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# $Br^+$-Induced Cyclization of γ,δ-Unsaturated Ketones: A New Approach to Bromopyrane Derivatives

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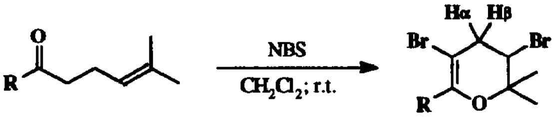
**Abstract:** 3,5-dibromo-3,4-dihydro-2,2-dimethyl-(2H)-pyrans **2**, are obtained through a simple and new procedure involving a bromoenol-etherification of γ,δ-unsaturated ketones **1**; the key step is the formation of mono-bromopyran intermediate **A**.

Processes of halo-cyclization[1,2,3] have been widely employed in organic synthesis for the preparation of oxygenated heterocyclic compounds. They usually involve the intramolecular addition of a nucleophile, such as -OH (alcoholic[4], enolic[5,6], phenolic[7]), -OR[8], -COOH[9], COOR[10] functions on C-C double bond, promoted by suitable sources of halonium ions ($I_2$, $Br_2$, NIS, NBS)[11,12].



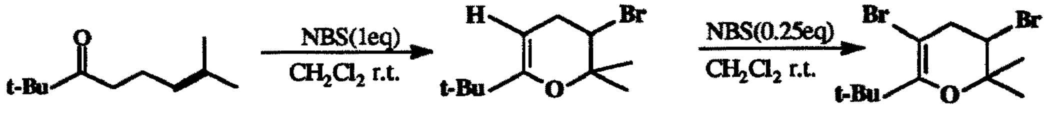
**1** **2**

| Entry | R | t(min) | %$^{a,b}$ | δ-CHBr ($J_1$; $J_2$) | δ-$CH_\alpha H_\beta$ (Jgem) |
|---|---|---|---|---|---|
| a | Me | 5 | 60 | 4.04 ( 9; 8) | 2.79-2.96 ( 17 ) |
| b | n-Pr | 3 | 31$^c$ | 4.05 (10; 10 ) | 2.81-2.94 ( 17 ) |
| c | i-Pr | 3 | 13$^c$ | 4.04 (8, 7 ) | 2.78-2.92 ( 17 ) |
| d | t-Bu | 1 | 50 | 3.99 (9; 6 ) | 2.81-2.96 ( 17 ) |
| e | Ph | 1 | 60 | 4.18 (9; 6 ) | 2.98-3.15 ( 17 ) |

a) All the yields refer to isolated, chromatographically pure compounds.
b) All compounds were fully characterized by $^1$H-NMR, IR, MS. The data are in agreement with proposed structures.
c) Low yields in entries **2b** and **2c** are due to marked decomposition during purification run.

We have found that, in spite of low nucleophilicity of the carbonyl function, γ,δ-unsaturated ketones **1a-e** undergo a very fast process of halocyclization by treatment with N-Bromosuccinimide (NBS) in methylene chloride solution at room temperature furnishing the dibromodihydropyrans **2a-e**. Moreover it has to be noted that the reaction runs in completely regioselective manner; in fact, in all cases no evidence of formation of dihydrofuran products was detected, although they could be easily distinguishable by $^1$H-NMR spectroscopy.

The conversion **1**$\rightarrow$**2** shows to proceed through formation of a mono-bromopyran compound. In fact **1d** furnishes compound **A**[13], in 25% yield, by reaction with 1eq. of NBS in $CH_2Cl_2$. Successively **A**, by treatment with 0.25 eq. of NBS, in the same solvent, gives dibromopyran **2d** in 20% yield.



**1d** **A** **2d**

In conclusion the showed procedure proved to be of a significant value since it represents the first general example of halo-enoletherification by $\gamma,\delta$-unsaturated ketones to give pyran-derivatives in efficent, rapid and regiospecific way.

In a tipical experiment a solution of NBS (2mmol) in dry $CH_2Cl_2$ (20ml) was added dropwise, at room temperature, to a solution of **1** (1mmol) in dry $CH_2Cl_2$ (1ml). After times listed in Table the solution was diluted with $Et_2O$ (50ml) and washed several times with brine (4x25ml). Organic phase was dried with $Na_2SO_4$. After solvent evaporation, the crude product was purified by chromatography on silica gel by elution with n-hexane.

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13. Compounds A has been isolated and purified by chromatography on silica gel. $^1$H-NMR ($CDCl_3$): 0.99 (s,9H); 1.25 (s,3H); 1.35 (s,3H); 2.42 (ddd,1H, $J_1$=3Hz, $J_2$=9Hz, $J_3$=17Hz); 2.57 (ddd,1H, $J_1$=4Hz, $J_2$=6Hz, $J_3$=17Hz); 4.02 (dd,1H $J_1$=6Hz, $J_2$=9Hz); 4.37 (dd,1H, $J_1$=3Hz, $J_2$=4Hz).

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