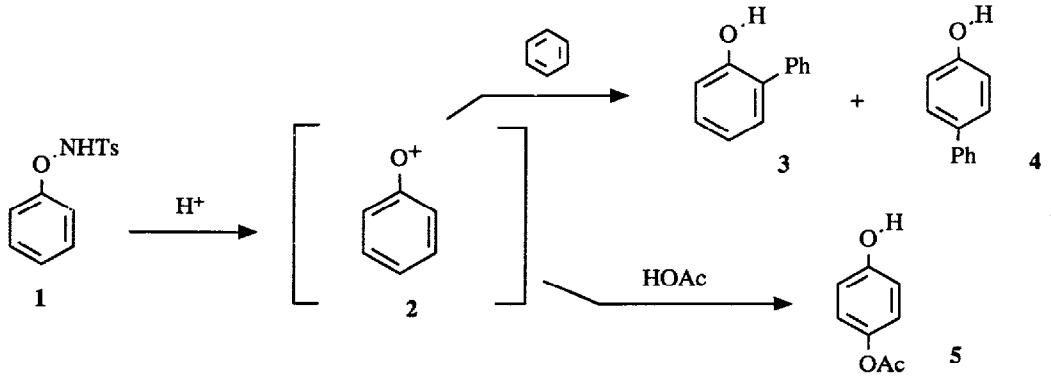
Tetrahedron Letters,Vol.30,No.37,pp 4929-4930,1989 0040-4039/89 $3.00 + .00
Printed in Great Britain Pergamon Press plc

Fluorination Reactions with HF/THF Medium
Solvolysis of N-Tosyl-O-Phenylhydroxylamine

William R. Dolbier, Jr.*, Lech Celewicz and Keiichi Ohnishi
Department of Chemistry, University of Florida
Gainesville, FL 32611

Abstract: Solvolysis of N-tosyl-O-phenylhydroxylamine in HF/THF leads to regiospecific formation of p-fluorophenol via umpolung strategy which induces nucleophilic aromatic fluorine/hydrogen substitution.

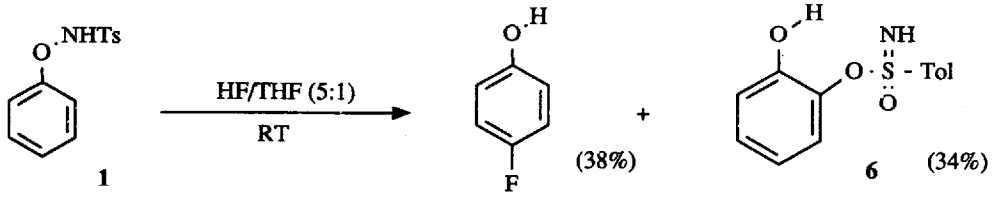
It has been reported by Okamoto that the acid-catalyzed solvolyses of N-tosyl-O-phenylhydroxylamine, **1**, lead to interception by nucleophiles of an intermediate, assumed to be a phenoxenium ion **2**, to give products such as **3**, **4** and **5**.[1] Among the nucleophiles which they found effective was Cl^- (from HCl) which gave as products



28% of a mixture of o- and p-chlorophenol.

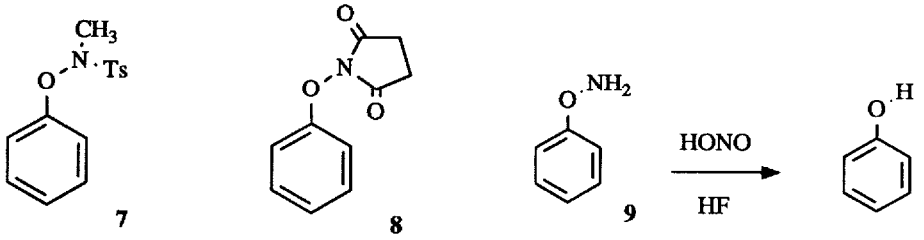
In view of such results, we considered the possibility of introducing fluorine into phenols via this reaction, using our recently reported HF/THF cosolvent medium,[2] which has been demonstrated to be an excellent source of nucleophilic fluoride ion, unlike anhydrous HF, while also being quite an acidic medium, unlike HF/pyridine.

Indeed it was found that **1** underwent acid-catalyzed solvolysis in HF/THF medium at room temperature to yield 38% of p-fluorophenol, along with 34% of what is presumed to be the nominal [3.3]-rearrangement (or internally trapped) product **6**.[1] A trace, at most, of o-fluorophenol could be detected.



A ratio of HF:THF of 5:1 proved to be optimum for the reaction. Yields of p-fluorophenol with other ratios were: 2.5:1 (24%), 3.5:1 (30%), 10:1 (5%). As expected, use of anhydrous HF, *not* a good source of nucleophilic fluoride, led only to rearrangement product **6**. On the other hand, HF/pyridine (10:1) was apparently not acidic enough to catalyze the solvolysis, and its use led only to recovery of starting material.

In the hope that modification of the leaving group might improve the yield, O-phenylhydroxylamine derivatives **7** and **8** were prepared and subjected to solvolysis.[3] It was hoped that the bulkier leaving group on **7**



7 **8** **9**

might inhibit formation of rearrangement product **6**, but, in fact, the yield of p-fluoropenol was actually reduced to 24%. Derivative **8**, on the other hand was found to be unreactive under the reaction conditions and was recovered unchanged.

Direct deamination of o-phenylhydroxylamine **9** was carried out both in anhydrous HF and in HF/THF in an attempt to generate **2** via a non-solvolytic pathway. However. such reactions led surprisingly only to the formation of phenol, perhaps via protonation of the benzene ring, followed by cleavage of the O-NH_2 bond.

In general, aromatic substitutions of phenols or phenol derivatives occur via attack by *electrophiles*. With regard to introduction of *fluorine* into aromatics, effective non-exotic electrophilic fluorination reagents are essentially non-existent.[4] The methodology presented in this paper creates an *umpolung* situation for phenol, thus enabling one to use a cheap, *nucleophilic* source of fluorine, i.e. anhydrous HF in THF. The reaction moreover is totally regiospecific, being the only case where phenol has been converted to p-fluorophenol, free of o-fluorophenol. In effect and in concept the reaction is reminiscent of the conversion of N-phenylhydroxylamine by anhydrous HF to p-fluoroaniline.[6] While the key to high yields in this reaction has still eluded discovery, the strategy shows significant potential. Work in this area continues.

Acknowledgement. Support of this research in part by the Mallincrodt Chemical Company and by Asahi Glass Co., Ltd., is gratefully acknowledged.

References and Footnotes.

1. Endo, Y.; Shudo, K.; Okamoto, T. *J. Am. Chem. Soc.* **1982**, *104*, 6393.
2. Dolbier, W. R., Jr.; Gray, T. A.; Ohnishi, K. *Synthesis* **1987**, *10*, 956.
3. N-methyl derivative **7** was prepared by the reaction of **1** with CH_3I in the presence of pyridine, while **8** was prepared from **9** by treatment with succinic anhydride, followed by heating with Ac_2O. Attempts were also made to prepare the N-triflyl derivative, but it was too unstable for isolation. In-situ utilization will be attempted.
4. The best of the available reagents for electrophilic aromatic fluorination is $(CF_3SO_2)_2NF$.[5]
5. Singh, S.; Des Marteau, D. D.; Zuberi, S. S.; Witz, M.; Huang, H.-N. *J. Am. Chem. Soc.* **1987**, *109*, 7194.
6. Titov, A. I.; Baryshnikova, A. N. *Zh. Obshch. Khim.* **1953**, *23*, 346; *Chem. Abstr.* **1954**, *48*, 2623 f.

(Received in USA 9 June 1989)