the ^1H NMR spectrum detected when any other signals were saturated.

Further rearrangement processes were observed by examination of the ^1H NMR spectrum of the cation formed by mixing perdeuteriated naphthalene and FSO_3H. Despite the presence of some extraneous peaks in the ^1H NMR spectrum (resulting from excess FSO_3H and from cation decomposition), no regions containing signals for any protons in the carbocation are obscured until higher temperatures are achieved (see the figure). The proton is initially delivered to position H (as expected from literature precedent[7]), and at −100 °C, the protons corresponding to types H and G are the only major signals (tiny singlets for protons of types A–F are detectable and undoubtedly arise from the residual protons in the 98% perdeuteriated naphthalene used as precursor in the cation preparation). The appearance of G is consistent with the known fast process that intercoverts α- and β-protonated naphthalene. The relative intensity ratio of protons type H to type G is about 2:1. With increasing temperature, the signals broaden, as seen in the nondeuteriated cation.

At −50 °C, there is a definite and simultaneous increase in the intensity of proton type B and F. At −30 °C, the signals originally corresponding to protons G and H are gone from view and the intensities of proton types B and F has greatly increased with relative intensities of about 1:1. This indicates the presence of a, previously unreported, second 1,2 shift occurring in the carbocation. This shift interconverts the β- and β'-protonated naphthalene and also results in the production of α'-protonated naphthalene (all of ring A). All the protons of ring A are thus able to interconvert by −40 °C. At −20 °C, signals corresponding to proton types A, C, D, and E simultaneously increase in intensity at the expense of proton types B and F. When allowed to come to equilibrium at −20 °C, proton types A–F are represented by singlets of essentially equal intensity in the ^1H NMR spectrum. This suggests that there is also a process taking place at elevated temperatures that allows for shifts *between the rings* of the protonated naphthalene, presumably by two successive 1,2 shifts via the quarternary carbon. This allows for the production of α-, β-, and β'-protonated naphthalene (all of ring B). Rings A and B have changed identities, and thus protons of ring A and ring B are able to interconvert at −20 °C. This cation solution appears to be less stable than that prepared from fluorobullvalene and antimony pentafluoride; because of the presence of FSO_3H, the cation rapidly and irreversibly decomposes to unidentifiable products at 0 °C.

Thus, attempted preparations of the bullvalenyl cation from fluorobullvalene and SbF_5 in SO_2ClF with the molecular beam method at low temperatures did not produce a detectably stable solution of this cation. If it is formed as such, the bullvalenyl cation quickly rearranges to α-protonated naphthalene at temperatures below −100 °C. High-field NMR and the 2D heteronuclear COSY pulse sequence allows for unambiguous ^1H NMR and ^{13}C NMR spectral assignments of the cation. A series of 1,2 hydride shifts are detected (at elevated temperatures) in the ^1H NMR spectrum of a sample prepared by mixing perdeuteriated naphthalene with FSO_3H/SbF_5 in SO_2ClF. These processes result in *complete* proton scrambling in protonated naphthalene, below 0 °C (the temperature where the sample irreversibly decomposes to unidentifiable products).

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Registry No. Fluorobullvalene, 27576-97-2; α-protonated naphthalene, 41636-41-3.

Stereoselective Synthesis of *cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic Acid[1]

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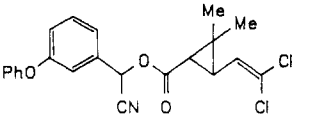
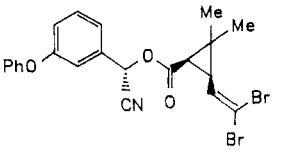
The synthetic pyrethroid insecticides play an important role in modern methods of insect control in agriculture.[2] Among the more important members of this class are cypermethrin (1) and deltamethrin (2).[2] A key structural element of these materials is the 2,2-dimethyl-3-(2,2-dihalovinyl)cyclopropanecarboxylic acid (3). The relative



1



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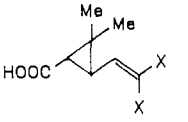

3a: X=Cl
3b: X=Br

and absolute stereochemistry about the cyclopropane ring influences both the spectrum and level of insecticidal activity exhibited by these compounds.[2,3] Consequently, methods for the stereoselective synthesis of **3** are highly desirable.

Numerous imaginative approaches to compounds of general structure **3** have been described.[4] Conceptually, one of the simplest approaches involves the formation of the cyclopropane ring by an intramolecular alkylation of an enolate anion derived from an appropriate carbonyl compound as the key step (Scheme I). Significant levels of stereochemical control have been achieved with this approach.[4] Stereoselection has been observed in the cyclization of methyl ketone **4** (R = Me, X = Cl) and ester **4** (R = OEt, X = Br).[5,6] The solvent effect in the reaction of ester **4** (R = OEt, X = Br) suggests that stereoselection in enolate formation influences the stereochemical outcome of the ring closure.[7]

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(3) Burt, P. E.; Elliot, M.; Farnham, A. W.; Janes, N. F.; Needham, P. H.; Pulman, D. A. *Pestic. Sci.* **1974**, *5*, 791.
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(5) Itaya, N.; Matsuo, T.; Ohno, N.; Mizutani, T.; Fujita, F.; Yoshioka, H. in *Synthetic Pyrethroids*; ACS Symposium Series 42; American Chemical Society: Washington, DC, 1977; p 45.
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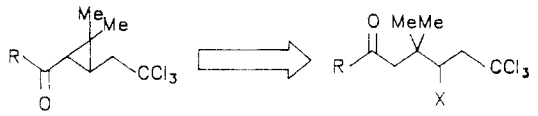
0022-3263/86/1951-5429$01.50/0

Scheme I



4

We have chosen to explore further the intramolecular alkylation approach to **3** by investigating the cyclization of amide enolates.[9] If the relationship between the stereoselection in enolate formation and stereoselection in the ring closure is operable, amides should serve as an excellent means of controlling the relative stereochemistry about the cyclopropane ring.[10] Furthermore, recent advances in asymmetric synthesis via the intermolecular alkylation of chiral amides should provide potential methods for the control of the absolute stereochemistry in **3**.[11] This report details our early studies toward this end culminating in the stereoselectives synthesis of **3a**.

We initially chose to examine the cyclization of simple *N,N*-dialkylamide enolates. Amide **5** prepared by the Meerwein–Eschenmoser variation of the claisen rearrangement[12] failed to yield suitable cyclization precursors upon reaction with haloalkanes under free radical conditions or epoxidation (Scheme II). Mild reaction conditions[13,14] led to the recovery of **5**, and more vigorous conditions[15,16] resulted in the formation of lactones **6** and **8**, presumably through intermediates arising from intramolecular alkylation of the amide oxygen (e.g., **7**).

On the basis of our experience with attempted functionalization of **5**, we chose to explore a system which more closely models a compound of interest for our ultimate goal of preparing optically active **3a**.[11e] Consequently we prepared acid chloride **11** in three steps frm 3-methyl-2-buten-1-ol in 44–57% overall yield (Scheme III).[17] Reaction of **11** with the sodium salt of 2-oxazolidinone gave **12** in 67–77% yield. After initial difficulty in affecting the addition of CCl_4 to **12** catalyzed by Cu(I) salts, we found that reaction catalyzed by iron pentacarbonyl proceeded smoothly to give **13** in 75–87% yield.

After some experimentation it was found that sodium hydride was a suitable base to promote the cyclization of **13** to form a cyclopropane ring.[18] Many other conventional bases were less satisfactory due to competing dehydrochlorination or oxazolidinone ring-opening reactions. Treatment of **13** with sodium hydride in THF–DMF gave a mixture of cis and trans cyclopropanes (**14** and **15**, respectively) in a ratio of 85:15. The overall yield for the process was 89%, and the desired cis diastereomer was isolated in pure form in 62% yield. The final proof of the structure of **14** was the conversion to **3a**. This was accomplished by two different procedures. The first involves the three-step procedure involving sequential treatment with KOH to open the oxazolidinone ring, aqueous HCl to rearrange the hydroxy amide to the amino ester, and KOH to promote hydrolysis of the amino ester and dehydrochlorination.[19] This sequence afforded **3a** identical with previously described material[20] in 70% yield. Alternatively, **14** could be treated with LiOMe to form the corresponding methyl ester, which was hydrolyzed and dehydrochlorinated without purification with KOH to form **3a** in 72% yield.[11e]

We have developed a new stereoselective synthesis of **3a** based on the intramolecular alkylation of an enolate anion. Future publications will describe our results in the extension of this methodology to the synthesis of **3a** in optically active form.[21]

Experimental Section

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.

Ethyl 3,3-Dimethyl-4-pentenoate (9). Following a previously described procedure,[17] a solution of 147 g (1.70 mol) of 3-methyl-2-buten-1-ol and 7.5 mL of propionic acid in 2.3 L of triethyl orthoacetate was heated at 120–130 °C for 11 h. The reaction mixture was cooled to room temperature and poured onto a mixture of 3 L of ice and 5% H_2SO_4. After being stirred overnight (17 h), the mixture was extracted with Et_2O. The Et_2O extract was washed with saturated $NaHCO_3$ (aqueous) and saturated NaCl (aqueous) and dried (Na_2SO_4). The solvent was removed by distillation at atmospheric pressure, and the residue was distilled at reduced pressure to yield 221 g (83%) of **9** as a colorless liquid, bp 94–98 °C (72 mm) [lit.[23] bp 81–83 °C (47 mm), lit.[14] bp 35–45 °C (0.10 mm)]: ^1H NMR ($CDCl_3$) δ 5.95 (1 H, d of d, J = 18.0 and 10.0 Hz), 4.97 (1 H, d of d, J = 18.0 and 1.6 Hz), 4.93 (1 H, d of d, J = 10.0 and 1.6 Hz), 4.13 (2 H, q), 2.30 (2 H, s), 1.23 (3 H, t), 1.15 (6 H, s); IR ($CHCl_3$) 1724 cm^{-1}.

3,3-Dimethyl-4-pentenoic Acid (10). Following a previously described procedure,[17] ester **9** (238 g, 1.53 mol) was added over

(7) The formation of the cis diastereomer is favored in the presence of polar aprotic solvents (i.e., HMPA). From the work of Ireland[8] it would be predicted that the predominant enolate diastereometer under these conditions would contain the oxygen atom bearing the charge and the aliphatic residue at the 2-position of the ester in a cis arrangement. This leads to the supposition that enolates of this configuration cyclize selectively to form the cis-cyclopropanecarboxylate.

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(17) Acid **10** was prepared by a modification of a previously described procedure: Jager, V.; Gunther, H. J. *Tetrahedron Lett.* **1977**, 2543.

(18) We have made numerous attempts to trap by silylation the enolate formed upon treatment of **13** with base to determine the diastereomer composition. In all cases we were unsuccessful due to competing ring closure to the cyclopropane.

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(22) 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.

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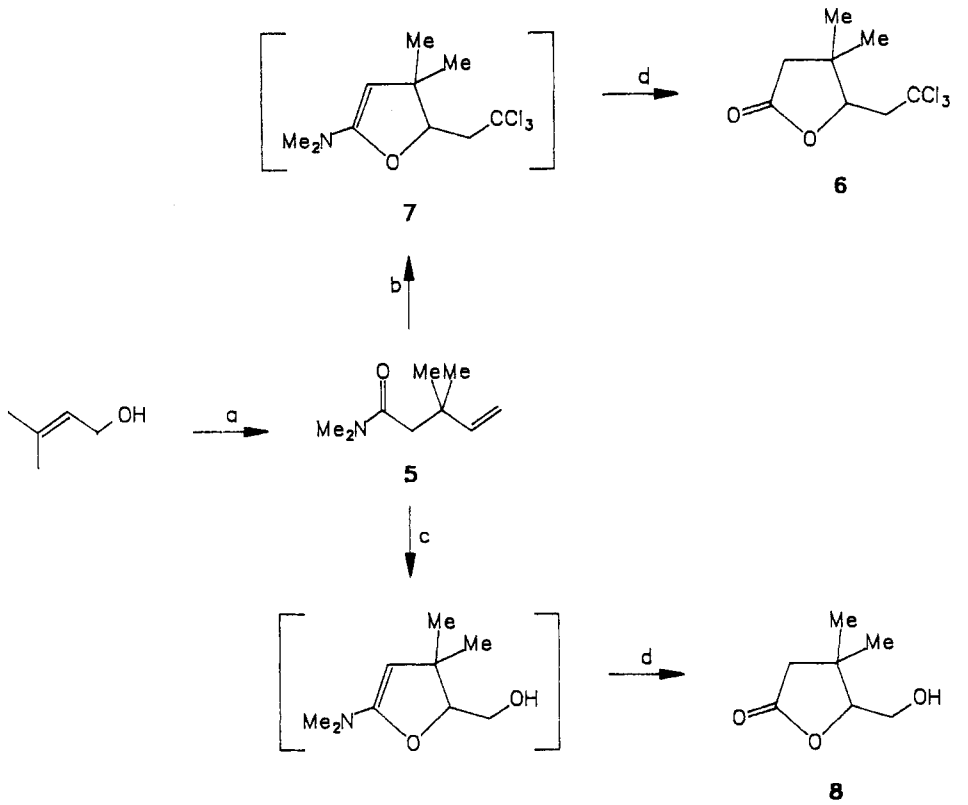
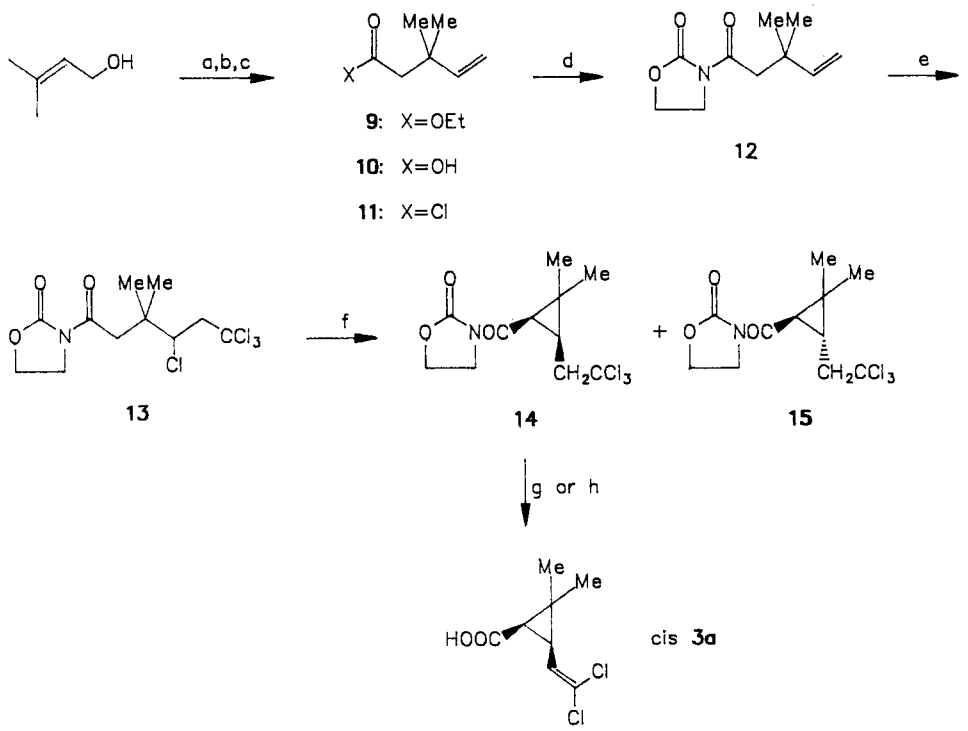
Scheme II[a]



[a] (a) $MeC(OMe)_2NMe_2$, xylene, reflux; (b) $CuBr_2 \cdot SMe_2$, $CBrCl_3$, 80 °C; (c) $(CF_3)_2C(OH)_2$, H_2O_2, $ClCH_2CH_2Cl$, reflux; (d) H_2O.

Scheme III[a]



[a] (a) $MeC(OEt)_3$, EtCOOH, 120–130 °C; (b) NaOH, EtOH–H_2O; (c) $SOCl_2$, DMF (catalyst), benzene; (d) NaH, 2-oxazolidinone, THF–DMF; (e) $Fe(CO)_5$, CCl_4, reflux; (f) NaH, THF–DMF; (g) KOH, THF–EtOH; 3 N HCl, reflux; KOH, EtOH, reflux; (h) LiOMe, THF; KOH, EtOH, reflux.

1 h to a solution of 488 g (6.10 mol) of 50% NaOH (aqueous) in 1530 mL of EtOH–H_2O (1:1, v/v) at 5 °C. After the addition was complete, the reaction mixture was warmed to room temperature, stirred for 4 h, and partitioned between Et_2O and H_2O. The organic phase was washed with 5% KOH, and the combined aqueous phases were cooled in an ice bath, acidified with concentrated HCl, and extracted with three portions of CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4), and the solvent was removed by distillation at atmospheric pressure. The residue was distilled at reduced pressure through a 15-cm Vigreux column to afford 145 g (74%) of **10** as a colorless liquid, bp 83–85 °C (4 mm): ^1H NMR ($CDCl_3$) δ 10.93 (1 H, s), 5.93 (1 H, d of d, J =

17.8 and 10.2 Hz), 5.00 (1 H, d of d, J = 17.8 and 1.4 Hz), 4.97 (1 H, d of d, J = 10.2 and 1.6 Hz), 2.35 (2 H, s), 1.17 (6 H, s); IR ($CHCl_3$) 3080, 1708 cm^{-1}. Anal. Calcd for $C_7H_{12}O_2$: C, 65.60; H, 9.44. Found: C, 65.30; H, 8.98.

3,3-Dimethyl-4-pentenoyl Chloride (11). A solution of 143 g (1.12 mol) of **10**, 90 mL (150 g, 1.2 mol) of thionyl chloride, and 0.5 mL of DMF in 550 mL of benzene was heated at reflux for 2.5 h. The excess thionyl chloride and benzene were removed by distillation at atmospheric pressure, and the residue was distilled at reduced pressure through a 10-cm Vigreux column to afford 143 g (87%) of **11** as a pale yellow liquid, bp 71–72 °C (45 mm): ^1H NMR ($CDCl_3$) δ 5.92 (1 H, d of d, J = 18.0 and 9.8 Hz), 5.02 (1 H, d of d, J = 18.0 and 1.2 Hz), 5.02 (1 H, d of d, J = 9.8 and 1.4 Hz), 2.95 (2 H, s), 1.17 (6 H, s); IR ($CHCl_3$) 1807, 1725 cm^{-1}.

3-(3,3-Dimethyl-4-pentenoyl)-2-oxazolidinone (12). Sodium hydride (50% in oil, 14.4 g, 0.300 mol) was washed free of oil with three 50-mL portions of hexane and suspended in 300 mL of anhydrous THF–DMF (3:1, v/v). To this suspension was added 21.8 g (0.250 mol) of 2-oxazolidinone, and the resulting suspension was stirred at room temperature for 48 h. The reaction mixture was cooled to 5 °C, and 36.7 g (0.250 mol) of **11** was added dropwise over 20 min. After the addition was complete the reaction mixture was allowed to warm to room temperature and was stirred overnight (24 h). The reaction mixture was quenched by cautious addition of saturated NH_4Cl (aqueous), diluted with H_2O, and extracted twice with Et_2O. The combined organic phases were dried (Na_2SO_4) and evaporated at reduced pressure to afford a yellow liquid containing (TLC, silica gel coating, EtOAc–hexane eluent, 1:1, v/v) **12** (R_f 0.47) and various impurities (R_f 0.34, 0.22, 0.10, and 0.04). HPLC (nine portions) on silica gel eluting with EtOAc–hexane (1:3, v/v) gave 33.2 g (67%) of **12** as a yellow liquid, n_D 1.4828: ^1H NMR ($CDCl_3$) δ 6.02 (1 H, d of d, J = 18.2 and 10.2 Hz), 4.97 (1 H, d of d, J = 18.2 and 1.6 Hz), 4.95 (1 H, d of d, J = 10.2 and 1.6 Hz), 3.8–4.6 (4 H, m), 3.02 (2 H, s), 1.17 (6 H, s); ^{13}C NMR ($CDCl_3$) 171.3 (s), 153.7 (s), 146.8 (d), 110.9 (t), 61.8 (t), 45.2 (t), 42.6 (t), 36.7 (s), 27.0 (q) ppm; IR ($CHCl_3$) 1781, 1694 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO_3$: C, 60.90; H, 7.67; N, 7.10. Found: C, 60.69; H, 7.37; N, 6.96.

3-(4,6,6,6-Tetrachloro-3,3-dimethylhexanoyl)-2-oxazolidinone (13). A solution of 32.9 g (0.167 mol) of **12** and 2.2 mL (3.3 g, 17 mmol) of $Fe(CO)_5$ in 82 mL of CCl_4 was heated at reflux for 27 h. The reaction mixture was cooled to room temperature and filtered through a 6-in. column of silica gel by eluting with Et_2O. The Et_2O washings were concentrated by evaporation at reduced pressure, and the residue was taken up in $CHCl_3$ and filtered through a 6-in. column of alumina (activity I). The $CHCl_3$ washings were concentrated by evaporation at reduced pressure to yield a residue containing (TLC, silica gel coating, EtOAc eluent, 1:1, v/v) **13** (R_f 0.55). HPLC of the residue eluting with EtOAc–hexane (1:3, v/v) gave 44.2 g (75%) of **13** as a viscous, nearly colorless oil, which crystallized on standing, mp 57.5–59.5 °C: ^1H NMR ($CDCl_3$) δ 4.73 (1 H, d of d, J = 6.4 and 2.6 Hz), 3.8–4.7 (4 H, m), 2.7–3.7 (4 H, m), 1.27 (3 H, s), 1.13 (3 H, s); ^{13}C NMR ($CDCl_3$) 170.8 (s), 153.4 (s), 97.8 (s), 64.7 (d), 61.9 (t), 57.9 (t), 42.4 (t), 42.4 (t), 39.1 (s), 23.8 (q), 23.3 (q) ppm; IR ($CHCl_3$) 1780, 1705, 1694 cm^{-1}. Anal. Calcd for $C_{11}H_{15}Cl_4NO_3$: C, 37.64; H, 4.31; N, 3.99. Found: C, 37.39; H, 4.26; N, 4.01.

***cis*- and *trans*-3-[(2,2-Dimethyl-3-(2,2,2-trichloroethyl)-cyclopropyl)carbonyl]-2-oxazolidinone (14 and 15).** Sodium hydride (50% in oil, 2.26 g, 47 mmol) was washed free of oil with three 25-mL portions of hexane and suspended in 54 mL of anhydrous THF–DMF (1:1, v/v). A solution of 15.0 g (42.7 mmol) of **13** in 42 mL of anhydrous THF was added, and the resultant mixture was stirred at room temperature for 39.5 h. The reaction was quenched by cautious addition of saturated NH_4Cl (aqueous) and partitioned between Et_2O and H_2O. The aqueous phase was washed with Et_2O, and the combined Et_2O extracts were dried (Na_2SO_4). The Et_2O solution was evaporated at reduced pressure to afford a yellow solid containing (HPLC, Waters 10-μm Porasil column, 3.9 mm × 30 cm, EtOAc–hexane eluent, 1:4, v/v) **14** (85%) and **15** (15%). HPLC on silica gel eluting with EtOAc–hexane (1:3, v/v) gave 11.9 g (89%) of a mixture of **14** and **15** as a colorless solid, mp 104.5–116 °C: ^1H NMR ($CDCl_3$) δ 3.7–4.6 (4 H, m) 2.6–3.5 (3 H, m), 0.7–2.5 (7 H, m including s at δ 1.30 and 1.20); IR ($CHCl_3$) 1782, 1687 cm^{-1}. Anal. Calcd for $C_{11}H_{14}Cl_3NO_2$: C, 42.00; H, 4.49; N, 4.45; Cl, 33.81. Found: C, 42.00; H, 4.68; N, 4.37; Cl, 33.49.

The product was fractionally crystallized from benzene at 0 °C, and the solid obtained was recrystallized from benzene to obtain pure **14**. After three cycles, 6.42 g (48%) of **14** was obtained as colorless plates, mp 123–124 °C: ^1H NMR ($CDCl_3$) 3.7–4.7 (4 H, m), 3.0–3.4 (3 H, m including d of d at δ 3.30, J = 15.8 and 6.0 Hz, d at δ 3.12, J = 8.4 Hz, and d of d at 2.98, J = 15.8 and 6.4 Hz), 1.0–2.0 (7 H, m including s at δ 1.32 and 1.20); ^{13}C NMR ($CDCl_3$) 170.9 (s), 153.9 (s), 100.1 (s), 61.7 (t), 49.6 (t), 42.9 (t), 31.4 (d), 28.4 (q), 28.2 (d), 27.7 (s), 14.8 (q) ppm; IR ($CHCl_3$) 1780, 1687 cm^{-1}. Anal. Calcd for $C_{11}H_{14}Cl_3NO_2$: C, 42.00; H, 4.49; N, 4.45. Found: C, 41.64; H, 4.53; N, 4.44.

The combined mother liquors from the crystallizations were subjected to HPLC eluting with EtOAc–hexane (1:3, v/v). All fractions containing (HPLC analysis) greater than 85% of **14** were combined and concentrated at reduced pressure to afford 3.33 g of colorless solid, mp 108–117 °C. The solid was recrystallized from benzene to give 1.85 g (14%) of **14** as colorless plates, mp 122–124 °C.

The mother liquor from the recrystallization, and the remaining HPLC fractions were concentrated by evaporation at reduced pressure to give 1.20 g of colorless solid. Fractional crystallization from benzene afforded a crystalline solid, which was recrystallized from benzene to give pure **15**. After three cycles 421 mg (3.1%) of **15** was obtained as colorless plates, mp 127.5–128.5 °C: ^1H NMR ($CDCl_3$) δ 3.7–4.7 (4 H, m), 2.4–3.2 (3 H, m including d of d at δ 2.93, J = 14.4 and 6.2 Hz, d at δ 2.82, J = 14.5 Hz, and d of d at δ 2.65, J = 14.8 and 6.4 Hz), 1.7–2.3 (1 H, m), 1.27 (3 H, s), 1.17 (3 H, s); ^{13}C NMR ($CDCl_3$) 170.5 (s), 153.9 (s), 99.3 (s), 61.9 (t), 53.5 (t), 42.9 (t), 33.0 (d), 29.6 (d), 29.0 (s), 21.7 (q), 20.3 (q) ppm; IR ($CHCl_3$) 1780, 1685 cm^{-1}. Anal. Calcd for $C_{11}H_{14}Cl_3NO_2$: C, 42.00; H, 4.49; N, 4.45; Cl, 33.81. Found: C, 42.33; H, 4.57; N, 4.44; Cl, 33.56.

***cis*-3-(2,2-Dichlorovinyl)-2,2-dimethylcyclopropanecarboxylic Acid (3a).** Following a previously described general procedure,[19] a solution of 2.22 g (7.06 mmol) of **14** and 2.1 mL (15 mmol) of 7 N KOH (aqueous) in 35 mL of THF–EtOH (2:3, v/v) was stirred at room temperature for 24 h. This solvent was removed by evaporation at reduced pressure, and the residue was suspended in 35 mL of 3 N HCl (aqueous). The aqueous suspension was heated at reflux for 4 h. After cooling to room temperature, the reaction mixture was extracted three times with CH_2Cl_2. The combined organic extracts were dried ($MgSO_4$ for 1 min) and evaporated at reduced pressure. The residual amber oil was dissolved in 15 mL of EtOH, and 5 mL (35 mmol) of 7 N KOH (aqueous) was added. The solution was stirred at room temperature for 30 min and heated at reflux for 4 h. The solvent was removed by evaporation at reduced pressure, and the residue was partitioned between Et_2O and H_2O. The aqueous phase was acidified to pH 3 with concentrated HCl and extracted three times with CH_2Cl_2. The combined organic phases were dried (Na_2SO_4) and evaporated at reduced pressure to give 1.03 g (70%) of **3a** as a pale yellow solid identical with an authentic sample of **3a** by ^1H NMR. The product was recrystallized from hexane to afford 911 mg (62%) of **3a** as pale yellow plates, mp 85–88 °C (lit.[20] mp 88–89 °C): ^1H NMR ($CDCl_3$) δ 11.9 (1 H, br s), 6.18 (1 H, d, J = 8.4 Hz), 1.93 (1 H, t), 1.80 (1 H, d), 1.25 (6 H, s); IR (CCl_4) 3070, 1697 cm^{-1}.

As an alternative to the procedure described above and following a previously described general procedure,[11e] a solution of 4 mL of anhydrous MeOH in 4 mL of anhydrous THF was cooled to 5 °C, and 4.44 mL (6.00 mmol) of 1.35 M n-butyllithium in hexane was added over 10 min. After the mixture was stirred for 20 min, 629 mg (2.00 mmol) of **14** was added, and the solution was warmed to room temperature and stirred for 48 h. The solution was partitioned between Et_2O and pH 7 phosphate buffer, and the organic phase was separated, dried (Na_2SO_4), and evaporated at reduced pressure. The residue was Kugelrohr distilled at reduced pressure [oven temperature 80 °C (0.5 mm)] to afford 374 mg (72%) of methyl 2,2-dimethyl-3-(2,2,2-trichloroethyl)cyclopropanecarboxylate: ^1H NMR ($CDCl_3$) δ 3.62 (3 H, s), 2.7–3.4 (2 H, m), 1.3–1.8 (2 H, m), 1.22 (6 H, s); IR (CCl_4) 1729 cm^{-1}.

A solution of 273 mg (1.05 mmol) of methyl 2,2-dimethyl-3-(2,2,2-trichloroethyl)cyclopropane carboxylate and 0.36 mL (2.5

mmol) of 7 N KOH (aqueous) in 1.5 mL of EtOH was stirred at room temperature for 30 min and at reflux for 5 h. After the mixture was allowed to cool to room temperature, the solvent was removed by evaporation at reduced pressure, and the residue was partitioned between Et_2O and H_2O. The aqueous phase was acidified (concentrated HCl) and extracted twice with CH_2Cl_2. The combined organic extracts were dried (Na_2SO_4) and evaporated at reduced pressure to afford 220 mg (100%) of **3a** as a pale yellow crystalline solid identical with an authentic sample of **3a** by mp, ^1H NMR, and IR.

Registry No. **3a**, 59042-49-8; **5**, 78137-45-8; **6**, 64501-94-6; **8**, 78984-88-0; **9**, 7796-72-7; **10**, 7796-73-8; **11**, 88819-78-7; **12**, 95470-21-6; **13**, 95470-22-7; **14**, 95470-23-8; **15**, 95470-19-2; $MeC(OMe)_2NMe_2$, 18871-66-4; $CBrCl_3$, 75-62-7; $MeC(OEt)_3$, 122-51-0; $Fe(CO)_5$, 13463-40-6; CCl_4, 56-23-5; 3-methyl-2-buten-1-ol, 556-82-1; 2-oxazolidinone, 497-25-6; methyl *cis*-2,2-dimethyl-3-(2,2,2-trichloroethyl)cyclopropanecarboxylate, 64879-04-5.

Hydrolysis of Orthoisobutyrates. Rate-Determining Step and Effects of β-Methyl Substitution on Reactivity

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The acid-catalyzed hydrolysis of ortho esters is a three-stage process (eq 1–3), with the formation of an

$$RC(OR)_3 + HA \xrightarrow{k_1} RC^+(OR)_2 + ROH + A^- \quad (1)$$

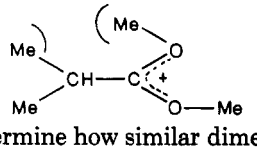
$$RC^+(OR)_2 + H_2O \rightleftharpoons RC(OH)(OR)_2 + H^+ \quad (2)$$

$$RC(OH)(OR)_2 \xrightarrow{k_3} RCO_2H + ROH \quad (3)$$

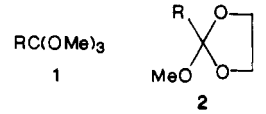
alkoxy carbocation (eq 1) being generally rate determining.[1] The formation of a similar carbocation intermediate is also the rate-determining step in the acid-catalyzed hydrolysis of ketene acetals (eq 4).[2-5] In the latter reaction, di-

$$R_1(R_2)C{=}C(OR)_2 + HA \rightarrow RC^+(OR)_2 + A^- \quad (4)$$

methylketene dimethyl acetal was found to be less reactive than the unsubstituted ketene acetal by a factor of 9×10^5.[5] This large reduction in reactivity was ascribed to steric interaction between the β-methyl and the methoxy groups in the dimethoxy carbocation, which inhibits resonance stabilization of the cation and hence its formation.



In order to determine how similar dimethyl substitution affected the reactivity of ortho esters, we have studied the kinetics of the acid-catalyzed hydrolysis of orthoisobutyrates **1b** and **2b**.



a, R = Me; **b**, R = Me_2CH; **c**, R = Me_3C; **d**, R = *p*-$MeOC_6H_4$

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Table I. Kinetic Results for the Hydrolysis of Ortho Esters

substrate	range of 10^3[HCl], M	$10^{-3}k_{H^+}$,[a] M^{-1} s^{-1}	$10^{-3}k_{H^+}$,[b] M^{-1} s^{-1}
1a[c]	1–2.5	12.0 (0.4)	
1b[c]	1–10	38.9 (0.5)	44.5 (1.6)
1c[c]	1–10	13.1 (0.2)[d]	12.9 (1.4)
1d[e]	0.45–50	0.307 (0.002)	0.325 (0.017)
2b[c]	5–50	0.858 (0.004)	22.0 (1.5)

[a] Calculated from k_{obsd} obtained in HCl solutions; standard deviations given in parentheses. [b] Calculated from data obtained at pH about 6.3 and 6.8 in biphosphate buffer solutions. The average of the two is given with the difference from the calculated k_{H^+}. [c] At 25 °C and 0.10 M ionic strength (KCl) in 1–1.5 vol % CH_3CN–H_2O. [d] $k_{D^+} = 2.20 \times 10^4$ M^{-1} s^{-1} in DCl solution; $k_{D^+}/k_{H^+} = 1.68$. [e] At 30 °C and 0.45 M ionic strength (KCl) in 10 vol % CH_3CN–H_2O.

It has recently been shown that the rate-determining step in the hydrolysis of cyclic ortho esters becomes the breakdown of the tetrahedral intermediate (eq 3) at low pH.[6-10] However, acyclic ortho esters, except for trimethyl orthocyclopropanecarboxylate, do not undergo this change.[10,11] This exception was attributed to the hydrophobicity of the cyclopropyl group.[10] We determined whether this change in the rate-determining step occurred with acyclic ortho esters **1** that have a bulky substituent.

Results

Rates of hydrolysis of **1** and **2** were measured in dilute HCl and in biphosphate buffer solutions. Pseudo-first-order rate constants k_{obsd} in 0.00005–0.05 M HCl were proportional to the acid concentration.[12] Catalytic constants k_{H^+} were determined by least-squares analysis and are given in Table I. The rate of the uncatalyzed reaction was essentially zero.

Buffer catalysis was observed for all the substrates, consistent with the general-acid catalysis usually observed for ortho ester hydrolysis.[1,12] The rate constants extrapolated to zero buffer concentration by least-squares treatment represent the hydronium ion contribution to the observed rates, $k_{H^+}[H^+]$, and were converted to k_{H^+} by using the pH of the buffer. The averages of the catalytic constants are given in Table I.

Discussion

The data in Table I show that the constants k_{H^+} for the hydrolysis of **1** are essentially equal to those determined at higher pH in biphosphate buffers. The rate constants in the two different pH regions should reflect the same reaction step (eq 1), indicating that the rate-determining step does not change with pH. In contrast, the catalytic constant for the cyclic ortho ester **2b** in HCl at pH 1.3–2.3 is about $^1/_{25}$ that in biphosphate buffers. Thus, the rate-determining step changes from that of eq 1 at high

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(12) Tables of observed rate constants are available as supplementary material.

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