

biosynthetic pathway to **6**. In order to test this prediction, a synthesis of **9** was devised. Formylation of ethyl 4-methylpentanoate with ethyl formate and ethoxide gave ethyl 2-formyl-4-methylpentanoate.⁶ Conversion of the formyl ester to its cyanohydrin^{5d,6} followed by acid hydrolysis^{3d} yielded **9** as a mixture of diastereomers.⁶ When carbon-14 labeled cyanide was employed in the synthesis, [1-¹⁴C]-**9** was obtained. The labeled sample of **9** was administered to *C. harringtonia* plants and the plants were harvested after 7 days. Radioinactive diacid **6** was added to the crude, alcoholic plant extract which was then subjected to acidic saponification.⁹ The crude mixture of acids resulting from the saponification was converted into methyl esters and the dimethyl ester of **6** was purified by repeated thin-layer chromatography using a system in which the dimethyl ester of the precursor **9** exhibited an *R_f* value considerably smaller than that for the dimethyl ester of **6**.¹⁰ The purified dimethyl ester of **6** was then hydrolyzed to the free diacid and converted to the bis(*p*-bromophenacyl) ester **14** (Scheme II) in the usual way. The bis(*p*-bromophenacyl) ester **14** was purified by repeated thin-layer chromatography using a system in which the bis(*p*-bromophenacyl) ester of the precursor **9** exhibited a lower *R_f* value than **14**.¹⁰ The labeled diester **14** was then recrystallized to constant activity to give the incorporation figure shown in Table I (expt 2). The specific incorporation of the diacid **9** into **6** was demonstrated by means of the degradative sequence outlined in Scheme II. The bis(*p*-bromophenacyl) ester **14** was reduced with lithium aluminum hydride and the resulting labeled 3-hydroxy-3-hydroxymethyl-6-methyl-1-heptanol (**15**) cleaved with periodate. The results of the degradation (Table I, expt 2) clearly show that **9** is incorporated into **6** with very little randomization of the label.

On the basis of the hypothesis suggested in Scheme I, 2-oxo-5-methylhexanoic acid (**10**) would be expected to be the immediate precursor of **6**. If this is the case, then homoleucine (**11**) should be specifically incorporated into **6** due to the facile interconversion between α -amino acids and the corresponding α -keto acids. DL-Homoleucine was conveniently prepared from 4-methylpentanal by condensation with potassium cyanide and ammonium carbonate followed by hydrolysis of the intermediate hydantoin. The resulting amino acid exhibited properties identical with those previously reported.¹¹ [1-¹⁴C]-DL-Homoleucine was then synthesized using ¹⁴C-labeled potassium cyanide. Administration of the labeled homoleucine to *Cephalotaxus* was followed by workup after 7 days in the usual way to give radioactive **6** as its bis(*p*-bromophenacyl) ester **14**. After purification by chromatography, and crystallization to constant activity, the incorporation figure shown in Table I (expt 3) was obtained. The incorporation level is considerably higher than is usually observed in biosynthetic experiments with higher plants and it demonstrates that homoleucine is a highly efficient precursor of **6**. The specific incorporation of **11** into **6** was verified by reduction of the labeled diester **14** and cleavage of the labeled triol **15** with periodate (Scheme II); the results of this degradation are shown in Table I (expt 3).

The experiments presented here provide compelling evidence that the acyl moiety of deoxyharringtonine (**2**) is biosynthesized via the pathway delineated in Scheme I. Similar pathways appear to be involved in the biogenesis of the so called mustard oil glycosides¹² and may prove to be widespread in higher plants. The operation of the pathway shown in Scheme I can also account for the biosynthesis of the acyl portions of the remaining antitumor alkaloids found in *Cephalotaxus*, including homoharringtonine (**5**). The acyl moiety of the latter alkaloid would be expected to arise from the diacid **6** by a series of steps closely analogous to the formation of **6** from the diacid **8**. Experiments are in progress to examine this possibility and to provide additional details concerning the biosynthesis of each of the four antitumor alkaloids **2-5**.

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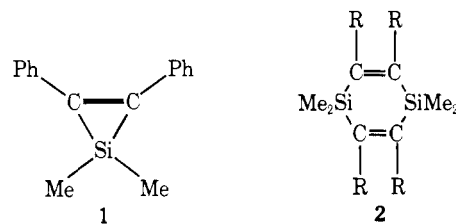
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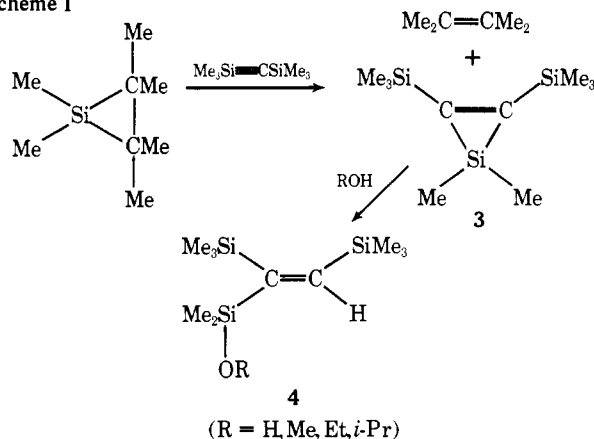
1,1-Dimethyl-2,3-bis(trimethylsilyl)-1-silirene, a Stable Silacyclopentene

Sir:

Some years ago, Vol'pin et al. predicted that silacyclopentenes should be a stable class of organosilicon compounds on the basis of analogies to the cyclopropenium cation.¹ However, the initial claim by these workers that they had prepared 1,1-dimethyl-2,3-diphenyl-1-silirene (**1**) by addition of dimethylsilylene to diphenylacetylene did not stand up to subsequent experimental scrutiny. The highly stable product of their reaction, which was claimed to be **1**, was shown to be the dimer, **2** (*R* = Ph).² At that time there had been no report of any three-membered ring compound containing only silicon and carbon atoms in the ring. Nevertheless, the concept of Vol'pin was an intriguing one and a residual interest in the possible existence of silirenes remained. Recently, Atwell and Weyenberg reported that the generation of dimethylsilylene by 1,2-dimethoxytetramethyldisilane pyrolysis in the presence of 2-butyne and methanol gave *cis*-MeCH=C(Me)Si-



Scheme I



Me_2OMe .³ The reasonable reaction course which they suggested involved initial formation of tetramethylsilirene followed by methanol cleavage of its Si-C bond.

In 1972, we were able to prepare and characterize the first stable silacyclopropanes⁴ and in succeeding years developed the chemistry of this novel class of compounds.⁵ The fair stability of the saturated SiC_2 ring, together with the original ideas about bonding in Vol'pin's paper, suggested to us that some silacyclopropenes should be stable at room temperature for times long enough to permit their properties and chemistry to be studied.

It was the basic reaction of Vol'pin which served in our preparation of the title compound. The dimethylsilylene source used was hexamethylsilirane, which we recently showed undergoes smooth decomposition to dimethylsilylene and tetramethylethylene at reasonable rates at temperatures as low as 60 °C.⁶ In a typical experiment, a solution of 1.3 mmol of hexamethylsilirane⁷ in 4 ml of bis(trimethylsilyl)acetylene was heated under nitrogen at 66 °C for 15 h. The solution subsequently was treated with 0.5 ml of anhydrous ethanol. An exothermic reaction ensued. After 15 min, the reaction mixture was analyzed by GLC (SE-30 silicone at 120 °C) to show the presence of tetramethylethylene (100%) and a product identified by ir and proton NMR spectroscopy, as well as combustion analysis, as **4** ($\text{R} = \text{Et}$). The high yield (75%) of this product demonstrated that **3**, the title compound, had been formed in high yield. The reactions which had occurred are shown in Scheme I. Similar products were obtained with other alcohols. Addition of water to the reaction mixture resulted in formation of the silanol **4** ($\text{R} = \text{H}$). The reactivity of bis(trimethylsilyl)acetylene toward dimethylsilylene is high. This was demonstrated by an experiment in which this acetylene and hexamethylsilirane were heated in benzene solution in only 1:1 molar ratio at 70–75 °C for 18 h. A 59% yield of the silacyclopropene-derived methanolysis product **4** ($\text{R} = \text{Me}$) was obtained.

In a subsequent experiment we were able to isolate and characterize the title compound, **3**. Another such hexamethylsilirane/bis(trimethylsilyl)acetylene reaction was carried out. GLC analysis of the reaction mixture directly (3 ft of 20% SE-30 at 125 °C) showed the presence of one major product which was collected by GLC. This material, like the silacyclopropanes, fumed profusely on exposure to air, and it must always be handled under an inert atmosphere. The mass spectrum (70 eV) of the isolated product showed a relatively strong (14%) molecular ion at m/e 228, the calculated molecular weight of the silirene **3**. There were no significant fragments with masses greater than $M + 2$. The parent ion (m/e 73) corresponded to $[\text{Me}_3\text{SiC}_2\text{SiMe}_2]^+$. A GLC-collected sample gave a correct combustion analysis. $\text{C}_{10}\text{H}_{24}\text{Si}_3$ calcd: C, 52.55; H, 10.58. Found: C, 52.19; H, 10.51.

The NMR spectra (^1H , ^{13}C , and ^{29}Si) were in agreement

with the structure shown for **3**, and, in particular, the ^{29}Si NMR spectrum was revealing. The proton NMR spectrum of **3** (in C_6D_6 , with cyclohexane internal standard) showed two singlets in 1:3 ratio, as expected, at δ 0.19 and 0.30 ppm, respectively. The proton-decoupled ^{13}C NMR spectrum of **3** showed three singlets at δ_{C} 189.6 ($\text{C}=\text{C}$), 0.40 (Me_3Si), and -2.2 ppm (Me_2Si) downfield from tetramethylsilane (Me_4Si). The olefinic carbon atom signal is at unusually low field. Trimethylsilyl substituents on a $\text{C}=\text{C}$ bond do cause downfield shifts in the olefinic carbon atom signals (compare *trans*- $\text{EtCH}=\text{CHEt}$, δ_{C} 130.4 ppm vs. *trans*- $\text{Me}_3\text{SiCH}=\text{CHSiMe}_3$, 151 ppm), but further experiments with other silacyclopropenes and cyclopropenes will be required before a better understanding of this question will be possible. In a fully proton-coupled ^{13}C NMR spectrum of **3** the $\text{CH}_3\text{-Si}$ resonances split into two overlapping quartets with $J(\text{C-H}) = 119$ Hz. The ^1H and ^{13}C NMR spectra thus are consistent with the silirene structure of **3**, but they do not by any means prove the structure. As in the case of silacyclopropanes,^{4,7} it is the ^{29}Si NMR spectrum which brings suggestive evidence that an unusual, atypical organosilicon compound is in hand. The ^{29}Si chemical shifts of cyclic and acyclic tetraalkylsilanes usually are found between 5 ppm upfield and 20 ppm downfield from Me_4Si ,⁸ except for silacyclopropanes, whose ^{29}Si resonances occur at about 50–55 ppm upfield from Me_4Si .^{4,7} The ring silicon atom signal in the ^{29}Si NMR spectrum of **3** was found at 106.2 ppm upfield from Me_4Si as a three-line pattern (seven lines theoretical) atop the broad glass signal. The Me_3Si resonance occurred at 8.5 ppm upfield from Me_4Si as the expected ten-line pattern. In a fully decoupled spectrum, both of these signals were singlets, with the 106.2 ppm line being inverted due to the negative nuclear Overhauser effect of the silicon nucleus. That the ring silicon atom is so highly shielded could be due to the three-membered ring effect as well as to π -bonding involving participation of vacant silicon 3d orbitals, as originally suggested by Vol'pin.¹

Compound **3** shows absorption in the ultraviolet region; λ_{max} (2×10^{-4} M in pentane) (ϵ): 205 (3450), 215 (2850), and 345 nm (37). Its ir spectrum shows bands of medium intensity at 1505 and 1500 cm^{-1} . These may possibly be due to the $\text{C}=\text{C}$ vibrations. The $\text{C}=\text{C}$ stretching frequencies in the ir spectra of alkyl-substituted cyclopropenes usually are found at 1755–1880 cm^{-1} ,⁹ but trimethylsilyl substituents are well-known to shift $\text{C}=\text{C}$ absorptions to lower frequency (note $\nu_{\text{C}=\text{C}}$ of 1499 cm^{-1} in $(\text{Me}_3\text{Si})_2\text{C}=\text{CHSiMe}_3$ ¹⁰).

The high chemical reactivity of **3**, its mass spectrum, and ^{29}Si NMR spectrum thus speak strongly in favor of the silirene structure. In view of the experience of previous workers,^{1,2} one must rule out conclusively the alternate 1,4-disilacyclohexadiene structure **2** ($\text{R} = \text{Me}_3\text{Si}$). We prepared **2** ($\text{R} = \text{Me}$), a close analogue, by the method of Atwell and Weyenberg¹¹ in order to measure its ^{13}C and ^{29}Si NMR spectra and to compare them with those of **3**. They were, we found, decisively different. The olefinic carbon atom resonance in **2** ($\text{R} = \text{Me}$) occurred at δ_{C} 148.3 ppm downfield from Me_4Si , while its ^{29}Si resonance was found at 19.0 ppm upfield from Me_4Si . Furthermore, compounds of type **2** do not fragment upon electron impact to give $\frac{1}{2}M^+$ species.^{2a} We may conclude that our product does not have the **2** ($\text{R} = \text{Me}_3\text{Si}$) structure.

The mode of decomposition of **3** requires more detailed study. In benzene solution at 70–75 °C this compound has a half-life of about 60 h. (It is thus more stable than hexamethylsilirane.⁷) During the course of this decomposition some bis(trimethylsilyl)acetylene is formed, but not in an amount comparable to the amount of **3** which has been consumed. Thus when 64% of silirene **3** had decomposed, the yield of the acetylene produced was only 20%. It seems likely that more than one decomposition pathway is available. At room temperature, benzene solutions of **3** are stable for periods of weeks. Neat

samples of **3** under argon at room temperature turned cloudy after several days, but major decomposition did not occur. It is evident that **3** is rather stable thermally, although it is highly reactive toward common reagents.

Our studies in this area are continuing with emphasis on the preparation of other silacycloprenes and on a broad scope study of the chemical reactivity of this novel class of compounds. It will be of special interest to determine if the trimethylsilyl substituents play an important role in the stability of **3**. We were prompted to disclose these preliminary results by a paper presented at the 10th Organosilicon Award Symposium by Gaspar and Conlin¹² in which the synthesis of tetramethylsilirene by the flow pyrolysis of 1,2-dimethoxytetramethyldisilane in the presence of 2-butyne was claimed.

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Electron-Transfer Reactions of Excited States: Direct Evidence for Reduction of the Charge-Transfer Excited State of Tris(2,2'-bipyridine)ruthenium(II)

Sir:

The charge-transfer excited state of tris(2,2'-bipyridine)ruthenium(II) ($^*Ru(bpy)_3^{2+}$)¹ is a more powerful reducing agent (eq 1) than the ground state molecule by ~2.1 V, the excitation free energy.^{2,3} Thus oxidants (e.g., $Co^{III}(NH_3)_5X^{2+}$,^{2,4} Fe^{3+} ,⁵⁻⁷ $Ru(NH_3)_6^{3+}$ ^{2,6}) can quench the emission from $^*Ru(bpy)_3^{2+}$ by an electron-transfer mechanism (eq 2) as has been demonstrated by product analyses,⁴ steady-state measurements,⁷ flash-photolysis experiments,⁶ and rate comparisons.^{2,3,7}

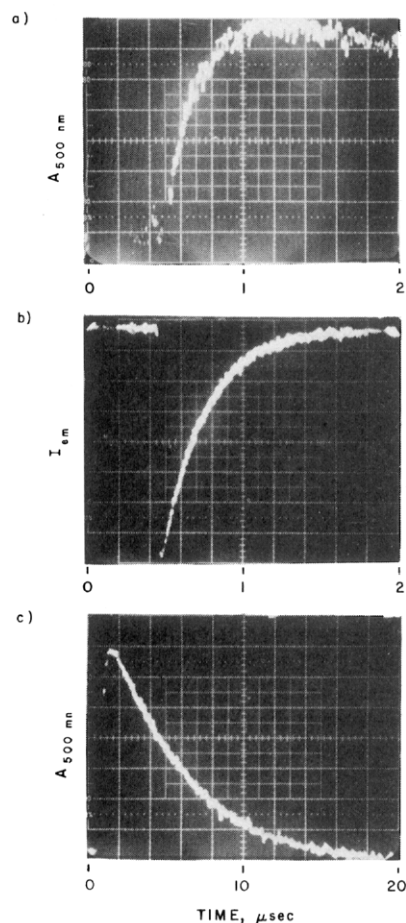
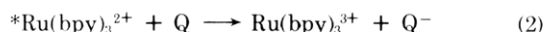
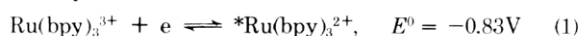
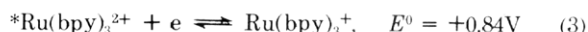


Figure 1. Flash photolysis of europium(II)- $Ru(bpy)_3^{2+}$ solution: (a) absorbance at 500 nm ($\Delta A \sim 0.02$ per major division) as a function of time (0.2 μs per major division); (b) emission intensity at 600 nm (I_{em} increases down the trace) in arbitrary units as a function of time (0.2 μs per major division); (c) same as (a), but 2 μs per major division.

The same excited state is also expected to possess oxidizing properties (eq 3). Evidence for reduction of $^*Ru(bpy)_3^{2+}$ (eq 4) to $Ru(bpy)_3^+$ (which has previously been produced by



electrochemical^{8,9} and pulse-radiolysis¹⁰ techniques) has recently been sought by studying the quenching of the $^*Ru(bpy)_3^{2+}$ emission by reductants such as $Eu(II)$,¹¹ $Ru(NH_3)_6^{2+}$ ¹¹ and metal cyanides (e.g., $Os(CN)_6^{4-}$).¹² Here we present results of flash-photolysis experiments which provide direct evidence for the reduction of the charge-transfer excited state to $Ru(bpy)_3^+$.

Flash-photolysis studies using a frequency-doubled neodymium laser as the excitation source^{7b} (λ 530 nm, pulse width ~30 ns) were undertaken for the Eu^{II} - $Ru(bpy)_3^{2+}$ system¹¹ ($Eu(II)$ 0.01-0.1 M; $Ru(bpy)_3^{2+}$ $0.3-3 \times 10^{-4}$ M; excitation intensities $10-10^2$ einstein $cm^{-2} s^{-1}$; 0.5 M Cl^- , 0.05 M H^+ , 25 °C). Examples of the traces obtained are shown in Figure 1. An increase in absorbance in the region 470-550 nm (Figure 1a) accompanied the decrease in emission intensity following the excitation flash (Figure 1b). The magnitude of the absorbance increase at 500 nm was linear in the excitation light intensity. The rate of decay of the transient (Figure 1c) was first-order in the transient and first-order with respect to added $Eu(III)$.¹³ These observations are interpreted in terms of the following sequence: reductive quenching of $^*Ru(bpy)_3^{2+}$ to yield $Ru(bpy)_3^+$ and $Eu(III)$ (eq 6, Figure 1a) is followed by $Eu(III)$ -oxidation of $Ru(bpy)_3^+$ to regenerate the preflash