RSC Advances

PAPER

View Article Online
View Journal | View Issue

Cite this: *RSC Adv.*, 2017, **7**, 49810

Fused multifunctionalized isoindole-1,3-diones *via* the coupled oxidation of imidazoles and tetraynes†

Qiong Hu,‡ Lidong Li,‡ Fei Yin, Hao Zhang, Yadong Hu, Baohua Liu and Yimin Hu *

Received 9th August 2017
Accepted 13th October 2017

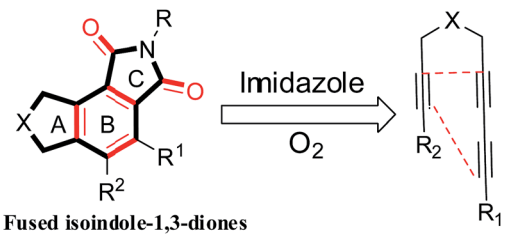
DOI: 10.1039/c7ra08817e

rsc.li/rsc-advances

The facile synthesis of fused multifunctionalized isoindole-1,3-diones by a hexadehydro-Diels–Alder domino reaction of various substituted tetraynes and imidazole derivatives is reported. The overall transformation involved the formation of three new C–C bonds and two new C_{aryl}–O bonds *via* intramolecular cyclization and intermolecular coupling oxidation reactions.

Introduction

Isoindole-1,3-dione derivatives, commonly known as phthalimides, represent an important class of biological and pharmaceutical compounds, including indole alkaloids.[1] Multifunctionalized isoindole-1,3-dione derivatives are widespread structural motifs in a plethora of different natural products.[2] They are usually synthesized by the condensation of a phthalic anhydride with primary amines. An efficient strategy to construct isoindole-1,3-dione building blocks is convenient for the preparation of multifunctionalized isoindole-1,3-dione cores,[3] and various synthetic methods have been documented in the literature.[4] Sheykhan reported a method to form two C–C bonds *via* consecutive activation of four C–H bonds in the reaction of maleimides/maleic anhydride with styrenes.[5] Bhanage presented a CO-free protocol for the synthesis of isoindole-1,3-diones.[6] Zhang reported the reaction of benzyne with *N*-substituted imidazoles to afford arylamines containing anthracene.[7] Zhang reported the cobalt-catalyzed carbonylation of C(sp^2)–H bonds with azodicarboxylate as the carbonyl source.[8] Although alkylarenes are generally thought to be relatively easy to oxygenate, the development of a selective, high-yield reaction to convert isoindole-1,3-dione into fused highly substituted isoindole-1,3-dione derivatives remains challenge.[9] The skeletal representation of the fused heterocyclic ring system shown in Scheme 1 depicts the common planes in the A–B and B–C ring system.[10] Surprisingly, the benzannulation of tetraynes and imidazole derivatives in a green, waste-free transformation with a high atom economy in toluene yielded isoindole-1,3-dione derivatives as the major product. Compared with ordinary isoindole-1,3-dione derivatives, tricyclic isoindole-1,3-dione derivatives prepared in the present report have multiple rings, complex and variable structures, and a broad potential for use in chemical production and clinical medicine.



Scheme 1 Target multifunctionalized isoindole-1,3-dione core structures.

Here, we report the reaction of tetraynes with imidazole derivatives and oxygen to produce various multifunctionalized tricyclic isoindole-1,3-diones in good to excellent yields in the absence of metals, catalysts, and bases. This approach did not require directing groups and can produce highly substituted isoindole-1,3-diones in good to excellent yields *via* a hexadehydro-Diels–Alder (HDDA) reaction[11] and intermolecular oxygen-coupling oxidation (**1a–g**) (Table 1). Thus, this method provides a direct, efficient, and economical way of constructing tricyclic isoindole-1,3-dione compounds.

Results and discussion

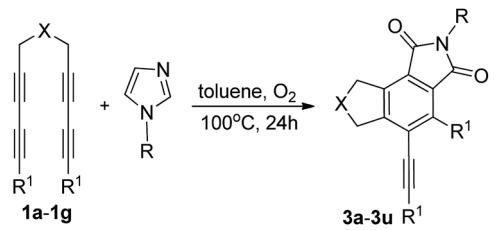
The reaction of tetrayne **1a** with *N*-ethylimidazole was used as a test experiment (Table 1). Several phenomena were observed when the experimental conditions were modified. The efficiency of the reaction was greatly enhanced by increasing the reaction temperature to 100 °C. An investigation of various catalysts indicated that palladium(II) acetate was the most effective catalytic system in the cross-coupling reactions; however, the reaction proceeded well without metal catalysts or other

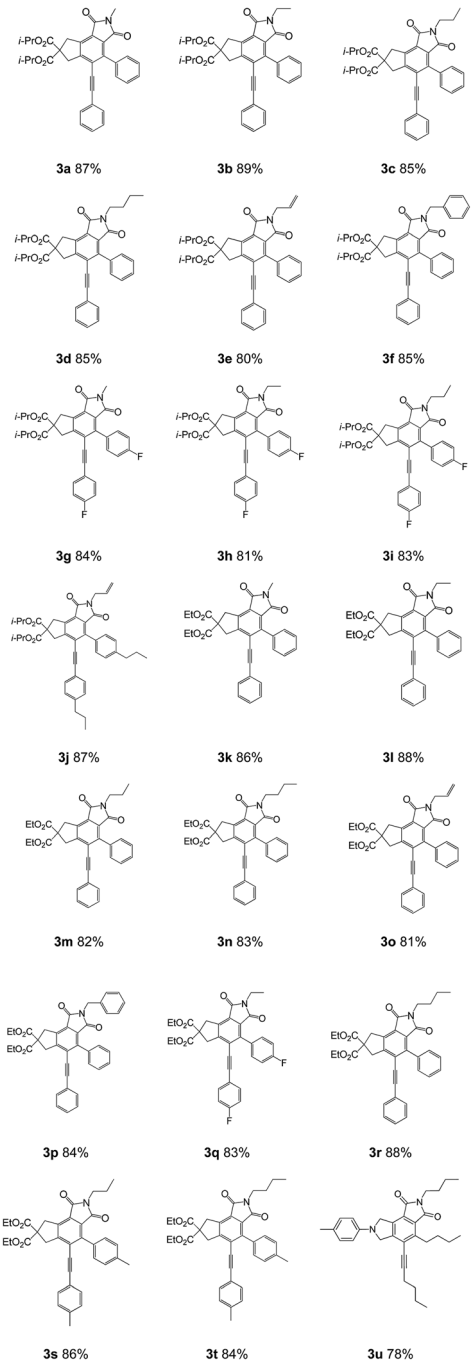
Laboratory of Functional Molecular Solids, Ministry of Education, Anhui Key Laboratory of Molecular-Based Materials, School of Chemistry and Materials Science, Anhui Normal University, Wuhu, Anhui 241000, China. E-mail: yiminhu@ahnu.edu.cn

† Electronic supplementary information (ESI) available: Experimental procedures and characterization of all new compounds. CCDC 1520526 and 992692. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra08817e

‡ Q. H. and L. L. contributed equally to this work.

Table 1 One-pot formation of fused isoindole-1,3-diones[a,b]





[a] Reaction conditions: **1a–g** (1.0 equiv.), imidazole (1.1 equiv.), toluene (2 mL), 100 °C. [b] Yield of the isolated product after flash column chromatography.

additives, such as bases. In addition, the reaction also worked well if not protected. But we could hardly get any product under oxygen-free conditions. By blowing oxygen through the system the best results were obtained. Thus, the following standard reaction conditions were used for the subsequent experiments: 1 equiv. of **1** was reacted with 1.1 equiv. of *N*-ethylimidazole vent with O_2 (1 atm) at 100 °C for 24 h.

Illustrative examples of the scope of this study are presented in Table 1. Various substituted tetraynes were compatible with this reaction. Compounds ranging from diisopropyl 2-methyl-1,3-dioxo-4-phenyl-5-(phenylethynyl)-2,3,6,8-tetrahydrocyclopenta[*e*] isoindole-7,7(1*H*)-dicarboxylate to 2,4-dibutyl-5-(hex-1-yn-1-yl)-7-(*p*-tolyl)-7,8-dihydropyrrolo[3,4-*e*]isoindole-1,3(2*H*,6*H*)-dione were readily isolated with good to excellent yields from various substituted tetraynes. The substituents in the aryl ring of the tetraynes could be either electron donating or electron withdrawing. For instance, methyl, *n*-propyl and fluoro groups were all acceptable. Substituents, such as methyl, ethyl, propyl, *n*-butyl, benzyl, and allyl, in the *N*-substituted imidazoles were also suitable for the reaction. Reactions of different tetraynes with various substituted imidazoles and oxygen afforded the 4-phenyl-5-(phenylethynyl)-7,8-dihydrocyclopenta[*e*]isoindole-1,3(2*H*,6*H*)-dione cores in excellent yields (for instance, Table 1 indicates that **3a**, **3b**, **3j**, **3k**, **3l**, **3r**, and **3s** had yields up to 85%). Compound **3b** was produced in the highest isolated yield (89%) among the examined products. Compounds **3e**, **3h**, **3i**, **3m**, **3o**, **3q**, and **3t** were also obtained in good yields between 80-85%.

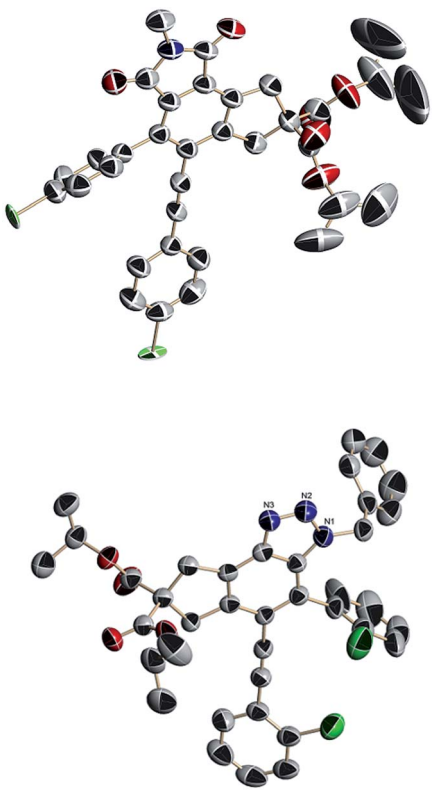
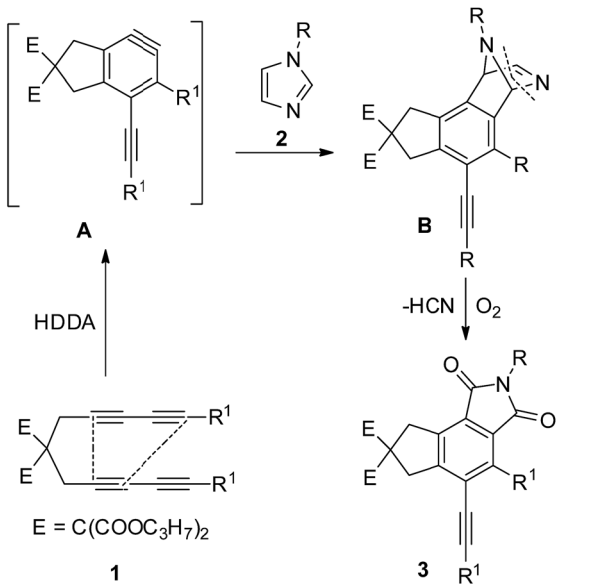


Fig. 1 Molecular structure of the fused isoindole-1,3-dione **3g** (top) and the molecular structure of the trapped intermediate **4a** (bottom).



Scheme 2 Tentative mechanism for the HDDA annulation to produce tricyclic isoindole-1,3-diones **3**.

These results demonstrate the potential of the direct functionalization of existing unsaturated hydrocarbons with substituted imidazoles and oxygen for the synthesis of multifunctionalized cyclopenta[*e*]isoindole-1,3(2*H*,6*H*)-diones. Using another substrate, alkyl-substituted *N*-tetrayne (**3u**, 78%), instead of alkyl-substituted *C*-tetrayne also generated the corresponding product in good yield.

All the resulting tricyclic isoindole-1,3-dione compounds were verified *via* various spectroscopic techniques (^{1}H NMR, ^{13}C NMR, IR spectroscopy and/or HRMS). The molecular structures and relative configurations of **3g** and **4a** were confirmed unambiguously by X-ray diffraction (Fig. 1). Further details are provided in the ESI.†[12]

Scheme 2 indicates the sequence of steps involved in the synthesis of highly substituted tricyclic isoindole-1,3-diones by a cascade HDDA reaction, the formation of an intermolecular cycloaddition and an oxidation by oxygen. A HDDA reaction of tetrayne **1** produces the aryne[13] intermediate **A**, which subsequently reacts with the imidazole derivative by a formal [4 + 2] cycloaddition to produce the unstable bridge-ring intermediate **B**.[14] An elimination reaction occurs on the C–N double bond in **B**, which was easy to be oxidized to take off HCN for isoindolones skeleton structure, followed by an oxidation reaction by oxygen to afford the final product **3**. Fortunately, the aryne-trapped[15] product was isolated by adding a small quantity of RN_3 to the reaction system, and this product was characterized by X-ray crystallography (Fig. 1, bottom, **4a**).

Conclusions

In conclusion, we developed a convenient and general method for synthesizing highly substituted tricyclic isoindole-1,3-diones *via* the reaction of tetraynes with imidazoles and oxygen. The formation of C–C and C=O bonds involved a cascade HDDA reaction, the formation of an intermolecular imidazole cycloaddition and an oxygen-coupling oxidation. This approach required no metals, catalysts, additives, or directing groups and could apply to a range of substrates. The reaction also exhibited excellent regioselectivity, producing all types of highly substituted tricyclic isoindole-1,3-diones under mild conditions in good to excellent yields. The primary evaluation of the photoluminescence property of the novel extended p-systems indicated that these heteroarenes could be potentially used in the field of optoelectronic materials.

Experiment

General information

All the catalytic reactions were performed under an argon atmosphere using the oven-dried Schlenk flask. The chemicals were purchased from Alfa Aesar and Acros Chemicals. All solvents and materials were pre-dried, redistilled or recrystallized before use. ^{1}H NMR (300 MHz) and ^{13}C NMR (125 MHz) spectra were recorded on a Bruker Avance 300 spectrometer with $CDCl_3$ as the solvent. Chemical shifts are reported in ppm by assigning TMS resonance in the ^{1}H NMR spectra as 0.00 ppm and $CDCl_3$ resonance in the ^{13}C spectra as 77.0 ppm. All coupling constants (*J* values) were reported in Hertz (Hz). Column chromatography was performed on silica gel 300–400 mesh. Melting points were determined using a Gallenkamp melting point apparatus and are uncorrected. The FT-IR spectra were recorded from KBr pellets or thin film from $CHCl_3$ on the NaCl window in the 4000–400 cm^{-1} ranges on a Nicolet 5DX spectrometer. All HRMS spectra were record using EI at 70 eV. X-ray crystallography diffraction data of **3g** and **4a** were collected at room temperature with a Bruker SMART Apex CCD diffractometer with Mo-Kα radiation (λ = 0.71073 Å) with a graphite monochromator using the ω-scan mode. Data reductions and absorption corrections were performed with SAINT and SADABS software, respectively. The structure was solved by direct methods and refined on F^2 by full-matrix least squares using SHELXTL. All non-hydrogen atoms were treated anisotropically. The positions of hydrogen atoms were generated geometrically.

General procedures

Typical experimental procedure: tetraynes (1.0 equiv.), imidazole (1.1 equiv.), were added to toluene (2 mL), the reaction was vented 3 times to eliminate argon which was connected to a tank of O_2 and pressurized to 1 atm, the mixture was stirred at room temperature for half an hour and then heated at 100 °C for 10 hours. The reaction mixture was cooled to room temperature, and the solvent was evaporated *in vacuo*. The residue was purified by preparative thin-layer chromatography (TLC) on silica gel with the appropriate mixture of petroleum ether and ethyl acetate to give the fused multifunctionalized isoindole-1,3-diones.

Diisopropyl 2-methyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3a). White solid, 478 mg (87% yield); m.p. 210–211 °C; FT-IR (KBr): 3481, 2983, 2360, 1701, 1654, 1433, 1382, 1269, 1101,

910, 688, 486 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.36–7.16 (m, 8H), 5.09 (dt, J = 12.3, 6.1 Hz, 2H), 3.97 (s, 2H), 3.80 (s, 2H), 3.09 (s, 3H), 1.28 (d, J = 6.1 Hz, 12H); ^{13}C NMR (75 MHz, C_6D_6) δ 170.63, 150.67, 137.13, 134.84, 131.66, 129.81, 129.04, 128.43, 127.59, 126.31, 125.39, 122.34, 100.42, 85.75, 77.48, 77.06, 76.63, 69.80, 59.96, 40.85, 38.94, 23.83, 21.57 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{34}H_{31}NO_6$: 550.2220; found: 551.2251.

Diisopropyl 2-ethyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3b). White solid, 501 mg (89% yield); m.p. 220–221 °C; FT-IR (KBr): 3456, 2980, 2208, 1766, 1710, 1442, 1400, 1261, 1190, 1101, 908, 758, 688, 493 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.26 (dd, J = 13.4, 7.5 Hz, 8H), 5.10 (dt, J = 12.4, 6.2 Hz, 2H), 3.97 (s, 1H), 3.80 (s, 1H), 3.65 (dd, J = 14.1, 6.9 Hz, 4H), 1.39–1.10 (m, 15H); ^{13}C NMR (75 MHz, MeOD) δ 170.67, 167.45, 150.61, 141.30, 137.09, 134.86, 131.66, 129.84, 129.03, 128.41, 127.70, 126.35, 125.34, 122.36, 100.35, 85.79, 77.71, 76.76, 76.62, 69.79, 59.94, 40.84, 38.92, 32.84, 21.57, 13.87 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{35}H_{33}NO_6$: 564.2375; found: 565.2407.

Diisopropyl 1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2-propyl-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3c). White solid, 491 mg (85% yield); m.p. 164–165 °C; FT-IR (KBr): 3431, 2980, 2935, 2360, 2341, 1718, 1708, 1400, 1259, 1192, 1101, 908, 881, 756, 688 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 6.6 Hz, 4H), 7.45 (d, J = 13.2 Hz, 2H), 7.26 (dd, J = 13.5, 6.2 Hz, 4H), 5.20–5.01 (m, 2H), 3.98 (s, 2H), 3.81 (s, 2H), 3.55 (t, J = 6.4 Hz, 2H), 1.64 (d, J = 6.9 Hz, 2H), 1.28 (d, J = 5.0 Hz, 12H), 0.95 (dt, J = 30.3, 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.78, 167.90, 150.75, 141.42, 137.21, 134.99, 131.77, 131.07, 129.97, 129.50, 129.12, 128.52, 128.34, 127.75, 127.36, 126.80, 122.51, 85.92, 77.39, 77.17, 77.01, 69.88, 69.42, 60.08, 45.50, 41.41, 40.99, 39.69, 39.06, 22.82, 21.93, 21.68, 11.70, 11.48 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{36}H_{35}NO_6$: 577.2504; found: 577.6726.

Diisopropyl 2-butyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3d). White solid, 503 mg (85% yield); m.p. 187–188 °C; FT-IR (KBr): 3466, 2980, 2939, 2875, 2374, 1708, 1400, 1708, 1259, 1190, 1107, 921, 752, 684, 478 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.26 (dd, J = 13.2, 7.4 Hz, 8H), 5.10 (dt, J = 12.3, 6.1 Hz, 2H), 3.97 (s, 1H), 3.80 (s, 1H), 3.59 (t, J = 7.1 Hz, 4H), 1.67–1.51 (m, 2H), 1.28 (d, J = 6.2 Hz, 14H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 170.68, 167.79, 167.52, 150.62, 141.29, 137.08, 134.86, 131.66, 129.86, 129.03, 128.42, 127.66, 126.30, 125.34, 122.37, 100.35, 85.82, 77.50, 77.08, 76.65, 69.79, 59.93, 40.86, 38.93, 37.78, 30.56, 21.58, 20.15, 13.66 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{37}H_{37}NO_6$: 592.2687; found: 593.2721.

Diisopropyl 2-allyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3e). White solid, 460 mg (80% yield); m.p. 205–206 °C; FT-IR (KBr): 3448, 2980, 2924, 2360, 2341, 2208, 1766, 1712, 1419, 1390, 1282, 1261, 1192, 1101, 1055, 933, 918, 756, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.31–7.17 (m, 8H), 5.82 (ddd, J = 16.0, 10.0, 5.0 Hz, 1H), 5.28–5.02 (m, 2H), 4.20 (d, J = 5.0 Hz, 4H), 3.98 (s, 2H), 3.81 (s, 2H), 1.31–1.25 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.75, 167.37, 167.06, 150.89, 141.60, 137.39, 134.92, 131.75, 129.95, 129.15, 128.53, 127.76, 126.31, 125.65, 122.47, 118.18, 100.61, 85.88, 77.39, 77.05, 76.88, 69.90, 60.06, 41.00, 40.23, 39.06, 21.67 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{36}H_{33}NO_6$: 575.2394; found: 575.6586.

Diisopropyl 2-benzyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3f). White solid, 531 mg (85% yield); m.p. 123–125 °C; FT-IR (KBr): 3446, 2978, 2926, 2854, 1734, 1701, 1490, 1386, 1340, 1257, 1190, 1103, 1068, 910, 756, 688, 486, 459 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.81–7.16 (m, 15H), 5.08 (dd, J = 7.8, 4.6 Hz, 2H), 4.75 (s, 1H), 4.44 (s, 1H), 3.97 (s, 2H), 3.80 (s, 2H), 1.29–0.82 (m, 12H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.16, 170.72, 169.62, 150.90, 132.71, 132.00, 131.64, 130.10, 129.15, 128.92, 128.91, 126.79, 127.83, 127.74, 127.83, 126.79, 127.74, 126.95, 126.31, 126.05, 125.68, 122.04, 77.28, 77.14, 76.88, 69.87, 69.41, 60.06, 41.81, 40.98, 39.06, 29.81, 21.65, 21.38 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{40}H_{35}NO_6$: 625.2519; found: 625.7156.

Diisopropyl 4-(4-fluorophenyl)-5-(2-(4-fluorophenyl)ethynyl)-2-methyl-1,3-dioxo-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3g). White solid, 491 mg (84% yield); m.p. 234–235 °C; FT-IR (KBr): 3446, 2981, 2360, 1722, 1629, 1382, 1269, 1101, 833, 484 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42 (dd, J = 19.0, 8.2 Hz, 4H), 7.35–7.22 (m, 2H), 7.16 (d, J = 8.2 Hz, 2H), 5.09 (dt, J = 12.2, 6.0 Hz, 2H), 3.97 (s, 2H), 3.77 (s, 2H), 3.09 (s, 3H), 1.28 (d, J = 6.1 Hz, 12H); ^{13}C NMR (75 MHz, C_6D_6) δ 170.53, 167.42, 150.99, 137.56, 135.37, 134.67, 133.12, 132.81, 131.30, 128.88, 127.89, 126.55, 124.86, 120.55, 86.30, 77.46, 77.04, 76.62, 69.90, 59.94, 40.81, 38.92, 23.90, 21.56 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{34}H_{29}F_2NO_6$: 586.2033; found: 587.2065.

Diisopropyl 2-ethyl-4-(4-fluorophenyl)-5-(2-(4-fluorophenyl)ethynyl)-1,3-dioxo-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3h). White solid, 485 mg (81% yield); m.p. 223–225 °C; FT-IR (KBr): 3448, 2981, 2933, 1764, 1726, 1708, 1506, 1436, 1400, 1350, 1259, 1232, 1190, 1101, 1053, 840, 761, 520 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.49–7.39 (m, 4H), 7.30–7.10 (m, 2H), 6.99 (t, J = 8.2 Hz, 2H), 5.09 (dt, J = 12.1, 6.0 Hz, 2H), 3.96 (s, 2H), 3.77 (s, 2H), 3.65 (dd, J = 13.7, 6.7 Hz, 2H), 1.26 (t, J = 8.8 Hz, 12H), 1.20 (t, J = 7.0 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.72, 167.46, 150.86, 140.13, 137.46, 133.72, 131.91, 128.02, 126.54, 125.29, 116.06, 115.89, 114.87, 114.68, 99.52, 85.44, 77.40, 77.15, 76.89, 69.97, 60.07, 40.93, 39.02, 33.00, 21.66, 13.94 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{35}H_{31}F_2NO_6$: 599.2124; found: 599.6244.

Diisopropyl 4-(4-fluorophenyl)-5-(2-(4-fluorophenyl)ethynyl)-1,3-dioxo-2-propyl-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3i). White solid, 509 mg (83% yield); m.p. 184–186 °C; FT-IR (KBr): 3448, 2978, 2937, 2210, 1718, 1602, 1458, 1436, 1400, 1382, 1344, 1269, 1193, 1155, 1101, 1060, 906, 881, 839, 756, 657, 524, 399 cm^{-1}; $_1H$ NMR (300 MHz, $CDCl_3$) δ 7.51–7.37 (m, 2H), 7.29–7.11 (m, 4H), 7.05–6.94 (m, 2H), 5.09 (dd, J = 7.7, 4.5 Hz, 2H), 3.97 (s, 2H), 3.78 (s, 2H), 3.56 (d, J = 7.7 Hz, 2H), 1.64 (d, J = 7.0 Hz, 2H), 1.28 (dd, J = 5.8, 3.1 Hz, 12H), 0.90 (dd, J = 8.8, 5.8 Hz, 3H); $_{13}C$ NMR (126 MHz, $CDCl_3$) δ 170.71, 167.73, 150.87, 137.47, 133.69, 131.88, 130.78, 127.93, 125.30, 118.43, 115.97, 114.76, 77.38, 77.00, 76.76, 76.41, 69.95, 60.07, 40.96,

39.74, 39.04, 21.92, 21.66, 11.46 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{36}H_{33}F_2NO_6$: 613.2313; found: 613.6587.

Diisopropyl 2-allyl-1,3-dioxo-4-(4-propylphenyl)-5-(2-(4-propylphenyl)ethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3j). White solid, 574 mg (87% yield); m.p. 138–139 °C; FT-IR (KBr): 3431, 2981, 2374, 1724, 1674, 1394, 1259, 1101, 920, 677, 480 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 21H), 7.27 (d, J = 10.9 Hz, 2H), 7.10 (dd, J = 16.7, 7.7 Hz, 4H), 5.82 (d, J = 6.5 Hz, 1H), 5.30–5.03 (m, 2H), 4.20 (d, J = 4.9 Hz, 4H), 3.96 (s, 2H), 3.79 (s, 2H), 2.68 (t, J = 7.2 Hz, 2H), 2.56 (t, J = 7.3 Hz, 2H), 1.73 (dd, J = 14.4, 7.2 Hz, 2H), 1.60 (dd, J = 15.8, 8.4 Hz, 2H), 1.28 (d, J = 6.1 Hz, 12H), 0.95 (dt, J = 25.7, 7.2 Hz, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 170.69, 167.25, 150.48, 144.13, 142.88, 141.64, 137.00, 132.09, 131.63, 129.77, 128.52, 127.70, 119.62, 118.00, 100.84, 85.59, 77.47, 77.04, 76.62, 69.76, 59.91, 40.88, 40.09, 38.93, 38.00, 24.43, 21.56, 13.83 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{42}H_{45}NO_6$: 660.3314; found: 661.3346.

Diethyl 2-methyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3k). White solid, 448 mg (86% yield); m.p. 195–196 °C; FT-IR (KBr): 3462, 1708, 1637, 1425, 1382, 1261, 1070, 761, 692, 472 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 2H), 7.26 (dd, J = 12.8, 7.0 Hz, 8H), 4.27 (dd, J = 14.0, 6.9 Hz, 4H), 4.01 (s, 2H), 3.84 (s, 2H), 3.09 (s, 3H), 1.30 (t, J = 7.0 Hz, 6H); ^{13}C NMR (75 MHz, C_6D_6) δ 171.07, 167.76, 150.53, 141.36, 136.97, 134.80, 131.67, 129.81, 129.08, 128.45, 127.60, 126.34, 122.29, 100.48, 85.74, 77.49, 77.07, 76.64, 62.24, 59.92, 40.90, 38.97, 23.84, 14.07 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{27}NO_6$: 522.1914; found: 523.1945.

Diethyl 2-ethyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3l). White solid, 471 mg (88% yield); m.p. 178–180 °C; FT-IR (KBr): 2926, 2854, 2360, 2341, 1734, 1707, 1637, 1400, 1384, 1257, 1186, 1105, 754, 704, 688, 478 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 4H), 7.34–7.17 (m, 6H), 4.33–4.17 (m, 4H), 4.01 (s, 2H), 3.83 (s, 2H), 3.67 (dt, J = 21.4, 7.1 Hz, 2H), 1.24 (ddd, J = 31.7, 17.1, 10.0 Hz, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.20, 131.77, 129.94, 129.14, 128.51, 127.69, 77.25, 77.11, 77.10, 76.87, 62.30, 41.02, 39.09, 32.96, 32.03, 29.63, 29.39, 28.78, 27.32, 22.79, 14.15, 13.95 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{29}NO_6$: 535.2334; found: 535.5987.

Diethyl 1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2-propyl-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3m). White solid, 450 mg (82% yield); m.p. 177–178 °C; FT-IR (KBr): 3446, 2968, 2935, 2875, 1759, 1734, 1707, 1440, 1400, 1367, 1253, 1184, 1087, 1068, 866, 744, 688, 520, 476 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (s, 4H), 7.26 (dd, J = 13.0, 6.2 Hz, 6H), 4.27 (dd, J = 14.0, 6.9 Hz, 4H), 4.02 (s, 2H), 3.84 (s, 2H), 3.56 (t, J = 7.1 Hz, 2H), 1.64 (dd, J = 14.2, 7.1 Hz, 2H), 1.30 (t, J = 7.0 Hz, 6H), 0.90 (t, J = 7.3 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.13, 167.66, 150.50, 141.32, 136.92, 134.78, 131.67, 129.86, 129.08, 128.44, 127.59, 126.30, 125.37, 122.31, 100.40, 85.79, 77.50, 77.07, 76.65, 62.25, 59.87, 40.89, 39.59, 38.96, 21.85, 14.09, 11.41 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{34}H_{31}NO_6$: 549.2223; found: 549.6165.

Diethyl 2-butyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3n). White solid, 467 mg (83% yield); m.p. 185–186 °C; FT-IR (KBr): 3446, 2960, 2935, 2873, 1757, 1730, 1707, 1440, 1398, 1363, 1278, 1253, 1186, 1159, 1089, 1068, 933, 864, 744, 688, 522, 478 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 7.4 Hz, 2H), 7.45 (d, J = 13.2 Hz, 4H), 7.32–7.20 (m, 4H), 4.26 (p, J = 6.8 Hz, 4H), 4.02 (s, 2H), 3.84 (s, 2H), 3.59 (t, J = 7.2 Hz, 2H), 1.59 (dt, J = 15.0, 7.4 Hz, 2H), 1.32 (dd, J = 14.3, 7.2 Hz, 8H), 0.89 (dd, J = 15.4, 8.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.21, 167.86, 167.57, 150.60, 141.44, 137.03, 134.96, 131.78, 129.97, 129.15, 128.52, 127.80, 126.45, 125.49, 122.47, 100.53, 85.91, 77.40, 77.15, 76.89, 62.31, 60.03, 41.03, 39.09, 37.90, 30.67, 20.25, 14.21, 13.95 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{35}H_{33}NO_6$: 563.2376; found: 563.6448.

Diethyl 2-allyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3o). White solid, 443 mg (81% yield); m.p. 196–197 °C; FT-IR (KBr): 3448, 2987, 2926, 2360, 2341, 1761, 1734, 1707, 1436, 1394, 1255, 1184, 1091, 931, 862, 758, 688, 474 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (s, 4H), 7.32–7.18 (m, 6H), 5.82 (ddd, J = 15.9, 11.0, 5.8 Hz, 1H), 5.19 (dd, J = 21.2, 13.6 Hz, 2H), 4.24 (dt, J = 12.4, 6.4 Hz, 6H), 4.02 (s, 2H), 3.84 (s, 2H), 1.30 (t, J = 7.1 Hz, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.19, 167.20, 150.76, 141.63, 137.22, 134.87, 131.74, 129.95, 129.18, 128.54, 127.78, 126.33, 125.68, 122.43, 118.18, 100.67, 85.86, 77.39, 77.14, 76.88, 62.32, 60.03, 41.05, 40.23, 39.10, 14.16 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{34}H_{29}NO_6$: 547.2328; found: 547.6339.

Diethyl 2-benzyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3p). White solid, 502 mg (84% yield); m.p. 124–125 °C; FT-IR (KBr): 3448, 2956, 2924, 2852, 1718, 1707, 1637, 1560, 1396, 1259, 1078, 756, 690, 472 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53–7.19 (m, 15H), 4.75 (s, 2H), 4.26 (dd, J = 14.2, 7.1 Hz, 4H), 4.01 (s, 2H), 3.83 (s, 2H), 1.36–1.21 (m, 6H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.16, 167.50, 167.10, 150.77, 141.64, 137.25, 136.53, 134.90, 132.72, 131.78, 131.54, 129.98, 129.45, 129.31, 129.10, 129.00, 128.97, 128.82, 128.55, 128.21, 127.79, 127.69, 127.52, 126.34, 125.70, 122.42, 100.69, 85.87, 77.40, 77.15, 76.90, 62.31, 60.03, 41.71, 41.04, 39.10, 32.04, 29.82, 29.52, 27.33, 22.81, 21.91, 20.33, 14.16 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{38}H_{31}NO_6$: 597.2227; found: 597.6606.

Diethyl 2-ethyl-4-(4-fluorophenyl)-5-(2-(4-fluorophenyl)ethynyl)-1,3-dioxo-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3q). White solid, 474 mg (83% yield); m.p. 198–199 °C; FT-IR (KBr): 3446, 2374, 1718, 1637, 1500, 1400, 1085, 837, 489 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46 (d, J = 5.6 Hz, 2H), 7.33–7.12 (m, 4H), 7.01 (d, J = 8.3 Hz, 2H), 4.26 (dd, J = 14.0, 6.9 Hz, 4H), 4.00 (s, 2H), 3.81 (s, 2H), 3.65 (d, J = 7.0 Hz, 2H), 1.30 (t, J = 6.8 Hz, 6H), 1.21 (t, J = 6.9 Hz, 3H); ^{13}C NMR (75 MHz, C_6D_6) δ 214.59, 214.32, 191.40, 191.13, 171.02, 167.38, 164.67, 161.34, 150.60, 140.05, 137.17, 133.62, 131.79, 130.62, 130.35, 128.44, 128.44, 124.71, 125.07, 124.71, 118.38, 117.11, 115.87, 115.20, 115.09, 114.81, 114.52, 99.46, 85.31, 79.24, 78.98, 77.73, 76.81, 76.59, 62.24, 59.91, 40.87, 38.94, 34.47, 34.21, 32.90, 13.94 ppm; HRMS (APCI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{27}F_2NO_6$: 572.1874; found: 573.1906.

Diethyl 2-butyl-1,3-dioxo-4-phenyl-5-(2-phenylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3r). White solid, 496 mg (88% yield); m.p. 153–154 °C; FT-IR (KBr): 3446, 2935, 2374, 1710, 1602, 1508, 1398, 1236, 1087, 835, 669,

468 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43 (d, J = 5.3 Hz, 2H), 7.22 (dt, J = 17.7, 12.2 Hz, 4H), 7.00 (t, J = 8.2 Hz, 2H), 4.27 (dd, J = 13.9, 6.9 Hz, 4H), 4.01 (s, 2H), 3.81 (s, 2H), 3.59 (t, J = 7.0 Hz, 2H), 1.67–1.51 (m, 2H), 1.30 (t, J = 6.9 Hz, 8H), 0.90 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, DMSO) δ 171.03, 167.60, 167.34, 164.67, 161.47, 161.21, 150.61, 140.04, 137.16, 133.63, 131.80, 131.00, 130.61, 127.85, 126.40, 125.19, 118.43, 118.16, 116.39, 116.17, 115.87, 115.08, 114.67, 99.45, 85.31, 77.44, 76.83, 76.59, 62.24, 59.89, 52.54, 52.27, 40.88, 38.39, 37.38, 36.75, 30.55, 20.02, 14.05, 13.62 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{35}H_{33}NO_6$: 600.2186; found: 601.2217.

Diethyl 1,3-dioxo-2-propyl-4-*p*-tolyl-5-(2-*p*-tolylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3s). White solid, 496 mg (86% yield); m.p. 175–177 °C; FT-IR (KBr): 2360, 2341, 1734, 1701, 1627, 1400, 1257, 1186, 1105, 1085, 1085, 1051, 817, 759, 659, 474 cm^{-1}; ^1H NMR (300 MHz, C_6D_6) δ 7.37 (d, J = 7.7 Hz, 2H), 7.27 (d, J = 10.2 Hz, 2H), 7.13 (dd, J = 17.2, 7.7 Hz, 4H), 4.26 (dd, J = 14.0, 6.9 Hz, 4H), 4.00 (s, 2H), 3.82 (s, 2H), 3.55 (t, J = 7.0 Hz, 2H), 2.44 (s, 3H), 2.34 (s, 3H), 1.63 (dd, J = 14.1, 7.1 Hz, 2H), 1.30 (t, J = 7.0 Hz, 6H), 0.89 (t, J = 7.2 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.15, 167.73, 150.39, 141.32, 139.35, 138.20, 136.62, 131.65, 129.82, 129.13, 128.25, 127.96, 124.07, 124.71, 124.71, 119.38, 100.66, 98.74, 96.92, 98.74, 70.78, 76.59, 76.59, 62.17, 59.87, 40.94, 39.55, 38.96, 22.11, 20.90, 14.05, 11.38 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{36}H_{35}NO_6$: 577.2514; found: 577.6746.

Diethyl 2-butyl-1,3-dioxo-4-*p*-tolyl-5-(2-*p*-tolylethynyl)-2,3-dihydrocyclopenta[*e*]isoindole-7,7(1*H*,6*H*,8*H*)-dicarboxylate (3t). White solid, 497 mg (84% yield); m.p. 157–159 °C; FT-IR (KBr): 3446, 2933, 2868, 1734, 1707, 1500, 1438, 1398, 1251, 1184, 1151, 1082, 1049, 933, 858, 813, 761, 731, 663, 509 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37 (d, J = 7.6 Hz, 2H), 7.27 (d, J = 10.7 Hz, 2H), 7.12 (dd, J = 17.0, 7.7 Hz, 4H), 4.26 (dd, J = 13.9, 6.9 Hz, 4H), 4.00 (s, 2H), 3.79 (m, 2H), 3.58 (t, J = 7.0 Hz, 2H), 2.44 (s, 3H), 2.34 (s, 3H), 1.59 (m, 2H), 1.30 (t, J = 6.9 Hz, 8H), 0.89 (t, J = 7.1 Hz, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 171.25, 167.93, 167.71, 150.49, 141.43, 139.45, 138.29, 136.73, 131.87, 131.69, 129.93, 129.23, 128.37, 126.29, 125.72, 119.51, 100.77, 85.58, 77.39, 77.13, 76.88, 62.27, 60.00, 41.06, 39.08, 37.87, 30.66, 21.65, 20.25, 14.16, 13.75 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{37}H_{37}NO_6$: 591.2651; found: 591.6923.

2,4-Dibutyl-5-(hex-1-ynyl)-7-*N*-*p*-tolyl-7,8-dihydrocyclopenta[*e*]-isoindole-1,3(2*H*,6*H*)-dione (3u). White solid, 389 mg (78% yield); m.p. 129–130 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.80 (d, J = 7.9 Hz, 2H), 7.36–7.27 (m, 1H), 7.26 (s, 1H), 4.84 (s, 2H), 4.64 (s, 2H), 3.65–3.52 (m, 2H), 3.15 (d, J = 6.2 Hz, 2H), 2.57–2.44 (m, 2H), 2.40 (s, 3H), 1.65–1.24 (m, 16H), 1.01–0.83 (m, 9H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 168.51, 167.33, 146.00, 144.81, 144.03, 133.76, 130.86, 130.06, 128.02, 125.33, 124.79, 124.45, 103.64, 102.72, 77.24, 76.81, 75.66, 75.42, 53.91, 52.76, 37.84, 32.64, 30.67, 29.13, 22.99, 21.87, 21.63, 19.89, 19.59, 14.29, 12.96 ppm; HRMS (APCI): m/z $[M + H]^+$ calcd for $C_{31}H_{38}N_2O_2$: 470.2905; found: 470.6516.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

The authors thank the National Natural Science Foundation of China (21572002, 21272005), The Research Culture Funds of Anhui Normal University (2016XJJ020), and Department of Human Resources of Anhui Province for financial support.

Notes and references

1 For reviews on this topic, see: (*a*) B. Baire, D. W. Niu, P. H. Willoughby, B. P. Woods and T. R. Hoye, *Nat. Protoc.*, 2013, **8**, 501–509; (*b*) S. W. M. Crossley and R. A. Shenvi, *Chem. Rev.*, 2015, **115**, 9465–9531; (*c*) S. Ziegler, V. Pries, C. Hedberg and H. Waldmann, *Angew. Chem., Int. Ed.*, 2013, **52**, 2744–2792.

2 For reviews on this topic, see: (*a*) M. S. Chen and M. C. A. White, *Science*, 2007, **318**, 783–787; (*b*) S. P. Ross and T. R. Hoye, *Nat. Chem.*, 2017, **9**, 523–530; (*c*) H. Pellissier and H. Clavier, *Chem. Rev.*, 2014, **114**, 2275–2823.

3 For selected examples of syntheses of isoindole-1,3-diones derivatives, see: (*a*) A. R. Katritzky and S. Rachwal, *Chem. Rev.*, 2011, **111**, 7063–7120; (*b*) J. R. Kong and M. J. Krische, *J. Am. Chem. Soc.*, 2006, **128**, 16040–16041; (*c*) J. Shen, T. T. Nguyen, Y. P. Goh, W. P. Ye, X. Fu, J. Y. Xu and C. H. Tan, *J. Am. Chem. Soc.*, 2006, **128**, 13692–13693.

4 (*a*) X. S. Wu, Y. Zhao and H. B. Ge, *J. Am. Chem. Soc.*, 2015, **137**, 4924d–4927; (*b*) S. Inoue, H. Shiota, Y. Fukumoto and N. Chatani, *J. Am. Chem. Soc.*, 2009, **131**, 6898–6899; (*c*) H. Li, R. P. Hughes and J. Wu, *J. Am. Chem. Soc.*, 2014, **136**, 6288–6296.

5 M. Sheykhan, M. Shafiee-Pour and M. Abbasnia, *Org. Lett.*, 2017, **19**, 1270–1273.

6 (*a*) D. N. Sawant, Y. S. Wagh, K. D. Bhatte and B. M. Bhanage, *Eur. J. Org. Chem.*, 2011, **33**, 6719–6724; (*b*) M. V. Khedkara, A. R. Shindea, T. Sasakib and B. M. Bhanage, *J. Mol. Catal. A: Chem.*, 2014, **385**, 91–97.

7 (*a*) C. S. Xie and Y. H. Zhang, *Org. Lett.*, 2007, **9**, 781–784; (*b*) R. Kranthikumar, R. Chegondi and S. Chandrasekhar, *J. Org. Chem.*, 2016, **81**, 2451–2459; (*c*) C. R. Wu, Y. S. Fang, R. C. Larock and F. Shi, *Org. Lett.*, 2010, **12**, 2234–2237.

8 (*a*) J. Ni, J. Li, Z. Fan and A. Zhang, *Org. Lett.*, 2016, **18**, 5960–5963; (*b*) L. Grigorjeva and O. Daugulis, *Angew. Chem., Int. Ed.*, 2014, **53**, 10209–10212.

9 (*a*) F. Sandfort, M. J. O'Neill, J. Cornella, L. Wimmer and P. S. Baran, *Angew. Chem., Int. Ed.*, 2017, **56**, 3319–3323; (*b*) X. G. Liu, Q. L. Qiao, W. M. Tian, W. J. Liu, J. Chen, M. J. Lang and Z. C. Xu, *J. Am. Chem. Soc.*, 2016, **138**, 6960–6963; (*c*) K. M. M. Huihui, J. A. Caputo, Z. Melchor, A. M. Olivares, A. M. Spiewak, K. A. Johnson, T. A. DiBenedetto, S. Kim, L. K. G. Ackerman and D. J. Weix, *J. Am. Chem. Soc.*, 2016, **138**, 5016–5019.

10 (*a*) Y. M. Hu, Y. D. Hu, Q. Hu, J. Ma, S. Lv and S. Wang, *Chem.–Eur. J.*, 2017, **23**, 4065–4072; (*b*) Y. M. Hu, J. Ma, L. D Li, Q. Hu, S. Lv, B. H Liu and S. Wang, *Chem. Commun.*, 2017, **53**, 1542–1545; (*c*) X. Z. Meng, S. Lv, D. Cheng, Q. Hu, J. Ma, B. H. Liu and Y. M. Hu, *Chem.–*

Eur. J., 2017, **23**, 6264–6271; (*d*) Y. M. Hu, C. L. Yu, D. Ren, Q. Hu, L. D. Zhang and D. Cheng, *Angew. Chem., Int. Ed.*, 2009, **48**, 5448–5451.

11 (*a*) A. Z. Bradley and R. P. Johnson, *J. Am. Chem. Soc.*, 1997, **119**, 9917–9918; (*b*) T. R. Hoye, B. Baire, D. Niu, P. H. Willoughby and B. P. Woods, *Nature*, 2012, **490**, 208–212; (*c*) S. Y. Yun, K. P. Wang, N. K. Lee, P. Mamidipalli and D. Lee, *J. Am. Chem. Soc.*, 2013, **135**, 4668–4671; (*d*) R. Karmakar, S. Y. Yun, K. P. Wang and D. Lee, *Org. Lett.*, 2014, **16**, 6–9.

12 CCDC-1520526 (**3g**), CCDC-992692 (**4a**) contain the supplementary crystallographic data for this paper.†

13 (*a*) P. H. Willoughby, D. W. Niu, T. Wang, M. K. Haj, C. J. Cramer and T. R. Hoye, *J. Am. Chem. Soc.*, 2014, **136**, 13657–13665; (*b*) J.-A. Garcia-Lopez and M. F. Greaney, *Chem. Soc. Rev.*, 2016, **45**, 6766–6798.

14 (*a*) Z. J. Liu and R. C. Larock, *J. Org. Chem.*, 2006, **71**, 3198–3209; (*b*) L. Grigorjeva and O. Daugulis, *Org. Lett.*, 2014, **16**, 4688–4690; (*c*) E. Yoshioka and H. Miyabe, *Tetrahedron*, 2012, **68**, 179–189; (*d*) E. Yoshioka, S. Kohtani and H. Miyabe, *Molecules*, 2014, **19**, 863–880.

15 (*a*) T. Wang and H. R. Hoye, *J. Am. Chem. Soc.*, 2016, **138**, 13870–13873; (*b*) H. Miyabe, *Molecules*, 2015, **20**, 12558–12575; (*c*) T. R. Hoye, B. Baire and T. Wang, *Chem. Sci.*, 2014, **5**, 545–550; (*d*) A. E. Goetz, T. K. Shah and N. K. Garg, *Chem. Commun.*, 2015, **51**, 34–45; (*e*) I. Pozo, A. Cobas, D. Pena, E. Guitianab and D. Perez, *Chem. Commun.*, 2016, **52**, 5534–5537.