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Synthesis of a New β-Mercaptoalcohol

Jian Feng GE[1,2], Li Fen ZHANG[1], Zong Xuan SHEN[1], Ya Wen ZHANG[1*]

[1]Department of Chemistry and Chemical Engineering, Suzhou University, Suzhou 215006
[2]Department of Material and Engineering, Suzhou University, Suzhou 215006

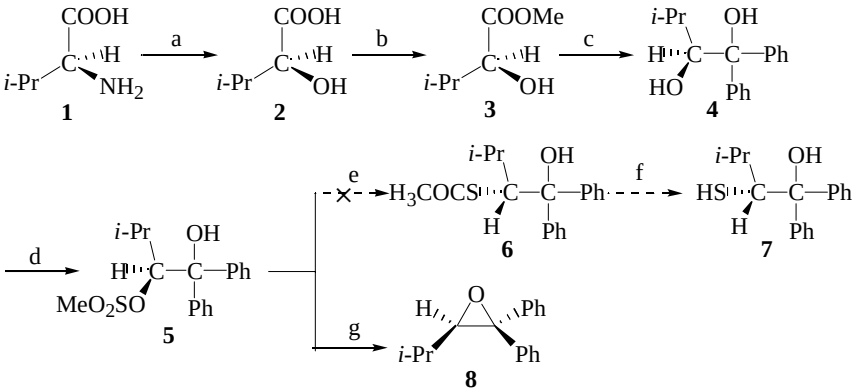
Abstract: In this letter, (R)-1,1-diphenyl-2-mercapto-3-methyl-1-butanol was synthesized from L-valine and two synthetic routes have been tried.

Keywords: (R)-1,1-Diphenyl-2-mercapto-3-methyl-1-butanol, asymmetric synthesis, L-valine.

Mercaptoalcohols are a rare class of natural products. Some optically active mercaptoalcohols have been used as catalysts in asymmetric reduction of prochiral Ketone[1,2]. In this letter, we report the synthesis of a new optically active β-mercaptoalcohols, (R)-1,1-diphenyl-2-mercapto-3-methyl-1-butanol **7**, from L- valine.

Our first attempt is showed in **Scheme 1**. According to literature's method L-valine was converted to (S)-2-Hydroxy-3-methylbutanoic acid **2**[1,2]. **2** was treated with MeOH/$SOCl_2$ to obtain (S) -2-hydroxy-3-methylbutanoic acid methyl ester **3**, which was treated with excess of phenyl magnesium bromide to give (S)-1, 1-diphenyl-3-methyl-1, 2-butanediol **4**[1]. Then **4** was mesylated to obtain **5**.

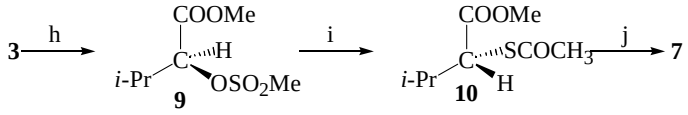
Scheme 1



Reagents: a. $NaNO_2/H_2SO_4$; b. MeOH/$SOCl_2$; c. PhMgBr/Et_2O; d. MsCl/pyridine;
e. $KSCOCH_3$/DMF(fail); f. NH_3/H_2O(untried); g. $HSCOCH_3$/pyridine reflux

Unfortunately, conversion of **5** to **6** was unsuccessful. When **5** was refluxed with thioacetic acid in pyridine[1], instead of compound **6**, an optical active epoxy **8** was obtained[1], probably due to the steric hindrance around the reaction center.

Scheme 2



Reagents: h. MsCl/pyridine; i. $KSCOCH_3$ / DMF; j. $PhMgBr/Et_2O$

A successful synthetic route is showed in **Scheme 2**. **3** was mesylated to obtain (S)-3-methyl-2-(methylsulfonyloxy)butanoic acid methyl ester **9**, which was treated with $KSCOCH_3$ in DMF to give **10**. Treating **10** with phenyl magnesium bromide gave the desired compound (R)-1,1-diphenyl-2-mercapto-3-methyl-1-butanol **7**[1]. Synthesis of others β-mercapto-alcohols is on going.

References and notes

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6. Selected data of **8**: White solid, mp 95~96°C, yield: 28% based on **5**. $[\alpha]_D^{20}$ =+94.3 ($CHCl_3$, c=0.55). Calce. for $C_{17}H_{18}O$: C, 85.67, H, 7.61; found C, 85.79, H, 7.58. IR (*v*, KBr): 1671 (C_6H_5), 1241 (C-O-C) cm^{-1}. ^{1}H-NMR (δ_H, $CDCl_3$): 0.75 (d, 3H, J=6.8, CH_3), 1.01 (d, 3H, J=6.4, CH_3), 2.55~2.64 (m, 1H, $(CH_3)_2CH$), 4.21 (d, 1H, J=10.4, CH), 7.20~8.00 (m, 10H, $2\times C_6H_5$).
7. Selected data of **7**: Slight yellow solid, mp 78~80°C, yield: 20% based on **10**. $[\alpha]_D^{25}$ = +135.0 (C_6H_6, c=0.78). Calce. for $C_{17}H_{20}OS$: C, 74.96, H, 7.40; found C, 75.05, H, 7.46. IR (*v*, KBr): 3482(OH), 2576 (SH), 1598, 1485,1477 (C_6H_5) cm^{-1}. ^{1}H-NMR (δ_H, $CDCl_3$): 0.97 (d, 3H, J=6.8, CH_3), 1.03 (d, 3H, J=6.8, CH_3), 1.11 (d, 1H, J=4.8, SH), 1.84~1.96 (m, 1H, $(CH_3)_2CH$), 3.45 (2, 1H, OH), 4.14 (dd, 1H, CHCHSH), 7.26~7.58 (m, 10H, $2\times C_6H_5$).

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