CIMS (isobutane), m/z (rel intensity) 245 (19, $M^+ + H$); HRMS m/z calcd for $C_9H_{19}O_2Si$ ($M^+ - C_4H_9$) 187.1154, found 187.1154; $[\alpha]^{25}_D$ +40.0 (c 1.27, CH_2Cl_2). Also isolated by the chromatographic purification was the corresponding alcohol as an overreduction product (6% yield). To a solution of **15** (0.019 g, 0.078 mmol) in CH_2Cl_2 (2.5 mL) at 25 °C under nitrogen was added a solution of methyl (triphenylphosphoranylidene)acetate (0.026 g, 0.078 mmol; Aldrich) in CH_2Cl_2 (2.5 mL). The solution was then heated at reflux for 4 weeks. The mixture was poured into brine (5 mL), and the resulting mixture was extracted with CH_2Cl_2 (3 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo, leaving a yellow oil. The *E*:*Z* ratio in the crude reaction mixture was 18:1 under these conditions. Flash chromatography on silica gel (99.5:0.5 hexane/ethyl acetate) gave 0.016 g (70%) of pure (2*E*)-(4*R*,5*R*)-**10** as a colorless oil having spectroscopic data identical with that of the racemic material prepared above but having $[\alpha]^{25}_D$ +25.0 (c 0.58, CH_2Cl_2). Through use of the chiral NMR shift reagent tris(3-((heptafluoropropyl)hydroxymethylene)-(+)-camphorato)europium(III) (Eu(hfc)$_3$, Aldrich), none of the 4*S*,5*S* enantiomer could be detected. By addition of Eu(hfc)$_3$ to samples of racemic **10**, (4*R*,5*R*)-**10**, and mixtures of racemic **10** and (4*R*,5*R*)-**10**, the minimum detection limit for (4*S*,5*S*)-**10** was found to be 0.5%, and therefore, an enantiomeric excess of at least 99% can be claimed for (4*R*,5*R*)-**10**.

With shorter reaction times and with benzene as the solvent instead of CH_2Cl_2 in the final condensation step with the phosphonium ylide, significantly larger amounts of the 2*Z* isomer of (4*R*,5*R*)-**10** were obtained. In an extreme case, when the condensation of **15** was done with trimethyl phosphonoacetate and potassium *tert*-butoxide in THF at −78 °C rather than with the ylide used above, the *E* and *Z* isomers were isolated in 18% and 47% yields, respectively. (2*Z*)-(4*R*,5*R*)-**10**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.12 (dd, 1 H, J = 11.60, 10.43 Hz, C*H*=CHCO$_2$CH$_3$), 5.70 (dd, 1 H, J = 11.60, 0.85 Hz, CH=C*H*CO$_2$CH$_3$), 3.71 (s, 3 H, CO$_2$C*H*$_3$), ca. 3.7 (m, difficult to detect, overlapped with the strong CO$_2$C*H*$_3$ singlet, and probably strongly deshielded by the carbomethoxy group, 1 H, C*H*CH$_3$), 3.32 (dd, 1 H, J = 5.13, 5.13 Hz, C*H*OSi), 1.71 (qqd, 1 H, J = 6.80, 6.76, 5.13 Hz, C*H*(CH$_3$)$_2$), 1.05 (d, 3 H, J = 6.95 Hz, CH$_3$), 0.91 (s, 9 H, C(C*H*$_3$)$_3$), 0.87 (d, 3 H, J = 6.80 Hz, CH(C*H*$_3$)CH$_3$), 0.82 (d, 3 H, J = 6.76 Hz, CH(CH$_3$)C*H*$_3$), 0.036 (s, 3 H, Si(C*H*$_3$)CH$_3$), 0.023 (s, 3 H, Si(CH$_3$)C*H*$_3$); EIMS, m/z (rel intensity) 300 (1, M^+), 285 (4, $M^+ - CH_3$), 257 (36, $M^+ - C_3H_7$), 243 (100, $M^+ - C_4H_9$); HRMS m/z calcd for $C_{12}H_{23}O_3Si$ ($M^+ - C_4H_9$) 243.1416, found 243.1414.

Acknowledgment. We thank Dr. James T. Carey for assistance with NMR data in the initial stages of this work and Dr. B. Plashko for assistance with MS data, and we express our gratitude to the National Institutes of Health for generous support of this research.

Alkaline Hydrolysis of 1,3-Dibromo-1,1-difluoroalkanes: A Two-Step Vinyl Carboxylation

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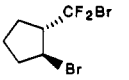
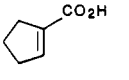
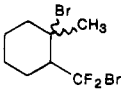
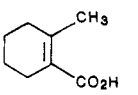
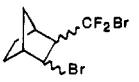
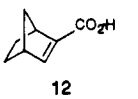
Received January 3, 1989

In a recent attempt to prepare 3-(difluoromethylene)-cyclohexene, **1**, we found that refluxing 1-(bromodifluoromethyl)-2-bromocyclohexanes, **2**, with aqueous potassium hydroxide followed by acidic workup produced 1-cyclohexene-1-carboxylic acid, **3**. Subsequent investigations showed that diene **1** is an intermediate but is converted to **3** under the reaction conditions.[1] Inasmuch as dibromides **2** were obtained from addition of CF_2Br_2 to cyclohexene, this reaction sequence amounts to a two-step vinyl carboxylation strategy. We therefore sought to demonstrate the generality of these conversions.

Table I. Dibromodifluoromethane-Alkene Adducts and Their Alkaline Hydrolysis Products

CF_2Br_2–alkene adduct	unsaturated acid	% yield[a]
2	**3**	93[b]
$CH_3(CH_2)_3CHBrCH_2CF_2Br$	$CH_3(CH_2)_3CH{=}CHCO_2H$	96
4	**9**	
		69
5	**10**	
		53
6	**11**	
		73
7	**12**	
$PhCH_2CHBrCH_2CF_2Br$	$PhCH{=}CHCH_2CO_2H$	72
8	**13**	

[a] Based on unrecovered haloalkane. [b] Reference 1.

Scheme I

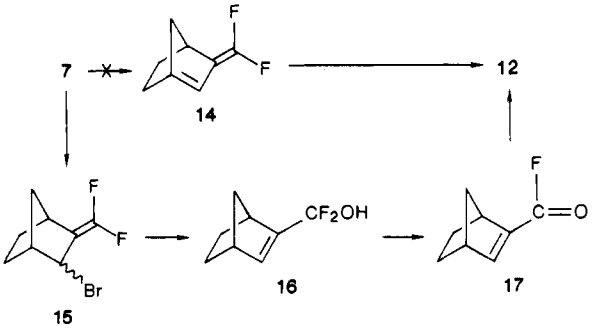


Table I summarizes the results of this study. Mono-, di-, and trisubstituted alkenes all give CuCl-initiated free-radical addition products with CF_2Br_2. When the adducts were refluxed with aqueous potassium hydroxide and then acidified, α,β-unsaturated carboxylic acids were produced in good yield.

One noteworthy exception is 1,3-dibromo-1,1-difluoro-4-phenylbutane, **8**, which gave 4-phenyl-3-butenoic acid, **13**, upon alkaline hydrolysis. This presumably reflects a thermodynamic advantage for the alkene to be conjugated with the aryl ring rather than the carboxy carbonyl.[2]

The mechanistically significant observation that **7** is converted to **12** suggests the existence of an alternative pathway which does *not* involve a diene intermediate.[3]

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(2) The isomerization of (*E*)-4-phenyl-2-butenoic acid to (*E*)-4-phenyl-3-butenoic acid was estimated to be exothermic by 1.64 kcal/mol at 150 °C. ASTM Chemical Thermodynamics and Energy Release Evaluation Program.

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0022-3263/89/1954-3992$01.50/0

Although 1 was observed in the conversion of 2 to 3,[1] an analogous route to 12 would require the bridgehead diene 14. We propose that initial dehydrobromination of 7 to 15[5] is followed by S_N2' attack by hydroxide to yield the unstable difluoro alcohol 16. Spontaneous loss of HF produces 17, which further reacts to yield 12 (Scheme I).

Experimental Section

General Methods. All NMR spectra were obtained in $CDCl_3$ solutions at ambient temperature on a Varian Gemini 200 spectrometer. Chemical shifts (δ) are reported in parts per million downfield of internal tetramethylsilane. Infrared spectra were obtained from neat liquids or solutions as capillary films between KBr plates on a Perkin-Elmer 1420 ratio recording infrared spectrophotometer. All reagents and solvents were commercial samples used without purification. Elemental analyses were performed by Robertson Laboratory, Inc., Madison, NJ.

Addition of CF_2Br_2 to Alkenes. General Procedure. The procedure was patterned after that reported by Burton and Kehoe.[4] A mixture of 300 mmol of CF_2Br_2, 150 mmol of olefin, 75 mmol of ethanolamine, 2 mmol of CuCl, and 150 mL of *tert*-butyl alcohol was refluxed for at least 24 h. Adducts were worked up as described previously for the isolation of 2.[1]

1,3-Dibromo-1,1-difluoroheptane (4): yield 23%; ^1H NMR δ 4.20 (quint, J = 6.4 Hz, 1 H, CHBr), 2.8–3.25 (mult, 2 H), 1.7–2.0 (mult, 2 H), 1.2–1.6 (mult, 4 H), 0.9 (t, 3 H); ^{13}C NMR δ 121.1 (t, J_{FC} = 308 Hz, CF_2Br), 52.9 (t, J_{FC} = 21.4 Hz), 47.1, 38.4, 29.4, 22.1, 14.0; IR 2960, 2940, 2870, 1460, 1430, 1380, 1337, 1218, 1197, 1170, 1130, 1085, 1070, 1025, 995, 937, 915, 789, 766 cm^{-1}. Anal. Calcd for $C_7H_{12}Br_2F_2$: C, 28.60; H, 4.11. Found: C, 29.31; H, 4.25.

***trans*-1-(Bromodifluoromethyl)-2-bromocyclopentane (5):** yield 20%; ^1H NMR δ 4.4 (ddd, J = 6.6 Hz, J' = 5.2 Hz, J'' = 4.7 Hz, 1 H, CHBr), 3.25 (mult, 2 H, $CHCF_2Br$), 1.7–2.4 (unresolved mults, 6 H); ^{13}C NMR δ 124.8 (t, J_{FC} = 309 Hz, CF_2Br), 62.3 (t, J_{FC} = 20.2 Hz, C(1)), 48.0, 38.8, 28.0 (d, J = 2.6 Hz), 24.1; IR 2959, 2866, 1775, 1445, 1347, 1302, 1212, 1095, 1061, 1028, 985, 958, 908, 865, 769, 703 cm^{-1}. Anal. Calcd for $C_6H_8Br_2F_2$: C, 25.93; H, 2.90. Found: C, 26.52; H, 2.92.

1-Bromo-1-methyl-2-(bromodifluoromethyl)cyclohexane (6): yield 25%; ^1H NMR δ 2.99 (ddt, J = 22.6 Hz, J' = 9.1 Hz, J'' = 3.7 Hz, 1 H, $CHCF_2Br$), 2.20 (t, J = 10.1 Hz, 2 H), 19.3 (t, J = 2 Hz, 3 H, CH_3) 1.88–1.39 (complex mults, 6 H); ^{13}C NMR δ 125.4 (t, J_{FC} = 316 Hz, CF_2Br), 65.6, 60.4 (dd, J_{FC} = 18.3 Hz, $J_{FC'}$ = 15.3 Hz), 46.3, 28.6, 27.1 (d, J_{FC} = 2.6 Hz), 24.0, 23.5; IR 3006 (w), 2932, 2852, 1742, 1705, 1442, 1358, 1215, 1142, 1098, 908, 758 cm^{-1}.

***trans*-2-(Bromodifluoromethyl)-3-bromobicyclo[2.2.1]heptanes (7).** Two isomers were produced in 47% total yield. The ratio of **7a** (exo CF_2Br) to **7b** (endo CF_2Br) was 4.4 to 1: IR 2960, 2875, 1470 (w), 1450, 1350, 1265, 1250, 1235, 1220, 1205, 1190, 1175, 1150, 1115, 1090 (s), 1020, 980, 965, 940, 900, 835, 815, 800, 765, 745, 675 cm^{-1}; ^1H NMR δ 4.16 (t, J = 5 Hz, **7a**, CHBr, 0.815 H), 4.03 (dd, J = 7.7 Hz, J' = 2.6 Hz, **7b**, CHBr, 0.185 H), 2.9–2.3 (mult, 3 H), 2.1–1.9 (mult, 1 H), 1.8–1.5 (mult, 3 H), 1.4–1.2 (mult, 2 H); ^{13}C NMR **7a** δ 123.5 (t, J_{FC} = 309 Hz), 65.2 (t, J_{FC} = 20.5 Hz), 52.0, 44.5, 40.0, 36.0, 29.8, 23.8; **7b** δ 122.6 (t, J_{FC} = 312 Hz), 60.6 (t, J_{FC} = 19.8 Hz), 51.2, 48.5, 41.0, 35.4, 30.3, 27.1. Anal. Calcd for $C_8H_{10}Br_2F_2$: C, 31.61; H, 3.32. Found: C, 31.88; H, 3.32.

1,1-Difluoro-1,3-dibromo-4-phenylbutane (8). The standard procedure described above produced a mixture of 8 and unreacted allylbenzene. Pure 8 was isolated in 33% yield by flash chromatography on silica gel with hexane elution: ^1H NMR δ 2.9–3.4 (mult, 4 H), 4.35 (quintet, 1 H, CHBr), 7.2–7.5 (mult, 5 H); ^{13}C NMR δ 137.7, 129.9, 129.3, 128.0, 121.3 (t, J_{FC} = 308 Hz, CF_2Br), 51.9 (t, J_{FC} = 21.5 Hz), 46.5, 45.3; IR 3075 (w), 3055 (w), 3020, 2915, 1600, 1493, 1450, 1370, 1340, 1307, 1260, 1200 (s), 1165, 1104 (s), 1077, 1028, 980, 940, 917, 860, 1165, 1104 (s), 1077, 1028, 980, 940, 917, 860, 770, 745, 700 (s), 647 cm^{-1}.

Reaction of CF_2Br_2–Alkene Adducts with Potassium Hydroxide. General Procedure. Into a 10-mL screw-topped test tube were placed 5 mmol of KOH, 2 mL of deionized water, 1 mmol of the dibromodifluoro compound, and a small stirring magnet. The vessel was closed, and the lower half was suspended in an oil bath while the mixture was stirred and heated until it appeared homogeneous. Afterward the cooled reaction mixture was extracted with three 2-mL portions of chloroform to remove any unreacted alkyl halide. The reaction mixture was then acidified wth 3 M HCl and extracted with three 2-mL portions of chloroform. These second chloroform extracts were dried over anhydrous calcium sulfate and rotary evaporated to give the carboxylic acid.

2-Heptenoic Acid (9). A reaction of 4 with KOH was carried out as described above for 7 h at 130–140 °C to yield 96% **9**: ^1H NMR δ 10.62 (br s, 1 H, CO_2H), 7.10 (dt, J = 15.6 Hz, J' = 7.1 Hz, 1 H), 5.82 (d, J = 15.6 Hz, 1 H), 2.24 (quart., J = 7.1 Hz, 2 H), 1.65–1.25 (mult, 4 H), 0.92 (t, J = 7 Hz); the ^{13}C NMR agreed with the liteature;[6] IR 3300–2500 (br, OH), 2946, 2912, 2855, 2665, 1095, (s, C=O), 1642 (C=C), 1419, 1285, 1225, 981, 925 cm^{-1}.

1-Cyclopentene-1-carboxylic Acid (10). A reaction of 5 with KOH was carried out as described above for 6.5 h at 140 °C to yield 69% **10**: mp 117–119 °C (lit.[7] mp 119–120 °C); the ^1H NMR and IR spectra agreed with the literature;[7] ^{13}C NMR δ 171.5, 147.4, 136.5, 33.7, 31.1, 23.2.

2-Methyl-1-cyclohexene-1-carboxylic Acid (11). Reaction of 6 with KOH was carried out as described above for 41 h at 160 °C to yield 65% **11**. The crude material was recrystallized from methanol and water to give white needles, mp 84–85 °C. The ^1H NMR, ^{13}C NMR, and IR spectra agreed with those previously reported.[8]

Bicyclo[2.2.1]hept-2-ene-2-carboxylic Acid (12). Reaction of 7 with KOH was carried out as described above for 17 h at 130 °C to yield 73% **12**. The ^1H NMR and IR spectra were identical to those previously reported:[9] ^{13}C NMR δ 171.1 (CO_2H), 150.5, 140.9, 48.4, 44.0, 41.8, 24.7, 24.6.

4-Phenyl-3-butenoic Acid (13). Reaction of 8 with KOH was carried out as described above for 5 h at 130 °C to yield 72% **13**. The ^1H NMR spectrum agreed with that previously reported[10] and indicated an *E*:*Z* ratio of 5:1: IR 3400–2400 (br OH), 2890, 1695 (C=O), 1647 (C=C), 1457, 1375, 1290, 1220, 973, 912, 736, 680 cm^{-1}.

Acknowledgment. We gratefully acknowledge financial support from the National Science Foundaton through Instrument Grant No. CHE-8608881 and from the University of Central Florida Division of Sponsored Research through Research Grant Nos. 11-64-907 and 11-64-908. We also acknowledge Prof. J. T. Gupton for helpful discussions and Prof. G. R. Hertel for carrying out the thermochemical calculations.

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Kinetic Medium Effects in *N*-Cyclohexyl-2-pyrrolidone–Water Mixtures. Evidence for a Low Critical Hydrophobic Interaction Concentration

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Received February 2, 1989

Binary mixtures of water with a relatively hydrophobic cosolvent have been defined as typically aqueous (TA) solutions.[1] Sufficiently hydrophobic solutes, dissolved in

0022-3263/89/1954-3993$01.50/0