

Sodium-Modified Fluorapatite: A Mild and Efficient Reusable Catalyst for the Synthesis of α,α' -Bis(Substituted Benzylidene) Cycloalkanones under Conventional Heating and Microwave Irradiation

Bahija Mounir¹, Fathallaah Bazi², Abdelfetah Mounir³, Hamid Toufik¹, Mohamed Zahouily⁴

¹Laboratoire Matériaux, Substances Naturelles, Environnement & Modélisation (LMSNEM), Faculté Polydisciplinaire de Taza, Université Sidi Mohamed Ben Abdellah, Fès, Maroc

²Laboratoire de Chimie Analytique et physicochimie des Matériaux, Faculté des Sciences Ben M'Sik de Casablanca, Université Hassan II, Casablanca, Maroc

³Higher Institute of Nursing Professions and Health Techniques, Marrakech, Morocco

⁴Laboratoire de Matériaux, Catalyse et Valorisation des Ressources Naturelles, Faculté des Sciences et Techniques de Mohammedia, Université Hassan II, Casablanca, Maroc

Email: bahija.mounir@usmba.ac.ma

How to cite this paper: Mounir, B., Bazi, F., Mounir, A., Toufik, H. and Zahouily, M. (2018) Sodium-Modified Fluorapatite: A Mild and Efficient Reusable Catalyst for the Synthesis of α,α' -Bis(Substituted Benzylidene) Cycloalkanones under Conventional Heating and Microwave Irradiation. *Green and Sustainable Chemistry*, 8, 156-166. <https://doi.org/10.4236/gsc.2018.82011>

Received: January 25, 2018

Accepted: May 7, 2018

Published: May 10, 2018

Copyright © 2018 by authors and Scientific Research Publishing Inc. This work is licensed under the Creative Commons Attribution International License (CC BY 4.0). <http://creativecommons.org/licenses/by/4.0/>



Open Access

Abstract

A versatile and environmentally friendly method for α,α' -bis(substituted benzylidene) cycloalkanones has been developed using a heterogeneous catalysis technology. We have synthesized a series of the α,α' -bis(substituted benzylidene) cycloalkanones, a biologically important class of compounds, via the cross aldol condensation between arylaldehydes and cycloketones using sodium-modified fluorapatite (Na/FAP) as a highly efficient solid catalyst under conventional heating in aqueous media and solventless conditions under microwave. Catalyst reuse, ease of separation of the pure product, and high yields are some of the unique features of this process. Shorter reaction times (4 - 7 min) and higher yields (80% - 94%) were achieved under microwave irradiation conditions.

Keywords

Green Chemistry, α,α' -Bis(Substituted Benzylidene) Cycloalkanones, Microwaves Irradiation, Conventional Heating, Aqueous Media, Fluorapatite Activated by Sodium Nitrate (Na/FAP)

1. Introduction

The concept of “green chemistry” has been widely adopted to meet the fundamental

scientific challenges of protecting human health and the environment while simultaneously achieving commercial viability [1]. The emerging area of green chemistry envisages minimum hazard as the performance criteria while designing new chemical processes. One of the thrust areas for achieving this target is to explore alternative reaction conditions and reaction media to accomplish the desired chemical transformations with minimum byproducts and waste generation, as well as eliminating the use of volatile and toxic organic solvents [2] [3].

Organic reactions in aqueous media have become one of the most challenging areas in organic synthesis due to the environmental benefits and favorable effects of water on chemical transformations [4] [5] [6] [7]. Especially, the reactions mediated by heterogeneous catalysts in aqueous media are of current interest for their considerable applications in organic synthesis [8] [9]. In other cases, organic reactions accelerated under the influence of microwave (MW) irradiation assisted heterogeneous reactions that various solid inorganic supports have attracted considerable attention in the past decade for the efficient and relatively friendlier synthesis of a variety of organic compounds [10] [11] [12] [13]. The use of MW irradiation for the formation of several carbon heteroatom and carbon-carbon bonds has been successfully demonstrated [14] [15].

A general method for the formation of a carbon-carbon bond in many classes of carbonyl compounds is aldol condensation [16] [17]. Due to the importance of the methylene structural unit, which is found in many naturally occurring compounds and antibiotics, and the use of α,α' -bis(substituted benzylidene) cycloalkanones as precursors for the synthesis of bioactive pyrimidine derivatives [18], the condensation of cycloalkanones with aldehydes and ketones is of special interest, and cross-aldol condensation is an effective pathway for these preparations. This reaction is classically carried out using strong acid or base [19]. Indeed, different organometallic complexes [20], Lewis acid such as RuCl_3 [21], $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ [22], $\text{Mg}(\text{HSO}_4)_2$ [23], $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ [24], $\text{Cu}(\text{OTf})_2$ [25], and other catalysts such as, $\text{SiO}_2\text{-Pr-SO}_3\text{H}$ [26], under micellar medium [27], Polymer-supported sulfonic acid (NKC-9) [28], $\text{TiCl}_3(\text{SO}_3\text{CF}_3)$ [29], I_2 [30], LiOH [31], BMPTO [32], and $\text{KF/Al}_2\text{O}_3$ [33] are found to be able to catalyze this reaction. However, these methods of synthesis suffer from some drawbacks such as the use of toxic reagents, unfeasibility of recovering the catalyst, modest yields and long reaction time. Thus, it is significant to exploit clean and efficient catalysts for the synthesis of α,α' -bis(substituted benzylidene) cycloalkanones.

The last few years have witnessed considerable resurgence of interest in the activity of fluorapatite activated by sodium nitrate (Na/FAP), induced organic transformations. In a series of publications from our group, we have exploited the catalytic potential of Na/FAP for various organic transformations, e.g. Knoevenagel condensation [34], synthesis of α -hydroxy phosphonates [9] and hydration of nitriles to amides [35]. In continuation, we wish to report a mild, convenient and green methodology for the synthesis of α,α' -bis(substituted benzylidene) cycloalkanones using Na/FAP in aqueous media under conventional

heating (Method A) or in solventless system under microwave irradiation (Method B) (**Scheme 1**).

2. Result and Discussion


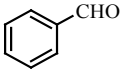
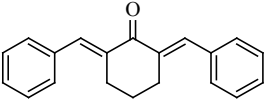

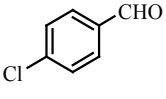
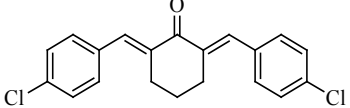

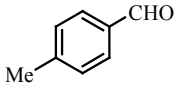
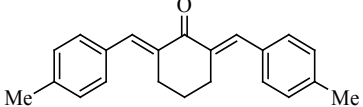
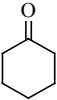
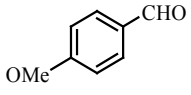
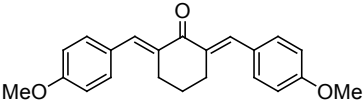

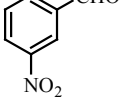
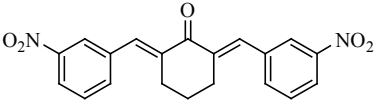

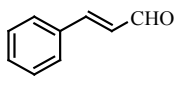
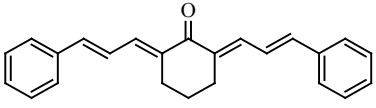

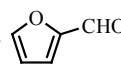
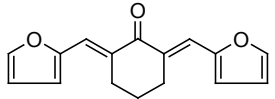

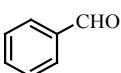
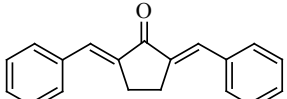

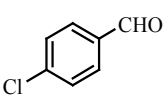
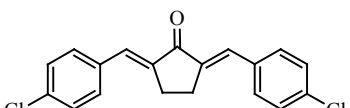

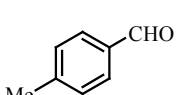
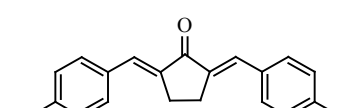

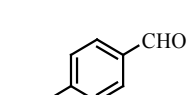
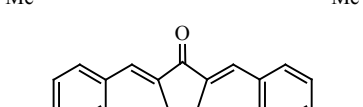

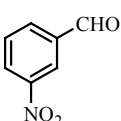
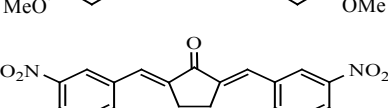

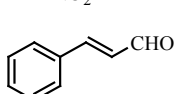
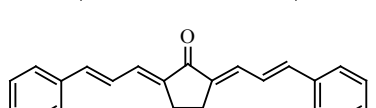
Crossed aldol was first carried out in water using FAP as a catalyst under conventional heating. In general, the yields obtained are poor. Thus, in 48 h reaction, the obtained recoveries in 3a, 3b, 3c, 3d, 3e, 3f, 3g, 3h, 3i, 3j, 3k, 3l, 3m and 3n were 10%, 08%, 13%, 11%, 07%, 10%, 20%, 20%, 16%, 13%, 12%, 10%, 11% and 25% respectively. To increase its catalytic activity, FAP was impregnated by sodium nitrate to yield a more efficient catalyst (Na/FAP), as described previously [9] [34] [35]. The cross-aldol condensation between benzaldehyde (1a, 2 mmol) and cyclohexanone (2a, 1 mmol) were chosen as model substrates to determine suitable reaction conditions for synthesis α,α' -bis(substituted benzyldene) cycloalkanones with Na/FAP under classical heating. At first, various solvent were tested. Thus, after 2.5 h the yields of product 3a obtained were 91%, 78%, 50% and 30% in the presence of water, methanol, ethanol and n-butanol, respectively. It can be concluded that water is the best solvent for this reaction. The reaction was quite sensitive to the reflux temperature. In the absence of the solvent, no product was observed but only the starting material was recovered. This behaviour indicates that some solvent is needed to facilitate the contact between the reagents and active site.

The study of the influence of the volume of the solvent showed that 5 mL of water resulted in optimal yield (**Figure 1**). An increase in the volume of up to 6mL slightly decreased the reaction yield (84%), and this was reduced further to 38% when a volume of 10mL was used. The large solvent volume reduced the overall reaction concentration, which explains the decreased yield (**Figure 1**).

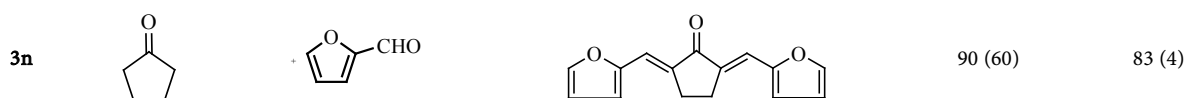
Based on the results obtained above, other substrates have also been studied for the preparation of α,α' -bis(substituted benzyldene) cycloalkanone derivatives (**Scheme 1**). The results are summarized in the **Table 1**. The reactions were completed within 60 - 255 min and high yields of α,α' -bis(substituted benzyldene, furfurylidene and cinnamylidene) cyclopentanone and cyclohexanone were obtained (entries 3a - 3n). Under these conditions, no self-condensation of the starting materials was observed. Monocondensation from one side of cycloalkanones in the presence of small amounts of the aldehydes was attempted but was not successful. It can be noticed that the condensation of various aldehydes with cyclopentanone is faster than the condensation with cyclohexanone. This may be due to the removal of the eclipsing effect of adjacent hydrogen atoms in cyclopentanone after the formation of arylmethylidene derivative [36].

The development of a more sustainable and benign strategy that minimizes energy consumption and time for reaction completion maximizing the conversions and/or yields has been reported through the use of microwaves [37]. Indeed, the best results of the present work were obtained under microwave irradiation. The effect of the microwave in the cross aldol was investigated employing the

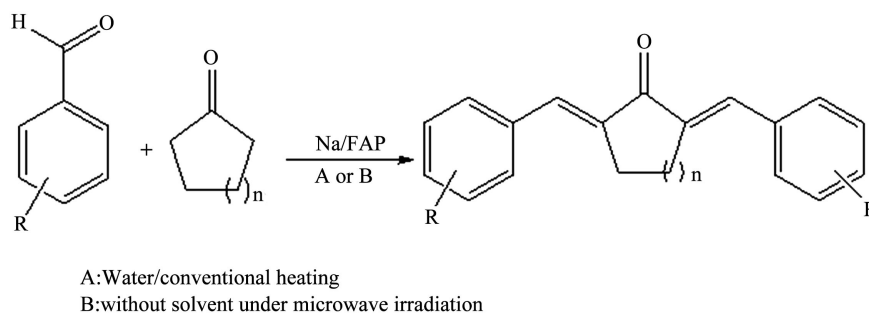
Table 1. Crossed aldol condensation of cycloalkanones with aromatic aldehydes in the presence of Na/FAP.

| Entry | Ketone | Aldehyde | Product ^d | Isolated yield ^a (%) | |
|-------|---|---|--|---------------------------------|-----------------------|
| | | | | Method A ^b | Method B ^c |
| 3a |  |  |  | 91 (150) | 90 (6) |
| 3b |  |  |  | 98 (180) | 80 (6) |
| 3c |  |  |  | 88 (150) | 94 (7) |
| 3d |  |  |  | 80 (180) | 88 (7) |
| 3e |  |  |  | 86 (255) | 87 (7) |
| 3f |  |  |  | 90 (180) | 86 (6) |
| 3g |  |  |  | 98 (90) | 80 (5) |
| 3h |  |  |  | 95 (120) | 92 (5) |
| 3i |  |  |  | 96 (150) | 82 (5) |
| 3j |  |  |  | 98 (150) | 89 (6) |
| 3k |  |  |  | 91 (120) | 83 (6) |
| 3l |  |  |  | 87 (240) | 85 (7) |
| 3m |  |  |  | 97 (150) | 80 (6) |

Continued



^aValues given in parentheses denote the time in minutes. ^bReaction carried out in water under conventional heating. ^cSolvent-free synthesis under microwave irradiation. ^dAll products are reported in the literature.



Scheme 1. Cross-aldol condensation over sodium-modified fluorapatite.

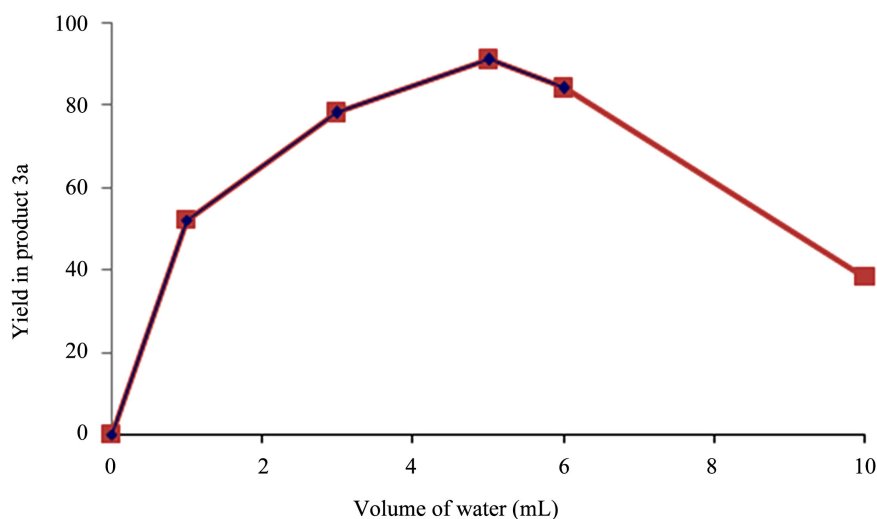


Figure 1. Volume of water effect in product **3a**.

catalyst (Na/FAP). The results are summarized in **Table 1**. The reactions were completed within 4 - 7 min and α,α' -bis(substituted benzylidene, furfurylidene and cinnamylidene) cyclopentanone and cyclohexanone obtained in good to high yields (entries 3a - 3n).

The results of the reactions at microwave irradiation conditions are compared with the reflux conditions and short reaction times were observed, which is more economic in terms of time. It was noticed that there was no reaction under microwave without catalyst, and to what was observed in traditional heating without solvent. This shows a certain synergy between catalyst and the microwave. It is thus completely reasonable to think that the effect of the temperature is a determining factor to promote this condensation. Unfortunately, domestic microwave was used and therefore it was impossible to measure the exact

temperature during the reaction. The structures of α,α' (EE)-bis-(benzylidene)-cycloalkanones (3a - 3n) were characterized by comparison of their spectroscopic data (^1H NMR and IR) and melting points with those reported in the literature.

One of the most important features of a heterogeneous catalyst is the ease of the recovery and reuse. Na/FAP was recovered and dried at 150°C before being tested for the synthesis of 3a. After a 4 cycle run, a progressive decrease in yield was observed as shown in **Figure 2**, indicating catalyst exhaustion. This behavior can be explained by the accumulation of organic substrates over the active sites of the catalyst. However, we were able to achieve a complete regeneration of the catalyst when washed by acetone and then calcined at 500°C before its reuse. **Figure 2** shows the activity profile of the catalyst after a 4 cycle run.

3. Experimental

3.1. Preparation and Characterisation of Fluorapatite (FAP)

The synthesis of fluorapatite [$\text{Ca}_{10}(\text{PO}_4)_6\text{F}_2$] is carried out by a co-precipitation method. An amount of 250 mL of an aqueous solution containing 7.92 g of diammonium phosphate and 1.00 g of NH_4F , maintained at a pH greater than 12 by addition of ammonium hydroxide (15 mL), was dropped under constant stirring into 150 mL of an aqueous solution containing 23.6 g of calcium nitrate [$\text{Ca}(\text{NO}_3)_2, \text{H}_2\text{O}$]. The suspension was then refluxed for 4 h. The obtained FAP was filtered, washed with doubly distilled water, dried overnight at 80°C , and calcined at 700°C . The final product is identified by X-ray diffraction (space group hexagonal system; $a = 9364 \text{ \AA}$ and $c = 6893 \text{ \AA}$), infrared spectra IR and chemical analysis (Ca = 38.29%, P = 17.78% and Ca/P = 1.66). The BET specific surface area was found to be $S = 15.4 \text{ m}^2/\text{g}$. The total pore volume was calculated by the BJH method at $P/P_0 = 0.98$ ($V_t = 0.0576 \text{ cm}^3/\text{g}$) [34] [35].

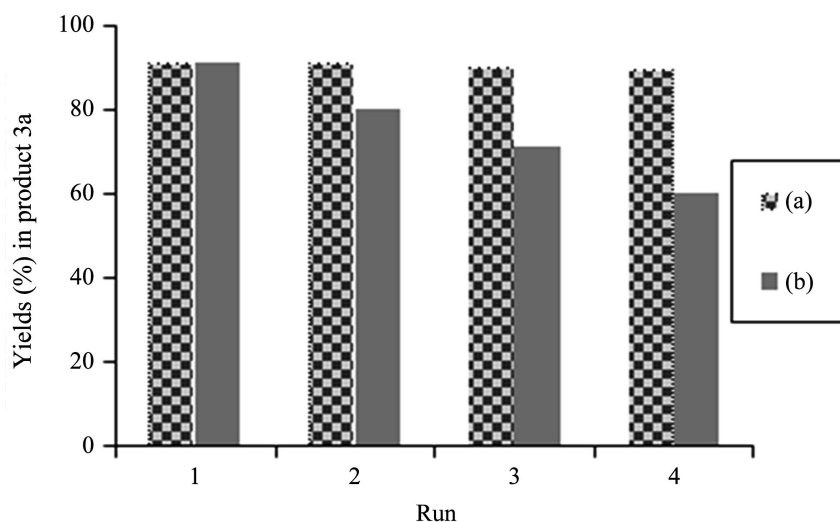


Figure 2. Recycling of the Na/FAP catalyst in the synthesis of 3a. (a) The recovered Na/FAP was reactivated by calcinations at 500°C for 1 h after being acetone washed; (b) Catalyst recoverable dried at 150°C for 2 h.

3.2. Preparation and Characterisation of Na/FAP

The modified FAP (Na/FAP = 1/2 w/w) was prepared by addition of FAP (10 g) to an aqueous sodium nitrate solution (50 mL, 1.17 M). The mixture was stirred at room temperature for 15 min and then the water evaporated under vacuum. The resulting solid was calcined under air for 1 h at 650 °C. The XRD patterns of calcined Na/FAP showed the apparition of new phases, so the CaO phase ($2\theta = 32.2, 37.5$ and 54.0) is clearly identified [9]. Two new phases are probably CaNaPO_4 and $\text{Na}_2\text{Ca}_4(\text{PO}_4)_3\text{F}$ obtained by an exchange of sodium with calcium. No crystalline phases of Na_2O and CaF_2 were observed. The surface area of the new catalyst Na/FAP was determined by the BET method as $S = 5.4 \text{ m}^2/\text{g}$ and the total pore volume obtained by BJH method is $0.0032 \text{ cm}^3/\text{g}$ [34] [35].

3.3. General Procedure for the Synthesis of the α, α' -(EE)-Bis(Benzylidene)-Cycloalkanones

The typical reaction procedure for the cross-aldol condensation of aldehydes with cycloalkanones catalyzed by fluorapatite alone or modified was as follows.

Method A: to a 5 mL of distilled water in a round bottom flask, was added arylaldehydes **1** (2 mmol), cycloalkones **2** (1 mmol) and 1g of the catalyst, and the mixture was refluxed in water.

Method B: to a solution of aldehydes **1** (2 mmol) and cycloalkanes **2** (1 mmol), 1 g of the Na/FAP was added and the mixture was stirred with a spatula at room temperature and was irradiated by domestic microwave for the appropriate time at (450 W). Hot water ($2 \times 20 \text{ mL}$) was added, followed by simple filtration. For both methods, after filtration and extraction with hot water, the solutions were concentrated and purified by silica gel chromatography (n hexane/ethyl acetate: 7 mL/3mL). The products were identified by melting points, ^1H NMR, and IR spectroscopies. Na/FAP was reactivated by drying at 150 °C or, alternatively washed with acetone and calcined at 500 °C for 1 h.

Effect of solvent for the synthesis of the α, α' -(EE)-bis(benzylidene)-cyclohexanone

To a 5 mL of solvent (methanol, ethanol, n-butanol and water) of different solvents such as methanol, ethanol, n-butanol and water in a round bottom flask, was added benzaldehyde **1** (2 mmol), cyclohexanone **2** (1 mmol) and 1 g of the catalyst, and the mixture was refluxed for 2.5 h.

Spectral data of the products

Melting points were measured on Electro thermal 9100 apparatus. Fourier transform infrared (FT-IR) spectra of samples in KBr pellets were measured on a Bruker Vector 22 spectrometer. ^1H NMR spectra were determined on a Bruker ARX 300 spectrometer as CDCl_3 solutions. Chemical shifts (δ) were expressed in ppm downfield from the internal standard tetramethylsilane and coupling constants J were given in Hz.

3a: mp 116 °C - 118 °C ; IR (KBr, $\nu \text{ cm}^{-1}$): 773; 1144; 1268; 1440; 1570; 1609; 1675; 2926; 3024.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.76 - 1.83 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.95 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, t, $J = 5.6$ Hz); 7.30 - 7.48 (10H, arom, m); 7.80 (2H, =CH, s).

3b: mp: 148°C - 149°C, IR (KBr, $\nu \text{ cm}^{-1}$): 828; 1262; 1576; 1440; 1606; 1665; 2930.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.78 - 1.84 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.89 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, t, $J = 6$ Hz); 7.36 - 7.41 (8H, arom, m); 7.73 (2H, =CH, s).

3c: mp: 167°C - 169°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1600; 1660; 2918; 2942.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.75 - 1.79 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.39 (3H, $-\text{CH}_3$, s); 2.92 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, t, $J = 5.6$ Hz); 7.18 - 7.39 (8H, arom, m); 7.78 (2H, =CH, s).

3d: mp: 203°C - 204°C, IR (KBr, $\nu \text{ cm}^{-1}$): 833; 1021; 1248; 1505; 1552; 1595; 1661; 2937.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.80 - 1.83 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.94 (3H, $-\text{CH}_3$, s); 2.92 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, t, $J = 6$ Hz); 3.86 (s, 6H, OCH_3); 6.94 (4H, arom, d, $J = 8.6$ Hz); 7.47 (4H, arom, d, $J = 8.6$ Hz); 7.77 (2H, =CH, s).

3e: mp: 189°C - 190°C, IR (KBr, $\nu \text{ cm}^{-1}$): 807; 1346; 1525; 1576; 1606; 1633; 2925.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.84 - 1.90 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.97 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, t, $J = 6$ Hz); 7.58 - 7.81 (6H, arom, m); 8.22 (2H, arom, d, $J = 8$ Hz); 8.33 (s, 2H, =CH).

3f: mp: 177 - 178°C; IR (KBr, $\nu \text{ cm}^{-1}$): 1600, 1690, 2900, 3050.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.75 (m, 2H), 2.91 - 2.74 (t, 4H, $J = 5.6$ Hz), 7.35 - 7.02 (s, 2H), 7.65 (m, 10H).

3g: mp: 140°C - 142°C, IR (KBr, $\nu \text{ cm}^{-1}$): 752; 1594; 1643; 2903; 3183.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 1.95 - 2.05 (2H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 2.95 - 2.72 (4H, $\text{CH}_2\text{-CH}_2\text{-CH}_2\text{-}$, m); 6.95 - 7.63 (8H, furyl et = CH, m).

3h: mp: 188°C - 189°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1600; 1625; 1688; 2910; 3017; 3052.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 3.13 (4H, $-\text{CH}_2\text{-CH}_2\text{-}$, s); 7.36 - 7.45 (6H, arom, m); 7.58 - 7.60 (6H, arom et = CH, m).

3i: mp: 228°C - 229°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1587; 1604; 1620; 1693; 2912.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 3.03 (4H, $-\text{CH}_2\text{-CH}_2\text{-}$, s); 7.33 - 7.36 (4H, arom, m); 7.45 - 7.47 (6H, arom et = CH, m).

3j: mp: 243°C - 244°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1589; 1602; 1622; 1686; 2912.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 2.32 (6H, $-\text{CH}_3$, s); 3.03 (4H, $-\text{CH}_2\text{-CH}_2\text{-}$, s); 7.17 - 7.18 (4H, arom, m); 7.43 - 7.55 (4H, arom, m); 7.58 (2H, =CH, s).

3k: mp: 211°C - 212°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1590; 1684; 2851; 3080.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 3.07 (4H, $-\text{CH}_2\text{-CH}_2\text{-}$, s); 3.88 (6H, $-\text{OCH}_3$, s); 6.89 (4H, arom, d, $J = 8$ Hz); 7.58 (2H, =CH, s); 7.59 (4H, arom, d, $J = 8$ Hz).

3l: mp: 224°C - 226°C, IR (KBr, $\nu \text{ cm}^{-1}$): 1528; 1613; 1691; 2922.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 3.26 (4H, $-\text{CH}_2\text{-CH}_2\text{-}$, s); 7.67 (4H, arom, m); 7.91 (2H, arom, d, $J = 7.5$ Hz); 8.28 (2H, arom, d, $J = 6.3$ Hz); 8.49 (2H, =CH, s).

3m: mp: 213°C - 214°C; IR (KBr, $\nu \text{ cm}^{-1}$): 1585, 1616, 1671, 3027.

$^1\text{H NMR}$ (CDCl_3 , 300 MHz) δ : 2.95 (s, 4H); 6.98 - 7.02 (m, 4H), 7.25 - 7.42 (m, 8H), 7.53 (d, 4H, $J = 7.2$ Hz).

3n: mp: 162°C - 163°C, IR (KBr, ν cm⁻¹): 1600; 1620; 1681; 2917; 3115.
¹H NMR (CDCl₃, 300 MHz) δ : 3.09 (s, 4H, -CH₂-CH₂-); 6.54 (2H, furyl, s); 6.71 (2H, furyl, d, J = 3.2 Hz); 7.36 (2H, furyl, s); 7.60 (.s, 2H, = CH).

4. Conclusion

In conclusion, we have developed a clean and easy method for the synthesis of α,α' -bis(substituted benzylidene, furfurylidene and cinnamylidene) cyclopentanone and cyclohexanone using an inexpensive, reusable, easy to handle, noncorrosive, and environmentally benign catalyst (sodium-modified fluorapatite). The reaction can be carried out in water under classical heating. The microwave-assisted procedure in solvent-free system has provided a soft and cleaner approach for the cross-aldol condensation. The use of Na/FAP offers diverse advantages including simplicity of operation due to the heterogeneous nature of reaction, easy workup, high yields, and catalyst reusability.

References

- [1] Anastas, P.T. and Warner, J.C. (1998) *Green Chemistry: Theory and Practice*; Oxford University Press: Oxford.
- [2] Darr, J.A. and Poliakoff, M. (1999) New Directions in Inorganic and Metal-Organic Coordination Chemistry in Supercritical Fluids. *Chemical Reviews*, **99**, 495-542. <https://doi.org/10.1021/cr970036i>
- [3] Clifford, A.A. and Rayer, C.M. (2001) Suppression of Double Bond Isomerisation in Intramolecular Heck Reactions Using Supercritical Carbon Dioxide. *Tetrahedron Letters*, **42**, 323-325. [https://doi.org/10.1016/S0040-4039\(00\)01917-1](https://doi.org/10.1016/S0040-4039(00)01917-1)
- [4] Li, C.J. (1993) Organic Reactions in Aqueous Media—With a Focus on Carbon-Carbon Bond Formation. *Chemical Reviews*, **93**, 2023-2035. <https://doi.org/10.1021/cr00022a004>
- [5] Lubineau, A., Aug, J. and Queneau, Y. (1994) Water-Promoted Organic Reactions. *Synthesis*, **8**, 741-760. <https://doi.org/10.1055/s-1994-25562>
- [6] Li, C.J. and Chan, T.H. (1997) *Organic Reactions in Aqueous Media*. Wiley, New York.
- [7] Grieco, P.A. (1998) *Organic Synthesis in Water*. Blackie Academic & Professional, London.
- [8] Wan, Y., Wang, H., Zhao, Q., Klingstedt, M., Terasaki, O. and Zhao, D. (2009) Ordered Mesoporous Pd/Silica-Carbon as a Highly Active Heterogeneous Catalyst for Coupling Reaction of Chlorobenzene in Aqueous Media. *Journal of the American Chemical Society*, **131**, 4541-4550. <https://doi.org/10.1021/ja808481g>
- [9] Ramanarivo, H.R., Solhy, A., Sebt, J., Smahi, A., Zahouily, M., Clark, J. and Sebt, S. (2013) An Eco-Friendly Paradigm for the Synthesis of α -Hydroxyphosphonates Using Sodium-Modified Fluorapatite under Solventless Conditions. *Sustainable Chemistry & Engineering*, **1**, 403-409. <https://doi.org/10.1021/sc3001417>
- [10] Kappe, C.O. (2004) Controlled Microwave Heating in Modern Organic Synthesis. *Angewandte Chemie International Edition*, **43**, 6250-6284. <https://doi.org/10.1002/anie.200400655>
- [11] Lidstrom, P., Tierney, J., Wathey, B. and Westman, J. (2001) Microwave Assisted Organic Synthesis—A Review. *Tetrahedron*, **57**, 9225-9283.

- [https://doi.org/10.1016/S0040-4020\(01\)00906-1](https://doi.org/10.1016/S0040-4020(01)00906-1)
- [12] Varma, R.S. (1999) Solvent-Free Organic Syntheses using Supported Reagents and Microwave Irradiation. *Green Chemistry*, **1**, 43-55.
<https://doi.org/10.1039/a808223e>
- [13] Gabriel, C., Gabriel, S., Grant, E.H., Halstead, B.S.J. and Mingos, D.M.P. (1998) Dielectric Parameters Relevant to Microwave Dielectric Heating. *Chemical Society Reviews*, **27**, 213-224. <https://doi.org/10.1039/a827213z>
- [14] Larhed, M., Moberg, C. and Hallberg, A. (2002) Microwave-Accelerated Homogeneous Catalysis in Organic Chemistry. *Accounts of Chemical Research*, **35**, 717-727. <https://doi.org/10.1021/ar010074v>
- [15] Varma, R.S. (1999) Solvent-Free Synthesis of Heterocyclic Compounds Using Microwaves. *Journal of Heterocyclic Chemistry*, **36**, 1565-1571.
<https://doi.org/10.1002/jhet.5570360617>
- [16] Smith, M.B. and March, J. (2001) March's Advanced Organic Chemistry: Reactions, Mechanisms, and Structure. John Wiley & Sons, New York, 1218.
- [17] Trost, B.M. and Fleming, I. (1991) Comprehensive Organic Synthesis: 9-Volume Set. Pergamon, Oxford, Vol. 2, 1.4-1.7.
- [18] Deli, J., Lorand, T., Szabo, D. and Foldesi, A. (1984) Potentially Bioactive Pyrimidine Derivatives. 1,2-Amino-4-aryl-8-arylidene-3,4,5,6,7,8-hexahydroquinazoline. *Pharmazie*, **39**, 539-540. <http://europepmc.org/abstract/med/6504976>
- [19] Hathaway, B.A. (1987) An Aldol Condensation Experiment Using a Number of Aldehydes and Ketones. *Journal of Chemical Education*, **64**, 367-368.
<https://doi.org/10.1021/ed064p367>
- [20] Nakano, T. and Migita, T. (1993) A Convenient Synthesis of α,α' Bis(Substituted Benzylidene) Cycloalkanones. *Chemistry Letters*, **22**, 2157-2158.
<https://doi.org/10.1246/cl.1993.2157>
- [21] Iranpoor, N. and Kazemi, F. (1998) RuCl₃ Catalyses Aldol Condensations of Aldehydes and Ketones. *Tetrahedron*, **54**, 9475-9480.
[https://doi.org/10.1016/S0040-4020\(98\)00575-4](https://doi.org/10.1016/S0040-4020(98)00575-4)
- [22] Zhang, X.Y., Fan, X.S., Niu, H.Y. and Wang, J.J. (2003) An Ionic Liquid as a Recyclable Medium for the Green Preparation of α,α' -Bis(Substituted Benzylidene) Cycloalkanones Catalyzed by FeCl₃·6H₂O. *Green Chemistry*, **5**, 267-269.
<https://doi.org/10.1039/b212155g>
- [23] Salehi, P., Khodaei, M.M., Zolfigol, M.A. and Keyvan, A. (2002) Solvent-Free Crossed Aldol Condensation of Ketones with Aromatic Aldehydes Mediated by Magnesium Hydrogensulfate. *Chemical Monthly*, **133**, 1291-1295.
<https://link.springer.com/article/10.1007%2Fs007060200107?LI=true>
- [24] Deng, G. and Ren, T. (2003) Indium Trichloride Catalyzes Aldol-Condensations of Aldehydes and Ketones. *Synthetic Communications*, **33**, 2995-3001.
<https://doi.org/10.1081/SCC-120022473>
- [25] Li, J., Su, W. and Li, N. (2006) Copper Triflate-Catalyzed Cross-Aldol Condensation: A Facile Synthesis of α,α' -Bis(Substituted Benzylidene) Cycloalkanones. *Synthetic Communications*, **35**, 3037-3043.
<https://doi.org/10.1080/00397910500278735>
- [26] Ziarani, G.M., Badieli, A., Abbasi, A. and Farahani, Z. (2009) Cross-Aldol Condensation of Cycloalkanones and Aromatic Aldehydes in the Presence of Nanoporous Silica-Based Sulfonic Acid (SiO₂-Pr-SO₃H) under Solvent Free Conditions. *Chinese Journal of Chemistry*, **27**, 1537-1542. <https://doi.org/10.1002/cjoc.200990259>

- [27] Shrikhande, J.J., Gawande, M.B. and Jayaram, R.V. (2008) Cross-Aldol and Knoevenagel Condensation Reactions in Aqueous Micellar Media. *Catalysis Communication*, **9**, 1010-1016. <https://doi.org/10.1016/j.catcom.2007.10.001>
- [28] An, L.T., Zou, J.P. and Zhang, L.L. (2008) Polymer-Supported Sulphonic Acid Catalyzed Cross-Aldol Condensation: An Expedient Synthesis of α,α' -Bis(Substituted Benzyldiene) Cycloalkanones. *Catalysis Communications*, **9**, 349-354. <https://doi.org/10.1016/j.catcom.2007.06.004>
- [29] Iranpoor, N., Zeynizadeh, B. and Aghapour, A. (1999) Aldol Condensation of Cycloalkanones with Aromatic Aldehydes Catalysed with $TiCl_3(SO_3CF_3)$. *Journal of Chemical Research, Synopses*, **9**, 554-555. <https://doi.org/10.1039/a809827a>
- [30] Das, B., Thirupathi, P., Mahender, I. and Reddy, K.R. (2006) Convenient and Facile Cross-Aldol Condensation Catalyzed by Molecular Iodine: An Efficient Synthesis of α,α' -Bis(Substituted-Benzyldiene) Cycloalkanones. *Journal of Molecular Catalysis A: Chemical*, **247**, 182-185. <https://doi.org/10.1016/j.molcata.2005.11.044>
- [31] Bhagat, S., Sharma, R. and Chakraborti, A.K. (2006) Dual-Activation Protocol for Tandem Cross-Aldol Condensation: An Easy and Highly Efficient Synthesis of α,α' -bis(aryl/alkylmethylidene)ketones. *Journal of Molecular Catalysis A: Chemical*, **260**, 235-240. <https://doi.org/10.1016/j.molcata.2006.07.018>
- [32] Zheng, M., Wang, L., Shao, J. and Zhong, Q. (1997) A Facile Synthesis of α,α' -bis(Substituted Benzyldiene) Cycloalkanones Catalyzed by Bis(*p*-ethoxyphenyl) Telluroxide (Bmpto) under Microwave Irradiation. *Synthetic Communications*, **27**, 351-354. <https://doi.org/10.1080/00397919708005039>
- [33] Yadav, J.S., Subba Reddy, B.V., Nagaraju, A. and Sarma, J.A.R.P. (2002) Microwave Assisted Synthesis of α,α' -bis(Benzyldiene)ketones in Dry Media. *Synthetic communications*, **32**, 893-896. <https://doi.org/10.1081/SCC-120002700>
- [34] Zahouily, M., Salah, M., Bahlaouan, B., Mounir, B., Rayadh, A. and Sebti, S. (2004) Sodium/Fluorapatite as a New Solid Support for the Synthesis of α,β -Unsaturated Arylsulfones. *Catalysis Letters*, **96**, 57-61. <https://doi.org/10.1023/B:CATL.0000029529.98306.5f>
- [35] Solhy, A., Smahi, A., El Badaoui, H., Elaabar, B., Amoukal, A., Tikad, A., Sebti, S. and Macquarrie, D.J. (2003) Efficient Hydration of Nitriles to Amides Catalysed by Sodium Nitrate Modified Fluorapatite. *Tetrahedron Letters*, **44**, 4031-4033. [https://doi.org/10.1016/S0040-4039\(03\)00872-4](https://doi.org/10.1016/S0040-4039(03)00872-4)
- [36] Carey, F.A. and Sundberg, R.J. (1984) *Advanced Organic Chemistry, Part A*. 2nd Edition, Plenum Press, New York, Chapter 8.
- [37] Chang, W. and Ahn, B.J. (2004) Microwave-Assisted Mesoporous Molecular Sieve-Catalyzed Knoevenagel Condensation and Imine Formation Reactions under Solvent-Free Conditions. *Journal of Industrial and Engineering Chemistry*, **10**, 690-693. <https://www.cheric.org/research/tech/periodicals/view.php?seq=442269>