JOC The Journal of Organic Chemistry

Note

Synthesis of Isoindoles from Intramolecular Condensation of Benzyl Azides with #-Aryldiazoesters

Jing Zhu, Rui Li, Yan Su, and Peiming Gu

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.8b03180 • Publication Date (Web): 21 Mar 2019

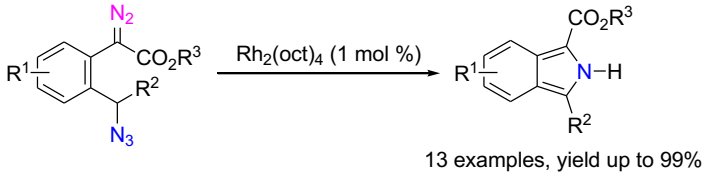
ACS Publications

is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Synthesis of Isoindoles from Intramolecular Condensation of Benzyl Azides with α-Aryldiazoesters

Jing Zhu, Rui Li, Yan Su, Peiming Gu*
Department of Chemistry, Ningxia University, Yinchuan 750021, China
Phone: +86(951)206-2274
Fax: +86(951)206-2323
E-mail: gupm@nxu.edu.cn

Tables of contents



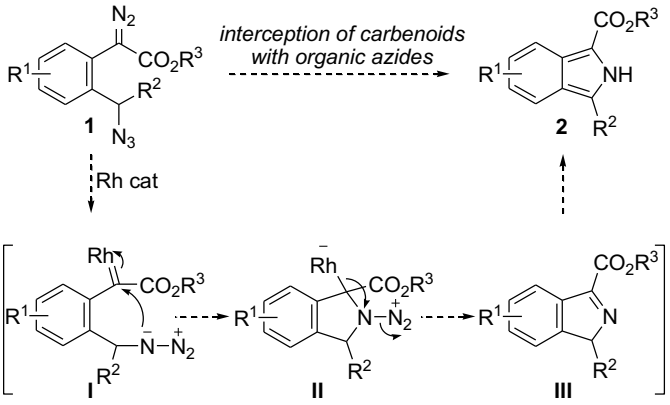
13 examples, yield up to 99%

Abstract

Rh-catalyzed intramolecular condensation of the benzyl azides with α-aryldiazoesters was explored. The reaction proceeded through the nucleophilic attack of the organic azide onto a rhodium carbenoid while releasing nitrogen gas, affording the α-imino esters as the primary product. Tautomerization of the imino esters efficiently gave thirteen desired isoindoles with good to excellent yields.

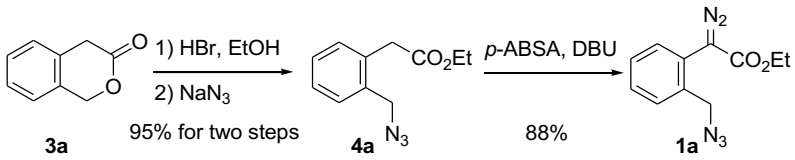
The isoindoles and their derivatives are very reactive compounds, and they have been widely applied in multi-disciplinary research fields. For examples, the isoindoles are employed as synthetic building blocks for tetracenes,[1] and also they are embedded in the material chemistry.[2] Due to their important usage, quite a few synthetic methods towards the isoindoles have been reported.[3,4] The organic azides are very powerful materials for synthesizing aza-cycles compounds, however it was less involved in isoindoles chemistry, and only Chiba's group had reported an intramolecular 1,3-dipolar cycloaddition of azides onto alkenes for synthesis of isoindoles.[4c] In this paper, we will report the Rh-catalyzed intramolecular condensation of benzyl azides with α-aryldiazoesters for addressing the isoindoles.

The rhodium(II) catalyzed interception of the diazo compounds with organic azides was initially reported by Wee and co-workers, and two unexpected imines were observed during their exploration of the C-H insertion with indoline diazoamides.[5] Then the conversion was confirmed by Lecourt and Micouin,[6] and further explored in our group[7] and Doyle group,[8] demonstrating its excellent efficiency in synthesis of α-imine esters. We envisioned that the isoindole **2a** could be accessed with the interception reaction of **1a**, featuring an azidomethyl moiety attached on the *ortho*-position of the α-aryldiazoester (Scheme 1). The rhodium catalyst would promote the formation of carbenoid **I** from the diazo compound, then the azide would attack on to the rhodium complex with the nucleophilic inner nitrogen atom, resulting in an intermediate **II**. Rhodium-carbon bond cleavage and nitrogen extrusion of intermediate **II** would give the α-imino ester **III**, which would rapidly proceed *via* a tautomerization process for producing the desired isoindole **2**.



Scheme 1. Designed process for synthesis of isoindoles

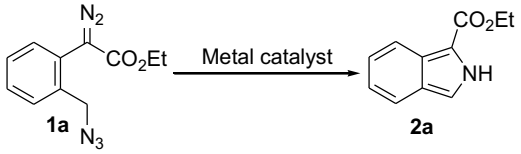
With the above vision in mind, the first substrate **1a** was prepared from the commercially available 3-isochromanone **3a** (Scheme 2). Treatment of **3a** with HBr gas in EtOH at 50°C for 5 h gave the corresponding ethyl 2-(2-(bromomethyl)phenyl)acetate as a sole product according to Vincent's procedure,[9] then azidation of the corresponding bromide with sodium azide in DMF delivered the benzyl azide **4a** with 95% yield for two steps. Further Regitz diazo transfer reaction[10] of **4a** with 4-acetamidobenzenesulfonyl azide (*p*-ABSA) in the presence of DBU gave the desired substrate **1a**[11] with 88 % yield.



Scheme 2. Synthesis of substrate**1a**.

The substrate **1a** was a bit sensitive to the natural light, and it should be kept in dark place. Otherwise, trace isoindole **2a** could be observed if the sample was exposed to natural light for several days. The rhodium(II) salts[5, 6, 7a] and copper salts[7b, 7c] had been employed as the catalysts for the interception reaction, therefore, $Cu(OTf)_2$, $CuPF_6(MeCN)_4$, $Rh_2(OAc)_4$ and $Rh_2(oct)_4$ were selected for promoting the reaction of **1a**. All the experiments were performed with 0.2 mmol of **1a** in the presence of 1 mol % of copper salts or rhodium salts in dichloromethane at room temperature (entries 1-4, Table 1). To our delight, the known isoindole **2a**[12] could be observed with each case. $Rh_2(oct)_4$ was demonstrated as the best catalyst, and the isoindole **2a** was isolated in 97% yield. It should be noted that the isoindole was regarded as a potentially instable substance, therefore purification of the isoindoles by flash column chromatography should be quickly finished. Otherwise, the yield would be reduced. Further evaluation of the solvents did not improve the yield (entries 4-7, Table 1), and the halogenated hydrocarbon solvents seemed to be more suitable for the conversion. The conversion failed to give isoindole **2a** if the reaction of **1a** was carried without catalyst in DCM at room temperature (entry 8, Table 1) or at refluxing DCM (entry 9, Table 1). Themolysis of the substrate **1a** in refluxing DCE (at about 80 ºC) for 17 h could be successful, where the isoindole **2a** was produced with only 56% yield (entry 10, Table 1).

Table 1. Optimization reaction conditions for synthesis of isoindole **2a**[a].



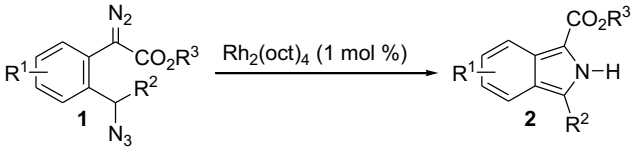
Entry	Catalyst	Solvent	Time (h)	Yield (%)[b]
1	$Cu(OTf)_2$	DCM	18	31
2	$CuPF_6(MeCN)_4$	DCM	4	62
3	$Rh_2(OAc)_4$	DCM	12	74
4	**$Rh_2(oct)_4$**	**CH_2Cl_2**	**4**	**97**
5	$Rh_2(oct)_4$	DCE	10	64
6	$Rh_2(oct)_4$	THF	24	38
7	$Rh_2(oct)_4$	$CHCl_3$	4	82
8	no catalyst	DCM	48	-
9[c]	no catalyst	DCM	12	trace
10[d]	no catalyst	DCE	17	56

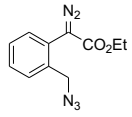
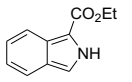
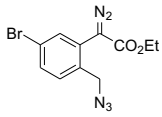
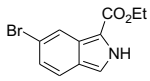
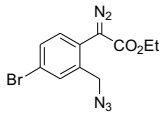
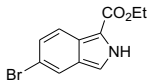
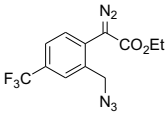
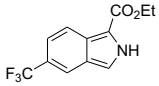
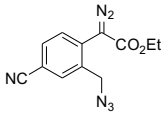
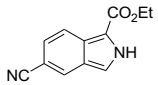
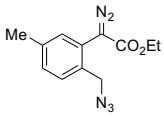
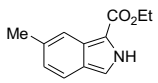
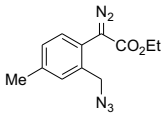
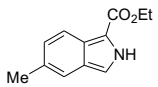
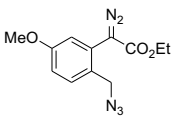
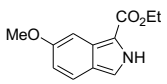
a) Reaction of **1a** (0.2 mmol) with metal catalyst (0.002 mmol) in the solvent (2.0 mL) for the above mentioned time; b) Isolated yield; c) At refluxing DCM; d) At refluxing DCE.

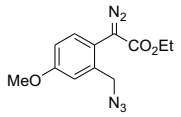
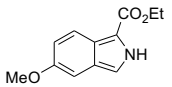
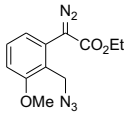
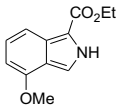
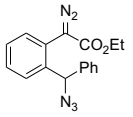
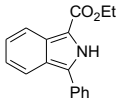
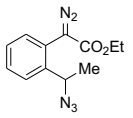
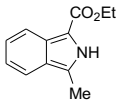
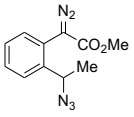
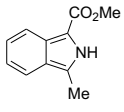
Then the scope of substrates was examined with $Rh_2(oct)_4$, and the results were summarized in Table 2. As disclosed, isoindoles are very reactive compounds, especially in solution.[3] Therefore, the handling time for the isoindoles and their stability would affect the isolated yields. All the azides **1** examined here could be converted into the corresponding isoindoles **2** with good to excellent yields, and generally the isoindole was observed as the sole product from the NMR of the each crude reaction mixture (entries 1-4 and entries 7-13, Table 2), which demonstrated the powerful efficiency of reaction. All the isoindoles were purified as soon as possible, then the yield difference should be mainly due to the stability of the products during the purification process. The reaction of azide **1a** (0.4 mmol) was re-examined in CH_2Cl_2, and **2a** was isolated in 92% yield (entry 1, Table 2). It was reported that stabilization of the isoindoles could be accessed by introduction of electron withdrawing groups,[3] which would be beneficial to good isolated yield. Isoindoles **2b** and **2c**, both attaching a bromo substituent, were obtained with excellent isolated yields from the substrates **1b** and **1c**, and the reaction time was 3 h and 6 h, respectively (entries 2 and 3, Table 2). The reaction of 4-CF_3 substrate **2d** for 5 h afforded the isoindole **1d** with 82% yield. Though the isoindole **1e** with a cyano group was supposed to be more stable, but the substrate **2e** was less reactive, which might be due to the long-distance л-л conjugation between the cyano group and the diazo group. It took 20 h for the substrate **2e** to be consumed, where the long reaction time led to the reduced yield (entry 5, Table 2). The electron donating substituents at the aryl ring were supposed to be negative for the stability, and the reactions of the substrates with a methyl or a methoxyl group in 2 h to 7 h gave the isoindoles in 75%-88% yields. It should be noted that there was still a bit of azide **1f** left when the reaction was stopped at 4 h. If the reaction was prolonged to 16 h, the **2f** was produced with only 66% yield, and excessive reaction of the isoindole might be proceeded. The **2f** had been isolated with 98% yield when the substrate was employed as 0.29 mmol, where all the material **1f** was consumed. The azide **1k** bearing an additional phenyl group at the benzylic carbon were converted into a 1,3-disubstituted isoindole **2k** with 88% yield, and **2k** could be produced with 99% yield when 0.8 mmol of **1k** was applied for the conversion (entry 11, Table 2), where the structure

assignment was supported by an X-ray crystallographic structure determination. Also, the reaction of azide **1l** with a methyl group at the benzylic carbon gave **2l** with 74% yield, and the yield difference between **2k** and **2l** might be due to the conjugated system (entry 11 *vs* entry 12, Table 2). Fortunately, the yield of **2l** could be improved to 85% if the reaction was performed in $CHCl_3$. Then the methyl α-aryldiazoester **1m** was also successfully converted into the isoindole **2m** with 87% yield (entry 13, Table 2).

Table 2. Conversion of azide **1** to isoindole **2**[a].



entry	Azide**1**	Time (h)	Isoindole **2**	Yield (%)[b]
1		4		92
	1a		**2a**	
2		3		93
	1b		**2b**	
3		6		90
	1c		**2c**	
4		5		82
	1d		**2d**	
5		20		70[c]
	1e		**2e**	
6		16 4 4		66 75[d] 98[e]
	1f		**2f**	
7		2		86
	1g		**2g**	
8		4		88

	1h		2h	
9		4		82%[c]
	1i		2i	
10		7		80%
	1j		2j	
11		3 4		88 99[f]
	1k		2k	
12		8 10		74 85[g]
	1l		2l	
13		17		87
	1m		2m	

a) Reaction of azide **1** (0.4 mmol) with $Rh_2(oct)_4$ (3 mg, 0.004 mmol) in CH_2Cl_2 (4.0 mL) for the above mentioned time; b) isolated yield; c) 0.2 mmol azide **1** was employed; d) a bit of azide **1f** was left; e) 0.29 mmol azide **1f** was employed; f) 0.8 mmol azide **1** was employed; g) reaction in $CHCl_3$.

In summary, a synthetic method toward isoindoles has been designed and developed, and the intramolecular interception of benzyl azides with α-aryldiazoesters is practical and efficient, affording thirteen isoindoles with good to excellent yields.

EXPERIMENTAL SECTION

All the reagents were purchased from *Acros*, *Sigma-Aldrich*, *Alfa-Aesar*, *Aladdin*, *Accela* or *Adamas*, and they were used as received. All the solvents were distilled using the classic method before use. The reactions were monitored by thin layer chromatography (TLC) on 2.5*10 cm, 250 μm analytical plates coated with silica gel 60 F254, and they were purchased from *Qingdao Haiyang Chemical Co. Ltd*. The thin layer chromatography plates were visualized by exposure to the ultraviolet light (UV, 254 nm) or Phosphomolybdic acid. Purification of the synthetic compounds by the flash column chromatography employed the neutral Silica gel (200-300 mesh or 300-400 mesh), which were purchased from *Qingdao Haiyang Chemical Co. Ltd*. The NMR spectra were recorded on a Bruker 400 MHz spectrometer, and the tetramethylsilane (δ = 0 and δ = 7.26 for $CDCl_3$, δ = 0 and δ = 2.05 for acetone-d6, δ = 0 and δ = 2.50 for DMSO-d6) was used as an internal standard for ^1H NMR (400MHz) and $CDCl_3$ (δ = 77.16), acetone-d6 (δ = 29.84), DMSO-d6(δ = 39.92) for ^{13}C NMR(100 MHz), and the ^{13}C NMR were plus APT [methyl and methine (down), methylene and quaternary carbon (up)]. The IR spectra were recorded on a Perkein Elmer with potassium bromide crystal optic rectangle. High-resolution mass spectra (HRMS) were measured on a LTQ Orbitrap

XL Domain35A (Thermo Fisher) spectrometer, and the electro spray ionization (ESI) was used as the ion source. The isoindole **4a** had been previously prepared by Mathias's procedure[13]. And azides **4b-4m** were prepared according to the method that our previously reported procedure[7], and isochromanones **3a** was purchased from Accela. The lactone **3b** was prepared from the known dicarboxylic acid.[14] The lactones **3c** and **3h** were prepared from the known dicarboxylic acids.[15] The lactone **3e** was prepared from the known dicarboxylic acid.[16] The lactones **3f** and **3g** were prepared from the known dicarboxylic acids.[17] The lactone **3i** was prepared from the known dicarboxylic acid.[18] The lactones **3k** and **3l** were prepared from the known dicarboxylic acids.[19] And the isoindoles **2a**, **2k** and **2l** had been previously prepared by SatoshiItoa's procedure[12]. All the reaction of the benzyl azides with α-aryldiazoesters were carried out in dry reaction vessels or flasks under a positive pressure of nitrogen or argon.

6-bromoisochroman-3-one(3b). To a stirred solution of the known 4-bromo-2-(2-methoxy-2-oxoethyl) benzoic acid[14] (3.10 g, 11.4 mmol) in THF (36.0 ml) was added 2.0 M $BH_3{\cdot}Me_2S$ (6.3 ml, 12.6 mmol), and the mixture was heated to 40ºC for 4 h. Then it was cooled to room temperature and 4.0 M HCl (30 ml) was added to quench the reaction. The mixture was extracted with ethyl acetate (20 mL × 3), and washed with brine (20 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography to give the lactone **3b** as a white solid (1.80 g, 70% yield), known compound[20(a)]; R_f = 0.62 (Et_2O/0.5 M aqueous NaH_2PO_4/HOAc/PE = 0.9/0.09/0.01/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.45 (d, J = 8.0 Hz, 1H), 7.40 (s, 1 H), 7.14 (d, J = 8.0 Hz, 1H), 5.27 (s, 2H),3.70 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 169.9, 133.3, 130.7, 122.8, 69.7, 35.9, δ (down) 130.7, 130.2, 126.5.

7-bromoisochroman-3-one(3c). The lactone **3c** (2.03 g) was prepared from the known 5-bromo-2-(2-methoxy-2-oxoethyl)benzoic acid[15] (3.22 g, 11.8 mmol) by the procedure for the preparation of lactone **3b**, and the yield was 76%, known compound[20(a)], R_f= 0.44 (EtOAC/PE = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.47 (d, J = 8.0 Hz, 1H), 7.40 (s, 1H), 7.11 (d, J = 8.0 Hz, 1H), 5.27 (s, 2H), 3.66 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.0, 133.6, 130.0, 121.1, 69.3, 35.8, δ (down) 131.9, 128.8, 127.9.

7-(trifluoromethyl)-1H-isochromen-3(4H)-one(3d). The lactone **3d** (1.81 g) was prepared from the known 2-(carboxymethyl)-5-(trifluoromethyl)benzoic acid[14] (2.87 g, 11.6 mmol) by the procedure for the preparation of lactone **3b**, and the yield was 72%, Mp: 158-159 ºC, R_f= 0.63 (EtOAC/PE = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63 (d, J = 8.0 Hz, 1H), 7.53 (s, 1H), 7. 37 (d, J = 8.0 Hz, 1H), 5.37 (s, 2H), 3.79 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 169.6, 135.2, 132.5, 130.1 (q, J_{CF} = 33 Hz), 123.8 (q, J_{CF} = 270 Hz), 69.6, 36.2, δ (down) 127.8, 125.9 (q, J_{CF} = 3 Hz), 121.9 (q, J_{CF} = 3 Hz). IR (film) 1734 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{10}H_7F_3O_2Na$ 239.0290, found 239.0290.

3-oxoisochromane-7-carbonitrile(3e). The lactone **3e** (705.0 mg) was prepared from the known 5-cyano-2-(2-methoxy-2-oxoethyl)benzoic acid[16] (1.23 g, 5.6 mmol) by the procedure for the preparation of lactone **3b**, and the yield was 72%, Mp:147-149 ºC, R_f= 0.26 (Et_2O/0.5 M aqueous NaH_2PO_4/HOAc/PE = 2.7/0.27/0.03/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.68 (dd, J = 8.0 Hz and 1.6 Hz, 1H), 7.59 (s, 1H), 7.39 (d, J = 8.0 Hz, 1H), 5.36 (s, 2 H), 3.81 (s, 2H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 169.3, 136.5, 133.0, 118.1, 111.5, 69.1, 36.3, δ (down) 132.7, 128.4, 128.2. IR (film) 1737 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{10}H_7NO_2Na$ 196.0369, found 196.0369.

6-methylisochroman-3-one(3f). The **3f** (413.0 mg) was prepared from the known 2-

((methoxycarbonyl) methyl)-4-methylbenzoic acid[17](1.33 g, 6.3 mmol) by the procedure for the preparation of lactone **3b**, and the yield was 40%, known compound,[20(a)] R_f= 0.37(EtOAC/PE = 1/3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.09-7.15 (m, 2H), 7.04 (s, 1H), 5.28 (s, 2H), 3.67 (s, 2H), 2.37 (s, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.0, 138.8, 131.0, 128.7, 70.1, 36.3, δ (down) 128.0, 127.7, 124.6, 21.3.

7-methylisochroman-3-one(3g). The **3g** (614.0 mg) was prepared from the known 2-(2-methoxy-2-oxoethyl)-5-methylbenzoic acid[16] (1.22 g, 5.8 mmol) by the procedure for the preparation of lactone **3b**, and the yield was 65%, known compound[20(b)], R_f= 0.36(EtOAC/PE = 1/3); ^{1}H NMR (acetone-d6, 400 MHz) δ 7.15-7.20 (m, 3H), 5.31 (s, 2H), 3.70 (s, 2H), 2.33 (s, 3H); $^{13}C\{^1H\}$ NMR (acetone-d6, 100 MHz, plus APT) δ (up) 170.3, 136.6, 132.5, 129.0, 69.4, 35.4, δ (down) 128.9, 126.6, 125.2, 20.1.

6-methoxyisochroman-3-one(3h). The **3h** (430.0 mg) was prepared from the known 4-methoxy-2-(2-methoxy-2-oxoethyl) benzoic acid[15] (2.00 g, 8.9 mmol) by the procedure for the preparation of **3b**, and the yield was 27%, known compound [20(c)], R_f= 0.46 (EtOAC/PE = 1/2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.16 (d, J = 8.0 Hz, 1H), 6.82 (dd, J = 8.0 Hz and 2.4 Hz, 1H), 6.76 (d, J = 2.4 Hz, 1 H), 5.27 (s, 2 H), 3.82 (s, 3 H), 3.69 (s, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.9, 160.2, 132.7, 123.8, 69.9, 36.7, δ (down) 126.0, 112.9, 112.7, 55.6.

7-methoxy-1H-isochromen-3(4H)-one(3i). The **3i** (697.0 mg) was prepared from the known 2-(carboxymethyl)-5-methoxybenzoic acid[15] (1.87 g, 8.9 mmol) by the procedure for the preparation of **3b**, and the yield was 44%, known compound [18], R_f= 0.48 (EtOAC/PE = 1/2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.13 (d, J = 8.4 Hz, 1H), 6.87 (dd, J = 8.4 Hz and 2.8 Hz, 1H), 6.79 (d, J = 2.8 Hz, 1 H), 5.27 (s, 2 H), 3.82 (s, 3 H), 3.65 (s, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.0, 158.9, 132.7, 122.6, 70.1, 35.3, δ (down) 128.1, 114.2, 110.4, 55.5.

8-methoxy-1H-isochromen-3(4H)-one(3j). The **3j** (539.0 mg) was prepared from the known 2-(carboxymethyl)-6-methoxybenzoic acid[15] (1.81 g, 8.6 mmol) by the procedure for the preparation of **3b**, and the yield was 35%, R_f= 0.47 (EtOAC/PE = 1/2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.28 (t, J = 8.4 Hz, 1H), 6.80 (t, J = 8.4 Hz, 2H), 5.40 (s, 2 H), 3.85 (s, 3 H), 3.67 (s, 2 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.9, 155.2, 132.4, 119.7, 65.4, 35.7, δ (down) 129.8, 119.2, 109.1, 55.6. IR (film) 1750 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{10}H_{11}O_3$ 179.0703, found 179.0701.

1-phenylisochroman-3-one(3k). To a stirred solution of known 2-(2-benzoylphenyl) acetic acid[18](1.20 g, 5.0 mmol) in EtOH (4 ml) was added $NaBH_4$ (209.0 mg 5.5 mmol) in small portion, and the reaction temperature was controlled bellow 10 ºC. The mixture was warmed to room temperature for 8 h, and the EtOH was removed under vacumn. Then 10% aqueous HCl (2 ml) was added, and the mixture was extracted with CH_2Cl_2 (2 mL× 3), washed by water (3 mL), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography to give the lactone **3k** (1.20 g, 92% yield) as a pale-yellow solid, known compound [20(d)], R_f= 0.71 (EtOAC/PE = 1/1); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.23-7.46 (m, 8 H), 6.96 (d, J = 7.6 Hz, 1 H), 6.39 (s, 1 H), 3.74 (d, J = 18.0 Hz, 1H), 3.63 (d, J = 18.0 Hz, 1H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.7, 137.0, 134.7, 131.1, 36.6, δ (down) 129.1, 129.0, 128.9 (2), 127.6 (2), 127.4 (2), 126.1, 82.2.

1-methylisochroman-3-one(3l). The lactone **3l** (844.0 mg) was prepared from the known 2-(2-acetylphenyl) acetic acid[18] (1.00 g, 5.6 mmol) by the procedure for the preparation of lactone **3h**, and the yield was 93%, known compound [20(d)], R_f= 0.33 (EtOAC/PE = 1/3); ^{1}H NMR ($CDCl_3$, 400

MHz) δ 7.20-7.36 (m, 4H), 5.48 (q, J = 6.8 Hz, 1H), 3.74 (d, J = 18.4 Hz, 1H), 3.68 (d, J = 18.4 Hz, 1H), 1.76 (d, J = 6.8 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.8, 135.8, 130.7, 36.2, δ (down) 128.6, 127.5, 127.1, 123.6, 76.4, 19.1.

ethyl 2-(2-(azidomethyl)phenyl)acetate(4a). To a stirred solution of 3-isochromanone **3a** (1.80 g, 12.1 mmol) in dry EtOH (30 mL) was introduced HBr gas for 5 h, then EtOH was evaporated to afford the ethyl 2-(2-(bromomethyl) phenyl)acetate (3.05 g) as a brown oil. Then the crude ethyl 2-(2-(bromomethyl) phenyl) acetate was dissolved in DMF (40 ml), and NaN_3 (1.50 g, 23.0 mmol) was added into the mixture. The mixture was kept at 70 ºC for 40 min, then it was partitioned between EtOAc (15 mL) and H_2O (10 mL). The organic phase was separated and the aqueous phase was extracted with EtOAc (30 mL × 2). The combined organic phase was washed with water (30 ml × 4), dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography to give the azide **4a** as a yellow oil (2.53 g, 95% yield from **3a**), known compound[13], ^1H NMR ($CDCl_3$, 400 MHz) δ 7.28-7.36 (m, 4H), 4.42 (s, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.71 (s, 2H), 1.25 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.3, 134.1, 133.4, 61.2, 53.0, 38.7, δ (down) 131.3, 130.1, 129.0, 127.9, 14.3.

ethyl 2-(2-(azidomethyl)-5-bromophenyl)acetate(4b). The azide **4b** (1.46 g) was prepared from **3b** (1.80 g, 7.9 mmol) by the procedure for the preparation of azide **4a**, and the yield was 97%, R_f = 0.52 (EtOAC/PE = 1/6); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.43 (d, J = 2.0 Hz, 1H), 7.39 (dd, J = 8.4 Hz and 2.0 Hz, 1H), 7.17 (d, J = 8.4 Hz, 1H), 4.34 (s, 2H), 4.13 (q, J = 7.2 Hz, 2H), 3.64 (s, 2H), 1.23 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.3, 135.2, 133.1, 122.4, 61.2, 52.0, 38.0, δ (down) 133.9, 130.6, 131.2, 14.0. IR (film) 2102, 1733 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{11}H_{12}BrN_3O_2Na$ 320.0005, found 320.0003.

ethyl 2-(2-(azidomethyl)-4-bromophenyl)acetate(4c). The azide **4c** (1.43 g) was prepared from **3c** (1.98 g, 8.7 mmol) by the procedure for the preparation of azide **4a**, and the yield was 59%, R_f= 0.37 (EtOAC/PE = 1/7); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.48 (d, J = 2.0 Hz, 1H), 7.44 (dd, J = 8.0 Hz and 2.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 1H), 4.38 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 3.64 (s, 2H), 1.24 (t, J = 7.2 Hz, 3H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.6, 136.3, 132.1, 121.5, 61.3, 52.3, 38.1, δ (down) 132.8, 132.5, 131.8, 14.2. IR (film) 2102, 1732 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{11}H_{12}BrN_3O_2Na$ 320.0005, found 320.0004.

ethyl 2-(2-(azidomethyl)-4-(trifluoromethyl)phenyl)acetate(4d). The azide **4d** (597.0 mg) was prepared from **3d** (900.0 mg, 4.2 mmol) by the procedure for the preparation of azide **4a**, and the yield was 50%, R_f= 0.72 (EtOAC/PE = 1/3); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.60 (s, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 4.49 (s, 2H), 4.17 (q, J = 7.2 Hz, 2H), 3.76 (s, 2H), 1.26 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.4, 137.2, 135.3, 130.2 (q, J_{CF} = 33 Hz), 123.93 (q, J_{CF} = 270 Hz), 61.6, 52.5, 38.5, δ (down) 131.8, 126.4 (q, J_{CF} = 3 Hz), 125.7 (q, J_{CF} = 3 Hz), 14.2. IR (film) 2102, 1734 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{12}F_3N_3O_2Na$ 310.0774, found 310.0775.

ethyl 2-(2-(azidomethyl)-4-cyanophenyl)acetate(4e). The azide **4e** (175.0 mg) was prepared from **3e** (326.0 mg, 1.2 mmol) by the procedure for the preparation of azide **4a**, and the yield was 62%, R_f= 0.42(EtOAC/PE = 1/3); ^1H NMR ($CDCl_3$, 400 MHz) δ 7.66 (s, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.42 (d, J = 8.0 Hz, 1H), 4.48 (s, 2H), 4.17 (q, J = 7.2 Hz, 2H), 3.76 (s, 2H), 1.26 (t, J = 7.2 Hz, 3 H); $^{13}C\{^1H\}$ NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 170.0, 138.4, 135.9, 118.3, 111.9, 61.7, 52.1, 38.7, δ (down) 132.8, 132.3, 132.1, 14.2. IR (film) 2100, 1732 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{12}N_4O_2Na$ 267.0853, found 267.0851.

ethyl 2-(2-(azidomethyl)-5-methylphenyl)acetate(4f). The azide **4f** (465.0 mg) was prepared from **3f** (413.0 mg, 2.5 mmol) by the procedure for the preparation of azide **4a**, and the yield was 78%, R_f= 0.60 (EtOAC/PE = 1/5); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.20 (d, J = 7.6 Hz, 1H), 7.10-7.12 (m, 2H), 4.37 (s, 2H), 4.15 (q, J = 7.2 Hz, 2H), 3.67 (s, 2H), 2.35 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.3, 138.8, 133.1, 130.9, 61.1, 52.6, 38.5, δ (down) 132.0, 130.1, 128.4, 21.1, 14.2. IR (film) 2096, 1733 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3O_2Na$ 256.1057, found 256.1054.

ethyl 2-(2-(azidomethyl)-4-methylphenyl)acetate(4g). The azide **4g** (700.0 mg) was prepared from **3g** (610.0 mg, 3.8 mmol) by the procedure for the preparation of azide **4a**, and the yield was 80%, R_f= 0.53 (EtOAC/PE = 1/10); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.13-7.20 (m, 3H), 4.38 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 3.67 (s, 2H), 2.36 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.5, 137.6, 133.8, 130.2, 61.2, 53.0, 38.3, δ (down) 131.2, 130.8, 129.7, 21.2, 14.3. IR (film) 2098, 1733 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3O_2Na$ 256.1057, found 256.1055.

ethyl 2-(2-(azidomethyl)-5-methoxyphenyl)acetate(4h). The azide **4h**(200.0 mg) was prepared from **3h** (430.0 mg, 2.4 mmol) by the procedure for the preparation of azide **4a**, and the yield was 32%, R_f= 0.72 (EtOAC/PE = 1/2); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.21 (d, J = 8.4 Hz, 1H), 6.85 (d, J = 2.4 Hz, 1H), 6.80 (dd, J = 8.4 Hz and 2.4 Hz, 1H), 4.33 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 3.79 (s, 3H), 3.67 (s, 2H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.0, 159.8, 134.8, 126.0, 61.1, 52.4, 38.7, δ (down) 131.5, 116.9, 112.6, 55.3, 14.1. IR (film) 2097, 1732 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3O_3Na$ 272.1006, found 272.1004.

ethyl 2-(2-(azidomethyl)-4-methoxyphenyl)acetate(4i). The azide **4i** (238.0 mg) was prepared from **3i** (348.0 mg, 1.9 mmol) by the procedure for the preparation of azide **4a**, and the yield was 49%, R_f= 0.72 (EtOAC/PE = 1/5); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.19 (d, J = 8.4 Hz, 1H), 6.87 (d, J = 2.4 Hz, 1H), 6.83 (dd, J = 8.4 Hz and 2.4 Hz, 1H), 4.37 (s, 2H), 4.12 (q, J = 7.2 Hz, 2H), 3.78 (s, 3H), 3.62 (s, 2H), 1.23 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.4, 158.9, 135.2, 125.0, 61.0, 52.8, 37.7, δ (down) 132.2, 115.4, 113.7, 55.3, 14.1. IR (film) 2100, 1733 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3O_3Na$ 272.1006, found 272.1000.

ethyl 2-(2-(azidomethyl)-3-methoxyphenyl)acetate(4j). The azide **4j** (369.0 mg) was prepared from **3j** (539.0 mg, 3.0 mmol) by the procedure for the preparation of azide **4a**, and the yield was 49%, R_f= 0.70 (EtOAC/PE = 1/5); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.23 (d, J = 8.0 Hz, 1H), 6.85 (t, J = 8.0 Hz, 2H), 4.43 (s, 2H), 4.10 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H), 3.65 (s, 2H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.2, 158.5, 135.3, 122.8, 61.2, 45.4, 38.8, δ (down) 129.8, 123.2, 109.9, 55.8, 14.2. IR (film) 2097, 1735 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{15}N_3O_3Na$ 272.1006, found 272.0996.

ethyl 2-(2-(azido(phenyl)methyl)phenyl)acetate(4k). The azide **4k** (485.0 mg) was prepared from **3k** (998.0 mg, 4.5 mmol) by the procedure for the preparation of azide **4a**, and the yield was 40%, R_f= 0.28 (EtOAC/PE = 1/5); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.38-7.42 (m, 1H), 7.24-7.34 (m, 8H), 6.00 (s, 1H), 4.03 (q, J = 7.2 Hz, 2H), 3.58 (s, 2H), 1.17 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.0, 138.8, 137.8, 132.4, 61.0, 38.7, δ (down) 131.5, 128.7 (2), 128.5, 128.4, 128.1, 127.8, 127.5 (2), 65.3, 14.1. IR (film) 2098, 1732 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{17}H_{17}N_3O_2Na$ 318.1213, found 318.1213.

ethyl 2-(2-(1-azidoethyl)phenyl)acetate(4l). The azide **4l** (983.0 mg) was prepared from **3l** (844.0 mg, 5.2 mmol) by the procedure for the preparation of azide **4a**, and the yield was 81%, R_f=

0.68 (EtOAC/PE = 1/3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.42 (d, J = 7.6 Hz, 1H), 7.22-7.32 (m, 3H), 4.91 (q, J = 6.8 Hz, 1H), 4.15 (q, J = 7.2 Hz, 2H), 3.73 (d, J = 15.6 Hz, 1H), 3.63 (d, J = 15.6 Hz, 1H), 1.53 (d, J = 6.8 Hz, 3H), 1.25 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.3, 139.5, 131.9, 61.3, 38.7, δ (down) 131.3, 128.3, 128.2, 126.5, 57.2, 21.1, 14.3. IR (film) 2103, 1733 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{15}N_3O_2Na$ 256.1057, found 256.1054.

methyl 2-(2-(1-azidoethyl)phenyl)acetate(4m). To a stirred solution of ethyl 2-(2-(1-azidoethyl) phenyl)acetate **4m** (337.0 mg, 1.4 mmol) in THF/H_2O (1:1, 5.0 ml) was added LiOH·H_2O (14.4 mmol). The mixture was heated to 70°C for 12 h, then it was cooled to room temperature and acidified with aqueous HCl (2.0 M) to pH = 1−2. The mixture was extracted with ethyl acetate (4 mL×3), and washed by brine, dried over anhydrous Na_2SO_4, and concentrated. The residue was purified by flash chromatography to give the corresponding 2-(2-(1-azidoethyl) phenyl) acetic acid (290.0 mg) as a colorless oil. The sample was dissolved in MeOH (5 ml), and AcCl (0.2 ml, 2.0 mmol) was added at 0 ºC. The reaction mixture was kept for 5 h, then MeOH was removed. The residue was purified by flash chromatography to give the azide **4m** (260.0 mg, 70% yield) as a colorless oil, R_f= 0.44 (EtOAC/PE = 1/6); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.24-7.46 (m, 4H), 4.90 (q, J = 6.8 Hz, 1H), 3.73 (q, J = 16.0 Hz, 2H), 3.70 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.7, 139.6, 131.8, 38.6, δ (down) 131.3, 128.4, 128.3, 126.6, 57.3, 52.4, 21.1. IR (film) 2104, 1738 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{13}N_3O_2Na$ 242.0900, found 242.0903.

ethyl 2-(2-(azidomethyl)phenyl)-2-diazoacetate(1a). To a stirred solution of **4a** (1.00 g, 4.6 mmol) in CH_3CN (15 ml) under nitrogen atmosphere was added DBU (1.04 g, 6.8 mmol). 30 min later, the *p*-ABSA (1.63 g, 6.8 mmol) was added into the mixture. The reaction was kept for an additional 18 h, then CH_3CN was removed. The residue was purified by flash chromatography to afford **1a** (1.00 g, 90% yield) as a yellow oil, R_f= 0.61 (EtOAC/PE = 1/4); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36-7.46 (m, 4H), 4.40 (s, 2H), 4.29 (q, J = 7.2 Hz, 2H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 165.7, 135.8, 124.6, 61.4, 52.9, δ (down) 131.2, 129.7, 129.5, 128.8, 14.5. IR (film) 2096, 1704 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{11}N_5O_2Na$ 268.0805, found 268.0810.

ethyl 2-(2-(azidomethyl)-5-bromophenyl)-2-diazoacetate(1b). The **1b** (358.0 mg) was prepared from **4b** (434.0 mg, 1.5 mmol) by the procedure for the preparation of **1a**, and the yield was 76%, R_f= 0.59 (EtOAC/PE = 1/7); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.57 (d, J = 2.0 Hz, 1H), 7.52 (dd, J = 8.4 Hz and 2.0 Hz, 1H), 7.34 (d, J = 8.4 Hz, 1H), 4.37 (s, 2H), 4.30 (q, J = 7.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 165.2, 134.7, 126.6, 122.4, 61.7, 52.4, δ (down) 133.8, 132.5, 131.2, 14.6. IR (film) 2094, 1694 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{10}BrN_5O_2Na$ 345.9910, found 345.9913.

ethyl 2-(2-(azidomethyl)-4-bromophenyl)-2-diazoacetate(1c). The **1c** (473.0 mg) was prepared from **4c** (403.0 mg, 1.4 mmol) by the procedure for the preparation of **1a**, and the yield was 92%, R_f= 0.43 (EtOAC/PE = 1/7); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.63 (d, J = 2.0 Hz, 1H), 7.52 (dd, J = 8.4 Hz and 2.0 Hz, 1H), 7.27 (d, J = 8.4 Hz, 1H), 4.40 (s, 2H), 4.14 (q, J = 7.2 Hz, 2H), 1.32 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 160.1, 137.9, 123.7, 123.5, 61.7, 52.4, δ (down) 132.6, 132.5, 132.0, 14.6. IR (film) 2091, 1695 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{10}BrN_5O_2Na$ 345.9910, found 345.9919.

ethyl 2-(2-(azidomethyl)-4-trifluoromethyl)-2-diazoacetate(1d). The **1d** (597.0 mg) was

prepared from **4d** (597.0 mg, 2.1 mmol) by the procedure for the preparation of **1a**, and the yield was 93%, R_f= 0.68 (EtOAC/PE = 1/3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.74 (s, 1H), 7.63 (dd, J = 8.4 Hz and 1.6 Hz, 1H), 7.54 (d, J = 8.4 Hz, 1H), 4.49 (s, 2H), 4.32 (q, J = 7.2 Hz, 2H), 1.33 (t, J = 7.2 Hz, 3 H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 165.0, 136.5, 131.3 (q, J_{CF} = 33 Hz), 128.5, 123.7 (q, J_{CF} = 270 Hz), 61.8, 52.5, δ (down) 131.2, 126.4 (q, J_{CF} = 3 Hz), 125.5 (q, J_{CF} = 3 Hz), 14.4. IR (film) 2095, 1699 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{10}F_3N_5O_2Na$ 336.0679, found 336.0676.

ethyl 2-(2-(azidomethyl)-4-cyanophenyl)-2-diazoacetate(1e). The **1e** (109.0 mg) was prepared from **4e** (175.0 mg, 0.7 mmol) by the procedure for the preparation of **1a**, and the yield was 56%, R_f= 0.46 (EtOAC/PE = 1/3); ^{1}H NMR (acetone-d6, 400 MHz) δ 7.93-7.96 (m, 1H), 7.83 (dd, J = 8.4 Hz and 1.6 Hz, 1H), 7.77 (d, J = 8.4 Hz, 1H), 4.67 (s, 2H), 4.29 (q, J = 7.2 Hz, 2H), 1.29 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (acetone-d6, 100 MHz, plus APT) δ (up) 164.2, 136.9, 130.2, 117.8, 112.0, 61.2, 51.6, δ (down) 132.8, 131.7, 131.4, 13.8. IR (film) 2092, 1694 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{10}N_6O_2Na$ 293.0757, found 293.0757.

ethyl 2-(2-(azidomethyl)-5-methylphenyl)-2-diazoacetate(1f). The **1f** (467.0 mg) was prepared from **4f** (465.0 mg, 2.0 mmol) by the procedure for the preparation of **1a**, and the yield was 90%, R_f= 0.70 (EtOAC/PE = 1/5); ^{1}H NMR (acetone-d6, 400 MHz) δ 7.42 (d, J = 8.0 Hz, 1H), 7.36 (s, 1H), 7.27 (d, J = 8.0 Hz, 1H), 4.47 (s, 2H), 4.26 (q, J = 7.2 Hz, 2H), 2.42 (s, 3H), 1.27 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (acetone-d6, 100 MHz, plus APT) δ (up) 165.1, 138.7, 133.0, 124.8, 60.9, 52.2, δ (down) 131.8, 130.0, 129.9, 20.0, 13.9. IR (film) 2090, 1697 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_2Na$ 282.0962, found 282.0961.

ethyl 2-(2-(azidomethyl)-4-methylphenyl)-2-diazoacetate(1g). The **1g** (506.0 mg) was prepared from **4g** (600.0 mg, 2.6 mmol) by the procedure for the preparation of **1a**, and the yield was 76%, R_f= 0.30 (EtOAC/PE = 1/10); ^{1}H NMR (DMSO-d6, 400 MHz) δ 7.24-7.42 (m, 3H), 4.45 (s, 2H), 4.20 (q, J = 7.2 Hz, 2H), 2.35 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 165.7, 139.7, 135.9, 121.7, 61.4, 52.3, δ (down) 132.0, 130.9, 129.8, 21.2, 14.7. IR (film) 2090, 1698 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_2Na$ 282.0962, found 282.0959.

ethyl 2-(2-(azidomethyl)-5-methoxyphenyl)-2-diazoacetate(1h). The **1h** (216.0 mg) was prepared from **4h** (200.0 mg, 0.80 mmol) by the procedure for the preparation of **1a**, and the yield was 98%, R_f= 0.72 (EtOAC/PE = 1/2); ^{1}H NMR (DMSO-d6, 400 MHz) δ 7.44 (d, J = 8.8 Hz, 1H), 7.12 (d, J = 2.8 Hz, 1H), 7.03 (dd, J = 8.8 Hz and 2.8 Hz, 1H), 4.40 (s, 2H), 4.22 (q, J = 7.2 Hz, 2H), 3.78 (s, 3H), 1.22 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 165.4, 159.6, 127.8, 126.1, 61.4, 52.0, δ (down) 132.1, 117.2, 115.3, 55.8, 14.7. IR (film) 2087, 1692 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_3Na$ 298.0911, found 298.0912.

ethyl 2-(2-(azidomethyl)-4-methoxyphenyl)-2-diazoacetate(1i). The **1i** (172.0 mg) was prepared from **4i** (238.0 mg, 0.9 mmol) by the procedure for the preparation of **1a**, and the yield was 66%, R_f= 0.71 (EtOAC/PE = 1/5); ^{1}H NMR (DMSO-d6, 400 MHz) δ 7.45 (d, J = 8.4 Hz, 1H), 7.10 (d, J = 2.8 Hz, 1H), 7.02 (dd, J = 8.4 Hz and 2.8 Hz, 1H), 4.45 (s, 2H), 4.20 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz) δ 165.8, 160.5, 138.0, 133.8, 116.3, 115.9, 114.5, 61.3, 55.8, 52.3, 14.8. IR (film) 2087, 1692 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_3Na$ 298.0911, found 298.0913.

ethyl 2-(2-(azidomethyl)-3-methoxyphenyl)-2-diazoacetate(1j). The **1j** (195.0 mg) was prepared from **4j** (200.0 mg, 0.8 mmol) by the procedure for the preparation of **1a**, and the yield

was 89%, R_f= 0.68 (EtOAC/PE = 1/5); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.36 (t, J = 8.0 Hz, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.96 (d, J = 8.0 Hz, 1H), 4.43 (s, 2H), 4.29 (q, J = 7.2 Hz, 2H), 3.87 (s, 3H), 1.30 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 165.9, 158.8, 127.0, 124.0, 61.4, 47.1, δ (down) 130.0, 123.4, 111.3, 55.8, 14.5. IR (film) 2091, 1699 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_3Na$ 298.0911, found 298.0911.

ethyl 2-(2-(azido(phenyl)methyl)phenyl)-2-diazoacetate(1k). The **1k** (368.0 mg) was prepared from **4k** (414.0 mg, 1.4 mmol) by the procedure for the preparation of **1a**, and the yield was 82%, R_f= 0.44 (EtOAC/PE = 1/4); ^{1}H NMR (DMSO-d6, 400 MHz) δ 7.22-7.60 (m, 9H), 6.14 (s, 1H), 4.12 (t, J = 6.8 Hz, 2H), 1.15 (t, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 165.58, 140.73, 139.01, 123.98, 61.39, δ (down) 133.3, 130.7, 129.2, 129.1 (2), 128.6 (2), 127.5 (2), 65.3, 14.8. IR (film) 2094, 1694 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{15}N_5O_2Na$ 344.1118, found 344.1118.

ethyl 2-(2-(1-azidoethyl)phenyl)-2-diazoacetate(1l). The **1l** (450.0 mg) was prepared from **4l** (646.0 mg, 2.8 mmol) by the procedure for the preparation of **1a**, and the yield was 63%, R_f= 0.44 (EtOAC/PE = 1/6); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.54 (d, J = 7.6 Hz, 1H), 7.36-7.50 (m, 3H), 4.81 (q, J = 6.8 Hz, 1H), 4.29 (q, J = 7.2 Hz, 2H), 1.53 (d, J = 6.8 Hz, 3H), 1.31 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 161.0, 141.7, 123.9, 61.6, δ (down) 131.7, 130.3, 128.8, 127.1, 58.0, 21.3, 14.6. IR (film) 2090, 1699 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}N_5O_2Na$ 282.0962, found 282.0961.

methyl 2-(2-(1-azidoethyl)phenyl)-2-diazoacetate(1m). The **1m** (233.0 mg) was prepared from **4m** (260.0 mg, 1.2 mmol) by the procedure for the preparation of **1a**, and the yield was 80%, R_f= 0.46 (EtOAC/PE = 1/6); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.24-7.46 (m, 4H), 4.81 (q, J = 6.8 Hz, 1H), 3.83 (s, 3H), 1.53 (d, J = 6.8 Hz, 3H); ^{13}C{^{1}H} NMR ($CDCl_3$, 100 MHz, plus APT) δ (up) 171.1, 141.8, 120.8, δ (down) 131.7, 130.4, 128.8, 127.2, 58.0, 52.5, 21.3. IR (film) 2092, 1698 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{11}H_{11}N_5O_2Na$ 268.0805, found 268.0804.

ethyl 2H-isoindole-1-carboxylate(2a). To a stirred solution of $Rh_2(oct)_4$ (3.0 mg, 0.004 mmol) in DCM (4 ml) was added **1a** (100.0 mg, 0.40 mmol), and the mixture was keep for 4 h. Then the mixture was concentrated and the residue was purified by flash chromatography to give the isoindole **2a** (73.0 mg, 97% yield from **1a**) as a white soild, Mp:120-122 ºC, R_f= 0.28 (EtOAC/PE = 1/4); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.28 (s, 1H), 7.96 (d, J = 8.8, 1H), 7.64-7.71 (m, 2H), 7.19-7.23 (m, 1H), 7.02-7.06 (m, 1H), 4.33 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.1, 127.4, 125.6, 110.7, 59.7, δ (down) 125.3, 121.8, 121.7, 120.5, 117.6, 14.8. IR (film) 3195, 1645 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{11}H_{12}NO_2$ 190.0863, found 190.0862.

ethyl 6-bromo-2H-isoindole-1-carboxylate(2b). The **2b** (100.0 mg) was prepared from **1b** (130.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 93%, Mp:140-141 ºC, R_f= 0.25 (EtOAC/PE = 1/3); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.50 (s, 1H), 8.11 (s, 1H), 7.71 (s, 1H), 7.69 (d, J = 8.8, 1H), 7.14 (dd, J = 8.8 Hz and 2.0 Hz, 1H), 4.34 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 160.8, 128.1, 123.9, 119.1, 110.5, 60.0, δ (down) 124.8, 124.3, 122.4, 118.5, 15.0. IR (film) 3231, 1666 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{11}H_{11}BrNO_2$ 267.9968, found 267.9977.

ethyl 5-bromo-2H-isoindole-1-carboxylate(2c). The **2c** (96.5 mg) was prepared from **1c** (130.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 90%, Mp:141-142 ºC, R_f= 0.25 (EtOAC/PE = 1/3); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 11.15 (s, 1H), 7.95 (d, J = 8.8 Hz, 1H),

7.82 (s, 1H), 7.43 (s, 1H), 7.31 (d, J = 8.8 Hz, 1H), 4.47 (q, J = 7.2 Hz, 2H), 1.47 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 160.9, 126.5, 125.4, 114.6, 111.4, 60.0, δ (down) 128.2, 123.9, 122.7, 117.2, 15.0. IR (film) 3225, 1665 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{11}H_{11}BrNO_2$ 267.9968, found 267.9963.

ethyl 5-(trifluoromethyl)-2H-isoindole-1-carboxylate(2d). The **2d** (84.0 mg) was prepared from **1d** (125.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 82%, Mp:171-172 ºC, R_f= 0.44 (EtOAC/PE = 1/3); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.75 (s, 1H), 8.17 (s, 1H), 8.13 (d, J = 8.8 Hz, 1H), 7.88 (s, 1H), 7.39 (dd, J = 8.8 Hz and 1.6 Hz, 1H), 4.36 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 160.9, 127.6, 125.5 (q, J_{CF} = 270 Hz), 123.8, 122.3 (q, J_{CF} = 33 Hz), 111.7, 61.3, δ (down) 122.0, 120.7 (q, J_{CF} = 5Hz), 120.4 (q, J_{CF} = 3Hz), 120.0, 15.0. IR (film) 3221, 1685 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{11}F_3NO_2$ 258.0736, found 258.0734.

ethyl 5-cyano-2H-isoindole-1-carboxylate(2e). The **2e** (34.0 mg) was prepared from **1e** (54.0 mg, 0.20 mmol) by the procedure for the preparation of **2a**, and the yield was 72%, Mp:178-180 ºC, R_f= 0.21 (EtOAC/PE = 1/2); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.90 (s, 1H), 8.36 (s, 1H), 8.07 (d, J = 8.8 Hz, 1H), 7.90 (s, 1H), 7.41 (d, J = 8.8 Hz, 1H), 4.35 (q, J = 7.2 Hz, 2H), 1.37 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 160.8, 127.1, 124.1, 120.6, 112.1, 130.9, 60.3, δ (down) 130.0, 125.3, 121.9, 120.2, 14.9. IR (film) 3216, 1678 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{10}N_2O_2Na$ 237.0635, found 237.0633.

ethyl 6-methyl-2H-isoindole-1-carboxylate(2f). The **2f** (53.0 mg) was prepared from **1f** (104.0 mg, 0.40 mmol) for 16 h by the procedure for the preparation of **2a**, and the yield was 66%. Further, the **2f** (60.0 mg) could be produced from **1f** (104.0 mg, 0.40 mmol) for 4 h, and the yield was 75%. In addition, the **2f** (58.0 mg) had been prepared from **1f** (75.0 mg, 0.29 mmol) for 4 h, and the yield was 98%. Mp:115-116 ºC, R_f= 0.23 (EtOAC/PE = 1/5); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.10 (s, 1H), 7.73 (s, 1H), 7.59 (d, J = 8.8 Hz, 2H), 6.89 (dd, J = 8.8 Hz and 1.2 Hz, 1H), 4.32 (q, J = 7.2 Hz, 2H), 2.39 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.2, 134.4, 128.1, 124.3, 110.0, 59.6, δ (down) 124.5, 121.6, 119.1, 117.7, 22.4, 15.1. IR (film) 3237, 1657 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{14}NO_2$ 204.1019, found 204.1016.

ethyl 5-methyl-2H-isoindole-1-carboxylate(2g). The **2g** (70.0 mg) was prepared from **1g** (104.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 86%, Mp:147-148 ºC, R_f= 0.44 (EtOAC/PE = 1/5); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.14 (s, 1H), 7.86 (d, J = 8.8 Hz, 1H), 7.52 (d, J = 3.6 Hz, 1H), 7.43 (s, 1H), 7.06 (dd, J = 8.8 Hz and 3.6 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 2.34 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.1, 130.4, 126.1 (2), 110.6, 59.6, δ (down) 128.0, 120.3, 120.1, 116.7, 21.8, 15.1. IR (film) 3215, 1646 cm^{-1}; HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{12}H_{13}NO_2Na$ 226.0839, found 226.0832.

ethyl 6-methoxy-2H-isoindole-1-carboxylate(2h). The **2h** (77.0 mg) was prepared from **1h** (110.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 88%, Mp:150-151 ºC, R_f= 0.46 (EtOAC/PE = 1/2); ^{1}H NMR (DMSO-d6, 400 MHz) δ 12.94 (s, 1H), 7.52-7.62 (m, 2H), 7.28 (s, 1H), 6.71 (d, J = 8.8 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.80 (s, 3H), 1.36 (t, J = 7.2 Hz, 3H); $^{13}C\{^{1}H\}$ NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.2, 157.9, 128.8, 121.5, 110.1, 59.5, δ (down) 123.3, 118.2, 116.0, 98.0, 55.2, 15.1. IR (film) 3207, 1649 cm^{-1}; HRMS (ESI-TOF) m/z $[M + H]^+$ calcd for $C_{12}H_{14}NO_3$ 220.0968, found 220.0969.

ethyl 5-methoxy-2H-isoindole-1-carboxylate(2i). The **2i** (36.0 mg) was prepared from **1i** (55.0 mg, 0.20 mmol) by the procedure for the preparation of **2a**, and the yield was 82%, Mp:121-122 ºC, R_f= 0.50 (EtOAC/PE = 1/2); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.05 (s, 1H), 7.85 (d, J = 9.2 Hz, 1H), 7.48 (d, J = 3.2 Hz, 1H), 7.01 (d, J = 2.4 Hz, 1H), 6.89 (dd, J = 9.2 Hz and 2.4 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.76 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.0, 154.9, 125.9, 123.5, 110.9, 59.7, δ (down) 121.8, 119.5, 116.2, 98.75, 55.5, 15.0. IR (film) 3239, 1667 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{12}H_{13}NO_3Na$ 242.0788, found 242.0786.

ethyl 4-methoxy-2H-isoindole-1-carboxylate(2j). The **2j** (70.0 mg) was prepared from **1j** (110.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 80%, Mp:117-118 ºC, R_f= 0.51 (EtOAC/PE = 1/2); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.16 (s, 1H), 7.54 (d, J = 3.2 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.12 (t, J = 8.0 Hz, 1H), 6.89 (d, J = 7.2 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 3.88 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.2, 154.0, 129.1, 118.8, 111.3, 59.7, δ (down) 126.5, 115.2, 112.9, 99.3, 55.3, 15.0. IR (film) 3235, 1660 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{12}H_{14}NO_3$ 220.0968, found 220.0968.

ethyl 3-phenyl-2H-isoindole-1-carboxylate(2k). The **2k** (94.0 mg) was prepared from **1k** (129.0 mg, 0.40 mmol) for 3 h by the procedure for the preparation of **2a**, and the yield was 88%. Further, the **2k** (210.0 mg) could be prepared from **1k** (258.0 mg, 0.80 mmol) for 4 h, and the yield was 99%. Mp:142-143 ºC, R_f= 0.41 (EtOAC/PE = 1/4); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.45 (s, 1H), 8.06 (d, J = 8.8 Hz, 1H), 7.92 (d, J = 8.8 Hz, 1H), 7.85 (d, J = 7.6 Hz, 2H), 7.53 (t, J = 8.0 Hz, 2H), 7.41 (t, J = 7.2 Hz, 1H), 7.28 (t, J = 8.0 Hz, 1H), 7.14 (t, J = 7.6 Hz, 1H), 4.37 (q, J = 7.2 Hz, 2H), 1.39 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.2, 131.4, 129.3, 129.1, 123.1, 111.4, 59.9, δ (down) 129.3 (2), 128.5 (2), 128.2, 125.7, 123.0, 121.2, 121.0, 15.1. IR (film) 2925, 1660 cm^{-1}; HRMS (ESI-TOF) m/z [M + Na]$^+$ calcd for $C_{17}H_{15}NO_2Na$ 288.0995, found 288.0991.

ethyl 3-methyl-2H-isoindole-1-carboxylate(2l). The **2l** (69.0 mg) was prepared from **1l** (104.0 mg, 0.40 mmol) for 10 h by the procedure for the preparation of **2a**, and the yield was 85% where the solution was $CHCl_3$. Further, the **2l** (60.0 mg) could be produced from **1l** (104.0 mg, 0.40 mmol) for 8 h, and the yield was 74% where the solution was CH_2Cl_2. R_f= 0.31 (EtOAC/PE = 1/4); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.05 (s, 1H), 7.89 (d, J = 8.4 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.20 (t, J = 7.6 Hz, 1H), 6.99 (t, J = 7.6 Hz, 1H), 4.30 (q, J = 7.2 Hz, 2H), 2.58 (s, 3H), 1.35 (t, J = 7.2 Hz, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.1, 127.9, 123.9 (2), 108.2, 59.3, δ (down) 125.6, 121.0, 120.7, 120.4, 15.1, 11.2. IR (film) 3231, 1666 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{12}H_{14}NO_2$ 204.1019, found 204.1013.

methyl 3-methyl-2H-isoindole-1-carboxylate(2m). The **2m** (66.0 mg) was prepared from **1m** (98.0 mg, 0.40 mmol) by the procedure for the preparation of **2a**, and the yield was 87%, Mp:186-187 ºC, R_f= 0.29 (EtOAC/PE = 1/4); ^{1}H NMR (DMSO-d6, 400 MHz) δ 13.10 (s, 1H), 7.89 (d, J = 8.8 Hz, 1H), 7.66 (d, J = 8.8 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 6.99 (t, J = 7.2 Hz, 1H), 3.82 (s, 3H), 2.58 (s, 3H); ^{13}C{^{1}H} NMR (DMSO-d6, 100 MHz, plus APT) δ (up) 161.3, 128.1, 123.9 (2), 107.9, δ (down) 125.7, 121.1, 120.7, 120.3, 51.0, 11.2. IR (film) 3226, 1640 cm^{-1}; HRMS (ESI-TOF) m/z [M + H]$^+$ calcd for $C_{11}H_{12}NO_2$ 190.0863, found 190.0858.

ACKNOWLEDGMENT

This work was supported by the National Natural Science Foundation of China (No 21662027),

and the Program for Leading Talents of Ningxia Province (KJT2015002).

SUPPORTING INFORMATION

The Supporting Information (copies of NMR spectra for the key compounds and X-ray crystallographic data for **4a**) is available free of charge on the ACS Publications website

References

1. (a) Chen, Z.; Müller, P.; Swager, T. M. Syntheses of Soluble, π-Stacking Tetracene Derivatives.*Org. Lett.* **2006**, 8 (2), 273. (b) Hsu, D.-T.; Lin, C.-H. Synthesis of Benzo[c] and Naphtho[c]heterocycle Diesters and Dinitriles via Homoelongation. *J. Org. Chem*. **2009**, 74 (23), 9180–9187.
2. Application in material chemistry, see: (a) Sole, D.; Vallverdu, L.; Solans, X.; Font-Bardia, M.; Bonjoch, J. Intramolecular Pd-Mediated Processes of Amino-Tethered Aryl Halides and Ketones: Insight into the Ketone α-Arylation and Carbonyl-Addition Dichotomy. A New Class of Four-Membered Azapalladacycles. *J. Am. Chem. Soc.* **2003**, 125 (6), 1587–1594. (b) Howard-Jones, A. R.; Walsh, C. T. Nonenzymatic Oxidative Steps Accompanying Action of the Cytochrome P450 Enzymes StaP and RebP in the Biosynthesis of Staurosporine and Rebeccamycin. *J. Am. Chem. Soc.* **2007**, 129 (36), 11016–11017. (c) Neumann, C. S.; Walsh, C. T. Biosynthesis of (-)-(1S,2R)-Allocoronamic Acyl Thioester by an Fe^{II}-Dependent Halogenase and a Cyclopropane-Forming Flavoprotein. *J. Am. Chem. Soc*. **2008**, 130 (43), 14022–14023. (d) Shiraki, T.; Morikawa, M.-A.; Kimizuka, N. Amplification of Molecular Information through Self-Assembly: Nanofibers Formed from Amino Acids and Cyanine Dyes by Extended Molecular Pairin. *Angew. Chem. Int. Ed.* **2008**, 47 (1), 106–108.
3. For a review on the synthesis of isoindoles, see: Heugebaert, T. S. A.; Roman, B. I.; Stevens, C.V. Synthesis of isoindoles and related iso-condensed heteroaromatic pyrroles. *Chem. Soc. Rev.* **2012**, 41, 5626–5640.
4. For several representative method, see: (a) Yeom, H.-S.; Lee, J.-E.; Shin, S. Gold-Catalyzed Waste-Free Generation and Reaction of Azomethine Ylides: Internal Redox/Dipolar Cycloaddition Cascade. *Angew. Chem. Int. Ed.* **2008**, 47, 7040–7043. (b) Ohmura, T.; Kijima, A.; Suginome, M. Synthesis of 1-Borylisoindoles via Palladium-Catalyzed Dehydrogenation/C−H Borylation of Isoindolines. *J. Am. Chem. Soc.* **2009**, 131, 6070–6071. (c) Hui, B. W.-Q.; Chiba, S. Orthogonal Synthesis of Isoindole and Isoquinoline Derivatives from Organic Azides. *Org. Lett.* **2009**, 11, 729–732.
5. Wee, A. G. H.; Slobodian, J. Metal-Catalyzed Reaction of Indoline Diazoamides Possessing a C-2 CH_2X Substituent: Site-Selectivity, Diastereoselectivity, and Chemoselectivity. *J. Org. Chem.* **1996**, 61, 2897−2900.
6. Blond, A.; Moumné, R.; Bégis, G.; Pasco, M.; Lecourt, T.; Micouin, L. Rhodium(II) carbene-mediated modification of 2-deoxystreptamine surrogates. *Tetrahedron Lett.* **2011**, 52, 3201−3203.
7. (a) Gu, P.; Wu, X.-P.; Su, Y.; Li, X.-Q.; Xue, P.; Li, R. Rhodium-Catalyzed Intermolecular Reaction of Alkyl Azides with Diazo(aryl)acetates. *Synlett.* **2014**, 25, 535−538. (b) Wu, X.-P.; Su, Y.; Gu, P. Catalytic Enantioselective Desymmetrization of 1,3-Diazido-2-propanol via Intramolecular Interception of Alkyl Azides with Diazo(aryl)acetates. *Org. Lett.* **2014**, 16, 5339−5341. (c) Qiao, J.-B.; Zhao, Y.-M.; Gu, P. Asymmetric Intramolecular Desymmetrization of meso-α,α′-Diazido Alcohols with Aryldiazoacetates: Assembly of

Chiral C3 Fragments with Three Continuous Stereocenters. *Org. Lett.* **2016**, 18, 1984−1987

8. Mandler, M. D.; Truong, P. M.; Zavalij, P. Y.; Doyle, M. P. Catalytic Conversion of Diazocarbonyl Compounds to Imines: Applications to the Synthesis of Tetrahydropyrimidines and β-Lactams. *Org. Lett.* **2014**, 16, 740−743.
9. For synthesis of **4a**, see: Philippe, N.; Levacher, V.; Dupas, G.; Que´guiner, G.; Bourguignon, J. Diastereoselective Protonation of Lactam Enolates Derived from (R)-Phenylglycinol. A Novel Asymmetric Route to 4-Phenyl-1,2,3,4-tetrahydroisoquinolines. *Org. Lett.* **2000**, 2 (15), 2185-2187.
10. Regitz diazo transfer reaction, see: Regitz, M. New Methods of Preparative Organic Chemistry. Transfer of Diazo Groups. *Angew. Chem. Int. Ed.* **1967**, 6, 733-749.
11. Caution: the azides are suggested to be potentially explosive compounds, special precautions must be taken in its handling. From the TGA and DSC experiments, the azide **1a** was found to be decomposed at about 80 ºC.
12. isoindole **2a**, a known compound, see: Ito, S.; Akaki, M.; Shinozaki, Y.; Iwabe, Y.; Furuya, M.; Tobata, M.; Roppong, M.; Sato, T.; Itoh, N.; Oba, T. Efficient synthesis of isoindoles using supercritical carbon dioxide. *Tetrahedron Lett.* **2017**, 58 (13), 1338-1342.
13. Hanna, A.; Heidi, D.; Georges, V.; Gunnar, L.; Anders, K.; Mathias, H. Ligands to the (IRAP) /AT4 receptor encompassing a 4-hydroxydiphenylmethane scaffold replacing Tyr2. *Bioorg. Med. Chem.* **2008**, 16 (14), 6924-6935.
14. Trost, B. M.; Kalnmals, C. A. Sulfones as Synthetic Linchpins: Transition-Metal-Free sp^3–$sp^2$and sp^2–sp^2 Cross-Couplings Between Geminal Bis(sulfones) and Organolithium Compounds. *Chem. –Eur. J.* **2018**, 24 (36), 9066-9074.
15. Kilikli, A. A.; Dengiz, C.; Özcan, S.; Balci, M. Synthesis of Indolin-2-one, Isoindolin-1-one, and Indole Derivatives from Homophthalic Acid. *Synthesis*. **2011**, (22), 3697-3705.
16. Borsche, W.; Diacont, K.; Hanau, H. Über 5-Carboxyhomophthalsaure, 6-Nitro-phthalid und 6-Nitro-phthalimidin. *Ber. Dtsch. Chem. Ges.* **1934**, 67B, 675-86.
17. Peter A. S. S.; Robert O. K. Cyclization of Isothiocyanates as a Route to Phthalic and Homophthalic Acid Derivatives. *J. Org. Chem*. **1964**, 29 (8), 2261-2265.
18. Kanapure, S. P.; Das, K. G.; Bhawal, B. M. An Improved Synthesis of 7-Methoxyisochroman-3-one: A Synthon for Generation of *o*-Quinodimethanes. *Synth. Commun.* **1984**, 14 (13), 1205-1211.
19. Martin, S.; Peter, J. W. Light-Induced Decarboxylation of (o-Acylphenyl)acetic Acids. *Org. Lett.* **2002**, 4 (3), 379-382.
20. (a) Li, T.-T.; Xiang,C.-B.; Zhang, B.-J.; Yan, J. Hypervalent Iodine Catalyzed Cyclization of Aryl–Substituted Alkanoic Acids. *Helv. Chim. Acta.* **2014**, 97 (6), 854-860. (b) Zhang, B.-J.; Han, L.-Q.; Li, T.-T.; Yan, J.; Yang, Z.-P. Ammonium Iodide–Promoted Cyclization of Aryl-Substituted Carboxylic Acids. *Synth. Commun.* **2014**, 44 (11), 1608-1613. (c) Brancaccio, G.; Larizza, A.; Lettieri, G.; Monforte, P. 2-(Arylmethyl)arylacetic acids as potential antiinflammatory agents. *J. Med. Chem.* **1981**, 24 (8), 998-1000. (d) Shigehisa, H.; Hayashi, M.; Ohkawa, H.; Suzuki, T.; Okayasu, H.; Mukai, M.; Yamazaki, A.; Kawai, R.; Kikuchi, H.; Satoh, Y.; Fukuyama, A.; Hiroya, K. Catalytic Synthesis of Saturated Oxygen Heterocycles by Hydrofunctionalization of Unactivated Olefins: Unprotected and Protected Strategies. *J. Am. Chem. Soc.* **2016**, 138 (33), 10597-10604.