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LETTERS

Intramolecular electrophilic aromatic substitution reactions with methyl vinyl ethers for the synthesis of dihydronaphthalenes

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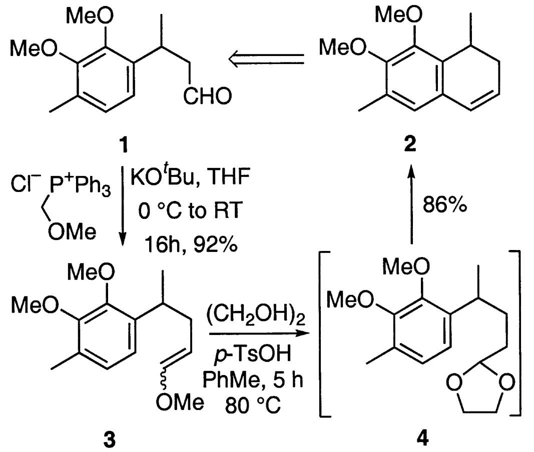
Abstract—A simple and inexpensive method to effect the conversion of 4-arylalk-1-en-1-yl methyl ethers to dihydronaphthalenes has been developed. Cyclisation is accomplished by warming a toluene solution of the substrate with 1,2-ethanediol and *para*-toluenesulfonic acid and proceeds via in situ formation of a 1,3-dioxolane. Reactions generally give good yields and have been successful with electron rich, unsubstituted and halogenated arenes. They display excellent regioselectivity; appearing to follow the course of lowest steric demand. © 2002 Elsevier Science Ltd. All rights reserved.

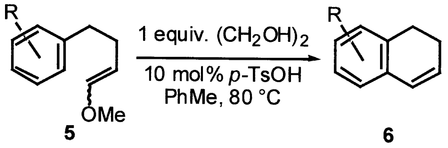
During studies directed towards the marine diterpene pseudopterosin, we had cause to prepare dihydronaththalene **2**.[1] The route envisioned involved homologation of aldehyde **1** followed by a cyclodehydration to **2**. In the event this proved troublesome. However, through the simple expedient of warming a toluene solution of methyl vinyl ether **3** at 80°C in the presence of 1,2-ethanediol and *para*-toluenesulfonic acid, cyclisation to **2** could be achieved in high yield (Scheme 1).[2] In this letter we highlight that transformation together with some studies on its scope and limitations.

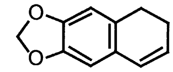
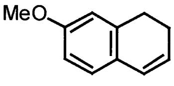
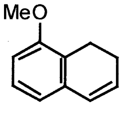
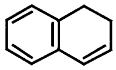
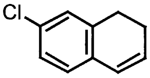
A series of methyl vinyl ethers were prepared in order to examine the transformation's generality. Pleasingly, all gave the reaction in yields ranging from 66% to 91% (Table 1). In each case a transient 1,3-dioxolane intermediate could be detected by thin layer chromatography, though these were not isolated.[3] As expected, it was necessary to extend reaction times from 4 to ca. 24



Scheme 1.

Table 1. Further examples



entry	Substrate (R) Reaction time & yield[a]	Product
a	3,4-methylenedioxy 4 h, 71%	
b	3-methoxy 4 h, 91%	
c	2-methoxy 16 h, 71%	
d	H 24 h, 86%	
e	3-chloro 24 h, 66%	

a: isolated yield, all compounds were characterised by ^{1}H and ^{13}C NMR, IR, UV, LRMS and HRMS.

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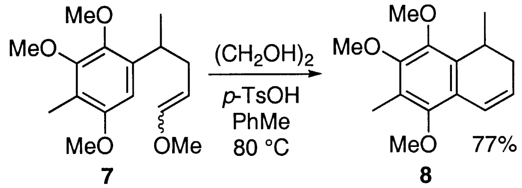

Scheme 2.

hours for the 2-methoxy-, unsubstituted and 3-chloro-derivatives, **5c** to **5e**, respectively. Notably, when both *ortho*- positions were unsubstituted, reactions displayed excellent regioselectivity, seemingly favouring cyclisation through the course of lowest steric demand (Table 1 entries **a**, **b** and **e**).

Finally, we have also shown the method's potential for constructing heavily substituted arenes. Thus, *cyclo*-dehydration of the pentasubstituted arene **7**, which is of relevance to our work on the synthesis of colombiasin A,[4] gave **8** in 77% yield after 16 hours (Scheme 2).

In conclusion, a simple and inexpensive method has been developed to effect the conversion of 4-arylalk-1-en-1-yl methyl ethers to the corresponding dihydronaphthalene.[2] Cyclisation is accomplished by warming a toluene solution of the substrate with 1,2-ethanediol and *para*-toluenesulfonic acid. The reaction proceeds via the in situ formation of a 1,3-dioxolane.[2,3] Where two cyclisation pathways are possible reactions follow the course of lowest steric demand. Electron rich, unsubstituted and halogenated arenes all give the reaction, the latter requiring extended reaction times.

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References

1. Harrowven, D. C.; Wilden, J. D.; Tyte, M. J.; Hursthouse, M. B.; Coles, S. J. *Tetrahedron Lett.* **2001**, *42*, 1193.
2. Related cyclisations of methyl vinyl ethers for the synthesis of condensed polyaromatics have been reported using tris-(4-bromophenyl)aminium hexachloroantimonate and methanesulfonic acid. See (a) Lapouyade, R.; Villeneuve, P.; Nourmamode, A.; Morand, J.-P. *J. Chem. Soc., Chem. Commun.* **1987**, 776; (b) Kumar, S. *J. Org. Chem.* **1997**, *62*, 8535; (c) Zhang, J.-T.; Harvey, R. G. *Tetrahedron* **1999**, *55*, 625.
3. Related cyclisations of acetals akin to **4** are well precedented. See (a) Meyers, A. I.; Schmidt, W.; Santiago, B. *Heterocycles* **1995**, *40*, 525; (b) Hallinan, K. O.; Honda, T. *Tetrahedron* **1995**, *51*, 12211; (c) van Dijk, J. T. M.; Hartwijk, A.; Bleeker, A. C.; Lugtenburg, J.; Cornelisse, J. *J. Org. Chem.* **1996**, *61*, 1136; (d) Shimizu, M.; Kamikubo, T.; Ogasawara, K. *Heterocycles* **1997**, *46*, 21; (e) Zhang, F.-J.; Cortez, C.; Harvey, R. G. *J. Org. Chem.* **2000**, *65*, 3952.
4. Harrowven, D. C.; Tyte, M. J. *Tetrahedron Lett.* **2001**, *42*, 8709.