

Research article

The potassium pyrophosphate $K_2CaP_2O_7$, a new and efficient catalyst for the conjugate addition of thiols onto chalcones

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Abstract

The synthetic potassium pyrophosphate $K_2CaP_2O_7$ is a new solid support, catalyse the Michael addition of mercaptans onto α,β -unsaturated carbonyl compounds in heterogeneous media, leading to quantitative yields in a short reaction time. Products of undesirable side reactions resulting from 1,2-addition, polymerisation and bis-addition are not observed. The work-up procedure is simplified so she gives a cleaner product.

Keywords: Heterogeneous catalysis, $K_2CaP_2O_7$, Conjugate addition, Carbon-sulphur bond; Thiols, Chalcones derivatives

Introduction

The conjugate addition[1] of thiols to electron deficient alkenes is one of the most effective methods for carbon-sulphur bond formation[2] and has been the subject of a number of studies about various uses involving synthesis of anti-tuberculosis drug[3], biochemistry[4], agrochemistry[5], anti-corrosion[6] and lubrication[7] among others.

In classic methods[8], this reaction catalysed by strong bases such as alkali metal alkoxides, hydroxides and transition metal complexes. The limitation of these strong bases in these reactions is mainly the formation of undesirable side products by polymerisation, bis-addition and self-condensation.

A new methodology to overcome these problems has been devised by the use of heterogeneous catalyst like alumina[9], zeolites[10], montmorillonite[11], Mg-Al hydrotalcite[12], animal bone meal[13], $\text{Na}_2\text{CaP}_2\text{O}_7$ [14], fluorapatite[15], hydroxyapatite[16], natural phosphate[17].

In continuation of our investigations on the use of heterogeneous catalysts for fine chemicals preparation, we wish to report here a mild, heterogeneous catalytic method for the Michael addition between chalcones derivatives **1** and mercaptans **2** catalyzed by synthetic potassium pyrophosphate $\text{K}_2\text{CaP}_2\text{O}_7$ in mild reaction condition (Figure 1).

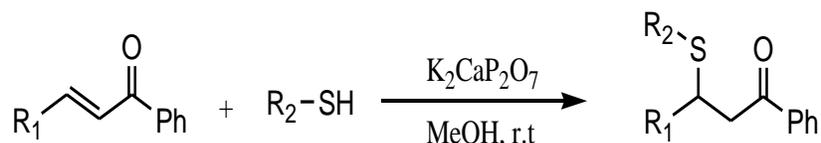


Figure 1. Thia-Michael addition catalyzed by $\text{K}_2\text{CaP}_2\text{O}_7$

Materials and Method

Chemicals and instrumentations

All commercial reagents and solvents were used without further purification. Potassium pyrophosphate $\text{K}_2\text{CaP}_2\text{O}_7$ is prepared in powder state. X-ray diffraction (XRD) patterns of the catalysts were obtained on a Philips 1710 diffractometer using $\text{Cu-K}\alpha$ radiation. Surface areas were determined at 77 K using a Coulter SA 31000 instrument with an automated gas volumetric method employing nitrogen as the adsorbate. NMR spectra were recorded on a Bruker ARX 300 spectrometer. Mass spectra were recorded on a VG Autospec spectrometer. FTIR spectra were recorded on an ATI Mattson-Genesis Series spectrophotometer using the KBr disc method.

Preparation of the catalyst and structural characteristics

The Potassium pyrophosphate $\text{K}_2\text{CaP}_2\text{O}_7$ [18] was synthesized by heating stoichiometric quantities of K_2CO_3 , CaCO_3 and $\text{NH}_4\text{H}_2\text{PO}_4$ (purity greater than 99%). The starting materials were carefully mixed in an agate mortar and heated by steps of 150°C in a porcelain crucible up to 800°C . This solid state technique allows ammonia, water and carbon dioxide to evolve progressively according to the following equation (Figure 2).

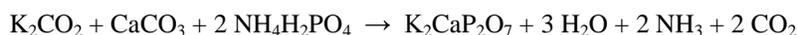


Figure 2. Preparation of potassium pyrophosphate

After the final grinding, the powder is heated at 820°C for 48 hours. The purity of the final powder was controlled by X-ray diffraction, using a D 500 Diffractometer ($\text{CuK}\alpha$ radiation, $1,540 \text{ \AA}$).

The powder pattern of $\text{K}_2\text{CaP}_2\text{O}_7$ available in the literature (monoclinic system, space group $\text{P2}_1/\text{n}$, $a = 9.79 \text{ \AA}$, $c = 12.97 \text{ \AA}$, $\beta = 104.3^\circ$), and by comparison to those of its two isomorphous diphosphates $\text{Cs}_2\text{CaP}_2\text{O}_7$ and $\text{Rb}_2\text{CaP}_2\text{O}_7$ [19].

The powder was dried for 2 hours at 100°C before use in order to eliminate possible water molecules adsorbed on the surface of the sample which may affect catalytic.

Results and Discussion

Thiophenol **2a** and chalcone **1a** catalyzed by the potassium pyrophosphate $K_2CaP_2O_7$ (0.1g), were chosen as model substrates to determine suitable reaction conditions for thia-Michael addition.

Firstly, various solvents (1.5ml) were tested. Thus, after 25 min of reaction the yields obtained of product **3a** are in presence of methanol (92%) and ethanol (93%), respectively. In the cases of hexane, THF, dichloromethane, or butanol, no product **3a** was observed under the reaction conditions, only the starting material was isolated. Thus, methanol was chosen as a solvent for further study.

Therefore, we carried out the reaction in various quantities of methanol. The yields obtained of product **3a** are 71%; 92%; 93%; 87%; and 53% with 0.75; 1.5; 3; 5; and 10 ml of methanol, respectively.

This result confirms the crucial role played by the solvent used to carry out the reaction. It would appear that best solvent for this reaction is the methanol and ethanol. The same result has been observed with natural phosphate [20].

To determine the scope and limitation of Michael addition, the optimum conditions were applied to other substrates as shown in Table 1. For this study, we carried out the Michael addition of chalcones as acceptors with various mercaptans such as thiophenol, ethyl thioglycolate and 2-aminothiophenol, catalysed by $K_2CaP_2O_7$ (0.1g) in the presence of methanol (1.5 ml) at room temperature. The products of undesirable side reactions resulting from 1,2 addition, polymerization and bis-addition are not observed.

Table 1. Synthesis of products **3** catalyzed by $K_2CaP_2O_7$

Products	X ₁	R	Yield (%/min)
3a	H	-Ph	92 (25)
3b	H	-2-NH ₂ -Ph	98 (03)
3c	H	-CH ₂ -CO ₂ -Et	78 (60)
3d	<i>p</i> -NO ₃	-Ph	92 (02)
3e	<i>p</i> -NO ₃	-2-NH ₂ -Ph	91 (01)
3f	<i>p</i> -NO ₃	-CH ₂ -CO ₂ -Et	86 (60)
3g	<i>p</i> -Cl	-Ph	92 (02)
3h	<i>p</i> -Cl	-2-NH ₂ -Ph	94 (01)
3i	<i>p</i> -Cl	-CH ₂ -CO ₂ -Et	83 (60)
3j	<i>p</i> -Me	-Ph	90 (35)
3k	<i>p</i> -Me	-2-NH ₂ -Ph	94 (05)
3l	<i>p</i> -Me	-CH ₂ -CO ₂ -Et	64 (60)
3m	<i>p</i> -OMe	-Ph	91 (120)
3n	<i>p</i> -OMe	-2-NH ₂ -Ph	92 (06)
3o	<i>p</i> -OMe	-CH ₂ -CO ₂ -Et	57 (60)

The use of synthetic diphosphate $K_2CaP_2O_7$ as heterogeneous catalyst for Michael reaction has allowed the isolation of products **3** rapidly and with good yields (83 % to 97 %), except for products (**3c**, **3l**, **3o**).

The results observed with different Michael acceptors shown that the presence of an electron-donors group (-OMe, -CH₃) decreases their activity (**3l**, **3o**, **3n**) whereas the electron-acceptors group (NO₂, Cl) increases the activity of the Michael acceptors.

In order to test their possible synthetic application, ketone **3a** was converted to oxime **4a** catalyzed by the Potassium pyrophosphate K₂CaP₂O₇. The oxime was subjected to the reaction by thionyl chloride and the chemoselective Beckmann rearrangement gave the anilide of 3,*N*-Diphenylsulfanyl-propan-1-one **5a**. Its alcoholysis furnished the corresponding ethyl ester **6a**. While compound **6a** is a direct precursor of β-thio acid **7a** (Figure 3).

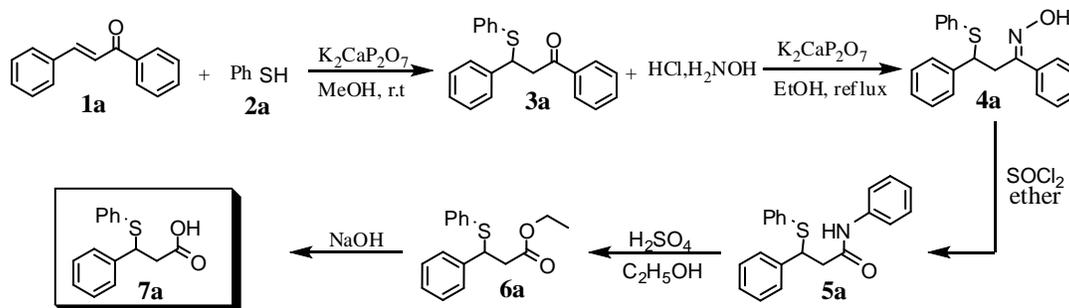


Figure 3. A simple route to synthesis of β-thio acid

Thus, we estimate that the surface of K₂CaP₂O₇ presents certainly multicycatalytic active sites [21]. The basic sites (oxygens of P₂O₇ group and CaO₆ octahedra) abstract the proton from the thiophenol. The acidic sites (phosphorus of P₂O₇ group, K⁺ and Ca²⁺ cations) coordinate with the oxygen of chalcone that increase the enone moiety polarization. Consequently, the C-S bond formation is facilitated and the sulfanyl product is obtained by transfer of a proton (Figure 4).

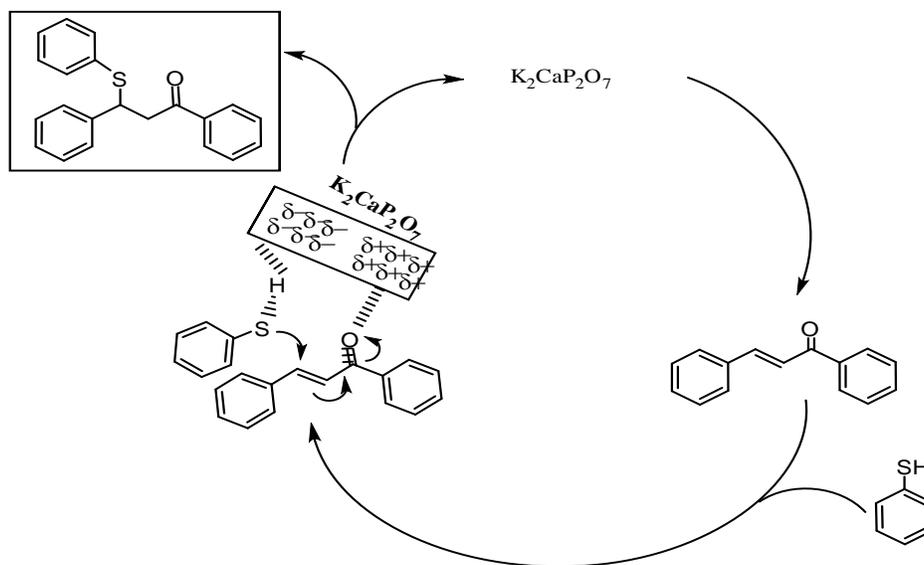


Figure 4. Mechanism of heterogeneous catalytic for conjugate addition using K₂CaP₂O₇

We next investigated the stability of the catalyst in order to recycle it. The used and recovered $K_2CaP_2O_7$ has been shown to be reusable after drying at 150 °C in vacuum, and more efficiently after washing with acetone followed by calcinations at 600 °C. In the last case, the catalyst can be recovered and reused at least five times without appreciable loss of activity.

Conclusion

In summary, we believe that $K_2CaP_2O_7$ is a new heterogeneous catalytic for effecting carbon-sulphur bond formation and represent an important breakthrough in the development of solid catalysts. The high reactivity and specificity of our catalyst coupled with their ease of use and reduced environmental problems makes them attractive alternatives to homogeneous basic reagents.

Acknowledgement

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References

- [1] Abrouki, Y., Anouzla, A., Loukili, H., Saida, K., Bennazha, J., Loukili, A., Rayadh, A., Sebti, S., and Zahouily, M., 2013, Sodium Pyrophosphate: A Novel and Efficient Catalyst for Sulfa-Michael additions., *American Journal of Biological Chemical and Pharmaceutical Sciences*, 1(5), 16-21.
- [2] Abrouki, Y., Anouzla, A., Loukili, H., Lotfi, R., Rayadh, A., Bahlaoui, M.A., Sebti, S., Zakarya, D., and Zahouily, M., 2013, Central Composite Experimental Design Applied to the Catalytic Carbon-Sulfur Bond Formation by Fluorapatite Catalyst., *American Journal of Applied Chemistry*, 1(2), 22-27.
- [3] Abrouki, Y., Anouzla, A., Loukili, H., Lotfi, R., Rayadh, A., Bahlaoui, M.A., Sebti, S., Zakarya, D., and Zahouily, M., 2013, Process Optimization for Synthesis of Anti-Tuberculosis Drug Catalyzed by Fluor apatite Supported Potassium Fluoride., *American Journal of Theoretical and Applied Statistics*, 2(3), 81-86.
- [4] Elzagheid, MI., Tedeschi, AL., and Damha, MJ., 2003, Synthesis of 2',3'-dideoxy-2'-fluoro-3'-thioarabinothymidine and its 3'-phosphoramidite derivative., *Nucleosides Nucleotides Nucleic Acids*, 22(5-8):1343-1346.
- [5] Fest, C., and Schmidt, KJ., 1982, *The Chemistry of Organophosphorus Pesticides*, Springer-Verlag, New York.
- [6] Desforges, E., Grysan, A., Oget, N., Sindt, M., and Mieloszynski, JL., 2003, A quantitative synthesis of β -carboxylated thiophosphates via a Michael reaction., *Tetrahedron Letters*, 44 (33) 6273-6276.
- [7] Zinke, H., and Schumaker, R., 1994, The thermal stability and antiwear performance of some thiophosphoric acid derivatives., *Wear*, 179(1), 45-48.
- [8] Ceylan, M., Gürdere, MB., Gezegen, H., and Budak, Y., 2010, Potassium-tertiary butoxide-assisted Addition of thioglycolic acid to chalcone derivatives under solvent-free conditions., *Synthetic Communication*, 40, 2598-2606.
- [9] Ahammed, S., Bhadra, S., Kundu, D., Sreedhar, B., and Ranu, BC., 2012, An efficient and general procedure for the synthesis of alkynyl chalcogenides (selenides and tellurides) by alumina-supported Cu(II)-catalyzed reaction of alkynyl bromides and diphenyl dichalcogenides., *Tetrahedron*, 68(51), 10542-10549.
- [10] Uguina, MA., Sotelo, JL., and Serrano, DP., 1991, Toluene disproportionation over ZSM-5 zeolite: Effects of crystal size, silicon-to-aluminum ratio, activation method and pelletization., *Applied Catalysis*, 76(2), 183-198.
- [11] Sharma, G., Kumar, R., and Chakraborti, AK., 2007, A novel environmentally friendly process for carbon-sulfur bond formation catalyzed by montmorillonite clays., *Journal of Molecular Catalysis A: Chemical*, 263, 143-148.

- [12] Wang, YB., and Jehng, JM., 2011, Hydrotalcite-like compounds containing transition metals as solid base catalysts for transesterification., *Chemical Engineering Journal*, 175(1), 548-554.
- [13] Riadi, Y., Mamouni, R., Abrouki, Y., El Haddad, M., Saffaj, N., El Antri, S., Routier, S., Guillaumet, G., and Lazar, S., 2010, Animal Bone Meal (ABM): a novel natural catalyst for thia-Michael addition., *Letters in Organic Chemistry*, 7(3), 269-271.
- [14] Zahouily, M., Abrouki, Y., and Rayadh, A., 2002, $\text{Na}_2\text{CaP}_2\text{O}_7$, a new catalyst for Michael addition., *Tetrahedron Letters*, 43(43), 7729-7730.
- [15] Zahouily, M., Abrouki, Y., Rayadh, A., Sebti, S., Dhimane, H., and David, M., 2003, Fluorapatite: efficient catalyst for the Michael addition., *Tetrahedron Letters*, 44(12), 2463-2465.
- [16] Zahouily, M., Abrouki, Y., Bahlaouan, B., Rayadh, A., and Sebti, S., 2003, Hydroxyapatite: new efficient Catalyst for the Michael addition., *Catalysis Communications*, 4(10), 521-524.
- [17] Abrouki, Y., Zahouily, M., Rayadh, A., Bahlaouan, B., and Sebti, S., 2002, A natural phosphate and doped-catalyzed Michael addition of mercaptans to α,β -unsaturated carbonyl compounds., *Tetrahedron Letters*, 43(49), 8951-8953.
- [18] Brown, EH., Lehr, JR., Smith, JP., Frazier, AW., and Agr, J., 1963, Preparation and characterization of some calcium pyrophosphates., *Agricultural and Food Chemistry*, 11, 214-222.
- [19] Song, HJ., Yim, DK., Cho, IS., Roh, HS., Kim, JS., Kim, DW., and Hong, KS., 2012, Luminescent Properties of Phosphor Converted LED Using an Orange-emitting $\text{Rb}_2\text{CaP}_2\text{O}_7:\text{Eu}^{2+}$ Phosphor., *Materials Research Bulletin*, 47(12), 4522-4526.
- [20] Zahouily, M., Charki, H., Abrouki, Y., Mounir, B., Bahlaouan, B., Rayadh A., and Sebti, S., 2005, Natural Phosphate Modified with Sodium Nitrate: New Efficient Catalyst for the Construction of a Carbon-Sulfur and Carbon-Nitrogen Bonds, *Letters in Organic Chemistry*, 2(4), 354-359.
- [21] Abrouki, Y., Anouzla, A., Loukili, H., Lotfi, R., Rayadh, A., Bahlaoui, M.A., Zakarya, D., Zahouily, M., and Sebti, S., 2013, Response Surface Methodology for the Optimization of Thia-Michael Addition Reaction Catalyzed by Doped Fluorapatite., *Open Journal of Advanced Materials Research*, 1(2), 29-34.