Tetrahedron Letters,Vol.24,No.48,pp 5303-5304,1983 0040-4039/83 $3.00 + .00
Printed in Great Britain

SYNTHESIS OF 2-ALKYL-2,3-DIHYDRO-γ-PYRONES FROM 1-METHOXY-1-BUTEN-3-YNE

Michael T. Crimmins* and Danuté M. Bankaitis
Venable and Kenan Laboratories
University of North Carolina
Chapel Hill, N.C. 27514

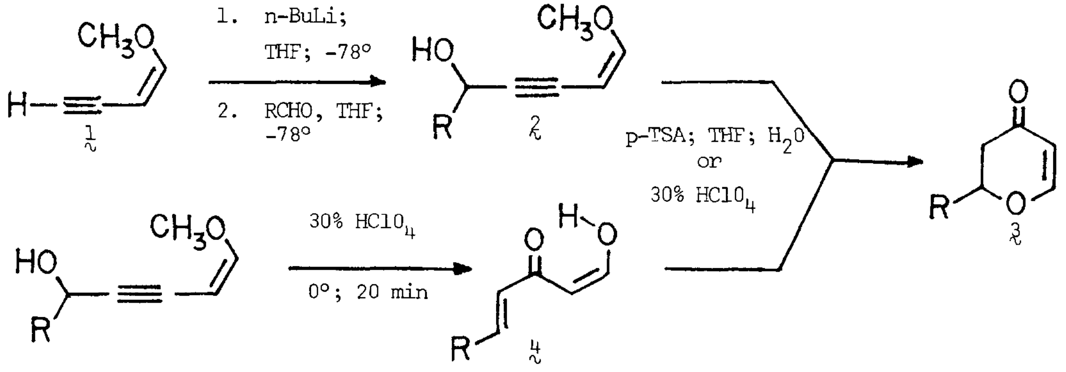
Abstract

A method for the preparation of 2-alkyl-2,3-dihydro-γ-pyrones from 1-methoxy-1-buten-3-yne **1** and aliphatic aldehydes is reported.

We recently reported that addition of the lithium acetylide of 1-methoxy-1-buten-3-yne **1** to lactones followed by acid hydrolysis provides high yields of dihydropyrone spiroketal systems.[1] Others have utilized the addition of the enolate of 4-methoxy-3-buten-2-one to acid chlorides to prepare 2-alkyl-γ-pyrones.[2] The synthetic importance of substituted dihydropyrones has been illustrated by Danishefsky through his elegant studies on dihydropyrones derived from Lewis acid catalyzed additions of oxygenated dienes to aldehydes.[3-6] Additionally, many natural products which contain dihydropyrone or related systems have displayed important biological properties.[7] A short, efficient synthesis of alkyl substituted dihydropyrones is described here.

Addition of various simple, inactivated aldehydes to the lithium acetylide of **1** results in the isolation of acetylenic alcohols **2**. When these acetylenes are treated for either 24 h at 25 °C with 30% $HClO_4$ in a biphase in dichloromethane, or for 48 h at 65 °C with p-toluene sulfonic acid in 4:1 THF:H_2O, dihydropyrones **3** are obtained in very good yield. We have subjected several aldehydes to this sequence and the results are given in the Table below.

The mechanism of this hydrolysis-cyclization is presently unclear. However, if the 30% $HClO_4$ hydrolysis is carried out at 0 °C for only 10-20 min, high yields of formyl ketones **4** result. These can be resubjected to the more strenuous hydrolysis conditions above to produce the dihydropyrones.



Table

	RCHO	yield of pure, distilled dihydropyrone [8]
R =	CH_3	40
	CH_3CH_2	63
	$CH_3CH_2CH_2$	80
	$(CH_3)_2CH$	71
	$(CH_3)_2CHCH_2$	70

General Procedure for the Preparation of Dihydropyrones: To a solution of 1-methoxy-1-buten-3-yne (10 mmol) in 15 mL of dry tetrahydrofuran at -78 °C was added slowly a solution of *n*-butyllithium (10 mmol) in hexane. The mixture was stirred for 15 min whereupon the aldehyde (12 mmol) in 2 mL tetrahydrofuran was added. After stirring for 1 h at -78 °C the mixture was quenched with saturated ammonium chloride, extracted with ether, dried and concentrated to afford the crude alcohol. Without purification this material was dissolved in 50 mL of 4:1 THF:H_2O and the mixture was acidified with *p*-toluene sulfonic acid. The mixture was refluxed for 48 h, cooled, diluted with ether and washed with saturated $NaHCO_3$. The organic layer was dried and concentrated, and the residue was distilled at reduced pressure to provide the pure dihydropyrones.[9]

References and Notes

1. Crimmins, M. T.; Bankaitis, D. M. *Tetrahedron Lett.* in press.
2. Koreeda, M.; Akagi, H. *Tetrahedron Lett.* **1980**, 1197. Ganem, B.; Morgan, T. A. *ibid.* **1980**, 2773.
3. Danishefsky, S.; Kerwin, J. F., Jr.; Kobayashi, S. *J. Amer. Chem. Soc.* **1982**, *104*, 358.
4. Danishefsky, S.; Kato, N.; Askin, D.; Kerwin, J. F., Jr. *J. Amer. Chem. Soc.*, **1982**, *104*, 360 and references therein.
5. Danishefsky, S.; Larson, E. R.; Askin, D. *J. Amer. Chem. Soc.* **1982**, *104*, 6457.
6. Larson, E. R.; Danishefsky, S. *J. Amer. Chem. Soc.* **1982**, *104*, 6458.
7. For example see: Pseudomonic Acid: Chaim, E. B.; Mellows, G. *J. Chem. Soc., Perkin trans. 1* **1977**, 294. Trichadione: Ireland, C.; Faulkner, J. D.; Solheim, B. A.; Clardy, J. *J. Amer. Chem. Soc.* **1978**, *100*, 1003. Compactin: Brown, A. G.; Smole, T. C.; King, T. J.; Hasenkamp, R.; Thompson, R. H. *J. Chem. Soc. Perkin trans. 1* **1976**, 1165.
8. All dihydropyrones gave satisfactory (± 0.4%) elemental analyses and consistent ^1H NMR and IR spectra.
9. We gratefully acknowledge financial assistance from the National Institutes of Health (AI-19544-01) and the Merck Sharp and Dohme Company.

(Received in USA 11 August 1983)