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A New Approach to Dihydrobenzofurans by Intramolecular Trapping of Benzynes by Hydroxyl Functions

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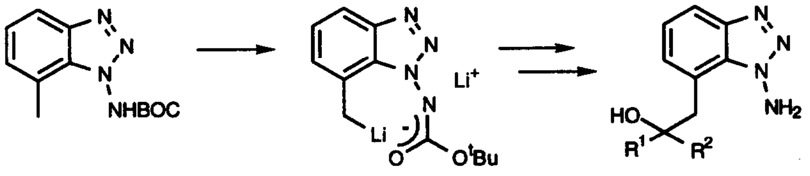
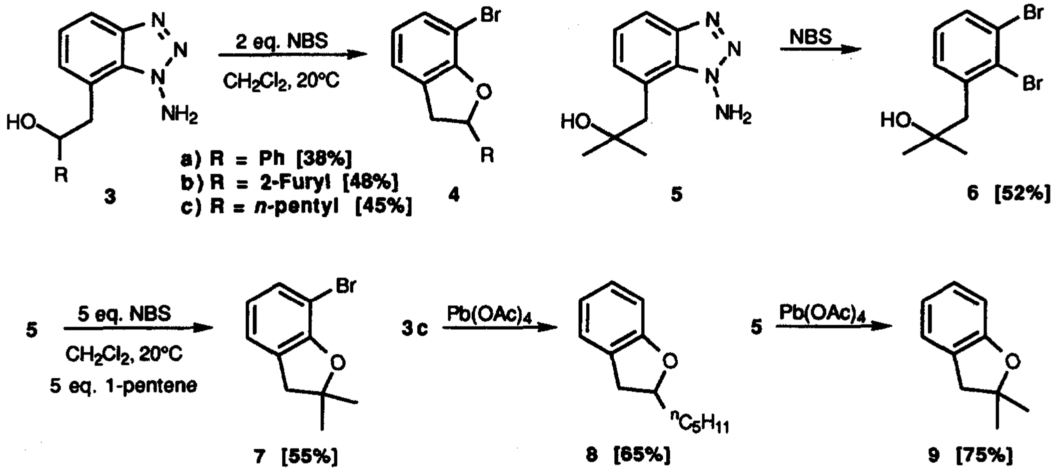
Abstract:- *The adducts **3**, derived from condensations of the 1-aminobenzotriazole dianion **2** and aldehydes or ketones, are converted into the corresponding benzynes upon exposure to either N-bromosuccinimide or lead(IV) acetate; intramolecular trapping by the hydroxyl group then leads to the dihydrobenzofurans **4**, **7**, **8** and **9** in 38-75% isolated yields.*

In the foregoing paper, we describe the generation of the dianion **2** by double deprotonation of the *N*-BOC-1-aminobenzotriazole **1**, and subsequent condensations with aldehydes and ketones leading to the adducts **3**.[1] Herein, we report that these can be smoothly converted into the corresponding benzynes which are then trapped *in situ* by the flanking hydroxy function. The two major synthetic uses of benzynes are as Diels-Alder dienophiles and as electrophiles. Following the classic studies of Bunnett and his colleagues, the types of nucleophilic partners have been largely limited to amines (usually after deprotonation), enolates and α-lithionitriles.[1,2] As arynes are soft acids, alcohols and alkoxides should be less reactive partners;[2] however, benzynes have been trapped efficiently by simple examples of both these types of nucleophiles[2,3] as well as intramolecularly by phenoxides.[4]



1 **2** **3**

The attraction of generating benzynes from 1-aminobenzotriazoles is the simplicity and mildness of suitable reagents, either *N*-bromosuccinimide or lead(IV) acetate.[3] We were pleased to find that exposure of the aminobenzotriazoles **3a-c** to two equivalents of NBS at ambient temperature in dichloromethane led rapidly to the *bromo*-dihydrobenzofurans **4a-c**, which were isolated in the yields indicated.[5] By contrast, the adduct **5** derived from acetone failed to cyclise under these conditions and instead, the dibromo derivative **6** was isolated in 52% yield. We reasoned that the more hindered hydroxyl function was not competing successfully with the bromine present in the reaction mixture. Therefore, 1-pentene (5 eq.) was added as a bromine trap prior to the addition of NBS. Now that the latter was the major bromonium ion source, *ca.* 5 equivalents were required to drive the reaction to completion leading to the bromo-dihydrobenzofuran **7**. As an alternative, oxidation of the aminobenzotriazoles **3c** and **5** using lead(IV) acetate [1.1 eq., CH_2Cl_2, 20°C]^4 led smoothly to the less functionalised dihydrobenzofurans **8** and **9** respectively, in somewhat greater yields than with NBS.



This relatively brief approach appears to have considerable potential for the elaboration of a wide range of dihydrobenzofurans.^{6} The incorporation of an additional bromine atom in the final products **4** and **7** is a significant bonus as this should allow for the incorporation of a variety of additional substituents at the 7-position using either Pd- or Ni-catalysed coupling reactions or radical chemistry. Studies of these possibilities are in progress.

Acknowledgements

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3. *Eg*. Lera, A. R.; Aubourg, S.; Suau, R.; Castedo, L. *Heterocycles*, **1987**, *26*, 675.
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5. All yields refer to material showing correct analytical and spectroscopic data.
6. For an alternative, see Kim, K. M.; Kim, H. R.; Ryu, E. K. *Heterocycles*, **1993**, *36*, 497.

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