Facile and Highly Regiospecific Synthesis of 2-Aryl-Substituted Pyrazolidin-3-ones from α,β-Unsaturated *N*-Acylbenzotriazoles and Arylhydrazines

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Received 4 June 2008; revised 4 July 2008

Abstract: The bis-addition of arylhydrazines to α,β-unsaturated *N*-acylbenzotriazoles to form heterocyclic compounds was achieved in refluxing THF by using triethylamine as promoter. The reaction was highly regioselective and various 2-aryl-substituted pyrazolidin-3-ones were obtained in moderate to good yields.

Key words: bis-addition, regioselectivity, arylhydrazine, α,β-unsaturated *N*-acylbenzotriazole, pyrazolidinone

The importance of pyrazolidin-3-ones has increased significantly in the last decade, due to their applicability in industrial processes, and also because several pyrazolidin-3-one derivatives exhibit biological activities or excellent antibacterial activities and are pharmaceutically useful.[1]

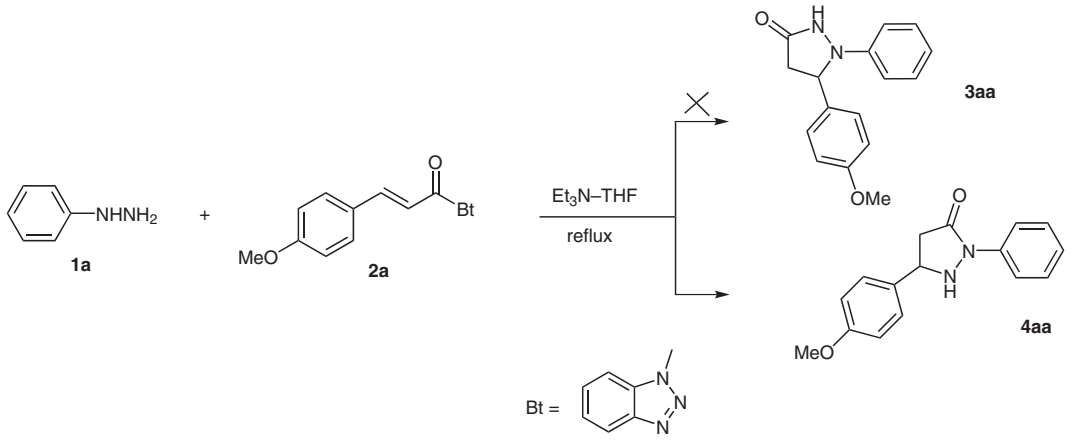
The addition of hydrazines as bisnucleophilic donors to α,β-unsaturated carboxylic acids or their derivatives such as α,β-unsaturated esters,[1c,2] amides,[1i] nitriles,[1i] and imides,[3] can provide direct access to pyrazolidin-3-ones. However, usually harsh basic conditions such as sodium or sodium alkoxide were required. Although 1-substituted pyrazolidin-3-ones could be prepared smoothly from the above reactions, to the best of our knowledge, 2-substituted pyrazolidin-3-ones could not be obtained or were only formed as a by-product, and therefore the synthesis of 2-substituted pyrazolidin-3-one may necessitate multistep reactions.[4] Herein, we wish to report a direct and regiospecific access to 2-aryl-substituted pyrazolidin-3-ones from readily available α,β-unsaturated *N*-acylbenzotriazoles and arylhydrazines.

α,β-Unsaturated *N*-acylbenzotriazole is a class of special unsaturated amide, which contains an active amide moiety[5] (useful for acylation) as well as an electron-deficient carbon–carbon double bond. Correspondingly, it could act as an acylating agent (1,2-addition) and a Michael addition acceptor (1,4-addition). For example, they could efficiently acylate N-nucleophiles such as anhydrous hydrazine[6] and amines[7] to afford cinnamoylhydrazines and cinnamoylamides. We recently found that *N*-cinnamoylbenzotriazoles were good acylating agents for thiolates.[8] Katritzky's group also reported that α,β-unsaturated *N*-acylbenzotriazoles were useful as C-acylating agents. Thus, lithium enolates of ketones[9] and Grignard reagents[10] underwent 1,2-addition and several γ,δ-unsaturated β-diketones and α,β-unsaturated ketones were prepared, respectively. The potential of α,β-unsaturated *N*-acylbenzotriazole to act as a Michael addition acceptor was first demonstrated by us in its regioselective Friedel–Crafts alkylation of indoles.[11] In light of these combined observations, it occurred to us that both 1,2- and 1,4-addition of a binucleophile may proceed concurrently with α,β-unsaturated *N*-acylbenzotriazoles and thereby providing a useful route for the construction of small-ring heterocycles. We now report that with arylhydrazine as a binucleophile, the 5-membered heterocyclic compounds could be constructed in high regioselectivity and satisfactory yields.

We began our experiments with the goal of identifying conditions that would allow for the ring formation. Phenylhydrazine (**1a**) was first chosen as a model substrate to react with *N*-cinnamoylbenzotriazole **2a** in THF at room temperature without any additive in light of the mild reaction conditions previously reported.[5,12] Since no product could be formed, triethylamine was then added as a base promoter. Fortunately, a reaction was observed albeit in low conversion in 24 hours. When the reaction was carried out under refluxing conditions, the conversion increased drastically even in shorter time and **2a** disappeared in 6 hours. Structure characterization of the isolated product showed the absence of the benzotriazolyl group. Combined with the presence of three characteristic doublet-doublet peaks in the ^{1}H NMR spectrum it could be deduced that both 1,2- and 1,4-addition, as expected, did occur between the *N*-cinnamoylbenzotriazole and phenylhydrazine, thus the ring formation was realized. However, it should be noted that the two nitrogen atoms in the monosubstituted hydrazine may possess different nucleophilicity and undergo two possible pathways of cyclization,[3,13] which correspond to two regioisomers, namely **3aa** and **4aa** (Scheme 1).

We then set out to identify the structure of the product, which has a melting point between 102–104 °C, much lower than the known isomer **3a**a, which melted at 162–164 °C.[2c] Besides, a broad peak at 4.73 ppm in the ^{1}H NMR spectrum indicates the presence of a more active amine NH rather than an amide NH, which usually displays a peak at 7–10 ppm. All the above data supported that the product obtained here should be **4aa** rather than

SYNTHESIS 2008, No. 20, pp 3223–3228
Advanced online publication: 25.09.2008
DOI: 10.1055/s-0028-1083159; Art ID: F123080SS



Scheme 1

3aa. To ascertain the structure unambiguously, an X-ray diffraction analysis[14] was conducted. As shown in Figure 1, the structure of **4aa** was finally confirmed, where the more nucleophilic nitrogen atom of the phenylhydrazine attaches on the β-position of the *N*-cinnamoylbenzotriazole while the phenyl-substituted nitrogen atom prefers to be acylated. The more nucleophilic nitrogen atom of the arylhydrazines tended to undergo 1,4-addition preferably, which has been observed in pyrazole synthesis.[15]

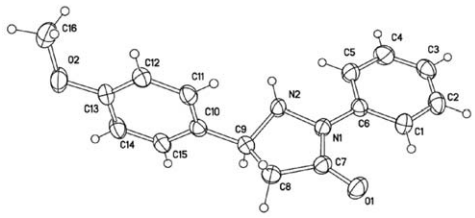
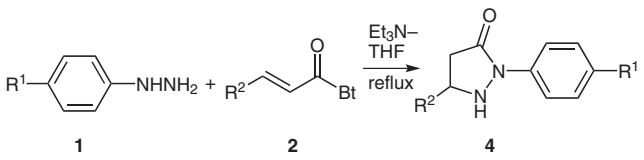


Figure 1 X-ray structure of 5-(4-methoxyphenyl)-2-phenylpyrazolidin-3-one (**4aa**)

Under the above established conditions, a variety of α,β-unsaturated *N*-acylbenzotriazoles and arylhydrazines with either electron-donating or electron-withdrawing groups on the phenyl ring were allowed to react together (Scheme 2 and Table 1).



Scheme 2

As could be summarized from Table 1, phenylhydrazine and the arylhydrazines substituted with 4-methyl, 4-choro, and 4-bromo all afforded pyrazolidin-3-ones **4** in moderate to good yields. 4-Nitrophenylhydrazine was unreactive (Table 1, entry 21).

The α,β-unsaturated *N*-acylbenzotriazoles substituted at the β-position with an aryl such as phenyl, 4-methoxyphenyl, 4-methylphenyl, 4-chlorophenyl and 2-furyl generally afforded the products in moderate to good yields. However, with 4-nitro-substituted aryl **2g**, no product could be obtained (Table 1, entries 7 and 17). In comparison with *N*-cinnamoylbenzotriazoles, *N*-crotonylbenzotriazole reacted with arylhydrazines more readily and afforded better yields of the expected heterocyclic compounds in shorter time (Table 1, entries 4, 10, 13, and 20). The higher reactivity may result from the less steric hindrance at the β-position.

Products **4** were formed exclusively and no isomers were detected. The analogous absorption pattern (a broad peak at 4.5–5.0 ppm) indicated the presence of a more active amine NH in all the compounds obtained here.

In conclusion, arylhydrazines can undergo acylation and Michael addition concurrently with α,β-unsaturated *N*-acylbenzotriazoles to afford 2-aryl-substituted pyrazolidin-3-ones in moderate to good yields under mild basic conditions. The reaction is in contrast to that between *N*-cinnamoylbenzotriazoles and anhydrous hydrazine where only amidated products were obtained.[6] In addition, it shows completely different regioselectivity from the reaction between α,β-unsaturated esters and arylhydrazines[2b,c] and is a useful addition to the methods for the preparation of pyrazolidin-3-one derivatives.

THF was distilled from sodium-benzophenone immediately prior to use. Petroleum ether used refers to the fraction boiling at 60–90 °C. ^{1}H NMR spectra were recorded on a Bruker AV400 instrument as $CDCl_3$ solutions using TMS as an internal standard. Chemical shifts (d) were reported in ppm and coupling constants *J* are given in Hz. IR spectra were recorded as films or using KBr disks with a NEXUS 670 FTIR spectrometer. Mass spectra (MeCN solutions) were recorded on a Waters ZQ4000 spectrometer operating in ESI mode. Single crystal X-ray diffraction analysis was performed on Bruker SMART APEX II instrument. Elemental analyses were performed on a Vario-ELIII instrument. Phenylhydrazine and arylhydrazines were commercially available and α,β-unsaturated *N*-acylbenzotriazoles were synthesized from α,β-unsaturated carboxylic acids according to literature procedures.[6,16]

Table 1 5-Substituted 2-Arylpyrazolidin-3-ones **4** Prepared

Entry	R^1	R^2	Product **4**	Time (h)	Yield (%)[a]
1	H **1a**	4-$MeOC_6H_4$ **2a**	**4aa**	6	63
2	H **1a**	4-MeC_6H_4 **2b**	**4ab**	4	75
3	H **1a**	4-ClC_6H_4 **2c**	**4ac**	6	60
4	H **1a**	Me **2d**	**4ad**	0.5	76
5	H **1a**	2-furyl **2e**	**4ae**	5	74
6	H **1a**	Ph **2f**	**4af**	4.5	61
7	H **1a**	4-$O_2NC_6H_4$ **2g**	**4ag**	10	–[b]
8	Me **1b**	4-MeC_6H_4 **2b**	**4bb**	2	78
9	Me **1b**	Ph **2f**	**4bf**	6	80
10	Me **1b**	Me **2d**	**4bd**	1	81
11	Me **1b**	4-ClC_6H_4 **2c**	**4bc**	4.5	78
12	Me **1b**	4-$MeOC_6H_4$ **2a**	**4ba**	3	59
13	Cl **1c**	Me **2d**	**4cd**	1	95
14	Cl **1c**	4-MeC_6H_4 **2b**	**4cb**	8	90
15	Cl **1c**	4-$MeOC_6H_4$ **2a**	**4ca**	7.5	63
16	Cl **1c**	Ph **2f**	**4cf**	9	85
17	Cl **1c**	4-$O_2NC_6H_4$ **2g**	**4cg**	10	–[b]
18	Br **1d**	Ph **2f**	**4df**	14	58
19	Br **1d**	4-MeC_6H_4 **2b**	**4db**	12	59
20	Br **1d**	Me **2d**	**4dd**	1.5	74
21	NO_2 **1e**	Ph **2f**	**4ef**	10	–[b]

[a] Isolated yields based on α,β-unsaturated *N*-acylbenzotriazoles.
[b] No reaction.

5-Substituted 2-Arylpyrazolidin-3-ones 4; General Procedure

A mixture of arylhydrazine **1** (1.1 mmol), α,β-unsaturated *N*-acylbenzotriazole **2** (1 mmol), and Et_3N (1 mL) was refluxed in anhyd THF (10 mL) for the time indicated in Table 1 (monitored by TLC). Then the mixture was washed with aq sat. Na_2CO_3 (10 mL) and extracted with EtOAc (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by column chromatography using EtOAc and petroleum ether (1:2) as eluent to afford pure **4**.

5-(4-Methoxyphenyl)-2-phenylpyrazolidin-3-one (4aa)

Colorless plates from EtOAc; mp 103–104 °C.

IR (KBr): 3221, 3066, 2998, 2962, 2930, 2837, 1683, 1594, 1514 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 2 H, ArH), 7.37–7.34 (m, 4 H, ArH), 7.10–7.14 (m, 1 H, ArH), 6.92 (d, *J* = 8.8 Hz, 2 H, ArH), 4.77–4.73 (m, 2 H, H-5, NH), 3.81 (s, 3 H, CH_3), 3.06 (dd, *J* = 6.0, 16.4 Hz, 1 H, H-4a), 2.99 (dd, *J* = 8.4, 16.4 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 159.7, 138.8, 128.8, 127.8, 124.3, 118.32, 118.31, 114.3, 57.6, 55.4, 41.5.

MS (ESI$^+$): *m*/*z* (%) = 291 (100, $[M + Na]^+$), 269 (75.5, $[M + H]^+$), 267 (62.2, $[M – H]^+$).

Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.78; H, 5.98; N, 10.40.

2-Phenyl-5-*p*-tolylpyrazolidin-3-one (4ab)

White powder; mp 85–87 °C.

IR (KBr): 3210, 3028, 2921, 1698, 1596, 1496 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.90–7.88 (m, 2 H, ArH), 7.37–7.29 (m, 4 H, ArH), 7.25–7.19 (m, 2 H, ArH), 7.13–7.10 (m, 1 H, ArH), 4.77–4.76 (m, 2 H, H-5, NH), 2.95–3.10 (m, 2 H, H-4a, H-4b), 2.35 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 138.8, 138.3, 129.6, 128.8, 126.5, 124.3, 118.3, 57.7, 41.5, 21.2.

MS (ESI$^+$): *m*/*z* (%) = 275 (70.0, $[M + Na]^+$), 253 (100, $[M + H]^+$).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.48; H, 6.31; N, 11.15.

5-(4-Chlorophenyl)-2-phenylpyrazolidin-3-one (4ac)

Light purple powder; mp 119–122 °C.

IR (KBr): 3242, 2977, 2925, 1702, 1592, 1486 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.0 Hz, 2 H, ArH), 7.43–7.32 (m, 6 H, ArH), 7.15–7.12 (m, 1 H, ArH), 4.89 (br d, *J* = 8.0 Hz, 1 H, NH), 4.77 (dd, *J* = 8.0, 16.0 Hz, 1 H, H-5), 3.16 (dd, *J* = 8.0, 16.0 Hz, 1 H, H-4a), 2.90 (dd, *J* = 8.0, 16.0 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 138.6, 134.2, 129.1, 128.9, 128.8, 127.8, 124.5, 118.3, 56.9, 41.6.

MS (ESI$^+$): *m*/*z* (%) = 297 (26.4, $[M(^{37}Cl) + Na]^+$), 295 (58.4, $[M(^{35}Cl) + Na]^+$), 273 (78.6, $[M(^{35}Cl) + H]^+$ or $[M(^{37}Cl) – H]^+$), 271 (100, $[M(^{35}Cl)^+ – H]$).

Anal. Calcd for $C_{15}H_{13}ClN_2O$: C, 66.06; H, 4.80; N, 10.27. Found: C, 65.77; H, 4.88; N, 10.20.

5-Methyl-2-phenylpyrazolidin-3-one (4ad)

Light brown powder; mp 74–76 °C.

IR (KBr): 3214, 2977, 2921, 1691, 1594 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 8.1 Hz, 2 H, ArH), 7.37–7.33 (m, 2 H, ArH), 7.11 (t, *J* = 7.4 Hz, 1 H, ArH), 4.46 (br, 1

H, NH), 3.82–3.74 (m, 1 H, H-5), 2.83 (dd, *J* = 6.6, 16.1 Hz, 1 H, H-4a), 2.45 (dd, *J* = 8.5, 16.3 Hz, 1 H, H-4b), 1.34 (d, *J* = 6.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.0, 138.9, 128.7, 124.2, 118.3, 51.1, 42.8, 18.7.

MS (ESI$^+$): *m*/*z* (%) = 199 (100, $[M + Na]^+$), 177 (48.3, $[M + H]^+$), 175 (66.1, $[M – H]^+$).

Anal. Calcd for $C_{10}H_{12}N_2O$: C, 68.16; H, 6.86; N, 15.90. Found: C, 67.95; H, 6.91; N, 15.93.

5-(Furan-2-yl)-2-phenylpyrazolidin-3-one (4ae)
White powder; mp 70–72 °C.

IR (KBr): 3223, 3118, 2901, 1694, 1595, 1489 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85–7.83 (m, 2 H, ArH), 7.44–7.26 (m, 3 H, ArH), 7.16–7.12 (m, 1 H, ArH), 6.42–6.37 (m, 2 H, ArH), 4.93–4.80 (m, 2 H, H-5, NH), 3.15 (dd, *J* = 8.8, 16.5 Hz, 1 H, H-4a), 3.00 (dd, *J* = 7.4, 16.6 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.5, 143.0, 138.7, 128.8, 124.5, 118.5, 110.6, 108.4, 52.4, 39.4.

MS (ESI$^+$): *m*/*z* (%) = 251 (100, $[M + Na]^+$), 229 (48.6, $[M + H]^+$), 227 (19.2, $[M – H]^+$).

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.41; H, 5.30; N, 12.27. Found: C, 68.62; H, 5.22; N, 12.21.

2,5-Diphenylpyrazolidin-3-one (4af)
Viscous oil.

IR (KBr): 3212, 3063, 2927, 1695, 1596, 1495 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.85 (m, 2 H, ArH), 7.35–7.30 (m, 7 H, ArH), 7.10–7.08 (m, 1 H, ArH), 4.85 (br, 1 H, NH), 4.69–4.64 (m, 1 H, H-5), 3.00 (dd, *J* = 7.2, 16.4 Hz, 1 H, H-4a), 2.85 (dd, *J* = 8.4, 16.4 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 138.8, 128.9, 128.8, 128.3, 126.5, 124.3, 118.3, 118.2, 57.6, 41.5.

MS (ESI$^+$): *m*/*z* (%) = 238 (18.1, $[M]^+$), 237 (100, $[M – H]^+$).

Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.37; H, 5.94; N, 11.70.

2,5-Di(*p*-tolyl)pyrazolidin-3-one (4bb)
Light brown powder; mp 78–80 °C.

IR (KBr): 3128, 1687, 1509, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.0 Hz, 2 H, ArH), 7.30 (d, *J* = 8.0 Hz, 2 H, ArH), 7.20–7.14 (m, 4 H, ArH), 4.75 (br, 2 H, H-5, NH), 3.08–3.04 (m, 1 H, H-4a), 2.97 (dd, *J* = 8.0, 16.0 Hz, 1 H, H-4b), 2.35 (s, 3 H, CH_3), 2.32 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.7, 138.2, 136.3, 134.0, 129.6, 129.3, 126.5, 118.4, 57.5, 41.5, 21.1, 20.8.

MS (ESI$^+$): *m*/*z* (%) = 289 (100, $[M + Na]^+$), 267 (50.5, $[M + H]^+$), 265 (13.9, $[M – H]^+$).

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.85; H, 6.77; N, 10.42.

5-Phenyl-2-*p*-tolylpyrazolidin-3-one (4bf)
Viscous oil.

IR (KBr): 3217, 3031, 2922, 2856, 1682, 1614, 1510 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (d, *J* = 8.4 Hz, 2 H, ArH), 7.45–7.33 (m, 5 H, ArH), 7.15 (d, *J* = 8.4 Hz, 2 H, ArH), 4.80–4.76 (m, 2 H, H-5, NH), 3.11 (dd, *J* = 7.2, 16.0 Hz, 1 H, H-4a), 2.96 (dd, *J* = 8.4, 16.4 Hz, 1 H, H-4b), 2.32 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.6, 136.3, 134.1, 129.3, 128.9, 128.3, 126.5, 118.4, 41.5, 29.7, 20.9.

MS (ESI$^+$): *m*/*z* (%) = 275 (27.1, $[M + Na]^+$), 251 (100, $[M – H]^+$).

Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.32; H, 6.42; N, 11.14.

5-Methyl-2-*p*-tolylpyrazolidin-3-one (4bd)
White powder; mp 76–79 °C.

IR (KBr): 3475, 3415, 3128, 1682, 1618, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.8 Hz, 2 H, ArH), 7.13 (d, *J* = 8.8 Hz, 2 H, ArH), 4.48 (br s, 1 H, NH), 3.75–3.74 (m, 1 H, H-5), 2.79 (dd, *J* = 6.8, 16.3 Hz, 1 H, H-4a), 2.41 (dd, *J* = 8.4, 16.3 Hz, 1 H, H-4b), 2.31 (s, 3 H, CH_3), 1.31 (d, *J* = 6.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.7, 136.6, 133.8, 129.2, 118.4, 51.0, 42.7, 20.9, 18.6.

MS (ESI$^+$): *m*/*z* (%) = 213 (76.8, $[M + Na]^+$), 191 (25.1, $[M + H]^+$), 189 (100, $[M – H]^+$).

Anal. Calcd for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.73. Found: C, 69.58; H, 7.37; N, 14.77.

5-(4-Chlorophenyl)-2-*p*-tolylpyrazolidin-3-one (4bc)
White powder; mp 92–95 °C.

IR (KBr): 3413, 3132, 1674, 1619, 1509, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75–7.73 (m, 2 H, ArH), 7.40–7.31 (m, 4 H, ArH), 7.15 (d, *J* = 8.3 Hz, 2 H, ArH), 4.89 (br d, *J* = 6.8 Hz, 1 H, NH), 4.77–4.73 (m, 1 H, H-5), 3.14 (dd, *J* = 7.6, 16.3 Hz, 1 H, H-4a), 2.86 (dd, *J* = 7.4, 16.3 Hz, 1 H, H-4b), 2.32 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.3, 136.1, 134.2, 129.9, 129.4, 129.3, 129.1, 127.8, 118.4, 56.9, 41.6, 20.9.

MS (ESI$^+$): *m*/*z* (%) = 309 (33.9, $[M(^{35}Cl) + Na]^+$), 287 (47.2, $[M(^{35}Cl) + H]^+$ or $[M(^{37}Cl) – H]^+$), 285 (100, $[M(^{35}Cl) – H]^+$).

Anal. Calcd for $C_{16}H_{15}ClN_2O$: C, 67.02; H, 5.27; N, 9.77. Found: C, 66.87; H, 5.32; N, 9.81.

5-(4-Methoxyphenyl)-2-*p*-tolylpyrazolidin-3-one (4ba)
Light brown powder; mp 89–91 °C.

IR (KBr): 3475, 3414, 3128, 1685, 1615, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.5 Hz, 2 H, ArH), 7.32 (d, *J* = 8.6 Hz, 2 H, ArH), 7.14 (d, *J* = 8.3 Hz, 2 H, ArH), 6.90 (d, *J* = 8.8 Hz, 2 H, ArH), 4.72 (br, 2 H, H-5, NH), 3.80 (s, 3 H, CH_3), 3.01–2.95 (m, 2 H, H-4), 2.31 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 170.8, 159.6, 136.3, 133.9, 129.28, 129.26, 127.8, 118.4, 114.3, 57.5, 55.3, 41.4, 20.9.

MS (ESI$^+$): *m*/*z* (%) = 305 (100, $[M + Na]^+$), 283 (65.3, $[M + H]^+$).

Anal. Calcd for $C_{17}H_{18}N_2O_2$: C, 72.32; H, 6.43; N, 9.92. Found: C, 72.21; H, 6.47; N, 9.89.

2-(4-Chlorophenyl)-5-methylpyrazolidin-3-one (4cd)
Light brown powder; mp 103–104 °C.

IR (KBr): 3130, 2930, 1692, 1492, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.5 Hz, 2 H, ArH), 7.29 (d, *J* = 8.5 Hz, 2 H, ArH), 4.45 (br, s, 1 H, NH), 3.82-3.75 (m, 1 H, H-5), 2.84 (dd, *J* = 6.4, 16.4 Hz, 1 H, H-4a), 2.46 (dd, *J* = 8.4, 16.4 Hz, 1 H, H-4b), 1.34 (d, *J* = 6.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.1, 137.6, 129.1, 128.7, 119.4, 51.1, 42.6, 18.5.

MS (ESI$^+$): *m*/*z* (%) = 235 (20.5, [M(^{37}Cl) + Na]$^+$), 233 (100, [M(^{35}Cl) + Na]$^+$), 213 (26.8, [M(^{37}Cl) + H]$^+$), 211 (93.1, [M(^{35}Cl) + H]$^+$ or [M(^{37}Cl) – H]$^+$), 209 (90.5, [M(^{35}Cl) – H]$^+$).

Anal. Calcd for $C_{10}H_{11}ClN_2O$: C, 57.01; H, 5.26; N, 13.30. Found: C, 56.83; H, 5.20; N, 13.35.

2-(4-Chlorophenyl)-5-*p*-tolylpyrazolidin-3-one (4cb)
Light brown powder; mp 135–137 °C.

IR (KBr): 3129, 1694, 1488, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.85 (m, 2 H, ArH), 7.33–7.29 (m, 4 H, ArH), 7.21 (d, *J* = 8.0 Hz, 2 H, ArH), 4.82–4.74 (m, 2 H, H-5, NH), 3.10 (dd, *J* = 6.6, 16.4 Hz, 1 H, H-4a), 3.02 (dd, *J* = 8.8, 16.4 Hz, 1 H, H-4b), 2.36 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 137.4, 129.7, 129.2, 128.8, 126.4, 119.4, 58.2, 41.4, 21.2.

MS (ESI$^+$): *m*/*z* (%) = 311 (12.4, [M(^{37}Cl) + Na]$^+$), 309 (28.8, [M(^{35}Cl) + Na]$^+$), 289 (38.8, [M(^{37}Cl) + H]$^+$), 287 (100, [M(^{35}Cl) + H]$^+$ or [M(^{37}Cl) – H]$^+$).

Anal. Calcd for $C_{16}H_{15}ClN_2O$: C, 67.02; H, 5.27; N, 9.77. Found: C, 67.25; H, 5.31; N, 9.72.

2-(4-Chlorophenyl)-5-(4-methoxyphenyl)pyrazolidin-3-one (4ca)
Light brown powder; mp 98–100 °C.

IR (KBr): 3475, 3414, 3129, 1695, 1614, 1489, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (d, *J* = 8.4 Hz, 2 H, ArH), 7.34–7.26 (m, 4 H, ArH), 6.92 (d, *J* = 7.9 Hz, 2 H, ArH), 4.78–4.71 (m, 2 H, H-5, NH), 3.81 (s, 3 H, CH_3), 3.06–2.97 (m, 2 H, H-4).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.4, 159.7, 137.4, 130.2, 129.2, 128.7, 127.8, 119.4, 114.3, 57.6, 55.4, 41.3.

MS (ESI$^+$): *m*/*z* (%) = 327 (13.2, [M(^{37}Cl) + Na]$^+$), 325 (35.7, [M(^{35}Cl) + Na]$^+$), 305 (43.7, [M(^{37}Cl) + H]$^+$), 303 (100, [M(^{35}Cl) + H]$^+$ or [M(^{37}Cl) – H]$^+$).

Anal. Calcd for $C_{16}H_{15}ClN_2O_2$: C, 63.47; H, 4.99; N, 9.25. Found: C, 63.23; H, 4.93; N, 9.29.

2-(4-Chlorophenyl)-5-phenylpyrazolidin-3-one (4cf)
White powder; mp 103–105 °C.

IR (KBr): 3129, 1697, 1641, 1489, 1400 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88 (d, *J* = 8.8 Hz, 2 H, ArH), 7.42–7.26 (m, 7 H, ArH), 4.84–4.81 (m, 2 H, H-5, NH), 3.14–3.12 (m, 1 H, H-4a), 3.02 (dd, *J* = 7.0, 15.0 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 137.3, 129.3, 129.0, 128.8, 128.5, 126.6, 119.4, 57.9, 41.4.

MS (ESI$^+$): *m*/*z* (%) = 297 (13.1, [M(^{37}Cl) + Na]$^+$), 295 (49.8, [M(^{35}Cl) + Na]$^+$), 275 (28.6, [M(^{37}Cl) + H]$^+$), 273 (100, [M(^{35}Cl) + H]$^+$ or [M(^{37}Cl) – H]$^+$).

Anal. Calcd for $C_{15}H_{13}ClN_2O$: C, 66.06; H, 4.80; N, 10.27. Found: C, 65.86; H, 4.83; N, 10.22.

2-(4-Bromophenyl)-5-phenylpyrazolidin-3-one (4df)
Light brown powder; mp 119–121 °C.

IR (KBr): 3413, 3130, 1695, 1485, 1401 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.7 Hz, 2 H, ArH), 7.44 (d, *J* = 8.8 Hz, 2 H, ArH), 7.39–7.34 (m, 5 H, ArH), 4.79 (m, 2 H, H-5, NH), 3.11 (dd, *J* = 6.8, 16.0 Hz, 1 H, H-4a), 2.98 (dd, *J* = 8.4, 16.2 Hz, 1 H, H-4b).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.1, 137.8, 131.7, 129.0, 128.5, 126.4, 119.7, 117.0, 57.8, 41.4.

MS (ESI$^+$): *m*/*z* (%) = 341 (47.8, [M(^{81}Br) + Na]$^+$), 339 (60.9, [M(^{79}Br) + Na]$^+$), 319 (92.3, [M(^{81}Br) + H]$^+$), 317 (100, [M(^{79}Br) + H]$^+$ or [M(^{81}Br) – H]$^+$).

Anal. Calcd for $C_{15}H_{13}BrN_2O$: C, 56.80; H, 4.13; N, 8.83. Found: C, 56.95; H, 4.11; N, 8.79.

2-(4-Bromophenyl)-5-*p*-tolylpyrazolidin-3-one (4db)
Light brown powder; mp 148–149 °C.

IR (KBr): 3413, 3128, 1694, 1485, 1401 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.81 (d, *J* = 8.8 Hz, 2 H, ArH), 7.45 (d, *J* = 9.2 Hz, 2 H, ArH), 7.29 (d, *J* = 8.0 Hz, 2 H, ArH), 7.20 (d, *J* = 8.0 Hz, 2 H, ArH), 4.78 (t, *J* = 8.4 Hz, 1 H, H-5), 3.08 (dd, *J* = 7.6, 16.0 Hz, 1 H, H-4a), 3.00 (dd, *J* = 8.8, 16.0 Hz, 1 H, H-4b), 2.36 (s, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 171.2, 138.4, 137.9, 131.7, 129.7, 126.4, 119.7, 116.9, 57.8, 41.4, 21.1.

MS (ESI$^+$): *m*/*z* (%) = 355 (49.8, [M(^{81}Br) + Na]$^+$), 353 (39.9, [M(^{79}Br) + Na]$^+$), 333 (84.1, [M(^{81}Br) + H]$^+$), 331 (100, [M(^{79}Br) + H]$^+$ or [M(^{81}Br) – H]$^+$).

Anal. Calcd for $C_{16}H_{15}BrN_2O$: C, 58.02; H, 4.56; N, 8.46. Found: C, 58.19; H, 4.58; N, 8.41.

2-(4-Bromophenyl)-5-methylpyrazolidin-3-one (4dd)
Light brown powder; mp 81–83 °C.

IR (KBr): 3415, 3128, 1689, 1487, 1401 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, *J* = 8.9 Hz, 2 H, ArH), 7.43 (d, *J* = 8.8 Hz, 2 H, ArH), 4.48 (br s, 1 H, NH), 3.76 (dd, *J* = 6.8, 14.1 Hz, 1 H, H-5), 2.81 (dd, *J* = 6.4, 16.2 Hz, 1 H, H-4a), 2.42 (dd, *J* = 8.4, 16.4 Hz, 1 H, H-4b), 1.33 (d, *J* = 6.4 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 172.2, 138.1, 131.6, 119.8, 116.7, 51.1, 42.6, 18.5.

MS (ESI$^+$): *m*/*z* (%) = 279 (21.3, [M(^{81}Br) + Na]$^+$), 277 (100, [M(^{79}Br) + Na]$^+$), 257 (28.1, [M(^{81}Br) + H]$^+$), 255 (74.9, [M(^{79}Br) + H]$^+$ or [M(^{81}Br) – H]$^+$), 253 (50.0, [M(^{79}Br) – H]$^+$).

Anal. Calcd for $C_{10}H_{11}BrN_2O$: C, 47.08; H, 4.35; N, 10.98. Found: C, 46.94; H, 4.31; N, 11.03.

Acknowledgment

We thank the Department of Science and Technology, Zhejiang Province (Project No. 2006C11262) and the National Natural Science Foundation of China (No. 20802070) for financial support.

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(14) Crystal data for **4aa**: $C_{16}H_{16}N_2O_2$, M_r = 268.31, colorless crystal (0.41 × 0.15 × 0.05 mm), monoclinic, space group $P2_1/c$, a = 8.6609(4) Å, b = 6.0272(3) Å, c = 27.1719(13) Å, β = 105.494(4)°, V = 1366.85(11) Å^3, Z = 4, T = 296(2) K, ρ_{calcd} = 1.304 g·cm^{-3}, $F(000)$ = 568, μ = 0.087 mm^{-1}, $R1$ = 0.0594, $wR2$ = 0.1527 and S = 1.048 for 1810 reflections with $I > 2\sigma(I)$. The structure was solved by direction methods and difference Fourier syntheses. Nonhydrogen atoms were refined anisotropically, and all hydrogen atoms were placed at ideal positions and allowed to ride. The crystallographic calculations were conducted using the SHELXL-97 programs. Detail crystallographic data of **4aa** have been deposited at Cambridge Crystallographic Data Center under CCDC-687432. These data can be obtained free of charge from www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; e-mail: deposit@ccdc.cam.ac.uk.

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