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Rh(III)-catalyzed aromatic C–H bond carbenoid functionalization of triazenes by α -diazomalonate

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ARTICLE INFO

Article history:

Received 24 April 2015

Received in revised form 2 June 2015

Accepted 5 June 2015

Available online xxx

Keywords:

C–H activation

Rh(III) catalysis

Triazene

Carbenoid

Divergent synthesis

ABSTRACT

A Rh(III)-catalyzed aromatic C–H bond carbenoid functionalization of triazenes by α -diazomalonates has been developed, with features of mild reaction condition and high efficiency. Furthermore, the functionalized triazenes could be subject to divergent synthesis.

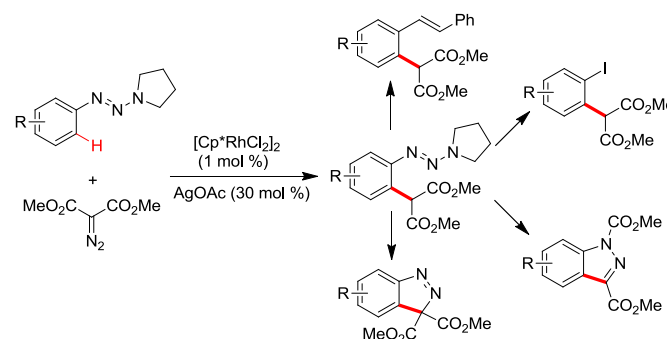
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1. Introduction

Recently, Rh(III)-catalyzed functionalization of aryl C–H bond has enjoyed tremendous advance owing to their wide applications to the rapid assembly of various complex molecular structures, particular in the fields of medicinal chemistry.¹ The direct C–H functionalization has advantages over classical cross coupling reactions, avoiding the preactivation of coupling partners thus leads to a more atom-economical process.² In particular, diazo compounds have acted as alkylation precursors in Rh(III)-catalyzed C–H functionalization. For example, Yu reported a seminal work of Rh(III)-catalyzed carbenoid functionalization of oximes and *N*-Methylbenzylamines with diazomalonates.³ Diazo compounds have also been investigated as coupling-cyclization components under Rh(III) catalysis.⁴ Therefore, the development of Rh(III)-catalyzed C–H functionalization using diazo compounds as coupling partners remains interesting.

Triazenes are versatile building blocks in organic synthesis, which could be transformed to diverse compounds under acidic condition and transition-metal-catalysis.⁵ Recently, Huang and co-workers explored the Rh(III)-catalyzed C–H activation of arenes using triazene as substrates,⁶ which provides a versatile and removable directing group in C–H functionalization and useful synthetic utility. In continuation of our interest in Rh(III)-catalyzed

C–H functionalization for biologically interesting small molecule synthesis,⁷ herein we report a Rh(III)-catalyzed aromatic C–H bond carbenoid functionalization of triazenes by α -diazomalonate. Moreover, the functionalized triazenes could be subject to various transformations to access divergent compounds (Scheme 1).



Scheme 1. Rh(III)-catalyzed carbenoid functionalization of triazenes.

2. Results and discussions

We commenced our study by investigating the coupling of pyrrolidine-derived triazene **1a** and α -diazomalonate **2** using $[\text{Cp}^*\text{RhCl}_2]_2$ as catalyst. When the reaction was conducted in methanol at 70 °C without additives, the Rh(III) catalyzed C–H

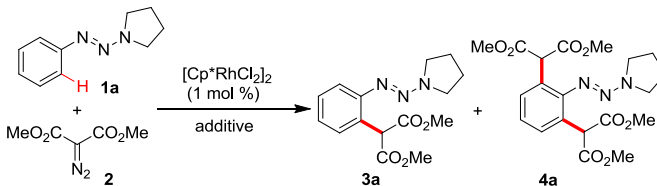
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<http://dx.doi.org/10.1016/j.tet.2015.06.024>

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functionalized was completely shut down (Table 1, entry 1), gratifyingly, catalytic addition of CsOAc led to the formation of mono-alkylation triazene **3a** in 21% yield and di-alkylation triazene product **4a** in 10% yield (Table 1, entry 2). This encouraged us to screen other additives and found AgOAc was superior to afford **3a** in 48% yield and **4a** in 23% yield (Table 1, entries 3–4). The next survey of silver salts showed that Ag₂CO₃ and AgSbF₆ were inferior to afford trace products (Table 1, entries 5–6). Further screening of solvents were revealed that the use of EtOH would result in lower yield (Table 1, entry 7), while other solvents was inferior to generate trace products (Table 1, entries 8–11). Moreover, decreasing the temperature to 30 °C would result in trace product formation (Table 1, entry 12).

Table 1
Optimization of reaction conditions^a



Entry	Additive	Solvent	T [°C]	Yield [%] ^b	
				3a	4a
1	none	MeOH	70	0	0
2	CsOAc	MeOH	70	21	10
3	Cu(OAc) ₂	MeOH	70	16	7
4	AgOAc	MeOH	70	48	23
5	Ag ₂ CO ₃	MeOH	70	Trace	Trace
6	AgSbF ₆	MeOH	70	Trace	Trace
7	AgOAc	EtOH	70	25	11
8	AgOAc	<i>t</i> -Amyl alcohol	70	Trace	Trace
9	AgOAc	CH ₃ CN	70	Trace	Trace
10	AgOAc	DCE	70	Trace	Trace
11	AgOAc	DMF	70	Trace	Trace
12	AgOAc	MeOH	30	Trace	Trace

^a Reaction conditions: **1a** (0.2 mmol), **2** (0.2 mmol), [Cp*RhCl₂]₂ (1 mol %), additives (30 mol %), solvent (2 mL).

^b Yields of isolated products.

With the optimized reaction condition in hand, we next the scope of this Rh(III)-catalyzed carbenoid functionalization using various triazenes. As depicted in Table 2, various *para*-substituted triazenes with valuable functional groups like methyl, chloro, acetyl, ethoxycarbonyl, could react smoothly with **2** in this process to furnish the mono-alkylation products (**3b–3e**) and di-alkylation products (**4b–4e**) in moderate yields. The *ortho*-substituted triazenes were also applicable to exclusively furnish the mono-alkylation product in moderate to excellent yields (**3f–3i**), with functionalized group such as bromo, ethoxycarbonyl, cyano, trifluoromethoxy, thus offering ample opportunity for further derivatization. Additionally, polysubstituted triazenes were also tolerated to afford the mono-alkylation products in moderate to excellent yields (**3j–3m**). Interestingly, when 3,5-dimethoxy substituted triazene **1n** was used, the reaction only delivered the mono-alkylation product **3n** in 53% yield, and the reaction of 2-naphthenyl substituted triazene exclusively generate the 3-alkylation product **3o** in 42% yield. Moreover, the structure of **3g** was unambiguously confirmed by X-ray analysis (Fig. 1).⁸ As mentioned before, triazenes were versatile building block and could be subject to divergent transformations. The unique features were then studied using **3a** as modeling substrate. As shown in Scheme 2, when **3a** was treated with styrene in the presence of Pd(OAc)₂, the Heck reaction occurred to form *E*-stilbene derivative **5** in 73% yield, in which triazene served as leaving group. **3a** could also be transformed into an iodobenzene derivative **6** in the presence of NaI under acidic condition. Interestingly, **3a** would undergo

divergent intramolecular cyclization to afford indazole compounds **7** and **8**.⁹

A proposed mechanism is depicted in Scheme 3. The initial rhodium diacetate was generated from [Cp*RhCl₂]₂ and AgOAc, and a carboxylate-assisted C–H activation of triazenes occurred to form intermediate **A** with release of AcOH. Then **A** takes diazo insertion with α -diazomalonate **2** to generate **B**, which sequentially takes migratory insertion to provide **C**, with extrusion of N₂. The final protonation of **C** furnishes the carbenoid functionalized product **3**, with regeneration of Rh(III) catalysis. And another carbenoid functionalization of **3** would lead to dialkylation product **4**.

3. Conclusions

In conclusion, we have developed a Rh(III)-catalyzed aromatic C–H bond carbenoid functionalization of triazenes by α -diazomalonate under mild reaction condition. Furthermore, the functionalized triazenes could take divergent transformations to access a variety of small molecules.

4. Experimental section

4.1. General

All commercially available reagents were used without purification unless otherwise noted. Column chromatography was performed using silica gel (100–200 mesh). Visualization of the compounds was accomplished with UV light (254 nm) and iodine. ¹H NMR and ¹³C NMR spectra were recorded in CDCl₃ operating at 400 MHz and 100 MHz, respectively. Proton chemical shifts are reported relative to the residual proton signals of the deuterated solvent CDCl₃ (7.26 ppm) or TMS. Carbon chemical shifts were internally referenced to the deuterated solvent signals in CDCl₃ (77.16 ppm). Chemical shifts are reported in δ (parts per million) values. Coupling constants *J* are reported in Hertz. Proton coupling patterns were described as singlet (s), doublet (d), triplet (t), quartet (q), and multiple (m). High-resolution mass spectra were recorded on Waters GCT Premier Time of Flight Mass Spectrometer (EI).

General procedure for the synthesis of compounds **3a–3o** and **4a–4e**. A mixture of Triazenes (0.2 mmol) and dimethyl diazomalonate (0.2 mmol) was dissolved in MeOH (2 mL), and [Cp*RhCl₂]₂ (1.2 mg, 1 mol %) and AgOAc (10 mg, 30% mmol) was added. Then the reaction was proceeded in a sealed tube at a temperature of 70 °C for 10 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 15–20 % ethyl acetate in petroleum ether to afford the desired products **3** and **4** as solid.

4.2. Compound (3a)

(*E*)-Dimethyl-2-(2-(pyrrolidin-1-yl)diazanyl)phenyl)malonate **3a**. White solid (29.3 mg, 48%); Mp 87–93 °C; ¹H NMR (CDCl₃, 400 MHz), δ : 7.48 (dd, *J*₁=8.4 Hz, *J*₂=1.2 Hz, 1H), 7.32–7.30 (m, 1H), 7.29–7.25 (m, 1H), 7.15–7.11 (m, 1H), 5.55 (s, 1H), 3.92 (s, 2H), 3.74 (s, 6H), 3.59 (s, 2H), 2.01 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ : 169.6, 148.4, 129.0, 128.8, 127.5, 125.2, 116.2, 52.7, 52.6, 51.0, 46.7, 24.0, 23.7; IR (KBr) ν : 2952, 2930, 2879, 1745, 1728, 1416, 1259, 1224, 1028, 768 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₅H₁₉N₃O₄ (M⁺): 305.1376; Found: 305.1377.

4.3. Compound (3b)

(*E*)-Dimethyl-(5-methyl-2-(pyrrolidin-1-yl)diazanyl)phenyl)malonate **3b**. Pale yellow solid (21.7 mg, 34%); Mp 97–99 °C; ¹H NMR (CDCl₃, 400 MHz), δ : 7.39 (d, *J*=8.4 Hz, 1H), 7.11–7.07 (m, 2H),

Table 2Rh(III)-catalyzed C–H carbenoid functionalization^a

Entry		Starting Material	Product / Yield [%] ^b
1		 1a , R = H 1b , R = Me 1c , R = Cl 1d , R = Ac 1e , R = CO ₂ Et	 3a , 48% 3b , 34% 3c , 42% 3d , 38% 3e , 52%
			 4a , 23% 4b , 14% 4c , 14% 4d , 13% 4e , 22%
2		 1f	 3f , 99%
3		 1g	 3g , 57%
4		 1h	 3h , 41%
5		 1i	 3i , 69%
6		 1j	 3j , 42%
7		 1k	 3k , 94%
8		 1l	 3l , 66%
9		 1m	 3m , 61%
10		 1n	 3n , 53%
11		 1o	 3o , 42%

^a Reaction Conditions: **1** (0.2 mmol), **2** (0.2 mmol), [Cp*RhCl₂]₂ (1 mol %), AgOAc (30 mol %), MeOH (2 mL), 70 °C, 8 h. ^b Isolated yields.

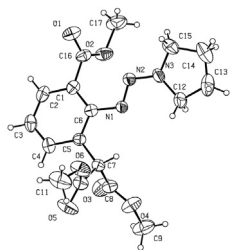
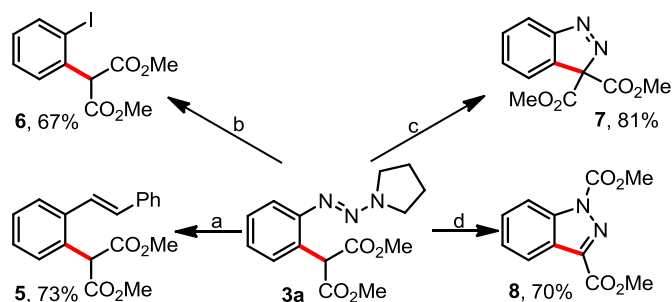
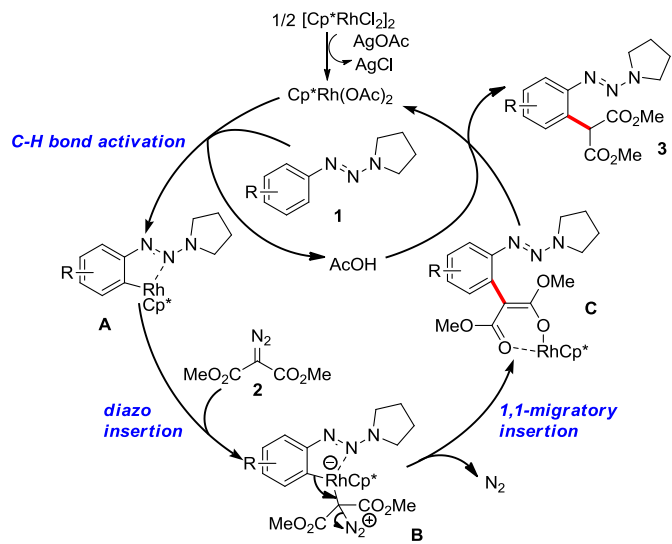


Fig. 1. ORTEP representation of the X-ray crystal structure of compound **3g**.



Scheme 2. Divergent transformation of **3a**. Reaction conditions: (a) Pd(OAc)₂ (10 mol %), styrene (2 equiv), TFA (2 equiv), MeOH, 60 °C; (b) NaI (3 equiv), TFA (10 equiv), acetone, 0 °C; (c) TFA (1 equiv), CH₃CN, 65 °C; (d) BF₃·Et₂O (2.8 equiv), CH₃CN, 0 °C.



Scheme 3. Proposed mechanism.

5.53 (s, 1H), 3.86 (s, 2H), 3.74 (s, 6H), 3.60 (s, 2H), 2.32 (s, 3H), 2.00 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 169.7, 146.1, 134.9, 129.6, 129.4, 127.3, 116.0, 52.7, 52.6, 50.8, 46.6, 23.9, 21.2; IR (KBr) v: 2953, 2872, 1760, 1735, 1405, 1315, 1148, 1032, 827 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₆H₂₁N₃O₄ (M⁺): 319.1532; Found: 319.1532.

4.4. Compound (3c)

(*E*)-Dimethyl-2-(5-chloro-2-(pyrrolidin-1-yl)diazenyl)phenyl malonate **3c**. Pale yellow solid (28.5 mg, 42%); Mp 83–88 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.43 (d, *J*=8.8 Hz, 1H), 7.32 (d, *J*=2.4 Hz, 1H), 7.22 (dd, *J*₁=8.4 Hz, *J*₂=2.4 Hz, 1H), 5.51 (s, 1H), 3.91 (s, 2H), 3.74 (s, 6H), 3.57 (s, 2H), 2.02 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 169.1, 147.1, 130.3, 129.03, 128.95, 128.8, 117.4, 52.9, 52.4, 51.2, 46.9, 24.1, 23.6; IR (KBr) v: 2954, 2877, 1749, 1435, 1316, 1211, 1026, 905, 834 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₅H₁₈ClN₃O₄ (M⁺): 339.0986; Found: 339.0984.

4.5. Compound (3d)

(*E*)-Dimethyl-2-(5-acetyl-2-(pyrrolidin-1-yl)diazenyl)phenyl malonate **3d**. Pale yellow solid (26.4 mg, 38%); Mp 126–129 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.92 (d, *J*=2.0 Hz, 1H), 7.87 (dd, *J*₁=8.4 Hz, *J*₂=2.0 Hz, 1H), 7.55 (d, *J*=8.8 Hz, 1H), 5.49 (s, 1H), 3.95 (t, *J*=6.4 Hz, 2H), 3.74 (s, 6H), 3.61 (t, *J*=6.4 Hz, 2H), 2.56 (s, 3H), 2.07–2.00 (m, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 197.2, 169.1, 152.2, 133.5, 130.1, 129.1, 127.4, 115.9, 52.7, 51.4, 47.2, 26.5, 24.0, 23.5; IR (KBr) v: 2954, 2882, 1738, 1674, 1596, 1343, 1205, 1026, 834 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₇H₂₁N₃O₅ (M⁺): 347.1481; Found: 347.1480.

4.6. Compound (3e)

(*E*)-Dimethyl-2-(5-(ethoxycarbonyl)-2-(pyrrolidin-1-yl)diazenyl)-phenyl malonate **3e**. Pale yellow solid (39.2 mg, 52%); Mp 75–78 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.97–7.92 (m, 2H), 7.53 (d, *J*=8.8 Hz, 1H), 5.46 (s, 1H), 4.33 (q, *J*=6.8 Hz, 2H), 3.93 (t, *J*=6.4 Hz, 2H), 3.73 (s, 6H), 3.59 (t, *J*=6.0 Hz, 2H), 2.05–1.98 (m, 4H), 1.36 (t, *J*=7.2 Hz, 3H); ¹³C NMR (CDCl₃, 100 MHz), δ: 169.2, 166.4, 152.0, 130.9, 130.3, 127.4, 126.6, 115.8, 60.8, 53.0, 52.7, 51.3, 47.1, 24.0, 23.5, 14.4; IR (KBr) v: 2955, 2884, 1742, 1711, 1605, 1432, 1208, 1027, 779 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₈H₂₃N₃O₆ (M⁺): 377.1587; Found: 377.1587.

4.7. Compound (3f)

(*E*)-Dimethyl-2-(3-bromo-2-(pyrrolidin-1-yl)diazenyl)phenyl malonate **3f**. White solid (76.0 mg, 99%); Mp 72–78 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.57 (dd, *J*₁=8.0 Hz, *J*₂=1.2 Hz, 1H), 7.29 (dd, *J*₁=7.6 Hz, *J*₂=1.2 Hz, 1H), 7.01 (t, *J*=7.6 Hz, 1H), 4.94 (s, 1H), 3.89 (s, 2H), 3.72 (s, 6H), 3.68 (s, 2H), 2.04 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 169.0, 148.2, 133.3, 129.6, 128.7, 127.3, 125.9, 117.6, 53.9, 52.8, 51.1, 46.6, 24.1, 23.6; IR (KBr) v: 2950, 2873, 1752, 1733, 1432, 1407, 1314, 1147, 1028, 758 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₅H₁₈BrN₃O₄ (M⁺): 383.0481; Found: 383.0477.

4.8. Compound (3g)

(*E*)-Dimethyl-2-(3-(methoxycarbonyl)-2-(pyrrolidin-1-yl)diazenyl)-phenyl malonate **3g**. Pale yellow solid (41.4 mg, 57%); Mp 101–104 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.45–7.43 (m, 2H), 7.15 (t, *J*=8.0 Hz, 1H), 5.48 (s, 1H), 3.83–3.82 (m, 2H), 3.76 (s, 3H), 3.71 (s, 6H), 3.63 (s, 2H), 2.03–2.00 (m, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 170.3, 169.1, 147.6, 131.4, 129.3, 128.0, 124.5, 124.2, 52.7, 52.5, 51.8, 51.1, 46.8, 23.9, 23.6; IR (KBr) v: 2954, 2879, 1755, 1732, 1409, 1309, 1201, 1157, 771, 626 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₇H₂₁N₃O₆ (M⁺): 363.1430; Found: 363.1428.

4.9. Compound (3h)

(*E*)-Dimethyl-2-(3-cyano-2-(pyrrolidin-1-yl)diazenyl)phenyl malonate **3h**. Yellow gel (27.1 mg, 41%); ¹H NMR (CDCl₃, 400 MHz), δ: 7.57 (dd, *J*₁=8.0 Hz, *J*₂=1.2 Hz, 1H), 7.29 (dd, *J*₁=7.6 Hz, *J*₂=1.2 Hz, 1H), 7.01 (t, *J*=7.6 Hz, 1H), 4.94 (s, 1H), 3.89 (s, 2H), 3.72 (s, 6H), 3.68 (s, 2H), 2.04 (s, 4H); ¹³C NMR (CDCl₃, 100 MHz), δ: 168.8, 151.1, 134.7, 133.6, 128.3, 124.5, 119.2, 102.7, 52.9, 52.7, 51.3, 47.1, 24.0, 23.5; IR (KBr) v: 2954, 2919, 2879, 2221, 1736, 1405, 1310, 1153, 1031, 760 cm⁻¹; HRMS (EI) (*m/z*): calcd for C₁₆H₁₈N₄O₄ (M⁺): 330.1328; Found: 330.1325.

4.10. Compound (3i)

(*E*)-Dimethyl-2-(2-(pyrrolidin-1-yl)diazenyl)-3-(tri-fluoromethoxy)phenyl malonate **3i**. Pale yellow solid (53.7 mg, 69%); Mp 90–92 °C; ¹H NMR (CDCl₃, 400 MHz), δ: 7.29–7.27 (m,

1H), 7.25–7.23 (m, 1H), 7.12 (t, $J=8.0$ Hz, 1H), 5.18 (s, 1H), 3.90 (s, 2H), 3.74 (s, 6H), 3.62 (s, 2H), 2.03 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.0, 142.8, 140.8 (q, $J=2.0$ Hz), 128.9, 127.8, 124.8, 122.5, 120.8 (q, $J=255.0$ Hz), 53.4, 52.8, 51.2, 46.3, 24.0, 23.6; IR (KBr) ν : 2972, 2881, 1754, 1738, 1410, 1310, 1145, 754 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{16}\text{H}_{18}\text{F}_3\text{N}_3\text{O}_5$ (M^+): 389.1199; Found: 389.1199.

4.11. Compound (3j)

(*E*)-Dimethyl-2-(4-chloro-3-fluoro-2-(pyrrolidin-1-ylidiazanyl)-phenyl)malonate **3j**. Pale brown solid (30.0 mg, 42%); Mp 63–68 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.14–7.10 (m, 1H), 7.05 (dd, $J_1=8.4$ Hz, $J_2=1.6$ Hz, 1H), 5.21 (s, 1H), 3.93 (t, $J=6.4$ Hz, 2H), 3.73 (s, 6H), 3.61 (t, $J=6.0$ Hz, 2H), 2.09–2.01 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 168.8, 150.2 (d, $J=252.0$ Hz), 138.9 (d, $J=8.0$ Hz), 127.8 (d, $J=2.0$ Hz), 125.5, 124.5 (d, $J=4.0$ Hz), 122.1 (d, $J=18.0$ Hz), 52.91, 52.87, 51.4, 46.5, 24.1, 23.6; IR (KBr) ν : 2955, 2877, 1747, 1434, 1410, 1024, 792, 728 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{15}\text{H}_{17}\text{ClF}_2\text{N}_3\text{O}_4$ (M^+): 357.0892; Found: 357.0888.

4.12. Compound (3k)

(*E*)-Dimethyl-2-(5-chloro-3-methyl-2-(pyrrolidin-1-ylidiazanyl)-phenyl)malonate **3k**. Yellow solid (66.5 mg, 94%); Mp 98–102 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.14 (d, $J=2.0$ Hz, 1H), 7.12 (s, 1H), 5.02 (s, 1H), 3.83 (s, 2H), 3.72 (s, 6H), 3.59 (s, 2H), 2.24 (s, 3H), 2.02 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.0, 146.9, 132.5, 130.8, 129.4, 127.3, 126.7, 53.6, 52.8, 51.0, 46.3, 23.9, 23.8, 19.4; IR (KBr) ν : 2951, 2873, 1743, 1301, 1267, 1038, 769, 615 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{16}\text{H}_{20}\text{ClN}_3\text{O}_4$ (M^+): 353.1142; Found: 353.1144.

4.13. Compound (3l)

(*E*)-Dimethyl-2-(5-iodo-3-methyl-2-(pyrrolidin-1-ylidiazanyl)-phenyl)malonate **3l**. Yellow solid (58.7 mg, 66%); Mp 116–120 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.48 (d, $J=1.2$ Hz, 1H), 7.44 (d, $J=1.6$ Hz, 1H), 4.98 (s, 1H), 3.83 (s, 2H), 3.72 (s, 6H), 3.59 (s, 2H), 2.21 (s, 3H), 2.02 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.0, 148.0, 139.7, 135.5, 133.0, 127.9, 88.6, 53.4, 52.8, 51.0, 46.3, 23.9, 23.7, 19.2; IR (KBr) ν : 2950, 2873, 1740, 1725, 1299, 1264, 1037, 862, 770 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{16}\text{H}_{20}\text{IN}_3\text{O}_4$ (M^+): 445.0499; Found: 445.0500.

4.14. Compound (3m)

(*E*)-Dimethyl-2-(6-fluoro-3-(methoxycarbonyl)-2-(pyrrolidin-1-ylidiazanyl)phenyl)malonate **3m**. White solid (46.5 mg, 61%); Mp 128–131 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.46 (dd, $J_1=8.4$ Hz, $J_2=6.0$ Hz, 1H), 6.88 (t, $J=8.8$ Hz, 1H), 5.36 (s, 1H), 3.83 (t, $J=6.4$ Hz, 2H), 3.75 (s, 3H), 3.71 (s, 6H), 3.61 (t, $J=6.8$ Hz, 2H), 2.06–1.97 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.5, 168.2, 162.4 (d, $J=250.0$ Hz), 150.1 (d, $J=7.0$ Hz), 130.7 (d, $J=11.0$ Hz), 120.4 (d, $J=3.0$ Hz), 116.6 (d, $J=16.0$ Hz), 111.5 (d, $J=23.0$ Hz), 52.8, 51.9, 51.3, 48.4, 47.0, 24.0, 23.6; IR (KBr) ν : 2981, 2878, 1751, 1604, 1590, 1309, 1116, 786 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{17}\text{H}_{20}\text{FN}_3\text{O}_6$ (M^+): 381.1336; Found: 381.1339.

4.15. Compound (3n)

(*E*)-Dimethyl-2-(2,4-dimethoxy-6-(pyrrolidin-1-ylidiazanyl)phenyl)malonate **3n**. Yellow solid (38.7 mg, 53%); Mp 115–116 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 6.72 (d, $J=2.4$ Hz, 1H), 6.30 (d, $J=2.4$ Hz, 1H), 5.44 (s, 1H), 3.90 (s, 2H), 3.81 (s, 3H), 3.79 (s, 3H), 3.68 (s, 6H), 3.53 (s, 2H), 1.99 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.9, 160.6, 158.7, 150.2, 110.7, 96.4, 92.5, 56.0, 55.4, 52.3, 51.0, 47.9, 47.0, 24.0, 23.6; IR (KBr) ν : 2952, 2855, 1741, 1720, 1363, 1143, 709, 604 cm^{-1} ;

HRMS (EI) (m/z): calcd for $\text{C}_{17}\text{H}_{23}\text{N}_3\text{O}_6$ (M^+): 365.1587; Found: 365.1590.

4.16. Compound (3o)

(*E*)-Dimethyl-2-(3-(pyrrolidin-1-ylidiazanyl)naphthalen-2-yl)malonate **3o**. Red solid (29.8 mg, 42%); Mp 92–96 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 8.25–8.23 (m, 1H), 7.81–7.79 (m, 1H), 7.66 (d, $J=8.8$ Hz, 1H), 7.48–7.45 (m, 3H), 5.23 (s, 1H), 3.88 (s, 4H), 3.75 (s, 6H), 2.09 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.7, 134.1, 128.3, 127.8, 126.7, 126.3, 125.9, 125.1, 124.6, 120.6, 54.0, 52.8, 51.1, 46.6, 24.0, 23.8; IR (KBr) ν : 2952, 2872, 1759, 1733, 1359, 1263, 1152, 754 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{19}\text{H}_{21}\text{N}_3\text{O}_4$ (M^+): 355.1532; Found: 355.1532.

4.17. Compound (4a)

(*E*)-Tetramethyl-2,2'-(2-(pyrrolidin-1-ylidiazanyl)-1,3-phenylene)dimalonate **4a**. Pale red solid (20.0 mg, 23%); Mp 131–133 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.29 (s, 1H), 7.27 (s, 1H), 7.15 (t, $J=7.6$ Hz, 1H), 5.09 (s, 2H), 3.82 (s, 2H), 3.72 (s, 12H), 3.58 (s, 2H), 2.02–2.01 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.4, 147.6, 129.4, 125.9, 124.9, 54.2, 52.7, 50.8, 46.5, 24.0, 23.6; IR (KBr) ν : 2984, 2958, 1756, 1735, 1406, 1309, 1150, 1027, 769 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{20}\text{H}_{25}\text{N}_3\text{O}_8$ (M^+): 435.1623; Found: 435.1626.

4.18. Compound (4b)

(*E*)-Tetramethyl-2,2'-(5-methyl-2-(pyrrolidin-1-ylidiazanyl)-1,3-phenylene)dimalonate **4b**. Yellow solid (12.6 mg, 14%); Mp 146–149 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.07 (s, 2H), 5.05 (s, 2H), 3.80 (s, 2H), 3.73 (s, 12H), 3.57 (s, 2H), 2.33 (s, 3H), 2.01 (s, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.6, 145.3, 134.6, 130.1, 125.7, 54.2, 52.7, 50.8, 46.5, 24.1, 23.7; IR (KBr) ν : 2955, 1762, 1733, 1437, 1416, 1311, 1149, 1030, 779 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{21}\text{H}_{27}\text{N}_3\text{O}_8$ (M^+): 449.1798; Found: 449.1801.

4.19. Compound (4c)

(*E*)-Tetramethyl-2,2'-(5-chloro-2-(pyrrolidin-1-ylidiazanyl)-1,3-phenylene)dimalonate **4c**. Yellow solid (13.2 mg, 14%); Mp 121–125 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.28 (s, 2H), 5.06 (s, 2H), 3.83–3.81 (m, 2H), 3.74 (s, 12H), 3.57–3.56 (m, 2H), 2.05–2.00 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 168.9, 146.4, 130.1, 129.5, 127.4, 54.0, 53.0, 51.0, 46.7, 24.1, 23.6; IR (KBr) ν : 2918, 2881, 1755, 1732, 1347, 1157, 1029, 803, 787 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{20}\text{H}_{24}\text{ClN}_3\text{O}_8$ (M^+): 469.1252; Found: 469.1248.

4.20. Compound (4d)

(*E*)-Tetramethyl-2,2'-(5-acetyl-2-(pyrrolidin-1-ylidiazanyl)-1,3-phenylene)dimalonate **4d**. Pale yellow solid (12.4 mg, 13%); Mp 135–139 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.89 (s, 2H), 5.10 (s, 2H), 3.86 (t, $J=6.4$ Hz, 2H), 3.74 (s, 12H), 3.61 (t, $J=6.4$ Hz, 2H), 2.57 (s, 3H), 2.08–2.01 (m, 4H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 196.7, 169.0, 151.3, 133.2, 130.0, 126.3, 54.4, 52.9, 51.2, 47.0, 26.6, 24.0, 23.5; IR (KBr) ν : 2990, 2955, 1731, 1682, 1402, 1162, 1033, 797, 784 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{22}\text{H}_{27}\text{N}_3\text{O}_9$ (M^+): 477.1747; Found: 477.1747.

4.21. Compound (4e)

(*E*)-Tetramethyl-2,2'-(5-(ethoxycarbonyl)-2-(pyrrolidin-1-ylidiazanyl)-1,3-phenylene)dimalonate **4e**. Brown solid (22.3 mg, 22%); Mp 113–118 °C; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.93 (s, 2H), 5.07 (s, 2H), 4.34 (q, $J=7.2$ Hz, 2H), 3.84 (t, $J=6.8$ Hz, 2H), 3.73 (s,

12H), 3.59 (t, $J=6.4$ Hz, 2H), 2.07–1.99 (m, 4H), 1.36 (t, $J=7.2$ Hz, 3H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 169.1, 165.9, 151.1, 131.0, 126.6, 126.2, 61.1, 54.6, 52.8, 51.1, 46.9, 24.1, 23.5, 14.5; IR (KBr) ν : 2957, 1741, 1708, 1403, 1275, 1217, 1024, 787, 770 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{23}\text{H}_{29}\text{N}_3\text{O}_{10}$ (M^+): 507.1853; Found: 507.1853.

Typical procedure for the synthesis of compounds **5**. A mixture of **3a** (20 mg, 0.0656 mmol, 1 equiv), palladium acetate (1.5 mg, 0.00656 mmol, 10 mol %) and styrene (15 μL , 0.1312 mmol, 2 equiv) was dissolved in MeOH (1 mL), TFA (10 μL , 0.1312 mmol, 2 equiv) was added. Then the reaction was proceeded in a sealed tube at a temperature of 60 $^\circ\text{C}$ for 1 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 15–20 % ethyl acetate in petroleum ether to afford the desired products **5** as solid.

4.22. Compound (5)

(*E*)-Dimethyl-2-(2-styrylphenyl)malonate **5**. Pale yellow solid (14.8 mg, 73%); Mp 58–68 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.61–7.58 (m, 1H), 7.52 (s, 1H), 7.50 (s, 1H), 7.44–7.42 (m, 1H), 7.39–7.36 (m, 3H), 7.34–7.30 (m, 2H), 7.29–7.26 (m, 1H), 6.95 (t, $J=16$ Hz, 1H), 5.07 (s, 1H), 3.75 (s, 6H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 168.9, 137.6, 137.2, 133.1, 130.7, 129.7, 128.9, 128.7, 128.2, 128.0, 127.1, 126.8, 125.6, 54.6, 53.1; IR (KBr) ν : 3003, 2951, 1750, 1732, 1496, 1434, 1207, 1148, 965, 763, 745 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{19}\text{H}_{18}\text{O}_4$ (M^+): 310.1205; Found: 310.1203.

Typical procedure for the synthesis of compounds **6**. A mixture of sodium iodide (78.3 mg, 0.522 mmol, 3 equiv) was dissolved in acetone (1 mL), TFA (129.6 μL , 1.74 mmol, 10 equiv) and **3a** (53 mg, 0.174 mmol, 1 equiv) was added. Then the reaction was proceeded in a sealed tube at a temperature of 0 $^\circ\text{C}$ for 8 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 15–20 % ethyl acetate in petroleum ether to afford the desired products **6** as solid.

4.23. Compound (6)

Dimethyl-2-(2-iodophenyl)malonate **6**. Pale yellow solid (38.9 mg, 67%); Mp 57–61 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz), δ : 7.87 (dd, $J_1=8.0$ Hz, $J_2=1.2$ Hz, 1H), 7.47 (dd, $J_1=7.6$ Hz, $J_2=1.6$ Hz, 1H), 7.39–7.35 (m, 1H), 7.04–7.00 (m, 1H), 5.18 (s, 1H), 3.78 (s, 6H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 168.3, 139.8, 136.2, 130.0, 129.8, 128.8, 101.7, 62.0, 53.2; IR (KBr) ν : 2955, 2929, 1754, 1738, 1434, 1263, 1151, 1019, 747 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{11}\text{H}_{11}\text{IO}_4$ (M^+): 333.9702; Found: 333.9710.

Typical procedure for the synthesis of compounds **7**. A mixture of **3a** (20 mg, 0.0656 mmol, 1 equiv) was dissolved in CH_3CN (1 mL) and TFA (4.9 μL , 0.0656 mmol, 1 equiv) was added. Then the reaction was proceeded in a sealed tube at a temperature of 65 $^\circ\text{C}$ for 8 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 15–20 % ethyl acetate in petroleum ether to afford the desired products **7** as solid.

4.24. Compound (7)

Dimethyl-3*H*-indazole-3,3-dicarboxylate **7**. Brown solid (12.4 mg, 81%); Mp 78–92 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz), δ : 8.16–8.14 (m, 1H), 7.85–7.83 (m, 1H), 7.65–7.57 (m, 2H), 3.83 (s, 6H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 163.2, 158.5, 134.2, 131.4, 130.9, 124.7, 122.2, 54.2; IR (KBr) ν : 2957, 2917, 2849, 1735, 1461, 1437, 1215, 1056, 752 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_4$ (M^+): 234.0641; Found: 234.0644.

Typical procedure for the synthesis of compounds **8**. A mixture of **3a** (62 mg, 0.203 mmol, 1 equiv) was dissolved in CH_3CN (1 mL) and $\text{BF}_3\text{--Et}_2\text{O}$ (70.3 μL , 0.568 mmol, 2.8 equiv) was added. Then the reaction was proceeded in a sealed tube at 0 $^\circ\text{C}$ for 2 h. The resulting reaction mixture was loaded on a silica gel column and flashed with 15–20 % ethyl acetate in petroleum ether to afford the desired products **8** as solid.

4.25. Compound (8)

Dimethyl 1*H*-indazole-1,3-dicarboxylate **8**. White solid (29.3 mg, 70%); Mp 167–170 $^\circ\text{C}$; ^1H NMR (CDCl_3 , 400 MHz), δ : 8.29 (t, $J=8.8$ Hz, 2H), 7.64–7.60 (m, 1H), 7.48–7.44 (m, 1H), 4.16 (s, 3H), 4.06 (s, 3H); ^{13}C NMR (CDCl_3 , 100 MHz), δ : 162.2, 150.9, 141.2, 141.0, 130.0, 125.6, 124.5, 122.5, 114.6, 55.1, 52.8; IR (KBr) ν : 2920, 2851, 1766, 1732, 1607, 1261, 1131, 809, 771 cm^{-1} ; HRMS (EI) (m/z): calcd for $\text{C}_{11}\text{H}_{10}\text{N}_2\text{O}_4$ (M^+): 234.0641; Found: 234.0640.

Acknowledgements

The authors are grateful for financial supports from National Natural Science Foundation of China (21202143, 21402163).

Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.tet.2015.06.024>.

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