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SYNTHESIS OF α-METHYLENE MONOSUBSTITUTED δ-LACTONES FROM α-PHOSPHONOLACTONES NEW WITTIG-HORNER COMPOUNDS

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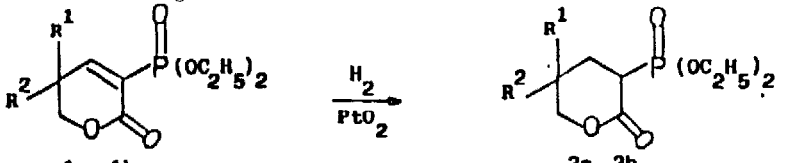
Abstract- The synthesis of the α-methylene monosubstituted δ-lactones 6-10 and 14-18 from the α-phosphonolactones 2a,2b and the aldehydes 3-5 and 11-13 is described.

The reaction of α-halolactones with trialkylphosphites[1-3] (Arbuzov reaction) represents a facile and elegant procedure for the synthesis of Wittig-Horner reagents. The general use of this reaction is limited by the small number of the α-halolactones obtainable[4,5]. By hydrogenation of the α-phosphonolactones α,β- unsaturated 1a,1b, obtained in our laboratory[6], we have opened a new route to a class of compounds of synthetic interest.

The hydrogenation of the compounds 1a and 1b in the presence of platinium (IV) oxide in isobutyl alcohol (r.t) led to the unknown α-diethylphosphonolactones 2a ($R^1 = CH_3$ $R^2 = C_3H_7$) and 2b ($R^1 = R^2 = CH_3$) in 100% yields.



1a, 1b 2a, 2b

Scheme 1

The EI mass spectra of the α-phosphonolactones show the presence of molecular ions at m/z =292 of 2a and m/z =264 of 2b supporting the complete hydrogenation of the starting compounds 1a,1b. Olefination of the 2a with the aldehydes 3-5 and of 2b with the aldehydes 11-13 under Wittig-Horner conditions gives the α-methylene monosubstituted δ-lactones 6-10 ($R^1 = CH_3, C_3H_7$) and 14-18 ($R^1 = R^2 = CH_3$) in 50-70% yields; (E/Z=3/2) (Scheme 2).

We have observed that the reaction of 2b with 4-nitrobenzaldehyde 11 and of 2a with the 5-methyl-thiophene-carbaldehyde 4 afforded only pure E-isomeres 8 and 14. In the other reactions E/Z-isomers *have been always obtained and separated by flash chromatography.*

In the ^{1}H-NMR spectra exocyclic protons are at a lower field - at δ = 7,98 - 8.13 ppm for aromatic derivates; δ = 6.70 - 7.10 ppm for aliphatic derivates - (s.Table 1) in the E-isomers by respect to Z-isomers - at δ = 6.23 ppm for 6 and δ = 5.73 - 6.03 ppm for aliphatic derivates -. This difference in the chemical shifts of the olefinic protons in the E-

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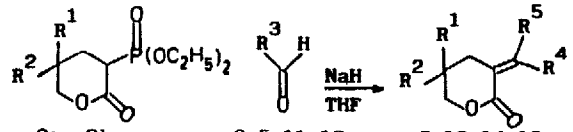
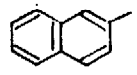
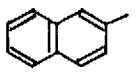
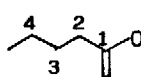
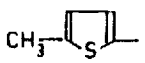
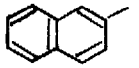
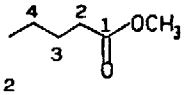
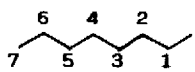
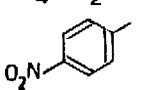
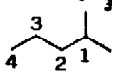
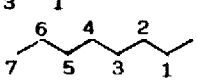
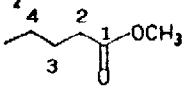
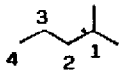
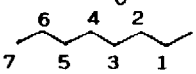
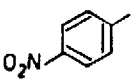
isomers might be attributable, besides, to a mesomeric effect. This effect is also observed in the ^{13}C-NMR spectra of the carbonyl groups of lactones (s. Table 1).[7,8]

By comparison of the EI mass spectra of the aromatic E-compounds 7,8,14 a prevailing cleavage between the C-2,C-3 and C-4,C-5 of the lactone ring under formation of the conspicuos fragments ions (m/z = 165,70%; 166,70.5%; for 7; m/z = 136,100% for 8; m/z = 161, 94% for 4) was observed. In the aliphatic derivates 15-18 prevail the fragment at m/z = 167,90% of the Z-isomers; m/z=167,40-50% of the E-isomers. The presence of the secondary methyl group in the side chain of the isomeric compounds 9 and 10 affords in the MS spectra the fragments at m/z=124 + H, 77,6% of Z-isomers 9 and at m/z=156, 75.5% of E-isomers 10.



2a, 2b 3-5,11-13 6-10,14-18

	R^3		R^4	R^5		R^4	R^5
3		6		H	15		H
4		7	H		16	H	
5		8	H		17		H
11		9		H	18	H	
12		10	H				
13		14	H				

Scheme 2. (Procedure: 20 mmol NaH in 70 ml THF, 20 mmol 2a,2b under N_2-atmosphere was added and 1h reflux; 20 mmol 3-5 and 11-13 in 10 ml THF was added and 2h reflux).

Table 1. Chemical Shifts ^{1}H (ppm) of the Olefinic Protons and ^{13}C (ppm) of the Carbonyl Groups Lactones 6-10 and 14-18.

Z-isomers			E-isomers			Z-isomers			E-isomers		
Compd.	H	C	Compd.	H	C	Compd.	H	C	Compd.	H	C
6	6.23	164.30	7	8.13	166.35				14	7.98	165.13
			8	8.30	166.88	15	6.00	164.9	16	7.03	165.80
9	5.73	165.13	10	6.70	166.18	17	6.03	164.29	18	7.10	165.90

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