** in 94% yield (entry 1, Table 2). Encouraged by this result, other MBH-acetates **1b** to **1f** were also examined for the reaction with



Scheme 2 Hypothesis for the reaction of alkyl azide with MBH-acetate of acetylenic aldehyde.

Table 2 Synthesis of *N*-benzyl pyrroles[a]

Entry	MBH-Acetate (**1**)	Time (h)	Product (**3**)[b]	Yield[c] (%)
1	**1a**	10	 R = Ph, **3g**	94
2	**1b**	08	R = 2-Thiophenyl, **3h**	88
3	**1c**	10	R = n-Propyl, **3i**	77
4	**1d**	05	R = *4-MeO*-Ph, **3j**	81
5	**1e**	04	R = *4-NO*$_2$-Ph, **3k**	72
6	**1f**	24	 **3l**	85

[a] *Reaction conditions*: MBH-Acetate (1 mmol), BnN_3 (1.2 mmol), Ph_3P (1.25 mmol), THF–H_2O (8 : 2, 6 mL), rt. [b] All the products were characterized by ^1H, ^{13}C NMR, IR and MS spectra. [c] Isolated yield.

benzyl azide (**2b**) and the results are summarized in Table 2. All the substrates **1b** to **1f** participated smoothly to afford the corresponding *N*-benzyl pyrroles **3h–3l** in good yields (entries 2–6, Table 2).

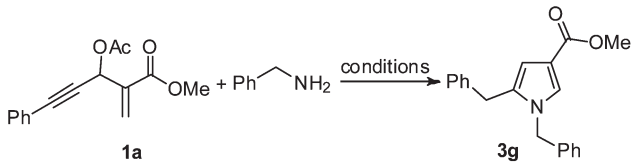
To compare the newly developed reaction conditions with the earlier method,[9] the reaction of benzyl amine with **1a** was carried out. Interestingly, the reaction proceeded cleanly in the presence of Ph_3P in THF–H_2O to provide the pyrrole **3g** in 95% yield and in the absence of Ph_3P it gave only 61% (entries 1 and 2, Table 3). This result represents a distinct improvement, when compared to the reaction of benzyl amine with **1a** under K_2CO_3/DMF/45 °C (entry 2, Table 3).

Later, we extended the scope of various azides as nitrogen precursors for the synthesis of *N*-substituted pyrroles under the

conditions described by treating them with MBH-acetates of acetylenic aldehydes and the results are compiled in Table 4. Initially, the reaction of cinnamyl azide (**2c**) with **1a** was performed using Ph_3P in THF–H_2O at room temperature, which provided the corresponding *N*-cinnamyl pyrrole **3m** in 79% yield (entry 1, Table 4). Likewise, MBH-acetate **1b** also reacted with **2c** to furnish **3n** in 81% yield (entry 2, Table 4). Ethyl azidoacetate **2d** was reacted with **1a** as well as **1b** to obtain the corresponding trisubstituted pyrroles **3o** and **3p** in 86 and 88% yields, respectively. Azides obtained from furano-sugars **2e** and **2f** were effectively employed in the reaction with **1a** and **1b** to offer the corresponding pyrroles **3q** to **3t** in good yields (entries 5 to 8, Table 4). The observed result clearly demonstrates that the method developed is useful for the conversion of azides to the corresponding *N*-substituted pyrroles in one pot under mild reaction conditions[14] which accordingly may find a wide range of applications.

Further, our interest in investigating the applicability of the pyrrole obtained resulted in a novel access to 6,11-dihydro-5*H*-indolizino[6,7-*b*]indoles and 5,10-dihydropyrrolo[1,2-*b*]isoquinolines *via* an acid-catalyzed tandem carbon–carbon bond forming reaction. These are attractive frameworks for drug discovery.[15] Thus, the MBH-acetate **1a** was treated with azide **2g** to obtain the corresponding pyrrole **3u** in 72% yield. This pyrrole **3u** can be used as a versatile scaffold for the preparation of 6,11-dihydro-5*H*-indolizino[6,7-*b*]indoles, by reacting with aldehydes. Accordingly, **3u** was treated with 4-nitrobenzaldehyde in presence of *p*TSA (5 mol%) in CH_2Cl_2 at room temperature and

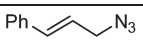
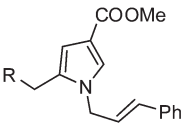
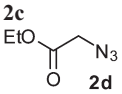
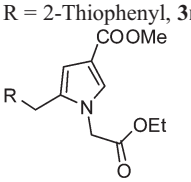
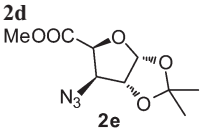
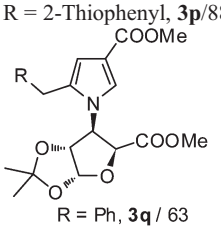
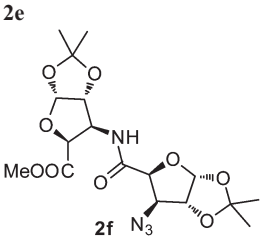
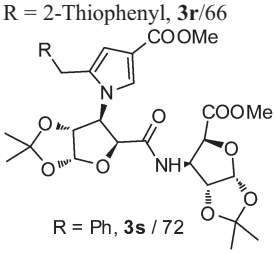
Table 3 Reaction of MBH-acetate **1a** with benzyl amine



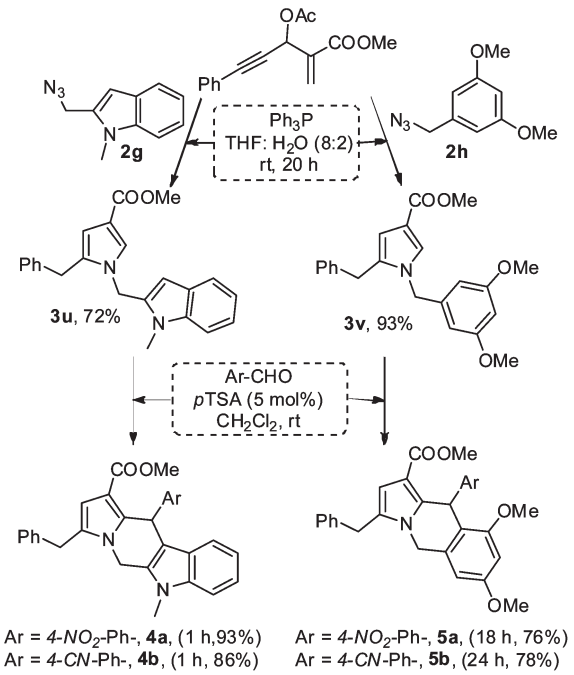
Entry	Reagent	Solvent	*T* (°C)	Time (h)	Yield[a] [%]
1	**Ph_3P**	**THF–H_2O**	**rt**	**14**	**95**
2	—	THF–H_2O	rt	20	61
3[9]	K_2CO_3	DMF	45	12	86

[a] Isolated yield.

Table 4 Synthesis of pyrroles from alkyl azides[a]

Entry	Azide (**2**)	MBH-Acetate/time (h)	Product (**3**)[b]/yield[c] (%)
1	 **2c**	**1a**/8	 R = Ph, **3m** / 79
2	**2c**	**1b**/11	R = 2-Thiophenyl, **3n**/81
3	 **2d**	**1a**/8	 R = Ph, **3o** / 86
4	**2d**	**1b**/9	R = 2-Thiophenyl, **3p**/88
5	 **2e**	**1a**/30	 R = Ph, **3q** / 63
6	**2e**	**1b**/36	R = 2-Thiophenyl, **3r**/66
7	 **2f**	**1a**/33	 R = Ph, **3s** / 72
8	**2f**	**1b**/34	R = 2-Thiophenyl, **3t**/78

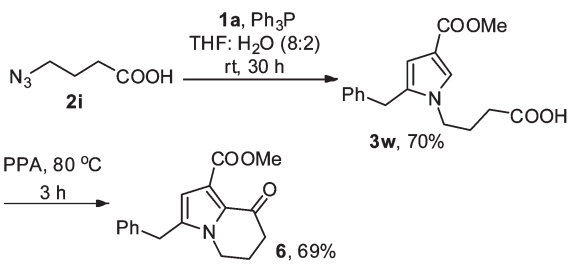
[a] *Reaction conditions*: MBH-acetate (1 mmol), RN_3 (1.2 mmol), Ph_3P (1.25 mmol), THF–H_2O (8 : 2, 6 mL), rt. [b] All the products were characterized by ^1H, ^{13}C NMR, IR and MS spectra. [c] Isolated yield.



Scheme 3 Synthesis of indolizino[6,7-*b*]indoles and pyrrolo[1,2-*b*] isoquinolines.

to our satisfaction the desired indolizino[6,7-*b*]indole **4a** was obtained in 93% yield. Similarly, the reaction of **3u** with 4-cyanobenzaldehyde gave the indole derivative **4b** in 86% yield. Another interesting scaffold **3v**, obtained from the reaction of **1a** with azide **2h**, was also successfully examined for the synthesis of 5,10-dihydropyrrolo[1,2-*b*]isoquinoline derivatives **5a** and **5b** but after longer reaction times (Scheme 3). To the best of our knowledge, this is the first demonstration of one-step synthesis of indolizino[6,7-*b*]indoles and pyrrolo[1,2-*b*]isoquinolines from *N*-benzylated pyrroles.

Additionally, the synthesis of 8-oxo-5,6,7,8-tetrahydroindolizine, a useful bio-active framework and precursor for indolizidine alkaloids,[16] has also been accomplished using the described methodology. The treatment of azido carboxylic acid **2i** with **1a** afforded the corresponding pyrrole **3w** (70% yield), which was subsequently treated with polyphosphoric acid at 80 °C for 3 h to afford indolizidone **6** in 69% yield (Scheme 4).[17]



Scheme 4 Synthesis of indolizidone **6**.

Conclusions

In summary, we have developed a new cascade reaction for the synthesis of substituted pyrroles from the reaction of azides with MBH-acetates of acetylenic aldehydes under metal-free reaction conditions. The use of sodium azide in the reaction provided *N*-unsubstituted pyrroles and alkyl azide afforded *N*-alkylated pyrroles. The mild reaction conditions and use of easily accessible azides as well as MBH-acetate of acetylenic aldehydes give the present method potential in pyrrole synthesis. Further, this approach led us to develop a facile and novel entry to indolizino indoles, pyrrolo isoquinolines and 8-oxo-5,6,7,8-tetrahydroindolizine, which are useful for generating libraries of new molecular entities.

Experimental

General

Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using UV-light and anisaldehyde or potassium permanganate or β-naphthol for visualization. Column chromatography was performed on silica gel (60–120 mesh) using *n*-hexane and ethyl acetate as eluent. Evaporation of solvents was conducted under reduced pressure at temperatures less than 45 °C. IR spectra were recorded on Perkin-Elmer 683 or Nicolet Nexus 670 spectrometers. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, DMSO-d_6 solvents on a 300 MHz or 500 MHz NMR spectrometer. Chemical shifts δ and coupling constants J are given in ppm (parts per million) and Hz (hertz) respectively. Chemical shifts are reported relative to residual solvent as an internal standard for ^{1}H and ^{13}C ($CDCl_3$: δ 7.26 ppm for ^{1}H and 77.0 ppm for ^{13}C). Mass spectra were obtained on Finnigan MAT1020B, Micromass VG 70–70H or LC/MSD trapSL spectrometer operating at 70 eV using direct inlet system.

Morita–Baylis–Hillman acetate adducts have been prepared using the literature procedure[9,12a] to obtain **1a** to **1h**. Alkyl azides and other starting materials have been prepared using the literature procedure.[18]

Methyl 3-acetoxy-5-(4-methoxyphenyl)-2-methylenepent-4-ynoate (1d). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40 (d, J = 8.7 Hz, 2H), 6.83 (d, J = 8.7 Hz, 2H), 6.52 (s, 1H), 6.51 (s, 1H), 6.33 (s, 1H), 3.80 (s, 3H), 3.79 (s, 3H), 2.11 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 164.8, 159.9, 136.6, 133.3, 128.9, 113.8, 113.7, 87.1, 82.3, 62.1, 55.1, 52.1, 20.7; IR (KBr): 2942, 2851, 2447, 1955, 1735, 1515, 1343, 1223, 980, 854, 691 cm^{-1}; MS (ESI): *m*/*z* 311 (M + Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{16}H_{16}NaO_5$ (M + Na)$^+$: 311.0890, found: 311.0893.

Methyl 3-acetoxy-2-methylene-5-(4-nitrophenyl)pent-4-ynoate (1e). Yellow solid; mp: 92–93 °C; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 8.20 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 6.51 (s, 1H), 6.47 (s, 1H), 6.26 (s, 1H), 3.84 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.2, 164.6, 147.5, 136.0, 132.7, 129.4, 129.3, 123.5, 89.0, 84.8, 61.8, 52.4, 20.8; IR (KBr): 2929, 2358, 1734, 1515, 1222, 1157, 980, 854, 689 cm^{-1}; MS (ESI): *m*/*z* 326 (M + Na)$^+$; HRMS (ESI): *m*/*z* calcd for $C_{15}H_{13}NaNO_6$ (M + Na)$^+$: 326.0635, found: 326.0608.

Procedure for the preparation of 2-(azidomethyl)-1-methyl-1*H*-indole (2g). To a solution of (1-methyl-1*H*-indol-2-yl)methanol (1 g, 6.21 mmol) in THF (12 mL) at room temperature was

added sequentially triphenylphosphine (2.44 g, 9.32 mmol), diisopropyl azodicarboxylate (1.5 mL, 9.32 mmol), and diphenylphosphonic azide (2.7 mL, 12.42 mmol). The reaction was stirred for 5 hours before the volatiles were concentrated *in vacuo*. The residue was purified by column chromatography over silica gel (hexanes–ethyl acetate: 98 : 2) to afford azide **2g** (0.75 g, 65%) as a brown oil.

2-(Azidomethyl)-1-methyl-1*H*-indole (2g). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.60 (d, J = 7.7 Hz, 1H), 7.35–7.22 (m, 2H), 7.12 (t, J = 7.5 Hz, 1H), 6.54 (s, 1H), 4.46 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 138.1, 132.8, 126.9, 122.3, 120.8, 119.7, 109.2, 103.2, 46.8, 29.6; IR (KBr): 2930, 2171, 2100, 1476, 1205, 965, 743 cm^{-1}; MS (EI): *m*/*z* 186.

General procedure for the preparation of *N*-unsubstituted pyrroles. To a solution of MBH-acetate (1.0 mmol) and sodium azide (1.2 mmol) in 5 mL of THF–H_2O (8 : 2) was added triphenyl phosphine (1.25 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 6 to 22 h. After the completion of the reaction, the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding product.

Spectral data for all new compounds

Methyl 5-benzyl-1*H*-pyrrole-3-carboxylate (3a).[9] White solid; mp: 125–127 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.06 (brs, 1H), 7.31–7.13 (m, 6H), 6.37 (s, 1H), 3.93 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.6, 138.5, 131.9, 128.7, 128.6, 126.6, 123.1, 116.1, 107.6, 50.9, 33.8; IR (KBr): 3238, 2919, 1686, 1517, 1451, 1218, 1026, 994, 747, 707 cm^{-1}; MS (ESI): *m*/*z* 216.0 (M + H)$^+$. HRMS (ESI): *m*/*z* calcd for $C_{13}H_{14}NO_2$ (M + H)$^+$: 216.1019, found: 216.1020.

Methyl 5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3b). White solid; mp: 104–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.33 (br, 1H), 7.31 (dd, J = 1.5, 2.6 Hz, 1H), 7.18 (d, J = 5.1 Hz, 1H), 6.94 (dd, J = 5.1, 3.5, 1H), 6.84 (d, J = 3.5 Hz, 1H), 6.45 (s, 1H), 4.14 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 141.1, 130.9, 127.0, 125.5, 124.5, 123.1, 116.3, 107.5, 51.0, 28.1; IR (KBr): 3460, 2922, 1640, 1516, 1205, 997, 699 cm^{-1}; MS (ESI): *m*/*z* 222 (M + H); HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}NO_2S$ (M + H)$^+$: 222.0583, found: 222.0588.

Methyl 5-butyl-1*H*-pyrrole-3-carboxylate (3c). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.65 (br, 1H), 7.29 (s, 1H), 6.31, (s, 1H), 3.80 (s, 3H), 2.56 (t, J = 7.3 Hz, 2H), 1.63–1.55 (m, 2H), 1.40–1.30 (m, 2H), 0.91 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.0, 134.0, 122.4, 115.7, 106.0, 51.0, 31.3, 27.0, 22.1, 13.7; IR (KBr): 3449, 2929, 1635, 1517, 1207, 1129, 726, 562 cm^{-1}; MS (ESI): *m*/*z* 204 (M + Na); HRMS (ESI): *m*/*z* calcd for $C_{10}H_{15}NNaO_2$ (M + Na)$^+$: 204.0995, found: 204.0992.

Methyl 5-(4-methoxybenzyl)-1*H*-pyrrole-3-carboxylate (3d). White solid; mp: 95–97 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.09 (br, 1H), 7.27 (s, 1H), 7.09 (d, J = 8.9 Hz, 2H), 6.84 (d, J = 8.9 Hz, 2H), 6.37 (s, 1H), 3.87 (s, 2H), 3.78 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 158.4, 132.3, 130.8, 130.4, 129.7, 122.9, 114.2, 107.4, 55.3, 51.0, 32.9; IR (KBr): 3251, 2926, 2860, 1724, 1688, 1511, 1214, 1032, 757 cm^{-1}; MS (ESI): *m*/*z* 268 (M + Na); HRMS (ESI): *m*/*z* calcd for $C_{14}H_{16}NO_3$ (M + H)$^+$: 246.1125, found: 246.1124.

Methyl 5-(4-nitrobenzyl)-1*H*-pyrrole-3-carboxylate (3e). White solid; mp: 148–150 °C; ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.38 (d, J = 8.5 Hz, 2H), 8.08–8.04 (m, 3H), 7.71 (s, 1H), 7.13 (s, 1H), 3.78 (s, 3H), 3.35 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 163.2, 149.0, 142.7, 130.0, 129.3, 128.1, 123.2, 119.7, 117.0, 50.6, 28.8; IR (KBr): 3349, 2924, 2854, 1689, 1513, 1248, 1121, 1034, 764 cm^{-1}; MS (ESI): *m*/*z* 261 (M + H); HRMS (ESI): *m*/*z* calcd for $C_{13}H_{13}N_2O_4$ (M + H)$^+$: 261.0870, found: 261.0867.

2-Benzyl-6,7-dihydro-1*H*-indol-4(5*H*)-one (3f). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.14 (m, 4H), 7.11 (d, J = 6.7 Hz, 2H), 6.29 (s, 1H), 3.91 (s, 2H), 2.69 (t, J = 6.6 Hz, 2H), 2.42 (t, J = 6.0 Hz, 2H), 2.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.0, 144.3, 133.3, 128.5, 128.4, 128.3, 128.1, 126.4, 104.5, 32.8, 30.6, 23.4, 21.8; IR (KBr): 3440, 2925, 2849, 1646, 1481, 1036, 750 cm^{-1}; MS (ESI): *m*/*z* 226 (M + H); HRMS (ESI): *m*/*z* calcd for $C_{15}H_{16}NO$ (M + H)$^+$: 226.1226, found: 226.1221.

General procedure for the preparation of *N*-substituted pyrroles. To a solution of alkyl azide (1.2 mmol) in 5 mL of THF–H_2O (8 : 2) was added triphenyl phosphine (1.25 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 3 h. A solution of MBH-acetate (1.0 mmol) in 1 mL of THF was added to it, and stirred for 1–32 h. After the completion of the reaction, the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding product.

Methyl 1,5-dibenzyl-1*H*-pyrrole-3-carboxylate (3g).[9] White solid; mp: 99–101 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.32–7.14 (m, 7H), 7.05 (d, J = 7.1 Hz, 2H), 6.91 (d, J = 7.3 Hz, 2H), 6.37 (s, 1H), 4.84 (s, 2H), 3.76 (s, 3H), 3.75 (s, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 138.2, 136.6, 132.7, 128.8, 128.5, 128.3, 127.7, 127.1, 126.5, 126.4, 114.5, 109.9, 50.99, 50.93, 32.6; IR (KBr): 2925, 1706, 1518, 1445, 1217, 1090, 714, 617 cm^{-1}; MS (ESI): *m*/*z* 306 (M + H); HRMS (ESI): *m*/*z* calcd for $C_{20}H_{20}NO_2$ (M + H)$^+$: 306.1489, found: 306.1493.

Methyl 1-benzyl-5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3h).[9] White solid; mp: 104–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.23 (m, 4H), 7.13 (dd, J = 1.3, 5.1 Hz, 1H), 7.0–6.92 (m, 2H), 6.88 (dd, J = 3.6, 5.1, 1H), 6.72–6.67 (m, 1H), 6.47 (s, 1H), 4.93 (s, 2H), 3.94 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 141.5, 136.5, 132.1, 128.9, 127.8, 127.3, 126.8, 126.6, 125.1, 124.1, 114.7, 109.7, 51.0, 50.9, 27.1; IR (KBr): 2925, 2853, 1703, 1518, 1444, 1362, 1212, 1179, 1001, 762, 712 cm^{-1}; MS (ESI): *m*/*z*

312 (M + H)$^+$; HRMS (ESI): *m/z* calcd for $C_{18}H_{18}NO_2S$ (M + H)$^+$: 312.1053, found: 312.1056.

Methyl 1-benzyl-5-butyl-1*H*-pyrrole-3-carboxylate (3i). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26–7.16 (m, 4H), 6.93–6.84 (m, 2H), 6.30 (s, 1H), 4.94 (s, 2H), 3.70 (s, 3H), 2.33 (t, J = 7.3 Hz, 2H), 1.52–1.41 (m, 2H), 1.31–1.21 (m, 2H), 0.79 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.5, 136.9, 134.9, 128.8, 127.7, 126.5, 126.3, 114.5, 107.4, 50.9, 50.7, 30.4, 25.6, 22.3, 13.7; IR (KBr): 2952, 2864, 1707, 1640, 1215, 761, 611 cm^{-1}; MS (ESI): *m/z* 272 (M + H); HRMS (ESI): *m/z* calcd for $C_{17}H_{22}NO_2$ (M + H)$^+$: 272.1645, found: 272.1626.

Methyl 1-benzyl-5-(4-methoxybenzyl)-1*H*-pyrrole-3-carboxylate (3j). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30–7.21 (m, 4H), 6.96–6.89 (m, 4H), 6.74 (d, J = 8.9 Hz, 2H), 6.32 (s, 1H), 4.84 (s, 2H), 3.75 (s, 6H), 3.68 (s, 2H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.0, 146.7, 145.9, 136.2, 130.9, 129.2, 128.9, 127.9, 127.6, 126.4, 123.7, 115.0, 110.6, 51.4, 51.2, 51.0, 32.5; IR (KBr): 2946, 1705, 1518, 1345, 1219, 1101, 761 cm^{-1}; MS (ESI): *m/z* 358 (M + Na)$^+$; HRMS (ESI): *m/z* calcd for $C_{21}H_{21}NNaO_3$ (M + Na)$^+$: 358.1414, found 358.1417.

Methyl 1-benzyl-5-(4-nitrobenzyl)-1*H*-pyrrole-3-carboxylate (3k). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 8.08 (d, J = 9.1 Hz, 2H), 7.32–7.23 (m, 4H), 7.19 (d, J = 9.1 Hz, 2H), 6.93–6.86 (m, 2H), 6.36 (s, 1H), 4.88 (s, 2H), 3.85 (s, 2H), 3.78 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): 165.3, 158.3, 136.7, 133.3, 130.3, 129.4, 128.8, 127.8, 127.1, 126.6, 114.6, 114.0, 109.8, 55.2, 51.0, 31.8; IR (neat): 2924, 2851, 1707, 1514, 1449, 1218, 1004, 822, 760 cm^{-1}; MS (ESI): *m/z* 373 (M + Na)$^+$; HRMS (ESI) *m/z* calcd for $C_{20}H_{18}N_2NaO_4$ (M + Na)$^+$: 373.1159, found: 373.1165.

1,2-Dibenzyl-6,7-dihydro-1*H*-indol-4(5*H*)-one (3l).Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.15 (m, 6H), 7.13–7.07 (m, 2H), 6.93–6.82 (m, 2H), 6.37 (s, 1H), 4.92 (s, 2H), 3.77 (s, 2H), 2.61 (t, J = 6.0 Hz, 2H), 2.47 (t, J = 6.4 Hz, 2H), 2.15–2.04 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.3, 144.7, 138.0, 136.5, 133.7, 128.9, 128.5, 128.4, 127.5, 126.5, 125.5, 120.0, 105.3, 47.2, 37.6, 32.7, 23.6, 21.9; IR (KBr): 2933, 2864, 1711, 1654, 1474, 1170, 697 cm^{-1}; MS (ESI): *m/z* 316 (M + H); HRMS (ESI): *m/z* calcd for $C_{22}H_{22}NO$ (M + H)$^+$: 316.1696, found: 316.1683.

Methyl 5-benzyl-1-cinnamyl-1*H*-pyrrole-3-carboxylate (3m). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.09 (m, 11H), 6.37 (d, J = 1.5 Hz, 1H), 6.30 (dt, J = 15.8, 1.5 Hz, 1H), 6.05 (dt, J = 15.8, 5.3 Hz, 1H), 4.42 (dd, J = 1.5, 5.3 Hz, 2H), 3.93 (s, 2H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 138.3, 135.8, 132.6, 132.4, 128.5, 128.3, 128.0, 126.7, 126.6, 126.5, 126.4, 124.1, 114.5, 109.7, 50.9, 49.1, 32.5; IR (KBr): 2925, 1705, 1520, 1444, 1214, 1095, 1003, 757, 699 cm^{-1}; MS (ESI): *m/z* 332 (M + H)$^+$, HRMS (ESI): *m/z* calcd for $C_{22}H_{22}NO_2$ (M + H)$^+$: 332.1645, found: 332.1660.

Methyl 1-cinnamyl-5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3n). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35–7.24 (m, 6H), 7.16 (d, J = 4.2 Hz, 1H), 6.93 (t, J = 4.2 Hz, 1H), 6.79 (d, J = 15.6 Hz, 1H), 6.50 (s, 1H), 6.31 (d, J = 15.6 Hz, 1H), 6.13 (dt, J = 15.6, 6.2 Hz, 1H), 4.51 (d, J = 6.2 Hz, 2H), 4.12 (s, 2H), 3.80 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 141.6, 135.8, 132.7, 131.8, 128.5, 128.0, 126.8, 126.6, 126.4, 125.1, 124.1, 124.0, 114.6, 109.5, 50.9, 49.2, 27.0; IR (KBr): 2924, 2885, 1706, 1519, 1443, 1215, 1097, 1004, 759, 698 cm^{-1}; MS (ESI): *m/z* 338 (M + H)$^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{20}NO_2S$ (M + H)$^+$: 338.1209, found: 338.1230.

Methyl 5-benzyl-1-(2-ethoxy-2-oxoethyl)-1*H*-pyrrole-3-carboxylate (3o). Yellow solid; mp: 94–96 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.09 (m, 6H), 6.36 (s, 1H), 4.37 (s, 2H), 4.08 (q, J = 7.5 Hz, 2H), 3.87 (s, 2H), 3.77 (s, 3H), 1.22 (t, J = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 165.0, 137.8, 132.7, 128.6, 128.4, 127.6, 126.6, 115.3, 109.9, 61.8, 50.9, 48.7, 32.5, 14.0; IR (KBr): 2921, 2851, 1734, 1715, 1528, 1216, 721 cm^{-1}; MS (ESI): *m/z* 302 (M + H)$^+$; HRMS (ESI): *m/z* calcd for $C_{17}H_{20}NO_4$ (M + H)$^+$: 302.1387, found: 302.1378.

Methyl 1-(2-ethoxy-2-oxoethyl)-5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3p). White solid; mp: 99–101 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.26 (d, J = 1.5 Hz, 1H), 7.16 (d, J = 5.1 Hz, 1H), 6.91 (dd, J = 1.5, 3.6 Hz, 1H), 6.75 (d, J = 3.6 Hz, 1H), 6.47 (s, 1H), 4.48 (s, 2H), 4.15 (q, J = 7.2 Hz, 2H), 4.06 (s, 2H), 3.78 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.7, 164.9, 140.9, 132.1, 127.8, 126.8, 125.3, 124.4, 115.3, 109.6, 61.8, 50.9, 48.7, 27.0, 14.0; IR (KBr): 2922, 1706, 1685, 1194, 1119, 998, 721, 541 cm^{-1}; MS (ESI): *m/z* 308 (M + H); HRMS (ESI): *m/z* calcd for $C_{15}H_{18}NO_4S$ (M + H)$^+$: 308.0951, found: 308.0969.

Methyl 5-benzyl-1-((3a*R*,5*S*,6*R*,6a*R*)-5-(methoxycarbonyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)-1*H*-pyrrole-3-carboxylate (3q). White solid; mp: 165–166 °C; $[\alpha]_D^{20}$ = −24.0 (*c* 0.42, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.12 (m, 6H), 6.26 (s, 1H), 6.20 (d, J = 3.6 Hz, 1H), 5.03 (d, J = 4.7 Hz, 1H), 4.81 (d, J = 4.7 Hz, 1H), 4.47 (d, J = 3.6 Hz, 1H), 3.97 (q, J = 11.7 Hz, 2H), 3.75 (s, 3H), 3.53 (s, 3H), 1.51 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.1, 164.8, 137.7, 133.4, 128.7, 128.5, 126.7, 123.8, 116.4, 112.7, 109.6, 105.3, 84.7, 78.5, 62.5, 52.4, 51.0, 32.5, 26.6, 25.9; IR (neat): 2948, 1710, 1515, 1437, 1242, 1195, 759, 697 cm^{-1}; MS (ESI): *m/z* 416 (M + H)$^+$; HRMS (ESI): *m/z* calcd for $C_{22}H_{26}NO_7$ (M + H)$^+$: 416.1704, Found: 416.1714.

Methyl 1-((3a*R*,5*S*,6*R*,6a*R*)-5-(methoxycarbonyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)-5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3r). White solid; mp: 130–131 °C; $[\alpha]_D^{20}$ = −20.2 (*c* 0.36, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.19–7.14 (m, 2H), 6.93 (t, J = 5.3 Hz, 1H), 6.80 (d, J = 3.0 Hz, 1H), 6.37 (s, 1H), 6.19 (d, J = 3.0 Hz, 1H), 4.99 (d, J = 4.5 Hz, 1H), 4.80 (d, J = 4.5 Hz, 1H), 4.49 (d, J = 3.8 Hz, 1H), 4.15 (s, 2H), 3.78 (s, 3H), 3.56 (s, 3H), 1.52 (s, 3H), 1.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.0, 164.7, 140.8, 132.6, 127.0, 125.4, 124.5, 123.9, 116.5, 112.7, 109.4, 105.3, 84.8, 78.5, 62.6, 52.5, 51.0, 27.0, 26.6, 26.0; IR (neat): 2955, 1699, 1523, 1216, 1081, 1030, 764 cm^{-1}; MS (ESI): *m/z* 444 (M + Na)$^+$; HRMS (ESI): *m/z* calcd for $C_{20}H_{24}NO_7S$ (M + H)$^+$: 422.1268, found: 422.1253.

Methyl 5-benzyl-1-((3a*R*,5*S*,6*R*,6a*R*)-5-(((3a*R*,5*S*,6*R*,6a*R*)-5-(methoxycarbonyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)carbamoyl)-2,2-dimethyltetrahydrofuro[2,3-*d*][1,3]

dioxol-6-yl)-1*H*-pyrrole-3-carboxylate (3s). White solid; mp: 149–150 °C; $[\alpha]_D^{20}$ = +37.2 (*c* 0.5, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.55 (s, 2H), 7.38–7.29 (m, 3H), 6.24 (s, 1H), 6.98 (s, 1H), 6.89 (d, *J* = 9.0 Hz, 1H), 5.95 (d, *J* = 3.3 Hz, 1H), 5.86 (d, *J* = 3.2 Hz, 1H), 4.83–4.72 (m, 2H), 4.68 (d, *J* = 4.3 Hz, 1H), 4.60 (d, *J* = 3.2 Hz, 1H), 4.48 (d, *J* = 3.4 Hz, 1H), 3.83 (s, 3H), 3.78–3.72 (m, 5H), 1.51 (s, 3H), 1.42 (s, 3H), 1.29 (s, 3H), 1.25 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 168.2, 168.1, 166.4, 138.7, 131.8, 129.3, 128.4, 122.6, 122.1, 112.7, 112.2, 105.4, 104.9, 102.3, 84.9, 83.8, 83.0, 80.9, 62.4, 55.9, 52.6, 52.2, 44.8, 29.6, 26.9, 26.6, 26.1, 26.0; IR (KBr): 3122, 2944, 1695, 1525, 1229, 769 cm^{-1}; MS (ESI): *m*/*z* 601 $(M + H)^+$; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{37}N_2O_{11}$ $(M + H)^+$: 601.2392, found: 601.2438.

Methyl 1-((3a*R*,5*S*,6*R*,6a*R*)-5-(((3a*R*,5*S*,6*R*,6a*R*)-5-(methoxycarbonyl)-2,2 dimethyltetrahydrofuro[2,3-*d*][1,3]dioxol-6-yl)carbamoyl)-2,2-dimethyltetrahydrofuro[2,3*d*][1,3]dioxol-6-yl)-5-(thiophen-2-ylmethyl)-1*H*-pyrrole-3-carboxylate (3t). White solid; mp: 98–99 °C; $[\alpha]_D^{20}$ = −49.2 (*c* 0.64, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): δ 7.14 (d, *J* = 4.9 Hz, 1H), 6.94–6.87 (m, 2H), 6.86–6.78 (m, 2H), 6.25 (s, 1H), 6.22 (d, *J* = 3.2 Hz, 1H), 5.87 (d, *J* = 3.2 Hz, 1H), 4.84–4.78 (m, 2H), 4.63–4.57 (m, 2H), 4.48 (d, *J* = 3.0 Hz, 1H), 4.18 (dd, *J* = 17.5, 4.15 Hz, 2H), 3.75 (s, 3H), 3.68 (s, 3H), 1.51 (s, 3H), 1.46 (s, 3H), 1.28 (s, 3H), 1.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 167.6, 166.5, 164.6, 141.0, 133.9, 126.9, 125.3, 124.2, 122.9, 116.5, 112.8, 108.9, 105.1, 104.7, 84.9, 83.4, 79.6, 75.7, 61.7, 56.8, 52.5, 50.9, 31.5, 29.5, 26.8, 26.4, 26.3, 26.0; IR (KBr): 2920, 1713, 1214, 1082, 1033, 764 cm^{-1}; MS (ESI): *m*/*z* 629 $(M + Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{28}H_{34}$ Na $N_2O_{11}S$ $(M + Na)^+$: 629.1776, found: 629.1726.

Methyl 5-benzyl-1-((1-methyl-1*H*-indol-2-yl)methyl)-1*H*-pyrrole-3-carboxylate (3u). Pale yellow solid; mp: 128–129 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.56 (d, *J* = 8.3 Hz, 1H), 7.33–7.04 (m, 9H), 6.46 (d, *J* = 1.5 Hz, 1H), 6.33 (s, 1H), 4.93 (s, 2H), 3.96 (s, 2H), 3.72 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 138.2, 138.1, 133.2, 132.5, 128.8, 128.5, 127.2, 126.8, 126.2, 122.2, 120.8, 119.9, 114.8, 110.2, 109.2, 103.3, 51.0, 43.7, 32.9, 29.4; IR (KBr): 2925, 1706, 1520, 1214, 1004, 770 cm^{-1}; MS (ESI): *m*/*z* 359 $(M + H)^+$; HRMS (ESI): *m*/*z* calcd for $C_{23}H_{23}N_2O_2$ $(M + H)^+$: 359.1754, found: 359.1749.

Methyl 5-benzyl-1-(3,5-dimethoxybenzyl)-1*H*-pyrrole-3-carboxylate (3v). Pale green oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.36–7.18 (m, 4H), 7.11 (s, 1H), 7.10 (s, 1H), 6.39 (s, 1H), 6.36 (t, *J* = 1.9 Hz, 1H), 6.08 (d, *J* = 1.9 Hz, 2H), 4.81 (s, 2H), 3.80 (s, 2H), 3.78 (s, 3H), 3.72 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 161.1, 139.0, 138.2, 131.6, 128.5, 128.3,127.1, 126.5, 121.8, 109.8, 106.6, 104.5, 99.3, 55.2, 50.9, 50.8, 32.5; IR (KBr): 2944, 2842, 1708, 1602, 1459, 1347, 1063, 757 cm^{-1}; MS (ESI): *m*/*z* 366 $(M + H)^+$; HRMS (ESI): *m*/*z* calcd for $C_{22}H_{24}NO_4$ $(M + H)^+$: 366.1700, found: 366.1710.

4-(2-Benzyl-4-(methoxycarbonyl)-1*H*-pyrrol-1-yl)butanoic acid (3w). Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.26–7.08 (m, 6H), 6.30 (s, 1H), 3.90 (s, 2H), 3.80–3.72 (m, 5H), 2.23 (t, *J* = 7.0 Hz, 2H), 1.88 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 177.0, 165.5, 138.3, 132.5, 132.0, 128.5, 128.3, 126.7, 114.4, 109.5, 51.0, 45.9, 32.5, 30.5, 25.7; IR (KBr): 3450, 2950, 1706, 1442, 1219, 1003, 761, 722 cm^{-1}; MS (ESI): *m*/*z* 324 $(M + Na)^+$; HRMS (ESI): *m*/*z* calcd for $C_{17}H_{19}NNaO_4$ $(M + Na)^+$: 324.1206, found: 324.1203.

1-*tert*-Butyl 3-methyl 5-benzyl-1*H*-pyrrole-1,3-dicarboxylate (3a′). Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, *J* = 2.2 Hz, 1H), 7.23–7.03 (m, 5H), 6.04 (s, 1H), 4.10 (s, 2H), 3.71 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.5, 148.6, 138.7, 135.5, 128.8, 128.3, 126.4, 126.3, 117.0, 112.5, 84.8, 51.3, 34.8, 27.8; IR (KBr): 2961, 1752, 1720, 1634, 1526, 1269, 1205, 1155, 1086, 760, 708 cm^{-1}; MS (ESI): *m*/*z* 338 (M + Na). HRMS (ESI): *m*/*z* calcd for $C_{18}H_{21}$ Na NO_4 $(M + Na)^+$: 338.1363, found: 338.1376.

General procedure for the preparation of compounds 4 and 5. To a solution of *N*-substituted pyrrole (1.0 mmol) and aldehyde (1.1 mmol) in 5 mL dichloromethane was added *p*TSA (5 mol%) at room temperature. The reaction mixture was stirred at the same temperature for 1 to 24 h. After the completion of reaction, the reaction mixture was diluted with water (5 mL) and extracted with dichloromethane (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding product.

Methyl 3-benzyl-6-methyl-11-(4-nitrophenyl)-6,11-dihydro-5*H*-indolizino[6,7-*b*]indole-1-carboxylate (4a). Pale yellow solid; mp: 236–237 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.7 Hz, 2H), 7.47 (d, *J* = 7.9 Hz, 1H), 7.39–7.15 (m, 9H), 7.06 (t, *J* = 7.4 Hz, 1H), 6.50 (s, 1H), 6.16 (s, 1H), 5.08 (td, *J* = 16.4, 2.5 Hz, 2H), 4.14 (s, 2H), 3.71 (s, 3H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 152.3, 146.0, 137.9, 136.7, 130.4, 128.9, 128.7, 128.3, 127.6, 127.5, 127.4, 126.9, 124.7, 123.5, 122.3, 119.9, 118.6, 110.8, 110.6, 109.0, 50.7, 41.0, 38.9, 32.9, 29.6; IR (KBr): 2924, 2853, 1745, 1685, 1515, 1442, 1343,1110, 1050, 743 cm^{-1}; MS (ESI): *m*/*z* 492 $(M + H)^+$; HRMS (ESI): *m*/*z* calcd for $C_{30}H_{26}N_3O_4$ $(M + H)^+$: 492.1918, found: 492.1900.

Methyl 3-benzyl-11-(4-cyanophenyl)-6-methyl-6,11-dihydro-5*H*-indolizino[6,7-*b*]indole-1-carboxylate (4b). Pale yellow solid; mp: 245–246 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.61–7.04 (m, 13H), 6.49 (s, 1H), 6.12 (s, 1H), 5.07 (td, *J* = 14.2, 2.6 Hz, 2H), 4.13 (s, 2H), 3.71 (s, 3H), 3.61 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.7, 150.2, 137.9, 136.9, 132.0, 130.3, 128.8, 128.6, 128.3, 127.6, 127.5, 126.8, 124.7, 122.3, 119.8, 119.0, 118.6, 110.8, 110.5, 109.6, 109.2, 109.0, 50.7, 41.0, 39.0, 32.9, 29.6; IR (KBr): 2924, 2854, 2225, 1744, 1697, 1460, 1220, 1163, 1057, 741 cm^{-1}; MS (ESI): *m*/*z* 472 $(M + H)^+$; HRMS (ESI): *m*/*z* calcd for $C_{31}H_{26}N_3O_2$ $(M + H)^+$: 472.2020, found: 472.2037.

Methyl 3-benzyl-7,9-dimethoxy-10-(4-nitrophenyl)-5,10-dihydropyrrolo[1,2-*b*]isoquinoline-1-carboxylate (5a). White solid; mp: 120–122 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 8.01 (d, *J* = 8.9 Hz, 2H), 7.36–7.15 (m, 7H), 6.41 (s, 2H), 6.40 (s, 1H), 6.28 (s, 1H), 4.89 (d, *J* = 16.1 Hz, 1H), 4.73 (d, *J* = 16.1 Hz, 1H), 4.06 (dd, *J* = 16.1, 8.1 Hz, 2H), 3.82 (s, 3H), 3.78 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 159.8, 157.6, 151.0, 146.1,

138.0, 136.6, 132.8, 129.9, 128.7, 128.5, 128.3, 126.6, 123.4, 116.7, 109.9, 109.6, 102.2, 97.8, 55.5, 55.4, 50.7, 45.9, 37.3, 32.6; IR (KBr): 2937, 1697, 16.4, 1520, 1345, 1211, 1057, 827, 697 cm^{-1}; MS (ESI): *m/z* 499 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{29}H_{27}N_2O_6$ $(M + H)^+$: 499.1864, found: 499.1883.

Methyl 3-benzyl-10-(4-cyanophenyl)-7,9-dimethoxy-5,10-dihydropyrrolo[1,2-*b*]isoquinoline-1-carboxylate (5b). White solid; mp: 190–191 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.44 (d, J = 8.3 Hz, 2H), 7.35–7.14 (m, 7H), 6.39 (s, 2H), 6.37 (s, 1H), 6.16 (d, J = 1.5 Hz, 1H), 4.86 (d, J = 16.6 Hz, 1H), 4.69 (d, J = 16.6 Hz, 1H), 4.04 (dd, J = 16.6, 2.7 Hz, 2H), 3.82–3.75 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 159.8, 157.7, 148.8, 138.1, 136.8, 133.0, 131.9, 129.8, 128.7, 128.5, 128.3, 126.6, 119.0, 117.0, 109.9, 109.8, 109.6, 102.3, 97.9, 55.5, 55.4, 50.7, 46.0, 37.5, 32.7; IR (KBr): 2924, 2845, 2226, 1699, 1609, 1496, 1211, 1142, 1056, 775, 553 cm^{-1}; MS (ESI): *m/z* 479 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{30}H_{27}N_2O_4$ $(M + H)^+$: 479.1965, found: 479.1955.

Procedure for the preparation of compound 6. 4-(2-Benzyl-4-(methoxycarbonyl)-1*H*-pyrrol-1-yl)butanoic acid (301 mg, 1 mmol) was stirred in polyphosphoric acid (>84% phosphate as P_2O_5) (1 mL) at 75 °C for 3 h. The reaction mixture was quenched with water (5 mL), and the resulting solution was extracted with dichloromethane (3 × 5 mL). The organic phases were combined, dried over Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography on silica gel (EtOAc–hexanes) to afford the corresponding product **6** (195 mg, 69%) as a colorless oil.

Methyl 3-benzyl-8-oxo-5,6,7,8-tetrahydroindolizine-1-carboxylate (6). ^1H NMR (500 MHz, $CDCl_3$): δ 7.34–7.22 (m, 3H), 7.12 (d, J = 7.9 Hz, 2H), 6.43 (s, 1H), 3.97 (s, 2H), 3.88–3.81 (m, 5H), 2.58 (t, J = 5.9 Hz, 2H), 2.22–2.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 186.0, 165.1, 136.8, 135.5, 132.0, 128.9, 128.4, 126.9, 120.1, 113.3, 52.0, 43.1, 36.7, 32.7, 22.8; IR (KBr): 2956, 2926, 1728, 1670, 1488, 1278, 1134, 773 cm^{-1}; MS (ESI): *m/z* 306 $(M + Na)^+$; HRMS (ESI): *m/z* calcd for $C_{17}H_{17}NNaO_3$ $(M + Na)^+$: 306.1101, found: 306.1097.

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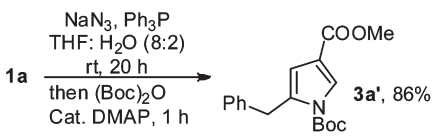

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