Stereoselective Synthesis of Trans Isomers of a Volatile Compound Isolated from the Elm Bark Beetle "*Pteleobius vittatus*" via Stereospecific Cyclodehydration Route

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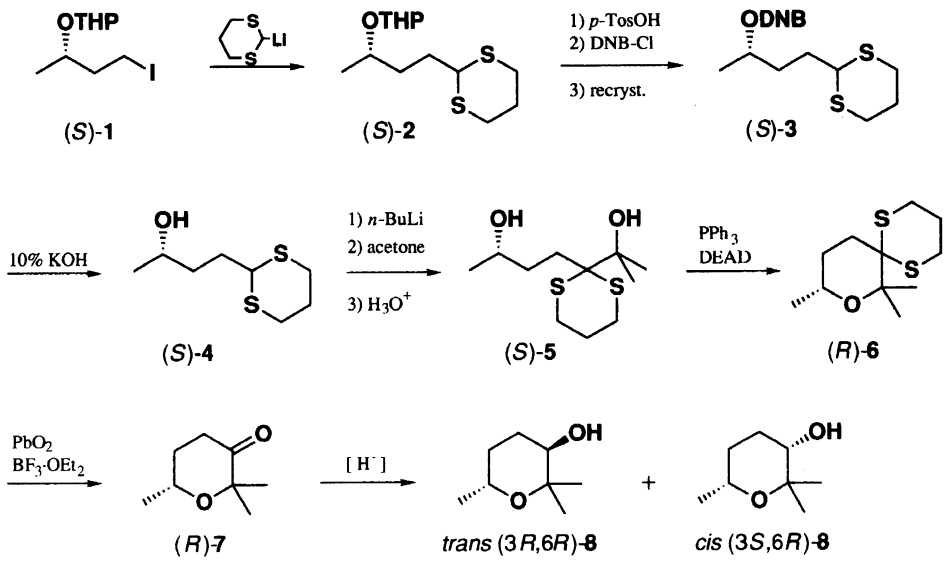
The stereoselective asymmetric synthesis of two trans isomers of the title natural product, (3*R*,6*R*)- and (3*S*,6*S*)-tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-ol, was achieved by starting with easily obtainable ethyl (*S*)-3-hydroxybutanoate, via the stereospecific asymmetric construction of substituted tetrahydropyran skeletons by the one-step cyclodehydration process of dithioacetal-functionalized chiral 1,5-diols with PPh_3 and diethyl azodicarboxylate in THF at room temperature.

Tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-ol (**8**) is a volatile compound from the elm bark beetle "*Pteleobius vittatus*", which was recently isolated by Francke and Klimetzek.[1] Although all four of its stereoisomers have already been synthesized from (*S*)- and (*R*)-sulcatol by Mori and Puapoomchareon in order to clarify the stereochemistry of the natural product, their synthesis has not emerged as a method that would allow stereocontrolled access to these isomers.[2] In previous papers, we have reported a new route to the stereocontrolled asymmetric construction of substituted tetrahydrofurans via the highly stereospecific one-step cyclodehydration of dithioacetal-functionalized chiral 1,4-diols.[3] In this paper, as an application of this cyclization process to the synthesis of cyclic ethers from 1,*n*-diols, we report the stereoselective asymmetric synthesis of the two trans isomers of the natural product, (3*R*,6*R*)- and (3*S*,6*S*)-**8** via the stereospecific one-step cyclization of dithioacetal-functionalized chiral 1,5-diols to the corresponding substituted tetrahydropyrans.

Results and Discussion

The present route to the trans isomer (3*R*,6*R*)-**8** starting with the tetrahydropyranyl (THP) ether (*S*)-**1**[4] of optically pure (*S*)-4-iodo-2-butanol is illustrated in Scheme 1. The alkylation of (*S*)-**1** with 2-lithio-1,3-dithiane in THF at −40 to 0 °C efficiently proceeded to give the THP ether (*S*)-**2** in 95% yield. The hydrolysis of (*S*)-**2** with *p*-TosOH in ethanol, followed by treatment with 3,5-dinitrobenzoyl chloride (DNB-Cl), gave the pure crystalline DNB-ester (*S*)-**3** in 52% yield after recrystallization three times from ethanol. This DNB-ester was then hydrolyzed with 10% aqueous KOH to give the optically pure alcohol (*S*)-**4** in 86% yield. Optical purity of (*S*)-**4** was determined to be >99% e.e. by the ^{1}H NMR analysis of the corresponding (+)-α-methoxy-α-(trifluoromethyl)phenylacetyl (MTPA) ester.[5] The dianion produced from (*S*)-**4** by treatment with 2.1 equiv of *n*-BuLi in THF at −40 to 0 °C was allowed to react with acetone to give the dithioacetal-functionalized 1,5-diol (*S*)-**5** in 50% yield.[6] The transformation of (*S*)-**5** into the corresponding substituted tetrahydropyran (*R*)-**6** by the one-step cyclodehydration process was examined by employing several different methods, with the results summarized in Table 1. Recently, we have reported that a similar one-step cyclodehydration of optically active 1,4-diols to the corresponding optically active tetrahydrofurans proceeded stereospecifically without racemization and epimerization by the simple treatment with *p*-TosCl in pyridine at room temperature.[3] However, the cyclization of (*S*)-**5** with *p*-TosCl in pyridine at room temperature (Method **A**) showed a loss in optical activity of the product (*R*)-**6**, while the reaction with PPh_3 and K_2CO_3 in CCl_4 (Method **B**) also gave (*R*)-**6** with worse stereospecificity. On the other hand, the cyclization employing the Mitsunobu type of intramolecular substitution reaction[7] with PPh_3 and diethyl azodicarboxylate (DEAD) in THF at room temperature (Method **C**) was found to show excellent stereospecificity. The optical purity and the absolute stereochemistry of (*R*)-**6** were determined based on those of the final product (3*R*,6*R*)-**8** transformed from the product obtained by Method **C** which will be discussed later. We have already demonstrated that a similar cyclization of 1,4-diols to substituted tetrahydrofurans by Method **A** proceeds via a S_N2 mechanism promoted by the chemoselective activation at the hydroxyl group more distant from the dithioacetal group due to steric and electrosteric effects of the dithioacetal group. On the basis of this mechanism, the present results could be rationalized such that the chiral center of the hydroxylated carbon, being more distant from the dithioacetal group, is considerably recemized via a S_N1 type of mechanism due to the entropical disadvantage in the six-membered ring (tetrahydropyran) formation when compared with the five-membered ring (tetrahydrofuran) formation of similar 1,4-diols. Although racemization by the concerted S_N1 or S_N2 type of mechanism starting with the activation of the tertiary alcohol position is not likely, this possibility can not be denied by the present data.

Thus, the dithioacetal group of the tetrahydropyran (*S*)-**6** obtained by Method **C** was then hydrolyzed with PbO_2 and $BF_3{\cdot}OEt_2$ in aqueous THF at 0 °C to give



Scheme 1.

Table 1. Stereospecific One-Step Cyclodehydration of the 1,5-Diol (*S*)-**5**

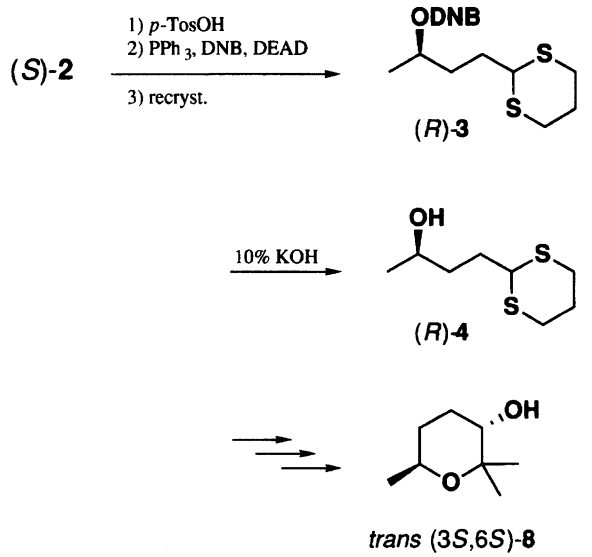
Method	Reagents (Conditions)	Tetrahydropyran (*R*)-**6**		
		Yield/%[a]	$[\alpha]_D$/° [b]	O.P.(e.e.)/%
A	*p*-TosCl (pyridine, r.t., 36 h)	30	−20.3	83[c]
B	PPh_3, K_2CO_3 (CCl_4, reflux, 24 h)	35	−19.0	78[c]
C	PPh_3, DEAD (THF, r.t., 2 d)	32	−24.4	>99[d]

a) Yield of isolated, pure product after MPLC. b) Measured at 24 °C in $CHCl_3$.
c) Calculated based on the specific rotation of the product obtained by Method **C**.
d) Determined based on the optical purity of (3*R*,6*R*)-**8** transformed from this product.

the ketone (*R*)-**7** in 80% yield. The hydride reduction of (*R*)-**7** was finally examined under a variety of reaction conditions: $LiAlH_4$, THF, −78 °C, 3 h (98%); $NaBH_4$, ethanol, 0 °C, 4 h (100%); diisobutylaluminum hydride (DIBAL-H), THF, −40—0 °C, 3 h (89%); lithium tri-*s*-butylhydroborate (L-Selectride), THF, −78 °C, 3 h (79%); *t*-BuMgCl, toluene, −78—0 °C, 4 h (64%); diisobutylaluminum-2,6-di-*t*-butyl-4-methylphenoxide, toluene, −78 °C (20 h)——10 °C (4 h) (44%).[8] We have found that all these reductions afford the trans isomer (3*R*,6*R*)-**8** with >99 : 1 selectivity without exception. Although specific rotation of (3*R*,6*R*)-**8** showed a somewhat smaller value ($[\alpha]_D^{21}$ +11.8° (*c* 1.00, ether)) than the reported value ($[\alpha]_D^{25}$ +12.6° (*c* 0.99, ether)),[2] the optical purity of the product was determined to be >99% e.e. by ^{1}H NMR analysis of the corresponding (+)-MTPA ester. These results could be well-understood based on the difficulty of the equatorial attack of a hydride to the carbonyl group, because of the high steric hindrance due to the axial α-methyl group. Recently, bulky Lewis acids such as methylaluminum bis(2,6-di-*t*-butyl-4-methylphenoxide) (MAD)[9] have been reported to be useful for blocking the less hindered carbonyl face. We thus tried the reduction of (*R*)-**7** with *t*-BuMgCl in the presence of MAD and with $LiAlH_4$ in the presence of MAD with the aim of synthesizing the corresponding cis isomer. However, even in these cases, (3*R*,6*R*)-**8** was obtained in 58 and 52% yields, respectively, without concomitant production of the cis isomer.

We have applied the present method to the synthesis of the enantiomer (3*S*,6*S*)-**8** by starting from (*R*)-**4** (Scheme 2). The alcohol obtained by the hydrolysis of (*S*)-**2** was treated under the Mitsunobu-inversion conditions with PPh_3, DNB, and DEAD and then recrystallized three times from ethanol to give the DNB ester (*R*)-**3**. This DNB ester was hydrolyzed with 10% KOH to give the alcohol (*R*)-**4** in 37% yield from (*S*)-**2** with >99% e.e. (by (+)-MTPA method). Based on the method for the synthesis of (3*R*,6*R*)-**8** from (*S*)-**4**, the alcohol (*R*)-**4** could be stereoselectively transformed into (3*S*,6*S*)-**8** of optically pure form: hydroxyalkylation with acetone, 49%; cyclization with PPh_3 and DEAD, 31%; hydrolysis with PbO_2 and BF_3·OEt_2, 80%; and $LiAlH_4$ reduction, 50%, 100% stereoselectivity.

In summary, the trans isomers of the natural prod-



Scheme 2.

uct (3*R*,6*R*)- and (3*S*,6*S*)-**8** of high enantiomeric purity could be synthesized in a stereoselective manner via the stereospecific one-step cyclodehydration route of dithioacetal-functionalized chiral 1,5-dioles. Spectroscopic data of these compounds were in good agreement with the reported values.[2)]

Experimental

Melting points were measured with a Yanagimoto micro melting-point apparatus and are uncorrected. Optical rotations were determined with an Othuka Photal PM-101 polarimeter. IR spectra were obtained on a Perkin–Elmer Model 1600 FT-IR spectrophotometer. ^{1}H NMR spectra were measured with JEOL JNM-GX400 spectrometer at 400 MHz with tetramethylsilane as an internal reference. Medium-pressure liquid chromatography (MPLC) was carried out on silica gel (Merck silica gel 60, 230—400 mesh ASTM). TLC was carried out on Merck precoated silica-gel plates (Merck silica gel 60 F_{254}).

Materials. The solvents were purified by the usual methods and freshly distilled before use. (*S*)-1-Iodo-3-(2-tetrahydropyranyloxy)butane (*S*)-**1** was prepared from ethyl 3-oxobutanoate according to the literature method.[4)] 1,3-Dithiane was prepared according to the literature method.[10)] The other reagents were supplied as high grade commercial products and used without further purification.

(*S*)-1-(1,3-Dithian-2-yl)-3-(2-tetrahydropyranyloxy)butane ((*S*)-2). To a stirred and cooled solution of 1,3-dithiane (26.8 g, 221 mmol) in THF (320 ml) at −40 °C, a 15% hexane solution of *n*-BuLi (143 ml, 231 mmol) was added dropwise at −40 °C under nitrogen. The mixture was stirred for 1 h at −40 °C and then for 2 h at 0 °C. The mixture was again cooled to −40 °C and (*S*)-**1** (60 g, 211 mmol) was added dropwise. After stirring for 1 h at −40 °C and for 2 h at 0 °C, the reaction mixture was quenched by the addition of water at 0 °C. The aqueous layer was extracted with ether and the combined organic layers were washed with water, dried over $MgSO_4$, and then concentrated under reduced pressure to give (*S*)-**2** as a pale yellow oil (55.2g, 95%). This product was used for the next reaction without purification.

(*S*)-1-(1,3-Dithian-2-yl)-3-(3,5-dinitrobenzoyloxy)-butane ((*S*)-3). To a solution of (*S*)-**2** (55.0 g, 199 mmol) in ethanol (1.1 l), was added *p*-toluenesulfonic acid monohydrate (2.5 g, 13 mmol) at room temperature. After stirring for 1 h at room temperature, the reaction mixture was neutralized with saturated aqueous $NaHCO_3$ solution and then concentrated under reduced pressure. The residue was diluted with water and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$, and then concentrated under reduced pressure. The residue was diluted with hexane–ethyl acetate (16:1 v/v). The solution was filtered through a silica-gel pad (Wakogel C-300) and the pad was then washed with ethyl acetate. Concentration of the filtrate under reduced pressure gave almost TLC-pure (*S*)-4-(1,3-dithian-2-yl)-2-butanol as a colorless oil (35.9 g, 93%): $[\alpha]_D^{24}$ +9.6° (*c* 1.04, $CHCl_3$). To a solution of this alcohol (10.0 g, 52 mmol) in pyridine (120 ml) was added 3,5-dinitrobenzoyl chloride (15.0 g, 65 mmol) at 0 °C. After stirring for 2 h at room temperature, water was added to the mixture at 0 °C. The aqueous layer was extracted with ether and the combined organic layers were successively washed with saturated aqueous $CuSO_4$, saturated aqueous $NaHCO_3$ and water, and then dried over $MgSO_4$. The crystalline residue obtained after concentration of the solution under reduced pressure was recrystallized three times from ethanol to give pure (*S*)-**3** as yellow needles (11.6 g, 58% from (*S*)-**2**): Mp 84.8—85.2 °C; $[\alpha]_D^{25}$ +35.1° (*c* 1.00, $CHCl_3$); IR (KBr) 3081, 2912, 1720, 1630, 1540, 1463, 1345, 1295, 1174, 1132, 1081, 926, 731, and 722 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.44 (d, *J*=6.4 Hz, 3H), 1.81—1.93 (m, 3H), 1.93—2.08 (m, 2H), 2.09—2.18 (m, 1H), 2.83—2.94 (m, 4H), 4.08 (t, *J*=6.6 Hz, 1H), 5.29 (tq, *J*=6.4, 6.4 Hz, 1H), 9.16 (s, 2H), and 9.23 (s, 1H). Calcd for $C_{14}H_{18}O_6N_2S_2$: C, 45.90; H, 4.85; N, 7.48%. Found: C, 46.68; H, 4.57; N, 7.28%.

(*S*)-4-(1,3-Dithian-2-yl)-2-butanol ((*S*)-4). To a solution of (*S*)-**3** (11.0 g, 28.5 mmol) in THF–H_2O (550 ml, 1:1 v/v), 1 M KOH (88 ml) (1 M=1 mol dm^{-3}) was added dropwise at 0 °C. The mixture was stirred for 1 h at 0 °C and then concentrated under reduced pressure. The residue was diluted with water and the aqueous layer was extracted with ether. The combined organic layers were washed with water, dried over $MgSO_4$ and then concentrated under reduced pressure. Purification of the residue by MPLC (hexane–ethyl acetate 1:1 v/v) gave pure (*S*)-**4** as a colorless oil (4.7 g, 86%): $[\alpha]_D^{24}$ +9.9° (*c* 1.01, $CHCl_3$); IR (NaCl) 3385, 2931, 1450, 1422, 1373, 1276, 1244, 1181, 1129, 1082, 956, 908, and 855 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.21 (d, *J*=6.8 Hz, 3H), 1.62 (br, 1H), 1.62—1.75 (m, 2H), 1.75—1.98 (m, 3H), 2.09—2.16 (m, 1H), 2.81—2.92 (m, 4H), 3.84 (quint, *J*=6.2 Hz, 1H) and 4.07 (t, *J*=7.5 Hz, 1H). Calcd for $C_8H_{16}OS_2$: C, 49.95; H, 8.38%. Found: C, 49.81; H, 8.38%.

(*S*)-2-Methyl-3-(1,3-dithian-2-yl)-2,6-heptanediol ((*S*)-5). To a stirred and cooled solution of (*S*)-**4** (4.61 g, 24.0 mmol) in THF (41 ml) at −40 °C, 15% hexane solution of *n*-BuLi (33 ml, 53 mmol) was added dropwise at −40 °C under nitrogen. The mixture was stirred for 1 h at −40 °C and then for 2 h at 0 °C. The mixture was again cooled to −40 °C and acetone (3.2 ml, 44 mmol) was added dropwise. After stirring for 4 h at −40 °C, the reaction mixture was quenched by the addition of water at 0 °C. The aqueous

layer was extracted with ether and the combined organic layers were washed with water, dried over $MgSO_4$ and concentrated under reduced pressure. Purification of the residue by MPLC (hexane–ethyl acetate 1:1 v/v) gave pure (*S*)-**5** as colorless needles (3.00 g, 50%): Mp 98.0—98.5 °C; $[\alpha]_D^{21}$ +13.3° (*c* 1.05, $CHCl_3$); IR (NaCl) 3383, 2986, 1458, 1379, 1296, 1274, 1239, 1179, 1152, 1028, 1000, 961, 912, 881, 866, 790, and 534 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.23 (d, J=5.5 Hz, 3H), 1.43 (d, J=2.3 Hz, 6H), 1.82—1.97 (m, 2H), 1.94 (t, J=5.5 Hz, 2H), 2.13 (m, 1H), 2.79—2.96 (m, 4H), and 3.78 (ddq, J=6.2, 12.3, 6.2 Hz, 1H). Calcd for $C_{11}H_{22}O_2S_2$: C, 52.75; H, 8.86%. Found: C, 52.70; H, 8.82%.

(*R*)-Tetrahydro-2,2,6-trimethyl-3,3-trimethylenedithio-2*H*-pyran ((*R*)-6). To a stirred and cooled solution of (*S*)-**5** (4.21 g, 18.1 mmol) and PPh_3 (11.4 g, 43 mmol) in THF (25 ml) at −40 °C, diethyl azodicarboxylate (7.6 g, 44 mmol) was added dropwise. The mixture was stirred for 2 d at room temperature and then concentrated under reduced pressure. The residue was diluted with hexane and filtered through a silica-gel pad (Wakogel C-300). The filtrate was concentrated under reduced pressure and the residue was purified by MPLC (hexane–ethyl acetate 6:1 v/v) to give pure (*R*)-**6** as a colorless oil (1.25 g, 32%): $[\alpha]_D^{24}$ −24.4° (*c* 1.03, $CHCl_3$); IR (NaCl) 2939, 1421, 1380, 1242, 1177, 1118, 1086, 1064, 975, 905, 844, and 799 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.16 (d, J=5.9 Hz, 6H), 1.43 (s, 3H), 1.44—1.48 (m, 1H), 1.52 (s, 3H), 1.76—1.90 (m, 2H), 2.00—2.07 (m, 1H), 2.18 (dt, J=4.0, 13.6 Hz, 1H), 2.56—2.71(m, 3H), 2.87 (ddd, J=3.2, 11.4, 14.8 Hz, 1H), 3.05 (ddd, J=3.6, 12, 14.5 Hz, 1H), and 3.83 (ddq, J=2.8, 11.8, 5.9 Hz, 1H). Calcd for $C_{11}H_{20}OS_2$: C, 56.84; H, 8.67%. Found: C, 56.59; H, 8.62%.

(*R*)-Tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-one ((*R*)-7). To a stirred and cooled solution of PbO_2 (1.70 g, 7.11 mmol) and BF_3·OEt_2 (4.7 mmol, 38 mmol) in THF–H_2O (4:1 v/v, 11 ml) at 0 °C, (*R*)-**6** (1.1 g, 4.7 mmol) was added dropwise. After stirring for 30 min at 0 °C, the mixture was filtered through a Cerite pad. The filtrate was diluted with ether, washed with saturated aqueous $NaHCO_3$ and water, and then dried over $MgSO_4$. The residue obtained by concentration of the organic layer under reduced pressure was filtered through a Cerite pad and purified by MPLC (hexane–ethyl acetate 4:1 v/v) to give pure (*R*)-**7** as a colorless syrup (0.53 g, 78%): $[\alpha]_D^{22}$ +43.1° (*c* 1.03, ether); IR (NaCl) 2978, 2937, 1718, 1448, 1377, 1229, 1170, 1142, 1079, and 999 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (d, J=5.8 Hz, 3H), 1.32 (s, 3H), 1.36 (d, 3H), 1.81—1.90 (m, 1H), 2.00—2.07 (m, 1H), 2.49—2.54 (m, 2H), and 4.06 (ddq, J=2.5, 12, 6 Hz, 1H). Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92%. Found: C, 67.44; H, 9.67%.

(3*R*,6*R*)-Tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-ol ((3*R*,6*R*)-8). To a suspension of $LiAlH_4$ (0.31 g, 2.8 mmol) in THF (35 ml), (*R*)-**7** (0.40 g, 2.8 mmol) was added dropwise at −78 °C under nitrogen. The mixture was stirred for 3 h at −78 °C and then quenched by the addition of water at room temperature. The aqueous layer was extracted with ether several times and the combined organic layers were washed with water, dried over $MgSO_4$ and then concentrated under reduced pressure. Purification of the residue by MPLC (hexane–ethyl acetate 1:1 v/v) gave pure (3*R*,6*R*)-**8** as colorless needles (0.31 g, 79%): $[\alpha]_D^{21}$ +11.8° (*c* 1.00, ehter) [lit,[2] $[\alpha]_D^{25}$ +12.6° (*c* 0.99, ether)]; IR (KBr) 3418, 2937, 1381, 1167, 1088, and 977 cm^{-1}; ^1H NMR δ=1.12 (d, J=6 Hz, 3H), 1.18 (s, 3H), 1.27 (s, 3H), 1.34 (dddd, J=4, 12, 12, 14 Hz, 1H), 1.57 (dddd, J=4, 12, 13, 14 Hz, 1H), 1.68 (ddd, J=2.5, 4, 13 Hz, 1H), 1.81 (ddd, J=2.5, 4.5, 12 Hz, 1H), 3.42 (dd, J=4.8, 14 Hz, 1H), and 3.65 (ddq, J=2.5, 12, 6 Hz, 1H). Calcd for $C_8H_{16}O_2$: C, 66.53; H, 11.18%. Found: C, 66.67; H, 11.35%.

(*R*)-1-(1,3-Dithian-2-yl)-3-(3,5-dinitrobenzoyloxy)butane ((*R*)-3). To a stirred solution of (*S*)-**2** (4.00 g, 20.8 mmol), 3,5-dinitrobenzoic acid (8.84 g, 41.7 mmol) and PPh_3 (10.9 g, 41 mmol) in THF (24 ml), diethyl azodicarboxylate (7.24 g, 42 mmol) was added dropwise at 0 °C. After stirring for 20 h at room temperature, additional 3,5-dinitrobenzoic acid (4.42 g, 20.9 mmol), PPh_3 (5.50 g, 21 mmol) and diethyl azodicarboxylate (3.62 g, 21 mmol) was added to the reaction mixture. The mixture was stirred for additional 20 h at room temperature and then concentrated under reduced pressure. The residue was diluted with chloroform and filtered through a silica-gel pad (Wakogel C-300). The residue obtained by concentration of the filtrate under reduced pressure was recrystallized three times from ethanol to give pure (*R*)-**3** as yellow needles (4.12 g, 46%): Mp 84.5—85.5 °C; $[\alpha]_D^{23}$ −35.2° (*c* 0.98, $CHCl_3$); IR (KBr) 3081, 2932, 1720, 1630, 1540, 1463, 1345, 1295, 1174, 1132, 1081, 926, 731, and 722 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.44 (d, J=6.4 Hz, 3H), 1.81—1.93 (m, 3H), 1.93—2.08 (m, 2H), 2.09—2.18 (m, 1H), 2.83—2.94 (m, 4H), 4.08 (t, J=6.6 Hz, 1H), 5.29 (tq, J=6.4, 6.4 Hz, 1H), 9.16 (s, 2H), and 9.23 (s, 1H). Calcd for $C_{14}H_{18}O_6N_2S_2$: C, 45.90; H, 4.85; N, 7.48%. Found: C, 46.59; H, 4.62; N, 7.31%.

(*R*)-4-(1,3-Dithian-2-yl)-2-butanol ((*R*)-4). This compound was prepared with (*R*)-**3** (4.00 g, 10.4 mmol) according to the procedure described for (*S*)-**4** to give pure (*R*)-**4** as a colorless oil (1.64 g, 81%): $[\alpha]_D^{24}$ −9.8° (*c* 1.00, $CHCl_3$); IR (NaCl) 3387, 2900, 1422, 1374, 1275, 1243, 1181, 1129, 959, 908, and 854 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.21 (d, J=6.8 Hz, 3H), 1.62 (br, 1H), 1.62—1.75 (m, 2H), 1.75—1.98 (m, 3H), 2.09—2.16 (m, 1H), 2.81—2.92 (m, 4H), 3.84 (quint, J=6.2 Hz, 1H), and 4.07 (t, J=7.5 Hz, 1H). Calcd for $C_8H_{16}OS_2$: C, 49.95; H, 8.38%. Found: C, 49.90; H, 8.42%.

(*R*)-2-Methyl-3-(1,3-dithian-2-yl)-2,6-heptanediol ((*R*)-5). This compound was prepared with (*R*)-**4** (1.61 g, 8.4 mmol) according to the procedure described for (*S*)-**5** to give pure (*R*)-**5** as colorless needles (1.02 g, 49%): Mp 98.1—98.7 °C; $[\alpha]_D^{22}$ −13.1° (*c* 0.99, $CHCl_3$); IR (NaCl) 3384, 2986, 1458, 1378, 1296, 1274, 1238, 1179, 1152, 1028, 1000, 961, 912, 881, 866, 790, and 534 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.23 (d, J=5.5 Hz, 3H), 1.43 (d, J=2.3 Hz, 6H), 1.82—1.97 (m, 2H), 1.94 (t, J=5.5 Hz, 1H), 2.13 (m, 1H), 2.79—2.96 (m, 4H), and 3.78 (ddq, J=6.2, 12.3, 6.2 Hz, 1H). Calcd for $C_{11}H_{22}O_2S_2$: C, 52.75; H, 8.86%. Found: C, 52.78; H, 8.70%.

(*S*)-Tetrahydro-2,2,6-trimethyl-3,3-trimethylenedithio-2*H*-pyran ((*S*)-6). This compound was prepared with (*R*)-**5** (1.88 g, 8.08 mmol) according to the procedure described for (*R*)-**6** to give (*S*)-**6** as a colorless oil (0.54 g, 31%): $[\alpha]_D^{24}$ +23.8° (*c* 0.99, $CHCl_3$); IR (NaCl) 2975, 2940, 1417, 1380, 1243, 1177, 1118, 1086, 1065, 975, 906, 844, and 799 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.16 (d, J=5.9 Hz, 6H), 1.43 (s, 3H), 1.44—1.48 (m, 1H), 1.52 (s, 3H), 1.76—1.90 (m, 2H), 2.00—2.07 (m, 1H), 2.18 (dt, J=4.0, 13.6 Hz, 1H),

2.56—2.71 (m, 3H), 2.87 (ddd, J=3.2, 11.4, 14.8 Hz, 1H), 3.05 (ddd, J=3.6, 12, 14.5 Hz, 1H), and 3.83 (ddq, J=2.8, 11.8, 5.9 Hz, 1H). Calcd for $C_{11}H_{20}OS_2$: C, 56.84; H, 8.67%. Found: C, 56.93; H, 8.73%.

(*S*)-Tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-one ((*S*)-7). This compound was prepared with (*S*)-**6** (0.40 g, 1.7 mmol) according to the procedure described for (*R*)-**7** to give pure (*S*)-**7** as a colorless syrup (0.20 g, 80%): $[\alpha]_D^{24}$ −43.1° (*c* 0.99, ether); IR (NaCl) 2977, 2936, 1719, 1447, 1377, 1229, 1170, 1142, 1077, and 999 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.26 (d, J=5.8 Hz, 3H), 1.32 (s, 3H), 1.36 (d, 3H), 1.81—1.90 (m, 1H), 2.00—2.07 (m, 1H), 2.49—2.54 (m, 2H), and 4.06 (ddq, J=2.5, 12, 6 Hz, 1H). Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92%. Found: C, 67.51; H, 10.19%.

(3*S*,6*S*)-Tetrahydro-2,2,6-trimethyl-2*H*-pyran-3-ol ((3*S*,6*S*)-8). This compound was prepared with (*S*)-**7** (0.10 g, 0.70 mmol) according to the procedure described for (3*R*,6*R*)-**8** to give pure trans (3*S*,6*S*)-**8** as colorless needles (27 mg, 50%): $[\alpha]_D^{21}$ −9.8° (*c* 0.18, ether) [lit,[2]) $[\alpha]_D^{24}$ −11.8° (*c* 0.99, ether)]; IR (KBr) 3418, 2937, 1381, 1167, 1088, and 977 cm^{-1}; ^1H NMR ($CDCl_3$) δ=1.12 (d, J=6 Hz, 3H), 1.18 (s, 3H), 1.27 (s, 3H), 1.34 (dddd, J=4, 12, 12, 14 Hz, 1H), 1.57 (dddd, J=4, 12, 13, 14 Hz, 1H), 1.68 (ddd, J=2.5, 4, 13 Hz, 1H), 1.81 (ddd, J=2.5, 4.5, 12 Hz, 1H), 3.42 (dd, J=4.8, 14 Hz, 1H), and 3.65 (ddq, J=2.5, 12, 6 Hz, 1H). Calcd for $C_8H_{16}O_2$: C, 66.63; H, 11.31%. Found: C, 66.77; H, 11.18%.

References

1) W. Francke and D. Klimetzek, unpublished results.
2) K. Mori and P. Puapoomchareon, *Liebigs Ann. Chem.*, **1988**, 175.
3) H. Chikashita, H. Yasuda, Y. Kimura, and K. Itoh, *Chem. Lett.*, **1992**, 195; H. Chikashita, Y. Nakamura, H. Uemura, and K. Itoh, *Chem. Lett.*, **1992**, 439; H. Chikashita, T. Fukushima, H. Uemura, and K. Itoh, *Chem. Lett.*, **1992**, 599.
4) K. Mori and K. Tanida, *Tetrahedron*, **37**, 3221 (1981).
5) J. A. Dale and H. S. Mosher, *J. Am. Chem. Soc.*, **95**, 512 (1973).
6) We have already used a similar dianion of 1-(1,3-dithian-2-yl)-2-propanol in the stereoselective synthesis of insect pheromone isomers: H. Chikashita, E. Kittaka, Y. Kimura, and K. Itoh, *Bull. Chem. Soc. Jpn.*, **62**, 833 (1989).
7) O. Mitsunobu and M. Eguchi, *Bull. Chem. Soc. Jpn.*, **44**, 3427 (1971).
8) H. Haubenstock, *Tetrahedron*, **46**, 6633 (1990).
9) K. Maruoka, M. Sakurai, and H. Yamamoto, *Tetrahedron Lett.*, **1985**, 3853.
10) D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975).