solvent removal under vacuum and analyzed by NMR and GLC. A 10-ft 10% THEED on 60/80-mesh Chromosorb W column was used to separate the products of reduction of 2-methylcyclohexanone (90 °C), 3-methylcyclohexanone (90 °C), and 4-methylcyclohexanone (80 °C). A 12-ft 10% Carbowax 20M on 60/80-mesh Chromosorb W column was used to separate the products in the cases of 2-*tert*-butylcyclohexanone (110 °C), 4-*tert*-butylcyclohexanone (130 °C), 3,3,5-trimethylcyclohexanone (135 °C), norcamphor (110 °C), and camphor (135 °C).

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Registry No. $Li(i\text{-}Bu)_2(t\text{-}Bu)AlH$, 62779-60-6; 4-*tert*-butylcyclohexanone, 98-53-3; 4-methylcyclohexanone, 589-92-4; 3-methylcyclohexanone, 591-24-2; 2-methylcyclohexanone, 583-60-8; 2-*tert*-butylcyclohexanone, 1728-46-7; 3,3,5-trimethylcyclohexanone, 873-94-9; norcamphor, 497-38-1; camphor, 76-22-2.

A Convenient Procedure for Upgrading Commercial (+)- and (–)-α-Pinene to Material of High Optical Purity

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α-Pinene, readily available in the (+) and (–) isomeric forms, is becoming of considerable importance for directed chiral synthesis. Hydroboration produces diisopinocampheylborane, which achieves asymmetric hydroboration of cis alkenes with high optical induction.[2] This reagent is readily transformed into monoisopinocampheylborane, suitable for the chiral hydroboration of trans and trisubstituted alkenes.[3] Hydroboration of α-pinene with 9-BBN produces *B*-pinanyl-9-BBN, a reagent that reduces deuterioaldehydes to primary alcohols, RCHDOH, with remarkably high enantiomeric purities.[4] This reagent also reduces acetylenic ketones to acetylenic alcohols with excellent results.[5] More recently it has been extended to many simple ketones.[6] A derivative of α-pinene, 2-hydroxypinan-3-one, is used for the asymmetric synthesis of α-amino acids.[7] Finally, α-pinene is readily converted to pinanediol,[8] and the latter compound has been used to form esters with boronic acids and converted to products with very high optical purities.[9]

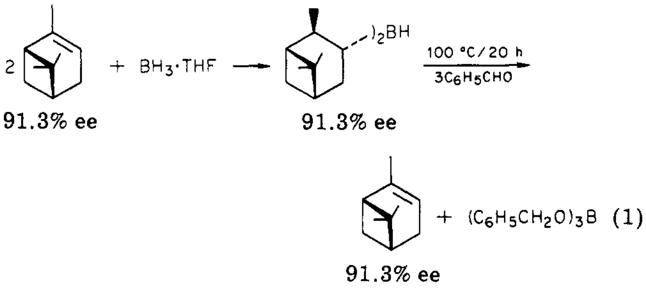
These promising applications make it desirable to have available α-pinene with high optical purity (if possible, a purity approaching 100%).

Regretably, the best available commercial (+)-α-pinene is 91.3% enantiomerically pure.[10] The commercially available (–)-α-pinene is comparatively expensive and is only 81.3% optically pure.[10] Fortunately, commercial (–)-β-pinene[10] of 92.1% ee is available and is readily isomerized by treatment with potassium 3-aminopropylamide[11] (KAPA) to (–)-α-pinene of 92% ee. We set ourselves the goal of finding a simple procedure that would upgrade such (+)- and (–)-α-pinene of ~92% to material approaching 100% ee.

A reasonable starting place for (–)-α-pinene appeared to be commercial (–)-β-pinene. The isomerization of (–)-β-pinene (92.1% ee) to (–)-α-pinene (92% ee) by KAPA was carried out on a 1-mol scale without any experimental difficulties. For (+)-α-pinene, the commerical material (91.3% ee) is satisfactory. Hydroboration of α-pinene with $BH_3\cdot THF$[2c] or $BH_3\cdot SMe_2$[2d] provides diisopinocampheylborane (Ipc$_2$BH). We had observed[2c] that the digestion of the product suspended in THF with 15% excess α-pinene causes the major isomer to become incorporated into the crystalline Ipc$_2$BH, with the minor isomer accumulating in the solution. Filtration of the solution removed the minor isomer and gave crystalline Ipc$_2$BH containing 99% of one isomer.

The problem was to find a convenient method to liberate α-pinene from Ipc$_2$BH. Elimination of up to two alkyl groups from trialkylboranes on treatment with aldehydes has been reported.[12] However, the elimination of the third alkyl group usually does not take place, even under very vigorous conditions.[12a] We have now discovered that, in the case of Ipc$_2$BH, even the last alkyl group on the boron can be eliminated on treatment with benzaldehyde under relatively mild conditions. The elimination of the alkyl group on boron depends on the structure of the alkyl group.[12] The 3-pinanyl group on boron appears especially favorable for such eliminations.[4-6]

Thus, treatment of Ipc$_2$BH with 3 mol of benzaldehyde, allowing the temperature to rise to 100 °C, displaces the α-pinene quantitatively, with the formation of tribenzyl borate (eq 1). The α-pinene is readily distilled away from the tribenzyl borate. Small amounts of benzaldehyde in the product are readily removed by distilling the product from a small excess of lithium aluminum hydride. The product thus obtained is 100% chemically pure (GLC), with no trace of β-pinene, indicating that thermal isomerization[13] does not occur at the displacement temperature (100 °C). Similarly, no racemization has been noted under



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(10) (+)-α-Pinene [$[\alpha]^{22}_D$ +47.1° (neat)], (–)-α-pinene [$[\alpha]^{22}_D$ –42.0° (neat)], and (–)-β-pinene [$[\alpha]^{20}_D$ –21.0° (neat)] are available from Aldrich Chemical Co.

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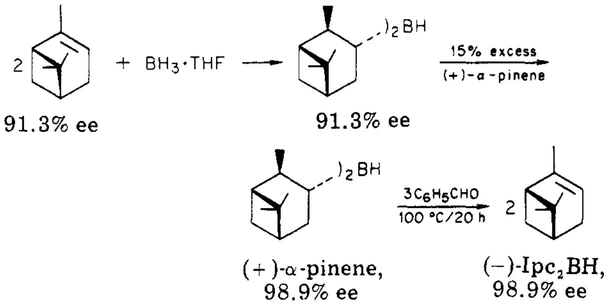
Table I. Summary of Rotations for α- and β-Pinene of High Optical Purities

compd	temp, °C	$[\alpha]^T{}_D$, deg (neat)	% ee[a]	ref
(+)-α-pinene	20	+51.60	100.0	14
(+)-α-pinene	20	+51.14	99.1	15
(+)-α-pinene	25	+51.0	98.9	2c
(+)-α-pinene	23	+51.0	98.9	[b]
(−)-α-pinene	20	−51.28	99.4	15
(−)-α-pinene	23	−51.1	99.0	[b]
(+)-β-pinene	25	+22.80	100.0	17
(−)-β-pinene	25	−22.70	99.6	16

[a] Percent ee of (+)- and (−)-α-pinene based on maximum rotation $[\alpha]^{20}{}_D$ 51.6° (neat); percent ee of (+)- and (−)-β-pinene based on maximum rotation $[\alpha]^{25}{}_D$ −22.8° (neat). [b] Present study.

these conditions, with the optical purity of the product α-pinene, 91.3% ee, the same as that of the α-pinene used to prepare the Ipc$_2$BH.

By combining the digestion procedure with this displacement procedure, we have been able to obtain (+)-α-pinene in optical purity of 98.9% from commercial (+)-α-pinene of 91.3% ee (eq 2).



(2)

In order to prepare (−)-α-pinene, the commercial (−)-β-pinene, 92% ee, is first isomerized by KAPA into (−)-α-pinene, 92% ee.[11] This material is hydroborated to form the (+)-Ipc$_2$BH, digested, and converted to 99% ee (−)-α-pinene.

It is desirable to summarize pertinent data for the rotations of α- and β-pinene (Table I).

Experimental Section

All operations were carried out under a nitrogen atmosphere, with ovendried glassware. GLC analyses were carried out on a Hewlett-Packard 5750 gas chromatograph with a 10 ft × 0.25 in. column packed with (a) 10% SE-30 on Chromosorb W (60–80 mesh) or (b) 10% Carbowax 20M on Chromosorb W (60–80 mesh). The ^{11}B NMR spectra were obtained on a Varian FT-80A instrument. Rotations were measured on a Rudolph Polarimeter Autopol III.

Materials. (+)-α-Pinene and (−)-β-pinene (Aldrich Chemical Co.) were distilled from a small excess of lithium aluminum hydride.

3-Aminopropylamine (APA) was distilled from a small excess of calcium hydride.

Conversion of (−)-β-Pinene to (−)-α-Pinene. In a dry 50-mL centrifuge tube fitted with a rubber septum and magnetic stirring bar was placed 1.78 mL (10 mmol) of 22.4% potassium hydride in oil. The oil was removed by washing with dry *n*-pentane (3 × 10 mL). After centrifugation, the pentane layer was removed by a double-ended needle. The residual pentane was removed under a stream of nitrogen. To the oil-free potassium hydride was rapidly added 10 mL of 3-aminopropylamine (APA). Hydrogen evolution subsided after 1.5 h, indicating that the formation of KAPA had been completed. Meanwhile, in a 500-mL round-bottom flask fitted with a septum inlet, a magnetic stirring bar, and a bent tube adaptor, connected to a mercury bubbler, was placed dry (−)-β-pinene (158.8 mL, 1 mol, $[\alpha]^{23}{}_D$ −21.0°, 92.1% ee, $n^{20}{}_D$ 1.4782), cooled to 0 °C in an ice bath. The KAPA in APA (1 mol %) was added dropwise to the vigorously stirred β-pinene with the help of a double-ended needle. The reaction mixture, light yellow initially, turns brown after about 30 min. Aliquots (0.1 mL) were withdrawn at intervals, quenched in a vial containing ice-cold water and 0.5 mL of pentane, separated, and dried. The GLC analysis showed that the equilibration was complete after 24 h with α-pinene/β-pinene (99.4:0.6). The reaction mixture was poured into ice–water, washed with brine (2 × 50 mL), dried over anhydrous calcium chloride, and filtered, the filtrate was distilled from a small excess of lithium aluminum hydride to provide 126.5 g (93% yield) of (−)-α-pinene: bp 72 °C (46 mm); $[\alpha]^{23}{}_D$ −47.47° (neat); 92.0% ee.

Conversion of (−)-α-Pinene of 92% ee to (−)-α-Pinene of 99% ee. A 250-mL flask, equipped with a septum inlet, magnetic stirring bar, and a distillation condenser, connected to a receiver cooled in a dry ice–acetone bath was charged with 5.0 mL (50 mmol) of $BH_3{\cdot}SMe_2$ and 15 mL of THF. It was cooled to 0 °C in an ice bath and 15.9 mL (100 mmol) of (−)-α-pinene, $[\alpha]^{23}{}_D$ −47.47° (neat), 92% ee, was added dropwise with stirring. After the contents were stirred at 0 °C for 3 h, a mixture of DMS and THF (13 mL) was removed under vacuum [0 °C (30 mm)], and the flask was brought to atmospheric pressure by flushing with nitrogen gas and charged with 18 mL of THF and 2.4 mL (15 mmol) of (−)-α-pinene. The distillation condenser was replaced by a bent tube adaptor under positive pressure of nitrogen. The flask was then stored in the cold room at 0 °C for 3 days to permit equilibration. The slurry of Ipc$_2$BH was transferred to a 125-mL centrifuge tube cooled in an ice bath. The upper layer containing excess α-pinene and THF was removed after centrifugation, and the solid Ipc$_2$BH was washed with cold (−10 °C) THF (2 × 20 mL). The solid Ipc$_2$BH was then transferred as a suspension in THF (15 mL) to a 100-mL flask fitted with a septum inlet, a magnetic stirring bar, and a distillation condenser connected to a mercury bubbler. The solvent was removed under reduced pressure [25 °C (2 mm), 2 h] to provide Ipc$_2$BH (10.86 g, 76% yield). It was then treated with benzaldehyde (11.6 mL, 114 mmol) at 25 °C. After the reaction mixture was stirred at 25 °C for 15 min, it was heated in an oil bath maintained at 100 °C for 20 h, whereby the elimination of α-pinene with the formation of tribenzyl borate [δ 18 (^{11}B NMR)] was complete. The liberated α-pinene was distilled. The distillate was stirred with a small excess of $LiAlH_4$ to remove traces of benzaldehyde and redistilled to provide α-pinene (8.3 g, 61% yield): bp 82 °C (60 mmHg); $[\alpha]^{23}{}_D$ −51.10° (neat); 99% ee. Alternatively, the distillate containing a mixture of α-pinene and benzaldehyde was dissolved in pentane, and the pentane solution was washed with 10% aqueous sodium bisulfite (3 × 30 mL), followed by water (30 mL). The organic layer, after drying over anhydrous magnesium sulfate, was distilled to provide pure α-pinene.

Conversion of (+)-α-Pinene of 91.3% ee to (+)-α-Pinene of 99% ee. The experimental procedure described for (−)-α-pinene is followed. (+)-α-Pinene, $[\alpha]^{23}{}_D$ +47.1° (neat); 91.3% ee, was used to provide (+)-α-pinene (8.15 g, 60% yield), bp 82 °C (60 mmHg), $[\alpha]^{23}{}_D$ +51.0° (neat), 98.9% ee.

Registry No. KAPA, 56038-00-7; $BH_3{\cdot}SMe_2$, 13292-87-0; Ipc$_2$BH, 21947-87-5; (+)-α-pinene, 7785-70-8; (−)-β-pinene, 18172-67-3; (−)-α-pinene, 7785-26-4; benzaldehyde, 100-52-7.

Diphthalimido Carbonate: A New Reagent for Active Ester Synthesis

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Active amino acid esters from *N*-hydroxyphthalimide/dicyclohexylcarbodiimide have found wide use in peptide chemistry.[1] During the study on the reactions of