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**PAPER**

# Iodine catalyzed four-component reaction: a straightforward one-pot synthesis of functionalized pyrroles under metal-free conditions†

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An iodine-catalyzed four-component reaction of 1,3-dicarbonyl compounds, amines, aldehydes and nitroalkanes afforded polysubstituted pyrroles under a metal free condition. Simplicity, low cost and good yields are the key features of this methodology. The mechanism of this four component process is discussed and structural elaboration of one of the compounds synthesized using Suzuki and Sonogashira coupling is presented.

## Introduction

The pyrrole framework in addition to its occurrence in many natural products has found wide applications in the area of drug discovery.[1] A range of pharmacological properties *e.g.* anti-tumor, *anti*-inflammatory, antibacterial, antioxidant and anti-fungal activities of this important class of heterocycle are known in the literature. Thus, a number of synthetic methods have been developed for the construction of a pyrrole ring. The classical methods used frequently for the synthesis of pyrroles include Hantzsch,[2] Knorr,[3] and Paal–Knorr[4] reactions. While these methods are very useful and effective their uses however suffer from several drawbacks such as functional group compatibility, regiospecificity, harsh reaction conditions and multistep synthetic operation. Among the various strategies[1] developed to overcome these problems, multi-component reactions (MCRs) have found wide applications in the synthesis of pyrroles.[5] MCRs allow the union of three or more starting materials in a single synthetic operation leading to increased molecular diversity and complexity in a fast and experimentally simple fashion. MCRs have become an important tool in organic synthesis especially for diversity-oriented synthesis. The advantages of MCRs over classical stepwise methods include (i) high atom economy and bond-forming efficiency, (ii) avoids isolation and purifications of any intermediates thereby (iii) minimizing waste, labor, and cost.[6] Thus, synthesis of functionalized pyrroles has been reported *via* a Fe(III)-catalyzed four-component coupling reaction of 1,3-dicarbonyl compounds, amines, aldehydes, and nitroalkanes.[7] More recently, we have reported a Pd-mediated MCR for the synthesis of functionalized pyrroles of potential medicinal value.[8] All these methods however, involve the use of a metal catalyst the removal of which often requires cumbersome workup and purifications. As an inexpensive and commercially available reagent iodine has attracted considerable interest due to its non-hazardous nature and efficiency in various organic transformations.[9] Herein we report a metal free synthesis of polysubstituted pyrroles *via* a four component reaction catalyzed by molecular iodine.

## Results and discussion

It is known that generation of (i) *β*-enaminocarbonyl derivatives from *β*-dicarbonyl and amines[10a] and (ii) nitroalkenes from aldehyde and nitroalkane can be catalyzed by molecular iodine.[10b] Moreover, the iodine catalyzed Michael reaction is well known.[10c] It was therefore hypothesized that construction of a pyrrole ring *via* Michael reaction of *β*-enamino ketones or esters and nitroalkenes followed by cyclization could be facilitated by iodine (Fig. 1).[10d]

Accordingly, we examined the reaction of benzylamine (**1a**), acetyl acetone (**2a**), benzaldehyde (**3a**) and nitromethane (**4**) in the presence of a catalyst under nitrogen. Since our initial goal was to identify an alternative catalyst—preferably non-metal—a range of relevent agents were examined (Table 1). All the reactions were generally carried out at 90–95 °C without using an

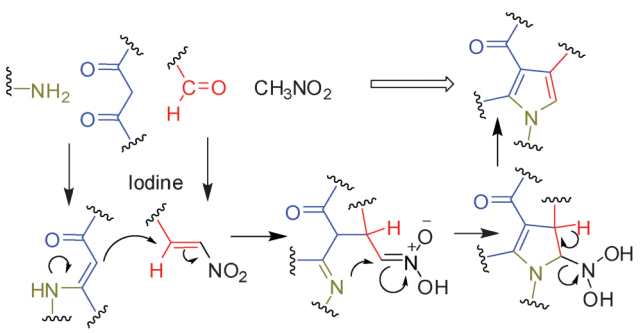


**Fig. 1** Probable route to construct a pyrrole ring catalyzed by $I_2$.

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† Electronic Supplementary Information (ESI) available: Copies of spectra for all new compounds. See DOI: 10.1039/c2ra00982j/

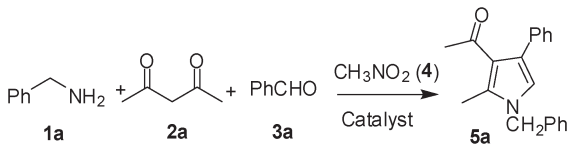
additional solvent. The use of *p*-toluenesulfonic acid (*p*-TSA) (entry 1, Table 1), $CF_3SO_3H$ (entry 2, Table 1) and solid supported catalyst such as $NaHSO_3$-$SiO_2$ (entries 3 and 4, Table 1) was examined but found to be less effective. The desired product **5** was isolated only in 25–30% yield. The use of iodine however accelerated the MCR and increased the product yield significantly (entry 5, Table 1) affording compound **5** in 85% yield. The reaction was carried out using 0.1 mmol of iodine. The yield of the product was decreased when 0.05 mmol of iodine was used (entry 6, Table 1) or suppressed when the reaction was performed at room temperature (entry 7, Table 1). The effect of using a solvent *e.g.* DMF (entry 8, Table 1) or THF, was also examined and found to be counter productive. The MCR did not proceed well in the absence of iodine (entry 9, Table 1) or when Amberlyst-15 was used as a catalyst (entry 10, Table 1).

To demonstrate the utility of the present MCR a variety of polyfunctionalized pyrroles (**6**) was synthesized (Table 2) in good yields. Both aryl and alkyl amines *e.g.* benzyl, (*R*)- and (*S*)-phenylethyl, 1-naphthyl, 2-hydroxyethyl and cyclohexyl amine were employed in the present MCR. Both acetyl acetone (**2a**) and ethyl acetoacetate (**2b**) participated well in this reaction. The MCR proceeded smoothly with a number of aryl aldehydes containing various substitution patterns.

To expand the scope of the present solvent free MCR, structural elaboration of one of the compounds synthesized *e.g.* **5g** was carried out using Suzuki (Table 3) and Sonogashira coupling (Table 4). A number of boronic acids were employed to couple with compound **5** in the presence of $PdCl_2(dppf)\cdot CH_2Cl_2$, $PPh_3$ and $K_2CO_3$ in 1,4-dioxane-$H_2O$ at 90–95 °C. The desired product **6** was isolated in 75–83% yield. Similarly, a number of terminal alkynes were coupled with **5** in the presence of $PdCl_2(dppf)\cdot CH_2Cl_2$, $PPh_3$, CuI and $Et_3N$ in DMF at 90–95 °C to give desired alkynes **7** in 78–83% yield.

Mechanistically, the reaction seems to proceed *via* the path shown in Fig. 1. While the precise role of iodine in the present MCR was not clearly understood possibly the Michael reaction[11] of *β*-enamino carbonyl compounds with nitroalkene (both generated *in situ*) was accelerated in presence of iodine. To gain further evidences the *β*-enamino ketone (**8a**) prepared from **1a** and **2a** was reacted with nitroalkene (**9a**) prepared separately from the benzaldehyde (**3a**) and the nitromethane (**4**) in the presence and absence of iodine. While the reaction proceeded well in the first case (< 80% conversion after 6 h) but it was sluggish in the second case (> 40% conversion after 6 h) indicating the key role played by iodine in the Michael addition step. The formation of *β*-enamino carbonyl compound *via* the reaction of amine and the 1,3-dicarbonyl compound could also be accelerated by iodine.[12] The interaction of molecular iodine with carbonyl oxygen perhaps played a vital role here. This type of interaction has been described in the literature earlier.[13a] For example, nucleophilic addition of indole to a carbonyl compound was catalyzed efficiently by molecular iodine.[13b] Additionally, the Michael reaction of indole and imidazole with unsaturated carbonyl compound has also been carried out successfully in the presence of a catalytic amount of iodine.[10c] It was therefore suggested that a halogen bond between the carbonyl oxygen and iodine molecule plays a key role in the remarkable catalytic effect of iodine observed in these reactions.[13a] A halogen bond is defined as intermolecular uncovalent interaction between a halogen atom and electron-donor atom such as O or N (similar to hydrogen bond).[14] Nevertheless, once again to gain further evidence the nitroalkene **9a** was reacted with **1a** and **2a** in the presence and absence of iodine. The reaction was completed within 6 h in the first case affording the desired product **5a** whereas very little product was formed in the second case. Overall, all these observations not only suggested that the reaction proceed *via* formation of a nitroalkene but the central role played by iodine in facilitating the MCR.

**Table 1** Effect of reaction conditions on 4-component reaction for the preparation of a pyrrole derivative[a]




| Entry | Catalyst (mmol) | *T*/°C | Time (h) | %Yield[b] |
|---|---|---|---|---|
| 1 | *p*-TSA (0.1) | 90–95 | 14 | 30 |
| 2 | $CF_3SO_3H$ (0.1) | 90–95 | 14 | 30 |
| 3 | $NaHSO_3$-$SiO_2$ (0.1) | 90–95 | 24 | 25 |
| 4 | $NaHSO_3$-$SiO_2$ (0.15) | 90–95 | 24 | 30 |
| 5 | $I_2$ (0.1) | 90–95 | 6.0 | 85 |
| 6 | $I_2$ (0.05) | 90–95 | 6.0 | 65 |
| 7 | $I_2$ (0.1) | Room temp | 24 | 15 |
| 8 | $I_2$ (0.1) | 90–95 | 6.0 | 60[c] |
| 9 | No catalyst | 90–95 | 24 | 11 |
| 10 | Amberlyst-15 (10%w/w) | 90–95 | 24 | 10 |

[a] All the reactions were carried out using compound **1** (1.5 mmol), **2** (1.0 mmol), **3a** (1.0 mmol) and **4** (3.0 mL) in presence of a catalyst under nitrogen. [b] Isolated yield. [c] The reaction was carried out in DMF.

## Conclusions

In conclusion, a facile and efficient synthesis of multisubstituted pyrroles derivatives has been developed *via* a $I_2$-mediated MCR. The methodology employs readily available and inexpensive starting materials under metal and solvent free conditions. To the best of our knowledge this is the first example of Grob and Camenisch's pyrrole synthesis[11a] catalyzed by iodine *via* one-pot four-component reactions. The methodology should find wide usage both in academia and pharma industries.

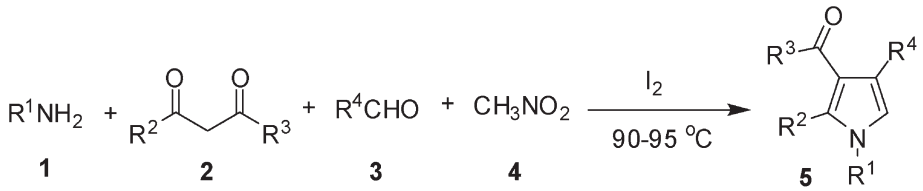
## Experimantal

### General methods

Unless stated otherwise, reactions were performed under nitrogen atmosphere using oven dried glassware. Reactions were monitored by thin layer chromatography (TLC) on silica gel plates (60 F254), visualizing with ultraviolet light or iodine spray. Flash chromatography was performed on silica gel (230–400 mesh) using distilled hexane, ethyl acetate, dichloromethane. $^1H$ NMR and $^{13}C$ NMR spectra were recorded in $CDCl_3$ or DMSO-$d_6$ solution by using 400 or 200 and 100 MHz spectrometers, respectively. Proton chemical shifts ($\delta$) are relative to tetramethylsilane (TMS, $\delta$ = 0.00) as internal standard and expressed in ppm. Spin multiplicities are given as s (singlet), d (doublet), t (triplet) and m (multiplet) as well as b (broad). Coupling constants (*J*) are given in hertz. Infrared spectra were recorded on a FT-IR spectrometer. Melting points were

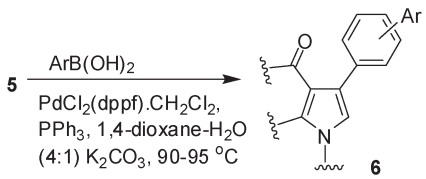
**Table 2** Iodine-mediated 4-component reaction for the synthesis of functionalized pyrrole derivatives[a]

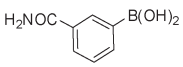
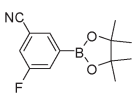
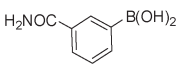
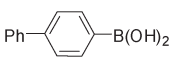
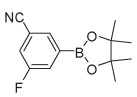
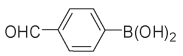



| Entry | 1; $R^1$ | 2; $R^2$; $R^3$ | 3; $R^4$ | Time (h) | Products | %Yield[b] |
|---|---|---|---|---|---|---|
| 1 | **1a**; $PhCH_2$ | **2a**; $CH_3$; $CH_3$ | **3a**; Ph | 6 | **5a** | 85 |
| 2 | **1a** | **2b**; $CH_3$; OEt | **3a** | 8 | **5b** | 76 |
| 3 | **1b**; (*R*)-Ph($CH_3$)CH | **2b** | **3a** | 8 | **5c** | 75 |
| 4 | **1b** | **2a** | **3a** | 7 | **5d** | 85 |
| 5 | **1b** | **2a** | **3b**; 2,6-diF-4-$BrC_6H_2$ | 7.5 | **5e** | 72 |
| 6 | **1a** | **2a** | **3b** | 6.5 | **5f** | 81 |
| 7 | **1a** | **2a** | **3c**; 3-$BrC_6H_4$ | 6.0 | **5g** | 85 |
| 8 | **1a** | **2a** | **3d**; 4-$BrC_6H_4$ | 7.5 | **5h** | 80 |
| 9 | **1c**; (*S*)-Ph($CH_3$)CH | **2b** | **3e**; 2-$IC_6H_4$ | 8.0 | **5i** | 70 |
| 10 | **1d**; 1-Naphthyl | **2a** | **3a** | 6.5 | **5j** | 60 |
| 11 | **1a** | **2a** | **3f**; 4-$FC_6H_4$ | 6.5 | **5k** | 80 |
| 12 | **1b** | **2a** | **3f** | 7.0 | **5l** | 75 |
| 13 | **1a** | **2b** | **3f** | 8.0 | **5m** | 77 |
| 14 | **1b** | **2b** | **3c** | 7.5 | **5n** | 69 |
| 15 | **1e**; $HOCH_2CH_2$– | **2b** | **3a** | 8.0 | **5o** | 70 |
| 16 | **1f**; c-Hexyl | **2b** | **3a** | 7.0 | **5p** | 65 |

[a] All the reactions were carried out using amine **1** (1.5 mmol), 1,3-dicarbonyl compound **2** (1.0 mmol), aryl aldehyde **3** (1.0 mmol) and nitromethane **4** (3.0 mL) in presence of iodine (0.10 mmol) at 90–95 °C under nitrogen. [b] Isolated yield.

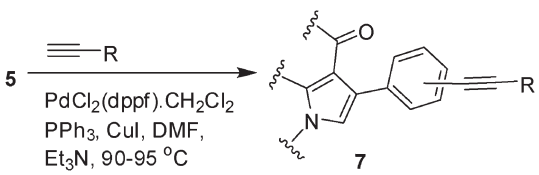
**Table 3** Synthesis of 4-biaryl substituted pyrroles (**6**)[a]




| Entry | Halide **5** | $ArB(OH)_2$ or ester | Products (**6**) | Time[b](h) | %Yield[b] |
|---|---|---|---|---|---|
| 1 | **5e** |  | **6a** | 6.5 | 75 |
| 2 | **5e** |  | **6b** | 7.0 | 79 |
| 3 | **5g** |  | **6c** | 6.0 | 77 |
| 4 | **5g** |  | **6d** | 6.5 | 75 |
| 5 | **5i** |  | **6e** | 7.0 | 76 |
| 6 | **5h** |  | **6f** | 6.0 | 84 |

[a] All the reactions were carried out using compound **5** (1.0 mmol), aryl boronic acid (1.5 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (0.10 mmol), $PPh_3$ (0.10 mmol) and $K_2CO_3$ (2.0 mmol) in 1,4-dioxane-$H_2O$ (4 : 1) (5.0 mL) at 90–95 °C under nitrogen. [b] Isolated yield.

**Table 4** Synthesis of alkynyliaryl substituted pyrroles (**7**)[a]




| Entry | Halide **5** | Alkynes | Products (**7**) | Time[b](h) | %Yield[b] |
|---|---|---|---|---|---|
| 1 | **5h** | ≡–$CH_2CH_2CH_2Cl$ | **7a** | 8.0 | 80 |
| 2 | **5h** | ≡–$CH_2(CH_2)_6CH_3$ | **7b** | 7.0 | 81 |
| 3 | **5g** | ≡–$C(CH_3)_2OH$ | **7c** | 7.5 | 83 |
| 4 | **5g** | ≡–$CH_2(CH_2)_6CH_3$ | **7d** | 8.5 | 79 |
| 5 | **5f** | ≡–$C(CH_3)_2OH$ | **7e** | 9.0 | 78 |

[a] All the reactions were carried out using compound **5** (1.0 mmol), a terminal alkyne (1.5 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (0.10 mmol), $PPh_3$ (0.10 mmol), CuI (0.1 mmol) and $Et_3N$ (3.0 mmol) in DMF (6 mL) at 90–95 °C under nitrogen. [b] Isolated yield.

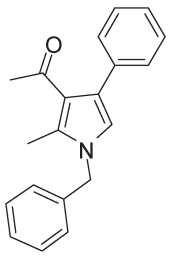
determined using Buchi B-540 melting point apparatus and are uncorrected. MS spectra were obtained on a Agilent 6430 series Triple Quard LC-MS/MS spectrometer. High-resolution mass spectra (HRMS) were recorded using a Waters LCT Premier XE instrument.

### General method for the synthesis of functionalized pyrrole derivatives (5)

To a solution of amine **1** (1.5 mmol), 1,3-dicarbonyl compound **2** (1.0 mmol), aryl aldehyde **3** (1.0 mmol) and nitromethane **4** (3.0 mL) was added $I_2$ (0.10 mmol) with stirring under nitrogen at room temp. The mixture was then stirred at 90–95 °C and the

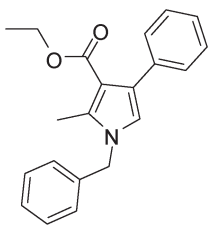
progress was monitored by TLC. After completion of the reaction the mixture was cooled to room temp, diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The organic layers were collected, combined, washed with brine (5 mL), dried over $Na_2SO_4$, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel using 1 : 9–4 : 6 ethyl acetate–petroleum ether to afford the desired compound.

**1-(1-Benzyl-2-methyl-4-phenyl-1*H*-pyrrol-3-yl)ethanone (5a).**



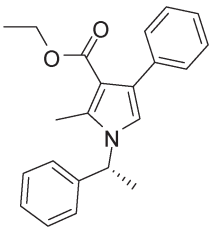
Brown colour solid (245 mg, 0.85 mmol, 85%); mp 52–54 °C; IR (neat) 3585, 3019, 2929, 1887, 1647, 1560, 1453, 1354, 1215, 1073 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.03 (s, 3H), 2.43 (s, 3H), 5.05 (s, 2H), 6.53 (s, 1H), 7.09 (d, $J$ = 6.8 Hz, 2H), 7.25–7.55 (m, 8H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 31.0, 120.0, 121.9, 125.8, 126.6, 127.3, 128.1, 129.0, 135.0, 136.2, 197.5; HRMS: $m/z$ calcd for $C_{20}H_{19}NO$ (M + 1) 290.1467; found 290.1541.

**Ethyl-1-benzyl-2-methyl-4-phenyl-1*H*-pyrrole-3-carboxylate (5b).**



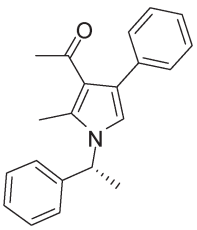
Dark brown sticky liquid (242 mg, 0.76 mmol, 76%); IR (neat) 3405, 3017, 2982, 1949, 1687, 1527, 1454, 1284, 1216 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.13 (t, $J$ = 6.8 Hz, 3H), 2.47 (s, 3H), 4.17 (q, $J$ = 6.8 Hz, 2H), 5.06 (s, 2H), 6.58 (s, 1H), 7.08 (d, $J$ = 6.8 Hz, 2H), 7.23–7.38 (m, 8H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.4, 14.0, 50.5, 59.3, 111.0, 120.3, 126.0, 127.4, 128.8, 129.2, 135.8, 136.3, 165.8; HRMS: $m/z$ calcd for $C_{21}H_{21}NO_2$ (M + 1) 320.1572; found 320.1646.

**Ethyl-2-methyl-4-phenyl-1-((*R*)-1-phenylethyl)-1*H*-pyrrole-3-carboxylate (5c).** Off white solid (250 mg, 0.75 mmol, 75%); mp 47–49 °C; IR (neat) 3384, 3060, 2981, 1949, 1802, 1693, 1527, 1412, 1276 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.12 (t, $J$ = 6.8 Hz, 3H), 1.83 (d, $J$ = 6.8 Hz, 3H), 2.44 (s, 3H), 4.16 (q, $J$ = 6.8 Hz, 2H), 5.39 (q, $J$ = 6.8 Hz, 1H), 6.72 (s, 1H), 7.08 (d, $J$ = 7.2 Hz, 2H), 7.23–7.40 (m, 8H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$



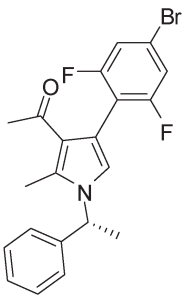
11.3, 13.9, 22.1, 55.0, 59.3, 110.8, 116.7, 125.7, 126.0, 127.4, 128.8, 129.2, 136.1, 142.0, 165.9; HRMS: $m/z$ calcd for $C_{22}H_{23}NO_2$ (M + 1) 334.1729; found 334.1809.

**1-(2-Methyl-4-phenyl-1-((*R*)-1-phenylethyl)-1*H*-pyrrol-3-yl) ethanone (5d).**



Off-white solid (257 mg, 0.85 mmol, 85%); mp 126–129 °C; IR (neat) 3401, 3013, 2401, 1950, 1647, 1511, 1406, 1272, 1215, 1029 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.83 (d, $J$ = 7.2 Hz, 3H), 2.03 (s, 3H), 2.41 (s, 3H), 5.40 (q, $J$ = 7.2 Hz, 1H), 6.67 (s, 1H), 7.10 (d, $J$ = 7.2 Hz, 2H), 7.24–7.38 (m, 8H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.4, 22.0, 54.8, 116.5, 121.9, 125.6, 126.5, 127.6, 128.1, 129.2, 134.9, 136.5, 141.9, 197.8; HRMS: $m/z$ calcd for $C_{21}H_{21}NO$ (M + 1) 304.1623; found 304.1694.

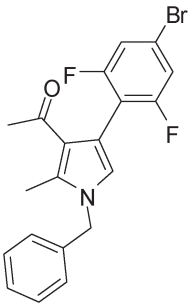
**1-(4-(4-Bromo-2,6-difluorophenyl)-2-methyl-1-((*R*)-1-phenylethyl)-1*H*-pyrrol-3-yl)ethanone (5e).**



Brown sticky liquid (300 mg, 0.72 mmol, 72%); IR (neat) 3400, 3089, 2927, 1651, 1557, 1417, 1269, 1216, 1026, 851, 687 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.83 (d, $J$ = 7.6 Hz, 3H), 2.10 (s, 3H), 2.41 (s, 3H), 5.41 (q, $J$ = 7.6 Hz, 1H), 6.77 (s, 1H), 7.07 (d, $J$ = 7.6 Hz, 2H), 7.12–7.18 (m, 2H), 7.26–7.35 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.7, 22.2, 29.6, 55.2, 108.7, 113.3, 115.1, 116.3, 118.6, 120.1, 122.2, 125.4, 127.6, 128.9, 135.6, 141.7, 159.0, 161.1, 195.7; HRMS: $m/z$ calcd for $C_{21}H_{18}F_2NO$ (M + 1) 418.0540; found 418.0633.

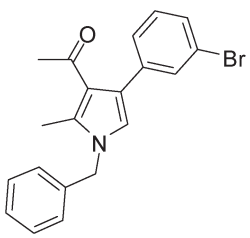
 

**1-(1-Benzyl-4-(4-bromo-2,6-difluorophenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (5f).**



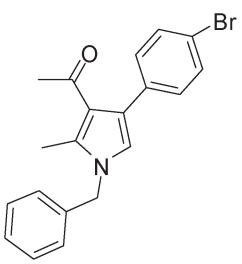

Brown colour solid (326 mg, 0.81 mmol, 81%); mp 96–99 °C; IR (neat) 3390, 3031, 2925, 1807, 1651, 1557, 1417, 1353, 1181, 1025, 852, 752 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.10 (s, 3H), 2.45 (s, 3H), 5.08 (s, 2H), 6.62 (s, 1H), 7.07 (d, $J$ = 7.2 Hz, 2H), 7.09–7.17 (m, 2H), 7.25–7.37 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.7, 29.4, 50.4, 108.9, 113.0, 115.8, 116.4, 120.2, 122.1, 126.5, 127.7, 128.8, 129.2, 135.7, 136.1, 161.4, 195.4; HRMS: *m/z* calcd for $C_{20}H_{16}BrF_2NO$ (M + 1) 404.0383; found 404.0461.

**1-(1-Benzyl-4-(3-bromophenyl)-2-methyl-1*H*-pyrrol-3-yl) ethanone (5g).**



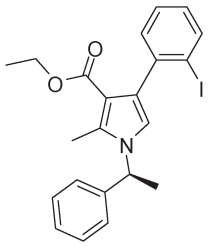

Off-white solid (312 mg, 0.85 mmol, 85%); mp 105–107 °C; IR (neat) 3397, 2941, 2400, 1949, 1806, 1653, 1559, 1420, 1215, 1180, 1071, 755 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.06 (s, 3H), 2.42 (s, 3H), 5.05 (s, 2H), 6.54 (s, 1H), 7.08 (d, $J$ = 6.8 Hz, 2H), 7.21–7.42 (m, 6H), 7.49 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 31.0, 50.2, 120.3, 121.8, 122.1, 124.2, 126.5, 127.8, 128.1, 129.2, 131.9, 135.3, 136.2, 138.3, 196.9; HRMS: *m/z* calcd for $C_{20}H_{18}BrNO$ (M + 1) 368.0572; found 368.0638.

**1-(1-Benzyl-4-(4-bromophenyl)-2-methyl-1*H*-pyrrol-3-yl) ethanone (5h).**



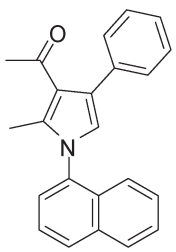

Dark brown sticky liquid (293 mg, 0.80 mmol, 80%); mp 115–117 °C; IR (neat) 3399, 3031, 2923, 1646, 1555, 1454, 1377, 1279, 1010, 701 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.05 (s, 3H), 2.42 (s, 3H), 5.05 (s, 2H), 6.52 (s, 1H), 7.08 (d, $J$ = 6.8 Hz, 2H), 7.20–7.28 (m, 2H), 7.29–7.41 (m, 4H), 7.48 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 31.0, 50.3, 120.0, 121.9, 124.5, 126.6, 127.3, 128.8, 129.0, 130.8, 131.2, 132.2, 134.1, 135.2, 136.3, 197.1; HRMS: *m/z* calcd for $C_{20}H_{18}BrNO$ (M + 1) 368.0572; found 368.0626.

**Ethyl-4-(2-iodophenyl)-2-methyl-1-((*S*)-1-phenylethyl)-1*H*-pyrrole-3-carboxylate (5i).**



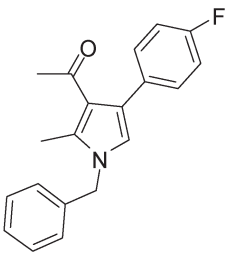

Pale yellow colour solid (321 mg, 0.70 mmol, 70%); mp 77–80 °C; IR (neat) 3436, 3045, 2977, 1686, 1531, 1409, 1283, 1155, 1090, 1016, 637 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.94 (t, $J$ = 7.2 Hz, 3H), 1.83 (d, $J$ = 7.2 Hz, 3H), 2.46 (s, 3H), 4.03 (q, $J$ = 7.2 Hz, 2H), 5.41 (q, $J$ = 7.2 Hz, 1H), 6.67 (s, 1H), 6.93–6.97 (m, 1H), 7.09 (d, $J$ = 6.8 Hz, 2H), 7.23–7.34 (m, 5H), 7.87 (d, $J$ = 7.6 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.2, 13.6, 22.2, 55.0, 59.0, 102.5, 111.7, 116.8, 125.6, 127.1, 128.7, 130.5, 135.8, 138.1, 142.2, 165.4; HRMS: *m/z* calcd for $C_{22}H_{22}INO_2$ (M + 1) 460.0695; found 460.0794.

**1-(2-Methyl-1-(naphthalen-1-yl)-4-phenyl-1*H*-pyrrol-3-yl)ethanone (5j).**



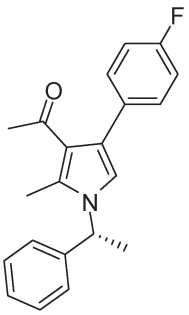

Dark brown sticky liquid (195 mg, 0.60 mmol, 60%); IR (neat) 3584, 3352, 3051, 2933, 1922, 1601, 1573, 1514, 1434, 1313, 1281 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.87 (s, 3H), 2.17 (s, 3H), 6.76 (s, 1H), 7.24–7.32 (m, 5H), 7.42–7.55 (m, 3H), 7.75–7.88 (m, 3H), 8.02–8.03 (m, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 19.4, 29.0, 97.4, 109.5, 118.8, 120.7, 122.6, 123.3, 124.7, 126.2, 128.1, 129.8, 134.1, 142.0, 196.3; HRMS: *m/z* calcd for $C_{23}H_{19}NO$ (M + 1) 326.1467; found 326.1547.

**1-(1-Benzyl-4-(4-fluorophenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (5k).**



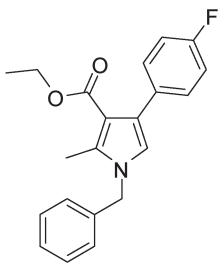
Dark brown sticky liquid (245 mg, 0.80 mmol, 80%); IR (neat) 3684, 3019, 2927, 2400, 1645, 1557, 1511, 1281, 1215, 1016, 835 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.02 (s, 3H), 2.43 (s, 3H), 5.05 (s, 2H), 6.50 (s, 1H), 7.02–7.09 (m, 3H), 7.21–7.38 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 30.9, 50.2, 114.8, 115.0, 120.0, 121.9, 124.6, 126.5, 127.2, 128.1, 129.4, 130.7, 132.2, 135.0, 136.4, 163.0, 197.1; HRMS: *m/z* calcd for $C_{20}H_{18}FNO$ (M + 1) 308.1372; found 308.1443.

**1-(4-(4-Fluorophenyl)-2-methyl-1-((*R*)-1-phenylethyl)-1*H*-pyrrol-3-yl)ethanone (5l).**



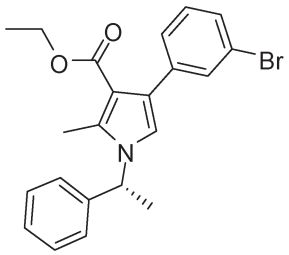

Brown colour solid (240 mg, 0.75 mmol, 75%); mp 131-133 °C; IR (neat) 3430, 3019, 2400, 1645, 1510, 1420, 1215, 1016, 756, 669 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.83 (d, $J$ = 6.8 Hz, 3H), 2.01 (s, 3H), 2.40 (s, 3H), 5.40 (q, $J$ = 6.8 Hz, 1H), 6.64 (s, 1H), 7.02–7.10 (m, 4H), 7.22–7.37 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.4, 22.0, 31.0, 54.8, 114.9, 115.1, 116.5, 121.9, 124.5, 125.4, 127.1, 128.8, 130.7, 132.5, 135.1, 141.7, 162.6, 197.4; HRMS: *m/z* calcd for $C_{21}H_{20}FNO$ (M + 1) 322.1529; found 322.1594.

**Ethyl-1-benzyl-4-(4-fluorophenyl)-2-methyl-1*H*-pyrrole-3-carboxylate (5m).**



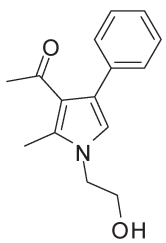

Brown sticky liquid (259 mg, 0.77 mmol, 77%); IR (neat) 3681, 3018, 2937, 1951, 1887, 1686, 1605, 1528, 1424, 1284, 1065, 756, 668 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.13 (t, $J$ = 6.8 Hz, 3H), 2.46 (s, 3H), 4.17 (q, $J$ = 6.8 Hz, 2H), 5.05 (s, 2H), 6.54 (s, 1H), 6.99–7.07 (m, 3H), 7.25–7.35 (m, 6H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.1, 14.0, 50.4, 59.3, 110.9, 114.0, 120.2, 125.1, 126.0, 127.4, 128.8, 129.2, 130.6, 131.7, 136.4, 162.0, 165.6; HRMS: *m/z* calcd for $C_{21}H_{20}FNO_2$ (M + 1) 338.1478; found 338.1541.

**Ethyl-4-(3-bromophenyl)-2-methyl-1-((*R*)-1-phenylethyl)-1*H*-pyrrole-3-carboxylate (5n).**



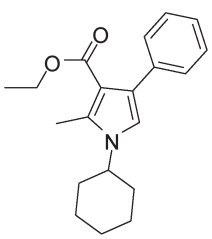

Off-White solid (283 mg, 0.69 mmol, 69%); mp 103–105 °C; IR (neat) 3677, 3019, 2984, 1686, 1605, 1527, 1425, 1302, 1260, 1215, 1027, 668 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.15 (t, $J$ = 6.8 Hz, 3H), 1.83 (d, $J$ = 7.2 Hz, 3H), 2.45 (s, 3H), 4.17 (q, $J$ = 7.2 Hz, 2H), 5.37 (q, $J$ = 6.8 Hz, 1H), 6.71 (s, 1H), 6.96 (d, $J$ = 7.2 Hz, 2H), 7.07 (d, $J$ = 7.2 Hz, 2H), 7.17–7.37 (m, 4H), 7.60 (d, $J$ = 8.8 Hz, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.3, 13.9, 22.0, 55.0, 59.4, 110.7, 114.6, 117.0, 121.3, 124.3, 125.3, 127.0, 128.8, 132.1, 133.9, 136.8, 138.2, 141.8, 165.6; HRMS: *m/z* calcd for $C_{22}H_{22}BrNO_2$ (M + 1) 412.0834; found 412.0915.

**1-(1-(2-Hydroxyethyl)-2-methyl-4-phenyl-1*H*-pyrrol-3-yl)ethanone (5o).**




Dark brown sticky liquid (170 mg, 0.70 mmol, 70%); IR (neat) 3390, 2924, 1702, 1632, 1551, 1413, 1282, 1070 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.01 (s, 3H), 2.49 (s, 3H), 3.90 (t, $J$ = 5.2 Hz, 2H), 4.01 (t, $J$ = 5.2 Hz, 2H), 6.57 (s, 1H), 7.26–7.48 (m, 5H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 30.8, 48.4, 61.6, 120.6, 121.5, 126.5, 128.2, 129.1, 133.0, 135.2, 136.0, 198.0; HRMS: *m/z* calcd for $C_{15}H_{17}NO_2$ (M + 1) 244.1259; found 244.1333.

**Ethyl-1-cyclohexyl-2-methyl-4-phenyl-1*H*-pyrrole-3-carboxylate (5p).**




Dark brown sticky liquid (202 mg, 0.65 mmol, 65%); IR (neat) 3018, 2983, 2858, 1889, 1687, 1603, 1557, 1449, 1379, 1278, 1215, 1068 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.08 (t, $J$ = 7.2 Hz, 3H), 1.19–1.48 (m, 4H), 1.56–1.70 (m, 2H), 1.74–1.77 (m, 2H), 1.89–2.01 (m, 2H), 2.54 (s, 3H), 3.91 (m, 1H), 4.16 (q, $J$ = 7.2 Hz,

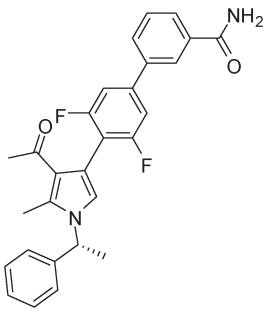
 

2H), 6.62 (s, 1H), 7.20–7.39 (m, 5H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 11.0, 13.9, 25.2, 33.8, 55.1, 59.1, 109.9, 115.8, 125.7, 127.3, 128.9, 135.2, 136.2, 166.0; HRMS: *m/z* calcd for $C_{20}H_{25}NO_2$ (M + 1) 312.1885; found 312.1951.

**General method for the synthesis of 4-biaryl substituted pyrroles (6)**

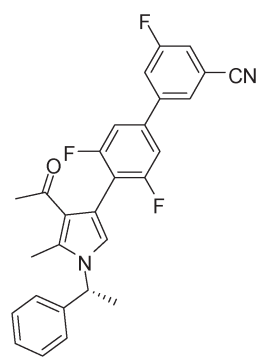
To a stirring solution of compound **5** (1.0 mmol) in 1,4-dioxane (4.0 mL) and water (1.0 mL) was added arylboronic acid (1.5 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (0.10 mmol), $PPh_3$ (0.10 mmol) and $K_2CO_3$ (2.0 mmol) with stirring. The mixture was then stirred at 90–95 °C under nitrogen for the time indicated in Table 3. After completion of the reaction the mixture was cooled to room temp, diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The organic layers were collected, combined, washed with brine (5 mL), dried over $Na_2SO_4$, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel using 1 : 9–3 : 7 ethyl acetate–petroleum ether to afford the desired compound.

**(*R*)-4′-(4-Acetyl-5-methyl-1-(1-phenylethyl)-1*H*-pyrrol-3-yl)-3′,5′-difluoro-[1,1′-biphenyl]-3-carboxamide (6a).**



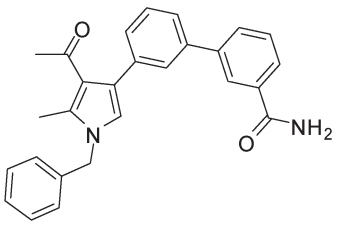

Brown sticky liquid (383 mg, 0.75 mmol, 75%); IR (neat) 3467, 3177, 3017, 2929, 1670, 1604, 1517, 1483, 1267, 1215, 1071, 855, 667 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.85 (d, *J* = 6.8 Hz, 3H), 2.14 (s, 3H), 2.44 (s, 3H), 5.41 (q, *J* = 6.8 Hz, 1H), 6.84 (s, 1H), 7.10 (d, *J* = 7.6 Hz, 2H), 7.22–7.32 (m, 4H), 7.34–7.36 (m, 1H), 7.44–7.51 (m, 1H), 7.52–7.57 (m, 1H), 7.64–7.75 (m, 2H), 7.82 (d, *J* = 4.8 Hz, 1H), 8.10 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 11.7, 22.1, 29.6, 55.1, 109.7, 112.8, 114.4, 118.7, 119.3, 122.3, 125.6, 126.1, 128.8, 129.1, 131.6, 132.0, 134.2, 135.4, 138.8, 140.8, 141.7, 161.7, 169.1, 196.2; HRMS: *m/z* calcd for $C_{28}H_{24}F_2N_2O_2$ (M + 1) 459.1806; found 459.1877.

**(*R*)-4′-(4-Acetyl-5-methyl-1-(1-phenylethyl)-1*H*-pyrrol-3-yl)-3′,5,5′-trifluoro-[1,1′-biphenyl]-3-carbonitrile (6b).**



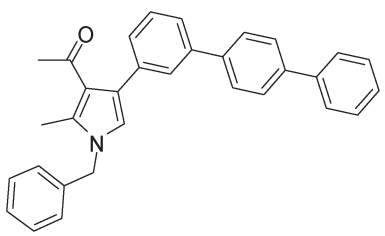

Light brown solid (362 mg, 0.79 mmol, 79%); mp 66–68 °C; IR (neat) 3683, 3019, 2926, 2229, 1951, 1737, 1652, 1569, 1409, 1354, 1271, 1029, 865, 668 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 1.86 (d, *J* = 6.8 Hz, 3H), 2.16 (s, 3H), 2.44 (s, 3H), 5.43 (q, *J* = 6.8 Hz, 1H), 6.85 (s, 1H), 7.09 (d, *J* = 7.6 Hz, 2H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.26–7.39 (m, 4H), 7.54 (d, *J* = 6.0 Hz, 1H), 7.68 (s, 1H) ; $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 11.7, 22.2, 29.7, 55.2, 108.9, 109.8, 110.1, 114.5, 117.2, 118.6, 122.4, 125.7, 126.4, 127.7, 128.9, 135.4, 137.9, 141.7, 142.5, 159.6, 161.3, 162.0, 163.8, 195.7; HRMS: *m/z* calcd for $C_{28}H_{21}F_3N_2O$ (M + 1) 459.1606; found 459.1684.

**3′-(4-Acetyl-1-benzyl-5-methyl-1*H*-pyrrol-3-yl)-[1,1′-biphenyl]-3-carboxamide (6c).**



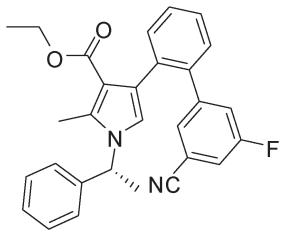

Dark brown sticky liquid (314 mg, 0.77 mmol, 77%); IR (neat) 3686, 3019, 2400, 1625, 1523, 1423, 1215, 1016, 669 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.09 (s, 3H), 2.45 (s, 3H), 5.08 (s, 2H), 6.60 (s, 1H), 7.11 (d, *J* = 7.6 Hz, 2H), 7.24–7.39 (m, 6H), 7.44–7.62 (m, 5H), 7.83 (d, *J* = 7.6 Hz, 1H), 7.88 (s, 1H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 11.6, 31.9, 50.3, 112.9, 118.7, 120.3, 122.0, 125.2, 126.6, 127.8, 128.9, 129.3, 130.6, 131.4, 135.4, 136.4, 137.2, 138.8, 142.2, 163.8, 197.1; HRMS: *m/z* calcd for $C_{27}H_{24}N_2O_2$ (M + 1) 409.1838; found 409.1920.

**1-(4-([1,1′:4′,1′′-Terphenyl]-3-yl)-1-benzyl-2-methyl-1*H*-pyrrol-3-yl)ethanone (6d).**



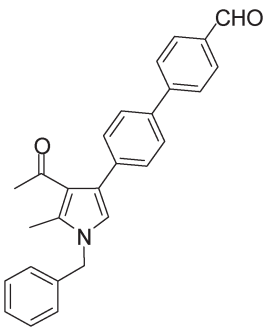

Off-White solid (331 mg, 0.75 mmol, 75%); mp 135–136 °C; IR (neat) 3018, 2938, 2401, 1688, 1605, 1527, 1424, 1384, 1284, 1216, 1029 cm$^{-1}$; $^1$H NMR ($CDCl_3$, 400 MHz) $\delta$ 2.11 (s, 3H), 2.45 (s, 3H), 5.07 (s, 2H), 6.60 (s, 1H), 7.11 (d, *J* = 6.8 Hz, 2H), 7.25–7.37 (m, 5H), 7.42–7.56 (m, 3H), 7.58–7.70 (m, 8H); $^{13}$C NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 31.1, 50.3, 120.2, 122.0, 125.3, 126.6, 127.0, 128.3, 135.2, 136.4, 139.7, 140.1, 197.4; HRMS: *m/z* calcd for $C_{32}H_{27}NO$ (M + 1) 442.2093; found 442.2185.

**(*R*)-Ethyl-4-(3′-cyano-5′-fluoro-[1,1′-biphenyl]-2-yl)-2-methyl-1-(1-phenylethyl)-1*H*-pyrrole-3-carboxylate (6e).**




Pale yellow viscous liquid (343 mg, 0.76 mmol, 76%); IR (neat) 3310, 3070, 2937, 2233, 1694, 1606, 1591, 1417, 1329, 1259, 1152, 860, 691 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.02 (t, $J$ = 7.2 Hz, 3H), 1.73 (d, $J$ = 6.8 Hz, 3H), 2.36 (s, 3H), 3.99 (q, $J$ = 7.2 Hz, 2H), 5.32 (q, $J$ = 6.8 Hz, 1H), 6.40 (s, 1H), 6.91 (d, $J$ = 7.6 Hz, 2H), 7.17–7.20 (m, 2H), 7.26–7.37 (m, 8H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.3, 12.9, 14.0, 29.6, 54.8, 59.4, 110.8, 115.2, 116.4, 117.6, 121.4, 123.8, 125.4, 127.2, 128.0, 129.2, 131.5, 136.1, 141.7, 163.7, 165.6; HRMS: *m*/*z* calcd for $C_{29}H_{25}FN_2O_2$ (M + 1) 453.1900; found 453.1981.

**4′-(4-Acetyl-1-benzyl-5-methyl-1*H*-pyrrol-3-yl)-[1,1′-biphenyl]-4-carbaldehyde (6f).**

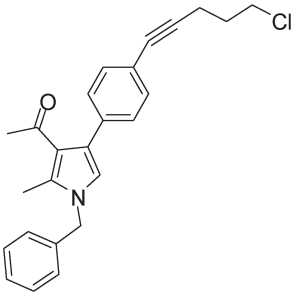



White solid (330 mg, 0.84 mmol, 84%), mp 119–120 °C; IR (neat) 3584, 3368, 2710, 2400, 1603, 1424, 1217, 1021 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 2.12 (s, 3H), 2.45 (s, 3H), 5.08 (s, 2H), 6.60 (s, 1H), 7.11 (d, $J$ = 7.2 Hz, 2H), 7.26–7.45 (m, 5H), 7.66 (d, $J$ = 8.0 Hz, 2H), 7.80 (d, $J$ = 7.6 Hz, 2H), 7.97 (d, $J$ = 8.4 Hz, 2H), 10.06 (s, 1H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 31.1, 50.3, 55.3, 120.3, 122.0, 125.0, 126.6, 127.1, 128.9, 130.2, 136.3, 137.7, 146.6, 191.8, 197.3 ; HRMS: *m*/*z* calcd for $C_{27}H_{23}NO_2$ (M + 1) 394.1729; found 394.1803.

**General method for the synthesis of alkynyliaryl substituted pyrroles (7)**

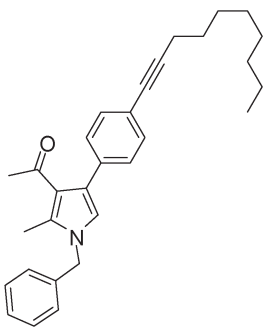
To a stirring solution of aryl halide (1.0 mmol), DMF (6.0 mL), was added a terminal alkyne (1.5 mmol), CuI (0.1 mmol), $PdCl_2$ (dppf)·$CH_2Cl_2$ (0.1 mmol), $PPh_3$ (0.1 mmol) and $Et_3N$ (3.0 mmol) with stirring. The mixture was then stirred at 90–95 °C under nitrogen for the time indicated in Table 4. After completion of the reaction the mixture was cooled to room temp, diluted with water (5 mL) and extracted with ethyl acetate (3 × 5 mL). The organic layers were collected, combined, washed with brine (5 mL), dried over $Na_2SO_4$, filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel using 1 : 9–2 : 8 ethyl acetate–petroleum ether to afford the desired compound.

**1-(1-Benzyl-4-(4-(5-chloropent-1-yn-1-yl)phenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (7a).**



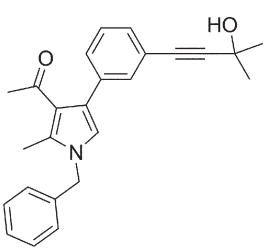

Pale yellow colour solid (311 mg, 0.80 mmol, 80%); mp 152–153 °C; IR (neat) 3443, 2962, 2236, 1915, 1648, 1513, 1421, 1261, 1095, 802 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 500 MHz) $\delta$ 2.04 (s, 3H), 2.08 (t, $J$ = 7.0 Hz, 2H), 2.42 (s, 3H), 2.63 (t, $J$ = 7.0 Hz, 2H), 3.74 (t, $J$ = 6.5 Hz, 2H), 5.05 (s, 2H), 6.54 (s, 1H), 7.09 (d, $J$ = 7.0 Hz, 2H), 7.24–7.39 (m, 7H) ; $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.5, 16.9, 20.8, 29.7, 31.1, 43.7, 50.3, 80.3, 88.3, 120.1, 122.0, 125.2, 126.6, 127.8, 128.9, 129.0, 131.4, 135.8, 136.4, 197.4; HRMS: *m*/*z* calcd for $C_{25}H_{24}ClNO$ (M + 1) 390.1546; found 390.1629.

**1-(1-Benzyl-4-(4-(dec-1-yn-1-yl)phenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (7b).**




Brown colour liquid (344 mg, 0.81 mmol, 81%); IR (neat) 3283, 3011, 2928, 2232, 1949, 1648, 1510, 1419, 1378, 1216, 1029 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.89 (t, $J$ = 6.8 Hz, 3H), 1.21–1.39 (m, 4H), 1.43–1.47 (m, 2H), 1.57–1.64 (m, 6H), 2.04 (s, 3H), 2.39–2.43 (m, 5H), 5.05 (s, 2H), 6.53 (s, 1H), 7.09 (d, $J$ = 6.8 Hz, 2H), 7.22–7.39 (m, 7H) ; $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.3, 13.9, 19.3, 22.5, 28.6, 29.0, 30.9, 31.7, 50.1, 80.3, 90.7, 120.0, 121.8, 122.2, 125.2, 126.5, 127.7, 128.8, 131.2, 135.1, 136.3, 197.4; HRMS: *m*/*z* calcd for $C_{30}H_{35}NO$ (M + 1) 426.2719; found 426.2790.

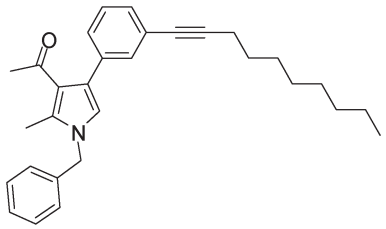
**1-(1-Benzyl-4-(3-(3-hydroxy-3-methylbut-1-yn-1-yl)phenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (7c).**



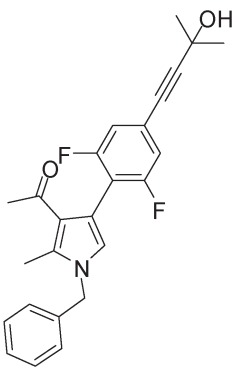
Brown colour liquid (308 mg, 0.83 mmol, 83%); IR (neat) 3670, 3394, 3011, 2228, 1950, 1647, 1509, 1420, 1216, 1133, 1029, $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.61 (s, 6H), 2.04 (s, 3H), 2.43 (s, 3H), 5.05 (s, 2H), 6.53 (s, 1H), 7.08 (d, $J$ = 6.8 Hz, 2H), 7.24–7.40 (m, 7H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 11.5, 31.0, 50.2, 65.5, 81.9, 93.9, 120.2, 121.9, 122.6, 124.9, 126.5, 127.8, 128.0, 129.3, 132.2, 135.2, 136.4, 197.3; HRMS: $m/z$ calcd for $C_{25}H_{25}NO_2$ (M + 1) 372.1885; found 372.1955.

**1-(1-Benzyl-4-(3-(dec-1-yn-1-yl)phenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (7d).**



Brown colour liquid (337 mg, 0.79 mmol, 79%); IR (neat) 3678, 3015, 2928, 2226, 1949, 1648, 1599, 1420, 1216, 1078 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 0.89 (t, $J$ = 6.8 Hz, 3H), 1.25–1.31 (m, 8H), 1.44–1.58 (m, 2H), 1.59–1.61 (m, 2H), 2.04 (s, 3H), 2.41 (t, $J$ = 7.2 Hz, 2H), 2.42 (s, 3H), 5.05 (s, 2H), 6.53 (s, 1H), 7.07 (d, $J$ = 6.8 Hz, 2H), 7.20–7.38 (m, 7H); $^{13}C$ NMR ($CDCl_3$, 50 MHz) $\delta$ 11.5, 14.1, 19.4, 22.6, 28.7, 29.1, 31.1, 50.2, 80.3, 90.6, 120.1, 121.9, 124.0, 125.1, 127.8, 129.7, 132.2, 135.1, 136.3, 197.3; HRMS: $m/z$ calcd for $C_{30}H_{35}NO$ (M + 1) 426.2719; found 426.2817.

**1-(1-Benzyl-4-(2,6-difluoro-4-(3-hydroxy-3-methylbut-1-yn-1-yl)phenyl)-2-methyl-1*H*-pyrrol-3-yl)ethanone (7e).**



Brown colour solid (317 mg, 0.78 mmol, 78%); mp 79–81 °C; IR (neat) 3672, 3364, 3014, 2926, 2227, 1912, 1643, 1561, 1455, 1377, 1216, 860 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) $\delta$ 1.53 (s, 3H), 1.61 (s, 3H), 2.08 (s, 3H), 2.45 (s, 3H), 5.08 (s, 2H), 6.65 (s, 1H), 7.01 (d, $J$ = 7.6 Hz, 2H), 7.08 (d, $J$ = 6.8 Hz, 2H), 7.26–7.37 (m, 3H); $^{13}C$ NMR ($CDCl_3$, 100 MHz) $\delta$ 11.7, 29.6, 30.9, 31.2, 50.4, 65.4, 83.9, 95.8, 109.3, 114.1, 122.2, 123.2, 126.5, 127.8, 128.9, 135.7, 136.2, 161.0, 195.8; HRMS: $m/z$ calcd for $C_{25}H_{23}F_2NO_2$ (M + 1) 408.1697; found 408.1774.

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