

7-Oxabicyclo[2.2.1]heptadiene derivatives: reactivity towards Brønsted acids

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7-Oxabicyclo[2.2.1]heptadiene derivatives can be converted to phenols, fulvenes and/or the products from a retro-Diels–Alder-like reaction by treatment with Brønsted acids; the outcome of the reaction depends on the experimental conditions and the nature of the Brønsted acid used.

During the course of our investigations we have synthesised a large variety of arylphenols. These compounds are easily obtained *via* Diels–Alder reaction between arylfurans and dimethyl acetylenedicarboxylate (DMAD).¹ However, in most cases a mixture of the phenolic and the oxabicyclic derivatives is obtained. The proportions of the two species depend on the nature and the position of the substituent on the phenyl group. 7-Oxabicyclo[2.2.1]heptadiene derivatives are often used in organic synthesis as synthons for natural product elaboration.^{2,3} We have shown previously that dimethyl 1-aryl-7-oxabicyclo[2.2.1]heptadiene-2,3-dicarboxylates **1** can be converted to phenols **2** or to 6-hydroxyfulvenes **3** by reaction with Lewis acids.⁴ Depending on the acid used, **2** or **3** can be formed in a totally selective and quantitative way (Scheme 1). Never in the past have such high yields and such a selectivity been

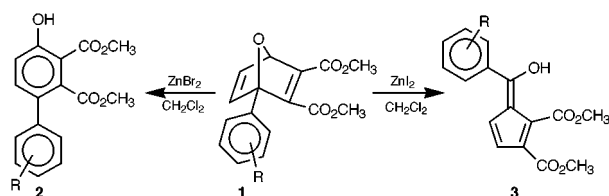
described.^{5–8} We report here the results obtained when **1** is reacted with Brønsted acids.

As with Lewis acids, depending on the nature of the Brønsted acid, phenols **2** and/or hydroxyfulvenes **3** are formed. However, another reaction was observed: a retro-Diels–Alder like reaction (retro-DA) leading to **4** and DMAD **5** (Scheme 2).

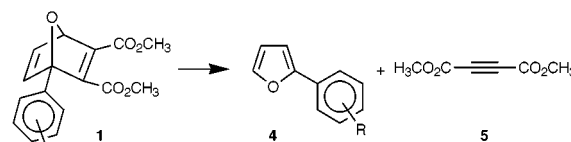
Our results are reported in Table 1. These results were obtained using 1-(2-chlorophenyl)-7-oxabicyclo[2.2.1]heptadiene-2,3-dicarboxylate as a model compound, but similar results were observed with **1** for R = *p*-nitro or *p*-acyl.

In the presence of gaseous HCl or with glacial AcOH (entries 4, 6–9) the retro-DA reaction is totally regioselective and is the only process observed. In AcOH, the conversion rate increases with the temperature. However, the retro-DA reaction is not a purely thermal one, as exemplified by the absence of conversion when **1** is heated at reflux in a CHCl₃–CCl₄ mixture (entry 10).

When mineral aqueous acids are used (HCl or H₂SO₄) the results depend on the experimental conditions and particularly on the solvent and temperature (entries 1–3, 5). In Et₂O, at room temperature, only the phenol **2** is formed. In CH₂Cl₂, with H₂SO₄, only tars are formed starting from compound **1**. With aqueous HCl, under heating, the reaction is not selective and the



Scheme 1



Scheme 2

Table 1 Influence of the Brønsted acids nature on the behaviour of **1**^a

Entry	Acid	Solvent	T/°C	t/h	Yield (%) ^b			
					1	2	3	4 + 5
1	HCl (aq.)	CH ₂ Cl ₂	55	24		44–37	6–0	50–63
2	HCl (aq.)	CH ₂ Cl ₂	reflux	24	9	8	72	11
3	HCl (aq.)	Et ₂ O	25	24	11	89		
4 ^c	HCl (g)	CH ₂ Cl ₂	25	48				100
5	H ₂ SO ₄	Et ₂ O	25	24	5	95		
6	AcOH	—	25	48	100			
7	AcOH	—	60	48	40			60
8	AcOH	—	90	48	25			75
9	AcOH	—	reflux	48	18			82
10	None	CHCl ₃ –CCl ₄	reflux	48	100			

^a Reagents and conditions: i, aq. HCl or H₂SO₄, Et₂O, room temp.; ii, aq. HCl, CH₂Cl₂, reflux; iii, anhydrous HCl, Et₂O or CH₂Cl₂, room temp. (or AcOH, reflux.) ^b The indicated yields are based on pure isolate compounds. ^c Ref. 9.

retro-DA process is observed along with the formation of **2** and **3**. The ratio of the different compounds depends on the temperature, and the yield of the retro-DA reaction increases with the temperature (entries 1, 2) while the yield of fulvene **3** decreases. It must be noted that the formation of the fulvene **3** and the retro-DA reaction are totally regioselective processes: only the 6-hydroxyfulven **3** and the 2-arylfurane **4** are formed, without any traces of another regioisomers.

With Lewis acids, **2** and **3** can be obtained selectively as unique compounds. Similarly with gaseous HCl or AcOH, the retro-DA-like reaction is the only one observed. Although we have no evidence for the mechanism of that reaction, we have observed, by thin layer chromatography, that an intermediate compound is formed during the reaction with gaseous HCl. This compound could not be isolated as it is rapidly converted to arylfuran and DMAD. This suggest that the retro-DA-like process could occur by chlorination (or acetoxylation in the case of AcOH) of the starting compound followed by subsequent rearrangements.

Our results show the great reactivity of 7-oxabicyclo-[2.2.1]heptadiene derivatives towards Brønsted acids. This was also demonstrated with Lewis acids. However, although with Lewis acids it is possible to synthesise phenols and/or 6-hydroxyfulvenes, we have shown that with Brønsted acids it is also possible to observe a quantitative and totally regioselective retro-Diels–Alder like reaction in AcOH or with gaseous HCl. Although, in our case, the retro-DA products are the same as the ones used for preparing the starting compound **1**, our observations may be applied to other 7-oxabicyclo-[2.2.1]heptadiene derivatives and thus could be very useful, as

interest in retro-Diels–Alder reactions as a tool in organic synthesis is increasing.¹⁰

Notes and references

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- 9 *General procedure* for the retro-DA reaction induced by anhydrous HCl: a stirred solution of the oxabicyclic derivative **1** in CH₂Cl₂ (0.5 ml per 0.1 mmol of substrate) was saturated with anhydrous HCl (between 1.5 and 2 h). The solution was stirred at room temperature for 48 h. The solution was washed with water to neutrality. The organic layer was dried over MgSO₄ and then concentrated under vacuum. The crude product was purified by flash chromatography (eluent: hexane–Et₂O).
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