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TETRAHEDRON: *ASYMMETRY*

A new access to β-methyl substituted secondary alcohols. Application to the synthesis of 4-methylheptan-3-ol

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Abstract

All four stereoisomers of 4-methylheptan-3-ol were synthesized by a five-step route starting from 4-thianones. Key steps in the synthesis include: (a) reduction of 3-propyl-4-thianone to yield an easily separable isomeric mixture of *cis*- and *trans*-3-propyl-4-thianols; and (b) a highly efficient resolution of the particular *cis*/*trans*-isomers through a chromatographic separation of their respective esters with (*S*)-chlorofluoroacetic acid. Subsequent hydrolysis and desulfurization gave the required compounds in 18% overall yield. All the stereoisomers are obtained with purities better than 90%.

1. Introduction

The -CH(OH)-CH(CH_3)- motifs with two stereogenic centers represent a common structural feature for a variety of biologically important natural products. Among them, pheromones of the general type **A** have gained considerable attention due to their potential use in insect pest management strategies. Consequently, the development of synthetic routes to these compounds and their precursors has become an important part of natural product chemistry, as well as chemical ecology and related disciplines.[1] Searching for a simple and efficient method for preparing compounds of the type **A** with defined stereochemistry, we turned our attention to substituted 4-thianols **B** and **C** whose general ability to serve as synthetic equivalents of corresponding acyclic compounds has been well-documented.[2]

The present work was undertaken as a model study in order to demonstrate the utility of the synthon **B** (R_1=*n*-C_3H_7, R_2=H; Scheme 1) in conjunction with our chlorofluoroacetic acid (CFA)-based method[3,4] for the resolution of chiral alcohols for the synthesis of 4-methylheptan-3-ol (**1**, **A**: R_1=*n*-C_3H_7, R_2=H). The synthetic usefulness of the keto group in structure **B** has already been shown by Hoffmann et al.,[16] who used it as a substrate for an enzymatic reduction, leading finally to (3*S*,4*S*)-**A** (R_1=*n*-C_3H_7,

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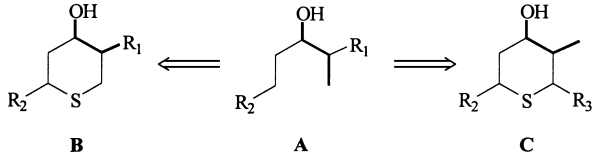
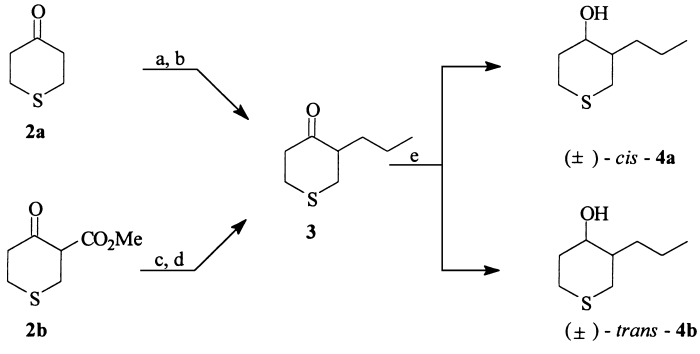
R_2=H). In our experiments, we selected alcohol **1** as a model compound for two reasons: (i) at least two isomers of **1** are insect pheromones of considerable interest, i.e. the (3*R*,4*S*)-isomer which has been identified[5] as a trail pheromone of the ponerinae ant *Leptogenys diminuta*, and the (3*S*,4*S*)-isomer which is known[6] as an aggregation pheromone component of the smaller European elm bark beetle, *Scolytus multistriatus*; and (ii) the syntheses of **1**, although rather extensively studied,[7] have been primarily directed towards the (3*S*,4*S*)-isomer using either a suitable chiral substrate or applying stereoselective enzymatic reactions such as reductive and/or resolution steps. To the best of our knowledge, only three methods have been designed to prepare all the four possible stereoisomers of **1**. These methods include: (a) multiple HPLC separations of the corresponding MTPA esters on an analytical scale;[8] (b) sequential constructions of stereogenic carbon centers via the (α-haloalkyl) boronic esters of chiral *vic*-diols;[9] and (c) fractional crystallization of racemic dinitrobenzoates followed by hydrolysis and enzymatic resolution of enantiomeric pairs.[10] These methods suffer from rather circuitous routes,[9] poor enantiomeric excesses[8,10] and/or the use of difficult-to-access starting material.[9]



Scheme 1.

Considering the above limitations of the earlier syntheses of **1**, the need to develop a short and efficient synthesis is apparent. We report herein a method for the synthesis of all four stereoisomers of **1** which provides an important extension to known methodology in that it allows for: (i) the use of an easily accessible common intermediate **4** (Scheme 2) for preparing all possible isomers; and (ii) the use of (*S*)-chlorofluoroacetic acid (CFA) as an excellent derivatizing agent for resolving the enantiomeric pairs of **4**.



Scheme 2. (a) CH_2=$CHCH_2OH$, TsOH, C_6H_6; (b) H_2, PtO_2, EtOH; (c) *n*-PrI, NaH; (d) H_2O; (e) $LiAlH_4$

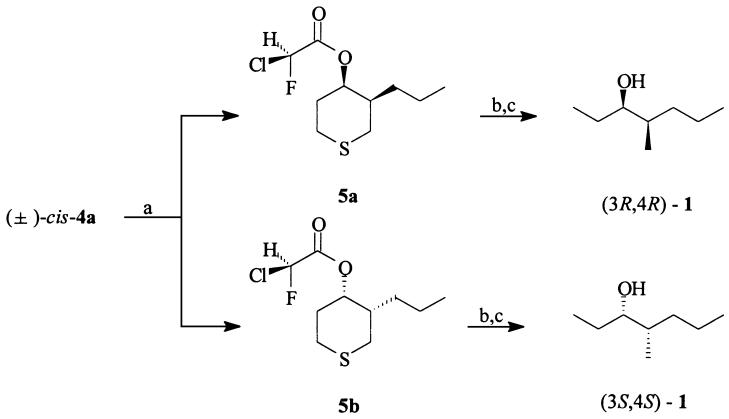
2. Results and discussion

Following the strategy shown in Scheme 1, the standard method[11,12] of introducing a C-3 substituent into the 4-thianones, i.e. alkylation with *n*-propyliodide of the readily available ketoester **2b**[17] followed by decarboxylation, was first used to prepare 3-propyl-4-thianone **3**. Unfortunately, using this method, the overall yield of **3** was lower than 30%. An alternative two-step method based[13,14] on the Claisen rearrangement of the allyl vinyl ether derived from commercially available 4-thianone **2a** with subsequent

hydrogenation of the preformed 3-allyl-4-thianone was found to be more favorable, affording **3** in about 90% overall yield.

The reduction of **3** with lithium aluminium hydride at −30°C in dry diethyl ether furnished the alcohol **4** as an approximately 1:1 mixture of two (R_f ≅0.55 vs. 0.48, TLC silica gel, diethyl ether:hexane, 1:1) compounds. The mixture was readily separated into its individual components by flash chromatography and the compounds were identified as *cis*- and *trans*-isomers of **4** by ^{1}H NMR spectroscopic comparisons of the chemical shifts of the C-4 protons. The orientation of propyl/hydroxyl groups was found to be either equatorial/axial **4a** or axial/axial **4b**. The diastereomeric 1:1 ratio of **4a**:**4b** demonstrates almost negligible influence of the cyclic thiane auxiliary with regard to the diastereoselectivity of the reduction. On the other hand, the presence of the thiane ring appears to be responsible for exceptionally good separation and, in turn, purification of the **4a**/**4b** diastereomers.

We have recently shown[3,4] that enantiopure chlorofluoroacetic acids (CFA) can be used to efficiently resolve many of the secondary alcohols and/or amines. Considering that (*S*)-CFA may be readily synthesized[15] from trifluorochloroethylene in >100 g quantities and its analytical potential has been shown in several respects to be even superior to the frequently used Mosher's acid, we found it reasonable to extend its applicability to synthetic purposes. Thus, treatment of **4a** with (*S*)-CFA in the presence of DCC gave rise to two diastereomeric acetates **5a** and **5b** (Scheme 3). The diastereomers, showing R_f=0.62 and 0.53, respectively (TLC, silica gel, 10% diethyl ether in hexane), were separated by flash chromatography and their configuration identified as (3*R*,4*R*)-**5a** and (3*S*,4*S*)-**5b**. Characteristic doublets in ^{1}H NMR spectra δ≈6.2 ppm ($J_{H–F}$=50 Hz) together with $\Delta\delta_{(S,R/S,S)}$=2 Hz allow their easy assignment. It is to be noted that, although the (*S*)-CFA is readily accessible, the procedure is designed in such a way that this acid can be recovered and reused. Each of the isomers **5a** and **5b** was in turn converted into the corresponding (3*S*,4*S*)- and (3*R*,4*R*)-**1** by desulfurization with Raney Ni in methanol.[16] Other cleavage methods available for ring fission according to Scheme 1, e.g. the use of Ni_2B,[14] failed to give better results, probably as a consequence of some isolation problems emerging from the use of larger methanol volumes required. The stereochemistry of the final products as well as that of reaction intermediates was subsequently confirmed by comparing the specific rotations with available literature values.



Scheme 3. (a) (*S*)-CFA, DCC, 0°C, CH_2Cl_2; (b) NaOH, MeOH; (c) RaNi, MeOH

Related sequences as depicted in Scheme 2 for **4a** paved the way to (3*S*,4*R*)-**1** and (3*R*,4*S*)-**1** starting from **4b**. The stereochemistry of (3*S*,4*R*)-**1** and (3*R*,4*S*)-**1** enantiomers as well as their chlorofluoroacetate precursors was elucidated in a similar manner as described above for the (3*S*,4*S*)-**1** and (3*R*,4*R*)-**1**.

Table 1
The product composition

Product	Content of stereoisomers (%)			
	(3*R*,4*R*)-**1**	(3*S*,4*S*)-**1**	(3*R*,4*S*)-**1**	(3*S*,4*R*)-**1**
(3*R*,4*R*)-**1**	94.10	5.59	0.31	-
(3*S*,4*S*)- **1**	4.98	94.67	-	0.33
(3*R*,4*S*)-**1**	2.91	0.18	92.06	4.85
(3*S*,4*R*)-**1**	0.21	3.46	5.2	91.13

In order to determine the purity of the products, the prepared 4-methylheptan-3-ols were esterified with (*S*)-CFA/DCC, and the thus formed esters were subjected to GC investigation under the given conditions. The elution order of the respective ester stereoisomers corresponds to (3*R*,4*R*)-, (3*S*,4*S*)-, (3*R*,4*S*)- and (3*S*,4*R*)-4-methylheptan-3-ols. Composition of the products can be found in Table 1.

In conclusion, we have presented a facile synthetic access to the four stereoisomers of **1**, demonstrating that resolution may still play an important role in the preparation of chiral pheromone-like compounds. Major advantages of our methodology are its conceptual simplicity and ease of designing and executing straightforward routes to a wide variety of chiral compounds of the general type **A** by using rationally designed R_1–R_3 substituted thianones **B** and/or **C** as starting materials. Research along these lines is being carried out in this laboratory.

3. Experimental

All compounds were characterized by elemental analyses with ±0.2% accuracy. NMR data were taken either on Varian Unity-200 or 500 spectrometers (200.04 or 499.8 MHz, respectively, in deuterochloroform with TMS as an internal standard). Chemical shifts are expressed in δ scale while *J* values are given in hertz. For IR (CCl_4) and mass recordings, a Perkin–Elmer spectrometer and ZAB EQ instrument (VG, Great Britain; EI 70 eV) were used, respectively. GC analyses were performed on a Hewlett–Packard chromatograph (DB5 column: 30 m×0.25 mm i.d.) with helium as the carrier gas. Activated Raney nickel (Merck, 820876) was used without any further treatment.

*3.1. 3-Propyltetrahydro-2*H*-thiopyran-4-ol **4***

To a suspension of lithium aluminium hydride (0.21 g, 5.37 mmol) in dry diethyl ether (8 ml) cooled to −30°C was slowly added a solution of 3-propyltetrahydro-2*H*-thiopyran-4-one (0.85 g, 5.37 mmol) in 5 ml of diethyl ether. The reduction is over within minutes (TLC) and the reaction mixture was then decomposed by adding a solution of NaOH (0.45 g) in water (2 ml). Stirring was continued for 2 h at the room temperature. Then the solid was removed by filtration and diethyl ether evaporated using the evaporator. The rest was chromatographed (MPLC, column 90×180 mm, silica gel 60, 0.063–0.2 μ, Merck, 30% of diethyl ether in light petroleum, flow rate: 10 ml min^{-1}) in order to separate the isomers. Repeated chromatography afforded almost pure isomers whose stereochemistry was determined by ^{1}H NMR (500 MHz).

3.1.1. cis-*3-Propyltetrahydro-2*H-*thiopyran-4-ol* ***4a***

Yield: 0.235 g; $R_f \approx 0.55$ (TLC, silica gel, 50% of diethyl ether in hexane; contained 0.7% of *trans*-isomer (GC)); δ_H: 0.92 (t, *J*=6.9, 3H, CH_3), 1.34–1.38 (m, 2H, 2×CH_2), 1.79 (m, *J*=2.6, 3.4, 6.0, 7.4, 10.4, 1H, CH_2CH(propyl) ax.), 1.89 (dddd, *J*=2.6, 3.5, 11.5, 13.9, 1H, HOCHCH_2 eq.), 2.08 (ddt, *J*=2.9, 5.4, 5.4, 13.9, 1H, HOCHCH_2 ax.), 2.31 (ddd, *J*=1.7, 3.4, 13.8, 1H, SCH_2CH eq.), 2.75 (dd, *J*=10.4, 13.8, 1H, SCH_2CH ax.), 2.96 (ddd, *J*=2.9, 11.5, 13.8, 1H, SCH_2CH_2 ax.), 2.32 (dddd, *J*=1.7, 3.5, 5.2, 13.8, 1H, SCH_2CH_2 eq.), 3.91 (dt, *J*=2.6, 2.6, 5.5); ν_{max}/cm^{-1}: 3625, 3382, 1380, 1048, 1022, 678; *m*/*z*: 160, 151, 143, 134 (BP), 117, 99, 61, 41.

3.1.2. trans-*3-Propyltetrahydro-2*H-*thiopyran-4-ol* ***4b***

Yield: 0.266 g; $R_f \approx 0.48$ (TLC, silica gel, 50% of diethyl ether in hexane; contained 6% of *cis*-isomer (GC)); δ_H: 0.93 (t, *J*=7.1, 3H, CH_3), 1.22–1.51 (m, 4H, 2×CH_2), 1.71 (dddd, *J*=3.6, 9.7, 10.7, 13.2, 1H, HOCHCH_2 ax.), 2.23 (dddd, *J*=2.9, 3.5, 5.7, 13.2, 1H, HOCHCH_2 eq.), 1.77 (m, *J*=3.4, 7.3, 9.8, 10.8, 1H, CH_2CH(propyl) ax.), 2.31 (dd, *J*=9.8, 13.9, 1H, SCH_2CH eq.), 2.79 (ddd, *J*=2.2, 3.4, 13.9, 1H, SCH_2CH ax.), 2.61 (ddd, *J*=2.9, 10.7, 13.7, 1H, SCH_2CH_2 ax.), 2.70 (dddd, *J*=2.2, 3.6, 5.7, 13.7, 1H, SCH_2CH_2 eq.); ν_{max}/cm^{-1}: 3625, 3421, 1429, 1380, 1272, 1023, 678; *m*/*z*: 160, 142, 113, 99 (BP), 59, 41.

*3.2. Synthesis of (3*R,*4*R*)- and (3*S,*4*S*)-3-propyltetrahydro-2*H*-thiopyran-4-yl (2*S*)-2-chloro-2-fluoro-ethanoate*

To a mixture of **4a** (0.235 g, 1.47 mmol), (*S*)-chlorofluoroacetic acid (0.18 g, 1.6 mmol) and 4-dimethylamino pyridine (0.150 g, 1.6 mmol) in dry methylene chloride (15 ml) was added dropwise a solution of dicyclohexylcarbodiimide (0.33 g, 1.6 mmol) in 5 ml of the same solvent, under stirring, N_2 and at 0°C. Then the reaction mixture was checked by TLC (silica gel, 10% of diethyl ether in light petroleum) and when **4a** disappeared (about 45 min), the solid (dicyclohexylurea) was removed by filtration through Celite 545 (5 g), and the solvent evaporated. The rest was covered several times with light petroleum and the solid (dicyclohexylurea) removed by filtration again. The yellowish oil was chromatographed (column 30×300 mm, silica gel 60, 0.063–0.2 μ, Merck, 10% of diethyl ether in light petroleum, flow rate: 10 ml min^{-1}) in order to separate the diastereoisomers. Repeated chromatography afforded almost pure diastereoisomers whose stereochemistry was determined by correlation with the known structure of the final products as follows.

*3.2.1. (3*R,*4*R*)-3-Propyltetrahydro-2*H-*thiopyran-4-yl (2*S*)-2-chloro-2-fluoroethanoate* ***5a***

Yield: 0.119 g; $R_f \approx 0.62$ (TLC, silica gel, 10% of diethyl ether in hexane; contains 0.7% of (3*S*,4*S*)-**5**, (GC)); $[\alpha]_D^{21}$ −30 (*c* 1.1, pentane); δ_H: 0.90 (t, *J*=7.0, 3H, CH_3), 1.18–1.42 (m, 4H, 2×CH_2), 1.94 (dddd, *J*=2.3, 3.9, 12.2, 14.5, 1H ax., SCH_2CH_2), 2.29 (ddt, *J*=2.6, 5.0, 5.0, 14.5, 1H eq., SCH_2CH_2), 2.29 (m, 1H, CH_2CH), 2.42 (ddd, *J*=1.7, 3.4, 13.8, 1H, SCH_2CH eq.), 2.76 (dd, *J*=11.1, 13.8, 1H, SCH_2CH ax.), 5.22 (dt, *J*=2.3, 2.3, 5.2, 1H, OCH), 6.314 (d, *J*=50.5, 1H, CHClF); ν_{max}/cm^{-1}: 1771, 1754, 1429, 1297, 1286, 1268, 1109, 665; *m*/*z*: 254, 142, 113 (BP), 99, 95, 87, 67, 55, 41.

*3.2.2. (3*S,*4*S*)-3-Propyltetrahydro-2*H-*thiopyran-4-yl (2*S*)-2-chloro-2-fluoroethanoate* ***5b***

Yield: 0.142 g; $R_f \approx 0.53$ (TLC, silica gel, 10% of diethyl ether in hexane; contains 6% of (3*R*,4*R*)-**5**, (GC)); $[\alpha]_D^{24}$ +36 (*c* 1.2, pentane); δ_H: 0.89 (t, *J*=7.2, 3H, CH_3), 1.18–1.42 (m, 2H, 2×CH_2), 1.96 (dddd, *J*=2.3, 3.8, 12.0, 14.5, 1H, SCH_2CH_2 ax.), 2.29 (m, 1H, SCH_2CH_2 eq.), 2.29 (m, 1H, SCH_2CH ax.), 2.42 (m, 1H, SCH eq.), 2.40 (m, 1H, SCH_2 eq.), 2.86 (m, 1H, SCH ax.), 6.310 (d, *J*=50.5, 1H,

CHClF); ν_{max}/cm^{-1}: 1771, 1752, 1430, 1297, 1291, 1268, 1082; *m*/*z*: 254, 142, 113 (BP), 99, 87, 67, 55, 41.

*3.3. Synthesis of (3*R,*4*S*)- and (3*S,*4*R*)-3-propyltetrahydro-2*H*-thiopyran-4-yl (2*S*)-2-chloro-2-fluoro-ethanoate*

According to the above-mentioned procedure, **4b** (0.266 g, 1.66 mmol) was subjected to esterification with (*S*)-CFA. The obtained diastereoisomers were separated as follows.

*3.3.1. (3*R,*4*S*)-3-Propyltetrahydro-2*H*-thiopyran-4-yl (2*S*)-2-chloro-2-fluoroethanoate*

Yield: 0.114 g; $R_f \approx 0.61$ (TLC, silica gel, 10% of diethyl ether in hexane; contains 5.1% of (3*S*,4*R*)-**5** (GC)); $[\alpha]_D^{21}$ −34.0 (*c* 0.32, pentane); δ_H: 0.92 (t, *J*=7.2, 3H, CH_3), 1.20–1.61 (m, 2H, 2×CH_2), 1.90 (dddd, *J*=3.6, 9.2, 10.5, 13.5, 1H, SCH_2CH_2), 1.94 (dddt, *J*=3.6, 7.3, 7.3, 8.6, 10.8, 1H, SCH_2CH_2), 2.40 (m, 2H, SCH_2), 2.62 (m, 2H, SCH_2), 2.29 (m, 1H, SCH_2CH ax.), 4.77 (dt, *J*=3.6, 8.6, 8.6, 1H, OCH), 6.294 (d, *J*=50.5, 1H, CHClF); ν_{max}/cm^{-1}: 1770, 1754, 1428, 1297, 1285, 1268, 1091; *m*/*z*: 254, 142, 113, 99 (BP), 87, 67, 55, 41.

*3.3.2. (3*S,*4*R*)-3-Propyltetrahydro-2*H*-thiopyran-4-yl (2*S*)-2-chloro-2-fluoroethanoate*

Yield: 0.144 g; $R_f \approx 0.55$ (TLC, silica gel, 10% of diethyl ether in hexane; contains 5.4% of (3*R*,4*S*)-**5** (GC)); $[\alpha]_D^{21}$ +34.5 (*c* 0.74, pentane); δ_H: 0.91 (t, *J*=7.2, 3H, CH_3), 1.18–1.59 (m, 2H, 2×CH_2), 1.87 (dddd, *J*=3.6, 8.5, 10.3, 13.5, 2H, SCH_2CH_2), 1.94 (dddt, *J*=3.5, 7.2, 7.2, 8.7, 10.6, 1H, SCH_2CH_2), 2.40 (m, 2H, SCH_2), 2.64 (m, 2H, SCH_2), 4.75 (dt, *J*=3.6, 8.7, 8.7, 1H, OCH), 6.289 (d, *J*=50.5, 1H, CHClF); ν_{max}/cm^{-1}: 1772, 1752, 1430, 1380, 1297, 1293, 1268, 1030, 659; *m*/*z*: 254, 142, 113, 99 (BP), 87, 67, 55, 41.

3.4. General procedure for the synthesis of 4-methylheptan-3-ols

Esters **5** (0.142 g, 0.56 mmol) were hydrolyzed first in the mixture of sodium hydroxide (0.026 mg, 0.65 mmol), methanol (0.4 ml) and water (0.8 ml). The hydrolysis is over almost immediately under rt. The obtained substrate was desulfurized by the procedure as follows while the water solution of (*S*)-CFA–sodium salt served for the later isolation of an acid.[3] Thus, alcohols **4** (0.082 g, 0.51 mmol) in methanol (1 ml) and Raney nickel (0.15 g) were vigorously stirred for several minutes at 90°C. When the reaction was complete (TLC), about the same volume of CH_2Cl_2 was added and the catalyst was removed by filtration through Celite 545 (5 g). The solution was extracted with water (3×2 ml), the water layer with CH_2Cl_2 (1×2 ml) and the combined organic solution dried with $MgSO_4$. The crude product was re-chromatographed (Pasteur pipet, silica gel, 5% of diethyl ether in pentane). We obtained the following products.

*3.4.1. (3*S,*4*S*)-4-Methylheptan-3-ol*

Starting from (3*S*,4*S*)-**5** (0.142 g, 0.56 mmol) and using the above procedure, 0.034 g (51%) of the product was obtained. $[\alpha]_D^{21}$ −21.1 (*c* 0.28, pentane) (lit.:[6] $[\alpha]_D^{22}$ −21.7 (*c* 0.57, hexane)); δ_H: 0.86 (d, *J*=6.8, 3H, CH_3), 0.89 (t, *J*=6.6, $CH_3(CH_2)_2$), 0.96 (t, *J*=7.4, $CH_3(CH_2)$), 1.04–1.56 (m, 7H, 3×CH_2, CH), 3.35 (ddd, *J*=3.5, 5.2, 8.8, C*H*OH); ν_{max}/cm^{-1}: 3638, 3383, 2967, 2935, 2875, 1466, 1457, 1380, 1102, 969, 950; *m*/*z*: 112, 97, 83, 70, 59 (BP), 45, 41, 32, 28.

*3.4.2. (3*R*,4*R*)-4-Methylheptan-3-ol*

Compound (3*R*,4*R*)-**5** (0.119 g, 0.47 mmol) was subjected to the same procedure as described for the preparation of (3*S*,4*S*)-4-methylheptan-3-ol. Yield: 0.030 g (56%). $[\alpha]_D^{25}$ +19.6 (*c* 0.26, pentane) (lit.:[9] $[\alpha]_D^{25}$ +22.05 (*c* 1.4, hexane)); δ_H: 0.86 (d, *J*=6.8, 3H, CH_3), 0.89 (t, *J*=6.6, C*H*$_3$(CH$_2$)$_2$), 0.96 (t, *J*=7.4, C*H*$_3$(CH$_2$)), 1.04–1.56 (m, 7H, 3×CH$_2$, CH), 3.35 (ddd, *J*=3.5, 5.2, 8.8, C*H*OH); ν_{max}/cm^{-1}: 3635, 3381, 2967, 1467, 1455, 1102, 969, 950; *m*/*z*: 112, 97, 83, 70, 59 (BP), 45, 41, 32, 28.

*3.4.3. (3*S*,4*R*)-4-Methylheptan-3-ol*

(3*S*,4*R*)-**5** (0.144 g, 0.57 mmol) was subjected to the same procedure as described for the preparation of (3*S*,4*S*)-4-methylheptan-3-ol. Yield: 0.028 g (45%). $[\alpha]_D^{21}$ +7.5 (*c* 0.2, pentane) (lit.:[18] $[\alpha]_D^{23}$ +9 (*n*-hexane)); δ_H: 0.86 (d, *J*=6.8, 3H, CH_3), 0.90 (t, *J*=7.2, C*H*$_3$(CH$_2$)$_2$), 0.95 (t, *J*=7.8, C*H*$_3$(CH$_2$)), 1.04–1.56 (m, 7H, 3×CH$_2$, CH), 3.41 (dt, *J*=4.3, 4.3, 8.4, C*H*OH); ν_{max}/cm^{-1}: 3633, 2967, 2934, 2875, 1381, 969, 950; *m*/*z*: 112, 97, 83, 70, 59 (BP), 45, 41, 32, 28.

*3.4.4. (3*R*,4*S*)-4-Methylheptan-3-ol*

(3*R*,4*S*)-**5** (0.114 g, 0.45 mmol) was subjected to the same procedure as described for the preparation of (3*S*,4*S*)-4-methylheptan-3-ol. Yield: 0.025 g (48%). $[\alpha]_D^{21}$ −6.8 (*c* 0.34, pentane) (lit.:[9] $[\alpha]_D^{25}$ −11.98 (*n*-hexane)); δ_H: 0.86 (d, *J*=6.8, 3H, CH_3), 0.90 (t, *J*=7.2, C*H*$_3$(CH$_2$)$_2$), 0.95 (t, *J*=7.8, C*H*$_3$(CH$_2$)), 1.04–1.56 (m, 7H, 3×CH$_2$, CH), 3.41 (dt, *J*=4.3, 4.3, 8.4, C*H*OH); ν_{max}/cm^{-1}: 3635, 2966, 2934, 2877, 1380, 1102, 969, 950; *m*/*z*: 112, 97, 83, 70, 59 (BP), 45, 41, 32, 28.

3.5. Determination of the purity of the products

Prepared 4-methylheptan-3-ols (2 mg) were esterified with (*S*)-CFA/DCC according to the procedure mentioned above and the arising esters were subjected to GC investigation under conditions described as follows: splitless injector (200°C), DB5 column (30 m×0.25 mm), helium: 0.6 ml min^{-1}, temperature program: 50°C (5 min delay), 0.5°C/min, 60°C (15 min delay), 0.5°C/min, 70°C. FID: 180°C. The elution order of respective ester stereoisomers corresponds to: (*R*,*R*)-, (*S*,*S*)-, (*R*,*S*)- and (*S*,*R*)-4-methylheptan-3-ols.

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