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

## Alain Maggiani, Arlette Tubul and Pierre Brun\*

Laboratoire de Synthèse Organique Sélective, GCOPL, ESA 6114, Université de la Méditerranée, Faculté des Sciences de Luminy, 163 Avenue de Luminy, case 901, F-13288 Marseille Cedex 9, France. E-mail: brun@chimlum.univ-mrs.fr

Received (in Liverpool, UK) 22nd October 1999, Accepted 4th November 1999

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).<sup>1</sup> 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.<sup>2,3</sup> 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.<sup>4</sup> 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



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

described.<sup>5–8</sup> 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 CHCl<sub>3</sub>–CCl<sub>4</sub> mixture (entry 10).

When mineral aqueous acids are used (HCl or  $H_2SO_4$ ) the results depend on the experimental conditions and particularly on the solvent and temperature (entries 1–3, 5). In Et<sub>2</sub>O, at room temperature, only the phenol **2** is formed. In CH<sub>2</sub>Cl<sub>2</sub>, with  $H_2SO_4$ , only tars are formed starting from compound **1**. With aqueous HCl, under heating, the reaction is not selective and the





 $CI \qquad \qquad$									
				Yield $(\%)^b$					
Entry	Acid	Solvent	T/°C	t/h	1	2	3	4 + 5	
 1	HCl (aq.)	CH <sub>2</sub> Cl <sub>2</sub>	55	24		44–37	6–0	50-63	
2	HCl (aq.)	$CH_2Cl_2$	reflux	24	9	8	72	11	
3	HCl (aq.)	$Et_2O$	25	24	11	89			
$4^c$	HCl (g)	$CH_2Cl_2$	25	48				100	
5	$H_2SO_4$	$Et_2O$	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	CHCl3-CCl4	reflux	48	100				

<sup>*a*</sup> Reagents and conditions: i, aq. HCl or H<sub>2</sub>SO<sub>4</sub>, Et<sub>2</sub>O, room temp.; ii, aq. HCl, CH<sub>2</sub>Cl<sub>2</sub>, reflux; iii, anhydrous HCl, Et<sub>2</sub>O or CH<sub>2</sub>Cl<sub>2</sub>, room temp. (or AcOH, reflux.) <sup>*b*</sup> The indicated yields are based on pure isolate compounds. <sup>*c*</sup> 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

- 1 A. Maggiani, A. Tubul and P. Brun, Synthesis, 1997, 631.
- R. D. Little and G. N. Muller, J. Am. Chem. Soc., 1981, 103, 2744.
  R. D. Little, G. L. Caroll and J. L. Petersen, J. Am. Chem. Soc., 1983,
- 105, 928. 4 A. Maggiani, A Tubul and P. Brun, *Tetrahedron Lett.*, 1998, **39**,
- 4485. 5 P. Vogel, B. Willhalm and H. Prinzbach, *Helv. Chim. Acta*, 1969, **52**,
- 584. 6 D. S. Stusche and H. Prinzbach, *Chem. Ber.*, 1973, **106**, 3817.
- 7 A. Bruggink, H. Hogeveenh and T. B. Middlekoop, *Tetrahedron Lett.*,
- 1972, 4961.
- 8 R. K. Bansal, A. W. McCulloch, P. W. Rasmussen and A. G. McInnes, *Can. J. Chem.*, 1975, **53**, 138.
- 9 General procedure for the retro-DA reaction induced by anhydrous HCI: a stirred solution of the oxabicyclic derivative 1 in CH<sub>2</sub>Cl<sub>2</sub> (0.5 ml per 0.1 mmol of substrate) was saturated with anhydrous HCI (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 MgSO<sub>4</sub> and then concentrated under vacuum. The crude product was purified by flash chromatography (eluent: hexane–Et<sub>2</sub>O).
- 10 R. Bloch and G. Mandville, Novel strategies for the use of retro-Diels-Alder reactions in stereoselective synthesis, in Recent research developments in organic chemistry, ed. S. G. Pandalai, TRN, Trivadrum, India, 1998, vol. 2, pp. 411-452.

Communication 9/08451G