The Titanium(III)- and Samarium(II)-Promoted Rearrangement of a Vinylcyclobutene 1,2-Diester to 1,2-, 1,3-, and 1,4-Phthalates

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Received August 17, 1999

We have discovered a novel rearrangement of a vinylcyclobutene 1,2-diester into a mixture of 1,2-, 1,3-, and 1,4-phthalates. On the basis of deuterium labeling studies, a mechanism for this rearrangement is proposed.

For the past few years, we have studied the nickel(I)-catalyzed rearrangement of the vinylcyclobutene derivative **1** to the corresponding cyclohexadiene **2** (Scheme 1).[1−3] In an effort to find other metals which will promote a similar rearrangement reaction, we have investigated titanium(III) and samarium(II). Unlike the nickel reaction, with these two metals, a subsequent oxidation takes place to generate aromatic compounds. (Due to the oxidation state change, the titanium and samarium reactions, unlike the nickel rearrangement reaction, cannot be catalytic.) In this paper, we report a very unusual rearrangement—the reaction of **1** with Ti(III) and Sm(II) generates not only the *o*-phthalate **3** but also the meta (**4**) and para (**5**) isomers.

Specifically, when vinylcyclobutene **1** is treated with Cp_2TiCl, generated from the reaction of Cp_2TiCl_2 with Zn,[4] or with SmI_2, which can be purchased, compound **3** is the major product. However, meta isomer **4** and para isomer **5** are also generated. The combined yield of these three compounds is 72% with Cp_2TiCl and 89% with SmI_2. The products are formed in approximately an ortho:meta:para ratio of 10:2:1, regardless of which of the two metals is used.

To better understand what is happening in these reactions, a number of control experiments were run.

1. Cp_2TiCl_2, $SmCl_3$, Zn, and $ZnCl_2$ have no effect on starting material **1**.

2. The product ratio and yield for the Cp_2TiCl reaction are approximately the same whether or not the Zn and $ZnCl_2$ are filtered off prior to the reaction of Cp_2TiCl with compound **1**.

3. When cyclohexadiene **2** is subject to the Cp_2TiCl or the SmI_2 reaction conditions, only ortho isomer **3** is formed. Not even a trace of meta isomer **4** or para isomer **5** can be observed by ^{1}H NMR spectroscopy or by gas chromatography.

4. In a recent publication,[5] aromatic compounds similar to **3**−**5** rearranged photochemically to generate a mixture of the ortho, meta, and para isomers. Approximately a 10:1.3:0.3 (ortho:meta:para) ratio was obtained regardless of which isomer was used as the starting material. In contrast, when any one of the three aromatic compounds **3**−**5** is subjected to either the titanium or the samarium reaction conditions, only that isomer is recovered. In other words, all the aromatic compounds are stable and do *not* rearrange under the titanium or samarium reaction conditions.

When these last two points are taken together, it is only vinylcyclobutene **1** which generates the meta and the para products.

To help determine the mechanism of the rearrangement reaction, a deuterium labeling experiment was performed. With compound **1**-d_4[2] as the starting material, ortho, meta, and para isomers **3**-d_2, **4**-d_2, and **5**-d_2 were formed. The fact that there are two deuterium atoms in each product was determined by mass spectrometry, and the position of these two deuterium atoms was determined by ^{1}H NMR spectroscopy.

As shown in Scheme 2, the ortho isomer (**3**) has the deuterium atoms at the 3- and 6-positions. For our Ni(I)-catalyzed rearrangement of **1**-d_4 to cyclohexadiene **2**-d_4, the deuterium atoms are at analogous positions in the product. For the meta isomer (**4**), the deuterium atoms are at the 2- and 4-positions. For the para isomer (**5**), the positions of the two deuterium atoms in the product could not be determined. Regardless of whether the deuterium atoms are 2,3, 2,5, or 2,6, they are chemically equivalent; therefore, there is no obvious loss of a peak in the ^{1}H NMR spectrum upon deuteration as with the ortho and meta isomers. We attempted to use ^{13}C satellite peaks to help with this analysis, but this proved unsuccessful. Thus, we do not know which labeled isomer of the para product is formed.

Taking all these data together, we wish to propose the mechanism shown in Scheme 3 for this rearrangement. The circles represent the deuterated carbon atoms. The Ti(III) or Sm(II), represented as M$^\bullet$, coordinates to the ring double bond of **1**, as has been observed previously for nickel,[1,6] to give **6**. The vinyl group then attacks to give the bicyclic ring system **7**. When the bond between the two bridgehead atoms breaks, the six-membered ring **8** is formed. Loss of the metal then gives cyclohexadiene **2**, which we know will aromatize to **3** under these reaction conditions.

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(1) Choi, H.; Hershberger, J. W.; Pinhas, A. R.; Ho, D. M. *Organometallics* **1991**, *10*, 2930.

(2) DiFrancesco, D.; Pinhas, A. R. *J. Org. Chem.* **1986**, *51*, 2098.

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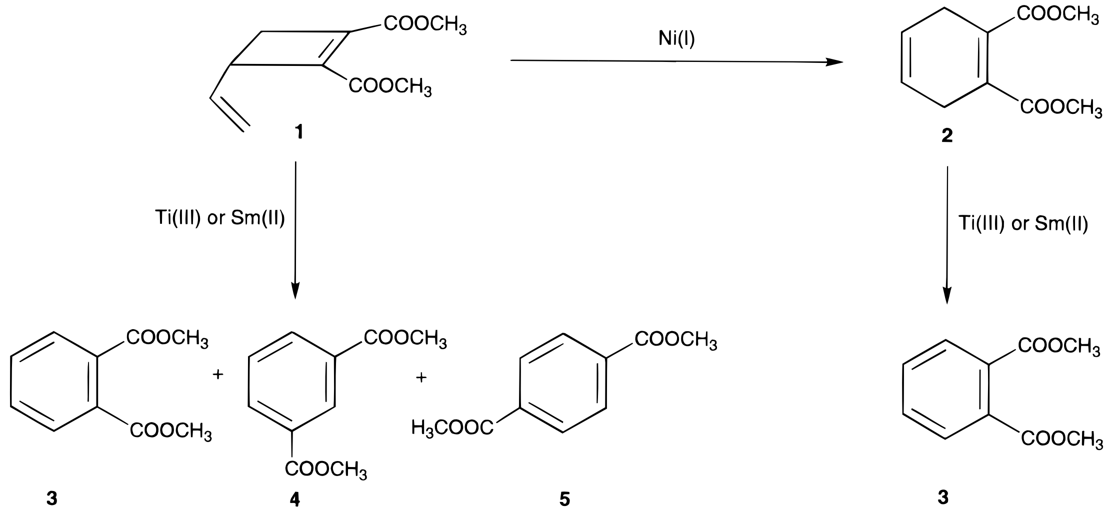
(4) RajanBabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1994**, *116*, 986.

(5) Foster, J.; Pincock, A. L.; Pincock, J. A.; Thompson, K. A. *J. Am. Chem. Soc.* **1998**, *120*, 13354.

10.1021/om990668q CCC: $18.00

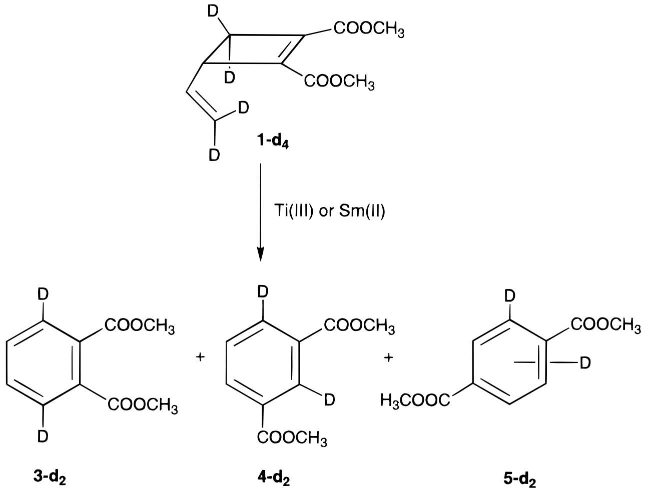
Scheme 1



If instead of the bond between the bridgehead atoms breaking in compound **7**, the bond between the two carbons bearing the esters breaks, a new bicyclic compound, **9**, is formed. As with any bicylobutane, **9** has two ways to generate a diene derivative. One gives **10**, which upon cyclization and the net loss of $MH_2^{\bullet}$ gives the meta isomer, and one gives **12**, which upon cyclization and the net loss of $MH_2^{\bullet}$ gives the para isomer.

Experimental Section

Scheme 2



All glassware was dried in an oven at 120 °C. THF and dioxane were freshly distilled from either benzophenone ketyl or potassium metal stills. Reactions were carried out at room temperature with magnetic stirring unless otherwise specified. All reactions were carried out under an argon atmosphere, and when vacuum evaporation was utilized, argon was used to reestablish atmospheric pressure. **1**, **1**-d_4, Zn, and Cp_2TiCl were prepared by literature methods.[1,2,4] SmI_2 is commercially available. Spectroscopic data for compounds **1** and **2**, and their deuterated analogues, have been previously reported.[2]

Analyses of reactants and products were conducted using a Perkin-Elmer 1600 Series FTIR spectrophotometer with KBr cells for solutions or KBr plates for neat samples. All NMR spectra were recorded on a Bruker 250 MHz spectrometer and referenced to TMS (tetramethylsilane) at 0.00 ppm. Deuterated chloroform ($CDCl_3$) was used exclusively as the solvent for all NMR analyses. Mass spectroscopic data were obtained using a Hewlett-Packard (HP) Model 6890 instrument with an injector port temperature of 170 °C and a split ratio of 10:1 with a flow of helium of 1.0 mL/min through a Supelco SPB-1 column (15 m $\times$ 250 μm $\times$ 0.25 μm). The column oven was set at an initial temperature of 70 °C, held for 1 min, and then ramped at 15 °C/min until a final temperature of 280 °C was reached; this temperature was held until the entire run time of 22 min had elapsed.

Reaction of 2 with Ti(III). A 10 mL portion of 1,4-dioxane was added to a 25 mL flask containing a magnetic stir bar. A 250 mg (0.25 g, 1.3 mmol) amount of **2** was added, and the mixture was stirred under an argon atmosphere for 10 min to complete solution. The flask was then sealed with a rubber septum. A 2 mL amount of a zinc suspension (0.2 g/mL, 0.4 g, 6 mmol) was added by syringe to the flask. A 250 mg amount of Cp_2TiCl_2 (0.25 g, 1.0 mmol) dissolved in 2 mL of 1,4-dioxane was added by syringe in the same way as the zinc suspension. The mixture was allowed to react for 240 h at room temperature with constant stirring. Samples were taken at 48 h

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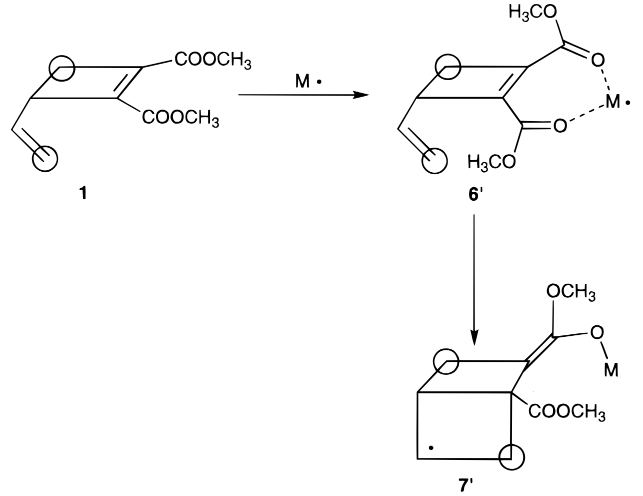
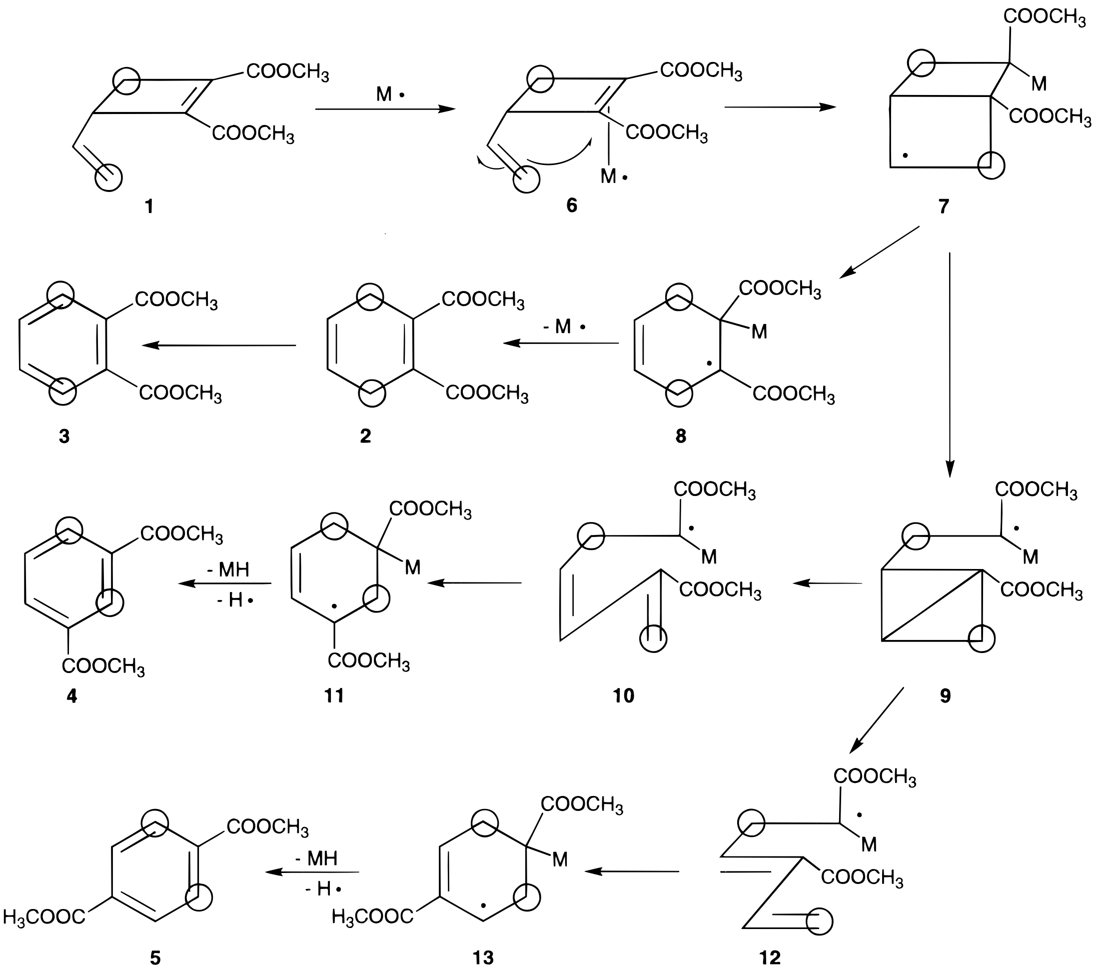
(6) One of the reviewers felt the "proposal that the oxophilic Lewis acids Cp_2TiCl and SmI_2 will coordinate to the C=C double bond is incorrect" and that "both metals will coordinate to the carbonyl functionality". We totally agree that titanium and samarium are much more oxophilic than nickel. The mechanism in Scheme 3 is proposed in an attempt to unify the nickel, titanium, and samarium chemistry. Since we have observed a compound similar to **6** in the nickel case,[1] we have proposed this as the initial intermediate. However, for titanium and samarium, the first-formed intermediate could be **6′**, which then isomerizes to **7′**. In a manner similar to that shown in Scheme 3, **7′** could generate **8′** and **9′**, compounds similar to **8** and **9** but in which the metal is coordinated to the oxygen instead of the carbon.



Scheme 3



intervals. A 155 mg amount (0.155 g, 0.798 mmol) of 1,2-dimethyl phthalatedicarboxylate (**3**) was produced. The yield for this reaction was 80%. ^{1}H NMR: δ 3.88 (s, 3 H), 3.90 (s, 3 H), 7.50−7.60 (m, 2 H), 7.70−7.80 (m, 2 H). ^{13}C NMR: δ 29.2, 128. 4, 134.2, 140.2, 167.1. IR (THF): 3005 (m), 2960 (s), 1747 (vs), 1375 (s), 1160 (s), 1043 (s) cm^{-1}. MS (EI): *m*/*z* (%) 59 (40), 77 (50), 82 (40), 91 (40), 107 (100), 166 (50), 194 (5).

Reaction of 1 with Ti(III). The above experimental procedure was usedd, substituting compound **1** (0.25 g, 1.3 mmol) for compound **2**. The reaction produced only **3**−**5** as determined by GC/MS. The overall yield was 0.14 g (0.72 mmol, 72%) with a distribution ratio of isomers equaling 10:2:1, respectively, on the basis of GC/MS. The remainder of the material is mainly unreacted starting material **1**. Compound **4**: ^{1}H NMR δ 3.90 (s, 6 H), 7.55 (t, $J = 3.5$ Hz, 1 H), 8.20 (d, $J = 3.5$ Hz, 2 H), 8.70 (s, 1 H); ^{13}C NMR δ 28.7, 128.3, 130.4, 131.5, 134.0, 167.0; IR (THF): 3005 (m), 2895 (s), 1745 (vs), 1372 (s), 1150 (s), 1040 (s) cm^{-1}; MS (EI) *m*/*z* (%) 59 (48), 67 (50), 82 (60), 91 (61), 107 (85), 163 (95), 194 (3). Compound **5**: ^{1}H NMR δ 3.90 (s, 6H), 8.0 (s, 4 H); ^{13}C NMR δ 25.3, 128.6, 134.8, 167.0; IR (THF) 2957 (w), 1745 (s), 1380 (s), 1145 (w) cm^{-1}; MS (EI) *m*/*z* (%) 59 (41), 68 (50), 82 (41), 91 (55), 107 (90), 163 (100), 194 (10).

Reaction of 1 with Sm(II). The above experimental procedure was used, substituting SmI_2 (1.0 M, 2.0 mL, 2.0 mmol) for the titanium. The reaction produced **3**−**5**. None of the reactant **1** remained. The overall yield was 89% (0.225 g, 1.16 mmol total) with a distribution ratio of isomers equaling 10:2:1, on the basis of GC/MS.

Reaction of 1-*d*$_4$ with Ti(III). The above experimental procedure was used, substituting compound **1**-*d*$_4$ (0.185 g, 0.925 mmol) for compound **2**. The reaction produced **3**-*d*$_2$, **4**-*d*$_2$, and **5**-*d*$_2$. The overall yield was 0.098 g (0.50 mmol, 54%) with a distribution ratio of isomers equaling 10:2:1, respectively, on the basis of GC/MS. **3**-*d*$_2$: ^{1}H NMR δ 3.88 (s, 3 H), 3.90 (s, 3 H), 7.36−7.48 (m, 2 H), 7.75−7.85 (m, <0.1 H); ^{13}C NMR δ 29.2, 128.4, 134.2, 140.2, 167.1; IR (THF) 3005 (m), 2960 (s), 2207 (w), 1747 (vs), 1375 (s), 1160 (s), 1043 (s) cm^{-1}; MS (EI) *m*/*z* (%) 59 (40), 77 (50), 84 (40), 92 (40), 108 (100), 168 (50), 196 (5). **4**-*d*$_2$: ^{1}H NMR δ 3.88 (s, 3 H), 3.90 (s, 3 H), 7.54−7.6 (m, 1.1 H), 8.25−8.36 (m, 1.2 H), 8.65−8.85 (s, <0.1 H); ^{13}C NMR δ 29.2, 128. 4, 134.2, 140.2, 167.1; IR (THF) 3005 (m), 2960 (s), 2205 (m), 1747 (vs), 1375 (s), 1160 (s), 1043 (s) cm^{-1}; MS (EI) *m*/*z* (%) 59 (40), 77 (52), 84 (40), 93 (40), 109 (100), 165 (50), 196 (5). **5**-*d*$_2$: ^{1}H NMR δ 3.90 (s, 6 H), 7.90−8.22 (d, $J = 11$ Hz, 2.4 H); ^{13}C NMR δ 29.2, 128. 4, 134.2, 140.2, 167.1; IR (THF) 2965 (m), 2960 (s), 2195 (w), 1747 (vs), 1375 (s), 1160 (s), 1045 (s) cm^{-1}; MS (EI) *m*/*z* (%) 59 (40), 77 (53), 84 (40), 94 (40), 108 (100), 164 (50), 196 (4).

Reaction of 1-*d*$_4$ with Sm(II). The above experimental procedure was used, substituting **1**-*d*$_4$ (0.185 g, 0.925 mmol) for **3** and SmI_2 (1.0 M, 2.0 mL, 2.0 mmol) for the titanium complex. The reaction only took 72 h. The reaction produced **3**-*d*$_2$, **4**-*d*$_2$, and **5**-*d*$_2$. The overall yield was 33% (0.061 g, 0.31 mmol) with a distribution ratio of isomers equaling 10:2:1, respectively, on the basis of GC/MS.

Acknowledgment. We wish to thank Dr. Herman Holt, Jr. (UNC-Asheville), and Dr. Barry Carpenter (Cornell) for valuable discussions.

OM990668Q