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Synthesis, structure and cytotoxicity of new 2-[(3-aminopropyl)dimethylsilyl]-5-furfural diethylacetals and 2-[(3-aminopropyl) dimethylsilyl]-5-phenylfurans

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Novel 2-[(3-aminopropyl)dimethylsilyl]-5-furfural diethylacetals and 2-[(3-aminopropyl)di-methylsilyl]-5-phenylfurans have been synthesized by a hydrosilylation reaction of aliphatic and heterocyclic *N*-allylamines in the presence of the Speier's catalyst. The effects of the structure of the amine and nature of organic substituent at the furan ring on the cytotoxicity of the new compounds have been studied. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: 2-[(3-aminopropyl)dimethylsilyl]-5-furfural diethylacetals; 2-[(3-aminopropyl)-dimethylsilyl]-5-phenylfurans; hydrosilylation; ^{1}H, ^{13}C, ^{29}Si NMR; cytotoxic activity

Introduction

Previously we studied the synthesis and cytotoxic activity of 2-[(3-aminopropyl)-dimethylsilyl]-5-trialkylsilyl(germyl)furans.[1,2] Our investigations have demonstrated that these types of compounds have high cytotoxic activity on two cell tumor lines, viz. HT-1080 (human fibrosarcoma) and MG-22A (mouse hepatoma), but unfortunately these compounds possess high cytotoxic activity towards normal NIH 3 T3 cells (normal mouse embryonic fibroblasts) as well as relatively high toxicity. In order to search for new substances with low toxicity (LD_{50}) that are highly toxic to cancer cells but not toxic to normal cells, we synthesized a new series of aminopropylsilylfurans with organic substituent in the furan ring and studied the cytotoxicity of the obtained novel compounds.

Experimental

Materials and Methods

The ^{1}H, ^{13}C and ^{29}Si NMR spectra were recorded on a Varian 400 Mercury spectrometer at 400, 100 and 80 MHz, respectively, in $CDCl_3$ as a solvent, with $(Me_3Si)_2O$ as a standard for ^{1}H, tetramethylsilane (external) as the standard for ^{29}Si, and the signal on the residual proton of the solvent (δ 77.05 ppm) for ^{13}C. The mass-spectra under electron impact conditions were recorded on an Agilent Technologies 7890 gas chromatography–mass spectrometry (GC-MS) system with 5975C EI/CI MSD (70 eV) on an HP-5 capillary column. High-resolution mass spectra were recorded by Q-TOF micromass electrospray ionization (ESL^{+}). Elemental analyses were recorded on a CARLO ERBA EA-1108 element analyzer.

All solvents were dried over CaH_2 and metallic sodium and distilled prior to use. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} with various eluents. Column chromatography was performed on silica gel (0.060–0.200 mm, pore diameter 6 nm ('Acros'). 5-Dimethylsilylfurfural diethylacetal (**1**) has been prepared by known methods.[3]

Cytotoxicity *In Vitro*

Monolayer tumor cell lines MG-22A (mouse hepatoma), HT-1080 (human connective tissue fibrosarcoma) and NIH 3 T3 (normal mouse fibroblasts) were cultivated for 72 h in standard Dulbecco's modified Eagle's medium (Sigma) without indicator and antibiotics.[4] After the ampoule was thawed not more than four passages were performed. The control cells and cells with tested substances in the range of 2–5 $\times$ 10^4 cells ml^{-1} concentration (depending on line nature) were placed on separate 96-well plates. Solutions containing test compounds were diluted and added to wells to give final concentrations of 50, 25, 12.5 and 6.25 $\mu g\ ml^{-1}$. The control cells were treated in the same manner but in the absence of test compounds. Plates were cultivated for 72 h. The quantity of surviving cells was determined using Crystal Violet (CV), Neutral Red (NR) or 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide (MTT) coloration, which was assayed by multiscan spectrophotometer (Tetretek Multiscan MCC/340). The quantity of living cells on the control plate was taken in calculations as 100% (IC_{50} determination).[4,5] The concentration of NO was determined according to Fast *et al.*[5] The mean lethal dose (LD_{50}) was determined on NIH 3 T3 cells (alternative to LD *in vivo* test) according to the protocols of the Interagency

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Coordinating Committee on the Validation of Alternative Methods and the National Toxicology Program of the Interagency Center for the Evaluation of Alternative Toxicological Methods.[6]

Chemistry

*Synthesis of 2-dimethylsilyl-5-phenylfuran (**2**)*

A solution of 2-phenylfuran (16.6 mmol) in dry ether (35 ml) was placed in a three-necked flask fitted with a reflux condenser, thermometer, magnetic stirrer and a rubber stopper in a stream of argon. The flask with the solution was cooled to −30 °C, and a solution of 2.5 N *n*-BuLi (16.6 mmol) in hexane was added dropwise slowly to maintain the temperature below −25 °C. When all the *n*-BuLi had been added, the mixture was stirred for 30 min at −25 °C, and for 2 h at 20 °C. Then, dimethylchlorosilane (16.6 mmol) was added dropwise at −10 ÷ −15 °C. After the addition of dimethylchlorosilane the mixture was stirred for 10 min at −15 °C, the temperature was slowly raised to room temperature and the mixture was stirred for 12 h. The precipitate was filtered through Al_2O_3, the solvents were evaporated and the residue was distilled under reduced pressure at 106–108 °C (5 mmHg), to give 1.93 g (57.6%) of compound **2**.^{1}H NMR δ ppm (*J*, Hz): 0.38 (6H, s, Si-CH_3); 4.44–4.48 (1H, m, Si-H); 6.64 (1H, d, H^4, *J* = 3.6 Hz); 6.74 (1H, d, H^3, *J* = 3.6 Hz); 7.23–7.26 (1H, m, C_6H_5), 7.35–7.40 (2H, m, C_6H_5), 7.62–7.72 (2H, m, C_6H_5); ^{13}C NMR δ ppm: −4.46 Si-CH_3, 105.29 C^4, 122.98 C^3, 124.16 C_6H_5, 127.47 C_6H_5, 128.65 C_6H_5, 131.04 C_6H_5, 156.88 C^5, 158.47 C^2. ^{29}Si NMR, δ ppm: −28.49. GC-MS, *m/z* (%): 202 (M^+, 37), 187 (M^+ − Me, 100), 171 (5), 161 (40), 145 (9), 127 (13), 115 (25), 105 (11), 87 (11), 77 (33), 61 (12), 51 (14). Anal. Calcd for $C_{12}H_{14}OSi$: C, 71.24; H, 6.97. Found: C, 71.08; H, 6.88.

General Synthetic Procedure and Structural Elucidation

To a solution of 5-dimethylsilyl-2-furfural diethylacetal or 5-dimethylsilyl-5-phenylfuran (1 mmol) and corresponding allylamine (1 mmol) two drops of 0.1% $H_2PtCl_6.6H_2O$ solution in 2-PrOH were added to a flask equipped with a reflux condenser and magnetic stirrer. The reaction course was monitored by TLC and GC-MS. In some cases an exothermic reaction occurred immediately and in other cases by heating for 15–150 min. The product was separated and purified using a chromatography column with CH_2Cl_2–MeOH (10:1) as eluent. These experimental conditions led to expected products in good yields. The new compounds were identified by NMR (^{1}H, ^{13}C and ^{29}Si), GC-MS, elemental analysis and high-resolution mass spectrometry (HR-MS).

N,N-Diethyl-{3-[dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}amine (**3**)

Compound **3** was prepared from compound **1** and *N,N*-diethylallylamine by stirring for 30 min at room temperature (during the first 10 min a violent reaction took place), followed by heating at 90 °C for 1 h, then cooling and analysis by GC-MS. After purification by column chromatography using CH_2Cl_2–MeOH (10:1) as eluent and removal of the solvents a light-brown oil was obtained. Yield: 61.2%. ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.67–0.71 (m, 2H, Si-CH_2), 1.00 (t, 6H, C-CH_3, *J* = 7.2 Hz), 1.21 (t, 6H, C-CH_3, *J* = 7.2 Hz), 1.44–1.52 (m, 2H, C-CH_2), 2.37–2.41 (m, 2H, N-CH_2), 2.45–2.52 (m, 4H, N-CH_2), 3.50–3.67 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.37 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.38 Si-CH_3, 11.66 C-$\underline{C}H_3$, 12.88 C-$\underline{C}H_3$, 15.18 Si-CH_2, 21.27 C-$\underline{C}H_2$, 46.89 N-CH_2, 56.42 N-CH_2, 61.15 O-CH_2, 96.57 O-CH, 107.91 C^3, 120.46 C^4, 156.25 C^5, 159.43 C^2. ^{29}Si NMR δ ppm: −9.40. GC-MS, *m/z* (%): 341 (M+, 12), 296 (M + − OEt, 28), 238 (6), 155 (45), 142 (12), 112 (20), 97 (7), 86 (100), 59 (20). HR-MS calcd for $C_{18}H_{36}NO_3Si$ (M^+, 10) 342.2067, found 342.2057. Anal. Calcd for $C_{18}H_{35}NO_3Si$: C, 63.30; H, 10.33; N 4.10. Found: C, 63.08; H, 10.18; N, 3.98.

Compounds **4–21** were isolated and purified in the same manner as described for compound **3**.

N,N-Dibutyl-{3-[dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}amine (**4**)

Compound **4** was prepared from compound **1** and *N,N*-di-*n*-butylallylamine by stirring for 1 h at room temperature (during the first 45 min a violent reaction took place). Yield: 70.4% (light-brown oil). ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.66–0.71 (m, 2H, Si-CH_2), 0.90 (t, 6H, C-CH_3, *J* = 7.2 Hz), 1.19–1.23 (t, 6H, C-CH_3, *J* = 7.2 Hz), 1.25–1.48 (m, 10H, C-CH_2), 2.35–2.40 (m, 6H, N-CH_2), 3.53–3.65 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.38 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.38 Si-CH_3, 12.77 C-$\underline{C}H_3$, 14.08 C-$\underline{C}H_3$, 15.17 Si-CH_2, 20.76 C-$\underline{C}H_2$, 21.23 $\underline{C}H_2$-CH_3, 29.17 C-$\underline{C}H_2$, 53.88 N-CH_2 , 57.59 N-CH_2, 61.12 O-CH_2, 96.56 O-CH, 107.90 C^3, 120.41 C^4, 156.23 C^5, 159.48 C^2. ^{29}Si NMR δ ppm: −9.24. GC-MS, *m/z* (%): 397 (M+, 11), 382 (M^+ − Me, 5), 352 (M^+ – Me, 65), 294 (11), 228 (5), 183 (66), 170 (46), 153 (89), 142 (100), 128 (33), 119 (53), 109 (32), 100 (88), 41 (83), 75 (41), 59 (39). HR-MS calcd for $C_{22}H_{44}NO_3Si$ (M^+, 100) 398.3090, found 398.3133. Anal. Calcd for $C_{22}H_{43}NO_3Si$: C, 66.45; H, 10.90; N 3.52. Found: C, 66.28; H, 10.79; N, 3.40.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}pyrrolidine (**5**)*

Compound **5** was prepared from compound **1** and *N*-allylpyrrolidine by stirring for 1.2 h at room temperature (during the first15 min a violent reaction took place) followed by heating at 90 °C for 15 min. Yield 73.2% (light-brown oil). ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.72–0.76 (m, 2H, Si-CH_2); 1.21 (t, 6H, C-CH_3, *J* = 7.2 Hz,), 1.49–1.60 (m, 2H, C-CH_2); 1.70–1.80 (m, 4H, C-CH_2); 2.39–2.55 (m, 6H, N-CH_2), 3.55–3.67 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.37 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.45 Si-CH_3, 13.00 C-$\underline{C}H_3$, 15.16 Si-CH_2, 23.18 C-$\underline{C}H_2$, 23.35 C-$\underline{C}H_2$, 54.11 N-CH_2, 59.82 N-CH_2, 61.12 O-CH_2, 96.54 O-CH, 107.89 C^3, 120.45 C^4, 156.22 C^5, 159.350 C^2. ^{29}Si NMR δ ppm: −9.35. GS-MS, *m/z* (%): 294 (M^+ – EtO, 9), 153 (8), 110 (7), 84 (100), 59 (5). HRMS calcd for $C_{18}H_{34}NO_3Si$ (M^+, 10) 340.2308, found 340.2307. Anal. Calcd for $C_{18}H_{33}NO_3Si$: C, 63.67; H, 9.80; N 4.13. Found: C, 63.38; H, 9.98; N, 4.03.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}piperidine (**6**)*

Compound **6** was prepared from compound **1** and *N*-allylpiperidine by stirring for 1.2 h at room temperature (during the first 10 min a violent reaction took place) followed by heating at 90 °C for 15 min. Yield 78.8 % (light-brown oil). ^{1}H NMR δ ppm: 0.22 (s, 6H, Si-CH_3), 0.65–0.70 (m, 2H, Si-CH_2); 1.20 (t, 6H, C-CH_3 *J* = 7.2 Hz), 1.34–1.60 (m, 8H, C-CH_2); 2.23–2.40 (m, 6H, N-CH_2), 3.55–3.65 (m, 4H, O-CH_2), 5.53 (s, 1H, CH), 6.36 (d, 1H, , H^4, $J_{3,4}$ = 3.2 Hz), 6.53 (d, 1H, , H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.40 Si-CH_3, 12.96 C-$\underline{C}H_3$, 15.18 Si-CH_2, 21.10 C-$\underline{C}H_2$, 24.49 C-$\underline{C}H_2$, 25.98 C-$\underline{C}H_2$, 54.62 N-CH_2, 61.14 N-CH_2, 62.93 O-CH_2, 96.56 O-CH, 107.91 C^3, 120.46 C^4, 156.24 C^5, 159.40 C^2. ^{29}Si NMR δ ppm: −9.34. GS-MS, *m/z* (%): 353 (M+, 5), 338 (M^+ − Me, 4), 308 (M^+ − EtO, 16), 250 (6), 182 (5) 153 (17), 124 (11), 98 (100), 75 (9), 59 (9). HR-MS calcd for $C_{19}H_{36}NO_3Si$ (M^+, 12) 354.2464, found 354.2453. Anal. Calcd for $C_{19}H_{35}NO_3Si$: C, 64.54; H, 9.98; N 3.36. Found: C, 64.36; H, 9.68; N, 3.29.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}-2-methylpiperidine (**7**)*

Compound **7** was prepared from compound **1** and *N*-allyl-2-methylpiperidine by stirring for 20 min at room temperature (during the first 5 min a violent reaction took place) followed by heating at 90 °C for 1 h. Yield: 66.1% (light-brown oil). ^{1}H NMR δ ppm: 0.21 (s, 6H, Si-CH_3), 0.61–0.66 (m, 2H, Si-CH_2); 1.01(d, 3H, CH_3, J = 6.0 Hz), 1.20 (t, 6H, C-CH_3, J = 7.0 Hz), 1.25–1.30 (m, 2H, C-CH_2), 1.41–1.66 (m, 6H, C-CH_2), 2.03–2.40 (m, 3H, N-CH_2), 2.55–2.65 (m, 1H, N-CH_2), 2.79–2.85 (m, 1H, N-CH), 3.51–3.63 (m, 4H, O-CH_2), 5.52 (s, 1H, CH), 6.36 (d,1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.53 (d,1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.39 Si-CH_3, 12.96 C-CH_3, 15.17 Si-CH_2, 19.53 C-CH_3, 24.07 C-CH_2, 26.16 C-CH_2, 34.64 C-CH_2, 52.27 N-CH_2, 55.84 N-CH_2, 57.60 CH_2-CH_3, 61.13 O-CH_2, 96.55 O-CH, 107.91 C^3, 120.455 C^4, 156.24 C^5, 159.39 C^2. ^{29}Si NMR δ ppm:− 9.37. GS-MS, *m/z* (%): 367 (M^+, 6), 352 (M^+ − Me, 7), 322 (M^+ − EtO, 19), 153 (14), 112 (100), 83 (6), 55 (8). HRMS calcd for $C_{20}H_{38}NO_3Si$ (M^+, 100) 368.2621, found 368.2582. Anal. Calcd for $C_{20}H_{37}NO_3Si$: C, 65.35; H, 10.15; N 3.81. Found: C, 65.16; H, 10.09; N, 3.72.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}azepane (**8**)*

Compound **8** was prepared from compound **1** and *N*-allylhexamethyleneimine by stirring for 25 min at room temperature (during the first 10 min a violent reaction took place) followed by heating at 90 °C for 1 h. Yield: 72.5% (light-brown oil). ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.66–0.70 (m, 2H, Si-CH_2), 1.21 (t, 6H, C-CH_3, J = 6.8 Hz), 1.45–1.67 (m, 10H, C-CH_2), 2.42–2.50 (m, 2H, N-CH_2), 2.55–2.63 (m, 4H, N-CH_2), 3.55–2.65 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.37 (d, 1H, H^4, $J_{3,4}$ = 3.0 Hz), 6.55 (d, 1H, d, H^3, $J_{3,4}$ = 3.0 Hz). ^{13}C NMR δ ppm: −3.37 Si-CH_3, 12.77 C-CH_3, 15.16 Si-CH_2, 21.55 C-CH_2, 27.00 C-CH_2, 27.86 C-CH_2, 55.50 N-CH_2, 61.12 N-CH_2, 61.62 O-CH_2, 96.54 O-CH, 107.89 C^3, 120.42 C^4, 156.21 C^5, 159.44 C^2. ^{29}Si NMR δ ppm: −9.33. GS-MS, *m/z* (%): 367 (M^+, 20), 352 (M^+ − Me, 6), 338 (M^+ − Et, 6), 322 (M^+ − EtO, 49), 292 (11), 264 (14), 196 (8), 153 (32), 142 (26), 112 (100), 95 (6), 75 (15), 58 (19). HRMS calcd for $C_{20}H_{38}NO_3Si$ (M^+, 50) 368.2621, found 368.2582. Anal. Calcd for $C_{20}H_{37}NO_3Si$: C, 65.35; H, 10.15; N 3.81. Found: C, 65.06; H, 10.09; N, 3.61.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}morpholine (**9**)*

Compound **9** was prepared from compound **1** and *N*-allylmorpholine by stirring for 20 min at room temperature (during the first 5 min a violent reaction took place) followed by heating at 90 °C for 1 h. Yield: 65.3% (yellow). ^{1}H NMR δ ppm: 0.24 (s, 6H, Si-CH_3), 0.70–0.74 (m, 2H, Si-CH_2), 1.21 (t, 6H, C-CH_3, J = 7.2 Hz), 1.45–1.60 (m, 2H, C-CH_2); 2.30 (t, 2H, N-CH_2, J = 8.0 Hz), 2.35–2.45 (m, 4H, N-CH_2), 3.50–3.65 (m, 4H, O-CH_2), 3.69–3.75 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.38 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.43 Si-CH_3, 12.73 C-CH_3, 15.16 Si-CH_2, 20.76 C-CH_2, 53.72 N-CH_2, 61.12 N-CH_2, 62.30 O-CH_2, 66.98 O-CH_2, 96.51 O-CH, 107.91 C^3, 120.51 C^4, 156.27 C^5, 159.22 C^2. ^{29}Si NMR δ ppm: −9.34. GS-MS, *m/z* (%): 355 (M+, 13), 340 (M^+ − Me, 5), 310 (M^+ − EtO, 22), 280 (9), 252 (14), 186 (9), 153 (34), 142 (10), 126 (23), 100 (100), 75 (21), 59 (23). HR-MS calcd for $C_{18}H_{34}NO_4Si$ (M^+, 5) 356.2257, found 356.2282. Anal. Calcd for $C_{18}H_{33}NO_4Si$: C, 60.81; H, 9.36; N 3.94. Found: C, 60.96; H, 9.29; N, 3.65.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}thiomorpholine (**10**)*

Compound **10** was prepared from compound **1** and *N*-allylthiomorpholine by stirring for 30 min at room temperature (during the first 5 min a violent reaction took place) followed by heating at 90 °C for 1.5 h. Yield: 61.5% (yellow oil). ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.66–0.70 (m, 2H, Si-CH_2), 1.21 (t, 6H, C-CH_3, J = 7.0 Hz), 1.43–1.60 (m, 2H, C-CH_2), 2.31–2.34 (m, 2H, N-CH_2), 2.62–2.72 (m, 8H, N-CH_2, S-CH_2), 3.52–3.67 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.38 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d,1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.41 Si-CH_3, 12.74 C-CH_3, 15.17 Si-CH_2, 20.66 C-CH_2, 27.96 S-CH_2, 54.98 N-CH_2, 61.12 N-CH_2, 62.61 O-CH_2, 96.51 O-CH, 107.91 C^3, 120.50 C^4, 156.27 C^5, 159.22 C^2, ^{29}Si NMR δ ppm: −9.35. GS-MS, *m/z* (%): 371 (M^+, 36), 356 (M^+ − Me, 7), 342 (9), 326 (M^+ − EtO, 40), 296 (10), 268 (16) 252 (6), 202 (14), 174 (7), 153 (58), 142 (30), 128 (17), 116 (100), 103 (14), 88 (30), 75 (26), 59 (29). HR-MS calcd for $C_{18}H_{34}NO_3SSi$ (M^+, 10) 372.2029, found 372.2057. Anal. Calcd for $C_{18}H_{33}NO_3SSi$: C, 58.18; H, 8.95; N 3.77; S 8.63. Found: C, 58.04; H, 9.09; N, 3.63; S, 8.55.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}-4-methylpiperazine (**11**)*

Compound **11** was prepared from compound **1** and *N*-allyl-4-methypiperazine by stirring for 1 h at room temperature (during the first 50 min a violent reaction took place). Yield: 64.0% (yellow oil). ^{1}H NMR δ ppm: 0.23 (s, 6H, Si-CH_3), 0.68–0.72 (m, 2H, Si-CH_2); 1.21 (d, 6H, C-CH_3, J = 7.0 Hz), 1.40–1.55 (m, 2H, C-CH_2), 2.20–2.58 (m, 13H, N-CH_2, CH_3), 3.54–3.63 (m, 4H, O-CH_2), 5.54 (s, 1H, CH), 6.38 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.56 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz). ^{13}C NMR δ ppm: −3.40 Si-CH_3, 12.81 C-CH_3, 15.15 Si-CH_2, 21.08 C-CH_2, 46.04 C-CH_3, 53.17 N-CH_2, 55.12 N-CH_2, 61.10 N-CH_2, 61.94 CH_2-CH_3, 96.51 CH-O, 107.89 C^3, 120.47 C^4, 156.24 C^5, 159.26 C^2. ^{29}Si NMR δ ppm: −9.35. GS-MS, *m/z* (%): 368 (M^+, 14), 339 (M^+, 14), 323 (M^+ − EtO, 49), 197 (6), 153 (16), 141 (13), 129 (8), 113 (100), 97 (12), 85 (7), 70 (82), 59 (17). HR-MS calcd $C_{19}H_{37}N_2O_3Si$ (M^+, 20) 369.257, found 369.2552. Anal. Calcd for $C_{19}H_{36}N_2O_3Si$: C, 61.91; H, 9.85; N 7.60. Found: C, 61.76; H, 9.79; N, 7.46.

*1-{3-[Dimethyl(5-diethoxymethylfuran-2-yl)silyl]propyl}-4-phenylpiperazine (**12**)*

Compound **12** was prepared from compound **1** and *N*-allyl-4-phenylpiperazine by stirring for 45 min at room temperature (during the first 30 min a violent reaction took place) followed by heating at 90 °C for 1 h. Yield: 75.3% (yellow oil). ^{1}H NMR δ ppm: 0.24 (s, 6H, Si-CH_3), 0.71–0.76 (m, 2H, Si-CH_2); 1.21 (t, 6H, C-CH_3, J = 7.0 Hz), 1.50–1.60 (m, 2H, C-CH_2), 2.30–2.39 (m, 2H, N-CH_2), 2.50–2.58 (m, 4H, N-CH_2), 3.17–3.20 (m, 4H, N-CH_2), 3.50–3.63 (m, 4H, O-CH_2), 5.55 (s, 1H, CH), 6.38 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.57 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.82–6.85 (m, 1H, C_6H_5), 6.90–6.95 (m, 2H, C_6H_5), 7.23–7.27 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.38 Si-CH_3, 12.86 C-CH_3, 15.20 Si-CH_2, 21.10 C-CH_2, 49.13 N-CH_2, 53.26 N-CH_2, 61.16 N-CH_2, 61.97 O-CH_2, 96.56 O-CH, 107.95 C^3, 116.01 C_6H_5, 119.61 C_6H_5, 120.55 C^4, 129.07 C_6H_5, 151.38 C_6H_5, 156.31 C^5, 159.28 C^2. ^{29}Si NMR δ ppm: −9.30. GS-MS, *m/z* (%): 430 (M^+, 76), 385 (M^+ − EtO, 18), 327 (10), 259 (12), 201 (27), 175 (100), 153 (34), 142 (11), 132 (52), 120 (10), 104 (35), 70 (71), 59 (26). HR-MS calcd for $C_{24}H_{39}N_2O_3Si$ (M^+, 50) 431.2730, found 431.2708. Anal. Calcd for $C_{24}H_{38}N_2O_3Si$: C, 66.94; H, 8.89; N 6.51. Found: C, 66.93; H, 9.07; N, 3.43.

N,N-Diethyl-{3-[dimethyl(5-phenylfuran-2-yl)silyl]propyl}amine (**13**)

Compound **13** was prepared from compound **2** and *N,N*-diethylallylamine by stirring and heating at 90 °C for 1 h. Yield: 65.4% (light-brown oil). ^{1}H NMR δ ppm: 0.28 (s, 6H, Si-CH_3), 0.71–0.75 (m, 2H, Si-CH_2), 0.98 (t, 6H, C-CH_3, J = 7.2 Hz), 1.50–1.58 (m, 2H, C-CH_2), 2.38–2.42 (m, 2H, N-CH_2), 2.46–2.52 (m, 4H, N-CH_2), 6.61 (d, 1H, H^3, $J_{3,4}$ = 3.6 Hz), 6.66 (d, 1H, H^4, $J_{3,4}$ = 3.6 Hz), 7.19–7.23 (m, 1H, C_6H_5), 7.32–7.36 (m, 2H, C_6H_5), 7.66–7.68 (m, 2H, C_6H_5). ^{13}C

NMR δ ppm: −3.30 Si-CH_3, 11.68 C-CH_3, 13.00 Si-CH_2, 21.38 C-CH_2, 46.91 N-CH_2, 56.47 N-CH_2, 105.10 C^4, 121.93 C^3, 124.01 C_6H_5, 127.24 C_6H_5, 128.55 C_6H_5, 131.16 C_6H_5, 157.88 C^5, 159.28 C^2. ^{29}Si NMR δ ppm: −9.28. GC-MS, *m/z* (%): 315 (M+, 15), 300 (M + − Me, 5), 201 (11), 157 (18), 127 (11), 99 (10), 86 (100), 75 (17), 58 (21). HRMS calcd for $C_{19}H_{30}NOSi$ (M^+, 20) 316.2097, found 316.2105. Anal. Calcd for $C_{19}H_{29}NOSi$: C, 72.33; H, 9.27; N 4.44. Found: C, 72.26; H, 9.30; N, 4.36.

N,N-Dibutyl-{3-[dimethyl(5-phenylfuran-2-yl)silyl]propyl}amine (**14**)

Compound **14** was prepared from compound **2** and *N,N*-di-*n*-butylallylamine by stirring and heating at 90 °C for 1 h. Yield: 72.6% (brown oil). ^{1}H NMR δ ppm: 0.28 (s, 6H, Si-CH_3), 0.71–0.75 (m, 2H, Si-CH_2), 0.87 (t, 6H, C-CH_3, J = 7.2 Hz), 1.21–1.57 (m, 10H, C-CH_2), 2.35–2.45 (m, 6H, N-CH_2), 6.61 (d, 1H, H^3, $J_{3,4}$ = 3.6 Hz), 6.67 (d, 1H, H^4, $J_{3,4}$ = 3.6 Hz), 7.20–7.24 (m, 1H, C_6H_5), 7.33–7.37 (m, 2H, C_6H_5), 7.66–7.69 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.25 Si-CH_3, 12.95 C-CH_3, 14.11 Si-CH_2, 20.79 CH_2-CH_3, 21.42 C-CH_2, 29.29 C-CH_2, 54.00 N-CH_2, 57.70 N-CH_2, 105.12 C^4, 121.92 C^3, 124.05 C_6H_5, 127.27 C_6H_5, 128.59 C_6H_5, 131.21 C_6H_5, 157.91 C^5, 159.42 C^2. ^{29}Si NMR δ ppm: −9.25. GC-MS, *m/z* (%): 371 (M^+, 8), 356 (M^+ − Me, 3), 328 (4), 201 (8), 168 (10), 157 (61), 142 (100), 127 (7), 115 (7), 100 (16), 86 (6), 75 (8), 57 (6). HR-MS calcd for $C_{23}H_{38}NO_3Si$ (M^+, 100) 372.2723, found 372.2721. Anal. Calcd for $C_{23}H_{37}NOSi$: C, 74.34; H, 10.04; N 3.77. Found: C, 74.16; H, 9.89; N, 3.63.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}pyrrolidine (***15***)

Compound **15** was prepared from compound **2** and *N*-allylpyrrolidine by stirring and heating at 90 °C for 1 h. Yield 65.1% (brown oil). ^{1}H NMR δ ppm: 0.29 (s, 6H, Si-CH_3), 0.77–0.81 (m, 2H, Si-CH_2); 1.56–1.64 (m, 2H, C-CH_2), 1.73–1.78 (m, 4H, C-CH_2), 2.41–2.50 (m, 6H, N-CH_2), 6.62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.67 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 7.22–7.25 (m, 1H, C_6H_5), 7.34–7.38 (m, 2H, C_6H_5), 7.67–7.69 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.33 Si-CH_3, 13.15 Si-CH_2, 23.29 C-CH_2, 23.39 C-CH_2, 54.18 N-CH_2, 59.90 N-CH_2, 105.12 C^4, 121.97 C^3, 124.04 C_6H_5, 127.27 C_6H_5, 128.58 C_6H_5, 131.17 C_6H_5, 157.90 C^5, 159.25 C^2. ^{29}Si NMR δ ppm: −9.26. GS-MS, *m/z* (%): 313 (M^+, 9), 298 (M^+ − Me), 201 (15), 185 (8), 168 (22), 154 (5), 141 (36), 110 (40), 99 (17), 84 (100), 75 (32), 55 (30). HR-MS calcd for $C_{19}H_{28}NOSi$ (M^+, 10) 314.1940, found 314.1954. Anal. Calcd for $C_{19}H_{27}NOSi$: C, 72.79; H, 8.68; N 4.47. Found: C, 72.54; H, 8.66; N, 4.31.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}piperidine (***16***)

Compound **16** was prepared from compound **2** and *N*-allylpiperidine by stirring and heating at 90 °C for 1 h. Yield 65.29% (light-brown oil). ^{1}H NMR δ ppm: 0.28 (s, 6H, Si-CH_3), 0.71–0.76 (m, 2H, Si-CH_2); 1.40–1.41 (m, 2H, C-CH_2), 1.54–1.64 (6H, m, C-CH_2), 2.26–2.34 (m, 6H, N-CH_2), 6.62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.67 (d,1H, H^4, $J_{3,4}$ = 3.2 Hz), 7.19–7.27 (m, 1H, C_6H_5), 7.34–7.38 (m, 2H, C_6H_5), 7.67–7.69 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.31 Si-CH_3, 13.07 Si-CH_2, 21.17 C-CH_2, 24.51 C-CH_2, 26.00 C-CH_2, 54.65 N-CH_2, 62.95 N-CH_2, 105.10 C^4, 121.94 C^3, 124.03 C_6H_5, 127.25 C_6H_5, 128.56 C_6H_5, 131.16 C_6H_5, 157.88 C^5, 159.25 C^2. ^{29}Si NMR δ ppm: −9.27. GS-MS, *m/z* (%): 327 (M^+, 11), 312 (M^+ − Me, 4), 155 (6), 145 (9), 124 (8), 98 (100), 75 (12), 55 (12). Calcd for $C_{20}H_{30}NOSi$ (M^+, 20) 328.2097, found, 328.2112. Anal. Calcd for $C_{20}H_{29}NOSi$: C, 73.34; H, 8.92; N 4.28. Found: C, 73.16; H, 8.96; N, 4.24.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}-2-methylpiperidine (***17***)

Compound **17** was prepared from compound **2** and *N*-allyl-2-methylpiperidine by stirring and heating at 90 °C for 1 h. Yield: 67.5 % (brown oil). ^{1}H NMR δ ppm: 0.29 (s, 6H, Si-CH_3), 0.68–0.73 (m, 2H, Si-CH_2), 1.02 (d, 3H, C-CH_3, J = 6.4 Hz), 1.25–1.28 (m, 2H, C-CH_2), 1.50–1.68 (m, 6H, C-CH_2), 2.13–2.38 (m, 3H, N-CH_2), 2.62–2.68 (m, 1H, N-CH_2), 2.83–2.86 (m, 1H, N-CH) 6.62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.68 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 7.22–7.27 (m, 1H, C_6H_5), 7.34–7.38 (m, 2H, C_6H_5), 7.67–7.70 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.23 Si-CH_3, 13.13 Si-CH_2, 19.31 C-CH_3, 24.18 C-CH_2, 26.20 C-CH_2, 34.74 C-CH_2, 52.37 N-CH_2, 55.92 N-CH_2, 57.69 C-CH_3, 105.16 C^4, 121.99 C^3, 124.09 C_6H_5, 127.32 C_6H_5, 128.62 C_6H_5, 131.21 C_6H_5, 157.94 C^5, 159.33 C^2. ^{29}Si NMR δ ppm: −9.26. GS-MS, *m/z* (%): 341 (M^+, 24), 326 (M^+ − Me, 18), 201 (19), 182 (12), 155 (7), 145 (30), 127 (20), 112 (100), 99 (23), 75 (39), 55 (53). HR-MS calcd for $C_{21}H_{32}NOSi$ (M^+, 100), 342.2253, found 342.2266. Anal. Calcd for $C_{21}H_{31}NOSi$: C, 73.85; H, 9.15; N 4.01. Found: C, 73.66; H, 9.23; N, 4.00.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}azepane (***18***)

Compound **18** was prepared from compound *2* and *N*-allylhexamethyleneimine by stirring and heating at 90 °C for 1.5 h. Yield: 67.0% (brown oil). ^{1}H NMR δ ppm: 0.28 (s, 6H, Si-CH_3), 0.71–0.75 (m, 2H, Si-CH_2); 1.57–1.65 (m, 10H, C-CH_2), 2.44–2.48 (m, 2H, N-CH_2), 2.59–2.62 (m, 4H, N-CH_2), 6.61 (d, 1H, H^3, $J_{3,4}$ = 3.0 Hz), 6.67 (d, 1H, H^4, $J_{3,4}$ = 3.0 Hz), 7.20–7.24 (m, 1H, C_6H_5), 7.33–7.37 (m, 2H, C_6H_5), 7.67–7.69 (m, 2H, C_6H_5) ^{13}C NMR δ ppm: −3.25 Si-CH_3, 12.91 Si-CH_2, 21.64 C-CH_2, 27.03 C-CH_2, 27.87 C-CH_2, 55.54 N-CH_2, 61.51 N-CH_2, 105.12 C^4, 121.94 C^3, 124.03 C_6H_5, 127.26 C_6H_5, 128.58, C_6H_5 131.17 C_6H_5, 157.88 C^5, 159.33 C^2. ^{29}Si NMR δ ppm: −9.25. GS-MS, *m/z* (%): 341 (M^+, 6), 326 (M^+ − Me, 4), 207 (5), 112 (100), 75 (7), 58 (11). HR-MS calcd for $C_{21}H_{32}NOSi$ (M^+, 40) 342.2253, found 342.2271. Anal. Calcd for $C_{21}H_{31}NOSi$: C, 73.85; H, 9.15; N 4.10. Found: C, 73.76; H, 9.04; N, 3.97.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}morpholine (***19***)

Compound **19** was prepared from compound **2** and *N*-allylmorpholine by stirring and heating at 90 °C for 1 h. Yield: 76.6% (yellow oil). ^{1}H NMR δ ppm: 0.29 (s, 6H, Si-CH_3), 0.75–0.79 (m, 2H, Si-CH_2); 1.54–1.62 (m, 2H, C-CH_2), 2.31–2.45 (m, 6H, N-CH_2), 3.67–3.70 (m, 4H, O-CH_2), 6,62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.68 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 7.22–7.26 (m, 1H, C_6H_5), 7.35–7.38 (m, 2H, C_6H_5), 7.67–7.70 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: −3.32 Si-CH_3, 12.87 Si-CH_2, 20.81 C-CH_2, 53.75 N-CH_2, 62.30 N-CH_2, 67.00 O-CH_2, 105.12 C^4, 122.04 C^3, 124.02 C_6H_5, 127.33 C_6H_5, 128.60 C_6H_5, 131.12 C_6H_5, 157.94 C^5, 159.08 C^2. ^{29}Si NMR δ ppm: −9.25. GS-MS, *m/z* (%): 329 (M^+, 47), 314 (M^+ − Me, 59), 300 (12), 256 (6), 242 (8), 224 (17), 201 (52), 185 (50), 185 (50), 171 (15), 157 (59), 145 (71), 135 (16), 127 (85), 115 (40), 100 (100), 86 (15), 75 (81), 68 (31), 56 (82). HRMS calcd for $C_{19}H_{28}NO_2Si$ (M^+, 5), 330.1889, found 330.1916. Anal. Calcd for $C_{19}H_{27}NO_2Si$: C, 69.26; H, 8.26; N 4.25. Found: C, 69.09; H, 8.26; N, 4.16.

1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}-4-methylpiperazine (***20***)

Compound **20** was prepared from compound **2** and *N*-allyl-4-methylpiperazine by stirring and heating at 90 °C for 1 h. Yield: 68.4% (yellow oil). ^{1}H NMR δ ppm: 0.28 (s, 6H, Si-CH_3), 0.73–0.78 (m, 2H, Si-CH_2); 1.54–1.65 (m, 2H, C-CH_2), 2.26 (s, 3H, CH_3), 2.32–2.57 (m, 8H, N-CH_2), 6.62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.68 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 7.22–7.25 (m, 1H, C_6H_5), 7.34–7.38 (m, 2H, C_6H_5), 7.67–7.69 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: - 3.33 Si-CH_3, 12.93 Si-CH_2, 21.13 C-CH_2, 46.05 N-CH_3, 53.21 N-CH_2, 55.13 N-CH_2, 61.95 N-CH_2, 105.10 C^4, 121.99 C^3, 124.02 C_6H_5, 127.27 C_6H_5, 128.57 C_6H_5, 131.13 C_6H_5, 157.90 C^5, 159.12 C^2. ^{29}Si NMR δ ppm: −9.29. GS-MS, *m/z* (%): 342 (M^+, 16), 327 (M^+ − Me,

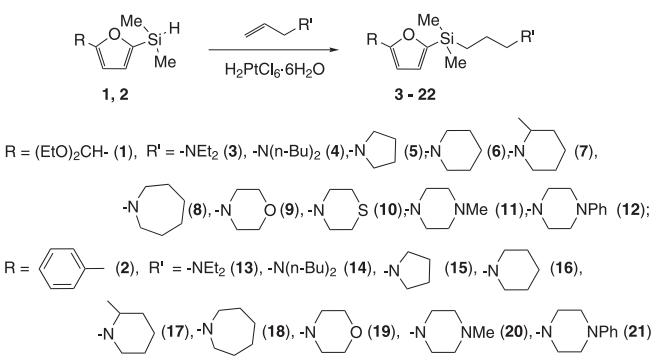
4), 207 (6), 157 (5), 128 (7), 113 (100), 98 (5), 77 (5), 70 (40). HR-MS calcd for $C_{20}H_{31}N_2OSi$ (M^+, 10) 343.2206, found 343.2225. Anal. Calcd for $C_{20}H_{30}N_2OSi$: C, 70.13; H, 8.23; N 8.18. Found: C, 69.99; H, 8.39; N, 8.01.

*1-{3-[Dimethyl(5-phenylfuran-2-yl)silyl]propyl}-4-phenylpiperazine (**21**)*

Compound **21** was prepared from compound **2** and *N*-allyl-4-phenylpiperazine by stirring and heating at 90 °C for 2.5 h. Yield: 71.3% (light-brown). ^{1}H NMR δ ppm: 0.29 (s, 6H, Si-CH_3), 0.76–0.80 (m, 2H, Si-CH_2); 1.58–1.66 (m, 2H, C-CH_2), 2.37–2.41 (m, 2H, N-CH_2), 2.55–2.58 (m, 4H, N-CH_2), 3.15–3.18 (m, 4H, N-CH_2), 6.62 (d, 1H, H^3, $J_{3,4}$ = 3.2 Hz), 6.68 (d, 1H, H^4, $J_{3,4}$ = 3.2 Hz), 6.81–6.90 (m, 3H, C_6H_5), 7.21–7.25 (m, 3H, C_6H_5), 7.34–7.38 (m, 2H, C_6H_5), 7.67–7.69 (m, 2H, C_6H_5). ^{13}C NMR δ ppm: - 3.30 Si-CH_3, 12.94 Si-CH_2, 21.09 C-CH_2, 49.07 N-CH_2, 53.23 N-CH_2, 61.90 N-CH_2, 105.15 C^4, 116.00 C_6H_5, 119.59 C^3, 122.07 C_6H_5, 124.04 C_6H_5, 127.32 C_6H_5, 128.61 C_6H_5, 129.06 C_6H_5, 131.13 C_6H_5, 151.34 C_6H_5, 157.95 C^5, 159.10 C^2. ^{29}Si NMR δ ppm: −9.20. GS-MS, *m/z* (%): 404 (M^+, 30), 389 (M^+ − Me, 5), 327 (5), 259 (5), 201 (9), 175 (100), 157 (9), 145 (9), 132 (19), 115 (6), 104 (14), 70 (25), 56 (9). HR-MS calcd for $C_{25}H_{33}N_2OSi$ (M^+, 20) 405.2362, found 405.2343. Anal. Calcd for $C_{25}H_{32}N_2OSi$: C, 74.21; H, 7.97; N 6.92. Found: C, 74.06; H, 8.09; N, 7.01.

Results and Discussion

In a continuation of our studies we have examined hydrosilylation of a series of allylamines with dimethyl(2-furyl)silane containing a diethylacetal group at C-5 of the furan ring. After removal of the protective group new synthesized compounds can serve as synthons in the synthesis of new biologically active compounds. The choice of aromatic substituent for our investigations was associated with the fact that numerous phenyl-substituted derivatives had been studied as anticancer compounds and a lot of them had been already used for treatment of cancer.[7–10] The starting 5-dimethylsilylfurfural diethyl acetal (**1**) has been prepared by known methods.[3] The 2-dimethylsilyl-5-phenylfuran (**2**) has been obtained by using the organolithium method. They were used for the hydrosilylation of heterocyclic allylamines in the presence of Speier's catalyst (Scheme 1). The hydrosilylation reaction of all studied allyamines by hydrosilanes **1** and **2** occurred smoothly over 1–2.5 h (in some cases an exothermic reaction occurred immediately; in other cases, it required heating for 15–150 min) at the presence a drop of Speier's catalyst. The reaction afforded a series of silylamines **3–21** in good or moderate yield.



Scheme 1. Synthesis of 2-[(3-aminopropyl)dimethylsilyl]-5-organylfurans.

In order to reveal the effect of a heterocyclic amino group and an organic substituent at the furan ring in the furylsilylpropylamines **3–21** on their antitumor activity, we studied their cytotoxicity *in vitro* on two cell tumor lines, viz. HT-1080 (human fibrosarcoma) and MG-22A (mouse hepatoma). In comparison, we studied the cytotoxicity (IC_{50}) of these compounds towards normal NIH 3 T3 cells (normal mouse embryonic fibroblasts – Swiss Albino mice) and also their toxicity (LD_{50}). The experimental evaluation of cytotoxic properties is presented in Table 1. The investigations showed that, regardless of the structure of the amine (R^1), all of the compounds studied (**3–21**) possessed moderate toxicity (lethal doses for them are in the range 102–756 mg kg^{-1}, with the exception of compounds **14** and **17**). The amines **14** and **17** showed high cytotoxic activity in cancer cells accompanied by the highest cytotoxic activity on normal cells 3 T3 (IC_{50} 0.3 μg ml^{-1}). It is interesting to note that all of the derivatives with a phenyl substituent in position 5 of the furan ring (compounds **13–21**) were more active than compounds with a diethoxymethyl substituent in position 5 of the furan ring (compounds **3–12**) (Table 1). However, some amino derivatives of diethoxymethylfuran (**3**, **7**, **11**) exhibit high cytotoxic activity on MG-22A cancer cells (IC_{50} 2–4 μg ml^{-1}) and at the same time they were much less cytotoxic on normal fibroblasts (IC_{50} 20–67 μg ml^{-1}). Silylpropylamino derivatives of diethoxymethylfuran **3–12** have a certain cytoselectivity: compounds of this type exhibited high cytotoxicity to MG-22 tumor cell lines (compounds **9** and **12** are an exception) and at the same time they were less toxic to HT-1080. It should be noted that compounds with the phenyl substituent in position 5 of the furan ring generally

Table 1. Cytotoxic activity (IC_{50}) of compounds **3–21**

Compound	IC_{50} (μg ml^{-1})							LD_{50} (mg kg^{-1})
	HT-1080			MG-22A			NIH3T3	
	CV	MTT	NO	CV	MTT	NO	NR	
3	33	34	200	2	3	100	33	512
4	6	10	100	3	4	100	17	756
5	20	30	150	3	10	100	44	577
6	15	30	200	3	10	200	27	495
7	17	27	100	3	3	100	20	405
8	4	10	200	2	3	133	10	331
9	33	32	150	13	22	100	72	747
10	21	24	100	2	6	100	32	520
11	32	30	150	3	4	150	67	737
12	4	4	150	3	3	150	10	345
13	1	3	150	2	2	250	5	221
14	3	3	300	1	1	250	0.3	74
15	3	2	200	1	1	200	4	188
16	3	1	150	1	1	150	3	164
17	1	2	200	1	2	200	0.3	68
18	1	1	150	1	1	250	11	102
19	3	3	200	1	2	150	60	659
20	3	3	200	1	3	200	6	240
21	4	4	150	8	8	75	6	283

IC_{50}, the concentration providing 50% cell death; LD_{50}, the calculated values of expected toxicity; CV, crystal violet (action on the cell membrane); MTT, 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl-2*H*-tetrazolium bromide (influence on the activity of mitochondrial enzymes in the cell); NR, neutral red; NO, degree of generation of the NO radical determined and calculated by the method of Fast *et al.*[5]

have more pronounced cytotoxic activity on tumor cell lines compared to the analogues with Et_3Si group[2] and Et_3Ge group in the furan ring.[1] Morpholino derivative **19** is the more promising compound among the studied amines: moderate toxicity (LD_{50} 659 mg kg^{-1}), high cytotoxicity on both cancer cell lines (IC_{50} 1–3 μg ml^{-1}) and low cytotoxicity on normal fibroblasts (IC_{50} 60 μg ml^{-1}).

Conclusions

Our investigations have shown that by variations of the substituents (organosilicon, organogermanium or organic) at position 5 of the furan ring in 2,5-substituted furylsilylpropylamines we can achieve a high cytotoxicity against cancer cells and low toxicity and cytotoxicity on normal fibroblasts. The effect of the nature of the amine on the cytotoxic activity is not so large in the studied compounds.

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