in an oil bath preheated to 160 °C, was passed through the solution in a stream of nitrogen for 5 min. The color of the solution changed from brownish red to bright yellow during this period. Water (2 mL) was then added, the mixture was allowed to warm to room temperature, and the solvent was removed under reduced pressure. The residue was partitioned between 100 mL of ether and 50 mL of water, and the ether solution was washed with three 25-mL portions of saturated NaCl and dried over $MgSO_4$. Removal of the solvent in vacuo gave 1.1 g (85%) of the hydroxymethyl derivatives of **9**: IR ($CHCl_3$) 3450 (OH), 1757 cm^{-1} (H-bonded γ-lactone).

To a solution of 1 g (3.2 mmol) of the hydroxymethyl derivatives of **9** in 25 mL of dry pyridine at 0 °C was added 0.7 g (6 mmol) of methanesulfonyl chloride with stirring under nitrogen. The mixture was then heated at reflux for 6 h. The pyridine was removed under reduced pressure and the residue partitioned between 50 mL of ether and 25 mL of water. The ether solution was washed with three 25-mL portions of saturated NaCl and dried over anhydrous $MgSO_4$. Removal of the solvent in vacuo gave 0.69 g (74%) of the α-methylene derivatives of **9** as a dark oil: IR (thin film) 1761 (conjugated γ-lactone), 1622 cm^{-1} (conjugated C=C); NMR ($CDCl_3$) δ 6.14 and 5.61 (2 d, J = 2.0 Hz, 1 H each, $=CH_2$), 5.11 (m, 0.5 H, vinyl H), 4.70 (m, 1 H, >CHO), 3.86 (s, 4 H, OCH_2CH_2O), 1.15 (s, 3 H, angular CH_3's).

A solution of 0.54 g (1.8 mol) of the α-methylene derivatives of **9** in 75 mL of dry acetone containing 50 mg of PTSA was heated at reflux under nitrogen for 12 h. The solution was cooled to room temperature, 0.5 g of solid $NaHCO_3$ was added, and the acetone was removed under reduced pressure. The residue was partitioned between ether and water and worked up in the usual way. The crude product was then chromatographed on a column containing 20 g of Florisil. Elution with 30–50% $CHCl_3$/benzene gave 200 mg (45%) of *dl*-3-oxodiplophyllin (**1a**): mp 168–169 °C; UV (95% C_2H_5OH) 246 nm (ε 14 500); IR ($CHCl_3$) 1764 (α,β-unsaturated γ-lactone C=O), 1660 (α,β-unsaturated (C=O), 1625 cm^{-1} (conjugated C=C); NMR δ 1.25 (s, 3 H, angular CH_3), 1.83 (br s, 3 H, vinyl CH_3), 4.64 (m, 1 H, >CHO), 6.40 and 5.78 (2 d, J = 2.8 Hz, 1 H each, $=CH_2$; mass spectrum (70 eV), m/e (relative intensity) 246.1245 (100; EMC = 246.1255); 204 (68), 108 (60), 93 (42), 91 (61), 79 (45), 77 (44), 53 (50), 41 (47). These spectral properties were in close agreement with those reported by Asakawa and co-workers[5,16] for natural 3-oxodiployphyllin.

Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.14; H, 7.37. Found: C, 73.03; H, 7.36.

***dl*-Yomogin (1b).** A solution of 160 mg (0.65 mmol) of the α-methylene lactone **1a** in 30 mL of dry dioxane (freshly distilled from sodium metal) containing 160 mg (0.71 mmol) of DDQ was heated at reflux with stirring under nitrogen for 18 h. The mixture was cooled to room temperature and filtered, and the solvent was removed in vacuo. The residue was dissolved in 50 mL of benzene, and the solution was extracted with four 25-mL portions of 1% aqueous NaOH and one 25-mL portion of water. The organic phase was dried over anhydrous $MgSO_4$ and the solvent removed under reduced pressure. The residue was recrystallized from diethyl ether to give 100 mg (62%) of *dl*-yomogin (mp 170–172 °C) with IR, NMR, and mass spectral properties identical with those of an authentic sample.[6,17] The synthetic and natural material also showed identical R_f values on TLC in ether, chloroform, and benzene.

Registry No. (±)-**1a**, 56393-93-2; (±)-**1b**, 56393-94-3; (±)-**2**, 56393-88-5; (±)-**3**, 56393-91-0; (±)-**5**, 73986-30-8; (±)-**6**, 73986-31-9; **9** (4,5-ene), 56393-92-1; (±)-**9** (5,6-ene), 56393-95-4; **9** (hydroxymethyl derivative), 73986-39-7; **9** (α-methylene derivative), 56396-20-4; (±)-2-methyl-4-(ethylenedioxy)cyclohexanone, 54316-77-7; ethyl vinyl ketone, 1629-58-9; 6,6-(ethylenedioxy)-1,10-dimethyl-1(9)-octalin-2-one, 13944-80-4; ethyl bromoacetate, 105-36-2.

Stereospecific Total Synthesis of the Potent Synthetic Pyrethroid NRDC 182[1]

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A highly stereospecific synthesis of (1*R*,3*R*)-*cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid was devised which allowed for a total synthesis of the potent synthetic pyrethroid insecticide (*S*)-cyano-(3-phenoxyphenyl)methyl (1*R*,3*R*)-*cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (NRDC 182). Asymmetric reduction of 1,1,1-trichloromesityl oxide with an LAH–ephedrine complex produced (2*R*)-1,1,1-trichloro-2-hydroxy-4-methylpent-3-ene which was transformed to a diazoacetate ester via the corresponding diazoacetoacetate. Copper-catalyzed thermal decomposition of the diazoacetate resulted in internal carbenoid cyclization onto the olefin in nearly quantitative stereoselectivity. The resultant bicyclic lactone was ring opened via a Boord-type reaction to give the requisite cyclopropane acid which was esterified with racemic 3-phenoxybenzaldehyde cyanohydrin followed by crystallization and epimerization of the mother liquor to produce NRDC 182.

Since the discovery in the early seventies of the photostable and highly active synthetic pyrethroid permethrin, **1a** (Table I), by Elliott et al.,[2] synthetic pyrethroids have emerged as a new and important class of agricultural insecticides. They combine both low mammalian toxicity and biodegradibility with high activity against a large number of insect types, including the important Lepidoptera cotton pests.

Subsequent to Elliott's initial report, a number of even more active materials have been found, including decamethrin[4] (**1b**) and its dichloro analogue NRDC 182 (**1c**). While esters **1b** and **1c** are both highly potent insecticides, **1c** offers the advantage of being more stable chemically and significantly less toxic to mammals. Our recent in-

(1) (a) Presented in part at the 177th National Meeting of the American Chemical Society, Honolulu, Hawaii, Apr 1979, No. PEST 103 (C. Hatch). (b) For a communication on earlier related work see: K. Kondo, T. Takashima, and D. Tunemoto, *Chem. Lett.*, 1185 (1979).

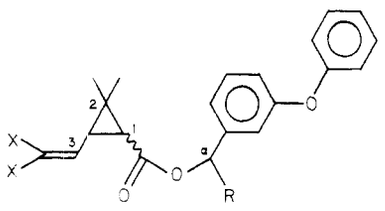
(2) M. Elliott, A. Farnham, N. Janes, R. Needham, D. Pulman, and J. Stevenson, *Nature (London)*, **246**, 169 (1973).

(3) Average topical data against several Lepidopterous insects relative to permethrin.

(4) M. Elliott, A. Farnham, N. Janes, R. Needham, and D. Pulman, *Nature (London)*, **248**, 710 (1974).

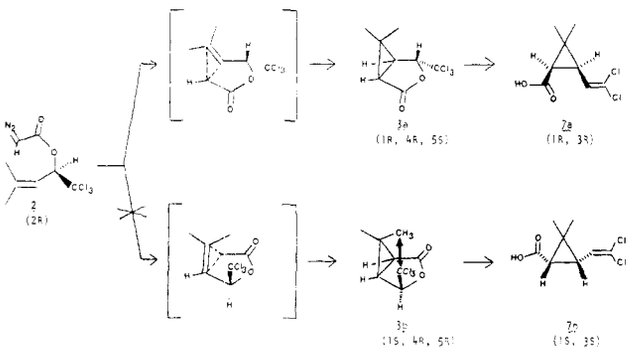
0022-3263/80/1945-3281$01.00/0

Table I

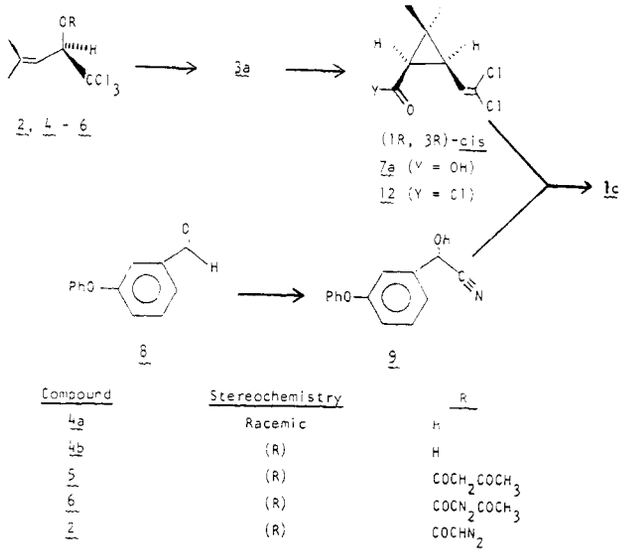


compd	X	R	stereochemistry	rel[3] activity
1a, permethrin	Cl	H	40/60 cis/trans	1
1b, decamethrin	Br	CN	(1*R*,3*R*)-cis, α *S*	10-11
1c, NRDC 182	Cl	CN	(1*R*,3*R*)-cis, α *S*	13

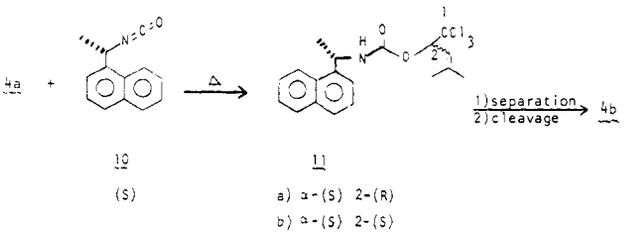
Scheme I



Scheme II



Scheme III

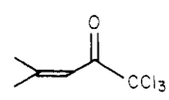


terest in this area has been in developing a commercially feasible synthesis of the dichlorovinyl ester **1c**. This report describes our novel stereospecific process to **1c**, which is also applicable to **1b**.

Ester **1c** offers an interesting synthetic challenge in that it contains three asymmetric centers in addition to a multifunctionalized cyclopropane ring. The approach taken was to prepare stereospecifically the requisite acid, esterify it with racemic cyanohydrin, separate the two resultant diastereomers, and recycle the undesired isomer. The key stereochemical control feature of the acid synthesis rests in the bicyclic lactone **3** which was generated stereospecifically from the diazo ester **2** (see Scheme I). Steric hindrance between the CCl_3 group and the CH_3 group which overlies the lactone ring prevents formation of diasteriomer **3b**. As a result, the optically active C-2 carbon in **2**, which ultimately becomes achiral in the final product, induces chirality into the two bridgehead carbon atoms of bicyclic lactone **3**.[5] The integration of this key step into the total synthesis of ester **1c** is outlined in Scheme II.

The racemic allylic alcohol **4a** was readily prepared from isobutylene and chloral in two steps via a Prins reaction followed by acid-catalyzed isomerization of the terminal olefin.[6] This material was surprisingly unreactive at the alcohol functionality, undoubtedly due to the strong electron-withdrawing nature of the adjacent trichloromethyl group. After examination of a number of possible reagents, most of which were eliminated due to unreactivity, it was found that **4a** could be resolved by using as a derivatizing agent the optically active isocyanate **10**[7] (see Scheme III). Reaction of equimolar quantities of **4a** and **10** at 80 °C for 2 days gave in high yield as a sticky solid the expected two diastereomers of carbamate **11** which could be separated by high-pressure LC. However, a more facile separation was effected simply by triturating the crude reaction mixture with hexane prior to cooling to precipitate a 60% yield of a single diastereomer, **11a** (mp 120–123 °C), of >98% isomeric purity as assayed by high-pressure LC. Cleavage of **11a** using the literature conditions of trichlorosilane–triethylamine in toluene[7] followed by column chromatography gave a 60–70% yield of the desired **4b** [mp 79–81 °C, $[\alpha]_D$ −12.1° ($CHCl_3$)], the optical purity of which was >98% as assayed by derivatization to the corresponding ester by condensation with (+)-(1*R*,3*R*)-*cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid chloride (**12**)[8] followed by GLC analysis. The identity of this (−) alcohol isomer, **4b**, as the desired *R* isomer, which leads to (1*R*,3*R*)-cis acid **7a** as indicated in Scheme I, was, in fact, determined by transforming **4b** into **7a**. A number of attempts to also utilize the (+) alcohol isomer, **4c**, from the above resolution by either inversion or racemization under both acidic and basic conditions were unsuccessful. In almost all cases the alcohol was recovered unchanged.

As an alternative approach, other than resolution, to the optically active alcohol **4b**, asymmetric reduction of 1,1,1-trichloromesityl oxide (**13**) was examined. The ketone



13

13 was obtained in good yield by a Moffat-type oxidation of **4a** using dicyclohexylcarbodiimide and dimethyl sulf-

(5) For related ring closures, see: G. Gannic, G. Linstrumelle, and S. Julia, *Bull. Soc. Chim. Fr.*, 4413 (1968); S. Danishefsky, R. McKee, and R. K. Singh, *J. Am. Chem. Soc.*, **99**, 7711 (1977); D. Tunemoto, T. Takahatake, and K. Kondo, *Chem. Lett.*, 189 (1978).

(6) E. Klimora, A. Abramov, N. Antonova, and Y. Arbuzov, *Russ. J. Org. Chem. (Engl. Transl.)*, **5** (8), 1308 (1969).

(7) W. Pirkle and M. Hoekstra, *J. Org. Chem.*, **39**, 3904 (1974).

(8) This acid chloride was found to be a very good reagent for the GLC enantiomeric excess determination of a variety of different alcohols.

Table II. Asymmetric Reduction of 1,1,1-Trichloromesityl Oxide (13) to Allylic Alcohol 4

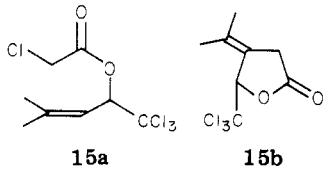
run	chiral ligand (amt, equiv)	reducing agent (amt, equiv)	solvent[e]	reaction conditions	isolated yield, %	enantiomeric[f] ratio (ee)
1	α-pinene (1.2)	9-BBN[c] (1.1)	THF	reflux for several h	0	
2	Pyr[a] (2.5)	$LiAlH_4$[d] (2.5)	Et_2O	−78 °C, 1-3 h	78	63/37 (26% *S*)
3	Pyr·HCl (2.5)				97	20/80 (60% *R*)
4	Eph[b] (2.5)				85	51/49 (2% *S*)
5	Eph·HCl (2.5)				86	14/86 (72% *R*)

[a] Pyr = (+)-(*S*)-2-(phenylaminomethyl)pyrrolidine, $[\alpha]_D$ +30.1° (*c* 1, $CHCl_3$).[13] [b] Eph = (+)-ephedrine, $[\alpha]_D$ +13.9° (*c* 1, $CHCl_3$). [c] Reagent prepared at reflux for 2 h. [d] Reagent prepared by addition of the ligand solution at −10 °C over 30 min to a suspension of the $LiAlH_4$. [e] About 1 mmol of **13** in 10 mL of solvent (total after addition). [f] By derivatization with the acid chloride **12** followed by GLC analysis on 15% QF-1. The second ester to elute contains the desired (−)-**4b** (*R* enantiomer).

oxide.[9] Several attempts at oxidation of **4a** with either $KMnO_4$ or CrO_3 were totally unsuccessful, due to preferential attack at the olefin. Initially, reduction of **13** back to racemic **4a** was demonstrated to occur cleanly and in good yield with both $NaBH_4$ and $LiAlH_4$ without concomitant olefin reduction. Following these racemic experiments, chiral reduction of **11** was examined with several reagents as outlined in Table II. As has been previously reported in the literature for related reductions, the stereoselectivity of the ligand–lithium aluminum hydride complex is quite subject to the conditions of its preparation and aging. Run 5 in Table II represents our best reduction conditions, and the optical purity of this alcohol could be improved to >95% by one recrystallization from hexane. One very interesting point from these experiments is the reversal of stereoselectivity of aluminum hydride based reagents (runs 3 and 5) over the lithium aluminum hydride based reagents (runs 2 and 4).

The *R* alcohol **4b**, which was obtained above via both resolution and reduction, was next transformed by treatment with diketene to the corresponding acetoacetate, **5** ($[\alpha]_D$ +13.7° ($CHCl_3$)), which could be purified by careful distillation. Diazo transfer to **5** to give diazoacetoacetate **6** could be effected by using *p*-toluenesulfonyl azide.[10] However, the less toxic and much less shock-sensitive reagent *p*-acetamidobenzenesulfonyl azide was found to be comparable in diazo-transfer ability and was routinely utilized to prepare **6**. Although **6** could be isolated and characterized, it was normally cleaved in situ in good yield by using sodium hydroxide in water–dioxane to the diazoacetate **2** which was purified by column chromatography on silica gel ($[\alpha]_D$ +63.0° ($CHCl_3$)). Even under best conditions, however, this reaction was always accompanied by a few percent of undesired ester hydrolysis product.

The critical ring closure of diazoacetate **2** to lactone **3a** was next examined by using a variety of catalysts and solvents. The best conversion of **2** to **3a** (65% isolated yield) was performed by using copper(II) acetylacetonate catalyst (5 mol %) and high dilution in dioxane solvent (1 g of **2**/75 mL of solvent). Under other conditions a number of byproducts were observed, including **4b**, **15a**, **15b**, and dimeric materials. However, in no case was any



15a **15b**

of the diastereomeric lactone **3b** detected or isolated, indicating the stereospecificity in the ring closure to be close to quantitative. The lactone **3a** which was isolated by column chromatography on silica gel (mp 74–76 °C, $[\alpha]_D$ −28.3° ($CHCl_3$)), as well as esters **5** and **2**, were all shown by using the optically active NMR shift reagent $Eu(hfc)_3$ to have >98% optical purity.

Opening of the lactone **3a** via a Boord-type reaction with zinc dust in acetic acid proceeded smoothly to give a crude solid which upon recrystallization from hexane gave the desired acid **7a** in 90% isolated yield: mp 90–91 °C; $[\alpha]_D$ +28.9° ($CHCl_3$). The enantiomeric purity of **7a** could be ascertained by esterification of it, via the corresponding acid chloride **12**, with (−)-2-octanol followed by GLC analysis on a 3.7-m, 15% QF-1 column.[11] The acid **7a** from the above process was shown by this means to have a >98% optical purity, once again supporting the nearly quantitative stereospecificity in the ring closure.

The final step in the preparation of **1c**, namely, esterification of acid **7**, was accomplished in good yield and purity (both chemical and optical) by addition of **12**, the acid chloride of **7a**, to preformed racemic **9** in toluene–pyridine solvent at 30 °C to give ester **16** (NRDC 168) which was composed of a mixture of two diastereomers (racemic at the α-carbon). The acid chloride **12** was readily prepared from acid **7a** via standard thionyl chloride treatment and found to be stable to careful purification by distillation, while the cyanohydrin **9** was easily prepared from the corresponding aldehyde **8** via its bisulfite addition product. In 2-propanol–ammonia solution at ice-bath temperature, the desired α*S* diastereomer, **1a**, could be selectively crystallized from **16** in 40–60% yield based on the amount of **1c** present. The remaining mother liquor could be either racemized at the α-carbon in the presence of an amine base[12] back to **14** or hydrolyzed, using aqueous sodium hydroxide to aldehyde **8** and acid **7a** with no loss of chirality in the acid moiety, thus allowing the entire diastereomeric ester to be converted to the desired **1c**.

We are currently investigating improvements in this synthesis as well as extensions of this work to the synthesis of other pyrethroids and pyrethroid intermediates.

Experimental Section

Melting points were taken on a Thomas-Hoover melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 727 spectrometer. NMR spectra were recorded either on a Varian T-60 or XL-100 instrument using $CDCl_3$ as solvent and a tetramethylsilane reference. Mass spectra (70 eV) were recorded on a Du Pont 21-490B instrument. Microanalyses were determined by the Analytical Department of FMC Corp. Gas chromatography was performed on a Hewlett-Packard 5840 instrument equipped with a flame-ionization detector and either a 3.7-m, ss, 15% QF-1 column or a 0.9-m, glass, 3% UCW 982

(9) E. J. Corey and C. U. Kim, *J. Am. Chem. Soc.*, **94**, 7586 (1972).
(10) M. Regitz, *Angew. Chem., Int. Ed. Engl.*, **6**, 733 (1967).
(11) Essentially the method of M. Horiba, A. Kobayshi, and A. Murano, *Agric. Biol. Chem.*, **41**, 581 (1977).
(12) Belgium Patent 853-866, Oct 1977, assigned to Roussel-Uclaf.
(13) T. Mukaiyama, M. Asami, J. Hanna, and S. Kobayashi, *Chem. Lett.*, 783 (1977).

column. Liquid chromatography was performed on a Waters Associates instrument equipped with a 254-nm fixed-wavelength UV photometer detector and a 25 cm × 4.6 mm id, stainless steel Zorbax-Sil silica column. In all cases hexane was a mixture of isomers.

(*R*,*S*)-1,1,1-Trichloro-2-hydroxy-4-methyl-3-pentene (4a). To a stirred solution of chloral (221.1 g, 1.5 mol, 1.0 equiv) in hexane (500 mL) cooled to 15 °C under a nitrogen atmosphere was added all at once stannic chloride (13.38 g, 0.51 mol, 0.03 equiv). To the resultant mixture was added over 30 min a stream of isobutylene (138.0 g, 2.45 mol, 1.6 equiv) during which the solution turned pale yellow and warmed slightly. The reaction was stirred at 15–20 °C an additional 30 min, after which it was diluted with water (500 mL). The resultant organic layer was separated, after which the water was back-extracted with hexane (250 mL). The combined organics were washed twice with water (400 mL each), dried over Na_2SO_4, and concentrated to give 290.35 g of a pale yellow liquid which was distilled to give 216.72 g (71%) of colorless 1,1,1-trichloro-2-hydroxy-4-methyl-4-pentene: bp 80–90 °C (2–3 mm); NMR ($CDCl_3$) δ 1.85 (s, 3, CH_3), 2.05–3.05 (m, 2, CH_2), 2.90 (br s, 1, OH), 4.05–4.30 (m, 1, Cl_3CCH), 4.90 (s, 2, $C{=}CH_2$).

A solution of the above 4-pentene (197.80 g, 1.00 mol, 1.0 equiv) and *p*-toluenesulfonic acid (10.00 g, 0.05 mol, 0.05 equiv) in hexane (500 mL) was heated at 50 °C overnight under a nitrogen atmosphere, after which GLC analysis on QF-1 showed ~75% of a new material which had a slightly longer retention time than the starting material and ~15% alcohol. The reaction was cooled, washed three times with water (500 mL each), dried over Na_2SO_4, and concentrated to give an off-white semisolid product which was recrystallized from hexane to give 86.10 g (43%) of a colorless solid: mp 79–81 °C (lit.[6] 78–80 °C); NMR ($CDCl_3$) δ 1.85 (s, 6, $C{=}C(CH_3)_2$), 2.75 (d, 1, J = 5 Hz, OH), 4.75 (dd, 1, J = 5, 9 Hz, Cl_3CCH), 5.35 (d with allylic coupling, J = 9 Hz, 1, C=CH).

(*R*)-1,1,1-Trichloro-4-methyl-3-penten-2-yl (*S*)-*N*-[1-(1-Naphthyl)ethyl]carbamate (11). A stirred mixture of (*S*)-(−)-1-(1-naphthyl)ethyl isocyanate (**10**; 7.50 g, 0.038 mol, 1.0 equiv), (*R*,*S*)-1,1,1-trichloro-2-hydroxy-4-methyl-3-pentene (**4a**; 7.75 g, 0.038 mol, 1.0 equiv), and toluene (1 mL) was heated at 80 °C under a nitrogen atmosphere for 43 h and then cooled to room temperature. GLC analysis of the crude product on UCW 982 showed 80% of the desired carbamate, but it did not resolve the two diastereomers which could be distinguished by high-pressure LC on silica gel with an isooctane/methylene chloride mobile phase. Addition of hexane (30 mL) to the crude product during cooling caused precipitation of 4.85 g (32%) of a colorless powder which was shown by high-pressure LC to be >99% of the title diastereomer (mp 117–119 °C) which could be used directly. Recrystallization of a portion of the powder from hexane gave crystalline **11**: mp 121–122 °C; $[\alpha]_D$ +10.51° (*c* 1, $CHCl_3$); IR (KBr) 1700 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.40–2.00 (m, 9, $C{=}C(CH_3)_2$ and $NCCH_3$), 5.00–6.10 (m, 4, NH, NCH, C=CH, and Cl_3CCH), 7.30–8.30 (m, 7, aromatic H).

Anal. Calcd for $C_{19}H_{20}NO_2Cl_3$: C, 56.95; H, 5.03; N, 3.49. Found: C, 57.00; H, 5.04; N, 3.22.

For reference purposes, the mother liquor from the original precipitation was concentrated and cooled to give a second crop of colorless powder which was predominately the undesired diastereomer (*S*)-1,1,1-trichloro-4-methyl-3-penten-2-yl (*S*)-*N*-[1-(1-naphthyl)ethyl]carbamate by high-pressure LC (mp 98–101 °C). Recrystallization of this powder from hexane gave the material in >99% diastereomeric purity: mp 104–105 °C; $[\alpha]_D$ −58.79° (*c* 1, $CHCl_3$).

Anal. Calcd for $C_{19}H_{20}NO_2Cl_3$: C, 56.95; H, 5.03; N, 3.49. Found: C, 57.20; H, 4.85; N, 3.45.

(*R*)-(−)-1,1,1-Trichloro-2-hydroxy-4-methyl-3-pentene (4b). To a stirred solution of (*R*)-1,1,1-trichloro-4-methyl-3-penten-2-yl (*S*)-*N*-[1-(1-naphthyl)ethyl]carbamate (**11**; 1.00 g, 0.0025 mol, 1.0 equiv) and triethylamine (0.63 g, 0.0062 mol, 2.5 equiv) in toluene (15 mL) under a nitrogen atmosphere was added dropwise over 10 min a solution of trichlorosilane (0.85 g, 0.0062 mol, 2.5 equiv) in toluene (5 mL). A white solid formed, and fuming occurred during this addition. The mixture was stirred overnight at room temperature and then heated at 40 °C for 4 h, at which time a mini workup indicated no carbamate remaining. The reaction mixture was cooled and poured into a separatory funnel containing Et_2O (40 mL) and saturated NH_4Cl (40 mL). The layers were separated, and the water layer was extracted twice with Et_2O (40 mL each) after which the combined organics were washed with saturated NH_4Cl (50 mL) and water (50 mL), dried over Na_2SO_4, and concentrated to give 0.91 g of a sticky white solid. Preparative TLC on silica gel with hexane/chloroform (1/3) eluant gave 0.41 g (82%) of white solid which was 96% pure by GLC analysis on UCW 982. Derivatization of part of the alcohol with *cis*-(1*R*,3*R*)-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid chloride (**12**) in toluene containing several equivalents of pyridine to produce the corresponding ester followed by GLC analysis on QF-1 showed that the material was >99% one diastereomer. The alcohol was therefore >98% optically pure. For **4b**: mp 79–81 °C; $[\alpha]_D$ −12.10° (*c* 1, $CHCl_3$); NMR same as for **4a**.

1,1,1-Trichloro-2-oxo-4-methyl-3-pentene (13). To a stirred solution of 1,1,1-trichloro-2-hydroxy-4-methyl-3-pentene (**4a**; 10.20 g, 0.05 mol, 1.0 equiv) in anhydrous dimethyl sulfoxide (75 mL) was added a solution of pyridine (3.98 g, 0.05 mol, 1.0 equiv) and trifluoroacetic acid (2.85 g, 0.025 mol, 0.5 equiv) in benzene (75 mL) followed by dicyclohexylcarbodiimide (31.00 g, 0.15 mol, 3.0 equiv). The resultant mixture was stirred under a nitrogen atmosphere at room temperature overnight and then diluted with Et_2O (500 mL) and a solution of oxalic acid (13.50 g, 0.15 mol, 3.0 equiv) in methanol (50 mL). After gas evolution had ceased, water (500 mL) was added, and the resultant precipitate of dicyclohexylurea was filtered off. The organic layer was washed twice with saturated aqueous $NaHCO_3$ (250 mL each) and twice with saturated aqueous NaCl (250 mL each), dried over $MgSO_4$, and concentrated to give a crude yellow liquid which was distilled to give 8.23 g (82%) of colorless liquid which was identified as the title compound **13**: bp 85–86 °C (0.1–0.2 mm); IR (thin film) 1720 (C=O), 1620 (C=C) cm^{-1}; NMR ($CDCl_3$) δ 2.10 (s, allylic coupling, 3, CH_3), 2.30 (s, allylic coupling, 3, CH_3), 6.60 (s, allylic coupling, 1, C=CH); mass spectrum (70 eV), *m/e* 200 (M^+, 3-Cl).

Anal. Calcd for $C_6H_7OCl_3$: C, 35.77; H, 3.50. Found: C, 36.33; H, 3.59.

(*R*)-(+)-1,1,1-Trichloro-4-methyl-3-penten-2-yl Acetoacetate (5). To a stirred melt of (*R*)-(−)-1,1,1-trichloro-2-hydroxy-4-methyl-3-pentane (**4b**; 2.00 g, 0.0098 mol, 1.0 equiv) and sodium acetate (~50 mg) at 80–90 °C under a nitrogen atmosphere was added dropwise over 15 min diketene (0.92 g, 0.0109 mol, 1.1 equiv). The resultant mixture was stirred at 80–85 °C for 4 h, cooled, taken up in Et_2O (20 mL), washed with aqueous 1 N HCl (20 mL), saturated aqueous $NaHCO_3$ (20 mL), and twice with water (20 mL each), dried over Na_2SO_4, and concentrated to give 2.76 g of a yellow liquid which was distilled to give 2.15 g (76%) of colorless liquid which was identified as the title compound **5**: bp 84–86 °C (0.01–0.02 mm); $[\alpha]_D$ +13.69° (*c* 1, $CHCl_3$); IR (thin film) 1755 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.90 (s with allylic coupling, 6, $C{=}C(CH_3)_2$), 2.3 (s, 3, $COCH_3$), 3.5 (s, 2, CH_2), 5.30 (d with allylic coupling, J = 9 Hz, 1, C=CH), 6.10 (d, J = 9 Hz, 1, Cl_3CCH). Approximately 10–15% enol content was indicated by additional signals at δ 1.95 (s), 5.05 (s), and 10.00 (s).

Anal. Calcd for $C_{10}H_{13}O_3Cl_3$: C, 41.77; H, 4.56. Found: C, 41.96; H, 4.62.

(*R*)-(+)-1,1,1-Trichloro-4-methyl-3-penten-2-yl Diazoacetate (2). To a stirred solution of (*R*)-(+)-1,1,1-trichloro-4-methyl-3-penten-2-yl acetoacetate (**5**; 1.00 g, 0.0035 mol, 1.0 equiv) and triethylamine (0.35 g, 0.0035 mol, 1.0 equiv) in acetonitrile (10 mL) under a nitrogen atmosphere was added at room temperature over 30 min a solution of *p*-acetamidobenzenesulfonyl azide (0.83 g, 0.0035 mol, 1.0 equiv) in acetonitrile (4 mL), during which a solid white precipitate of byproduct *p*-acetamidobenzenesulfonyl amide formed. Stirring was continued for 2 h at which time GLC analysis of the reaction mixture on UCW 982 showed no starting material and one major product of longer retention time which was (*R*)-1,1,1-trichloro-4-methyl-3-penten-2-yl diazoacetoacetate (**6**). To the crude reaction mixture was added at room temperature in one portion aqueous 1 N NaOH (10 mL; 0.010 mol of NaOH, 2.9 equiv) which resulted in disappearance of the byproduct amide precipitate. Stirring was continued an additional 1 h, at which time the reaction was diluted with Et_2O (10 mL), and the resultant layers were separated. The aqueous layer was extracted with additional Et_2O (10 mL), after

which the combined organics were washed with saturated aqueous NaCl (25 mL), dried over Na_2SO_4, and concentrated to give 0.82 g of yellow semisolid material. GLC analysis of this material indicated 82% of the title compound 1 and 10% of the alcohol **4b** resulting from undesired ester hydrolysis. The crude product was column chromatographed on silica gel (75 g) with $CHCl_3$ as eluant to give 0.69 g (73%) of a yellow oil which was ~94% pure **2** by GLC on UCW 982. For **2**: $[\alpha]_D$ +63.0° (*c* 1, $CHCl_3$); IR (thin film) 2140 (C=N_2), 1710 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.90 (s with allylic coupling, 6, C=$C(CH_3)_2$), 4.85 (s, 1, CHN_2), 5.35 (d with allylic coupling, J = 9 Hz, 1, C=CH), 6.15 (d, J = 9 Hz, 1, Cl_3CCH).

Anal. Calcd for $C_8H_9N_2Cl_3O_2$: C, 35.39; H, 3.34; N, 10.31. Found: C, 35.35; H, 3.44; N, 10.05.

(1*R*,4*R*,5*S*)-(−)-6,6-Dimethyl-4-(trichloromethyl)-3-oxobicyclo[3.1.0]hexan-2-one (3a). To a refluxing solution of copper(II) acetylacetonate (0.005 g, 2×10^{-5} mol, 0.02 equiv) in dioxane (15 mL) under nitrogen atmosphere was added over 1.5 h a solution of (*R*)-(+)-1,1,1-trichloro-4-methyl-3-penten-2-yl diazoacetate (**2**; 0.302 g, 0.001 mol, 1.0 equiv) in dioxane (5 mL). The reaction was heated an additional 2 h at reflux and then cooled to room temperature. TLC analysis on silica gel with hexane/ethyl acetate (9/1) as eluant showed very little of the starting material **3a** (R_f 0.27) and one new component (R_f 0.44). The reaction mixture was concentrated, diluted with Et_2O (30 mL), washed with aqueous $NaHCO_3$ (15 mL) and saturated aqueous NaCl (15 mL), dried over Na_2SO_4, and concentrated to give 0.26 g of a yellow oil. Column chromatography on silica gel (10 g) with CH_2Cl_2 as eluant gave 0.17 g (70%) of tan solid **3a**: mp 74–76 °C; $[\alpha]_D$ −28.27° (*c* 1, $CHCl_3$); IR (thin film on crude product) 1790 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.25 (s, 6, $C(CH_3)_2$), 2.10 (d, J = 5 Hz, 1, bridgehead proton), 2.30 (d, J = 5 Hz, 1, bridgehead proton), 4.55 (s, 1, Cl_3CCH).

Anal. Calcd for $C_8H_9O_2Cl_3$: C, 39.46; H, 3.73. Found: C, 39.65; H, 3.70.

(1*R*,3*R*)-(+)-*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic Acid (7a). To a stirred solution of (1*R*,4*R*,5*S*)-(−)-6,6-dimethyl-4-(trichloromethyl)-3-oxobicyclo-[3.1.0]hexan-2-one (**3a**; 0.500 g, 0.0021 mol, 1.0 equiv) in a mixture of acetic acid (1.23 g, 0.021 mol, 10 equiv) and Et_2O (10 mL) at 15–20 °C under a nitrogen atmosphere was added all at once zinc dust (1.37 g, 0.021 mol, 10 equiv). The resultant mixture was allowed to warm to room temperature and was then stirred an additional 5 h after which it was filtered through Celite, washed with water, and concentrated to give a 0.40 g (91%) of solid product which was identified as the title compound **7a**: mp 90–91 °C; $[\alpha]_D$ +28.9° (*c* 1, $CHCl_3$); IR (KBr) strong OH, 1680 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.30 (s, 6, $C(CH_3)_2$), 1.75–2.35 (m, 2, cyclopropane ring protons), 6.25 (d, 1, J = 8 Hz, C=CH), 11.95 (s, 1, OH).

Anal. Calcd for $C_8H_{10}O_2Cl_2$: C, 45.96; H, 4.82. Found: C, 45.67; H, 4.73.

Treatment of a small sample of the above **7a** with thionyl chloride followed by (−)-2-octanol in toluene containing several equivalents of pyridine gave the expected ester which was shown by GLC analysis on QF-1[9] to be 98% of the desired (1*R*)-cis configuration.

(1*R*,3*R*)-(+)-*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic Acid Chloride (12). To (1*R*,3*R*)-(+)-*cis*-3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (**7a**; 5.00 g, 0.024 mol, 1.0 equiv) was added all at once thionyl chloride (5.69 g, 0.048 mol, 2.0 equiv) under a nitrogen atmosphere at room temperature. The resultant mixture was stirred for 1 h, heated to 35–40 °C for 1 h, and then carefully distilled to give 4.86 g (89%) of colorless liquid which was identified as the title compound **12**: bp 74–75 °C (0.1 mm); $[\alpha]_D$ +14.75° (*c* 1, $CHCl_3$); IR (thin film) 1800 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.25, 1.33 (2 s, 6, $C(CH_3)_2$), 2.13–2.53 (m, 2, cyclopropane ring protons), 5.90–6.10 (m, 1, C=CH).

(*R*,*S*)-Cyano-(3-phenoxyphenyl)methyl Alcohol (9). To a solution of sodium metabisulfite (19.00 g, 0.10 mol, 1.0 equiv) in water (100 mL) with vigorous stirring was added dropwise at room temperature under a nitrogen atmosphere 3-phenoxybenzaldehyde (19.80 g, 0.10 mol, 1.0 equiv). The resultant mixture was cooled to 15 °C, after which a solution of sodium cyanide (9.80 g, 0.20 mol, 2.0 equiv) in water (25 mL) was added over 30 min. The bath was removed and stirring continued for 3 h, after which time it was extracted twice with methylene chloride (100 mL each). The combined organics were dried over Na_2SO_4 and concentrated to leave 19.60 g (88%) of a yellow oil which was used without further purification. The material could be analyzed by GLC on UCW 982 after silylation with *O*,*N*-bis(trifluorosilyl)acetamide (BSTFA). For **9**: IR (thin film) strong OH, no C=O; NMR ($CDCl_3$) δ 3.80 (br s, 1, OH), 5.40 (s, 1, CHCN), 6.8–7.5 (m, 9, aromatic H's).

(*R*,*S*)-Cyano-(3-phenoxyphenyl)methyl (1*R*,3*R*)-*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (14, NRDC 168). To a mixture of alcohol **9** (2.25 g, 0.01 mol, 1.0 equiv), pyridine (2 mL), and toluene (25 mL) at 30 °C under a nitrogen atmosphere was added over 30 min a solution of acid chloride **12** (2.28 g, 0.01 mol, 1.0 equiv) in toluene (5 mL). The resultant mixture was stirred for an additional hour, cooled, washed with water (25 mL), aqueous 2 N HCl (25 mL), and water (25 mL), dried over Na_2SO_4, and concentrated to give 3.71 g (89%) of a yellow oil which was identified as the title compound. High-pressure LC analysis of the crude ester indicated approximately a 50/50 [(1*R*-cis,αR/(1*R*)-cis,αS] diastereomeric ratio. For **14**: $[\alpha]_D$ +7.76° (*c* 0.4, $CHCl_3$); IR (thin film) 1740 (C=O) cm^{-1}; NMR ($CDCl_3$) δ 1.10–1.30 (4 s, 6, $C(CH_3)_2$), 1.65–2.40 (m, 2, cyclopropane ring protons), 6.1–6.45 (m, 2, C=CH and CHCN), 6.9–7.55 (m, 9, aromatic H's).

Anal. Calcd for $C_{22}H_{19}NO_3Cl_2$: C, 63.47; H, 4.60; N, 3.36. Found: C, 63.32; H, 4.65; N, 3.30.

Crystallization of (*S*)-Cyano-(3-phenoxyphenyl)methyl (1*R*,3*R*)-*cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylate (1c, NRDC 182). A mixture of **14** (1.28 g, 0.003 mol), 2-propanol (2.5 mL), and aqueous ammonia (22° Bé, 0.2 mL) was slowly stirred for 2 days at 0 °C. The initial contact of the ammonia caused a reddish pink color which slowly dissipated after 1 day. After the 2-day period the reaction was rapidly suction filtered and the resultant oily solid washed with cold 2-propanol (2 mL). The dried solid (0.53 g, 41%) was shown by high-pressure LC to be predominantly the desired **1c**: mp 53–55 °C; $[\alpha]_D$ +30.25° (*c* 1.0, $CHCl_3$); NMR ($CDCl_3$) δ 1.15–1.25 (2 s, 6, $C(CH_3)_2$), 1.85–2.25 (m, 2, cyclopropane ring protons), 6.15 (d, 1, J = 8 Hz, C=CH), 6.35 (s, 1, CHCN), 6.9–7.55 (m, 9, aromatic H's).

Anal. Calcd for $C_{22}H_{19}NO_3Cl_2$: C, 63.47; H, 4.60; N, 3.36. Found: C, 63.73; H, 4.62; N, 3.34.

Racemization Back to 14 of the Mother Liquor from the Crystallization of 1c. A solution of the concentrated mother liquor from the crystallization of **1c** (see above; 0.50 g, 0.0012 mol, 1.0 equiv) and triethylamine (0.07 g, 0.0007 mol, 0.6 equiv) in dioxane (2 mL) was stirred at room temperature for 70 h. Concentration gave a yellow oil (0.54 g) which was shown by high-pressure LC analysis to be **14** composed of approximately a 50/50 [(1*R*)-cis, αR/(1*R*)-cis, αS] diastereomeric ratio.

Hydrolysis of the Mother Liquor from the Crystallization of 1c Back to 7a. A mixture of the concentrated mother liquor (2.00 g, 0.0048 mol, 1.0 equiv), potassium hydroxide (1.61 g, 0.0288 mol, 6 equiv), water (16 mL), and ethanol (16 mL) was refluxed under a nitrogen atmosphere for 2 h. The resulting solution was cooled, diluted with water (50 mL), and extracted four times with Et_2O (50 mL each). The resultant water layer was cooled in an ice bath, acidified with concentrated HCl to pH ~1 and extracted three times with Et_2O (50 mL each). The three acid extracts were combined, dried over Na_2SO_4, and concentrated to give 0.66 g (66%) of pale yellow solid **7a**, identical with **7a** described above.

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Registry No. **1c**, 65731-84-2; **2**, 72800-54-5; **3a**, 72843-77-7; **4a**, 72800-48-7; **4b**, 72843-76-6; **5**, 72800-50-1; **6**, 73986-06-8; **7a**, 55667-40-8; **8**, 39515-51-0; **9**, 52315-06-7; **10**, 73671-79-1; (*R*,*S*)-**11**, 72812-59-0; (*S*,*S*)-**11**, 74007-18-4; **12**, 69831-14-7; **13**, 73986-07-9; **14** [(1*R*)-*cis*-αR], 65731-83-1; chloral, 75-87-6; isobutylene, 115-11-7; 1,1,1-trichloro-2-hydroxy-4-methyl-4-pentene, 25308-82-1.