

# Palladium-catalyzed Hydroarylation of Bicyclic Alkenes: A Polymer-supported Approach I

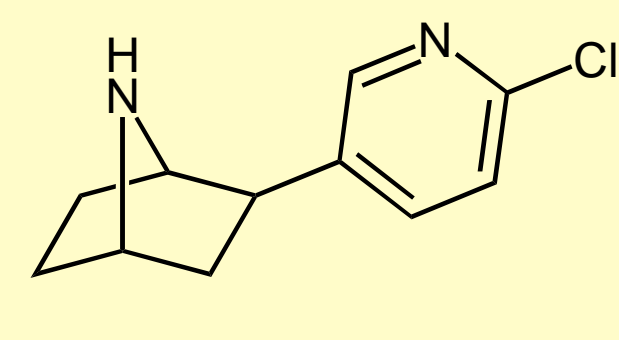
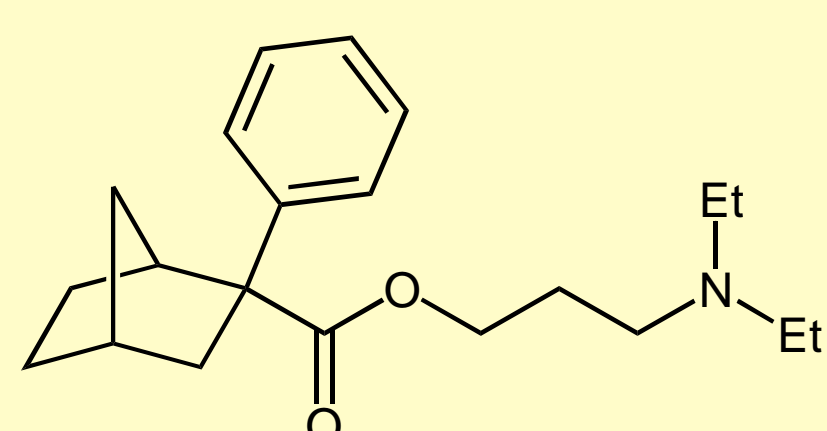
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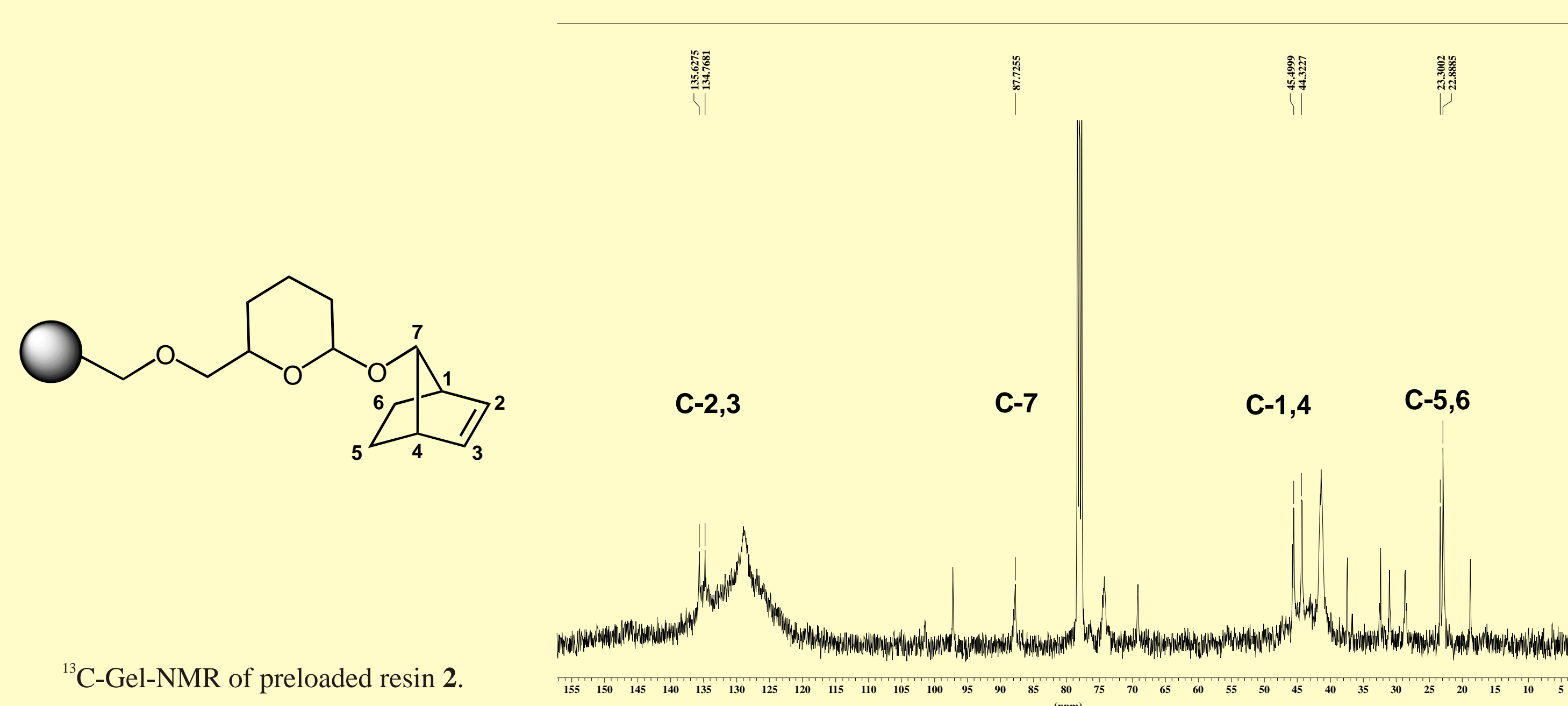
## Introduction

An important goal of contemporary organic chemistry is the transition metal-catalyzed arylation<sup>[1]</sup> of bicyclic (hetero)-alkenes, leading to structures with several pharmacological properties like Epibatidin. This nicotigenic acetylcholin receptor antagonist, which was first reported by *Daly*<sup>[2]</sup> in 1992, gave rise to numerous chemical investigations during the past years<sup>[3]</sup>. Also new derivatives like *Bornaprin*<sup>[4]</sup> have been developed as pharmaceuticals against the *Parkinson* disease.

An important scope was the synthesis of variations of the structure, first racemic by *Clayton* and *Regan*<sup>[5]</sup> and finally also asymmetric, for example by *Achiwa*<sup>[6]</sup> and *Kaufmann*<sup>[7]</sup>. Among the published work only little is found concerning the use of the solid-phase technique in the synthesis of these structures. The most interesting work in this field appeared 1996 by *Ellmann*<sup>[8]</sup>, who investigated the arylation of resin attached tropane derivatives. In this context, solid-phase supported synthesis of [2.2.1]bicyclic alkenes should also be investigated.

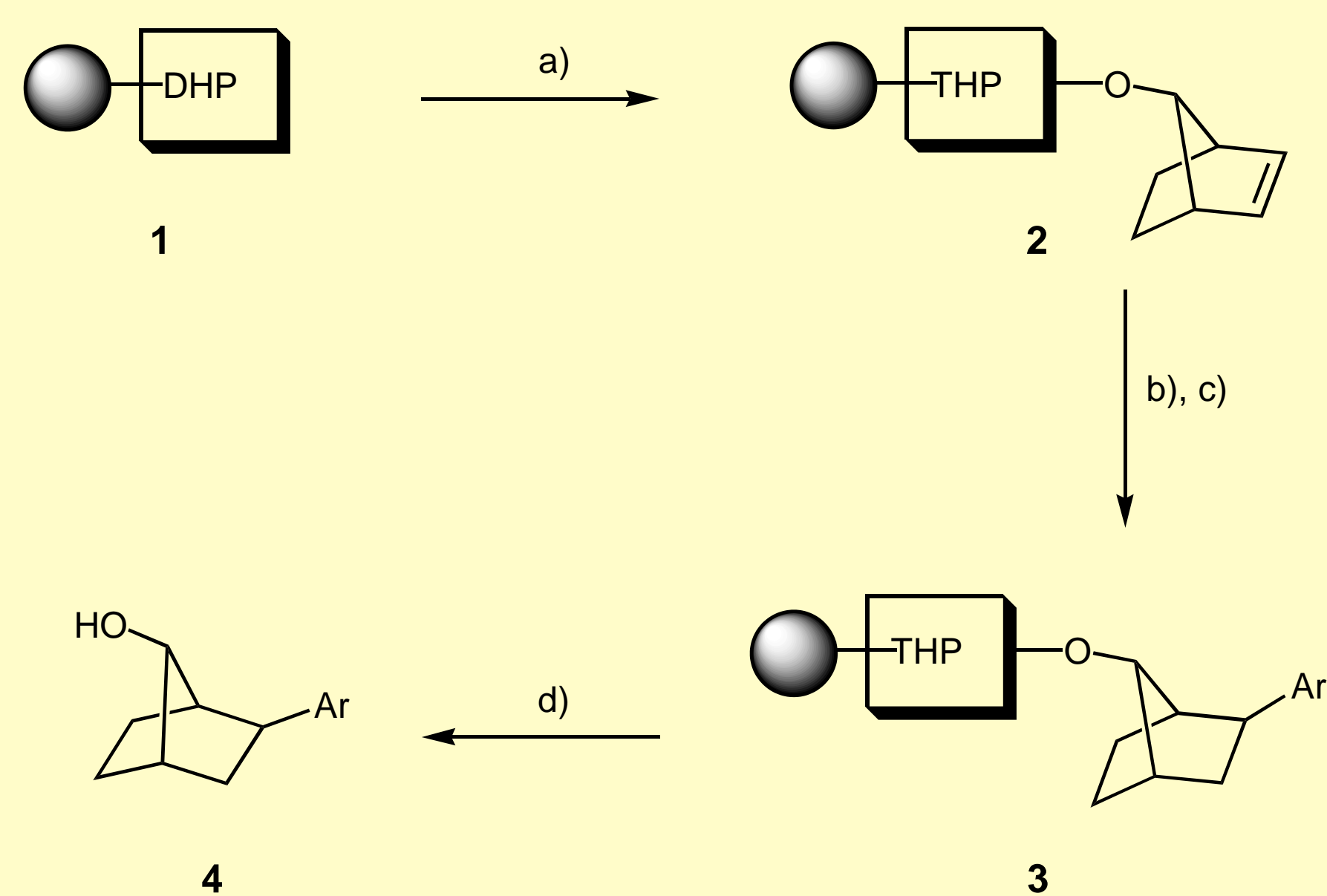


## NMR-Data



## Approach

In order to find a simple and stable test system for the polymer supported hydroarylation of [2.2.1]bicyclic alkenes, we have chosen to attach 7-hydroxy-norbornene to a DHP-linked *Merrifield* resin. Starting from this preloaded resin, we have successfully coupled several arenes to the attached alkene and cleaved the resulting substrates.



- a) 5 eq. anti-bicyclo-2-en-7-ol, 2 eq. PPTs, 1,2-dichloroethane, 80 °C, 24 h, 0.34 mmol/g;  
 b) 3 eq. Pd(PPh<sub>3</sub>)<sub>4</sub>, 4 eq. ArX, THF, 66 °C, 24 h;  
 c) 2 eq. PPh<sub>3</sub>, 9 eq. Et<sub>3</sub>N, 4.3 eq. HCOOH, 66 °C, 12 h.  
 d) TFA/H<sub>2</sub>O (95/5), rt, 30 min.

## Results

Reaction	ArX	Product *	Yield [%]
1	4-iodoaniline		<1 (22)**
2	2-chloro-5-iodopyridine		1-2
3	4-bromoanisole		12
4	iodobenzene		24
5	4-iodoanisole		33
6	4-iodotoluene		32
7	5-iodo- <i>m</i> -xylene		38

\* Isolated yield

\*\* Only *exo*-Phenylnorbornane was detected (yield 22%)

## Literature

- <sup>[1]</sup> M. Nogrady, *Stereoselective Synthesis* **1995**, 2. Auflage, VCH Verlag Weinheim.  
<sup>[2]</sup> T. F. Spande, H. M. Garraffo, M. W. Edwards, L. Pannell, J. W. Daly, *J. Am. Chem. Soc.* **1992**, 114, 3475-3478.  
<sup>[3]</sup> K.-C. Kong, C.-H. Cheng, *J. Am. Chem. Soc.* **1991**, 113, 6313-6315.  
<sup>[4]</sup> H.-P.-Bächthold, A. Fürst, T. Struller, H. Kreiskott, *Ullmanns Encycl. d. techn. Chemie* **1980**, 21, 628.  
<sup>[5]</sup> S. C. Clayton, A. C. Regan, *Tetrahedron Lett.* **1993**, 34, 7493-7496.  
<sup>[6]</sup> S. Sakuraba, T. Okada, T. Morimoto, K. Achiwa, *Chem. Pharm. Bull.* **1995**, 43, 927-934.  
<sup>[7]</sup> A. Otten, J. C. Namyslo, M. Stoermer, D. E. Kaufmann, *Eur. J. Org. Chem.* **1998**, 1997-2001.  
<sup>[8]</sup> J. S. Koh and J. A. Ellmann, *J. Org. Chem.* **1996**, 61, 233-235.

## Conclusion

The present approach shows the ability to attach the bicyclic 7-hydroxy-norbornene to DHP-linked *Merrifield* resin and the successful use of this preloaded solid support in palladium-catalyzed reductive Heck arylation. As a first result, it can be observed that the achieved yield show a strong dependence on the nature of substitution of the arene compound. In fact, methylaryliodides lead to best results in this transition metal catalyzed reaction (reaction 6 and 7). Employing 4-iodoaniline in the present reaction, only unsubstituted *exo*-phenylnorbornane was isolated. This result, due to so-called "phosphanescrambling", was first observed by *Cheng*<sup>[9]</sup> in 1991. Further work is in progress to light and optimize the processes in solid-phase supported reductive arylation of bicyclic alkenes.