



## Intramolecular C–H insertion in ring-expanded *N*-heterocyclic carbenes

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### ABSTRACT

Mild heating of the ring-expanded *N*-heterocyclic carbenes 7-Mes and 6-Mes results in intramolecular insertion of the carbene into an *ortho*-methyl C–H bond. In the presence of traces of acid, the resulting products ring-open to afford *N*-alkyl indoles.

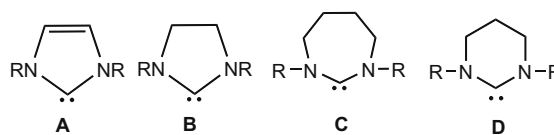
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*N*-Heterocyclic carbenes (NHCs) are a well-established class of compounds of considerable importance due to their roles as ligands in metal-mediated catalysis and as organocatalysts in their own right.<sup>1</sup> While the majority of studies have focused on the unsaturated and saturated five-membered ring species **A** and **B** (Scheme 1), the so-called ring-expanded carbenes that is, those containing seven- and six-membered rings, such as **C** and **D** have recently started to receive some attention.<sup>2</sup> These species display a significantly wider N–C–N angle than their five-membered counterparts, which in turn considerably increases their basicity.<sup>3</sup> We now report another remarkable difference with the observation that mild heating of the seven- and six-membered carbenes with *N*-mesityl substituents (7-Mes, **1**; 6-Mes, **2**; Scheme 2) leads to insertion of the carbene into one of its own *ortho*-methyl C–H bonds. Although such intramolecular C–H activation has been observed with unstable acyclic monoaminocarbenes, we believe it to be unknown for diaminocarbenes.<sup>4</sup> Indeed there is only one example of this class of carbenes reacting with non-acidic C–H bonds,<sup>5</sup> that being the low yielding insertion of a mixed *N*-Et/*N*-<sup>*i*</sup>Pr six-membered carbene into a methyl C–H bond of toluene.<sup>6</sup>

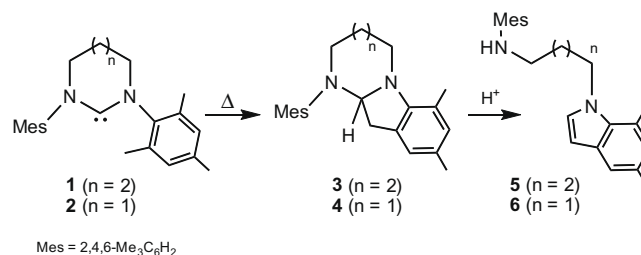
Substitution of the five-membered carbenes IMes and SIMes (Scheme 1: **A** and **B**, R = mesityl) into a range of ruthenium complexes, including Ru(PPh<sub>3</sub>)<sub>3</sub>(CO)H<sub>2</sub>, Ru(PPh<sub>3</sub>)<sub>3</sub>(CO)HX (X = F, Cl) and Ru(PPh<sub>3</sub>)<sub>3</sub>HCl has been previously described.<sup>7</sup> Efforts to react these same precursors with 7-Mes **1** at elevated temperatures failed to generate any Ru–NHC containing products but instead, in all cases, gave the C–H insertion product **3** (Scheme 2).<sup>8</sup> Further examination revealed that **3** could be formed by simply heating an in situ-generated solution of **1** by itself in benzene at 70 °C for 24 h.<sup>9</sup> Similarly, heating the six-membered ring carbene **2** at

70 °C gave the insertion product **4**, although the reaction proceeded a lot more slowly, requiring 72 h to go to completion.<sup>10</sup>

Proton NMR spectroscopy provided unequivocal evidence for the structures of **3** and **4** with the appearance of a doublet of doublets resonance for the unique aminal proton at the C2 position (**3**: δ 4.97; **4**: δ 4.87) and two doublets of doublets arising from the diastereotopic protons of the activated arm (**3**: δ 2.77, 2.62; **4**: δ 2.55, 2.46). In contrast to the <sup>1</sup>H NMR spectra of **1** and **2**, which display only two methyl signals, four and five methyl resonances were seen for **3** and **4**, respectively, consistent with the activation of one of the mesityl rings. The high frequency quaternary C2 resonances of **1** (δ 257.3) and **2** (δ 244.9) in the <sup>13</sup>C{<sup>1</sup>H} PENDANT

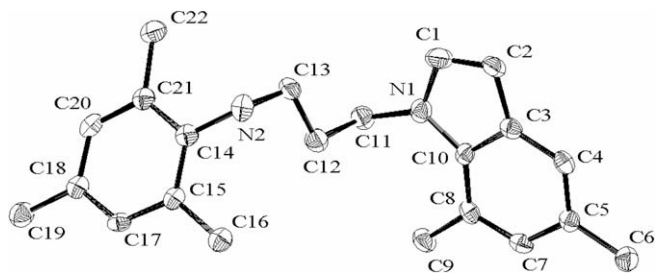


Scheme 1.



Scheme 2.

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**Figure 1.** ORTEP diagram of **6**. Ellipsoids are shown at 50% probability while all hydrogen atoms have been removed for clarity.

spectra were replaced by signals at  $\delta$  82.6 (**3**) and  $\delta$  81.8 (**4**) for the newly formed methine C2 carbon centres.<sup>11</sup> Despite a number of attempts, **3** and **4** could only be isolated as viscous oils, excluding any possibility of crystallographic characterisation.

Dissolution of either **3** or **4** in  $\text{CDCl}_3$  resulted in opening of the saturated seven- and six-membered rings to afford the *N*-alkyl indole products **5** and **6**.<sup>12</sup> Proton NMR spectra revealed the presence of two new high frequency doublets for both **5** ( $\delta$  6.86, 6.26) and **6** ( $\delta$  6.70, 6.51), characteristic of the indolyl protons. The structure of **6** was confirmed unequivocally by X-ray crystallography (Fig. 1) following the successful crystallisation of the compound from a concentrated MeOH solution at  $-78^\circ\text{C}$ .<sup>13</sup> Exposure of **3** and **4** to a silica gel column led to their conversion into **5** and **6**, which along with the chloroform result, suggests that traces of acid are likely to be responsible for the ring-opening reaction.<sup>14</sup>

Further work is necessary to elucidate fully the factors that govern the insertion chemistry seen for **1** and **2**. The order of basicity (7-NHC > 6-NHC > 5-NHC)<sup>15</sup> makes it very likely that this is an important contributor. In line with this, thermolysis of SIMes (Scheme 1: **B**, R = mesityl) at  $70^\circ\text{C}$  for 72 h resulted in no insertion chemistry. The proximity of the carbene lone pair of electrons to a C–H bond does not appear to be paramount given that the distance from the carbenic carbon to the nearest methyl substituent is in fact longer in the more reactive species **1** (3.348 Å) than it is in **2** (3.281 Å).<sup>3</sup> The same two structures show quite different CMe<sub>3</sub>–N–N–CMe<sub>3</sub> torsion angles, and it may be that these are altered upon generating the bicyclic ring systems present in **3** and **4**. It is also worth noting that upon changing the *N*-substituent on the seven-membered carbene from mesityl to 2,6-diisopropylphenyl, no activation of an isopropyl methyl C–H bond was observed even after heating at  $70^\circ\text{C}$  for 48 h, implying that it is unfavourable to form a second six- rather than five-membered ring.

In conclusion, we have demonstrated that increasing the ring size (5  $\rightarrow$  6  $\rightarrow$  7) in *N*-heterocyclic carbenes results in the unprecedented observation of intramolecular C–H insertion in a diamino-carbene. We believe that these results have ramifications not only in organocarbene chemistry, but also in the application of these ligands in transition metal catalysis.

## Acknowledgement

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## Supplementary data

Supplementary data (NMR numbering schemes for compounds **3–6**) associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2009.11.090.

## References and notes

- (a) Bourissou, D.; Guerret, O.; Gabba, F. P.; Bertrand, G. *Chem. Rev.* **2000**, *100*, 39; (b) Enders, D.; Balensiefer, T. *Acc. Chem. Res.* **2004**, *37*, 534; (c) *N-Heterocyclic*
- Nolan, S. P., Ed.; Wiley-VCH: Weinheim, 2006; (d) Glorius, F. *Top. Organomet. Chem.* **2007**, *21*; (e) Enders, D.; Niemeier, O.; Henseler, A. *Chem. Rev.* **2007**, *107*, 5606; (f) Hahn, F. E.; Jahnke, M. C. *Angew. Chem., Int. Ed.* **2008**, *47*, 3122.
- (a) Mayr, M.; Wurst, K.; Organia, K.-H.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 1256; (b) Yang, L. R.; Mayr, M.; Wurst, K.; Buchmeiser, M. R. *Chem. Eur. J.* **2004**, *10*, 5761; (c) Scarborough, C. C.; Grady, M. J. W.; Guzei, I. A.; Gandhi, B. A.; Bunel, E. E.; Stahl, S. S. *Angew. Chem., Int. Ed.* **2005**, *44*, 5269; (d) Bantu, B.; Wang, D. R.; Wurst, K.; Buchmeiser, M. R. *Tetrahedron* **2005**, *61*, 12145; (e) Rogers, M. M.; Wendlandt, J. E.; Guzei, I. A.; Stahl, S. S. *Org. Lett.* **2006**, *8*, 2257; (f) Iglesias, M.; Beetstra, D. J.; Stasch, A.; Horton, P. N.; Hursthouse, M. B.; Coles, S. J.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Organometallics* **2007**, *26*, 4800; (g) Scarborough, C. C.; Bergant, A.; Sazama, G. T.; Guzei, I. A.; Spencer, L. C.; Stahl, S. S. *Tetrahedron* **2009**, *65*, 5084; (h) Binobaid, A.; Iglesias, M.; Beetstra, D. J.; Kariuki, B.; Dervisi, A.; Fallis, I. A.; Cavell, K. J. *Dalton Trans.* **2009**, 7099.
- Iglesias, M.; Beetstra, D. J.; Knight, J. C.; Ooi, L. L.; Stasch, A.; Coles, S. J.; Male, L.; Hursthouse, M. B.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Organometallics* **2008**, *27*, 3279.
- (a) Goumri, S.; Leriche, Y.; Gornitzka, H.; Baceiredo, A.; Bertrand, G. *Chem. Eur. J. Inorg. Chem.* **1998**, 1539; (b) Solé, S.; Gornitzka, H.; Schoeller, W. W.; Bourissou, D.; Bertrand, G. *Science* **2001**, *292*, 1901; (c) Canac, Y.; Conejero, S.; Soleilhavoup, M.; Donnadieu, B.; Bertrand, G. *J. Am. Chem. Soc.* **2006**, *128*, 459; (d) Vignolle, J.; Asay, M.; Miqueu, K.; Bourissou, D.; Bertrand, G. *Org. Lett.* **2008**, *10*, 4299; (e) Vignolle, J.; Cattoën, X.; Bourissou, D. *Chem. Rev.* **2009**, *109*, 3333. While this manuscript was being refereed, there have been reports of intramolecular C–H insertion in a free diamidocarbene (Hudnall, T. W.; Bielawski, C. W. *J. Am. Chem. Soc.* **2009**, *131*, 16039) and a free abnormal *N*-heterocyclic carbene (Aldeco-Perez, E.; Rosenthal, A. J.; Donnadieu, B.; Parameswaran, P.; Frenking, G.; Bertrand, G. *Science* **2009**, *326*, 556).
- For examples of NHC insertion into acidic ( $\text{p}K_{\text{a}} \leq 25$ ) C–H bonds see: (a) Arduengo, A. J., III; Calabrese, J. C.; Davidson, F.; Dias, H. V. R.; Goerlich, J. R.; Krafczyk, R.; Marshall, W. J.; Tamm, M.; Schmutzler, R. *Helv. Chim. Acta* **1999**, *82*, 2348; (b) Korotkikh, N. I.; Ytayanenko, G. F.; Shvaika, O. P.; Pekhtereva, T. M.; Cowley, A. H.; Jones, J. N.; Macdonald, C. L. B. *J. Org. Chem.* **2003**, *68*, 5762; (c) Nyce, G. W.; Csihony, S.; Waymouth, R. M.; Hedrick, J. L. *Chem. Eur. J.* **2004**, *10*, 4073.
- Lloyd-Jones, G. C.; Alder, R. W.; Owen-Smith, G. J. *J. Chem. Eur. J.* **2006**, *12*, 5361.
- (a) Jazzar, R. F. R.; Macgregor, S. A.; Mahon, M. F.; Richards, S. P.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2002**, *124*, 4944; (b) Abdur-Rashid, K.; Fedorkiw, T.; Lough, A. J.; Morris, R. H. *Organometallics* **2004**, *23*, 86; (c) Dharmasena, U. L.; Foucault, H. M.; dos Santos, E. N.; Fogg, D. E.; Nolan, S. P. *Organometallics* **2005**, *24*, 1056; (d) Reade, S. P.; Mahon, M. F.; Whittlesey, M. K. *J. Am. Chem. Soc.* **2009**, *131*, 1847.
- A suspension of **1**·HBF<sub>4</sub> (528 mg, 1.25 mmol) and KN(SiMe<sub>3</sub>)<sub>2</sub> (250 mg, 1.25 mmol) in benzene (10 mL) was heated at  $70^\circ\text{C}$  for 24 h. The solution was cooled, filtered to remove KBF<sub>4</sub> and the volatiles were removed in vacuo to yield a pale yellow oil corresponding to **3** (418 mg, 99% yield). <sup>1</sup>H NMR (see Supplementary data for assignments; 500 MHz, C<sub>6</sub>D<sub>6</sub>, 298 K):  $\delta$  6.79 (s, 1H, CH<sup>m</sup>), 6.76 (s, 1H, CH<sup>m</sup>), 6.69 (s, 1H, CH<sup>7</sup>), 6.59 (s, 1H, CH<sup>5</sup>), 4.97 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 8.2 Hz, <sup>2</sup>J<sub>HH</sub> = 5.6 Hz, CH<sup>2</sup>), 3.92 (m, 1H, CH<sub>2</sub><sup>1</sup>), 3.21 (m, 1H, CH<sub>2</sub><sup>1</sup>), 3.00 (m, 2H, CH<sub>2</sub><sup>4</sup>), 2.77 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 16.2 Hz, <sup>3</sup>J<sub>HH</sub> = 5.6 Hz, CH<sub>2</sub><sup>3</sup>), 2.62 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 16.2 Hz, <sup>3</sup>J<sub>HH</sub> = 8.2 Hz, CH<sub>2</sub><sup>3</sup>), 2.29 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.21 (s, 6H, C<sup>6</sup>CH<sub>3</sub>), 2.18 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.15 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 1.73 (m, 1H, CH<sub>2</sub><sup>2</sup>), 1.60 (m, 1H, CH<sub>2</sub><sup>2</sup>), 1.53 (m, 1H, CH<sub>2</sub><sup>2</sup>), 1.46 (m, 1H, CH<sub>2</sub><sup>2</sup>). <sup>13</sup>C{<sup>1</sup>H}:  $\delta$  147.7 (s, C<sup>9</sup>), 145.0 (s, C<sup>9</sup>), 138.6 (s, C<sup>9</sup>), 137.7 (s, C<sup>9</sup>), 135.0 (s, C<sup>9</sup>), 132.0 (s, C<sup>7</sup>), 130.6 (s, C<sup>7</sup>), 130.3 (s, C<sup>7</sup>), 130.0 (s, C<sup>4</sup>), 127.8 (s, C<sup>6</sup>), 123.4 (s, C<sup>2</sup>), 118.7 (s, C<sup>8</sup>), 82.6 (s, C<sup>2</sup>), 53.7 (s, C<sup>4</sup>), 48.8 (s, C<sup>1</sup>), 35.2 (s, C<sup>3</sup>), 31.4 (s, C<sup>3</sup>), 29.2 (s, C<sup>2</sup>), 21.2 (s, C<sup>6</sup>CH<sub>3</sub>), 21.1 (s, C<sup>6</sup>CH<sub>3</sub>), 20.5 (s, C<sup>6</sup>CH<sub>3</sub>), 20.4 (s, C<sup>6</sup>CH<sub>3</sub>), 20.0 (s, C<sup>6</sup>CH<sub>3</sub>). ESI-TOF MS: [M+H]<sup>+</sup> *m/z* = 335.2495 (theoretical 335.2487).
- The in situ route was adopted simply for convenience, as isolation of **1** and **2** (see Ref. 3 for their reported preparation and isolation) in our hands proved possible only in low yields. Nevertheless, thermolysis of an isolated crystalline sample of **1** in benzene generated **3**, although the conversion was slower.
- A suspension of **2**·HBF<sub>4</sub> (510 mg, 1.25 mmol) and KN(SiMe<sub>3</sub>)<sub>2</sub> (250 mg, 1.25 mmol) in benzene (10 mL) was heated at  $70^\circ\text{C}$  for 72 h. The solution was cooled, filtered to remove KBF<sub>4</sub> and the volatiles were removed in vacuo to yield an oil, which was purified by distillation under vacuum (100 °C,  $6 \times 10^{-2}$  mmHg) to afford **4** as a pale yellow oil (304 mg, 76% yield). <sup>1</sup>H NMR (see Supplementary data for assignments; 500 MHz, C<sub>6</sub>D<sub>6</sub>, 298 K):  $\delta$  6.78 (s, 1H, CH<sup>m</sup>), 6.68 (s, 1H, CH<sup>m</sup>), 6.64 (s, 1H, CH<sup>7</sup>), 6.59 (s, 1H, CH<sup>5</sup>), 4.87 (dd, 1H, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, <sup>2</sup>J<sub>HH</sub> = 4.5 Hz, CH<sup>2</sup>), 4.12 (m, 1H, CH<sub>2</sub><sup>1</sup>), 3.13 (m, 1H, CH<sub>2</sub><sup>1</sup>), 3.00 (m, 1H, CH<sub>2</sub><sup>4</sup>), 2.79 (m, 1H, CH<sub>2</sub><sup>4</sup>), 2.55 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 15.0 Hz, <sup>3</sup>J<sub>HH</sub> = 6.1 Hz, CH<sub>2</sub><sup>3</sup>), 2.46 (dd, 1H, <sup>2</sup>J<sub>HH</sub> = 15.0 Hz, <sup>3</sup>J<sub>HH</sub> = 4.5 Hz, CH<sub>2</sub><sup>3</sup>), 2.26 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.18 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.15 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.13 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 2.10 (s, 3H, C<sup>6</sup>CH<sub>3</sub>), 1.92 (m, 1H, CH<sub>2</sub><sup>2</sup>), 1.12 (m, 1H, CH<sub>2</sub><sup>2</sup>). <sup>13</sup>C{<sup>1</sup>H}:  $\delta$  146.5 (s, C<sup>9</sup>), 144.2 (s, C<sup>9</sup>), 140.3 (s, C<sup>9</sup>), 137.1 (s, C<sup>9</sup>), 135.5 (s, C<sup>9</sup>), 132.1 (s, C<sup>7</sup>), 130.9 (s, C<sup>4</sup>), 130.6 (s, C<sup>7</sup>), 130.0 (s, C<sup>4</sup>), 127.6 (s, C<sup>6</sup>), 124.3 (s, C<sup>2</sup>), 117.9 (s, C<sup>8</sup>), 81.8 (s, C<sup>2</sup>), 50.6 (s, C<sup>4</sup>), 47.4 (s, C<sup>1</sup>), 34.3 (s, C<sup>3</sup>), 26.3 (s, C<sup>2</sup>), 21.2 (s, C<sup>6</sup>CH<sub>3</sub>), 21.1 (s, C<sup>6</sup>CH<sub>3</sub>), 20.4 (s, C<sup>6</sup>CH<sub>3</sub>), 20.3 (s, C<sup>6</sup>CH<sub>3</sub>), 19.6 (s, C<sup>6</sup>CH<sub>3</sub>). ESI-TOF MS: [M+H]<sup>+</sup> *m/z* = 321.2325 (theoretical 321.2331). Analysis found: C, 81.01; H, 8.63; N, 8.63. C<sub>22</sub>H<sub>28</sub>N<sub>2</sub>·0.33 MeOH requires: C, 81.02; H, 8.93; N, 8.46.
- (a) Chen, Y.-T.; Jordan, F. *J. Org. Chem.* **1991**, *56*, 5029; (b) Alder, R. W.; Blake, M. E.; Chaker, L.; Harvey, J. N.; Paolini, F.; Schutz, J. *Angew. Chem., Int. Ed.* **2004**, *43*, 5896.
- Solutions of **3** or **4** (1.10 mmol) were stirred in CHCl<sub>3</sub> (10 mL) for 24 h. These solutions were reduced to dryness, redissolved in MeOH (2 mL) and cooled at

–78 °C overnight to afford white crystals of the products (**5**, 86%; **6**, 90%). Data for **5**:  $^1\text{H}$  NMR (see Supplementary data for assignments; 500 MHz,  $\text{CDCl}_3$ , 298 K):  $\delta$  7.14 (s, 1H,  $\text{CH}^3$ ), 6.86 (d, 1H,  $^3J_{\text{HH}} = 3.0$  Hz,  $\text{CH}^2$ ), 6.70 (s, 2H,  $\text{CH}^m$ ), 6.65 (s, 1H,  $\text{CH}^7$ ), 6.26 (d, 1H,  $^3J_{\text{HH}} = 3.0$  Hz,  $\text{CH}^3$ ), 4.20 (t, 2H,  $^3J_{\text{HH}} = 7.3$  Hz,  $\text{CH}_2^1$ ), 2.80 (t, 2H,  $^3J_{\text{HH}} = 7.3$  Hz,  $\text{CH}_2^4$ ), 2.56 (s, 3H,  $\text{C}^8\text{CH}_3$ ), 2.28 (s, 3H,  $\text{C}^6\text{CH}_3$ ), 2.11 (s, 3H,  $\text{C}^p\text{CH}_3$ ), 2.10 (s, 6H,  $\text{C}^o\text{CH}_3$ ), 1.76 (m, 2H,  $\text{CH}_2^2$ ), 1.49 (m, 2H,  $\text{CH}_2^3$ ).  $^{13}\text{C}\{^1\text{H}\}$ :  $\delta$  143.6 (s,  $\text{C}^1$ ), 133.0 ( $\text{C}^9$ ), 131.6 (s,  $\text{C}^p$ ), 130.4 (s,  $\text{C}^o$ ), 129.9 (s,  $\text{C}^4$ ), 129.7 (s,  $\text{C}^2$ ), 129.6 (s,  $\text{C}^m$ ), 128.9 (s,  $\text{C}^6$ ), 126.5 (s,  $\text{C}^7$ ), 120.5 (s,  $\text{C}^8$ ), 118.9 (s,  $\text{C}^5$ ), 101.1 (s,  $\text{C}^3$ ), 48.9 (s,  $\text{C}^1$ ), 48.7 (s,  $\text{C}^4$ ), 30.6 (s,  $\text{C}^2$ ), 28.7 (s,  $\text{C}^3$ ), 21.2 (s,  $\text{C}^6\text{CH}_3$ ), 20.8 (s,  $\text{C}^p\text{CH}_3$ ), 20.0 (s,  $\text{C}^8\text{CH}_3$ ), 18.5 (s,  $\text{C}^o\text{CH}_3$ ). ESI-TOF MS:  $[\text{M}+\text{H}]^+$   $m/z = 335.2473$  (theoretical 335.2487). Data for **6**:  $^1\text{H}$  NMR (see Supplementary data for assignments; 500 MHz,  $\text{C}_6\text{D}_6$ , 298 K):  $\delta$  7.39 (s, 1H,  $\text{CH}^3$ ), 6.80 (s, 1H,  $\text{CH}^7$ ), 6.77 (s, 2H,  $\text{CH}^m$ ), 6.70 (d, 1H,  $^3J_{\text{HH}} = 2.9$  Hz,  $\text{CH}^2$ ), 6.51 (d, 1H,  $^3J_{\text{HH}} = 2.9$  Hz,  $\text{CH}^3$ ), 3.88 (t, 2H,  $^3J_{\text{HH}} = 7.2$  Hz,  $\text{CH}_2^1$ ), 2.62 (t, 2H,  $^3J_{\text{HH}} = 7.2$  Hz,  $\text{CH}_2^3$ ), 2.48 (s, 3H,  $\text{C}^8\text{CH}_3$ ), 2.42 (s, 3H,  $\text{C}^6\text{CH}_3$ ), 2.17 (s, 3H,  $\text{C}^p\text{CH}_3$ ), 2.07 (s, 6H,  $\text{C}^o\text{CH}_3$ ), 1.58 (m, 2H,  $\text{CH}_2^2$ ).  $^{13}\text{C}\{^1\text{H}\}$ :  $\delta$  144.2 (s,  $\text{C}^9$ ), 134.1 (s,  $\text{C}^9$ ), 131.8 (s,  $\text{C}^1$ ), 131.5 (s,  $\text{C}^4$ ), 130.4 (s,  $\text{C}^p$ ), 130.2 (s,  $\text{C}^m$ ), 129.6 (s,  $\text{C}^2$ ), 129.1 (s,  $\text{C}^6$ ), 127.2 (s,  $\text{C}^7$ ), 120.6 (s,  $\text{C}^8$ ), 119.9 (s,  $\text{C}^5$ ), 102.0 (s,  $\text{C}^3$ ), 47.4 (s,  $\text{C}^1$ ), 46.4 (s,  $\text{C}^3$ ), 34.3 (s,  $\text{C}^2$ ), 21.7 (s,  $\text{C}^6\text{CH}_3$ ), 21.1 (s,  $\text{C}^p\text{CH}_3$ ), 20.3 (s,  $\text{C}^8\text{CH}_3$ ), 18.8 (s,  $\text{C}^o\text{CH}_3$ ). ESI-TOF MS:  $[\text{M}+\text{H}]^+$   $m/z = 321.2303$  (theoretical 321.2331). Analysis found: C, 82.50; H, 8.78; N, 8.63.  $\text{C}_{22}\text{H}_{28}\text{N}_2$  requires: C, 82.45; H, 8.81; N, 8.74.

13. Crystal data for **6**:  $\text{C}_{22}\text{H}_{28}\text{N}_2$ ,  $M = 320.46$ ,  $\lambda = 0.71073$  Å, triclinic, space group  $P\bar{1}$  (No. 2),  $a = 8.6573(16)$ ,  $b = 14.410(3)$ ,  $c = 15.828(4)$  Å,  $\alpha = 100.81(2)$ ,  $\beta = 105.834(18)$ ,  $\gamma = 98.632(16)^\circ$ ,  $U = 1823.1(7)$  Å<sup>3</sup>,  $Z = 4$ ,  $D_c = 1.168$  g cm<sup>-3</sup>,  $\mu = 0.068$  mm<sup>-1</sup>,  $F(000) = 696$ , crystal size  $0.30 \times 0.09 \times 0.07$  mm, unique reflections = 6102 [ $R_{\text{int}} = 0.0246$ ], observed  $I > 2\sigma I = 3199$ , data/restraints/parameters = 6102/2/452,  $R_1 = 0.0433$ ,  $wR_2 = 0.0879$  (obs. data),  $R_1 = 0.0862$ ,  $wR_2 = 0.0942$  (all data), max peak/hole 0.251 and  $-0.197$  e Å<sup>-3</sup>, software used, SHELXS, SHELXL and ORTEP. Sheldrick, G. M. *Acta Crystallogr.* **1990**, 467–473, A46. Sheldrick, G. M. SHELXL-97, a computer program for crystal structure refinement, University of Göttingen, 1997. Crystallographic data for **6** has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 741905. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax(+44) 1223 336033, e-mail: deposit@ccdc.cam.ac.uk].
14. For examples of acid-induced ring-opening of amins, see: (a) Shinohara, T.; Deng, H.; Snapper, M. L.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2005**, 127, 7334; (b) López-Alvarado, P.; Caballero, E.; Avendaño, C.; Menéndez, J. C. *Org. Lett.* **2006**, 8, 4303.
15. (a) Magill, A. M.; Cavell, K. J.; Yates, B. F. *J. Am. Chem. Soc.* **2004**, 126, 8717; (b) See Ref. 3.; (c) Iglesias, M.; Beetstra, D. J.; Kariuki, B.; Cavell, K. J.; Dervisi, A.; Fallis, I. A. *Eur. J. Inorg. Chem.* **2009**, 1913.