



Investigation of the basis of catalytic activity of solid state phosphate complexes in the Knoevenagel condensation

Jamal Bennazha^{a,b}, Mohamed Zahouilly^b, Ali Boukhari^c, Elizabeth M. Holt^{d,*}

^a *Laboratoire Matériaux Catalyse et Environnement (LMCE), Faculté des Sciences et Techniques, Mohammedia, Université Hassan-II, BP 146, Mohammedia 20650, Morocco*

^b *Département de Chimie, Faculté des Sciences et Techniques, UFR de Chimie Appliquée, Mohammedia, Université Hassan-II, BP 146, Mohammedia 20650, Morocco*

^c *Laboratoire de Chimie du Solide Appliquée (LSCA), Laboratoire Associé Francophone (LAF N° 501), Département de Chimie, Faculté des Sciences, Université Mohammed-V, Avenue Ibn-Batouta, Rabat, Morocco*

^d *Department of Chemistry, Oklahoma State University, Stillwater, OK 74078, USA*

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Abstract

The Knoevenagel condensation of benzaldehyde and ethyl cyanoacetate in ethanol at ambient temperature was catalyzed with range of mono-, meta- and diphosphate complexes. Comparison of the results shows that the catalytic activity of those phosphates is related to the electropositivity of the cation present in the structure and to the availability of the phosphate moiety to serve as a base.

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1. Introduction

The Knoevenagel condensation of an active methylene compound and an aldehyde is a convenient route to the synthesis of substituted alkenes [1]. This condensation is normally carried out in the presence of a base to remove the somewhat acidic or 'active' hydrogen atom. Often alkoxides, secondary amines or piperidine are used as the base. Of late there has been interest in carrying out synthetic organic reactions under conditions which do not require separation of the product from other organic materials (such as the base), which are fast, effective and which do

not require heating or the use of large quantities of solvent.

In an attempt to meet these conditions for the Knoevenagel reaction, attention has turned to the use of heterogeneous catalysts which can be removed from the reaction mixture by filtration. Alumina [2], silica [3], zinc and magnesium oxides [4], resins [5], zeolites [6,7], and other catalysts have been tried with some success [7–16].

Other researchers have augmented the effect of the catalyst with the addition of ultrasound [17–19] and microwave [20–22] radiation.

We are interested in the application of solid state phosphate complexes in catalysis. We have shown, earlier, that the diphosphate $\text{Na}_2\text{CaP}_2\text{O}_7$ has activity similar to that of the best catalysts for the Knoevenagel reaction [23]. Alkali and alkaline earth containing

* Corresponding author. Tel.: +405-744-5949;

fax: +405-744-6007.

E-mail address: betsy@biochem.okstate.edu (E.M. Holt).

phosphate materials ($\text{Na}_2\text{CaP}_2\text{O}_7$, $\text{Na}_4\text{P}_2\text{O}_7$, $\text{Ca}_2\text{P}_2\text{O}_7$) have shown effectiveness in Knoevenagel catalysis [24]. Natural phosphate (similar to $\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$) doped with KF and/or sodium nitrate has been reported to catalyze Knoevenagel reactions [25]. Magnesium phosphates, $\text{NaMg}_4(\text{PO}_4)_3$, $\text{Mg}_3(\text{PO}_4)_2$, $\alpha\text{-Mg}_2\text{P}_2\text{O}_7$ and NaMgPO_4 have been studied as catalysts in this kind of reaction [26]. Phosphates containing transition metals such as $\text{K}_2\text{NiP}_2\text{O}_7$, etc. have also shown effectiveness [27,28].

In the present work, our goal is to understand the influence of phosphate structure on the effective basicity of phosphate materials by comparison of their respective catalytic activity towards the Knoevenagel reaction between benzaldehyde and ethyl cyanoacetate.

2. Experimental

2.1. Preparation of the phosphate materials used as heterogeneous catalysts

The identity of all phosphates used was confirmed by X-ray powder diffraction using a Siemens D8 Advance diffractometer equipped with Diffrac Plus software [29] and $\lambda(\text{Cu K}\alpha) = 1.5406 \text{ \AA}$. The powder patterns measured were identified by comparison to those of the known compounds in the JCPDS data base (Joint Committee for Powder Diffraction (JCPD)) except where indicated below.

$\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$, $\text{Na}_3\text{PO}_4 \cdot 8\text{H}_2\text{O}$, $(\text{NaPO}_3)_n$, LiPO_3 , Li_3PO_4 and $\text{Mg}_3(\text{PO}_4)_2 \cdot x\text{H}_2\text{O}$ were obtained commercially. Other phosphates were prepared synthetically:

- $\alpha\text{-Na}_4\text{P}_2\text{O}_7$: Prepared by the dehydration of $\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$ at 600°C .
- $\gamma\text{-Na}_3\text{PO}_4$: Prepared by the dehydration of $\text{Na}_3\text{PO}_4 \cdot 12\text{H}_2\text{O}$ at 720°C .

- $\gamma\text{-Ca}_2\text{P}_2\text{O}_7$: Obtained by the dehydration of CaHPO_4 at 600°C .
- $\text{Na}_2\text{CaP}_2\text{O}_7$: Prepared from Na_2CO_3 , CaCO_3 and $\text{NH}_4\text{H}_2\text{PO}_4$ at 700°C [30]. The structure was verified by comparison of the powder pattern recorded with that calculated on the basis of the single crystal structure reported earlier.
- $\alpha\text{-Co}_2\text{P}_2\text{O}_7$: Prepared from $\text{Co}(\text{NO}_3)_2 \cdot 6\text{H}_2\text{O}$ and $(\text{NH}_4)_2\text{HPO}_4$ at 850°C .
- $\alpha\text{-Ni}_2\text{P}_2\text{O}_7$: Prepared from NiO and $(\text{NH}_4)_2\text{HPO}_4$ at 910°C .
- $\text{Mn}_2\text{P}_2\text{O}_7$: Prepared from MnO and $(\text{NH}_4)_2\text{HPO}_4$ at 910°C .

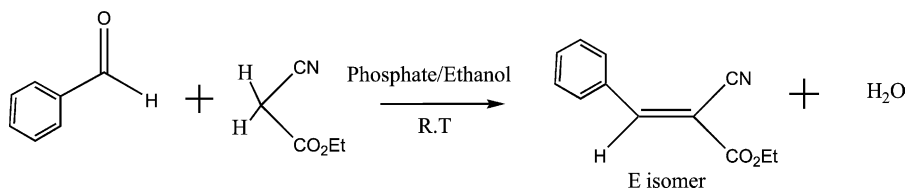
A sample of each catalyst with particle size of less than $90 \mu\text{m}$ was obtained by passing each powderous product through a sieve of that size. Thus, the effect of large differences in particle size on the catalytic activity of these phosphates was eliminated.

All the samples were dried for 2 h at 100°C before use in order to eliminate water molecules adsorbed on the surface of the samples which may affect catalytic activity.

2.2. Reaction procedure

The Knoevenagel condensation between benzaldehyde and ethyl cyanoacetate in the presence of 95% ethanol at room temperature was chosen as the standard reaction (Scheme 1).

The general procedure was as follows. To a flask containing 200 mg of the phosphate were added, successively, benzaldehyde (3 mmol), ethyl cyanoacetate (3.2 mmol) and the solvent (95% ethanol: 1.6 ml). The mixture was then stirred vigorously at room temperature for 40 min. At the end of the reaction time, the catalyst was removed by gravity filtration and washed with 6 ml of 95% ethanol. The progress of the reaction was observed by use of a Hewlett-Packard G1800A



Scheme 1.

GCD System gas chromatograph coupled to a mass spectrometer (carrier gas—helium; flow, 1 ml/min; oven, 70–290 °C; injector, 150 °C; detector, 280 °C; high performance capillary siloxane packed column, 30 m length, 0.25 mm in thickness). Spectra of pure benzaldehyde and ethyl cyanoacetate were previously determined to ascertain their retention times under the conditions used.

The single product of the reaction, ethyl (*E*)- α -cyanocinnamate, was identified by allowing reaction product mixtures to concentrate in air whereupon a solid material crystallized. This material was shown to be ethyl (*E*)- α -cyanocinnamate, with properties comparable to those previously reported for this solid material [31]. There was no *Z*-isomer formed and no further Michael addition of ethyl cyanoacetate to ethyl (*E*)- α -cyanocinnamate took place. Under the conditions used for GC analysis, the retention times observed were: benzaldehyde, 12.30; ethyl cyanoacetate, 11.80; ethyl (*E*)- α -cyanocinnamate, 37.95 min.

mp: 50–51 °C; reported 50 °C [32]. IR: 2230 (C=N), 1730 (C=O), 1610 (C=C) cm^{-1} . ^1H NMR spectrum: 1.40 (t, 3H ethyl), 4.40 (q, 2H ethyl), 7.50 (m, 3H *m*- and *p*-aromatic protons), 8.00 (d, 2H *o*-aromatic protons), 8.25 (s, 1H alkene proton). Varian Gemini 300 mH NMR spectrometer. ^{13}C NMR spectrum: 14.09 (ethyl), 62.67 (ethyl), 102.96 (CN), 115.42 (CH=C(CN)), 129.22, 131.01, 131.42, 133.24 (aromatic carbon atoms), 155.28 (Ph-CH=C), 162.42

(C=O). Mass spectrum: M^+ 201, 156, 172, 128, 200, 102.

3. Result and discussion

Table 1 presents the results of the standard reaction catalyzed by the 13 phosphate catalysts. Results are presented in the form of a ratio of the area of the GC peak seen for the product, ethyl (*E*)- α -cyanocinnamate to that seen for unreacted benzaldehyde. The heterogeneous phosphate catalysts are grouped according to the structure of the phosphate: monophosphates (PO_4^{3-}), polymeric meta phosphates (PO_3^{1-}) and diphosphates ($\text{P}_2\text{O}_7^{4-}$) are represented.

The mechanism of the Knoevenagel condensation involves abstraction of one of the active methylene protons by a base, followed by attack of the resulting anion on the carbonyl carbon of the benzaldehyde. The resulting O^- abstracts a hydrogen atom from the base. Elimination of a molecule of water results in the formation of a system of extended conjugation Scheme 2 [33].

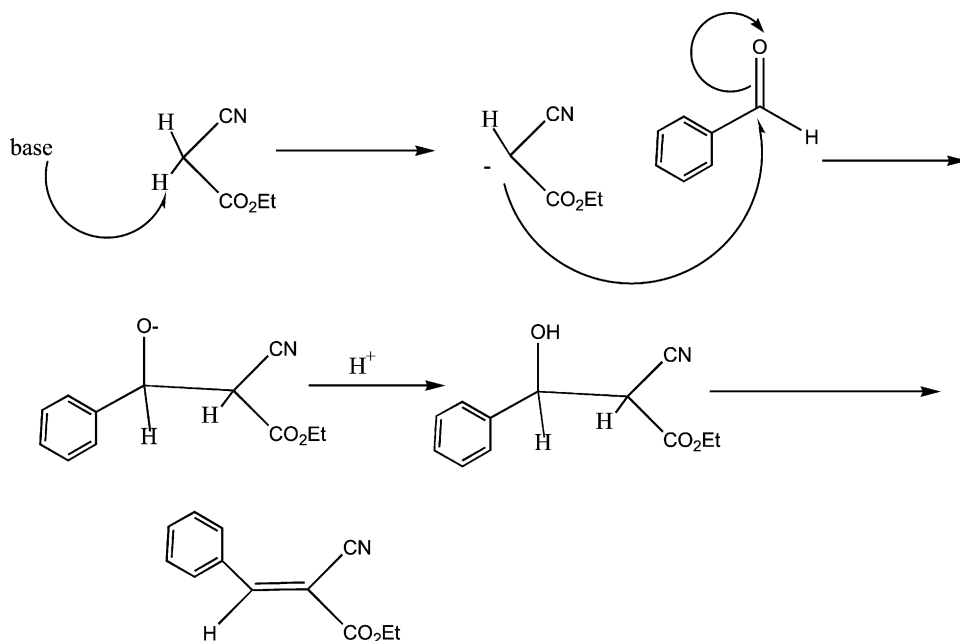
Thus the role of the phosphate catalyst can be presumed to be the initial abstraction of the proton from the active methylene group of the ethylcyanoacetate by a negatively charged oxygen atom of a phosphate group. The effectiveness of the catalyst may be related to the number of negative sites available, to the

Table 1

Results of phosphate catalysis of the Knoevenagel reaction between benzaldehyde and ethylcyanoacetate^a

Entry	Catalyst	Phosphate group (negative charge per oxygen atom)	Total moles of atoms of oxygens present	Ratio product/benzaldehyde
1	Li_3PO_4	$(\text{PO}_4)^{3-}$ (−3/4)	0.00690	0.785
2	Na_3PO_4	–	0.00487	0.547
3	$\text{Na}_3\text{PO}_4 \cdot 8\text{H}_2\text{O}$	–	0.00260	0.826
4	$\text{Mg}_3(\text{PO}_4)_2 \cdot 5\text{H}_2\text{O}$	–	0.00227	0.811
5	$(\text{NaPO}_3)_n$	$(\text{PO}_3)^{1-}$ (−1/2)	0.00392	0.666
6	$(\text{LiPO}_3)_n$	–	0.00465	0.204
7	$\text{Na}_2\text{CaP}_2\text{O}_7$	$(\text{P}_2\text{O}_7)^{4-}$ (−4/6)	0.00461	0.708
8	$\text{Na}_4\text{P}_2\text{O}_7$	–	0.00451	0.876
9	$\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$	–	0.00268	0.843
10	$\text{Ca}_2\text{P}_2\text{O}_7$	–	0.00472	0.299
11	$\text{Co}_2\text{P}_2\text{O}_7$	–	0.00411	0.036
12	$\text{Ni}_2\text{P}_2\text{O}_7$	–	0.00411	0.001
13	$\text{Mn}_2\text{P}_2\text{O}_7$	–	0.00422	0.011

^a Ratio of areas of the peaks (product/(product+benzaldehyde)) seen in the GC spectrum of the reaction mixture after removal of catalyst.



Scheme 2.

availability of each of these negative sites considering their involvement with cations in the structure or to the intensity of the negative charge at these sites.

Table 1 shows that for the most part phosphates with alkali or alkali earth cations behave as good catalysts for the Knoevenagel reaction between benzaldehyde and ethyl cyanoacetate. Their product/benzaldehyde ratios range from 0.299 to 0.876. The exception is LiPO_3 which shows a very low product ratio. Phosphates containing transition metal cations (entries 11–13) show weak activity as catalysts.

Only small differences are also noted in the effectiveness of the three categories of phosphates represented: monophosphates (PO_4^{3-}), polymeric meta phosphates (PO_3^{1-}) and diphosphates ($\text{P}_2\text{O}_7^{4-}$).

The question can be asked if the difference in catalyst behavior is 1. The number of oxygen atoms available for catalytic activity or 2. Their relative basicity (negative charge per oxygen atom) or 3. Their availability (degree of involvement with the cationic metal atom) which is important in the effectiveness of an individual catalyst. Another issue is the influence of waters of hydration on the effectiveness of the catalyst.

Since 200 mg of catalyst were used, the molar presence of each catalyst was not equal. Since the bridg-

ing oxygen atoms of the phosphate moieties are neutral and presumably do not participate in catalysis, the number of negatively charged oxygen atoms is four for a monophosphate, two for a polymeric meta phosphate and six for a diphosphate. Column 3 shows the number of moles of negatively charged oxygen atoms that were available for each phosphate catalyst. Since the charges shared by the 'available' or terminal oxygen atoms differ between the three groups, column 3 shows the effective charge resident on each terminal oxygen atom of the catalyst.

1. The number of moles of oxygen atoms available per 0.2 g of catalyst (column 4) does not play a role in the efficiency of the phosphate as a base. $\text{Na}_3\text{PO}_4 \cdot 8\text{H}_2\text{O}$ and $\text{Mg}_3(\text{PO}_4)_2 \cdot 5\text{H}_2\text{O}$ with the lowest numbers of oxygen atoms available to serve as catalytic sites in 200 mg of catalyst are among the most active catalysts. This is reasonable considering that not all oxygen sites are needed to serve as catalytic sites at any one point in time. In most cases, the number of oxygen sites exceeds the number of active methylene hydrogen atoms (0.0032 mol). However, it is not to be expected that all oxygen atoms are at the surface of the

particles used and thus available to act as basic sites.

- The negative charge per oxygen atom (column 3) varies with the form of the phosphate moiety with the oxygen atoms of monophosphate groups, PO_4^{3-} groups being marginally more negative ($-3/4$) than those of diphosphate groups, $\text{P}_2\text{O}_7^{4-}$ groups ($-4/6$). Both of these forms have a more concentrated negative charge on terminal oxygens than the polymeric metaphosphate (PO_3) $^{1-}$ with two terminal oxygen atoms (charge per oxygen = $-1/2$). In general these differences in electronegativity are reflected in the product yields within the series 1–10.
- Character of bonding between cation and terminal oxygen atoms of catalyst.

Phosphates containing alkali and alkaline earth cations are dramatically more effective as catalysts than those with transition cations. The character of the interaction between cation and terminal phosphate oxygen atom must be involved. The more electropositive the cation, the more ionic the character of its interaction with neighboring oxygen atoms. Highly ionic cation–oxygen interactions leave the basicity of the oxygen atoms intact. Transition metals with more covalent character to their interactions with phosphate oxygen atoms tie up the negative charge and render it less effective in a catalytic mechanism. Similarly, the series, $\text{Na}_4\text{P}_2\text{O}_7$, $\text{Na}_2\text{CaP}_2\text{O}_7$, $\text{Ca}_2\text{P}_2\text{O}_7$ represents a transition from more electropositive to a less electropositive cation and catalytic efficiency declines in the series, 0.876, 0.708, 0.299.

- Involvement of water.

The presence of water molecules at the surface of the catalyst has recently shown to be an activator of the catalytic properties of phosphate materials [28].

One can note that the hydrated phosphates (entries 3, 4 and 9) are more active than many of the anhydrous compounds. The number of terminal oxygen atoms is reduced when the 0.2 g includes water molecules of hydration as well as phosphate terminal oxygen atoms. Since all reactions were run in 95% ethanol, all reactions had water molecules in the solution and presumably at the surface of the catalyst particles.

The crystal structure of $\text{Na}_4\text{P}_2\text{O}_7 \cdot 10\text{H}_2\text{O}$ [34] shows the two sodium atoms per asymmetric unit to

be six-fold coordinate. Of the 12 oxygen atoms coordinated to sodium atoms, only two are phosphate oxygen atoms. Thus, the presence of the water in the matrix serves to remove the other two phosphate oxygen atoms from involvement with sodium and to leave them free to serve as catalytic sites, with their negativity undiminished by proximity to a positive cation. The water crystallized in the matrix thus serves as an insulator. Similarly in $\text{Na}_3\text{PO}_4 \cdot 8\text{H}_2\text{O}$ [35] the six independent sodium atoms are coordinated largely to water oxygen atoms. Only two of the eight phosphate oxygen atoms per asymmetric unit are coordinated to sodium atoms. Thus in this structure as well, water molecules serve to insulate phosphate atoms from sodium atoms. Thus the catalytic activity of the hydrated material is greater than that of the unhydrated Na_3PO_4 . The crystal structure of $\text{Mg}_3(\text{PO}_4)_2 \cdot 5\text{H}_2\text{O}$ is unknown but the same insulation may be assumed to exist.

4. Conclusion

The Knoevenagel reaction between benzaldehyde and ethyl cyanoacetate in ethanol has been carried out in the presence of various phosphate compounds at room temperature for a 40 min period. The catalytic activity of the phosphates tested appears largely related to the availability of the phosphate oxygen atoms to remove active methylene hydrogen atoms at the start of the mechanism. Two factors have been observed to influence this availability: increased electropositivity of the cation present in the structure leads to a more ionic bond between cation and terminal phosphate oxygen atoms and thus to a more available basic catalytic site. Secondly, alkali and alkaline earth cations appear to coordinate to water molecules included in the solid state matrix in preference to phosphate oxygen atoms. The presence of water molecules in the solid matrix thus ‘occupies’ the cation, leaving the phosphate oxygen atoms greater freedom to serve as catalytic sites.

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