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AN EFFECTIVE METHOD FOR THE SYNTHESIS OF UNSYMMETRICAL DIFURYLMETHANE DERIVATIVES AND 1,1-DIFURYL OLEFINS

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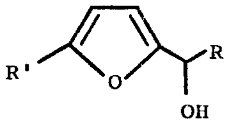
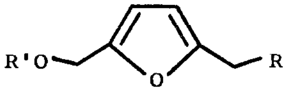
Summary: Unsymmetrical difurylmethane derivatives 9 and the unknown difuryl alkenes 10 were selectively obtained from carbinols 1a and 1b in two steps and with excellent yields.

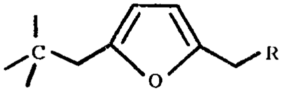
During the course of our studies on the reactivity of furyl-phosphinyl-carbinols and their use as intermediates in the synthesis of rethrolone- and prostaglandin-related compounds[1], we observed that 5-alkoxymethyl-furfurylphosphonates 2 can be easily obtained in very good yields when 5-methylfuryl-phosphinyl carbinol 1a and the suitable alcohol are allowed to react in the presence of dry gaseous hydrochloric acid[2]. Prompted by this finding, we considered synthetically interesting and profitable for our purposes the extension of this method that could afford the structure 3 in order to find a general procedure for the synthesis of 2,5-dialkylsubstituted furans. Results achieved in reaching this goal, lead now to report a new synthetic application of furyl-phosphinyl carbinols 1a and 1b as valuable starting materials for a facile and convenient synthesis of difurylmethane derivatives and unknown 1,1-difuryl olefins.



1a R=PO(OEt)$_2$, R'=Me
1b R=PO(OEt)$_2$, R'=H



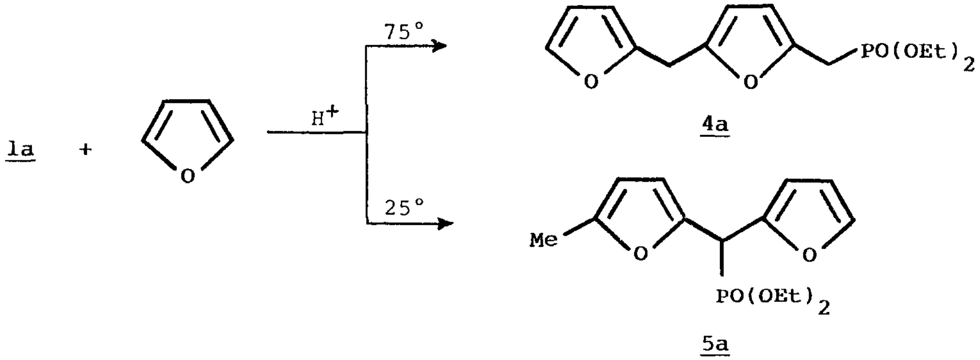
2 R=PO(OEt)$_2$, R'=alkyl



3 R=PO(OEt)$_2$

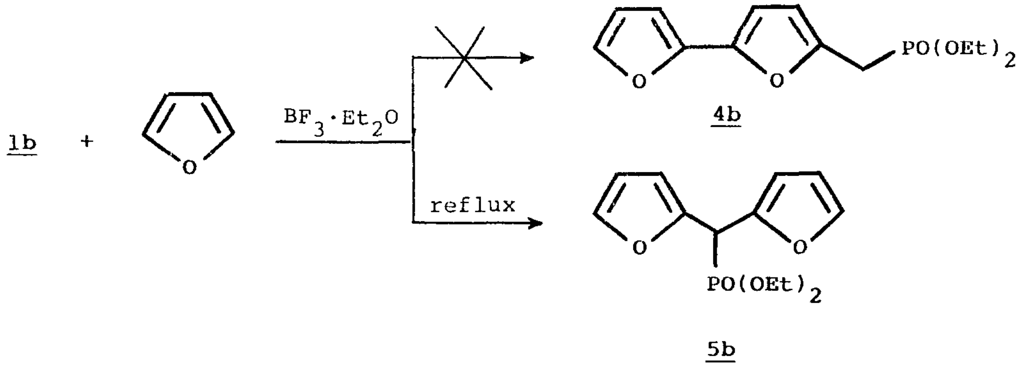
Difurylalkanes have been hitherto prepared by condensation of furans with carbonyl compounds[3] or by acid-catalyzed fission of furfuryl alcohol[4]. Both the methods are ineffective for a satisfying preparation of difurylmethane derivatives because of the complex mixtures from which these were isolated with exceedingly poor yields (1.7-4%). The lack of more effective synthetic procedures caused these compounds to be sparely employed, in spite of their potential importance for the insecticides industry.

Under protic conditions, 2-(diethoxyphosphinylmethyl)-5-furfuryl-furan 4a[5] has been obtained in 77% yield[6] from carbinol 1a and furan at 75°C[7].

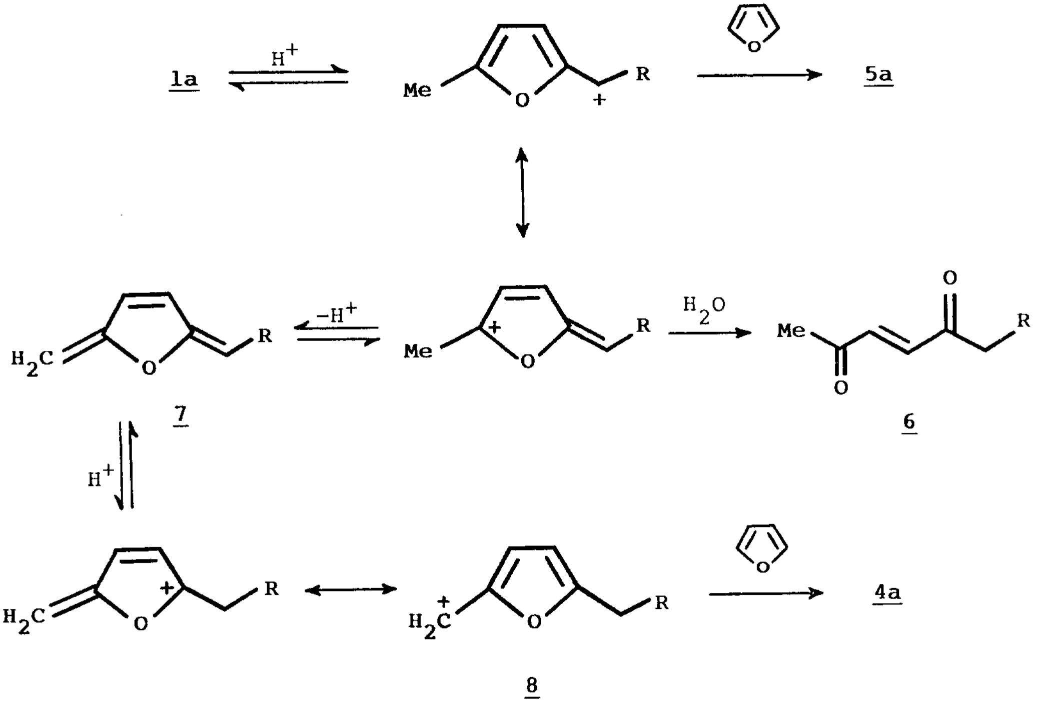


Solvent and temperature influence the yield and the nature of the products. Temperature effects are notable: a decrease in the reaction temperature below 70°C led to an increase in the formation of phosphonate 5a[5] arising from direct substitution of the hydroxy group of 1a, so that 5a was obtained regioselectively at 25°C in 83% yield[7]. The best results were observed carring out the reaction in dipolar aprotic solvents; in CH_3CN the yields of 4a and 5a were not less than 75% when water was rigorously excluded from the medium to avoid cleavage of the furan ring that consequently affords γ-diketone 6[1] (see Scheme I). The formation of 4a can be explained with the hypothesis that the undetected intermediate 7, under thermodynamically proper conditions, undergoes protonation and rearrangement into the cation 8 (Scheme I).

Attempts to obtain 4b and 5b in analogous manner from furyl-phosphinyl-carbinol 1b, were unfruitful. 5b[5] has been otherwise prepared (81%) by treating 1b with $BF_3 \cdot Et_2O$ in CH_3CN at gentle reflux for 3 hr[7].



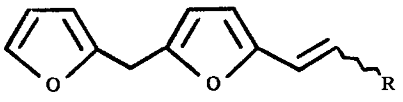
Scheme I



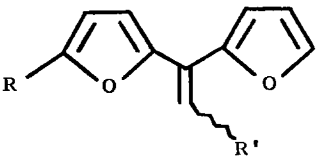
R=$PO(OEt)_2$

In all experiments, no significant amount of 4b has been detected.

As expected, compounds such as 4a, 5a and 5b take part in Wittig-Horner reactions. Thus, using NaH in THF at 0°C, the novel difuryl derivatives 9 and 10 were achieved in 15 min with excellent yields from formaldehyde or 2-furyl carbaldehyde and the suitable phosphonate.



9a R=H, 83%
9b R=2-furyl, 90%



10a R=R'=H, 78%
10b R=H, R'=2-furyl, 92%
10c R=Me, R'=2-furyl, 88%

In conclusion, the method here described represents a new and effective synthetic approach towards two different classes of compounds, which can be easily prepared in selective ways and using simple procedures: on the one hand, 5-furfuryl-2,2'(1,2-ethenediyl)-bis-furan **9b**[5] and 5-furfuryl-2-ethenyl-furan 9a, patterns of otherwise difficultly obtainable unsymmetric difurylmethane derivatives, on the other hand, 1,1-bis(2'-furyl)-ethene **10a**[5] and 1,1,2-tris(2'-furyl)-ethene **10b**[5], the first examples of 1,1-difuryl and trifuryl olefins.

Studies on the application of new compounds 9 and 10 to organic synthesis are now in progress.

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5) All products gave mass spectra in accord with the proposed structures. ^{1}H-NMR spectra were taken at 90 MHz in $CDCl_3$. Chemical shifts of protons of furan rings and phosphinyl group, are omitted.
   ^{1}H-NMR (δ). 4a: 4.00, s, 2H; 3.20, d, 2H, $J_{H,P}$=21 Hz; 5a: 4.68, d, 1H, $J_{H,P}$= = 26.5 Hz; 2.28, s, 3H; 5b: 4.74, d, 1H, $J_{H,P}$= 26 Hz; 9b: 6.73, s, 2H; 4.03, s, 2H; **10a**: 5.55, s, 2H; **10b**: 7.05, s, 1H.
6) All yields refer to isolated, chromatographically pure products.
7) Experimental procedure. 4a (5a): 10 mmoles of freshly distilled furan were added dropwise to a dry gaseous HCl saturated CH_3CN solution of 4 mmoles of 1a and 4 mmoles of N,N'-dicyclohexylcarbodiimide. The solution was stirred at 75°C (25°C) for 15 min (25 min), then cooled to 0°C and filtered. Solvent evaporation gave a crude residue that was submitted to chromatographic purification on silica gel short column using Et_2O as eluent.
   5b: 12 mmoles of furan were slowly added during two hours to a refluxing dry CH_3CN solution of 4 mmoles of 1b and 4 mmoles of $BF_3 \cdot Et_2O$. The resulting mixture was kept at refluxing temperature for about one hour more, after this time the reaction being complete (TLC analysis). The solution was poured onto ice-cold water, extracted with Et_2O and the organic layer was dried and evaporated. The crude product was then purified as reported above for 4a.

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