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METALLOID DERIVATIVES FOR SYNTHESIS
THE PREPARATION OF MACROCYCLIC TETRATHIOLACTONES

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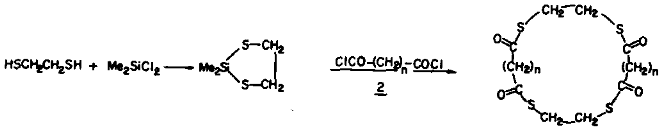
Summary: The preparation of macrocyclic thiolactones by condensation of diacyl chlorides with siladithianes is described.

We have recently reported on the use of tin derivatives for the preparation of macrocyclic compounds[1, 2]. Specifically, macrocyclic tetralactones have been prepared in good yields by condensation of stannoxanes with diacyl chlorides[2]. In this communication we wish to report on an expansion of this approach and describe the preparation of macrocyclic thiolactones via the use of silicon. The selection of silicon in this case has been based on its notoriously weak bonds with sulfur which renders silathianes susceptible to a large range of condensation reactions[3].

The method involves transformation of 1,2-ethanedithiols to the cyclic silathiane 1 [4] and condensation of the latter with diacyl chlorides 2. The detailed reaction conditions are given below for the preparation of the macrocyclic glutarate derivative 3d .



1

3

a, n = 8
b, n = 7
c, n = 5
d, n = 3

A solution of 1.5 ml ($1.11.10^{-2}$m) 2,2-dimethyl-2-sila-1,3-dithiacyclopentane in 25 ml toluene was treated with a solution of 1.41 ml ($1.11.10^{-2}$ m) glutaryl dichloride 2d in 5 ml toluene. The reaction mixture was subsequently heated under reflux for 45 hours

Addition of 2ml pyridine, concentration in vacuo and chromatography on silica gel afforded analytically pure 1,7,10,16-tetrathiocyclooctadecane-2,6,11,15-tetrone (3d) in 38 % yield. The structure of the product was identified by its analytic and spectroscopic properties. Compound 3d exhibited: mp 118-120°C; ir (KBr) 2920, 1685, 1450, 1405, 1250, 1210, 1140, 1040, 975, 760 and 720 cm^{-1}; nmr ($CDCl_3$) 3.06 (s, 8H, CH_2-S), 2.71 (t, J = 7 Hz, 8H, CH_2-CO) and 2.27 ppm (q, J = 6 Hz, 4H, CH_2CH_2-CO); mass spectrum, molecular ion m/e = 380, base peak m/e = 191; elemental analysis: found, C 44.38, H 5.49, S 33.68, calculated for $C_{14}H_{20}O_4S_4$: C 44.21, H 5.30, S 33.68.

Following similar reaction procedures but omitting pyridine provided ethylene sebacate 3a, azelate 3b and pimelate 3c in 18, 14 and 9 % yields respectively without optimizing the reaction conditions. All compounds have been characterized by their analytic and spectroscopic properties which were in agreement with the assigned structures. No evidence for the formation of the corresponding dithiolactones has been found in any of the cases studied. Moreover, treatment of sodium dithiolates with the respective acyl chloride provided macrocyclic products in trace amounts only.

The exclusive formation of tetrathiolactones in preference to the corresponding dithiolactones and the substantially enhanced yields observed when using silicon derivatives indicate the potential of the metalloid element as both, guiding and activating unit. The expansion of this method to other systems, the mechanistic implications of these transformations and the applications of the novel macrocycles as heavy metal ligands[5] are under current investigation.

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