A Preparatively Viable *in Situ* Synthesis of Methyl 1-Cyclopropenecarboxylate[†]

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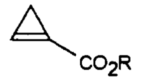
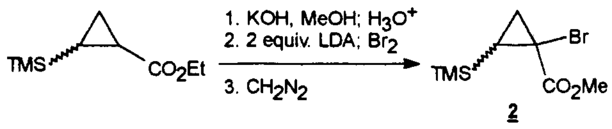
In our work on the preparation of functionalized cyclopropenes of structural and synthetic usefulness, we became interested in 1-cyclopropenecarboxylate esters without substitution in the 3-position. Owen[1a] reported the isolation of methyl cyclopropenecarboxylate from the treatment of methyl γ-bromocrotonate with sodium methoxide in benzene; however, Dreiding[1b] later demonstrated the product to be dimethyl 2,4,6-octatrienedioate. The alkoxide-induced dehydrohalogenation of ethyl 2-bromocyclopropane carboxylate, reported by Wiberg,[1c] was believed to generate cyclopropene **1b** which succumbed to nucleophilic addition by the base. A later attempt at preparing **1b** via the thermal elimination of acetic acid from ethyl 2-acetoxycyclopropanecarboxylate[1d] produced no cyclopropene derivatives. The elusiveness of these strained esters has prompted a statement[1e] of their unattainability as synthetic goals. We report, herein, an efficient and preparatively useful *in situ* approach to cyclopropene carboxylate esters which we have used to synthesize the methyl ester of the parent acid **1**.



1a, R = CH_3
1b, R = CH_2CH_3

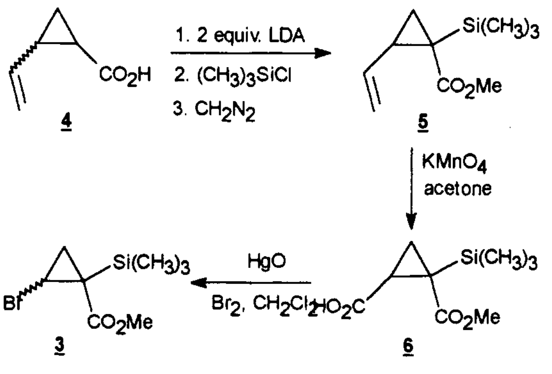
Results and Discussion

As noted by Wiberg,[1c,d] nonsterically protected cyclopropenes of type **1** must be generated in the absence of nucleophiles. The fluoride-induced dehalosilylation[2] reaction has been very successful in the generation of reactive cyclopropenes without the presence of nucleophiles because of the highly silophilic nature of the fluoride with relatively little or no carbophilicity observed. Application of this type of elimination reaction to the preparation of **1** requires the preparation of suitable β-halocyclopropylsilanes **2** or **3**. Halosilane **2**[3] was readily prepared from the adduct of ethyl diazoacetate and vinyltrimethylsilane (45%). However, we found that **2** was unreactive to treatment with tetra-*n*-butylammonium fluoride (TBAF) in tetrahydrofuran. Treatment with TBAF at various temperatures from −30 to 45 °C produced only recovered **2**.



A preparation for **3** was not possible via a simple carbenoid addition to vinyl bromide or α-(trimethylsilyl)acrylate esters. Retrosynthetic analysis led to the choice of 2-vinylcyclopropanecarboxylic acid (**4**) as our starting point. The vinyl group would serve as a masked halogen via oxidation to the carboxylic acid and then subsequent halodecarboxylation. Compound **4** was readily available from the rhodium(II)-catalyzed cyclopropanation of 1,3-butadiene with ethyl diazoacetate.[4] Silylation of the acid, **4**, was performed by conversion to the enediolate with 2.3 equiv of lithium dicyclohexylamide (−35 to 0 °C) and then addition of 2.3 equiv of chlorotrimethylsilane.[5] Acidic workup provided the α-silyl acid, which was converted directly to the ester **5** (93% from **4**, bp 72–75 °C, 10 mmHg) by treatment with ethereal diazomethane. NMR exhibited the presence of a single diastereomer in the resulting β-vinyl-α-silyl ester, **5**, which we believe to be the *cis*-vinyl ester on the basis of steric arguments.

Oxidative cleavage of the vinyl group with 4 molar equiv of $KMnO_4$ in acetone[6] provided the potassium salt of acid ester **6** which adhered to the resulting MnO_2. Aqueous washing and acidification provided **6** in 60% yield as colorless needles of mp 150–51 °C (subl. ∼145 °C). It is notable that neither hydrolysis of the ester nor desilylation was observed. Bromodecarboxylation with bromine and red mercuric oxide[7] in methylene chloride yielded the desired bromide **3** in $\geq$90% isolated yield (chromatography on Florisil with 10:3 hexane/chloroform) as a viscous colorless oil.



Treatment of silyl bromide **3** with a solution of TBAF in THF in the presence of cyclopentadiene effected complete conversion and a virtually quantitative yield (94%, isolated) of the Diels–Alder adduct, **7**, was obtained. Only one of the two possible adducts was observed. The

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(6) Kokke, W. C. M. C.; Varkvisser, F. A. *J. Org. Chem.* **1974**, *39*, 1535.

(7) Paquette, L. A.; Wells, G. J.; Horn, K. A.; Yan, T.-H. *Tetrahedron* **1983**, *39*, 913.

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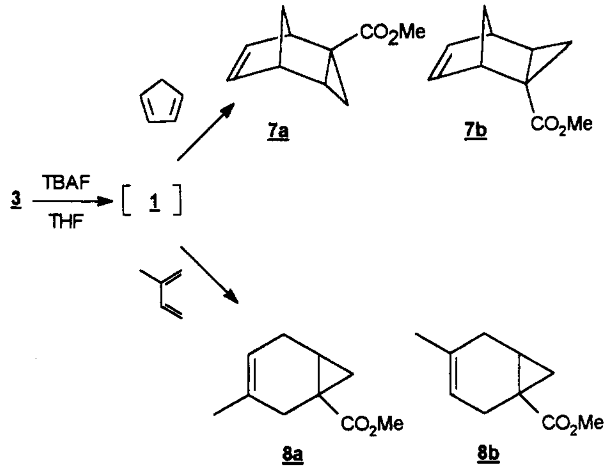

proton NMR shift of the vinylic hydrogens[8] and the deshielding (~14.7 ppm) of the bridging methylene carbon[9] (relative to norbornene) strongly suggests structure **7a**. This assignment is consistent with the general behavior of cyclopropene adduct formation with cyclopentadiene.[1e] A more definitive assignment has been procured via NOE-difference experiments. A small NOE enhancement was shown for the ester $-CH_3$ group ($\delta = 3.72$ ppm) when one of the norbornyl methylene hydrogens ($\delta = 1.81$ ppm) was irradiated. No NOE enhancement was observed for interaction between the cyclopropyl protons and the norbornyl methylene.

Use of isoprene as the enophile, under identical conditions, provided an excellent yield of adducts (92%) to which we have assigned structures **8a** and **8b** (43:57, respectively). These trapping experiments were performed at 0 °C (0.5 h) suggesting that **1** is a synthetically viable reagent even with weak enophiles.

Solutions of **1a** allowed to "decompose" displayed the physical and spectral characteristics of extensive polymerization. We believe that an ene-type dimerization was the mode of decompostion as we observe no indications of carbene-addition products or $2\pi + 2\pi$ cycloaddition products.

The extreme difference in reactivities of precursors **2** and **3** toward dehalosilylation was expected. Electron-withdrawing groups α to the silyl group vastly enhance the lability of the carbon–silicon bond, possibly through stabilization of the developing localized charge. Even an α bromide is sufficient to induce spontaneous desilylation of (α-bromovinyl)trimethylsilane[10] with aqueous hydroxide, while vinyltrimethylsilane readily undergoes phase-transfer carbene[11] additions with 50% aqueous sodium hydroxide or methoxide without significant decomposition.

We found this approach to be quite convenient with the yield and purity of the crude product at each step being sufficient for continuing to the next without additional purification. Overall yield of precursor **3** from ethyl 1-vinylcyclopropanecarboxylate (five steps) is 45–50%, with room for improvement, and scale-up to multigram quantities did not degrade the yield. We are using this synthesis as the starting point for further developments in the preparation and chemistry of cyclopropene esters and as an entry into the preparation of materials incorporating the bicyclo[4.1.0]heptane moiety.

Experimental Section

All reagents were used as received without further purification or prepared as previously reported. Only reactions involving alkyllithium reagents were performed under a maintained inert atmosphere. All others were conducted under ambient atmospheric conditions. Melting and boiling points are uncorrected. J values are given in Hz.

Methyl 1-(Trimethylsilyl)-2-ethenylcyclopropanecarboxylate (5). A solution of **4** (9.25 g, 82.5 mmol) in 8 mL of THF was added dropwise, via syringe, to a suspension of lithium dicyclohexylamide at 0 °C, prepared from 42 g of $(C_6H_{11})_2NH$ (231.6 mmol), 100 mL of THF, and 150 mL of butyllithium (1.6 M). The addition was performed over 15 min, and the mixture was stirred at 0 °C for an additional 30 min. A CCl_4 slush bath was used to cool the dark mixture to −35 °C, chlorotrimethylsilane (29.0 mL, 312 mmol) was added rapidly over 3 min via syringe, and the mixture was stirred for 1 h while warming to room temperature. H_2SO_4 (2M, 120 mL) was added to the yellow mixture, and then 200 mL of ether was added. The layers were separated, and the aqueous layer was adjusted to pH ~2 and reextracted with the ether layer. The aqueous extract was washed with ether (4 × 50 mL). The ethereal extracts were combined, washed once with 0.1 M H_2SO_4, and dried (anhydrous $MgSO_4$), and the volume was reduced to about 25 mL. Addition of CH_2N_2 (generated from 20 g of methylurea via the *N*-nitrosomethylurea) was performed until N_2 evolution was not evident, and then the volume was reduced to 50 mL and the addition continued. When no reaction was noted with excess CH_2N_2, the solvent was removed *in vacuo* to give a light yellow oil which was purified by column chromatography on Florisil (hexane/dichloromethane (8:2)) (17.6 g, 90%): 60-MHz H-NMR ($CDCl_3$) δ 0.02 (s, 9H), 1.03 (d of d, $J = 4.1, 7.5$, 1H), 1.43 (d of d, $J = 4.1, 6.2$, 1H), 1.77 (m, 1H), 3.6 (s, 3H), 4.85–5.9 (m, 3H); 15-MHz C-NMR ($CDCl_3$) δ 2.83, 16.66, 21.21, 27.41, 51.35, 115.75, 136.32, 173.65; IR (neat) 3061 (m), 2996 (m), 2940 (m), 2887 (m), 1714 (s), 1631 (m) cm^{-1}; MS (EI) *m/e* 198 (4), 183 (4), 167 (7), 147 (41), 131 (48), 94 (82), 89 (84), 73 (100); HRMS (EI) *m/e* calcd for $C_{10}H_{18}O_2Si$ 198.1076, found 198.1076, calcd for $C(13)C_9H_{18}O_2Si$ 199.1110, found 199.1112.

2-Carbomethoxy-2-(trimethylsilyl)cyclopropanecarboxylic Acid (6). To a stirred solution of **5** (10.0 g, 50.5 mmol) in 200 mL of anhydrous acetone was added in one portion finely powdered $KMnO_4$ (28.0 g, 178 mmol). The deep purple mixture slowly began to reflux under its own heat and was stirred for 1.5 h more after reflux subsided. The solids were vacuum filtered and repeatedly washed with acetone until the washings were almost colorless. The solids were then washed with 5% aqueous $NaHCO_3$ three times (120 mL each). The aqueous washings were then acidified to pH 1~2 with 2 M H_2SO_4 and extracted with CH_2Cl_2 (5 × 25 mL). The combined extracts were dried (anhydrous $MgSO_4$) and filtered and the solvent removed *in vacuo* to give virtually pure **6** (6.68 g, 61%) as white needles: mp 150–151 °C (subl. ~145 °C). An additional 5–10% of impure **6** can be isolated from the acetone washings after destroying the excess $KMnO_4$ with 2-propanol: 60-MHz H-NMR ($CDCl_3$) δ 0.05 (s, 9H), 1.15 (d of d, $J = 6.2, 10.4$, 1H), 1.72 (m, 2H), 3.63 (s, 3H), 10.5 var. (bs, 1H); 15-MHz C-NMR ($CDCl_3$) δ 3.47, 16.56, 22.18, 26.38, 51.84, 172.04, 177.90; IR MS (EI) *m/e* 201 (85), 185 (48), 169 (100), 97 (95), 89 (79); HRMS (EI) calcd for $C_9H_{16}O_4Si$ 216.0818, found 216.0817, calcd for $C(13)C_8H_{16}O_4Si$ 217.0851, found 217.0855.

Methyl 2-Bromo-1-(trimethylsilyl)cyclopropanecarboxylate (3). A mixture of **6** (3.00 g, 13.9 mmol) and red mercuric oxide (2.24 g, 10.3 mmol) were suspended in 25 mL of anhydrous CH_2Cl_2 at 0 °C, with stirring. A solution of bromine (2.36 g, 14.7 mmol) in 25 mL of anhydrous CH_2Cl_2 was then added dropwise over 1 h, and the red suspension was stirred for an additional 1.5 h at 0 °C. The solids were removed by filtration and rinsed twice with hexane (20 mL). The combined organics were concentrated *in vacuo*, and the residue was applied to a Florisil column with hexane and eluted with 15% (v/v) CH_2Cl_2/hexane. Bromide **3**

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[11] Miller, R. B. *Synth. Commun.* **1974**, *4*, 341.

was obtained as a colorless oil (3.22 g, 90.2%): 60-MHz H-NMR ($CDCl_3$) δ 1.24 (t, *J* = 5.3, 1H), 1.78 (d of d, *J* = 5.3, 7.8, 1H), 3.35 (d of d, *J* = 5.3, 7.8, 1H), 3.68 (s, 3H); 15-MHz C-NMR ($CDCl_3$) δ 1.07, 17.83, 19.25, 19.79, 22.13, 26.68 (2C), 51.74 (2C), 171.21, 173.50; IR (neat) 2958 (m), 2902 (w), 1721 (s); MS (EI) *m/e* ($M^+ - CH_3$) 237 (7), 235 (8), 171 (7), 148 (16), 146 (16), 89 (100), 73 (62), 67 (79); HRMS (EI) *m/e* calcd for $C_8H_{15}Br(79)O_2Si$ 250.0025, found 250.0026, calcd for $C(13)C_7H_{15}Br(79)O_2Si$ 251.0058, found 251.0062, calcd for $C_8H_{15}Br(81)O_2Si$ 252.0004, found 252.0007.

Reaction of Methyl 1-Cyclopropenecarboxylate (3) with Cyclopentadiene. A stirred mixture of 3 (510 mg, 2.03 mmol) and cyclopentadiene (1.2 mL) was stirred 0 °C while a 1 M solution of TBAF in THF (3.5 mL, 3.5 mmol) was added dropwise via syringe over 15 min. The resulting green-black mixture was stirred 1 additional h at 0 °C, and then the excess cyclopentadiene and THF were removed *in vacuo*. The dark residue was chromatographed on Florisil with hexane until the dicyclopentadiene had completely eluted, and then 15% (v/v) CH_2Cl_2/hexane was used as the eluent. Adduct 7 (330 mg, 94%) was obtained as a colorless oil characterized by an extremely sweet but irritating odor: 250-MHz H-NMR ($CDCl_3$) δ 1.1 (d of d, *J* = 8.2, 4.5 Hz, 1H), 1.68 (m, 1H), 1.81 (d of m, *J* = 7.3 Hz, 1H), 1.92 (d of m, *J* = 7.3 Hz, 1H), 2.08 (m, 1H), 2.92 (m, 1H), 3.31 (m, 1H), 3.72 (s, 3H), 5.80 (m, 1H), 5.96 (m, 1H); 15-MHz C-NMR ($CDCl_3$) δ 26.63, 28.34, 28.88, 43.14, 43.58, 51.50, 63.52, 132.46, 132.80, 175.99; IR (neat) 3043 (w), 2938 (m), 2852 (w), 1712 (s); MS (EI, 70 eV) *m/e* 164 (5), 149 (3), 133 (3), 105 (15), 91 (7), 77 (12), 28 (100); HRMS (EI) *m/e* calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0833, calcd for $C(13)C_9H_{12}O_2$ 165.0871, found 165.0868.

Reaction of 3 with Isoprene. Use of isoprene (2.0 mL) in place of cyclopentadiene, as above, gave a 92% yield of adduct, as a mixture of isomers **8a** and **8b**: 60-MHz H-NMR ($CDCl_3$) δ 5.24 (m, 1H), 3.70 (s, 3H), 2.8–2.2 (m, 4H), 1.68 (m, 2H), 1.30 (m, 3H), 0.92 (m, 3H); 15-MHz C-NMR ($CDCl_3$) δ 16.5 (2C), 20.4, 21.4, 23.4, 24.0, 24.6, 28.5, 29.1, 51.5 (2C), 115.9, 117.3, 128.8, 130.3, 176.2 (2C); HRMS (EI) *m/e* calcd for $C_{10}H_{14}O_2$ 166.0993, found 166.0988.

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Supplementary Material Available: ^1H NMR spectra for compounds 3, 5, 6, 7, 8a, and 8b and NOE difference spectra for compound 7 (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.