Synthesis of Biologically Important Guanidine-Containing Molecules Using Triflyl-Diurethane Protected Guanidines

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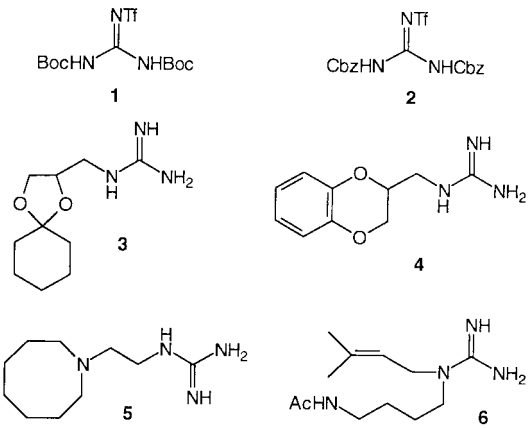
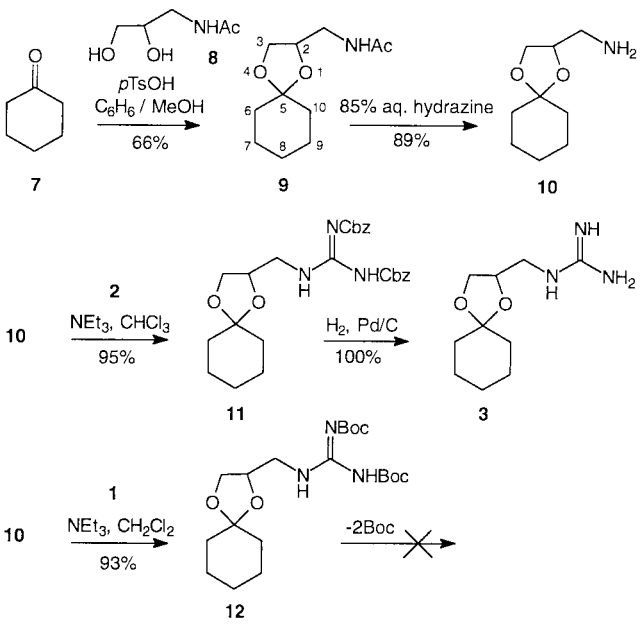
Abstract: The guanidine-containing biologically important molecules, guanadrel, guanoxan, guanethidine and smirnovine have been synthesized using the recently developed triflyl-diurethane protected guanidines.

Key words: guanadrel, guanoxan, guanethidine, smirnovine, guanidinylation

Numerous natural and non-natural guanidine-containing compounds have had an significant impact on agricultural and medicinal chemistry. Moreover, many of these novel molecules have shown unprecedented activity ranging from antimicrobial, antiviral, antifungal to neurotoxic making these compounds and their derivatives clear targets for drug design and discovery.[1] With increasing numbers of bioactive molecules containing the guanidine moiety, there is a continuing need for a general and efficient method for their syntheses. We have recently reported the use of *N*,*N*'-di-Boc-*N*''-triflylguanidine (**1**) and *N*,*N*'-di-Cbz-*N*''-triflylguanidine (**2**) for the guanidinylation of amines under mild conditions and in high yields.[2] Application of this procedure has now been extended to the facile syntheses of the therapeutic agents, guanadrel (**3**),[3] guanoxan (**4**),[4] and guanethidine (**5**).[5] We have also applied this method to the preparation of the *N*,*N*-dialkylated guanidino-alkaloid, smirnovine (**6**).[6]



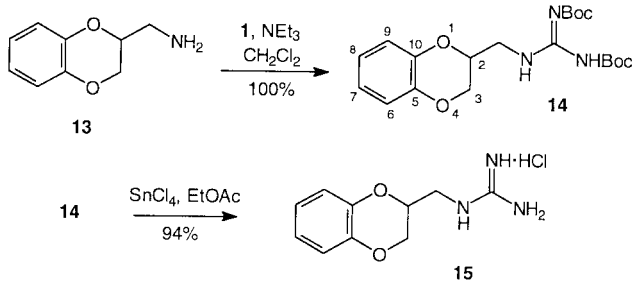
To date, the preparation of compounds **3**, **4**, and **5** involves either treatment of the appropriate amine with *S*-methylisothiourea[4–6] or reaction of a tosylate derivative with guanidine.[5] Both methods often require elevated temperatures and extended periods of time in polar solvents, such as H_2O, methanol, *tert*-butanol, or DMF for reasons of solubility. The precursor amine **10** of guanadrel (**3**) was prepared through ketalization of cyclohexanone (**7**) with diol **8**[7] to provide intermediate **9** (Scheme 1). The subsequent removal of the acetyl group of compound **9** using aqueous hydrazine afforded amine **10** in a reasonable overall yield for the two steps. Using either reagent **1** or **2**, the guanidinylation step was carried out with a slight excess of amine **10** at room temperature in the presence of Et_3N. After an aqueous workup, derivatives **11** and **12** were isolated in 95 and 93% yield, respectively. Catalytic hydrogenolysis under parr conditions led to the deprotection of the Cbz groups of compound **11** in quantitative yield to give guanadrel (**3**) as the free base. Deprotection of the Boc groups of compound **12** was not possible in the presence of the labile ketal (Scheme 1).



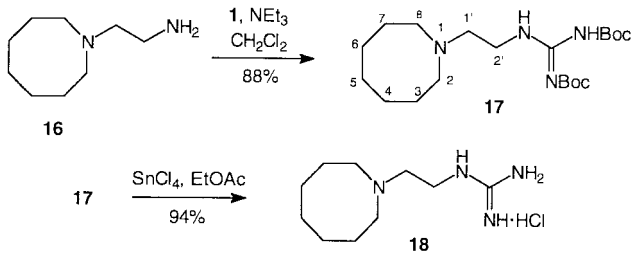
Scheme 1

The precursor amine **13** of guanoxan hydrochloride (**15**) was prepared following literature procedure.[8] In an analogous process to the guanidinylation of compound **12**, excess amine **13** was treated with reagent **1** in the presence of Et_3N to afford diBoc guanoxan (**14**) in quantitative yield. After deprotection with $SnCl_4$[9] followed by crystal-

lization, guanoxan hydrochloride (**15**) was isolated in 94% yield (Scheme 2). Guanethidine hydrochloride (**18**) was also prepared in a parallel method to that described for compound **12** by guanidinylation of amine **16**[10] followed by deprotection with $SnCl_4$ providing target compound **18** in 83% overall yield for the two steps (Scheme 3).

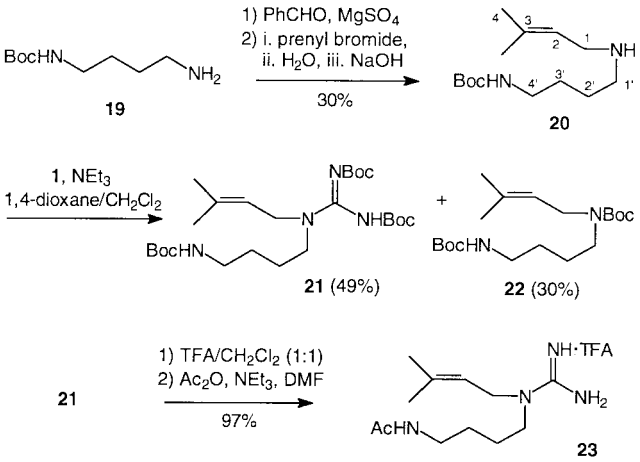


Scheme 2



Scheme 3

The only published synthesis of smirnovine (**6**) employs the conversion of the *N*-acetyl derivative of secondary amine **20** to a nitrocarboxylic ester intermediate followed by ammonolysis and acidification to give the picrate salt of smirnovine (**6**) in modest yield.[6] The synthesis of smirnovine using *S*-methylisothiourea as the guanidinylation agent was unsuccessful.[6] The secondary amine **20** was prepared according to literature procedure[11] from compound **19**. The readily available monoBoc-protected amine **19**[12] was used as our starting material rather than the corresponding acetyl derivative as used by Hessing and co-worker.[11] The guanidinylation of amine **20** was successfully carried out in a mixture of 1,4-dioxane/CH_2Cl_2 using excess reagent **1** (Scheme 4). The target compound **21** was isolated in 49% yield along with an unexpected side product **22** which presumably was formed by nucleophilic attack of amine **20** at the carbonyl carbon of a Boc group rather than the imine of the guanidinylation reagent. (This side product **22** may be easily recycled if the acetyl or Cbz derivative of compound **19** is used as the starting material.) The Boc protecting groups were removed with TFA followed by selective acylation with acetic anhydride to give the trifluoroacetate salt of smirnovine (**23**) in 97% yield (Scheme 4).



Scheme 4

In summary, the guanidinylation methods described above constitute a novel, simple and efficient route to biologically important guanidine-containing molecules.

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. CH_2Cl_2 and $CHCl_3$ were dried first with neutral alumina (Brockman activity I, Fisher Scientific) and NEt_3 with KOH then distilled from CaH_2. Analytical thin-layer chromatography was carried out on precoated silica gel plates (Kieselgel 60 F254, E. Merck & Co., Germany). Flash column chromatography was performed using silica gel (230–400 mesh) from J. T. Baker. All NMR spectra were obtained on a 360 MHz spectrometer assembled at UCSD with a pulse programmer, digitizer, and an Oxford Instruments superconducting magnet and a 400 MHz Varian Mercury spectrometer. Mass spectra were obtained at the Scripps Research Institute, La Jolla, CA. Elemental analysis was performed by Desert Analytics, Tucson, AZ. Melting points were determined with a uni-melt capillary melting apparatus.

***N*-(1,4-dioxaspiro[4.5]dec-2-ylmethyl)acetamide (9)**

To diol **8** (323 mg, 2.43 mmol) in benzene/MeOH (5:1, 15 mL) was added *p*-toluenesulfonic acid (5 mg, 0.024 mmol) and cyclohexanone (**7**, 357 mg, 3.64 mmol) at r.t. The reaction flask was equipped with a Dean–Stark trap, condenser and drying tube and heated to reflux. After 24 h, the solution was cooled to r.t. and concentrated under reduced pressure. The resulting residue was dissolved in CH_2Cl_2 (25 mL) and washed with H_2O (30 mL), sat. $NaHCO_3$ (30 mL), and brine (30 mL) and dried ($MgSO_4$). After removal of the solvent under reduced pressure, purification on silica gel (95:5 $CHCl_3$/MeOH) provided compound **9** (341 mg, 66%).

^{1}H NMR ($CDCl_3$; 360 MHz): δ = 1.26–1.45 (m, 2H, H-8), 1.46–1.55 (m, 4H, H-7,9), 1.56–1.60 (m, 4H, H-6,10), 1.97 (s, 3H, Ac), 3.21 (ddd, 1H, *J* = 14.0, 6.1, 6.1 Hz, C*H*$_2$NHAc), 3.51 (ddd, 1H, *J* = 14.0, 6.1, 3.2 Hz, C*H*$_2$NHAc), 3.57 (dd, 1H, *J* = 8.3, 6.1 Hz, H-3), 3.99 (dd, 1H, *J* = 8.3, 6.5 Hz, H-3), 4.18 (dddd, 1H, *J* = 6.5, 6.1, 6.1, 3.2 Hz, H-2), 5.93 (br s, 1H, NH).

^{13}C NMR ($CDCl_3$; 100 MHz): δ = 23.0, 23.6, 23.9, 25.0, 34.6, 36.4, 41.8, 66.3, 74.0, 109.6, 170.2.

HRMS (FAB) calcd for $C_{11}H_{19}NO_3$ (M_r) 214.1443 $(M+H)^+$, found 214.1440 Δ = 1.4 ppm.

1,4-Dioxaspiro[4.5]dec-2-ylmethanamine (10)

Compound **9** (724 mg, 3.40 mmol) was dissolved in 85% aq. hydrazine (10 mL) and heated at 100 °C for 18 h. The solution was cooled to r.t. and diluted with H_2O (35 mL) then extracted with $CHCl_3$

(2 × 30 mL), washed with H_2O (35 mL) and brine (35 mL) and dried ($MgSO_4$). After removal of the solvent under reduced pressure, amine **10** (517 mg, 89%) was purified on silica gel (3:1 $CHCl_3$/MeOH).

^{1}H NMR (**10**, $CDCl_3$; 400 MHz): δ = 1.30–1.37 (m, 2H, H-8), 1.49–1.54 (m, 8H, H-6,7,9,10), 2.68 (dd, 1H, *J* = 13.2, 6.8 Hz, C*H*$_2$NH$_2$), 2.75 (dd, 1H, *J* = 13.2, 4.0 Hz, C*H*$_2$NH$_2$), 3.57 (dd, 1H, *J* = 7.2, 6.8 Hz, H-3), 3.94 (dd, 1H, *J* = 7.2, 7.2 Hz, H-3), 4.03 (dddd, 1H, *J* = 7.2, 6.8, 6.8, 4.0 Hz, H-2)

^{13}C NMR (**10**, $CDCl_3$; 100 MHz): δ = 23.7, 24.0, 25.1, 34.8, 36.5, 44.8, 66.4, 76.7, 109.4.

HRMS (FAB) calcd for $C_9H_{17}NO_2$ (M_r) 172.1338 $(M+H)^+$, found 172.1339 Δ = 0.6 ppm.

_N_-(1,4-Dioxaspiro[4.5]dec-2-ylmethyl)-_N'_,_N"_-bis(benzyloxycarbonyl)guanidine (11)

Reagent **2** (490 mg, 1.07 mmol) in $CHCl_3$ (2 mL) was added to a solution of amine **10** (200 mg, 1.18 mmol) and Et_3N (0.16 mL, 1.18 mmol) in $CHCl_3$ (5 mL) at r.t. After 8 h, the mixture was diluted with $CHCl_3$ (15 mL) and washed with 2M $NaHSO_4$ (15 mL), sat. $NaHCO_3$ (15 mL) and brine (15 mL) and dried ($MgSO_4$) (standard workup). After removal of the solvent under reduced pressure, the product (**11**, 488 mg, 95%) was purified on silica gel (4:1 hexanes/EtOAc).

^{1}H NMR ($CDCl_3$; 400 MHz): δ = 1.39–1.41 (m, 2H, H-8), 1.54–1.69 (m, 8H, H-6,7,9,10), 3.58 (ddd, 1H, *J* = 13.6, 6.0, 5.6 Hz, CH_2-guan), 3.66 (dd, 1H, *J* = 8.4, 6.0 Hz, H-3), 3.68 (ddd, 1H, *J* = 13.6, 4.8, 4.0 Hz, CH_2-guan), 4.02 (dd, 1H, *J* = 8.4, 6.8 Hz, H-3), 4.29 (dddd, 1H, *J* = 6.8, 6.0, 6.0, 4.8 Hz, H-2), 5.12 (s, 2H, CH_2Ar), 5.19 (s, 2H, CH_2Ar), 7.28–7.39 (m, 10H, ArH), 8.65 (s, 1H, CH_2N*H*), 11.72 (s, 1H, N*H*Boc).

^{13}C NMR ($CDCl_3$; 100 MHz): δ = 23.9, 24.1, 25.2, 34.7, 36.4, 43.2, 66.1, 67.2, 68.2, 73.3, 110.1, 127.8, 128.0, 128.2 (2C), 128.4 (2C), 128.5 (2C), 128.6 (2C), 134.4, 136.5, 153.4, 156.2, 163.3.

HRMS (FAB) calcd for $C_{26}H_{31}N_3O_6$ (M_r) 482.2291 $(M+H)^+$, found 482.2280 Δ = 2.3 ppm.

_N_-(1,4-Dioxaspiro[4.5]dec-2-ylmethyl)-_N'_,_N"_-bis(*tert*-butoxycarbonyl)guanidine (12)

Reagent **1** (421 mg, 1.08 mmol) was added as a solid to a solution of amine **10** (203 mg, 1.18 mmol) and Et_3N (0.17 mL, 1.18 mmol) in CH_2Cl_2 (6 mL) at r.t. After 1.5 h and standard workup, the solvent was evaporated in vacuo. The product (**12**, 413 mg, 93%) was shown to be greater than 95% pure by ^{1}H NMR but could be further purified on silica gel (99:1 $CHCl_3$/MeOH) or by recrystallization from hexanes, mp 127–129 °C.

^{1}H NMR ($CDCl_3$; 360 MHz): δ = 1.34–1.41 (m, 2H, H-8), 1.47 (s, 18H, 2Boc), 1.51–1.68 (m, 8H, H-6,7,9,10), 3.53–3.67 (m, 3H, CH_2-guan+H-3), 4.01 (dd, 1H, *J* = 7.9, 6.8 Hz, H-3), 4.26 (m, 1H, H-2), 8.66 (br s, 1H, CH_2N*H*), 11.46 (br s, 1H, N*H*Boc).

MS(FAB): m/z (%) = 436 (7, $\{M+Na\}^+$), 414 (100, $\{M+H\}^+$).

(1,4-Dioxaspiro[4.5]dec-2-ylmethyl)guanidine (Guanadrel, 3)

Compound **11** (133 mg, 0.276 mmol) was dissolved in MeOH/THF (3:1, 10 mL) and transferred to a high pressure flask. After 10% Pd/C (40 mg) was added, the solution was shaken under a pressure of 50 psi for 3 h. The resulting solution was filtered through Celite, rinsed with MeOH, and the solvent removed under reduced pressure to give guanadrel (**3**, 59 mg, 100%) as the free base. Compound **3** was shown to be greater than 95% pure by ^{1}H NMR.

^{1}H NMR (DMSO; 400 MHz): δ = 1.29–1.34 (m, 2H, H-8), 1.45–1.54 (m, 8H, H-6,7,9,10), 3.19 (dd, 1H, *J* = 14.4, 6.0 Hz, CH_2-guan), 3.30 (dd, 1H, *J* = 14.4, 4.8 Hz, CH_2-guan), 3.60 (dd, 1H, *J* = 8.4, 6.0 Hz, H-3), 3.98 (dd, 1H, *J* = 8.4, 6.4 Hz, H-3), 4.13 (dddd, 1H, *J* = 6.4, 6.0, 6.0, 4.8 Hz, H-2).

^{13}C NMR (DMSO; 100 MHz): δ = 23.4, 23.6, 24.7, 34.5, 36.0, 43.2, 65.8, 73.4, 109.1, 157.6.

HRMS (FAB) calcd for $C_{10}H_{19}N_3O_2$ (M_r) 214.1556 $(M+H)^+$, found 214.1558 Δ = 0.9 ppm.

_N_-(1,4-Benzodioxan-2-ylmethyl)-_N'_,_N"_-bis(*tert*-butoxycarbonyl)guanidine (14)

Method as for compound **12**: reagent **1** (284 mg, 0.73 mmol), amine **13** (132 mg, 0.80 mmol) and Et_3N (0.11 mL, 0.80 mmol). After 40 min and standard workup, the product (**15**, 296 mg, 100%) was shown to be greater than 95% pure by ^{1}H NMR then recrystallized from hexanes, mp 124–127 °C.

^{1}H NMR ($CDCl_3$; 360 MHz): δ = 1.48 (s, 18H, 2Boc), 3.61 (ddd, 1H, *J* = 14.0, 7.2, 5.2, CH_2-guan), 3.86 (ddd, 1H, *J* = 14.0, 5.2, 4.0, CH_2-guan), 3.97 (dd, 1H, *J* = 11.3, 7.2 Hz, H-3), 4.29 (dd, 1H, *J* = 11.3, 2.2 Hz, H-3), 4.34 (dddd, 1H, *J* = 7.2, 7.2, 4.0, 2.2 Hz, H-2), 6.81–6.92 (m, 4H, ArH), 8.71 (br s, 1H, CH_2N*H*), 11.46 (br s, 1H, N*H*Boc).

MS (FAB): m/z (%) = 430 (14, $\{M+Na\}^+$), 408 (100, $\{M+H\}^+$).

(1,4-Benzodioxan-2-ylmethyl)guanidine Hydrochloride (Guanoxan•HCl, 15)

Neat $SnCl_4$ (0.09 mL, 0.76 mmol) was added dropwise to compound **14** (143 mg, 0.356 mmol) in anhyd EtOAc (2 mL) at r.t. After 3 h, the solvent and excess $SnCl_4$ were removed under reduced pressure. The resulting solid was dissolved in MeOH and precipitated by the addition of Et_2O. On standing at r.t., guanoxan•HCl (**15**, 43.3 mg, 94%) crystallized from solution, mp 145–147 °C (Lit.[13] 147–148 °C)

^{1}H NMR (D_2O; 360 MHz): δ = 3.36 (dd, 1H, *J* = 14.8, 6.8 Hz, CH_2-guan), 3.44 (dd, 1H, *J* = 14.8, 4.3 Hz, CH_2-guan), 3.94 (dd, 1H, *J* = 11.5, 5.8 Hz, H-3), 4.18 (dd, 1H, *J* = 11.5, 2.3 Hz, H-3), 4.28 (dddd, 1H, *J* = 6.8, 5.8, 4.3, 2.3 Hz, H-2), 6.79 (br s, 4H, ArH).

^{13}C NMR (DMSO; 100 MHz): δ = 40.9, 64.7, 71.1, 116.8, 116.9, 121.2, 121.4, 142.1, 142.5, 157.0.

_N_-(2-Azocan-1-ylethyl)-_N'_,_N"_-bis(*tert*-butoxycarbonyl)guanidine (17)

Method as for compound **12**: reagent **1** (260 mg, 0.66 mmol), amine **16** (114 mg, 0.73 mmol) and Et_3N (0.10 mL, 0.73 mmol). Compound **17** (233 mg, 88%) was purified on silica gel (98:2 $CHCl_3$/MeOH).

^{1}H NMR ($CDCl_3$; 360 MHz): δ = 1.46 (s, 9H, Boc), 1.48 (s, 9H, Boc), 1.53–1.60 (m, 10H, H-3,4,5,6,7), 2.48–2.53 (m, 4H, H-2,8), 2.58 (t, 2H, *J* = 4.7 Hz, H-1'), 3.42 (dt, 2H, *J* = 4.7, 4.7 Hz, H-2'), 8.73 (br s, 1H, CH_2N*H*), 11.43 (br s, 1H, N*H*Boc).

^{13}C NMR ($CDCl_3$; 100 MHz) δ = 25.7 (5C), 28.1 (3C), 28.4 (3C), 29.8, 39.6, 54.8, 57.6, 79.1, 82.6, 152.6, 155.9, 163.4.

HRMS (FAB) calcd for $C_{20}H_{38}N_4O_4$ (M_r) 399.2971 $(M+H)^+$, found 399.2982 Δ = 2.8 ppm.

(2-Azocan-1-ylethyl)guanidine Hydrochloride (Guanethidine•HCl, 18)

Method as for compound **15**: $SnCl_4$ (0.04 mL, 0.36 mmol), compound **17** (36 mg, 0.09 mmol). Guanethidine•HCl (**18**, 19.8 mg, 94%) was crystallized from MeOH/Et_2O. Compound **18** was neutralized with NaOH and acidified with H_2SO_4 to give guanethidine sulfate,[5] mp 275–279 °C (Lit.[5] 276–281 °C {dec.}).

^{1}H NMR (**18**, D_2O; 360 MHz): δ = 1.50–1.59 (m, 2H, CH_2 of ring), 1.67–1.81 (m, 6H, CH_2 of ring), 1.90–2.00 (m, 2H, CH_2 of ring),

3.19–3.24 (m, 2H, H-2), 3.37 (t, 2H, *J* = 6.4 Hz, H-1'), 3.43–3.50 (m, 2H, H-8), 3.61 (t, 2H, *J* = 6.4, H-2').

^{13}C NMR (**18**, DMSO; 100 MHz): δ = 22.0 (2C), 23.9, 25.2 (2C), 36.0 (2C), 50.7, 53.4, 156.7.

HRMS (FAB) calcd for $C_{10}H_{22}N_4$ (M_r) 199.1923 $(M+H)^+$, found 199.1921 Δ = 1.0 ppm.

_N_-(4'-_tert_-Butoxycarbonylaminobutyl)-_N_-(3-methylbuten-2-yl)amine (20)

Compound **20** was prepared according to literature procedure[11] in 30% overall yield from amine **19**, mp 133–135 °C.

^{1}H NMR ($CDCl_3$; 360 MHz): δ = 1.43 (s, 9H, Boc), 1.50–1.56 (m, 4H, H-2',3'), 1.64 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 2.14 (br s, 1H, NH), 2.62 (t, 2H, *J* = 7.6 Hz, H-1'), 3.11 (br s, 2H, H-4'), 3.21 (d, 2H, *J* = 6.8 Hz, H-1), 4.88 (br s, 1H, N*H*Boc), 5.25 (t, 1H, *J* = 6.8 Hz, H-2).

^{13}C NMR ($CDCl_3$; 100 MHz): δ = 17.6, 25.2, 25.3, 27.2, 28.0 (3C), 39.6, 45.7, 47.1, 78.1, 118.8, 136.5, 155. 5.

HRMS (FAB) calcd for $C_{14}H_{28}N_2O_2$ (M_r) 257.2229 $(M+H)^+$, found 257.2233 Δ = 1.6 ppm.

_N_-(4'-Boc-aminobutyl)-_N_-(3-methylbuten-2-yl)-_N'_,_N''_-bis(Boc-carbonyl)guanidine (21)

Method as for compound **12**: reagent **1** (82.0 mg, 0.209 mmol), amine **20** (44.7 mg, 0.175 mmol) and Et_3N (0.06 mL, 0.420 mmol) in 1,4-dioxane/CH_2Cl_2 (5:1, 3 mL). After 10 d and standard workup, the product (**21**, 42.6 mg, 49%) was isolated and purified on silica gel (100% $CHCl_3$, 5:1 hexanes/EtOAc) to give a pale yellow oil along with compound **22** (18.6 mg, 30%).

^{1}H NMR ($CDCl_3$; 400 MHz): δ = 1.39 (s, 9H, Boc), 1.44 (s, 18H, 2Boc), 1.53–1.56 (m, 4H, H-2',3'), 1.62 (s, 3H, CH_3), 1.69 (s, 3H, CH_3), 3.09 (dt, 2H, *J* = 5.6, 5.6 Hz, H-4'), 3.35 (t, 2H, *J* = 6.8 Hz, H-1'), 3.92 (d, 2H, *J* = 7.2 Hz, H-1), 4.87 (br s, 1H, BocN*H*CH_2), 5.14 (t, 1H, *J* = 7.2 Hz, H-2), 9.60 (br s, 1H, N = CN*H*Boc).

^{13}C NMR ($CDCl_3$; 100 MHz): δ = 17.9, 24.3, 25.7, 27.0, 28.2 (6C), 28.5 (3C), 29.7, 39.8, 47.0, 78.8, 119.3, 136.5, 154.7, 155.7 (These were the resonances observed. The resonances of the quaternary carbons of two *t*-Bu groups may be overlapping with 78.8 or $CHCl_3$, and resonances corresponding to carbons of the imine and one carbonyl may be overlapping with 154.7 and 155.7. The ^{13}C NMR spectrum in DMSO did not resolve the peaks).

HRMS (FAB) calcd for $C_{25}H_{46}N_4O_6$ (M_r) 499.3496 $(M+H)^+$, found 499.3506 Δ = 2.0 ppm.

_N_-(4'-Acetaminobutyl)-_N_-(3-methylbuten-2-yl)guanidine Trifluoroacetate (Smirnovine•TFA, 23)

A solution of TFA/CH_2Cl_2 (1:1, 2 mL) was added to compound **21** (44.7 mg, 0.090 mmol) at r.t. The mixture was stirred for 1.5 h and the volatiles removed under reduced pressure. The resulting residue was dissolved in DMF (3 mL) and Et_3N (10 μL, 0.072 mmol) was added at r.t. After 10 min, Ac_2O (8 μL, 0.081 mmol) was added and allowed to stir for 1 h. The solution was concentrated under reduced pressure and compound **23** (30.8 mg, 97%) was recrystallized from MeOH/hexanes, mp 108–110 °C.

^{1}H NMR (DMSO; 400 MHz): δ = 1.30–1.38 (m, 2H, CH_2), 1.44–1.51 (m, 2H, CH_2), 1.66 (s, 3H, CH_3), 1.71 (s, 3H, CH_3), 1.78 (s, 3H, Ac), 3.01 (dt, 2H, *J* = 6.0, 5.6 Hz, H-4'), 3.18 (t, 2H, *J* = 7.2 Hz, H-1'), 3.89 (d, 2H, *J* = 6.4 Hz, H-1), 5.10 (t, 1H, *J* = 6.4 Hz, H-2), 7.37 (br s, 4H,+H_2N = CNH_2), 9.46 (br s, 1H, NH).

^{13}C NMR (DMSO; 100MHz): δ = 17.8, 22.6, 24.2, 25.4, 26.3, 37.9, 45.6, 47.0, 118.2, 136.5, 155.5, 168.9.

HRMS (FAB) calcd for $C_{12}H_{24}N_4O$ (M_r) 241.2028 $(M+H)^+$, found 241.2030 Δ = 0.8 ppm.

Acknowledgement

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