



A Novel C-H Insertion via Deoxygenation of Amides by a Sm/SmI₂ Mixed System

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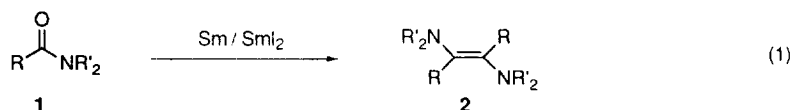
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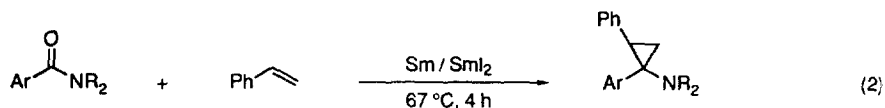
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Abstract: A samarium/samarium diiodide mixed system successfully effects novel aminocyclopropanation and C-H insertion via the deoxygenation of amides. Styrenes undergo aminocyclopropanation by the reaction with aromatic amides, samarium metal, and samarium diiodide. Furthermore, the reaction of aliphatic amides with Sm/SmI₂ in the presence of alkylbenzenes like toluene causes benzylic C-H insertion giving the corresponding phenylethylamine derivatives in good yields. © 1997 Elsevier Science Ltd.

Recently it has been reported that the use of low-valent samarium species (Sm, Sm(Hg), and SmI₂) in conjunction with dihalomethanes leads to the efficient cyclopropanation of allylic alcohols¹ and metal enolates.² In these reactions, samarium-based carbenoids are proposed to act as key species. We have recently revealed that a samarium/samarium diiodide mixed system successfully effects the deoxygenative coupling of amides to provide *vic*-diaminoalkenes (**2**) in high yields (eq 1).^{3,4} The coupling reaction is suggested to involve an α -aminocarbene species⁵⁻⁷ which undergoes dimerization giving **2**. In this article, we wish to report novel aminocyclopropanation and C-H insertion reaction based on the Sm/SmI₂-induced deoxygenation of amides.

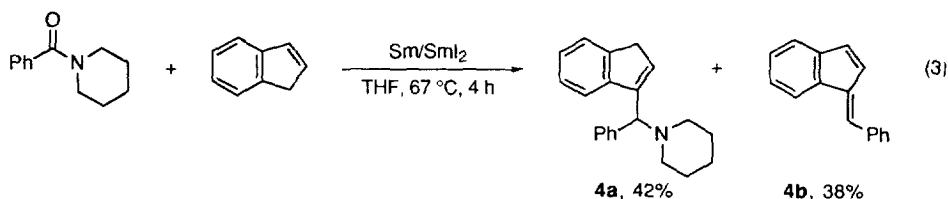


To capture the α -aminocarbene species with olefins, we examined the reaction of *N,N*-disubstituted aromatic amides with Sm/SmI₂ in the presence of several olefinic compounds such as ethyl acrylate, styrene, and butyl vinyl ether. In the case of electron-deficient olefins like ethyl acrylate, the reduction of the olefins with Sm/SmI₂ took place in preference to the desired reduction of amides,⁸ whereas electron-rich olefins like butyl vinyl ether could not capture the α -aminocarbene species (the deoxygenative coupling of amides proceeded exclusively). As the result, the desired aminocyclopropanation was found to occur successfully in the presence of excess styrene (eq 2).^{9,10}

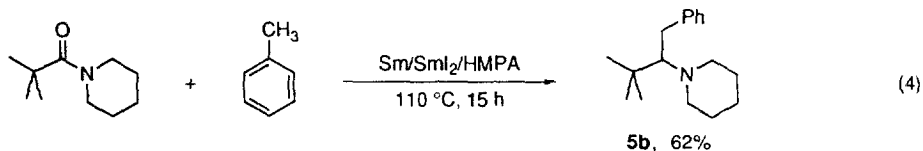


| | Ar = | R ₂ N = | |
|------------|--|--------------------|-----|
| 3 a | Ph | 1-piperidino | 45% |
| 3 b | <i>p</i> -Me-C ₆ H ₄ | 1-piperidino | 56% |
| 3 c | β -naphthyl | 1-piperidino | 58% |
| 3 d | Ph | diethylamino | 42% |

In the case of indene, the desired aminocyclopropanation did not proceed at all, and more interestingly, novel insertion reaction of aminocarbene species to the benzylic C-H bond of indene took place affording **4a** and **4b** in 42% and 38% yields, respectively (eq 3).

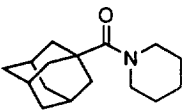

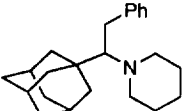
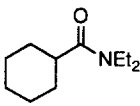

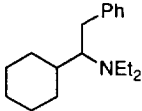
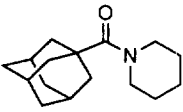

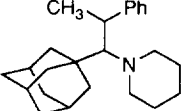
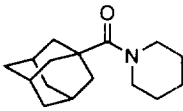
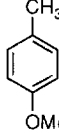
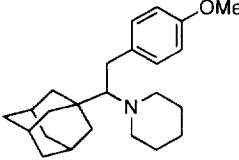
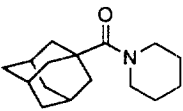
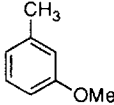
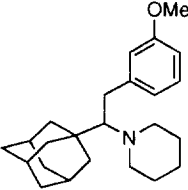


This result prompted us to examine the C-H insertion reaction¹¹ with several benzylic compounds. In the reaction of aromatic amides with toluene by using Sm/SmI₂, the deoxygenative coupling to give vic-diaminoalkenes proceeded in preference to the desired C-H insertion reaction. Contrary to this, the Sm/SmI₂-induced reduction of aliphatic amides like pivaloylpiperidine in the presence of toluene successfully provided the corresponding benzylic insertion product (**5b**) in good yields (eq 4). Compared with the case of aromatic amides, relatively slow generation of aliphatic α -aminocarbene species might contribute to suppression of the dimerization of α -aminocarbene species.



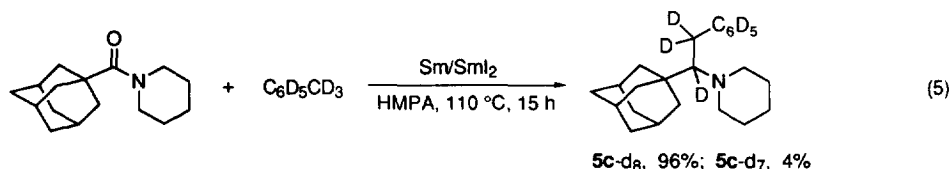
With aliphatic amides bearing a bulky substituent like 1-adamantyl groups, the benzylic C-H insertion proceeded efficiently: the reduction of 1-adamantanecarbonylpiperidine with Sm/SmI₂ in the presence of HMPA¹² in toluene at 110 °C for 15 h selectively afforded the insertion product **5c** in 76% yield (entry 1 in Table 1). Similarly, the benzylic C-H insertion reaction with ethylbenzene (entry 3) and methoxytoluenes (entries 4 and 5) occurred efficiently. In contrast, the use of secondary alkyl amides like *N,N*-diethylcyclohexylamide resulted in the low yield of the desired benzylic insertion product (**5d**), due to the competitive intramolecular insertion to give enamines like *N,N*-(diethylamino)methylenecyclohexane and also to the formation of **2d** (entry 2).

Table 1. Sm/SmI₂-Induced C-H Insertion Reaction^a

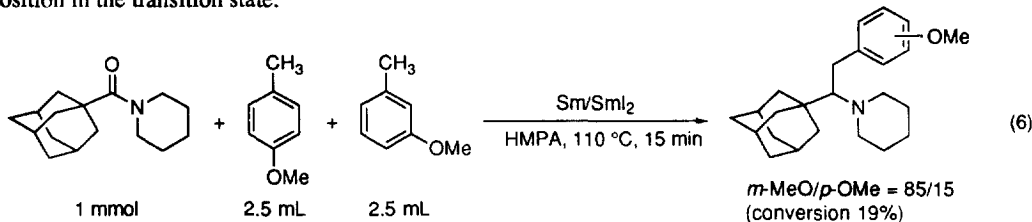
| entry | amide | benzylic compound | product (yield,%) |
|-------|---|---|--|
| 1 |  |  |  5c (76) |
| 2 |  |  |  5d (25) ^b |
| 3 |  |  |  5e (50) ^{c,d} |
| 4 |  |  |  5f (53) |
| 5 |  |  |  5g (81) |

^aAmide (1 mmol), benzylic compound (5 mL), Sm (0.5 mmol), SmI₂ (2.2 mmol), HMPA (0.5 mL), 110 °C, 15 h. ^bBis(*N,N*-diethylamino)-1,2-dicyclohexylethane (**2d**, 12%) was also obtained. ^cObtained as a diastereoisomeric mixture [67/33]. ^d136 °C.

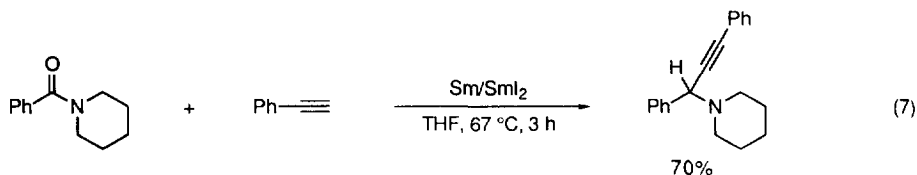
To get insight into the reaction pathway, we examined the C-H insertion reaction by using toluene labeled with deuteriums: Sm/SmI₂-induced reaction of 1-adamantanecarbonylpiperidine with toluene-d₈ afforded the benzylic C-D insertion product (**5c**-d₈) mainly, as indicated in eq 5.



Interestingly, the competitive reaction using *m*- and *p*-methoxytoluenes provided the corresponding *m*- and *p*-methoxyl substituted insertion products with the ratio of 85/15 (eq 6). Although the mechanistic details of this insertion reaction have not been clarified yet, this result suggests the anionic character at the benzylic position in the transition state.



The present C-H insertion reaction is applicable to terminal acetylenes. For example, the Sm/SmI₂-induced reaction of benzoylpiperidine with phenylacetylene afforded the corresponding propargylic piperidine in good yield (eq 7).



In summary, this work describes a novel example of C-H insertion into alkylbenzenes *via* the deoxygenation of amides by Sm/SmI₂. Further studies on the scope and precise mechanism are underway.

EXPERIMENTAL

General Comments.

¹H NMR spectra were recorded on a JEOL JNM-GSX-270 (270 MHz) spectrometer using CDCl₃ as the solvent with Me₄Si as the internal standard. ¹³C NMR spectra were taken on a JEOL JNM-GSX-270 using CDCl₃ as the solvent. Chemical shifts in ¹³C NMR were measured relative to CDCl₃ and converted to δ(Me₄Si) value by using δ(CDCl₃) = 76.9 ppm. IR spectra were determined on a Perkin Elmer Model 1600 spectrometer. Melting points were determined on a Yanagimoto micro melting point apparatus. Mass spectra were obtained on a JEOL JMS-DX303 in the analytical section of our department. Elemental analyses were also performed there.

Samarium powder in oil (99.9%) was purchased from High Purity Chemicals, and was used after washing with dry pentane, followed by drying for 4 h under reduced pressure.

The C–H insertion reaction was performed as follows. In a 20 mL two-necked flask equipped with a condenser were placed under argon atmosphere samarium powder (2 mmol), freshly distilled (sodium / benzophenone ketyl) THF (5 mL), and 1,2-diiodoethane (1 mmol). Heating of the mixture at 67 °C for 1 h with magnetic stirring provided samarium metal / samarium diiodide mixed reagent (Sm/SmI₂). Then the solvent (THF) was removed under reduced pressure. To the resulting dark-black solid were added toluene (5 mL), HMPA (0.5 mL), and amide (1 mmol). The mixture was stirred under reflux for 16 h. After the reaction was complete, saturated NaHCO₃ (40 mL) was added to the reaction mixture, and the products were extracted with diethyl ether (20 mL x 3). The combined extracts were dried (MgSO₄), and the solvent was removed in vacuo. Purification by column chromatography on silica gel using hexane/Et₂O/Et₃N = 90/9/1 as an eluent provided the desired insertion products. Alternatively, Sm/SmI₂/HMPA in toluene can be prepared conveniently by the reaction of samarium metal (2.1 mmol) with diiodoethane (1.1 mmol) in a mixed solvents of toluene (5 mL) and HMPA (0.5 mL) at the refluxing temperature for 8 h.

The aminocyclopropanation of olefins was performed as follows. The Sm/SmI₂ reagent was prepared as described above. To the THF solution of Sm/SmI₂ were added an amide (1 mmol) and styrene (5 mL), and the resulting solution was stirred at 67 °C for 4 h. After similar workup as described in the C–H insertion reaction, the desired aminocyclopropanation product was purified by column chromatography on silica gel (φ 2 cm x length 10 cm, Fuji silisia, BW-820MH) using hexane/Et₂O = 10/1 as an eluent.

The following spectroscopic and elemental analyses were performed on these samples.

1-Piperidino-1,2-diphenylcyclopropane (3a). A pale yellow oil: ¹H NMR (270 MHz, CDCl₃) δ 1.16 (m, 2 H), 1.26 (m, 4 H), 1.38 (dd, 2 H, *J* = 8.3, 1.0 Hz), 2.11 (m, 2 H), 2.33 (t like, 3 H), 7.14–7.32 (m, 8 H), 7.45 (d, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 21.5, 24.4, 26.1, 32.0, 50.8, 55.8, 125.4, 126.9, 127.1, 127.5, 128.3, 130.5, 138.8, 138.8; IR (neat) 3056, 3023, 2932, 2801, 1601, 1497, 1443, 1319, 1247, 1118, 1032, 767, 748, 696 cm⁻¹; MS (EI), *m/z* = 277 (M⁺, 27). Anal. Calcd for C₂₀H₂₃N: C, 86.59; H, 8.36; N, 5.05. Found: C, 86.25; H, 8.43; N, 4.92.

1-Piperidino-1-(*p*-tolyl)-2-phenylcyclopropane (3b). A pale yellow oil: ¹H NMR (270 MHz, CDCl₃) δ 1.16 (m, 2 H), 1.26 (m, 4 H), 1.35 (d, 2 H, *J* = 8.3 Hz), 2.10 (m, 2 H), 2.35 (m, 6 H), 7.11–7.28 (m, 7 H), 7.42–7.45 (m, 2 H); ¹³C NMR (68 MHz, CDCl₃) δ 21.1, 21.6, 24.4, 26.1, 32.1, 50.8, 55.5, 125.3, 127.1, 128.2, 128.3, 130.4, 135.9, 136.4, 138.9; IR (neat) 3020, 2932, 2802, 1603, 1498, 1456, 1246, 1117, 910, 748, 733, 695 cm⁻¹; MS (EI), *m/z* = 291 (M⁺, 39); HRMS calcd for C₂₁H₂₅N 291.1987, found 291.1970.

1-Piperidino-1-(2'-naphthyl)-2-phenylcyclopropane (3c). An orange solid: mp 51–52 °C; ¹H NMR (270 MHz, CDCl₃) δ 1.08 (brs, 2 H), 1.29 (brs, 4 H), 1.52 (brs, 2 H), 2.22 (brs, 2H), 2.45 (brs, 3 H), 7.27–7.54 (m, 9 H), 7.77–7.87 (dd, 2 H, *J* = 7.4, 18.4 Hz), 8.48, (brs, 1 H); ¹³C NMR (68 MHz, CDCl₃) δ 22.7, 24.1, 26.3, 33.7, 51.2, 53.4, 124.8, 125.1, 125.3, 125.6, 126.0, 127.4, 127.8, 128.3, 128.6, 130.1, 133.4, 133.9, 135.1, 138.7; IR (KBr) 3037, 2931, 2802, 1603, 1496, 1441, 1237, 801, 775, 695 cm⁻¹; MS (EI), *m/z* = 327 (M⁺, 61); HRMS calcd for C₂₄H₂₅N 327.1987, found 327.2003.

1-Diethylamino-1,2-diphenylcyclopropane (3d). A yellow oil: ¹H NMR (270 MHz, CDCl₃) δ 0.83 (t,

6 H, $J = 7.3$ Hz), 1.54, (dd, 1 H, $J = 4.9, 9.2$ Hz), 1.64, (dd, 1 H, $J = 4.9, 7.0$ Hz), 2.32–2.50 (m, 5 H), 7.21–7.49 (m, 10 H); ^{13}C NMR (68 MHz, CDCl_3) δ 14.2, 22.6, 30.8, 46.4, 55.1, 125.4, 126.8, 127.2, 127.7, 128.5, 128.6, 130.0, 138.9; IR (neat) 3024, 2968, 2818, 1601, 1498, 1444, 1257, 1030, 910, 767, 696 cm^{-1} ; MS (EI), $m/z = 265$ (M^+ , 57); HRMS calcd for $\text{C}_{19}\text{H}_{23}\text{N}$ 265.1830, found 265.1830. Anal. Calcd for $\text{C}_{19}\text{H}_{23}\text{N}$: C, 86.05; H, 7.67; N, 6.27. Found: C, 86.11; H, 7.88; N, 5.99.

3-(α -Piperidinobenzyl)indene (4a). A yellow oil: ^1H NMR (270 MHz, CDCl_3) δ 1.43 (m, 2 H), 1.57 (m, 4 H), 2.42 (brs, 4 H), 3.31 (s, 2 H), 4.46 (s, 1 H), 6.48 (brs, 1 H) 7.10–7.28 (m, 5 H), 7.38 (d, 1 H, $J = 7.3$ Hz), 7.46 (d, 2 H, $J = 6.0$ Hz), 7.69 (d, 1 H, $J = 7.3$ Hz); ^{13}C NMR (68 MHz, CDCl_3) δ 24.7, 26.3, 37.7, 53.0, 71.1, 121.2, 123.5, 124.4, 125.8, 126.8, 128.1, 128.6, 130.3, 141.1, 144.2, 144.7, 145.7; IR (neat) 3061, 3024, 2932, 2795, 1600, 1452, 1117, 909, 771, 726, 699 cm^{-1} . MS (EI), $m/z = 289$ (M^+ , 10); HRMS calcd for $\text{C}_{21}\text{H}_{23}\text{N}$ 289.1830, found 289.1834.

1-(Phenylmethylenyl)indene (4b). A yellow solid: mp 82–83 °C; ^1H NMR (270 MHz, CDCl_3) δ 7.02 (s, 1 H), 7.18–7.48 (m, 9 H), 7.60 (dd, 1 H, $J = 7.3$ Hz), 7.69 (dd, 1 H, $J = 6.2$ Hz); ^{13}C NMR (68 MHz, CDCl_3) δ 119.1, 121.0, 125.1, 126.1, 127.6, 128.3, 128.7, 128.7, 130.2, 134.5, 136.9, 137.5, 140.1, 142.1; IR (KBr) 3110, 1495, 1444, 1336, 795, 750, 697 cm^{-1} ; MS (EI), $m/z = 204$ (M^+ , 92); HRMS calcd for $\text{C}_{16}\text{H}_{12}$ 204.0939, found 204.0949.

2-Piperidino-3,3-dimethylbutylbenzene (5b). A pale yellow oil: ^1H NMR (270 MHz, CDCl_3) δ 0.96 (s, 9 H), 1.29–1.39 (m, 6 H), 2.51–2.58 (m, 5 H), 2.77–2.81 (m, 2 H), 7.17–7.26 (m, 5 H); ^{13}C NMR (68 MHz, CDCl_3) δ 25.1, 27.2, 28.1, 32.5, 37.6, 53.1, 75.5, 125.3, 127.9, 129.3, 143.1; IR (neat) 3026, 2931, 1604, 1495, 1452, 1440, 1100, 1032, 1008, 729, 698 cm^{-1} ; MS (EI), $m/z = 245$ (M^+ , 0.3); HRMS (M^+) calcd for $\text{C}_{17}\text{H}_{27}\text{N}$ 245.2143, found 245.2165.

1-(α -Piperidinophenethyl)adamantane (5c). A white solid: mp 59.5–60.5 °C; ^1H NMR (270 MHz, CDCl_3) δ 1.29–1.41 (m, 6 H), 1.51–1.73 (m, 12 H), 1.96 (brs, 3 H), 2.35 (t like, 1 H, $J = 7.08$ Hz), 2.51 (brs, 4 H), 2.77 (m, 2 H), 7.14–7.25 (m, 5 H); ^{13}C NMR (68 MHz, CDCl_3) δ 25.1, 27.2, 28.9, 31.0, 37.5, 39.6, 40.2, 53.5, 76.4, 125.3, 127.9, 129.4, 143.4; IR (KBr) 3024, 2904, 2846, 1603, 1494, 1452, 1099, 1031, 723, 697 cm^{-1} ; MS (EI), $m/z = 323$ (M^+ , 0.4). Anal. Calcd for $\text{C}_{23}\text{H}_{33}\text{N}$: C, 85.39; H, 10.28; N, 4.33. Found: C, 85.15; H, 10.19; N, 4.60.

[α -(Diethylamino)phenethyl]cyclohexane (5d). A pale yellow oil: ^1H NMR (270 MHz, CDCl_3) δ 0.93 (t, 6 H, $J = 7.1$ Hz), 1.07–1.38 (m, 5 H), 1.65 (m, 5 H), 1.99 (d, 1 H, $J = 12.7$ Hz), 2.36–2.77 (m, 7 H), 7.14–7.27 (m, 5 H); ^{13}C NMR (68 MHz, CDCl_3) δ 15.0, 26.7, 30.9, 31.6, 34.4, 41.3, 44.7, 67.0, 125.2, 128.0, 129.2, 142.8; IR (neat) 3025, 2924, 2852, 1602, 1494, 1449, 1379, 1200, 1068, 724, 698 cm^{-1} ; MS (CI), $m/z = 260$ ($\text{M}^+ + 1$, 27); HRMS ($\text{M}^+ + 1$) calcd for $\text{C}_{18}\text{H}_{29}\text{N}$ 260.2379, found 260.2371.

(E)-1,2-Bis(diethylamino)-1,2-di(cyclohexyl)ethene (2d). A colorless solid: mp 79–80 °C; ^1H NMR (270 MHz, CDCl_3) δ 0.97 (t, 12 H, $J = 7.1$ Hz), 1.03–1.75 (m, 20 H), 2.26 (m, 2 H), 2.59–2.90 (m, 8 H); ^{13}C

NMR (68 MHz, CDCl_3) δ 16.0, 26.5, 27.2, 31.6, 42.5, 49.8, 151.6; IR (KBr) 2965, 2923, 2848, 1450, 1189, 1046, 892, 806, 745, 627 cm^{-1} ; MS (EI), m/z = 334 (M^+ , 79); HRMS (M^+) calcd for $\text{C}_{22}\text{H}_{42}\text{N}_2$ 334.3348, found 334.3339.

1-(α -Piperidino- β -methylphenethyl)adamantane (5e). Isolated as a diastereoisomeric mixture (67:33). Thus, the following spectral and analytical data were obtained by using this sample: ^1H NMR (270 MHz, CDCl_3) δ 1.15-1.45 (m, 9 H), 1.55-1.75 (m, 12 H), 1.89-1.94 (brs, 3 H), 2.21-2.29 (d, 1 H, J = 6.1, 4.9 Hz), 2.56-2.61 (m, 2 H), 2.77 (m, 1 H), 2.93 (m, 1 H), 3.08-3.19 (m, 1 H), 7.13-7.30 (m, 5 H); ^{13}C NMR (68 MHz, CDCl_3) major isomer: δ 23.6, 24.9, 26.8, 29.0, 37.3, 39.9, 41.3, 41.8, 53.7, 80.4, 125.1, 127.4, 128.6, 148.6; minor isomer: δ 20.5, 25.2, 27.4, 29.0, 37.2, 40.1, 41.4, 42.1, 54.1, 80.1, 125.3, 127.5, 127.9, 149.9; IR (neat) 3060, 3024, 2904, 2847, 1601, 1451, 1171, 1101, 759, 699 cm^{-1} ; MS (EI), m/z = 335 (M^+ -2, 0.6), 232 (M^+ -PhCHCH₃, 100), 202 (M^+ -adamantyl, 72); HRMS (M^+ -2) calcd for $\text{C}_{24}\text{H}_{35}\text{N}$ -2 335.2613, found 335.2609.

1-(α -Piperidino-*p*-methoxyphenethyl)adamantane (5f). A white solid: mp 122.5-123.5 $^\circ\text{C}$; ^1H NMR (270 MHz, CDCl_3) δ 1.29-1.47 (m, 6 H), 1.53-1.72 (m, 12 H), 1.95 (brs, 3 H), 2.28 (t like, 1 H, J = 7.1 Hz), 2.50 (brs, 4 H), 2.70 (d like, 2 H, J = 7.8 Hz), 3.77 (s, 3 H), 6.79 (d, 2 H, J = 8.5 Hz), 7.15 (d, 2 H, J = 8.5 Hz); ^{13}C NMR (68 MHz, CDCl_3) δ 25.1, 27.2, 28.9, 29.9, 37.4, 39.4, 40.2, 53.5, 55.2, 76.4, 113.3, 130.1, 135.2, 157.4; IR (KBr) 2904, 2846, 1612, 1512, 1246, 1177, 1100, 1040, 1004, 819 cm^{-1} ; MS (CI), m/z = 354 (M^+ +1, 21). Anal. Calcd for $\text{C}_{24}\text{H}_{35}\text{NO}$: C, 81.54; H, 9.98; N, 3.96. Found: C, 81.72; H, 10.18; N, 3.92.

1-(α -Piperidino-*m*-methoxyphenethyl)adamantane (5g). An colorless oil: ^1H NMR (270 MHz, CDCl_3) δ 1.30-1.44 (m, 6 H), 1.47-1.80 (m, 12 H), 1.94 (brs, 3 H), 2.34 (t, 1 H, J = 6.8 Hz), 2.53 (brs, 4 H), 2.75 (d, 2 H, J = 6.8 Hz), 3.79 (s, 3 H), 6.70 (d, 1 H, J = 7.8 Hz), 6.79 (d, 2 H, J = 12.2 Hz), 7.18 (t, 1 H, J = 7.8 Hz); ^{13}C NMR (68 MHz, CDCl_3) δ 25.1, 27.2, 28.8, 31.0, 37.4, 39.5, 40.2, 53.4, 55.1, 76.14, 110.3, 115.3, 121.9, 128.7, 145.0, 159.3; IR (neat) 2906, 2846, 1601, 1491, 1453, 1263, 1151, 1100, 1054, 1006, 908, 777, 756, 734, 694 cm^{-1} ; MS (CI), m/z = 354 (M^+ +1, 16); HRMS (M^+ +1) calcd for $\text{C}_{24}\text{H}_{35}\text{NO}$ 354.2797, found 354.2785.

1,3-Diphenyl-3-piperidino-propyne. A yellow oil: ^1H NMR (270 MHz, CDCl_3) δ 1.35 (m, 2 H), 1.51 (m, 4 H), 2.46 (t, 4 H, J = 5.4 Hz), 4.71 (s, 1 H), 7.19-7.35 (m, 6 H), 7.43 (m, 2 H), 7.55 (d, 2 H, J = 7.3 Hz); ^{13}C NMR (68 MHz, CDCl_3) δ 24.3, 25.9, 50.5, 62.2, 85.8, 87.8, 127.4, 127.8, 127.9, 128.1, 128.4, 129.6, 131.6, 138.3; IR (neat) 3060, 3030, 2933, 1599, 1490, 1450, 1262, 1096, 1027, 803, 756, 692 cm^{-1} ; MS (EI), m/z = 275 (M^+ , 11).

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