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PAPER

Tandem allylic substitution–5-*exo*-dig-carbocyclization: a [4 + 1]-annulation approach to arylidene cyclopentenes from MBH-acetates of acetylenic aldehydes†

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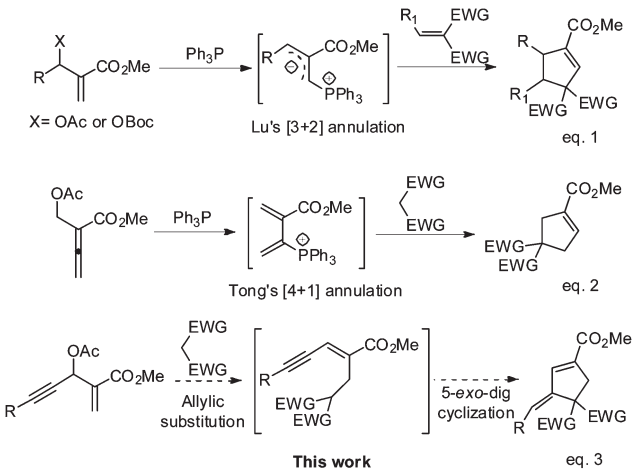
A new entry for the synthesis of functionalized arylidene cyclopentenes under metal-free reaction conditions is disclosed *via* the base-promoted [4 + 1]-annulation of Morita–Baylis–Hillman acetates of acetylenic aldehydes with active methylene derivatives involving tandem allylic substitution followed by 5-*exo*-dig-carbocyclization.

Introduction

Morita–Baylis–Hillman (MBH) adducts and their derivatives have been proven to be some of the most flexible synthons in the rapid formation of useful synthetic products including heterocycles and carbocycles through various transformations.[1] Among these, the phosphine-catalyzed annulation reaction of MBH-acetates/carbonates or allenes with electron-deficient olefins is one of the useful methods for the synthesis of substituted cyclopentenes.[2–4] In these reactions, MBH-adducts served as a C_3 synthon, which has been extensively studied by Lu and co-workers in various phosphine-catalyzed [3 + *n*] annulations (eqn (1), Scheme 1).[3] In 2010, Tong *et al.* described a different MBH-acetate, derived from allenoate, as a C4 synthon for phosphine-catalyzed [4 + *n*] annulations to provide cyclopentene and tetrahydropyridazine derivatives (eqn (2), Scheme 1).[5]

We envisioned a new [4 + 1] annulation approach to substituted cyclopentenes using MBH-acetates of acetylenic aldehydes as C_4 synthons.[6] This MBH-acetate is expected to participate in allylic substitution with 1,1′-bisnucleophile to give an ε-acetylenic carbonyl compound, which would undergo 5-*exo*-dig-carbocyclization to provide the corresponding cyclopentene (eqn (3), Scheme 1). However, in contrast to the former annulations, the present envisioned strategy is expected to provide an alkyl/arylidene cyclopentenes. Commonly, this type of alkyl/arylidene cyclopentyl is obtained *via* ene-carbocyclization reactions such as the Conia-ene reaction, which is one of the useful carbon–carbon bond forming methods to provide an atom-economical synthesis of carbocycles by the thermal cyclization of an alkyne bearing an enolizable carbonyl group.[7,8] In addition, a few other methods are also available to obtain alkyl/arylidene cyclopentyls.[9] Nevertheless, these methods are usually multistep reactions (preparation of the ω-alkynyl substrate and cyclization) and require the use of metal catalyst or strong base and/or high temperature to promote the cyclization. Herein, we present a mild base-mediated metal-free tandem allylic substitution–5-*exo*-dig-carbocyclization of MBH-acetates of acetylenic aldehydes to arylidene cyclopentenes at room temperature.



Scheme 1 Access to cyclopentenes from MBH-adducts.

Results and discussion

Initial investigation was aimed to determine the optimal reaction conditions for the proposed approach by the reaction of MBH-acetate **1a** with ethyl cyanoacetate (**2a**) in the presence of readily available bases and solvents (Table 1). Firstly, the reaction of **1a**

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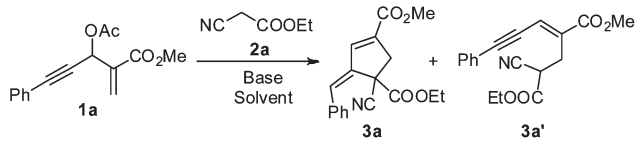
†Electronic supplementary information (ESI) available: Copies of ^{1}H NMR and ^{13}C NMR spectra of all the new compounds. See DOI: 10.1039/c2ob26934a

Table 1 Screening different bases and solvents



Entry	Base (1 equiv.)	Solvent	*T* (°C)	Time (h)	Yield[a] (%) 3a	3a′
1	Et_3N	CH_2Cl_2	rt	16	14	62
2	DABCO	CH_2Cl_2	rt	36	46	0
3	K_2CO_3	THF	rt	24	0	0
4	K_2CO_3	CH_3CN	rt	24	0	0
5	K_2CO_3	DMF	rt	16	74	0
6	Cs_2CO_3	DMF	rt	24	38	0

[a] Isolated yield.

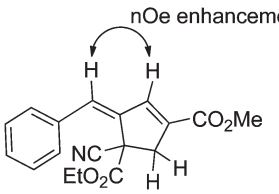


Fig. 1 Key NOE enhancements of compound **3a**.

with **2a** using Et_3N in CH_2Cl_2 at room temperature provided the expected cyclopentene **3a** (14% yield) along with the allylic substituted product **3a′** (entry 1, Table 1). Continuation of the reaction at 50 °C for another 6 h did not help in improvement of the yield. Later, other bases such as DABCO, K_2CO_3 and Cs_2CO_3 were tested for the above reaction (entries 2 to 6, Table 1). Among the examined reaction conditions, K_2CO_3 in DMF at room temperature was found to be the best condition to obtain **3a** in 74% yield. It is important to reveal that, a prolonged reaction time or an increase in reaction temperature leads to the decomposition of the MBH-adduct or allylic intermediate.

The geometry of the exocyclic olefin in compound **3a** was confirmed as exclusively the *Z*-isomer using NOE experiments (Fig. 1).

Under the optimized conditions for the present [4 + 1]-annulation reaction, the scope of other 1,1′-bisnucleophiles was studied using MBH-acetate **1a** as a C_4 synthon and the results are summarized in Table 2. The results suggested that diethyl malonate (**2b**) was successfully reacted with **1a** to afford the corresponding cyclopentene **3b** in 68% yield (entry 1, Table 2). Whereas, the reaction of dibenzoylmethane (**2c**) with **1a** was sluggish to give the corresponding cyclopentene **3c** (entry 2) and it was observed that the initial allylic substitution takes place smoothly at room temperature to the corresponding ε-acetylenic carbonyl compound but not the carbocyclization. However, when the reaction was carried out at 60 °C it provided the desired cyclopentene **3c** albeit with low yield (54%, entry 1, Table 2). The low yield may be due to the decomposition of the allylic intermediate at a higher temperature. The reactions of other active methylene carbonyl compounds such as ethyl acetoacetate (**2d**), ethyl nitroacetate (**2e**) and ethyl 2-tosylacetate (**2f**) with **1a** ensued efficiently to give the corresponding benzylidene cyclopentene derivatives **3d** to **3f** in good yields (entries 3 to 5, Table 2). To our delight, Meldrum's acid (**2g**) also underwent the present tandem reaction with **1a** to give the desired spirocyclic product **3g** in 62% yield (entry 6, Table 2). A notable example for the efficiency of the present [4 + 1]-annulation was the use of a non-carbonyl compound, 1-nitropropane (**2h**), as the bis-nucleophilic agent to obtain the corresponding nitro substituted cyclopentene **3h** in 73% yield (entry 7, table 2).

We also explored the influence of substitution on the alkyne functionality of MBH-acetates in providing the cyclopentene annulation products under the developed reaction conditions. As shown in Table 3, a smooth [4 + 1]-annulation was observed in MBH-acetate **1b** having *p*-nitro-phenyl (an electron withdrawing group on the phenyl ring) substitution on the alkyne with ethyl cyanoacetate (**2a**) to give the corresponding products **3i** in 66% yield. The MBH-acetate (**1c**) bearing 4-methoxyphenyl (an electron donating group on the phenyl ring) was successful in reacting with **2a** to provide the cyclopentene **3j** although it took a longer reaction time and gave 53% yield. Thiophenyl MBH-acetate **2d** also proved to be a suitable substrate in reacting with **2a** to give the corresponding cyclopentene derivative **3k** in 61% yield. The above success encouraged us to study the reactions of **1b** to **1d** with different 1,1′-bis-nucleophiles **2b** and **2h** and found that all the reactions gave the corresponding cyclopentenes **3l** to **3q** in convincingly good yields (Table 3). It was observed that the MBH-acetate **1c** bearing an electron donating group on the phenyl ring is less reactive compared to others. Whereas, the reaction of MBH-acetate **1e** bearing an *n*-propyl group on the alkyne functionality with **2a** provided the dialkylated product **4a** instead of the expected cyclopentene (Scheme 2).

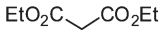
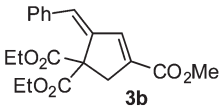
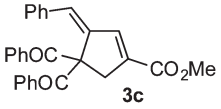
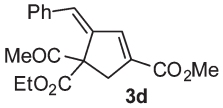
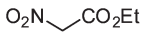
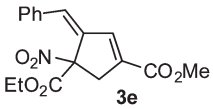
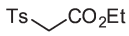
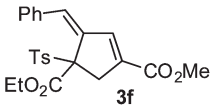
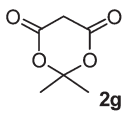
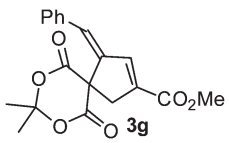
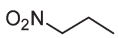
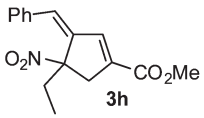
The above reactivity variations depending on the groups present on the aromatic ring and the formation of the *Z*-isomer, suggests that the 5-*exo*-dig carbocyclization proceeds through an *anti*-addition of nucleophile on to the alkyne, whereas the Conia-ene reaction proceeds through a concerted transition state, wherein the ene partner will undergo *syn*-addition to the alkyne.

In addition, the construction of spirocyclopentene oxindole, a core structure in many complex bioactive natural products and an important pharmacophore in medicinal chemistry,[10] has also been investigated. Thus, the reaction of oxindole **2i** with MBH acetate **1a** under the optimized reaction conditions was carried out and the successful formation of spiro-oxindole **3r** in good yields was observed (Scheme 3).

Conclusions

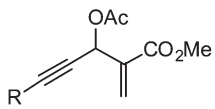
In conclusion, we have successfully developed a novel strategy for the construction of substituted cyclopentenes through the use of MBH-acetates of acetylenic aldehydes as attractive C4-synthons. A simple base (K_2CO_3) promotes the [4 + 1]-annulation of various 1,1′-bis carbon nucleophiles (active methylene compounds including non-carbonyl compounds) with MBH-acetates through tandem reaction of allylic substitution–5-*exo*-dig carbocyclization. To the best of our knowledge, this is a first method

Table 2 Synthesis of benzyledene-cyclopentenes from **1a**[a]

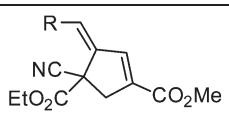
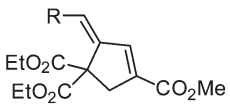
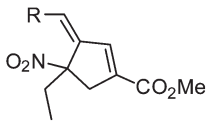
Entry	Bis-nucleophile (**2**)	Time (h)	Product (**3**)[b]	Yield[c] (%)
1	 **2b**	16	 **3b**	68
2	 **2c**	16	 **3c**	54
3	 **2d**	10	 **3d**	67
4	 **2e**	8	 **3e**	68
5	 **2f**	8	 **3f**	85
6	 **2g**	16	 **3g**	62
7	 **2h**	8	 **3h**	73

[a] *Reaction conditions*: MBH-acetate (1 mmol), bis-nucleophile (1.1 mmol), K_2CO_3 (2.5 mmol), DMF (6 mL), rt. [b] All the products were characterized by ^1H, ^{13}C NMR, IR and MS spectra. [c] Isolated yield.

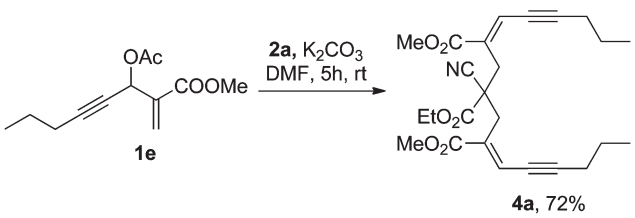
Table 3 Synthesis of arylidene cyclopentenes[a]



R= *p*NO_2-Ph, **1b**
R= *p*MeO-Ph, **1c**
R= 2-Thiophenyl, **1d**

	Product[b]/reaction time/yield[c]
2a 	R = *p*-NO_2-Ph (**3i**)/6 h/66% R = *p*-MeO-Ph (**3j**)/24 h/53% R = 2-Thiophenyl (**3k**)/14 h/61%
2b 	R = *p*-NO_2-Ph (**3l**)/16 h/63% R = *p*-MeO-Ph (**3m**)/16 h/51% R = 2-Thiophenyl (**3n**)/14 h/64%
2h 	R = *p*-NO_2-Ph (**3o**)/72 h/54% R = *p*-MeO-Ph (**3p**)/72 h/46% R = 2-Thiophenyl (**3q**)/72 h/65%

[a] *Reaction conditions*: MBH-acetate (1 mmol), bis-nucleophile (1.1 mmol), K_2CO_3 (2.5 mmol), DMF (6 mL), rt. [b] All the products were characterized by ^1H, ^{13}C NMR, IR and MS spectra. [c] Isolated yield.



Scheme 2 Reaction of **1e** with **2a**.

Scheme 3 Synthesis of spiro-oxindole **3r**.

where arylidene cyclopentenes have been accomplished through the 5-*exo*-dig-cyclization of an ε-acetylenic carbonyl compound, while all the literature methods provide cyclopentanes.

Experimental

General

Reactions were monitored by thin-layer chromatography carried out on silica plates (silica gel 60 F254, Merck) using UV-light and anisaldehyde or potassium permanganate or β-naphthol for visualization. Column chromatography was performed on silica gel (60–120 mesh) using *n*-hexane and ethyl acetate as eluent. Evaporation of solvents was conducted under reduced pressure at temperatures less than 45 °C. IR spectra were recorded on a Perkin-Elmer 683, Nicolet Nexus 670 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$, DMSO-d_6 solvents 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). Mass spectra were obtained on a Finnigan MAT1020B, micromass VG 70–70H or LC/MSD trapSL spectrometer operating at 70 eV using a direct inlet system.

Morita–Baylis–Hillman acetates, **1a** to **1e**, were prepared using the literature procedure.[6,11]

General procedure for the preparation of cyclopentenes

To a solution of MBH-acetate (**1a**, 0.48 mmol) and active methylene compound (**2a**, 0.53 mmol) in DMF (3 mL) was added K_2CO_3 (1.2 mmol) at room temperature. The reaction mixture was stirred at the same temperature for 6 to 22 h. After the completion of reaction, the reaction mixture was diluted with water (10 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic extracts were washed with brine (20 mL), dried over Na_2SO_4 and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel (EtOAc : hexanes) to afford the corresponding product.

Spectral data for all new compounds

(*Z*)-1-Ethyl 3-methyl 5-benzylidene-1-cyanocyclopent-3-ene-1,3-dicarboxylate (3a). Brown liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.48–7.28 (m, 5H), 7.09 (t, J = 1.9 Hz, 1H), 6.94 (s, 1H), 3.93–4.10 (m, 2H), 3.81 (s, 3H), 3.58 (d, J = 17.8 Hz, 1H), 3.38 (d, J = 17.8, 1H), 1.10 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.9, 164.0, 143.4, 140.7, 133.4, 134.0, 129.0, 128.9, 128.6, 118.1, 114.2, 68.1, 63.3, 52.0, 45.8, 13.6; IR (KBr): 2954, 2851, 2243, 1742, 1713, 1607, 1438, 1357, 1257, 1203, 1163, 1092, 1044, 930, 854, 742 cm^{-1}; MS (ESI): m/z 334 (M + Na)$^+$; HRMS (ESI): m/z calcd for $C_{18}H_{17}NNaO_4$ (M + Na)$^+$: 334.1050, Found: 334.1043.

(*E*)-1-Ethyl 5-methyl 2-cyano-4-(3-phenylprop-2-yn-1-ylidene)-pentanedioate (3a′). Colourless liquid, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.55–7.50 (m, 2H), 7.38–7.30 (m, 3H), 7.11 (s, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.82 (d, J = 2.6 Hz, 1H), 3.78 (s, 3H), 3.41 (dd, J = 12.0, 13.7 Hz, 2H), 1.28 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.0, 166.4, 136.1, 132.0, 129.5, 128.4, 124.9, 122.0, 117.2, 103.6, 85.3, 63.3, 52.3, 35.8, 29.1, 13.8; IR (KBr): 2952, 2851, 2195, 1743, 1716, 1609, 1489, 1437, 1368, 1251, 1128, 1059, 899, 842, 757, 689, 532; MS (ESI): m/z 334 (M + Na)$^+$; HRMS (ESI): m/z calcd for $C_{18}H_{18}NO_4$ (M + H)$^+$: 312.1230, Found: 312.1218.

(*Z*)-1,1-Diethyl 3-methyl 5-benzylidenecyclopent-3-ene-1,1,3-tricarboxylate (3b). Colourless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.40 (d, J = 7.9 Hz, 2H), 7.30–7.20 (m, 3H), 7.02 (t, J = 1.9 Hz, 1H), 6.90 (s, 1H), 4.07–3.96 (m, 4H), 3.79 (s, 3H), 3.44 (d, J = 1.9 Hz, 2H), 1.09 (t, J = 6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.5, 164.8, 145.0, 142.7, 135.3, 134.2, 133.2, 129.1, 128.0, 127.9, 62.6, 61.9, 51.7, 43.7, 13.7; IR (KBr): 2984, 2926, 2853, 1727, 1605, 1439, 1358, 1254, 1182, 1093, 1061, 930, 750, 697 cm^{-1}; MS (ESI): m/z 381 (M + Na)$^+$; HRMS (ESI): m/z calcd for $C_{20}H_{22}O_6Na$ (M + Na)$^+$: 381.0522, Found: 381.0504 (M + Na)$^+$.

(*Z*)-Methyl 4,4-dibenzoyl-3-benzylidenecyclopent-1-enecarboxylate (3c). Brown liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 7.75–7.64 (m, 5H), 7.56–7.40 (m, 4H), 7.38–7.29 (m, 5H), 7.21–6.99 (m, 3H), 3.76 (s, 3H), 3.70 (s, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 195.6, 196.5, 166.8, 146.8, 144.3, 138.7, 136.3, 133.4, 132.8, 131.9, 129.5, 129.2, 128.2, 127.5, 122.5, 68.1, 51.8, 44.3; IR (KBr): 3061, 2925, 2854, 1709, 1602, 1441, 1255, 1182, 1094, 756, 692 cm^{-1}; MS (ESI): m/z 445 (M + Na)$^+$; HRMS (ESI): m/z calcd for $C_{28}H_{22}O_4Na$ (M + Na)$^+$: 445.1410, Found 445.1393.

(*Z*)-1-Ethyl 3-methyl 1-acetyl-5-benzylidenecyclopent-3-ene-1,3-dicarboxylate (3d). Pale yellow liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28–7.15 (m, 5H), 7.05 (s, 1H), 6.92 (s, 1H), 4.15–3.91 (m, 2H), 3.78 (s, 3H), 3.50 (d, J = 17.8 Hz, 1H), 3.16 (d, J = 17.8 Hz, 1H), 2.15 (s, 3H), 1.07 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 202.2, 169.9, 164.8, 146.0, 142.8, 134.9, 133.7, 131.8, 129.1, 128.4, 122.2, 61.9, 52.2, 51.8, 42.4, 26.7, 13.6; IR (KBr): 2953, 1712, 1604, 1438, 1358, 1254, 1165, 1093, 753, 695 cm^{-1}; MS (ESI): m/z 351 (M + Na)$^+$; HRMS (ESI): m/z calcd for $C_{19}H_{20}O_5Na$ (M + Na)$^+$: 351.1227, Found: 351.1224.

(*Z*)-1-Ethyl 3-methyl 5-benzylidene-1-nitrocyclopent-3-ene-1,3-dicarboxylate (3e). Brown liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.52–7.29 (m, 5H), 7.20 (s, 1H), 7.11 (bs, 1H), 3.97 (dd, J = 18.5, 2.0 Hz, 1H), 3.89–3.67 (m, 5H), 3.56 (dd, J = 18.5, 2.0 Hz, 1H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 165.2, 163.9, 142.9, 138.7, 137.5, 134.0, 132.9, 129.1, 128.9, 128.3, 97.6, 63.4, 52.0, 44.8, 13.3; IR (KBr): 2925, 2856, 1746, 1608, 1555, 1449, 1254, 1087, 1021, 845, 745, 694 cm^{-1}; MS (ESI): m/z 354 (M + Na)$^+$.

(*Z*)-1-Ethyl 3-methyl 5-benzylidene-1-tosylcyclopent-3-ene-1,3-dicarboxylate (3f). Brown solid, m.p.: 135–136 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.85 (d, J = 8.1 Hz, 2H), 7.62–7.40 (m, 2H), 7.36–7.15 (m, 5H), 7.01 (s, 1H), 7.80 (s, 1H), 4.20–3.64 (m, 6H), 3.32 (d, J = 19.2 Hz, 1H), 2.40 (s, 3H), 0.89 (t, J = 6.9 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.9, 164.0, 146.3, 145.3, 138.5, 136.9, 134.1, 133.6, 132.8, 131.1, 129.5, 129.0, 128.8, 128.1, 78.5, 62.4, 51.7, 43.1, 21.5, 13.4; IR (KBr): 2925, 1738, 1692, 1597, 1441, 1321, 1227, 1143, 1085, 588, 644 cm^{-1}; MS (ESI): m/z 458 (M + NH_4)$^+$; HRMS (ESI): m/z calcd for $C_{24}H_{28}NO_6S$ (M + NH_4)$^+$: 458.1636, found 458.1984.

(*Z*)-Methyl 4-benzylidene-8,8-dimethyl-6,10-dioxo-7,9-dioxaspiro[4.5]dec-2-ene-2-carboxylate (3g). White solid, m.p.: 168–170 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37–7.22 (m, 3H), 7.20 (s, 1H), 7.07 (d, J = 6.9 Hz, 2H), 6.98 (s, 1H), 3.80 (s, 3H), 3.26 (s, 2H), 1.67 (s, 3H), 1.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.0, 164.1, 146.9, 143.6, 134.9, 134.4, 131.6, 128.5, 128.3, 128.2, 105.6, 52.03, 53.1, 46.1, 29.6, 27.6; IR (KBr): 2997, 2942, 1746, 1691, 1604, 1443, 1363, 1275, 1200, 1095, 1038, 946, 751, 685 cm^{-1}; MS (ESI): *m/z* 365 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{19}H_{18}O_6Na$ $(M + Na)^+$: 365.1001, Found, 365.0992.

(*Z*)-Methyl 3-benzylidene-4-ethyl-4-nitrocyclopent-1-enecarboxylate (3h). Colourless liquid, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.38–7.27 (m, 3H), 7.14 (t, J = 1.8 Hz, 1H), 7.13–7.07 (m, 2H), 7.05 (s, 1H), 3.81 (s, 3H), 3.30 (dd, J = 18.6, 1.8 Hz, 1H), 3.10 (dd, J = 18.6, 1.8 Hz, 1H), 2.21–2.05 (m, 1H), 2.03–1.88 (m, 1H), 0.75 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.3, 144.6, 143.2, 134.6, 134.7, 133.5, 128.4, 128.33, 128.3, 94.0, 51.88, 45.64, 26.4, 8.37; IR (KBr): 2972, 2953, 2879, 2843, 1713, 1610, 1549, 1436, 1283, 1257, 1217, 1134, 1034, 771, 689, 531 cm^{-1}; MS (ESI): *m/z* 288 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{16}H_{17}NO_4Na$ $(M + Na)^+$: 310.1054, Found 310.0955.

(*Z*)-1-Ethyl 3-methyl 1-cyano-5-(4-nitrobenzylidene)cyclopent-3-ene-1,3-dicarboxylate (3i). Light brown solid, m.p.: 102–104 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.26 (d, J = 8.3 Hz, 2H), 7.60 (d, J = 8.3 Hz, 2H), 7.06 (t, J = 2.2 Hz, 1H), 6.97 (s, 1H), 4.33–3.97 (m, 4H), 3.85 (s, 3H), 3.69 (dd, J = 18.1, 2.2 Hz, 1H), 3.40 (dd, J = 18.1, 2.2 Hz, 1H), 1.18 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.3, 163.5, 147.3, 144.1, 142.3, 140.2, 136.7, 130.4, 129.6, 123.7, 117.4, 63.7, 52.2, 48.0, 45.8, 13.7; IR (KBr): 3081, 2955, 2245, 1743, 1716, 1599, 1520, 1438, 1345, 1259, 1206, 1092, 861, 744 cm^{-1}; MS (ESI): *m/z* 374 $(M + NH_4)^+$; HRMS (ESI): *m/z* calcd for $C_{18}H_{16}N_2O_6Na$ $(M + Na)^+$: 379.0906, Found 379.0899.

(*Z*)-1-Ethyl 3-methyl 1-cyano-5-(4-methoxybenzylidene)cyclopent-3-ene-1,3-dicarboxylate (3j). Light brown liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.38 (d, J = 8.8 Hz, 2H), 7.07 (s, 1H), 6.89 (d, J = 8.8 Hz, 3H), 4.18–4.00 (m, 2H), 3.79 (s, 3H), 3.77 (s, 3H), 3.58 (d, J = 18.1 Hz, 1H), 3.58 (d, J = 18.1 Hz, 1H), 1.11 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 167.0, 164.0, 160.1, 144.0, 138.2, 133.1, 132.3, 130.7, 126.5, 118.0, 114.0, 63.2, 60.2, 55.2, 51.8, 45.8, 13.6; IR (KBr): 2953, 2843, 2191, 1742, 1714, 1594, 1509, 1437, 1300, 1250, 1174, 1108, 1032, 834, 752, 538 cm^{-1}; MS (ESI): *m/z* 359 $(M + NH_4)^+$. HRMS (ESI): *m/z* calcd for $C_{20}H_{24}NO_4$ $(M + H)^+$: 342.1699, Found: 342.1691.

(*Z*)-1-Ethyl 3-methyl 1-cyano-5-(thiophen-2-ylmethylene) cyclopent-3-ene-1,3-dicarboxylate (3k). Light brown liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40 (d, J = 4.9 Hz, 1H), 7.34 (d, J = 4.7 Hz, 1H), 7.08 (dd, J = 4.9, 4.7 Hz, 1H), 7.04 (t, J = 1.1 Hz, 1H), 7.00 (s, 1H), 4.29–4.12 (m, 2H), 3.79 (s, 3H), 3.64 (dd, J = 18.1, 1.1 Hz, 1H), 3.39 (dd, J = 18.1, 1.1 Hz, 1H), 1.23 (t, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 166.2, 164.6, 144.9, 140.7, 135.3, 134.0, 133.3, 129.5, 127.4, 124.4, 117.0, 63.2, 62.0, 52.2, 43.5, 13.6; IR (KBr): 3106, 2952, 2852, 2186, 1715, 1604, 1436, 1368, 1318, 1266, 1238, 1203, 1128, 1048, 1002, 849, 749, 710; HRMS (ESI): *m/z* calcd for $C_{16}H_{15}NNaO_4S$ $(M + Na)^+$: 340.0619, Found: 340.0628.

(*Z*)-1,1-Diethyl 3-methyl 5-(4-nitrobenzylidene)cyclopent-3-ene-1,1,3-tricarboxylate (3l). Pale yellow liquid, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.15 (d, J = 9.0 Hz, 2H), 7.60 (d, J = 9.0 Hz, 2H), 7.02 (t, J = 2.2 Hz, 1H), 6.91 (s, 1H), 4.09–3.99 (q, J = 6.7 Hz, 4H), 3.80 (s, 3H), 3.48–3.45 (d, J = 2.2 Hz, 2H), 1.17–1.10 (t, J = 6.7 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.9, 164.3, 146.1, 143.8, 141.7, 140.8, 135.9, 130.3, 129.3, 123.1, 68.0, 62.3, 51.9, 43.6, 13.6; IR (KBr): 2981, 1726, 1598, 1519, 1439, 1342, 1253, 1181, 1091, 1058, 860, 747 cm^{-1}; MS (ESI): *m/z* 404 $(M + H)^+$.

(*Z*)-1,1-Diethyl 3-methyl 5-(4-methoxybenzylidene)cyclopent-3-ene-1,1,3-tricarboxylate (3m). Colourless liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40 (d, J = 9.0 Hz, 2H), 7.04 (s, 1H), 6.82–6.69 (m, 3H), 4.08 (q, J = 7.0 Hz, 4H), 3.81 (s, 3H), 3.78 (s, 3H), 3.49 (d, J = 1.5 Hz, 2H), 1.1 (t, J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.6, 164.8, 159.5, 145.6, 140.6, 133.0, 131.9, 130.9, 127.8, 113.3, 62.4, 61.9, 55.1, 51.6, 43.7, 13.6; IR (KBr): 2982, 1730, 1599, 1510, 1439, 1360, 1254, 1178, 1089, 1034, 828, 748, 527 cm^{-1}; MS (ESI): *m/z* 389 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{21}H_{24}O_7Na$ $(M + Na)^+$: 411.1414, Found, 411.1414.

(*Z*)-1,1-Diethyl 3-methyl 5-(thiophen-2-ylmethylene)cyclopent-3-ene-1,1,3-tricarboxylate (3n). Colourless liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.28 (d, J = 4.0 Hz, 1H), 7.20 (d, J = 4.0 Hz, 1H), 6.99–6.92 (m, 3H), 4.12 (q, J = 7.0 Hz, 4H), 3.77 (s, 3H), 3.44 (d, J = 2.0 Hz, 2H), 1.13 (t, J = 7.0 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.9, 164.6, 144.8, 140.6, 138.6, 133.8, 129.6, 127.46, 127.4, 125.0, 62.0, 61.4, 51.6, 43.5, 13.6; IR (KBr): 2983, 1728, 1592, 1437, 1357, 1257, 1182, 1091, 1059, 858, 755, 704, 499 cm^{-1}; MS (ESI): *m/z* 387 $(M + Na)^+$; HRMS (ESI): *m/z* calcd for $C_{18}H_{20}O_6NaS$ $(M + Na)^+$: 387.0878, found: 387.0879.

(*Z*)-Methyl 4-ethyl-4-nitro-3-(4-nitrobenzylidene)cyclopent-1-enecarboxylate (3o). Pale yellow liquid, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 8.20 (d, J = 8.3 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.14 (s, 1H), 7.05 (s, 1H), 3.83 (s, 3H), 3.36 (d, J = 18.8 Hz, 1H), 3.10 (d, J = 18.8 Hz, 1H), 2.22–2.07 (m, 1H), 1.95–1.74 (m, 1H), 0.77 (t, J = 7.3 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.0, 146.1, 143.3, 141.1, 137.1, 135.4, 129.2, 130.3, 123.7, 94.8, 52.1, 45.3, 27.0, 8.3; IR (KBr): 2921, 1710, 1518, 1342, 1219, 1085, 772, 1594, 1253; MS (ESI): *m/z* 333 $(M + H)^+$.

(*Z*)-Methyl 4-ethyl-3-(4-methoxybenzylidene)-4-nitrocyclopent-1-enecarboxylate (3p). Pale yellow liquid, ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.12 (t, J = 2.2 Hz, 1H), 7.05 (d, J = 9.0 Hz, 2H), 6.96 (s, 1H), 6.85 (d, J = 9.0 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 3.30 (dd, J = 18.8, 2.2 Hz, 1H), 3.10 (dd, J = 18.8, 2.2 Hz, 1H), 2.27–2.04 (m, 2H), 0.74 (t, J = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.5, 159.7, 145.4, 141.5, 133.5, 132.9, 130.2, 127.0, 114.0, 95.1, 55.2, 51.8, 45.9, 26.2, 8.46; IR (KBr): 3452, 2957, 1711, 1599, 1543, 1511, 1438, 1255, 1176, 1030, 831, 529; MS (ESI): *m/z* 318 $(M + H)^+$; HRMS (ESI): *m/z* calcd for $C_{17}H_{19}NNaO_5$ $(M + Na)^+$: 340.1161, Found: 340.1170.

(*Z*)-Methyl 4-ethyl-4-nitro-3-(thiophen-2-ylmethylene)cyclopent-1-enecarboxylate (3q). Light red liquid; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.37 (d, J = 4.8 Hz, 1H), 7.07 (s, 1H), 7.06 (s, 1H), 7.04–6.97 (m, 2H), 3.80 (s, 3H), 3.37 (d, J = 18.3 Hz, 1H), 3.18 (d, J = 18.3 Hz, 1H), 2.63–2.53 (m, 1H), 2.43–2.33 (m, 1H), 0.85 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 164.2, 145.1, 140.7, 137.2, 133.6, 130.8, 128.6, 128.0, 125.3, 95.2, 51.9, 46.2, 26.7, 8.5; IR (KBr): 2944, 1710, 1592, 1542, 1436, 1356, 1257, 1088, 707; MS (ESI): m/z 294 $(M + H)^+$.

(*Z*)-Methyl 2-benzylidene-1′-methyl-2′-oxospiro[cyclopent[3]-ene-1,3′-indoline]-4-carboxylate (3r). Yellow semi solid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.28–7.10 (m, 3H), 7.08–6.94 (m, 4H), 6.88 (s, 1H), 6.58–6.50 (m, 3H), 3.81 (s, 3H), 3.34 (dd, J = 17.5, 1.7 Hz, 1H), 2.94 (dd, J = 17.5, 1.7 Hz, 1H), 2.80 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 177.5, 164.9, 148.2, 143.7, 142.9, 137.0, 135.3, 130.8, 130.6, 128.7, 128.1, 127.8, 127.1, 126.9, 122.8, 122.3, 108.0, 68.0, 51.7, 45.4, 38.6; IR (KBr): 2927, 1713, 1609, 1467, 1437, 1349, 1251, 1205, 1127, 1085, 1025, 975, 921, 749, 698, 541, 486; MS (ESI): m/z 346 $(M + H)^+$; HRMS (ESI): m/z calcd for $C_{22}H_{20}NO_3$ $(M + H)^+$: 346.1437, found 346.1438.

(6*E*,11*E*)-9-Ethyl 11,7-dimethyl 9-cyanoheptadeca-6,11-dien-4,13-diyne-7,9,11-tricarboxylate (4a). Colourless liquid; ^{1}H NMR ($CDCl_3$, 400 MHz): δ 6.86 (t, J = 2.0 Hz, 2H), 4.19 (q, J = 7.1 Hz, 2H), 3.76 (s, 6H), 3.26 (d, J = 13.6 Hz, 2H), 3.13 (d, J = 13.6 Hz, 2H), 2.41 (dt, J = 7.3, 2.0 Hz, 4H), 1.62 (q, J = 7.3 Hz, 4H), 1.32 (t, J = 7.1 Hz, 3H), 1.02 (t, J = 7.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 168.0, 166.7, 135.3, 125.9, 117.1, 106.3, 77.1, 62.9, 52.0, 48.5, 35.3, 29.6, 21.9, 13.8, 13.5; IR (KBr): 2962, 2934, 2874, 2217, 2250, 1747, 1716, 1611, 1439, 1371, 1266, 1203, 1098, 1033, 855, 756 cm^{-1}; MS (ESI): m/z 459 $(M + NH_4)^+$; HRMS (ESI): m/z calcd for $C_{25}H_{35}N_2O_6$ $(M + NH_4)^+$: 459.2490, Found 459.2488.

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