A Convenient Synthesis of (+)-β-Pinene from (+)-α-Pinene

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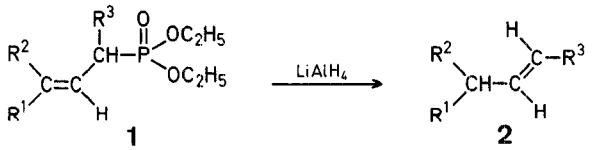
A convenient four-step procedure for the conversion of α-pinene to β-pinene in 25% overall yield via stable, easily purified intermediates is described. This route renders accessible the scarce (+)-β-pinene possessing high isomeric and enantiomeric purity.

In connection with recent studies, we required access to appreciable quantities of (+)-β-pinene of high optical purity. Unfortunately, (−)-β-pinene is produced almost exclusively in nature, the (+)-antipode having been reported in very few cases[1,2]. In contrast, (+)-α-pinene, which possesses the same absolute configuration at C-1 and C-5 as (+)-β-pinene, is readily available and this fact led us to search for a simple means of obtaining β-pinene from α-pinene.

Although equilibration between α- and β-pinenes occurs readily β-pinene is usually the minor constituent of the product mixture[3]. Attempts to increase the amount of β-pinene in the product have lead to racemisation[4]. A method previously described[5] involves the thermal rearrangement of the hydroboration product of α-pinene followed by displacement of β-pinene by a second alkene. However, this work gives no information on the optical activity of the materials. (+)-β-Pinene, $[\alpha]_D$: +22.8°, has been obtained in low yield from (+)-10-camphensulphonyl chloride after separation from the major component of the reaction mixture by preparative G.L.C.[6]. (This is the highest optical activity reported for (+)-β-pinene and compares with a value of $[\alpha]_D$: −22.7° for (−)-β-pinene purified by complexation with silver tetrafluoroborate[7]). None of these approaches appeared suitable for our needs.

3-Substituted 2-alkenephosphonates of type **1** have been reported to undergo reductive fission with lithium aluminium hydride to yield *trans*-alkenes[8] **(2)**. The observation that this reduction step is accompanied by a transposition of the double bond prompted us to apply this technique to our problem.

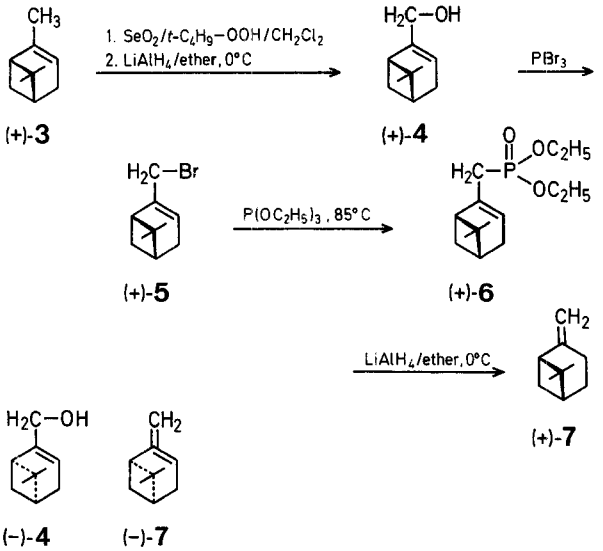


1 **2**

R^1 = alkyl
R^2, R^3 = H, alkyl

Preliminary investigations were carried out in the (−)-series using the commercially available (−)-myrtenol [(−)-**(4)**; $[\alpha]_D^{22}$: −47.5°, enantiomeric purity: 88%[2]]. This was converted to (−)-myrtenyl bromide [(−)-**5**; $[\alpha]_D^{22}$: −22.2°, enantiomeric purity: 88%[9]] in 74% yield of distilled product using phosphorus tribromide/pentane[10]. Compound (−)-**5** was converted into the key intermediate diethyl (−)-myrtene-10-phosphonate [(−)-**6**; 91% yield of distilled product; $[\alpha]_D^{22}$: −19.1°] by heating with a slight excess of triethyl phosphite for 12 h at 85 °C under nitrogen. Compound (−)-**6** was reduced by stirring with lithium aluminium hydride in ether to give, after filtration through silica gel, (−)-β-pinene [(−)-**7**; (99% pure by G.L.C.] in 93% yield [60% overall yield from (−)-**4**]. Distillation afforded a product possessing $[\alpha]_D^{22}$: −18.6°, corresponding to an enantiomeric purity of 82%[2,7]. The overall yield from (−)-**4** thus was 63%, the overall optical yield was 93%.

In the (+)-series, (+)-α-pinene[9] [(+)-**3**; $[\alpha]_D^{22}$: +46.5°, enantiomeric purity: 89%], was converted to (+)-myrtenol [(+)-**4**; $[\alpha]_D^{22}$: +44.3°, enantiomeric purity: 82%], in 25% yield (43% based on recovered starting material) using selenium dioxide/*t*-butyl hydroperoxide[11], followed by reduction of the crude product with lithium aluminium hydride, and distillation. Compound (+)-**4** was in turn converted, via (+)-myrtenyl bromide [(+)-**5**; $[\alpha]_D^{22}$: +20.8°, enantiomeric purity: 83%[9]], to diethyl (+)-myrtene-10-phosphonate [(+)-**6**; $[\alpha]_D^{22}$: +20.1°] in 90% yield of distilled product [62% yield from (+)-**4**]. Reduction of (+)-**6** with lithium aluminium hydride gave (+)-β-pinene [(+)-**7**] in 99% purity (G.L.C.) and 93% yield; the distilled product had $[\alpha]_D^{22}$: +18.3°, enantiomeric purity: 80%. The overall yield of (+)-β-pinene [(+)-**7**] from (+)-α-pinene [(+)-**3**] is thus 25% in four steps, with an overall optical yield of 90%. The only impurity (0.5%) detectable in the product by G.L.C. analysis was α-pinene.



In contrast, the reaction of myrtenyl bromide with lithium aluminium hydride[10], myrtenyl chloride with sodium/ethanol[12], or myrtenol with sodium/ethanol[10] gives only α-pinene with none of the β-isomer being detected.

The procedures described here are amenable to medium or large scale work. The intermediates are all stable and may be easily purified by distillation. The preparation of quantities of (+)-β-pinene useful for laboratory work is thus henceforth a practical proposition.

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Commercial starting materials were purchased from Aldrich-Europe division and were used without further purification (purity: >98%, by G.L.C. analysis). All G.L.C. analyses were performed using 5% carbowax on chromosorb (3 × 1.5 mm internal diameter) between 70° and 210 °C.

(+)-Myrtenol [(+)-4]:
A solution of (+)-α-pinene [(+)-**3**; 27.2 g, 0.2 mol; $[\alpha]_D^{22}$: +46.5°], in dichloromethane (100 ml) is stirred at ambient temperature with selenium dioxide (11.0 g) and *t*-butyl hydroperoxide (44.0 ml) for 24 h. The mixture is washed with 10% aqueous potassium hydroxide (4 × 40 ml), the organic phase dried, and the solvent removed under reduced pressure. The residue is dissolved in dry ether and lithium aluminium hydride (1.0 g) is cautiously added to the stirred mixture at 0 °C. After 4 h, the excess hydride is carefully destroyed with water, the organic phase is separated, dried with sodium sulphate, and the solvent evaporated. The residue is distilled in vacuo to give (+)-α-pinene (9.0 g; b.p. 65 °C/35 torr) and (+)-myrtenol; yield: 8.75 g (25%); b.p. 69–75 °C/1.5 torr; $[\alpha]_D^{22}$: +44.3° (*c* 3.21, chloroform). The product thus obtained was identical with an authentic sample of (−)-myrtenol in every respect except optical rotation.

(+)-Myrtenyl Bromide [(+)-5]:
(+)-Myrtenol [(+)-**4**; 8.40 g, 58 mmol] is treated with phosphorus(III) bromide (5.90 g, 22 mmol) following the described method[9]. Distillation of the resultant product in vacuo gives (+)-**5** as a slightly lacrymatory oil; yield: 8.64 g (68%); b.p. 52–58 °C/0.6 torr; $[\alpha]_D^{22}$: +20.8° (*c* 3.46, chloroform); data identical to those previously reported.

Diethyl (+)-Myrtene-10-phosphonate [(+)-6]:
A mixture of (+)-myrtenyl bromide [(+)-**5**; 8.64 g, 40 mmol], and triethyl phosphite (7.15 g, 43 mmol) is heated at 85 °C for 12 h under a nitrogen atmosphere. Distillation under reduced pressure gives the pure phosphonate; yield: 9.84 g (90%); b.p. 114–118 °C/0.9 torr; $[\alpha]_D^{22}$: +20.1° (*c* 3.95, chloroform).

$C_{14}H_{25}O_3P$	calc.	C 61.75	H 9.25	P 11.37
(272.3)	found	61.79	9.53	11.13

M.S.: *m/e* = 272 (M^+); 257; 243; 229; 201; 173.

I.R. (neat): ν = 2980; 2900; 1245; 1025; 960 cm^{-1}.

^{1}H-N.M.R. (90 MHz, $CDCl_3$): δ = 0.87 (s, 3 H); 1.23 (s, 3 H); 1.28 (t, *J* = 7.0 Hz, 6 H); 1.90–2.45 (m, 6 H); 2.60 (broad d, *J* = 22.5 Hz, 2 H); 4.05 (quin, *J* = 7.3 Hz, 4 H); 5.23–5.48 ppm (m, 1 H).

(+)-β-Pinene [(+)-7]:
All manipulations prior to distillation of the product should be carried out under an efficient hood due to the formation of small amounts of toxic volatile by-products during the course of the reaction).

Lithium aluminium hydride (1.82 g, excess) is added in small portions during 10 min to a stirred solution of diethyl (+)-myrtene-10-phosphonate [(+)-**6**; 9.10 g] in dry ether (650 ml) cooled to 0 °C. The suspension is stirred at 0 °C under nitrogen for 4 h, and left overnight at ambient temperature. The excess hydride is carefully destroyed by the dropwise addition of water and the mixture dried with sodium sulphate. The solution is filtered through silica gel (30 g), washing the filtrant with ether (3 × 100 ml). The filtrate is evaporated at atmospheric pressure to give pure (T.L.C.) (+)-**7** as a colourless liquid; yield: 4.21 g (93%); purity (G.L.C.): 99.5%. Distillation of this product is accompanied by appreciable decomposition but gives only one fraction consisting of analytically pure (+)-β-pinene [(+)-**7**]; yield: 2.74 g (60%); b.p. 70–71 °C/28 torr (Ref.[13], b.p. 59.7 °C/20 torr); $[\alpha]_D^{22}$: +18.3° (*c* 4.20, chloroform); enantiomeric purity: 80%[2]. The product thus obtained was identical in all respects except optical rotation with authentic (−)-β-pinene.

We thank the Royal Society and the Centre National de La Recherche Scientifique for the award of a fellowship under the European Science Exchange Programme.

1 *Rodd's Chemistry of Carbon Compounds*, 2nd Edn., S. Coffey, Ed., Vol. IIc, Elsevier publishing Co., Amsterdam, 1969, p. 174.
2 D. V. Banthorpe, D. Whittaker, *Chem. Rev.* **66**, 643 (1966).
3 C. A. Brown, *Synthesis* **1978**, 754; and references cited therein.
4 G. A. Rudakov, L. S. Ivanova, A. G. Borovskaya, *Zh. Org. Khim.* **11**, 2275 (1975); *C. A.* **84**, 165037 (1976).
5 H. C. Brown, M. V. Bhatt, *J. Am. Chem. Soc.* **82**, 2074 (1960).
6 W. Kirmse, W. Gruber, *Chem. Ber.* **105**, 2764 (1972).
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10 G. Ohloff, H. Farnow, G. Schade, *Chem. Ber.* **89**, 1549 (1956).
11 M. A. Umbreit, K. B. Sharpless, *J. Am. Chem. Soc.* **99**, 5526 (1977).
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13 R. E. Fuguitt, W. D. Stallcup, J. E. Hawkins, *J. Am. Chem. Soc.* **64**, 2978 (1942).

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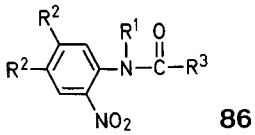
Errata and Addenda 1980

V. N. R. Pillai, *Synthesis* **1980** (1), 1–26;
The structure of compound **86** (p. 12) should be:

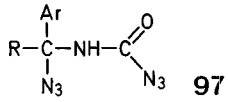


86

V. I. Cohen, *Synthesis* **1980** (1), 60–63;
The alternative name (in brackets) for compounds **1** (p. 62, first experimental procedure) should be ***S*-Methylpseudothiourea Hydroiodides.**

J. R. Mahajan, H. C. de Araújo, *Synthesis* **1980** (1), 64–66;
The authors have erroneously stated that "exaltolide" is a trivial name for pentadecanolide. In fact "exaltolide" is a trademark registered in the name of Firmenich SA, Geneva and should be designated as Exaltolide®.

V. I. Gorbatenko, L. I. Samarai, *Synthesis* **1980** (2), 85–110;
The structure of compound **97** (p. 99) should be:



97

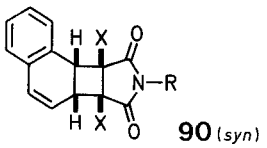
M. Mikołajczyk, P. Bałczewski, S. Grzejszczak, *Synthesis* **1980** (2), 127–129;
The correct name for compound **5a** (first procedure, p. 129) is **Diethyl 1-Phenylthioethanephosphonate.**

G. A. Olah, Y. D. Vankar, M. Arvanaghi, *Synthesis* **1980** (2), 141–142;
The correct name for compound **4** is ***N*-(Chlorosulfonyl)-dimethylsulfilimine.**

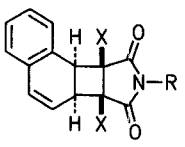
Abstract 5692, *Synthesis* **1980** (2), 159;
The title should be: **Phenols from Aryl Ethyl Ethers.**

Abstract 5698, *Synthesis* **1980** (2) 161;
The title should be: **Enals and Enones from Ketones.**

T. Wagner-Jauregg, *Synthesis* **1980** (3), 165–214;
The structures of compounds **90** (p. 175) should be:



90 (*syn*)



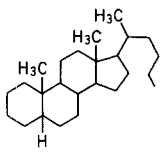
90 (*anti*)

The correct name for compound **251** (p. 188) is **2*H*-Cyclohepta[*gh*]pyrrolizin-Derivat.**

Abstract 5724, *Synthesis* **1980** (3), 254;
The title should be: **Carbamates, Thiocarbamates, and Carbonates from Alcohols or Thiols.**
The first line under the formula scheme should be: Y = O, S.

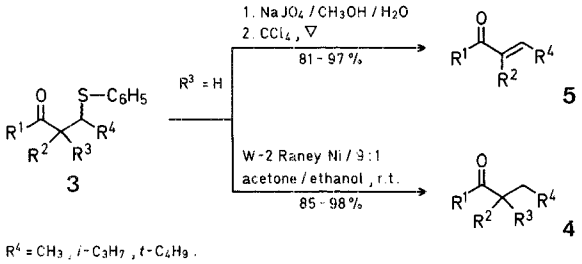
Abstract 5728, *Synthesis* **1980** (3), 256;
The title (and name for compound **3**) should be: ***N*-Sulphenylimines Derived from Amino Acids.**

C. R. Harrison, P. Hodge, *Synthesis* **1980** (4), 299–301;
The 3rd group in the Table, part B (p. 300) should have the structure:



Abstract 5745, *Synthesis* **1980** (4), 334;
The title should be: **Stereocontrolled *cis*-Addition of Organocopper Reagents to 2-Alkynals, 1-Alkynyl Ketones, 2-Alkynoic Acids, and 2-Alkynoic Esters.**

Abstract 5752, *Synthesis* **1980** (4), 336;
The title should be: **α-Alkylation and α-Alkylidenation of Carbonyl Compounds.**
The formula scheme for the conversion **3**→**4** or **5** should be:



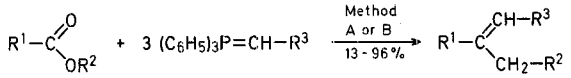
3 **5** **4**

R^4 = CH_3, *i*-C_3H_7, *t*-C_4H_9.

Abstract 5770, *Synthesis* **1980** (4), 342;
The title should be: **Claisen Rearrangement of Ketene Allyl Ethyl Acetals.**

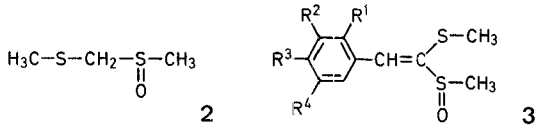
M. A. Alkhader, R. K. Smalley, B. Mohajerani, *Synthesis* **1980** (5), 381–383;
The correct name for compound **6** is **Indazolo[3,2-*b*]naphtho[2,3-*d*]-[1,3] oxazin-6-one.**

Abstract 5782, *Synthesis* **1980** (5), 418;
The formula scheme should be:



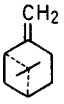
1 **2** **3**

Abstract 5799, *Synthesis* **1980** (5), 424;
The structures of compounds **2** and **3** should be:



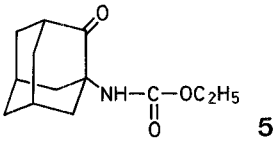
2 **3**

L. M. Harwood, M. Julia, *Synthesis* **1980** (6), 456–457;
The structure of compound (−)-**7** should be:



(−)-**7**

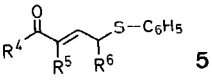
T. Sasaki, S. Eguchi, T. Okano, *Synthesis* **1980** (6), 472–475;
The structure of compound **5** should be:



5

Abstract 5804, *Synthesis* **1980** (6), 498;
The title should be: **Allylic Funtionalisation of Exomethylene Compounds.**

Abstract 5817, *Synthesis* **1980** (6), 503;
The structure of compound **5** should be:



5