Anal. Calcd for $C_{14}H_{16}ClN$: C, 71.94; H, 6.90; Cl, 15.17; N, 5.99. Found: C, 71.77; H, 6.62; Cl, 15.31; N, 6.12.

Acknowledgment. I am grateful to Mr. Gifford Marzoni for supplying the data on the cleavage of the dihydrolysergic ester derived cyanamide.

Synthesis of Optically Active *cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic Acid via Intramolecular Alkylation of a Chiral Enolate

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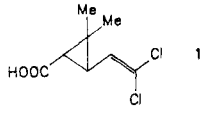
A large number of the agriculturally important synthetic pyrethroid insecticides are esters of 3-(2,2-dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic acid (1). The impact of stereochemistry about the cyclopropane ring on insecticidal activity necessitates the development of efficiednt methods for the stereoselective synthesis of the various enantiomers of 1.[2,3] We previously reported a new stereoselective synthesis of *cis*-1 using the intramolecular alkylation of an amide enolate to establish the relative stereochemistry.[4] We now report our observations in attempts to extend this methodology to the synthesis of optically active (1*R*,3*R*)-1 using a chiral enolate.[5]



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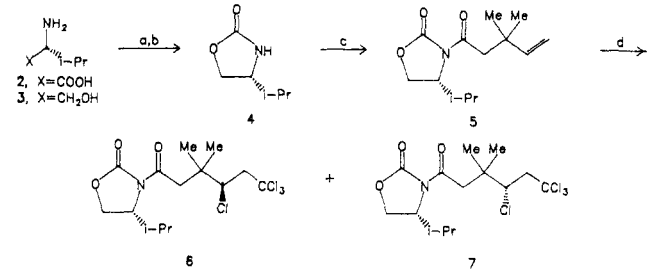
The synthesis of the appropriate starting materials for cyclization is illustrated in Scheme I. Oxazolidinone **4** was prepared in two steps from (*R*)-valine (**2**) by reduction with BH_3–SMe_2[6] followed by treatment of the resultant amino alcohol **3**[7] with carbonyldiimidazole. Oxazolidinone **4** was treated with NaH followed by addition of 3,3-dimethyl-4-pentenoyl chloride[4a] to yield **5**, in 85% yield. Compound **5** was reacted with $Fe(CO)_5$ in CCl_4 to afford a 3:2 mixture of addition products **6** and **7**, respectively, in 86% yield. The isomeric products were separated by preparative HPLC to afford the pure major isomer **6** and the minor

Scheme I[a]



[a] (a) BH_3–SMe_2; (b) carbonyldiimidazole; (c) NaH, $ClCOCH_2C(Me)_2CH{=}CH_2$; (d) $Fe(CO)_5$, CCl_4.

isomer **7**. The spectroscopic properties of **6** and **7** were nearly identical with the exception of the ^1H NMR resonances attributed to the diastereotopic protons adjacent to the carbonyl group. In **7** one resonance was shifted upfield by 0.15 ppm and the other was shifted downfield by 0.16 ppm relative to the corresponding resonances in **6**. Consequently, the stereochemistry of **6** was determined by single-crystal X-ray analysis.[1b]

The ring closures of **6** and **7** initiated by enolate formation were studied separately. It should be expected that in one instance (i.e., **7**) cyclization should be highly stereoselective due to the combined facial differentiation of the enolate and normal (*Z*)-enolate preference to yield cis stereochemistry in the ring closure through a backside S_N2 reaction.[4a] In the case of **6**, where these factors oppose each other, much poorer stereoselection should be anticipated. Treatment of **6** with NaH produced a 70% yield of a 1:23:74:2 mixture of cyclized products **8a**:**8b**:**8c**:**8d**, respectively, as determined by HPLC and NMR spectral analysis (Scheme II). Under indentical reaction conditions, compound **7** produced an 84% yield of a 92:1:2:5 mixture of products **8a**:**8b**:**8c**:**8d**, respectively.

Final confirmation of the isomeric composition of the cyclization mixtures was accomplished by conversion to **1** by hydrolysis and dehydrohalogenation. Each mixture was treated with LiOMe followed by treatment of the crude methyl esters with KOH.[5d] The mixture of isomers **8** derived from **6** gave **1**, $[\alpha]^{25}_D$ −13.2°, in 77% yield. The mixture of isomers **8** obtained from **7** gave **1**, $[\alpha]^{25}_D$ +18.9°, in 77% yield. The ratios of cis to trans products in each case were easily confirmed by examination of the relative intensities of the resonance for the vinyl proton in the ^1H NMR spectrum of crude product.[3] These data, combined with the magnitude and sign of the optical rotation of samples of **1** in comparison with literature values,[3] verified the ratios of isomers in **8** as shown above.

Experimental Section[8]

General Methods. Unless otherwise noted, materials were obtained from commercial suppliers and were used without further purification. Anhydrous tetrahydrofuran (THF) was obtained by distillation from sodium–benzophenone immediately prior to use. Anhydrous *N*,*N*-dimethylformamide (DMF) was obtained by distillation from CaH_2 immediately prior to use. Anhydrous MeOH was obtained by distillation from $Mg(OMe)_2$ immediately prior to use. All reactions involving strong bases or reactive organometallic intermediates were performed under a nitrogen atmosphere.

(*R*)-(−)-2-Amino-3-methyl-1-butanol (3). Following a previously described procedure for reduction of racemic valine,[6] **3**

(1) (a) Dow Chemical U.S.A. (b) North Carolina State University. Address correspondance regarding the X-ray structure of **6** to this author at Central Research, Pfizer Inc., Groton, CT 06340.

(2) Elliot, M. *Pestic. Sci.* **1980**, *11*, 119.

(3) Burt, P. E.; Elliot, M.; Farnham, A. W.; Janes, N. F.; Needham, P. H.; Pulman, D. A. *Pestic. Sci.* **1974**, *5*, 791.

(4) (a) Kleschick, W. A. *J. Org. Chem.* **1986**, *51*, 5429. (b) Kleschick, W. A. U.S. Pat. 4 479 005, 1984. (c) Kleschick, W. A. U.S. Pat. 4 515 956, 1985.

(5) (a) Evans, D. A.; Takacs, J. M.; McGee, L. R.; Ennis, M. D.; Mathre, D. J.; Bartroli, J. *Pure Appl. Chem.* **1981**, *53*, 1109. (b) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23. (c) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2230. (d) Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737.

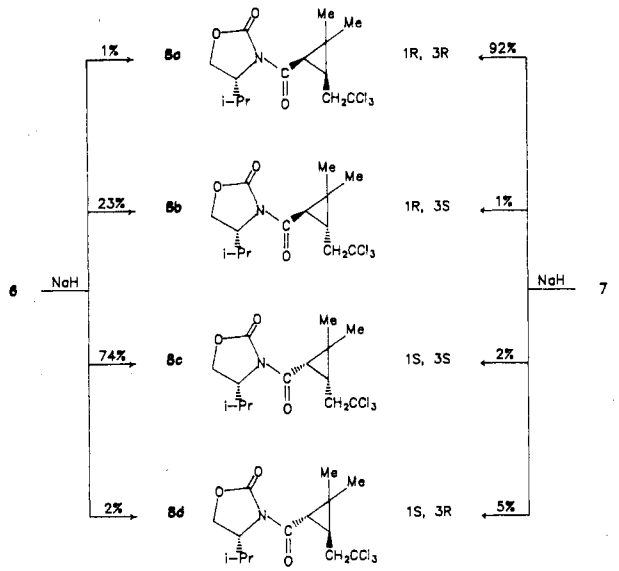
(6) Lane, C. F. U.S. Pat. 3 935 280, 1976.

(7) The optical purity of **3** was determined to be >98% ee by examination of the ^{19}F NMR spectra and HPLC resolution of diastereomeric α-methoxy-α-(trifluoromethyl)phenylacetamide derivatives: Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543.

(8) All melting points and boiling points are uncorrected. NMR chemical shifts are expressed as δ values (ppm) relative to a Me_4Si internal standard. Significant NMR data are tabulated in order: number of protons, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad), coupling constant(s) in hertz.

0022-3263/87/1952-3168$01.50/0

Scheme II



was obtained in 65% yield as a hygroscopic solid, mp 31.5–33 °C: $[\alpha]^{25}_D$ −16.6° (EtOH, *c* 0.0930 g/mL). The optical purity of **3** was determined to be >98% ee by conversion to the corresponding Mosher amide[7,9] and comparison with the resolved peaks in the ^{19}F NMR spectrum and HPLC chromatogram of the Mosher amide derived from racemic **3**.

(*R*)-(−)-4-(1-Methylethyl)-2-oxazolidinone (4). A solution of 21.3 g (0.206 mol) of **3** and 37.6 g (0.232 mol) of 1,1′-carbonyldiimidazole in 340 mL of toluene was heated at reflux for 18 h. After being cooled to room temperature, the reaction mixture was partitioned between CH_2Cl_2 and dilute aqueous HCl. The aqueous phase was washed four times with CH_2Cl_2, and the combined organic phases were dried (Na_2SO_4) and evaporated at reduced pressure to afford a solid residue. Recrystallization from Et_2O gave 9.73 g (36%) of **4** as a colorless crystalline solid, mp 70–72 °C: $[\alpha]^{25}_D$ −15.5° ($CHCl_3$, *c* 0.0706 g/mL); IR ($CHCl_3$) 1760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.1 (1 H, br s), 4.41 (1 H, t), 4.07 (1 H, dd), 3.4–3.8 (1 H, m), 1.3–2.0 (1 H, m), 0.96 (3 H, d), 0.80 (3 H, d). Anal. Calcd for $C_{16}H_{11}NO_2$: C, 55.80; H, 8.58; N, 10.84. Found: C, 56.05; H, 8.43; N, 10.95.

(*R*)-(−)-3-(3,3-Dimethyl-4-pentenoyl)-4-(1-methylethyl)-2-oxazolidinone (5). A solution of 6.00 g (46.3 mmol) of **4** in 25 mL of dry THF was added dropwise to a suspension of 2.44 g (51 mmol) of 50% NaH in oil (washed free of oil with three 10-mL portions of hexane) in 35 mL of dry THF. The resulting mixture was stirred at room temperature overnight and cooled in an ice bath. 3,3-Dimethyl-4-pentenoyl chloride[4a] (6.79 g, 46.3 mmol) was added dropwise, and the resulting mixture was warmed to room temperature and stirred for 24 h. The reaction mixture was partitioned between Et_2O and saturated aqueous $NaHCO_3$. The organic layer was dried (Na_2SO_4) and evaporated at reduced pressure to afford a pale yellow oil. Kugelrohr distillation gave 9.47 g (85%) of **5** as a colorless liquid, bp 95 °C (oven temperature) at 0.1–0.5 mm: n_D 1.4735; $[\alpha]^{25}_D$ −69.3° (acetone, *c* 0.0275 g/mL); IR ($CHCl_3$) 1790, 1700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.00 (1 H, dd, *J* = 18 and 10 Hz), 4.93 (1 H, d of d, *J* = 18 and 2 Hz), 4.91 (1 H, dd, *J* = 10 and 2 Hz), 4.0–4.6 (3 H, m), 3.18 (1 H, d, *J* = 14 Hz), 2.85 (1 H, d, *J* = 14 Hz), 1.18 (6 H, s), 0.89 (3 H, d), 0.85 (3 H, d). Anal. Calcd for $C_{13}H_{21}NO_3$: C, 65.24; H, 8.85; N, 5.85. Found: C, 65.36; H, 8.86; N, 5.85.

(4*R*,4′*R*)-(−)- and (4*R*,4′*S*)-(−)-4-(1-Methylethyl)-3-(4,6,6,6-tetrachloro-3,3-dimethylhexanoyl)-2-oxazolidinone (6 and 7). A solution of 5.42 g (22.7 mmol) of **5** and 0.35 mL (0.52 g, 2.7 mmol) of $Fe(CO)_5$ in 13.6 mL of CCl_4 was heated at reflux for 6 h. After being cooled to room temperature, the reaction mixture was filtered through a 4-in. column of alumina. The column was thoroughly washed with CH_2Cl_2, and the filtrate was evaporated at reduced pressure to afford a yellow oil. HPLC on silica gel, eluting with EtOAc–hexane (1:9, v/v), gave 7.67 g (86%) of a 3:2 mixture of **6** and **7** (HPLC, Altex Ultrasphere Si, 4.6 mm × 25 cm, EtOAc–hexane eluent, 1:9, v/v). Careful HPLC on silica gel, eluting with EtOAc–hexane (1:9 v/v), followed by recrystallization from hexane afforded pure samples of **6** and **7**.

Isomer **6** was obtained as colorless solid, mp 70.5–72 °C: $[\alpha]^{25}_D$ −5.50° (acetone, *c* 0.0294 g/mL); IR ($CHCl_3$) 1789, 1700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.72 (1 H, dd, *J* = 7 and 1 Hz), 4.47 (1 H, ddd, *J* = 9, 3, and 3 Hz), 4.28 (1 H, dd, *J* = 9 and 9 Hz), 4.21 (1 H, dd, *J* = 9 and 3 Hz), 3.31 (1 H, dd, *J* = 16 and 1 Hz), 3.25 (1 H, d, *J* = 17 Hz), 3.11 (1 H, dd, *J* = 16 and 7 Hz), 3.06 (1 H, d, *J* = 17 Hz), 2.3–2.5 (1 H, m), 1.28 (3 H, s), 1.15 (3 H, s), 0.93 (3 H, d), 0.88 (3 H, d). Anal. Calcd for $C_{14}H_{21}Cl_4NO_3$: C, 42.77; H, 5.38; N, 3.56. Found: C, 42.91; H, 5.39; N, 3.62.

Isomer **7** was obtained as a colorless crystalline solid, mp 69–70 °C: $[\alpha]^{25}_D$ −87.9° (acetone, *c* 0.0399 g/mL); IR ($CHCl_3$) 1787, 1700 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 4.74 (1 H, dd, *J* = 7 and 1 Hz), 4.46 (1 H, ddd, *J* = 9, 3, and 3 Hz), 4.27 (1 H, dd, *J* = 9 and 9 Hz), 4.21 (1 H, dd, *J* = 9 and 3 Hz), 3.41 (1 H, d, *J* = 17 Hz), 3.30 (1 H, dd, *J* = 16 and 1 Hz), 3.11 (1 H, dd, *J* = 16 and 7 Hz), 2.91 (1 H, d, *J* = 17 Hz), 2.3–2.5 (1 H, m), 1.27 (3 H, s), 1.14 (3 H, s), 0.93 (3 H, d), 0.89 (3 H, d). Anal. Calcd for $C_{14}H_{21}Cl_4NO_3$: C, 42.77; H, 5.38; N, 3.56. Found: C, 42.77; H, 5.31; N, 3.51.

Cyclization of 6 and 7. To a suspension of 0.35 g (7.1 mmol) of 50% NaH in oil (washed free of oil with three 5-mL portions of hexane) in 14 mL of anhydrous THF–DMF (3:1, v/v) was added 2.56 g (6.50 mmol) of **6**. The resulting mixture was stirred at room temperature for 48 h and partitioned between Et_2O and saturated aqueous NH_4Cl. The organic phase was separated, dried (Na_2SO_4), and evaporated at reduced pressure to afford a pale yellow solid containing **8a**, **8b**, **8c**, and **8d** in a ratio of 1:23:74:2 (HPLC, Altex Ultrasphere ODS, 4.6 mm × 25 cm, MeCN–H_2O eluent, 4:1, v/v). HPLC on silica gel, eluting with EtOAc–hexane (1:9, v/v), gave 1.63 g (70%) of a mixture of **8a–d** as a colorless solid mp 85.5–91 °C: IR (CCl_4) 1784, 1689 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.0–4.6 (3 H, m), 2.7–3.5 (3 H, m), 2.1–2.7 (1 H, m), 0.7–2.1 (13 H, m including s at 1.32 and 1.19 and d at 0.89 and 0.86). Anal. Cald for $C_{14}H_{20}Cl_3NO_3$: C, 47.14; H, 5.65; N, 3.93; Cl, 29.82. Found: C, 47.28; H, 5.55; N, 3.83; Cl, 30.02.

With the same procedure described above for the cyclization of **6**, 2.56 g (6.50 mmol) of **7** afforded a crude mixture containing **8a**, **8b**, **8c**, and **8d** in a ratio of 92:1:2:5. HPLC on silica gel, eluting with EtOAc–hexane (1:9, v/v), gave 1.95 g (84%) of a mixture of a **8a–d** as a colorless solid, mp 112.5–116.5 °C: IR (CCl_4) 1784, 1688 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.0–4.6 (3 H, m), 2.7–3.5 (3 H, m), 0.6–2.6 (14 H, m including s at 1.30 and 1.17 and d at 0.88 and 0.84). Anal. Calcd for $C_{14}H_{20}Cl_3NO_3$: C, 47.14; H, 5.65; N, 3.93; Cl, 29.82. Found: C, 47.24; H, 5.54; N, 3.83; Cl, 30.06.

Hydrolysis of 8. The mixtures of **8a–d** obtained from the cyclization of **6** and **7** were hydrolized and dehydrohalogenated to afford **1** using a previously described procedure.[4a]

Starting with 1.07 g (3.00 mmol) of the mixture of **8a–d** derived from **6**, 482 mg (77%) of **1** was obtained as a waxy solid, $[\alpha]^{25}_D$ −13.2° ($CHCl_3$, *c* 0.0210 g/mL).[10] The ^1H NMR spectrum of **1** was consistent with a 88:12 mixture of cis/trans isomers.[11]

Starting with 1.07 g (3.00 mmol) of the mixture of **8a–d** derived from **7**, 481 mg (77%) of **1** was obtained as a waxy solid, $[\alpha]^{25}_D$ +18.9° ($CHCl_3$, *c* 0.0132 g/mL).[10] The ^1H NMR spectrum of **1** was consistent with a 91:9 mixture of cis/trans isomers.[11]

Acknowledgment. We thank Professor Andrew S. Kende for helpful discussions and providing 400-MHz ^1H NMR spectra of intermediates **6** and **7**.

(9) Meyers, A. I.; Poindexter, G. S.; Brich, Z. *J. Org. Chem.* **1978**, *43*, 892.

(10) Based on literature values for the $[\alpha]_D$ of the optical isomers of **1**,[3] the predicted value for $[\alpha]_D$ of **1** derived from the isomeric composition of the crude mixture of **8a–d** obtained from the cyclization of **6** and **7** are −12.7° and +23.1°, respectively. Deviation from the predicted value is consistent with fractionation that occurred during chromatographic purification of the crude mixture of **8a–d**. When a correction is made the predicted values of $[\alpha]_D$ are −19.7° and +20.6°, respectively.

(11) The assignment was made by integration of the resonances for the vinyl proton which are characteristic for each isomer.[3] Differences in the cis/trans ratios determined for **1** and those quoted in the text and experimental section for crude mixtures of **8a–d** are due to fractionation which occured upon chromatographic purification of the crude mixtures of **8a–d**.