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# Synthesis of Functionalized 2-Aminopyrroles by Lewis Acid Catalyzed Ring-opening of 1,1,2,3-Tetrasubstituted Cyclopropanes with Arylamines

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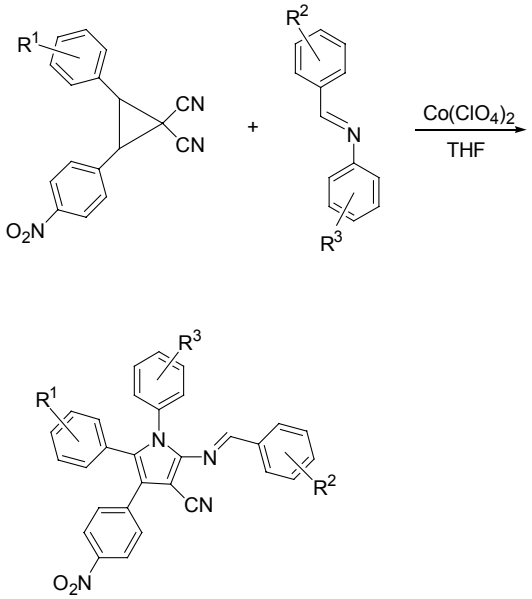
Under the catalysis of Lewis acid $Co(ClO_4)_2$ the reaction of the sterically hindered 1,1,2,3-tetrasubstituted cyclopropanes with arylamines in refluxing THF gave the functionalized 2-aminopyrroles with sequential ring-opening of cyclopropane, nucleophilic substitution, nucleophilic addition of cyano group and recyclization processes.

**Keywords** cyclopropane, pyrrole, ring-opening reaction, catalysis, domino reaction

## Introduction

The ring-opening reactions of functionalized cyclopropane have proven to be very valuable tool in synthetic organic chemistry.[1,2] The presence of both electron-donating groups and electron-withdrawing groups in cyclopropane core produces a synergistic electron 'push-pull' relationship and thus increases the reactivity of cyclopropane.[3,4] Although the ring-opening reactions of activated cyclopropane derivatives with nucleophiles, double bonds, triple bonds and 1,3-dipoles are well established,[5-9] most of the reported works were focused on using donor-acceptor cyclopropanes having at least one unsubstituted methylene unit in order to avoid sterically hindrance and to finish the ring-opening of cyclopropyl moiety in mild condition.[10-15] The reactivity of the sterically hindered polysusbstituted cyclopropanes, in which no unsubstituted methylene unit exists, was rarely investigated.[16-20] Our group recently found that Lewis acid catalyzed reactions of 1,1-dicyano-2,3-diarylcyclopropanes with aromatic imines give the novel polysubstituted pyrrole-3-carbonitriles bearing an 2-arylideneimino group (Scheme 1).[21] Even there have been several reports about Lewis acid-catalyzed reactions of imines with the activated cyclopropane to form pyrrolidine derivatives.[22-26] In our reaction the combination of ring-opening of cyclopropane with addition of cyano group produced new reaction pattern. This protocol not only provids an effective methodology for the preparation of functionalized pyrroles, but also opens a broad way for employing the sterically hindered cyclopropane to develop new ring-opening reaction. The investigation of reaction mechanism indicated that the aromatic imine did not react with cyclopropane directly, while it firstly decomposed to aldehyde and amine, and then the generated amine attacked the cyclopropyl ring to finish the reaction. Thus it is logical to examine the reactivity of amine with sterically hindered polysusbstituted cyclopropanes and to explore the generality and scope of this domino reaction. Herein we wish to report the results on the ring-opening reactions of 1,1,2,3-tetrasubstituted cyclopropanes with aromatic amines under Lewis acid catalysis and the syntheses of the functionalized 2-aminopyrrole deivatives.

**Scheme 1** Reaction of cyclopropane with aromatic imine

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## Experimental

All reactions were monitored by TLC. Melting points were taken on a hot-plate microscope apparatus. IR spectra were obtained on a Bruker Tensor 27 spectrometer (KBr disc). NMR spectra were recorded with a Bruker AV-600 spectrometer with DMSO-$d_6$ as solvent and TMS as internal standard (600 and 150 MHz for $^1$H and $^{13}$C NMR spectra, respectively). Elemental analyses were obtained on Thermo Flash 2000 instrument. HPLC/MS were measured at Fennigan LCQ Deca XP MAX instrument. The substituted cyclopropanes were synthesized by our previous reported method.[27] Arylamines and other reagents are commercial reagents and used as received. Solvents were purified by standard techniques.

**General procedure for the preparation of polysubstituted 2-aminopyrroles via reactions of cyclopropanes with arylamines**

A mixture of 1,1-dicyano-2,3-diarylcyclopropane (2.0 mmol) and arylamine (2.0 mmol) and $Co(ClO_4)_2$ (0.2 mmol) in 20 mL THF was refluxed for about 36 h (TLC analysis). After cooling the reaction was quenched with water and extracted with methylene dichloride. The solvent was evaporated under reduced pressure. The residue was purified by thin-layer chromatography ($SiO_2$) with light petroleum and ethyl acetate ($V/V$=3/1) as developing reagent to give the pure product for analysis.

**2-Amino-5-*p*-methoxyphenyl-1-*p*-methylphenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3a)** Yellow solid, yield 63%, m.p. 203—204 ℃; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.09 (d, $J$=8.4 Hz, 2H, ArH), 7.41 (d, $J$=8.4 Hz, 2H, ArH), 7.19 (d, $J$=8.4 Hz, 2H, ArH), 7.02 (d, $J$=8.4 Hz, 2H, ArH), 6.82 (d, $J$=7.8 Hz, 2H, ArH), 6.66 (d, $J$=7.8 Hz, 2H, ArH), 4.16 (bs, 2H, $NH_2$), 3.73 (s, 3H, $OCH_3$), 2.36 (s, 3H, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 159.2, 147.3, 146.0, 142.5, 140.6, 139.4, 132.2, 132.1, 130.5, 129.2, 128.0, 126.9, 123.6, 122.1, 118.2, 114.0, 55.1, 21.2; IR (KBr) $v$: 3429 (m), 3325 (m), 3226 (w), 2928 (w), 2200 (m), 1631 (m), 1561 (m), 1509 (s), 1334 (s), 1248 (m), 1178 (w), 1106 (m), 1032 (w), 840 (m) cm$^{-1}$. Anal. calcd for $C_{25}H_{20}N_4O_3$: C 70.74, H 4.75, N 13.20; found C 70.58, H 5.19, N 12.86. MS (ESI$^-$) $m/z$: 423.60.

**2-Amino-1,5-di(*p*-methylphenyl)-4-*p*-nitrophenylpyrole-3-carbonitrile (3b)** Yellow solid, yield 71%, m.p. 214—216 ℃; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.08 (d, $J$=8.8 Hz, 2H, ArH), 7.41 (d, $J$=8.8 Hz, 2H, ArH), 7.19 (d, $J$=8.1 Hz, 2H, ArH), 7.03 (d, $J$=8.1 Hz, 2H, ArH), 6.92 (d, $J$=7.9 Hz, 2H, ArH), 6.79 (d, $J$=7.9 Hz, 2H, ArH), 3.73 (d, $J$=7.0 Hz, 1H, NH), 3.71 (d, $J$=7.0 Hz, 1H, NH), 2.36 (s, 3H, $CH_3$), 2.25 (s, 3H, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 147.3, 146.0, 140.6, 139.4, 137.8, 132.1, 130.6, 130.5, 129.3, 129.2, 128.0, 127.0, 126.9, 123.6, 118.6, 117.4, 212 (2C); IR (KBr) $v$: 3451 (w), 3338 (m), 2198 (m), 2611 (m), 1557 (m), 1508 (s), 1338 (s), 1176 (w), 1107 (m), 822 (w), 750 (w) cm$^{-1}$. Anal. calcd for $C_{25}H_{20}N_4O_2$: C 73.51, H 4.94, N 13.72; found C 73.36, H 5.30, N 13.61. MS (ESI$^-$) $m/z$: 407.33.

**2-Amino-5-*p*-*t*-butylphenyl-1-*p*-methylphenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3c)** Yellow solid, yield 68%, m.p. 280—282 ℃; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.08 (d, $J$=8.7 Hz, 2H, ArH), 7.42 (d, $J$=8.7 Hz, 2H, ArH), 7.19 (d, $J$=7.8 Hz, 2H, ArH), 7.12 (d, $J$=7.8 Hz, 2H, ArH), 7.03 (d, $J$=7.8 Hz, 2H, ArH), 6.82 (d, $J$=7.8 Hz, 2H, ArH), 2.37 (s, 3H, $CH_3$), 1.23 (s, 9H, $C(CH_3)_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 150.0, 145.1, 139.6, 138.3, 131.2, 130.7, 130.6, 129.4, 129.3, 128.6, 128.3, 127.0, 125.8, 124.3, 122.6, 119.0, 33.6, 30.2, 20.2; IR (KBr) $v$: 3433 (s), 3337 (m), 2960 (w), 2205 (m), 1637 (m), 1561 (w), 1512 (s), 1342 (s), 1265 (w), 1106 (w), 831 (m) cm$^{-1}$. Anal. calcd for $C_{28}H_{26}N_4O_2$: C 74.65, H 5.82, N 12.44; found C 74.53, H 6.25, N 12.07. MS (ESI+) $m/z$: 450.47.

**2-Amino-5-*p*-bromophenyl-1-*p*-methylphenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3d)** Yellow solid, yield 80%, m.p. 221—222 ℃. $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.12 (d, $J$=8.8 Hz, 2H, ArH), 7.41 (d, $J$=8.8 Hz, 2H, ArH), 7.25 (d, $J$=8.5 Hz, 2H, ArH), 7.22 (d, $J$=8.5 Hz, 2H, ArH), 7.03 (d, $J$=8.2 Hz, 2H, ArH), 6.76 (d, $J$=8.2 Hz, 2H, ArH), 2.38 (s, 3H, $CH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 146.6, 145.3, 139.1, 138.8, 136.1, 131.2, 130.9, 130.8, 130.7, 130.5, 129.9, 129.8, 129.7, 129.5, 128.5, 128.0, 126.9, 126.8, 124.2, 122.8, 122.0, 121.2, 118.5, 20.2; IR (KBr) $v$: 3447 (w), 3332 (m), 3229 (w), 2202 (m), 1631 (m), 1557 (m), 1513 (s), 1340 (s), 1170 (w), 1108 (m), 1014 (w), 824 (m) cm$^{-1}$. Anal calcd for $C_{24}H_{17}BrN_4O_2$: C 60.90, H 3.62, N 11.84; found C 60.72, H 3.70, N 11.47. MS (ESI$^-$) $m/z$: 472.73.

**2-Amino-1,5-di(*p*-methoxyphenyl)-4-*p*-nitrophenyl pyrrole-3-carbonitrile (3e)** Yellow solid, yield 59%, m.p. 216—218 ℃; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.08 (d, $J$=8.9 Hz, 2H, ArH), 7.42 (d, $J$=8.9 Hz, 2H, ArH), 7.08 (d, $J$=8.8 Hz, 2H, ArH), 6.93 (d, $J$=8.8 Hz, 2H, ArH), 6.89 (d, $J$=8.9 Hz, 2H, ArH), 6.79 (d, $J$=8.8 Hz, 2H, ArH), 3.81 (s, 3H, $OCH_3$), 3.73 (s, 3H, $OCH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 159.9, 147.5, 146.0, 140.7, 137.8, 130.7, 130.4, 129.5, 129.3, 129.2, 129.1, 127.2, 127.1, 127.0, 123.6, 123.3, 118.5, 115.3, 115.0, 55.6, 55.5; IR (KBr) $v$: 3425 (m), 3329 (m), 3231 (w), 2922 (w), 2200 (m), 1634 (m), 1559 (m), 1509 (s), 1334 (s), 1247 (m), 1107 (m), 1027 (w), 833 (m) cm$^{-1}$. Anal. calcd for $C_{24}H_{20}N_4O_4$: C 68.17, H 4.58, N 12.72; found C 67.78, H 4.88, N 12.45. MS (ESI$^+$) $m/z$: 441.45.

**2-Amino-1-*p*-methoxyphenyl-4-*p*-nitrophenyl-5-phenylpyrrole-3-carbonitrile (3f)** Yellow solid, yield 76%, m.p. 190—192 ℃; $^1$H NMR (600 MHz, $CDCl_3$) $\delta$: 8.07 (d, $J$=8.4 Hz, 2H, ArH), 7.42 (d, $J$=8.4 Hz, 2H, ArH), 7.17 (t, $J$=7.1 Hz, 1H, ArH), 7.12 (t, $J$=7.1 Hz, 2H, ArH), 7.08 (d, $J$=8.5 Hz, 2H, ArH), 6.92 (d, $J$=7.3 Hz, 2H, ArH), 6.88 (d, $J$=8.4 Hz, 2H, ArH), 3.80 (s, 3H, $OCH_3$); $^{13}$C NMR (150 MHz, $CDCl_3$) $\delta$: 159.9, 146.1, 140.4, 132.4, 130.8, 130.5, 130.0, 129.4, 129.3

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(2C), 128.7, 128.5, 127.9, 127.5, 127.1, 126.9, 123.7, 123.3, 118.8, 115.4, 115.0, 55.5; IR (KBr) *v*: 3419 (m), 3223 (w), 2205 (m), 1632 (m), 1557 (m), 1511 (s), 1340 (s), 1249 (m), 1177 (w), 1109 (w), 1029 (w), 846 (m), 703 (w) $cm^{-1}$. Anal. calcd for $C_{24}H_{18}N_4O_3$: C 70.23, H 4.42, N 13.65; found C 79.42, H 4.64, N 13.38. MS ($ESI^-$) *m*/*z*: 409.60.

**2-Amino-1-*p*-chlorophenyl-5-*p*-methylphenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3g)** Yellow solid, yield 66%, m.p. 226—228 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 8.08 (d, *J*=8.6 Hz, 2H, ArH), 7.41 (d, *J*=8.6 Hz, 2H, ArH), 7.37 (d, *J*=8.5 Hz, 2H, ArH), 7.11 (d, *J*=8.5 Hz, 2H, ArH), 6.95 (d, *J*=7.8 Hz, 2H, ArH), 6.78 (d, *J*=7.8 Hz, 2H, ArH), 4.23 (bs, 2H, $NH_2$), 2.27 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 146.9, 146.2, 140.2, 138.2, 135.3, 133.4, 130.6, 130.1, 129.6, 129.4, 129.3 (3C), 129.0, 126.6, 123.7, 119.0, 21.2; IR (KBr) *v*: 3428 (m), 3316 (m), 3226 (m), 2206 (m), 1635 (m), 1561 (m), 1505 (s), 1340 (s), 1103 (m), 835 (m) $cm^{-1}$. Anal. calcd for $C_{24}H_{17}ClN_4O_2$: C 67.21, H 4.00, N 13.06; found C 66.85, H 4.47, N 12.73. MS ($ESI^+$) *m*/*z*: 429.33.

**2-Amino-1-*p*-chlorophenyl-5-*m*-chlorophenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3h)** Yellow solid, yield 55%, m.p. 197—198 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 8.13 (d, *J*=7.6 Hz, 2H, ArH), 7.42 (s, 3H, ArH), 7.19 (d, *J*=7.8 Hz, 1H, ArH), 7.13—7.08 (m, 3H, ArH), 6.89 (s, 1H, ArH), 6.79 (d, *J*=7.3 Hz, 1H, ArH); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 147.3, 146.5, 139.5, 135.7, 134.5, 132.9, 131.4, 130.6, 130.4, 129.9, 129.5, 129.4 (2C), 128.9, 128.4, 124.6, 123.9, 123.6, 120.2, 58.5, 18.4; IR (KBr) *v*: 3417 (s), 3324 (s), 3226 (m), 2201 (m), 1712 (m), 1637 (m), 1596 (m), 1559 (m), 1497 (w), 1339 (s), 1227 (w), 1096 (w), 1014 (w), 834 (w) $cm^{-1}$. Anal. calcd for $C_{23}H_{14}Cl_2N_4O_2$: C 61.49, H 3.14, N 12.47; found C 61.35, H 3.52, N 12.27. MS ($ESI^-$) *m*/*z*: 449.29.

**2-Amino-1-phenylmethyl-5-*p*-methylphenyl-4-*p*-nitrophenylpyrrole-3-carbonitrile (3i)** Yellow solid, yield 50%, m.p. 208—210 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 8.05 (d, *J*=8.6 Hz, 2H, ArH), 7.38 (t, *J*=8.5 Hz, 4H, ArH), 7.33 (t, *J*=7.3 Hz, 1H, ArH), 7.12 (d, *J*=7.8 Hz, 2H, ArH), 7.07 (d, *J*=7.8 Hz, 2H, ArH), 7.03 (d, *J*=7.8 Hz, 2H, ArH), 4.91 (s, 2H, $CH_2$), 3.96 (s, 2H, $NH_2$), 2.35 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 150.5, 149.9, 144.4, 143.1, 139.6, 134.9, 134.8, 133.9, 133.6, 133.4, 132.9, 132.2, 131.7, 130.9, 129.8, 129.5, 127.9, 127.6, 122.6, 118.7, 51.0, 25.3; IR (KBr) *v*: 3447 (w), 3356 (m), 2200 (m), 1628 (m), 1557 (m), 1512 (s), 1342 (s), 1110 (w), 864 (w), 746 (w) $cm^{-1}$. Anal calcd for $C_{25}H_{20}N_4O_2$: C 73.51, H 4.94, N 13.72; found C 73.26, H 5.29, N 13.64. MS ($ESI^-$) *m*/*z*: 407.47.

**2-Amino-1-*p*-naphthyl-4-*p*-nitrophenyl-5-phenylpyrrole-3-carbonitrile (3j)** Yellow solid, yield 82%, m.p. 214—216 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 8.11 (d, *J*=8.6 Hz, 2H, ArH), 7.91 (d, *J*=8.0 Hz, 2H, ArH), 7.61—7.55 (m, 3H, ArH), 7.49 (d, *J*=8.6 Hz, 2H, ArH), 7.45 (t, *J*=7.5 Hz, 1H, ArH), 7.34 (d, *J*=7.2 Hz, 1H, ArH), 7.04 (t, *J*=7.3 Hz, 1H, ArH), 6.96 (t, *J*=7.8 Hz, 2H, ArH), 6.86 (d, *J*=7.8 Hz, 2H, ArH), 4.07 (bs, 2H, $NH_2$); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 147.9, 146.2, 140.3, 134.3, 131.0, 130.5, 130.3, 129.9, 129.3, 128.7, 128.3, 128.2, 128.0, 127.9, 127.7, 127.3, 125.3, 123.7, 122.3, 119.5; IR (KBr) *v*: 3411 (w), 3359 (w), 3228 (w), 3059 (w), 2202 (m), 1600 (m), 1560 (m), 1508 (m), 1337 (s), 1108 (m), 854 (w) $cm^{-1}$. Anal. calcd for $C_{27}H_{18}N_4O_2$: C 75.34, H 4.21, N 13.02; found C 75.27, H 4.50, N 12.75. MS ($ESI^+$) *m*/*z*: 431.05.

**2-Amino-1,5-di(*p*-methylphenyl)-4-phenacylpyrrole-3-carbonitrile (4a)** Light yellow solid, yield 74%, m.p. 204—206 ℃; $^1H$ NMR (600 MHz, DMSO-$d_6$) *δ*: 7.18—6.93 (m, 7H, ArH), 6.48 (s, 4H, ArH), 5.64 (s, 2H, ArH), 3.10 (s, 2H, $NH_2$), 2.04 (s, 3H, $CH_3$), 1.79 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, DMSO-$d_6$) *δ*: 190.1, 149.2, 136.7, 131.9, 131.6, 130.5, 129.9, 128.9, 128.6, 128.5, 127.9, 127.6, 126.9, 20.6, 20.5; IR (KBr) *v*: 3353 (m), 3196 (s), 2216 (s), 1614 (s), 1571 (s), 1514 (m), 1495 (m), 1469 (m), 1396 (m), 1352 (w), 1289 (m), 1190 (s), 1076 (m), 1020 (w), 928 (s), 811 (s) $cm^{-1}$. Anal. calcd for $C_{26}H_{21}N_3O$: C 79.77, H 5.41, N 10.73; found C 79.52, H 5.65, N 10.80. MS ($ESI^+$) *m*/*z*: 392.59.

**2-Amino-5-*p*-chlorophenyl-1-*p*-methylphenyl-4-phenacylpyrrole-3-carbonitrile (4b)** Light yellow solid, yield 70%, m.p. 276—278 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 7.63 (d, *J*=7.2 Hz, 2H, ArH), 7.35 (s, 1H, ArH), 7.20 (s, 4H, ArH), 7.02 (d, *J*=8.4 Hz, 2H, ArH), 6.92 (d, *J*=9.0 Hz, 2H, ArH), 6.81 (d, *J*=8.4 Hz, 2H, ArH), 4.25 (s, 2H, $NH_2$), 2.36 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 190.3, 139.9, 137.9, 134.0, 132.2, 131.9, 130.7, 129.5, 128.0, 127.9, 127.8, 100.0, 21.2; IR (KBr) *v*: 3315 (w), 3228 (w), 2211 (s), 1624 (s), 1569 (s), 1538 (m), 1514 (m), 1477 (m), 1398 (s), 1354 (s), 1266 (m), 1175 (m), 1085 (m), 926 (s), 818 (m) $cm^{-1}$. Anal. calcd for $C_{25}H_{18}ClN_3O$: C 72.90, H 4.40, N 10.20; found C 72.66, H 4.81, N 10.46. MS ($ESI^+$) *m*/*z*: 412.64.

**2-Amino-1-*p*-methylphenyl-4-phenacyl-5-phenylpyrrole-3-carbonitrile (4c)** Light yellow solid, yield 60%, m.p. 216—218 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) *δ*: 7.60 (d, *J*=7.2 Hz, 2H, ArH), 7.33 (s, 1H, ArH), 7.28 (d, *J*=7.8 Hz, 1H, ArH), 7.18 (d, *J*=8.4 Hz, 2H, ArH), 7.13 (b, 2H, ArH), 7.03 (d, *J*=8.4 Hz, 2H, ArH), 6.98 (s, 1H, ArH), 6.92 (b, 2H, ArH), 6.86 (d, *J*=7.2 Hz, 2H, ArH), 4.25 (s, 2H, $NH_2$), 2.34 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) *δ*: 190.5, 147.3, 139.6, 138.0, 132.9, 131.9, 131.7, 130.8, 130.5, 129.5, 128.0, 127.8, 127.6, 120.4, 21.2; IR (KBr) *v*: 3057 (m), 3029 (m), 2924 (m), 2209 (s), 1624 (w), 1538 (m), 1512 (m), 1473 (m), 1394 (m), 1071 (m), 925 (s), 836 (m), 811 (m) $cm^{-1}$. Anal. calcd for $C_{25}H_{19}N_3O$: C 79.55, H 5.07, N 10.13; found C 79.22, H 5.42, N 9.84. MS ($ESI^+$) *m*/*z*: 378.30.

**2-Amino-5-*p*-fluorophenyl-1-*p*-methylphenyl-4-phenacylpyrrole-3-carbonitrile (4d)** Light yellow solid, yield 75%, m.p. 265—267 ℃; $^1H$ NMR (600 MHz, DMSO-$d_6$) *δ*: 7.62 (d, *J*=7.2 Hz, 2H, ArH), 7.33 (s, 1H, ArH), 7.19 (m, 4H, ArH), 7.02 (d, *J*=8.4 Hz, 2H,

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ArH), 6.86 (s, 2H, ArH), 6.64 (s, 2H, ArH), 4.23 (b, 2H, $NH_2$), 2.36 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, DMSO-$d_6$) $\delta$: 189.9, 160.4, 149.4, 138.5, 138.1, 133.0, 132.9, 131.5, 130.0, 128.9, 127.6, 126.3, 119.7, 116.5, 114.3, 114.1, 20.6; IR (KBr) $v$: 3226 (m), 3193 (m), 2214 (s), 1642 (m), 1610 (m), 1570 (m), 1515 (m), 1469 (m), 1257 (m), 1189 (s), 1074 (m), 930 (s), 848 (m) $cm^{-1}$. Anal. calcd for $C_{25}H_{19}FN_3O$: C 75.93, H 4.59, N 10.63; found C 79.78, H 4.61, N 10.27. MS ($ESI^+$) $m/z$: 397.04.

**2-Amino-5-*p*-fluorophenyl-1-*p*-methylphenyl-4-(piperidine-4-carbonyl)pyrrole-3-carbonitrile (4e)** Light yellow solid, yield 77%; m.p. 235—236 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$: 7.21 (s, 2H, ArH), 7.03 (s, 4H, ArH), 6.86 (s, 2H, ArH), 3.61 (s, 2H, $NCH_2$), 3.23 (s, 2H, $NCH_2$), 2.37 (s, 3H, $CH_3$), 1.51 (b, 4H, $2CH_2$), 1.25—1.12 (m, 2H, $CH_2$); IR (KBr) $v$: 3437 (m), 3314 (w), 2935 (w), 2205 (m), 1623 (s), 1558 (m), 1505 (m), 1443 (m), 1228 (w), 847 (w) $cm^{-1}$. Anal. calcd for $C_{24}H_{23}FN_4O$: C 71.62, H 5.76, N 13.92; found C 71.52, H 6.17, N 13.66.

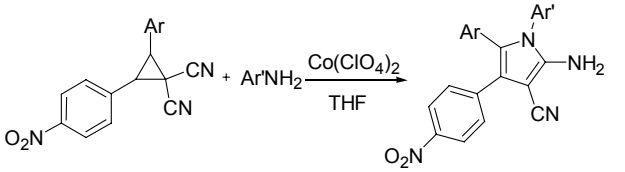
**2-Amino-5-*p*-fluorophenyl-1-*p*-methylphenyl-4-(morpholine-4-carbonyl)pyrrole-3-carbonitrile (4f)** Light yellow solid, yield 68%, m.p. 202 ℃; $^1H$ NMR (600 MHz, $CDCl_3$) $\delta$: 7.21 (d, $J$=7.9 Hz, 2H, ArH), 7.02 (q, $J$=8.6 Hz, 4H, ArH), 6.88 (t, $J$=8.6 Hz, 2H, ArH), 3.64—3.25 (m, 10H, $NH_2$, $2CH_2CH_2$), 2.37 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, $CDCl_3$) $\delta$: 164.1, 163.0, 161.3, 147.0, 139.6, 131.8, 131.2, 131.1, 130.7, 127.8, 125.9, 125.2, 115.8, 115.7, 115.6, 115.5, 72.8, 64.4, 58.4, 21.2, 18.4; IR (KBr) $v$: 3414 (m), 3319 (s), 2855 (m), 2209 (s), 1609 (s), 1505 (s), 1477 (m), 1363 (w), 1270 (m), 1231 (m), 1115 (m), 852 (m), 805 (m) $cm^{-1}$. Anal. calcd for $C_{23}H_{21}FN_4O_2$: C 68.30, H 5.23, N 13.85; found C 68.12, H 5.37, N 13.50. MS ($ESI^+$) $m/z$: 405.87.

**2-Amino-5-*p*-bromophenyl-1-*p*-methylphenyl-4-(morpholine-4-carbonyl)pyrrole-3-carbonitrile (4g)** Light yellow solid, yield 54%, m.p. 286—288 ℃; $^1H$ NMR (600 MHz, DMSO-$d_6$) $\delta$: 7.57 (d, $J$=8.6 Hz, 2H, ArH), 7.44 (d, $J$=8.6 Hz, 2H, ArH), 7.18—7.11 (m, 4H, ArH), 3.72—3.32 (m, 10H, $NH_2$, $CH_2CH_2$), 2.25 (s, 3H, $CH_3$); $^{13}C$ NMR (150 MHz, DMSO-$d_6$) $\delta$: 167.9, 167.5, 165.4, 140.8, 140.0, 139.9, 139.5, 136.2, 136.1, 134.8, 134.6, 134.5, 128.5, 126.8, 126.7, 121.0, 70.7, 69.5, 58.8, 52.3, 50.5, 25.6; IR (KBr) $v$: 3449 (m), 3310 (s), 2173 (s), 1655 (s), 1628 (s), 1541 (s), 1489 (m), 1439 (m), 1396 (w), 1274 (m), 1219 (m), 1116 (m), 1074 (m), 1011 (m), 969 (m), 825 (m) $cm^{-1}$. Anal. calcd for $C_{23}H_{21}BrN_4O_2$: C 59.36, H 4.55, N 12.04; found C 59.27, H 4.80, N 11.75. MS ($ESI^+$) $m/z$: 466.84.

## Results and Discussion

According to the previously established reactions for the reactions of imines with polysubstituted cyclopropanes,[21] a THF solution of 1,1-dicyano-2,3-diarylcyclopropane (2.0 mmol) and *p*-toluidine (2.0 mmol) in the presence of $Co(ClO_4)_2$ (0.2 mmol) as catalyst was heated to reflux for about 36 h. After work up, the desired funationalized 2-aminopyrrole **3a** was obtained in 63% yield. The structure of **3a** is very similar to the related reaction product of imine with cyclopropane,[21] which clearly indicated that arylamine could replace imine as a nucleophilic reagent to cause the ring-opening of polysubstituted cyclopropane. Then the generality of the reaction was evaluated using various arylamines and 1,1-dicyano-2,3-diaryl cyclopropanes. The results of the reaction were listed in Table 1. 1,1-Dicyano-2,3-diarylcyclopropanes having different kinds of groups such as alkyl, alkoxyl, chloro and bromo substituted phenyl groups were used in reactions, from which polysubstituted 2-aminopyrroles **3a**—**3o** were obtained in good yields (55%—82%). On the other hand arylamines bearing electron-donating alkyl, methoxyl groups gave relatively higher yields of product than that of *p*-chloroaniline. Under this reaction conditions *m*-nitro- and *p*-nitroanilines did not show any reactivity and no desired products were separated from their reactions, which might be due to the much weak nucleophilic ability of nitroaniline. Benzylamine and $\alpha$-naphthylamine also gave satisfactory yields of products (Table1, Entries 9—10). The structures of the prepared functionalized 2-aminopyrroles **3a**—**3j** were fully characterized by $^1H$ and $^{13}C$ NMR, MS, IR spectra, and were further confirmed by single-crystal studies performed for the representative compounds **3a** (Figure 1) and **3g** (Figure 2).

**Table 1** Synthesis of polysubstituted 2-aminopyrroles **3a**—**3j**




| Entry | Comp. | Ar | Ar' | Yield/% |
|---|---|---|---|---|
| 1 | **3a** | *p*-$CH_3OC_6H_4$ | *p*-$CH_3C_6H_4$ | 63 |
| 2 | **3b** | *p*-$CH_3C_6H_4$ | *p*-$CH_3C_6H_4$, | 71 |
| 3 | **3c** | *p*-$(CH_3)_3CC_6H_4$ | *p*-$CH_3C_6H_4$ | 68 |
| 4 | **3d** | *p*-$BrC_6H_4$ | *p*-$CH_3C_6H_4$ | 80 |
| 5 | **3e** | *p*-$CH_3OC_6H_4$ | *p*-$CH_3OC_6H_4$ | 59 |
| 6 | **3f** | $C_6H_5$ | *p*-$CH_3OC_6H_4$ | 76 |
| 7 | **3g** | *p*-$CH_3C_6H_4$ | *p*-$ClC_6H_4$ | 66 |
| 8 | **3h** | *m*-$ClC_6H_4$ | *p*-$ClC_6H_4$ | 55 |
| 9 | **3i** | *p*-$CH_3C_6H_4$ | $C_6H_5CH_2$ | 50 |
| 10 | **3j** | $C_6H_5$ | $\alpha$-$C_{10}H_7$ | 82 |

To extend the utility of this reaction, the reactivity of other polysubstituted cyclopropanes was also explored. Under similar reaction conditions 1,1-dicyanocyclopropanes with phenacyl group (Table 2, Entries 1—4), piperidine-4-carbonyl and morphine-4-carnonyl groups

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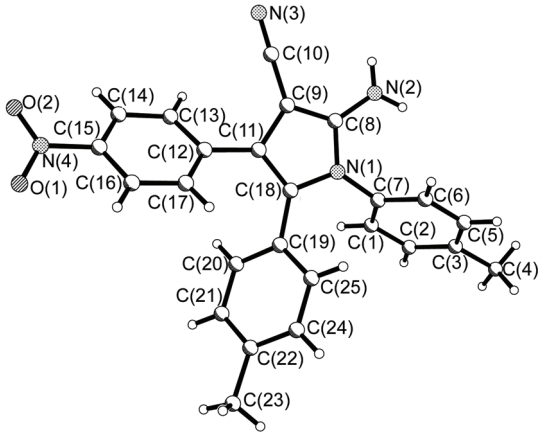



**Figure 1** Molecular structure of compound **3b**.

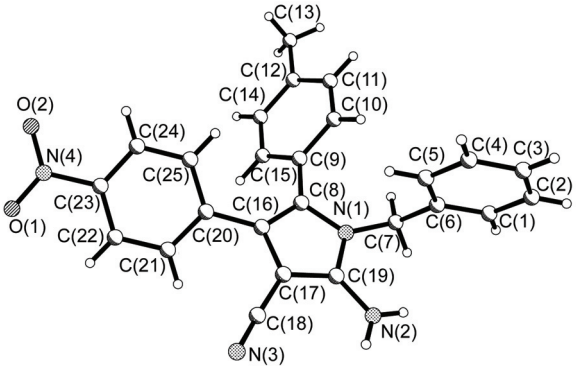
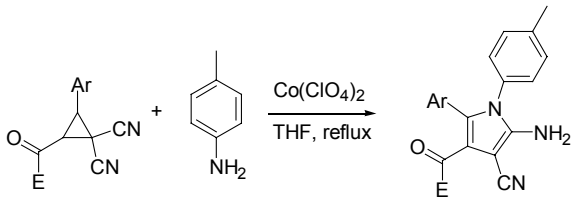



**Figure 2** Molecular structure of compound **3g**.

(Table 2, Entries 5—7) reacted smoothly with *p*-toluidine to give the more functionalized 2-aminopyrrole derivatives **4a**—**4g** in good yields (Table 2). These results showed that this reaction is quite general and has a very broad substrate scope. It should be pointed out that there is no any ring-opening product observed when the polysubstituted cycloproanes in which one cyano group is replaced by an ester group were used in this reaction. The exact reasons of this are not very clear at present and more detailed works should be made in future.

To explain the formation mechanism of functionalized 2-aminopyrroles, we proposed a plausible reaction mechanism (Scheme 2) based on our previously established mechanism for the reaction of cyclopropanes with aromatic imine.[21] Firstly the cyclopropane ring underwent a heterolytic ring-cleavage to give a 1,3-zwitterionic intermediate (**A**) due to the combinatorial activation of aryl groups and two stronger electron-withdrawing cyano groups in cyclopropane **1** and the catalysis of Lewis acid $Co(ClO_4)_2$. Secondly the nucleophilic amine attracks the carbocation in intermediate (**A**) to give an adduct intermediate (**B**). Thirdly the intramolecular addition of the amino group to one of cyano group results in a ring intermediate (**C**), from which 2-aminodihydropyrrole (**D**) was formed by the imine-enamine tautomerization. At last, 2-aminodihydropyrrole (**D**) was dehydrogenated by heating in air to give

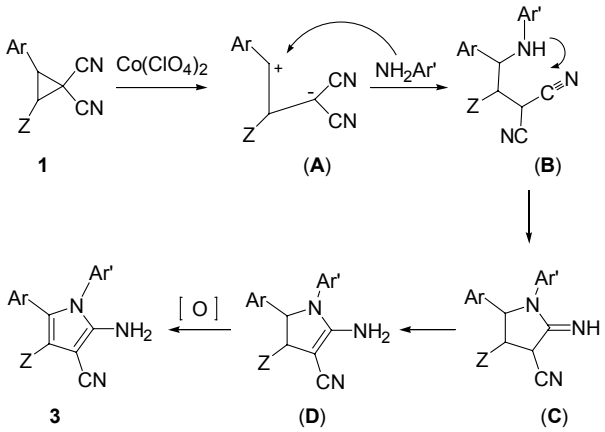
**Table 2** Synthesis of polysubstituted 2-aminopyrroles **4a**—**4g**




| Entry | Compd | Ar | E | Yield/% |
|---|---|---|---|---|
| 1 | **4a** | *p*-$CH_3C_6H_4$ | $C_6H_5$ | 74 |
| 2 | **4b** | *p*-$ClC_6H_4$ | $C_6H_5$ | 70 |
| 3 | **4c** | $C_6H_5$ | $C_6H_5$ | 60 |
| 4 | **4d** | *p*-$FC_6H_4$ | $C_6H_5$ | 75 |
| 5 | **4e** | *p*-$FC_6H_4$ | $N(CH_2)_5$ | 77 |
| 6 | **4f** | *p*-$FC_6H_4$ | $N(CH_2)_4O$ | 68 |
| 7 | **4g** | *p*-$BrC_6H_4$ | $N(CH_2)_4O$ | 54 |

the 2-aminopyrrole (**3**) as the separated product **3**. In this reaction mechanism a sequential process of ring-opening of cyclopropane, nucleophilic substitution, addition to cyano group and recyclization are observed.

**Scheme 2** The formation mechanism of 2-aminopyrrole




## Conclusions

In conclusion an efficient synthetic procedure for the functinalized 2-aminopyrroles was established by Lewis acid catalyzed ring-opening reaction of the sterically hindered cyclopropanes with arylamines. This protocol has advantages of mild reaction conditions, easily accessible starting material and easy purification of the products, which makes it a useful and attractive method for the synthesis of the polysubstituted pyrroles and also opens a brand way for employing the sterically hindered cyclopropane to design new ring-opening reaction. The potential uses of the reaction in synthetic and medicinal chemistry might be quite significant. Further expansion of the reaction scope and synthetic applications of this methodology are in progress in our laboratory.

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## Supplementary Information

Single crystal data for compounds **3b** (CCDC 865228) and **3g** (CCDC 865229) have been deposited in the Cambridge Crystallographic Data Center.

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