EurJOC European Journal of Organic Chemistry

FULL PAPER

DOI: 10.1002/ejoc.201300737

Palladium-Catalysed Synthesis of 9*H*-Pyrrolo[1,2-*a*]indol-9-ones and the Isomeric Indeno[2,1-*b*]pyrrol-8-ones

Shuyang Wang,[a] Qinghua Yang,[a] Jingjing Dong,[a] Changwei Li,[a] Li Sun,[a] Chuanjun Song,*[a] and Junbiao Chang*[a]

Keywords: Amination / C–H activation / Palladium / Nitrogen heterocycles / Cyclization

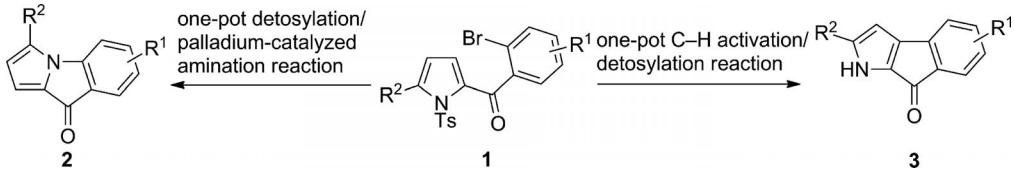
9*H*-Pyrrolo[1,2-*a*]indol-9-ones and isomeric indeno[2,1-*b*]pyrrol-8-ones could be obtained in moderate to good isolated yields, by subjecting the same substrates, 2-bromophenyl *N*-tosyl-2-pyrrolyl ketones, to different palladium catalysts.

Introduction

9*H*-Pyrrolo[1,2-*a*]indol-9-one (fluorazone) and its analogues have shown a wide range of biological activities.[1] Moreover, fluorazone itself is the key precursor to the cytostatic mitomycin family.[2] Among the many strategies developed to date for the synthesis of fluorazones, the most appealing seems to be the intramolecular acylation of 2-(pyrrol-1-yl)benzoic acid derivatives.[3] However, this route requires multiple steps, including the transformation of 2-aminobenzoic acids into 2-aminobenzoate derivatives, Clauson–Kaas pyrrole synthesis, ester hydrolysis to reveal the free carboxylic acid functionalities (in most cases followed by activation to an acyl chloride), and cyclization. Other less well-proven methods include the palladium-catalysed cyclocarbonylation of *N*-(2-iodophenyl)pyrrole,[4] the direct double metallation of *N*-phenylpyrrole followed by treatment of the resulting dilithium salt with ethyl *N*,*N*-dimethylcarbamate,[5] the hydrolysis of 9-arylimino-9*H*-pyrrolo[1,2-*a*]indoles, which in turn were obtained by the reaction of 2-(pyrrol-1-yl)benzaldehydes with arylamines,[6] or the annulation of pyrrole-2-carboxylates with benzyne.[7]

The palladium-catalysed amination reaction has found widespread application in the construction of heterocycles, as well as in natural-product synthesis.[8] However, to the best of our knowledge, this reaction has never been used for fluorazone synthesis. In this paper, we report a one-pot process consisting of a detosylation and a palladium-catalysed intramolecular amination reaction of 2-bromophenyl *N*-tosyl-2-pyrrolyl ketones **1** for the synthesis of fluorazones **2** (Scheme 1). The required precursors **1** can be easily obtained by regioselective acylation of *N*-tosylpyrroles[9] with 2-bromobenzoic acid derivatives in the presence of TFAA.

With the same substrates **1**, palladium-catalysed intramolecular C–H activation followed by detosylation would result in the formation of isomeric indeno[2,1-*b*]pyrrol-8-ones **3**. Fluorenone analogues of this type have barely been reported in the literature, although many examples are known in which one or both of the phenyl rings are replaced by other heterocycles, such as thiophene, benzothiophene, furan, benzofuran, indole, etc.[1a,2,3e,4,10]



Scheme 1. Synthesis of 9*H*-pyrrolo[1,2-*a*]indol-9-ones **2** and isomeric indeno[2,1-*b*]pyrrol-8-ones **3**.

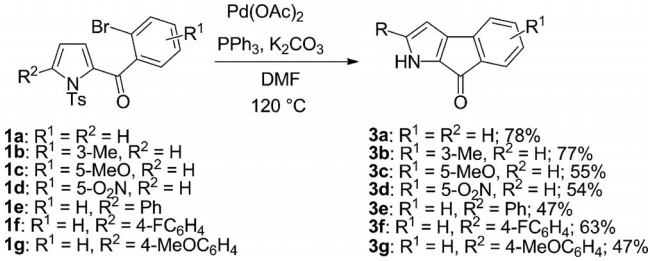
Results and Discussion

The palladium-catalysed intramolecular C–H activation reaction was examined first. $Pd(OAc)_2$ was found to be the

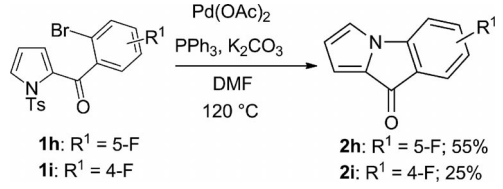
[a] College of Chemistry and Molecular Engineering, Zhengzhou University,
100 Science Avenue, Zhengzhou 450001, P. R. of China
E-mail: chjsong@zzu.edu.cn
changjunbiao@zzu.edu.cn
http://hxx.zzu.edu.cn

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201300737.

best catalyst. In the presence of $Pd(OAc)_2$, Ph_3P, and K_2CO_3 in DMF as solvent, a variety of 2-bromophenyl *N*-tosyl-2-pyrrolyl ketones including those with sterically hindered (**1b**), electron-donating (**1c**), or electron-withdrawing (**1d**) substituents on the phenyl ring, as well as those with a 5-aryl-substituted pyrrolyl moiety (**1e**–**g**) underwent a one-pot palladium-catalysed C–H activation/detosylation reaction to give indeno[2,1-*b*]pyrrol-8-ones **3a**–**g** in moderate to good isolated yields (Scheme 2).[9e] When substrates with a fluorinated phenyl ring (**1h**, **1i**) were subjected to the same reaction conditions, instead of indeno[2,1-*b*]pyrrol-8-ones, the corresponding 9*H*-pyrrolo[1,2-*a*]indol-9-ones (i.e., **2h** and **2i**) were isolated in 55 and 25% yields, respectively (Scheme 3). It appears that the presence of a fluorine atom on the phenyl ring hampered the oxidative addition process, and **2h** and **2i** were produced by sequential deprotection of the tosyl group and in situ palladium-catalysed intramolecular amination reaction.[11] This was further confirmed by the fact that only 9*H*-pyrrolo[1,2-*a*]indol-9-one **2a** (see Scheme 4) was obtained when 2-bromophenyl pyrrol-2-yl ketone was subjected to the same reaction conditions.[9e]

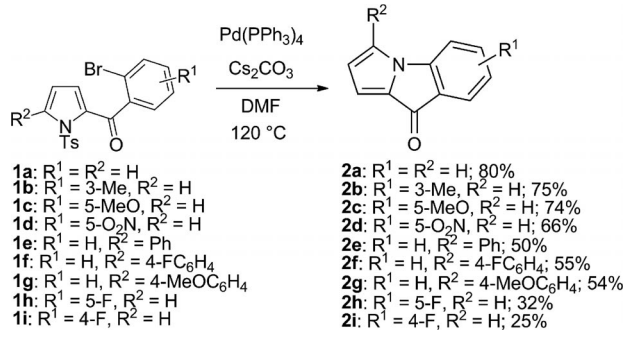


Scheme 2. One-pot $Pd(OAc)_2$-catalysed C–H activation/detosylation for the synthesis of indeno[2,1-*b*]pyrrol-8-ones **3a**–**g**.



Scheme 3. One-pot detosylation/$Pd(OAc)_2$-catalysed intramolecular amination for the synthesis of 9*H*-pyrrolo[1,2-*a*]indol-9-ones **2h** and **2i**.

The above results indicated that a one-pot detosylation/palladium-catalysed intramolecular amination of other 2-bromophenyl *N*-tosyl-2-pyrrolyl ketones to produce 9*H*-pyrrolo[1,2-*a*]indol-9-ones is possible if a suitable catalyst, which can efficiently catalyse the amination reaction but not the C–H activation, is used. When $Pd(PPh_3)_2Cl_2$ or $Pd_2(dba)_3$ were tested as catalysts under a variety of conditions, they failed to deliver either indeno[2,1-*b*]pyrrol-8-ones or indeno[2,1-*b*]pyrrol-8-ones in acceptable yields. To our delight, when $Pd(PPh_3)_4$ was used as catalyst, the one-pot reaction proceeded smoothly with all the 2-bromophenyl *N*-tosyl-2-pyrrolyl ketones tested (i.e., **1a**–**i**) to give 9*H*-pyrrolo[1,2-*a*]indol-9-ones **2a**–**i** in moderate to good isolated yields, uncontaminated by the corresponding indeno[2,1-*b*]pyrrol-8-ones (Scheme 4). We assume that the



Scheme 4. One-pot detosylation/$Pd(PPh_3)_4$-catalysed intramolecular amination for the synthesis of 9*H*-pyrrolo[1,2-*a*]indol-9-ones **2a**–**i**.

different regioselectivity observed with the different catalyst might be due to the ability of the acetate anion from $Pd(OAc)_2$ to facilitate the oxidative addition process.

Conclusions

We have developed a valuable approach to 9*H*-pyrrolo[1,2-*a*]indol-9-ones and isomeric indeno[2,1-*b*]-pyrrol-8-ones by subjecting the same substrates to different palladium catalysts. The former compounds were produced in a one-pot detosylation/palladium-catalysed intramolecular amination reaction, the latter by a palladium-catalysed C–H activation/detosylation sequence.

Experimental Section

General Remarks: Solvents were dried according to standard procedures where necessary. Melting points were determined with an XT4A hot-stage apparatus. IR spectra were obtained with an IFS25 FTIR spectrometer. ^1H and ^{13}C NMR spectra were obtained with Bruker AV300 or AV400 instruments. Mass spectra were recorded with a Micromass Q-TOF mass spectrometer.

General Procedure for the Synthesis of Compounds 2a–i: A mixture of **1a**–**i** (1.0 mmol), $Pd(PPh_3)_4$ (0.01 mmol), and Cs_2CO_3 (2.0 mmol) in dry DMF (20 mL) under N_2 was heated to 120 °C for 12 h, and then the mixture was allowed to cool. The mixture was partitioned between EtOAc (100 mL) and H_2O (200 mL). The separated aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with brine (200 mL), then dried (Na_2SO_4) and filtered, and the solvents were evaporated. The residue was purified by column chromatography.

9*H*-Pyrrolo[1,2-*a*]indol-9-one (2a): Yellow solid (78%); m.p. 112–113 °C (ref.[5] m.p. 121–122 °C). IR: $\tilde{\nu}$ = 1681, 1617, 1546, 1478, 1469, 1449, 1403, 1359, 1338, 1262, 1181, 1076 cm^{-1}. ^1H NMR (400 MHz, [D$_6$]DMSO): δ = 6.38 (t, J = 3.2 Hz, 1 H), 6.84 (d, J = 4.0 Hz, 1 H), 7.21 (td, J = 7.2, 1.2 Hz, 1 H), 7.52–7.61 (m, 3 H), 7.68 (d, J = 2.8 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 111.2, 113.8, 115.7, 121.6, 123.6, 125.4, 129.0, 130.5, 134.6, 143.1, 178.4 ppm. MS (ESI): *m*/*z* (%) = 192 (50) $[M + Na]^+$, 170 (100) $[M + H]^+$. HRMS: calcd. for $C_{11}H_8NO$ $[M + H]^+$ 170.0606; found 170.0589.

5-Methyl-9*H*-pyrrolo[1,2-*a*]indol-9-one (2b): Yellow solid (75%); m.p. 129–132 °C (ref.[3a] m.p. 137–139 °C). ^1H NMR (400 MHz,

$CDCl_3$): δ = 2.43 (s, 3 H), 6.27 (dd, J = 3.6, 2.7 Hz, 1 H), 6.80 (d, J = 3.6 Hz, 1 H), 7.03 (t, J = 7.6 Hz, 1 H), 7.13 (d, J = 2.7 Hz, 1 H), 7.16 (d, J = 7.6 Hz, 1 H), 7.38 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 17.5, 113.3, 115.6, 121.8, 122.04, 122.2, 125.2, 130.1, 132.1, 136.7, 142.0, 179.8 ppm. MS (ESI): *m*/*z* (%) = 206 (100) $[M + Na]^+$, 184 (38) $[M + H]^+$. HRMS: calcd. for $C_{12}H_{10}NO$ $[M + H]^+$ 184.0726; found 184.0749.

7-Methoxy-9*H*-pyrrolo[1,2-*a*]indol-9-one (2c): Yellow solid (74%); m.p. 120–121 °C (ref.[3a] m.p. 124–125 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.79 (s, 3 H), 6.23 (dd, J = 3.6, 2.7 Hz, 1 H), 6.74 (d, J = 3.6 Hz, 1 H), 6.89 (dd, J = 8.4, 2.7 Hz, 1 H), 7.00 (m, 2 H), 7.11 (d, J = 2.7 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.8, 109.6, 110.9, 114.1, 115.3, 119.2, 119.5, 131.5, 132.1, 137.3, 157.8, 179.4 ppm. MS (ESI): *m*/*z* (%) = 222 (100) $[M + Na]^+$, 200 (28) $[M + H]^+$. HRMS: calcd. for $C_{12}H_9NNaO_2$ $[M + Na]^+$ 222.0531; found 222.0540.

7-Nitro-9*H*-pyrrolo[1,2-*a*]indol-9-one (2d): Yellow solid (66%); m.p. 198–200 °C (ref.[3a] m.p. 200–201 °C). ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 6.49 (dd, J = 3.6, 2.7 Hz, 1 H), 6.99 (d, J = 3.6 Hz, 1 H), 7.48 (d, J = 8.4 Hz, 1 H), 7.81 (d, J = 2.7 Hz, 1 H), 8.12 (d, J = 2.1 Hz, 1 H), 8.48 (dd, J = 8.4, 2.1 Hz) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 112.2, 116.2, 17.9, 118.9, 123.3, 130.2, 131.0, 132.1, 145.0, 147.1, 176.1 ppm. MS (ESI): *m*/*z* (%) = 237 (71) $[M + Na]^+$, 215 (100) $[M + H]^+$. HRMS: calcd. for $C_{11}H_7N_2O_3$ $[M + H]^+$ 215.0457; found 215.0455.

3-Phenyl-9*H*-pyrrolo[1,2-*a*]indol-9-one (2e): Yellow solid (50%); m.p. 91–92 °C. $\tilde{\nu}$ = 1690, 1612, 1540, 1515, 1474, 1448, 1391, 1354, 1338, 1310, 1267, 1237, 1216 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.27 (d, J = 3.9 Hz, 1 H), 6.86 (d, J = 3.9 Hz, 1 H), 6.95 (d, J = 7.8 Hz, 1 H), 7.09 (t, J = 7.8 Hz, 1 H), 7.26 (td, J = 7.8, 1.2 Hz, 1 H), 7.49–7.62 (m, 6 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.8, 114.0, 116.3, 123.9, 124.9, 128.3, 128.7, 128.8, 130.4, 132.7, 133.6, 137.5, 143.8, 178.8 ppm. MS (ESI): *m*/*z* (%) = 268 (26) $[M + Na]^+$, 246 (100) $[M + H]^+$. HRMS: calcd. for $C_{11}H_{12}NO$ $[M + H]^+$ 246.0919; found 246.0932.

3-(4-Fluorophenyl)-9*H*-pyrrolo[1,2-*a*]indol-9-one (2f): Yellow solid (55%); m.p. 162–164 °C. $\tilde{\nu}$ = 1689, 1613, 1546, 1522, 1478, 1442, 1418, 1384, 1353, 1311, 1267, 1238, 1218, 1158, 1101, 1072 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.26 (d, J = 3.6 Hz, 1 H), 6.86–6.88 (m, 2 H), 7.10 (td, J = 8.1, 0.6 Hz, 1 H), 7.20–7.29 (m, 3 H), 7.56–7.63 (m 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 111.5, 113.9, 115.3, 115.9 (d, J = 45.0 Hz), 124.1, 125.0, 126.5 (d, J = 3.0 Hz), 130.3, 130.5 (d, J = 7.5 Hz), 132.6, 133.6, 136.1, 143.6, 162.8 (d, J = 225.0 Hz), 178.7 ppm. MS (ESI): *m*/*z* (%) = 286 (100) $[M + Na]^+$, 264 (55) $[M + H]^+$. HRMS: calcd. for $C_{17}H_{11}FNO$ $[M + H]^+$ 264.0825; found 264.0795.

3-(4-Methoxyphenyl)-9*H*-pyrrolo[1,2-*a*]indol-9-one (2g): Yellow solid (54%); m.p. 152–154 °C. $\tilde{\nu}$ = 1681, 1606, 1580, 1546, 1504, 1458, 1417, 1373, 1327, 1312, 1294, 1246, 1185, 1157, 1114, 1071 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.92 (s, 3 H), 6.23 (d, J = 3.9 Hz, 1 H), 6.86 (d, J = 3.9 Hz, 1 H), 6.97 (d, J = 7.8 Hz, 1 H), 7.04 (d, J = 8.4 Hz, 2 H), 7.10 (t, J = 7.8 Hz, 1 H), 7.27 (t, J = 7.8 Hz, 1 H), 7.52 (d, J = 8.4 Hz, 2 H), 7.61 (d, J = 7.8 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.0, 111.7, 113.7, 114.2, 115.9, 122.7, 123.9, 124.8, 130.1, 130.6, 132.4, 133.5, 137.6, 143.8, 160.0, 178.7 ppm. MS (ESI): *m*/*z* (%) = 298 (100) $[M + Na]^+$, 276 (60) $[M + H]^+$. HRMS: calcd. for $C_{18}H_{14}NO_2$ $[M + H]^+$ 276.1025; found 276.1009.

7-Fluoro-9*H*-pyrrolo[1,2-*a*]indol-9-one (2h): Yellow solid (32%); m.p. 118–119 °C (ref.[3a] m.p. 124 °C). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.30 (dd, J = 3.6, 2.7 Hz, 1 H), 6.80 (d, J = 3.6 Hz, 1 H), 7.04–7.14 (m, 3 H), 7.27 (dd, J = 7.2, 2.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 110.7 (d, J = 7.5 Hz), 111.7 (d, J = 22.5 Hz), 114.4, 115.6, 119.4, 119.7, 131.4 (d, J = 7.5 Hz), 131.9, 139.3, 160.3 (d, J = 244.5 Hz), 177.6 ppm. MS (ESI): *m*/*z* (%) = 210 (100) $[M + Na]^+$, 188 (17) $[M + H]^+$. HRMS: calcd. for $C_{11}H_6FNNaO$ $[M + Na]^+$ 210.0331; found 210.0339.

6-Fluoro-9*H*-pyrrolo[1,2-*a*]indol-9-one (2i): Yellow solid (25%); m.p. 121–123 °C. $\tilde{\nu}$ = 1682, 1617, 1528, 1484, 1434, 1400, 1361, 1297, 1244, 1201, 1134, 1066 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.33 (dd, J = 3.6, 2.7 Hz, 1 H), 6.78–6.87 (m, 3 H), 7.06 (m, 1 H), 7.56 (dd, J = 8.4, 5.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 99.1 (d, J = 28.5 Hz), 111.4 (d, J = 22.5 Hz), 113.8, 115.9, 119.0, 125.8 (d, J = 7.5 Hz), 132.1, 145.1 (d, J = 12.6 Hz), 166.3 (d, J = 244.5 Hz), 177.8 ppm. MS (ESI): *m*/*z* (%) = 210 (100) $[M + Na]^+$, 188 (47) $[M + H]^+$ HRMS: calcd. for $C_{11}H_6FNNaO$ $[M + Na]^+$ 210.0331; found 210.0331.

General Procedure for the Synthesis of Compounds 3a–g: A mixture of **1a–g** (1.0 mmol), $Pd(OAc)_2$ (0.05 mmol), PPh_3 (0.1 mmol), and K_2CO_3 (3.0 mmol) in dry DMF (20 mL) under N_2 was heated to 120 °C for 11 h, and then the mixture was allowed to cool. The mixture was partitioned between EtOAc (100 mL) and H_2O (200 mL). The separated aqueous phase was extracted with EtOAc (3 × 100 mL). The combined organic extracts were washed with brine (200 mL), then dried (Na_2SO_4) and filtered, and the solvents were evaporated. The residue was purified by column chromatography.

Indeno[2,1-*b*]pyrrol-8(1*H*)-one (3a): Red solid (80%); m.p. 205–206 °C. $\tilde{\nu}$ = 3222, 1690, 1632, 1607, 1509, 1450, 1357, 1319, 1272, 1098 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 6.19 (m, 1 H), 6.99–7.27 (m, 5 H), 12.00 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]-DMSO): δ = 103.8, 119.0, 122.6, 126.9, 131.2, 131.7, 133.2, 138.0, 139.1, 142.9, 180.0 ppm. MS (ESI): *m*/*z* (%) = 192 (100) $[M + Na]^+$, 170 (53) $[M + H]^+$. HRMS: calcd. for $C_{11}H_7NNaO$ $[M + Na]^+$ 192.0425; found 192.0416.

4-Methylindeno[2,1-*b*]pyrrol-8(1*H*)-one (3b): Red solid (77%); m.p. 198–200 °C. $\tilde{\nu}$ = 3180, 1690, 1677, 1607, 1599, 1474, 1462, 1394, 1357, 1322 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 2.23 (s, 3 H), 6.19 (m, 1 H), 6.88–7.10 (m 4 H), 12.00 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 17.8, 105.0, 120.2, 126.9, 129.1, 130.9, 131.4, 134.9, 137.2, 137.8, 142.5, 180.2 ppm. MS (ESI): *m*/*z* (%) = 206 (100) $[M + Na]^+$, 184 (100) $[M + H]^+$. HRMS: calcd. for $C_{12}H_{10}NO$ $[M + H]^+$ 184.0762; found 184.0747.

6-Methoxyindeno[2,1-*b*]pyrrol-8(1*H*)-one (3c): Red solid (55%); m.p. 198–200 °C. $\tilde{\nu}$ = 3162, 1679, 1618, 1513, 1463, 1431, 1365, 1313, 1277, 1259, 1215, 1193 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]-DMSO): δ = 3.72 (s, 3 H), 6.09 (m, 1 H), 6.67 (dd, J = 7.8, 2.4 Hz, 1 H), 6.76 (d, J = 2.4 Hz, 1 H), 6.93 (d, J = 7.8 Hz, 1 H), 7.63 (t, J = 2.4 Hz), 11.91 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 55.4, 103.4, 111.3, 114.9, 119.7, 130.9, 131.4, 131.5, 140.3, 143.8, 158.9, 179.2 ppm. MS (ESI): *m*/*z* (%) = 222 (100) $[M + Na]^+$, 200 (18) $[M + H]^+$. HRMS: calcd. for $C_{12}H_9NNaO_2$ $[M + Na]^+$ 222.0531; found 222.0540.

6-Nitroindeno[2,1-*b*]pyrrol-8(1*H*)-one (3d): Red solid (54%); m.p. 252–254 °C. $\tilde{\nu}$ = 3119, 1682, 1617, 1528, 1484, 1400, 1361, 1337, 1297, 1273, 1244, 1201 cm^{-1}. ^{1}H NMR (300 MHz, [D$_6$]DMSO): δ = 6.28 (d, J = 2.7 Hz, 1 H), 7.04 (d, J = 2.7 Hz, 1 H), 7.24 (dd, J = 8.1, 0.9 Hz, 1 H), 7.80 (m, 1 H), 8.25 (m, 1 H), 12.22 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D$_6$]DMSO): δ = 105.9, 116.9, 117.2, 126.2, 128.2, 130.0, 140.3, 141.7, 146.6, 148.3, 182.8 ppm. MS (ESI): *m*/*z* (%) = 237 (100) $[M + Na]^+$, 215 (80) $[M + H]^+$. HRMS: calcd. for $C_{11}H_6N_2NaO_3$ $[M + Na]^+$ 237.0276; found 237.0282.

2-Phenylindeno[2,1-*b*]pyrrol-8(1*H*)-one (3e): Red solid (47%); m.p. 219–221 °C. $\tilde{\nu}$ = 3196, 1682, 1605, 1541, 1503, 1455, 1357, 1419, 1382, 1318, 1289, 1274, 1246 cm^{-1}. ^1H NMR (300 MHz, [D_6]-DMSO): δ = 6.74 (s, 1 H), 7.05–7.12 (m, 2 H), 7.21–7.46 (m, 3 H), 7.43 (t, J = 7.2 Hz, 2 H), 7.80 (d, J = 7.2 Hz, 2 H), 12.47 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 101.7, 119.1, 122.5, 124.9, 127.2, 128.1, 128.9, 131.0, 132.5, 133.1, 138.2, 138.6, 143.7, 143.8, 179.7 ppm. MS (ESI): *m*/*z* (%) = 268 (60) $[M + Na]^+$, 246 (100) $[M + H]^+$. HRMS: calcd. for $C_{11}H_{12}NO$ $[M + H]^+$ 246.0919; found 246.0921.

2-(4-Fluorophenyl)indeno[2,1-*b*]pyrrol-8(1*H*)-one (3f): Red solid (63%); m.p. 263–265 °C. $\tilde{\nu}$ = 3192, 1678, 1604, 1548, 1504, 1456, 1419, 1324, 1291, 12775, 1246, 1162, 1129, 1072 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 6.71 (s, 1 H), 7.02–7.09 (m, 2 H), 7.17–7.30 (m, 4 H), 7.79–7.84 (m, 2 H), 12.42 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 101.9, 116.0, 116.3, 119.3, 122.7, 127.2 (d, J = 7.5 Hz), 127.4, 127.8 (d, J = 3.0 Hz), 132.6, 133.3, 138.5 (d, J = 32.0 Hz), 142.8, 143.9, 161.9 (d, J = 244.5 Hz), 179.9 ppm. MS (ESI): *m*/*z* (%) = 264 (100) $[M + H]^+$. HRMS: calcd. for $C_{17}H_{11}FNO$ $[M + H]^+$ 264.0825; found 264.0798.

2-(4-Methoxyphenyl)indeno[2,1-*b*]pyrrol-8(1*H*)-one (3g): Red solid (47%); m.p. 257–258 °C. $\tilde{\nu}$ = 3191, 1681, 1606, 1580, 1546, 1504, 1458, 1417, 1373, 1327, 1312, 1294, 1246, 1185 cm^{-1}. ^1H NMR (300 MHz, [D_6]DMSO): δ = 3.79 (s, 3 H), 6.63 (s, 1 H), 6.99 (d, J = 8.7 Hz, 2 H), 7.05–7.09 (m, 2 H), 7.17 (d, J = 7.5 Hz, 1 H), 7.25 (t, J = 7.5 Hz, 1 H), 7.73 (d, J = 8.7 Hz, 2 H), 12.28 (s, 1 H) ppm. ^{13}C NMR (75 MHz, [D_6]DMSO): δ = 55.3, 100.9, 114.5, 119.0, 122.3, 123.6, 126.5, 127.2, 131.8, 133.0, 138.4, 138.5, 144.1, 144.2, 159.3, 179.2 ppm. MS (ESI): *m*/*z* (%) = 298 (53) $[M + Na]^+$, 276 (100) $[M + H]^+$. HRMS: calcd. for $C_{18}H_{14}NO_2$ $[M + H]^+$ 276.1025; found 276.0995.

Supporting Information (see footnote on the first page of this article): Copies of the ^1H and ^{13}C NMR spectra of compounds **2a**–**i** and **3a**–**g**.

Acknowledgments

We are grateful to the National Natural Science Foundation of China (Grant Nos. 20902085 and 21172202) for financial support.

[1] a) M. T. Tierney, M. W. Grinstaff, *J. Org. Chem.* **2000**, *65*, 5355–5359; b) S. Rault, J. C. Lancelot, L. Bouyazza, M. Robba, M. A. Quermonne, B. Nammathao, J. Louchahi-Raoul, R. Marcy, *Eur. J. Med. Chem.* **1991**, *26*, 939–946; c) C. Rochais, P. Dallemagne, S. Rault, *Anti-Cancer Agents Med. Chem.* **2009**, *9*, 369–380; d) P. Diana, A. Stagno, P. Barraja, A. Montalbano, A. Carbone, B. Parrino, G. Cirrincione, *Tetrahedron* **2011**, *67*, 3374–3379.

[2] V.-S. Li, D. Choi, Z. Wang, L. S. Jimenez, M.-S. Tang, H. Kohn, *J. Am. Chem. Soc.* **1996**, *118*, 2326–2331.

[3] a) F. Aiello, A. Garofalo, F. Grande, *Tetrahedron Lett.* **2010**, *51*, 6635–6636; F. Aiello, A. Garofalo, F. Grande, *Tetrahedron Lett.* **2011**, *52*, 5824–5826; F. Aiello, A. Garofalo, F. Grande, *Tetrahedron* **2010**, *66*, 274–277; b) A. D. Josey, E. L. Jenner, *J. Org. Chem.* **1962**, *27*, 2466–2470; c) V. J. Mazzola, K. F. Bernady, R. W. Franck, *J. Org. Chem.* **1967**, *32*, 486–489; d) A. S. Bailey, P. W. Scott, M. H. Vandrevala, *J. Chem. Soc. Perkin Trans. 1* **1980**, 97–101; e) V. Lisowki, S. Léonce, L. Kraus-Berthier, J. Sopkova-de Oliveira Santos, A. Pierré, G. Atassi, D.-H. Caignard, P. Renard, S. Rault, *J. Med. Chem.* **2004**, *47*, 1448–1464.

[4] M. A. Campo, R. C. Larock, *Org. Lett.* **2000**, *2*, 3675–3677; M. A. Campo, R. C. Larock, *J. Org. Chem.* **2002**, *67*, 5616–5620.

[5] I. A. Kashulin, I. E. Nifant'ev, *J. Org. Chem.* **2004**, *69*, 5476–5479.

[6] K. Kobayashi, Y. Himei, S. Fukamachi, M. Tanmatsu, O. Morikawa, H. Konishi, *Tetrahedron* **2007**, *63*, 4356–4359.

[7] R. D. Giacometti, Y. K. Ramtohul, *Synlett* **2009**, 2010–2016.

[8] For a recent review, see: D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438–6461; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338–6361.

[9] a) C. Song, D. W. Knight, M. A. Whatton, *Tetrahedron Lett.* **2004**, *45*, 9573–9576; b) C. Song, P. Zhao, Y. Liu, H. Liu, W. Li, S. Shi, J. Chang, *Tetrahedron* **2010**, *66*, 5378–5383; c) C. Song, Y. Liu, P. Zhao, X. Sun, W. Li, H. Liu, J. Chang, *Synthesis* **2011**, 45–50; d) M. Hong, H. Liu, L. Sun, F. Jia, Y. Liu, Q. Jiang, C. Song, J. Chang, *Synlett* **2011**, 2995–2996; e) J. Chang, L. Sun, J. Dong, Z. Shen, Y. Zhang, J. Wu, R. Wang, J. Wang, C. Song, *Synlett* **2012**, 2704–2706; f) C. Song, H. Liu, M. Hong, Y. Liu, F. Jia, L. Sun, Z. Pan, J. Chang, *J. Org. Chem.* **2012**, *77*, 704–706.

[10] a) G. Qabaja, G. B. Jones, *Tetrahedron Lett.* **2000**, *41*, 5317–5320; b) A. P. Kozikowski, D. Ma, *Tetrahedron Lett.* **1991**, *32*, 3317–3320; c) T.-P. Liu, Y.-X. Liao, C.-H. Xing, Q.-S. Hu, *Org. Lett.* **2011**, *13*, 2452–2455; d) Y. Matsuda, S. Kohra, K. Katou, T. Uemura, K. Yamashita, *Heterocycles* **2003**, *60*, 405–411; e) N. Chernyak, D. Tilly, Z. Li, V. Gevorgyan, *Chem. Commun.* **2010**, *46*, 150–152; f) R. Romagnoli, P. G. Baraldi, M. D. Carrion, C. L. Cara, O. Cruz-Lopez, M. Tolomeo, S. Grimaudo, A. D. Cristina, M. R. Pipitone, J. Balzarini, N. Zonta, A. Brancale, E. Hamel, *Bioorg. Med. Chem.* **2009**, *17*, 6862–6871; g) P. J. Perry, M. A. Read, R. T. Davies, S. M. Gowan, A. P. Reszka, A. A. Wood, L. R. Kelland, S. Neidle, *J. Med. Chem.* **1999**, *42*, 2679–2684; h) M. L. Greenlee, J. B. Laub, G. P. Rouen, F. DiNinno, M. L. Hammond, J. L. Huber, J. G. Sundelof, G. G. Hammond, *Bioorg. Med. Chem. Lett.* **1999**, *9*, 3225–3230; i) S. J. Gould, C. R. Melville, M. C. Cone, J. Chen, J. R. Carney, *J. Org. Chem.* **1997**, *62*, 320–324.

[11] N. Barbero, R. SanMartin, E. Domínguez, *Tetrahedron Lett.* **2009**, *50*, 2129–2131.

Received: May 18, 2013
Published Online: October 2, 2013

