ADDITIONS OF ANIONIC NUCLEOPHILES TO CARBONYL COMPOUNDS : CATION AND E-
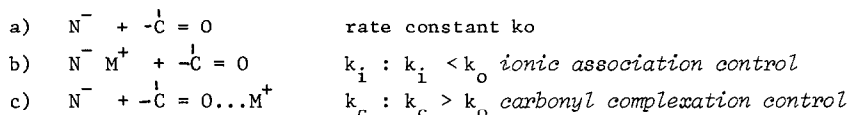LECTROPHILE NATURE INFLUENCE ON IONIC ASSOCIATION VS CARBONYL COMPLEXA-
TION CONTROL

A. LOUPY, M.C. ROUX-SCHMITT and J. SEYDEN-PENNE

GR 12 du CNRS, BP 28, 94320 THIAIS, France.

SUMMARY : the reaction of benzaldehyde with $LiCH_2CN$ in THF is controlled by carbonyl complexation while with KCH_2CN the reaction is controlled by ionic association. In the reaction of $m.Cl.C_6H_4CHCN^-/Li^+$ with substituted benzaldehydes, carbonyl complexation prevails with $p.CH_3OC_6H_4CHO$ while ionic association dominates with PhCHO and $p.CNC_6H_4CHO$.

During the nucleophilic addition of anionic reagents to carbonyl compounds, the as-
sociated cation can induce two opposite kinetic effects (scheme I) : either a rate decrease
due to interaction with the anion (case b)(ionic association) or a rate increase due to inter-
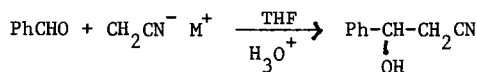action with the carbonyl compounds (case c)(complexation)(1-3)

a) N^- + $-\overset{|}{C} = O$ rate constant k_o

b) $N^- M^+$ + $-\overset{|}{C} = O$ k_i : $k_i < k_o$ *ionic association control*

c) N^- + $-\overset{|}{C} = O...M^+$ k_c : $k_c > k_o$ *carbonyl complexation control*

- Scheme I -

Consequently, the kinetic effect of a cation complexing agent (case ≃ a) can be of two types :
- if the reaction is controlled by carbonyl complexation a rate decrease is observed, as in
the case of the reduction of benzaldehyde by $LiAlH_4$ (1) -if the reaction is controlled by io-
nic association a rate increase is observed as in the case of alkaline enolate additions to
benzaldehyde, the magnitude of the effects being $Li^+ > Na^+ > K^+$ (4). Such opposite kinetic ef-
fects have also been observed for the initiation step of ethylene oxide polymerization by a-
nionic reagents depending on their nature (5).

These results show the dependency of the control on the nature of the nucleophile
for a given cation and electrophile. The dependency of the control with the associated cation
or the electrophile can also be considered. So, in a first set of experiments, we study the
influence of the cation, keeping the same anion and the same substrate ; the rate of addition
of MCH_2CN ($M^+ = Li^+$, Na^+, K^+) to benzaldehyde in the presence of complexing agents (cryptands)
is measured (Table I). In a second set of experiments the electrophile is changed while kee-
ping the cation and the anion constant : the rate of addition of lithiated m.chlorophenylace-
tonitrile is studied under the influence of a powerful cation solvating agent,   HMPA (6)
(Table II).

The reaction of PhCHO and $CH_2CN^- M^+$ $\underline{1}$ has been run at $-80°C$ using 0.1M solutions of each reagent (Table I).

<div align="center">TABLE I</div>

$$PhCHO + CH_2CN^- M^+ \xrightarrow[H_3O^+]{THF} \underset{\underset{OH}{|}}{Ph-CH-CH_2CN}$$

<div align="center">$\underline{1}$</div>

Run n°	M^+	adduct	Reaction Time (mn)	yield % [a]
1	Li^+	–	5	98
2	Li^+	$[2.1.1]$	60	90
3	Na^+	–	30	70
4	Na^+	$[2.2.1]$	30	60
5	K^+	–	150	80
6	K^+	$[2.2.2]$	30	90

a) the determinations were made by ^1H NMR of the crude reaction mixture after addition of $pCH_3OC_6H_4CHO$ as an internal standard. $[2.1.1]$, etc. refer to the corresponding cryptands.

The reaction of lithiated m.chlorophenylacetonitrile $\underline{2}$ with $pCH_3OC_6H_4CHO$, C_6H_5CHO, and $pCNC_6H_4CHO$, has been run at the same temperature and concentration (Table II).

In all the cases studied, we have checked that the reaction is univocal and goes to completion if the reaction time is long enough.

<div align="center">TABLE II</div>

$$ArCHO + mClC_6H_4CHCN^- Li^+ \xrightarrow[H_3O^+]{THF} \underset{\underset{CN\ OH}{|\ \ |}}{Ar-CH-CH-C_6H_4mCl}\ [a]$$
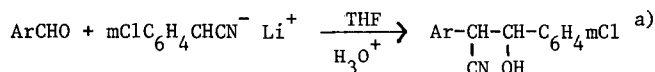
Run n°	Ar	adduct	t 1/2 [b]	$k_{THF-HMPA}/k_{THF}$
7	$pCH_3OC_6H_4$	–	5	0.1
8	$pCH_3OC_6H_4$	HMPA	45	
9	C_6H_5	–	10	5
10	C_6H_5	HMPA	2	
11	$pCNC_6H_4$	–	15	$\simeq 30$
12	$pCNC_6H_4$	HMPA	< 0.5	

a) two stereoisomers are formed in different amounts depending on the solvent. The stereochemistry of the reaction will be discussed in another paper (9).

b) t 1/2 is determined by ^1H NMR with an internal standard.

DISCUSSION

In the reaction of benzaldehyde with acetonitrile anion 1 (Table I), the influence of the cation is obvious : *when $M^+ = Li^+$ the reaction is faster when the cation participates* (runs 1, 2) : *lithium-oxygen carbonyl interaction (carbonyl complexation) prevails over ionic association.*
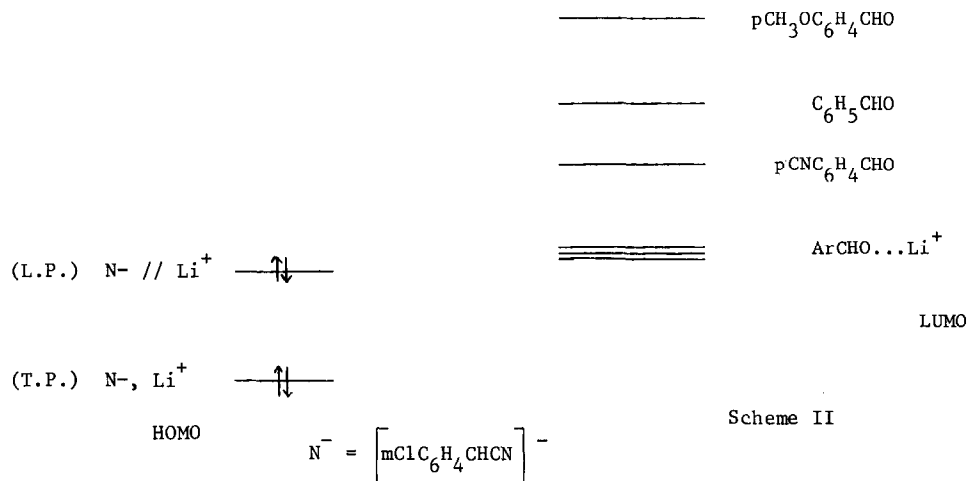
When $M^+ = K^+$, the reverse is observed as the reaction is slower when the cation participates (runs 5, 6) : *ionic association control is then the predominating factor.*

When $M^+ = Na^+$, the reaction rates are nearly the same in the different cases (runs 3, 4) : both effects are of the same order of magnitude. (10)

In the condensation of aromatic aldehydes with lithiated m.chlorophenylacetonitrile 2 (Table II), we notice either a rate decrease (runs 7, 8) or a rate increase (runs 9, 10, 11, 12) when HMPA is added to the reaction medium.

Thus, when the aromatic ring of the aldehyde is substituted by *an electron donating group* (pMeO) the reaction is faster *when Li^+ participates,* showing *the predominance of carbonyl complexation control* on this reaction process. On the reverse, *when the aromatic ring is unsubstituted or substituted by an electron withdrawing group (pCN),* reaction is slower in the presence of Li^+, *indicating a control by ionic association.*

In these cases, a perturbational Scheme (Scheme II) gives an account of the observed results : the closer the frontier orbitals, the faster the reaction.

$$pCH_3OC_6H_4CHO$$

$$C_6H_5CHO$$

$$pCNC_6H_4CHO$$

$$ArCHO...Li^+$$

LUMO

(L.P.) $N- // Li^+$

(T.P.) $N-, Li^+$

HOMO

$$N^- = \left[mClC_6H_4CHCN\right]^-$$

Scheme II

Li^+ complexation brings the levels of the aldehydes LUMO very close to each other (see Scheme II); thus the LUMO levels differences between complexed and uncomplexed carbonyl compounds are substituent dependent. The nucleophile HOMO level in the tight ion pair (T.P.) is lower in energy than in the loose ion pair (L.P.) ; therefore, frontier orbitals differences between T.P. HOMO and complexed aldehyde LUMO are larger than those of L.P. HOMO and free aldehyde LUMO for $p.CNC_6H_4CHO$ and C_6H_5CHO. The reverse situation occurs for $p.CH_3OC_6H_4CHO$.

In conclusion, the intervention of carbonyl complexation vs ionic association control in the reactions of anionic nucleophiles with carbonyl compounds not only depends on the nature of the nucleophile as previously observed, but also on the nature of the associated cation and of the electrophile.

REFERENCES and NOTES

1) - A. LOUPY, J. SEYDEN-PENNE and B. TCHOUBAR
     Tetrahedron Lett., 1976, 1677

2) - J.M. LEHN
     Accounts of Chem. Research, 1978, 11, 49 and quoted references.

3) - J.M. LEFOUR and A. LOUPY
     Tetrahedron 1978, 34, 2597.

4) - G. KYRIAKAKOU, A. LOUPY and J. SEYDEN-PENNE
     J. Chem. Research. (S), 1978, 8.

5) - S. BOILEAU, A. DEFFIEUX, D. LASSALLE, F. MENEZES and B. VIDAL
     Tetrahedron Lett., 1978, 1767 and quoted references.

6) - As the mean radius of Li^+ either complexed by $[2.1.1]$ (7) or solvated by HMPA (8) are very close, it seems that the strength of the electrostatic interaction is of the same order of magnitude in both cases.

7) -a) D. MORAS, B. METZ and R. WEISS
       Acta Cryst., 1973, B 29, 383
     b) D. MORAS and R. WEISS
       ibid, 1973, B 29, 400.

8) - E.M. HANNA, A.D. PETHYBRIDGE , J.E. PRUE and D.J. SPIERS
     J. Sol. Chem., 1974, 3, 563.

9) - A. LOUPY, M.C. ROUX-SCHMITT and J. SEYDEN-PENNE
     to be published
     Using lithiated phenylacetonitrile, association control operates with the three aldehydes.

10) - We can notice (runs 3,6,9) that the reactivities of the cryptated ion pairs are about the same in the case of $(Li^+, [2.1.1.])$ and $(Na^+, [2.2.1.])$ and slightly different for $(K^+, [2.2.2.])$
     This difference may be due to the strength of the electrostatic attraction of the anion and the complexed cation which depends upon the cation size (7) $(Li^+ [2,1,1] \bar{R} = 4,65$ Å ; $K^+, [2.2.2.] \bar{R} = 5,1$ Å).