the National Institutes of Health (Grant GM-18098) is gratefully acknowledged.

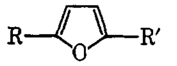
Stanley J. Opella, Donald J. Nelson, Oleg Jardetzky*
Department of Chemistry and
Stanford Magnetic Resonance Laboratory, Stanford University
Stanford, California 94305

Received August 5, 1974

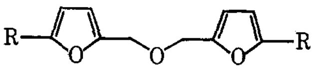
The Furanyl Unit in Host Compounds[1]

Sir:

The 2,5-dimethylyltetrahydrofuranyl unit is commonly encountered in antibiotics which complex cations and affect their permeability to natural and synthetic membranes.[2] Most of these antibiotics, generally isolated from various *Streptomyces* strains, uncouple oxidative phosphorylation in rat liver mitochondria. This paper reports the first synthesis of a series of 18-crown-6[3] compounds containing furanyl units spaced in many possible ways as part of the multiheteromacrocycles. These compounds are themselves hosts for binding organic and inorganic cations. More importantly, they serve as starting materials for preparing host compounds whose periphery is lined with a variety of binding and shaping units (*e.g.*, tetrahydrofuranyl).

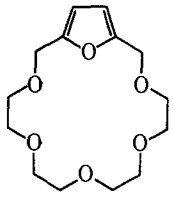


1, R = CHO, R′ = CH$_2$OH
2, R = R′ = CH$_2$OH
3, R = R′ = CH$_2$Cl
4, R = CHO; R′ = CH$_2$Cl
5, R = CHO; R′ = CH$_2$OCH$_2$CH$_2$Cl
6, R = CH$_2$OH; R′ = CH$_2$OCH$_2$CH$_2$Cl

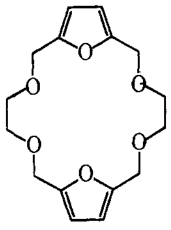


7, R = CHO
8, R = CH$_2$OH

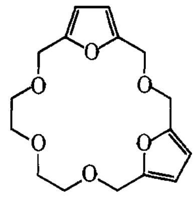
Key starting material, **1**, was prepared (41%) from sucrose[4] and in some cases was distilled (62%, mp 28–32°)[5] just before use.[6b,c] Reduction of crude **1** with sodium borohydride gave (92%) **2**,[6b,c,7] mp 75–76.5°. Dropwise addition with stirring of a solution of **2** in 2,6-lutidine to a stirred solution of thionyl chloride in ethyl acetate at −20° gave a frozen solid that was slowly warmed to 25° and stirred for 1 hr. Water and pentane were added, and the unstable **3**[6b,c,8] was isolated at low temperature without distillation and used immediately. Chloroaldehyde **4**[6b,c,9] was also prepared[4] (50%) from sucrose. Treatment of **4** with 2-chloroethanol and barium carbonate at 70° for 16 hr gave after distillation (bp 117° at 0.4 mm) **5**[6] (87%). Reduction of **5** in ethanol with sodium borohydride gave (97%) **6**[6], bp 104–105° at 0.2 mm. Water was azeotropically distilled (4 hr) from crude **1** in toluene containing 0.2% *p*-toluenesulfonic acid to give after chromatography, **7**,[6,10] mp 112–114° (44%). Reduction with sodium borohydride in ethanol of **7** gave (98%) of **8**,[6] mp 92–93°.



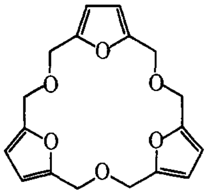
9



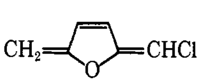
10



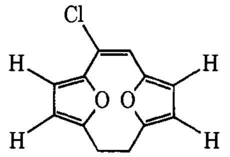
11



12



13



14

Multiheteromacrocycle **9** was prepared by treatment of tetraethyleneglycol ditosylate with diol **2** in tetrahydrofuran–potassium *tert*-butoxide (12 hr at 25°, 12 hr at reflux under nitrogen). The crude product was chromatographed on alumina (dichloromethane–ether) to give **9**[6] (36%), mp ∼0°. Treatment of a dimethylformamide solution of chloroalcohol **6** with sodium hydride in portions gave a mixture which was stirred for 48 hr at 25°. Cycle **10**[6] was isolated by extraction and chromatography (11%), mp 109–111°. Cycle **11**[6] was prepared from diol **8** and diethylene glycol ditosylate (see preparation of **9**) to give product (35%), mp 69–70°. Dropwise addition of a solution of **3** in tetrahydrofuran to a stirred tetrahydrofuran solution of **8** and potasssium *tert*-butoxide gave after 48 hr reaction time at 25° a mixture of materials. These were separated by chromatography (dichloromethane–pentane on alumina) to give 70% recovered **8**,[6c] 10% cycle **12**,[6] mp 124–126°, and **14**[6b,c] (29%), which required gel permeation chromatography for purification (oil). Above 52°, in the pmr spectrum of **14** (CDCl$_3$, 100 MHz, δ), the methylenes are a sharp singlet (2.60), which at 0° become an AB quartet, $V_A = 2.03$, $V_B = 3.23$ ($J_{AB} = 10$ Hz), the coalescence temperature being *ca.* 30°. Apparently the members of each pair of vicinal protons have the same chemical shifts, but the geminal protons do not for conformational reasons. The ring-system constraints inhibit equilibration of the geminal protons at lower temperatures. Cycle **14** probably arose by ring closure of a diradical formed by head-to-head dimerization of **13** (formed from **3**)[11] followed by elimination of 1 mol of hydrochloric acid from the product.

---

(1) This work was supported by a grant from the National Science Foundation, GP33533X, and by the U. S. Public Health Service, Research Grant No. GM 12640-10 from the Department of Health, Education and Welfare.

(2) For leading references on the actins, see (a) G. Eisenman, S. Ciani, and G. Szabo, *J. Membrane Biol.*, **1**, 294 (1969); (b) P. Lauger, *Science*, **178**, 24 (1972); (c) W. E. Morf and W. Simon, *Helv. Chim. Acta*, **54**, 286 (1971); (d) P. D. Shaw in "Antibiotics I," D. Gottlieb and P. D. Shaw Ed., Springer-Verlag, New York, N. Y., 1967, p 649; on grisorixin and nigericin, see (e) ref 2d, p 613; (f) L. K. Steinrauf, M. Pinkerton, and J. W. Chamberlin, *Biochem. Biophys. Res. Commun.*, **33**, 29 (1968); (g) P. Gachon, A. Kergomard, H. Veschambre, C. Esteve, and T. Staron, *Chem. Commun.*, 1421 (1970); on monensin see (h) B. C. Pressman, *Ann. N. Y. Acad. Sci.*, **147**, 829 (1968); on monensic acid see (i) A. Agtarap, J. W. Chamberlin, M. Pinkerton, and L. Steinrauf, *J. Amer. Chem. Soc.*, **89**, 5737 (1967); on antibiotic A-204A see (j) N. D. Jones, M. O. Chaney, J. W. Chamberlin, R. L. Hamill, and S. Chen, *ibid.*, **95**, 3399 (1973); on antibiotic X-537A see (k) J. W. Westly, R. H. Evans, Jr., T. Williams, and A. Stempel, *Chem. Commun.*, 71 (1970); on boromycin see (l) W. Marsh, J. D. Dunitz, and D. N. J. White, *Helv. Chim. Acta*, **57**, 10 (1974).

(3) C. J. Pedersen, *J. Amet. Chem. Soc.*, **89**, 7017 (1967).

(4) W. N. Haworth and W. G. M. Jones, *J. Chem. Soc.*, 667 (1944).

(5) M. L. Mednick, *J. Org. Chem.*, **27**, 398 (1962).

(6) (a) Carbon and hydrogen analyses were within 0.30% of theory; (b) mass spectra exhibited the molecular ion; (c) pmr spectra were consistent with the structures assigned.

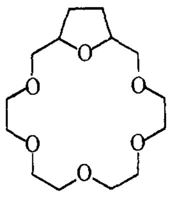
(7) P. A. Finan, *J. Chem. Soc.*, 3917 (1963).

(8) British Patent 911,221; *Chem. Abstr.*, **58**, 9027*f* (1963).

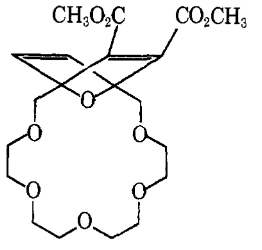
(9) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, **37**, 1056 (1959).

(10) British Patent 887,360; *Chem. Abstr.*, **57**, 2196*b* (1962).

(11 (a) H. E. Winberg, F. S. Fawcett, W. E. Mochel, and C. W. Theobald, *J. Amer. Chem. Soc.*, **82**, 1428 (1960); (b) D. J. Cram, C. S. Montgomery, and G. R. Knox, *ibid.*, **88**, 515 (1966).



15



16

Catalytic reduction of **9** with hydrogen in ethanol (Pd/C, 25°, 1 atm) gave **15**[6] as an oil, which appeared homogeneous on a variety of tlc plates. When mixed with dimethyl acetylenedicarboxylate, **9** gave a one-to-one complex, **17**[6a,c,12] (74%), mp 72–73°, which although sublimable from its melt separated into its components upon a gel permeation chromatographic column and in a mass spectrometer. When heated at 110° with excess dimethyl acetylenedicarboxylate, **9** gave **16**[6b,c] (~100%), mp 55–60°. The pmr spectrum of **16** is temperature dependent and consistent with a steric barrier at 25° for the carbon bridges of the bicyclic system passing through the center of the major ring. The complexing properties of these multiheteromacrocycles are reported elsewhere.[13] The reactions and properties of these and other furan-containing multiheteromacrocycles are under active investigation.

[12] The X-ray crystal structure will be reported by Drs. I. Goldberg and K. N. Trueblood.

[13] J. M. Timko, R. C. Helgeson, M. Newcomb, G. W. Gokel, and D. J. Cram, *J. Amer. Chem. Soc.*, **96**, 7097 (1974).

Joseph M. Timko, Donald J. Cram
Contribution No. 3356, Department of Chemistry
of the University of California at Los Angeles
Los Angeles, California 90024

Received July 18, 1974

Tin(II) Organosilylamines[1]

Sir:

Bis[*N*,*N*,-bis(trimethylsilyl)amino]tin(II) (A), a novel, dimeric organosilylamino derivative in which tin is stabilized as Sn(II), has been prepared analytically pure in 50% yield by the lithioamination of tin(II) chloride by hexamethyldisilazane in a 1:2 ratio. A is isochrom-

$$2[(CH_3)_3Si]_2NLi + SnCl_2 \longrightarrow (\{[(CH_3)_3Si]_2N\}_2Sn)_2 \qquad (1)$$

ous with Lappert's isoelectronic bis[bis(trimethylsilyl)-methyl]tin(II)[2] in being a chinese red (λ_{max} 3870 Å) distillable liquid (bp 109–110°, 0.75 Torr), which solidifies to an orange-yellow solid at room temperature, but not isostructural with it or the Zn,[3] Cd,[3] Hg,[3] or Be[4] analogs in being a dimer (mol wt 439.5, found 880 and 884 (osmometry in benzene); the highest observed ion at 70 eV in the mass spectrum is $2P^+$, with seven polyisotopic ditin fragments[5] appearing between P^+ and $2P^+$ associated with loss of CH_3, $Si(CH_3)_3$, $N[Si(CH_3)_3]_2$, etc., in various combinations). The ^{119m}Sn Mössbauer isomer shift (IS) of 2.88 mm/sec[6] confirms tin as Sn(II),[7] but the quadrupole splitting (QS) of 3.52 mm/sec[8] is among the largest ever recorded for a tin(II) species.[9] We have recorded the nmr couplings shown in the scheme. The trimethylsilyl protons give a singlet resonance at δ 0.23 ± 0.01 ppm in benzene, $CDCl_3$, THF, or in the neat liquid, and to −150° at 251 MHz in dimethyl ether,[10] giving no indication of a monomer–dimer equilibrium.

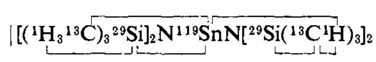
A reacts with methanol to give dimethoxytin(II),[11] and with oxygen to give bis[bis(trimethylsilyl)amino]-tin(IV) oxide as a white, infusible solid (IS = 0.56, QS = 0.83 mm/sec), and exchanges with stannocene to give η^5-cyclopentadienyl[bis(trimethylsilyl)amino]-tin(II)[12] which is also formed by lithioamination of η^5-

$$A + (\eta^5\text{-}C_5H_5)_2Sn \rightleftharpoons \eta^5\text{-}C_5H_5SnN[Si(CH_3)_3]_2 \longleftarrow$$
$$\eta^5\text{-}C_5H_5SnCl + LiN[Si(CH_3)_3]_2 \qquad (2)$$

cyclopentadienyltin(II) chloride,[13] but reverts to A and stannocene on attempted isolation.

Lithiobis(trimethylsilyl)amination of tin(II) chloride in a 1:1 ratio gives *N*,*N*-bis(trimethylsilyl)aminotin(II) chloride (B) as a white solid in 50% yield.

$$|{}^3J({}^{119}SnNSi{}^{13}C)| = 24.9\ Hz \quad |{}^4J({}^{119}SnNSiC{}^1H)| = 2.5\ Hz$$



$$[({}^1H_3{}^{13}C)_3{}^{29}Si]_2N{}^{119}SnN[{}^{29}Si({}^{13}C{}^1H)_3]_2$$

$$|{}^2J({}^{29}SiC{}^1H)| = 6.5\ Hz \quad |{}^2J({}^{119}SnN{}^{29}Si)| = 16.2\ Hz$$

$$|{}^1J({}^{29}Si{}^{13}C)| = 55.3\ Hz$$

$$|{}^1J({}^{13}C{}^1H)| = 116.0\ Hz$$

$$[(CH_3)_3Si]_2NLi + SnCl_2 \longrightarrow [(CH_3)_3Si]_2NSnCl \qquad (3)$$

The IS (3.18 mm/sec) confirms tin as Sn(II),[5] but the QS (2.64 mm/sec) is smaller by nearly 1 mm/sec than in the apparently symmetrical A.[14] The syntheses of other derivatives are underway using B as starting material.

The heterocyclic *N*,*N*′-bis(trimethylsilyl)tin(II) imidazolidine (mp 134–135°; IS = 2.66, QS = 2.50 mm/sec), perhydropyrimidine (mp 108–109°; IS = 2.71, QS = 2.34 mm/sec), and 1,3-perhydrodiazepin (mp 83.5–84.5°; IS = 2.67, QS = 2.24 mm/sec) form in *ca.* 50% yield from the lithioamination of tin(II)

---

[1] Preliminary reports of this work have been presented at the 1974 Organosilicon Award Symposium, St. Louis, Mo., March 1974 and at the 168th National Meeting of the American Chemical Society, Atlantic City, N. J., Sept 1974.

[2] P. J. Davidson and M. F. Lappert, *J. Chem. Soc., Chem. Commun.*, 317 (1973).

[3] H. Bürger, W. Sowodny, and U. Wannagat, *J. Organometal. Chem.*, 3, 113 (1965).

[4] A. H. Clark and H. Haaland, *Chem. Commun.*, 912 (1969).

[5] Intensity ratios clearly distinguish tin- and ditin-bearing fragments in mass spectra.

[6] IS error limits ±0.06 mm/sec at 77°K *vs.* $Ba^{119m}SnO_3$ at room temperature.

[7] J. J. Zuckerman, *Advan. Organometal. Chem.*, **9**, 21 (1970).

[8] QS error limits ±0.12 mm/sec.

[9] Among tin(II) species, only 3-stanna-1,2-dicarba-*closo*-dodecacarborane(II) (IS = 4.67 ± 0.04, QS = 3.84 ± 0.04 mm/sec) has a larger splitting (R. W. Rudolph and V. Chowdhry, *Inorg. Chem.*, **13**, 248 (1974). Dimethoxytin(II), for example, gives QS = 2.00 ± 0.12 mm/sec (W. D. Honnick and J. J. Zuckerman, unpublished results).

[10] We are grateful to Professor F. A. L. Anet of UCLA for carrying out this experiment.

[11] J. S. Morrison and H. M. Haendler, *J. Inorg. Nucl. Chem.*, **29**, 393 (1967).

[12] The tin-119 coupling to the protons of the cyclopentadienyl group changes from 15.9 Hz in stannocene (L. D. Dave, D. F. Evans, and G. Wilkinson, *J. Chem. Soc.*, 3684 (1959)) to 12.5 ± 0.3 Hz in the mixed derivative.

[13] K. D. Bos, E. J. Bulten, and J. G. Noltes, *J. Organometal. Chem.*, **39**, C52 (1972).

[14] The QS of stannocene (0.86 ± 0.12 mm/sec) (P. G. Harrison and J. J. Zuckerman, *J. Amer. Chem. Soc.*, **92**, 2577 (1970)) and of tin(II) chloride (none) (J. J. Zuckerman, *J. Inorg. Nucl. Chem.*, **29**, 2191 (1967)) are both smaller than that of the chloride, C_5H_5SnCl (1.05 mm/sec).[13]