The Formation of Ethers from Borneol and Isoborneol in the Presence of Boron Trifluoride Etherate

Kimiko NAGAI, Mitsuru NAKAYAMA, Akihiko MATSUO, Shizuko EGUCHI, and Shûichi HAYASHI

Department of Chemistry, Faculty of Science, Hiroshima University, Higashisenda-machi, Hiroshima 730

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dl-Borneol and *dl*-isoborneol, when separately submitted to the action of boron trifluoride etherate at room temperature, gave different ethers; the one from borneol was characterized as bornyl isobornyl ether, and the other from isoborneol, as diisobornyl ether. The ethers were also obtained from borneol and isoborneol in the reaction with zinc chloride. When *d*-borneol was used, an optically-active bornyl isobornyl ether was obtained.

In connection with a previous communication on the formation of cyclodiethers from 6-methyl-5-hepten-2-ol and citronellol,[1] the action of boron trifluoride etherate on borneol and isoborneol was examined in the present work; two kinds of ethers were obtained, whose structures were characterized as bornyl isobornyl and diisobornyl ethers.

Long years ago Ikeda obtained a condensation product in the reaction of borneol with zinc chloride; he described it as dibornyl ether. However, he did not attempt the reaction of isoborneol with zinc chloride, for this alcohol was more sensitive than borneol. Besides, in his work the structural characterization was not thoroughgoing enough; indeed, no consideration has yet been made[2] of the formation mechanism. In the present work, then, the reactions of borneol and isoborneol with zinc chloride were reexamined, and the reaction of borneol with camphene was examined in the presence of boron trifluoride etherate.

Results and Discussion

Reactions of dl-*Borneol and* dl-*Isoborneol with Boron Trifluoride Etherate.* *dl*-Borneol (I) and *dl*-isoborneol (II) were separately submitted to the action of boron trifluoride etherate under such conditions as are shown in Table 1. The reaction mixtures were subjected to fractional distillation followed by elution chromatography to separate individual components, which were characterized as tricyclene (III), camphene (IV), and C_{20}-hydrocarbons, together with the following two ethers.

dl-*Bornyl Isobornyl Ether (V)*: In the reaction of *dl*-borneol with boron trifluoride etherate (Experiment 3), the compound was isolated as feather-like crystals (mp 42.5—43.5 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$)) in a 14% yield. The molecular formula of this compound was determined to be $C_{20}H_{34}O$ from the molecular ion, *m/e* 290, and the molecular weight, 288, as taken by the Rast method. The IR spectrum showed characteristic ether bands at 1117, 1087, and 1078 cm^{-1}, while the NMR spectrum revealed the presence of two oxygen-carrying methine groups on the proton signals at δ 3.18 (1H, t) and 3.50 (1H, dq), but there was no indication of the presence of unsaturated bonds; the mass spectrum with characteristic ions at *m/e* 153 (8%, $C_{10}H_{17}O$), 152 (23, $C_{10}H_{16}O$), and 137 (base, $C_{10}H_{17}$) were reasonably explained as that of a di-monoterpene ether. Accordingly, the compound may be thought to be an ether consisting of two saturated bicyclic monoterpenes.

Together with the above signals, the NMR spectrum taken in a $CDCl_3$ solution showed methyl signals at δ 0.80, 0.90, 1.01 (each 3H, s) and 0.85 (9H, s). Among these, the first three were close to the separating methyl signals in the NMR spectrum of isoborneol (δ 0.81, 0.91 and 1.02; each 3H, s), while the last agreed with a combined methyl signal seen in the spectrum of borneol (δ 0.85, 9H, s). Regarding the NMR spectrum taken in a C_5D_5N solution, also, the methyl signals (δ 0.85, 9H, s; 0.95, 0.98, 1.09, each 3H, s) could be connected with those of borneol (δ 0.87, 6H, s; 0.98, 3H, s) and isoborneol (δ 0.85, 1.07, 1.28, each 3H, s), although the methyl signals to be assigned to the isobornyl moiety of the ether showed field shifts slightly higher than those of free isoborneol. These facts indicate that the compound is bornyl isobornyl ether.

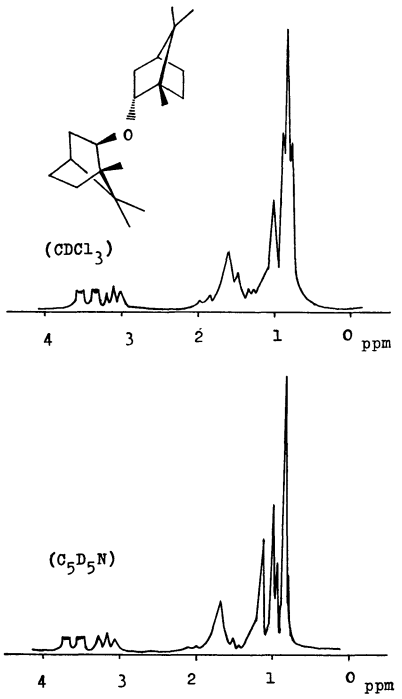


Fig. 1. NMR spectra of bornyl isobornyl ether (V).

This characterization of the ether was further supported by the signal patterns of the oxygen-carrying methine groups: according to Flautt[3] and Tori,[4] who have investigated in detail the NMR spectra of 2-substituted bornane derivatives, the α-methine proton of

the *endo*-substituted isomer (proton *exo*) appears as a quartet of two characteristic spacings split by a much smaller spacing, whereas that of the *exo*-substituted isomer (proton *endo*) appears as a triplet or a near triplet without any additional splitting; this difference gives a good test for the identification of the *exo* and *endo* isomers. The NMR spectrum taken in $CDCl_3$ showed two signals attributable to α-methine protons. That is, the one appeared as a quartet (δ 3.50) with a small splitting, and the other, as a triplet (δ 3.18). When the NMR spectrum taken in a C_5D_5N solution was compared with that in $CDCl_3$, both the α-methine signals were retained with nearly the same patterns, although the chemical shifts showed a slight down-field shift.

Thus, it is certain that the compound is optically-inactive bornyl isobornyl ether.

dl-*Diisobornyl Ether (VI)*: The compound was obtained as feather-like crystals (mp 87—88 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$)) in a 21% yield by the reaction of *dl*-isoborneol with boron trifluoride etherate at room temperature (Experiment 10). The molecular formula, $C_{20}H_{34}O$, was the same as that of bornyl isobornyl ether (V) discussed above, and the IR and mass spectra of the two compounds were nearly superimposable upon each other. In addition, the NMR spectrum was constituted of methyl, methylene, and α-methine signals with the same relative intensity as that of the above bornyl isobornyl ether, although these proton signals differed fairly much in pattern. Accordingly, this evidence seems to indicate that the compound is a stereo-isomer of bornyl isobornyl ether (V).

The proton signals of the two α-methine groups were overlapped as a triplet centering at δ 3.18 in a $CDCl_3$ solution, and as a near triplet centering at δ 3.20 in a C_5D_5N solution. Besides, the chemical shifts of the α-methine signals were in agreement with those in $CDCl_3$ and C_5D_5N solutions respectively of the α-methine proton belonging to the isobornyl moiety of bornyl isobornyl ether (V). Such proton signals of the α-methine group indicate that the ether-linkage of this compound is in the *exo-exo* conformation. Thus, the ether was characterized as diisobornyl ether (VI).

The methyl signals in $CDCl_3$ and C_5D_5N solutions of the ether were also reasonably connected with those of diisobornyl ether in comparison with the methyl signals of isoborneol[4] and the isobornyl moiety of bornyl isobornyl ether; besides, according to Tori's assignments for isoborneol, the methyl signals of δ 0.85 (6H, s, $C_{(9)}$ and $C_{(9')}$) and 1.02 (6H, s, $C_{(8)}$ and $C_{(8')}$) in $CDCl_3$ and of δ 0.81 (6H, s, $C_{(9)}$ and $C_{(9')}$) and 1.09 (6H, s, $C_{(8)}$ and $C_{(8')}$) in C_5D_5N were assigned to the two gem-dimethyls, and the methyl signals of δ 0.90 and 0.95 (each 3H, s) in $CDCl_3$ and of δ 0.91 and 0.95 (each 3H, s) in C_5D_5N, to $C_{(10)}$- and $C_{(10')}$-methyls.

Reactions of Borneol and Isoborneol with Zinc Chloride. When the structural elucidation was carried out on the products of the reaction with boron trifluoride etherate, we were especially interested in a *d*-dibornyl ether which had been obtained by Ikeda in the reaction of *d*-borneol with zinc chloride,[2] for its melting point agreed with that of our bornyl isobornyl ether and dibornyl ether was not obtained in our experiment.

The reaction of *dl*-borneol with zinc chloride was thus traced, and feather-like crystals whose melting point agreed with that reported by Ikeda were obtained. This compound, however, was identical with our *dl*-bornyl isobornyl ether in the IR, NMR, and mass spectra and in a gas-chromatographic comparison. Therefore, it was confirmed that Ikeda's ether was not dibornyl ether, but bornyl isobornyl ether.

Ikeda did not examine the reaction of isoborneol with zinc chloride. We tried this reaction under similar conditions and obtained diisobornyl ether. Thus, zinc chloride also acts similarly on borneol and isoborneol as boron trifluoride etherate.

Formation Mechanism of Bornyl Isobornyl and Diisobornyl Ethers. As has been mentioned above, camphene and tricyclene were detected in the monoterpene fraction of each reaction product in the reaction of borneol and isoborneol with boron trifluoride etherate. These compounds are thought to be produced *via* a non-

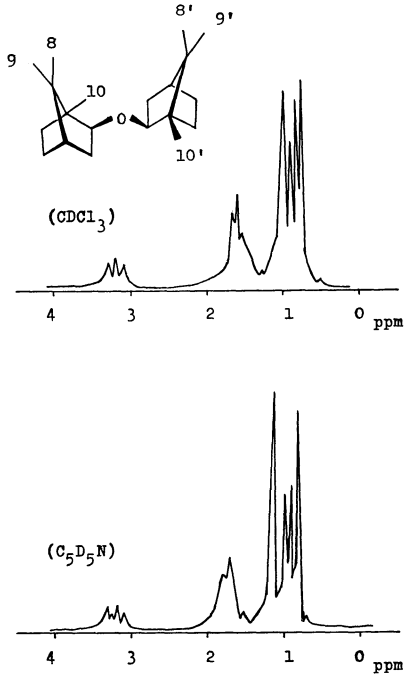
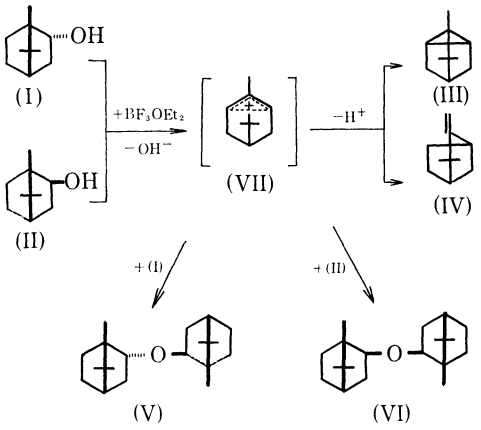


Fig. 2. NMR spectra of diisobornyl ether (VI).



Scheme 1.

classical carbonium ion (VII): a molecule of borneol or isoborneol undergoes the elimination of the hydroxyl group, followed by deprotonation, to give camphene or tricyclene.

The formation of the bornyl isobornyl and diisobornyl ethers mentioned above may be explained in terms of the nucleophilic attack of each molecule of borneol and isoborneol on the common carbonium ion (VII), in which the alcohol molecule approaches stereospecifically from the *exo*-side because of the steric hindrance and the asymmetric influence of the molecule. By the formation mechanism, the following experimental results can also be explained. When the *d*-borneol was submitted to the action of boron trifluoride etherate, we obtained optically-active bornyl isobornyl ether, $[\alpha]_D^{20}$ +53.8° ($CHCl_3$). Next, the reaction of *dl*-borneol or *d*-borneol with *d*-camphene was attempted in the presence of boron trifluoride etherate, because it has been established that camphene produces the carbonium ion in the acid-catalyzed reaction; from the reaction of *dl*-borneol and *d*-camphene, *dl*-bornyl isobornyl ether was obtained, while from that of *d*-borneol with *d*-camphene, we obtained optically-active bornyl isobornyl ether, $[\alpha]_D^{20}$ +54.6° ($CHCl_3$), whose specific rotation was equal to that of the above optically-active ether obtained in the reaction of *d*-borneol itself.

Experimental

Apparatus. For the analyses and preparative glc of monoterpenic hydrocarbons, a Shimadzu glc-apparatus was used: column temperature, 100 °C; stainless-steel separating column (3 m×3 mm) packed with Carbowax 6000 (30%) on Celite 545 (60—80 mesh); flow rate of the helium carrier, 60 ml/min. The mass spectra were taken on a Hitachi RMS-4 spectrometer at an ionization voltage of 80 eV, an ion-accelerating voltage of 1800 eV, and an ionization chamber temperature of 150 °C, or on a Hitachi-7L high-resolution spectrometer under the same conditions.

Materials. Commercial *dl*- and *d*-borneol and *dl*-isoborneol[5] were purified through repeated recrystallizations from benzene. They each showed one peak in glc; *dl*-Borneol mp 210 °C, $[\alpha]_D^{25}$ ±0° ($CHCl_3$); *d*-borneol: mp 205—206 °C, $[\alpha]_D^{22}$ +21.4° ($CHCl_3$). *dl*-Isoborneol: mp 212.0—212.3 °C, $[\alpha]_D^{25}$ ±0° ($CHCl_3$).

Commercial *d*-camphene was purified: mp 48.5—49.5 °C, $[\alpha]_D^{20}$ +5.3° ($CHCl_3$).

The chemical grade of boron trifluoride etherate (BF_3 47%) was used without any purification.

The zinc chloride was freshly dehydrated by fusion just before the experiment.

Reactions of Borneol and Isoborneol with Boron Trifluoride Etherate. To *dl*-borneol or *dl*-isoborneol, boron trifluoride etherate was added, drop by drop, in ether or with no solvent, as is shown in Table 1; the mixtures were then allowed to stand for a period from 7 min to 10 day at temperatures from 25 °C to 80 °C. The reaction mixtures were washed with a saturated aqueous solution of sodium carbonate and then with water, dried over anhydrous sodium sulfate, and fractionated under reduced pressure into a lower-boiling (bp 30—100 °C/4 mmHg) fraction, a higher-boiling (bp 100—150 °C/4 mmHg) fraction, and a residue.

Characterization of Monoterpene Compounds. The lower-boiling fractions from Experiments (1)—(5) and (7)—(10) showed two components except for the reactant in tlc using silica gel and hexane (R_f 0.91 and 0.78) and in glc (T_R 11.7 and 16.8). The components were isolated by means of preparative glc.

Tricyclene: The compound showing one peak with T_R 11.7 in glc and one spot with R_f 0.91 in tlc was isolated as colorless and pleasant odor crystals; mp 67.3—67.9 °C. The IR,[6] mass[7] spectra and gas chromatographic behavior coincided with those of tricyclene.

dl-*Camphene*: The compound showing one peak with T_R 16.8 in glc and one spot with R_f 0.78 on tlc was isolated as colorless and camphor-like-smelling crystals; mp 51.0—51.5 °C (lit,[8] 49—51 °C), $[\alpha]_D^{20}$ ±0° ($CHCl_3$). The IR[6] and mass spectra[7,9] with those of camphene, and the compound was gas-chromatographically identical with the authentic specimen.

Characterization of Dimerized Compounds. The higher-boiling fractions of the reaction products from borneol showed one or two components with T_R 10.9 and 18.8 on glc with the SE-30 column, while those from isoborneol showed such components with T_R 10.5 and 18.1. These components were isolated through elution chromatography with silica gel–benzene and then characterized.

C_{20}-*Hydrocarbon from* dl-*Borneol*: A colorless, viscous oil showing one peak with T_R 10.9 was isolated from the reaction mixture of *dl*-borneol. From the molecular ion (*m/e* 272) and the molecular weight (275) taken by the Rast method, the molecular formula of this compound was determined as $C_{20}H_{32}$. Although the mass spectrum showed abundant ions at *m/e*

Table 1. Reactions of borneol and isoborneol with boron trifluoride etherate

	Borneol[a]						Isoborneol[a]				
No. of experiment	1	2	3	4	5	6	7	8	9	10	11
BF_3OEt_2 (ml)	5.0	5.0	5.0	5.0	5.0	5.0	2.5	5.0	2.5	5.0	5.0
Et_2O (ml)	10	—	—	—	—	—	10	10	10	—	—
Reaction temp. (°C)	30	30	25	60	80	80	30	30	60	20	30
Reaction period (hr)	24	24	240	1	0.12	1	168	24	1	7	24
Unreacted alcohol (%)[b]	98.7	98.5	85.0	98.1	8.0	—	34.0	30.0	26.0	1.0	—
Tricyclene (%)	0.1	trace	—	0.1	6.0	—	8.0	6.0	2.0	1.0	—
Camphene (%)	1.2	1.5	1.0	1.8	21.0	—	58.0	64.0	72.0	19.0	—
$C_{20}H_{32}$ (%)	—	—	—	—	65.0	65.0	—	—	—	58.0	72.0
Bornyl isobornyl ether (%)	—	—	14.0	—	—	—	—	—	—	—	—
Diisobornyl ether (%)	—	—	—	—	—	—	—	—	—	21.0	—
Residue (%)	—	—	—	—	—	35.0	—	—	—	—	28.0

a) Five grams of the alcohol were used in each experiment. b) Relative amounts of reaction products were determined with the aid of gas chromatography.

257 (M^+-15, 4%), 229 (M^+-43, 10), 109 (31), 95 (base), 81 (57), and 41 (56), no further structural information was obtained from any of the mass, IR, or NMR spectra.

C_{20}-Hydrocarbon from dl-*Isoborneol*: The compound (T_R 10.5) was isolated from the reaction mixture of *dl*-isoborneol as a colorless, viscous oil. The hydrocarbon was determined to have the same molecular formula, $C_{20}H_{32}$, as that from the reaction mixture of borneol, and it had the same molecular ion (*m/e* 272) and the same molecular weight (270, Rast method), but a difference was observed between the IR and NMR spectra of the two hydrocarbons. The mass spectrum showed abundant ions at *m/e* 257 (M^+-15, 12%), 229 (M^+-43, 23), 162 (M^+-110, base), 147 (42), 109 (55), and 95 (66).

dl-*Bornyl Isobornyl Ether from* dl-*Borneol*: Colorless feather-like crystals, mp 42.5—43.5 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$), showing a peak with T_R 18.8 was obtained in a yield of 14% from a reaction mixture of *dl*-borneol. Found: C, 82.94; H, 11.92%. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80%. The mass spectrum showed ions at *m/e* 290 (M^+, 4%), 272 (M^+-18, 10), 153 ($C_{10}H_{17}O$, 8), 152 ($C_{10}H_{16}O$, 13), 137 ($C_{10}H_{17}$, base), 95 (C_7H_{11}, 29), 81 (C_6H_9, 90), 69 (27), 67 (30), 55 (28), and 41 (42).

d-*Bornyl Isobornyl Ether from* d-*Borneol*: *d*-Borneol was subjected to a reaction with boron trifluoride etherate under the same conditions as in Experiment (3) to give *d*-bornyl isobornyl ether as colorless feather-like crystals; mp 42.0—42.8 °C, $[\alpha]_D^{20}$ +53.8° ($CHCl_3$). The IR, NMR, and mass spectra were in good agreement with those of *dl*-bornyl isobornyl ether, and the compound was confirmed to be identical with the *dl*-ether in gas chromatography.

dl-*Diisobornyl Ether from* dl-*Isoborneol*: A crystalline portion of the reaction mixture from isoborneol was dried on a porous plate to separate colorless feather-like crystals in a yield of 21%, mp 87—88 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$). Found: C, 82.93; H, 11.91%. Calcd for $C_{20}H_{34}O$: C, 82.69; H, 11.80%. The IR and mass spectra were nearly superimposable on those of *dl*-bornyl isobornyl ether, but the NMR spectra were different between the two ethers.

Reactions of Borneol and Isoborneol with Zinc Chloride. dl-*Bornyl Isobornyl Ether*: *dl*-Borneol was submitted to a reaction with zinc chloride under conditions similar to those in Ikeda's report,[2] that is, 5 g of borneol were mixed with 2.5 g of zinc chloride in dried benzene (4 ml), and the mixture was boiled for 3 hr. The reaction mixture was then washed with 2M hydrochloric acid and water, dried over anhydrous sodium sulfate, and then chromatographed over a silica-gel column with a mixed solvent of hexane and ethyl acetate (95: 5) to isolate colorless crystals in a 25% yield; mp 42.5—53.0 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$). The IR, NMR, and mass spectra were superimposable on those of the *dl*-bornyl isobornyl ether obtained from the reaction of *dl*-borneol with boron trifluoride etherate, and their mixed-melting-point determination showed no depression.

d-*Bornyl Isobornyl Ether*: *d*-Borneol was also subjected to the reaction; we thus obtained *d*-bornyl isobornyl ether, which was identified by comparison with *d*-bornyl isobornyl ether obtained in the reaction of *d*-borneol with boron trifluoride etherate.

dl-*Diisobornyl Ether*: *dl*-Isoborneol was mixed with zinc chloride in dried benzene in the same ratio as in the case of borneol, and the mixture was then boiled for 50 min. Colorless crystals were obtained in a 16% yield; mp 87—88 °C, $[\alpha]_D^{20}$ ±0° ($CHCl_3$). This compound was identical in melting point and in the IR and NMR spectra with the *dl*-diisobornyl ether obtained from *dl*-isoborneol in the presence of boron trifluoride etherate.

Reaction of Borneol with Camphene in the Presence of Boron Trifluoride Etherate. dl-*Bornyl Isobornyl Ether*: To a mixed solution of *dl*-borneol (5 g) and *d*-camphene (5 g) in dried ether (20 ml), boron trifluoride etherate (2.5 ml) was added, drop by drop; the mixture was then allowed to stand at room temperature for 24 hr. The reaction mixture was treated with the usual procedure to give colorless crystals in a 30% yield; mp 42.5—43.5 °C; $[\alpha]_D^{20}$ ±0° ($CHCl_3$). This compound was identical with the ether drived by the above-described method.

d-*Bornyl Isobornyl Ether*: A mixed solution of *d*-borneol and *d*-camphene was treated with boron trifluoride etherate as has been described above; a colorless crystalline product was thus obtained; mp 42.0—42.8 °C, $[\alpha]_D^{20}$ +54.6° ($CHCl_3$). This compound was identical with the ether obtained in the reaction of *d*-borneol with boron trifluoride etherate.

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