Syntheses of Two Stereoselectively Trideuteriated Vinylcyclopropanes

John E. Baldwin* and Karla A. Villarica

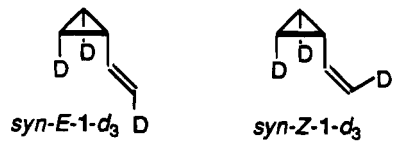
Department of Chemistry, Syracuse University, Syracuse, New York 13244

Received August 2, 1994[⊗]

Multigram quantities of methyl 2-cyclopropene-1-carboxylate have been converted in five steps to the *syn-E* and *syn-Z* isomers of 2,3,2′-d_3-vinylcyclopropane with high levels of deuterium incorporation and stereoselectivity.

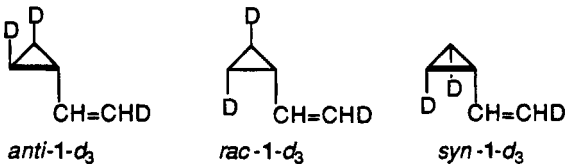
Introduction

An experimental determination of the stereochemistry of the thermal vinylcyclopropane to cyclopentene rearrangement[1–5] is of some importance, for whatever insights may be gained from computational and experimental studies on the stereochemistry of the rearrangement will be most readily compared for vinylcyclopropane and deuterium-labeled vinylcyclopropanes themselves. With this ambition in mind the deuterium-labeled vinylcyclopropanes *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 were selected as synthetic objectives.



While some progress has been made toward establishing the stereochemical characteristics of the thermal vinylcyclopropane to cyclopentene rearrangement for a few substituted yet geometrically unconstrained systems,[6–11] no experimental work relevant to the stereochemistry of the rearrangement of the parent hydrocarbon has ever been reported. The fact that the thermal stereomutations of deuterium-labeled vinylcyclopropanes[12–14] are very much faster than rearrangements to cyclopentenes, and thus that the stereochemistry of any stereoselectively labeled vinylcyclopropane will be compromised before appreciable amounts of deuterium-labeled cyclopentenes can be formed, constitutes one obvious impediment to such stereochemical studies. Another follows from the relative inaccessibility of sufficient quantities of appropriately labeled vinylcyclopropanes. The present work reports a synthetic route that overcomes the second obstruction in the path of informative stereochemical work.

As a point of comparison, Willcott and Cargle's classic kinetic studies of the thermal stereomutations of vinylcyclopropane depended in part on an adventitious synthesis of a d_3-vinylcyclopropane having labels at C(2) and C(3) in a cis,anti disposition.[13,14] A mixture of stereoisomers of 1-vinyl-2,3,2′-trichlorocyclopropane treated with sodium in CH_3OD gave *anti*-**1**-d_3 with substantial stereoselectivity; according to 100 MHz $^1H\{^2H\}$ NMR spectral indications, the product mixture contained about 88% *anti*-**1**-d_3 and 6% each of *rac*-**1**-d_3 and *syn*-**1**-d_3.[13,14]



One thus might aspire to at least this level of deuterium-labeling stereoselectivity at C(2) and C(3), to controlled definition of stereochemistry of the deuterium label at C(2′), and to securing substantially greater amounts of labeled vinylcyclopropanes: the synthetic work leading to *anti*-**1**-d_3 and minor amounts of *rac*-**1**-d_3 and *syn*-**1**-d_3 afforded only some 35 μL of these vinylcyclopropanes.[13,14]

Results and Discussion

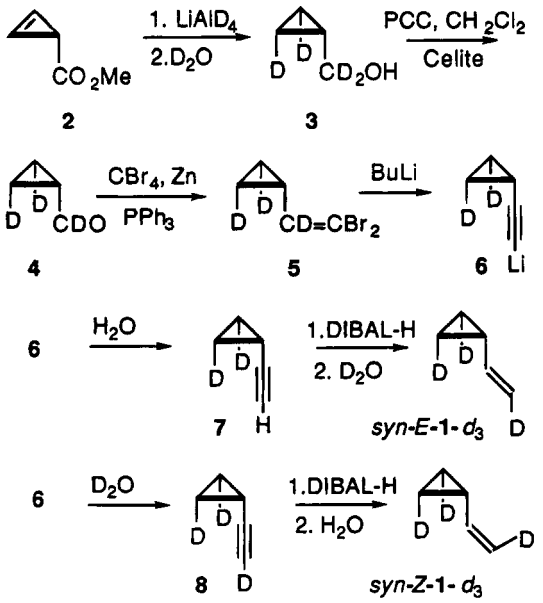
The overall strategy adopted to make vinylcyclopropanes *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 in useful quantities and the requisite degrees of deuterium incorporation and stereochemical control took advantage of prior experience gained while constructing related deuterium-labeled cyclopropanes, as outlined in Scheme 1. Were adequate amounts of a 2-cyclopropene-1-carboxylate such as **2** available, reduction with lithium aluminum deuteride followed by a D_2O workup would afford the alcohol **3** having deuterium labels at C(2) and C(3) in the syn orientation.[15,16] Application of the sequence developed by Ghatlia[9] would in turn convert the CD_2OH function of **3** into the corresponding deuterioaldehyde **4** and

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1994.

(1) Vogel, E.; Palm, R.; Ott, K. H. Unpublished. See Vogel, E. *Angew. Chem.* **1960**, *72*, 4–26.
(2) Overberger, C. G.; Borchert, A. E. *J. Am. Chem. Soc.* **1960**, *82*, 1007–1008; 4896–4899.
(3) Doering, W. von E.; Roth, W. R. *Angew. Chem. Int. Ed. Engl.* **1963**, *2*, 115–122.
(4) Ellis, R. J.; Frey, H. M. *J. Chem. Soc.* **1964**, 5578–5583.
(5) Woodward, R. B.; Hoffmann, R. *The Conservation of Orbital Symmetry*; Verlag Chemie: Weinheim, 1971; pp 120–122.
(6) von E. Doering, W.; Sachdev, K. *J. Am. Chem. Soc.* **1975**, *97*, 5512–5520. E. A. Barsa, Ph. D. Dissertation, Harvard University, 1977.
(7) Andrews, G. D.; Baldwin, J. E. *J. Am. Chem. Soc.* **1976**, *98*, 6705–6706.
(8) Gajewski, J. J.; Squicciarini, M. P. *J. Am. Chem. Soc.* **1989**, *111*, 6717–6728.
(9) Baldwin, J. E.; Ghatlia, N. D. *J. Am. Chem. Soc.* **1991**, *113*, 6273–6274.
(10) Gajewski, J. J.; Olson, L. P. *J. Am. Chem. Soc.* **1991**, *113*, 7432–7433.
(11) Baldwin, J. E.; Bonacorsi, S. J. *J. Am. Chem. Soc.* **1993**, *115*, 10621–10627.
(12) Willcott, M. R.; Cargle, V. H. *J. Am. Chem. Soc.* **1967**, *89*, 723–724.
(13) Willcott, M. R.; Cargle, V. H. *J. Am. Chem. Soc.* **1969**, *91*, 4310–4311.
(14) Cargle, V. H. Ph.D. Dissertation, University of Houston, 1969.
(15) Vidal, M.; Arnaud, P. *Bull. Soc. Chim. Fr.* **1972**, 675–681. Vincens, M.; Duimont, C.; Vidal, M.; Domnin, I. N. *Tetrahedron* **1983**, *39*, 4281–4289.
(16) Baldwin, J. E.; Selden, C. B. *J. Am. Chem. Soc.* **1993**, *115*, 2239–2248.

0022-3263/95/1960-0186$09.00/0

Scheme 1



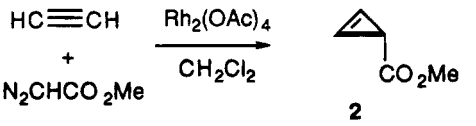
dibromovinyl derivative **5**. Two equivalents of butyllithium would give the lithioethynyl intermediate **6**, which could be quenched with H_2O or D_2O to give **7** or **8**. These ethynyl compounds could then be converted to *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 through reactions with diisobutylaluminum hydride, followed by D_2O or H_2O (Scheme 1).[9]

The first synthesis of methyl 2-cyclopropene-1-carboxylate was reported in 1956 by Doering and co-workers.[17] Pyrolysis of the Diels–Alder adduct from dimethyl acetylenedicarboxylate and the norcaradiene valence isomer of 7-(methoxycarbonyl)cycloheptatriene gave dimethyl phthalate and the cyclopropene ester. This ester was not isolated but its presence was inferred, for hydrogenation gave the known methyl cyclopropanecarboxylate.[17]

Myhre and co-workers[18] have published syntheses and spectroscopic characterizations of two $^{13}C_2$-labeled versions of **2** applying this fragmentation reaction and flash vacuum pyrolysis (FVP) techniques.[17,19–22] In attempts to adapt this precedent to larger-scale preparations of the ester, 7-(ethoxycarbonyl)cycloheptatriene was synthesized[23,24] by the reaction of benzene and ethyl diazoacetate in the presence of the rhodium(II) trifluoroacetate dimer[25,26] and combined with dimethyl acetylenedicarboxylate to give the tricyclo[3.2.2.$0^{2,4}$]nonadiene adduct. In FVP runs employing 10 g of this adduct, a packed quartz tube, and temperatures between 360 and 380 °C, only small amounts of the byproducts ethyl 2-butynoate and butadienoate were formed; from each run, 300 to 600 mg of the cyclopropenecarboxylate was obtained. Unconverted starting material was recovered and recycled. With this FVP route and a substantial investment of time and effort a total of some 5 g of ethyl 2-cyclopropene-1-carboxylate was secured. Alternative synthetic methods for preparing the ester remained of interest.

Photochemical decomposition of alkyl diazoacetates[15,16] in the presence of acetylene, in diethyl ether or dimethyl ether or methyl *tert*-butyl ether, did not give cyclopropene esters in adequate yields and purities; about 3 g of ethyl 2-cyclopropene-1-carboxylate was prepared in the course of these explorations. Analysis by ^1H and ^{13}C NMR spectroscopy of a GC purified sample of this ester confirmed its identity. Thermal reactions of bis(trimethylsilyl)acetylene with the rhodium-generated carbene from ethyl diazoacetate[27–31] did not seem sufficiently promising to warrant a sustained developmental effort.

Rhodium-catalyzed condensation of methyl diazoacetate with acetylene in methylene chloride was reported in 1992 by Shapiro and co-workers.[32] Only very small quantities of **2** were synthesized and the ester was not isolated; it was converted directly through reactions with cyclopentadiene or a thiol to give more stable compounds which could be isolated and characterized.



Initial implementations of this reaction gave **2** in 30–50% yields. An improved procedure was developed: the dropwise addition of the diazoacetate over 4 h to a cooled methylene chloride solution of rhodium acetate dimer that had been presaturated with purified acetylene gave **2** in yields as high as 70%, as determined by GC analyses against a standard. The identity of the product was confirmed by mass spectrometry. Approximately 20 g of **2** as a solution in methylene chloride was accumulated from several repetitions of this reaction.

This procedure is a substantial advance over the other methods tried for making multigram quantities of methyl 2-cyclopropene-1-carboxylate. Thanks to its efficacy, the projected syntheses of substantial amounts of *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 could be carried forward as planned.

Reduction of ethyl or methyl 2-cyclopropene-1-carboxylate with lithium aluminum deuteride in diethyl ether, followed by treatment of the reaction mixture with D_2O, gave the d_4-labeled alcohol **3**.[15,16] Ethyl 2-cyclopropene-1-carboxylate obtained by the FVP or the photochemical route was reduced directly, since it was available as an ethereal solution. The ester prepared using the rhodium acetate catalyst, available as a solution in methylene chloride, was filtered and concentrated by slowly remov-

(17) Doering, W. von E.; Laber, G.; Vonderwahl, R.; Chamberlain, N. F.; Williams, R. B. *J. Am. Chem. Soc.* **1956**, *78*, 5448.
(18) Myhre, P. C.; Maxey, C. T.; Bebout, D. C.; Swedberg, S. H.; Petersen, B. L. *J. Org. Chem.* **1990**, *55*, 3417–3421.
(19) Farnum, D. G.; Mehta, G.; Silberman, R. G. *J. Am. Chem. Soc.* **1967**, *89*, 5048–5049.
(20) Wiersum, U. E. *Aldrichim. Acta* **1981**, *14*, 53–59, and references therein.
(21) Wiersum, U. E. *Recl. Trav. Chim. Pays-Bas* **1982**, *101*, 317–364; 365–381.
(22) Staley, S. W.; Norden, T. D.; Su, C.-F.; Rall, M.; Harmony, M. D. *J. Am. Chem. Soc.* **1987**, *109*, 2880–2884.
(23) Anciaux, A. J.; Demonceau, A.; Noels, A. F.; Hubert, A. J.; Warin, R.; Teyssie, P. *J. Org. Chem.* **1981**, *46*, 873–876.
(24) Dzhemilev, U. M.; Dokichev, V. A.; Sultanov, S. Z.; Sadykov, R. A.; Tolstikov, G. A.; Nefedov, O. M. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1991**, 1063–1069.
(25) Johnson, S. A.; Hunt, H. R.; Neumann, H. M. *Inorg. Chem.* **1963**, *2*, 960–962.
(26) Tesler, J.; Drago, R. S. *Inorg. Chem.* **1984**, *23*, 2599–2606.
(27) Nefedov, O. M.; Dolgij, I. E.; Okonischnikova, G. P.; Schwedova, I. B. *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 929–930.
(28) Donaldson, W. A.; Hughes, R. P. *Synth. Commun.* **1981**, *11*, 999–1004.
(29) Maier, G.; Hoppe, M.; Resenauer, H. P.; Krüger, C. *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 437.
(30) Chen, P., 1993, personal communication. Clauberg, H., Ph.D. Dissertation, Harvard University, 1993.
(31) Sachs, R. K.; Kass, S. R. *J. Am. Chem. Soc.* **1994**, *116*, 783–784.
(32) Shapiro, E. A.; Kalinin, A. V.; Nefedov, O. M. *Org. Prep. Proced. Int.* **1992**, *24*, 517–520. For related syntheses utilizing 1-alkynes and 1,2-disubstituted acetylenes, see Protopopova, M. N.; Shapiro, E. A. *Russ. Chem. Rev.* **1989**, *58*, 667–681.

ing the solvent using a Kugelrohr transfer apparatus. The concentrated ester could be stored without serious decomposition in the refrigerator for days; it did not prove as labile as one might have supposed. Addition of diethyl ether to the concentrate caused the precipitation of a white solid, presumably dimethyl maleate and fumarate. Filtration gave an ethereal solution which was reduced with $LiAlD_4$ and then treated with D_2O to provide alcohol **3**.

Oxidation of the acid-sensitive cyclopropylcarbinol **3** to the readily air oxidized aldehyde **4** proved to be a troublesome step. Numerous methods were tried before this oxidation was accomplished with PCC and Celite.[33,34] Under these conditions the reaction was complete after 6 h and a nearly quantitative yield of the desired aldehyde **4** was achieved.

Aldehyde **4** was treated with carbon tetrabromide, zinc, and triphenylphosphine[35-39] to give **5** which, upon treatment with 2 equiv of butyllithium, gave the lithioethynyl intermediate **6**. This intermediate may be allowed to react with water to give the d_2-ethynylcyclopropane **7** or with D_2O to afford the d_3-analog **8**.

Reductions of the alkynes **7** and **8** to alkenes *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 were most successful when all traces of ether from the crude dibromide were carefully removed to minimize overreduction and the reaction time was not prolonged; reaction mixtures were monitored carefully and then worked up before overreduction became significant. The vinylcyclopropanes were distilled and then purified by preparative GC on an SE-30 column: 820 mg of *syn-E*-**1**-d_3 and 578 mg of *syn-Z*-**1**-d_3 were obtained.

Both samples contained a few percent of ethylcyclopropane-d_3, according to mass spectrometric and GC analyses and direct comparisons with an authentic sample of unlabeled ethylcyclopropane. This side-product stems from overreduction of the ethynylcyclopropane intermediates **7** and **8**. Further preparative GC on a β,β'-oxydipropionitrile (β,β'-OPDN) column provided pure *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3.

Figure 1 shows ^1H NMR spectra for an authentic sample of unlabeled vinylcyclopropane[40] and the final products *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 after the SE-30 chromatography. The very high stereochemical specificity and deuterium incorporation at C(2′) achieved through the synthetic route followed are evident in the second and third spectra. The ethylcyclopropane-d_3 impurities, about 2% in the *syn-E*-**1**-d_3 sample and 6% in the *syn-Z*-**1**-d_3 product, are apparent at δ 0.9, 1.3, and 1.55 ppm.[41]

Figure 2 records the upfield region of the ^1H NMR spectrum of the *syn-E*-**1**-d_3 product after purification through preparative GC on a β,β'-ODPN column. Some syn C(2) and C(3) hydrogen absorption intensity at δ 0.35–0.40 stems from lack of 100% deuterium incorporation. The C(1) hydrogen at δ 1.4 appears as an apparent quartet, for it is coupled with three vicinal hydrogens.

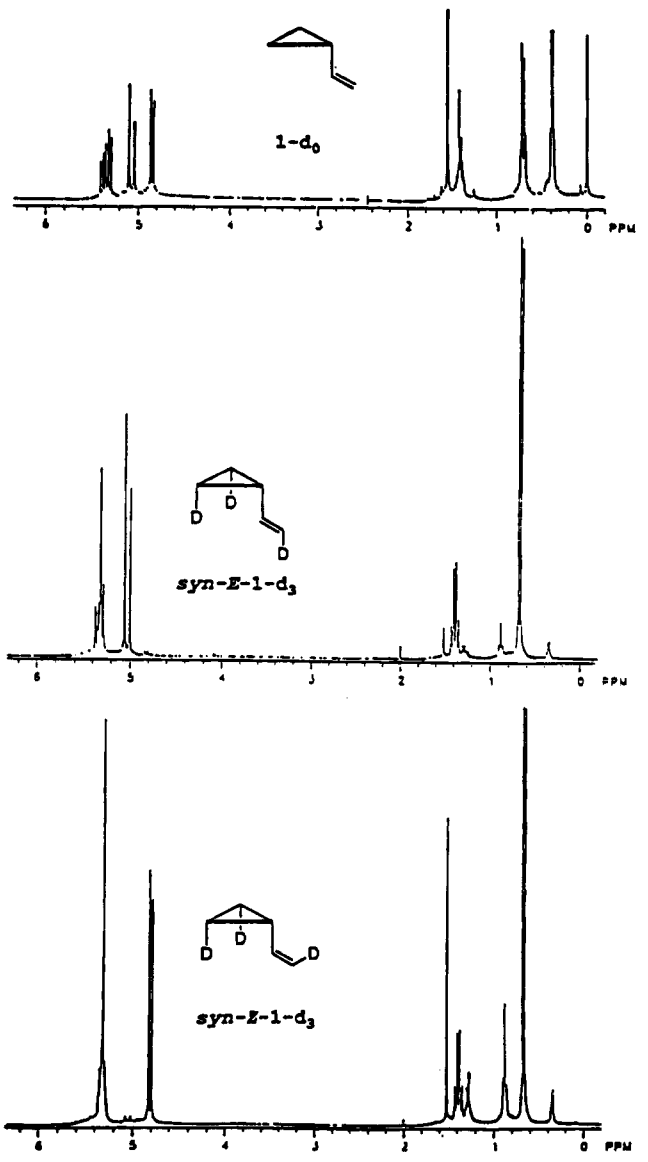


Figure 1. ^1H NMR (300 MHz) spectra for vinylcyclopropane (top), *syn-E*-**1**-d_3 (middle), and *syn-Z*-**1**-d_3 (bottom). The d_3-labeled vinylcyclopropanes, isolated by GC on an SE-30 column, are contaminated with some ethylcyclopropane-d_3.

Neither the small amounts of ethylcyclopropane-d_3 present in the samples after the SE-30 chromatography, nor the small amounts of incompletely deuteriated vinylcyclopropanes in the product mixtures, compromise the intended stereochemical and kinetic studies in which the *syn-E*-**1**-d_3 and *syn-Z*-**1**-d_3 vinylcyclopropanes are to be employed. The immediate synthetic objectives thus have been met, and methyl 2-cyclopropene-1-carboxylate may now be considered a readily available starting material for other synthetic applications.

Experimental Section

General. All ^1H and ^{13}C NMR spectra were obtained for $CDCl_3$ solutions. Chemical shifts are reported in ppm with respect to residual $CHCl_3$ at δ 7.26 downfield from Me_4Si, unless otherwise noted. Analytical gas chromatographic analyses were done utilizing two 25 m × 0.2 mm columns, Ultra 1 (cross-linked methyl silicone gum) and Ultra 2 (cross-linked 5% phenylmethyl silicone). Diethyl ether was dried

(33) Kurth, M. J.; O'Brien, M. J.; Hope, H.; Yanuck, M. *J. Org. Chem.* **1985**, *50*, 2626–2632.
(34) Shizuri, U.; Yamaguchi, S.; Terada, Y.; Yamamura, S. *Tetrahedron Lett.* **1987**, *28*, 1791–1794.
(35) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769–3772.
(36) Bestmann, H. J.; Frey, H. *Liebeigs Ann. Chem.* **1980**, 206–2071.
(37) Posner, G. H.; Loomis, G. L.; Sawaya, H. S. *Tetrahedron Lett.* **1975**, 1373–1376.
(38) Van Hijfte, L.; Kolb, M.; Witz, P. *Tetrahedron Lett.* **1989**, 3655–3656.
(39) Okamura, W. H.; Elnagar, H. Y.; Ruther, M.; Dobreff, S. *J. Org. Chem.* **1993**, *58*, 600–610.
(40) Kirmse, W.; von Bülow, B. G.; Schepp, H. *Liebigs Ann. Chem.* **1966**, *691*, 41–49.
(41) The ^1H NMR spectrum for ethylcyclopropane is reproduced in *Sadtler Standard Spectra: Nuclear Magnetic Resonance Spectra*; Sadtler Research Laboratories: Philadelphia, 1970; No. 8163.

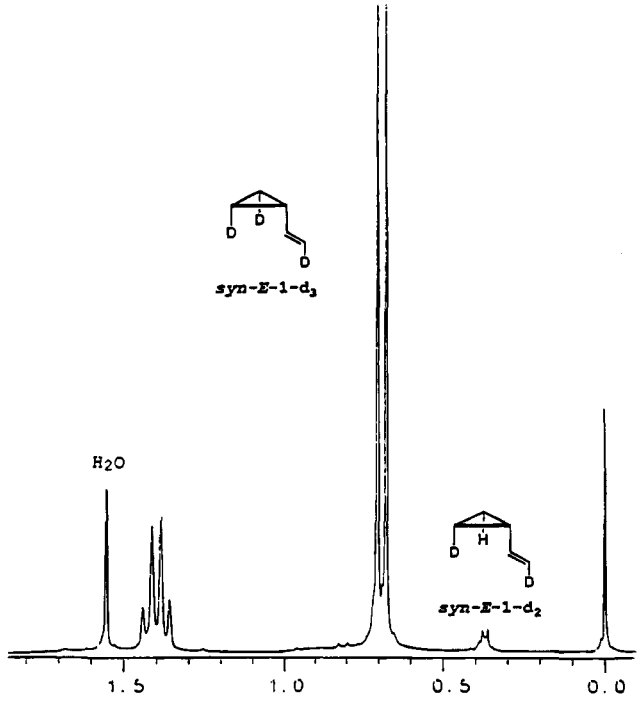


Figure 2. ^{1}H NMR (300 MHz) spectrum of the upfield absorptions of *syn-E*-**1**-d_3 after purification by GC on a β,β'-ODPN column. The absorption at δ 0.35–0.40 ppm is ascribed to a syn hydrogen in *syn-E*-**1**-d_2, an incompletely deuteriated version of the major synthetic product.

over sodium and benzophenone and distilled prior to use. Carbon tetrachloride and methylene chloride were dried over 3A molecular sieves and used without further purification. Cyclohexane was shaken with concentrated sulfuric acid, separated, dried over sodium, and then distilled through a Vigreux column. All reactions were carried out under a nitrogen atmosphere.

Ethyl 2-cyclopropene-1-carboxylate was synthesized using flash vacuum pyrolysis (FVP) techniques and preparative-scale glassware (Aldrich) from 3-(ethoxycarbonyl)-6,7-bis(methoxycarbonyl)tricyclo[3.2.2.0^{2,4}]nona-6,9-diene.[18] From a small portion of the product mixture in ether the ester was isolated by preparative GC using a 1-m 20% Carbowax 20M on Chromosorb P-NAW 60/80 column at 87 °C. ^{1}H NMR: δ 6.91 (d, J = 1.2 Hz, 2H), 4.16 (q, J = 6.9 Hz, 2H), 2.22 (t, 1H), 1.28 (t, J = 6.9 Hz, 3H). ^{13}C NMR: δ 103.7, 60.5, 16.8, 14.3, 14.2; lit.[42] (CCl_4) δ 6.84 (d, J = 1.8 Hz, 2H), 4.03 (q, 2H), 2.08 (t, 1H), 1.22 (t, 3H).

Methyl diazoacetate was prepared[18,43] and isolated as a fluorescent yellow oil. ^{1}H NMR: δ 4.74 (s, 1H), 3.74 (s, 3H); lit.[18] δ 4.77, 3.75.

Methyl 2-Cyclopropene-1-carboxylate (2). Rhodium acetate (100 mg, Strem, 2.3 × 10^{-4} mol, 0.2 mol % with respect to the diazoacetate) and 400 mL of reagent grade CH_2Cl_2 decanted from 3A molecular sieves were placed in a 1-L three-necked round-bottomed flask fitted with an addition funnel, a condenser, and a gas inlet tube. The flask was then cooled in an ice-water bath, and acetylene (Matheson, 99.6%) was bubbled into this green solution for 1 h, causing it to turn deeper green. A solution of 9.98 g of methyl diazoacetate (99.8 mmol) in 400 mL of CH_2Cl_2 was then added over 4 h via a pressure-equalizing addition funnel as acetylene was bubbled into the reaction mixture. The disappearance of the diazoacetate was followed by capillary GC analysis of aliquots filtered through a cotton plug to remove catalyst. When the reaction was complete, the reaction solution was filtered through filter paper to remove the catalyst. The yield of methyl 2-cyclopropene-1-carboxylate in the filtrate, determined using GC by analyzing a small weighed aliquot combined with methyl crotonate as a standard, was about 75%, or approximately 7.4 g. The solution also contained about 4% of fumarate and maleate esters. The cyclopropene ester was concentrated by removal of the solvent via Kugelrohr distillation at rt and atmospheric pressure. The distillation was continued, as the pressure was slowly decreased by opening the system to an aspirator; the concentrate of about 20 mL obtained was stored at −20 °C before it was used without further purification in the next step.

1-(d_2-Hydroxymethyl)-*syn*-2,3-d_2-cyclopropane (3). Into a 1-L three-necked round-bottomed flask fitted with an addition funnel and reflux condenser was placed a slurry of 7.00 g of $LiAlD_4$ (Aldrich, 167 mmol) in 100 mL of ether. About 7.4 g of **2** (75 mmol) dissolved in 50 mL of ether was then added over 2 h via a pressure-equalizing addition funnel. The reaction mixture was stirred overnight. In the morning, capillary GC analysis showed that the reaction was complete. The reaction flask was cooled in an ice bath and then 7 mL of D_2O was added slowly, which caused significant fizzing for a large excess of $LiAlD_4$ had been used. The hydrolysis mixture was stirred for another 30 min, and then it was treated with 7 mL of 15% NaOD/D_2O and an additional 7 mL of D_2O. Aluminum salts were removed by filtration through a sintered glass funnel and were rinsed with liberal portions of ether. Concentration of the filtrate by distillation of ether through a Vigreux column provided a solution weighing 16.13 g, 30% of which was alcohol **3** (about 85% yield, by analytical GC). The product had GC retention times identical with those characteristic of commercial cyclopropanemethanol.

A small aliquot of product from the $LiAlD_4$ reduction of ethyl 2-cyclopropene-1-carboxylate was isolated by preparative GC on a 2-m 10% XF-1150 on Chromosorb W-NAW 60/80 at 74 °C. ^{1}H NMR: δ 1.1 (t, J = 7.8 Hz, 1H) 0.5 (d, J = 7.8 Hz, 2H) 3.5 (s, 1H).

1-(d-Formyl)-*syn*-2,3-d_2-cyclopropane (4). To a 1-L round-bottomed flask was added 40.00 g of PCC (Aldrich, 186 mmol), 40.00 g of predried Celite, and 400 mL of CH_2Cl_2. The crude alcohol **3** (approximately 4.3 g, 57 mmol) was added via syringe, causing the solution to turn from orange to brown. After 4 h, analysis of an aliquot filtered through a Florisil plug by capillary GC indicated that the reaction was complete. The reaction mixture was then diluted with 1 L of ether and filtered through a 5-cm pad of Florisil in a sintered glass funnel; the solid was rinsed liberally with ether, until no more aldehyde was evident in the filtrate (by analytical GC). The slightly yellow organic filtrate was concentrated by slow distillation through a Vigreux column to about 100 mL. Capillary GC analysis confirmed the identity of aldehyde **4** by comparisons with commercial d_0-aldehyde.

1-(1′-d-2′,2′-Dibromoethenyl)-*syn*-2,3-d_2-cyclopropane (5). To a solution of 52.48 g of PPh_3 (Aldrich, 200 mmol) in 1 L of CH_2Cl_2 in a 3-L flask was added 13.11 g of purified zinc[44] (201 mmol). The resultant slurry was cooled in an ice–water bath and a solution of 66.38 g of CBr_4 (Aldrich, 200 mmol) in 200 mL of CH_2Cl_2 was added. The reaction mixture was stirred for 24 h at rt, and then about 4.2 g (approximately 57 mmol) of aldehyde **4** in ether and CH_2Cl_2 was added. After a minimum of 12 h, the progress of the reaction was checked by analytical GC of an aliquot. When the aldehyde was no longer evident, the reaction mixture was diluted with 1.8 L of pentane which caused an oil to separate. The pentane solution was then decanted from the oil into another reservoir. The residual oil was redissolved in 300 mL of CH_2Cl_2; 600 mL of pentane was added to it, and then the pentane solution was decanted from the separated oil. This procedure was done a total of five times. The combined pentane solutions were concentrated in batches by rotary evaporation until a very slightly yellow oil with some solid precipitate remained. Just enough CH_2Cl_2 was added to dissolve the oil, and then just enough pentane was added to cause the salts to precipitate. The solution was

(42) Kimura, K.; Horie, S.; Minato, I.; Odaira, Y. *Chem. Lett.* **1973**, 1209–1212.

(43) Searle, N. E. *Organic Syntheses*; Wiley: New York, 1963; *Coll. Vol. IV*; pp 424–426.

(44) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; Pergamon: Oxford, 1980; p 547.

filtered through a Celite plug into another flask. Rotary evaporation to remove the solvent provided a colorless oil and a small amount of solid. The latter was removed by the addition of pentane, filtration through a cotton plug, and then careful rotary evaporation to yield 11.00 g of an oil which, by analytical GC, contained 92.6% of the dibromide (78% for two steps from the alcohol). ^{1}H NMR: δ 1.84 (t, J = 8.1 Hz, 1H) 0.88 (d, J = 8.1 Hz, 2H).

1-(d-Ethynyl)-*syn*-2,3-d$_2$-cyclopropane (8). A 100-mL three-necked round-bottomed flask was fitted with a water condenser and then charged with 7.65 g (33 mmol) of (dibromoethenyl)cyclopropane **5** and 30 mL of dry cyclohexane. Using a syringe, 34 mL of 2.0 M *n*-BuLi (Aldrich, 68 mmol) in cyclohexane was added dropwise over 15 min to the reaction mixture cooled in a salt–ice water bath. Stirring was continued as the reaction mixture was held at −10 and 0 °C for 2 h and then at rt for 3 h, and then an aliquot was worked up and analyzed by capillary GC; the reaction was complete as evident by the absence of the dibromide. Both the reaction flask and a coil attached to the condenser were then cooled in an ice bath. A slow quench with 12 mL of D_2O (Aldrich, 99.9 atom % D) was added, and the layers were separated. The aqueous portion was extracted once with 30 mL of cyclohexane. The organic portions were combined, dried over $MgSO_4$, filtered, and analyzed by GC. This solution was used directly in the subsequent reduction. A small amount was isolated by preparative GC purification on a 3-m 20% SE-30 on Chromosorb P NAW column at 65 °C. ^{1}H NMR: δ 0.76 (d, J = 8.3 Hz, 2H) 1.22 (t, J = 8.3 Hz, 1H).

1-(2′-*Z*-d-Ethenyl)-*syn*-2,3-d$_2$-cyclopropane (*syn*-*Z*-1-d_3). A 250-mL three-necked round-bottomed flask was charged with the cyclohexane solution of **8** prepared immediately above. Using a syringe pump, 50 mL of 1.0 M DIBAL-H (Aldrich, 50 mmol) in cyclohexane was added over 1 h. The reaction mixture was stirred overnight and was then cooled in an ice–water bath. The addition of 8 mL of H_2O gave an emulsion which was eliminated by adding five 4-mL aliquots of 10% HCl. The layers were separated and the aqueous acidic layer was extracted with a 50-mL portion of cyclohexane. The combined organic material was washed with 50 mL portions of 5% aqueous $NaHCO_3$ and of H_2O. Analysis by GC indicated a 15:70:15 ratio of ethylcyclopropane to ethenylcyclopropane to ethynylcyclopropane. Concentration of this organic solution was achieved by distillation of the low-boiling components, including the desired compound through a 20-cm Vigreux column into a receiving flask cooled in a dry ice–acetone bath under a helium atmosphere. This distillate contained all three (ethyl, ethenyl, and ethynyl) cyclopropanes along with some butane from both the n-BuLi and DIBAL-H reactions. Preparative GC through a 3.5-m × 0.63-cm 25% SE-30 on Chromosorb P-NAW 60/80 column (oven at 45 °C) provided 578 mg of *syn*-*Z*-**1**-d_3 (ret time 22 min), 98% pure by analytical GC of the headspace (25% yield from 7.65 g of (dibromoethenyl)cyclopropane **6**); the remaining 6% was ethylcyclopropane-d_3. ^{1}H NMR: δ 5.32 (m, 1H) 4.81 (d, J = 10.2 Hz, 1H) 1.39 (q, J = 8.3 Hz, 1H) 0.67 (d, J = 8.3 Hz, 2H). The deuterium incorporation at the vinyl position was estimated to be better than 95% by dividing the integral of the residual proton signal at 5.0 ppm by that at 4.8, taken to be unity (Figure 1). Further preparative GC purification of a small portion using a β,β'-ODPN column provided an NMR sample free of ethylcyclopropane-d_3. The ratio of integrated ^{1}H NMR absorption intensities at 0.7 (anti C(2,3) H) and 0.4 ppm (syn C(2,3) H) was estimated to be 100:9.

1-(2′-*E*-d-Ethenyl)-*syn*-2,3-d$_2$-cyclopropane (*syn*-*E*-1-d_3). Treatment of 10.19 g of (dibromoethenyl)cyclopropane **5** (44.5 mmol) with 46 mL of 2.0 M *n*-BuLi in cyclohexane (Aldrich, 92 mmol), following the protocol and workup procedure described above but using shorter reaction times (about 4 h) and H_2O to quench the intermediate ethynyllithium compound, provided a cyclohexane solution of **7**. In the manner used to obtain the *Z* isomer, the ethynylcyclopropane **7** was converted to *syn*-*E*-**1**-d_3 utilizing a D_2O workup of the DIBAL-H reaction mixture immediately after analytical GC of an aliquot indicated nearly complete reaction but minimal overreduction (3 h). The ratio of ethylcyclopropane to ethenylcyclopropane to ethynylcyclopropane in the product mixture was 4:89:7 by analytical GC. Purification and isolation was achieved in the manner described above to afford 820 mg (26% yield from the (dibromoethenyl)cyclopropane **5**) of preparative GC purified material, with 2% contamination by ethylcyclopropane-d_3. ^{1}H NMR: δ 5.32 (m, 1H) 5.04 (d, J = 7.0 Hz, 1H) 1.40 (q, J = 8.3 Hz, 1H) 0.70 (d, J = 8.1 Hz, 2H). The deuterium incorporation at the vinyl position was estimated to be better than 95% by comparisons of the integrals for the residual proton signal at 4.8 ppm versus the 2′-H absorption at 5.04 ppm (Figure 1). As with the *Z* isomer, a small portion was subjected to preparative GC purification to provide an NMR sample that was free of ethylcyclopropane-d_3 (Figure 2). The ratio of integrated ^{1}H NMR absorption intensities at 0.7 (anti C(2,3) H) and 0.4 ppm (syn C(2,3) H) was about 100:5.

Ethylcyclopropane was synthesized according to literature methods[45–47] and purified through preparative GC purification on a 3.5-m × 0.63-cm 25% SE-30 on Chromosorb P-NAW 60/80 column. ^{1}H NMR: δ 0.02 (q, J = 4.8 Hz, 2H), 0.38 (2H), 0.63 (m, 1H), 0.95 (t, J = 7.2 Hz, 3H), 1.21 (m, 2H).

Acknowledgment. We thank the National Science Foundation for support of this work through CHE-9100246.

JO941318A

(45) Bloodworth, A. J.; Chan, K. H.; Cooksey, C. J. *J. Org. Chem.* **1986**, *51*, 2110–2115.
(46) Herr, C. H.; Whitmore, F. C.; Schiessler, R. W. *J. Am. Chem. Soc.* **1945**, *67*, 2061–2063.
(47) Van Volkenburgh, R.; Greenlee, K. W.; Derfer, J. M.; Boord, C. E. *J. Am. Chem. Soc.* **1949**, *71*, 172–175.