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SELECTIVE INTERCONVERSION OF STEREOISOMERIC CYCLOSILOXANES

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Summary

Reaction conditions have been determined which permit the highly selective interconversion of unsymmetrically substituted cyclosiloxanes. The *cis*- and *trans*-2,6-diphenylhexamethylcyclotetrasiloxanes can be cleanly interconverted while generating little or none of the isomeric 2,4-diphenyl cyclic compounds. A strained ring system, *cis*- or *trans*-$(PhMeSiO)_3$, can be interconverted to an equilibrium mixture of *cis*- and *trans*-$(PhMeSiO)_3$ without generating linear polymers or lower energy cyclic systems. These remarkably selective transformations are achieved with an electrophilic metal halide catalyst, such as $ZnCl_2$ or $FeCl_3$, in conjuction with a polar solvent such as a nitroalkane. A mechanism is presented which involved metal halide cleavage of siloxane bonds to yield short-lived linear intermediates which undergo racemization of the asymmetric chlorophenylmethylsiloxy termini before regeneration of the cyclosiloxane by intramolecular condensation.

Introduction

As reported elsewhere [1], 2,6-*cis*-diphenylhexamethylcyclotetrasiloxane (*cis*-I) has recently attracted considerable attention because of its endocrine activity. Therefore, it became of interest to devise an efficient synthesis to provide material for clinical evaluation. The series of reactions 1—3 was used to make the desired 2,6-diphenyl system. This sequence of reactions affords equal

$$PhMeSiCl_2 + 2\ HMe_2SiCl \xrightarrow{H_2O} \underset{(II)}{(HMe_2SiO)_2SiPhMe} \quad (1)$$

$$II \xrightarrow[H_2PtCl_6]{H_2O} \underset{(III)}{(HOMe_2SiO)_2SiPhMe} \quad (2)$$

$$PhMeSiCl_2 + III \xrightarrow[R_3N]{} \textit{cis}\text{- and } \textit{trans}\text{-I} \quad (3)$$

amounts of *cis*-and *trans*-I which can be separated from each other by fractional crystallization and/or distillation. A primary concern in the selection of the above route to *cis*- and *trans*-I was the necessity for precluding the formation of the isomeric 2,4-diphenyltetramers, since their presence makes the isolation of pure *cis*-I prohibitively inefficient. Properly executed, the above sequence produces *cis*/*trans*-I containing less than 0.2% of the combined 2,4-isomers.

The value of the above synthetic sequence would obviously be considerably enhanced were it possible to convert *trans*-I to *cis*-I, provided that the interconversion were efficient, selective, and did not simultaneously produce the 2,4-diphenyl isomers.

Experimental

Cyclosiloxanes bearing PhMeSiO and Me_2SiO moieties have been extensively characterized and documented in the literature [2]. In the present work, siloxane reactants and products were identified by comparison with authentic samples by GLC, NMR and mass spectral analysis. Solvents and other reactants were reagent grade; molecular sieves were added to the solvents to keep them dry and the metal halides were also protected from exposure to atmospheric moisture. The stereoisomeric interconversions were brought about by simply heating equal weights of the appropriate siloxane and nitroalkane in a closed container with the catalytic salt, and the rate of interconversion was determined by the amount of catalyst. To illustrate, 4.2 g nitromethane and 4.2 g of *trans*-2,6-diphenylhexamethylcyclotetrasiloxane were heated at 90°C in screw-cap vials with the amounts of $ZnCl_2$ shown in Table 1 and the isomeric composition was periodically assayed by GLC.

Strained cyclic compounds interconverted under much milder conditions. Thus *trans*-$(PhMeSiO)_3$ in nitromethane (50%) with 5% $ZnCl_2$ (based on the weight of siloxane compound) underwent complete interconversion to the equilibrium mixture (25% *cis*, 75% *trans*) in about 40 h at ambient temperature.

Discussion of results

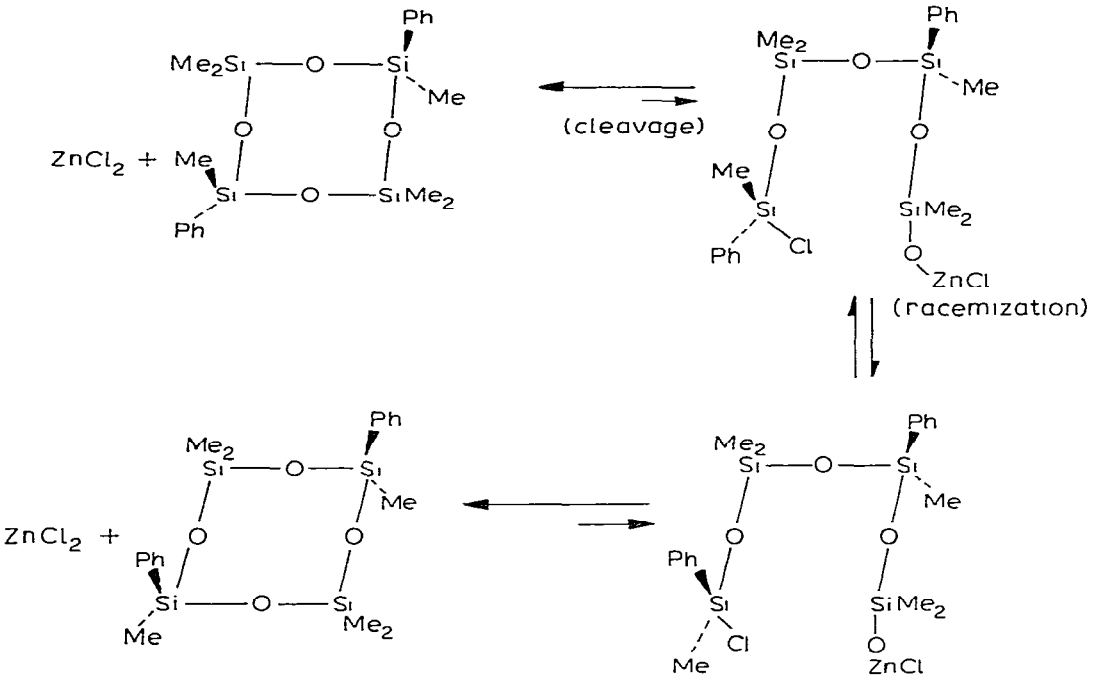
The desired stereoisomeric interconversions were achieved by the action of electrophilic metal halides on appropriate cyclosiloxanes in nitroalkane solvents. In the first successful example, it was determined that heating (90°C) a

TABLE 1

Run No.	Zinc chloride (%) based on weight of siloxane	64 h		82 h	
		cis (%)	*trans* (%)	*cis* (%)	*trans* (%)
1	10	54	46	52	48
2	1	12	88	15	85
3	5	51	49	—	—

solution of *trans*-I in nitromethane (50%) containing $ZnCl_2$ (1—10%) resulted in complete interconversion to a 1/1 mixture of *cis*/*trans*-I. Gas-liquid chromatography [3] unequivocally established the absence of 2,4-diphenyl cyclic compounds. It was also demonstrated that *cis*- or *trans*-$(PhMeSiO)_3$ could be converted to an equilibrium mixture of *cis*- and *trans*-$(PhMeSiO)_3$, without polymer formation, by the same salt/solvent, but under milder conditions (e.g., 2 days at room temperature). These results immediately posed a number of questions. If siloxane bonds were being broken (and it was obvious that they were), why weren't other cyclic and linear compounds being formed? What sort of mechanism would account for these interconversions, and, given a mechanistic rationale, what other catalysts and conditions might also be expected to function similarly? Our working hypothesis was that $ZnCl_2$ electrophilically cleaves the siloxane bond as shown in Scheme 1. This results in the formation of a

SCHEME 1

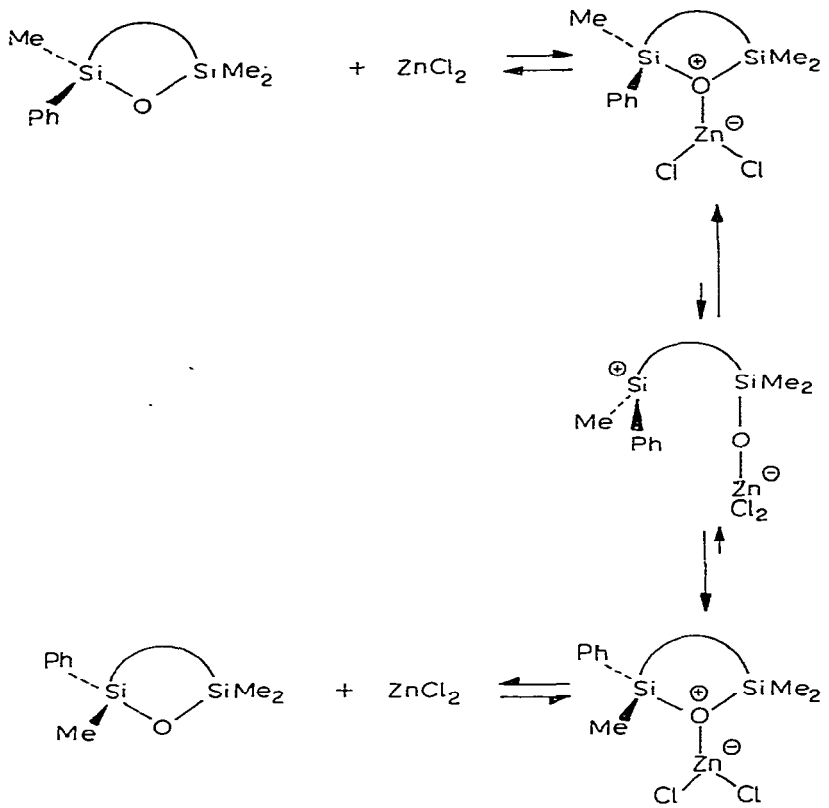


linear tetrasiloxane with an asymmetric chlorophenylmethylsiloxy terminus which can, under proper conditions, undergo racemization before ring closure regenerates *cis*/*trans*-I. It is known that optically active α-naphthylphenylmethylchlorosilane undergoes racemization in polar solvents such as nitromethane [4], and we think the chlorophenylmethylsiloxy site in our postulated linear intermediate is similarly racemized. Cleavage of the siloxane so as to form $ClMe_2$-siloxy and (ClZnO)PhMe-siloxy ends is presumably without stereochemical consequence since any ionization of the SiOZn linkage is not likely to break the Si—O bond. We are postulating that the above cleavage equilibria lie far to the left; i.e., that the concentration of the above ring-opened linear inter-

mediate is exceedingly low. Were this not the case, intermolecular processes would certainly be expected to result in polymerization as well as fragmentation and subsequent oligomerization; e.g., if the above linear intermediate were to react with additional $ZnCl_2$ to give disiloxane fragments, recombination would produce 2,4-diphenyl cyclic compounds as well as the 2,6-diphenyl cyclic compounds.

An interesting variation of the above mechanistic speculation involves siliconium ion intermediates. Thus, it could be argued that the cyclic forms a "donor–acceptor" complex with the electrophilic metal halide which, in a polar nitroalkane, then yields an ion pair with enough separation for free-rotation of the siliconium ion to yield racemization as shown in Scheme 2. Our

SCHEME 2



attempts to achieve selective interconversion with other materials are detailed elsewhere [5]. Although $CaCl_2$ and $HgCl_2$ were without effect in 2-nitropropane, $AlCl_3$ was moderately active and $FeCl_3$ was very effective in this solvent, small amounts (0.5%) resulting in complete interconversion of *cis*- or *trans*-I, in 2 h at 25°C, with little or no generation of 2,4-diphenyl isomers. Even protic electrophiles may be used, but with reduced selectivity. Thus, the use of tiny amounts of H_2SO_4 (100 ppm of siloxane) did indeed yield interconversion in 2-nitropropane after 3 h at 75°C; however, 4% of the 2,4-isomers were also formed. In toluene, the H_2SO_4 catalyzed conversion was only ~1% complete

after 3 h at 75°C. Other solvents were also employed, but none were as effective as the nitroalkanes. Acetonitrile, ketone and glymes were wholly ineffective; dimethyl formamide with $ZnCl_2$ resulted in the formation of other materials, apparently from indiscriminate siloxane rearrangement processes; aryl phosphates were effective, but required higher temperatures (220°C with $ZnCl_2$, 60°C with $FeCl_3$).

The selectivity of these stereoisomeric interconversions is truly remarkable. When pure *cis*- or *trans*-I is interconverted with $ZnCl_2$ or $FeCl_3$ in 2-nitropropane, the resulting *cis/trans*-I mixture contains no detectable amounts of the 2,4-isomers by surface-coated open tubular (SCOT) GLC analysis [3] (which gives complete base-line resolution of all four of the pertinent diphenylhexamethyl cyclic tetramers).

References

1 D.R. Bennett and B. Åberg (Eds.), Acta Pharmacol. Toxicol., Vol. 36, Suppl. III, 1975.
2 D.E. Williams, G.R. Ronk and D.E. Spielvogel, J. Organometal. Chem. 69 (1974) 69 and ref. therein.
3 D.E. Spielvogel and L.F. Hanneman, Acta Pharmacol. Toxicol., Vol. 36, Suppl. III (1975) p. 25—32.
4 L.H. Sommer, F.O. Stark and K.W. Michael, J. Amer. Chem. Soc., 86 (1964) 5683.
5 C.L. Frye and D.E. Spielvogel, U.S. Patent 3,954,832 May 4, 1976.