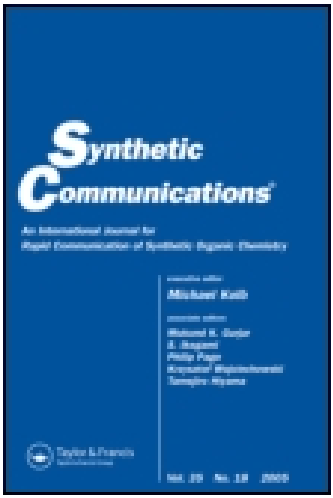

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Trimethylsilyl Trifluoromethanesul Fonate (Tmsotf) Catalyzed Amidoalkylation of Silylenolethers. Stereocontrolled Syntheses of (+/-)-Sedamine and (+/-)-Norsedamine

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TRIMETHYLSILYL TRIFLUOROMETHANESULFONATE(TMSOTf) CATALYZED AMIDOALKYLATION OF SILYLENOLETHERS. STEREOCONTROLLED SYNTHESES OF (+/-)-SEDAMINE AND (+/-)-NORSEDAMINE.

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Trimethylsilyl trifluoromethanesulfonate(TMSOTf) catalyzed addition of 1-trimethylsilyloxy-1-phenylethene to N-ethoxycarbonyl- and N-tert-butoxycarbonyl-2-ethoxypiperidines (3a and 3b, respectively) afforded the corresponding ketocarbamates 4a and 4b, in excellent yields. Stereoselective conversion to (±)-norsedamine (7) and (±)-sedamine (8) is described.

The attachment of an α-amidoalkyl group to nucleophiles is a well known transformation and a value le alternative to the Mannich reaction. Both its intermolecular and intramolecular version have been comprehensively reviewed and many examples of its application to the synthesis of biologically important molecules are known[1,2]. Among the nucleophiles amenable to α-amidoalkylation, silylenol-

ethers and silylketeneacetals have been explored as regioselective partners. Since the original report of ureidoalkylation of silylenolethers by Danishefsky et. al.[3] many novel routes to the preparation of N-acyl iminium ions have been described[2]. Heterolyses of α-heterosubstituted amides and carbamates is the most often employed method for **in situ** generation of N-acyl iminium ions where the heterosubstituent may be an oxygen, halogen, nitrogen, sulfur or phosphorous species[2].

Particularly relevant to this subject is the partial reduction of imides to cyclic hydroxy or alkoxylactams. Sodium borohydride in the presence of hydrochloric acid is the method of choice[4] although other reducing agents[5-7] and methodologies are also available[8]. Anhydrous titanium(IV) chloride is generally employed in stoichiometric amounts to generate the acyl iminium ion while better yields of amidoalkylation products are usually observed with acyl iminium ions derived from carbamates rather than from amides[9,10].

In 1984, Sekiya and coworkers[11] reported the **in situ** generation of N,N-bissilyliminium salts from N,N-bis(trimethylsilyl) methoxymethylamines and catalytic amounts of trimethylsilyl trifluoromethanesulfonate (TMSOTf), which reacted with silylketeneacetals to afford N,N-bis(trimethylsilyl)-β-aminoesters in high yields. We have described the TMSOTf promoted addition of silylenolethers to Schiff bases[12] and the diastereoselective reduction of the β-aminoketones[13].

Here we disclose our results on the addition of 1-trimethylsilyloxy-1-phenylethene to N-ethoxycarbonyl-2-ethoxypiperidine

(3a) and N-tert-butoxycarbonyl-2-ethoxypiperidine (3b) promoted by catalytic amounts of TMSOTf (Scheme 1) and its application to the total synthesis of (+/-)-norsedamine (7), (+/-)-sedamine (8) and (+/-)-allosedamine (9).

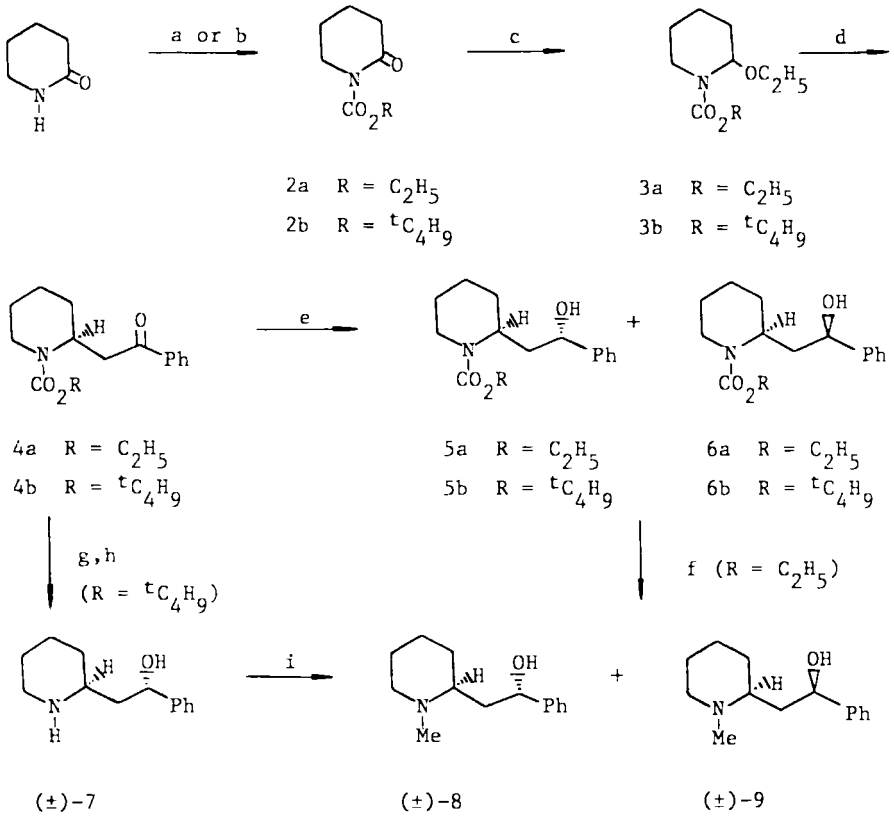
After extensive experimental optimization, the best yields of ketocarbamates 4a,b were achieved when 5-10 mol % of TMSOTf was added to a mixture of ethoxycarbamate 3a or 3b and 1-trimethylsilyloxy-1-phenylethene, in CH_2Cl_2 at -78°C. A smooth reaction took place and after quenching with aqueous $NaHCO_3$, the residue was purified by column chromatography to afford ketocarbamates 4a and 4b in 94% and 97% yield, respectively.

Although the preparation of α-phenacylpiperidine and its derivatives has long been known[9,14], the high yields and mild conditions employed in the TMSOTf catalyzed amidoalkylation seems to be appropriate for acid sensitive nucleophiles. As an initial application of this methodology, we prepared the racemic forms of norsedamine (7), sedamine (8) and allosedamine (9), alkaloids found in **Sedum acre**[15].

Attempts of stereoselective reduction of ketocarbamates 4a and 4b with several reducing agents (e.g., $LiAlH_4$, $Zn(BH_4)_2$, $LiBH(C_2H_5)_3$ and $KBH(C_2H_5)_3$) led only to modest diastereoselection (3:1 ratio of 5a,b/6a,b with $LiBH(C_2H_5)_3$ in THF, at -78°C). The relative configuration of 5a and 6a was assigned after $LiAlH_4$ reduction to (+/-)-sedamine (8) and (+/-)-allosedamine (9), respectively.

From our previous results in the diastereoselective reduction of β-aminoketones we reasoned that higher levels of stereocontrol

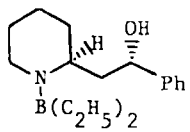
Scheme 1



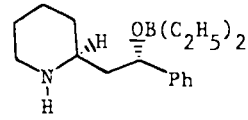
a) i. LDA,THF, -78°C; ii. $NCCO_2Et$, -78°C, 2h (67%) or i. LDA,THF, -78°C; ii. $ClCO_2Et$,-78°C (62%); b) $^tBuO\text{-}\overset{O}{\overset{\|}{C}}\overset{O}{\overset{\|}{C}}\text{-}O\text{-}^tBu$,$Et_3N$,DMAP,$CH_2Cl_2$, 25°C, 7h(83%) or i.LDA,THF,-78°C;ii.BOC-ON,THF,-78°C(80%);c)i.$NaBH_4$, EtOH,-23°C,3h;ii.2N HCl,EtOH,pH 3.0,1h,iii.KOH,EtOH,pH 7.0 (90--95%);d)$PhCH(OSiMe_3)CH_2$,TMSOTf(5mol%),CH_2Cl_2,-78°C(95-97%); e)$LiBH(C_2H_5)_3$,THF,-78°C(100%);f)$LiAlH_4$,THF,20h(100%);g)i.CF_3CO_2H 25°C,30 min,ii.aq. $NaHCO_3$(98%);h)$Zn(BH_4)_2$,THF,-78°C(95%) or i. $LiBH(C_2H_5)_3$,THF,-78°C, ii.H_2O_2,MeOH,pH 7.0(70%);i)HCHO,CH_3CN, $NaBH_3CN$,25°C(88%).

could be achieved if the reduction was carried out with α-phenacyl-piperidine itself. Trifluoroacetic acid treatment of ketocarbamate **4b** afforded the corresponding secondary β-aminoketone which was immediately reduced with $Zn(BH_4)_2$ to a 6:1 mixture of amino-alcohols from which (+/-)-norsedamine (7) (double doublet, δ 4.92 ppm, J = 10.8 and 2.7 Hz) cristallized as the major component (CH_2Cl_2-hexanes), in 75% yield.

Surprisingly, the reduction of α-phenacylpiperidine with $LiBH(C_2H_5)_2$ (2.0 equiv.) led to a 6:1 mixture of diastereoisomeric products to which structures **10a** or **10b** was tentatively assigned to the major isomer.



10a



10b

The incorporation of the $-B(C_2H_5)_2$ residue was evident from the ^{1}H-NMR (two triplets at δ 0.79 and 0.88 ppm), ^{13}C-NMR (two methyls at δ 8.31 and 8.83 ppm) and mass spectra (m/z 273). Attempted acetylation of **10** did not allow us to distinguish between structures **10a** and **10b**, since elimination of $-B(C_2H_5)_3$ ocurred under the conditions employed (Ac_2O/Et_3N/4-DMAP in CH_2Cl_2 at room temperature). Nevertheless, the relative configuration of the major isomer could be unambiguously established after H_2O_2 oxidation which afforded (+/-)-norsedamine (7), in 70% yield. These results were rationalized through chelation controlled hydride addition to α-phenacylpiperidine. (+/-)-Sedamine (8) was

uneventfully prepared[17], in 88% yield, by reductive methylation of (+/-)-norsedamine (**7**) using the formaldehyde/$NaBH_3CN$ protocol[18].

Experimental

Unless otherwise noted materials were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran (THF) and ether were distilled from sodium-benzophenone immediately prior to use. Diisopropylamine, triethylamine and dichloromethane were distilled from calcium hydride. All reactions involving organometallic reagents or trimethylsilyl trifluoromethanesulfonate (TMSOTf) were carried out under an argon atmosphere. Melting points were determined on a Kofler apparatus and are uncorrected. ^{1}H-NMR spectra were determined in $CDCl_3$ solution at 300 MHz and ^{13}C-NMR spectra in $CDCl_3$ solution at 75.5 MHz unless otherwise noted. Chemical shifts are expressed in ppm downfield from internal tetramethylsilane and ^{1}H-NMR data are tabulated in order: multiplicity (s, singlet; d, doublet; t, triplet; br, broad; dt, double triplet; q, quartet; dq, double quartet; m, multiplet), number of protons, coupling constants in hertz. Infrared spectra were recorded on a Perkin Elmer 399B spectrophotometer and mass spectra with a Varian MAT 311A spectrometer. Elemental analyses were performed on a Perkin Elmer 2400 CHN Analyser, at Instituto de Química, Unicamp.

N-Ethoxycarbonyl-2-ethoxypiperidine (**3a**) and N-tert-butoxycarbonyl-2-ethoxypiperidine (**3b**).

To a solution of **2a**[19] or **2b**[19] (1.0 mmol) in ethanol (10 ml) was added $NaBH_4$ (0.152 g; 4.0 mmol) in one portion at -23°C. This solution was kept at -23°C for 3 hours and quenched with aqueous HCl (1%) until pH 3.0. The mixture was stirred for an additional 30-45 min. period at -23°C, neutralized with ethanolic KOH (1%), poured into water and extracted with CH_2Cl_2.

The combined organic extracts were dried over anhydrous $MgSO_4$ and the solvent was removed under reduced pressure. The crude material was purified in silica gel (9:1 hexane-ethyl acetate with 1% of triethylamine) yielding 0.189 g (94% yield) of **3a** or 0.217 g (95% yield) of **3b** as colorless oils.

3a: ^{1}H-NMR: δ 1.18 (t, 3H, J = 6.9), 1.27 (t, 3H, J = 6.9); 1.4-1.9 (m, 6H), 3.0 (m, br, 1H), 3.42 (m, 2H), 3.95 (m, br, 1H), 4.0-4.3 (m, 2H), 5.6 (m, 1H).

^{13}C-NMR: δ 14.55, 14.65, 25.11, 30.47, 39.25, 60.64, 61.26, 66.49, 80.36, 155.36.

3b: ^{1}H-NMR: δ 1.19 (t, 3H, J = 7.0), 1.46 (s, 9H), 1.30-1.65 (m, 6H), 2.92 (m, br, 1H), 3.42 (m, 2H), 3.8 (m, 1H), 5.44 (m, 1H).

^{13}C-RMN: δ 155.23, 80.41, 79.70, 61.75, 39.18, 37.92, 28.34, 25.13, 18.49 and 15.00 ppm.

IR(film): 2868, 2969, 2934, 1701, 1414, 1261, 1166, 1091, 1076 cm^{-1}.

MS (70 eV): m/z 229 (M^+, 0.5%), 184 (27%), 144 (17%), 128 (100%), 100 (16%), 84 (87%), 83 (31%), 59 (25%), 57 (98%), 45 (36%), 43 (55%), 41 (45%).

N-Ethoxycarbonyl-2-phenacylpiperidine (**4a**) and N-tert--butoxycarbonyl-2-phenacylpiperidine (**4b**).

To a solution of **3a** or **3b** (1.0 mmol) and 1-trimethylsilyloxy--1-phenylethene (0.222 g, 1.15 mmol) in CH_2Cl_2 (2.0 ml) at -78°C and under an atmosphere of nitrogen was added trimethylsilyl trifluoromethanesulfonate (0.010 ml, 0.011 g, 0.05 mmol).

The resulting mixture was stirred for 1 hour at -78°C and quenched by the addition of saturated aqueous $NaHCO_3$. The resulting mixture was let to warm up to room temperature and it was extracted with CH_2Cl_2 (3 x 10 ml) and the combined organic extracts were dried over $MgSO_4$. The organci solvent was removed under reduced pressure and the crude material was purified by silica gel column chromatography (10:1 hexane-ether) to afford 0.258 g (0.94 mmol, 94% yield) of **4a**, as a colorless oil, and 0.294 g (0.97 mmol, 97% yield) of **4b** as a white solid (m.p. 81-82°C).

4a: ^{1}H-NMR: δ 1.19 (t. 3H, J = 6.6), 1.43 (m, 1H), 1.63 (m, 5H), 2.88 (t, 1H, J = 13.0), 3.13 (m, 2H), 4.03 (m, 3H), 4.77 (m, 1H), 7.42 (m, 2H), 7.51 (m, 1H), 7.98 (d, 2H, J = 7.8).

^{13}C-NMR: δ 14.57, 18.88, 25.33, 28.04, 39.36, 39.88, 48.35, 61.51, 128.74, 129.13, 133.68, 137.26, 156.16, 199.12.

IR(film): 2980, 2940, 2860, 1690, 1420 and 1260 cm^{-1}.

Elemental analysis calcd. for $C_{16}H_{21}NO_3$: C-69.81, H-7.64, N-5.09. Found: C-69.44, H-7.66, N-5.04.

4b: ^{1}H-NMR: δ 1.37 (s, 9H), 1.64 (m, 6H), 2.89 (ddd, 1H, J = 13.2, 12.6 and 2.7), 3.16 (dd, 1H, J = 14.4 and 6.1), 3.22

(1H, dd, J = 14.4 and 8.4), 4.05 (d, br, 1H, J = 12.6), 4.84 (m, 1H), 7.48 (m, 2H), 7.58 (m, 1H), 8.0 (d, 2H, J = 7.2).

^{13}C-NMR: δ 18.90, 25.34, 28.36, 28.55, 39.29, 39.49, 48.34, 79.84, 128.73, 129.08, 133.57, 137.29, 155.24, 199.13.

IR(KBr): 2975, 2945, 2875, 1770, 1715, 1295, 1250, 1160 and 1145 cm^{-1}.

MS (70 eV): 303 (M^+, 9%), 247 (11%), 229 (9%), 191 (62%), 128 (32%), 105 (39%), 84 (100%), 77 (16%), 57 (87%).

(1SR,2SR)- and (1RS,2SR) N-Ethoxycarbonyl-2-(ß-hydroxy-ß--phenylethyl)-piperidine (**5a** and **6a**).

To a stirred solution of **4a** (0.137 g, 0.5 mmol) in THF (3.0 ml), at -78°C and under nitrogen atmosphere, was added dropwise a 1.0 M solution of LiBH $(C_2H_5)_3$ in THF (0.7 ml, 0.7 mmol). After 2 hours at -78°C, the reaction was quenched by addition of water (2.0 ml) and allowed to warm up to room temperature.

After extraction with ether (3 x 2.0 ml), the combined organic phases were washed with brine (2 x 2.0 ml), dried over $MgSO_4$ and evaporated under reduced pressure. Column chromatography on silica gel (85:15 hexane-ether) afforded 0.102 g (0.37 mmol, 74% yield) of **5a** and 0.037 g (0.12 mmol, 24% yield) of **6a**.

5a: ^{1}H-NMR: δ 1.21 (t, 3H, J = 7.2), 1.38 (m, 2H), 1.59 (m, br, 5H), 1.89 (m, 1H), 2.16 (m, 1H), 2.85 (m, 1H), 3.89 (m, br, 1H), 4.09 (q, 2H, J = 7.2), 4.42 (m, br, 1H), 4.73 (m, br, 1H), 7.2-7.4 (m, 5H).

^{13}C-NMR: δ 14.58, 19.01, 25.39, 29.06, 39.50, 39.98, 48.51, 61.55, 72.48, 126.09, 127.65, 128.69, 145.04, 156.65.

IR(film): 3424, 3100, 3077, 3063, 3031, 2986, 2942, 2880, 1650, 1430, 1265 and 1170 cm^{-1}.

MS (70 eV) m/z 277 (M^+, 20%), 202 (5%), 156 (100%), 128 (17%), 105 (29%), 84 (26%), 45 (22%).

6a: ^{1}H-NMR: δ 1.29 (t, 3H, J = 7.2), 1.4-1.7 (m, 6H), 1.7-1.85 (m, 1H), 2.22 (dt, br, 1H, J = 13.2 and 2.4), 2.84 (dt, br, 1H, J = 13.2 and 2.4), 4.09 (d, br, 1H, J = 13.2), 4.18 (q, 2H, J = 7.2), 4.6-4.8 (m, 3H), 7.2-7.4 (m, 5H).

^{13}C-NMR: δ 14.61, 19.14, 25.46, 29.33, 39.33, 40.32, 47.49, 61.99, 70.01, 125.97, 127.48, 128.69, 144.48, 157.79.

(1SR,2SR)- and (1RS,2SR)-N-tert-Butoxycarbonyl-2-(β-Hydroxy--β-phenylethyl)-piperidine (**5b** and **6b**).

To a stirred solution of **4b** (0.151 g, 0.5 mmol) in THF (3.0 ml), at -78°C and under nitrogen atmosphere, was added dropwise a 1.0 M solution of LiBH $(C_2H_5)_3$ in THF (0.7 ml, 0.7 mmol). After 2 hours at -78°C, the reaction was quenched by addition of water (2.0 ml) and allowed to warm up to room temperature.

After extraction with ether (3 x 2.0 ml), the combined organic extracts were washed with brine (2 x 2.0 ml), dried over $MgSO_4$ and evaporated under reduced pressure. Column chromatography on silica gel (hexane-ether 95:5) afforded 5b (0.113 g, 0.37 mmol) as a colorless oil and **6b** (0.037 g, 0.12 mmol) as a colorless solid (m.p. 74.4-75.7°C).

5b: ^{1}H-NMR: δ 1.44 (s, 9H), 1.5-1.6 (m, br, 6H), 1.8-1.92 (m, 1H), 2.0-2.17 (m, 1H), 2.7-2.9 (m, 1H), 3.8-4.0 (m, 2H), 4.39 (m, br, 1H), 4.73 (m, br, 1H), 7.2-7.4 (m, 5H).

^{13}C-NMR: δ 19.09, 25.44, 28.48, 29.18, 39.55, 40.37, 48.56, 72.62, 79.77, 125.75, 127.25, 128.34, 144.74.

IR(film): 3400, 3085, 3064, 3029, 2980, 2940, 2925, 1690, 1665, 1420, 1364, 1274 and 1160 cm^{-1}.

MS (70 eV) m/z 305 (M^+, 6%), 249 (6%), 205 (7%), 184 (10%), 128 (94%), 84 (86%), 57 (100%).

6b: ^{1}H-NMR: δ 1.49 (s, 9H), 1.5-1.8 (m, br, 7H), 2.21 (m, 1H), 2.80 (m, 1H), 4.05 (m, br, 1H), 4.44 (m, br, 1H), 4.58 (m, br, 1H), 4.75 (s, br, 1H), 7.2-7.5 (m, 5H).

^{13}C-NMR: δ 19.20, 25.52, 28.44, 29.29, 39.54, 40.36, 46.80, 69.11, 80.38, 125.57, 127.04, 128.29, 128,65, 144.11.

IR(KBr): 3435, 3070, 3020, 2970, 2930, 2870, 2850, 1652, 1645, 1415, 1360, 1280, 1160 cm^{-1}.

MS (70 eV) m/z 305 (M^+, 12%), 249 (15%), 205 (16%), 184 (20%), 128 (100%), 104 (32%), 84 (98%), 77 (25%), 57 (97%), 43 (24%), 41 (54%).

(+/-)-Sedamine (**8**)

A solution of **5a** (0.138 g, 0.5 mmol) in THF (0.5 ml) was added dropwise to a stirred suspension of $LiAlH_4$ (0.030 g, 0.79 mmol) in ether (0.6 ml). The reaction mixture was refluxed for 20 hours and quenched by the addition of water (0.1 ml), 15% aqueous NaOH (0.1 ml) and water (0.3 ml), respectively. The resulting mixture was extracted with ether (3 x 1.0 ml), dried over $MgSO_4$ and the organic solvent was evaporated under reduced pressure. The crude material was recrystallized from CH_2Cl_2-hexane to afford

0.106 g (0.48 mmol, 96% yield) of a colorless solid (m.p. 89.6--90.1°C, lit. 14d: 90°C).

^{1}H-NMR ($CDCl_3/D_2O$) δ 1.2-1.8 (m, 7H), 2.12 (m, 1H), 2.50 (s, 3H), 2.4-2.7 (m, 1H), 2.82 (m, 1H), 3.04 (m, 1H), 4.90 (dd, 1H, J = 10.6 and 2.8), 7.2-7.4 (m, 5H).

^{13}C-NMR: δ 20.54, 22.45, 25.84, 39.90, 40.09, 51.44, 61.14, 75.01, 125.99, 127.46, 128.72, 146.15.

IR(KBr): 3396, 3166, 3076, 3016, 2985, 2945, 2925, 2915, 2915, 2846, 2814, 2786, 1456, 1376, 1196, 1075 and 1058 cm^{-1}.

MS (70 eV) m/z 219 (M^+, 11%), 112 (3%), 99 (13%), 98 (100%), 84 (2%), 79 (5%), 77 (5%), 70 (11%).

(+/-)-Allosedamine (**9**)

The same procedure described above afforded 0.017 g (0.08 mmol, 81% yield) of (+/-)-allosedamine (**9**) (m.p. 68.2-70.0°C, lit. 14d: 68-69°C) from 0.030 g (0.1 mmol) of **6a**.

^{1}H-NMR: δ 1.25-1.31 (m, 2H), 1.6-1.8 (m, 4H), 1.8-2.0 (m, 2H), 2.17 (m, 1H), 2.30 (m, 1H), 2.54 (s, 3H), 3.09 (m, 1H), 3.6-4.4 (s, br, 1H), 5.13 (dd, 1H, J = 10.5 and 3.3), 7.2-7.4 (m, 5H).

^{13}C-NMR: δ 24.28, 25.42, 29.22, 39.43, 43.85, 56.90, 62.60, 71.88, 125.58, 126.85, 128.20, 145.48.

IR(KBr): 3263, 3084, 3062, 3025, 2990, 2941, 2859, 2800, 1601, 1491, 1463, 1378 and 1061 cm^{-1}.

MS (70 eV) m/z 219 (M^+, 12%), 113 (5%), 99 (11%), 98 (100%), 70 (9%).

α-Phenacylpiperidine

A solution of **3b** (0.210 g, 0.69 mmol) in trifluoroacetic acid (1.5 ml) was stirred for 30 min. at room temperature. The mixture

was then diluted with CH_2Cl_2 (5.0 ml), neutralized with saturated aqueous $NaHCO_3$ and washed with water. The organic phase was dried over $MgSO_4$ and the organic solvent was removed under reduced pressure to give 0.199 g (0.67 mmol, 98% yield) of α-phenacylpiperidine as a pale yellow oil[21].

^{1}H-NMR: ($CDCl_3/D_2O$) δ 1.2-1.5 (m, 4H), 1.5-1.63 (m, 2H), 1.65-1.85 (m, 1H), 2.5-2.8 (m, 1H), 3.0-3.2 (m, 3H), 7.5-7.8 (m, 3H), 7.95 (d, 2H, J = 7.0).

^{13}C-NMR ($CDCl_3/D_2O$) δ 24.76, 25.96, 32.66, 45.53, 46.87, 52.96, 128.14, 128.69, 133.28, 137.14, 199.55.

IR(film): 3326, 3056, 3026, 2926, 2848, 1686, 1448, 1206, 1176 and 1136 cm^{-1}.

MS (70 eV) m/z 203 (M^+, 41%), 173 (23%), 105 (67%), 98 (29%), 91 (41%), 84 (100%), 77 (74%), 59 (96%), 43 (76%).

(+/-)-Norsedamine (7)

a) $Zn(BH_4)_2$ reduction

To a stirred solution of α-phenacylpiperidine (0.099 g, 0.49 mmol) in THF (2.0 ml), at -78°C and under a nitrogen atmosphere, was added dropwise a 0.16 M ethereal solution of $Zn(BH_4)_2$ (0.12 ml, 0.98 mmol). After 2 hours at -78°C the reaction was quenched with saturated aqueous NH_4Cl (2.0 ml). After extraction with ether (3 x 2.0 ml), the combined organic phases were washed with brine (2 x 2.0 ml), dried over $MgSO_4$ and evaporated under reduced pressure. Fractional crystallization of the residue (CH_2Cl_2-hexane) afforded 0.075 g (0.37 mmol, 75% yield) of (+/-)-norsedamine (7), m.p. 91-93°C (lit. 20: 92-93°C).

b) $LiBH(C_2H_5)_3$ reduction

To a stirred solution of α-phenacylpiperidine (0.099 g, 0.49 mmol) in THF (2.0 ml), at -78°C and under nitrogen atmosphere, was added dropwise a 1.0 M solution of $LiBH(C_2H_5)_3$ in THF (1.0 ml, 1.0 mmol). After 2 hours at -78°C, the reaction was quenched by addition of a saturated NH_4Cl solution (2.5 ml) and extracted with CH_2Cl_2 (3 x 3.0 ml). The combined organic extracts were dried over $MgSO_4$ and the solvent was removed under reduced pressure to afford 0.104 g (77% yield) of **10**, as a colorless solid (m.p. 93.5-96.0°C, after recrystallization from CH_2Cl_2-hexane.

^{1}H-NMR: δ 0.21 (m, 2H), 0.57 (m, 1H), 0.69 (m, 1H), 0.79 (t, 3H, J = 7.8). 0.88 (t, 3H, J = 7.8), 1.25 (m, 2H), 1.45 (m, 2H), 1.84 (m, 4H), 2.37 (m, 2H), 3.12 (m, 2H), 4.73 (d, 1H, J = 11.1), 7.18 (m, 1H), 7.29 (t, 2H, J = 7.2), 7.41 (d, 2H, J = 6.6).

^{13}C-NMR: δ 8.31, 8.83, 23.36, 26.10, 33.74, 44.07, 45.24, 55.82, 69.80, 125.75, 126.54, 128.10, 146.51.

IR(KBr): 3226, 3086, 3064, 3024, 2946, 2926, 2896, 2846, 2826, 1446, 1126 and 1111 cm^{-1}.

MS (70 eV) m/z 273 (M^+, 0.8%), 245 (16%), 244 (87%), 243 (23%), 104 (11%), 91 (7%), 84 (81%), 72 (22%), 59 (34%), 45 (100%).

0.104 g (0.38 mmol) were taken up in methanol (8.0 ml) and to this solution were added a solution containing 30% of H_2O_2 (2.5 ml) and phosphate buffer (5.0 ml). The mixture was stirred 30 min. at room temperature and the volatiles were removed under reduced pressure. The residue was extracted with CH_2Cl_2 (3 x 5.0 ml) and the combined organic phases were dried over $MgSO_4$ and the solvent

was removed underreduced pressure to afford, after recrystallization from CH_2Cl_2-hexane, 0.070 g (0.34 mmol, 70% overall yield) of (+/-)-norsedamine (7), m.p. 91-93°C (lit. 20: 92-93°C).

^{1}H-NMR: δ 1.10 (m, 1H), 1.31 (m, 2H), 1.46-1.71 (m, 5H), 1.82 (m, 1H), 2.63 (m, 1H), 2.88 (m, 1H), 3.06 (m, 1H), 4.92 (dd, 1H, J = 10.8 and 2.7), 7.22 (m, 1H), 7.34 (m, 4H).

^{13}C-NMR: δ 24.48, 27.32, 34.26, 45.19, 46.00, 58.25, 75.45, 125.54, 126.94, 128.15, 145.27.

IR(KBr): 3400, 3301, 3140, 3064, 3023, 1450, 1382, 1300, 1212, 1176, 1157, 742 cm^{-1}.

MS (70 eV m/z 205 (M^+, 11%), 149 (6%), 98 (6%), 85 (7%), 84 (100%), 77 (4%), 56 (10%).

(+/-)-Sedamine (8)

To a stirred solution of 7 (0.205 g, 1.0 mmol) and 37% aqueous formaldehyde (0.4 ml, 5.0 mmol) in acetonitrile (3.0 mmol) was added sodium cyanoborohydride (0.156 g, 2.5 mmol). The reaction mixture was stirred for 45 min. at room temperature and then glacial acetic acid was added dropwise until pH 5.0. Stirring was continued for an additional 20 min. when 1% aqueous KOH was added until pH 7.0 .

The resulting mixture was extracted with ether (3 x 5 ml), the combined organic extracts were washed with brine, dried over $MgSO_4$ and evaporated under reduced pressure to give an oil which was purified by column chromatography on silica gel (92:8 $CHCl_3$-MeOH) to give 0.193 g (0.88 mmol, 88% yield) of (+/-)-sedamine (8), m.p. 89.6-90.1°C (lit. 14d, 90°C).

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