Pergamon

Tetrahedron Letters 42 (2001) 7953–7955

TETRAHEDRON
LETTERS

Calcined sodium nitrate/natural phosphate: an extremely active catalyst for the easy synthesis of chalcones in heterogeneous media

Saïd Sebti,[a,*] Abderrahim Solhy,[a] Rachid Tahir,[a] Saïd Boulaajaj,[a] José A. Mayoral,[b,*]
José M. Fraile,[b] Abdelali Kossir[c] and Hammou Oumimoun[c]

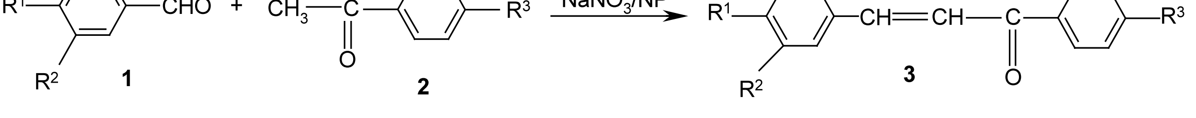
[a]*Laboratoire de Chimie Organique Appliquée et Catalyse, Université Hassan II, Faculté des Sciences Ben M'Sik, BP 7955, Casablanca, Morocco*
[b]*Departamento de Quimica Organica y Quimica Fisica, Instituto de Ciencia de Materiales de Aragon, Facultad de Ciencias, Universidad de Zaragoza-CSIC, E-50009 Zaragoza, Spain*
[c]*Centre d'Etudes et de Recherches sur les Phosphates Minéraux (CERPHOS), Groupe Office Chérifien des Phosphates (OCP), 37 Bd My Ismail, Casablanca, Morocco*

Received 20 May 2001; revised 7 September 2001; accepted 10 September 2001

Abstract—The modification of natural phosphate (NP) with sodium nitrate by calcination produces an extremely efficient basic catalyst for the Claisen–Schmidt condensation. A large variety of chalcones is easily obtained in high yield at room temperature using only a catalytic amount of $NaNO_3$/NP. © 2001 Elsevier Science Ltd. All rights reserved.

Some chalcones can be used as anti-oxidants,[1] anti-inflammatories,[2] pulmonary carcinogenesis inhibitors,[3] anti-malarials,[4] and anti-leishmanials.[5] These products can be obtained by Claisen–Schmidt condensation. For this reaction, the use of basic solids, such as alumina,[6] barium hydroxide,[7] hydrotalcite and zeolite,[8] has received much attention over the last years. Natural phosphates have been found to be interesting catalysts, able to promote Knoevenagel reactions,[9] hydrations of nitriles,[10] synthesis of α-hydroxyphosphonates,[11] Friedel–Crafts alkylations,[12] and Michael reactions.[13] Recently, we have reported that the Claisen–Schmidt condensation can be catalysed by natural phosphate, alone or activated with an ammonium salt.[14] In spite of the good results obtained, the utility of this method is limited by the need of using a large amount of catalyst.

In this paper, we describe a highly efficient method for the Claisen–Schmidt condensation catalysed by natural phosphate doped with sodium nitrate ($NaNO_3$/NP). Natural phosphate comes from an extracted ore in the region of Khouribga (Morocco). The fraction of 100–400 μm grain size has been washed with water, calcined at 900°C for 2 h, washed again, calcined at 900°C for 0.5 h and ground (63–125 μm). The structure of NP is similar to that of fluorapatite ($Ca_{10}(PO_4)_6F_2$), as shown by X-ray diffraction pattern and chemical analysis.[14] $NaNO_3$/NP was prepared by adding a mass (m_1) of natural phosphate to an aqueous solution of a mass (m_0) of sodium nitrate. The mixture was stirred vigorously at room temperature, evaporated to dryness and dried at 100°C for 2 h. The solid obtained was calcined for 1 h to give a new modified phosphate ($NaNO_3$/NP). The X-ray diffraction pattern of the modified phos-



Scheme 1.

Keywords: natural phosphate; sodium nitrate; heterogeneous catalysis; chalcones; Claisen–Schmidt condensation.

* Corresponding author. Fax: 212 22 24 96 72; e-mail: saidsebti@yahoo.fr

0040-4039/01/$ - see front matter © 2001 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(01)01698-7

phate calcined at 900°C, showed the apparition of two new phases which can be attributed to sodium phosphate and calcium oxide. This phenomenon can be due to a possible reaction in the solid state between sodium nitrate and the natural phosphate. On the contrary, the structures of NP and $NaNO_3$ are not modified by calcination of $NaNO_3$/NP at 300 or 500°C, in agreement with their low catalytic activity. It is worth noting that both sodium phosphate[9–11] and calcium oxide[15] have been used in heterogeneous catalysis. Thus, they can contribute to an increase in the basic activity of NP. However, the intensity of their peaks in X-ray pattern of $NaNO_3$/NP is very low.

The reactions were carried out between arylaldehydes **1** (2.5 mmol) and acetophenones **2** (2.5 mmol) at room temperature in the presence of a catalytic amount of $NaNO_3$/NP (0.1 g) in methanol (1–3 mL) (Scheme 1). First of all we tried to determine the best nitrate/NP ratio ($r = m_0/m_1$). With this aim, we carried out the synthesis of chalcone **3a** with 0.1 g of $NaNO_3$/NP using different nitrate/NP ratios ($r = 1/2$, 1/3, 1/5, 1/8, and 1/15 w/w). The yields obtained after 24 h of reaction (98, 78, 67, 8 and 2%, respectively) show that sodium nitrate/NP = 1/2 w/w is the optimal composition.

Thereafter, we carried out the synthesis of several chalcones **3** using 0.1 g of $NaNO_3$/NP (1/2) (Table 1). All products were isolated, purified, and analysed by ^{1}H, ^{13}C NMR, IR, and MS. Only the *E*-isomers were obtained. The yields were, in general, very high and exceeded 90% after 24 h of reaction, except for the chalcones obtained by condensation of arylaldehydes with *p*-methoxyacetophenone (**3f**, **3g** and **3h**). The low reactivity of this acetophenone, due to the presence of an electron-donor group, accounts for the yields in the range of 40–74% after 24 h, which can be increased to 70–93% with longer reaction times. It is important to note that, under the same conditions, unmodified natural phosphate displayed almost no activity, *p*-methoxyacetophenone did not react and with acetophenone yields did not exceed 10% after 24 h. It is even possible to further reduce the amount of catalyst. Thus, 78% yield of chalcone **3a** was obtained, after 48 h of reaction, with only 0.05 g of $NaNO_3$/NP. It is then clear that doping NP with sodium nitrate remarkably increases its catalytic activity.

To sum up, the modified natural phosphate ($NaNO_3$/NP) is a new inorganic reagent, which can represent an important breakthrough in the development of basic solid catalysts. Several chalcones have been synthesised with high yields using catalytic amounts of $NaNO_3$/NP. This phosphate is easily prepared from inexpensive precursors.

Table 1. Synthesis of chalcones by Claisen–Schmidt condensation

	Product			Yield/% (time/h)[a,b]	
	R^1	R^2	R^3	$NaNO_3$/NP	NP
3a	H	H	H	98 (18)	2 (24)
3b	Cl	H	H	94 (16)	5 (24)
3c	H	NO_2	H	94 (16)	9 (24)
3d	OCH_3	H	H	91 (36)	10 (24)
3e	H	H	OCH_3	90 (24)	0 (24)
3f	Cl	H	OCH_3	74 (24) 93 (48)	0 (24)
3g	H	NO_2	OCH_3	55 (24) 81 (48)	0 (24)
3h	OCH_3	H	OCH_3	40 (24) 70 (48)	0 (24)
3i	H	H	NO_2	92 (16)[c]	3 (24)
3j	Cl	H	NO_2	94 (16)[c]	5 (24)
3k	H	NO_2	NO_2	86 (16)[c] 95 (24)[c]	2 (24)
3l	OCH_3	H	NO_2	93 (16)[c]	2 (24)

[a] Yields in products isolated by distillation under vacuum or recrystallisation.

[b] All products have been identified by ^{1}H, ^{13}C NMR, IR and MS.

[c] Reaction carried out in presence of 3 mL of methanol.

Acknowledgements

Financial assistance of the Ministry of Education, Government of Morocco (PROTARS, P2T3/59) and CICYT (Project MAT99-1176) is gratefully acknowledged. We are also indebted to OCP for financial support and technical assistance.

References

1. (a) Mukherjee, S.; Kumar, V.; Prasad, A. K.; Raj, H. G.; Bracke, M. E.; Olsen, C. E.; Jain, S. C.; Parmar, V. S. *Bioorg. Med. Chem.* **2001**, *9*, 337; (b) Anto, R. J.; Sukumaran, K.; Kuttan, G.; Rao, M. N. A.; Subbaraju, V.; Kuttan, R. *Cancer Lett.* **1995**, *97*, 33.
2. (a) Hsieh, H.-K.; Tsao, L.-T.; Wang, J.-P.; Lin, C.-N. *J. Pharm. Pharmacol.* **2000**, *52*, 163; (b) Herencia, F.; Ferrandiz, M. L.; Ubeda, A.; Dominguez, J. N.; Charris, J. E.; Lobo, G. M.; Alcaraz, M. J. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 1169.
3. Wattenberg, L. *Lung Cancer* **1996**, *14*, 152.
4. Ram, V. J.; Saxena, A. S.; Srivastava, S.; Chandra, S. *Bioorg. Med. Chem. Lett.* **2000**, *10*, 2159.
5. Zhai, L.; Chen, M.; Blom, J.; Theander, T. G.; Christensen, S. B.; Kharazmi, A. *J. Antimicrob. Chemother.* **1999**, *43*, 793.
6. Varma, R. S.; Kabalka, G. W.; Evans, L. T.; Pagni, R. M. *Synth. Commun.* **1985**, *15*, 279.
7. (a) Sinisterra, J. V.; G-Raso, A.; Cabello, J. A.; Marinas, J. M. *Synthesis* **1984**, 502; (b) Alcantara, A. R.; Marinas, J. M.; Sinisterra, J. V. *Tetrahedron Lett.* **1987**, *28*, 1515; (c) Aguilera, A.; Alcantara, A. R.; Marinas, J. M.; Sinisterra, J. V. *Can. J. Chem.* **1987**, *65*, 1165; (d) Sathyanarayana, S.; Krishnamurty, H. G. *Curr. Sci.* **1988**, *57*, 1114; (e) Climent, M. S.; Marinas, J. M.; Mouloungui, Z.; Le Bigot, Y.; Delmas, M.; Gaset, A.; Sinisterra, J. V. *J. Org. Chem.* **1989**, *54*, 3695.
8. (a) Climent, M. J.; Garcia, H.; Primo, J.; Corma, A. *Catal. Lett.* **1990**, *4*, 85; (b) Tichit, D.; Lhouty, M. H.; Guida, A.; Chiche, B. H.; Figueras, F.; Auroux, A.; Bartalini, D.; Garrone, E. *J. Catal.* **1995**, *151*, 50; (c)

Climent, M. J.; Corma, A.; Iborra, S.; Primo, J. *J. Catal.* **1995**, *151*, 60; (d) Guida, A.; Lhouty, M. H.; Tichit, D.; Figueras, F.; Geneste, P. *Appl. Catal.* **1997**, *164*, 251.

9. Sebti, S.; Saber, A.; Rhihil, A. *Tetrahedron Lett.* **1994**, *35*, 9399.
10. Sebti, S.; Rhihil, A.; Saber, A.; Hannafi, N. *Tetrahedron Lett.* **1996**, *37*, 6555.
11. Sebti, S.; Rhihil, A.; Saber, A.; Laghrissi, M.; Boulaajaj, S. *Tetrahedron Lett.* **1996**, *37*, 3999.
12. Sebti, S.; Rhihil, A.; Saber, A. *Chem. Lett.* **1996**, *8*, 721.
13. Sebti, S.; Boukhal, H.; Hannafi, N.; Boulaajaj, S. *Tetrahedron Lett.* **1999**, *40*, 6207.
14. Sebti, S.; Saber, A.; Rhihil, A.; Nazih, R.; Tahir, R. *Appl. Catal. A* **2001**, *206*, 217.
15. Seki, T.; Akutsu, K.; Hattori, H. *Chem. Commun.* **2001**, 1000.