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Base-mediated isocyanide-based three-component reactions: divergent synthesis of spiro-substituted furans and pyrroles

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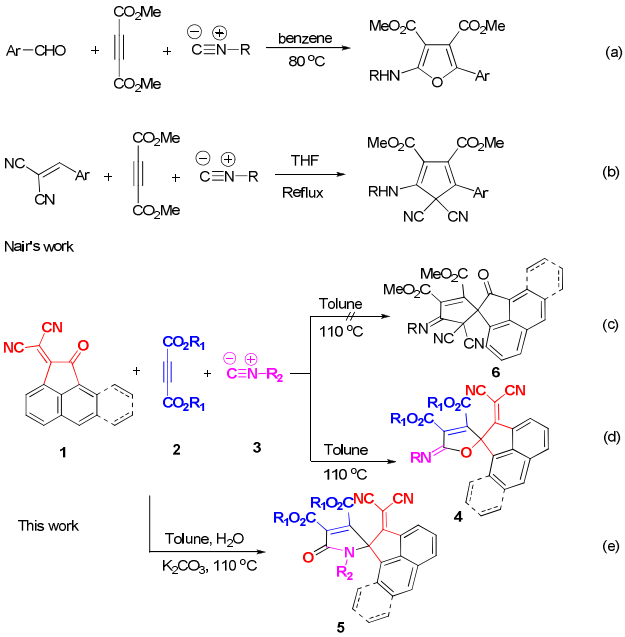
A facile base-mediated isocyanide-based three-component cycloaddition protocol for chemoselective formation of functionalized spiro-substituted furans and pyrroles derivatives has been developed. Fairly good yields of the products, the ready availability of the starting materials and the excellent chemoselectivity are the main advantages of this method.

Introduction

Isocyanide-based multicomponent reactions[1] (IMCRs) with efficient construction of complex molecules from the diversity of bond-forming processes available, inherent atom economy, and excellent selectivity (such as chemo-, regio-, and stereo-selectivity) become one of the most powerful and significant tools in modern synthetic chemistry.[2] These reactions can provide an attractive pathway toward the generation of structurally diverse molecules, especially unusual fused heterocyclic scaffolds.[3]

Spiroheterocyclic structures are common scaffolds of many natural products due to their significant biological activities,[4] including oxindole alkaloids,[5] shellfish toxins,[6] and marine macrolides.[7] Therefore, the synthesis of spirocyclic compounds has received continual attention from organic and medicinal chemists.[8] Among various efficient synthetic methodology, 1,3-dipolar cycloaddition reaction is one of the most efficient approaches for the synthesis of important spiroheterocyclic compounds.[9] The zwitterionic intermediates might undergo cycloaddition to activated acetylenes from nucleophiles, leading to a variety of novel highly substituted cyclopentadienoid systems.[10] For instance, Nair et al successfully developed a 1,3-dipolar cycloaddition in trapping the zwitterionic intermediates, derived from isocyanide and dimethyl acetylenedicarboxylates (DMAD), with dipolarophiles such as aryl aldehydes and activated styrenes leading to a facile synthesis of furan, pyrrole and cyclopentadienes derivatives (Schemes 1a and 1b).[11] To the best of our knowledge, the utilization of the zwitterion derived from isocyanide and dialkyl acetylenedicarboxylates to build important spiroheterocyclic compounds was seldom investigated. There is only limited number of studies on related spirocyclic system.[12]



Scheme 1. Three-component chemoselective synthesis of spiro-substituted furans **4** and pyrroles **5**.

As a consequence of our interest in 1,3-dipolar cycloaddition reactions, we decided to explore the feasibility of cycloaddition reactions between activated acrylonitrile and the zwitterion derived from isocyanide and DMAD, furnishing substituted spirocyclic compounds **6** *via* a three-component reaction. Interestingly, instead of the expected products **6** (Scheme 1c), the reaction underwent another direction to give access to functionalized spiro-substituted furans **4** and pyrroles **5** with good yields through isocyanide-based multicomponent reactions (Schemes 1d and 1e). Further investigations revealed that spiro-substituted furans **4** could be directly converted into spiro-substituted pyrroles **5** by Mumm rearrangement under suitable base conditions. Herein, we would like to elaborate these interesting transformations.

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Results and discussion

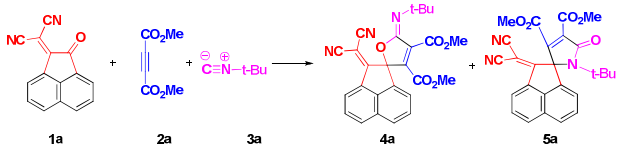
Initially, when a solution of equimolar amounts of 2-(2-oxoacenaphthylen-1(*2H*)-ylidene)malononitrile (**1a**), dimethyl acetylenedicarboxylate (**2a**), and *tert*-butyl isocyanide (**3a**) in toluene was stirred at 50 °C for 24 h, two identifiable products **4a** and **5a** were isolated with poor chemoselectivity (Table 1, entry 1). Subsequently, a series of other solvent (THF, CH_3CN, 1,4-dioxane, CH_3OH and $CHCl_3$) were screened and a range of different temperatures were examined to improve the yields. The result showed that toluene is the best solvent (Table 1, entries 1-11). Surprisingly, when using anhydrous toluene as a solvent and increasing the reaction temperature from 90 to 110 °C, the desired spirofuran product **4a** was obtained in 88% isolated yield without product **5a** (Table 1, entries 8-9).

Next, we set out to optimize the reaction conditions for the chemoselective synthesis of the spiropyrrol products **5a**. The organic or inorganic bases, including NEt_3, DMAP, pyridine, Quinoline, $KHCO_3$, K_2HPO_4, KOH and K_2CO_3 were screened in co-solvent of toluene and water at 110 °C for 24 h and the influence of volume ratio of toluene and water on the reaction was also investigated (Table 1, entries 12−19). Interestingly, when we treated 2-(2-oxoacenaphthylen-1(*2H*)-ylidene)malononitrile (**1a,** 1.0 equiv.), dimethyl acetylenedicarboxylate (**2a,** 1.0 equiv.), *tert*-butyl isocyanide (**3a,** 1.0 equiv.) and K_2CO_3 (0.5 equiv.) as the base in toluene and water (V_t/V_w = 100:1) at 110 °C for 24 h. A significant improvement in 80% isolated yield of the product **5a** was observed (Table 1, entry 19).

With the optimized reaction conditions in hand, we investigated the substrate scope of these transformations, the cyclohexyl- and benzyl- isocyanides (**3b, 3c**) were also utilized. As expected, the two isocyanides were efficiently converted into the corresponding products **4** and **5** in good yields under controlled conditions (Table 2, entry 4a-4f, entry 5a-5f). Furthermore, ethyl 2-(2-oxoaceanthrylen-1(2H)-ylidene)malononitrile (**1b**) and ethyl 2-(10-oxophenanthren-9(10H)-ylidene)malononitrile (**1c**) were also investigated as reaction partners for this reaction. Similarly, 2-(2-oxoaceanthrylen-1(2H)-ylidene)malononitrile (**1b**) showed high reactivity and efficiently afforded the corresponding products **4** and **5** in good yields under controlled conditions (Table 2, entry 4g-4l, entry 5g-5l). However, substrate **1c** only afforded spiropyrrole derivatives **5m-5o** (Table 2, entry 5m-5o,). The spiro-substituted furans were quickly transformed into spiro-substituted pyrroles in reaction process according to the TLC detection.

The structures of compounds **4** and **5** were deduced from their IR, ^{1}H NMR, ^{13}C NMR, and high-resolution mass spectrometry (HRMS) spectra. For example, ^{1}H NMR spectrum of **4a** exhibited three singlets due to the two MeO (3.99 and 3.52 ppm) and t-butyl (1.33 ppm) groups. The ^{1}H decoupled ^{13}C NMR spectrum of **4a** showed 23 distinct resonances that confirm the proposed structure.

Table 1 Optimization of the reaction conditions for the synthesis **4a** and **5a.**



Entry	Cat. (equiv)	Solvent	T (°C)	Yield (%)[a]	
				4a	**5a**
1	-	Toluene	50	45	5
2	-	THF	50	40	trace
3	-	CH_3CN	50	35	trace
4	-	1,4-dioxane	50	40	trace
5	-	CH_3OH	50	0	0
6	-	$CHCl_3$	50	20	trace
7	-	Toluene	70	64	8
8	-	Toluene[b]	90	73	0
9	-	Toluene[b]	110	88	0
10	-	Co-solvent[c]	110	70	5
11	-	Co-solvent[d]	110	74	7
12	NEt_3 (0.5)	Co-solvent[d]	110	67	12
13	DMAP (0.5)	Co-solvent[d]	110	72	14
14	Pyridine (0.5)	Co-solvent[d]	110	65	20
15	Quinoline (0.5)	Co-solvent[d]	110	61	18
16	$KHCO_3$ (0.5)	Co-solvent[d]	110	40	45
17	K_2HPO_4 (0.5)	Co-solvent[d]	110	47	40
18	KOH (0.5)	Co-solvent[d]	110	0	62
19	K_2CO_3 (0.5)	Co-solvent[d]	110	0	80
20	K_2CO_3 (0.2)	Co-solvent[d]	110	0	70
21	K_2CO_3 (1.0)	Co-solvent[d]	110	0	78
22	K_2CO_3 (0.5)	Toluene[b]	110	0	69

[a]Isolated yield. [b]Anhydrous toluene. [c]Co-solvent of toluene and H_2O (V_t:V_w=50:1). [d]Co-solvent of toluene and H_2O (V_t:V_w=100:1)

The HRMS spectrum of **4a** displayed the molecular ion peak at m/z = 454, which is consistent with the proposed 1:1:1 adduct of *t*-butyl isocyanide, dimethyl acetylenedicarboxylate, and 2-(2-oxoacenaphthylen-1(*2H*)-ylidene)malononitrile. The IR spectrum of **4a** showed strong absorptions at 2230 and 1736 cm^{-1} due to the cyan and ester carbonyls.

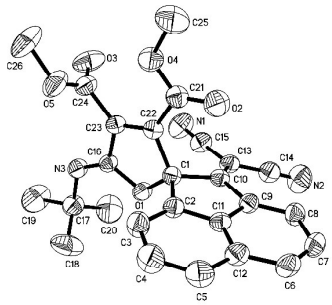
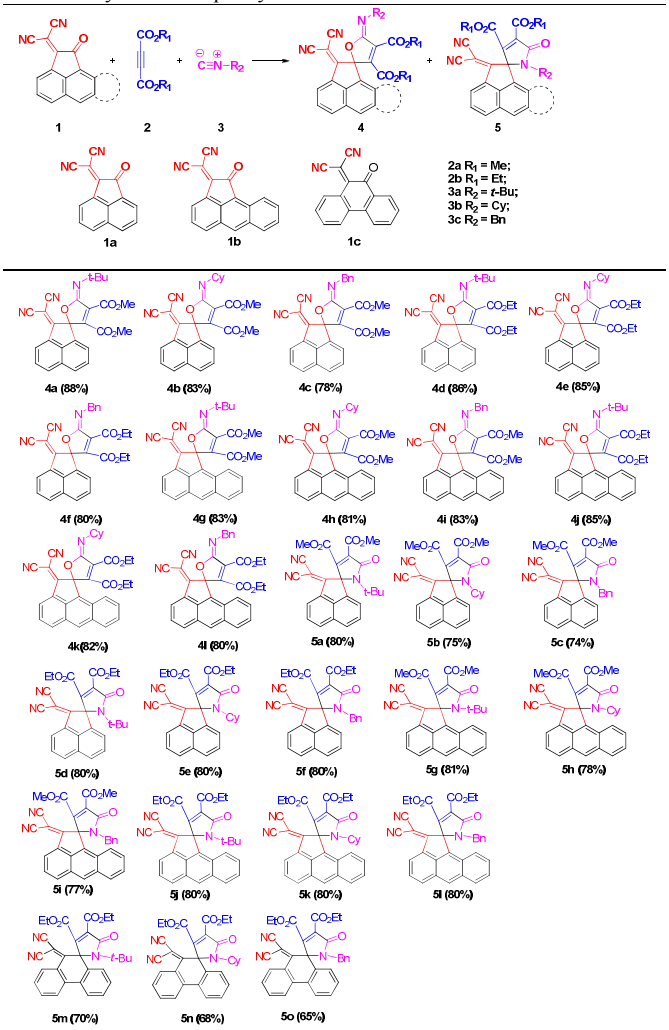


Fig. 1 ORTEP diagram of **4a**, displacement ellipsoids are shown with 40% probability.

Unambiguous evidence for the structure of **4a** and **5g** was obtained from single-crystal X-ray analysis. The ORTEP

diagram of the two compounds **4a** and **5g** were shown in Figure 1-2, respectively.

Table 2 Synthesis of spirocyclic derivatives **4**[a, c] and **5**[b, c].



[a] The reaction was performed with **1** (1.0 equiv), dialkyl acetylenedicarboxylate (**2**, 1.0 equiv) and isocyanide (**3**, 1.0 equiv) in anhydrous toluene. [b] The reaction was performed with **1** (1.0 equiv), dialkyl acetylenedicarboxylate (**2**, 1.0 equiv), isocyanide (**3**, 1.0 equiv) and K_2CO_3 (0.5 equiv) in toluene and water (V_t/V_w = 100:1). [c] Isolated yield.

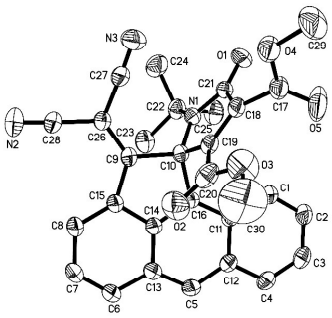
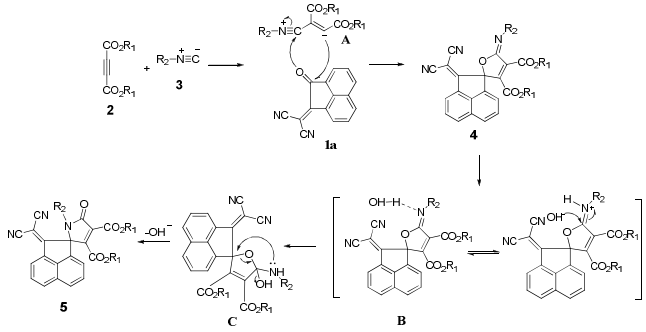


Fig. 2 ORTEP diagram of **5g**, displacement ellipsoids are shown with 40% probability.

Based on the experimental results and literature reports,[11c,13] a possible mechanism for the reaction is proposed in Scheme 2. The initial event is formation of the zwitterion **A** from the isocyanide **3** and dialkyl acetylenedicarboxylate **2**, which reacts with the carbon-oxygen double bond of 2-(2-oxoacenaphthylen-1(*2H*)-ylidene)malononitrile **1a** to yield spiro-substitute furan **4**. Subsequently, in the presence of H_2O and K_2CO_3, prodcut **4** undergoes a Mumm rearrangement to yield spiro-substitute pyrrol **5**. To verify the mechanism of the formation of **5**, the isolate compound **4c** was stirred in a mixture of toluene and water (Tolune:H_2O=100:1) or anhydrous toluene and in the presence of K_2CO_3 at 110 °C for 24 h. As expected, the conversion of spiro-furans **4c** to spiropyrrol **5c** under base-mediated conditions was proved.



Scheme 2 Plausible mechanistic pathway.

Among these compounds, the photophysical properties of **4a**, **4g**, **5a** and **5g** have been examined and reported as an example. The UV-vis absorption spectra of **4a**, **4g**, **5a** and **5g** are presented in Figure 3. As shown in Figure 3, The maximum UV–vis absorptions of all compounds are located in the range of 399–490 nm, which is attributed to the π-π* transition of the conjugated backbone.[14] By extended π-conjugated system in the compounds **4g**, **5g**, the absorption maxima (λmax) of the π-π* transition in MeCN solution are red shifted from 399 nm for **4a**, to 490 nm for **4g** and from 406 nm for **5a**, to 490 nm for **5g**, respectively.

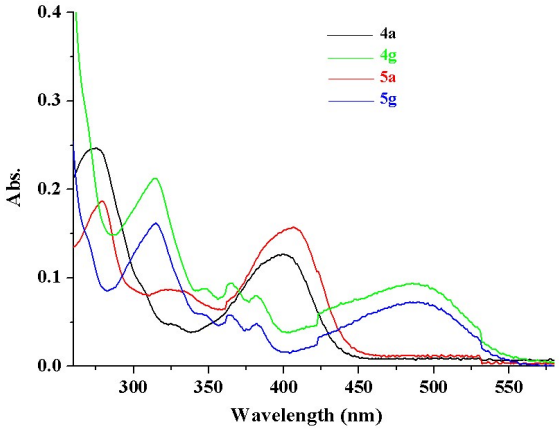


Fig. 3 Absorption spectra of **4a**, **4g**, **5a** and **5g** in MeCN (1.0×10^{-5} mol/L).

The emission spectra of **4a**, **4g**, **5a** and **5g** are depicted in Figure 4 with PL maxima at about 493, 498, 619 and 620 nm, respectively. In MeCN the **4g** and **5g** emit strong fluorescence

than **4a** and **5a** (Figure. 4). However, if water was added to MeCN, their emission intensities dramatically decrease with increasing concentrations and formation of aggregates (Figure S1 and Figure S2 in the ESI). This aggregation-caused quenching (ACQ) effect mainly results from strong intermolecular π–π stacking interactions and non-radiative decay.[15] The pH-dependent fluorescence response of **4g** and **5g** were also investigated (Figure S3 and Figure S4 in the ESI), which present slight change relative to the emission spectra of compound **4g** and **5g** in MeCN-H_2O.

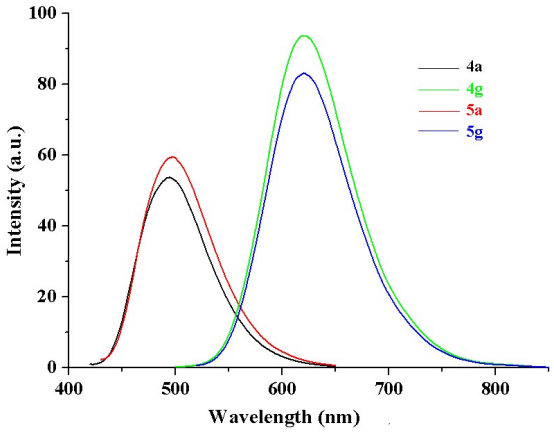


Fig. **4** Emission spectra of **4a**, **4g**, **5a** and **5g** (excited at 399, 406, 486 and 490 nm, respectively.) in MeCN (1.0×10^{-5} mol/L).

Conclusions

In summary, a facile method has been developed for chemoselective synthesis of polyfunctionalized spiroheterocyclic compounds (spirofurans and spiropyrroles) by base-mediated three-component protocol. Due to the importance of these spiroheterocyclic compounds, especially in pharmaceutical and medicinal chemistry, the present protocol can be extended for the synthesis of various biologically important spiroheterocyclic compounds.

Experimental section

General

All reagents and solvents were acquired from commercially available suppliers and used without further purification, unless specified. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer in $CDCl_3$ using TMS as the internal standard. IR spectra were recorded on a Nicollet 740 FT-IR spectrometer. HRMS were measured on an Agilent Technologies 6510, Q-TOFLC/MS ESI Technique. Melting points were determined in capillaries and are uncorrected. UV–vis spectra were recorded on a Shimadzu UV-2501PC spectrometer; fluorescence spectra were obtained on an Hitachi FL-4500 spectrofluorimeter. All reactions were monitored using thin layer chromatography (TLC) on pre-coated silica gel 60 F_{254} (mesh); spots were observed under UV light.

General procedure for the preparation of spiro-substituted furans 4

To a magnetically stirred solution of 2-(2-oxoacenaphthylen-1(*2H*)-ylidene)malononitrile (**1a**, 1 mmol) and the corresponding dialkyl acetylenedicarboxylate (**2**, 1 mmol) in anhydrous toluene (2 mL) was added dropwise a solution of corresponding isocyanide (**3**, 1 mmol) in anhydrous toluene (1 mL) at 25 °C for 5 min. The reaction mixture was then stirred at 110 °C for 24 h. The solvent was removed and the residue was purified by column chromatography using n-hexane–EtOAc (1:4) as eluent. The solvent was removed and the product was obtained.

(Z)-dimethyl 5'-(tert-butylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4a**): Mp 190-192 °C; pale yellow powder; IR(KBr): 2970, 2902, 2230, 1758, 1577, 1299, 779 cm^{-1} ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 7.4 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 8.3 Hz, 1H), 7.86-7.80 (m, 1H), 7.69 (dd, J = 8.2, 7.1 Hz, 1H), 7.46 (d, J = 7.0 Hz, 1H), 3.99 (s, 3H), 3.52 (s, 3H), 1.33 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 161.8, 159.8, 151.3, 140.0, 139.2, 138.3, 135.6, 132.7, 132.5, 130.8, 129.2, 127.2, 125.1, 120.2, 112.5, 110.4, 94.4, 79.7, 55.9, 53.5, 53.1; HRMS (ESI) calcd for $C_{26}H_{21}N_3O_5$ [M-H]$^-$ 454.1403, found 454.1397.

(Z)-dimethyl 5'-(cyclohexylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4b**): Mp 202-204 °C; pale yellow powder; IR (KBr): 2932, 2854, 2229, 1754, 1582, 1302, 780 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 7.4 Hz, 1H), 8.17 (d, J = 8.2 Hz, 1H), 7.97 (d, J = 8.2 Hz, 1H), 7.89-7.78 (m, 1H), 7.71 (dd, J = 8.2, 7.1 Hz, 1H), 7.49 (d, J = 6.9 Hz, 1H), 3.99 (s, 3H), 3.71-3.60 (m, 1H), 3.52 (s, 3H), 1.88 (d, J = 13.9 Hz, 1H), 1.79-1.68 (m, 3H), 1.60-1.41 (m, 3H), 1.32-1.17 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 161.5, 159.7, 153.5, 139.2, 139.2, 138.6, 135.5, 132.6, 132.4, 130.8, 129.2, 129.2, 127.2, 125.1, 120.5, 112.5, 110.5, 93.9, 79.9, 57.4, 53.5, 53.1, 33.3, 32.8, 25.6, 24.6; HRMS (ESI) calcd for $C_{28}H_{23}N_3O_5$[M-H]$^-$ 480.1559, found 480.1567.

(Z)-dimethyl 5'-(benzylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4c**): Mp 183-186 °C; pale yellow powder; IR (KBr): 2954, 2227, 1731, 1686, 1574, 1439, 1364, 1299, 1052, 776 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.4 Hz, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.70 (t, J = 7.7 Hz, 1H), 7.48 (dd, J = 6.8, 1.6 Hz, 1H), 7.34 (m, J = 15.0, 4.7 Hz, 4H), 7.23 (t, J = 7.1 Hz, 1H), 4.73 (d, J = 7.3 Hz, 2H), 4.01 (s, 3H), 3.54 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 161.2, 159.6, 155.9, 140.1, 139.2, 138.9, 138.0, 135.1, 132.5, 130.8, 129.3, 129.2, 128.3, 127.8, 127.4, 126.8, 125.2, 120.6, 112.4, 110.3, 94.5, 80.0, 62.9, 53.6, 53.2, 52.1, 14.2; HRMS (APCI) calcd for $C_{29}H_{19}N_3O_5$ [M+H]$^+$ 490.1403, found 490.1403.

(Z)-diethyl 5'-(tert-butylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4d**): Mp 204-206 °C; pale yellow powder; IR (KBr): 2988, 2968, 2229, 1747,

1685, 1580, 1335, 1276, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, J = 7.4 Hz, 1H), 8.16 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.82 (t, J = 7.8 Hz, 1H), 7.73-7.65 (m, 1H), 7.48 (d, J = 7.0 Hz, 1H), 4.46 (dd, J = 7.1, 5.5 Hz, 2H), 3.88 (dd, J = 7.1, 5.3 Hz, 2H), 1.41 (t, J = 7.1 Hz, 3H), 1.34 (s, 9H), 0.80 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 161.2, 159.2, 151.6, 140.1, 139.2, 138.4, 135.8, 132.8, 132.3, 130.8, 129.3, 129.1, 127.0, 124.9, 120.3, 112.6, 110.3, 94.3, 79.8, 62.6, 62.0, 55.9, 30.2, 29.5, 14.1, 13.2; HRMS (ESI) calcd for $C_{28}H_{25}N_3O_5$ $[M+Na]^+$ 506.1692, found 506.1691.

(Z)-diethyl 5'-(cyclohexylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4e**): Mp 213-215 °C; pale yellow powder; IR (KBr): 2982, 2927, 2230, 1749, 1689, 1578, 1335, 1260, 1023, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.59 (d, J = 7.4 Hz, 1H), 8.16 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.2 Hz, 1H), 7.82 (t, J = 7.8 Hz, 1H), 7.70 (t, J = 7.6 Hz, 1H), 7.50 (d, J = 6.9 Hz, 1H), 4.47 (dd, J = 6.9, 5.1 Hz, 2H), 3.88 (dd, J = 13.6, 6.8 Hz, 2H), 3.73-3.61 (m, 1H), 1.88 (d, J = 12.8 Hz, 1H), 1.73 (s, 3H), 1.52 (dd, J = 24.6, 13.5 Hz, 3H), 1.40 (t, J = 7.1 Hz, 3H), 1.26 (d, J = 21.1 Hz, 3H), 0.79 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.5, 161.0, 159.2, 153.5, 139.3, 139.2, 138.9, 135.7, 132.8, 132.3, 130.7, 129.2, 129.2, 127.1, 124.9, 120.5, 112.6, 110.4, 93.9, 79.9, 62.7, 62.0, 57.2, 33.3, 32.8, 25.7, 24.6, 14.1, 13.2; HRMS (ESI) calcd for $C_{30}H_{27}N_3O_5$ $[M+Na]^+$ 532.1848, found 532.1848.

(Z)-diethyl 5'-(benzylimino)-2-(dicyanomethylene)-2H,5'H-spiro[acenaphthylene-1,2'-furan]-3',4'-dicarboxylate (**4f**): Mp 191-194 °C; yellow powder; IR (KBr): 2987, 2950, 2223, 1735, 1686, 1570, 1440, 1367, 1230, 1045, 778 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.87-7.80 (m, 1H), 7.71 (m, 1H), 7.49 (d, J = 8.0 Hz, 1H), 7.38 (d, J = 8.0 Hz, 2H), 7.31 (m, 2H), 7.26-7.21 (m, 1H), 4.80-4.68 (m, 2H), 4.48 (m, 2H), 3.91 (m, 2H), 1.42 (t, J = 8.0 Hz, 3H), 0.82 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 160.8, 159.0, 156.0, 140.1, 139.3, 139.0, 138.3, 135.2, 132.7, 132.4, 130.8, 129.3, 129.2, 128.3, 127.7, 127.3, 126.7, 125.0, 120.7, 112.5, 110.3, 94.4, 80.0, 62.9, 62.2, 52.0, 14.1, 13.2; HRMS (ESI) calcd for $C_{31}H_{23}N_3O_5$ $[M+H]^+$ 518.1716, found 518.1713.

(Z)-dimethyl 5'-(tert-butylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4g**): Mp 190-193 °C; red powder; IR (KBr): 2961, 2904, 2228, 1758, 1732, 1571, 1429, 1279, 1029, 970 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.63 (d, J = 7.1 Hz, 1H), 8.58 (s, 1H), 8.29 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 7.79-7.80 (m, 2H), 7.72-7.64 (m, 1H), 7.61 – 7.55 (m, 1H), 4.02 (s, 3H), 3.43 (s, 3H), 1.35 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 161.8, 159.7, 151.7, 140.4, 138.5, 137.4, 134.4, 132.9, 132.6, 130.3, 128.6, 128.4, 128.0, 128.0, 127.8, 126.9, 126.3, 125.3, 122.0, 112.7, 110.5, 96.3, 79.3, 56.2, 53.4, 53.0, 29.4; HRMS (ESI) calcd for $C_{30}H_{23}N_3O_5$ $[M+Na]^+$ 528.1535, found 528.1535.

(Z)-dimethyl 5'-(cyclohexylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4h**): Mp 210-213 °C; red powder; IR (KBr): 2936, 2852, 2228, 1729, 1693, 1431, 1298, 1029, 979 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.66-8.55 (m, 2H), 8.27 (d, J = 8.5 Hz, 1H), 8.17 (d, J = 8.6 Hz, 1H), 7.78-7.79 (m, 2H), 7.69-7.64 (m, 1H), 7.62-7.56 (m, 1H), 4.02 (s, 3H), 3.76-3.68 (m, 1H), 3.43 (s, 3H), 2.00-1.88 (m, 1H), 1.81-1.65 (m, 3H), 1.53 (d, J = 14.3 Hz, 3H), 1.29-1.15 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 161.5, 159.7, 153.9, 139.5, 139.0, 137.4, 134.4, 132.9, 132.5, 130.4, 128.7, 128.2, 128.0, 127.9, 127.9, 127.0, 126.3, 125.3, 121.8, 112.7, 110.6, 95.8, 79.5, 57.6, 53.5, 53.0, 33.3, 33.0, 25.6, 24.6, 24.6; HRMS (ESI) calcd for $C_{32}H_{25}N_3O_5$ $[M+Na]^+$ 554.1692, found 554.1689.

(Z)-diethyl 5'-(tert-butylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4i**): Mp 182-185 °C; red powder; IR (KBr): 2974, 2935, 2227, 1748, 1730, 1686, 1574, 1428, 1335, 1275, 1030, 973 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.1 Hz, 1H), 8.58 (s, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 7.88-7.81 (m, 1H), 7.77 (dd, J = 8.4, 7.3 Hz, 1H), 7.71-7.64 (m, 1H), 7.62-7.54 (m, 1H), 4.55-4.43 (m, 2H), 3.85-3.72 (m, 2H), 1.43 (t, J = 7.1 Hz, 3H), 1.35 (s, 9H), 0.72 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 161.3, 159.1, 151.7, 140.7, 138.5, 137.4, 134.4, 133.1, 132.4, 130.2, 128.7, 128.5, 127.9, 127.7, 126.9, 126.3, 125.1, 122.1, 112.8, 110.5, 96.2, 79.4, 62.6, 62.0, 56.0, 29.5, 14.1, 13.1; HRMS (ESI) calcd for $C_{32}H_{27}N_3O_5$ $[M+Na]^+$ 556.1848, found 556.1843.

(Z)-diethyl 5'-(cyclohexylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4j**): Mp 208-211 °C; red powder; IR (KBr): 2932, 2856, 2230, 1720, 1696, 1575, 1429, 1335, 1276, 1020, 748 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.62 (d, J = 7.1 Hz, 1H), 8.58 (s, 1H), 8.28 (d, J = 8.5 Hz, 1H), 8.16 (d, J = 8.6 Hz, 1H), 7.88-7.81 (m, 1H), 7.77 (m, 1H), 7.71-7.64 (m, 1H), 7.62-7.54 (m, 1H), 4.55-4.43 (m, 2H), 3.85-3.72 (m, 2H), 1.43 (t, J = 7.1 Hz, 3H), 1.35 (s, 9H), 0.72 (t, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 161.0, 159.1, 153.9, 139.5, 139.3, 137.4, 134.4, 133.1, 132.4, 130.3, 128.7, 128.5, 127.9, 127.7, 126.9, 126.3, 125.1, 121.9, 112.8, 110.5, 95.7, 79.6, 62.7, 62.0, 57.4, 33.3, 33.0, 25.7, 24.6, 24.5, 14.1, 13.1; HRMS (APCI) calcd for $C_{34}H_{29}N_3O_5$ $[M+H]^+$ 560.2185, found 560.2187.

(Z)-dimethyl 5'-(benzylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4k**): Mp 211-214 °C; red powder; IR (KBr): 3031, 2954, 2229, 1720, 1686, 1570, 1440, 1300, 1048, 985, 734 cm^{-1}; ^1H NMR (400 MHz, DMSO) δ 8.86 (s, 1H), 8.55 (d, J = 8.4 Hz, 1H), 8.42 (d, J = 7.3 Hz, 1H), 8.28 (d, J = 8.4 Hz, 1H), 7.97 (t, J = 7.8 Hz, 1H), 7.62 (m, J = 15.2, 6.7 Hz, 2H), 7.38 (d, J = 8.3 Hz, 1H), 6.96 (t, J = 7.8 Hz, 1H), 6.80 (t, J = 7.4 Hz, 2H), 6.45 (d, J = 7.7 Hz, 2H), 4.70-4.64 (m, 1H), 3.96 (s, 3H), 3.85 (d, J = 14.8 Hz, 1H), 3.33 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 167.8, 165.6, 161.9, 159.6, 142.9, 138.9, 137.9, 134.3, 134.1, 133.9, 133.7, 131.1, 129.3, 128.8, 128.8, 128.3, 128.2, 128.1, 126.7, 126.7, 125.8, 125.7, 120.0, 113.0, 110.6, 79.0, 78.2, 53.9, 51.9, 44.8; HRMS (APCI) calcd for $C_{33}H_{21}N_3O_5$ $[M+H]^+$ 540.1559, found 540.1557.

(Z)-diethyl 5'-(benzylimino)-1-(dicyanomethylene)-1H,5'H-spiro[aceanthrylene-2,2'-furan]-3',4'-dicarboxylate (**4l**): Mp 200-203 °C; red powder; IR (KBr): 3030, 2954, 2220, 1731, 1686, 1575,

1435, 1364, 1299, 1052, 986, 735 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.65-8.57 (m, 2H), 8.29 (d, J = 8.0 Hz, 1H), 8.21-8.14 (m, 1H), 7.78 (t, J = 8.0 Hz, 2H), 7.60 (m, 2H), 7.39 (d, J = 4.0 Hz, 2H), 7.30 – 7.25 (m, 2H), 7.21 (t, J = 8.0 Hz, 1H), 4.85-4.72 (m, 2H), 4.55-4.43 (m, 2H), 3.88-3.74 (m, 2H), 1.43 (t, J = 8.0 Hz, 3H), 0.73 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 160.8, 159.0, 156.3, 140.4, 139.0, 138.9, 137.5, 134.4, 133.0, 132.5, 130.3, 128.9, 128.3, 128.0, 127.9, 127.9, 127.8, 127.0, 126.7, 126.4, 125.2, 121.8, 112.6, 110.3, 96.3, 79.7, 62.9, 62.2, 52.2, 14.1, 13.1; HRMS (ESI) calcd for $C_{35}H_{25}N_3O_5$ $[M+Na]^+$ 590.1692, found 590.1717.

General procedure for the preparation of spiro-substituted pyrroles 5

To a magnetically stirred solution of 2-(2-oxoaceanthrylen-1(2H)-ylidene)malononitrile (**1b**, 1 mmol), the corresponding dialkyl acetylenedicarboxylate (**2**, 1 mmol) and K_2CO_3 (0.5 mmol) in toluene and water (V_t/V_w = 100:1, 2.0 mL) was added dropwise a solution of corresponding isocyanide (**3**, 1 mmol) in toluene and water (V_t/V_w = 100:1, 1.0 mL) at 25 °C for 10 min. The reaction mixture was then stirred at 110 °C for 24 h. The solvent was removed and the residue was purified by column chromatography using n-hexane–EtOAc (1:4) as eluent. The solvent was removed and the product **5** was obtained.

Dimethyl 1'-tert-butyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5a**): Mp 219-222 °C; yellow powder; IR (KBr): 2930, 2849, 2225, 1745, 1690, 1570, 1438, 1346, 1274, 1089, 786 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (d, J = 7.4 Hz, 1H), 8.19 (d, J = 8.2 Hz, 1H), 7.96 (d, J = 8.3 Hz, 1H), 7.84 (t, J = 7.8 Hz, 1H), 7.69 (dd, J = 8.2, 7.1 Hz, 1H), 7.42 (d, J = 7.0 Hz, 1H), 3.95 (d, J = 5.3 Hz, 3H), 3.41 (d, J = 1.9 Hz, 3H), 1.23 (d, J = 7.1 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 166.4, 161.7, 159.5, 142.1, 139.3, 138.1, 135.4, 134.0, 132.8, 131.2, 129.3, 129.0, 127.0, 125.5, 120.6, 112.6, 110.1, 78.6, 77.9, 59.2, 53.3, 53.0, 27.7; HRMS (APCI) calcd for $C_{26}H_{21}N_3O_5$ $[M+H]^+$ 456.1559, found 456.1552.

Dimethyl 1'-cyclohexyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5b**): Mp 247-250 °C; yellow powder; IR (KBr): 2948, 2226, 1780, 1708, 1576, 1436, 1303, 1285, 1116, 784 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 7.4 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.87 (t, J = 7.8 Hz, 1H), 7.73-7.65 (m, 1H), 7.40 (d, J = 7.0 Hz, 1H), 3.98 (s, 3H), 3.48 (s, 3H), 2.59 (m, J = 15.8, 8.0, 3.8 Hz, 1H), 2.22-2.02 (m, 2H), 1.70 (t, J = 10.5 Hz, 2H), 1.58-1.49 (m, 1H), 1.46-1.33 (m, 2H), 0.98 (m, J = 18.8, 12.8, 3.2 Hz, 2H), 0.81-0.67 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 165.1, 161.7, 159.7, 141.3, 140.0, 139.8, 133.9, 133.7, 133.0, 131.2, 129.3, 128.9, 127.2, 125.5, 120.9, 112.5, 109.9, 79.1, 56.2, 53.3, 53.1, 29.7, 29.7, 25.9, 25.7, 24.7; HRMS (APCI) calcd for $C_{28}H_{23}N_3O_5$ $[M+H]^+$ 482.1716, found 482.1714.

Dimethyl 1'-benzyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5c**): Mp 173-175 °C; yellow powder; IR (KBr): 2957, 2231, 1708, 1576, 1445, 1383, 1270, 1109, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (d, J = 7.4 Hz, 1H), 8.20 (d, J = 8.2 Hz, 1H), 7.98 (d, J = 8.3 Hz, 1H), 7.87-7.78 (t, 1H), 7.65 (dd, J = 8.2, 7.1 Hz, 1H), 7.25-7.16 (m, 2H), 7.05 (t, J = 7.6 Hz, 2H), 6.66 (d, J = 7.3 Hz, 2H), 4.97 (d, J = 14.7 Hz, 1H), 4.01 (d, J = 1.7 Hz, 3H), 3.56 (d, J = 14.7 Hz, 1H), 3.49 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 165.5, 161.6, 159.7, 142.5, 139.7, 138.5, 134.3, 133.7, 133.5, 132.5, 131.0, 129.3, 129.1, 128.8, 128.4, 127.1, 125.1, 120.5, 111.9, 109.8, 79.5, 53.4, 53.1, 44.9; HRMS (APCI) calcd for $C_{29}H_{19}N_3O_5$ $[M+H]^+$ 490.1403, found 490.1422.

Diethyl 1'-tert-butyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5d**): Mp 214-217 °C; yellow powder; IR (KBr): 2935, 2850, 2227, 1740, 1686, 1574, 1439, 1340, 1280, 1070, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.67 (d, J = 8.0 Hz, 1H), 8.18 (d, J = 8..0 Hz, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.83 (t, J = 8.0 Hz, 1H), 7.74-7.66 (m, 1H), 7.44 (d, J = 8.0 Hz, 1H), 4.41 (q, J = 8.0 Hz, 2H), 3.85-3.73 (m, 2H), 1.38 (t, J = 8.0 Hz, 3H), 1.23 (s, 9H), 0.74 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 166.5, 161.3, 159.0, 142.0, 139.4, 138.5, 135.7, 134.2, 132.7, 131.2, 129.2, 129.0, 126.9, 125.4, 120.6, 112.6, 110.1, 78.6, 77.8, 62.5, 62.1, 59.1, 27.8, 14.1, 13.2; HRMS (ESI) calcd for $C_{28}H_{25}N_3O_5$ $[M+Na]^+$ 506.1692, found 506.1659.

Diethyl 1'-cyclohexyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5e**): Mp:164-167 °C; yellow powder; IR (KBr): 2950, 2222, 1750, 1700, 1574, 1439, 1364, 1283, 1110, 780 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.69 (d, J = 8.0 Hz, 1H), 8.22 (d, J = 8.0 Hz, 1H), 7.98 (d, J = 8.0 Hz, 1H), 7.86 (t, J = 8.0 Hz, 1H), 7.69 (m, 1H), 7.42 (d, J = 8.0 Hz, 1H), 4.45 (m, 2H), 3.93-3.77 (m, 2H), 2.60 (m, 1H), 2.12 (m, 2H), 1.83-1.65 (m, 3H), 1.58-1.48 (m, 2H), 1.40 (m, 3H), 0.90 (m, 3H), 0.78 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 165.3, 161.3, 159.1, 141.2, 140.3, 140.1, 134.1, 133.9, 132.9, 131.1, 129.2, 129.0, 127.1, 126.6, 125.4, 120.9, 112.6, 109.9, 62.6, 62.1, 56.2, 25.9, 25.8, 24.7, 14.1, 13.2; HRMS (ESI) calcd for $C_{30}H_{27}N_3O_5$ $[M+Na]^+$ 532.1848, found 532.1829.

Diethyl 1'-benzyl-2-(dicyanomethylene)-5'-oxo-1',5'-dihydro-2H-spiro[acenaphthylene-1,2'-pyrrole]-3',4'-dicarboxylate (**5f**): Mp 207-210 °C; yellow powder; IR (KBr): 2960, 2229, 1710, 1686, 1574, 1440, 1375, 1285, 1111, 776 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, J = 8.0 Hz, 1H), 8.20 (d, J = 8.0 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.84 – 7.78 (m, 1H), 7.65 (m, 1H), 7.25 (d, J = 8.0 Hz, 1H), 7.19 (t, J = 8.0 Hz, 1H), 7.05 (t, J = 8.0 Hz, 2H), 6.67 (d, J = 8.0 Hz, 2H), 4.98 (d, J = 16.0 Hz, 1H), 4.51 – 4.44 (m, 2H), 3.92 – 3.81 (m, 2H), 3.58 (d, J = 16.0 Hz, 1H), 1.42 (t, J = 8.0 Hz, 3H), 0.78 (t, J = 8.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 165.6, 161.2, 159.1, 142.4, 139.7, 138.9, 134.3, 133.8, 133.7, 132.4, 131.0, 129.3, 129.2,

129.1, 128.8, 128.3, 127.0, 124.9, 120.6, 112.0, 109.7, 79.5, 62.7, 62.2, 44.9, 31.9, 22.7, 14.1, 13.2; HRMS (ESI) calcd for $C_{31}H_{23}N_3O_5$ $[M+Na]^+$ 540.1535, found 540.1561.

Dimethyl 1'-tert-butyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5g**): Mp 264-267 °C; red powder; IR (KBr): 2951, 2222, 1700, 1561, 1425, 1274, 1197, 1092, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 7.2 Hz, 1H), 8.59 (s, 1H), 8.31 (d, J = 8.5 Hz, 1H), 8.20-8.13 (m, 1H), 7.83-7.73 (m, 2H), 7.65-7.56 (m, 2H), 3.98 (s, 3H), 3.32 (s, 3H), 1.17 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.2, 166.6, 161.6, 159.5, 142.2, 138.6, 137.3, 134.3, 134.2, 133.1, 130.4, 128.6, 128.3, 128.2, 128.0, 127.8, 126.7, 126.5, 126.1, 121.8, 112.8, 110.3, 79.1, 78.2, 59.5, 53.3, 53.0, 27.7; HRMS (APCI) calcd for $C_{30}H_{23}N_3O_5$ $[M+H]^+$ 506.1716, found 506.1726.

Dimethyl 1'-cyclohexyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5h**): Mp 256-259 °C; red powder; IR (KBr): 2933, 2220, 1706, 1550, 1429, 1339, 1276, 1156, 1031, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, J = 7.2 Hz, 1H), 8.62 (s, 1H), 8.35 (d, J = 8.5 Hz, 1H), 8.21-8.13 (m, 1H), 7.83 (m, 1H), 7.78-7.71 (m, 1H), 7.65-7.55 (m, 2H), 4.01 (s, 3H), 3.39 (s, 3H), 2.71 (m, 1H), 2.17-1.91 (m, 2H), 1.68 (m, 2H), 1.41-1.31 (m, 2H), 1.09 (d, J = 12.4 Hz, 1H), 0.99-0.85 (m, 2H), 0.56 (m, J = 13.2, 6.7 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 165.3, 161.7, 159.7, 141.7, 140.3, 138.1, 134.2, 133.9, 133.3, 130.4, 128.8, 128.3, 128.0, 127.1, 126.5, 126.0, 121.6, 112.7, 110.1, 79.0, 78.7, 56.3, 53.3, 53.0, 29.4, 29.0, 25.9, 25.7, 24.7; HRMS (APCI) calcd for $C_{32}H_{25}N_3O_5$ $[M+H]^+$ 532.1872, found 532.1876.

Dimethyl 1'-benzyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5i**): Mp 203-206 °C; red powder; IR (KBr): 3025, 2960, 2222, 1703, 1655, 1565, 1427, 1278, 1110, 745 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.45 (d, J = 7.2 Hz, 1H), 8.32 (d, J = 8.5 Hz, 1H), 8.20-8.12 (m, 1H), 7.77 (dd, J = 8.4, 7.3 Hz, 1H), 7.64-7.54 (m, 3H), 7.08 (t, J = 7.4 Hz, 1H), 6.92 (t, J = 7.7 Hz, 2H), 6.60-6.51 (m, 2H), 4.99 (d, J = 14.6 Hz, 1H), 4.04 (s, 3H), 3.56 (d, J = 14.6 Hz, 1H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 165.7, 161.6, 159.7, 143.0, 138.9, 138.0, 134.2, 133.8, 133.7, 132.7, 130.4, 129.4, 129.1, 128.6, 128.2, 128.0, 127.1, 126.5, 125.8, 125.5, 120.6, 112.2, 109.9, 78.9, 78.3, 53.4, 53.1, 45.2; HRMS (APCI) calcd for $C_{33}H_{21}N_3O_5$ $[M+H]^+$ 540.1559, found 540.1580.

Diethyl 1'-tert-butyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5j**): Mp 239-242 °C; red powder; IR (KBr): 2954, 2222, 1705, 1574, 1420, 1275, 1120, 1087, 750 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.0 Hz, 1H), 8.59 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 8.16 (d, J = 8.0 Hz, 1H), 7.84-7.75 (m, 2H), 7.65-7.56 (m, 2H), 4.49-4.40 (m, 2H), 3.75-3.63 (m, 2H), 1.40 (t, J = 8.0 Hz, 3H), 1.17 (s, 9H), 0.64 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 166.8, 161.2, 159.1, 142.0, 138.9, 137.3, 134.4, 134.3, 133.0, 130.3, 128.6, 128.5, 128.3, 128.0, 127.6, 126.7, 126.6, 126.0, 121.9, 112.9, 110.2, 79.1, 78.3, 62.6, 62.0, 59.4, 27.7, 14.1, 13.0; HRMS (ESI) calcd for $C_{32}H_{27}N_3O_5$ $[M+Na]^+$ 556.1848, found 556.1858.

Diethyl 1'-cyclohexyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5k**): Mp 182-185 °C; red powder; IR (KBr): 2930, 2220, 1712, 1550, 1435, 1345, 1276, 1155, 1031, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.0 Hz, 1H), 8.61 (s, 1H), 8.35 (d, J = 8.0 Hz, 1H), 8.19-8.14 (m, 1H), 7.83 (m, 1H), 7.76 (d, J = 8.0 Hz, 1H), 7.65-7.56 (m, 2H), 4.53-4.44 (m, 2H), 3.83-3.67 (m, 2H), 2.72 (m, 1H), 2.19-1.92 (m, 2H), 1.78-1.60 (m, 2H), 1.42 (t, J = 8.0 Hz, 3H), 1.39-1.32 (m, 2H), 1.10 (d, J = 8.0 Hz, 1H), 1.00-0.91 (m, 2H), 0.68 (t, J = 8.0 Hz, 3H), 0.57 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 165.5, 161.3, 159.1, 141.5, 140.7, 138.1, 134.2, 134.1, 133.2, 130.3, 128.7, 128.2, 128.0, 127.9, 127.2, 126.8, 126.5, 125.8, 121.7, 112.8, 110.0, 78.9, 62.6, 62.1, 56.3, 29.4, 29.1, 25.9, 25.7, 24.7, 14.2, 13.1; HRMS (ESI) calcd for $C_{34}H_{29}N_3O_5$ $[M+Na]^+$ 582.2005, found 582.2025.

Dimethyl 1'-benzyl-1-(dicyanomethylene)-5'-oxo-1',5'-dihydro-1H-spiro[aceanthrylene-2,2'-pyrrole]-3',4'-dicarboxylate (**5l**): Mp 158-161 °C; red powder; IR (KBr): 3032, 2960, 2227, 1700, 1660, 1574, 1420, 1299, 1111, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.61 (s, 1H), 8.44 (d, J = 8.0 Hz, 1H), 8.32 (d, J = 8.0 Hz, 1H), 8.20-8.13 (m, 1H), 7.80-7.73 (m, 1H), 7.62-7.56 (m, 3H), 7.08 (t, J = 8.0 Hz, 1H), 6.92 (t, J = 8.0 Hz, 2H), 6.56 (d, J = 8.0 Hz, 2H), 5.01 (d, J = 16.0 Hz, 1H), 4.51 (m, 2H), 3.83-3.71 (m, 2H), 3.57 (d, J = 16.0 Hz, 1H), 1.44 (t, J = 8.0 Hz, 3H), 0.69 (t, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 165.9, 161.2, 159.2, 142.8, 139.3, 138.0, 134.1, 134.0, 133.8, 132.6, 130.3, 129.4, 129.1, 128.6, 128.1, 127.9, 127.8, 127.1, 126.5, 126.1, 125.3, 120.7, 112.3, 109.8, 79.0, 78.3, 62.8, 62.2, 45.2, 14.1, 13.1; HRMS (ESI) calcd for $C_{35}H_{25}N_3O_5$ $[M+Na]^+$ 590.1692, found 590.1681.

General procedure for the synthesis of compound 5m-5o.

To a magnetically stirred solution of 2-(10-oxophenanthren-9(10H)-ylidene)malononitrile (**1c**, 1 mmol), the corresponding dialkyl acetylenedicarboxylate (1 mmol) and K_2CO_3 (0.5 mmol) in toluene and water (V_t/V_w = 100:1, 2.0 mL) was added dropwise a solution of corresponding isocyanide (1 mmol) in toluene and water (V_t/V_w = 100:1, 1.0 mL) at 25 °C for 10 min. The reaction mixture was then stirred at 110 °C for 24 h. The solvent was removed and the residue was purified by column chromatography using n-hexane–EtOAc (1:4) as eluent. The solvent was removed and the product **5m** was obtained.

Dimethyl 1'-t-Butyl-10-(dicyanomethylene)-5'-oxo-1',5'-dihydro-10H-spiro[phenanthrene-9,2'-pyrrole]-3',4'-dicarboxylate (**5m**): Mp 231-234 °C; yellow powder; IR (KBr): 2980, 2953, 2220, 1702, 1670, 1531, 1445, 1286, 1197, 1093,

764 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.74 (d, J = 8.3 Hz, 1H), 8.17 (d, J = 8.1 Hz, 1H), 8.08 (d, J = 8.0 Hz, 1H), 7.79-7.73 (m, 1H), 7.49 (m, J = 9.3, 8.2, 4.3 Hz, 2H), 7.38 (t, J = 7.6 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H), 4.00-3.92 (m, 3H), 3.46 (d, J = 1.7 Hz, 3H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 166.4, 161.7, 159.4, 144.1, 137.7, 135.9, 133.8, 130.7, 130.0, 129.8, 129.6, 128.7, 127.0, 126.6, 124.6, 124.0, 115.4, 113.0, 82.4, 69.7, 59.2, 53.3, 53.1, 27.9; HRMS (APCI) calcd for $C_{28}H_{23}N_3O_5$ $[M+H]^+$ 482.1716, found 482.1730.

Dimethyl 1'-cyclohexyl-10-(dicyanomethylene)-5'-oxo-1',5'-dihydro-10H-spiro[phenanthrene-9,2'-pyrrole]-3',4'-dicarboxylate (**5n**): Mp 196-199 °C; yellow powder; IR (KBr): 2926, 2855, 2220, 1700, 1661, 1525, 1447, 1278, 1091, 762 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.45 (d, J = 8.1, 1H), 8.07 (t, J = 7.9 Hz, 2H), 7.83-7.73 (m, 1H), 7.55-7.45 (m, 2H), 7.40-7.32 (m, 1H), 7.14 (d, J = 8.0, 1H), 3.99 (s, 3H), 3.57 (s, 3H), 2.81 (m, J = 12.0, 3.6 Hz, 1H), 1.91-1.92 (m, 2H), 1.63 (d, J = 10.1 Hz, 2H), 1.51 (dd, J = 13.4, 1.6 Hz, 1H), 1.40 (d, J = 11.2, 1H), 1.16 (d, J = 12.3 Hz, 1H), 1.03-0.91 (m, 1H), 0.89-0.71 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 165.2, 161.7, 159.8, 143.9, 139.7, 135.9, 134.2, 131.3, 130.4, 130.0, 129.9, 128.7, 128.6, 127.0, 126.9, 124.7, 124.1, 114.9, 112.5, 83.9, 69.3, 56.8, 53.3, 53.2, 29.8, 29.0, 26.0, 25.9, 24.8; HRMS (APCI) calcd for $C_{30}H_{25}N_3O_5$ $[M+H]^+$ 508.1872, found 508.1872.

Dimethyl 1'-benzyl-10-(dicyanomethylene)-5'-oxo-1',5'-dihydro-10H-spiro[phenanthrene-9,2'-pyrrole]-3',4'-dicarboxylate (**5o**): Mp 233-236 °C; yellow powde; IR (KBr): 2951, 2219, 1707, 1661, 1538, 1448, 1363, 1270, 1099, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.08-7.99 (m, 3H), 7.75-7.67 (m, 1H), 7.49-7.40 (m, 1H), 7.38-7.32 (m, 1H), 7.24-7.14 (m, 2H), 7.09 (t, J = 7.3 Hz, 2H), 6.91 (d, J = 7.1 Hz, 2H), 6.83 (d, J = 8.0, 1H), 4.73 (d, J = 14.8 Hz, 1H), 3.99 (s, 3H), 3.92 (d, J = 14.8 Hz, 1H), 3.44 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.5, 164.0, 161.5, 159.8, 146.0, 136.5, 135.6, 133.8, 133.7, 131.8, 130.4, 130.3, 130.1, 129.4, 128.7, 128.4, 128.4, 127.6, 126.8, 126.5, 124.4, 123.9, 114.5, 112.4, 84.0, 69.8, 53.4, 53.1, 45.8; HRMS (APCI) calcd for $C_{31}H_{21}N_3O_5$ $[M+H]^+$ 516.1559, found 516.1558.

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Graphical Abstract

Base-mediated isocyanide-based three-component reactions: divergent synthesis of spiro-substituted furans and pyrroles

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A facile base-mediated isocyanide-based three-component cycloaddition protocol for the chemoselective preparation of functionalized spiro-substituted furans and pyrroles derivatives has been designed. Fairly good yields of the products, the ready availability of the starting materials and the excellent chemoselectivity are the main advantages of this method.