

PREPARATION AND CHARACTERIZATION OF (TRIMETHYLSILYL)BICYCLO[2.2.1]HEPTANONES

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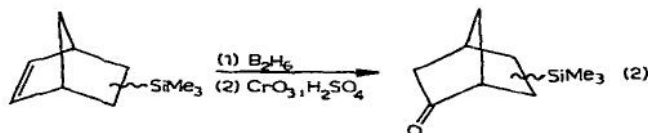
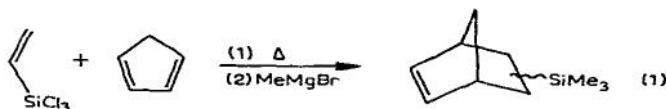
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SUMMARY

Five (trimethylsilyl)bicyclo[2.2.1]heptanones [(trimethylsilyl)norbornanones] have been synthesized. Three of these have been characterized unambiguously, and two, tentatively, by chemical and spectral methods. Addition of vinyltrichlorosilane to cyclopentadiene followed by reaction with methylmagnesium iodide yields a mixture of 5-(trimethylsilyl)norbornenes. Hydroboration, followed by chromic acid oxidation provided a mixture of the four 5- and 6-(trimethylsilyl)norbornan-2-ones. Reaction of *exo*-2,3-epoxy-5-(trimethylsilyl)norbornane with lithium aluminum hydride in *N*-methylmorpholine provided *endo*-5-(trimethylsilyl)norbornan-2-one and *exo*-2-(trimethylsilyl)norbornan-7-one.

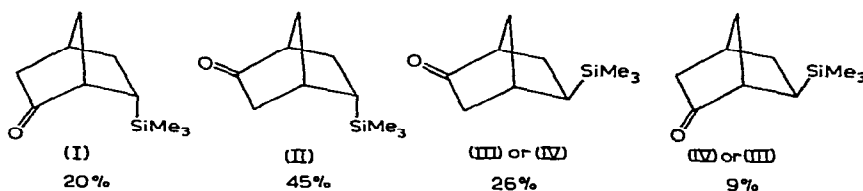
RESULTS AND DISCUSSION

In connection with photochemical studies on ketosilanes^{1,2} we wished to compare the photochemistry of 5- and 6-(trimethylsilyl)bicyclo[2.2.1]heptan-2-ones with that of norcamphor. The *endo* and *exo*-5-(trimethylsilyl)bicyclo[2.2.1]heptenes have been well characterized³ and seemed to be the logical starting materials. Preparation of a mixture of isomeric ketones is outlined in eqns. (1) and (2).



The Diels–Alder reaction of vinyltrichlorosilane and cyclopentadiene, after methylation, resulted in a mixture containing 70–80% of *endo*-5-(trimethylsilyl)norbornene and 20–30% of *exo*-5-(trimethylsilyl)norbornene. Hydroboration/oxidation⁴ of the olefin gave a mixture of the four possible ketones, (I), (II), (III) and

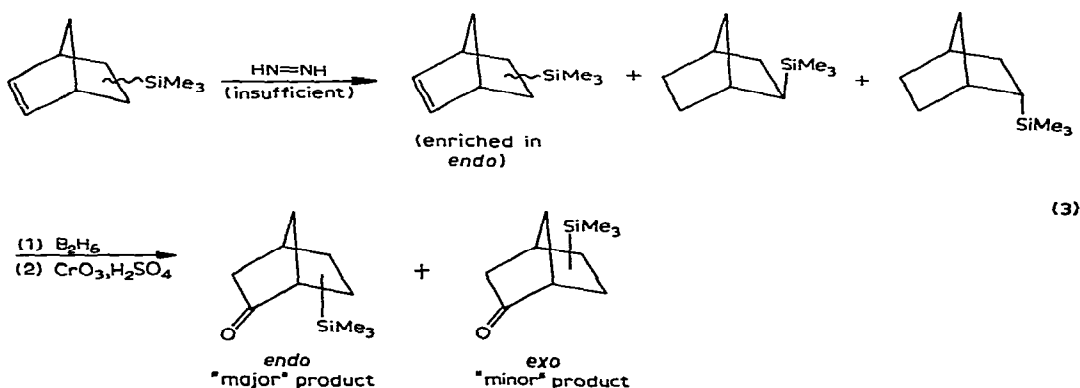
(IV), as shown by gas liquid partition chromatography (GLC) analysis with the relative percentages shown.



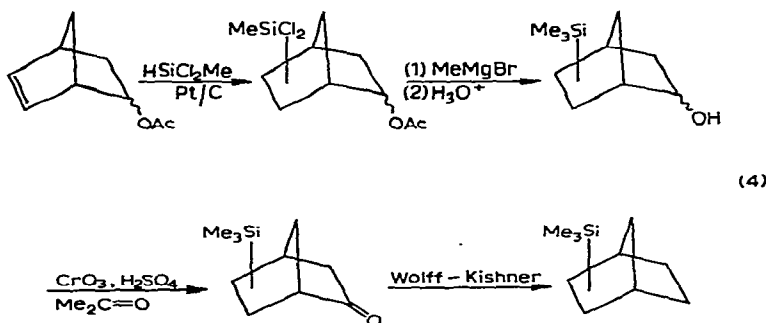
Structural assignments were made on the basis of spectral and chemical properties. That the desired ketones might be present was verified by the IR spectrum of the mixture which showed a strong carbonyl absorption at 1742 cm^{-1} and the trimethylsilyl group absorptions (in cm^{-1}) at 1250, 840 and 765^5 . It was possible to collect (I) by preparative GLC but retention times of the others were too close together to make effective separation possible.

The first series of characterization experiments was designed to differentiate between the *exo* and *endo* isomers. It was thought that if a sample of *endo*-5-(trimethylsilyl)norbornene could be obtained, hydroboration/oxidation would lead to the *endo* ketones. Attempts to prepare this compound pure were unsuccessful. Another approach was to prepare a sample considerably enriched in the *endo* isomer. If this sample were converted to the ketone mixture, the two components corresponding to the *endo* ketones should be present in increased amounts compared to the *exo* ketones. Examination of models indicated that *endo*-5-(trimethylsilyl)norbornene might be more resistant to $sp^2 \rightarrow sp^3$ rehybridization of the vinyl carbons than the *exo* isomer. The reason for this is that the increase in non-bonded 3,5 *endo* interactions would be more severe in the case of *endo*-trimethylsilyl group.

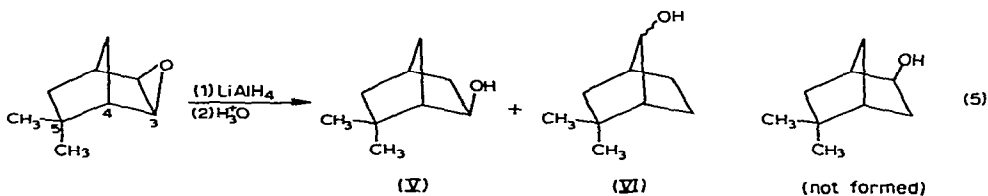
Partial hydrogenation of a mixture of *endo* and *exo*-5-(trimethylsilyl)norbornene by the Brown method⁶ indicated that there was some reactivity difference between the *exo* and *endo* isomers; however the difference was not large enough to provide a sample containing enough of the olefin for further reaction. A more selective hydrogenating agent is diimide⁷. Partial hydrogenation of a mixture of *exo* and *endo*-5-(trimethylsilyl)norbornene with this reagent showed the reactivity ratio to be: $k_{exo}/k_{endo} \cong 4$. Hydroboration/oxidation of a mixture of the partially hydrogenated



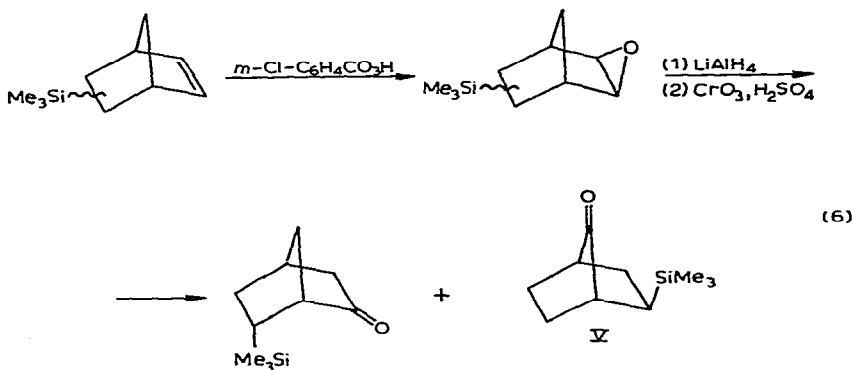
products gave a ketone mixture in which the proportions of (I) and (II) had increased considerably relative to those of (III) and (IV), eqn. (3). Hence, components (I) and (II) were assigned the *endo* configuration. In order to verify this, a sample of *exo*-5- and *exo*-6-(trimethylsilyl)norbornyl acetates was prepared. Addition of silanes to norbornenes has been shown to result in *exo* silylnorbornanes⁸. Methylchlorosilane was added to norbornenyl acetate; the reaction mixture was methylated and oxidized by chromic acid, eqn. (4), to yield a 50/50 mixture of two ketones which were shown to be the same as compounds (III) and (IV). The configuration of the trimethylsilyl group was verified by Wolff-Kishner reduction of the ketone mixture which gave 100% *exo*-2-(trimethylsilyl)norbornane³.



It was then necessary to differentiate between the *endo*-6 isomer, (I), and the *endo*-5 isomer, (II). Schleyer has reported that reduction of 5,5-dimethylbicyclo[2.2.1]heptene oxide with lithium aluminum hydride gave only the *exo*-2-norborneol, (V), and rearranged 7-norborneol, (VI), eqn. (5)⁹. It was proposed that the bulky

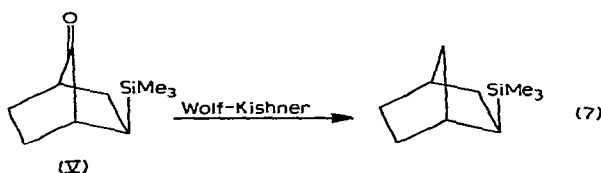


endo methyl group on C-5 prevented *endo* attack by the hydride on C-3. If a methyl group is sufficient to prevent attack of hydride at this carbon, a trimethylsilyl group should be even more effective. Preparation of 5-(trimethylsilyl)norbornene oxide was carried out by reaction of the olefin with *m*-chloroperoxybenzoic acid. Reduction of the oxide with lithium aluminum hydride in refluxing *N*-methylmorpholine, followed by chromic acid oxidation gave two ketones, eqn. (6), one of which was identical to (I) as shown by identity of GLC retention times and IR spectra. The second ketone was different from all of the other ketones previously obtained. IR analysis indicated it was the expected 7-oxo isomer (carbonyl absorption band at 1767 cm^{-1})¹⁰. The configuration of the trimethylsilyl group was determined by Wolff-Kishner reduction which resulted in formation of *exo*-2-(trimethylsilyl)norbornane as the only product, eqn. (7).

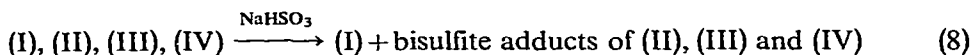


Unambiguous structural and configurational assignments have thus been made to three of the ketones. Assignments to (III) and (IV) are based on the expected addition of diborane away from the bulky trimethylsilyl group¹¹.

Sufficient quantities of (I) could be obtained for further study by taking advantage of the proximity of the trimethylsilyl group to the carbonyl group. It was found that a mixture of (I), (II), (III) and (IV) would react readily with sodium bi-



sulfite or Girard's T Reagent, with (II), (III) or (IV) forming the water soluble compounds. However, (I) resisted change in the hybridization of the carbonyl carbon from sp^2 to sp^3 due presumably to the resultant increase in 2,6-endo interactions, eqn. (8)¹².



EXPERIMENTAL

IR spectra were determined on liquid films using Perkin-Elmer 337 spectrophotometer. GLC analyses were performed using an F and M Model 5750 chromatograph employing helium as the carrier gas. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee.

Preparation of a mixture of (I), (II), (III) and (IV)

Into a 2-liter 3-necked flask equipped with stirrer, condenser with nitrogen inlet and addition funnel were placed 83 g (0.5 mole) of 5-(trimethylsilyl)norbornene³, 500 ml anhydrous tetrahydrofuran, and 16.7 g (0.46 mole) of sodium borohydride. While stirring and cooling at 0°, 20 ml (0.15 mole) of freshly distilled boron trifluoride etherate was added dropwise. After addition, the mixture was stirred at room temperature for 12 h. While cooling at 0°, 25 ml of water was added to destroy excess hydride

followed by slow addition of 800 ml of chromic acid solution prepared from 220 g sodium dichromate, 173 ml concentrated sulfuric acid and diluted to 800 ml with water². Stirring was continued at room temperature for 6 h. The mixture was extracted with 500 ml of ether. The ether layer was separated, washed five times with distilled water and once with saturated sodium chloride solution, and dried with magnesium sulfate. The ether was removed on a rotary evaporator and the reaction mixture distilled under reduced pressure to give 43 g (48%) of the ketone mixture, b.p. 103–108° (18 mm). IR analysis showed a strong absorption at 1742 cm^{-1} and other pertinent absorptions at 1250, 840 and 756 cm^{-1} . GLC analysis was carried out on a $\frac{1}{4}$ " \times 15 ft. column packed with 10% TCEP on 60–80 mesh Chromosorb P at 160°, with a flow rate of 80 cc helium a minute. Component (I) and a mixture of (II), (III) and (IV) were collected by preparative GLC for analysis. The retention times increased from (I) to (IV), but the last three peaks were not completely resolved. (Found [(I)]: C, 65.75; H, 9.73; Si, 15.42. Found [(II), (III) and (IV)]: C, 65.81; H, 9.87; Si, 15.24. $\text{C}_{10}\text{H}_{18}\text{SiO}$ calcd.: C, 65.93; H, 9.89; Si, 15.38%.)

*Partial hydrogenation of 5-(trimethylsilyl)norbornene with diimide*¹³

Into a 125 ml Erlenmeyer flask equipped with a magnetic stirrer were placed 50 ml of ethanol, 10 ml of 95% hydrazine solution, 3.3 g (0.02 mole) of the (trimethylsilyl)norbornene and 1 ml of 1% cupric sulfate solution. To the stirred solution at 0°, was added 1.7 g of 30% hydrogen peroxide solution (0.015 mole) slowly from a capillary dropping tube. The reaction mixture was extracted with 50 ml ether, washed 5 times with water and once with saturated sodium chloride solution. The ether was removed by rotary evaporator and the product analyzed by GLC on a $\frac{1}{4}$ " \times 20 ft. column packed with 15% Apiezon L on 60–80 mesh Chromosorb P, at 120°, with a flow rate of 80 cc helium/min. Integration of peak areas for *exo*- and *endo*-(trimethylsilyl)norbornanes³ and the unreacted olefin indicated the *exo* had been preferentially hydrogenated. The percentages of *exo* and *endo* olefins in the starting material were determined by complete hydrogenation³.

Preparation of a mixture of (III) and (IV)

To a 200 ml roundbottomed flask equipped with condenser and drying tube was added 15.2 g (0.1 mole) of norbornenyl acetate, 14 g (0.13 mole) of methylchlorosilane and 0.05 g of chloroplatinic acid. The reaction mixture was heated slowly to reflux and became exothermic at one point. After refluxing for one h, the reaction mixture was methylated³ with 0.6 mole of methylmagnesium bromide in 500 ml of ether, hydrolyzed, the ether layer separated and washed twice with water. The ether layer was concentrated to 100 ml with a rotary evaporator and placed in a 250 ml flask equipped with stirrer, condenser and addition funnel. While cooling and stirring at 0°, 120 ml of chromic acid solution prepared from 33 g sodium dichromate, 25 ml of concentrated sulfuric acid and diluted to 125 ml, was added over one h. After addition was complete, the reaction mixture was stirred at room temperature for four h, and the ether layer was separated, washed twice with water, once with saturated sodium chloride solution and dried with magnesium sulfate. The ether was removed by rotary evaporator and the product distilled under reduced pressure to give 10.9 g (61%) of product, b.p. 102–104° (19 mm). GLC analysis showed two products with the same retention times as (III) and (IV).

Preparation of 5-(trimethylsilyl)norbornene oxide

Into a 2-liter 3-necked flask equipped with stirrer, condenser and 500 ml addition funnel were added 41.5 g (0.25 mole) of olefin and 100 ml methylene chloride. While stirring at 0°, 51.6 g (0.3 mole) 85% *m*-chloroperoxybenzoic acid in 450 ml methylene chloride was added over a period of four h. After removal of the cooling bath, the reaction mixture was stirred at room temperature for two h and refluxed for one h. In order to decompose any unreacted peracid, 50 ml of 10% sodium sulfite solution was added to the reaction mixture, followed by 15% sodium bicarbonate solution until all of the precipitated benzoic acid had dissolved. The reaction mixture was then poured into a separatory funnel. The methylene chloride layer was separated, washed twice with water, once with saturated sodium chloride solution and dried over magnesium sulfate. After removal of the methylene chloride by rotary evaporator, the remaining liquid was eluted through a 18" × 1" column of alumina using benzene as eluent. The oxide was found in fractions 5 through 9 (35 ml fractions). Only fractions 5 and 6 were used; yield, 30 g (64%). IR analysis showed that the characteristic norbornene double bond absorption at 1575 cm⁻¹ had disappeared and a carbon-oxygen absorption at 1050 cm⁻¹ had appeared. Bands assigned to the trimethylsilyl group remained unchanged.

Reduction of 5-(trimethylsilyl)norbornene oxide with lithium aluminum hydride

To a 500 ml 3-necked flask equipped with stirrer, condenser and drying tube were added 30 g (0.165 mole) oxide, 200 ml *N*-methylmorpholine distilled from potassium hydroxide and 3.0 g (0.08 mole) lithium aluminum hydride. (Note: add lithium aluminum hydride slowly and cautiously.) The reaction mixture was slowly brought to reflux behind a safety shield and stirred for 4 h at that temperature. After cooling, hydrolysis was carried out by very slow addition of 10% ammonium chloride solution while stirring at 0°. The reaction mixture was then transferred to a one liter beaker and treated with concentrated hydrochloric acid until acid to litmus in order to remove the *N*-methylmorpholine. The mixture was then filtered, extracted with ether, washed twice with water and once with saturated sodium chloride solution; and dried over magnesium sulfate. Removal of the ether by rotary evaporator yielded 26 g of residue. IR analysis showed the presence of an alcohol band and a trimethylsilyl group. The intermediate alcohols were not characterized further and were immediately oxidized as described below.

Oxidation of alcohol mixture

Into a 500 ml 3-necked flask equipped with stirrer, condenser and addition funnel were placed 26 g of product from lithium aluminum hydride reduction and 75 ml acetone. While stirring at 0°, 0.25 mole of chromic acid solution prepared from 25 g chromium trioxide, 21 ml concentrated sulfuric acid and 180 ml water, was added over three h, followed by stirring at room temperature for four h. The reaction mixture was extracted with ether, washed with 5% sodium bicarbonate solution and dried with magnesium sulfate. Removal of the ether yielded 10 g of product containing (I), (52%) and *exo*-2-(trimethylsilyl)bicyclo[2.2.1]heptan-7-one (V) (48%) as shown by GLC analysis described above for the ketone mixture. No (II), (III) or (IV) was observed in the reaction mixture. (Found [(V)]: C, 66.08; H, 9.97; Si, 15.21. C₁₀H₁₈SiO calcd.: C, 65.93; H, 9.89; Si, 15.38%.) IR spectrum, ν_{\max} in cm⁻¹: 2950 s, 2900 m, 2870 s,

1767 s, 1447 m, 1444 m, 1395 m, 1260 s, 1250 s, 1189 m, 1160 s, 1135 s, 1100 m, 1025 s, 990 m, 980 m, 905 s, 840 s, 775 m, 750 s, 715 s, 690 s.

*Isolation of (I) with sodium bisulfite*¹⁴

To 3 g of sodium bisulfite in 10 ml water was added 7 ml of ethanol. While stirring magnetically, additional (about 5 ml) water was added to dissolve the sodium bisulfite. The ketone mixture, 4.5 g (0.025 mole) was added, and the mixture stirred for two h. A voluminous precipitate appeared. The mixture was filtered and the filtrate was poured into a 125 ml separatory funnel with 50 ml of ether and 25 ml of water. The ether layer was separated, washed three times with water, once with saturated sodium chloride solution and dried with magnesium sulfate. After removal of the ether by rotary evaporation, 3.3 g of product was obtained which was shown to consist of (I) and traces of ketones (II), (III) and (IV).

*Isolation of (I) with Girard's T Reagent*¹⁵

Into a 250 ml roundbottomed flask were placed 25.5 g (0.125 mole) of ketone mixture, 17.8 g (0.106 mole) Girard's T Reagent, 32 ml glacial acetic acid and 90 ml of 95% ethanol. The reaction mixture was heated at reflux on a steam bath for one h, cooled to room temperature and poured into a 500 ml separatory funnel with 75 ml ether and 100 ml water. The water layer was separated and the ether layer was washed twice with water. The ether layer was then neutralized with 10% sodium bicarbonate solution, washed successively with water, saturated sodium chloride solution and dried. The ether layer was removed by rotary evaporator to give 3 g of pure (I). IR spectrum, ν_{\max} in cm^{-1} units: 2950 s, 2902 m, 2989 m, 2870 s, 1742 s, 1460 w, 1452 w, 1405 m, 1300 w, 1260 m, 1250 s, 1212 w, 1180 m, 1140 m, 1107 w, 1070 m, 1005 m, 962 m, 938 m, 903 s, 838 s, 754 s, 690 m.

ACKNOWLEDGEMENT

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