# Notes

## Synthesis of the Two Epimeric 6-Carbomethoxy-1,5-dimethyl-*endo*-tricyclo-[5.2.1.$0^{2,6}$]dec-8-en-3-ones. Unequivocal Structural Assignment of the 5$\alpha$- and 5$\beta$-Isomers via Two-Dimensional NMR Spectroscopy

William B. Smith*

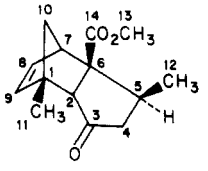
*Department of Chemistry, Texas Christian University, Ft. Worth, Texas 76129*

Alan P. Marchand,* Suresh Chander Suri, and Pei-wen Jin

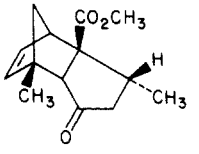
*Department of Chemistry, North Texas State University, Denton, Texas 76203*

*Received January 17, 1986*

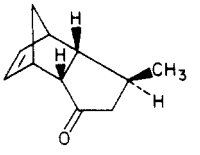
We recently completed the synthesis of **1**, which is needed as an intermediate in the total synthesis of (±)-silphinene.[1] Our synthetic approach to **1** involves $\beta$-alkylation of intermediate ketone **4**, (Scheme I). However, alkylation of **4** with $Me_2CuLi$[2] was found to afford a mixture of epimeric products **1** and **2**. The two products



**1**



**2**



**3**

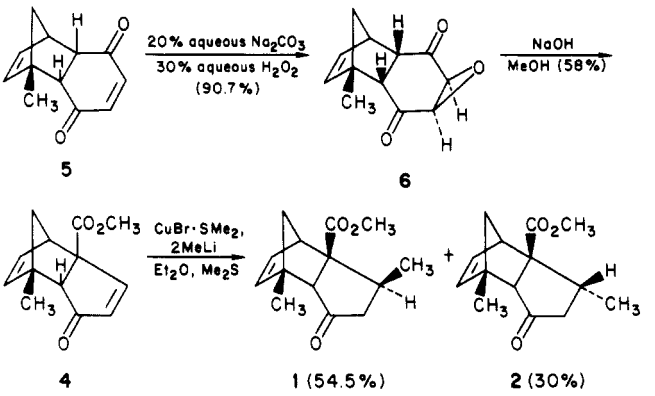
could be separated readily via flash column chromatography (see Experimental Section). However, the structures of the individual isomers **1** and **2** could not be assigned unequivocally simply via examination of their respective one-dimensional $^1H$ and $^{13}C$ NMR spectra. Accordingly, 2-D NMR and 1-D NOE studies of **1** and **2** were undertaken to complete the required structural assignments. We now report the results of these studies along with the results of corresponding NMR studies performed on a closely related tricyclic ketone **3**.

The configurations of the carbon–methyl bonds at C-5 (i.e., $\alpha$ or $\beta$) in compounds **1–3** cannot be established until the proton NMR signals corresponding to the nearby protons in each of these molecules respectively have been completely and correctly assigned. In practice, this requires complete assignment of the $^1H$ and $^{13}C$ NMR spectra of these molecules. This task has now been accomplished with the aid of 2-D correlation spectroscopy and NOE-difference spectra.

The $^{13}C$ and $^1H$ chemical shifts for **1–3** are given in Table I. Heteronuclear $^1H$–$^{13}C$ shift correlation data were utilized to assign proton signals to their respective carbon signals in each case. The task of assigning $^1H$ and $^{13}C$ signals in **1–3** was greatly facilitated via examination of proton coupling patterns in the COSY spectrum of each compound.

The procedure is illustrated by using data for **3**. The double quantum filtered phase-sensitive COSY spectrum

**Scheme I**




of **3** reveals that the olefinic proton absorptions at $\delta$ 6.15 (H-8) and 6.10 (H-9) are mutually coupled, and they are also coupled to the bridgehead proton signals at $\delta$ 3.06 (H-7) and 3.10 (H-1), respectively. In turn, H-1 and H-7 are each coupled to the bridge methylene protons (H-10a and H-10s) as well as to the neighboring exo protons [H-2 ($\delta$ 2.94) and H-6 ($\delta$ 2.56), respectively]. Further differentiation is made possible by the observation that proton H-6 is also coupled with methine proton H-5 ($\delta$ 1.82).

The assignments of the corresponding $^{13}C$ NMR signals in **3** follow directly from the above considerations in conjunction with information contained in the heteronuclear shift correlation spectrum. The methyl protons at $\delta$ 1.09 are split by H-5 into a doublet ($^3J_{HH}$ = 7.3 Hz). Protons H-4a and H-4s are associated with the $^{13}C$ NMR signal at $\delta$ 49.74. The four-peak multiplet at $\delta$ 2.22 was assigned tentatively to H-4s on the basis of (i) its observed large vicinal coupling to H-5 (0° dihedral angle) and (ii) its large geminal coupling to H-4a. This conclusion is substantiated via examination of the NOE-difference spectrum that was obtained with double irradiation at H-6. This experiment produced positive enhancements for the protons at $\delta$ 1.09, 1.34, 1.87, 2.94, and 3.06, thereby confirming the assignments of H-10a, H-4a (and, therefore, H-10s and H-4s indirectly), H-2 and H-7. Confirmation of the assigned $\beta$ configuration of the methyl group at C-5 in **3** follows from inspection of the NOE difference spectrum that was obtained with double irradiation of that methyl group. This experiment produced positive enhancements for the protons at $\delta$ 1.87 and 2.56 (H-4a and H-6, respectively).

Essentially the same procedure was followed to derive the corresponding $^1H$ and $^{13}C$ NMR spectral assignments for **1** and **2**. Of particular interest was the NOE-difference spectrum of **2** that was obtained with double irradiation of the C-5 methyl group. Positive enhancement of the signals corresponding to proton H-7 and the vinyl proton H-8 were thereby obtained. Examination of a Dreiding model with the C-5 methyl group in the $\alpha$ configuration confirms that the C-5 methyl group protons are situated in relatively close proximity to H-7 and H-8, (ca. 2 and 1.7 Å, respectively).

### Experimental Section

Melting points and boiling points are uncorrected. Routine $^1H$ NMR spectra (60 MHz) were obtained on a Hitachi-Perkin-Elmer Model R-24B NMR spectrometer. Routine $^1H$ NMR

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(2) House, H. O.; Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.

0022-3263/86/1951-3052$01.50/0 

Table I. $^{13}C$ ($^1H$) NMR Chemical Shifts (ppm) for Compounds 1-3[a]

| position | compound 1 | | compound 2 | | compound 3 | |
|---|---|---|---|---|---|---|
| 1 | 56.66 | | 55.85 | | 46.39 | (3.10) |
| 2 | 64.11 | (3.06) | 64.45 | (2.99) | 54.73 | (2.94) |
| 3 | | | | | 220.85 | |
| 4 | 49.60[b] | (4s, 2.24) | 48.26 | (4s, 2.18) | 49.74 | (4s, 2.22) |
| | | (4a, 2.18) | | (4a, 1.80) | | (4a, 1.87) |
| 5 | 34.55 | (2.08) | 35.10 | (2.30) | 31.18 | (1.82) |
| 6 | 66.13 | | 64.84 | | 50.41 | (2.56) |
| 7 | 49.66[b] | (3.35) | 48.90 | (3.25) | 46.68 | (3.06) |
| 8 | 135.52 | (6.16) | 135.63 | (6.21) | 135.99 | (6.15) |
| 9 | 142.60 | (6.04) | 142.07 | (5.80) | 135.14 | (6.10) |
| 10 | 58.48 | (10s, 1.50) | 57.40 | (10s, 1.35) | 52.28 | (10s, 1.56) |
| | | (10a, 1.29) | | (10a, 1.24) | | (10a, 1.34) |
| 11 | 17.83 | (1.43) | 17.74 | (1.34) | | |
| 12 | 17.76 | (0.96) | 15.47 | (1.08) | 23.41 | (1.09) |
| 13 | 51.73 | (3.74) | 52.25 | (3.64) | | |
| 14 | 175.67 | | 176.82 | | | |

[a] The stereochemical designations s and a indicate that the relevant carbon–hydrogen bond is either syn or anti, respectively, to the norbornene double bond. [b] May be interchanged.

spectra (90 MHz) and $^{13}C$ NMR spectra (22.5 MHz) were recorded on a JEOL FX-900 NMR spectrometer. In all cases, signals are reported in parts per million ($\delta$) downfield from internal tetramethylsilane. Compound 3 was synthesized via $\beta$-methylation of *endo*-tricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one[3] by following a previously reported procedure.[4]

**Selective Epoxidation of 5.**[5] To a mixture of 1-methyl-1,4,4a,8a-tetrahydro-*endo*-1,4-methanonaphthalene-5,8-dione (**5**,[6] 21.53 g, 114.5 mmol) in acetone (300 mL) and 20% aqueous sodium carbonate solution (20 mL) was added 30% aqueous hydrogen peroxide solution (40 mL, excess) dropwise at room temerature. After the addition of hydrogen peroxide had been completed, the reaction mixture was stirred at room temperature for 30 min and then concentrated in vacuo. The residue was dissolved in ether (300 mL), and the ethereal solution was washed repeatedly with water until the washings became neutral to litmus. The ether layer was then washed with brine, dried (anhydrous sodium sulfate), and filtered, and the filtrate was concentrated in vacuo. A colorless solid was thereby obtained. Recrystallization of this material from ethanol afforded **6** (21.2 g, 90.7%) as a colorless microcrystalline solid; mp 104.5–105.0 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.28–1.32 (m, 2 H), 1.5 (s, 3 H), 3.1–3.2 (m, 2 H), 3.5 (s, 2 H), 3.59 (dd, $J_1$ = 3.5 Hz, $J_2$ = 7.25 Hz, 1 H), 5.8–6.0 (m, 2 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 18.0 (q), 42.8 (d), 52.0 (d), 52.2 (s), 53.2 (d), 53.5 (t), 57.5 (d), 57.8 (d), 136.0 (d), 140,8 (d), 203.6 (s), 203.9 (s); IR (KBr) 2970 (m), 1710 (vs), 1690 (vs), 1340 (m), 1295 (s), 1260 (s), 840 (vs), 735 (vs), 640 $cm^{-1}$ (s). Anal. Calcd for $C_{12}H_{12}O_2$: C, 70.58; H, 5.92. Found: C, 70.71; H, 6.05.

**1-Methyl-*exo*-6-carbomethoxytricyclo[5.2.1.$0^{2,6}$]deca-4,8-dien-3-one (4).**[7] A saturated solution of sodium hydroxide in methanol was prepared by dissolving sodium hydroxide (6.25 g) in dry methanol (25 mL); the mixture was allowed to stand at room temperature for 2 days before use. To a warm solution (38 °C) of **5** (5.0 g, 24.5 mmol) in methanol (100 mL) was added saturated methanolic sodium hydroxide solution (2.5 mL). The reaction mixture was stirred at 38 °C for 1 h, at which time thin-layer chromatographic examination of the reaction mixture indicated that starting material **5** was no longer present. The reaction mixture was then concentrated in vacuo, and the residue was diluted with water and extracted with ether (200 mL). The ether layer was washed with water until the washings became neutral to litmus. The ether layer was then washed with brine, dried (anhydrous sodium sulfate), and filtered, and the filtrate was concentrated in vacuo. The crude product was adsorbed onto silica gel and repeatedly extracted with 3% ethyl acetate–hexane mixed solvent. The combined extracts were concentrated in vacuo, and the residue was distilled under reduced pressure. Pure **4** (3.0 g, 58%), bp 67 °C (0.01 mm), was thereby obtained. This material solidified on standing to afford a colorless microcrystalline solid: mp 68 °C; $^1H$ NMR ($CDCl_3$) $\delta$ 1.53 (s, 3 H), 1.72 (d, $J$ = 8.8 Hz, 1 H), 1.89 (d, $J$ = 8.8 Hz, 1 H), 2.95 (s, 1 H), 3.14 (m, 1 H), 3.78 (s, 3 H), 5.7–6.0 (m, 3 H), 7.35 (d, $J$ = 5.7 Hz, 1 H); $^{13}C$ NMR ($CDCl_3$) $\delta$ 17.3 (q), 49.9 (d), 52.4 (d), 54.2 (s), 57.3 (t), 58.0 (q), 66.2 (s), 133.3 (d), 135.7 (d), 138.7 (d), 160.4 (d), 172.9 (s), 207.4 (s); IR (film) 3060 (w), 2960 (m), 1715 (vs), 1680 (vs), 1340 (s), 1285 (s), 1220 (m), 1200 (m), 1185 (m), 1040 (m), 800 $cm^{-1}$ (s).

Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.47. Found: C, 71.57; H, 6.28.

**Alkylation of 4.**[2] To a colorless solution of copper(I) bromide–dimethyl sulfide complex (9.88 g, 48.1 mmol) and dimethyl sulfide (50 mL) in dry ether (50 mL) was added a 1.6 N solution of methyllithium in ether (61 mL, 96 mmol) at 20 °C. To the resulting clear, pale green solution was added a solution of enone **4** (7.68 g, 35.3 mmol) in ether (15 mL) dropwise with stirring during 5 min. The resulting mixture was stirred for 1 h at 20 °C after the addition of **4** had been completed. The reaction mixture was then diluted with ether, and the ether layer was washed repeatedly with saturated aqueous ammonium chloride solution (pH 8) until the washings became colorless. The ether layer was then washed successively with water and with brine, dried (anhydrous sodium sulfate), and filtered, and the filtrate was concentrated in vacuo. The residual pale yellow oil was purified via careful column chromatography (silica gel stationary phase, 2% ethyl acetate–hexane eluent). Two products were thereby obtained: **1** (4.50 g, 54.5%), bp 85 °C (0.02 mm), and **2** (2.5 g, 30%) bp 80 °C (0.02 mm). Proton and $^{13}C$ NMR spectra for **1** and **2** are described in the text.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found for **1**: C, 71.63; H, 7.79. Found for **2**: C, 71.51; H, 7.87.

**2-D NMR Studies on 1–3.** Proton NMR spectra (300 MHz) and $^{13}C$ NMR spectra (75 MHz) were obtained on a Varian XL-300 NMR spectrometer. WALTZ-16 decoupling was employed for all $^{13}C$ NMR spectra and in the appropriate 2-D NMR experiments. All spectra were obtained for solutions in deuteriochloroform with tetramethylsilane as the internal standard. Spectra were obtained for solutions in 5-mm NMR sample tubes in the $^1H$–$^{13}C$ switchable probe. The 90° pulses were determined by standard methods at $^1H$ = 21 $\mu$s, $^{13}C$ = 23.5 $\mu$s, and 83 $\mu$s on the proton decoupler coil.

Homonuclear proton correlation spectra (COSY)[8] and heteronuclear correlation spectra (HETCOR)[9] were run with the standard Varian 5.1-version software. COSY spectra were run

(3) Yamashita, Y.; Mukai, T. *Chem. Lett.* **1984**, 1741.
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(6) Compound **5** was synthesized via Diels–Alder addition of methylcyclopentadiene to *p*-benzoquinone; see: Marchand, A. P.; Suri, S. C.; Earlywine, A. D.; Powell, D. R.; van der Helm, D. *J. Org. Chem.* **1984**, *49*, 670. We thank the Exxon Corporation for the gift of a generous sample of methylcyclopentadiene dimer.
(7) Herz, W.; Iyer, V. S.; Nair, M. G. *J. Org. Chem.* **1975**, *40*, 3519

(8) (a) Bax, A.; Freeman, R.; Morris, G. *J. Magn. Reson.* **1983**, *53*, 313. (b) Marion, D.; Wüthrich, K. *Biochem. Biophys. Res. Commun.* **1983**, *113*, 967.
(9) Bax, A.; Morris, G. *J. Magn. Reson.* **1981**, *42*, 501.

with a 1024 × 1024 data matrix by using either 256 or 512 increments in the first dimension. An initial delay of 1 s was used. These data were processed by "pseudoecho" shaping prior to transformation. HETCOR spectra were acquired with sweep widths dictated by the appearance of the $^{13}C$ and $^{1}H$ spectra by using a 1024 × 512 data matrix and 128 increments in the first dimension. NOE-difference spectra were obtained with the decoupler gated off during acquisition time. A delay of 5 s was set between pulses. Spectra were obtained in an arrayed experiment with the decoupler set 10000 Hz off-resonance and then with the decoupler cycled over the multiplet structure of the desired proton for irradiation; the procedure of Kinns and Saunders[10] was followed in this connection. The two resultant free induction decays (FIDs) were then subtracted and transformed.

**Acknowledgment.** Financial support of our study by the Air Force Office of Scientific Research, Air Force System Command (Grant AFOSR-84-0085, to A.P.M.), the Robert A. Welch Foundation (Grant P-093, to W.B.S., Grant B-963, to A.P.M.), and the North Texas State University Faculty Research Committee (to A.P.M.) is gratefully acknowledged.

**Supplementary Material Available:** The phase-sensitive, double quantum filtered COSY spectrum of **3** and the normal proton NMR spectrum of **3** with the NOE-difference spectra resulting from irradiation of the methyl group and irradiation of H-6 (4 pages). Ordering information is given on any current masthead page.

(10) Kinns, M.; Saunders, J. K. M. *J. Magn. Reson.* **1984**, *56*, 518.

## Isomerization and Thermolysis of Bis(9-borabicyclo[3.3.1]nonane)

Roland Köster and Mohamed Yalpani*

*Max-Planck-Institut für Kohlenforschung, D-4330 Mülheim a.d. Ruhr, FRG*

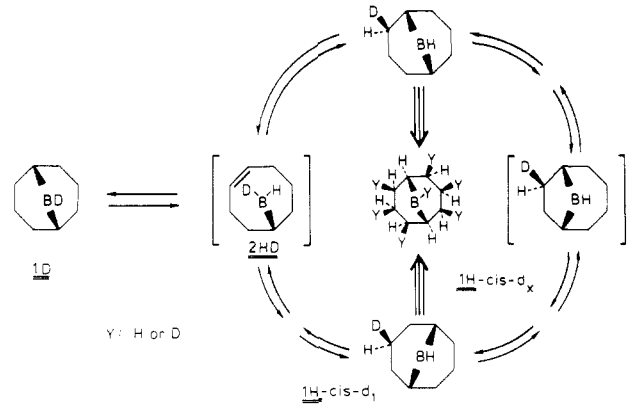
*Received December 13, 1985*

We recently reported that the spontaneous reaction of $Fe(CO)_5$ with bis(9-deuterio-9-borabicyclo[3.3.1]nonane) [(9-D-9-BBN)$_2$, **(1D)$_2$**][1] at temperatures above ≈140 °C leads to the formation of 9-alkyl-9-BBN derivatives **3** having only partially deuterated alkyl residues.[2] In contrast, at ≈100 °C $Co_2(CO)_8$ and **(1D)$_2$** form the 9-alkyl-BBN derivatives with practically only perdeuterated alkyl substituents. The reduced number of deuterium atoms incorporated into the alkyl groups of the 9-alkyl-BBN's in the course of the reductive carbon monoxide oligomerizations at ≳140 °C was said to be the result of the fast reversible dehydroboration-deuteroborations of **(1D)$_2$**.[2]

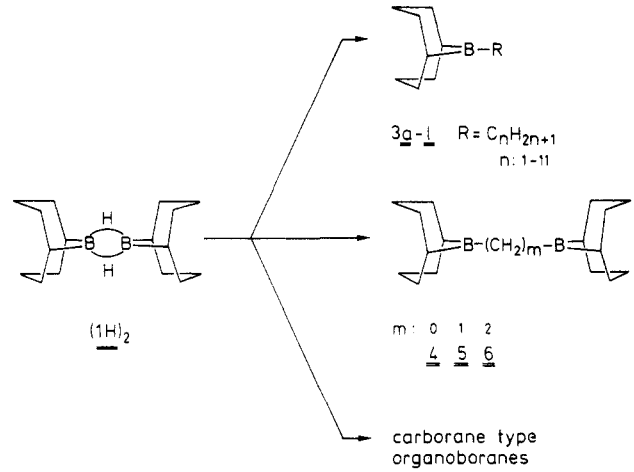
### Results and Discussion

We have now found, that **(1D)$_2$** reacts regio- and stereospecifically both in solution (>140 °C, 1 h) and in the molten state (≈160 °C, 5 min.). Reversible >BD/>CH and >BH/>CD at the $C_8$ ring gives mixtures of **(1H-$d_x$)$_2$** and **(1D-$d_{x-1}$)$_2$**, which on protolysis of the >BH and >BD functions gives a gas consisting of 85.8% of $H_2$ and to 14.2% of HD. This HD/$H_2$ ratio remains unchanged on prolonged heating of the solutions (>5 h) or of the melt (≈0.5 h). Therefore it can be concluded that only 6 of the 14 ring H atoms of the $C_8$ ring are exchangeable.

**Scheme I. Thermal Isomerization of 9-Deuterio-9-borabicyclo[3.3.1]nonane (1D)**




**Scheme II. Thermolysis of Bis(9-borabicyclo[3.3.1]nonane) (1H)$_2$**




**(1H-$d_x$)$_2$** or **(1D-$d_{x-1}$)$_2$** with one to three D atoms per monomer molecule ($x$ = 1–3) are formed if **(1D)$_2$** is held for a short time in the molten state. Repetitions of the melting procedure, preceded by a >BH/>BD exchange with an appropriate deuterium-donating reagent [e.g., alkyldeuterodiborane(6)], lead to the sixfold deuteration of both eight-membered rings in **(1D)$_2$** (mass spectra). The $^{13}C$ NMR spectra reveal that each of the methylene carbons (C atoms 2–4 and 6–8) are exclusively monodeuterated. A topotactical walk mechanism of the boron atom around the $C_8$ ring (cf. Scheme I) ensures the stereoselective formation of the all-cis configuration (*cis*-**1D-$d_6$**)$_2$. The formation of monomeric **1H-$d_x$** or **1D-$d_{x-1}$** ($x$ > 1) with more than one deuterium atom after only a very short time in the molten state shows that intermolecular deuterium transfer between the two 9-BBN parts by way of the diborane(6) bridged species **(2HD)$_2$** or **2HD–1D** is also involved (cf. Scheme I).

The facile transformation of **(1D)$_2$** to (*cis*-**1D-$d_6$**)$_2$ enables the preparation of defined cis deuterated cyclooctane derivatives by way of known oxidative transformations to *cis*-cyclooctane-1,5-diol-*2,3,4,6,7,8-$d_6$*.

Furthermore, in contrast to some reports in the literature,[3] the thermal stability of **(1H)$_2$** and **(1D)$_2$** has been

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