Useful Synthetic Routes to Pure *exo*-5-Vinyl-2-norbornene and *endo*-5-Vinyl-2-norbornene

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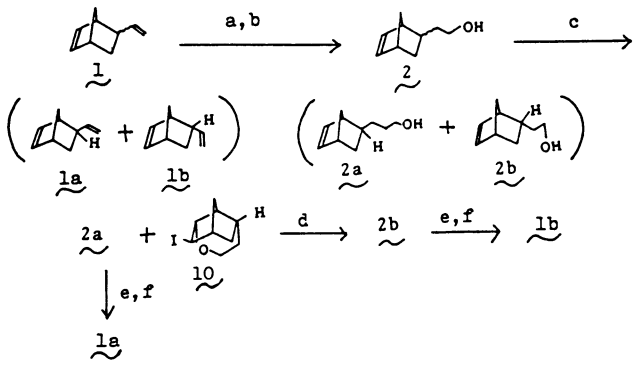
Synopsis. Hydroboration of 5-vinyl-2-norbornene (**1**) with 9-BBN mainly affords 5-(2-hydroxyethyl)-2-norbornene (**2**). The iodo ether cyclization of **2** can convert only *endo*-5-(2-hydroxyethyl)-2-norbornene (**2b**) to iodo ether **10**, followed by reductive elimination and subsequent dehydration to furnish *endo*-5-vinyl-2-norbornene (**1b**) which has not been isolated in pure form. Meanwhile, unreacted *exo*-5-(2-hydroxyethyl)-2-norbornene (**2a**) produces *exo*-5-vinyl-2-norbornene (**1a**) via dehydration.

5-Vinyl-2-norbornene (**1**), the principal product from the Diels–Alder reaction between cyclopentadiene and butadiene consists of *exo*-5-vinyl-2-norbornene (**1a**) and *endo*-5-vinyl-2-norbornene (**1b**).[1] Although a successful separation of these two isomers was accomplished by preparative gas chromatography,[1] the procedure encounters the difficulty in obtaining the isomers in pure form and in large quantities. As an alternative approach to the isolation of **1a**, of considerable utility is the thermal isomerization[2] in which **1b** was transformed into 4,7,3a,7a-tetrahydro-1*H*-indene whereas **1a** remained unchanged, allowing it to be isolated. It is difficult, however, to prevent the **1a** thus obtained from being contaminated by unreacted **1b**. Except these processes above mentioned, to the best of our knowledge no one appears to have reported on the stereoselective synthesis or isolation of **1a** and **1b**.

We now wish to report herein a convenient method for the isolation of **1a** and **1b** as well as the investigation of their chemical behavior.

Results and Discussion

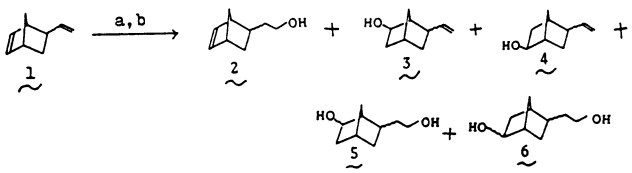
One of the most facile methods to separate **1a** and **1b** from **1**, the mixture of **1a** and **1b**, is outlined in Scheme 1.



Scheme 1.

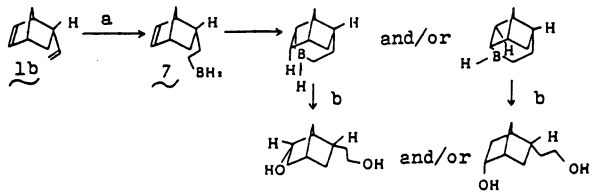
Reagents: a, 9-BBN, THF; b, H_2O_2, NaOH; c, I_2, KI, $NaHCO_3$, dioxane, H_2O; d, Zn, CH_3CO_2H; e TsCl, pyridine; f, pyridine, 100 °C.

Hydroboration of **1** with 9-borabicyclo[3.3.1]nonane (9-BBN), followed by oxidation with alkaline hydrogen peroxide, resulted in the formation of **2** in 70.7% yield, together with a 5.8% yield of a mixture of 6-vinyl-2-norbornanol (**3**) and 5-vinyl-2-norbornanol (**4**) and a 4.3% yield of a mixture of 6-(2-hydroxyethyl)-2-norbornanol (**5**) and 5-(2-hydroxyethyl)-2-norbornanol (**6**).



Reagents: a, 9-BBN, THF; b, H_2O_2, NaOH

Although this reaction could be achieved using B_2H_6 in THF, the selectivity of the hydroboration toward the vinyl group was decreased, resulting in the product ratio of **2**, the mixture of **3** and **4**, and the mixture of **5** and **6** being ca. 29:6:11. In this case, it was expected that the endo-isomer **7** of the initially formed [2-(5-norbornen-2-yl)ethyl]borane might undergo an intramolecular hydroboration[3] to give no *endo*-2-hydroxyethyl isomer **2b** as illustrated below, but in fact, evidence that this is not the case was presented by the experimental results on the formation of the iodo ether **10** from **2**, which will be described later.

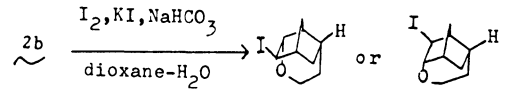


Reagents: a, B_2H_6, THF; b, H_2O_2, NaOH.

Further purification of **2** can be accomplished by utilizing the readily isolable intermediates, 2-(5-norbornen-2-yl)ethyl 3,5-dinitrobenzoate (**8**) and 2-(5-norbornen-2-yl)ethyl tetrahydro-2-pyranyl ether (**9**), which are, in turn, converted to **2**.

Turning here to Scheme 1, treatment of a solution of **2** in dioxane with iodine and KI in 0.5 M $NaHCO_3$ solution (1 M=1 mol dm^{-3}) led to the iodo ether cyclization of **2b** to form the iodo ether **10** in 42.1% yield, while **2a** remained unreacted. Separation of both products was readily achieved by a fractional distillation or recrystallization.

In considering possible modes of the iodo ether cyclization, examination of molecular models suggested that the seven-membered ring cyclization should be prohibited on steric grounds.[4]



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An attempt to follow the Kropp's procedure[5] where **2** was treated with I_2 and $N(C_2H_5)_3$ in methanol at a reflux temperature for 2 d failed to complete the iodo ether cyclization, providing 18% yield (based on **2b**) of **10** along with the unreacted starting material **2a** containing **2b**.

It was now ready to convert the iodo ether **10** to **2b** via a reductive elimination. Treatment of **10** with zinc in acetic acid furnished **2b** in 75.7% yield. Although the procedure for this reaction is similar to that applied to the reductive elimination of the iodo lactone[6] and the β-halo ether,[7] the observation that the β-halo ether compound in this system could be successfully effected by this treatment is noteworthy.

With these two stereoisomers **2a** and **2b** available, the dehydration step was now examined utilizing the conventional manners.[8] Both alcohols were converted individually to **1a** and **1b** in 26.8 and 28.3% yield, respectively, by treatment with tosyl chloride in pyridine, followed by elimination with pyridine at 100 °C. These two stereoisomers **1a** and **1b** thus obtained have a refractive index of n_D^{20} 1.4791 (lit,[2a] n_D^{20} 1.4794) and n_D^{20} 1.4806, respectively.

Experimental

Melting and boiling points are uncorrected. GC analysis was carried out on a Hitachi Model 163 gas chromatograph fitted with a FID detector, using a 5 mm×2 m stainless-steel column packed with 10% Silicone-30 on Chromosorb W. ^{1}H NMR spectra were recorded with a Hitachi Model R-24B, using $Si(CH_3)_4$ as an internal reference. IR spectra were obtained with a Hitachi Model 160-10 infrared spectrophotometer. Elemental analysis was performed by the Laboratory for Organic Elemental Microanalysis, Faculty of Pharmaceutical Science, Kyoto University.

Materials. 5-Vinyl-2-norbornene, obtained from Nippon Petrochemical Corp., was vacuum distilled before use. The 5-vinyl-2-norbornene employed, on the basis of ^{1}H NMR spectroscopy, consisted of *exo*- and *endo*-5-vinyl-2-norbornene in a ratio 2:3.[1]

5-(2-Hydroxyethyl)-2-norbornene (2). Method A. To a stirred solution of 5-vinyl-2-norbornene (**1**, 24.0 g, 0.200 mol) in dry THF (20 mL) at ambient temperature under a nitrogen stream was added dropwise 9-BBN (0.50 M THF solution, 400 mL) over about 1 h. The mixture was stirred at 25 °C for 2 h, and to this mixture was added dropwise water (5 mL), aq NaOH (3 M, 67 mL), then 30% aq H_2O_2 (67 mL). After being stirred at 40 °C for 2 h, the mixture was extracted three times with ether (150 mL). The ether layer was dried over $MgSO_4$ and concentrated in vacuo. The residue was distilled under reduced pressure to give a mixture of **3** and **4** (1.6 g, 5.8%) as the first fraction [64 °C/0.5 mmHg (1 mmHg=133.322 Pa) (lit,[9] 60—61 °C/0.35 mmHg)], **2** (19.5 g, 70.7%) as the second fraction (70 °C/0.5 mmHg), and then a mixture of **5** and **6** (1.3 g, 4.2%) as the third fraction (130—135 °C/1.5 mmHg). The spectroscopic data of the second and third fractions were as follows:

Alcohol **2**: IR (neat film) cm^{-1} 3350, 3080, 2930, 2870, 1640; ^{1}H NMR ($CDCl_3$) δ=6.20—5.80 (m, 2H), 3.60 (t, 2H), 2.80 (m, 2H), 2.40 (s, 1H), 2.60—1.10 (m, 7H). Found: C, 78.31; H, 10.19; O, 11.50%. Calcd for $C_9H_{14}O$: C, 78.26; H, 10.14; O, 11.60%.

A Mixture of **5** and **6**: IR (neat film) cm^{-1} 3345, 2935, 2870, 1100; ^{1}H NMR ($CDCl_3$) δ=4.75—4.50 (s, 1H), 4.35—3.75 (m, 1H), 3.60—3.20 (m, 1H), 2.45—0.80 (m, 13H). Found: C, 69.18; H, 10.35; O, 20.47%. Calcd for $C_9H_{16}O_2$: C, 69.23; H, 10.26; O, 20.51%.

Method B. To an ice-cooled, stirred solution of **1** (48.0 g, 0.400 mol) in dry THF (250 mL) was added $NaBH_4$ (4.2 g, 0.110 mol) and then added dropwise $BF_3 \cdot O(C_2H_5)_2$ (18.1 mL, 20.8 g, 0.147 mol). After being stirred at room temperature for 3 h, the reaction was quenched by adding water (32.5 mL), and then to the mixture was added aq NaOH (3 M, 44.0 mL) and 30% aq H_2O_2 (44.0 mL). After being allowed to stir at 40 °C for an additional 3 h, the reaction mixture was cooled to room temperature and then extracted three times with ether (200 mL). The organic extracts were washed with water and dried over $MgSO_4$. After removal of the solvent, the residue was distilled under reduced pressure to give a mixture of **3** and **4** (3.2 g, 5.8%), **2** (15.9 g, 28.8%), and a mixture of **5** and **6** (6.8 g, 10.9%).

Purification of 2. Via 3,5-Dinitrobenzoate 8. To an ice-cooled solution of **2** (5.0 g, 0.036 mol) in pyridine (20 mL) was added 3,5-dinitrobenzoyl chloride (7.5 g, 0.033 mol) with stirring. The reaction mixture was heated over a steam bath for 5 min and poured, with vigorous stirring, into water (50 mL). The precipitate was collected, washed with 5% aq Na_2CO_3 (25 mL), and recrystallized from a mixture of ethanol and water to give **8** (8.6 g, 78.5%): mp 68—69 °C; IR (nujol) cm^{-1} 3090, 2930, 2875, 1720, 1665, 1200; ^{1}H NMR ($CDCl_3$) δ=9.20 (s, 3H), 6.35—5.90 (m, 2H), 4.70—4.35 (t, 2H), 2.85 (broad s, 2H), 2.45—1.25 (m, 7H). Found: C, 57.92; H, 4.82; N, 8.32; O, 28.94%. Calcd for $C_{16}H_{16}O_6N_2$: C, 57.83; H, 4.85; N, 8.43; O, 28.89%.

The ester **8** (5.0 g, 0.015 mol) was added to a mixture of methanol (10 mL) and 20% aq NaOH (3.5 mL), and the mixture was refluxed for 1 h. After removal of methanol, the residue was extracted with ether–benzene (100 mL). The extract was washed with water, dried over $MgSO_4$, and concentrated in vacuo, and subsequent distillation afforded **2** (1.8 g, 87.0%) whose purity was determined to be more than 99.9% by GC analysis.

Via Tetrahydro-2-pyranyl Ether 9. A solution of **2** (10.0 g, 0.072 mol), 3,4-dihydro-2*H*-pyran (4.8 g, 0.057 mol), and *p*-toluenesulfonic acid (0.5 g) in ether (100 mL) was stirred at room temperature for 3 h and treated with 10% aq Na_2CO_3 (10 mL). The ethereal layer was washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residue was distilled (102—104 °C/2.0 mmHg) to yield **9** (8.5 g, 67.2%): IR (neat film) cm^{-1} 3050, 2930, 2870, 1660; ^{1}H NMR (CCl_4) δ=6.25—5.80 (m, 2H), 3.95—3.85 (t, 1H), 3.60—3.45 (m, 4H), 2.60—1.10 (m, 15H). Found: C, 75.48; H, 9.88; O, 14.64%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97; O, 14.40%.

A solution of the ether **9** (6.0 g, 0.027 mol), methanol (10 mL), and 2% aq HCl (3 mL) was refluxed for 3 h, and then this solution was treated with 5% aq $NaHCO_3$ (10 mL). After removal of methanol, the residual oil was extracted three times with ether–benzene (50 mL). The extracts were washed with water, dried over $MgSO_4$, and concentrated in vacuo. Distillation yielded **2** of more than 99.5% purity (2.8 g, 75.1%).

***exo*-7-Iodooctahydro-4,6-methanocyclopenta[*b*]pyran (10).** To a solution of **2** (16.2 g, 0.117 mol) in dioxane (30 mL), with stirring at room temperature, was added aq $NaHCO_3$ (0.5 M, 720 mL) and an aqueous solution (360 mL) of iodine (70.0 g, 0.276 mol) and potassium iodide (120.0 g, 0.723 mol). After being stirred at room temperature for 1 h, the mixture was extracted three times with ether–benzene (200 mL). The extracts were washed with sat. aq Na_2SO_3, water, and dried over $MgSO_4$. After removal of the solvent, the residue was distilled under reduced pressure to yield **2a** (4.4 g, 27.3%) as the first fraction (66 °C/0.2 mmHg) and then **10** (13.0 g, 42.1%) as the second fraction (100—103 °C/1.0 mmHg). The ester formed on treatment of **2a** with 3,5-dinitrobenzoyl chloride in pyridine had the mp of 72—74 °C.

The physical properties of **10** were as follows: IR (neat film) cm^{-1} 2925, 2870, 1470; ^1H NMR (CCl_4) δ=4.75—4.60 (broad s, 1H), 4.15—4.05 (t, 1H), 3.70—3.40 (m, 2H), 2.60—1.20 (m, 9H). Found: C, 41.06; H, 4.98%. Calcd for $C_9H_{13}OI$: C, 40.91; H, 4.92%.

Reaction of 2 with Iodine and Triethylamine in Methanol. A solution of **2** (10.0 g, 0.072 mol), iodine (17.9 g, 0.070 mol), and triethylamine (9.9 g, 0.098 mol) in methanol (55 mL) was refluxed for 2 d. After removal of the solvent, the reaction mixture was treated with water (35 mL), extracted twice with ether (50 mL). The extracts were washed with sat. aq Na_2SO_3, water, dried over $MgSO_4$, and concentrated in vacuo. Distillation gave **10** (2.3 g, 12.1%) and recovered **2** (6.0 g).

***endo*-5-(2-Hydroxyethyl)-2-norbornene (2b).** To an ice-cooled solution of **10** (12.0 g, 0.045 mol) in acetic acid (60 mL) was added slowly, with stirring, zinc dust (11.8 g, 0.183 mol), keeping the reaction temperature below 30 °C. Following the addition, the mixture was stirred at room temperature for 5 h, and then filtered. The resulting precipitate was washed with a 1:2 mixture of acetic acid and water (50 mL). The combined filtrates were concentrated in vacuo to remove the acetic acid. The residue was extracted with ether–benzene (200 mL), and then the extract was washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residual oil was distilled (62 °C/0.6 mmHg) to furnish **2b** (4.7 g, 75.7%). The ester formed on treatment of **2b** with 3,5-dinitrobenzoyl chloride in pyridine had the mp of 77 °C.

***exo*-5-Vinyl-2-norbornene (1a) and *endo*-5-Vinyl-2-norbornene (1b).** To an ice-cooled, stirred solution of **2a** (15.0 g, 0.109 mol) in pyridine (80 mL) was added in several portions of *p*-toluenesulfonyl chloride (22.8 g, 0.120 mol). After being stirred at room temperature overnight, the mixture was treated with water (5 mL), and the pyridine was evaporated in vacuo. The residue was treated with water (50 mL) and extracted with ether–benzene (200 mL). The organic extract was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure to give 2-(5-norbornen-*exo*-2-yl)ethyl *p*-toluenesulfonate (15.5 g, 48.7%) as an oil which was used in the next step without further purification: IR (neat film) cm^{-1} 3090, 2925, 2875, 1660, 1640, 1180; ^1H NMR ($CDCl_3$) δ=7.80—7.50 (m, 4H), 6.30—5.95 (m, 2H), 4.10—3.90 (t, 2H), 2.80 (broad s, 2H), 2.60 (s, 3H), 2.35—1.35 (m, 7H).

A solution of the above oil (15.5 g, 0.053 mol) in pyridine (50 mL) was refluxed for 12 h. Upon cooling to room temperature the mixture was poured into ice-water (50 mL) and extracted three times with pentane (100 mL), and the combined organic extracts were washed with water, dried over $MgSO_4$, and concentrated in vacuo. The residue was distilled [55—62 °C/25 mmHg (lit,[2a] 66.5 °C/66 mmHg)] to furnish **1a** (3.5 g, 55.0%): ^1H NMR (CCl_4) δ=6.05—6.00 (m, 2H), 5.95—5.70 (m, 1H), 5.30—4.85 (m, 2H), 2.85 (broad s, 1H), 2.70 (broad s, 1H), 2.25—1.95 (m, 2H), 1.45—1.35 (m, 3H); n_D^{20} 1.4791.

In place of **2a**, **2b** was treated in the identical manner described above to produce 2-(5-norbornen-*endo*-2-yl)ethyl *p*-toluenesulfonate (17.5 g, 55.0%) and **1b** (3.7 g, 51.4%), respectively. The physical properties of **1b** were as follows: bp 51—55 °C/20 mmHg; ^1H NMR (CCl_4) δ=6.05—5.95 (m, 2H), 5.80—5.40 (m, 1H), 5.10—4.70 (m, 2H), 2.95—2.65 (m, 3H), 2.10—1.80 (m, 1H), 1.50—1.30 (m, 2H), 1.00—0.80 (m, 1H); n_D^{20} 1.4806.

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References

1) T. Maeda, M. Muranaka, S. Hamanaka, and M. Ogawa, *Nippon Kagaku Kaishi*, **1974**, 1587.

2) a) A. A. Bobyleva, N. A. Belikova, A. N. Kalinichenko, A. T. Baryshnikov, N. F. Dubitskaya, T. I. Pekhk, E. T. Lippmaa, and A. F. Plate, *Zh. Org. Khim.*, **16**, 1645 (1980); b) G. Just, U. Linder, W. Pritzkow, and M. Roellig, *J. Prakt. Chem.*, **317**, 979 (1975).

3) H. C. Brown and E. Negishi, *J. Am. Chem. Soc.*, **89**, 5477 (1967).

4) H. O. House, R. G. Carlson, and H. Babad, *J. Org. Chem.*, **28**, 3359 (1963).

5) P. J. Kropp, P. R. Worsham, R. I. Davidson, and T. H. Jones, *J. Am. Chem. Soc.*, **104**, 3972 (1982).

6) B. M. Trost and P. G. McDougal, *J. Org. Chem.*, **49**, 458 (1984).

7) a) C. G. Schmitt and C. E. Boord, *J. Am. Chem. Soc.*, **54**, 751 (1932); b) D. C. Rowlands, K. W. Greenlee, J. M. Derfer, and C. E. Boord, *J. Org. Chem.*, **17**, 807 (1952).

8) a) J. P. Kutney and F. Bylsma, *J. Am. Chem. Soc.*, **92**, 6090 (1970); b) W. Reusch and D. W. Frey, *Tetrahedron Lett.*, **1967**, 5193; c) J. Schmutz and F. Künzle, *Helv. Chim. Acta*, **53**, 89 (1970); d) A. A. Bobyleva, A. N. Kalinichenko, N. A. Belikova, S. I. Korol'kov, N. F. Dubitskaya, and A. F. Platé, *Zh. Org. Khim.*, **10**, 1885 (1974).

9) E. A. Rick and S. W. Tinsley, U. S. Patent 3459775 (1969).