HETEROCYCLES, Vol. 98, No. 9, 2019, pp. 1189 - 1199. © 2019 The Japan Institute of Heterocyclic Chemistry
Received, 19th June, 2019, Accepted, 20th August, Published online, 20th September, 2019
DOI: 10.3987/COM-19-14113

FUNCTIONALIZATION OF BENZYLIC sp^3 C-H OF 2-METHYLAZAARENES IN DEEP EUTECTIC SOLVENT

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Abstract – The catalyst-free addition of 2-methylazaarene benzylic sp^3 C-H to electron-deficient olefins in deep eutectic solvents is reported. Moderate to good yields were obtained in 2 h at 80 °C in deep eutectic solvents. The method was operationally easy and involved mild reaction conditions. This expands the application of deep eutectic solvent in sp^3 C-H functionalization reaction.

INTRODUCTION

Nitrogen-containing heterocyclic compounds, such as pyridine and quinoline, have high biological activities and special cyclic structure. They are widely used in medicine intermediates, organic synthesis, and agriculture.[1-3] The functionalization of benzylic sp^3 C-H of azaarenes is one of the main methods for synthesizing nitrogen-containing heterocyclic compounds.[4-6] Meanwhile, it is also a common method for constructing C-C and C-X (X=O, N, S,) bonds in organic synthesis.[7-10] Therefore, the functionalization of benzylic sp^3 C-H of azaarenes have received extensive attention in the field of organic synthesis. The catalysts used at present for the functionalization of benzylic sp^3 C-H of azaarenes are mostly transition metals, Lewis acids, or Brønsted acids.[11-13] However, reactions using these catalysts have some disadvantages, such as complex post-treatment process, insufficient environmental protection, and high toxicity of the reaction media that comprise mainly organic solvents. Hence, an environmentally friendly and effective protocol for the functionalization of benzylic sp^3 C-H of azaarenes is highly desirable.

Deep eutectic solvent (DES) is a fluid generally composed of two or more components that are capable of self-association, usually through hydrogen bond interactions, to form an eutectic mixture with a melting point lower than the corresponding melting points of the individual components.[14-16] Reactions using DESs have simple synthesis steps; moreover, DESs are cheap, safe, and easily degradable. The

performance and application of DESs have been already reported in the past decade.[17-19] In this work, the catalyst-free addition of 2-methylazaarene benzylic sp^3 C-H to electron-deficient olefins in DES is reported. Good yields (87%) were obtained. To obtain the best reaction conditions, different solvents, reaction times, temperatures, and recycling ability of DES were evaluated in detail.

RESULTS AND DISCUSSION

First, the catalytic activities of six different choline chloride-based DESs were evaluated for the model reaction of *N*-phenylmaleimide and 2-methylquinoline, to optimize the reaction conditions and selectivity for the addition of the benzylic sp^3 C-H to electron-deficient olefins. The results are summarized in Table 1. The choline chloride–citric acid DES was the most effective (Table 1, entry 1), and up to 78% target product was obtained within 2 h. However, the reaction did not proceed at all in the choline chloride/*p*-toluenesulfonic acid DES (Table 1, entry 6). All the other DESs exhibited certain catalytic activities (Table 1, entries 2 ~ 5); however, the best yield was obtained for the choline chloride/citric acid DES. Therefore, the choline chloride/citric acid DES was used for the next stage of the investigation.

Table 1. Effect of different DESs on the yield[a]

Entry	DESs (molar ratio)	Yield(%)[b]
1	choline chloride/citric acid (1 : 1)	78
2	choline chloride/urea (1 : 2)	26
3	choline chloride/oxalic acid (1 : 1)	35
4	choline chloride/glycerol (1 : 2)	18
5	choline chloride/glucose (1 : 1)	13
6	choline chloride/*p*-toluenesulfonic acid (1 : 1)	trace

[a] Reaction condition: 0.5 mmol 2-methylquinoline, 0.75 mmol *N*-phenylmaleimide, 0.5 mL DES, the reaction mixture was stirred in oil bath at 60 ℃ for 2 h. [b] Yields of pure products isolated by chromatography.

Most of the DESs exhibit relatively high viscosities (>100 cP) at room temperature. Owing to their potential applications as green media, the development of DESs with low viscosities is highly desirable.[4] Water content can distinctly affect the viscosities of eutectic mixtures. Thus, the effect of different solvents in DES were investigated under the optimized reaction conditions. The results are show in Table 2. The yields in other solvents were lower than those in the solvent-free DES. No reaction took place in the DES with water (Table 2, entry 4). Therefore, the solvent-free DES was chosen to carry out the subsequent reaction.

Table 2. Effect of solvents on the yield[a]

Entry	Solvent	Yield(%)[b]
1	MeCOMe	24
2	MeCN	15
3	EtOH	46
4	H_2O	trace
5	DMSO	71
6	-	78

[a] Reaction condition: 0.5 mmol 2-methylquinoline, 0.75 mmol *N*-phenylmaleimide, 1 mL solvent, 0.5 mL DES, the reaction mixture was stirred in oil bath at 60 ℃ for 2 h. [b] Yields of pure products isolated by chromatography.

Next, the effects of the reaction temperature on functionalization of the benzylic sp^3 C-H of azaarenes were investigated. *N*-Phenylmaleimide was treated with 2-methylquinoline at various temperatures in the DES. The optimized reaction conditions are shown in Figure 1. Initially, the yields of the products increased rapidly with increasing temperature. The best result in DES was obtained at 80 °C, and the azaarene derivatives were afforded in 86% yield. However, the yield of the products decreased slightly with continuous increase in the temperature. Such a phenomenon could be attributed to the partial disruption of hydrogen bonds at high temperatures.

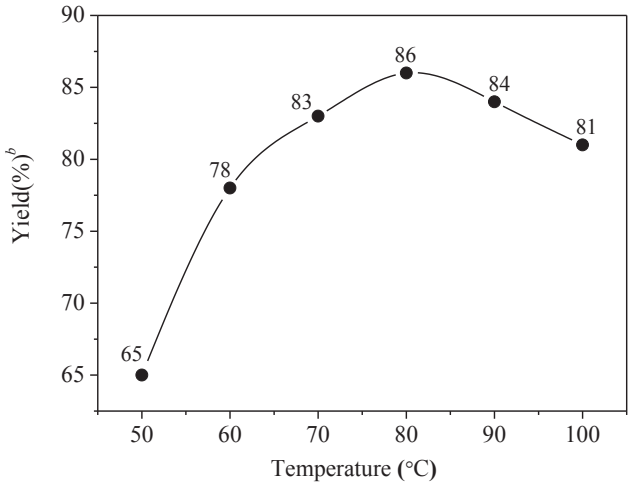


Figure 1. Effect of temperature on the yield[a]

[a] Reaction condition: 0.5 mmol 2-methylquinoline, 0.75 mmol *N*-phenylmaleimide, 0.5 mL DES, the reaction mixture was stirred in oil bath at different temperatures for 2 h. [b] Yields correspond to those of the pure products isolated by chromatography.

The effect of reaction time on the reaction of *N*-phenylmaleimide and 2-methylquinoline (Figure 2) was investigated after this. It was found that the yield of the target product increased markedly before 2 h, and the best yield (86%) was achieved when the reaction was carried out for 3 h. The yield of the reaction almost have no change by prolong the reaction time.

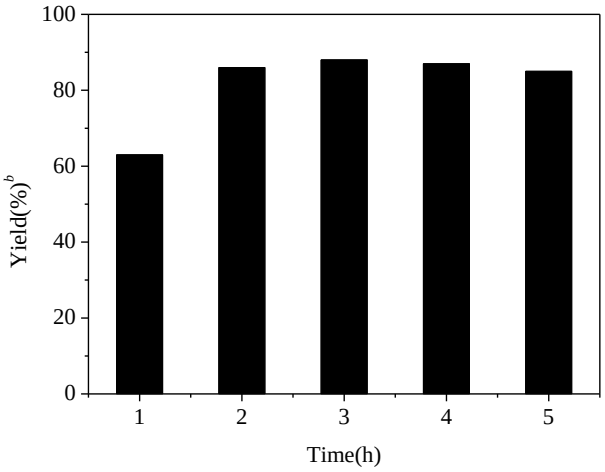


Figure 2. Effect of reaction time on the functionalization of benzylic sp^3 C-H of azaarene[a]

[a] Reaction condition: 0.5 mmol 2-methylquinoline, 0.75 mmol *N*-phenylmaleimide, 0.5 mL DES, the reaction mixture was stirred in oil bath at 80 °C for a certain period of time. [b] Yields correspond to those of the pure products isolated by chromatography.

The recycling ability of DES was also examined under the optimized condition. After the completion, the reaction mixture was cooled to room temperature, and water (5 mL) was added. The product was extracted with ethyl acetate, the combined organic phase was concentrated under reduced pressure and the residue was purified by silica gel column chromatography to give the corresponding product, and the DES was recovered from the filtrate by evaporating the water phase at 80 °C under vacuum. It was reused for the next batch and recycled again (Table 3, every time the mass of DES was lost 4% ~ 5%, at last the DES was lost 14%). Remarkably, the recovered DES could be used thrice without any significant loss of activity. Therefore, this method was a green protocol for the simple and fast functionalization of benzylic sp^3 C-H of azaarenes in DES.

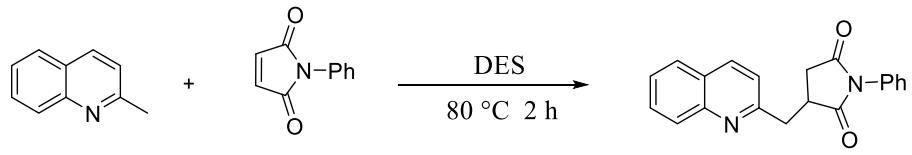
Table 3. Reusability of DES in the model reaction[a]

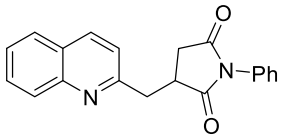
Entry	Cycle number	Yield(%)[b]
1	fresh	86
2	1st recycle	82
3	2nd recycle	79
4	3rd recycle	77

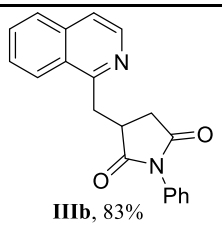
[a] Reaction condition: 0.5 mmol 2-methylquinoline, 0.75 mmol *N*-phenylmaleimide, 0.5 mL DES, the reaction mixture was stirred in oil bath at 80 °C for 2 h. [b] Yields of pure products isolated by chromatography.

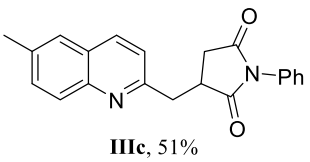
With the optimized catalytic system in hand, we continued to explore the scope and limitation of the reaction using various *N*-phenylmaleimide with 2-methylquinoline in the choline chloride–citric acid DES for obtaining the azaarene derivatives. The results are listed in Table 4. 2-Methylquinolines with different functional groups (methyl, chloro and nitro groups) react with *N*-phenylmaleimide, and moderate yields were obtained (Table 4, IIIb ~ IIIe). Other methyl-*N*-heterocycles such as 1-methylisoquinoline and 2-methylbenzimidazole were also examined for their compatibility under these reaction conditions in the DES; 83% and 69% isolated yields were obtained, respectively (Table 4, IIIb). In addition, 2-methylpyridine and 2,6-dimethylpyridine were reacted with *N*-phenylmaleimide; the yields of the products were only 22% and 27% (Table 4, IIIg, IIIh). This may be because of the fact that pyridine is monocyclic conjugated compound, and the electron cloud density at the α-position is lower compared with that in quinoline. Furthermore, different quinoline derivatives were examined under the optimized conditions, and the corresponding products were obtained in good yields (Table 4, IIIi ~ IIIn). Besides, *N*-phenylmaleimide, *N*-methylmaleimide, *N*-benzylmaleimide, *trans*-β-nitrostyrene, and benzylidenemalononitrile were tested for this reaction, and good yields were obtained in all the cases (Table 4, IIIo ~ IIIq). In summary, we have developed an effective and inexpensive protocol for the functionalization of benzylic sp^3 C-H. The advantages of this protocol are operational simplicity, short reaction times, and high yields. This method not only expands the application of the DESs in the functionalization of sp^3 C-H of the aza-aromatic hydrocarbons but also has a positive effect on the development of green chemistry.

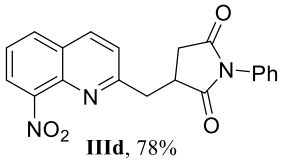
Table 4. Functionalization of benzylic sp^3 C-H of 2-methylazaarenes[a]

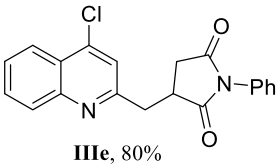


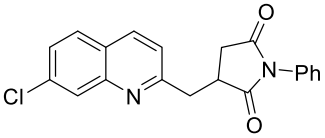

IIIa, 86%

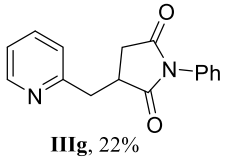

IIIb, 83%

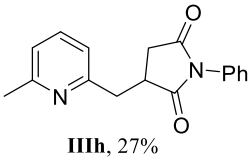

IIIc, 51%

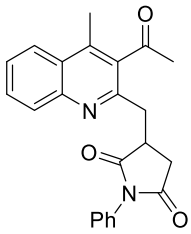

IIId, 78%

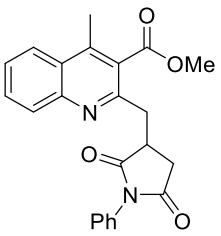

IIIe, 80%

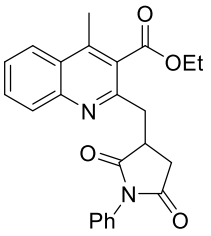

IIIf, 84%

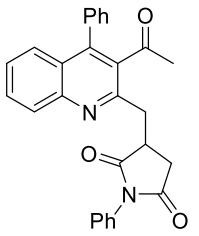

IIIg, 22%

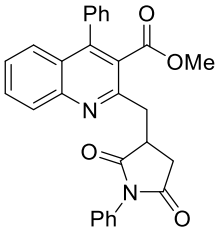

IIIh, 27%

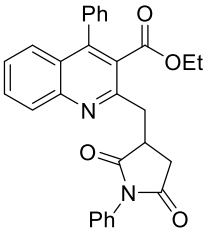

IIIi, 61%

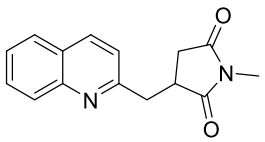

IIIj, 67%

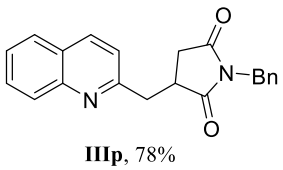

IIIk, 74%

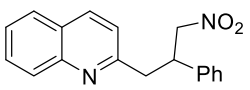

IIIl, 68%


IIIm, 76%


IIIn, 82%


IIIo, 60%


IIIp, 78%


IIIq, 54%

[a] Reaction condition: 0.75 mmol electron deficient olefin, 0.5 mmol 2-methylazaarene, 0.5 mL DES, the reaction mixture was stirred in an oil bath at 80 °C for 2 h.

EXPERIMENTAL

All the major chemicals were obtained from commercial sources and used without further purification. All the reactions were monitored by thin-layer chromatography with silica gel plates.

Preparation of deep eutectic solvent

The deep eutectic solvents, choline chloride/citric acid (1 : 1), chloride/urea (1 : 2), chloride/oxalic acid (1 : 1), chloride/glycerol (1 : 2), chloride/glucose (1 : 1), chloride/*p*-toluenesulfonic acid (1 : 1), were formed by stirring the two components at 100 °C until a homogeneous colorless liquid was formed.

General procedure:

2-Methylazaarene (0.5 mmol) and electron-deficient olefin (0.75 mmol) were dissolved in DES (0.5 mL). The mixture was stirred at 80 °C for 2 h. Then 10 mL of water was added to the reaction mixture. The resulting mixture was extracted by EtOAc (10 mL) for 3 times. The combined organic phase was concentrated under reduced pressure and the residue was purified by silica gel column chromatography to give the corresponding product.

1-Phenyl-3-(quinolin-2-ylmethyl)pyrrolidine-2,5-dione(IIIa):[20] a white solid; mp 124 ~ 125 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.08 (d, *J* = 8.4 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.77 (d, *J* = 7.8 Hz, 1H), 7.63 (t, *J* = 8.4 Hz, 1H), 7.51 ~ 7.45 (m, 3H), 7.41 ~ 7.34 (m, 3H), 7.29 (d, *J* = 8.4 Hz, 1H), 3.72 (dd, *J* = 17.4, 6.6 Hz, 1H), 3.56 ~ 3.48 (m, 2H), 3.06 (dd, *J* = 19.8, 7.8 Hz, 1H), 2.97 (dd, *J* = 18.6, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.15, 176.39, 157.48, 147.25, 136.36, 132.54, 129.55, 129.00, 128.73, 128.24, 127.47, 126.68, 126.46, 126.04, 121.50, 38.14, 36.99, 33.94.

3-(Isoquinolin-1-ylmethyl)-1-phenylpyrrolidine-2,5-dione(IIIb):[20] a white solid; mp 142 ~ 143 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.30 (d, *J* = 5.7 Hz, 1H), 8.03 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.60 (t, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.5 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 3H), 7.39 ~ 7.32 (m, 3H), 3.91 ~ 3.80 (m, 2H), 3.51 (td, *J* = 9.8, 5.1 Hz, 1H), 3.00 (dd, *J* = 18.2, 9.5 Hz, 1H), 2.79 (dd, *J* = 18.2, 5.2 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.51, 176.45, 156.23, 141.03, 135.87, 132.72, 129.99, 128.98, 128.23, 127.36, 127.02, 126.57, 124.16, 119.75, 37.58, 34.36, 33.64.

3-((6-Methylquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIc):[20] a white solid; mp 104 ~ 106 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 8.4 Hz, 1H), 7.74 (d, *J* = 8.5 Hz, 1H), 7.49 (s, 1H), 7.44 (dd, *J* = 13.4, 6.3 Hz, 3H), 7.35 (dd, *J* = 13.0, 7.6 Hz, 3H), 7.19 (d, *J* = 8.4 Hz, 1H), 3.65 (dd, *J* = 17.3, 6.9 Hz, 1H), 3.46 (d, *J* = 13.4 Hz, 2H), 3.00 (dd, *J* = 18.2, 9.0 Hz, 1H), 2.92 (dd, *J* = 18.2, 4.8 Hz, 1H), 2.47 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.19, 176.41, 156.38, 146.01, 136.04, 135.91, 132.58, 131.85, 129.07, 128.68, 128.31, 126.82, 126.53, 126.40, 121.52, 38.39, 37.13, 34.04, 21.49.

3-((8-Nitroquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIId):[20] a white solid; mp 148 ~

150 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.15 (d, *J* = 8.5 Hz, 1H), 7.96 (d, *J* = 7.6 Hz, 2H), 7.53 (t, *J* = 7.8 Hz, 1H), 7.44 (dd, *J* = 15.3, 7.9 Hz, 3H), 7.34 (dd, *J* = 12.6, 7.8 Hz, 3H), 3.73 ~ 3.64 (m, 2H), 3.49 (dd, *J* = 17.5, 9.2 Hz, 1H), 3.21 (dd, *J* = 18.3, 9.0 Hz, 1H), 3.01 (dd, *J* = 18.4, 5.6 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 178.74, 175.76, 160.66, 147.76, 138.71, 136.47, 132.26, 131.83, 129.02, 128.38, 127.68, 126.54, 125.00, 124.02, 123.52, 38.48, 37.59, 34.74.

3-((4-Chloroquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIe):[20] a white solid; mp 149 ~ 150 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.14 (d, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 8.4 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.58 ~ 7.54 (m, 1H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.36 (dd, *J* = 15.0, 9.4 Hz, 4H), 3.66 (dd, *J* = 17.6, 6.7 Hz, 1H), 3.45 (d, *J* = 13.7 Hz, 2H), 2.97 (ddd, *J* = 23.1, 18.0, 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 178.95, 176.30, 157.40, 148.14, 142.84, 132.45, 130.64, 129.21, 129.13, 128.40, 127.27, 126.45, 125.03, 123.95, 121.50, 38.03, 36.86, 34.12.

3-((7-Chloroquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIf):[20] a white solid; mp 128 ~ 130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.96 (d, *J* = 8.4 Hz, 1H), 7.82 (s, 1H), 7.62 (d, *J* = 8.7 Hz, 1H), 7.48 ~ 7.44 (m, 2H), 7.38 ~ 7.34 (m, 4H), 3.63 (dd, *J* = 17.7, 7.2 Hz, 1H), 3.50 ~ 3.41 (m, 2H), 3.01 (dd, *J* = 18.3, 9.2 Hz, 1H), 2.86 (dd, *J* = 18.3, 5.0 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 178.92, 176.19, 158.61, 147.52, 136.24, 135.25, 132.37, 129.00, 128.74, 128.29, 127.75, 127.08, 126.31, 125.02, 121.73, 38.16, 37.05, 33.93.

1-Phenyl-3-(pyridin-2-ylmethyl)pyrrolidine-2,5-dione(IIIg):[20] a white solid; mp 84 ~ 86 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.50 (d, *J* = 4.6 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.39 (t, *J* = 7.4 Hz, 1H), 7.28 (d, *J* = 7.7 Hz, 2H), 7.22 (d, *J* = 7.8 Hz, 1H), 7.19 ~ 7.15 (m, 1H), 3.49 ~ 3.43 (m, 2H), 3.37 (d, *J* = 10.7 Hz, 1H), 2.77 (dd, *J* = 18.3, 4.4 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.07, 175.98, 157.02, 149.08, 136.75, 132.39, 129.08, 128.45, 126.56, 123.80, 121.93, 42.65, 38.88, 37.22, 33.74.

3-((6-Methylpyridin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIh):[20] a white solid; mp 87 ~ 89 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.49 (dt, *J* = 30.5, 7.8 Hz, 3H), 7.40 ~ 7.36 (m, 1H), 7.30 (d, *J* = 9.6 Hz, 2H), 7.01 (d, *J* = 7.6 Hz, 2H), 3.47 ~ 3.41 (m, 2H), 3.32 (dd, *J* = 17.5, 6.7 Hz, 1H), 2.99 ~ 2.93 (m, 2H), 2.44 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 178.81, 176.02, 157.83, 156.22, 136.81, 132.34, 128.91, 128.29, 126.36, 121.23, 120.45, 42.60, 40.91, 38.82, 36.84, 33.76, 24.41.

3-((3-Acetyl-4-methylquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIi):[20] a white solid; mp 85 ~ 88 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.95 (d, *J* = 8.3 Hz, 1H), 7.79 (d, *J* = 8.3 Hz, 1H), 7.62 (t, *J* = 8.2 Hz, 1H), 7.52 (t, *J* = 7.6 Hz, 1H), 7.47 ~ 7.42 (m, 2H), 7.39 ~ 7.34 (m, 3H), 3.57 (dd, *J* = 17.2, 5.5 Hz, 1H), 3.47 (td, *J* = 9.4, 5.2 Hz, 1H), 3.37 (dd, *J* = 17.2, 3.9 Hz, 1H), 3.05 (dd, *J* = 18.1, 9.5 Hz, 1H), 2.94 (dd, *J* = 18.1, 5.3 Hz, 1H), 2.60 (s, 3H), 2.56 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 206.29, 179.14, 176.52, 151.35, 146.33, 139.14, 135.37, 132.61, 130.03, 129.63, 129.01, 128.27, 126.98, 126.42, 126.11,

123.61, 37.67, 34.52, 34.31, 32.89, 15.39;

Methyl 2-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-methylquinoline-3-carboxylate(IIIj):[20] a white solid; mp 107 ~ 109 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.4 Hz, 1H), 7.82 (d, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 7.6 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.49 ~ 7.46 (m, 2H), 7.40 ~ 7.37 (m, 3H), 4.02 (s, 3H), 3.69 (dd, *J* = 17.8, 6.5 Hz, 1H), 3.53 (dd, *J* = 17.9, 3.1 Hz, 2H), 3.08 (dd, *J* = 18.2, 9.5 Hz, 1H), 2.95 (dd, *J* = 18.2, 5.0 Hz, 1H), 2.66 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.33, 176.70, 169.22, 153.00, 146.68, 142.65, 132.74, 130.50, 129.77, 129.19, 128.40, 127.40, 127.02, 126.60, 126.05, 124.19, 52.70, 37.82, 35.25, 34.38, 16.14.

Ethyl 2-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-methylquinoline-3-carboxylate(IIIk):[20] a white solid; mp 93 ~ 95 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 8.00 (d, *J* = 8.3 Hz, 1H), 7.82 (d, *J* = 8.3 Hz, 1H), 7.65 (t, *J* = 8.1 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.49 ~ 7.46 (m, 2H), 7.39 (d, *J* = 7.0 Hz, 3H), 4.50 (q, *J* = 7.2 Hz, 2H), 3.70 (dd, *J* = 17.1, 6.0 Hz, 1H), 3.57 ~ 3.49 (m, 2H), 3.07 (dd, *J* = 18.2, 9.4 Hz, 1H), 2.96 (dd, *J* = 18.2, 5.2 Hz, 1H), 2.67 (s, 3H), 1.46 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.22, 176.65, 168.73, 152.94, 132.74, 130.42, 129.74, 129.19, 128.39, 127.68, 126.98, 126.60, 126.10, 124.15, 61.97, 37.91, 35.07, 34.31, 29.81, 15.91, 14.34.

3-((3-Acetyl-4-phenylquinolin-2-yl)methyl)-1-phenylpyrrolidine-2,5-dione(IIIl):[20] a white solid; mp 114 ~ 116 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 8.4 Hz, 2H), 7.52 (t, *J* = 9.6 Hz, 3H), 7.47 (d, *J* = 7.8 Hz, 3H), 7.42 ~ 7.37 (m, 4H), 7.33 (dd, *J* = 5.4, 3.0 Hz, 1H), 3.66 (dd, *J* = 18.0, 6.0 Hz, 1H), 3.61 ~ 3.48 (m, 2H), 3.11 (qd, *J* = 18.0, 7.2 Hz, 2H), 1.98 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.32, 176.74, 168.03, 153.24, 135.74, 132.79, 130.64, 129.54, 129.33, 129.21, 128.68, 128.42, 128.40, 128.38, 127.09, 127.09, 126.69, 126.63, 125.51, 61.69, 37.90, 35.02, 34.40, 13.61.

Methyl 2-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-phenylquinoline-3-carboxylate(IIIm):[20] a white solid; mp 121 ~ 122 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 8.3 Hz, 1H), 7.66 (t, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 8.4 Hz, 1H), 7.51 ~ 7.47 (m, 5H), 7.45 ~ 7.38 (m, 4H), 7.35 (dd, *J* = 10.1, 1.9 Hz, 2H), 3.79 (dd, *J* = 17.6, 5.9 Hz, 1H), 3.63 (dd, *J* = 17.6, 3.9 Hz, 1H), 3.57 (s, 3H), 3.56 ~ 3.53 (m, 1H), 3.13 (dd, *J* = 18.2, 9.5 Hz, 1H), 3.03 (dd, *J* = 18.2, 5.3 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 179.44, 176.74, 168.58, 153.17, 147.29, 135.66, 132.76, 130.71, 129.38, 129.33, 129.23, 128.78, 128.47, 128.43, 127.11, 126.97, 126.74, 126.64, 125.45, 52.41, 37.83, 35.06, 34.41, 29.82.

Ethyl 2-((2,5-dioxo-1-phenylpyrrolidin-3-yl)methyl)-4-phenylquinoline-3-carboxylate(IIIn):[20] a white solid; mp 106 ~ 108 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.87 (d, *J* = 8.4 Hz, 1H), 7.65 (t, *J* = 7.8 Hz, 1H), 7.58 (d, *J* = 8.4 Hz, 1H), 7.52 ~ 7.47 (m, 5H), 7.45 ~ 7.38 (m, 4H), 7.37 ~ 7.33 (m, 2H), 4.05 (q, *J* = 7.2 Hz, 2H), 3.81 (dd, *J* = 17.4, 6.0 Hz, 1H), 3.66 (dd, *J* = 17.4, 3.6 Hz, 1H), 3.56 (td, *J* = 9.6, 5.4 Hz, 1H), 3.13 (dd, *J* = 18.0, 9.6 Hz, 1H), 3.04 (dd, *J* = 18.0, 5.4 Hz, 1H), 0.92 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 205.50, 179.48, 176.78, 152.35, 135.16, 134.52, 132.79, 130.54, 130.25, 130.07, 129.28,

129.23, 129.12, 128.85, 128.43, 127.23, 126.65, 126.34, 125.31, 37.91, 34.89, 34.54, 32.12, 32.03, 29.76.

1-Methyl-3-(quinolin-2-ylmethyl)pyrrolidine-2,5-dione(IIIo):[20] a white solid; mp 104 ~ 106 °C; 1H NMR (600 MHz, $CDCl_3$) δ: 8.01 (d, *J* = 8.4 Hz, 1H), 7.84 (d, *J* = 8.4 Hz, 1H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.63 (t, *J* = 7.6 Hz, 1H), 7.45 (t, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 8.4 Hz, 1H), 3.46 (d, *J* = 5.6 Hz, 2H), 3.36 (dq, *J* = 10.5, 5.3 Hz, 1H), 3.04 (s, 3H), 2.86 (dd, *J* = 18.2, 9.2 Hz, 1H), 2.70 (dd, *J* = 18.2, 4.8 Hz, 1H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 180.00, 177.35, 157.47, 147.44, 136.37, 129.48, 128.76, 127.40, 126.53, 126.10, 121.50, 38.43, 37.53, 33.97, 24.80.

1-Benzyl-3-(quinolin-2-ylmethyl)pyrrolidine-2,5-dione(IIIp):[20] a white solid; mp 112 ~ 114 °C; ^1H NMR (600 MHz, $CDCl_3$) δ: 7.93 (d, *J* = 8.4 Hz, 1H), 7.68 (d, *J* = 8.3 Hz, 1H), 7.58 ~ 7.51 (m, 2H), 7.42 (t, *J* = 7.1 Hz, 1H), 7.39 ~ 7.35 (m, 2H), 7.26 ~ 7.21 (m, 3H), 7.14 (d, *J* = 8.4 Hz, 1H), 4.69 (q, *J* = 14.0 Hz, 2H), 3.43 (qd, *J* = 16.0, 5.6 Hz, 2H), 3.35 ~ 3.28 (m, 1H), 2.79 (qd, *J* = 18.2, 7.1 Hz, 2H); ^{13}C NMR δ: 179.63, 176.73, 157.35, 147.38, 136.39, 135.95, 129.42, 128.89, 128.48, 127.72, 127.33, 126.66, 126.15, 121.43, 42.42, 38.57, 37.20, 33.80.

2-(3-Nitro-2-phenylpropyl)quinoline(IIIq):[20] a black solid; mp 82 ~ 83 °C; ^1H NMR (600 MHz, $CDCl_3$) δ: 8.04 (dd, *J* = 20.1, 8.4 Hz, 2H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.70 (t, *J* = 8.2 Hz, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.29 ~ 7.22 (m, 5H), 7.13 (d, *J* = 8.4 Hz, 1H), 4.84 (dd, *J* = 12.7, 5.6 Hz, 1H), 4.78 ~ 4.71 (m, 1H), 4.25 ~ 4.15 (m, 1H), 3.36 (d, *J* = 7.6 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ: 158.51, 147.81, 139.40, 136.77, 129.84, 129.00, 128.95, 127.80, 127.67, 127.59, 126.89, 126.41, 121.79, 79.72, 43.97, 42.46.

ACKNOWLEDGEMENTS

We thank the National Natural Science Foundation of China (Nos. 21462001, 21465002, 11765002), the Science and Technology Projects of Jiangxi (No. 20161BCB24006) and the National Natural Science Foundation of Jiangxi (No. 20181BAB203019) for the financial support. We also appreciate the instrumentation for the experimental testing provided by other research groups in East China University of Technology.

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