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MICROWAVE IRRADIATION : WITTIG OLEFINATION OF LACTONES AND AMIDES

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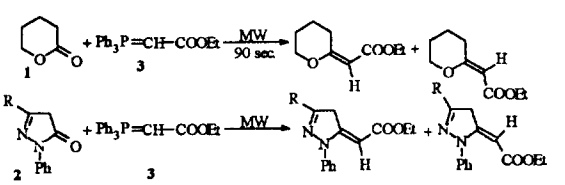
Abstract: Microwave assisted Wittig olefination of lactones and amides with a stabilised phosphorous ylide is described.

Key words : Microwave, lactones, amides, olefination, phosphorus ylide.

Wittig olefination[1] of carbonyl compounds has great importance in organic synthesis. In spite of the Peterson olefination[2] and the Tebbe methylenation,[3] the Wittig reaction is still the most widely used method for the formation of carbon-carbon double bonds from carbonyl compounds. Carbonyl groups of lactones and amides are not sufficiently reactive towards phosphoranes to undergo Wittig reactions as compared with aldehydes and ketones. Very recently, a preliminary report[4] appeared on the direct Wittig olefination of lactones derived from sugars by stabilised phosphoranes using forcing conditions. In contrast Wittig reactions of β-lactams[5] with phosphorous ylides even gave very poor yields after prolonged refluxing in toluene.

The enormous growth in the use of microwave irradiation[6] in synthetic organic chemistry inspired us to perform Wittig reactions of lactones and amides which are otherwise difficult to achieve under microwave conditions, significantly, remarkable rate enhancements, and drastic reduction of reaction time were observed. These reactions, when performed in refluxing toluene gave recovered starting materials. Herein we wish to report our observations with regard to Wittig olefination of lactones and amides under microwave irradiation (scheme) which occurs with excellent stereocontrol and in good yields.

Scheme



Thus, the lactone **1** or amide **2** and the two carbon stable ylide, ethoxycarbonylmethylene(triphenyl) phosphorane **3**, were mixed in 1:1.2 ratio and heated to 90°C in a microwave oven to give the products in 1 to 2 minutes, see table.

To test the generality of the reaction, several lactones and amides (see table) were reacted with the ylide. All reacted stereoselectively and configurational assignments were made on the basis of ^{1}H NMR[7] data or comparison with known compounds.[8] The products were purified by silica gel column chromatography.

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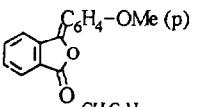
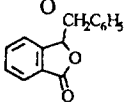
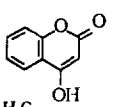
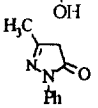
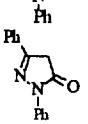
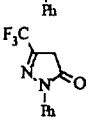
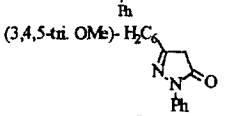
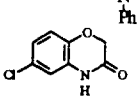
Table-1 : Wittig olefination of lactones and amides

Entry	Lactone/amide	Product	Product distribution (E/Z)	Reaction time (sec)	Total Yield (%)
1.		1E/1Z	20/80	90	80
2.		2E/2Z	15/85	100	89
3.		3E/3Z	20/80	110	72
4.		4E/4Z	25/75	140	66
5.		5E/5Z	10/90	110	82
6.		6E/6Z	10/90	90	86
7.		7E/7Z	15/85	100	82
8.		8E/8Z	10/90	90	80
9.		9E/9Z	10/90	100	86
10.		10E/10Z	15/85	95	76

In conclusion, our protocol demonstrates an efficient stereoselective method for making Wittig products from lactones and amides under microwave condition.

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[1] Maercker A. Org. React, 1965; 14: 270. [2] Ager DJ. Org. React. 1990; 38: 1. [3] Pine SH, Org. React. 1993; 43: 1. [4] Lakhrissi M and Chapleur Y. Angew. Chem. Int. Ed. Engl. 1996, 35: 750. [5] Gilpin ML, Harbridge JB. and Howarth TT. J. Chem. Soc., Perkin Trans I, 1987; 1369. [6] For recent review on Microwave assisted reactions, see a) Abramovich RA. Org. Prep. Proced. Int., 1991; 23: 683. b) Caddick S. Tetrahedron, 1995; 51: 10403. c) Galema SA. Chem. Soc. Rev., 1997; 26: 233. d) Sabitha G, Satheesh Babu R. and Yadav JS. Synth. Commun. (In press). [7] ^{1}H NMR (200 MHz, $CDCl_3$) : **2E** δ 1.3 (t, 3H), 4.16 (q, 2H), 5.5 (s, 1H), 5.62 (s, 2H), 7.3-7.6 (m, 4H), ms m/e 204 (M^+). **2Z** δ 1.35 (t, 3H), 4.2 (q, 2H), 5.3 (s, 1H), 5.71 (s, 2H), 7.3-7.6 (m, 4H), ms m/e 204 (M^+). **6E** δ 1.2-1.6 (m, 5H), 2.34 (s, 3H), 4.18 (q, 2H), 5.7 (s, 1H), 7.2-7.7 (m, 5H),ms m/e 212 (M^+). **6Z** δ 1.24-1.44 (m, 5H), 2.36 (s, 3H), 4.21 (q, 2H), 5.4 (s, 1H), 7.2-7.7 (m, 5H), ms m/e 212 (M^+). [8] Sauve G. and Deslongchamps P. Synth. Commun. 1985: 15(3): 201.