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PAPER

Morita–Baylis–Hillman acetates of acetylenic aldehydes: versatile synthons for substituted pyrroles *via* a metal-free tandem reaction†

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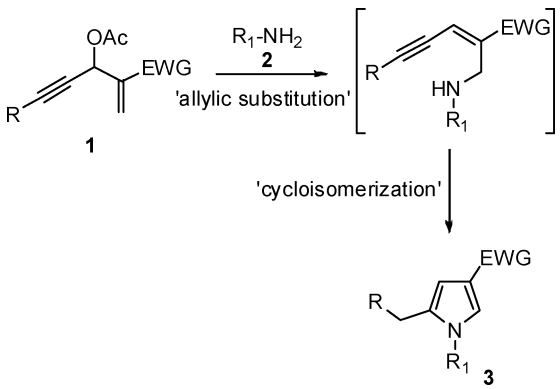
A mild and metal-free access to 1,2,4-tri or 1,2,4,5-tetrasubstituted pyrroles has been developed by the reaction of Morita–Baylis–Hillman acetates of acetylenic aldehydes with amines and sulfonamides. This new protocol is based on K_2CO_3-promoted tandem allylic substitution/cycloisomerization reactions.

Introduction

The Morita–Baylis–Hillman (MBH) reaction,[1] one of the most atom economic reactions, has become a powerful tool in current organic synthesis.[2] The products obtained from this reaction and their acetate derivatives serve as a versatile precursors for numerous useful compounds, particularly heterocycles.[2] In spite of these vast efforts, applications of acetylenic aldehydes in MBH reaction remains less investigated.[3] In continuation of our efforts towards the synthesis of bio-active natural products and heterocyclic compounds using alkyne chemistry,[4] we became interested in exploring the construction of substituted pyrroles using Morita–Baylis–Hillman acetates of acetylenic aldehydes. To the best of our knowledge, one-pot synthesis of pyrroles starting from MBH acetate has not been reported so far.[5]

Over the years considerable efforts have been made towards the synthesis of substituted pyrroles due to their wide occurrence in natural products and pharmaceuticals.[6–10] Among which cycloisomerization of substrates having alkyne and allene-functionalities are one of the useful approaches for forming pyrroles.[10] However, these cycloisomerization reactions, while offering some advantages also suffer from disadvantages such as a) the use of metal catalyst either in preparation of starting material or in cycloisomerization reaction,[10a,10c–10e] b) limitations in using the amines[10b] or c) multi-step reaction sequence.[10c] Hence, an efficient construction of substituted pyrroles using easily accessible starting materials and metal-free reagents is of high interest. Herein, we report a metal-free synthetic approach to substituted pyrroles (**3**) *via* K_2CO_3-mediated tandem allylic substitution/cycloisomerization reaction of MBH acetates (**1**) with various amines (**2**) (Scheme 1).



Scheme 1 Proposed route for the synthesis of pyrroles.

Results and discussion

We commenced our study with the use of Morita–Baylis–Hillman acetate **1a**, derived from the reaction of 3-phenylpropiolaldehyde with methyl acrylate,[3a] as starting material. As shown in Table 1, the reaction between **1a** and benzylamine (**2a**) was chosen as a model to identify the optimal condition. To begin with, the reaction was carried out using K_2CO_3 in DMF at room temperature which afforded only 14% of the desired product **3a** after 24 h (entry 1, Table 1). Subsequently, variety of reaction conditions were examined (Table 1) and we found, **3a** was obtained in excellent yield using K_2CO_3 in DMF at 45 °C (entry 5, Table 1). Whereas, other conditions carried out with change of base to Cs_2CO_3 and solvent to THF or CH_3CN at room temperature were not helpful in providing good yield for the desired product (entries 2 to 4, Table 1). As could be observed in the Table 1, increasing the reaction temperature to 45 °C offered good to excellent yield of **3a** either under K_2CO_3/DMF or CH_3CN conditions, (entries 5 and 6, Table 1). Absence of base however did not show any progress in the reaction (entry 7, Table 1). Now, having the optimized condition in hand, scope and limitations of both the amines (**2**) and MBH acetates (**1**) were investigated for this tandem reaction.

Firstly, the reactions of various amines with MBH acetate **1a** have been studied (Table 2). Aniline (**2b**), furfurylamine (**2c**) and

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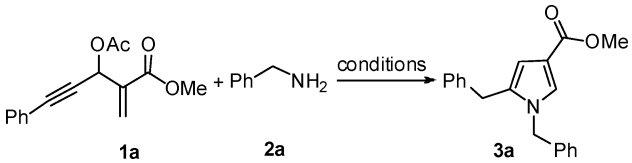
† Electronic supplementary information (ESI) available: Copies of ^1H NMR and ^{13}C NMR spectra of all the compounds. See DOI: 10.1039/c1ob05402c

Table 1 Optimization of reaction condition

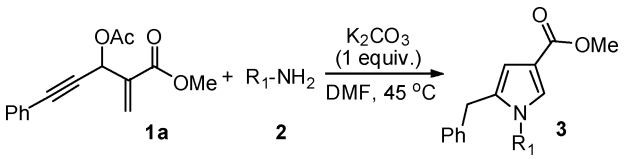


1a 2a 3a

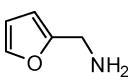
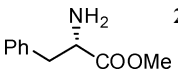
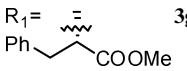
Entry	Base (1 equiv.)	Solvent	T (° C)	Time (h)	Yield (%)[a]
1	K_2CO_3	DMF	rt	24	14
2	Cs_2CO_3	DMF	rt	16	8
3	K_2CO_3	THF	rt	24	8
4	K_2CO_3	CH_3CN	rt	24	28
5	**K_2CO_3**	**DMF**	**45**	**12**	**86**
6	K_2CO_3	CH_3CN	45	16	68
7	—	DMF	45	14	0

[a] Isolated yield.

Table 2 Synthesis of pyrroles from **1a** using different amines



1a 2

Entry	Amine (**2**)	Time (h)	Product (**3**)[a]	Yield (%)[b]
1	$PhNH_2$ **2b**	6	R_1 = Ph; **3b**	77
2		4.5	R_1 = furfuryl; **3c**	82
3	$MeNH_2$ **2d**	15	R_1 = Me; **3d**	89
4	$TsNH_2$ **2e**	28	R_1 = Ts; **3e**	72
5	$PhSO_2NH_2$ **2f**	22	R_1 = $PhSO_2$, **3f**	65
6	 **2g**	28	R_1=  **3g**	62
7	$BocNH_2$ **2h**	48[c]	No reaction	—
8	$CbzNh_2$ **2i**	48[c]	No reaction	—

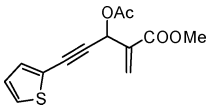
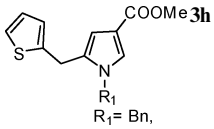
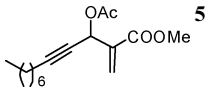
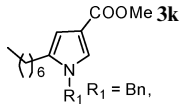
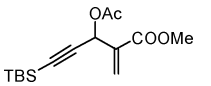
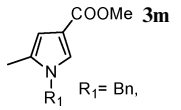
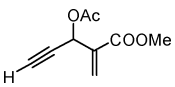
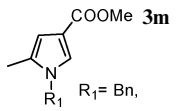
[a] All the products were characterized by ^1H, ^{13}C NMR, IR and mass spectra. [b] Isolated yield. [c] reaction at 90 °C.

methylamine (**2d**) were successfully participated in the tandem reaction to provide the corresponding pyrroles **3b**, **3c** and **3d** in 77%, 82% and 89% yields, respectively (entries 1 to 3, Table 2). Interestingly, the reactions of sulfonamides **2e** and **2f** led to the formation of *N*-sulfonyl pyrroles **3e** and **3f** in good yield (entry 4 and 5, Table 2), which is an added advantage for the present method to access the *N*-unsubstituted pyrroles *via* desulfonylation.[11] In addition, a chiral amino acid-methyl ester **2g** was employed as well, to afford pyrrole **3g** in 62% yield (entry 6, Table 2). However, no reaction was observed in the case of *tert*-butyl carbamate (**2h**) and benzyl carbamate (**2i**) even after 48 h at 90 °C, which may be due to their weak nucleophilic nature (entry 7 and 8, Table 2).

After the successful study in utilizing various amines as nucleophiles, we focused on the reactivity of MBH acetates bearing heteroaromatic, aliphatic, silyl group and no substitution on alkyne terminal (Table 3). Thus, thiophene-MBH acetate **1b** was treated with amines **2a**, **2b** and **2c**, which provided the corresponding 1,2,4-trisubstituted pyrroles **3h** to **3j** in 84–86% yield (entries 1 to 3, Table 3). Then, heptyl-MBH acetate **1c** in the presence of amines **2a** and **2b** also showed the same tendency to furnish the corresponding pyrroles **3k** and **3l** in 74% and 61%, respectively (entry 4 and 5, Table 3). The reaction of silyl-MBH acetate **1d** with amines **2a** and **2b** afforded desilylated pyrroles **3m** and **3n** in good yield (entry 6 and 7, Table 3).[12] Importantly, MBH acetate without substitution on alkyne terminal **1e** successfully participated in the tandem reaction with **2a** and **2c** to provide pyrroles **3m** and **3o** in 81% and 72%, respectively (entry 8 and 9, Table 3).

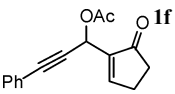
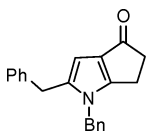
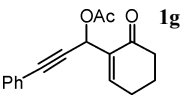
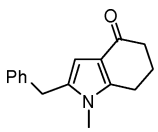
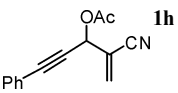
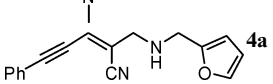
Further, we extended the scope of MBH acetates derived by varying activated alkenes towards the tandem reaction (Table 4). Hence, the substrate **1f**, prepared from 3-phenylpropiolaldehyde and cyclopentenone, was employed to react with amine **2a**. To our delight, the tandem reaction ensued well in 2 h to furnish a

Table 3 Synthesis of pyrroles from the reaction of MBH acetates with amines[a]

Entry	MBH acetate	Amine	Time (h)	Product[b]	Yield (%)[c]
1		**2a**	6	 **3h**	84
2	**1b**	**2b**	8	R_1 = Ph, **3i**	86
3	**1b**	**2c**	6	R_1 = Furfuryl, **3j**	85
4	 **5**	**2a**	16	 **3k**	74
5	**1c**	**2b**	16	R_1 = Ph, **3l**	61
6		**2a**	24	 **3m**	71
7	**1d**	**2b**	18	R_1 = Ph, **3n**	66
8		**2a**	20	 **3m**	81
9	**1e**	**2c**	16	R_1 = Furfuryl, **3o**	72

[a] Reaction conditions: MBH acetate (1 mmol), amine (1 mmol), K_2CO_3 (1 mmol), DMF (5 mL), 45 °C. [b] All the products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectra. [c] Isolated yield.

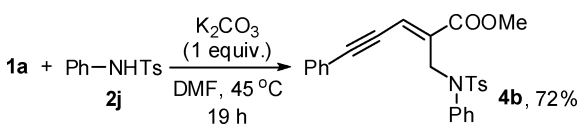
Table 4 Reactions of MBH acetates **1f–1h**[a]

Entry	MBH acetate	Amine	Time (h)	Product[b]	Yield (%)[c]
1	 **1f**	**2a**	2	 **3p**	61
2	 **1g**	**2d**	1	 **3q**	78
3	 **1h**	**2c**	24	 **4a**	64

[a] Reaction conditions: MBH acetate (1 mmol), amine (1 mmol), K_2CO_3 (1 mmol), DMF (5 mL), 45 °C. [b] All the products were characterized by ^{1}H, ^{13}C NMR, IR and mass spectra. [c] Isolated yield.

tetrasubstituted fused pyrrole **3p** in 61% yield (entry 1, Table 4). Then, **1g** also accomplished the desired fused pyrrole **3q** in 78% yield when treated with methyl amine **2d** (entry 2, Table 4). However, the MBH acetate **1h**, obtained from 3-phenylpropiolaldehyde and acrylonitrile, was unable to furnish the desired pyrrole even at elevated temperature (90 °C) for longer reaction time. Whereas, an allylic substituted product **4a** was obtained (entry 3, Table 4) which did not undergo further cycloisomerization. Extensive 2D NMR studies confirmed that the product **4a** was obtained, after initial allylic substitution, as *Z*-isomer,[13] in which the spatial arrangement of the substitutions on the double bond are not favorable for cycloisomerization. This suggests, MBH acetates **1a–1g** may provide the allylic amine intermediate with *E*-selectivity which was not isolated as they underwent immediate cycloisomerization to the corresponding pyrroles.

To verify the formation of (*E*)-isomer, the reaction of substrate **1a** with a secondary amine **2j** was performed, which afforded the product **4b** in 72% yield as anticipated (Scheme 2). Extensive 2D NMR studies established the stereochemistry of allylic amine **4b** as (*E*)-isomer.[14]



Scheme 2 Synthesis of **4b**.

Conclusions

In summary, we have developed a simple and novel method for the synthesis of substituted pyrroles starting from MBH acetates of acetylenic aldehydes with amine using a tandem reaction involving allylic substitution/cycloisomerization. The easy accessibility of the starting materials *via* an atom economic MBH-reaction and metal-free reaction condition makes the present method potentially useful in organic synthesis. Further development and synthetic applications of the described tandem reaction are under investigation.

Experimental

General

Reactions were monitored by thin-layer chromatography carried out on silica plates 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 either KBr pellets or as neat. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ solvent on a 300 MHz and 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).

Morita–Baylis–Hillman acetates have been prepared using the literature procedure[3a] to obtain **1a** to **1h**.

General procedure for the synthesis of substituted pyrroles

To a solution of MBH acetate (**1**, 1.0 mmol) and amine (**2**, 1.0 mmol) in 5 mL of dimethylformamide was added potassium carbonate (1.0 mmol) at room temperature. Then, the temperature was raised to 45 °C. The reaction mixture was stirred at the same temperature for 1 to 28 h (see Tables 1–3). After the completion of reaction, the 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 (**3**).

Spectral data for all new compounds

Methyl 3-acetoxy-2-methyleneundec-4-ynoate (1c). Pale yellow oil; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 6.41 (d, J = 1.5 Hz, 1H), 6.21 (s, 1H), 6.20 (d, J = 1.5 Hz, 1H), 3.79 (s, 3H), 2.23 (td, J = 6.7, 2.2 Hz, 2H), 2.08 (s, 3H), 1.59–1.46 (m, 2H), 1.45–1.22 (m, 6H), 0.90 (t, J = 6.8 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.3, 164.9, 136.9, 128.7, 88.5, 74.7, 61.9, 52.0, 31.1, 28.3, 28.1, 22.4, 20.7, 18.6, 13.9; IR (neat): 2930, 2858, 2236, 1744, 1638, 1225, 683 cm^{-1}; MS (ESI): m/z 289 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{15}H_{22}NaO_4$ (M+Na)$^+$: 289.1410 found: 289.1398.

Methyl 3-acetoxy-5-(*tert*-butyldimethylsilyl)-2-methylenepent-4-ynoate (1d). Pale yellow oil; ^{1}H NMR: (300 MHz, $CDCl_3$): δ 6.44 (d, J = 1.5 Hz, 1H), 6.25 (br, 1H), 6.23 (d, J = 1.5 Hz, 1H), 3.79 (s, 3H), 2.09 (s, 3H), 0.93 (s, 9H), 0.13 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 164.9, 136.4, 129.1, 100.1, 91.2, 61.9, 52.1, 25.9, 20.8, 16.4, –4.8; IR (KBr): 2956, 2926, 2078, 1731, 1639, 1396, 1056, 682 cm^{-1}; MS (ESI): m/z 297 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{15}H_{25}NaO_4Si$ (M+H)$^+$: 297.1517, found: 297.1525.

Methyl 3-acetoxy-2-methylenepent-4-ynoate (1e). ^{1}H NMR (500 MHz, $CDCl_3$): Pale yellow oil; δ 6.45 (d, J = 1.8 Hz, 1H), 6.24 (d, J = 1.8 Hz, 1H), 6.23 (s, 1H) 3.79 (s, 3H), 2.51 (br, 1H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 164.6, 135.8, 129.3, 75.5, 61.2, 52.2, 29.6, 20.7; IR (KBr): 3267, 2956, 2920, 2850, 2105, 1742, 1721, 1438, 1370, 1235, 1009 cm^{-1}; MS (ESI): m/z 205 (M+Na)$^+$.

2-Cyano-5-phenylpent-1-en-4-yn-3-yl acetate (1h). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.48 (dd, J = 7.2, 7.1 Hz, 2H), 7.40–7.29 (m, 3H), 6.30 (d, J = 1.1 Hz, 1H), 6.19 (d, J = 1.1 Hz, 1H), 6.18 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.1, 133.7, 132.0, 129.4, 128.3, 120.9, 120.3, 115.6, 89.1, 81.1, 63.3, 20.7; IR (KBr): 2923, 2232, 1750, 1214, 1020, 757, 606 cm^{-1}; MS (ESI): m/z 248 (M+Na)$^+$; HRMS (ESI): m/z calcd for $C_{14}H_{11}NNaO_2$ (M+Na)$^+$: 248.0682, found: 248.0682.

Methyl 1, 5-dibenzyl-*1H*-pyrrole-3-carboxylate (3a). White solid; M.P: 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 5-benzyl-1-phenyl-*1H*-pyrrole-3-carboxylate (3b). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40–7.32 (m, 4H), 7.21–7.08 (m, 5H), 6.96 (d, J = 6.7 Hz, 2H), 6.40 (s, 1H), 3.81 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 138.9, 138.6, 133.7, 129.1, 128.5, 128.3, 128.1, 127.2, 126.3, 126.23, 115.5, 109.7, 51.0, 32.9; IR (neat): 2948, 1710, 1515, 1437, 1242, 1195, 759, 697 cm^{-1}; MS (ESI): m/z 292 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{19}H_{18}NO_2$ (M+H)$^+$: 292.1332, Found: 292.1330.

Methyl 5-benzyl-1-(furan-2-ylmethyl)-*1H*-pyrrole-3-carboxylate (3c). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (s, 1H), 7.29–7.15 (m, 4H), 7.11 (d, J = 6.9 Hz, 2H), 6.32 (s, 1H), 6.26 (dd, J = 2.1, 1.7 Hz, 1H), 6.01 (d, J = 2.1 Hz, 1H), 4.78 (s, 2H), 3.94 (s, 2H), 3.75 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.2, 149.3, 142.9, 138.2, 132.4, 128.6, 128.4, 126.6, 126.5, 114.7, 110.4, 109.7, 108.5, 50.9, 43.8, 32.5; IR (neat): 2921, 1705, 1519, 1212, 753, 601 cm^{-1}; MS (ESI): m/z 296 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{18}H_{18}NO_3$ (M+H)$^+$: 296.1281, found: 296.1279.

Methyl 5-benzyl-1-methyl-*1H*-pyrrole-3-carboxylate (3d). White solid; M.P: 105–106 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29–7.14 (m, 4H), 7.09 (d, J = 6.9 Hz, 2H), 6.31 (s, 1H), 3.90 (s, 2H), 3.76 (s, 3H), 3.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.3, 138.2, 132.6, 128.5, 128.3, 127.3, 126.4, 114.0, 109.3, 50.8, 34.3, 32.6; IR (KBr): 3122, 2944, 1695, 1525, 1229, 769 cm^{-1}; MS (ESI): m/z 230 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{14}H_{16}NO_2$ (M+H)$^+$: 230.1176, found: 230.1174.

Methyl 5-benzyl-1-tosyl-*1H*-pyrrole-3-carboxylate (3e). White solid; M.P: 112–114 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.70 (d, J = 7.5, 2H), 7.60 (d, J = 8.1, 2H), 7.36–7.16 (m, 5H), 6.73 (s, 1H), 6.31 (s, 1H), 4.54 (s, 2H), 3.69 (s, 3H), 2.41 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 162.8, 144.3, 141.7, 140.1, 135.2, 132.8, 130.7, 129.7, 129.4, 128.97, 128.2, 127.9, 123.4, 56.9, 51.8, 21.6; IR (KBr): 2920, 1709, 1595, 1443, 1356, 1164, 1089, 697, 591 cm^{-1}; MS (ESI): m/z 370 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{20}H_{20}NO_4S$ (M+H)$^+$: 370.1108, found: 370.1111.

Methyl 5-benzyl-1-(phenylsulfonyl)-*1H*-pyrrole-3-carboxylate (3f). White solid; M.P: 56–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.98–7.88 (m, 2H), 7.62 (d, J = 7.3 Hz, 2H), 7.59–7.45 (m, 2H), 7.44–7.36 (m, 1H), 7.21–7.12 (m, 2H), 7.02–6.96 (m, 2H), 6.14 (s, 1H), 4.04 (s, 2H), 3.78 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 164.1, 141.8, 138.3, 137.4, 135.4, 134.3, 133.4, 129.7, 129.5, 129.1, 127.9, 127.3, 126.8, 118.5, 113.9, 51.7, 33.5; IR (neat): 2952, 2850, 1719, 1448, 1374, 1178, 730, 590 cm^{-1}; MS (ESI): m/z 356 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{19}H_{17}NNaO_4S$ (M+Na)$^+$: 378.0770, found: 378.0788.

(*S*)-Methyl-5-benzyl-1-(1-methoxy-1-oxo-3-phenylpropan-2-yl)-*1H*-pyrrole-3 carboxylate (3g). Pale yellow oil; $[\alpha]_D^{21}$ −13.9 (c 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.58 (d, J = 1.5 Hz, 1H), 7.29 (m, 6H), 7.01 (d, J = 1.5 Hz, 1H), 6.99 (s, 1H), 6.82–6.78 (m, 2H), 6.25 (s, 1H), 4.68 (dd, J = 9.1, 6.8 Hz, 1H), 3.80 (s, 3H), 3.60 (s, 5H), 3.34 (dd, J = 6.8, 13.6 Hz, 1H), 3.00 (dd, J = 9.1, 13.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 169.8, 165.2, 135.6, 133.1, 130.9, 128.9, 128.7, 128.6, 128.5, 127.2, 126.6, 124.3, 115.7, 109.3, 68.1, 52.7, 51.1, 39.4, 32.4; IR (KBr): 2925, 1723, 1711, 1519, 1454, 1272, 1217, 1005, 757, 700 cm^{-1}; MS (ESI): m/z 378.0 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{23}H_{24}NO_4$ (M+H)$^+$: 378.1700, found: 378.1706.

Methyl 1-benzyl-5-(thiophen-2-ylmethyl)-*1H*-pyrrole-3-carboxylate (3h). White solid; M.P: 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-phenyl-5-(thiophen-2-ylmethyl)-*1H*-pyrrole-3-carboxylate (3i). Yellow solid; M.P: 69–70 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.38 (dd, J = 1.3, 5.1 Hz, 1H), 7.31 (dd, J = 1.5, 3.6 Hz, 1H), 7.16–7.08 (m, 2H), 7.04 (dd, J = 3.7, 5.1 Hz, 1H), 6.93 (s, 1H), 6.74–6.58 (m, 4H), 4.25 (s, 2H), 3.79 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.5, 147.3, 138.8, 133.4, 129.2, 129.1, 127.4, 121.9, 121.4, 117.8, 113.5, 96.3, 89.4, 52.1, 42.4; IR (KBr): 2930, 1691, 1600, 1438, 1239, 1110, 753, 700, 599 cm^{-1}; MS (ESI): m/z 298 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{17}H_{16}NO_2S$ (M+H)$^+$: 298.0896, found: 298.0903.

Methyl 1-(furan-2-ylmethyl)-5-(thiophen-2-ylmethyl)-*1H*-pyrrole-3-carboxylate (3j). White solid; M.P: 63–65 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.35 (d, J = 2.3 Hz, 1H), 7.25 (d, J = 2.6 Hz, 1H), 7.14 (dd, J = 5.1, 1.2 Hz, 1H), 6.89 (dd, J = 5.1, 3.6 Hz, 1H), 6.74 (d, J = 2.3 Hz, 1H), 6.41 (s, 1H), 6.29 (dd, J = 1.9, 3.0 Hz, 1H), 6.10 (d, J = 3.1 Hz, 1H), 4.85 (s, 2H), 4.12 (s, 2H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 165.1, 149.2, 142.9, 141.4, 131.7, 126.9, 126.7, 125.2, 124.2, 114.8, 110.5, 109.5, 108.5, 50.9, 43.9, 29.6; IR (KBr): 2924, 2854, 1703, 1438, 1385, 1211, 1011, 761, 708 cm^{-1}; MS (ESI): m/z 302 (M+H); HRMS (ESI): m/z calcd for $C_{16}H_{16}NO_3S$ (M+H)$^+$: 302.0845, found: 302.0838.

Methyl 1-benzyl-5-heptyl-*1H*-pyrrole-3-carboxylate (3k). White solid; M.P: 56–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.36–7.18 (m, 4H), 6.97 (d, J = 7.1 Hz, 2H), 6.32 (s, 1H), 5.02 (s, 2H), 3.76 (s, 3H), 2.37 (t, J = 7.3 Hz, 2H), 1.60–1.49 (m, 2H), 1.36–1.18 (m, 8H), 0.87 (t, J = 6.4 Hz, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.4, 136.9, 134.9, 128.7, 127.6, 126.4, 126.2, 122.8, 107.2, 50.8, 50.6, 31.6, 29.1, 28.9, 28.2, 25.9, 22.5, 13.9; IR (KBr): 2925, 2853, 2212, 1699, 1518, 1220, 702 cm^{-1}; MS (ESI): m/z 314 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{20}H_{28}NO_2$ (M+H)$^+$: 314.2115, found 314.2119.

Methyl 5-heptyl-1-phenyl-*1H*-pyrrole-3-carboxylate (3l). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.55–7.25 (m, 6H), 6.46 (s, 1H), 3.81 (s, 3H), 2.45 (t, J = 7.7 Hz, 2H), 1.54–1.40 (m, 2H), 1.33–1.14 (m, 8H), 0.85 (t, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.4, 139.3, 135.5, 129.2, 127.9, 126.6, 126.1, 115.4, 107.6, 51.0, 31.6, 29.1, 28.9, 28.6, 26.4, 22.5, 14.0; IR (neat): 2926, 2855, 1714, 1507, 1438, 1237, 1101, 756, 695 cm^{-1}; MS (ESI): m/z 300 (M+H)$^+$; HRMS (ESI) m/z calcd for $C_{19}H_{26}NO_2$ (M+H)$^+$: 300.1958, found: 300.1951.

Methyl 1-benzyl-5-methyl-*1H*-pyrrole-3-carboxylate (3m). Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–7.19 (m, 4H), 6.98 (d, J = 6.6 Hz, 2H), 6.30 (s, 1H), 5.01 (s, 2H), 3.76 (s, 3H), 2.11 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.3, 136.8, 130.0, 128.8, 127.7, 126.5, 126.3, 114.5, 108.5, 67.9, 50.9, 25.5; IR (KBr): 2921, 2851, 1704, 1526, 1443, 1218, 765, 725 cm^{-1}; MS (ESI): m/z 230 (M+H)$^+$; HRMS (ESI) m/z calcd for $C_{14}H_{16}NO_2$ (M+H)$^+$: 230.1176, found: 230.1177.

Methyl 5-methyl-1-phenyl-*1H*-pyrrole-3-carboxylate (3n). Colourless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49–7.22 (m, 6H), 6.39 (s, 1H), 3.79 (s, 3H), 2.17 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.3, 139.2, 130.3, 129.2, 127.8, 126.5, 125.7, 112.8, 108.9, 51.0, 12.7; IR (KBr): 2947, 2852, 1703, 1443, 1218, 1003, 725 cm^{-1}; MS (ESI): m/z 216 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{13}H_{14}NO_2$ (M+H)$^+$: 216.1019, found: 216.1021.

Methyl 1-(furan-2-ylmethyl)-5-methyl-*1H*-pyrrole-3-carboxylate (3o). Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.36 (s, 1H), 7.30 (s, 1H), 7.24 (s, 1H), 6.32 (s, 1H), 6.19 (s, 1H), 4.93 (s, 2H), 3.77 (s, 3H), 2.23 (s, 3H); ^{13}C NMR: (75 MHz, $CDCl_3$): δ 165.2, 149.6, 142.8, 129.7, 125.8, 124.4, 114.6, 110.4, 108.3, 50.8, 43.8, 11.8; IR (KBr): 2947, 2852, 1703, 1443, 1218, 1003, 725 cm^{-1}; MS (ESI): m/z 219 (M+H)$^+$; HRMS (ESI): m/z calcd for $C_{12}H_{14}NO_3$ (M+H)$^+$: 219.0968, found: 219.0953.

1, 2-Bibenzyl-5, 6-dihydrocyclopenta[b]pyrrol-4(*1H*)-one (3p). Pale yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.34–7.17 (m, 6H) 7.05 (d, J = 6.7 Hz, 2H), 6.90 (d, J = 6.2 Hz, 2H), 6.17 (s, 1H), 4.84 (s, 2H), 3.80 (s, 2H), 2.82 (t, J = 4.1 Hz, 2H), 2.71 (t, J = 4.1 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 197.4, 139.7, 136.1, 129.3, 128.9, 128.8, 128.6, 128.3, 127.8, 126.6, 126.2, 125.8, 102.5, 48.3, 40.8, 29.6, 20.7; IR (KBr): 2922, 2854, 1647, 1484, 1219, 772,

573 cm^{-1}; MS (ESI): *m/z* 302 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{21}H_{20}NO$ $(M+H)^+$: 302.1539, found: 302.1552.

2-Benzyl-1-methyl-6,7-dihydro-*1H*-indol-4(5H)-one (3q). Brown solid; M.P: 55–57 °C; ^1H NMR (300 MHz, $CDCl_3$): δ 7.29–7.14 (m, 3H), 7.11 (d, J = 6.8 Hz, 2H), 6.29 (s, 1H), 3.91 (s, 2H), 3.30 (s, 3H), 2.69 (t, J = 6.8 Hz, 2H), 2.42 (t, J = 6.0 Hz, 2H), 2.15 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.0, 144.3, 133.3, 128.5, 128.4, 128.3, 128.1, 126.4, 104.5, 37.5, 32.8, 30.6, 23.4, 21.8; IR (NEAT): 2925, 2845, 1649, 1489, 1396, 1041, 992, 758, 691 cm^{-1}; MS (ESI): *m/z* 240 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{16}H_{18}NO$ $(M+H)^+$: 240.1383, found: 240.1381.

(*Z*)-2-((Furan-2-ylmethylamino) methyl)-5-phenylpent-2-en-4-ynenitrile (4a). Pale yellow oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.55–7.49 (m, 2H), 7.38–7.31 (m, 4H), 6.49 (t, J = 1.5 Hz, 1H), 6.29 (dd, J = 3.0, 2.2 Hz, 1H), 6.18 (d, J = 3.0 Hz, 1H), 3.80 (s, 2H), 3.48 (d, J = 1.5 Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 152.6, 142.1, 132.0, 129.5, 128.4, 124.8, 122.7, 121.7, 116.9, 110.1, 107.6, 100.3, 84.6, 50.1, 44.4; IR (KBr): 3448, 2920, 2850, 2196, 1642, 758, 598 cm^{-1}; MS (ESI): *m/z* 263 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{17}H_{15}N_2O$ $(M+H)^+$: 263.1179, found: 263.1169.

(*E*)-Methyl 2-((4-methyl-*N*-phenylphenylsulfonamido) methyl)-5-phenylpent-2-en-4-ynoate (4b). Colorless oil; ^1H NMR (300 MHz, $CDCl_3$): δ 7.56–7.49 (m, 3H), 7.46 (d, J = 7.3 Hz, 2H), 7.42–7.32 (m, 3H), 7.25–7.16 (m, 5H), 7.02 (d, J = 6.3 Hz, 2H), 6.86 (s, 1H), 4.71 (s, 2H), 3.69 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 166.1, 143.3, 138.9, 136.2, 134.8, 132.0, 129.4, 129.3, 129.0, 128.5, 128.4, 128.0, 127.9, 124.3, 122.1, 103.9, 85.1, 52.1, 48.0, 21.5; IR (KBr): 2924, 2853, 2192, 1715, 1488, 1444, 1344, 1162, 1087, 758, 692 cm^{-1}; MS (ESI): *m/z* 446 $(M+H)^+$; HRMS (ESI): *m/z* calcd for $C_{26}H_{24}NO_4S$ $(M+H)^+$: 446.1421, found: 446.1426.

Methyl 5-benzyl-*1H*-pyrrole-3-carboxylate (3ea). White solid; M.P: 125–127 °C; ^1H 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.

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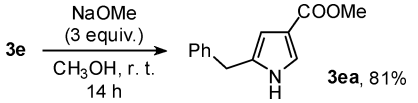
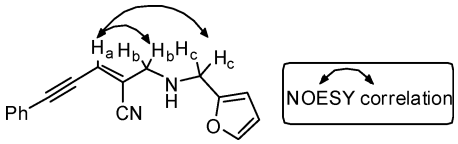


12 However, it is unclear whether the desilylation take place before allylic substitution, between substitution and cycloisomerization or after cycloisomerization.

13 The (*Z*)-stereochemistry of **4a** was supported by NOE cross peaks between H_a–H_b and H_a–H_c as shown below.



14 No NOE cross peaks were observed between H_a–H_b in compound **4b**.