concurrent addition of 1 mL of 3 M NaOH and 1 mL of 30% H_2O_2. The mixture was warmed to 50 °C for 20 min and was then salted out with NaCl. The organic phase was separated and dried over $MgSO_4$.

Registry No. 1, 53566-37-3; BMS, 13292-87-0; cyclohexene, 110-83-8; 2-methyl-2-butene, 513-35-9; 9-borabicyclo[3.3.1]nonane, 280-64-8; diborane, 18099-45-1; disiamylborane, 1069-54-1; dicyclohexylborane, 1568-65-6; 2-hexyne, 764-35-2.

Sex Pheromone of the White Peach Scale: Highly Stereoselective Synthesis of the Stereoisomers of Pentagonol Propionate

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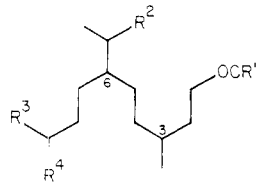
Sex pheromones of scale insects that have recently been identified are those of the white peach scale, *Pseudaulacaspis pentagona* (Targioni-Tozzetti)[1] (**1**), the yellow scale, *Aonidiella citrina* (Coquillett)[2] (**2**), and the California red scale, *A. aurantii* (Maskell)[3] (**3**). Compound **4** has also been isolated from the red scale, but is apparently not biologically active.[3] We report the details of a highly

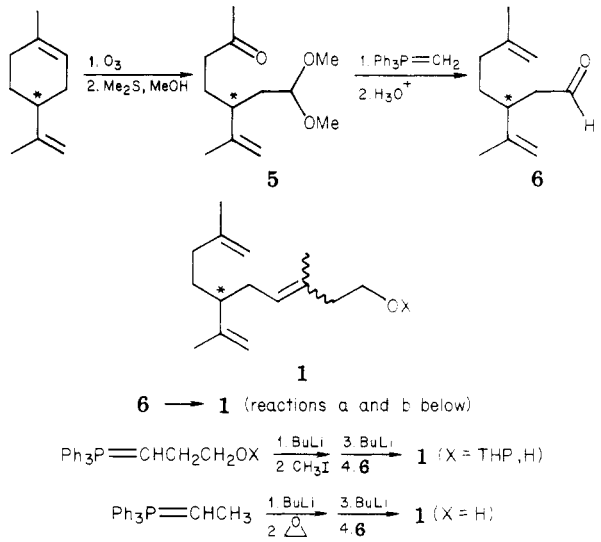


	R^1	R^2	R^3	R^4
1, Δ3(*Z*); 6*(*R*)	C_2H_5	$=CH_2$	CH_3	$=CH_2$
2, 3*(?); Δ5(*Z*); Δ8	CH_3	CH_3	CH_3	CH_3
3, Δ3(*Z*); 6*(*R*)	CH_3	$=CH_2$	H	$=CH_2$
4, 3*(?); 6*(?)	CH_3	$=CH_2$	H	$=CH_2$

stereoselective synthesis of the four stereoisomers of **1** (X = H) (Scheme I), pentagonol propionate [3,9-dimethyl-6-(1-methylethenyl)-3,9-decadien-1-ol propanoate].

A nonselective route was initially established from *dl*-limonene (see Scheme I). The ozonolysis of limonene in methanol was followed by a workup with dimethyl sulfide and *p*-toluenesulfonic acid to provide keto acetal **5** in 73% yield. Reaction of **5** with methylenetriphenylphosphorane followed by acid hydrolysis yielded the dienal **6** (80% yield). The trisubstituted olefinic linkage was then elaborated nonselectively in a multiple, single-pot alkylation in two ways: (1) The triphenylphosphonium salt derived from 3-bromo-1-propanol (hydroxyl either free or protected) was converted to an ylide, which was then alkylated with methyl iodide. The resulting salt was deprotonated and allowed to react with the dienal **6** to give **1** (X = H, 44% yield; or X = OTHP, 52% yield). (2) Alternatively,

Scheme I



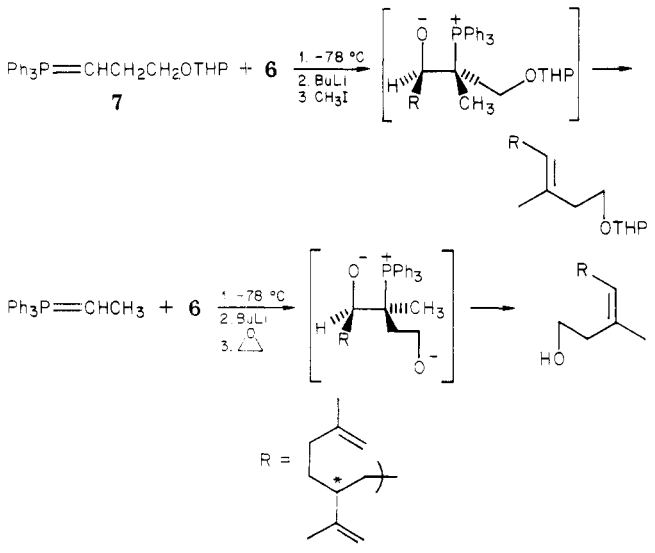
ethylidenetriphenylphosphorane was treated with ethylene oxide. The resulting hydroxyethylated betaine was treated with a second equivalent of butyllithium, producing an ylide that reacted with **6** to give **1** (X = H) in 67% yield. The geometrical compositions of the propionates were 54:46 (*Z*:*E*) by the first route and 70:30 by the second. Although we subsequently performed these reactions in a manner that provided **1** (X = H) very stereoselectively, we found that the reactions just described, if performed with readily available (*R*)-(+)-limonene and routed through the sequence using ethylene oxide for generating the trisubstituted olefin, could be coupled with preparative high-performance LC as an efficacious synthesis of gram quantities of very pure (≥99%) (*R*)-(+)-(*Z*)-**1** (X = H). In addition to providing a more favorable *Z*:*E* ratio, the ethylene oxide route generated no byproducts that were difficult to separate. In contrast, the first nonselective route employing methyl iodide and the hydroxypropyltriphenylphosphonium salt invariably provided substantial quantities (~7%) of the demethyl product, which limited the high-performance LC cleanup procedure.

Insect sex pheromones are generally isolated in quantities so limited that assessment of absolute configuration often hinges upon successful synthesis of all enantiomers and the subsequent biological evaluation.[4] The dienal **6** was therefore synthesized from both (*R*)-(+)-limonene and the (*S*)-(−)-isomer as outlined in Scheme I. The convenient method of Bergot et al.[5] was employed to determine enantiomeric purity of **6**. The dienals were oxidized to the acids and, after conversion to their acid halides, were allowed to react with (*R*)-(+)-1-(1-naphthyl)ethylamine. The diastereomer content was then determined by high-performance LC. Although complete analytical details for related compounds employing this useful procedure have been published, synthetic experimental details have not yet been reported. We have therefore incorporated the details of the derivatization in the experimental section. The (*R*)-(+)-dienal **6** was ≥99% *R*, while the enantiomer was ≥96.5% *S* (the limitations, of course, were inherent in the limonene starting material).

Successful completion of a stereoselective route required generation of the homoallylic trisubstituted linkage of **1**. Johnson's extension of the Julia method for homoallylic

(1) R. R. Heath, J. R. McLaughlin, J. H. Tumlinson, T. R. Ashley, and R. E. Doolittle, *J. Chem. Ecol.*, in press.
(2) M. J. Gieselmann, D. S. Moreno, J. Fargerlund, H. Tashiro, and W. L. Roelofs, *J. Chem. Ecol.*, **5**, 27 (1979).
(3) W. L. Roelofs, M. J. Gieselmann, A. M. Carde, H. Tashiro, C. A. Henrick, and R. J. Anderson, *Nature*, **267**, 698 (1977); *J. Chem. Ecol*, **4**, 211 (1978).
(4) The identification of the white peach scale pheromone, for example, was based upon 5 μg of material (ref 1).
(5) B. J. Bergot, R. J. Anderson, D. A. Schooley, and G. A. Henrick, *J. Chromatogr. Sci.*, in press.

Scheme II



bromides[6] and the recently published [2,3] sigmatropic rearrangement of a tin-derived methyl allyl ether anion by Still and Mitra[7] generated the required substitution patterns stereoselectively. Johnson's synthesis provided *E* geometry, while Still's produced *Z*. The latter elegant method was used to construct the related pheromone structure of the Caliornia red scale.[7]

In 1970, Corey and Yamamoto modified Schlosser and Christmann's method for *E* olefins by the Wittig reaction.[8] The intermediate betaine formed by the reaction of an ylide with an aldehyde was deprotonated at −78 °C. The resulting anion reacted very stereoselectively with certain electrophiles (H^+, formaldehyde, other aldehydes, methyl iodide) and ultimately produced trisubstituted olefins. This sequence, which has been dubbed the SCOOPY reaction,[9] was applied to obtain both the *Z* and *E* isomers of **1** (X = H) (Scheme II). Thus the betaines obtained from the reactions of (*R*)- and (*S*)-**6** with the phosphorane **7** were deprotonated and allowed to react with methyl iodide; after hydrolysis, they provided the enantiomeric *E* alkanes (35% yield of 97% *E*). The enantiomeric *Z* alkenes were obtained from the deprotonation of betaines derived from ethylidenetriphenylphosphorane with chiral **6** followed by reaction with ethylene oxide. This latter sequence appears to constitute a previously unreported and potentially useful synthesis for the *Z* homoallylic structure. The yield of *Z* alcohol was only 15% (no optimization); however, the product was 98% *Z*. The propionates were obtained from the alcohols with the customary propionyl chloride–triethylamine.

In summary, the sex pheromone of the white peach scale was synthesized very stereoselectively from (*R*)-(+)-limonene in overall 8.8% yield (≥99% *R* and 98% *Z*). Preparative high-performance LC afforded 100% *Z*. Alternatively, chiral limonene could be converted to **1** in 32.6% yield via a nonselective generation of the trisubstituted double bond with final high-performance LC separation.

(6) S. F. Brady, M. A. Ilton, and W. S. Johnson, *J. Am. Chem. Soc.*, **90**, 2882 (1968).
(7) W. C. Still and A. Mitra, *J. Am. Chem. Soc.*, **100**, 1927 (1978).
(8) (a) E. J. Corey and H. Yamamoto, *J. Am. Chem. Soc.*, **92**, 226 (1970); E. J. Corey, J. I. Shulman, and H. Yamamoto, *Tetrahedron Lett.*, 447 (1970); (b) M. Schlosser and K. F. Christmann, *Synthesis*, 38 (1969).
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Experimental Section

Gas–liquid chromatography was performed with a Varian 2400 instrument, an Ultrabond II column (3.2 mm × 1.5 m), and a Varian 3700 chromatograph using the following glass capillary columns: Carbowax 20M (0.25 mm × 35 m) and OV-101 (0.25 mm × 35 m). High-performance liquid chromatography was conducted with an analytical column of 5-μm Licrosorb Si-60, 6.3 mm × 25 cm, and a preparative column of 2–10-μm Biosil-A, 25 mm × 25 cm, as described below. Mass spectral data were obtained with a Finnegan Model 3200 chemical-ionization mass spectrometer that was equipped with a chromatographic inlet (Varian Model 1400) served by a 3% OV-101 column, 3.2 cm × 1.5 m, using either methane or isobutane as the reagent gas. Infrared data were recorded with a Nicolet 7199 FT-IR system as CCl_4 solutions, and ^1H and ^{13}C NMR data were obtained with a Bruker WHX-90 spectrometer (acetone-d_6). The ^{13}C data were collected by using a pulse width of 8 μs and 8K data points. Optical rotations were obtained with a Randolph Model 85 polarimeter with a sodium-vapor lamp.

(*R*)-(+)-7,7-Dimethoxy-5-(1-methylethenyl)-2-heptanone (5). (*R*)-(+)-Limonene, $[\alpha]^{25}_D$ +121.69 (neat) (20.4 g, 0.15 mol), was dissolved in 150 mL of MeOH and ozonized in a Welsbach T-408 generator at −72 °C (1.5 h, ca. 0.150 mol of ozone). After the solution had been purged (N_2), 0.5 g of *p*-TsOH and 25 mL of dimethyl sulfide were added. The resulting mixture was allowed to attain room temperature (0.5 h). The mixture was poured into 100 mL of cold saturated aqueous Na_2CO_3 and extracted thoroughly with petroleum ether. The organic layer was washed with water and dried (Na_2SO_4). The solvent was removed, and the residue was distilled through a short-path column to give 23.4 g (73%) of **5**: bp 74–78 °C (0.02 mm); $[\alpha]^{25}_D$ +12.14 (*c* 9.3, $CHCl_3$); IR (film) 1722 (C=O), 1190, 1158, 1127, 1067, 1056 (acetal), 890 cm^{-1} (CH_2=CR_2); NMR δ 1.59 (s, 3 H, CH_3C=), 2.03 (s, 3 H, CH_3C=O), 3.15 and 3.20 (s, 6 H, OCH_3), 4.25 (t, 1 H, $HCOCH_3]_2$), 4.75 (d, 2 H, H_2C=); chemical-ionization mass spectrum (isobutane), *m/e* (relative intensity) 215 (P +1, 2), 183 (P + 1 − CH_3OH, 100), 151 (P + 1 − $2CH_3OH$, 40). The *S* isomer, $[\alpha]^{25}_D$ −12.04 (*c* 9.3, $CHCl_3$), was obtained from (*S*)-(−)-limonene, $[\alpha]^{25}_D$ −99.04 (neat).

Anal. Calcd for $C_{12}H_{22}O_3$: C, 67.26; H, 10.35. Found: C, 67.29; H, 10.43.

(*R*)-(+)-6-Methyl-3-(1-methylethenyl)-6-heptenal (6). Methylenetriphenylphosphorane was prepared as usual from 0.11 mol each of the phosphonium bromide and butyllithium in 200 mL of THF (N_2). The ketone **5** (21.4 g, 0.10 mol) was added dropwise to the ylide solution while maintaining it at 0 °C. The resulting mixture was stirred for 1 h without cooling and was then worked up in the usual manner. The crude product was deposited onto a column of silica gel (225 g) and eluted with 300 mL of hexane and 100 mL of 5% ether–hexane. The solvent was removed and the crude diene acetal was distilled to give 16.8 g (80%): bp 57–67 °C (0.05 mm); $[\alpha]^{25}_D$ +0.12 (*c* 10.0, $CHCl_3$); IR (film) 890 cm^{-1} (H_2C=CR_2); NMR δ 1.59, 1.67 (s, 6 H, CH_3C=), 3.17, 3.20 (s, 6 H, OCH_3), 4.26 (t, 1 H, $HC(OCH_3)_2$), 4.75 (m, 4 H, H_2C=); chemical-ionization mass spectrum (isobutane), *m/e* (relative intensity) 213 (P + 1, 1), 181 (P + 1 − CH_3OH, 100).

Anal. Calcd for $C_{13}H_{24}O_2$: C, 73.54; H, 11.39. Found: C, 73.75; H, 11.44.

The acetal (14.2 g, 0.067 mol) was cleaved to the aldehyde **6** in 130 mL of THF to which had been added 1.8 mL of $HClO_4$ and water to saturate the solution. Hydrolysis was complete after 4 h at room temperature. The product was recovered in the usual manner and distilled (short path) to give 10.6 g (95%) of **6**: bp 48–52 °C (0.70 mm); $[\alpha]^{25}_D$ +22.15 (*c* 10.0, $CHCl_3$); IR (film) 2720, 1720 cm^{-1} (CH=O); NMR δ 1.63, 1.67 (s, 6 H CH_3C=), 4.73 (d, 4 H, H_2C=), 9.40 (s, 1 H, CH=O); chemical-ionization mass spectrum (isobutane), *m/e* (realative intensity) 167 (P + 1, 32), 149 (P + 1 − H_2O, 100). The *S* isomer has $[\alpha]^{25}_D$ −19.0 (*c* 10.0, $CHCl_3$).

Determination of Enantiomeric Purity of Dienal 6. The dienal (152 mg, 1.0 mmol) was dissolved in 20 mL of acetone and chilled in an ice bath. Jones reagent[10a] (0.45 mL, 1.0 mmol, 1.5

(10) (a) L. F. Fieser and M. Fieser, "Reagents for Organic Synthesis", Vol. 1, Wiley Interscience, New York, 1967, p 142; (b) p 286.

equiv) was added dropwise (2 min). The mixture was stirred for 20 min, diluted with aqueous $NaHSO_3$, and extracted thoroughly with ether. The organic phase was washed once with H_2O and then extracted with 10 mL of 1.25 N NaOH and 10 mL of H_2O. The aqueous extract was washed once with ether, acidified with 10 mL of 2 N HCl, and extracted with ether. The dried ($MgSO_4$) extract was concentrated (≤30 °C) and the residue was taken up in hexane (2 × 5 mL). The hexane solution was filtered through a pad of Na_2SO_4 and concentrated (≤30 °C), producing the liquid acid. Conversion to the acid halide was affected at room temperature with an ethereal solution of $SOCl_2$ (88 μL, 1.2 mmol) and DMF (10 μL, 0.12 mmol).[10b] After 4 h the mixture was concentrated (≤30 °C), and the residue was added dropwise as an etheral solution (1–2 mL) to a cooled solution of (*R*)-(+)-1-(1-naphthyl)ethylamine (0.5 g) in 5 mL of anhydrous ether. The chiral amine had been purchased from K and K Laboratories and was purified as a bitartrate by using (*S*)-tartaric acid. The bitartrate was recrystallized from 50% aqueous MeOH until the amide formed from (*R*)-**6** showed no further improvement in diastereomer composition. The amine was taken to be 100% *R* and the determined enantiomeric purity of **6** was thereby minimized. The amide preparation, which was quite clean judged by TLC and high-performance LC, was worked up in the usual manner and analyzed directly to avoid fractionation. The yield of amide was 211 mg (66%). Analysis by high-performance LC was done with the analytical column already described and 10% ethyl acetate–hexane (H_2O saturated) at 4 mL/min with UV detection (254 nm). The (*R*)-(+)-dienal **6** was judged to be ≥99%, and the (*S*)-(−)-isomer was ≥96.5%. The amide derivatives were collected by high-performance LC and showed the following spectral characteristics: IR (CCl_4) 3450 (amide NH), 1675 cm^{-1} (amide C=O); NMR (*R,R* diastereomer) 1.40, 1.48 (s, 6 H, CH_3C=), 1.51 (d, 3 H, J = 7 Hz, CH_3CH), 2.14 (d, 2 H, J = 7, $CHCH_2C$=O), 4.53, 4.58 (d, 4 H, H_2C=), 5.73 (m, 1 H, NH), 7–8 (m, 7 H, aryl H).

(*R*)-(+)-3,9-Dimethyl-6-(1-methylethenyl)-3,9-decadien-1-ol (Pentagonal) Propanoate (1, X = $OCCH_2CH_3$). Method A (Conventional Multiple Wittig Reaction Employing Ethylene Oxide). Ethylidenetriphenylphosphorane was prepared in the usual manner from the phosphonium bromide (19.7 g, 53 mmol) and 1 equiv of butyllithium in 100 mL of THF (N_2). The solution was chilled to −5 °C and ethylene oxide (2.65 mL, 53 mmol) was injected from a precooled syringe.

The temperature of the mixture rose to 25 °C. The mixture was stirred in an ice–MeOH bath for 0.5 h after which time another 53 mmol of butyllithium was added. The (*R*)-(+)-dienal **6** (4.4 g, 26.5 mmol) was added. The mixture was stirred for 0.25 h without cooling and was then worked up in the usual fashion (hexane extraction). A sample of the alcohol was purified by passage through a column of silica gel (5% loading) and eluted with 20% ether–hexane. GLC on OV-101 indicated a 70:30 ratio of *Z:E*. Preparative high-performance LC with 20% ether–hexane at 10 mL/min with refractive index (RI) detection resulted in collection of the *R,Z* and *R,E* alcohols: NMR (*R,Z*) δ 0.74, 1.80, 1.82 (s, 9 H, CH_3C=), 3.81 (t, 2 H, H_2COH), 4.90 (m, 4 H, H_2C=C), 5.4 (m, 1 H, HC=); NMR (*R,E*) was the same except that the allylic methyl signals were δ 1.74, 1.76, and 1.82 (s, 9 H, CH_3C=).

The propionate ester were prepared from the crude alcohol product above (presuming 26.5 mmol of alcohol) by using triethylamine (5.7 mL, 40 mmol) and proionyl chloride (3.5 mL, 40 mmol) in 125 mL of anhydrous ether in the usual fashion (ice-bath cooling while adding acid halide to the amine–alcohol solution). The crude product was purified by passage through silica gel (25 g), eluting with 5% ethyl acetate–hexane. Preparative high-performance LC with 3% ether–hexane at 10 mL/min with RI detection provided the *R,Z* propionate (3.95 g, 67%): $[\alpha]^{25}_D$ +7.10 (*c* 10, $CHCl_3$); IR (film) 1740 (ester C=O), 880 cm^{-1} (H_2C=CR_2); NMR δ 1.16 (s,CH_3), 1.74, 1.80, 1.82 (s, 9 H, CH_3C=), 4.28 (t, 2 H, CH_2O), 4.98 (m, 4 H, H_2C=), 5.55 (m, 1 H, HC=). *R,E* propionate: $[\alpha]^{25}_D$ +7.62 (*c* 10, $CHCl_2$); NMR was the same excepting δ 1.74, 1.74, 1.82, (s, 9 H, CH_3C=); chemical-ionization mass spectrum (isobutane), *m/e* (relative intensity) 270 (P + 1, 2), 205 (P + 1 − $C_2H_5CO_2H$, 100).

Anal. Calcd for $C_{18}H_{30}O_2$: C, 77.65; H, 10.86. Found: C, 77.81; H, 10.98.

Method B (Directed Wittig Reaction To Prepare the *R,E* Alcohol). The triphenylphosphonium salt of the tetrahydropyranyl ether of 3-iodo-1-propanol was obtained (as an oil) in the usual manner. The salt (7.3 g, 15 mmol) was dissolved in 75 mL of THF (N_2) and converted to the ylide with 1 equiv of butyllithium at 0 °C. The temperature was lowered to −75 °C, and the (*R*)-(+)-dienal **6** (2.28 g, 15 mmol) was added. Another equivalent of butyllithium (−75 °C) was added to the decolorized solution and, after 0.5 h, the temperature was allowed to rise to −5 °C. Methyl iodide (1.25 mL, 20 mmol) was added, and (after 0.5 h at 0 °C) the decolorized mixture was worked up in the usual fashion. Purification of the alcohol by chromatography on silica gel as described above gave 1.17 g (35%). GLC analysis of the alcohol or its propionate indicated ≥97% *E*.

Method C (Directed Wittig Reaction To Prepare the *R,Z* Alcohol). The procedure was identical with that of method B except that the phosphonium salt employed was ethyltriphenylphosphonium bromide (6.3 g, 15 mmol) and ethylene oxide (1 mL, 20 mmol) was used instead of methyl iodide. The chromatographically purified alcohol weighed 0.50 g (15%) and was ≥98% *Z*.[11]

Acknowledgment. We express our thanks to Mr. J. R. Jordan and Mr. A. T. Proveaux of this laboratory for their assistance in carrying out these experiments and for obtaining mass spectral data. We are also indebted to Dr. W. J. Ehmann of SCM Organic Chemicals, Jacksonville, FL, for generous samples of chiral limonene, and we express our appreciation to Drs. C. A. Henrick and R. J. Anderson and to Mr. B. J. Bergot of Zoecon Corp., Palo Alto, CA, for preprints of their articles and private communications regarding their synthesis of the California red scale pheromone.

Registry No. (*R,Z*)-1 (X = H), 73770-42-0; (*R,E*)-1 (X = H), 73770-43-1; (*R,E*)-1 (X = $OCCH_2CH_3$), 73770-44-2; (*R,Z*)-1 (X = $OCCH_2CH_3$), 73416-54-3; (*R*)-**5**, 73770-45-3; (*S*)-**5**, 73770-46-4; (*R*)-**6**, 73770-47-5; (*R*)-**6** (*R*)-1-(1-naphthyl)ethylamide, 73770-48-6; (*R*)-limonene, 5989-27-5; (*S*)-limonene, 5989-54-8; methylenetriphenylphosphorane, 3487-44-3; (*R*)-6-methyl-3-(1-methylethenyl)-6-hepten-1-one dimethyl acetal, 73770-49-7; ethylidenetriphenylphosphorane, 1754-88-7; ethylene oxide, 75-21-8; propionyl chloride, 79-03-8; 3-iodo-1-propanol THP ether triphenylphosphonium salt, 52103-13-6; ethyltriphenylphosphonium bromide, 1530-32-1.

(11) Mention of a commercial or proprietary product in this paper does not constitute an endorsement of that product by the USDA.

Resolution of α-Substituted Mandelic Acids via Chiral Oxazolines Using Pressurized Chromatography

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The advent of novel methods of asymmetric syntheses has led to many exciting new developments in the past few years. However, with the wide range of chiral products prepared arose the concurrent problem of determining enantiomeric purity. We have previously described,[1] along with others,[2] the separation of diastereomeric precursors, using medium- and high-pressure liquid chromatography,

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