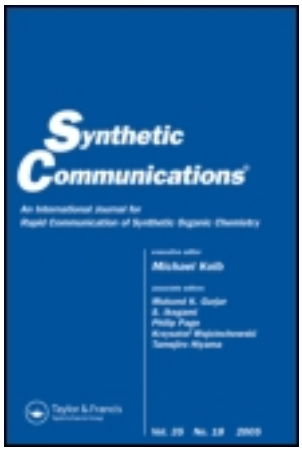

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Chemospecific Preparation of Both Enantiomers of α-Terpinyl Trifluoroacetate

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ABSTRACT

(*R*)- and (*S*)-α-Terpinyl trifluoroacetate can easily be prepared in 56–64% yield and high *ee* by the reaction of (*R*)- and (*S*)-limonene with trifluoroacetic acid in cyclohexane. The products were fully characterized by ^{1}H and ^{13}C NMR, IR and MS and theirs Chiral-HRGC analysis showed there is no loss of optical activity during the reaction.

Key Words: Limonene; *p*-Menthenes; Terpinyl trifluoroacetate.

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INTRODUCTION

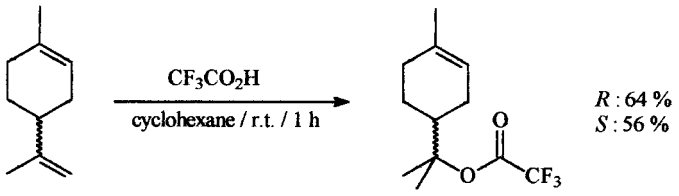
Electrophilic additions to limonene may suffer from issues of selectivity (1). Sometimes additions occur to both double bonds of a same molecule (e.g. bromination, acid-catalyzed hydration) or mixture of addition products to the disubstituted and trisubstituted double bonds are obtained (e.g. epoxidation, carbenoid addition).[1] Recently, we communicated that the surface-mediated hydrohalogenation of both enantiomers of limonene produced the α-terpinyl halides chemo- and regiospecifically.[2,3] The enantiomeric excess of the products were determined by Chiral-High Resolution Gas Chromatography (Chiral-HRGC).

In 1976, Roberts published a kinetic study on the reaction of limonene with trifluoroacetic acid and the product (α-terpinyl trifluoroacetate) was characterized by ^{1}H NMR only.[4] As part of our continuing interest in chemospecific functionalization of limonene,[1–3,5] we have revisited this reaction using both enantiomers of limonene and communicate our results here.

RESULTS

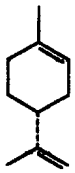
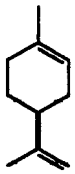
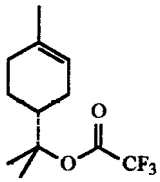
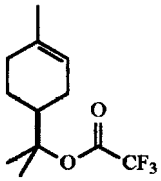
The reaction of (*R*)-limonene (10 mmol) with trifluoroacetic acid (10 mmol) in cyclohexane was performed at room temperature in an open flask for 1 h. After work up, (*R*)-α-terpinyl trifluoroacetate was obtained in 64% yield and >99% optical purity. The same reaction performed with (*S*)-limonene led to (*S*)-α-terpinyl trifluoroacetate in 56% yield (Sch. 1).

Chiral-HRGC of (*R*)-α-terpinyl trifluoroacetate showed *ee* > 99% [similar to the *ee* of the starting (*R*)-limonene], indicating that there is no loss of optical activity in this reaction. On the other hand, Chiral-HRGC of (*S*)-α-terpinyl trifluoroacetate showed the presence of small amount of the (*R*)-enantiomer, attributed to the fact that our (*S*)-limonene used was not



Scheme 1.

Table 1. Chiral-HRGC and polarimetric analysis of both enantiomers of limonene and α-terpinyl trifluoroacetate.

Compound	t_R (min)[a]	*ee* (%)[b]	$[\alpha]_D^{28}$
	22.2	>99	+118.7 (neat)
	21.6	>86	−103.4 (neat)
	159.8	>99	+44.5 (8.2%, cyclohexane)
	157.9	>87	−40.3 (8.2%, cyclohexane)

[a]See Experimental for chiral-HRGC conditions of analysis.
[b]Determined by integration of the areas of the peaks in Chiral-HRGC.

enantiomerically pure (*ee* > 86%). In fact, the stereoselectivity in both reactions are similar, as the products should have the same *ee* of the substrates. Table 1 summarizes the Chiral-HRGC and polarimetric analysis of substrates and products.

These results are important because in a protic media the enantiopurity of limonene can be totally or partially destroyed by protonation of the disubstituted double bond followed by 1,2-hydrogen shift from the stereogenic center.[6] Another possibility is the loss of optical activity by protonation-deprotonation of the trisubstituted double bond of limonene or product.

EXPERIMENTAL

General

(*R*)-limonene (Dierberger) and (*S*)-limonene (Aldrich) were distilled prior to use [b.p. 176–178°C, lit. 178°C][7] and other chemicals were used as received. ^{1}H NMR and ^{13}C NMR were acquired on a Bruker DRX-300 (300 MHz and 75 MHz, respectively) spectrometer in $CDCl_3$ solutions with TMS as internal standard. IR spectra were recorded on a Perkin–Elmer 1600 FT-IR spectrometer (KBr film). MS were obtained on a Hewlett–Packard HP5896-A HRGC-MS using electron impact (70 eV). Polarimetric analysis were done on a Jasco DIP 370 polarimeter. Chiral-HRGC analysis by FID were performed on a Varian 3400 CX chromatograph with a Cyclodex-B (J. & W. Scientific) with 30 m (length), 0.25 mm (i.d.) and 0.25 μm (film thickness) capillary silica column and He (50 cm/s) as carrier gas (split 1/20). Conditions of analysis: injector temperature: 240°C, detector temperature: 240°C, column temperature: 50°C.

(R)-α-Terpinyl trifluoroacetate. To a stirred solution of (*R*)-limonene (1.36 g, 10 mmol) in cyclohexane (10 mL), CF_3CO_2H (0.80 g, 10 mmol) was slowly added at room temperature. After 1 h, the solution was washed with water (5 mL), 5% $NaHCO_3$ (5 mL), water (5 mL) and then dried (Na_2SO_4). The solvent was removed under reduced pressure (2 Torr) and low heating (<50°C) to produce pure (*R*)-α-terpinyl trifluoroacetate (1.60 g, 64%).[a] ^{1}H NMR: δ 1.15–1.45 (m, 2H), 1.54 (s, 3H), 1.55 (s, 3H), 1.65 (s, 3H), 1.73–2.07 (m, 5H), 5.37 (broad s, 1H) ppm. RMN ^{13}C: δ 22.7, 23.0, 23.3, 23.7, 26.2, 30.6, 42.6, 91.9, 114.5 (q, J_{C-F} 285.4 Hz), 119.7, 134.1, 156.2 (q, J_{C-F} 40.8 Hz) ppm. IR: ν 2931, 1778, 1447, 1372, 1219, 1170, 1123, 861, 778 cm^{-1}. MS: m/z (%) 137 (M^+-CF_3CO_2, 13), 136 (49), 121 (100), 93 (75). Polarimetric and Chiral-HRGC analysis are shown in Table 1.

(S)-α-Terpinyl trifluoroacetate. Same as above, (*S*)-limonene used instead of (*R*)-enantiomer, obtained 1.40 g (56%). Polarimetric and Chiral-HRGC analysis are shown in Table 1.

[a]The purity of α-terpinyl trifluoroacetate (>99%) was checked by comparison of its analytical data with the previously reported (4) as well as by co-injection in HRGC with two chromatographic columns of different polarities (CARBOWAX and RTX-5) that showed only one peak.

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