Tetrahedron 66 (2010) 7743–7748

Contents lists available at ScienceDirect

Tetrahedron

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

Synthesis of zwitterionic salts via three-component reactions of pyridacylpyridinum iodide, aromatic aldehydes, and Meldrum acid or *N*,*N*-dimethylbarbituric acid

Ying Han, Jiao Chen, Li Hui, Chao-Guo Yan *

College of Chemistry & Chemical Engineering, Yangzhou University, Yangzhou 225002, China

ARTICLE INFO

Article history:
Received 20 May 2010
Received in revised form 20 July 2010
Accepted 26 July 2010
Available online 3 August 2010

Keywords:
Multicomponent reaction
Pyridinium salt
Zwitterionic salt
Meldrum acid
Barbituric acid

ABSTRACT

New zwitterionic salts of pyridinium–Meldrum acid and pyridinium–barbituric acid are conveniently synthesized from the three-component reactions of 2-, 3-, or 4-pyridacylpyridinum iodides, aromatic aldehydes, and Meldrum acid or *N*,*N*-dimethylbarbituric acid in the presence of triethylamine as base promoter in acetonitrile.

1. Introduction

N-Alkylpyridinium salts are one kinds of heterocyclic ammonium salts and have been used in a great variety of synthetic reactions.[1–4] Pyridinium salts derived from α-halogenocarbonyl compounds are easily deprotonated to give pyridinium ylide, which are prone to be high potential synthons and underwent versatile reactions, such as Kröhnke synthesis of oligopyridines and 1,3-dipolar cycloaddition for synthesis of indolizines.[2b–d,5–10] In the past years we have successfully developed some new multicomponent reactions by using the very easily in situ formed pyridinium salts as one component of the reactions.[11] Recently we found that the unusual charge-separated pyridinium–Meldrum acid and barbituric acid zwitterionic salts can be prepared by the four-component reaction of pyridine, *p*-nitrobenzyl bromide, aromatic aldehydes, and Meldrum acid or barbituric acid.[12] This work successfully provided one practical and efficient method for the preparation of the functionalized pyridinium zwitterions. In the literature pyridinium zwitterions are usually described as very reactive species and there are only few reports about the synthesis of them.[13–16] Huisgen addition reaction might be the most widely used reaction for the preparation of zwitterionic salts, in which the 1,4-dipolar zwitterionic species were generated by the addition of nucleophiles, such as triphenyl phosphine, pyridine, tertiary amine, and dimethyl sulfoxide to activated alkynes like dimethyl acetylenedicarboxylate generate and then captured by suitable substrates to give versatile heterocyclic compounds.[15a,17–19] In order to further explore the potential of our protocol and to evaluate the scope of this four-component reaction we tested the reactivity of three kinds of pyridacylpyridinium iodides in the reaction. Here we wish to report the synthesis of new kinds of pyridinium zwitterionic salts containing functional pyridacyl groups.

2. Results and discussion

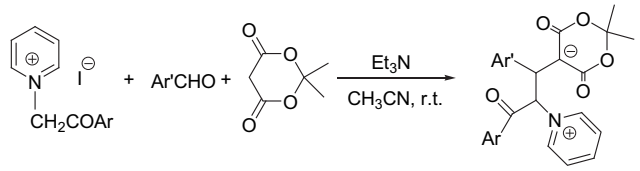
Our recently developed one-pot synthesis of zwitterionic salts involves in situ formation of pyridinium salts from the reaction of pyridine with reactive α-halogenocarbonyl compounds, such as phenacyl bromide and *p*-nitrobenzyl bromide.[12] But the corresponding pyridacyl halides are not available and are not readily accessible. It is well known that pyridacylpyridinium salts can be directly prepared by heating 2-, 3-, or 4-acetylpyridine with iodine in the solution of pyridine according to the Ortoleva–King reaction procedure.[1b,20] At first we think to combine Ortoleva–King reaction procedure and formation of zwitterionic salts into one-pot reaction and set out to test the multicomponent reaction by heating a mixture of 3-actylpyridine, iodine, benzaldehyde, Meldrum acid, and pyridine with triethylamine as base catalyst in acetonitrile. The result is very disappointed to us and no main product could be

* Corresponding author. E-mail address: cgyan@yzu.edu.cn (C.-G. Yan).

0040-4020/$ – see front matter © 2010 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2010.07.073

separated from the reaction mixture. After testing several base, solvent, and adding sequence of substrates we found that it is better to get firstly the isolated pyridacylpyridinium iodides (**1a**–**c**) by the Ortoleva–King reaction. Then we decided to test the three-component reaction of aromatic aldehydes, Meldrum acid and previously prepared 2-, 3-, or 4-pyridacylpyridinium salts in acetonitrile. After stirring the three reactants in solution of acetonitrile with triethylamine as base promoter for several hours, the expected pyridinium–Meldrum acid zwitterionic salts (**3a**–**q**) were formed as yellow precipitates in moderate to good yields, which are conveniently separated as pure products by filtration and washed with methanol. It should be pointed out that 3-pyridacylpyridinium iodide (**1b**) and 4-pyridacylpyridinium iodide (**1c**) reacted more smoothly than 2-pyridacylpyridinium iodide (**1a**), which need longer reaction time and gave lower yields of products (**3a**–**c**). Aromatic aldehydes carrying either electron-donating groups, such as *p*-methoxyl group or electron-withdrawing substituents, such as *m*-nitro and *p*-nitro groups showed similar reactivity and reacted efficiently to give the final products in satisfied yields. Thus our presented three-component reaction provides one practical procedure for the synthesis of reactive pyridinium zwitterions (Table 1).

Table 1
The synthesis of pyridinium–Meldrum acid zwitterionic salts



Entry	Compd	Ar	Ar′	*T* (h)	Yield (%)
1	**3a**	2-Py	*p*-ClC_6H_4	13	44
2	**3b**	2-Py	*p*-BrC_6H_4	14	52
3	**3c**	2-Py	*m*-$NO_2C_6H_4$	12	58
4	**3d**	3-Py	Ph	9	61
5	**3e**	3-Py	*p*-$CH_3C_6H_4$	9	74
6	**3f**	3-Py	*p*-$CH_3CH_2C_6H_4$	9	67
7	**3g**	3-Py	*p*- $CH_3OC_6H_4$	10	57
8	**3h**	3-Py	*p*-BrC_6H_4	8	71
9	**3i**	3-Py	*p*-ClC_6H_4	9	67
10	**3j**	3-Py	*m*-$NO_2C_6H_4$	8	80
11	**3k**	3-Py	*p*-$NO_2C_6H_4$	8	78
12	**3l**	4-Py	Ph	9	55
13	**3m**	4-Py	*p*-$CH_3C_6H_4$	8	70
14	**3n**	4-Py	*p*-$CH_3CH_2C_6H_4$	8	69
15	**3o**	4-Py	*p*-CH_3OC_6H	10	66
16	**3p**	4-Py	*p*-BrC_6H_4	8	72
17	**3q**	4-Py	*m*-$NO_2C_6H_4$	8	70

The structures of zwitterionic salts were fully characterized by ^1H and ^{13}C NMR, MS, IR spectra, and elemental analysis were further confirmed by single X-ray diffraction study performed for a representative compound **3d** (Fig. 1). In ^1H NMR spectra the methylene group connected with unit of Meldrum acid usually show one doublet at about δ 5.00 ppm with the vicinal coupling constant J=12.0 ppm. Due to connecting with two stronger electron-withdrawing pyridacyl and pyridinium groups the absorption beak of another methylene group greatly shifts to the range of 7–8 ppm and overlaps with signs of aromatic protons. From the Figure 1 it is clearly seen that the formed zwitterionic salt came from all three components of the reaction. The pyridyl group and Meldrum acid unit exist in the same side of molecule, which cause the positive charge and negative charge are in the shortest distance. The 3-pyridacyl and phenyl group exist on the other side. The methylene carbon atom in Meldrum acid unit adopts a sp^2 hybrid and the negative charge is delocalized to two carbonyl groups. The structure of this zwitterionic salt is very similar to that of our recently prepared pyridinium–Meldrum acid zwitterionic salts by one-pot three-component reaction of pyridine, acetylenedicarboxylate, and Meldrum acid.[19]

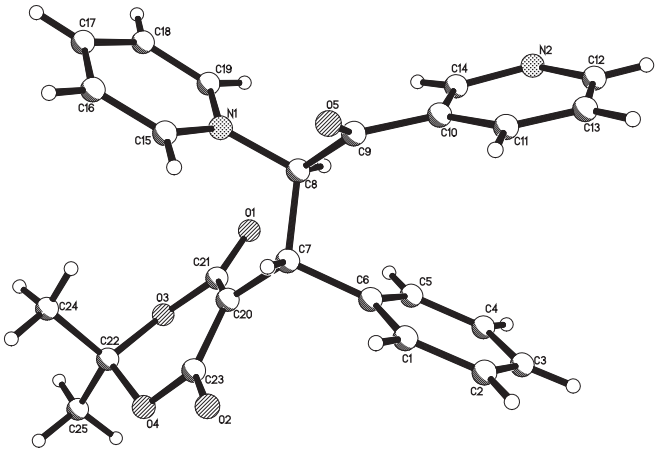
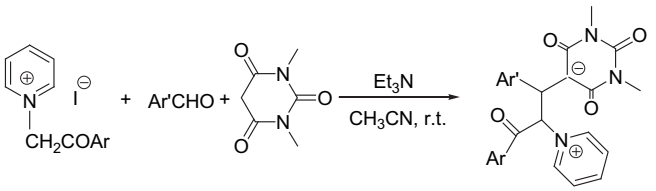


Figure 1. Molecular structure of zwitterionic salt **3d**.

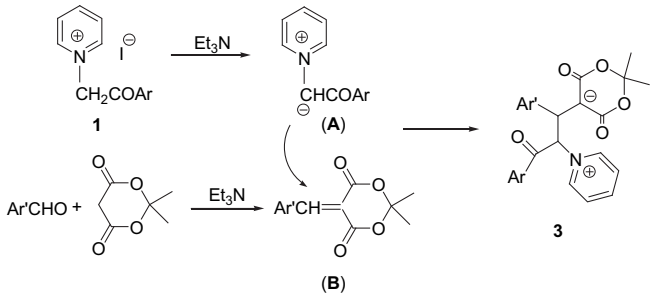
To evaluate the scope of this three-component reaction further, other reactive dicarbonyl compounds, such as *N*,*N*-dimethylbarbituric acid were also tested. The three-component reaction of aromatic aldehydes, *N*,*N*-dimethylbarbituric acid, and three kinds of pyridacylpyridinium iodides in acetonitrile with triethylamine as base catalyst went very smoothly at room temperature. A series of pyridinium–barbituric acid zwitterionic salts (**4a**–**l**) were obtained in good yields (Table 2). It should be indicated that the yields of pyridinium–barbituric acid zwitterionic salts (**4a**–**l**) are usually better than that of pyridinium–Meldrum acid zwitterionic salts (**3a**–**q**), which might be due to the effect of two bulk *ortho*-groups in *N*,*N*-dimethylbarbituric acid. The structures of the prepared pyridinium–barbituric acid zwitterionic salts were fully characterized by spectroscopic methods and elemental analysis. This result clearly demonstrated that this three-component reaction has great generality and can be developed to other active methylene compounds.

Table 2
The synthesis of pyridinium–barbituric acid zwitterionic salts



Entry	Compd	Ar	Ar′	*T* (h)	Yield (%)
1	**4a**	2-Py	Ph	10	52
2	**4b**	2-Py	*p*-$CH_3C_6H_4$	12	60
3	**4c**	2-Py	*p*-BrC_6H_4	10	64
4	**4d**	3-Py	Ph	8	70
5	**4e**	3-Py	*p*-$CH_3CH_2C_6H_4$	8	79
6	**4f**	3-Py	*p*-BrC_6H_4	7	85
7	**4g**	3-Py	*p*-ClC_6H_4	8	79
8	**4h**	4-Py	Ph	9	78
9	**4i**	4-Py	*p*-$CH_3CH_2C_6H_4$	9	67
10	**4j**	4-Py	*p*-$CH_3OC_6H_4$	10	74
11	**4k**	4-Py	*p*-BrC_6H_4	7	86
12	**4l**	4-Py	*p*-ClC_6H_4	8	80

This one-pot three-component reaction went very straightforward. The reaction mechanism is believed to be similar to our previously proposed course in recent work, which is illustrated in Scheme 1. The first step is the formation of pyridacylpyridinium ylide (**A**) from deprotonation of pyridacylpyridinium iodide by triethylamine. The second step is the formation of arylidene Meldrum



Scheme 1. The formation mechanism of zwitterionic salts.

acid (**B**) by the Knoevenagel condensation of aromatic aldehyde with Meldrum acid. The third step is Michael addition of a pyridinium ylide (**A**) to arylidene Meldrum acid (**B**) to afford the zwitterionic salt **3**. This proposed reaction mechanism is also applied to the formation of the pyridinium–barbituric acid zwitterionic salts **4a**–**l**.

In summary, we extend our new convenient synthesis of zwitterionic salts via four-component reactions to the three-component reaction of pyridacylpyridinium iodide, aromatic aldehyde, Meldrum acid or *N*,*N*-dimethylbarbituric acid. A series of new charge-separated pyridinium–Meldrum acid and barbituric acid zwitterionic salts are prepared in high yields in very convenient manner. The most attractive features of the presented reactions are the simplicity and one-pot multicomponent reaction procedure as well as using commercially available starting materials.

3. Experimental section

3.1. General

All reagents and solvents were commercially available with analytical grade and used as received. All evaporations of organic solvents were carried out with a rotary evaporator in conjunction with a water aspirator. 2-, 3-, and 4-Pyridacylpyridinum iodides (**1a**–**c**) were prepared according to the Ortoleva–King reaction method.[1,13] Melting points were taken on a hot-plate microscope apparatus and were uncorrected. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker AV-600 instrument. IR spectra were obtained on a Bruker Tensor27 spectrometer (KBr disc). HPLC/MS were measured at Fennigan LCQ Deca XP MAX instrument. Elemental analysis was determined on PE 240C instrument. X-ray data were collected on a Bruker Smart APEX-2 diffractometer.

3.1.1. The three-component reaction of pyridacylpyridinium iodide with aromatic aldehyde and Meldrum acid. To the mixture of pyridacylpyridinium iodide **1a**–**c** (2.4 mmol, 0.650 g), aromatic aldehydes (2.0 mmol), and Meldrum acid (2.0 mmol, 0.288 g) in acetonitrile (10.0 mL) was added triethylamine (3.0 mmol, 0.30 g) and the whole solution was stirred at room temperature for 8–14 h. The resulting precipitates were collected by filtration and washed with little methanol to give pure yellow solid for analysis.

Compound **3a** (Ar=2-pyridyl, Ar′=*p*-ClC_6H_4): yield: 44%. Mp 194–196 °C. IR (KBr) ν: 3138(m), 3053(m), 2997(m), 2823(w), 1705 (s), 1600(vs), 1491(s), 1384(s), 1258(s), 1015(m), 771(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.17 (d, *J*=6.0 Hz, 2H, ArH), 8.59 (s, 1H, ArH), 8.46 (d, *J*=12.0 Hz, 1H, CH), 8.35 (t, *J*=7.8 Hz, 1H, ArH), 7.91 (t, *J*=6.9 Hz, 2H, ArH), 7.81 (d, *J*=7.2 Hz, 1H, ArH), 7.75 (t, *J*=7.8 Hz, 1H, ArH), 7.53 (d, *J*=7.8 Hz, 2H, ArH), 7.45 (s, 1H, ArH), 6.99 (d, *J*=7.8 Hz, 2H, ArH), 5.13 (d, *J*=12.0 Hz, 1H, CH), 1.39 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.4, 149.2, 145.6, 145.0, 137.3, 130.5, 128.3, 128.2, 126.7, 123.2, 101.2, 44.9. MS (ESI$^-$): *m*/*z*=463.9. Anal. Calcd for $C_{25}H_{21}ClN_2O_5$: C 64.59, H 4.55, N 6.03; Found: C 64.71, H 4.81, N 5.68.

Compound **3b** (Ar=2-pyridyl, Ar′=*p*-BrC_6H_4): yield: 52%. Mp 180–182 °C. IR (KBr) ν: 3437(m), 3136(w), 3051(w), 1705(s), 1599(vs), 1489(s), 1383(w), 1257(m), 1010(m), 926(w), 770(m), 679(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.17 (d, *J*=5.4 Hz, 2H, ArH), 8.60 (d, *J*=3.6 Hz, 1H, ArH), 8.46 (d, *J*=12.0 Hz, 1H, CH), 8.36 (t, *J*=7.2 Hz, 1H, ArH), 7.92 (t, *J*=6.6 Hz, 2H, ArH), 7.82 (d, *J*=7.8 Hz, 1H, ArH), 7.76 (t, *J*=7.8 Hz, 1H, ArH), 7.48 (d, *J*=7.8 Hz, 3H, ArH), 7.15 (d, *J*=7.8 Hz, 2H, ArH), 5.12 (d, *J*=12.0 Hz, 1H, CH), 1.39 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.3, 149.2, 145.6, 145.1, 139.4, 137.4, 137.1, 130.8, 128.3, 126.8, 123.2, 101.2, 44.8. MS (ESI$^-$): *m*/*z*=509.6. Anal. Calcd for $C_{25}H_{21}BrN_2O_5$: C 58.95, H 4.16, N 5.50; Found: C 58.67, H 4.43, N 5.29.

Compound **3c** (Ar=2-pyridyl, Ar′=*m*-$NO_2C_6H_4$): yield: 58%. Mp 180–182 °C. IR (KBr) ν: 3132(w), 3083(w), 1702(w), 1671(w), 1610 (vs), 1521(m), 1392(s), 1354(m), 1262(m), 1207(m), 1129(w), 1098 (w), 1038(w), 993(w), 813(w), 736(w) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.18 (d, *J*=6.0 Hz, 2H, ArH), 8.59 (d, *J*=4.8 Hz, 1H, ArH), 8.52 (d, *J*=12.0 Hz, 1H, ArH), 8.39 (t, *J*=6.6 Hz, 2H, ArH), 8.03 (d, *J*=8.4 Hz, 1H, ArH), 7.95 (t, *J*=7.2 Hz, 2H, ArH), 7.86 (d, *J*=8.4 Hz, 2H, ArH), 7.75 (t, *J*=7.8 Hz, 1H, ArH), 7.44 (t, *J*=6.0 Hz, 1H, ArH), 7.25 (s, 1H, CH), 5.27 (d, *J*=12.6 Hz, 1H, CH), 1.38 (s, 6H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 195.0, 150.9, 149.4, 145.7, 145.2, 142.5, 137.5, 135.5, 129.1, 128.6, 126.8, 123.7, 123.6, 121.8, 101.4, 72.7, 71.8, 45.2. MS (ESI$^-$): *m*/*z*=474.4. Anal. Calcd for $C_{25}H_{21}N_3O_7$: C 63.15, H 4.45, N 8.84; Found: C 62.86, H 4.79, N 8.41.

Compound **3d** (Ar=3-pyridyl, Ar′=C_6H_5): yield: 61%. Mp 175–177 °C. IR (KBr) ν: 3433(m), 3053(m), 2996(w), 1694(s), 1575 (vs), 1489(s), 1388(s), 1263(m), 1118(m), 772(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.13 (d, *J*=6.0 Hz, 2H, ArH), 8.88 (s, 1H, ArH), 8.61 (d, *J*=4.8 Hz, 1H, ArH), 8.41 (t, *J*=7.8 Hz, 1H, ArH), 7.95 (t, *J*=7.2 Hz, 2H, ArH), 7.89–7.86 (m, 2H, ArH, CH), 7.54 (d, *J*=7.2 Hz, 2H, ArH), 7.15–7.13 (m, 1H, ArH), 7.05 (t, *J*=7.2 Hz, 2H, ArH), 6.98 (t, *J*=7.2 Hz, 1H, ArH), 5.01 (d, *J*=12.0 Hz, 1H, CH), 1.46 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 200.9, 194.6, 154.2, 150.0, 145.6, 145.3, 139.5, 135.9, 129.5, 129.4, 128.7, 127.6, 123.1, 101.5, 47.8, 27.6. MS (ESI$^-$): *m*/*z*=429.8. Anal. Calcd for $C_{25}H_{22}N_2O_5$: C 69.76, H 5.15, N 6.51; Found: C 69.40, H 5.33, N 6.27.

Compound **3e** (Ar=3-pyridyl, Ar′=*p*-$CH_3C_6H_4$): yield: 74%. Mp 164–166 °C. IR (KBr) ν: 3434(m), 3135(w), 3048(m), 2893(w), 1687 (s), 1577(vs), 1488(s), 1389(s), 1260(s), 1109(m), 699(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.20 (d, *J*=6.0 Hz, 2H, ArH), 8.89 (s, 1H, ArH), 8.61 (d, *J*=4.8 Hz, 1H, ArH), 8.40 (t, *J*=7.8 Hz, 1H, ArH), 7.94 (t, *J*=7.2 Hz, 3H, ArH), 7.89 (d, *J*=11.4 Hz, 1H, CH), 7.42 (d, *J*=7.8 Hz, 2H, ArH), 7.14–7.11 (m, 1H, ArH), 6.83 (d, *J*=7.8 Hz, 2H, ArH), 4.98 (d, *J*=11.4 Hz, 1H, CH), 2.12 (s, 3H, CH_3), 1.44 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.9, 167.1, 153.9, 150.0, 145.7, 145.3, 137.2, 136.6, 136.1, 130.4, 129.3, 126.6, 123.0, 101.3, 47.4, 20.9. MS (ESI$^-$): *m*/*z*=443.8. Anal. Calcd for $C_{26}H_{24}N_2O_5$: C 70.26, H 5.44, N 6.30; Found: C 69.85, H 5.67, N 5.74.

Compound **3f** (Ar=3-pyridyl, Ar′=*p*-$CH_3CH_2C_6H_4$): yield: 67%. Mp 170–172 °C. IR (KBr) ν: 443(m), 3133(w), 3048(m), 2967(w), 1686(m), 1581(vs), 1505(m), 1476(s), 1421(m), 1261(s), 1120(m), 819 (w), 757(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.15 (d, *J*=6.0 Hz, 2H, ArH), 8.89 (s, 1H, ArH), 8.58 (d, *J*=4.2 Hz, 1H, ArH), 8.40 (t, *J*=7.2 Hz, 1H, ArH), 7.95 (t, *J*=6.6 Hz, 2H, ArH), 7.88–7.86 (m, 2H, ArH, CH), 7.43 (d, *J*=7.2 Hz, 2H, ArH), 7.11 (t, *J*=6.9 Hz, 1H, ArH), 6.85 (d, *J*=7.8 Hz, 2H, ArH), 4.98 (d, *J*=12.0 Hz, 1H, CH), 2.40 (q, *J*=7.8 Hz, 2H, CH_2), 1.45 (s, 6H, $2CH_3$), 1.03 (t, *J*=7.8 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.8, 167.2, 153.9, 150.0, 145.6, 145.3, 143.7, 136.7, 136.0, 130.4, 129.4, 128.2, 126.6, 123.0 101.4, 47.5, 28.4, 15.7. MS(ESI$^-$): *m*/*z*=457.7. Anal. Calcd for $C_{27}H_{26}N_2O_5$: C 70.73, H 5.72, N 6.11; Found: C 70.65, H 5.90, N 5.72.

Compound **3g** (Ar=3-pyridyl, Ar′=*p*-$CH_3OC_6H_4$): yield: 57%. Mp 172–174 °C. IR (KBr) ν: 3427(m), 3136(m), 3066(w), 2996(w), 2937 (w), 2837(w), 1700(s), 1592(vs), 1512(s), 1423(m), 1388(s), 1247(m), 1116(m), 779(m) cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.10 (s, 2H, ArH), 8.91 (s, 1H, ArH), 8.63 (s, 1H, ArH), 8.41 (s, 1H, ArH),

7.95–7.82 (m, 4H, ArH, CH), 7.45 (d, *J*=7.8 Hz, 2H, ArH), 7.18 (s, 1H, ArH), 6.57 (d, *J*=7.8 Hz, 2H, ArH), 4.98 (d, *J*=11.4 Hz, 1H, CH), 3.63 (s, 3H, OCH_3), 1.44 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.8, 167.2, 158.9, 154.2, 150.0, 145.5, 145.3, 136.0, 130.5, 130.3, 126.6, 123.1 114.0, 101.4, 55.2, 47.1. MS(ESI^-): *m*/*z*=459.8. Anal. Calcd for $C_{26}H_{24}N_2O_6$: C 67.82, H 5.25, N 6.08; Found: C 67.55, H 5.84, N 5.80.

Compound **3h** (Ar=3-pyridyl, Ar′=*p*-BrC_6H_4): 71%. Mp 176–178 °C. IR (KBr) *ν*: 3430(m), 3048(w), 2924(w), 1681(m), 1587 (vs), 1482(s), 1390(s), 1119(s), 1218(m), 702(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.18 (d, *J*=6.0 Hz, 2H, ArH), 8.96 (s, 1H, ArH), 8.70 (d, *J*=4.8 Hz, 1H, ArH), 8.43 (t, *J*=7.8 Hz, 1H, ArH), 7.96 (d, *J*=6.6 Hz, 3H, ArH), 7.87 (d, *J*=11.4 Hz, 1H, CH), 7.45 (d, *J*=7.8 Hz, 2H, ArH), 7.22–7.16 (m, 3H, ArH), 4.98 (d, *J*=12.0 Hz, 1H, CH), 1.42 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.5, 167.1, 154.5, 150.0, 145.5, 138.8, 136.0, 131.7, 131.0, 130.2, 126.8, 123.3, 121.6, 101.5, 47.1. MS (ESI^-): *m*/*z*=508.6. Anal. Calcd for $C_{25}H_{21}BrN_2O_5$: C 58.95, H 4.16, N 5.50; Found: C 58.47, H 4.50, N 5.27.

Compound **3i** (Ar=3-pyridyl, Ar′=*p*-ClC_6H_4): yield: 67%. Mp 188–190 °C. IR (KBr) *ν*: 3432(m), 3041(m), 2990(m), 2958(m), 1692 (s), 1590(vs), 1487(s), 1420(m), 1390(s), 1258(m), 1105(s), 779 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.13 (d, *J*=6.0 Hz, 2H, ArH), 8.95 (s, 1H, ArH), 8.69 (d, *J*=4.2 Hz, 1H, ArH), 8.42 (t, *J*=7.8 Hz, 1H, ArH), 7.96–7.92 (m, 3H, ArH), 7.86 (d, *J*=12.0 Hz, 1H, CH), 7.51 (d, *J*=7.8 Hz, 2H, ArH), 7.22–7.19 (m, 1H, ArH), 7.01 (d, *J*=7.8 Hz, 2H, ArH), 4.99 (d, *J*=11.4 Hz, 1H, CH), 1.44 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.4, 182.9, 167.1, 154.6, 150.0, 145.5, 135.9, 130.7, 128.8, 126.8, 123.3, 101.6, 47.2. MS (ESI^-): *m*/*z*=464.1. Anal. Calcd for $C_{25}H_{21}ClN_2O_5$: C 64.59, H 4.55, N 6.03; Found: C 64.63, H 4.95, N 5.77.

Compound **3j** (Ar=3-pyridyl, Ar′=*m*-$NO_2C_6H_4$): yield: 80%. Mp 187–189 °C. IR (KBr) *ν*: 3141(w), 3066(m), 2985(w), 1696(m), 1573 (vs), 1536(s), 1499(m), 1391(s), 1350(m), 1268(m), 1203(m), 1115(w), 1015(w), 925(w), 805(w), 766(w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.21 (d, *J*=1.8 Hz, 1H, ArH), 8.85 (d, *J*=6.4 Hz, 1H, ArH), 8.63 (d, *J*=4.2 Hz, 2H, ArH), 8.32–8.27 (m, 3H, ArH), 8.04–8.01 (m, 1H, ArH), 7.76 (d, *J*=7.2 Hz, 1H, ArH), 7.71 (t, *J*=7.8 Hz, 1H, ArH), 7.62 (t, *J*=8.4 Hz, 1H, ArH), 7.51–7.49 (m, 1H, ArH), 7.33–7.29 (m, 1H, ArH, CH), 4.42 (d, *J*=9.0 Hz, 1H, CH), 1.80 (s, 3H, CH_3), 1.74 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 194.8, 164.9, 164.2, 153.5, 149.6, 147.3, 146.1, 136.1, 135.6, 129.5, 127.8, 126.7, 123.6, 123.1, 121.6, 99.7, 73.8, 72.0, 46.5, 25.3. MS (ESI^-): *m*/*z*=474.9. Anal. Calcd for $C_{25}H_{21}N_3O_7$: C 63.15, H 4.45, N 8.84; Found: C 63.40, H 4.66, N 8.67.

Compound **3k** (Ar=3-pyridyl, Ar′=*p*-$NO_2C_6H_4$): yield: 78%. Mp 158–160 °C. IR (KBr) *ν*: 3076(w), 1687(w), 1589(vs), 1510(m), 1384(s), 1343(s), 1260(m), 1201(m), 1112(s), 1001(w), 916(w), 780(w), 744 (w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.12 (d, *J*=6.0 Hz, 2H, ArH), 8.98 (s, 1H, ArH), 8.68 (d, *J*=4.8 Hz, 1H, ArH), 8.46 (d, *J*=8.4 Hz, 1H, ArH), 8.11–8.06 (m, 1H, ArH), 8.00 (t, *J*=6.6 Hz, 2H, ArH), 7.96 (d, *J*=8.4 Hz, 1H, ArH), 7.94–7.89 (m, 3H, ArH), 7.78 (d, *J*=8.4 Hz, 2H, ArH, CH), 5.13 (d, *J*=12.0 Hz, 1H, CH), 1.43 (s, 6H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 193.8, 164.0, 154.3, 150.1, 148.4, 146.5, 145.7, 145.2, 136.4, 130.2, 130.0, 129.0, 127.8, 126.7, 123.5, 123.1, 122.8, 99.4, 70.8, 69.7, 45.9, 25.4. MS(ESI^-): *m*/*z*=474.5. Anal. Calcd for $C_{25}H_{21}N_3O_7$: C 63.15, H 4.45, N 8.84; Found: C 62.70, H 4.83, N 8.55.

Compound **3l** (Ar=4-pyridyl, Ar′=C_6H_5): yield: 55%. Mp 192–194 °C. IR (KBr) *ν*: 3433(m), 3136(w), 3058(m), 2991(m), 1699 (s), 1664(m), 1631(s), 1570(vs), 1494(s), 1457(w), 1390(s), 1262(m), 1018(m), 773(w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.09 (d, *J*=6.0 Hz, 2H, ArH), 8.57 (d, *J*=6.0 Hz, 2H, ArH), 8.43 (t, *J*=7.2 Hz, 1H, ArH), 7.96 (t, *J*=7.2 Hz, 2H, ArH), 7.85 (d, *J*=11.4 Hz, 1H, CH), 7.52 (d, *J*=7.2 Hz, 2H, ArH), 7.38 (d, *J*=6.0 Hz, 2H, ArH), 7.04–6.98 (m, 3H, ArH), 5.01 (d, *J*=12.0 Hz, 1H, CH), 1.47 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 202.2, 195.6, 167.2, 150.7, 145.5, 129.4, 128.7, 127.8, 126.7, 121.1, 101.5, 48.0. MS (ESI^-): *m*/*z*=429.2. Anal. Calcd for $C_{25}H_{22}N_2O_5$: C 69.76, H 5.15, N 6.51; Found: C 69.36, H 5.49, N 5.86.

Compound **3m** (Ar=4-pyridyl, Ar′=*p*-$CH_3C_6H_4$): yield: 70%. Mp 184–187 °C. IR (KBr) *ν*: 3434(m), 3133(w), 3050(m), 2910(m), 1686 (s), 1589(vs), 1508(s), 1480(s), 1389(s), 1261(s), 1008(m), 751(m), 682(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.18 (d, *J*=6.0 Hz, 2H, ArH), 8.56 (d, *J*=6.0 Hz, 2H, ArH), 8.41 (t, *J*=7.2 Hz, 1H, ArH), 7.94 (t, *J*=7.2 Hz, 2H, ArH), 7.88 (d, *J*=11.4 Hz, 1H, CH), 7.45–7.39 (m, 4H, ArH), 6.82 (d, *J*=7.8 Hz, 2H, ArH), 4.99 (d, *J*=11.4 Hz, 1H, CH), 2.13 (s, 3H, CH_3), 1.46 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.9, 167.2, 150.6, 145.3, 137.5, 136.3, 129.3, 126.6, 121.3, 101.4, 47.6, 20.8. MS (ESI^-): *m*/*z*=443.8. Anal. Calcd for $C_{26}H_{24}N_2O_5$: C 70.26, H 5.44, N 6.30; Found: C 70.51, H 5.80, N 6.42.

Compound **3n** (Ar=4-pyridyl, Ar′=*p*-$CH_3CH_2C_6H_4$): 69%. Mp 168–170 °C. IR (KBr) *ν*: 3428(w), 3044(w), 2963(m), 1691(m), 1583 (vs), 1486(m), 1392(s), 1263(s), 1205(m), 1117(m), 1010(w), 826 (w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.10 (d, *J*=5.4 Hz, 2H, ArH), 8.55 (d, *J*=4.2 Hz, 2H, ArH), 8.42 (t, *J*=7.8 Hz, 1H, ArH) 7.95 (t, *J*=6.6 Hz, 2H, ArH), 7.85 (d, *J*=11.4 Hz, 1H, CH), 7.41–7.37 (m, 4H, ArH), 6.84 (d, *J*=7.2 Hz, 2H, ArH), 4.99 (d, *J*=12.0 Hz, 1H, CH), 2.41 (q, *J*=7.8 Hz, 2H, CH_2), 1.47 (s, 6H, $2CH_3$), 1.04 (t, *J*=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.8, 167.2, 150.5, 145.6, 129.4, 128.2, 126.7, 121.2, 101.5, 77.2, 77.0, 76.8, 75.9, 73.4, 47.7, 28.4, 15.8. MS (ESI^-): *m*/*z*=457.8. Anal. Calcd for $C_{27}H_{26}N_2O_5$: C 70.73, H 5.72, N 6.11; Found: C 70.55, H 5.48, N 6.40.

Compound **3o** (Ar=4-pyridyl, Ar′=*p*-$CH_3OC_6H_4$): yield: 66%. Mp 178–180 °C. IR (KBr) *ν*: 3436(w), 3030(m), 2879(w), 1709(w), 1592 (vs), 1510(m), 1488(m), 1391(s), 1263(m), 1028(w), 751(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.10 (d, *J*=6.0 Hz, 2H, ArH), 8.60 (d, *J*=4.8 Hz, 2H, ArH), 8.42 (d, *J*=7.8 Hz, 1H, ArH), 7.95 (t, *J*=7.2 Hz, 2H, ArH), 7.83 (d, *J*=12.0 Hz, 1H, CH), 7.44–7.41 (m, 4H, ArH, CH), 6.56(d, *J*=8.4 Hz, 2H, ArH), 4.98 (d, *J*=11.4 Hz, 1H, CH), 3.63 (s, 3H, OCH_3), 1.46 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.8, 167.2, 158.9, 154.2, 150.0, 145.5, 145.3, 136.0, 130.5, 130.3, 126.6, 123.1 114.0, 101.4, 55.2, 47.1. MS (ESI^-): *m*/*z*=459.8. Anal. Calcd for $C_{26}H_{24}N_2O_6$: C 67.82, H 5.25, N 6.08; Found: C 67.44, H 5.59, N 5.83.

Compound **3p** (Ar=4-pyridyl, Ar′=*p*-BrC_6H_4): 72%. Mp 186–188 °C. IR (KBr) *ν*: 3436(m), 3135(w), 3083(w), 1708(m), 1594 (vs), 1489(s), 1390(s), 1261(s), 1228(m), 1014(m), 827(w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.07 (s, 2H, ArH), 8.65 (s, 2H, ArH), 8.44 (t, *J*=7.2 Hz, 1H, ArH), 7.97 (t, *J*=6.0 Hz, 2H, ArH), 7.81 (d, *J*=11.4 Hz, 1H, CH), 7.42 (d, *J*=4.8 Hz, 4H, ArH), 7.17 (d, *J*=7.8 Hz, 2H, ArH), 4.97 (d, *J*=12.0 Hz, 1H, CH), 1.44 (s, 6H, $2CH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.5, 167.1, 154.5, 150.0, 145.5, 138.8, 136.0, 131.7, 131.0, 130.2, 126.8, 123.3, 121.6, 101.5, 47.1. MS (ESI^-): *m*/*z*=508.3. Anal. Calcd for $C_{25}H_{21}BrN_2O_5$: C 58.95, H 4.16, N 5.50; Found: C 58.47, H 4.51, N 5.27.

Compound **3q** (Ar=4-pyridyl, Ar′=*m*-$NO_2C_6H_4$): yield: 70%. Mp 179–181 °C. IR (KBr) *ν*: 3141(w), 3069(m), 2985(w), 1705(m), 1572 (vs), 1498(m), 1391(s), 1352(m), 1265(m), 1202(m), 1117(w), 1015 (w), 923(w), 867(w), 768(w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 8.88 (d, *J*=5.4 Hz, 2H, ArH), 8.64–8.62 (m, 2H, ArH), 8.33–8.27 (m, 2H, ArH), 8.03–7.92 (m, 1H, ArH), 7.56 (t, *J*=6.0 Hz, 4H, ArH), 7.63 (t, *J*=7.8 Hz, 1H, ArH), 7.49–7.44 (m, 1H, ArH), 7.35 (t, *J*=5.4 Hz, 1H, CH), 4.41 (d, *J*=9.6 Hz, 1H, CH), 1.78 (s, 3H, CH_3), 1.74 (s, 3H, CH_3). ^{13}C NMR (150 MHz, DMSO-d_6) δ (ppm): 196.8, 164.9, 164.1, 150.4, 150.0, 146.7, 146.1, 141.8, 135.7, 129.5, 127.8, 126.7, 123.7, 121.6, 121.6, 121.4, 99.7, 99.4, 74.0, 72.1, 46.3, 25.5. MS (ESI^-): *m*/*z*=474.5. Anal. Calcd for $C_{25}H_{21}N_3O_7$: C 63.15, H 4.45, N 8.84; Found: C 62.83, H 4.65, N 8.70.

3.1.2. The three-component reaction of pyridacylpyridinium iodides with aromatic aldehydes and N,N-dimethylbarbituric acid. To the mixture of *N*-pyridacylpyridinium iodides **1a–c** (2.4 mmol, 0.650 g), aromatic aldehydes (2.0 mmol), and *N*,*N*-dimethylbarbituric acid (2.0 mmol, 0.312 g) in acetonitrile (10.0 mL) was added triethylamine (3.0 mmol, 0.30 g) and the whole solution was stirred at room temperature for 7–12 h. The resulting precipitates were

collected by filtration and washed with little methanol to give pure yellow solid for analysis.

Compound **4a** (Ar=2-pyridyl, Ar′=C_6H_5): yield: 52%. Mp 178–180 °C. IR (KBr) ν: 3055(m), 2915(m), 1663(s), 1597(vs), 1492 (m), 1424(s), 1380(m), 1292(m), 1173(m), 776(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.17 (d, J=5.4 Hz, 2H, ArH), 8.83 (d, J=12.6 Hz, 1H, ArH), 8.62–8.59 (m, 2H, ArH), 8.29 (t, J=7.2 Hz, 1H, ArH), 7.82 (t, J=6.6 Hz, 2H, ArH), 7.74 (d, J=7.8 Hz, 1H, ArH), 7.64 (d, J=7.2 Hz, 2H, ArH), 7.36–7.33 (m, 2H, ArH), 7.01 (d, J=7.2 Hz, 2H, ArH), 5.35 (d, J=12.6 Hz, 1H, CH), 3.15 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.0, 153.5, 151.5, 149.1, 145.7, 144.9, 139.8, 137.2, 129.1, 128.2, 128.1, 126.8, 126.4, 123.0, 84.4, 45.9, 27.3. MS (ESI^+): m/z=443.2. Anal. Calcd for $C_{25}H_{22}N_4O_4$: C 67.86, H 5.01, N 12.66; Found: C 67.42, H 5.38, N 12.29.

Compound **4b** (Ar=2-pyridyl, Ar′=p-$CH_3C_6H_4$): yield: 60%. Mp 144–146 °C. IR (KBr) ν: 3136(w), 3051 (m), 2965(m), 2871(w), 1701 (m), 1660(s), 1597(vs), 1381(s), 1342(m), 1221(m), 1020(m), 773(m), 703(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.16 (d, J=6.0 Hz, 2H, ArH), 8.83 (d, J=12.6 Hz, 1H, ArH), 8.63 (d, J=4.2 Hz, 1H, ArH), 8.30 (t, J=7.8 Hz, 1H, ArH), 7.83 (t, J=6.9 Hz, 2H, ArH), 7.77–7.70 (m, 2H, ArH), 7.53 (d, J=7.8 Hz, 2H, ArH), 7.44 (t, J=6.0 Hz, 1H, ArH), 6.84 (d, J=7.8 Hz, 2H, ArH), 5.35 (d, J=12.6 Hz, 1H, CH), 3.15 (s, 6H, $2NCH_3$), 2.11 (s, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.9, 153.5, 149.1, 145.6, 144.8, 137.2, 128.9, 128.1, 126.5, 123.1, 84.6, 71.5, 45.2, 27.3, 20.9. MS (ESI^+): m/z=457.6. Anal. Calcd for $C_{26}H_{24}N_4O_4$: C 68.41, H 5.30, N 12.27; Found: C 68.60, H 5.75, N 11.86.

Compound **4c** (Ar=2-pyridyl, Ar′=p-BrC_6H_4): yield: 64%. Mp 196–198 °C. IR (KBr) ν: 3053(m), 2925(w), 1664(s), 1596(vs), 1485 (m), 1428(m), 1382(s), 1292(m), 1071(w), 774(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.13 (d, J=5.4 Hz, 2H, ArH), 8.79 (d, J=12.0 Hz, 1H ArH), 8.63 (s, 1H, ArH), 8.32 (t, J=7.2 Hz, 1H, ArH), 7.86–7.75 (m, 4H, ArH), 7.56 (d, J=7.8 Hz, 2H, ArH), 7.48 (s, 1H, ArH), 7.15 (d, J=7.2 Hz, 2H, ArH), 5.32 (d, J=12.0 Hz, 1H, CH), 3.15 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.5, 153.4, 151.1, 149.3, 145.6, 145.1, 139.0, 137.4, 131.2, 130.8, 128.4, 126.6, 123.2, 120.8, 84.1, 71.2, 45.2, 27.3. MS (ESI^+): m/z=521.6. Anal. Calcd for $C_{25}H_{21}BrN_4O_4$: C 57.59, H 4.06, N 10.75; Found: C 57.30, H 4.46, N 10.43.

Compound **4d** (Ar=3-pyridyl, Ar′=C_6H_5): yield: 70%. Mp 140–142 °C. IR (KBr) ν: 3067(m), 2955(w), 1663(s), 1589(vs), 1432 (s), 1386(m), 1293(m), 1164(m), 1029(w), 773(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.05(s, 2H, ArH), 8.92 (s, 1H ArH), 8.62 (s, 1H ArH), 8.38 (s, 1H, ArH), 8.16 (d, J=11.4 Hz, 1H, CH), 7.90–7.83 (m, 3H, ArH), 7.60 (d, J=6.6 Hz, 2H, ArH), 7.15(d, J=3.0 Hz, 1H, ArH), 7.03 (d, J=6.0 Hz, 2H, ArH), 6.96 (d, J=6.0 Hz, 1H, ArH), 5.17 (d, J=11.4 Hz, 1H, CH), 3.17 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.8, 154.3, 153.3, 150.0, 145.5, 139.3, 135.9, 130.3, 129.4, 128.8, 127.8, 126.5, 123.2, 84.5, 48.4, 27.4. MS (ESI^+): m/z=443.5. Anal. Calcd for $C_{25}H_{22}N_4O_4$: C 67.86, H 5.01, N 12.66; Found: C 67.65, H 4.83, N 12.91.

Compound **4e** (Ar=3-pyridyl, Ar′=p-$CH_3CH_2C_6H_4$): yield: 79%. Mp 130–132 °C. IR (KBr) ν: 3138(w), 3087(m), 2965(m), 2830(w), 1672(s), 1572(vs), 1384(s), 1269(m), 1237(w), 1166(m), 1027(m), 774 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.04 (d, J=5.4 Hz, 2H, ArH), 8.92 (s, 1H ArH), 8.60 (s, 1H ArH), 8.39 (s, 1H, ArH), 8.16 (d, J=11.4 Hz, 1H, CH), 7.90 (d, J=6.6 Hz, 3H, ArH), 7.49 (d, J=7.2 Hz, 2H, ArH), 7.13 (s, 1H, ArH), 6.85 (d, J=7.2 Hz, 2H, ArH), 5.14 (d, J=11.4 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$), 2.40–2.36 (m, 2H, CH_2), 1.00 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.0, 154.1, 153.4, 150.0, 145.6, 145.4, 143.9, 136.4, 136.0, 130.4, 129.4, 128.3, 126.4, 123.0, 84.5, 48.2, 28.4, 15.8. MS (ESI^+): m/z=471.5. Anal. Calcd for $C_{27}H_{26}N_4O_4$: C 68.92, H 5.57, N 11.91; Found: C 68.68, H 5.90, N 11.47.

Compound **4f** (Ar=3-pyridyl, Ar′=p-BrC_6H_4): yield: 85%. Mp 160–162 °C. IR (KBr) ν: 3072(w), 1669(s), 1583(vs), 1482(s), 1436 (vs), 1385(m), 1285(m), 1168(m), 1012(w), 775(s), 702(w) cm^{-1}; ^1H NMR(600 MHz, $CDCl_3$) δ (ppm): 9.07 (d, J=4.8 Hz, 2H, ArH), 9.00 (s, 1H, ArH), 8.70 (s, 1H, ArH), 8.41 (s, 1H, ArH), 8.14 (d, J=11.4 Hz, 1H, CH), 7.96–7.90 (m, 3H, ArH), 7.50 (d, J=7.2 Hz, 2H, ArH), 7.23 (s, 1H, ArH), 7.15 (d, J=7.2 Hz, 2H, ArH), 5.15 (d, J=11.4 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.6, 154.5, 153.2, 150.1, 145.5, 138.5, 136.0, 131.8, 130.3, 126.7, 123.4, 121.7, 84.2, 47.6, 27.4. MS (ESI^+): m/z=521.3. Anal. Calcd for $C_{25}H_{21}BrN_4O_4$: C 57.59, H 4.06, N 10.75; Found: C 57.28, H 4.33, N 10.69.

Compound **4g** (Ar=3-pyridyl, Ar′=p-ClC_6H_4): yield: 79%. Mp 180–181 °C. IR (KBr) ν: 3140(m), 3036(m), 2966(s), 1672(s), 1584 (vs), 1482(m), 1433(m), 1228(m), 1163(m), 1096(w), 776(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.04 (d, J=6.0 Hz, 2H, ArH), 8.98 (s, 1H, ArH), 8.70 (d, J=4.8 Hz, 1H, ArH), 8.42 (t, J=7.2 Hz, 1H, ArH), 8.16 (d, J=12.0 Hz, 1H, CH), 7.94–7.90 (m, 3H, ArH), 7.56 (d, J=8.4 Hz, 2H, ArH), 7.22 (d, J=12.6 Hz, 1H, ArH), 7.01 (d, J=8.4 Hz, 2H, ArH), 5.16 (d, J=12.0 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 194.6, 163.8, 154.7, 153.3, 150.0, 145.7, 145.5, 138.0, 135.9, 133.5, 130.1, 128.8, 126.6, 123.7, 123.3, 84.1, 47.8, 27.4. MS (ESI^+): m/z=478.9. Anal. Calcd for $C_{25}H_{21}ClN_4O_4$: C 62.96, H 4.44, N 11.75; Found: C 62.67, H 4.84, N 11.45.

Compound **4h** (Ar=4-pyridyl, Ar′=C_6H_5): yield: 78%. Mp 151–153 °C. IR (KBr) ν: 3428(m), 3054(w), 1672(s), 1567(vs), 1487 (s), 1433(s), 1263(m), 1227(m), 1026(w), 842(m), 682(w) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.05 (d, J=5.4 Hz, 2H, ArH), 8.58 (d, J=3.0 Hz, 2H, ArH), 8.40 (t, J=7.2 Hz, 1H, ArH), 8.18 (d, J=12.0 Hz, 1H, ArH), 7.90 (t, J=6.0 Hz, 2H, ArH), 7.56 (d, J=7.2 Hz, 2H, ArH), 7.43 (d, J=3.0 Hz, 2H, ArH), 7.02 (t, J=7.2 Hz, 2H, ArH), 6.98 (d, J=7.2 Hz, 1H, ArH), 5.17 (d, J=11.4 Hz, 1H, CH), 3.17 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 191.4, 151.5, 151.3, 150.7, 149.8, 145.5, 139.5, 138.8, 136.0, 129.5, 129.4, 129.0, 128.7, 128.6, 128.4, 127.2, 126.6, 123.7, 121.5, 121.1, 121.0, 91.7, 89.6, 48.8, 28.1. MS (ESI^-): m/z=441.8. Anal. Calcd for $C_{25}H_{22}N_4O_4$: C 67.86, H 5.01, N 12.66; Found: C 67.49, H 5.37, N 12.55.

Compound **4i** (Ar=4-pyridyl, Ar′=p-$CH_3CH_2C_6H_4$): yield: 67%. Mp 171 °C. IR (KBr) ν: 3432(m), 3050(m), 2963(m), 1699(s), 1662(s), 1593(vs), 1494(s), 1422(s), 1379(s), 1263(m), 1223(m), 1010(m), 830 (m), 772(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.03 (d, J=5.4 Hz, 2H, ArH), 8.56 (d, J=2.4 Hz, 2H, ArH), 8.39 (t, J=7.2 Hz, 1H, ArH), 8.18 (d, J=11.4 Hz, 1H, CH), 7.88 (t, J=6.6 Hz, 2H, ArH), 7.46–7.41 (m, 4H, ArH), 6.83 (d, J=7.8 Hz, 2H, ArH), 5.13 (d, J=11.4 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$), 2.39 (q, J=7.2 Hz, 2H, CH_2), 1.01 (t, J=7.2 Hz, 3H, CH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.1, 191.5, 161.6, 159.2, 151.3, 150.5, 149.8, 145.6, 144.5, 128.9, 123.8, 121.5, 91.8, 48.5, 29.9, 28.5, 28.0, 15.4. MS (ESI^-): m/z=470.0. Anal. Calcd for $C_{27}H_{26}N_4O_4$: C 68.92, H 5.57, N 11.91; Found: C 68.74, H 5.90, N 11.67.

Compound **4j** (Ar=4-pyridyl, Ar′=p-$CH_3OC_6H_4$): yield: 74%. Mp 134–138 °C. IR (KBr) ν: 3393(m), 3065(w), 2963(w), 1666(s), 1567 (vs), 1509(m), 1435(m), 1255(m), 1174(m), 1111(m), 829(w), 687 (m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.04 (d, J=6.0 Hz, 2H, ArH), 8.62 (d, J=4.2 Hz, 2H, ArH), 8.40 (t, J=7.8 Hz, 1H, ArH), 8.15 (d, J=11.4 Hz, 1H, CH), 7.91 (t, J=7.2 Hz, 2H, ArH), 7.49–7.46 (m, 4H, ArH), 6.55 (d, J=8.4 Hz, 2H, ArH), 5.14 (d, J=12.0 Hz, 1H, CH), 3.61 (s, 3H, OCH_3), 3.17 (s, 6H, $2NCH_3$) cm^{-1}. ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 196.1, 163.8, 159.3, 153.3, 150.7, 145.5, 140.6, 131.0, 130.7, 126.6, 121.2, 114.1, 84.7, 55.2, 47.9, 27.4. MS (ESI^-): m/z=471.9. Anal. Calcd for $C_{26}H_{24}N_4O_5$: C 66.09, H 5.12, N 11.86; Found: C 65.74, H 5.38, N 11.66.

Compound **4k** (Ar=4-pyridyl, Ar′=p-BrC_6H_4): yield: 86%. Mp 180–182 °C. IR (KBr) ν: 3429(m), 3135(w), 3059(m), 2979(m), 1674 (s), 1567(vs), 1483(s), 1430(s), 1379(s), 1264(m), 1229(m), 1009(m), 819(m), 771(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ (ppm): 9.03 (d, J=6.6 Hz, 2H, ArH), 8.66 (d, J=6.0 Hz, 2H, ArH), 8.42 (t, J=7.8 Hz, 1H, ArH), 8.15 (d, J=12.0 Hz, 1H, CH), 7.91 (t, J=7.2 Hz, 2H, ArH), 7.48–7.47 (m, 4H, ArH), 7.15 (d, J=8.4 Hz, 2H, ArH), 5.13 (d, J=12.0 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 193.8, 161.9, 151.4, 149.1, 143.9, 143.6, 138.6, 136.4, 129.9, 129.4, 124.8, 120.0, 119.2, 82.1, 72.7, 46.1, 25.5. MS(ESI^-): m/z=521.3.

Anal. Calcd for $C_{25}H_{21}BrN_4O_4$: C 57.59, H 4.06, N 10.75; Found: C 57.71, H 4.25, N 10.38.

Compound **4l** (Ar=4-pyridyl, Ar′=*p*-ClC_6H_4): yield: 80%. Mp 190–192 °C. IR (KBr) ν: 3434(m), 3088(w), 1667(s), 1589(vs), 1486(m), 1433(s), 1384(s), 1223(m), 1168(m), 1064(m), 821(w), 774(m) cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$) δ(ppm): 9.07 (d, J=5.4 Hz, 2H, ArH), 8.66 (d, J=3.6 Hz, 2H, ArH), 8.43 (t, J=7.2 Hz, 1H, ArH), 8.14 (d, J=12.0 Hz, 1H, CH), 7.93 (t, J=6.0 Hz, 2H, ArH), 7.54–7.49 (m, 4H, ArH), 7.00 (d, J=7.8 Hz, 2H, ArH), 5.16 (d, J=12.0 Hz, 1H, CH), 3.16 (s, 6H, $2NCH_3$). ^{13}C NMR (150 MHz, $CDCl_3$) δ (ppm): 195.7, 151.4, 151.2, 150.9, 149.8, 145.4, 130.9, 129.6, 128.8, 128.6, 126.7, 123.7, 121.4, 121.1, 120.9, 47.8, 27.4. MS (ESI^-): m/z=475.8. Anal. Calcd for $C_{25}H_{21}ClN_4O_4$: C 62.96, H 4.44, N 11.75; Found: C 62.83, H 4.69, N 11.55.

4. Supporting information

Crystallographic data (**3e**: CCDC 777602) have been deposited at the Cambridge Crystallographic Database Centre.

Acknowledgements

This work was financially supported by the National Natural Science Foundation of China (Grant No. 20972132).

References and notes

1. (a) Kröhnke, F.; Zecher, W. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 626; (b) Kröhnke, F. *Angew. Chem., Int. Ed. Engl.* **1963**, *2*, 225; (c) Kröhnke, F. *Synthesis* **1976**, 1.
2. (a) Yamada, S.; Yamamoto, J.; Ohta, E. *Tetrahedron Lett.* **2007**, *48*, 855; (b) Kojima, S.; Hiroikea, K.; Ohkata, K. *Tetrahedron Lett.* **2004**, *45*, 3565; (c) Kojima, S.; Fujitomo, K.; Shinohara, Y.; Shimizu, M.; Ohkata, K. *Tetrahedron Lett.* **2000**, *41*, 9847; (d) Vo, N. N.; Eyermann, C. J.; Hodge, C. N. *Tetrahedron Lett.* **1997**, *38*, 7951.
3. (a) Tsuge, O.; Kanemasa, S.; Takenaka, S. *Bull. Chem. Soc. Jpn.* **1985**, *58*, 3137; (b) Neve, F.; Crispini, A.; Campagna, S. *Inorg. Chem.* **1997**, *36*, 6150; (c) MacGillivray, L. R.; Diamente, P. R.; Reid, J. L.; Ripmeester, J. A. *Chem. Commun.* **2000**, 359; (d) Barrio, M. C. G.; Barrio, J. R.; Walker, G.; Novelli, A.; Leonard, N. J. *J. Am. Chem. Soc.* **1973**, *95*, 4891.
4. (a) Ulrich, G.; Ziessel, R. *J. Org. Chem.* **2004**, *69*, 2070; (b) Yam, V. W. W.; Wong, K. M. C.; Zhu, N. *Angew. Chem., Int. Ed.* **2003**, *42*, 1400; (c) Coppo, P.; Duati, M.; Kozhevnikov, V. N.; Hofstraat, J. W.; De Cola, L. *Angew. Chem., Int. Ed.* **2005**, *44*, 1806; (d) Pabst, G. R.; Pfüller, O. C.; Sauer, J. *Tetrahedron* **1999**, *55*, 5047; (e) Hovinen, J.; Hakala, H. *Org. Lett.* **2001**, *3*, 2473; (f) Kozhevnikov, V. N.; Kozhevnikov, D. M.; Nikitina, T. V.; Rusinov, V. L.; Chupakhin, O. N.; Zabel, M.; König, B. *J. Org. Chem.* **2003**, *68*, 2882; (g) Lai, S. W.; Chan, M. C. W.; Cheung, K. K.; Che, C. M. *Inorg. Chem.* **1999**, *38*, 4262.
5. (a) Eryazici, I.; Moorefield, C. N.; Durmus, S.; Newkone, G. R. *J. Org. Chem.* **2006**, *71*, 1009; (b) Tu, S. J.; Jia, R. H.; Jiang, B.; Zhang, J. Y.; Zhang, Y.; Yao, C. S.; Ji, S. J. *Tetrahedron* **2007**, *63*, 381; (c) Constable, E. C.; Edwards, A. J.; Martínez-Máñez, R.; Raithby, P. R. *J. Chem. Soc., Dalton Trans.* **1995**, 3253; (d) Constable, E. C.; Edwards, A. J.; Raithby, P. R.; Soto, J.; Tendero, M. J. L.; Martínez-Máñez, R. *Polyhedron* **1995**, *14*, 3061.
6. (a) Bora, U.; Saikia, A.; Boruah, R. C. *Org. Lett.* **2003**, *5*, 435; (b) Armstrong, R. W.; Combs, A. P.; Tempest, P. A.; Brown, S. D.; Keating, T. A. *Acc. Chem. Res.* **1996**, *29*, 123; (c) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168; (d) Sasaki, T.; Kanematsu, K.; Yukimoto, Y.; Ochiai, S. *J. Org. Chem.* **1971**, *36*, 813; (e) Xia, Z. Q.; Przewloka, T.; Koya, K.; Ono, M.; Chen, S. J.; Sun, L. J. *Tetrahedron Lett.* **2006**, *47*, 8817.
7. (a) Katritzky, A. R.; Grzeskowiak, N. E.; Alvarez-Buila, J. *J. Chem. Soc., Perkin Trans.* **1981**, 1180; (b) Druta, I. I.; Dinica, R. M.; Bacu, E.; Humelnicu, I. *Tetrahedron* **1998**, *54*, 10811; (c) Dinica, R. M.; Druta, I. I.; Pettinari, C. *Synlett* **2000**, 1013; (d) Druta, I. I.; Andrei, M. A.; Ganj, C. I.; Aburel, P. S. *Tetrahedron* **1999**, *55*, 13063; (e) Furdui, B.; Dinica, R.; Druta, I. I.; Demeunynck, M. *Synthesis* **2006**, *16*, 2640.
8. (a) Peng, W. M.; Zhu, S. Z. *J. Chem. Soc., Perkin Trans. 1* **2001**, 3204; (b) Zhu, S. Z.; Qin, C. Y.; Wang, Y. L.; Chu, Q. L. *J. Fluorine Chem.* **1999**, *99*, 183; (c) Zhang, X. C.; Huang, W. Y. *Synthesis* **1999**, *1*, 51; (d) Wu, K.; Chen, Q. Y. *Synthesis* **2003**, 35; (e) Chuang, C. P.; Tsai, A. I. *Synthesis* **2006**, *4*, 675.
9. (a) Zhang, X. D.; Hu, Y. F.; Hu, H. W. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2487; (b) Wang, B. X.; Zhang, X. C.; Li, J.; Jiang, X.; Hu, Y. F.; Hu, H. W. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1571; (c) Hu, J. X.; Jiang, X.; He, T.; Zhou, J.; Hu, Y. F.; Hu, H. W. *J. Chem. Soc., Perkin Trans. 1* **2001**, 1820.
10. (a) Shestopalov, A. M.; Litvinov, V. P.; Rodinovskaya, L. A.; Sharanin, Y. A. *Zh. Org. Khim.* **1991**, 146; (b) Kojima, S.; Suzuki, M.; Watanabe, A.; Ohkata, K. *Tetrahedron Lett.* **2006**, *47*, 9061.
11. (a) Yan, C. G.; Cai, X. M.; Wang, Q. F.; Wang, T. Y.; Zheng, M. *Org. Biomol. Chem.* **2007**, *5*, 945; (b) Yan, C. G.; Song, X. K.; Wang, Q. F.; Sun, J.; Siemeling, U.; Bruhn, C. *Chem. Commun.* **2008**, 1440; (c) Wang, Q. F.; Song, X. K.; Chen, J.; Yan, C. G. *J. Comb. Chem.* **2009**, *11*, 1007; (d) Wang, Q. F.; Hou, H.; Hui, L.; Yan, C. G. *J. Org. Chem.* **2009**, *74*, 7403; (e) Yan, C. G.; Wang, Q. F.; Song, X. K.; Sun, J. *J. Org. Chem.* **2009**, *74*, 710.
12. Wang, Q. F.; Hui, L.; Hou, H.; Yan, C. G. *J. Comb. Chem.* **2010**, *12*, 260.
13. (a) Visser, P.; Zuhse, R.; Wong, M. W.; Wentrup, C. *J. Am. Chem. Soc.* **1996**, *118*, 12598; (b) Kuhn, A.; Pluüg, C.; Wentrup, C. *J. Am. Chem. Soc.* **2000**, *122*, 1945; (c) Zia-Ebrahimi, M.; Reutzel, S. M.; Dorman, D. E.; Spangle, L. A.; Deeter, J. B. *Chem. Mater.* **1994**, *6*, 822; (d) Wenkert, E.; Michelotti, E. L.; St. Pyrek, J. *J. Org. Chem.* **1984**, *49*, 1832.
14. (a) Curtz, J.; Dach, R.; Duchardt, K. H.; Kröhnke, F. *Chem. Ber.* **1979**, *112*, 2199; (b) Jursic, B. S.; Neumann, D. M.; Moore, Z.; Stevens, E. D. *J. Org. Chem.* **2002**, *67*, 2372.
15. (a) Shaabani, A.; Rezayan, A. H.; Sarvary, A.; Heidary, M.; Ng, S. W. *Tetrahedron* **2009**, *65*, 6063; (b) Varga, L.; Nagy, T.; Dormán, G.; Kálmán, F.; Urge, L.; Darvas, F. *J. Comb. Chem.* **2006**, *8*, 338; (c) Wamhoff, H.; Schmidt, A. *J. Org. Chem.* **1993**, *58*, 6976.
16. (a) Jursic, B. S.; Neumann, D. M.; Martin, K. L.; Stevens, E. D. *Org. Lett.* **2002**, *4*, 811; (b) Sosnovskikh, V. Y.; Usachev, B. I.; Sizov, A. Y.; Vorontsov, I. I.; Shklyaev, Y. V. *Org. Lett.* **2003**, *5*, 3123; (c) Zhang, S. L.; Huang, Z. S.; An, L. K.; Bu, X. Z.; Ma, L.; Li, Y. M.; Chan, A. S. C.; Gu, L. Q. *Org. Lett.* **2004**, *6*, 4853.
17. (a) Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003**, *36*, 899; (b) Nair, V.; Menon, R. S.; Sreekanth, A. R.; Abhilash, N.; Biju, A. T. *Acc. Chem. Res.* **2006**, *39*, 520.
18. (a) Yavari, I.; Mokhtarporyani-Sanandaj, A.; Moradi, L. *Tetrahedron Lett.* **2007**, *48*, 6709; (b) Yavari, I.; Mirzaei, A.; Moradi, L.; Hosseini, N. *Tetrahedron Lett.* **2008**, *49*, 2355; (c) Yavari, I.; Anary-Abbasinejad, M.; Alizadeh, A. *Monatsh. Chem.* **2002**, *133*, 1331.
19. Xia, E. Y.; Sun, J.; Yao, R.; Yan, C. G. *Tetrahedron* **2010**, *66*, 3569.
20. (a) King, L. C. *J. Am. Chem. Soc.* **1944**, *66*, 894; (b) Dodso, R. M.; King, L. C. *J. Am. Chem. Soc.* **1946**, *68*, 871; (c) Kröhnke, F.; Gross, K. F. *Chem. Ber.* **1959**, *92*, 22.