

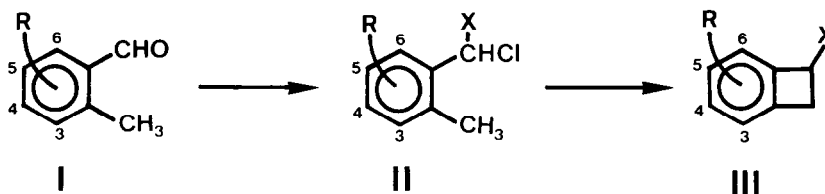
# FORMATION OF SUBSTITUTED BENZOCYCLOBUTENES THROUGH FLASH VACUUM PYROLYSIS

Peter Schiess <sup>\*</sup>, Suzanne Rutschmann & Van Vien Toan  
 Institut für Organische Chemie der Universität  
 St. Johannis-Ring 19, CH-4056 Basel, Switzerland.

Summary: Benzocyclobutenes carrying a substituent in the four membered ring are obtained in high yield from 2-methyl benzaldehydes through a reaction sequence involving a pyrolytic 1,4-elimination of HCl in the crucial step.

Flash vacuum pyrolysis (FVP) [1] has been shown recently to be the method of choice for the preparation of benzocyclobutenones from 2-methyl-benzoylchlorides [2] and of benzocyclobutenes from 2-methyl-benzylchlorides [3] through uncatalysed 1,4-elimination of HCl.

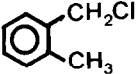


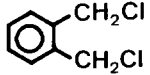

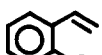
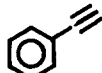
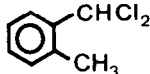


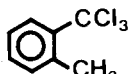
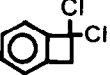
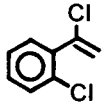
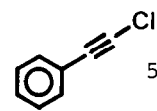
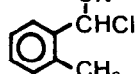

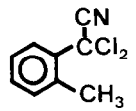
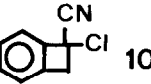
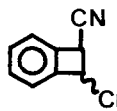
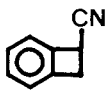
We now wish to report that  $\alpha$ -cyano- and  $\alpha$ -chloro-substituted 2-methyl-benzylchlorides II (X = Cl, CN) prepared from 2-methyl-benzaldehydes I yield the expected HCl-elimination products III upon flash vacuum pyrolysis. This constitutes a simple and versatile access to a variety of substituted benzocyclobutenes III which have gained importance as building blocks for the synthesis of polycyclic natural products through intramolecular Diels-Alder reaction [4].



The 2-methyl-benzylchlorides 1 - 6 (Table 1) were subjected to pyrolysis on a 1 - 5 g scale by distillation at a pressure of 0.1 mbar through a hot quartz tube (1 x 30 cm), the pyrolysis products being collected at the exit of the hot tube on a cold finger at -78° as described previously [3a]. The products were separated and characterised by comparison with authentic material. Analytical pyrolysis runs were carried out in a nitrogen flow reactor coupled to a vapor phase chromatograph as described in the preceding communication [5]. In this reactor the pyrolysis temperature was determined at which 50% conversion to products was observed. At this temperature,  $T_{50\%}$ , the residence time of the substrate in the reactor equals its half life in the unimolecular elimination

process. At constant flow  $T_{50\%}$ -values therefore constitute a measure of relative reactivity for the compounds investigated.

**Table 1**  $\alpha$ -substituted benzocyclobutenes through flash vacuum pyrolysis.

Starting material	$T_{50\%}$ <sup>a)</sup>	benzocyclobutenes <sup>b)</sup>	other products <sup>b)</sup>
 <b>1</b>	647°		77%  3%
 <b>2</b>	647°	 <b>7</b>	53%  ,  27%
 <b>3</b>	541°		80%  ,  4%
 <b>4</b>	514°	 <b>8</b>	35%  ,  55%
 <b>5</b>	561°	 <b>9</b>	42% not identified 3%
 <b>6</b>	520°	 <b>10</b>	19%  ,  30%

a) Pyrolysis temperature at which 50% inversion is reached in the  $N_2$ -flow reactor; residence time: 0.1 s; carrier gas pressure: 2 bar [5].

b) Formed in preparative runs; conversion: 90%; pressure: 0.1 mbar [6].

The rate of HCl elimination from 2-methyl-benzylchloride **1** is not affected by substitution of hydrogen through chlorine in the  $\alpha'$ -position, whereas it is greatly enhanced by chlorine in the  $\alpha$ -position as revealed by the lower  $T_{50\%}$ -values for **3** and **4** than for **1** and **2**. A similar but weaker rate enhancement is observed in  $\alpha$ -cyano-substituted benzylchlorides **5** and **6**. In spite of their high reactivity,  $\alpha$ -persubstituted benzylchlorides **4** and **6** upon pyrolysis gave the expected  $\alpha,\alpha$ -disubstituted benzocyclobutenes **8** and **10** in only modest yield and contaminated with thermal decomposition products which proved difficult to remove. The  $\alpha$ -monosubstituted benzocyclobutenes **7** and **9** however, were formed in fair to high yield and in a high state of purity from their precursors **3** and **5**, which in turn are easily obtained from 2-methyl-benzaldehyde by standard procedures. We have prepared  $\alpha$ -chloro-benzocyclobutene **7** through pyrolysis of **3** on a 100 g-scale. Compound **7** forms a Grignard reagent in THF in excellent yield and thus allows the preparation of a variety of thermolabile,  $\alpha$ -functionalised benzocyclobutenes (Table 2).

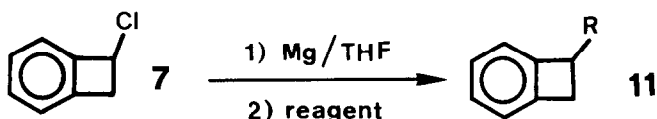


Table 2  $\alpha$ -functionalised benzocyclobutenes **11** from **7** through Grignard reaction<sup>a)</sup>

	reagent	R	bp/mbar (mp)	yield	
a)	CO <sub>2</sub>	COOH	(73-74°)	72%	[8]
b)	(CH <sub>3</sub> ) <sub>2</sub> NCHO	CHO	70-88°/0.1	74%	
c)	(CH <sub>3</sub> CO) <sub>2</sub> O	COCH <sub>3</sub>	60-70°/0.1	38%	[9]
d)	(CH <sub>3</sub> ) <sub>3</sub> SiCl	Si(CH <sub>3</sub> ) <sub>3</sub>	105-115°/17	82%	
e)	CH <sub>3</sub> J/Li <sub>2</sub> CuCl <sub>4</sub>	CH <sub>3</sub>	85-105°/105	66%	
f)	C <sub>4</sub> H <sub>9</sub> Br/Li <sub>2</sub> CuCl <sub>4</sub>	C <sub>4</sub> H <sub>9</sub>	75-90°/0.1	51%	
g)	C <sub>2</sub> H <sub>3</sub> Br/FeCl <sub>3</sub>	CH=CH <sub>2</sub>	60-75°/0.1	68%	[10]

a) New compounds have been characterized by analytical and spectral data.

The pyrolytic pathway to  $\alpha$ -chloro-benzocyclobutene **7** is as simple and straightforward as the synthesis recently described for the analogous bromo compound [7]. Its versatility is demonstrated by the preparation of several  $\alpha$ -cyano-benzocyclobutenes **III** (X=CN) carrying additional substituents, especially ether functions in the aromatic ring through the reaction sequence shown in scheme 2 (see table 3). The availability of appropriately substituted 2-methyl-benzaldehydes **I** and the good yield obtained in the pyrolytic formation of the four membered ring render this reaction sequence competitive with other synthetic pathways [11]-[14] to highly functionalised benzocyclobutenes **III**.

Scheme 2

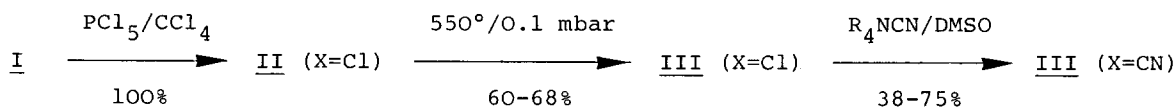


Table 3 Substituted benzocyclobutenes III prepared from 2-methylbenzaldehydes I.

substituents R				<u>III</u> (X=Cl) <sup>a)</sup>		<u>III</u> (X=CN) <sup>a)</sup>		
3	4	5	6	bp/mbar (mp)	yield	mp	yield	
H	CH <sub>3</sub> O	H	H	90-105°/0.1	67%	58-60°	52%	[11]
H	CH <sub>3</sub> O	CH <sub>3</sub> O	H	110-125°/0.1	60%	83-84°	38%	[12]
H	O-CH <sub>2</sub> -O		H	(54-55°)	62%	86-88°	75%	[13]
CH <sub>3</sub>	CH <sub>3</sub> O	H	H	(33-35°)	68%	79-81°	54%	
H	CH <sub>3</sub> O	CH <sub>3</sub>	H	(43-44°)	63%	69-70°	58%	

a) New compounds have been characterized by analytical and spectral data.

We wish to thank the Swiss National Science Foundation (project Nr. 2.887-0.80) and CIBA-GEIGY Co. for their generous support.

#### Notes and References

- [1] For a recent, comprehensive review see: R.F.C. Brown, "Pyrolytic Methods in Organic Chemistry", Academic Press, New York, 1980.
- [2] P. Schiess & M. Heitzmann, *Angew. Chem.* **89**, 485 (1977); *Angew. Chem. Int. Ed. Engl.* **16**, 469 (1977).
- [3] a) P. Schiess & M. Heitzmann, *Helv. Chim. Acta* **61**, 844 (1978); P. Schiess, M. Heitzmann, S. Rutschmann & R. Stäheli, *Tetrahedron Lett.* **1978**, 4569.  
b) R. Gray, L.G. Harruff, J. Krymowski, J. Peterson & V. Boekelheide, *J. Amer. Chem. Soc.* **100**, 2892 (1978); L.G. Harruff, M. Brown & V. Boekelheide, *J. Amer. Chem. Soc.* **100**, 2893; G.D. Ewing & V. Boekelheide, *Synthesis* **1979**, 427.
- [4] W. Oppolzer, *Synthesis*, **1978**, 793; T. Kametani & H. Nemoto, *Tetrahedron* **37**, 3 (1981).
- [5] P. Schiess, S. Rutschmann & V.V. Toan, *Tetrahedron Lett.*, preceding communication.
- [6] Pyrolysis temperatures in preparative experiments were 80-90° higher than the T<sub>50%</sub>-values found in analytical tests since residence times were shorter and conversions higher in preparative than in analytical runs.
- [7] M.R. DeCamp & L.A. Viscogliosi, *J. Org. Chem.* **46**, 3918 (1981).
- [8] L. Horner, W. Kirmse & K. Muth, *Chem. Ber.* **91**, 430 (1958).
- [9] R. Hug, H.J. Hansen & H. Schmid, *Helv. Chim. Acta* **55**, 10 (1972).
- [10] M.R. DeCamp, R.H. Levin & M. Jones, *Tetrahedron Lett.* **1974**, 3575.
- [11] T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama & K. Fukumoto, *J. Amer. Chem. Soc.* **98**, 3378 (1976).
- [12] T. Kametani, K. Ogasawara & T. Takahashi, *Tetrahedron* **29**, 73 (1973).
- [13] E.F. Jenny & K. Schenker, Swiss patent 485647, *Chem. Abstr.* **72**, p. 132 388 d (1970).
- [14] J.F. Bunnett & J.A. Skorcz, *J. Org. Chem.* **27**, 3836 (1962).

(Received in Germany 7 June 1982)