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Lactonization of 5-Phenylfuran-4-arylcarbinol-3-carboxylic Acids under the Catalysis of Boron Trifluoride Etherate

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Abstract: 5-Phenyl-4-aroylfuran-3-carboxylic acids were reduced in aqueous alkaline solutions of $NaBH_4$ to afford hydroxy acids in excellent yields. Under the catalysis of boron trifluoride etherate, the hydroxy acids were converted to lactones smoothly.

Keyword: Lactonization; boron trifluoride etherate; hydroxy acid.

Many kinds of natural products which have a moiety of lactone ring exhibit various biological activities, and some furofuran lignans fall into this category[1]. In our continuous study of furofuran lignans, we have recently described a convenient method for the synthesis of 5-phenyl-4-aroylfuran-3-carboxylic acids **1**[2]. To accomplish the synthesis of the analog of the lactone lignans, the hydroxy acids **2** , which were obtained in excellent yields of approximation 91% from the reduction of keto acids **1** in aqueous alkaline solutions of $NaBH_4$ (reflux, 4 h) , must be cyclized to lactones **3** according to our strategy.

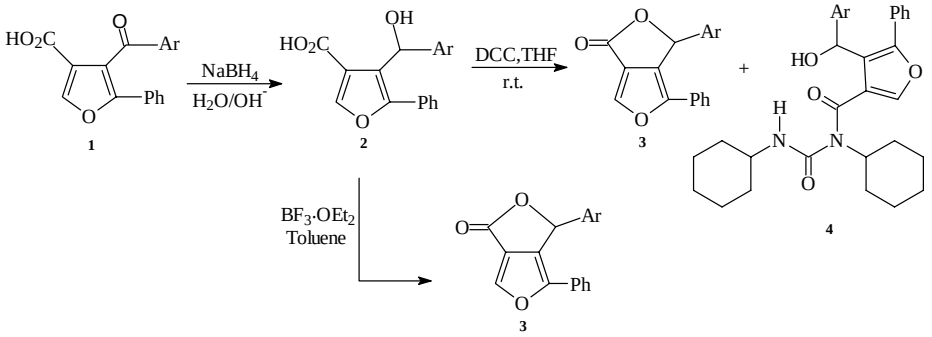
Some of the five-membered lactones are readily formed from hydroxy acids at room temperature after acitic work-up[3]. For those hydroxy acids which can not be converted spontaneously, the choices for lactonization are rather limited. They have been prepared by refluxing in acetic acid and acetic anhydride[4], or under the catalysis of PPTs (pyridinium p-toluenesulfonate) [5]. Other procedures appeared in literature were usually applied to small or large-membered lactone rings[6], for example, the Steglich approach[7] is a mild way of constructing macrolactone rings.

Since furan rings are susceptible to hydrolytic degradation in the presence of proton acids when heated, a mild lactonization procedure must be sought. Therefore, the Steglich method (DCC, THF, r. t., 24 h) was examined with or without adding DMAP (N,N-dimethyl amino pyridine) , but the experimental results were frustrating: 80% of the isolated products was by-product N-acylurea **4a** and the lactone **3a** only amounted to 20%. G.E.Kock, *et al.*[8], in their macrolactonization procedure, also found that adding DMAP as a catalyst had no significant effect on the proportion of the reaction mixture, *i.e.* N-acylurea remained the major product.

After many trials, it was eventually found that boron trifluoride etherate catalyzed the lactonization reaction of hydroxy acids **2a-c** very well (0.1 mol equivalent of boron trifluoride etherate[9], reflux in toluene, 2-3 h) , with yields ranging from 67% to 74%;

while hydroxy acid **2d** could not be transformed thoroughly even with lengthened reaction time, and moreover, we failed to get the pure form of **3d** owning to its liability to reverse to hydroxy acids **2d** during chromatography on silica gel.

Scheme



Ar: a, phenyl; **b**, 4-tolyl; **c**, 4-chlorophenyl; **d**, 4-methoxyphenyl

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References and Notes

1 For a review, see: R. S. Ward, *Natural Product Reports*, **1993,** *10*, 1; **1995**, *12*, 183; **1997**, *14*, 43.
2 X. P. Nie, X. L. Ye, *Chinese Chemical Letters*, **1998**, *9*, 103.
3 For a review, see: R. Ikan, V. Weinstein, *Org. Prep. Proc. Int.*, **1981**, *13* (1) , 59.
4 K. Inoue, T. Sugaya, T. Ogasa, S. Tomioka, *Synthesis*, **1997**, 113.
5 M. G. Constantino, L. G. O. .Matias, G. V. J. Silva, V. C. G. Heleno, M. T. P. Gambardella, *Syn. Commun.*, **1997**, *27* (24) , 4285.
6 R. C. Larock, *"Comprehensive Organic Transformation: A Guide to Functional Group Preparations*", VCH Publishers, Inc., New York, **1989,** p943.
7 B. Neises, W. Steglich, *Angew. Chem. Int. Ed. Eng.*, **1978**, *17*, 522.
8 E. P. Boden, G. E. Kock, *J. Org. Chem.*, **1985**, *50*, 2394.
9 More than 0.1 mol *equiv.* amount of catalyst would lower the yields of the lactones and no lactone was obtained with 1.0 mol equivalent amount of catalyst.

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