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Amide derivatives of 3-aminopropylsilatrane

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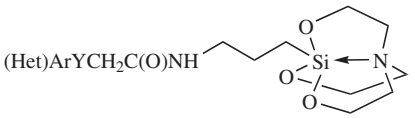
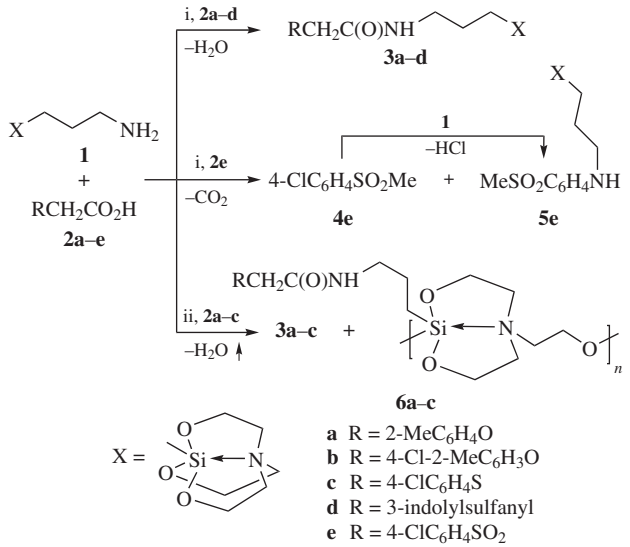
Silatranes bearing an amide group in the axial chain have been synthesized by the reaction of 1-(3-aminopropyl)silatrane with arylchalcogenylacetic acids (Het)ArYCH$_2$CO$_2$H [(Het)Ar = 2-MeC$_6$H$_4$, 4-Cl-2-MeC$_6$H$_3$, 4-ClC$_6$H$_4$, 3-indolyl; Y = O, S], and their structures have been established by ^{1}H, ^{13}C, ^{15}N, ^{29}Si NMR and IR spectroscopy. When 4-chlorophenylsulfonylacetic acid was employed, the reaction proceeded unexpectedly *via* the 4-chlorophenyl methyl sulfone intermediate and resulted in methyl 4-[3-(1-silatranyl)propylamino]-phenyl sulfone.



(Het)Ar = 2-MeC$_6$H$_4$, 4-Cl-2-MeC$_6$H$_3$, 4-ClC$_6$H$_4$, 3-indolyl
Y = O, S

1-Organylsilatranes are organosilicon derivatives of triethanolamine, which find application in agriculture, material science and medicine.[1] 1-(3-Aminopropyl)silatrane **1** was used as a precursor for the synthesis of advanced materials, such as siloxane surface anchors for heterogeneous catalysis and photoelectrochemical devices[2(*a*)] as well as chemical linkers for a particle plasmon resonance sensing.[2(*b*),(*c*)] Derivatives of compound **1** demonstrate antimicrobial activity,[3(*a*)] inhibition of hepatitis C[3(*b*)] and herpes[3(*c*)] viruses as well as an antitumor effect.[3(*d*)]

Earlier, we synthesized a number of pharmacologically active compounds of atrane class and their analogues, namely protatranes, hydrometallatranes, silatranes and quasisilatranes, starting from various combinations of ethanolamines, metal ions and biologically active arylchalcogenylacetic acids **2a–e**.[4] The obtained salts and complexes revealed synergistic effect of their bioactive precursors. An analogous reaction of silatrane **1** with acids **2a–d** under mild conditions (15 °C, 10 min) resulted in the corresponding [3-(1-silatranyl)propyl]ammonium arylchalcogenylacetates as promising physiologically active salts and ionic liquids.[5] It is known, that for this type of starting compounds, the formation of thermodynamically more stable amides, instead of ammonium carboxylate salts, can be achieved by catalytic and thermal routes or with various coupling reagents,[6] the resulting synthetic amides and polyamides being promising precursors for new functional materials.[7]



Scheme 1 *Reagents and conditions*: i, 160 °C, 24 h, MS 3 Å; ii, 160 °C, 8 h.

In this work, to synthesize new silatranes with an amide (peptide) group *via* the reaction of compounds **1** and **2** under the harsher conditions as compared with the above ones, we first attempted to carry out a test amidation using *N*-decylamine and (2-methylphenyloxy)acetic acid **2a** at 160 °C for 24 h in the presence of molecular sieves 3 Å. The reaction proceeds smoothly, affording *N*-decyl-2-(2-methylphenyloxy)acetamide as a model product. Then the analogous reactions of silatrane **1** with acids **2a–e** gave rise to a series of *N*-[3-(1-silatranyl)propyl]-2-(arylchalcogenyl)-acetamides **3a–d** as well as compounds **4e**, **5e** and **6a–c** (Scheme 1).[†]

Under the conditions employed, a reaction with 4-chlorophenylsulfonylacetic acid **2e** unexpectedly led to sulfone **5e** bearing the silatrane group. This result can be explained by the initial decarboxylation of acid **2e**, followed by the formation of intermediate 4-chlorophenyl methyl sulfone **4e**,[8] which reacted further with compound **1** affording sulfone **5e**.

Note that, when the amidation was carried out at 160 °C for 8 h in an open vessel with free evaporation of the liberated water and

[†] *General procedure for the synthesis of compounds* **3–6**. A mixture of compound **1** (10 mmol), arylchalcogenylacetic acid **2** (10 mmol) and highly activated molecular sieves 3 Å (2 g) was heated in a sealed ampoule at 160 °C for 24 h. Then the mixture was cooled, diluted with MeOH (15 ml), filtered through a thin pad of Celite, washed with MeOH (15 ml) and the filtrate was concentrated *in vacuo*, affording the product. Sulfones **4e** and **5e** were isolated from their mixture after its dissolution in CHCl$_3$–hexane (1 : 3). Crystals of sulfone **4e** precipitated within 24 h and were filtered off, for the crystallographic parameters of compound **4e**, see ref. 8. Oligomers **6a–c** were separated from compounds **3a–c** as a fraction insoluble in MeOH. The fraction was dissolved in CHCl$_3$, then oligomers **6a–c** were precipitated by MeOH and filtered off.

without molecular sieves, amides **3a–c** were obtained in lower yields due to the partial cleavage of the silatrane backbone with conversion to oligomers **6a–c**, which were in turn formed in 40–44% yields (see Scheme 1). The oligomeric structure of compounds **6a–c** bearing quasisilatrane and amide groups follows from a considerable change and significant broadening, compared with compounds **3**, of the ^{1}H NMR signals for both the propyl moiety and the quasisilatrane skeleton. For the details of spectra for all the compounds **2–6**, see Online Supplementary Materials.

In summary, new silatranes and quasisilatranes, bearing penta-coordinated silicon atom with amide group attached through a propylene linker, have been synthesized from physiologically active starting compounds, namely 1-(3-aminopropyl)silatrane and arylchalcogenylacetic acids. These products represent promising building blocks for further design of advanced materials and pharmaceuticals with synergistic effect of their bioactive precursors.

The main results were obtained using the equipment of Baikal Analytical Center of Collective Using, Siberian Branch of the Russian Academy of Sciences.

Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2019.11.029.

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