

## LEWIS ACID REVERSAL OF THE TORQUOSELECTIVITY OF THE ELECTROCYCLIC RING OPENING OF 3-ACETYLCYCLOBUTENE

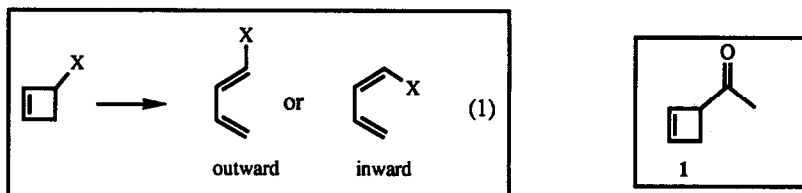
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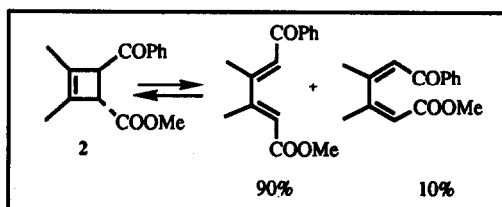
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**Summary:** Thermolysis of 3-acetylcyclobutene resulted in a mixture of E- and Z-dienes, favoring slightly the E-diene, in accord with theoretical prediction. This preference was reversed by the Lewis acid,  $ZnI_2$ , also predicted by ab initio calculations on a model system.

In the electrocyclic ring openings of substituted cyclobutenes, electron donors and mild electron acceptors rotate outward to form E-dienes, while powerful  $\pi$ -electron acceptors rotate inward to form Z-dienes.<sup>1-4</sup> Torquoselectivity is the stereoselectivity of the twisting of the breaking  $\sigma$ -bond, exemplified in this thermally-allowed conrotatory ring opening. As shown below, the twisting of the C<sub>3</sub>-C<sub>4</sub> bond during breaking can occur in two ways. We have predicted that substituents that rotate outward, such as esters and carboxylic acids, could be enticed to rotate inward by coordination with Lewis acids, due to the enhancement of the substituent electron-withdrawing properties.<sup>3</sup> Here, we present experimental proof of this prediction with 3-acetylcyclobutene, **1**.



Earlier, we found that 3-formylcyclobutene opens with rotation of the formyl group inward, in accord with our prediction.<sup>2</sup> Inward rotation permits the low-lying vacant orbital of the formyl group to overlap with the remote terminus of the breaking  $\sigma$ -bond. This stabilization overwhelms steric repulsions only with the most powerful  $\pi$ -acceptors such as formyl or dialkylboryl groups.<sup>1,4</sup> Alkylketo(X=RCO) groups are less powerful  $\pi$ -acceptors than formyl groups;



therefore, ketones should be on the borderline between inward and outward rotation. The thermolysis of the ketoester, **2**, gave a 90:10 preference for outward rotation of the phenylketo and ester groups, but this ratio reflects thermodynamic control, since the products rapidly equilibrate via the cyclobutene.<sup>5</sup>

In an earlier publication, we studied the rotational selectivity of cyclobutene-3-carboxylic acid computationally.<sup>3</sup> The carboxyl group is mildly electron-withdrawing and was predicted to prefer outward rotation by about 2 kcal/mol. The electron-withdrawing character is increased by protonation, and inward rotation of the protonated carboxylic acid is predicted to be favored by 5-6 kcal/mol.<sup>3</sup> These precedents have led us to undertake an experimental and theoretical study of the related 3-acetylcyclobutene, **1**.

RHF ab initio calculations on the thermal electrocyclic ring opening of **1** were carried out employing the GAUSSIAN 90 series of programs.<sup>6</sup> Four transition structures were located with the 3-21G basis set for the conversion of 3-acetylcyclobutene, **1**, to E- or Z-3,5-hexadiene-2-one, **3** or **4**. Single point calculations were carried out with the 6-31G\* basis set on these optimized structures. This procedure has been shown to give predictions of torquoselectivity in accord with experiment for many cases.<sup>2,4</sup> The structures and relative energies (6-31G\*//3-21G, kcal/mol) are shown in Figure 1.

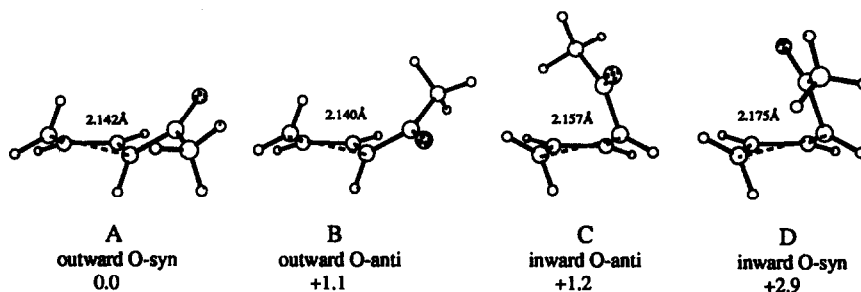


Figure 1. Transition structures of the 3-acetylcyclobutene electrocyclic ring opening

In the lowest energy outward transition state structure A, the carbonyl oxygen is syn to the cyclobutene ring. The carbonyl group points away from the cyclobutene ring for the lowest energy inward transition structure C. Outward rotation is predicted to be favored by 1.2 kcal/mol.

In order to evaluate the effects of Lewis acids on torquoselectivity,  $\text{BH}_3$ ,  $\text{ZnH}_2$  or  $\text{ZnF}_2$  were added to the four transition state structures with the 3-acetylcyclobutene geometries frozen.<sup>7</sup> The positions and geometries of each Lewis acid were fully optimized in each structure. Since the carbonyl oxygen has two lone pairs for coordination of a Lewis

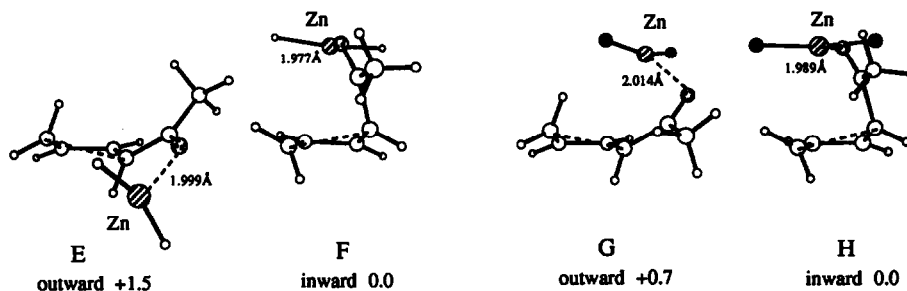
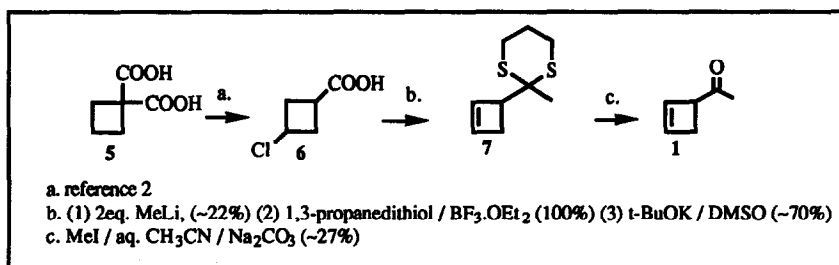


Figure 2. Transition structures of electrocyclic ring opening of 3-acetylcyclobutene coordinated to  $\text{ZnH}_2$  (E, F) or  $\text{ZnF}_2$  (G, H)

acid, eight structures were located altogether. For  $\text{BH}_3$ , 3-21G calculations indicate that inward rotation is now favored by 2.7 kcal/mol. The B-O distance is 0.02 Å shorter for inward rotation than for outward rotation. This signifies that the Lewis acid coordination is tighter for inward rotation. For  $\text{ZnH}_2$  and  $\text{ZnF}_2$ , the STO-3G\* basis set was used for the calculation.<sup>8</sup>

As summarized in Figure 2, inward rotation is calculated to be favored over outward rotation by 1.5 kcal/mol for  $\text{ZnH}_2$ . This energy difference corresponds to the ratio of 10:90(E:Z) at 80°C. In both modes of ring opening, the carbonyl oxygen of **1** is pointed in the direction opposite to that in the case of  $\text{BH}_3$ . In both cases,  $\text{ZnH}_2$  is coordinated from the side of the cyclobutene ring rather than the methyl group. Inward rotation with  $\text{ZnF}_2$  is favored by 0.7 kcal/mol over outward rotation. In both structures, the carbonyl oxygen is pointed toward cyclobutene ring and  $\text{ZnF}_2$  is also coordinated from the same side as the cyclobutene ring. The coordination of  $\text{ZnF}_2$  seems somewhat looser than of  $\text{ZnH}_2$  considering the coordination length between the Zn and O. The Zn-O distances are 2.01 Å (outward) and 1.99 Å (inward) for  $\text{ZnF}_2$ , while for  $\text{ZnH}_2$ , they are 2.00 Å (outward) and 1.98 Å (inward). In both cases, the Zn-O distance is slightly shorter by  $\sim 0.02$  Å for inward rotation, which signifies it is more tightly coordinated, as the case of  $\text{BH}_3$ .

In order to test these predictions, 3-acetylcyclobutene, **1**, was synthesized from the commercially available 1,1-cyclobutanedicarboxylic acid, **5**, as shown below.<sup>9</sup>

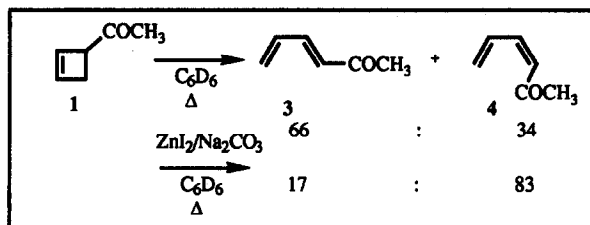


Thermolysis of **1** in benzene- $d_6$  in a sealed NMR tube overnight gave E-diene, **3**, almost exclusively. The diene has a  $^1\text{H-NMR}$  spectrum identical to the reported data.<sup>10</sup> However, this does not necessarily signify a kinetic preference of the ring opening of **1**, due to the expected ease of isomerization of **4**. In order to examine whether **4** was formed but lost by equilibration,  $^1\text{H-NMR}$  spectra were recorded periodically at very early stages of reflux of **1**. An authentic sample of **4** was prepared for comparison data in a separate experiment.<sup>11-14</sup> At 80°C in  $\text{C}_6\text{D}_6$ , judging from the relative intensities of integral curves corresponding to the singlet resonances of acetyl groups, the E/Z product ratio was observed to be 66:34( $\pm 5$ ) at the beginning of the ring opening and throughout the first  $\sim 100$  minute period. After this period the ratio gradually changed with increasing formation of the thermodynamically more stable E-diene, **3**. After about 6 hours, the E-diene, **3**, was the only detectable product. From this observation, we conclude that the kinetic ratio of 3:4 is approximately 66:34 at 80°C. This is similar to the theoretical prediction of 85:15(E:Z).

The influence of Lewis acids on this ratio was also studied. The Lewis acid  $\text{BF}_3 \cdot \text{OEt}_2$ , which is soluble in organic solvents, gave only the E-diene, **3**; the Z-diene, **4**, was not detected at all. However, Lewis acids readily isomerize the Z-diene to the E-diene. In a separate experiment, rapid isomerization of Z-diene, **4**, to E-diene, **3**, was observed at room temperature upon addition of  $\text{BF}_3 \cdot \text{OEt}_2$  to **4** in  $\text{C}_6\text{D}_6$  solution. In order to avoid product isomerization, a two-phase reaction with one equivalent of a solid Lewis acid,  $\text{ZnI}_2$ , was performed in the presence of  $\text{Na}_2\text{CO}_3$  in  $\text{C}_6\text{D}_6$ . Upon heating this mixture for 30 minutes at 80°C in a NMR probe, the reversed torquoselectivity was observed unambiguously. The product ratio was 17:83( $\pm 5$ ) favoring the Z-diene, **4**. Without  $\text{Na}_2\text{CO}_3$ , rapid isomerization to E-diene, **3**, occurs, and the solution turned brown, presumably due to the formation of HI and  $\text{I}_2$ .

Although we have also investigated other Lewis acids,  $\text{ZnI}_2$  turned out to be the only Lewis acid to reverse the torquoselectivity effectively. Silica gel did not affect the formation ratio.  $\text{AlCl}_3$  and TMSOTf afforded complex

mixtures, and  $\text{Sn}(\text{OTf})_2$  gave only E-diene, **3**.  $\text{ZnBr}_2$  slightly changed the ratio to ~50:50, but  $\text{ZnCl}_2$  did not change the torquoselectivity.

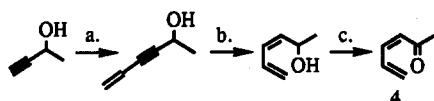


In conclusion, we have experimentally verified the torquoselectivity of thermal ring opening of 3-acetylcyclobutene, **1**, and its reversal from outward rotation to inward rotation by the soft Lewis acid,  $\text{ZnI}_2$ .

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#### Reference and Notes

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- 1**;  $^1\text{H-NMR}$ ( $\text{CDCl}_3$ , 200MHz): 2.142(3H, s), 2.617(1H, ddd,  $J=13.75$ , 1.00, 1.96), 2.785(1H, ddd,  $J=13.75$ , 0.89, 5.36), 3.705(1H, br.d), 6.086(1H, m), 6.248(1H, m);  $^{13}\text{C-NMR}$ ( $\text{CDCl}_3$ , 50MHz): 26.93(q), 33.92(t), 54.56(d), 135.77(d), 139.16(d), 208.90(s); MS:m/e 96.057515( $\text{M}^+$ )
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- The Z-diene, **4**, was prepared as follows. The  $^1\text{H-NMR}$  spectrum proved identical to the reported data.<sup>14</sup>



- vinyl bromide /  $\text{CuI}-(\text{Ph}_3\text{P})_2\text{PdCl}_2 / \text{Pr}_2\text{NH}$ ,  $25^\circ\text{C}$  (23%)<sup>12</sup>
- $\text{Zn}(\text{Cu}/\text{Ag})$ ,  $\text{MeOH-H}_2\text{O}$ ,  $25^\circ\text{C}$  (~73%)<sup>13</sup>
- activated  $\text{MnO}_2$ ,  $25^\circ\text{C}$  (-quant.)

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