Tetrahedron Letters No. 12, pp 959 - 962, 1974. Pergamon Press. Printed in Great Britain.

SOLVENT AND ION-PAIR EFFECTS ON THE AUTOCONDENSATION OF LINEAR ALIPHATIC ALDEHYDES

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(Received in UK 5 November 1973; accepted for publication 5 February 1974)

Our studies on the reactivity of phenoxymagnesium bromides in the presence of electrophiles have outlined a new series of highly regiospecific reactions.[1] We report now the results concerning the reactivity of magnesium enolates using phenates as metalating agents for linear aliphatic aldehydes.

Accordingly, 2,4,6-trimethylphenoxymagnesium bromide was used first since it cannot undergo electrophilic attack[1] by the carbonyl compound. Two completely different solvents, the former with low, the latter with high specific cationic coordinating power were utilized as reaction media: i.e. benzene and hexamethylphosphotriamide (HMPT). Although a different reaction course was observed in the two solvents, nevertheless a very high selectivity was maintained in both cases (see table 1). Crotonization products (III) were obtained quantitatively in benzene, whereas a mixture of the two 1,3-diols monoesters (IVa, IVb)[2] were produced quantitatively in HMPT.[3]

Scheme 1

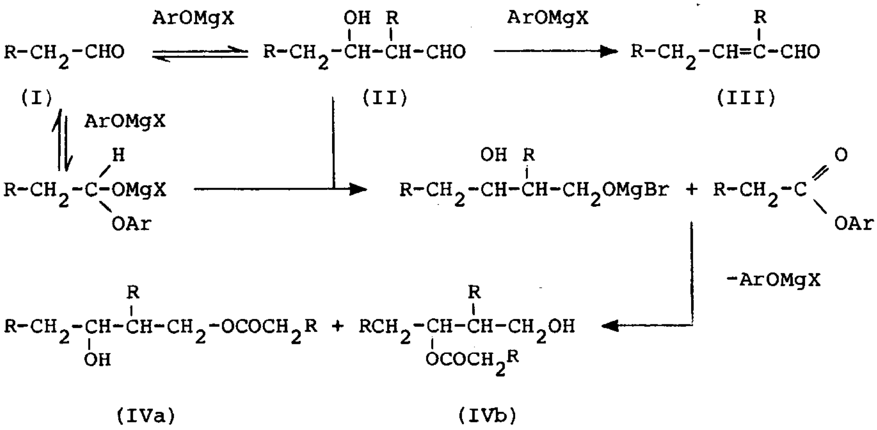

TABLE 1

Solvent effect in the autocondensation of linear aliphatic aldehydes in the presence of 2,4,6-trimethylphenoxymagnesium bromide at 40° for 24 hours

Solvent: C_6H_6				Solvent: HMPT			
	Total	Rel.yields%[§]			Total	Rel.yields%[§]	
R-CHO	conv.%	III	IV	R-CHO	conv.%	III	IV[¶]
C_2H_5CHO	80	95	0	C_2H_5CHO	95	0	94
C_3H_7CHO	70	94	0	C_3H_7CHO[†††]	90	0	95
C_3H_7CHO[†]	98	90	0	C_4H_9CHO	95	0	92
$C_6H_{13}CHO$	80	96	0	$C_5H_{11}CHO$	95	0	90
$C_6H_{13}CHO$[††]	80	90	0	$C_6H_{13}CHO$	95	0	96

[†] At 80° for 30 min. [††] At 80° for 3 hours. [†††] At 40° for 2 hours.

[§] Difference to 100 is represented by unidentified byproducts.

[¶] Ratio IVa : IVb = 60 : 40.

TABLE 2

Reaction of n-C_3H_7CHO in the presence of various magnesium phenoxides in C_6H_6 at 40° with different ion-pair:aldehydes molar ratios

	TMArOMgBr[†]				$(TMArO)_2Mg$[†]				$(C_6H_5O)_2Mg$			
Ion pair: aldehyde molar ratio	t[§]	Total conv.%	Rel. Yields%[¶] III	IV	t[§]	Total conv.%	Rel. Yields%[¶] III	IV	t[§]	Total conv.%[§]	Rel. Yields%[¶] III	IV
1 : 1	3	98	90	0	1	95	19	63	4	80	85	6
1 : 2	3	95	85	5	-	-	-	-	-	-	-	-
1 : 5	3	85	24	67	1	95	19	73	8	90	49	40
1 : 10	24	95	16	78	1	95	16	80	-	-	-	-
1 : 20	24	85	8	84	1	95	10	84	24	45	51	33
-[∫]	2	55	4	49	5'	90	10	58	-	-	-	-

[†] TMArO = 2,4,6-trimethylphenoxide.

[§] Times in hours unless stated otherwise.

[¶] Difference to 100 is represented by unidentified byproducts.

[∫] Reaction in aldehyde itself as solvent; ion-pair : aldehyde molar ratio 1 : 50.

According to what is known in the literature[4] and to some indirect tests we carried out, a common pathway leading to aldol (II), (see scheme 1), may be hypothesized for these reactions. In particular in benzene, probably because of the enhanced acid character of the cation present in the ion-pair, the dehydration process is favoured, affording the crotonic product (III). In contrast, in HMPT a Tischenko's type reaction[4] occurs because the acid character of the cation is strongly depressed in this solvent with consequent enhancement of the nucleophilic property of the phenate anion. In agreement with these results, in benzene itself, but with a decreased ion-pair:aldehyde ratio, i.e.favouring a greater coordination of the aldehyde to the cation, the yield in 1,3-diol monoesters (IV) increased as expected. This was verified in the reaction between n-butanal and 2,4,6-trimethylphenoxymagnesium bromide (see table 2), in which the ratio between the relative percentages of products IV and III (% IV : % III) varied from 0 (aldehyde : ion-pair = 1) to 10 (aldehyde : ion-pair = 1 : 20). Furthermore, in aldehyde itself as solvent, the ratio increased up to 15.

On the basis of these results, an analogous reaction course was to be expected for Mg^{2+} phenates also in solvents with low coordinating power.[5] Results obtained with 2,4,6-trimethylmagnesium phenate[5] are reported in table 2. A remarkable increase in the yield of 1,3-diol monoesters was observed also when a high aldehyde : ion-pair (1 : 1) ratio was used. In contrast, the ratios %IV : %III were no longer varied according to the different ratios ion-pair : aldehyde.

The high reactivity showed by aldehydes in the presence of magnesium salts, as well as their low electrophilicity towards the aromatic nucleus of magnesium phenates[1] allowed us to study the influence played by the structure of the phenoxidic anion on the reaction course. In the reaction with magnesium phenate, using a ratio ion-pair : aldehyde = 1, the crotonic product was obtained in high yield (see table 2). By varying the ratio ion-pair : aldehyde, we could observe variations much lower than those observed with 2,4,6-trimethylphenoxymagnesium bromide.

On the basis of these results, it is possible for the first time to emphasize the remarkable sensitivity of these reactions not only to small variations of the coordinating capability of the cation ($MgBr^{+}$, Mg^{2+}) but also to the structure of the anion, quite seldom observed in the reactions catalysed by ion-pairs.[6]

Acknowledgement: This work was partially supported by a C.N.R. grant.

Refences and foonotes

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[2] These products had already been obtained by autocondensation of aldehydes, but always as a mixture with other products: M. S. Kulpinsky and F. F. Nord, *J. Org. Chem.*, 8, 256 (1943); F. J. Villani and F. F. Nord, *J. Amer. Chem. Soc.*, 68, 1674 (1946); *ibidem*, 69, 2605 (1947); M. Hausermann, *Helv. Chim. Acta*, 34, 2172 (1951); G. Hesse and J. Mauer, *Ann.*, 658, 21 (1962).

[3] All the structures are based on analytical, mass spectral, n.m.r., and i.r. data.

[4] Y. Ogata and A. Kawasaki, *Tetrahedron*, 25, 929 (1969); Takeo Saegusa and Takashi Ueshima, *J. Org. Chem.*, 33, 3310 (1968); Takeo Saegusa, Takashi Ueshima, Kakutaroh Kauchi, and Sadao Kitagawa, *ibid.*, 33, 3657 (1968).

[5] Tests carried out with lithium and sodium 2,4,6-trimethylphenates evidenced loss of selectivity in the reaction, which leads to the formation of large precentages of side-products, in addition to products III and IV.

[6] See e.g.: H. C. Brown, H. Nambu, and M. M. Rogic, *J. Amer. Chem. Soc.*, 91, 6852, 6854, 6855 (1969); H. C. Brown, B. A. Carlson, R. M. Prager, *J. Amer. Chem. Soc.*, 92, 5790 (1970).