Tetrahedron 70 (2014) 239–244

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Synthesis of trisubstituted imidazoles via a convergent reaction network from methyl ketones and benzoins

Wei-Jian Xue [a], Hong-Zheng Li [a], Fang-Fang Gao [a], Anxin Wu [a,b,*]

[a] Key Laboratory of Pesticide & Chemical Biology, Ministry of Education, College of Chemistry, Central China Normal University, Wuhan 430079, PR China

[b] Department of Chemistry, State Key Laboratory of Applied Organic Chemistry, Lanzhou University, Lanzhou 730000, PR China

ARTICLE INFO

Article history:
Received 9 October 2013
Received in revised form 14 November 2013
Accepted 22 November 2013
Available online 27 November 2013

Keywords:
Reaction network
Imidazole
Convergent
Domino reaction

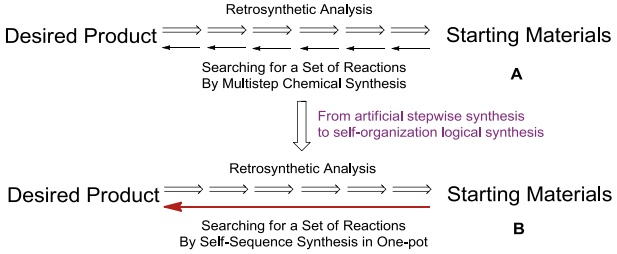
ABSTRACT

A novel method for constructing trisubstituted imidazoles has been created using simple and readily available aromatic ketones, benzoins, and ammonium acetate as starting materials. The new synthetic strategy utilized a convergent integration of two self-labor domino sequences, providing a typical example for logical self-organization synthesis.

1. Introduction

Retrosynthetic analysis, which searches a set of reactions for synthesizing complex molecule by multistep chemical synthesis, was devised by Corey in the mid 1960s (Scheme 1A).[1] Based on the same strategy, we attempt to find a set of compatible reactions, which can be integrated in one-pot to construct the desired product by self-sequence synthesis to achieve from artificial stepwise synthesis to self-organization logical synthesis (Scheme 1B). In view of this idea, we have been focusing on convergent integration of multipath reaction sequences, such as, self-sorting domino reaction,[2] a focusing domino reaction,[3] and a self-labor domino reaction.[4] This is because convergent synthesis was one of the most efficient methods in the construction of complex molecules.[5] To further verify the versatility of this strategy, an additional novel convergent self-labor reaction network for the construction of trisubstituted imidazoles from three simple and readily available starting substrates has been reported in this work.

Imidazoles are an important class of five-member heterocycles, which can be found in drug cores,[6] natural products,[7] important ligands,[8] ionic liquids,[9] etc.[10] Due to the significance of imidazoles, various methods have been developed for the construction of imidazole derivatives. These methods can be classified by their starting materials into amides,[11] imines,[12] nitriles,[13] amino acids,[14] isocyanides,[15] and other precursors.[16] Despite some recent interest, the direct cyclization of acyclic precursors has not yet been fully explored.[17]



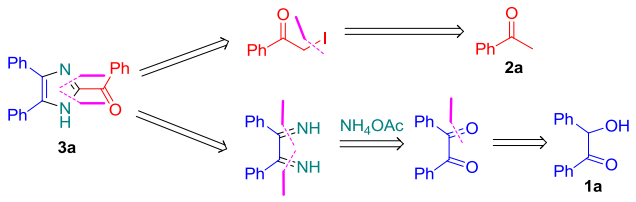
Scheme 1. Self-sequence synthesis strategy.

Retrosynthetically (Scheme 2), the synthesis of imidazole derivatives could be constructed from two different easily available starting substrates, methyl ketones and benzoins, based on a convergent integration of two parallel linear domino reactions.

In the previous literature, phenacyl iodine could be obtained by iodination of acetophenone.[18] In addition, benzoins could be oxidized to benzils under basic conditions catalyzed by iodine.[19] Phenacyl bromine could react with benzaldehyde to afford imidazoles in the presence of phenylamine and ammonium acetate.[17c]

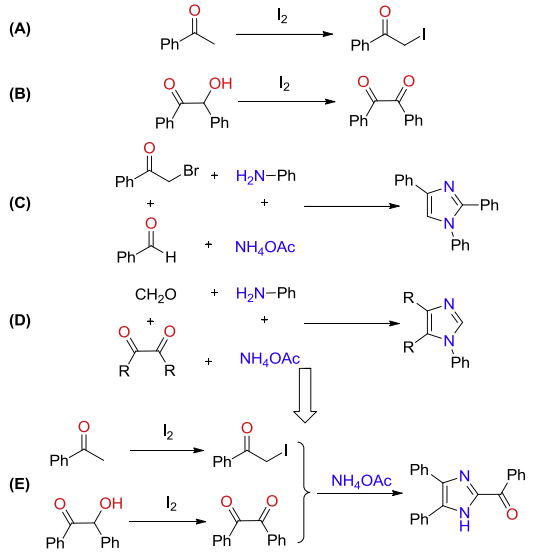
* Corresponding author. Tel./fax: +86 (0)27 6786 7773; e-mail address: chwuax@mail.ccnu.edu.cn (A. Wu).

0040-4020/$ – see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tet.2013.11.080



Scheme 2. Retrosynthetic analysis.

Moreover, benzyl could react with formaldehyde to afford imidazole in the presence of phenylamine and ammonium chloride.[20] In this study, we therefore tried to integrate two self-labor domino sequences in one-pot, which could merge the previous fundamental reactions (Scheme 3A–D) together to directly construct imidazole derivatives (Scheme 3E).



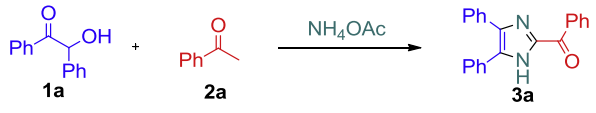
Scheme 3. Integration of two parallel linear domino reactions.

2. Results and discussion

The reaction conditions were initially optimized from benzoin (**1a**) and aryl methyl ketones (**2a**). As shown in Table 1, various catalysts, bases, solvents, and temperatures were examined. To our delight, the reaction of **1a** performed smoothly with **2a** to produce a 42% yield in the presence of I_2 (0.5 mmol) at 80 °C in CH_3CN without any catalyst. A series of bases were then screened for the reaction, such as Cs_2CO_3, K_2CO_3, DBU, and Na_2CO_3 (Table 1, entries 10–13). Pleasingly, the reaction was achieved in moderate yields with Cs_2CO_3. To our surprise, good yields were also obtained with a promotion in the dose of I_2. After several experimental optimizations, it was found that **1a** (0.5 mmol) could react with **2a** (0.5 mmol) and NH_4OAc (5 mmol) in the presence of I_2 (1.5 mmol) and Cs_2CO_3 (0.5 mmol) in CH_3CN at 80 °C to afford the desired product in 70% yield (Table 1, entry 18).

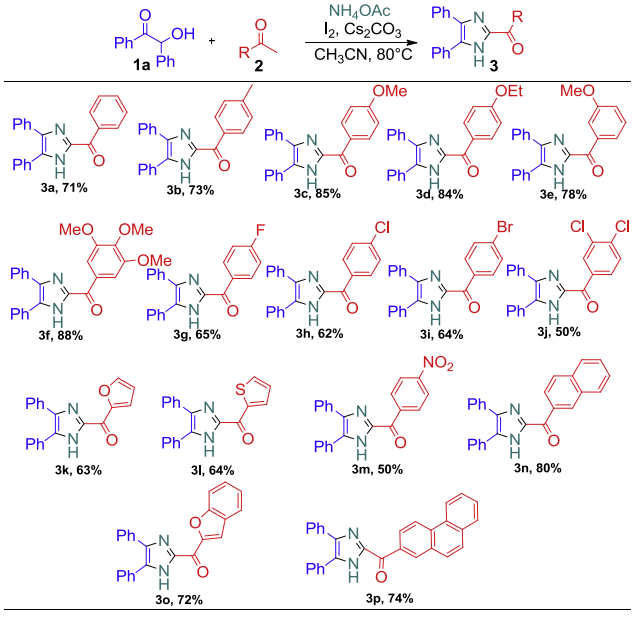
A wide range of aryl methyl ketones was investigated under the optimal conditions. As shown in Scheme 4, the substituted aryl methyl ketones performed smoothly with benzoin **1a** to afford the desired products in moderate to good yields (50–88%). The electron-donating groups attached to the phenyl rings of aryl methyl ketones, such as 4-Me, 4-OMe, 4-OEt, 3-OMe, and 3,4,5-$(OMe)_3$, exhibited good reactivity (Scheme 4, **3b**–**f**). However, the electron withdrawing groups, such as F, Cl, Br, and NO_2, decreased the reactivity (Scheme 4, **3g**–**j** and **3m**). In addition, 2-naphthyl methyl ketone and 2-acetylphenanthren reacted with benzoin **1a** to obtain satisfying results (80% and 74% yields). Encouraged by the results, the heteroaryl methyl ketones were then examined under the optimal conditions. To our delight, the substrates with heterocycle, such as furanyl (**2k**), thiophenyl (**2l**), and benzofuryl (**2o**), obtained the corresponding products in moderate yields (63–72%).

Table 1
Optimization of the reaction conditions[a]



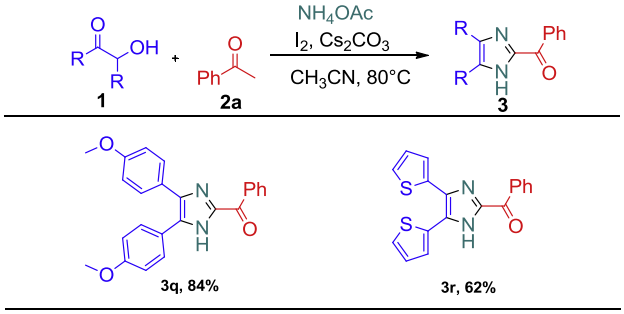
Entry	I_2 (equiv)	Catalyst (0.5 equiv)	Base (1.0 equiv)	Solvent	Temp (°C)	Yield[b] (%)
1	1.0	CuI		H_2O	80	12
2	1.0	CuI		MeOH	60	15
3	1.0	CuI		EtOH	78	16
4	1.0	CuI		*t*-Bu-OH	80	33
5	1.0	CuI		CH_3CN	80	39
6	1.0	CuCl		CH_3CN	80	36
7	1.0	$CuCl_2$		CH_3CN	80	24
8	1.0	$Cu(OAc)_2$		CH_3CN	80	25
9	1.0			CH_3CN	80	42
10	1.0		Cs_2CO_3	CH_3CN	80	53
11	1.0		K_2CO_3	CH_3CN	80	43
12	1.0		DBU	CH_3CN	80	21
13	1.0		Na_2CO_3	CH_3CN	80	34
14	1.0		Cs_2CO_3	CH_3CN	20	12
15	1.0		Cs_2CO_3	CH_3CN	40	23
16	1.0		Cs_2CO_3	CH_3CN	60	45
17	2.0		Cs_2CO_3	CH_3CN	80	60
18	*3.0*		*Cs_2CO_3*	*CH_3CN*	*80*	*70*
19	4.0		Cs_2CO_3	CH_3CN	80	71
20	5.0		Cs_2CO_3	CH_3CN	80	71

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.5 mmol), NH_4OAc (5 mmol) in 3 mL solvent for 4 h.
[b] Isolated yields.



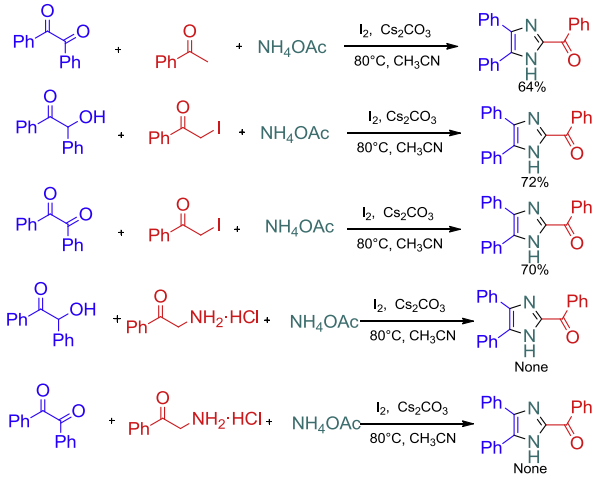
Scheme 4. Scope of aryl methyl ketones.

Different benzoins were then examined to further expand the scope of the substrates. As shown in Scheme 5, the benzoin with electron-donating groups could afford the desired product in good yield. Moreover, the target molecular could be obtained in moderate yield when heteroaryl benzoin was used as substrate. This implied that the electronic effect has a great influence on the reaction. Furthermore, the structure of **3a** was also confirmed by X-ray crystallography.[21]



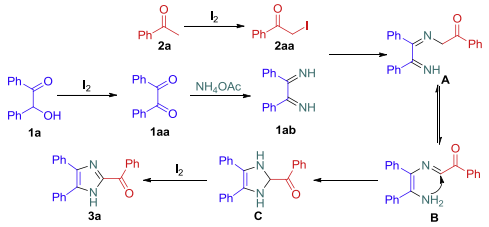
Scheme 5. Scope of benzoins.

To gain some insight into the mechanism of the reaction process, the following experiments were performed (Scheme 6). The target molecule was obtained from benzyl and acetophenone in 64% yield. The reaction of α-iodo ketone (0.5 mmol) and benzoin **1a** (0.5 mmol) with I_2 (1.5 mmol) and Cs_2CO_3 (0.5 mmol) were refluxed for 4.0 h in MeCN and the directed product was obtained in 72% yield. Then the mixture of α-iodo ketone (0.5 mmol) and benzil (0.5 mmol) with I_2 (1.5 mmol) and Cs_2CO_3 (0.5 mmol) was refluxed for 4.0 h in MeCN and the directed product was obtained in 70% yield. However, regardless of whether benzoin or benzil was used as substrate, the products could not be obtained when aryl methyl ketone **2a** was substituted with 2-aminoacetophenone hydrochloride. This result clearly confirmed α-iodo ketone and benzil as important intermediates in this reaction. In addition, 2-aminoacetophenone evidently could not participate in the reaction. Finally, GC–MS and ^{1}H NMR were used to detect the proposed intermediates for this reaction (Supplementary data). These also verified the significance of α-iodo ketone and benzil as important intermediates.



Scheme 6. Control experiments.

Based on the aforementioned experiments, it can be supposed that this reaction would be a novel self-labor reaction network. The possible mechanism for this reaction is illustrated with the example from benzoin (**1a**), acetophenone (**2a**), and ammonium acetate (as shown in Scheme 7). Firstly, α-iodo ketone **2aa** could be obtained by iodination of acetophenone (**2a**). Then, benzil (**1aa**) could be generated by oxidation of benzoin (**1a**) catalyzed by I_2. Subsequently, intermediate (**1ab**) could be formed as a product after the addition of ammonium acetate to benzil (**1aa**). Next, **A** or its enolizational isomer **B** could be obtained from **2aa** and **1ab**. When **B** underwent intramolecular nucleophilic reaction, **C** was obtained. Finally, **C** underwent dehydration reaction to afford the final product **3a**.



Scheme 7. Plausible mechanism of the present reaction.

3. Conclusion

In conclusion, this study has developed a novel method for the synthesis of polysubstituted imidazoles from methyl ketones and benzoins based on a convergent reaction network. This transformation is not only an efficient example to prove the versatile of the strategy but also a tool to discover novel reaction. Further studies on the applications of this reaction will be reported in due course.

4. Experimental

4.1. General

All substrates and reagents were commercially available and used without further purification. TLC analysis was performed using pre-coated glass plates. Flash column chromatography was performed on silica gel (200–300 mesh). IR spectra were recorded as KBr pellets with absorption in cm^{-1}. ^{1}H spectra were recorded in $CDCl_3$ on 600 MHz NMR spectrometers and resonances (δ) are given in parts per million (ppm) relative to tetramethylsilane. ^{13}C spectra were recorded in $CDCl_3$ on 100 MHz NMR spectrometers and resonances (δ) are given in parts per million (ppm). HRMS were obtained on an apex-Ultra MS spectrometer. MS was recorded using EI (70 eV). Melting points were determined using an electrothermal capillary melting point apparatus and not corrected. The X-ray crystal-structure determinations were obtained on a Bruker SMART APEX CCD system.

4.2. General procedure for synthesis of 3 (3a as an example)

A mixture of **1a** (106.0 mg, 0.5 mmol), acetophenone **2a** (60.0 mg, 0.5 mmol), NH_4OAc (385.0 mg, 5.0 mmol), Cs_2CO_3 (163.0 mg, 0.5 mmol) and iodine (381.0 mg, 1.5 mmol) in CH_3CN (3 mL) was stirred at 80 °C for 4 h. After disappearance of the reactant (monitored by TLC), and added 50 mL water to the mixture, then extracted with EtOAc three times (3×50 mL). The extract was washed with 10% $Na_2S_2O_3$ solution (w/w), dried over anhydrous Na_2SO_4, and evaporation. The residue was purified by column

chromatography on silica gel (petroleum ether/EtOAc=10:1) to yield the desired product **3a** as a yellow solid.

4.3. Characterization data

*4.3.1. (4,5-Diphenyl-1H-imidazol-2-yl)(phenyl)methanone (**3a**).*[22] Yield 71%, 115.0 mg; light yellow solid; mp 204.1–207.2 °C; IR (KBr): 3256, 3240, 1628, 1599, 1498, 1453, 1439, 1302, 1285, 907, 727 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.33 (s, 1H), 8.67 (d, J=7.2 Hz, 2H), 7.62 (t, J=7.8 Hz, 4H), 7.51 (t, J=7.8 Hz, 3H), 7.37 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.7, 144.2, 140.7, 135.6, 134.1, 133.3, 131.5, 129.8, 128.9, 128.8, 128.5, 128.4, 128.2, 127.9, 127.5; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{17}N_2O$: 325.13354; found: 325.13326.

*4.3.2. (4,5-Diphenyl-1H-imidazol-2-yl)(p-tolyl)methanone (**3b**).* Yield 73%, 123.4 mg; light yellow solid; mp 235.3–238.1 °C; IR (KBr): 3053, 1640, 1606, 1460, 1441, 1416, 1308, 1242, 1174, 910, 765, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.75 (s, 1H), 8.55 (d, J=7.2 Hz, 2H), 7.67 (d, J=6.6 Hz, 2H), 7.54 (d, J=5.4 Hz, 2H), 7.38 (s, 3H), 7.32 (d, J=6.6 Hz, 2H), 7.28 (d, J=6.6 Hz, 3H), 2.44 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.2, 144.4, 144.3, 133.1, 131.6, 129.0, 128.8, 128.6, 128.1, 21.8; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{19}N_2O$: 339.14919; found: 339.14890.

*4.3.3. (4,5-Diphenyl-1H-imidazol-2-yl)(4-methoxyphenyl)methanone (**3c**).*[22] Yield 85%; 150.5 mg light yellow solid; mp 192.3–195.8 °C; IR (KBr): 3058, 1622, 1602, 1571, 1459, 1442, 1411, 1314, 1260, 1248, 1164, 910, 778, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.56 (s, 1H), 8.73 (d, J=9.0 Hz, 2H), 7.68 (s, 2H), 7.54 (s, 2H), 7.39–7.29 (m, 6H), 6.98 (d, J=9.0 Hz, 2H), 3.90 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 163.9, 144.5, 140.3, 134.2, 133.9, 131.4, 129.9, 128.9, 128.6, 128.5, 128.3, 127.9, 127.4, 113.6, 55.5; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_2$: 355.14410; found: 355.14376.

*4.3.4. (4,5-Diphenyl-1H-imidazol-2-yl)(4-ethoxyphenyl)methanone (**3d**).* Yield 84%, 154.6 mg; light yellow solid; mp 205.3–208.9 °C; IR (KBr): 3251, 1616, 1599, 1564, 1461, 1450, 1260, 1237, 1181, 1168, 908, 808, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.88 (s, 1H), 8.67 (d, J=8.4 Hz, 2H), 7.68 (d, J=6.6 Hz, 2H), 7.54 (d, J=6.0 Hz, 2H), 7.37–7.27 (m, 6H), 6.94 (d, J=8.4 Hz, 2H), 4.14–4.10 (m, 2H), 1.45 (t, J=6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 163.4, 144.5, 133.9, 128.8, 128.5, 128.4, 128.3, 127.9, 127.8, 114.0, 63.7, 14.7; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{24}H_{21}N_2O_2$: 369.15975; found: 369.15937.

*4.3.5. (4,5-Diphenyl-1H-imidazol-2-yl)(3-methoxyphenyl)methanone (**3e**).* Yield 78%, 138.1 mg; light yellow solid; mp 169.4–172.8 °C; IR (KBr): 3054, 1651, 1603, 1578, 1498, 1484, 1441, 1418, 1258, 1226, 1054, 969, 764, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.48 (s, 1H), 8.31 (d, J=6.6 Hz, 1H), 8.23 (s, 1H), 7.67 (d, J=6.0 Hz, 2H), 7.53 (s, 2H), 7.41–7.29 (m, 7H), 7.16 (d, J=7.8 Hz, 1H), 3.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.3, 159.3, 144.2, 140.6, 136.8, 134.0, 131.8, 129.7, 129.3, 128.9, 128.4, 127.9, 127.5, 124.3, 120.2, 115.4, 55.4; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{23}H_{19}N_2O_2$: 355.14410; found: 355.14378.

*4.3.6. (4,5-Diphenyl-1H-imidazol-2-yl)(3,4,5-trimethoxyphenyl)methanone (**3f**).* Yield 88%, 182.2 mg; light yellow solid; mp 176.2–179.9 °C; IR (KBr): 3243, 1622, 1581, 1506, 1494, 1453, 1438, 1415, 1339, 1240, 1219, 1132, 996, 719 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.80 (s, 1H), 8.14 (s, 2H), 7.67 (d, J=7.2 Hz, 2H), 7.54 (d, J=6.6 Hz, 2H), 7.38–7.29 (m, 6H), 3.97 (s, 3H), 3.92 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 152.6, 144.3, 143.0, 140.4, 134.1, 131.6, 130.5, 129.7, 128.8, 128.3, 127.6, 127.5, 109.0, 60.9, 56.1; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{25}H_{23}N_2O_4$: 415.16523; found: 415.16486.

*4.3.7. (4,5-Diphenyl-1H-imidazol-2-yl)(4-fluorophenyl)methanone (**3g**).* Yield 65%, 111.2 mg; light yellow solid; mp 219.5–222.8 °C; IR (KBr): 3286, 1641, 1623, 1598, 1452, 1442, 1234, 1157, 911, 673 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.86 (s, 1H), 8.69 (t, J=6.6 Hz, 2H), 7.60 (s, 4H), 7.36 (s, 6H), 7.14 (t, J=7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 167.4, 164.8, 144.0, 134.3, 134.2, 131.9, 128.7, 128.2, 115.5, 115.3, 109.7; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{16}FN_2O$: 343.12412; found: 343.12378.

*4.3.8. (4-Chlorophenyl)(4,5-diphenyl-1H-imidazol-2-yl)methanone (**3h**).*[22] Yield 62%, 110.9 mg; light yellow solid; mp 207.6–210.9 °C; IR (KBr): 3257, 1620, 1585, 1451, 1441, 1302, 1229, 1091, 906, 766, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.48 (s, 1H), 8.63 (d, J=8.4 Hz, 2H), 7.66 (d, J=6.0 Hz, 2H), 7.53 (d, J=6.0 Hz, 2H), 7.46 (d, J=7.8 Hz, 2H), 7.41 (d, J=7.2 Hz, 3H), 7.34 (d, J=6.6 Hz, 2H), 7.31 (d, J=6.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 143.9, 140.8, 140.0, 133.9, 132.9, 131.9, 129.7, 129.0, 128.6, 128.4, 127.9, 127.7; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{16}ClN_2O$: 359.09457; found: 359.09424.

*4.3.9. (4-Bromophenyl)(4,5-diphenyl-1H-imidazol-2-yl)methanone (**3i**).* Yield 64%, 128.7 mg; light yellow solid; mp 228.5–231.8 °C; IR (KBr): 3268, 1625, 1584, 1452, 1442, 1425, 1237, 1214, 1070, 1101, 906, 767, 695 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.70 (s, 1H), 8.51 (d, J=8.4 Hz, 2H), 7.65 (d, J=7.2 Hz, 2H), 7.62 (d, J=7.2 Hz, 2H), 7.53 (d, J=7.2 Hz, 2H), 7.44–7.38(m, 3H), 7.35–7.29 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.0, 143.9, 134.3, 133.8, 132.9, 131.6, 129.7, 129.0, 128.9, 128.5, 127.9, 127.7; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{16}BrN_2O$: 403.04405; found: 403.04366.

*4.3.10. (3,4-Dichlorophenyl)(4,5-diphenyl-1H-imidazol-2-yl)methanone (**3j**).* Yield 50%, 98.0 mg; light yellow solid; mp 203.9–207.3 °C; IR (KBr): 3262, 1623, 1578, 1452, 1441, 1288, 1256, 1216, 1131, 940, 778, 695 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.53 (s, 1H), 8.71 (s, 1H), 8.60 (d, J=8.4 Hz, 1H), 7.65 (d, J=6.6 Hz, 2H), 7.56 (d, J=8.4 Hz, 1H), 7.52 (d, J=6.6 Hz, 2H), 7.41 (d, J=7.8 Hz, 3H), 7.34–7.31(m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 178.8, 143.6, 141.1, 138.0, 135.1, 133.6, 133.0, 130.7, 130.4, 129.4, 129.3, 129.1, 128.5, 128.4, 127.9; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{22}H_{15}Cl_2N_2O$: 393.05559; found: 393.05562.

*4.3.11. (4,5-Diphenyl-1H-imidazol-2-yl)(furan-2-yl)methanone (**3k**).* Yield 63%, 98.9 mg; light yellow solid; mp 252.7–255.2 °C; IR (KBr): 3177, 1619, 1557, 1468, 1443, 1426, 1253, 1216, 1011, 884, 768, 695 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 10.86 (s, 1H), 8.55 (d, J=8.4 Hz, 1H), 7.86 (s, 1H), 7.76 (d, J=7.2 Hz, 2H), 7.60 (s, 2H), 7.49 (s, 3H), 7.43–7.40 (m, 3H), 6.75 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.9, 150.3, 148.0, 143.0, 140.5, 134.0, 129.6, 129.0, 128.9, 128.4, 128.1, 127.9, 127.6, 124.3, 112.8; HRMS (ESI): m/z $[M+H]^+$ calcd for $C_{20}H_{15}N_2O_2$: 315.11280; found: 315.11255.

*4.3.12. (4,5-Diphenyl-1H-imidazol-2-yl)(thiophen-2-yl)methanone (**3l**).* Yield 64%, 105.6 mg; light yellow solid; mp 242.2–245.9 °C; IR (KBr): 3259, 1600, 1509, 1453, 1442, 1425, 1240, 1206, 1180, 820, 766, 691 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.33 (s, 1H), 9.36 (s, 1H), 7.93 (s, 1H), 7.68 (d, J=6.6 Hz, 2H), 7.54 (s, 2H), 7.40 (s, 3H), 7.34–7.28 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 175.1, 144.1, 139.2, 137.6, 134.1, 129.8, 129.0, 128.9, 128.7, 128.4, 128.3, 127.9, 127.6,

125.4; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{20}H_{15}N_2OS$: 331.08996; found: 331.08973.

*4.3.13. (4,5-Diphenyl-1H-imidazol-2-yl)(4-nitrophenyl)methanone (**3m**).* Yield 50%, 92.3 mg; red solid; mp 251.2–254.7 °C; IR (KBr): 3278, 1628, 1594, 1517, 1452, 1442, 1349, 1319, 1230, 912, 849, 768, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.11 (s, 1H), 8.85 (d, *J*=7.8 Hz, 2H), 8.35 (d, *J*=8.4 Hz, 2H), 7.67 (d, *J*=7.2 Hz, 2H), 7.54 (d, *J*=6.6 Hz, 2H), 7.45 (d, *J*=6.6 Hz, 2H), 7.38–7.34 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 179.3, 150.3, 143.5, 140.4, 132.3, 129.1, 128.9, 128.6, 128.5, 128.3, 127.9, 127.8, 125.2, 123.3; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{22}H_{16}N_3O_3$: 370.11862; found: 370.11835.

*4.3.14. (4,5-Diphenyl-1H-imidazol-2-yl)(naphthalen-2-yl)methanone (**3n**).* Yield 80%, 149.6 mg; light yellow solid; mp 215.3–218.9 °C; IR (KBr): 3245, 1635, 1612, 1591, 1451, 1442, 1416, 1250, 1219, 963, 829, 763, 708 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.34 (s, 1H), 9.52 (s, 1H), 8.53 (d, *J*=8.4 Hz, 1H), 8.07 (d, *J*=8.4 Hz, 1H), 7.94–7.89 (m, 2H), 7.73 (d, *J*=7.2 Hz, 2H), 7.62 (d, *J*=6.6 Hz, 1H), 7.58–7.56 (m, 3H), 7.42–7.31 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.3, 144.4, 140.7, 135.8, 134.4, 134.1, 132.9, 132.5, 131.7, 130.3, 129.8, 129.0, 128.9, 128.7, 128.4, 128.0, 127.7, 127.6, 126.4, 126.2; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{26}H_{19}N_2O$: 375.14919; found: 375.14883.

*4.3.15. Benzofuran-2-yl(4,5-diphenyl-1H-imidazol-2-yl)methanone (**3o**).* Yield 72%, 131.1 mg; light yellow solid; mp 257.3–260.9 °C; IR (KBr): 3278, 1625, 1547, 1513, 1513, 1463, 1451, 1442, 1326, 1259, 1228, 1185, 956, 768, 695 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.09 (s, 1H), 8.89 (s, 1H), 7.82 (s, 1H), 7.71 (s, 2H), 7.66 (d, *J*=6.6 Hz, 1H), 7.56–7.52 (m, 3H), 7.42–7.35 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 170.4, 156.2, 150.4, 143.2, 140.8, 133.9, 131.7, 129.5, 129.1, 128.7, 128.5, 128.1, 128.0, 127.8, 127.6, 124.0, 120.2, 112.5; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{17}N_2O_2$: 365.12845; found: 365.12802.

*4.3.16. (4,5-Diphenyl-1H-imidazol-2-yl)(phenanthren-2-yl)methanone (**3p**).* Yield 74%, 156.9 mg; light yellow solid; mp 269.6–273.8 °C; IR (KBr): 3240, 1627, 1607, 1584, 1568, 1462, 1449, 1425, 1234, 1218, 972, 848, 766, 698 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.14 (s, 1H), 9.44 (s, 1H), 8.87 (d, *J*=9.0 Hz, 1H), 8.78 (d, *J*=8.4 Hz, 1H), 8.75 (d, *J*=8.4 Hz, 1H), 7.94–7.90 (m, 2H), 7.81 (d, *J*=8.4 Hz, 1H), 7.75 (d, *J*=7.8 Hz, 2H), 7.72–7.66 (m, 2H), 7.57 (s, 2H), 7.43 (s, 2H), 7.39–7.32 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 180.9, 144.5, 140.7, 134.1, 133.7, 133.5, 133.3, 131.5, 129.8, 129.1, 129.0, 128.7, 128.4, 128.3, 128.0, 127.8, 127.6, 127.5, 126.9, 123.5, 122.8; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{30}H_{21}N_2O$: 425.16484; found: 425.16437.

*4.3.17. (4,5-Bis(4-methoxyphenyl)-1H-imidazol-2-yl)(phenyl)methanone (**3q**).*[22] Yield 84%, 161.3 mg; light yellow solid; mp 185.4–188.9 °C; IR (KBr): 3320, 1607, 1591, 1566, 1526, 1488, 1462, 1434, 1298, 1249, 1228, 1178, 904, 838, 693 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 11.61 (s, 1H), 8.62 (d, *J*=7.8 Hz, 2H), 7.60 (t, *J*=7.2 Hz, 2H), 7.54–7.48 (m, 5H), 6.88 (d, *J*=8.4 Hz, 4H), 3.82 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.4, 143.8, 135.8, 133.2, 131.4, 129.4, 128.2, 114.1, 112.3, 55.3; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{24}H_{21}N_2O_3$: 385.15467; found: 385.15426.

*4.3.18. (4,5-Di(thiophen-2-yl)-1H-imidazol-2-yl)(phenyl)methanone (**3r**).* Yield 62%, 104.2 mg; light yellow solid; mp 172.1–175.9 °C; IR (KBr): 3232, 1627, 1594, 1571, 1469, 1453, 1401, 1341, 1244, 1209, 1180, 901, 847, 696 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ (ppm) 10.86 (s, 1H), 8.68 (d, *J*=7.2 Hz, 2H), 7.63 (t, *J*=7.2 Hz, 1H), 7.53 (t, *J*=7.8 Hz, 2H), 7.46 (d, *J*=5.4 Hz, 1H), 7.42–7.38 (m, 2H), 7.32 (d, *J*=4.2 Hz, 1H), 7.15 (t, *J*=4.8 Hz, 1H), 7.04 (t, *J*=4.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 181.1, 143.9, 136.3, 135.4, 133.5, 131.4, 129.7, 128.5, 128.4, 127.8, 127.6, 127.3, 125.7, 125.6, 124.4; HRMS (ESI): *m/z* $[M+H]^+$ calcd for $C_{18}H_{13}N_2OS_2$: 337.04638; found: 337.04611.

Acknowledgements

We thank the National Natural Science Foundation of China (Grants 21032001 and 21272085). We also thank Dr. Xianggao Meng for his help with X-ray diffraction analysis and Dr. Chuanqi Zhou, Hebei University, for analytical support.

Supplementary data

Evidence in support of the hypothetic mechanism, and ^1H and ^{13}C NMR spectra and X-ray crystal data for **3a**. Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.11.080.

References and notes

1. Corey, E. J.; Cheng, X. M. *The Logic of Chemical Synthesis*; Wiley: New York, NY, 1989.
2. Yin, G. D.; Zhou, B. H.; Meng, X. G.; Wu, A. X.; Pan, Y. J. *Org. Lett.* **2006**, *8*, 2245.
3. Gao, M.; Yang, Y.; Wu, Y. D.; Deng, C.; Shu, W. M.; Zhang, D. X.; Cao, L. P.; She, N. F.; Wu, A. X. *Org. Lett.* **2010**, *12*, 4026.
4. Xue, W. J.; Li, Q.; Zhu, Y. P.; Wang, J. G.; Wu, A. X. *Chem. Commun.* **2012**, 3485.
5. Wang, Y.; Zhang, W. X.; Wang, Z. T.; Xi, Z. F. *Angew. Chem.* **2011**, *123*, 8272; *Angew. Chem., Int. Ed.* **2011**, *50*, 8122.
6. (a) Carini, D. J.; Duncia, J. V.; Johnson, A. L.; Chiu, A. T.; Price, W. A.; Wong, P. C.; Timmermans, P. *J. Med. Chem.* **1990**, *33*, 1330; (b) Lee, J. C.; Laydon, J. T.; McDonnell, P. C.; Gallagher, T. F.; Kumar, S.; McNully, D.; Blumenthal, M.; Heys, J. R. *Nature* **1994**, *372*, 739; (c) Atwell, G. A.; Fan, J.-Y.; Tan, K.; Denny, W. A. *J. Med. Chem.* **1998**, *41*, 4744.
7. (a) Jin, Z. *Nat. Prod. Rep.* **2009**, *26*, 382; (b) Jin, Z. *Nat. Prod. Rep.* **2006**, *23*, 464; (c) Jin, Z. *Nat. Prod. Rep.* **2005**, *22*, 196.
8. Holm, R. H.; Kennepohl, P.; Solomon, E. I. *Chem. Rev.* **1996**, *96*, 2239.
9. Dupont, J.; de Souza, R. F.; Suarez, P. A. Z. *Chem. Rev.* **2002**, *102*, 3667.
10. For selected examples, see: (a) Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2003**, *125*, 10580; (b) Kuwano, R.; Kameyama, N.; Ikeda, R. *J. Am. Chem. Soc.* **2011**, *133*, 7312; (c) Ueda, S.; Su, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2012**, *134*, 700; (d) Laroche, C.; Li, J.; Freyer, M.; Kerwin, W. S. M. *J. Org. Chem.* **2008**, *73*, 6462; (e) Bhandari, M. R.; Yousufuddin, M.; Lovely, C. J. *Org. Lett.* **2011**, *13*, 1382.
11. (a) Frantz, D. E.; Morency, L.; Soheili, A.; Murry, J. A.; Grabowski, E. J. J.; Tillyer, R. D. *Org. Lett.* **2004**, *6*, 843; (b) Zhong, Y. L.; Lee, J.; Reamer, R. A.; Askin, D. *Org. Lett.* **2004**, *6*, 929; (c) Lee, H. B.; Balasubramanian, S. *Org. Lett.* **2000**, *2*, 323.
12. For selected examples, see: (a) Siamaki, A. R.; Sakalauskas, M.; Arndtsen, B. A. *Angew. Chem.* **2011**, *123*, 6682; *Angew. Chem., Int. Ed.* **2011**, *50*, 6552; (b) Siamaki, A. R.; Arndtsen, B. A. *J. Am. Chem. Soc.* **2006**, *128*, 6050; (c) Piccionello, A. P.; Buscemi, S.; Vivona, N.; Pace, A. *Org. Lett.* **2010**, *12*, 3491.
13. (a) Giles, R. L.; Sullivan, J. D.; Steiner, A. M.; Looper, R. E. *Angew. Chem.* **2009**, *121*, 3162; *Angew. Chem., Int. Ed.* **2009**, *48*, 3116; (b) Shen, H.; Xie, Z. *J. Am. Chem. Soc.* **2010**, *132*, 11473; (c) Jiang, B.; Wang, X.; Shi, F.; Tu, S. J.; Ai, T.; Ballew, A.; Li, G. *J. Org. Chem.* **2009**, *74*, 9486; (d) Horneff, T.; Chuprakov, S.; Chernyak, N.; Gevorgyan, V.; Fokin, V. V. *J. Am. Chem. Soc.* **2008**, *130*, 14972.
14. (a) Attanasi, O. A.; Caselli, E.; Davoli, P.; Favi, G.; Mantellini, F.; Ori, C.; Prati, F. *Org. Lett.* **2009**, *11*, 2840; (b) Petit, S.; Fruit, C.; Bischoff, L. *Org. Lett.* **2010**, *12*, 4928.
15. (a) Bienaymé, H.; Bouzid, K. *Angew. Chem.* **1998**, *110*, 2349; *Angew. Chem., Int. Ed.* **1998**, *37*, 2234; (b) Lygin, A. V.; de Meijere, A. *Angew. Chem.* **2010**, *122*, 9280; *Angew. Chem., Int. Ed.* **2010**, *49*, 9094; (c) Kanazawa, C.; Kamijo, S.; Yamamoto, Y. *J. Am. Chem. Soc.* **2006**, *128*, 10662.
16. For selected examples, see: (a) Gainer, M. J.; Bennett, N. R.; Takahashi, Y.; Looper, R. E. *Angew. Chem.* **2011**, *123*, 710; *Angew. Chem., Int. Ed.* **2011**, *50*, 684; (b) Wang, H.; Wang, Y.; Liang, D.; Liu, L.; Zhang, J.; Zhu, Q. *Angew. Chem.* **2011**, *123*, 5796; *Angew. Chem., Int. Ed.* **2011**, *50*, 5678; (c) Smith, M. R.; Blake, A. J.; Hayes, C. J.; Stevens, M. F. G.; Moody, C. J. *J. Org. Chem.* **2009**, *74*, 9372; (d) Nie, Y. B.; Wang, L.; Ding, M. W. *J. Org. Chem.* **2012**, *77*, 696; (e) Zaman, S.; Mitsuru, K.; Abell, A. D. *Org. Lett.* **2005**, *7*, 609; (f) Attanasi, O. A.; Davoli, P.; Favi, G.; Filippone, P.; Forni, A.; Moscatelli, G.; Prati, F. *Org. Lett.* **2007**, *9*, 3461.
17. (a) Huang, H. W.; Ji, X. C.; Wu, W. Q.; Jiang, H. F. *Adv. Synth. Catal.* **2013**, *355*, 170; (b) Thomas, P. J.; Axtell, A. T.; Klosin, J.; Peng, W.; Rand, C. L.; Clark, T. P.; Landis, C. R.; Abboud, K. A. *Org. Lett.* **2007**, *9*, 2665; (c) Adib, M.; Ansari, S.; Feizi, S.; Damavandi, J. A.; Mirzaei, P. *Synlett* **2009**, 3263.

18. Okamoto, T.; Kakinami, T.; Nishimura, T.; Hermawan, I.; Kajigaeshi, S. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 1731.
19. Kidwai, M.; Mothsra, P. *Tetrahedron Lett.* **2006**, *47*, 5029.
20. Liu, J. P.; Chen, J. B.; Zhao, J. F.; Zhao, Y. H.; Li, L.; Zhang, H. B. *Synthesis* **2003**, 2661.
21. The details of the crystal data (**3a**) have been deposited with Cambridge Crystallographic Data Centre as Supplementary Publication, CCDC 949845.
22. (a) Kayağil, I.; Demirayak, Ş. *Turk. J. Chem.* **2011**, *35*, 13; (b) Dora, E. K.; Dash, B.; Panda, C. S. *J. Indian Chem. Soc.* **1988**, *65*, 784.