



# Unique formation of oxapentacycloundecanones by catalytic flash vacuum thermolysis of tricyclo[5.2.1.0<sup>2,6</sup>]decenone epoxides using mineral solid acids

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## Abstract

Tricyclodecenone *exo*- and *endo*-epoxides **1** and **9** underwent an unexpected isomerization to oxa-pentacycloundecanones **2** and **10**, respectively, under flash vacuum thermolysis conditions using various solid acid catalysts. The structure of a derivative of **2** (R = CO<sub>2</sub>Et) has been elucidated by X-ray diffraction analysis. A tentative mechanism for the formation of **2** from **1** is proposed. © 2000 Elsevier Science Ltd. All rights reserved.

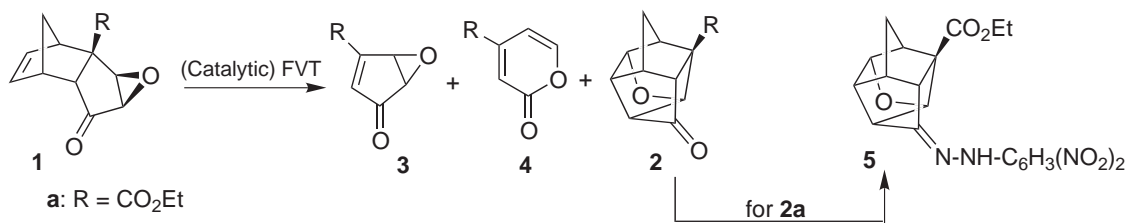
Recently, we described a novel dehydration reaction of stilbene oxides by concurrent use of flash vacuum thermolysis (FVT) and solid acid catalysts.<sup>1</sup> This catalytic FVT technique constitutes an attractive method to effect acid catalyzed rearrangement and fragmentation reactions in the gas phase. The retro Diels–Alder reaction is one of such conceivable fragmentation reactions. The use of solid acids as catalysts in combination with the FVT technique offers a unique possibility to lower the generally high temperatures required to achieve effective [4π+2π] cycloreversion thereby preventing consecutive thermal reactions and thus enabling access to kinetically labile products.

In continuation of earlier thermal gas phase studies<sup>2</sup> on the retro Diels–Alder reaction of 6-substituted tricyclodecenone epoxides **1** we considered catalytic FVT using mineral solid acids

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as a means to enhance the selectivity towards the synthetically valuable cyclopentadienone epoxides **3** at the expense of  $\alpha$ -pyrones **4**. These pyrones arise from a consecutive thermal rearrangement of initially formed **3**. Its formation may be considerably disfavored by lowering the temperature of the [4+2]-cycloreversion by Lewis or Brønsted catalysts. In contrast to the expectations, solid acid catalysts do not promote [4+2]-cycloreversion of tricyclodecadienone epoxides **3** but instead induce a rather effective formation of oxacage compounds **2** by a highly remarkable intramolecular isomerization/cyclization process.

Flash vacuum thermolysis of 6-functionalized *exo*-3,4-epoxy-5-oxo-*endo*-tricyclo-[5.2.1.0<sup>2,6</sup>]deca-8-en-2-ones **1** (Scheme 1) only leads to effective [4+2] cycloreversion at 400°C and higher temperatures.<sup>2</sup> Depending on the nature of R and the applied temperature, mixtures of cyclopentadienone epoxides **3** and pyrones **4** are obtained as the major products. Appreciable amounts of epoxides **3** are only obtained around 400°C. At higher temperatures these epoxides **3** are rapidly transformed into pyrones **4** via a stereospecific [ $4\pi_a+2\pi_a$ ] opening followed by recyclization.<sup>2</sup> In order to study the effect of strong solid mineral acids on the retro-Diels–Alder reaction these gas phase thermolysis experiments were reinvestigated in a flow batch reactor containing a small amount of a mineral solid acid.<sup>1</sup> Although complete conversion was indeed obtained at much lower temperatures ( $\geq 100^\circ\text{C}$  lower) hardly any cycloreversion product was obtained. Instead a major product was formed in appreciable quantities that was isomeric with the starting substrate. By carefully monitoring the thermolysis conditions using a variety of mineral acids optimum results were obtained for tricyclic ester **1a** as the starting substrate. A compilation of these results using Grade F-1 clay<sup>3</sup> and the amorphous silica-alumina B698D-24<sup>3</sup> as the most effective mineral acids is given in Table 1. For comparison the results of the gas phase thermolysis of **1a** in the absence of a catalyst are included. The selectivity with regard to the products **3a** and **4a** on one hand and the unknown compound **2a** on the other were dependent on the reaction temperature. Epoxide **3a** was not found at all under catalytic FVT conditions. The selectivity toward pyrone **4a** decreased sharply with decreasing reaction temperature. A maximum selectivity (73%) was attained at 250°C with amorphous alumina B698D-24<sup>3</sup> (entry 8). The mass balance is in most cases quite satisfactory and averages at 75%. Loss of cyclopentadiene and coke formation on the catalyst surface are responsible for loss of material.



Scheme 1.

The unknown compound **2a** could be isolated as a pure material and was extensively analyzed by 2D H NMR and <sup>13</sup>C NMR techniques. This analysis suggested the oxacage structure **2a**. Although all spectral information supported this structure, the formation of this unusual cage compound could not readily be rationalized. Therefore it was decided to secure this structure unequivocally by an X-ray diffraction analysis. As **2a** appeared to be an oil and its IR indicated the presence of a ketone function, attempts were made to obtain its 2,4-dinitrophenylhydrazone **5** which was indeed obtained after considerable experimentation as transparent orange platelet-

Table 1  
Reaction of tricyclodecenone epoxide **1a** under (catalytic) FVT conditions

Entry	Catalyst <sup>a</sup>	T <sup>b</sup> (°C)	Conversion <sup>c</sup> (%)	Selectivity <sup>c</sup> (%)		
				3a	4a	2a
1	None	500	100		100	
2		400	83	25	75	
3		300	0			
4	Grade F-1 <sup>3</sup>	400	98			33
5		350	75		24	52
6		300	22		23	50
7	B698D-24 <sup>3</sup>	300	87		12	72
8		250	74		4	73

<sup>a</sup> 400 mg of catalyst was used and 50 mg of substrate per run.

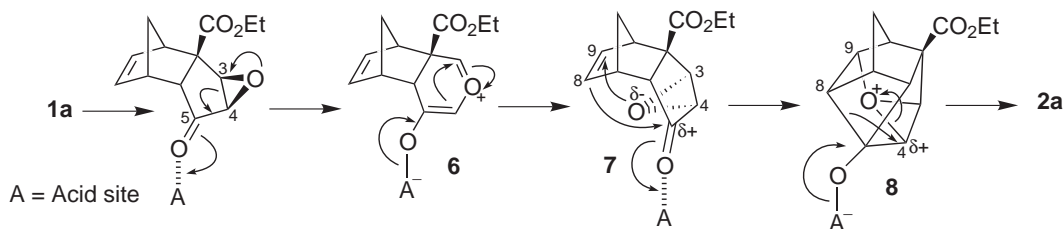
<sup>b</sup> Oven temperature; the substrate was vaporized at 150°C.

<sup>c</sup> Conversions and selectivities determined by GC.

like crystals after several crystallizations from ethanol and methanol. An X-ray diffraction analysis of **5** confirmed that the unknown pyrolysis product is oxapentacycloundecanone **2a**.

An intriguing question is how the formation of **2a** from **1a** can be explained in terms of an acceptable sequence of events. A prerequisite for such a rationale is the involvement of the solid acid. In the absence of this acid not a trace of such a cage compound is produced so its role is essential.

A tentative mechanism that might explain the formation of cage compound **2a** from **1a** under catalytic FVT conditions is presented in Scheme 2. The structure of **2a** dictates which bonds need to be formed during this process. Structural comparison of the starting tricyclic epoxide **1a** and the cage product **2a** leads to the conclusion that the oxygen bridge in **2a** originates from the epoxy oxygen. This conclusion inevitably requires inversion of configuration at the carbon to which this oxygen is attached (C<sub>3</sub> in epoxide **1a**), which can be accounted for by assuming a six-membered intermediate **6**. Such a transformation is conceivable by an initial coordination of



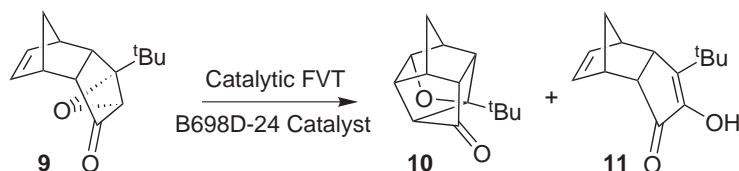
Scheme 2.

the carbonyl function in **1a** with the solid acid. Instead of promoting the  $[4\pi+2\pi]$  cycloreversion reaction, epoxide ring opening takes place to form carbonyl ylid type intermediate **6**. This carbonyl ylid may then reform the oxirane, but this can now result in either *exo*-epoxide **1a** or its isomeric *endo*-epoxide **7**. Epoxides are known to undergo isomerization via a C–C bond cleavage mechanism under certain thermal conditions,<sup>4,5</sup> but reports concerning a C–C bond cleavage of epoxy ketones giving 1,3-dipoles of the carbonyl ylid type are scarce.<sup>6</sup>

Calculations were performed on this unusual reaction from **7** to **2a**. Relatively simple AM1 calculations as implemented in the MOPAC93 program,<sup>7</sup> starting from the carbonyl protonated epoxy ketone **7** (A=H, CO<sub>2</sub>Et=H) and gradually decreasing the C<sub>8</sub>–C<sub>4</sub>/C<sub>5</sub> distance, suggested the occurrence of a mechanism as represented in Scheme 2. Considerable polarization of the C<sub>8</sub>–C<sub>9</sub>  $\pi$ -system takes place as a result of the approaching epoxide oxygen and the electron deficient carbonyl carbon C<sub>5</sub>. This results in the simultaneous formation of the C<sub>9</sub>–O and C<sub>5</sub>–C<sub>8</sub> bonds, leading to cyclobutanol **8** in a slightly exothermic process. The next step is the opening of the epoxide ring, by breaking of the C<sub>4</sub>–O bond and leaving a positive charge on C<sub>4</sub>. As the C<sub>4</sub>–O distance is about 2.1 Å, a transition state is reached, which allows the C<sub>8</sub>–C<sub>5</sub> bond to migrate to C<sub>4</sub>, thereby releasing a considerable amount of strain energy due to ring enlargement, viz. from a cyclobutanol to a cyclopentanone. The calculations show that this pathway has a favorable energy profile and probable geometric feasibility. Higher-level calculations (B3LYP 6-31G\*) confirmed the AM1 results, with proper characterization of the transition states between reactant, intermediate **8** and the product.

Catalytic FVT experiments were also performed with the dimethyl ketal of tricyclodecenone epoxide **1a**, viz. **1b**. As coordination of the solid acid with the basic carbonyl function in **1a** is essential in the above explanation, cage formation should now be blocked or at least hampered. Indeed, whereas **1a** gave an optimum yield of **2a** at 300°C, the major product obtained from **1b** turned out to be deketalized tricyclic ketone **1a**. Only minor amounts of cage compound **2a** were detected, which probably arise from **1a** after deketalization of **1b**. At higher temperatures a moderate selectivity towards pyrone **3a** was observed. The ketals of cyclopentadienone epoxide **3a** or of cage compound **2a** were not observed at all.

The mechanism proposed (Scheme 2) for the formation of oxacage **2a** from tricyclodecenone *exo*-epoxide **1a** requires inversion of the *exo*-epoxide function to *endo*-oxirane **7** in the first step. In order to further substantiate the occurrence of this unique epoxide inversion process, tricyclodecenonyl *endo*-epoxide **9** was synthesized independently and its thermal behavior studied under similar catalytic FVT conditions. As a consequence of the synthetic route to such an *endo*-epoxide a *tert*-butyl group at the C<sub>5</sub> position instead of an ester function at C<sub>6</sub>-bridge-head carbon atom had to be accepted.<sup>8</sup> Catalytic FVT experiments with tricyclodecenone *endo*-epoxide **9** were performed under identical conditions as applied for **1a** using amorphous alumina B698D-24 as the catalyst. At an optimum temperature of 300°C oxapentacycloundecanone cage structure **10** is indeed again produced with a relative high efficiency (78% selectivity at a conversion of 86%) (Scheme 3). This high yield of oxygen cage **10** clearly substantiates the intermediacy of such an *endo*-epoxide in the formation of cages **2** as proposed in Scheme 2.



Scheme 3.

In addition to cage compound **10** also 5-*tert*-butyl-4-hydroxy-tricyclodecadienone **11** was isolated (albeit in a low yield of 7%) and characterized (Scheme 3). A mechanism explaining the formation of **11** from **9** involves an acid-catalyzed epoxide rearrangement reaction<sup>9</sup> to form a 1,2-diketone, which leads to **11** after a keto-enol isomerization. According to spectral data the keto-enol equilibrium is completely on the enol side.

In conclusion, flash vacuum thermolysis of tricyclodecenone epoxides **1** applying mineral solid acids as the catalysts does not promote the expected retro Diels–Alder, but instead leads to a unique sequence of unusual transformations ultimately producing an oxapentacycloundecanone cage system **2**. This unconventional result together with our earlier work<sup>1</sup> in this new field of catalytic FVT clearly demonstrates the special effect of solid mineral acids on the chemical behavior of organic substrates in the gas phase at high temperatures. The strong Lewis acidity of these solid acids, which are completely free of water under these conditions, forms the basis of these novel transformations. Strong coordination of nucleophilic centers in the molecule, e.g. carbonyl and epoxide functions, on the active surface of the solid acid leads to unprecedented chemistry that is not feasible in homogeneous processes where solvents always interfere. In the present case, the use of Lewis acids such as BF<sub>3</sub> under homogeneous conditions indeed promotes the expected retro-Diels–Alder reactions,<sup>10</sup> thus underlining the remarkable contrasting behavior of substrates under catalytic FVT (CFVT) conditions.

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