COMPETITION BETWEEN ALLYLIC SUBSTITUTION AND MICHAEL ADDITION WITH CARBANIONS **<** TO NITRILES.

Catherine CHARDON, Alain PETIT, Marie-Claude ROUX-SCHMITT, Jacqueline SEYDEN-PENNE*

Unité Associée au C.N.R.S. 478, Institut de Chimie Moléculaire d'Orsay Université de Paris-Sud, 91405 ORSAY (France)

<u>Abstract.</u> The reaction of methyl 4-bromo-4-methylcrotonate <u>1</u> with anionic species \mathbf{Q}^{-} to nitriles does not lead to cyclopropanes via a MIRC process. Products originating from a SN' reaction, <u>3</u> and <u>6</u>, are predominantly formed from <u>2a-c</u>, while products resulting from SN and SN' reactions are obtained in equimolar amounts from aminonitrile <u>2d</u>.

The problem of allylic substitution with double bond migration (SN') in the absence of transition metals in still open (1). While the substitution of primary allylic halides by various nucleophiles obviously takes place via a SN_2 process (1-3) which can occasionally be followed by a [2,3] sigmatropic rearrangement, leading thus to transposed final products (3), things do not seem to be so simple from secondary and tertiary derivatives. Recently, JOUCLA <u>et al.</u> (4) have observed from tertiary bromocrotonate <u>1</u> and $Ph_2C=NCH_2COOEt$ with base in a dipolar aprotic solvent, the formation of a compound due to a SN' process. On the other hand, when this reaction was run in THF, cyclopropanes resulting from Michaël Addition - Ring Closure (MIRC) were obtained, as already found in similar conditions from other bromocrotonates and carbanionic reagents (4,5). One might wonder whether this SN' process could be induced by a S.E.T., in line with the proposals of PROSS and SHAIK (6) and the more recent work of BORDWELL (7) on nucleophilic substitutions.

In such an eventuality, carbanions \mathbf{Q} to nitriles formed from <u>2a-d</u> should be good candidate: as nucleophiles as they are prone to S.E.T. in dipolar aprotic media (8). The substrate <u>1</u> would also favor such a process since a) steric hindrance around the electrophilic carbon makes direct displacement highly improbable b) the electron withdrawing group decreases the LUMO level of the substrate thereby lowering the frontier orbital gap between the reagents.

Results (9)

The reactions have been run in THF in Et_2O or in the presence of dipolar aprotic solven (THF-HMPA or DMSO), the anionic reagents being preformed by action of nBuLi, $\text{LiN}(\text{SiMe}_3)_2$, KOtB or KN(SiMe_3)₂. Surprisingly, whatever the conditions, no cyclopropane was found. Only compounds resulting from SN' <u>3</u> or SN <u>4</u> reactions could be detected (see Table).



When R was H (2a,b), two other products were formed due to further evolution of the SN' products: in THF-HMPA, diallylated compounds $\underline{5}$ were obtained in amounts depending on the reaction temperature. When lithiated bases were used, a third compound $\underline{6}$ could be characterized : it was purified by column chromatography and its ¹H, ¹³C NMR spectrum (10) as well as IR, MS and analysis data allow the assignment of a cyclopentadienyl structure ; independent experiments showed its formation from <u>3</u> under basic conditions. Our results show that while <u>3a,b</u> could be predominantly obtained with a good yield using KN(SiMe₃)₂ in THF, it was not possible to find, until now, experimental conditions allowing to prepare <u>6a</u> or <u>6b</u> alone, with a satisfactory yield.



When R was NMe₂ (2d), the product analysis was carried out after treatment of the crude reaction mixture by aqueous AgNO₃ (11), leading thus to ketones $\underline{7}$ and $\underline{8}$.



This was necessary due to the known instability of aminonitriles on silica gel.

The reactions were also run in THF-HMPA in the dark or in the presence of p-dinitrobenzene: no change in yields were observed.

One interesting observation from our results is that contrary to previous data in the literature (4,5), no MIRC reaction takes place in these systems even in THF in the presence of lithiated bases.

The SN' process is highly favored from arylacetonitrile <u>2a-c</u> carbanions, showing again the similarity of their reactions to those of cuprates (13) or of the anion of 9-methylfluorene (1), whose pKa in DMSO (14) is close to that of arylacetonitrile (9-methylfluorene 22.3; <u>2a</u> : 21.9; <u>2c</u> : 23). From aminonitrile <u>2d</u>, SN and SN' processes compete and equal amounts of both regioisomers are obtained in THF-HMPA. No radical chain mechanism seems to be involved in these reactions (12). One could tentatively assume a concerted SN' pathway from arylacetonitriles <u>2a-c</u> and a radical coupling within a solvent cage from aminonitrile <u>2d</u> : theoretical calculations indicate that the coefficients of carbon 2 and 4 in the SOMO of radical <u>9</u> are very close in magnitude (15). We are currently investigating the scope of these reactions as well as their mechanism.



Table

Reaction of <u>1</u> with carbanion formed from <u>2</u> a)

Reagent	Solvent	Base	SN' (%)	SN (%)
<u>2a</u>	THF (r.t.)	nBuLi	78 ^{b)}	4
<u>2a</u>	THF (r.t.)	nBuLi ^{c)}	93 ^{b,c)}	4
<u>2a</u>	THF (r.t.)	KN(SiMe ₃) ₂	91 ^{b,d)}	1
<u>2a</u>	THF-HMPA (4:lv.v, r.t.)	nBuLi	85 ^{e)}	7
<u>2a</u>	Et ₂ 0	LiN(SiMe ₃) ₂	96 ^{b,f)}	2
<u>2b</u>	THF (-15°C)	nBuLi	66 ^{b,g)}	4
<u>2b</u>	THF (r.t.)	KNSi(Me ₃) ₂	₈₅ b,g)	5
<u>2c</u>	THF (r.t.)	nBuLi	98 ^{b)}	2
<u>2c</u>	THF-HMPA or DMSO (r.t.)	nBuLi or KOtBu	98 ^{h)}	2
<u>2d</u>	THF (r.t.)	nBuLi	10	10
<u>2d</u>	THF-HMPA (r.t.)	nBuLi	45	45

a) Yields determined by GPC with internal standard completion to 100% is arylacetonitrile $\underline{2}$; equimolar ratios of $\underline{1}$, $\underline{2}$ and base used unless quoted.

b) 3 : 1:1 mixture of stereoisomers (GPC),

c) 1/2a/base : 1/2/2 or 1/1.5/1.5 ; SN' product 3a + 6a in a 58/42 molar ratio.

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d) <u>3a</u> + <u>6a</u> in a 95/5 molar ratio.
e) <u>3a</u> + <u>5a</u> + <u>6a</u> in a 78/19/3 molar ratio.

f) 1/2a/base : 1/1.5/1.5 ; SN' product : 3a + 6a in a 50/50 molar ratio.

g) <u>3b</u> + <u>6b</u> in a 94/6 molar ratio.

h) 95/5 mixture of stereoisomers.

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