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SYNTHESIS OF FUNCTIONALIZED β-ENAMINO COMPOUNDS BY CARBON-FRAGMENT TRANSFER REACTION OF C(2)-SUBSTITUTED IMIDAZOLIDINES WITH AMINES

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Abstract –The substituted imidazolidines (**2**, **3**, **5**) and a ring-opening product, *N,N,N′*-trisubstituted 2-methyl-ethylenediamines (**4**), derived from addition of the carbon anions to 1-tosyl-3,4-dimethylimidazolinium iodide (**1**), were utilized to transfer substituted one-carbon units to various amines to yield a series of functionalized β-enamino compounds.

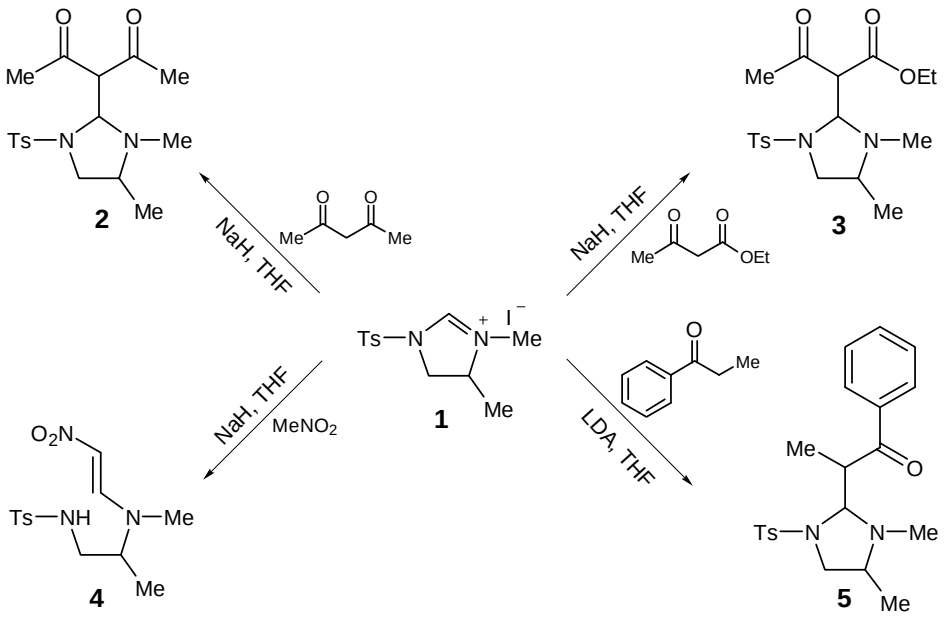
INTRODUCTION

β-Enamino compounds are versatile structures for the synthesis of natural therapeutic and synthetic biologically active analogues including taxol,[1-4] anticonvulsivant,[5,6] and antitumor agents,[5,7] as well as quinolone antibacterials and quinoline antimalarials.[8,9] Among the methods for generating β-enamino compounds, condensation of amines and β-dicarbonyl compounds is a classical method in which the azeotropic removal of water is affected by refluxing in aromatic solvent.[10-13] Treatment of amines with β,β-diactivated alkoxymethylene derivatives is another attractive method for the preparation of β-enamino compounds.[14-16] Under ultrasound in the presence of acetic acid, condensation of β-keto esters and amines gave good yields of the corresponding β-enamino esters.[17] A variety of other methods utilizing SiO_2, montmorillonite K10, and $NaAuCl_4$ as catalysts have also been revealed.[18-21] In this paper, we provide a novel method for preparing functionalized β-enamino compounds by the carbon-fragment transfer reactions of C(2)-substituted imidazolidines with amines.

RESULTS AND DISCUSSION

In our earlier research, a series of dihydroimidazolium iodides salts were synthesized as the tetrahydrofolate coenzyme model for the study of one-carbon unit transfer reactions.[22-25] Recently, we designed and synthesized a more activated model compound, 1-tosyl-3,4-dimethylimidazolinium iodide (**1**) by the adjusting the number of substituted methyl in imidazoline ring.[26] Furthermore, we found that

compound (**1**) could easily react with carbon anions to produce the substituted imidazolidines (**2**, **3**, **5**),[27] and a ring-opening products, *N*,*N*,*N*′-trisubstituted 2-methyl-ethylenediamines (**4**)[26] in good yields (Scheme 1). We speculated that compounds (**2-5**) can also be regarded as subsitituted folate models, and can transfer the *N*(1),*N*(3)-bonded carbon fragment to amines to produce functionalized β-enamino compounds. The observed results were found to be in agreement with our assumption. When compounds (**2-5**) were treated with tryptamine in refluxing acetonitrile, the corresponding complete carbon-fragment transfer product, β-enamino compounds, were produced, which have been used to prepare tetrahydro-β-carboline derivatives through Pictet-Spengler reaction by us.[27]

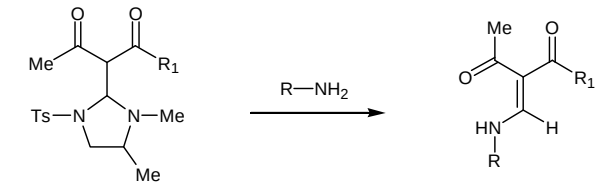


Scheme 1

In order to exploit the generality of this method for preparing various functionalized β-enamino compounds, a series of amines including aromatic amines, benzyl amine, amino acid methyl esters, and phenethylamine derivatives were tested in the current research, and results are summarized in Tables 1, 2. All reactions were refluxed in acetonitrile and easily followed by TLC. The reaction time was generally from 1 to 10 h and workup was straightforward. The results obtained suggested that compounds (**2**, **3**) are enough active and can react with all amines tested in moderate to good yields (Table 1); however, compounds (**4**, **5**) are less-active and fail to react with aromatic amines and amino acid methyl esters (Table 2). It is noteworthy that in the four compounds, low yields and incomplete reactions were only observed with compound **4** even in the lengthening time, and yields vary from 14% to 58%. For the compound **5**, the long reaction time are usually required in order to obtained good yields. All of the products obtained were identified by ^{1}H NMR, IR, MS, and Elemental Analysis. However, an effort in reacting a ring-opening product, derived from addition of the malononitrile carbon anions to

1-tosyl-3,4-dimethylimidazolinium iodide (**1**),[26] with various amines is unsuccessful due to its poor reactivity.

Table 1. Carbon-fragment transfer reactions of compounds (**2** and **3**) with various amine.



2, R = Me; **3**, R = OEt **6** - **25**

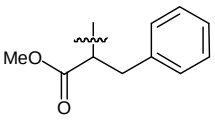
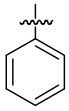
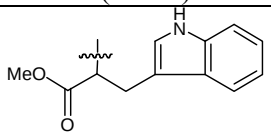
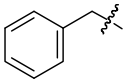
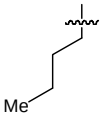
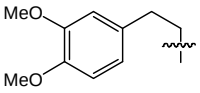
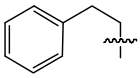
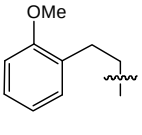
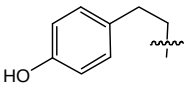
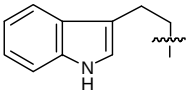
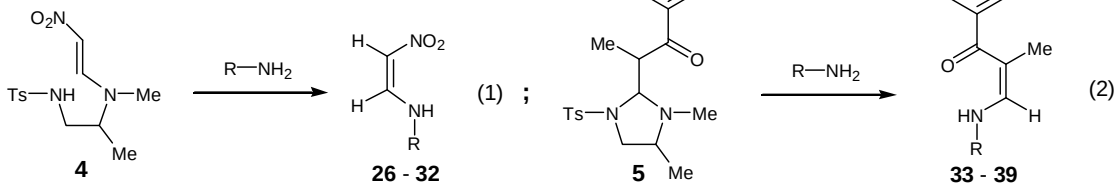
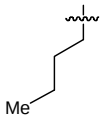
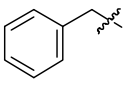
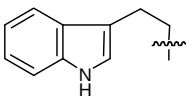
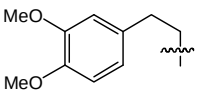
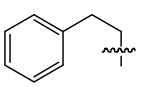
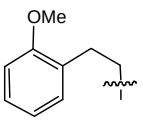
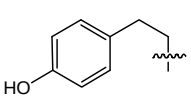
Product (Yield)					
R =					
R_1 = Me	**6**(79%)	**7**(77%)	**8**(73%)	**9**(78%)	**10**(71%)
R_1 = OEt	**16**(59%)	**17**(88%)	**18**(67%)	**19**(89%)	**20**(70%)
R =					
R_1 = Me	**11**(75%)	**12**(69%)	**13**(71%)	**14**(81%)	**15**(86%)
R_1 = OEt	**21**(75%)	**22**(77%)	**23**(68%)	**24**(82%)	**25**(86%)

Table 2. Carbon-fragment transfer reactions of compounds (**4** and **5**) with various amine.



4 **26** - **32** **5** **33** - **39**

Product (Yield)							
R =							
	26(39%)	**27**(35%)	**28**(58%)	**29**(14%)	**30**(40%)	**31**(44%)	**32**(24%)
	33(91%)	**34**(96%)	**35**(87%)	**36**(84%)	**37**(56%)	**38**(74%)	**39**(90%)

The stereochemistry of compounds (**16-25)** was deduced to be *E*-type by the intramolecular hydrogen bonding of N-H group and adjacent carbonyl group for each compound (in ^{1}H NMR, the NH hydrogen atom is shifted downfield, from 10.97 to 12.76), which can further be suggested by the crystal structures of compounds (**24, 25**) (for **24**, see Figure 1; for **25**, see reference 28). The *Z* geometry in compounds (**26-39**) is secured by intramolecular hydrogen bonding between nitro O atom (for **26-32**) or carbonyl O

atom (for **33-39**) and the adjacent N-H group (in ^{1}H NMR, the NH hydrogen atom is shifted downfield, from 9.12 to 10.92).

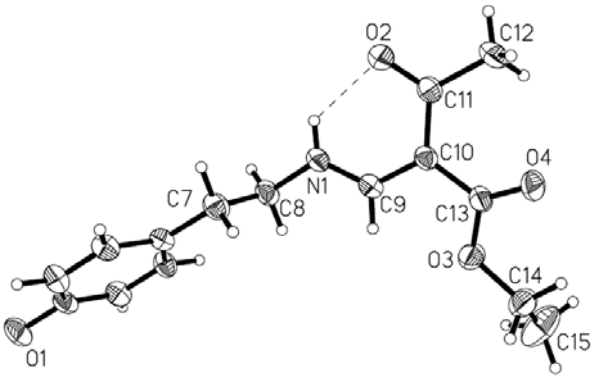
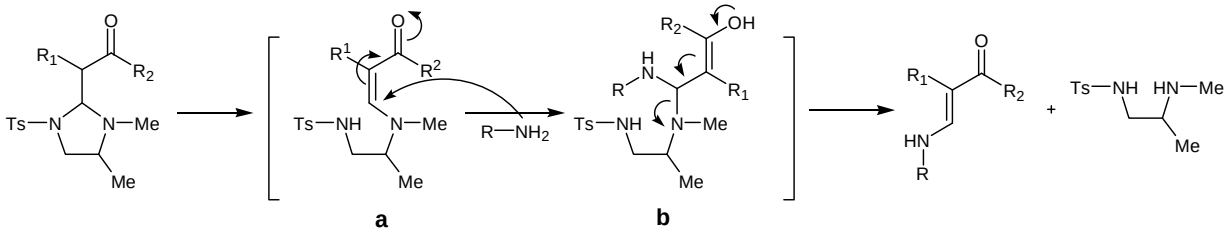


Figure 1 X-Ray structure of compound (**24**).

The possible mechanism of the transformation of the carbon fragment to amines is described in Scheme 2. According to this mechanism, the substituted imidazolidines (**2**, **3** and **5**) undergo ring opening to give enamine system (**a**). This is followed by addition of amines and, via the intermediate (**b**), results in the production of the β-enamino compounds. The thermodynamically favored form of **4** is a ring-opening product, which is possibly attacked straightforward by amines to give, via intermediate (**b**), β-enamino compounds.



Scheme 2

In conclusion, the present research revealed a new method for the synthesis of a series of functionalized β-enamino compounds by the carbon-fragment transfer reactions of C(2)-substituted imidazolidines, and may enable chemical and biological studies on these compounds.

EXPERIMENTAL

MS spectra were obtained on a JMS-D300 GC/MS spectrometer. The ^{1}H NMR spectra were recorded at 300MHz with TMS as a spectra standard. Combustion analyses were performed on a Perkin-Elmer 240C or a MOD 1106 instrument. IR spectra were obtained on a Shimadzu IR-1700 spectrophotometer. The TLC was carried out on silica gel GF-254 20*20 cm^2 plate. Melting points were uncorrected. All reagents and solvents were purified and dried as required. The synthesis procedures of compounds (**2-5**) and the spectrum datas of compounds (**15**, **25**, **28**, **35**) have been reported in our previous paper.[27] Products (**10**,[29]

19,[30] and **20**[29]) are known compounds, and the NMR spectra of the compounds are in agreement with reported data.

General procedure for the reaction of compounds (2-5) with a series of amines.

Compounds (**2-5**) (1 mmol) and amine (1 mmol) were refluxed in dry MeCN (10 mL) and monitored by TLC. Upon completion or after the indicated reaction time, the mixture was concentrated, and purified by column chromatography on silica gel to give the desired products (**6-39**).

***Compound (6)*:** yield 79% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.90 (s, 3H), 2.43 (s, 3H), 2.97 (m, 1H), 3.29 (m, 1H), 3.79 (s, 3H), 4.13 (m, 1H), 7.08-7.15 (m, 3H), 7.27-7.33 (m, 3H), 11.01 (br, 1H); IR (KBr) cm^{-1}: 2927, 1745, 1581, 1495, 1367, 1178, 979; MS m/z: 290 (M+1); *Anal*. Calcd for $C_{16}H_{19}NO_4$: C, 66.42; H, 6.62; N, 4.84. Found C, 66.23; H, 6.30; N, 4.88.

***Compound (7)*:** yield 77% as yellow oil. H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.39 (s, 3H), 2.57 (s, 3H), 7.23 (m, 3H), 7.42 (m, 2H), 8.22 (d, *J* = 12.7, 1H), 12.78 (br, 1H); IR (KBr) cm^{-1}: 3053, 2925, 1745, 1627, 1600, 1504, 1398, 1259, 1184, 1028; MS m/z: 203 (M^+); *Anal*. Calcd for $C_{12}H_{13}NO_2$: C, 70.92; H, 6.45; N, 6.89. Found C, 71.11; H, 6.54; N, 6.93.

***Compound (8)*:** yield 73%, recrystallized from EtOH as white crystals, mp 138~140 ^{o}C. H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.70 (s, 3H), 2.70 (s, 3H), 3.16 (m, 1H), 3.54 (m, 1H), 3.83 (s, 3H), 4.29 (m, 1H), 7.03 (d, *J* = 13.1, 2H), 7.15 (m, 2H), 7.37 (d, *J* = 7.9, 1H), 7.56 (d, *J* = 7.7, 1H), 8.29 (s, 1H), 11.22 (br, 1H); IR (KBr) cm^{-1}: 3190, 2922, 2873, 1739, 1625, 1562, 1398, 1178; MS m/z: 329 (M+1); *Anal*. Calcd for $C_{18}H_{20}N_2O_4$: C, 65.84; H, 6.14; N, 8.53. Found C, 65.75; H, 6.28; N, 8.83.

***Compound (9)*:** yield 78%, recrystallized from EtOH as white crystals, mp 81~83 ^{o}C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.25 (s, 3H), 2.49 (s, 3H), 4.55 (d, *J* = 5.9, 2H), 7.36 (m, 5H), 7.78 (d, *J* = 13.1, 1H), 11.32(br, 1H); IR (KBr) cm^{-1}: 3430, 3173, 2924, 1858, 1613, 1573, 1498, 1443, 1394, 1354, 1245, 1181, 1028; MS m/z: 217 (M^+); *Anal*. Calcd for $C_{13}H_{15}NO_2$: C, 71.87; H, 6.96; N, 6.45. Found C, 71.85; H, 7.07; N, 6.68.

***Compound (11)*:** yield 75% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.04 (s, 3H), 2.40 (s, 3H), 2.77 (m, 2H), 3.54 (m, 2H), 3.78 (s, 6H), 6.64 (m, 2H), 6.75 (d, *J* = 7.9, 1H), 7.44 (d, *J* = 13.2, 1H), 10.99 (br, 1H); IR (KBr) cm^{-1}: 3481, 3196, 2936, 1621, 1516, 1463, 1395, 1356, 1262, 1182, 1027; MS m/z: 291 (M^+); *Anal*. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found C, 65.77; H, 7.38; N, 4.97.

***Compound (12)*:** yield 69% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.04 (s, 3H), 2.45 (s, 3H), 2.90 (t, *J* = 6.7, 2H), 3.57 (m, 2H), 7.17 (d, *J* = 7.3, 2H), 7.32 (m, 3H), 7.36 (d, *J* = 13.2, 1H), 11.03 (br, 1H); IR (KBr) cm^{-1}: 3199, 3028, 2927, 1722, 1622, 1585, 1497, 1455, 1396, 1356, 1259, 1088; MS m/z: 231 (M^+); *Anal*. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found C, 72.76; H, 7.44; N, 6.17.

***Compound (13)*:** yield 71% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.99 (s, 3H), 2.39 (s, 3H), 2.86 (t, *J* = 6.6, 2H), 3.48 (m, 2H), 3.74 (s, 3H), 6.83 (m, 2H), 7.00 (d, *J* = 7.2, 1H), 7.17 (t, *J* = 7.8, 1H),

7.35 (d, *J* = 13.3, 1H), 11.02 (br, 1H); IR (KBr) cm^{-1}: 3433, 3198, 2926, 1722, 1622, 1586, 1495, 1463, 1439, 1394, 1246, 1183, 1028; MS m/z: 261 (M^+); *Anal*. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found C, 69.25; H, 7.63; N, 5.52.

***Compound (14)*:** yield 81%, recrystallized from EtOH as yellow crystals, mp 166~167 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.98 (s, 3H), 2.46 (s, 3H), 2.83 (t, *J* = 6.3, 2H), 3.55 (m, 2H), 6.22 (br, 1H), 6.78 (d, *J* = 7.9, 2H), 7.00 (d, *J* = 7.9, 2H), 7.38 (d, *J* = 13.3, 1H), 11.01 (br, 1H); IR (KBr) cm^{-1}: 3424, 3124, 3015, 2924, 1730, 1651, 1586, 1513, 1455, 1401, 1257, 1237, 1107; MS m/z: 247 (M^+); *Anal*. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found C, 67.94; H, 7.10; N, 6.14.

***Compound (16)*:** yield 59% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.26 (m, 3H), 2.44 (s, 3H), 3.11 (m, 2H), 3.76 (s, 3H), 4.11 (m, 2H), 4.25 (m, 1H), 7.08-7.30 (m, 5H), 7.60 (d, *J* = 13.3, 1H), 10.97 (br, 1H); IR (KBr) cm^{-1}: 2979, 1741, 1693, 1635, 1575, 1490, 1454, 1382, 1245, 1062; MS m/z: 319 (M^+); *Anal*. Calcd for $C_{17}H_{21}NO_5$: C, 63.94; H, 6.63; N, 4.39. Found C, 63.88; H, 6.58; N, 4.24.

***Compound (17)*:** yield 88% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.35 (t, *J* = 7.1, 3H), 2.54 (s, 3H), 4.28 (m, 2H), 7.27 (m, 3H), 7.40 (m, 2H), 8.52 (d, *J* = 13.1, 1H), 12.76 (br, 1H); IR (KBr) cm^{-1}: 3049, 2965, 1741, 1648, 1594, 1544, 1389, 1275, 1158, 1047; MS m/z: 233 (M^+); *Anal*. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found C, 67.21; H, 6.52; N, 6.17.

Compound (18)*:** yield 67%, recrystallized from EtOAc/petroleum ether as yellow crystals, mp 84~87 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.17 (t, *J* = 7.1, 3H), 2.46 (s, 3H), 3.27 (m, 1H), 3.47 (m, 1H), 3.75 (s, 3H), 4.07 (m, 2H), 4.30 (m, 1H), 7.02-7.58 (m, 6H), 8.33 (br, 1H), 11.03 (br, 1H); IR (KBr) cm^{-1}: 3435, 2976, 1730, 1699, 1635, 1566, 1419, 1386, 1178; MS m/z: 358 (M^+); ***Anal. Calcd for $C_{19}H_{22}N_2O_5$: C, 63.67; H, 6.19; N, 7.82. Found C, 63.51; H, 6.21; N, 7.69.

***Compound (21)*:** yield 75%, recrystallized from EtOAc/petroleum ether as white crystals, mp 88~90 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.26 (t, *J* = 7.1, 3H), 2.45 (s, 3H), 2.81 (t, *J* = 6.8, 2H), 3.53 (m, 2H), 3.85 (s, 6H), 4.16 (m, 2H), 6.72 (m, 3H), 7.85 (d, *J* = 13.6, 1H), 11.06 (br, 1H); IR (KBr) cm^{-1}: 3428, 3192, 2939, 1697, 1637, 1582, 1516, 1467, 1419, 1365, 1248, 1233, 1055; MS m/z: 321 (M^+); *Anal*. Calcd for $C_{17}H_{23}NO_5$: C, 63.54; H, 7.21; N, 4.36. Found C, 63.22; H, 7.15; N, 4.52.

***Compound (22)*:** yield 77% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.24 (t, *J* = 6.8, 3H), 2.43 (s, 3H), 2.85 (t, *J* = 6.5, 2H), 3.54 (m, 2H), 4.14 (m, 2H), 7.22 (m, 5H), 7.79 (d, *J* = 13.5, 1H), 11.01 (br, 1H); IR (KBr) cm^{-1}: 3184, 3028, 2980, 1694, 1633, 1583, 1497, 1455, 1418, 1383, 1250, 1071; MS m/z: 261 (M^+); *Anal.* Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found C, 68.56; H, 7.21; N, 5.76.

***Compound (23)*:** yield 68%, recrystallized from EtOAc/petroleum ether as white crystals, mp 49~51 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.28 (t, *J* = 7.1, 3H), 2.45 (s, 3H), 2.94 (t, *J* = 6.9, 2H), 3.54 (m, 2H), 3.83 (s, 3H), 4.15 (m, 2H), 6.88 (m, 2H), 7.11 (d, *J* = 7.2, 1H), 7.24 (m, 1H), 7.88 (d, *J* = 13.7, 1H), 11.00 (br, 1H); IR (KBr) cm^{-1}: 3430, 3191, 3028, 2926, 1693, 1636, 1587, 1494, 1461, 1419, 1386, 1251, 1067;

MS m/z: 291 (M^+); *Anal*. Calcd for $C_{16}H_{21}NO_4$: C, 65.96; H, 7.27; N, 4.81. Found C, 65.79; H, 7.22; N, 4.86.

***Compound (24)*:** yield 82%, recrystallized from EtOAc as yellow crystals, mp 116~117 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.31 (t, *J* = 7.1, 3H), 2.46 (s, 3H), 2.82 (t, *J* = 6.2, 2H), 3.55 (m, 2H), 4.18 (m, 2H), 6.78 (d, *J* = 8.0, 2H), 6.83 (s, 1H), 7.00 (d, *J* = 7.9, 2H), 7.87 (d, *J* = 13.7, 1H), 10.94 (br, 1H); IR (KBr) cm^{-1}: 3297, 3027, 2941, 1659, 1633, 1590, 1518, 1449, 1417, 1387, 1259, 1221, 1065; MS m/z: 278 (M+1); *Anal*. Calcd for $C_{15}H_{19}NO_4$: C, 64.97; H, 6.91; N, 5.05. Found C, 64.90; H, 6.89; N, 5.27.

***Compound (26)*:** yield 39% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.00 (t, *J* = 7.3, 3H), 1.40 (m, 2H), 1.64 (m, 2H), 3.37 (m, 2H), 6.47 (d, *J* = 5.6, 1H), 6.73 (m, 1H), 9.14 (br, 1H); IR (KBr) cm^{-1}: 3060, 2931, 2873, 1340, 1137; MS m/z: 144 (M^+); *Anal.* Calcd for $C_6H_{12}N_2O_2$: C, 49.98; H, 8.39; N, 19.43. Found C, 49.85; H, 8.35; N, 19.52.

***Compound (27)*:** yield 35% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 4.55 (s, 2H), 6.50 (d, *J* = 5.8, 1H), 6.81 (m, 1H), 7.28-7.44 (m, 5H), 9.34 (br, 1H); IR (KBr) cm^{-1}: 3031, 2875, 1622, 1558, 1456, 1338, 1141; MS m/z: 178 (M^+); *Anal.* Calcd for $C_9H_{10}N_2O_2$: C, 60.66; H, 5.66; N, 15.72. Found C, 60.75; H, 5.61; N, 15.43.

***Compound (29)*:** yield 14% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.88 (t, *J* = 6.5, 2H), 3.61 (m, 2H), 3.89 (s, 6H), 6.41 (d, *J* = 5.7, 1H), 6.54 (m, 1H), 6.70-6.87 (m, 3H), 9.16 (br, 1H); IR (KBr) cm^{-1}: 3057, 2935, 2837, 1622, 1593, 1517, 1465, 1093; MS m/z: 252 (M^+); *Anal.* Calcd for $C_{12}H_{16}N_2O_4$: C, 57.13; H, 6.39; N, 11.10. Found C, 57.26; H, 6.44; N, 11.25.

***Compound (30)*:** yield 40% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.96 (t, *J* = 6.8, 2H), 3.62 (m, 2H), 6.39 (d, *J* = 5.7, 1H), 6.54 (m, 1H), 7.12-7.38 (m, 5H), 9.13 (br, 1H); IR (KBr) cm^{-1}: 2927, 2864, 1622, 1541, 1454, 1141; MS m/z: 192 (M^+); *Anal.* Calcd for $C_{10}H_{12}N_2O_2$: C, 62.49; H, 6.29; N, 14.57. Found C, 62.35; H, 6.11; N, 14.38.

***Compound (31)*:** yield 44% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.96 (t, *J* = 6.6, 2H), 3.58 (m, 2H), 3.85 (s, 3H), 6.38 (d, *J* = 5.7, 1H), 6.52 (m, 1H), 6.90 (m, 2H), 7.17 (d, *J* = 7.0, 1H), 7.28 (m, 1H), 9.22 (br, 1H); IR (KBr) cm^{-1}: 2939, 2837, 1622, 1589, 1494, 1122; MS m/z: 222 (M^+); *Anal.* Calcd for $C_{11}H_{14}N_2O_3$: C, 59.45; H, 6.35; N, 12.60. Found C, 59.66; H, 6.47; N, 12.85.

***Compound (32)*:** yield 24% as yellow oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 2.87 (t, *J* = 6.6, 2H), 3.56 (m, 2H), 6.40 (d, *J* = 5.7, 1H), 6.53 (m, 1H), 6.83 (d, *J* = 8.1, 2H), 7.07 (d, *J* = 8.1, 2H), 9.12 (br, 1H); IR (KBr) cm^{-1}: 3020, 2925, 2854, 1618, 1595, 1550, 1515, 1444, 1143; MS m/z: 208 (M^+); *Anal.* Calcd for $C_{10}H_{12}N_2O_3$: C, 57.68; H, 5.81; N, 13.45. Found C, 57.59; H, 5.76; N, 13.37.

***Compound (33)*:** yield 91% as colorless oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 0.91 (t, *J* = 7.2, 3H), 1.31 (m, 2H), 1.49 (m, 2H), 1.83 (s, 3H), 3.25 (m, 2H), 6.98 (d, *J* = 13.7, 1H), 7.38 (m, 5H), 10.41 (br, 1H); IR (KBr) cm^{-1}: 3238, 2929, 2858, 1635, 1577, 1440, 1371, 1136; MS m/z: 217 (M^+); *Anal.* Calcd for

$C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found C, 77.44; H, 8.89; N, 6.51.

***Compound (34)*:** yield 96% as colorless oil. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.89 (s, 3H), 4.36 (d, *J* = 5.3, 2H), 7.05 (d, *J* = 13.4, 1H), 7.23-7.28 (m, 4H), 7.36-7.48 (m, 6H), 10.75 (br, 1H); IR (KBr) cm^{-1}: 3354, 2868, 2360, 1635, 1577, 1545, 1396, 1218, 1016; MS m/z: 251 (M^+); *Anal.* Calcd for $C_{17}H_{17}NO$: C, 81.24; H, 6.82; N, 5.57. Found C, 81.63; H, 6.97; N, 5.88.

***Compound (36)*:** yield 84%, recrystallized from EtOH as yellow crystals, mp 120~122 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.79 (s, 3H), 2.77 (t, *J* = 6.4, 2H), 3.40 (m, 2H), 3.86 (s, 3H), 3.90 (s, 3H), 6.65-6.86 (m, 4H), 7.34-7.44 (m, 5H), 10.79 (br, 1H); IR (KBr) cm^{-1}: 3350, 2931, 2837, 1635, 1539, 1514, 1440, 1365, 1137; MS m/z: 325 (M^+); *Anal*. Calcd for $C_{20}H_{23}NO_3$: C, 73.82; H, 7.12; N, 4.30. Found C, 73.79; H, 7.15; N, 4.29.

***Compound (37)*:** yield 56%, recrystallized from EtOH as white crystals, mp 153~154 °C. ^{1}H-NMR (300 MHz, δ ppm, DMSO-d_6): 1.68 (s, 3H), 2.73 (t, *J* = 6.0, 2H), 3.30 (m, 2H), 6.68 (d, *J* = 13.7, 1H), 6.95-7.36 (m, 10H), 10.92 (br, 1H); IR (KBr) cm^{-1}: 3238, 2922, 1630, 1581, 1548, 1497, 1446, 1392, 1230, 1012; MS m/z: 265 (M^+); *Anal*. Calcd for $C_{18}H_{19}NO$: C, 81.47; H, 7.22; N, 5.28. Found C, 81.11; H, 7.39; N, 5.14.

***Compound (38)*:** yield 74%, recrystallized from EtOH as yellow crystals, mp 120~121 °C. ^{1}H-NMR (300 MHz, δ ppm, $CDCl_3$): 1.79 (s, 3H), 2.84 (t, *J* = 6.3, 2H), 3.38 (m, 2H), 3.81 (s, 3H), 6.80-6.96 (m, 3H), 7.07 (d, *J* = 7.3, 1H), 7.28-7.41 (m, 6H), 10.76 (br, 1H); IR (KBr) cm^{-1}: 3307, 2933, 1635, 1598, 1539, 1446, 1396, 1375, 1226, 1118; MS m/z: 295 (M^+); *Anal*. Calcd for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17; N, 4.74. Found C, 77.17; H, 7.15; N, 4.69.

***Compound (39)*:** yield 90%, recrystallized from EtOH as white crystals, mp 189~190 °C. ^{1}H-NMR (300 MHz, δ ppm, DMSO-d_6): 1.68 (s, 3H), 2.68 (t, *J* = 7.1, 2H), 3.22 (m, 2H), 6.59-7.35 (m, 11H), 9.24 (br, 1H), 10.86 (br, 1H); IR (KBr) cm^{-1}: 3203, 2931, 1626, 1595, 1510, 1450, 1371, 1265, 1028; MS m/z: 281 (M^+); *Anal*. Calcd for $C_{18}H_{19}NO_2$: C, 76.84; H, 6.81; N, 4.98. Found C, 76.56; H, 7.08; N, 4.79.

Crystal data for compound (24).

Empirical formula: $C_{15}H_{19}NO_4$, crystal size: 0.40×0.20×0.20, Triclinic, a = 8.637(3)Å, b = 9.418(3)Å, c = 9.944(3)Å, α = 66.706 (4)°, β = 89.808(4)°, γ = 77.424(4)°, V = 722.0(4), T = 293(2)K, space group P-1, Z = 2, d_{calc} = 1.2767 g/cm^3, F(000) = 296, 3000 reflections measured, 2298 unique (R_{int}= 0.0187). The final R1 = 0.0762 ($I > 2\sigma$), 0.0974 (all data), wR2 = 0.1875 ($I > 2\sigma$), 0.2014 (all data).

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