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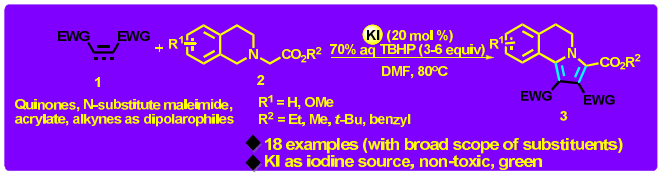


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Cite this: DOI: 10.1039/c0xx00000x

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ARTICLE TYPE

# A General, Simple and Green Access to Pyrrolo[2,1-a]isoquinolines Using KI/TBHP Catalytic System

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***Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX***

**DOI: 10.1039/b000000x**

A novel KI/TBHP-catalyzed 1,3-dipolar cycloaddition/oxidation/aromatization cascade reaction provided a general, efficient and green access to biologically important pyrrolo[2,1-a]isoquinolines. The product pyrrolo[2,1-a]isoquinolines were obtained from reactions between simple, readily available dipolarophiles and tetrahydroisoquinolines in moderate to excellent yields The reaction was environmentally benign in adoption of nontoxic KI as catalyst and IOH was generated *in situ* from the oxidation reaction of KI and TBHP.

## Introduction

Recently, various challenging metal-free reactions have been developed *via* hypervalent iodine,[1] molecular iodine,[2] DDQ,[3] strong base[4] etc. as catalysis. Very recently, a novel class of iodide-based oxidation catalysts was introduced by Ishihara and co-workers,[5] and the most important features of this catalytic system are the oxidation reactions require no metals and that water or *tert*-butyl alcohol is the only by-product derived from the co-oxidant. Comparing to molecular iodine, iodide is cheaper, non-toxic and safe to the environment. This green and efficient method has attracted various chemists to synthesize abundant important compounds such as 2-acyl-2,3-dihydrobenzofuran derivatives,[5b] 2-aminobenzoxazoles,[6] *N*-nitrosamines,[7] amides,[8] 2-aryl benzothiazoles,[9] sulfonated oxindoles,[10] α-amino acid esters,[11] *tert*-butyl peresters,[12] allylic ester,[13] *N*-sulfonyl formamidine,[14] benzylic esters,[15] highly functionalized [6,6,5] tricyclic frameworks[16] and iodophenols[17] et al.

The pyrrolo[2,1-a]isoquinoline structure occurs in lamellarin alkaloids, a newly discovered family of marine natural products that exhibit a wide spectrum of biological activities containing potent inhibitor of human topoisomerase I, inhibition of HIV integrase and potential antitumor activities (Figure 1).[18] So far, various approaches to the synthesis of this useful carbon skeleton have been developed,[19] especially the powerful 1,3-dipolar cycloaddition.[20m-s] Very recently, iodine-catalyzed 1,3-dipolar cycloaddition/oxidation/aromatization cascade with hydrogen peroxide as the terminal oxidant to pyrrolo[2,1-a]isoquinolines was reported by our group (Scheme 1, eq 1).[19s] As part of our ongoing research program the functionalized quinone structures[19s, 20] and inspired by the reported iodide-based oxidation catalysts, we herein report a general, simple and green access to pyrrolo[2,1-a]isoquinolines using KI/TBHP catalytic system (Scheme 1, eq 2). The reaction was environmentally benign in adoption of nontoxic KI as catalyst and IOH was generated *in situ* from the oxidation reaction of KI and TBHP.

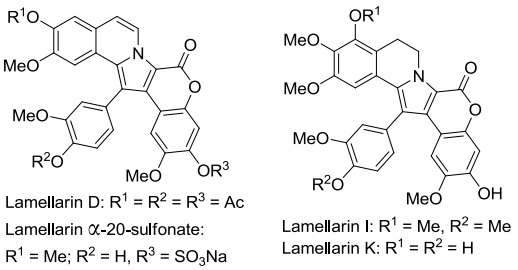
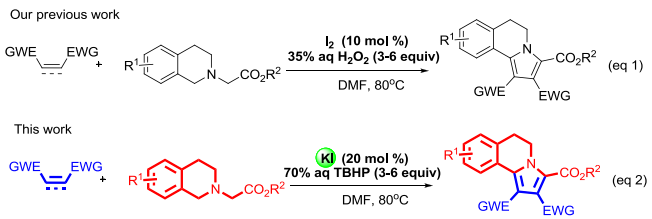



**Fig. 1** Biologically important pyrrolo [2, 1-*a*] isoquinoline lamellarin alkaloids



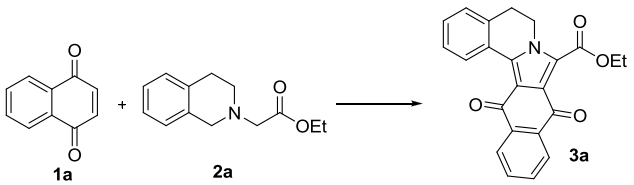

**Scheme 1** Methods for the construction of pyrrolo[2,1-a]isoquinolines.

## Results and discussion

Initially, we focused on examining the feasibility of the reaction of 1,4-naphthoquinone (**1a**) with ethyl 2-(3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2a**) and optimizing the reaction conditions. Excitingly, the proposed reaction between **1a** and **2a** did indeed occur in the presence of KI (20 mol%) and 70% aqueous TBHP (3 equiv) in DMF (80 $^{o}$C) for 10 h to afford the corresponding product (**3a**) in 60% yield (Table 1, entry 1). This result was due to iodine generated *in situ* from the oxidation reaction of iodide with TBHP. Several other solvents were also examined, but the

yield of **3a** was not improved in all these tested solvents comparing with DMF (entry 2-6). The yield of **3a** was still not increased when the amount of KI was up to 30 mol% (entry 7). However, the yield of **3a** was increased slightly when the amount of 70% aqueous TBHP was increased to 6 equiv (entry 8). When the amount of **2a** increased to 1.5 euqiv, the yield of **3a** was up to 73% (entry 9). Encouraged by these results, we further increased the amount of **2a** to 1.7 equiv, the yield of **3a** was obtained in 87% (entry 10). However, the yield of **3a** decreased slightly when the amount of **2a** increased to 2 equiv (entry 11). To further improve the economy of the reaction, the amount of KI decreased to 0.1 equiv, **3a** was only obtained in 70% yield (entry 12). Another oxidant (35% aqueous $H_2O_2$) was added instead of 70% aqueous TBHP, we only obtained **3a** in 50% yield (entry 13). Finally, the best yield of **3a** (87%) was obtained from the reaction of **1a** (1 mmol), **2a** (1.7 mmol), KI (20 mol %), and 70% aqueous TBHP (3 mmol) in DMF (5 mL) at 80 ℃ for 9 h (entry 10).

**Table 1** Optimization of reaction conditions[a]




| entry | solvent | temp (℃) | time (h) | KI (equiv) | **1a**:**2a** | yield of **3a** (%)[b] |
|---|---|---|---|---|---|---|
| 1 | DMF | 80 | 10 | 0.2 | 1:1.2 | 60 |
| 2 | EtOH | reflux | 15 | 0.2 | 1:1.2 | 57 |
| 3 | $CH_3CN$ | reflux | 30 | 0.2 | 1:1.2 | 51 |
| 4 | $CHCl_3$ | reflux | 28 | 0.2 | 1:1.2 | 47 |
| 5 | THF | reflux | 17 | 0.2 | 1:1.2 | 54 |
| 6 | 1,4-dioxane | reflux | 16 | 0.2 | 1:1.2 | 57 |
| 7 | DMF | 80 | 10 | 0.3 | 1:1.2 | 57 |
| 8[c] | DMF | 80 | 10 | 0.2 | 1:1.2 | 61 |
| 9 | DMF | 80 | 9 | 0.2 | 1:1.5 | 73 |
| 10 | DMF | 80 | 9 | 0.2 | 1:1.7 | **87** |
| 11 | DMF | 80 | 9 | 0.2 | 1:2.0 | 86 |
| 12 | DMF | 80 | 14 | 0.1 | 1:1.7 | 70 |
| 13[d] | DMF | 80 | 12 | 0.2 | 1:1.7 | 50 |

[a] Compound **1a** (1.0 mmol), **2a** (1.2-2.0 mmol), KI (10 mol%-30 mol%) and 70% aqueous TBHP (3-6 equiv) in solvent (5 mL) were stirred for several hours at the specified temperature until **1a** was consumed. [b]Isolated yield. [c]The amount of 70% aqueous TBHP was increased to 6 equiv. [d] 3 equiv. 35% aqueous $H_2O_2$ was added instead of 70% aqueous TBHP.

With the optimal reaction conditions established, we then examined the substrate scope of this KI/TBHP catalytic system to construct pyrrolo[2,1-a]isoquinolines (Scheme 2). As the reaction of **1a**, 1,4-anthraquinone (**1b**) was also reacted smoothly with **2a** and the corresponding products (**3b**) was yielded in 93%. However, when *N*-phenyl maleimides (**1c**) was employed under the optimal condition, the corresponding product (**3c**) was only obtained in 70% yield. When the amount of TBHP was up to 6 equiv, the yield of **3c** increased to 94%. Then several other *N*-substituted maleimides (**1d**–**1h**) reacted with **2a** in the presence of 6 equivTBHP and the corresponding products (**3d-3h**) were obtained in good yields (74%-94%). More importantly, other dipolarophiles, such as activated alkynes and acrylates, also reacted smoothly with **2a** to afford the desired products in moderate yields 78% and 50%. To further evaluate the substrate scope, we examined various tetrahydroisoquinoline derivatives **2**. Excitingly, **3k** was obtained in 90% yield when ethyl 2-(6,7-dimethoxy-3,4-dihydroisoquinolin-2(1H)-yl)acetate (**2b**) was employed. Similarly, the desired products **3l** and **3m** were both obtained in 80% when 1,4-anthraquinone (**1b**) and *N*-phenylmaleimide (**1c**) reacted with **2b**. Encouraged by these results, we prepared some tetrahydroisoquinoline derivatives containing various ester groups (methyl, ethyl, tertiary butyl, and benzyl) and allowed them to react with 1,4-naphthoquinone (**1a**) or *N*-phenylmaleimide (**1c**). The corresponding products **3m**-**3r** were also obtained in good yields, except the lower yield of **3p** and **3q** in 61% and 58% due to the steric of *tert*-butyl group. The yields obtained using the protocol described here were comparable to those reported in Ref. 19s (Scheme 2, yields in parentheses), indicating that the products can be synthesized effectively *via* 1,3-dipolar cycloaddition/oxidation/aromatization cascade reaction. This approach could therefore be considered a proper alternative to the reported process catalyzed by iodine reported in Ref. 19s. Moreover, the paper's merit lay in the adoption of environmentally benign catalyst (KI) which was favorable and highly pursued nowadays.

According to the above experimental results and previous reports,[5, 7, 8b, 11-14, 19s, 21] a plausible mechanism was proposed (Scheme 3). Initially tertiary amine (**2a**) was oxidized to isoquinolinium salt **A** by IOH, which was oxidized from KI by TBHP.[22] Then 1,3-dipole **B** was formed by elimination of HI with **2a** served as tertiary amine base, and then the 1,3-dipolar cycloaddition reaction between **B** and **1a** to afford the addition intermediate **D**. Finally, **3a** was formed through sequential oxidation. At the same time, intermediate **C** was reoxidized to IOH and **2a** in the presence of excess TBHP.[23]

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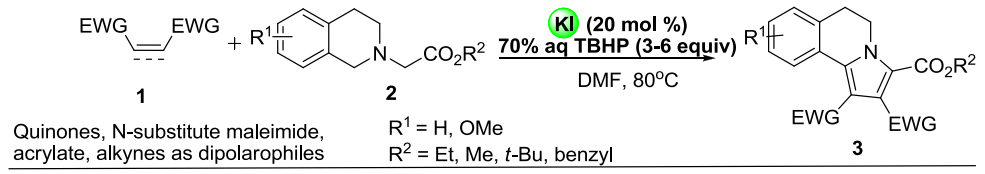


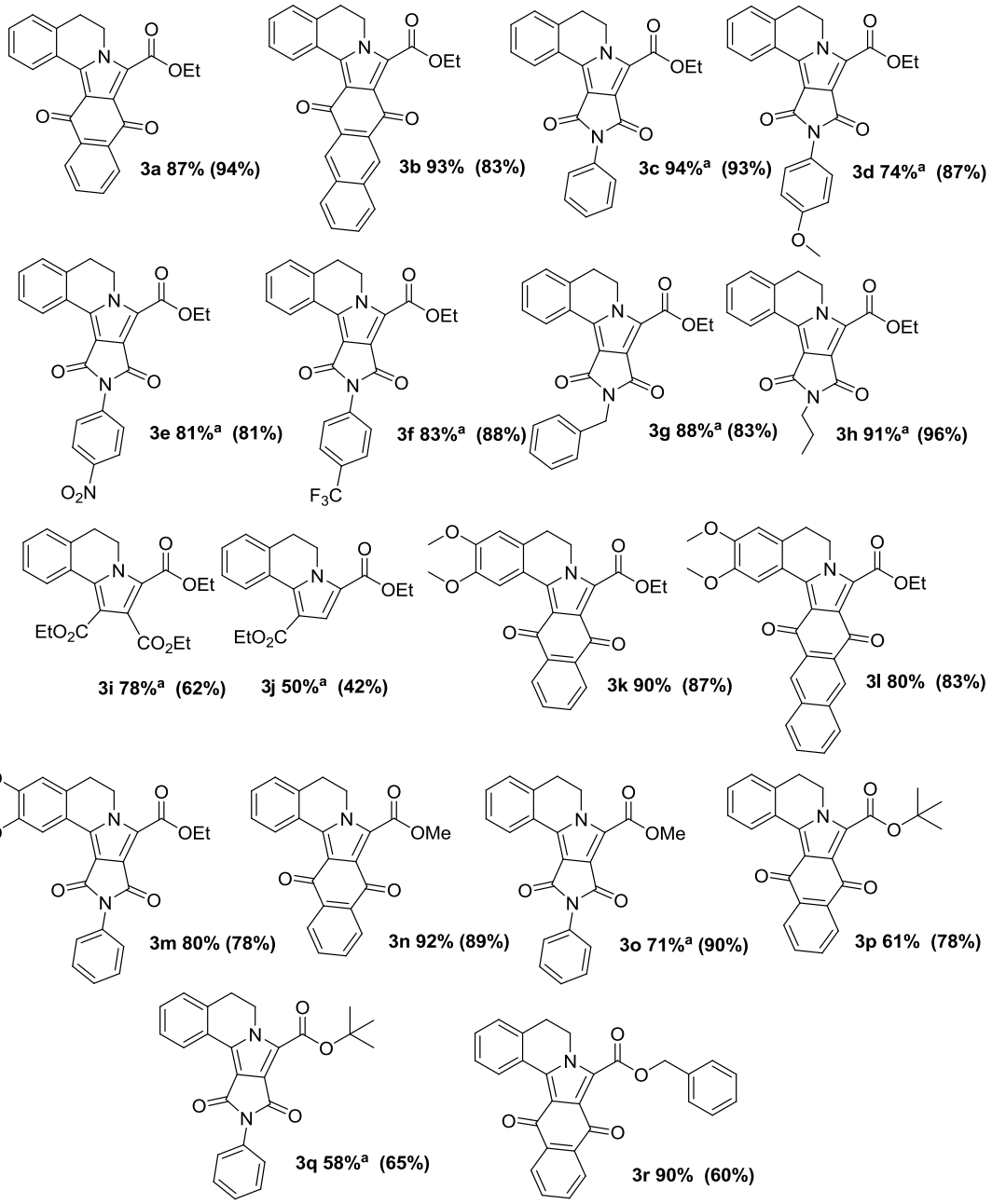


[a] 6 equiv 70% aq TBHP was added. Yields reported in Ref. 19s are given inparentheses

**Scheme 2** Reaction of different dipolarophiles with tetrahydroisoquinolines.

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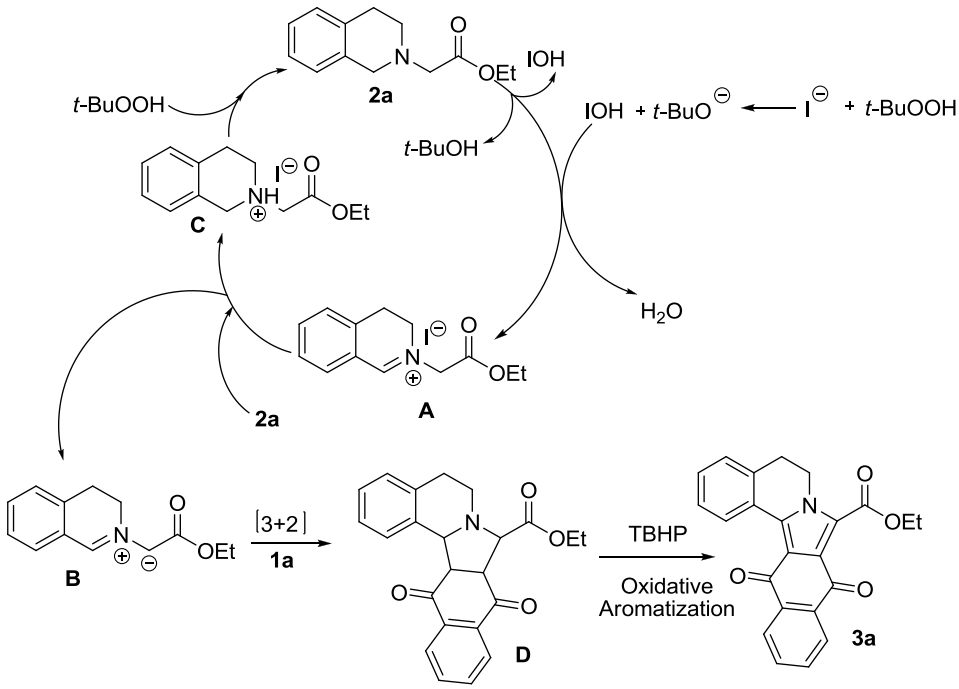



**Scheme 3** Proposed mechanism

## Conclusions

In summary, we have developed a novel protocol for the synthesis of pyrrolo[2,1-a]isoquinolines using KI/TBHP catalytic system. The reaction is environmentally benign in adoption of nontoxic KI as catalyst and IOH is generated *in situ* from the oxidation reaction of KI and TBHP. This novel KI/TBHP-catalyzed 1,3-dipolar cycloaddition/oxidation/aromatization cascade reaction provides a general, efficient and green access to biologically important pyrrolo[2,1-a]isoquinolines and more transformations by this useful catalytic system are currently underway in our laboratory.

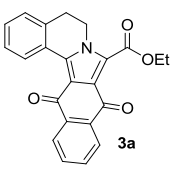
## Experimental

### General information

All solvents were purified and dried using standard methods prior to use. Commercially available reagents were used without further purification. $^{1}$H NMR spectra were recorded on an NMR instrument operated at 500 MHz. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 7.26 ppm). $^{13}$C NMR spectra were recorded on an NMR instrument operated at 125 MHz with complete proton decoupling. Chemical shifts are reported in ppm with the solvent resonance as the internal standard ($CDCl_3$: δ 77.1 ppm). MS and HRMS were measured in EI or ESI mode and the mass analyzer of the HRMS was TOF. Thin layer chromatography was performed on pre-coated glass back plates and visualized with UV light at 254 nm. Flash column chromatography was performed on silica gel.

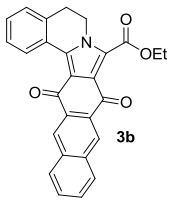
### Representative procedure for the synthesis of 3a

A dipolarophile **1a** (1.0 mmol) was added to a mixture of a tetrahydroisoquinoline **2a** (1.7 mmol), 70% aqueous TBHP (3-6 mmol), and potassium iodide (0.2 mmol) in DMF (5.0 mL). The solution was stirred for 9 h at 80 ℃. After **1a** was completely consumed (as indicated by TLC and GC-MS), the reaction mixture was washed with aqueous $Na_2S_2O_3$, dried over magnesium sulfate, and concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel with $CH_2Cl_2$ as the eluent provided desired products **3a**.

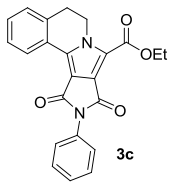



**Ethyl 9,14-dioxo-5,6,9,14-tetrahydrobenzo[5,6]isoindolo[1,2-a] isoquinoline-8-carboxylate (3a)** [19m]**:** yellow solid, yield 87% (0.323 g), mp 144-145°C; $^{1}$H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.01 (d, *J* = 8.0 Hz, 1H), 8.31-8.30 (m, 1H), 8.23-8.21 (m, 1H), 7.75-7.69 (m, 2H), 7.46 (t, *J* = 8.0 Hz, 1H), 7.39 (t, *J* = 6.5 Hz, 1H), 7.29-7.27 (m, 1H), 4.56 (q, *J* = 7.0 Hz, 2H), 4.30 (t, *J* = 6.5 Hz, 2H), 3.12 (t, *J* = 6.5 Hz, 2H), 1.51 (t, *J* = 7.0 Hz, 3H); IR

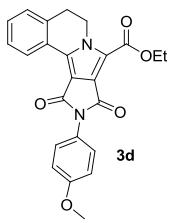
$\nu$/cm$^{-1}$ (KBr) 1704, 1660, 1524, 1465, 1413, 1384, 1311, 1268, 1227, 1141, 1108, 1047, 1010, 984, 790, 729, 711; GC-MS *m/z* 372.0 $[M+1]^+$, 326.7, 301.0, 243.6, 77.8, 51.0.



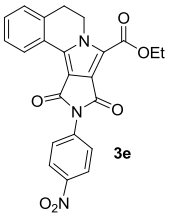

**Ethyl 9,16-dioxo-5,6,9,16-tetrahydronaphtho[5,6]isoindolo[1,2-a]isoquinoline-8-carboxylate (3b)** [19S]**:** orange solid, yield 93% (0.392 g), mp 234-235°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.00 (d, *J* = 8.0 Hz, 1H), 8.71 (s, 1H), 8.63 (s, 1H), 7.95-7.94 (m, 2H), 7.55-7.54 (m, 2H), 7.41 (t, *J* = 7.5 Hz, 1H), 7.32 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.5 Hz, 1H), 4.57 (q, *J* = 7.0 Hz, 2H), 4.22 (t, *J* = 6.5 Hz, 2H), 3.06 (t, *J* = 6.5 Hz, 2H), 1.54 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.4, 179.2, 161.6, 135.5, 134.8, 134.6, 133.5, 132.1, 131.2, 129.9, 129.8, 129.7, 129.2, 129.0, 128.8, 128.7, 128.5, 127.3, 127.3, 126.4, 126.1, 124.0, 118.2, 62.5, 43.1, 29.1, 14.1; IR $\nu$/cm$^{-1}$ (KBr) 1665, 1461, 1267, 1016, 751; HRMS (ESI-TOF) *m/z* Calcd for $C_{27}H_{20}NO_4$ $[M+H]^+$ 422.1392, found 422.1388.



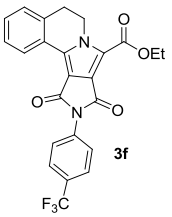

**Ethyl 9,11-dioxo-10-phenyl-6,9,10,11-tetrahydro-5H-pyrrolo[3',4':3,4]pyrrolo[2,1-a]isoquinoline-8-carboxylate (3c)** [19m]**:** white solid, yield 94% (0.363 g), mp 190-191°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.59 (d, *J* = 8.5 Hz, 1H), 7.50 (t, *J* = 7.0 Hz, 2H), 7.43-7.36 (m, 5H), 7.29 (d, *J* = 7.5 Hz, 1H), 4.77 (q, *J* = 8.0 Hz, 2H), 4.44 (q, *J* = 7.0 Hz, 2H), 3.18 (t, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 8.0 Hz, 3H); IR $\nu$/cm$^{-1}$ (KBr) 1759, 1709, 1551, 1482, 1421, 1384, 1341, 1301, 1279, 1198, 1155, 1111, 1090, 1051, 945, 895, 862, 823, 759; GC-MS *m/z* 386.8 $[M+1]^+$, 385.8, 339.9, 314.0, 270.1, 139.1.



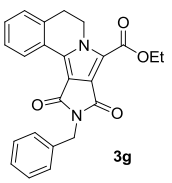

**Ethyl 10-(4-methoxyphenyl)-9,11-dioxo-6,9,10,11-tetrahydro-5*H*-pyrrolo-[3',4':3,4] pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3d)** [19n]**:** white solid, yield 74% (0.308 g), mp 168-169°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.57 (d, *J* = 7.5 Hz, 1H), 7.41-7.35 (m, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 7.28-7.27 (m, 1H), 7.00 (d, *J* = 9.0 Hz, 2H), 4.75 (t, *J* = 7.0 Hz, 2H), 4.42 (q, *J* = 7.5 Hz, 2H), 3.84 (s, 3H), 3.17 (t, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.5 Hz, 3H); IR $\nu$/cm$^{-1}$ (KBr) 1761, 1707, 1514, 1385, 1280, 1250, 1194, 1159, 1111, 1031, 809, 743; GC-MS *m/z* 417.3 $[M+1]^+$, 385.1, 325.6, 288.2, 236.1, 156.7, 71.1.



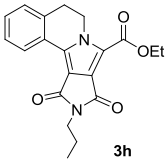

**Ethyl 10-(4-nitrophenyl)-9,11-dioxo-6,9,10,11-tetrahydro-5*H*-pyrrolo-[3',4':3,4] pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3e)** [19n]**:** yellow solid, yield 81% (0.349 g), mp 206-207°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.55 (d, *J* = 8.5 Hz, 1H), 8.35 (d, *J* = 9.0 Hz, 2H), 7.72 (d, *J*= 9.5 Hz, 2H), 7.46-7.40 (m, 2H), 7.32 (d, *J* = 7.0 Hz, 1H), 4.80 (t, *J* = 6.5 Hz, 2H), 4.46 (q, *J* = 7.5 Hz, 2H), 3.21 (t, *J* = 6.5 Hz, 2H), 1.49 (t, *J* = 7.5 Hz, 3H); IR $\nu$/cm$^{-1}$ (KBr) 1761, 1713, 1524, 1384, 1321, 1277, 1194, 1138, 1109, 1040, 1011, 893, 853, 817, 777; GC-MS *m/z* 432.5 $[M+1]^+$, 400.2, 333.8, 263.9, 200.9, 184.5, 85.1.



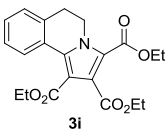

**Ethyl 10-(4-trifluoromethylphenyl)-9,11-dioxo-6,9,10,11-tetrahydro-5*H*-pyrrolo-[3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3f)** [19S]**:** white solid, yield 83% (0.377 g), mp 203-204°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.49-8.47 (m, 1H), 7.72 (d, *J* = 8.5 Hz, 2H), 7.58 (d, *J*= 8.5 Hz, 2H), 7.36-7.34 (m, 2H), 7.25 (t, *J* = 4.5 Hz, 1H), 4.70 (t, *J* = 7.0 Hz, 2H), 4.39 (q, *J* = 7.0 Hz, 2H), 3.13 (t, *J* = 7.0 Hz, 2H), 1.47 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 162.2, 160.6, 159.1, 135.8, 134.2, 133.5, 132.3, 130.3, 127.7, 127.6, 127.5, 126.8, 125.7, 125.6, 125.5, 125.1, 124.5, 122.8, 118.8, 115.6, 61.5, 43.2, 27.9, 13.9; IR $\nu$/cm$^{-1}$ (KBr) 1762, 1712, 1477, 1417, 1385, 1325, 1277, 1196, 1162, 1117, 1068, 1019, 947, 895, 845, 815; GC-MS *m/z* 454.7 $[M+1]^+$, 453.8, 371.0, 408.8, 381.8, 338.0, 139.0; HRMS (ESI-TOF) *m/z* Calcd for $C_{24}H_{18}F_3N_2O_4$ $[M+H]^+$ 455.1219, found 455.1216.



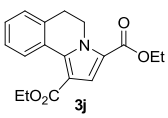

**Ethyl 10-benzyl)-9,11-dioxo-6,9,10,11-tetrahydro-5*H*-pyrrolo-[3',4':3,4]pyrrolo [2,1-*a*] isoquinoline-8-carboxylate (3g)** [19n]**:** white solid, yield 88% (0.352 g), mp 200-201°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.49 (d, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.0 Hz, 2H), 7.38-7.30 (m, 3H), 7.27-7.23 (m, 1H), 7.20 (d, *J* = 7.0 Hz, 1H), 4.77 (s, 2H), 4.68 (t, *J* = 7.0 Hz, 2H), 4.43 (q, *J* = 7.0 Hz, 2H), 3.10 (t, *J* = 7.0 Hz, 2H), 1.49 (t, *J* = 7.0 Hz, 3H); GC-MS *m/z* 401.0 $[M+1]^+$, 400.0, 371.0, 353.9, 325.9, 224.2, 195.1.



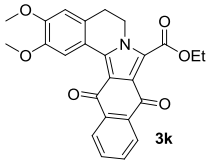

**Ethyl 10-propyl-9,11-dioxo-6,9,10,11-tetrahydro-5*H*-pyrrolo [3',4':3,4]pyrrolo[2,1-*a*] isoquinoline-8-carboxylate (3h)** [19S]: white solid, yield 91% (0.321 g), mp 188-189°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.53 (d, *J* = 8.5 Hz, 1H), 7.42-7.39 (m, 1H), 7.38-7.34 (m, 1H), 7.27 (d, *J* = 8.5 Hz, 1H), 4.72 (t, *J* = 7.0 Hz, 2H), 4.43 (q, *J* = 7.0 Hz, 2H), 3.59 (t, *J* = 7.0 Hz, 2H), 3.15 (t, *J* = 7.0 Hz, 2H), 1.72-1.67 (m, 2H), 1.49 (t, *J* = 7.0 Hz, 3H), 0.96 (t, *J* = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 164.2, 162.7, 159.7, 132.8, 132.4, 130.1, 127.9, 127.9, 127.6, 125.9, 125.7, 118.1, 116.7, 61.5, 43.3, 39.9, 28.4, 22.0, 14.2, 11.4; IR *ν*/cm$^{-1}$ (KBr) 1752, 1700, 1471, 1385, 1330, 1280, 1199, 1123, 1012, 779, 746; GC-MS *m/z* 353.0 $[M+1]^+$, 352.0, 323.1, 278.1, 266.2, 222.2, 139.2, 103.0; HRMS (ESI-TOF) *m/z* Calcd for $C_{20}H_{21}N_2O_4$ $[M+H]^+$ 353.1501, found 353.1498.



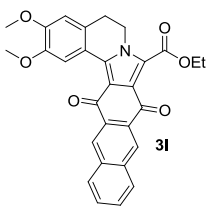

**3-Ethyl 1,2-diethyl 5,6-dihydropyrrolo[2,1-*a*]isoquinoline-1,2,3-tricarboxylate (3i)** [19S]: white solid, yield 78% (0.301 g), mp 112-113°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.20-8.18 (m, 1H), 7.32-7.30 (m, 2H), 7.25-7.24 (m, 1H), 4.54 (t, *J* = 7.0 Hz, 2H), 4.38 (q, *J* = 7.0 Hz, 2H), 4.34-4.30 (m, 4H), 3.00 (t, *J* = 7.0 Hz, 2H), 1.41 (t, *J* = 7.0 Hz, 3H), 1.37-1.32 (m, 6H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 166.0, 163.4, 159.9, 136.6, 134.3, 129.2, 128.5, 127.3, 126.9, 126.9, 126.5, 119.0, 110.8, 61.4, 61.0, 60.7, 42.6, 29.4, 14.12, 14.09, 14.05; IR *ν*/cm$^{-1}$ (KBr) 1673, 1581, 1431, 1366, 1155, 1043, 886; GC-MS *m/z* 385.5 $[M]^+$, 384.7, 339.7, 312.8, 265.7, 221.9, 139.0, 129.9; HRMS (ESI-TOF) *m/z* Calcd for $C_{21}H_{24}NO_6$ $[M+H]^+$ 386.1604, found 386.1598.



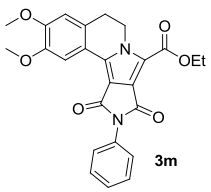

**Diethyl 5,6-dihydropyrrolo[2,1-*a*]isoquinoline-1,3-dicarboxylate (3j)** [19n]: yellow solid, yield 50% (0.157 g), mp 100-101°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.45 (d, *J* = 8.5 Hz, 1H), 7.50 (s, 1H), 7.36-7.30 (m, 2H), 7.25 (d, *J* = 6.0 Hz, 1H), 4.61 (t, *J* = 6.5 Hz, 2H), 4.37-4.32 (m, 4H), 3.03 (t, *J* = 6.5 Hz, 2H), 1.41-1.38 (m, 6H); GC-MS *m/z* 314.2 $[M+1]^+$, 312.9, 283.5, 155.9,73.5.



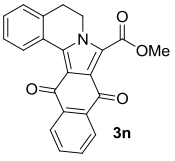

**Ethyl 2,3-dimethoxy-9,14-dioxo-5,6,9,14-tetrahydrobenzo[5,6]isoindolo[1,2-a] isoquinoline-8-carboxylate (3k)** [19S]: orange solid, yield 90% (0.388 g), mp 194-195°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.88 (s, 1H), 8.23 (t, *J* = 2.0 Hz, 1H), 8.12-8.10 (m, 1H), 7.66-7.60 (m, 2H), 6.67 (s, 1H), 4.51 (q, *J* = 7.0 Hz, 2H), 4.21 (t, *J* = 7.0 Hz, 2H), 4.06 (s, 3H), 3.89 (s, 3H), 3.01 (t, *J* = 7.0 Hz, 2H), 1.48 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.5, 179.4, 161.5, 150.2, 147.6, 136.2, 135.8, 134.6, 133.1, 132.7, 127.3, 126.9, 126.4, 125.9, 122.9, 119.1, 116.3, 112.4, 110.2, 62.4, 54.3, 55.9, 43.3, 28.5, 14.0; IR *ν*/cm$^{-1}$ (KBr) 1718, 1657, 1479, 1385, 1282, 1257, 1217, 1152, 1132, 1045, 1015, 705; HR MS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}NO_6$ $[M+H]^+$ 432.1447, found 432.1444.



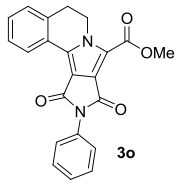

**Ethyl 2,3-dimethoxy-9,16-dioxo-5,6,9,16-tetrahydronaphtho[5,6]isoindolo[1,2-a] isoquinoline-8-carboxylate (3l)** [19S]: orange solid, yield 80% (0.433 g), mp 271-272°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.98 (s, 1H), 8.80 (s, 1H), 8.68 (s, 1H), 8.04-8.00 (m, 2H), 7.63-7.61 (m, 2H), 6.73 (s, 1H), 4.57 (q, *J* = 7.5 Hz, 2H), 4.26 (t, *J* = 7.0 Hz, 2H), 4.13 (s, 3H), 3.93 (s, 3H), 3.06 (t, *J* = 7.0 Hz, 2H), 1.54 (t, *J* = 7.5 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.6, 179.4, 161.8, 150.2, 147.7, 136.3, 134.9, 134.6, 132.4, 131.3, 129.83, 129.77, 129.3, 128.82, 128.76, 128.4, 127.0, 126.1, 123.8, 119.3, 117.2, 112.6, 110.2, 62.5, 56.3, 56.0, 43.3, 28.6, 14.1; IR *ν*/cm$^{-1}$ (KBr) 1719, 1659, 1479, 1384, 1271, 1240, 1222, 1186, 1133, 1038, 914, 763; HRMS (ESI-TOF) *m/z* Calcd for $C_{29}H_{24}NO_6$ $[M+H]^+$ 482.1604, found 482.1600.



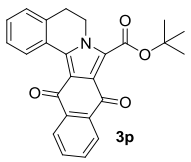

**Ethyl 2,3-dimethoxy-9,11-dioxo-10-phenyl-6,9,10,11-tetrahydro-5*H*-pyrrolo[3',4':3,4] pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3m)** [19n]: orange solid, yield 80% (0.357 g), mp 230-231°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.24 (s, 1H), 7.49-7.47 (m, 2H), 7.40-7.36 (m, 3H), 6.75 (s, 1H), 4.73 (t, *J* = 7.0 Hz, 2H), 4.41 (q, *J* = 7.0 Hz, 2H), 3.97 (s, 3H), 3.93 (s, 3H), 3.11 (t, *J* = 7.0 Hz, 2H), 1.46 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 163.46, 161.59, 159.59, 150.67, 148.57, 134.01, 132.60128.97 (2C), 127.84, 127.28 (2C), 125.55, 125.03, 118.29, 118.08, 114.75, 110.48, 110.26, 61.48, 56.14, 55.97, 43.42, 27.81, 14.12; GC-MS *m/z* 447.1 $[M+1]^+$, 445.0, 411.3, 385.4, 301.9, 254.3, 100.1, 56.4.



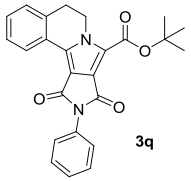
**Methyl 2,3-dimethoxy-9,14-dioxo-5,6,9,14-tetrahydrobenzo[5,6]isoindolo[1,2-a] isoquinoline-8-carboxylate (3n) [19S]:** orange solid, yield 92% (0.329 g), mp 205-206°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.95 (s, *J* = 8.0 Hz, 1H), 8.27-8.25 (m, 1H), 8.17-8.16 (m, 1H), 7.71-7.65 (m, 2H), 7.42 (t, *J* = 6.5 Hz, 1H), 7.36-7.33 (m, 1H), 7.23 (s, *J* = 7.0 Hz, 1H), 4.26 (t, *J* = 6.5 Hz, 2H), 4.06 (s, 3H), 3.08 (t, *J* = 6.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.51, 179.47, 161.8, 135.8, 135.6, 134.6, 133.7, 133.3, 132.9, 130.1, 128.9, 127.4 (2C), 127.2, 126.5, 126.3, 125.4, 123.4, 117.5, 53.0, 43.2, 29.0; IR *v*/cm$^{-1}$ (KBr) 1712, 1656, 1466, 1412, 1385, 1314, 1269, 1224, 1140, 1113, 1060, 1012, 799, 734; GC-MS *m/z* 358.1 $[M+1]^+$, 356.8, 333.6, 276.5, 139.8, 73.9; HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{16}NO_4$ $[M+H]^+$ 358.1079, found 358.1077.



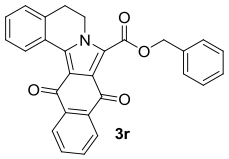

**Methyl 2,3-dimethoxy-9,11-dioxo-10-phenyl-6,9,10,11-tetrahydro-5*H*-pyrrolo[3',4':3,4] pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3o) [19S]:** orange solid, yield 71% (0.264 g), mp 217-218°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.58-8.57 (m, 1H), 7.49 (t, *J* = 7.5 Hz, 2H), 7.43-7.36 (m, 5H), 7.29-7.28 (m, 1H), 4.77 (t, *J* = 7.0 Hz, 2H), 3.98 (s, 3H), 3.18 (t, *J* = 7.0 Hz, 3H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 163.0, 161.5, 160.0, 133.6, 132.6, 132.4, 130.4, 128.8 (2C), 128.0, 127.9, 127.70, 127.65, 127.0 (2C), 125.5, 125.3, 118.2, 116.3, 52.3, 43.4, 28.3; IR *v*/cm$^{-1}$ (KBr) 1497, 1385, 1199, 756, 694, 620; GC-MS *m/z* 373.6 $[M+1]^+$, 372.1, 348.6, 303.2, 256.4, 202.1, 154.1, 54.6; HRMS (ESI-TOF) *m/z* Calcd for $C_{22}H_{17}N_2O_4$ $[M+H]^+$ 373.1188, found 373.1184.




***Tert*-butyl 2,3-dimethoxy-9,14-dioxo-5,6,9,14-tetrahydrobenzo[5,6]isoindolo[1,2-a] isoquinoline-8-carboxylate (3p) [19S]:** orange solid, yield 61% (0.244 g), mp 170-171°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.02 (d, *J* = 7.5 Hz, 1H), 8.30 (dd, $J_1$ = 2.0 Hz, $J_2$ = 6.5 Hz, 1H), 8.23 (dd, $J_1$ = 2.0 Hz, $J_2$ = 6.5 Hz, 1H), 7.72-7.69 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 8.5 Hz, 1H), 4.27 (t, *J* = 7.0 Hz, 2H), 3.11 (t, *J* = 7.0 Hz, 2H), 1.72 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.8, 179.3, 160.6, 135.8, 135.0, 134.9, 133.5, 133.1, 132.9 (2C), 129.9, 128.8, 127.7, 127.4, 127.4, 127.2, 126.5, 122.4, 117.2, 84.1, 43.0, 29.1, 28.1 (3C); IR *v*/cm$^{-1}$ (KBr) 1660, 1467, 1385, 1266, 1229, 1141, 1010, 714; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{21}NO_4Na$ $[M+Na]^+$ 422.1369, found 422.1365.




***Tert*-butyl 2,3-dimethoxy-9,11-dioxo-10-phenyl-6,9,10,11-tetrahydro-5*H*-pyrrolo [3',4':3,4]pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3q) [19S]:** orange solid, yield 58% (0.240 g), mp 234-235°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 8.59 (dd, $J_1$ = 1.5 Hz, $J_2$ = 8.0 Hz, 1H), 7.50 (t, *J* = 8.0 Hz, 2H), 7.43-7.35 (m, 5H), 7.28 (t, *J* = 6.5 Hz, 1H), 4.75 (t, *J* = 6.5 Hz, 2H), 3.16 (t, *J* = 6.5 Hz, 2H), 1.68 (s, 9H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 163.2, 161.6, 159.0, 133.0, 132.8, 132.4, 130.1, 128.9 (2C), 127.9, 127.9, 127.7, 127.6, 127.3 (2C), 125.7, 124.7, 120.2, 116.0, 83.4, 43.3, 28.4, 28.3 (3C); IR *v*/cm$^{-1}$ (KBr) 1759, 1703, 1481, 1415, 1385, 1349, 1305, 1289, 1154, 1135, 1112, 1089, 1051, 950, 889, 843, 762; HRMS (ESI-TOF) *m/z* Calcd for $C_{25}H_{22}N_2O_4Na$ $[M+Na]^+$ 437.1478, found 437.1475.




**Benzyl 2,3-dimethoxy-9,11-dioxo-10-phenyl-6,9,10,11-tetrahydro-5*H*-pyrrolo[3',4':3,4] pyrrolo[2,1-*a*]isoquinoline-8-carboxylate (3r) [19S]:** orange solid, yield 90% (0.390 g), mp 198-199°C; $^1$H NMR (500 MHz, $CDCl_3$): δ (ppm) 9.00 (d, *J* = 7.5 Hz, 1H), 8.30 (dd, $J_1$ = 2.5 Hz, $J_2$ = 6.0 Hz, 1H), 8.24 (dd, $J_1$ = 3.0 Hz, $J_2$ = 6.5 Hz, 1H), 7.74-7.70 (m, 2H), 7.57 (d, *J* = 6.5 Hz, 2H), 7.47-7.36 (m, 5H), 7.27 (d, *J* = 8.5 Hz, 1H), 5.53 (s, 2H), 4.26 (t, *J* = 6.5 Hz, 2H), 3.08 (t, *J* = 6.5 Hz, 2H); $^{13}$C NMR ($CDCl_3$, 125 MHz): δ (ppm) 179.8, 179.5, 161.4, 135.9, 135.8, 135.2, 134.9, 133.7, 133.4, 133.1, 130.2, 129.0, 128.8 (2C), 128.7 (2C), 128.7, 127.5, 127.5, 127.3, 126.7, 126.4, 125.5, 123.7, 117.7, 68.4, 43.3, 29.2; IR *v*/cm$^{-1}$ (KBr) 1642, 1384, 1262, 1097, 802; HRMS (ESI-TOF) *m/z* Calcd for $C_{28}H_{20}NO_4$ $[M+H]^+$ 434.1392, found 434.1390.

## Acknowledgements

This work was supported by the Natural Science Foundation of China (Grant no. 21176223), the National Natural Science Foundation of Zhejiang (Grant no. LY13B020016), and the Key Innovation Team of Science and Technology in Zhejiang Province (Grant no. 2010R50018).

## Notes and references

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† Electronic Supplementary Information (ESI) available: [Images of $^1$H and $^{13}$C NMR of all products]. See DOI: 10.1039/b000000x/

1 (a) A. De Mico, R. Margarita, L. Parlanti, A. Vescovi and G. Piancatelli, *J. Org. Chem*., 1997, **62,** 6974-6977; (b) D. Kalyani, N. R. Deprez, L. V. Desai and M. S. Sanford, *J. Am. Chem. Soc*., 2005, **127,** 7330-7331; (c) K. C. Nicolaou, T. Montagnon, P. S. Baran and Y. L. Zhong, *J. Am. Chem. Soc.* 2002, **124,** 2245-2258; (d) T. Wirth, *Angew. Chem. Int. Ed.* 2005, **44,** 3656-3665; (e) H. Tohma, H. Morioka, S. Takizawa, M. Arisawa and Y. Kita, *Tetrahedron* 2001, **57,** 345-352; (f) L. Pouységu, D. Deffieux and S. Quideau, *Tetrahedron* 2010, **66,** 2235-2261.

2 (a) P. T. Parvatkar, P. S. Parameswaran and S. G. Tilve, *Chem.–Eur. J.* 2012, **18,** 5460-5489; (b) H. Togo and S. Iida, *Synlett* 2006, **2006,** 2159-2175; (c) D. Fischer, H. Tomeba, N. K. Pahadi, N. T. Patil, Z. Huo and Y. Yamamoto, *J. Am. Chem. Soc.* 2008, **130,** 15720-15725; dD. Fischer, H. Tomeba, N. K. Pahadi, N. T. Patil and Y. Yamamoto, *Angew. Chem. Int. Ed*. 2007, **46,** 4764-4766; (e) Z. Huo, H. Tomeba and Y. Yamamoto, *Tetrahedron Lett.* 2008, **49,** 5531-5533; (f) F. C. Küpper, M. C. Feiters, B. Olofsson, T. Kaiho, S. Yanagida, M. B. Zimmermann, L. J. Carpenter, G. W. Luther, Z. Lu, M. Jonsson and L. Kloo, *Angew. Chem. Int. Ed.* 2011, **50,** 11598-11620; (g) Y. Kita, K. Morimoto, M. Ito, C. Ogawa, A. Goto and T. Dohi, *J. Am. Chem. Soc.* 2009, **131,** 1668-1669; (h) N. Fei, Q. Hou, S. Wang, H. Wang and Z.-J. Yao, *Org. Biomol. Chem.* 2010, **8,** 4096-4103; (i) S. Ali, H.-T. Zhu, X.-F. Xia, K.-G. Ji, Y.-F. Yang, X.-R. Song and Y.-M. Liang, *Org. Lett.* 2011, **13,** 2598-2601; (j) H. Batchu, S. Bhattacharyya and S. Batra, *Org. Lett.* 2012; (k) B. Alcaide, P. Almendros, G. Cabrero, R. Callejo , M. P. Ruiz, M. Arnó and L. R. Domingo, *Adv. Synth. Catal*. 2010, **352,** 1688-1700; (l) W.-B. Wu and J.-M. Huang, *Org. Lett.* 2012, **14,** 5832-5835; (m) W.-C. Lee, H.-C. Shen, W.-P. Hu, W.-S. Lo, C. Murali, J. K. Vandavasi and J.-J. Wang, *Adv. Synth. Catal*. 2012, **354,** 2218-2228; (n) Y.-X. Li, K.-G. Ji, H.-X. Wang, S. Ali and Y.-M. Liang, *J. Org. Chem.* 2010, **76,** 744-747; (o) Y.-X. Li, H.-X. Wang, S. Ali, X.-F. Xia and Y.-M. Liang, *Chem. Commun.* 2012, **48,** 2343-2345; (p) Y.-P. Zhu, M.-C. Liu, F.-C. Jia, J.-J. Yuan, Q.-H. Gao, M. Lian and A.-X. Wu, *Org. Lett.* 2012, **14,** 3392-3395; (q) H. Huang, X. Ji, W. Wu and H. Jiang, *Adv. Synth. Catal*. 2013, **355,** 170-180; (r) K. V. Sashidhara, A. Kumar, S. Agarwal, M. Kumar, B. Kumar and B. Sridhar, *Adv. Synth. Catal*. 2012, **354,** 1129-1140; (s) X. Zhang, Y. Zhou, H. Wang, D. Guo, D. Ye, Y. Xu, H. Jiang and H. Liu, *Adv. Synth. Catal*. 2011, **353,** 1429-1437.

3 (a) C.-J. Li, *Acc. Chem. Res.* 2008, **42,** 335-344; (b) Y. Oikawa, T. Yoshioka and O. Yonemitsu, *Tetrahedron Lett.* 1982, **23,** 885-888; (c) Y. Zhang and C.-J. Li, *J. Am. Chem. Soc.* 2006, **128,** 4242-4243.

4 V. P. Mehta and B. Punji, *RSC Adv.* 2013, **3,** 11957-11986.

5 (a) M. Uyanik and K. Ishihara, *ChemCatChem* 2012, **4,** 177-185; (b) M. Uyanik, H. Okamoto, T. Yasui and K. Ishihara, *Science* 2010, **328,** 1376-1379; (c) M. Uyanik, D. Suzuki, T. Yasui and K. Ishihara, *Angew. Chem. Int. Ed.* 2011, **50,** 5331-5334.

6 T. Froehr, C. P. Sindlinger, U. Kloeckner, P. Finkbeiner and B. J. Nachtsheim, *Org. Lett.* 2011, **13,** 3754-3757.

7 J. Zhang, J. Jiang, Y. Li and X. Wan, *J. Org. Chem.* 2013, **78,** 11366-11372.

8 (a) G. Wang, Q.-Y. Yu, J. Wang, S. Wang, S.-Y. Chen and X.-Q. Yu, *RSC Adv.* 2013, **3,** 21306-21310; (b) Z. Liu, J. Zhang, S. Chen, E. Shi, Y. Xu and X. Wan, *Angew. Chem. Int. Ed.* 2012, **51,** 3231-3235; (c) S. Zhang, L.-N. Guo, H. Wang and X.-H. Duan, *Org. Biomol. Chem.* 2013, **11,** 4308-4311; (d) M. Lamani and K. R. Prabhu, *Chem.–Eur. J.* 2012, **18,** 14638-14642; (e) H. Li, J. Xie, Q. Xue, Y. Cheng and C. Zhu, *Tetrahedron Lett.* 2012, **53,** 6479-6482; (f) W.-P. Mai, G. Song, J.-W. Yuan, L.-R. Yang, G.-C. Sun, Y.-M. Xiao, P. Mao and L.-B. Qu, *RSC Adv.* 2013, **3,** 3869-3872.

9 Y. Gao, Q. Song, G. Cheng and X. Cui, *Org. Biomol. Chem.* 2014, **12,** 1044-1047.

10 X. Li, X. Xu, P. Hu, X. Xiao and C. Zhou, *J. Org. Chem.* 2013, **78,** 7343-7348.

11 J. Zhang, J. Jiang, Y. Li, Y. Zhao and X. Wan, *Org. Lett.* 2013, **15,** 3222-3225.

12 W. Wei, C. Zhang, Y. Xu and X. Wan, *Chem. Commun.* 2011, **47,** 10827-10829.

13 E. Shi, Y. Shao, S. Chen, H. Hu, Z. Liu, J. Zhang and X. Wan, *Org. Lett.* 2012, **14,** 3384-3387.

14 S. Chen, Y. Xu and X. Wan, *Org. Lett.* 2011, **13,** 6152-6155.

15 G. Majji, S. Guin, A. Gogoi, S. K. Rout and B. K. Patel, *Chem. Commun.* 2013, **49,** 3031-3033.

16 Y.-C. Wong, C.-T. Tseng, T.-T. Kao, Y.-C. Yeh and K.-S. Shia, *Org. Lett.* 2012, **14,** 6024-6027.

17 K. Rajender Reddy, M. Venkateshwar, C. Uma Maheswari and P. Santhosh Kumar, *Tetrahedron Lett.* 2010, **51,** 2170-2173.

18 (a) H. Fan, J. Peng, M. T. Hamann and J.-F. Hu, *Chem. Rev.* 2007, **108,** 264-287; (b) D. Pla, F. Albericio and M. Alvarez, *MedChemComm* 2011, **2,** 689-697; (c)BT. Fukuda, F. Ishibashi and M. Iwaob, *Heterocycles* 2011, **83,** 491-529; (d) S. T. Handy and Y. Zhang, *Org. Prep. Proced. Int.* 2005, **37,** 411-445; (e) C. Bailly, *Curr. Med. Chem. Anti-Cancer Agents* 2004, **4,** 363-378; (f) F. A. M. A. D. Pla, *Anti-Cancer Agents Med. Chem.* 2008, **2008,** 746-760.

19 (a) M. Banwell and D. Hockless, *Chem. Commun.* 1997, **33,** 2259-2260; (b) A. Heim, A. Terpin and W. Steglich, *Angew. Chem. Int. Ed.* 1997, **36,** 155-156; (c) D. L. Boger, C. W. Boyce, M. A. Labroli, C. A. Sehon and Q. Jin, *J. Am. Chem. Soc.* 1998, **121,** 54-62; (d) C. P. Ridley, M. V. R. Reddy, G. Rocha, F. D. Bushman and D. J. Faulkner, *Bioorg. Med. Chem.* 2002, **10,** 3285-3290; (e) P. Ploypradith, C. Mahidol, P. Sahakitpichan, S. Wongbundit and S. Ruchirawat, *Angew. Chem. Int. Ed.* 2004, **43,** 866-868; (f) P. Cironi, I. Manzanares, F. Albericio and M. Álvarez, *Org. Lett.* 2003, **5,** 2959-2962; (g) S. T. Handy, Y. Zhang and H. Bregman, *J. Org. Chem.* 2004, **69,** 2362-2366; (h) P. Ploypradith, R. K. Kagan and S. Ruchirawat, *J. Org. Chem.* 2005, **70,** 5119-5125; (i) S. Su and J. A. Porco, *J. Am. Chem. Soc.* 2007, **129,** 7744-7745; (j) T. Ohta, T. Fukuda, F. Ishibashi and M. Iwao, *J. Org. Chem.* 2009, **74,** 8143-8153; (k) Q. Li, J. Jiang, A. Fan, Y. Cui and Y. Jia, *Org. Lett.* 2010, **13,** 312-315; (l) L. Ackermann, L. Wang and A. V. Lygin, *Chem. Sci.* 2012, **3,** 177-180; (m) C. Yu, Y. Zhang, S. Zhang, H. Li and W. Wang, *Chem. Commun.* 2011, **47,** 1036-1038; (n) Y.-Q. Zou, L.-Q. Lu, L. Fu, N.-J. Chang, J. Rong, J.-R. Chen and W.-J. Xiao, *Angew. Chem. Int. Ed.* 2011, **50,** 7171-7175; (o) M. Rueping, D. Leonori and T. Poisson, *Chem. Commun.* 2011, **47,** 9615-9617; (p) L. Huang and J. Zhao, *Chem. Commun.* 2013, **49,** 3751-3753; (q) H.-T. Wang and C.-D. Lu, *Tetrahedron Lett.* 2013, **54,** 3015-3018; (r) S. Guo, H. Zhang, L. Huang, Z. Guo, G. Xiong and J. Zhao, *Chem. Commun.* 2013, **49,** 8689-8691; (s) H.-M. Huang, Y.-J. Li, Q. Ye, W.-B. Yu, L. Han, J.-H. Jia and J.-R. Gao, *J. Org. Chem.* 2014, **79,** 1084-1092.

20 (a) H.-M. Huang, J.-R. Gao, L.-F. Hou, J.-H. Jia, L. Han, Q. Ye and Y.-J. Li, *Tetrahedron* 2013, **69,** 9033-9037; (b) H.-M. Huang, Y.-J. Li, Y.-P. Dai, W.-B. Yu, Q. Ye and J.-R. Gao, *J. Chem. Res.* 2013, **37,** 34-37; (c) H.-M. Huang, Y.-Jj. Li, J.-R. Yang, J.-H. Jia, Q. Ye, L. Han and J.-R. Gao, *Tetrahedron* 2013, **69,** 5221-5226; (d) Y.-J. Li, H.-M. Huang, H.-Q. Dong, J.-H. Jia, L. Han, Q. Ye and J.-R. Gao, *J. Org. Chem.* 2013, **78,** 9424-9430; (e) Y.-J. Li, H.-M. Huang, J. Ju, J.-H. Jia, L. Han, Q. Ye, W.-B. Yu and J.-R. Gao, *RSC Adv.* 2013; (f) Y.-J. Li, H.-M. Huang, Q. Ye, L.-F. Hou, W.-B. Yu, J.-H. Jia and J.-R. Gao, *Adv. Synth. Catal.* 2014, **356,** 421-427; (g) H.-M. Huang, J. Han, F. Xu, Y.-J. Li, H. Dong, W.-B. Yu and J.-R. Gao, *Chem. Lett.* 2013, **42,** 921-923; (h) H.-M. Huang, J.-R. Gao, Q. Ye, W.-B. Yu, W.-J. Sheng and Y.-J. Li, *RSC Adv.* 2014, **4,**15526–15533.

21 L. Chen, E. Shi, Z. Liu, S. Chen, W. Wei, H. Li, K. Xu and X. Wan, *Chem.–Eur. J.* 2011, **17,** 4085-4089.

22 T. Nobuta, N. Tada, A. Fujiya, A. Kariya, T. Miura and A. Itoh, *Org. Lett.* 2013, **15,** 574-577.

23 (a) J. Barluenga, M. Marco-Arias, F. Gonzalez-Bobes, A. Ballesteros and J. M. Gonzalez, *Chem. Commun.* 2004**,** 2616-2617; (b) J. Barluenga, M. Marco-Arias, F. González-Bobes, A. Ballesteros and J. M. González, *Chem.–Eur. J.* 2004, **10,** 1677-1682.