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Solvomercuration-Demercuration of Limonene with $Hg(BF_4)_2$; A Chemo-and Regiospecific Route to 8-Substituted p-Menthenes

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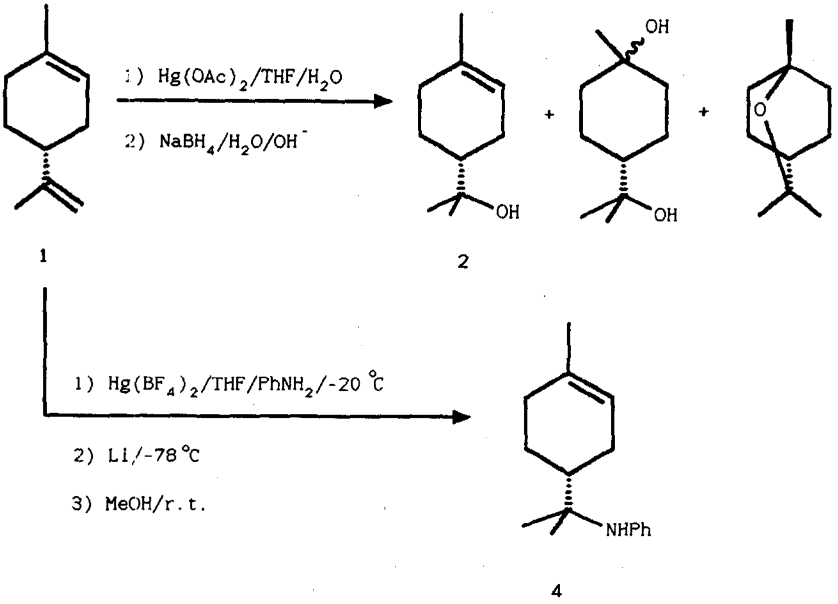
Key words: limonene; mercuration-demercuration; α-terpineol; mercuric tetrafluoroborate; p-menthenes

Abstract: Solvomercuration-demercuration of limonene with equimolar $Hg(BF_4)_2$ and excess nucleophile (-20°C) functionalizes the acyclic double bond and provides specifically 8-substituted p-menthenes.

Solvomercuration-demercuration, which furnishes a Markovnikov functionalization of olefins, has been studied for a long time.[1] The specific case of *R*-(+)-limonene (**1**) is known from early work of Brown[2] and Bambagiotti[3] in which α-terpineol (**2**) along with 1,8-diols and cineole were produced when limonene was mercurated with $Hg(OAc)_2$ in aqueous THF and the organomercurial reduced *in situ* with alkaline $NaBH_4$. Sukenik[4] showed that addition of sodium lauryl sulfate enhances the rate and selectivity for **2** and Einhorn[5] showed that similar selectivity in "oxymercuration" with ultrasound depends on the counterion of the mercury (II) salt. Recently we published[6] that the aminomercuration of **1** with an equimolar amount of $Hg(BF_4)_2$ (**3**) and excess aniline at -20°C gives specifically the secondary amine **4** (Scheme 1).

Scheme 1



It was decided to demonstrate the generality of this solvomercuration-demercuration methodology with **3** and limonene to prepare diverse p-menthene derivatives[7,8] (Scheme 2 and Table).

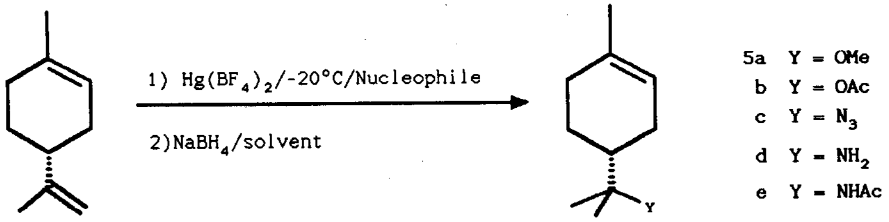
Hydroxymercuration of limonene was carried out by stirring with 1 eq of aqueous **3** in THF at -20°C. After addition of excess alkaline NaBH$_4$, **2** was isolated in 84% yield. Analysis of this crude reaction mixture with ^{13}C-NMR spectroscopy did not show the signals corresponding to the other products seen in previous work[2-5] and polarimetric analysis[10] indicated (as expected) more than 99% e.e.[12]

Similar results were obtained with anhydrous **3** in dry methanol (87% yield of **5a**[13]) and with acetic acid (5 eq) in THF (**5b** in 85% isolated yield). In this latter case the demercuration (only 3 min[14]) was followed by filtration on a short SiO$_2$ column.

The azidomercuration of **1** was carried out with aqueous **3** and NaN$_3$ (5 eq) in THF/H$_2$O (1/1). Reduction with alkaline NaBH$_4$ gave the azide **5c** in 80% isolated yield. Alternate treatment of the isolated organomercury intermediate with NaBH$_4$ (5 eq) at reflux in tetraglyme (2h) reduced both the azido and organomercury groups and lead to the primary amine **5d** in 75% isolated yield.

Using anhydrous **3** in dry acetonitrile and demercurating with aqueous alkaline NaBH$_4$ led to isolation of the acetamide **5e** in 80% yield.

Scheme 2



Table

Nucleophile	Product (%)	Hg° recovered(%)
H_2O	2 (84)	95
MeOH	5a (87)	98
HOAc	5b (85)	not determined
NaN_3	5c (80)	95
	5d (75)	91
MeCN	5e (80)	98

In conclusion, the solvomercuration of **1** with $Hg(BF_4)_2$ followed by reduction of the C-Hg bond provides a mild and regiospecific route for the preparation of chiral 8-substituted p-menthenes.

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7. Spectral data were in accord with the assigned structure.

8. Typical procedure, *e.g.* **5a**: to a solution of **1** (10 mmol) in dry MeOH (25 ml) was added **3**[9] (10 mmol) at -20°C (bath). When the mercuration was finished (negative test for Hg(II) with 10% NaOH in an aliquot), 10% NaOH (20 ml) was added followed by $NaBH_4$ (10 mmol) in 5% NaOH (10 ml) and the suspension was stirred overnight for complete coagulation of Hg°. After decantation, extraction (Et_2O), drying (Na_2SO_4) and high vacuum concentration, the crude product was analyzed with HRGC-MS, ^1H and ^{13}C-NMR and IR spectroscopy.

9. Prepared by stirring yellow HgO (10 mmol) and 40% HBF_4 (20 mmol) at r.t. Evaporation of the solvent from the yellow solution under high vacuum gave a white solid which was imediately used (Barluenga, J.; Alonso-Cires, L.; Asensio, G. *Synthesis* **1979**, 962-64).

10. Polarimetric analysis made on a Perkin-Elmer 241B polarimeter. **1**: $[\alpha]_D^{25}$ +126° (*c* 1.00, $CHCl_3$), lit. $[\alpha]_D^{20}$ +126.8[11]; **2**: $[\alpha]_D^{25}$ +100° (*c* 1.00, $CHCl_3$), lit. $[\alpha]_D^{20}$ +100.5[11].

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12. *R*-(+)-limonene (**1**) absolute configuration: Pawson, B.A.; Cheung, H.-C.; Gurbaxani, S.; Saucy, G. *J.Chem.Soc.Chem.Comm.* **1968**, 1057-58; *R*-(+)-α-terpineol (**2**) absolute configuration: Freudenberg, K.; Lwowski, W.; Hohmann, H. *Justus Liebigs Ann.Chem.* **1955**, *594*, 76-88.

13. Selected data, **5a**: ^{13}C-NMR ($CDCl_3$, 75 MHz): δ 133.1(s), 120.5(d), 79.5 (d)76.2(s), 48.0(d), 30.6(t), 26.4(t), 23.4(t), 21.9(q), 21.7(q), 21.2(q) ppm; ^1H-NMR ($CDCl_3$, 300 MHz): δ 5.3(s,1H), 3.1(s,3H), 1.9-1.0 (m,16H) ppm.

14. Longer reaction times led to the hydrolysis of **5b** to **2**.

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