Tetrahedron Letters,Vol.25,No.25,pp 2653-2654,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

THE SYNTHESIS OF 4-HALOTETRAHYDROPYRANS AND 4-HALO-5,6-DIHYDRO-2H-PYRANS VIA THE LEWIS ACID PROMOTED CYCLIZATION OF ACETALS OF HOMOALLYLIC AND HOMOPROPARGYLIC ALCOHOLS

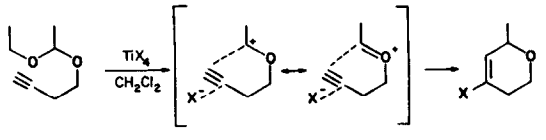
W. H. Bunnelle,* D. W. Seamon, D. L. Mohler, T. F. Ball and D. W. Thompson*

Department of Chemistry, College of William and Mary
Williamsburg, Virginia 23185

Ethyl vinyl ether, MEM chloride, and dihydropyran based acetals of homoallylic and homopropargylic alcohols cyclize in the presence of Lewis acids to give 4-halotetrahydropyrans and 4-halo-5,6-dihydro-2H-pyrans, respectively.

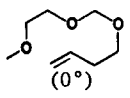
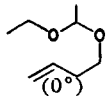
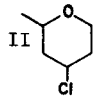
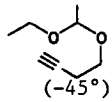
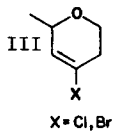
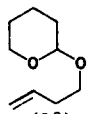
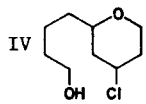
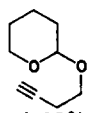
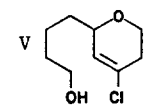
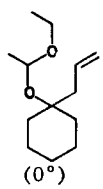
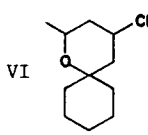
In this paper we report a facile synthesis of the title pyrans via a TiX_4 (X=Cl,Br) promoted cyclization of acetals derived from ethyl vinyl ether, 1-chloromethoxy-2-methoxyethane, and 3,4-dihydro-2H pyran with γ-unsaturated alcohols.[1] The synthetic results are summarized in the Table. The cyclizations were accomplished by dissolving 1-2 equivalents of TiX_4 in CH_2Cl_2 (5 mL per 1 mmol TiX_4) followed by dropwise addition of 1 equivalent of the acetal (1 mL per min). The reactions were allowed to proceed 15 min and then were quenched with methanol (5 mL per 10 mmol TiX_4) followed by 30-40 mL of 3N HCl saturated with NaCl. The product pyrans can be isolated from the organic layer by preparative GLC or distillation.

The reaction pathway most reasonably involves a cation-olefin cyclization step as illustrated for the acetal derived from ethyl vinyl ether and 3-butyn-1-ol:



These acetal cyclizations are related to Prins reaction chemistry yielding tetrahydropyrans.[2-4] However, the present approach gives higher yields and offers greater flexibility particularly in the cyclization of γ-alkynol based acetals. While our work was in progress a similar cyclization of the tetrahydropyranyl ether of 3-buten-1-ol catalyzed by $BF_3 \cdot OEt_2$ in trichloroethanol was reported.[5]

Products II, IV, and VI may exist as cis-trans isomers. GLC and NMR data for II indicate two isomers in the ratio 92:8 (presumable cis:trans). For products IV and VI

Acetal [7]	Product	Yield	^{13}C-NMR Data
 (0°)	 I	87	36.9($C_{3,5}$); 56.9(C_4); 66.1 ($C_{2,6}$)
 (0°)	 II	95 (92% cis 8% trans)	21.7(CH_3); 37.2,44.8(C_3 and C_5); 56.0(C_4); 67.3(C_2); 73.4(C_6)
 (-45°)	 III X=Cl,Br	95(Cl)	X=Cl: 20.8(CH_3); 32.8(C_5); 63.8(C_6); 71.0(C_2); 128.0(C_3); 129.4(C_4)
		98(Br)	X=Br: 21.1(CH_3); 35.5(C_5); 65.0(C_6); 72.3(C_2); 119.1(C_4); 133.2(C_3)
 (0°)	 IV	92	21.5, 32.5, 35.9, 37.1, 42.9, 62.5, 67.0(CH_2carbons); 55.9(C_4); 77.1(C_2)
 (-95°)	 V	65	21.6, 32.8, 33.3, 34.9, 62.8, 63.9(CH_2 carbons); 74.9(C_2); 127.7(C_3); 130.0(C_4)
 (0°)	 VI	94	24.8, 25.1, 25.4, 29.3, 34.0, 43.2, 47.8, 49.1, 57.0, 68.1, 77.1

the GLC and NMR data indicate a single isomer only.

The vinyl halide moiety resulting from the cyclization of the acetylenic acetals allows for further functional development, as demonstrated by the hydrolysis of III to 2-methyl-4-pyrone (aqueous $Hg(NO_3)_2$, 60°C).[6,8]

1. W. H. Bunnelle, D. W. Thompson, and D. W. Seamon, 35th Sourtheast Regional Meeting of the American Chemical Society, Charlotte, N.C., Nov. 1983; ORG 458.
2. E. Hanschke, Chem. Ber., 1955, 88, 1053.
3. J. Cologne and P. Boisde, Bull. soc. chim. France, 1956, 824.
4. P. R. Stapp, J. Org. Chem., 1969, 34, 479.
5. I. T. Kay and E. G. Williams, Tetrahedron Letters, 1983, 24, 5915.
6. H. Arzoumanian and J. Metzger, J. Organometal. Chem., 1973, 57, C1.

7. The temperature at which the acid promoted cyclization was run is listed under each acetal. Yields determined by GLC. NMR solvent: $CDCl_3$.

8. We thank the donors of the Petroleum Research Fund administered by the American Chemical Society and the Jeffress Memorial Trust for partial support of this work. We thank E. I. DuPont de Nemours and Company, Inc. and the National Science Foundation for funds with which to purchase gas chromatographs.

(Received in USA 24 February 1984)