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Effect of Aggregation of Nitrile Anions on the 1,2 versus 1,4 Regioselectivity towards Benzylideneacetone.

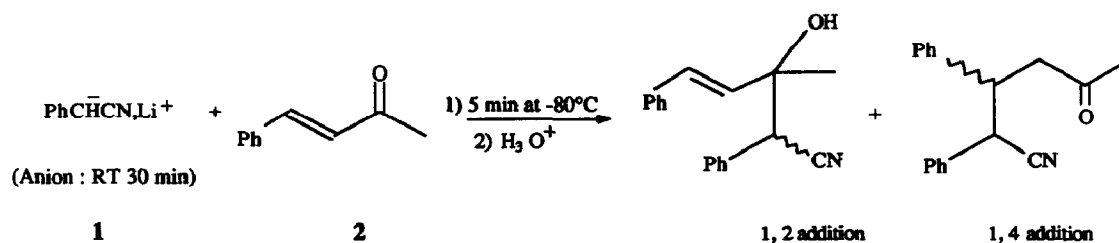
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Abstract : A direct evidence of the influence of aggregation state of lithiated phenylacetonitrile **1** on the 1,2 versus 1,4 regioselectivity towards benzylideneacetone **2** was established. Progressive addition of hexane to THF solutions raised the aggregates proportion of **1** as evidenced by IR ν_{CN} band and led to an increase of 1,4 adduct. Monomers afforded 1,2 addition in pure THF.

The knowledge of the state of aggregation of organolithiated species is an essential point in understanding their reactivity as it has been shown by the pioneer works of Seebach¹ and Collum² in the field of lithium enolates and amides respectively. However, few literature data of such studies are mentioned in the case of nitrile anions^{3,4}.

Recently, Heathcock demonstrated that the stereochemistry of enolate formation in THF/hexane solutions is highly depending on the solvent composition⁵. This prompted us to publish our results showing the influence of different THF/hexane media on the 1,2 versus 1,4 addition of $[\text{PhCHCN}]^-\text{Li}^+$ **1** to α -enone **2**.



IR and ^{13}C studies have evidenced that **1** exists in solution as monomeric, dimeric and tetrameric species which are in equilibrium according to the solvent nature, base, concentration and temperature⁶.

We report herein that the proportion of aggregates is growing up as the amount of hexane in THF solutions is increasing; this trend is shown by the relative IR ν_{CN} band intensities of the different species (Fig. 1a - e)⁷.

The results of the reaction of **1** ($n\text{BuLi}$; $c = 0.25\text{M}$; RT; 30 min.) with **2** (-80°C , 5 min.), in various THF/hexane mixtures (Table 1) indicate that the 1,2 versus 1,4 regioselectivity can be controlled by simple addition of progressive amounts of hexane to THF solutions.

Table 1 : Reaction of 1 with 2

Solvent THF/hexane : v/v	1,2/1,4 ^a	Yield % ^{a,b}
100 ^c -	95/5	92
80/20	75/25	78
70/30	47/53	41
60/40	25/75	43
50/50	8/92	53

^a) determined by ¹H NMR ; ^b) the complement to 100% being starting materials ; ^c) base : 1M HMDSL_i solution in THF.

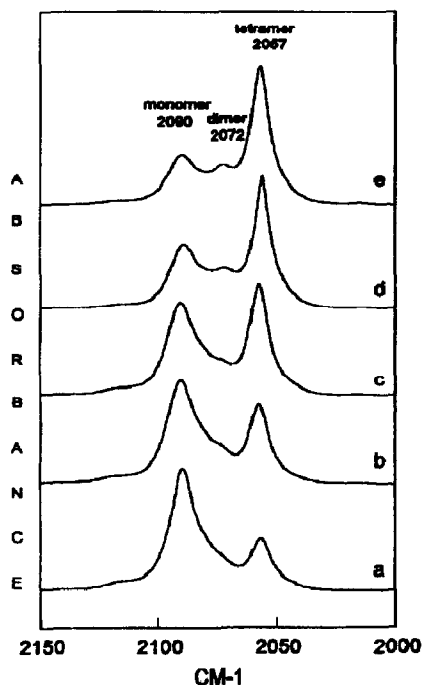


Fig.1. Infrared absorption spectra in the ν_{CN} vibration region of 1 : in various THF-hexane (v/v) mixtures : a = 100/0 ; b = 80/20 ; c = 70/30 ; d = 60/40 ; e = 50/50 ; base : a : HMDSL_i ; b-e : nBuLi ; c = 0.25M ; t = 25°C.

It appears that there is a striking parallelism between the regioselectivity and the aggregation state of 1, even if one assumes that at low temperature the reagents are less aggregated than at room temperature ⁸ ; moreover, this conclusion is strengthened by the fact that the rates of the 1,2 addition of monomers and of the 1,4 addition of aggregates are not very different.

References and notes

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