A SYNTHESIS OF 5-SILACYCLOTRIVERATRYLENES†

Hiroshi Hara, Hiroya Satoh, and Osamu Hoshino*

Faculty of Pharmaceutical Sciences, Science University of Tokyo, Shinjuku-ku, Tokyo 162, Japan

Abstract---- The dilithio compound (4), derived from 4,5-bis(6-bromoveratryl)-veratrol (3), reacted with dichlorodimethylsilane to give 5,5-dimethyl-5-silacyclo- triveratrylene (2a). Similarly, several 5-silacyclotriveratrylenes (2b, 2c, and 2d) and a methylenedioxy analogue (6) were prepared. On the basis of \(^1\)H-nmr spectra flexible conformation of the sila-heterocyclic system was elucidated.

Cyclotriveratrylene (1) and its analogues have been widely studied because of their interesting properties such as conformational behavior and host compounds.\(^1\) Although many investigations on their synthesis have been reported so far, a few cyclotribenzylene and cyclotriveratrylene derivatives, methylene groups in which were replaced with hetero atom such as oxygen,\(^2\) sulfur,\(^2,3\) or silicon, have been synthesized. Among them, only one example on synthesis of trisilacyclotribenzylene\(^4\) as a silicon containing compound has been reported. Therefore, we have been interested in synthesis of silacyclotriveratrylenes and their conformational behavior.

Here we wish to report a first synthesis of 5-silacyclotriveratrylenes (2). Previously, we have reported that bromination of cyclotriveratrylene (1) cleaves the ring to give rise to 4,5-bis(6-bromoveratryl)veratrole (3).\(^5\) The dibromide (3) is anticipated to be a key compound for synthesis of 5-silacyclotriveratrylene; dilithiated compound (4) generated from 3 could react with compounds containing silicon-halogen or silicon-oxygen bonds to give silacyclotriveratrylene system.\(^6\)

In order to confirm generation of 4 from 3, lithiation of 3 was carried out. After addition of \(n\)-BuLi (2.5 eq.) to tetrahydrofuran solution of 3\(^7\) at \(-50^\circ\)C the mixture was stirred at the same temperature, and then quenched

† Dedicated to Professor Emeritus Masatomo Hamana on the occasion of his 75th birthday.
1

3: X=Br

4: X=Li

5: X=D

2a: R=Me

2b: R=CH₂Cl

2c: R=CH=CH₂

2d: R=⁻

6

7
by excess deuteromethanol to afford a dideutero product (5). $^1$H-Nmr spectrum of 5 showed three singlets of aromatic protons demonstrating formation of the dilithiated compound (4).

Thus, reaction of 4 with dichlorodimethylsilane (1.1 eq.) at -50°C for 1 h and subsequent quenching with aqueous ammonium chloride afforded 5,5-dimethylsilacyclotraveratrylene (2a), $^8$ mp 174°C, in 54% yield, $^1$H-nmr spectrum of which showed six kinds of singlets ($\delta$ 0.54 (6H, SiMe$_2$), 3.73 (6H, OMe), 3.87 (12H, OMe), 6.58, 6.72, 6.98 (each 2H, ArH)]. The data verified the symmetrical structure of the sila compound (2a). Methylene protons in the $^1$H-nmr spectrum could not be observed clearly because of being overlapped by numerous protons of six methoxyl groups, while those of cyclotraveratrylene (1) appear characteristically as AB pattern to clarify the rigid conformation. This findings suggested that 2a might exist as a flexible conformation.$^1$

For the purpose of revealing the flexible conformation, we tried to synthesize a methylenedioxy analogue (6) having no obstructive protons in the region ($\delta$ 3.5-4.0) of resonance due to methoxyl protons in the $^1$H-nmr spectrum. By similar protocol as above, the dibromide (7)$^8,10$ (mp 204°C) was prepared from methylenedioxybenzene and 6-bromopiperonyl alcohol. Analogous treatment of the dibromide (7) as described above gave 5,5-dimethyl-5-silacyclotripiperonylene (6)$^8,10$ in 36% yield. As we would expect, in the $^1$H-nmr spectrum, methylene protons appeared clearly but as broad singlet at $\delta$ 3.80 without splitting pattern. Thus, conformation of these sila derivatives must be flexible undoubtedly.

Similarly, reaction of the dilithiated compound (4) with some dichlorosilane reagents produced 5-chloromethyl-(2b)$^8,10$ 5-vinyl- (2c)$^8,10$ and 5-phenyl- (2d)$^8,10$ 5-methyl-5-silacyclotraveratrylenes in the yields of 43, 40, and 23%, respectively. On the basis of $^1$H-nmr spectra, those sila-heterocycles (2b, 2c, and 2d) should be also flexible molecules.

Construction of other metal-containing cyclophanes could be engaged by this methodology.

ACKNOWLEDGEMENT

The authors are indebted to Takasago Perfumery Co., Ltd. for the supply of vanillin and piperonal, and to Sankyo Co., Ltd. for elemental analysis. Thanks are also due to Miss N. Sawabe and Mrs. F. Hasegawa, this faculty, for $^1$H-nmr and mass spectral measurements.
REFERENCES AND NOTES

7. The bromide (3) was practically prepared in 75% yield by reaction of 6-bromoveratryl alcohol (2 eq.) with veratrole (1 eq.) in the presence of concentrated sulfuric acid.
8. All new compounds described in the text gave satisfactory mass spectral and microanalytical data.
10. 2b: mp 141°C. $^1$H-Nmr δ 0.70 (3H, s, SiMe), 3.23 (2H, s, SiCH$_2$Cl), 3.76 (6H, s, 2xOMe), 3.89 (12H, s, 4xOMe), 6.61, 6.73, 7.09 (each 2H, s, ArH); 2c: mp 68°C. $^1$H-Nmr δ 0.67 (3H, s, SiMe), 3.76, 3.87, 3.90 (each 6H, s, 2xOMe), 6.61, 6.74, 7.00 (each 2H, s, ArH); 2d: mp 85°C. $^1$H-Nmr δ 0.85 (3H, s, SiMe), 3.70, 3.77, 3.90 (each 6H, s, 2xOMe), 6.68, 6.80, 6.88 (each 2H, s, ArH); 6: mp 236-237°C. $^1$H-Nmr δ 0.49 (6H, s, SiMe$_2$), 3.80 (4H, bs, 2xCH$_2$), 5.84 (4H, s, 2xOCH$_2$O), 5.88 (2H, s, OCH$_2$O), 6.60, 6.68, 6.96 (each 2H, s, ArH).

Received, 19th September, 1991