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Potassium Fluoride-Modified Clay as a Reusable Heterogeneous Catalyst for One-Pot Synthesis of 3,4-Dihydropyrimidin-2(1*H*)-ones

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Abstract—Potassium fluoride-modified clay collected from the region of Agadir (Morocco) was used as a heterogeneous catalyst in the one-pot synthesis of 3,4-dihydropyrimidine-2(1*H*)-one derivatives via the Biginelli reaction. The products were obtained with excellent yields (88–98%). The catalyst was characterized X-ray powder diffraction, Fourier-transform IR spectroscopy, scanning electron microscopy, differential thermal analysis, thermogravimetry, and Brunauer–Emmett–Teller (BET) analysis. Plausible reaction mechanisms for both reactions have been proposed. The catalyst can be recycled five times without loss of catalytic activity.

Keywords: KF-modified clay, heterogeneous catalysts, Biginelli reaction, substituted pyrimidines, 3,4-dihydropyrimidin-2(1*H*)-ones.

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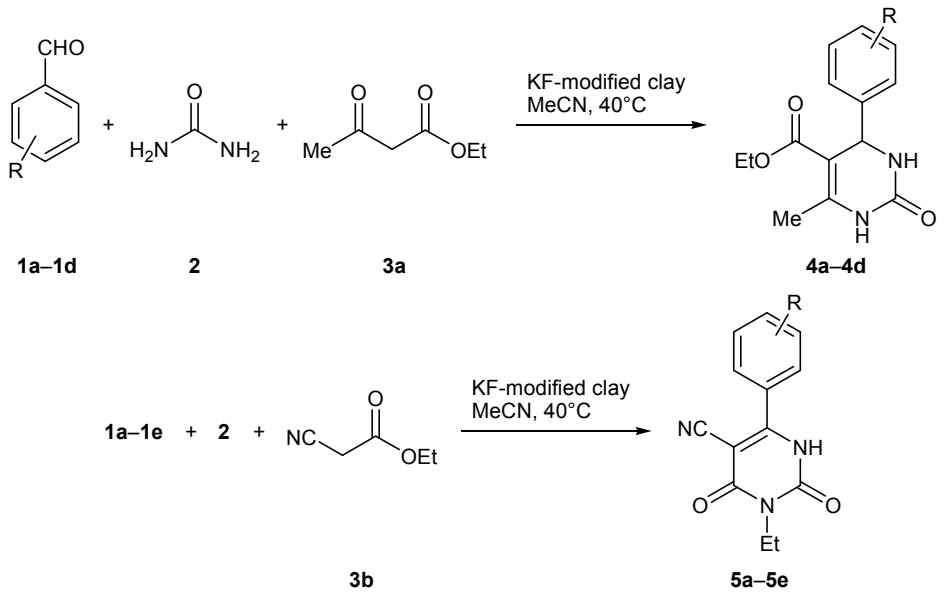
Multi-component reactions (MCRs) have become more and more important in organic synthesis [1]. They play a central role in the development of modern synthetic methodologies advocated by the pharmaceutical and biological sector. In addition, this type of approach has several advantages such as atom economy and higher overall yield than in sequential synthesis (notably due to the fact that the synthesis takes place in one step, ensuring that the number of purification steps is necessarily less) [2]. The Biginelli synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones [3] is a one-pot multicomponent condensation of an aldehyde, β-keto ester, and urea. This condensation is one of the most studied reactions because it leads to products with a wide range of biological and biomedical activities such as antibacterial [4], antifungal [5], antiviral [6], as well as anti-inflammatory and antioxidant properties [7]. In addition, 3,4-dihydropyrimidin-2(1*H*)-one derivatives behave as calcium channel blockers [8], exert antihypertensive effect [9], and act as coronary dilators. On the other hand, substituted pyrimidines can be prepared by condensation of aromatic aldehydes with urea and ethyl cyanoacetate. It should be noted that pyrimidines constitute an important class of compounds having widespread applications in the pharmaceutical field [10].

Several homogeneous catalysts (H_2SO_4 [11], $LiClO_4$ [12], H_3BO_3 [13], trifluoroacetic acid [14], boric acid [13]) and heterogeneous catalysts (mesoporous $NH_4H_2PO_4$/MCM-41 [15], zeolite-supported heteropolyacid [16], silica-bonded *S*-sulfonic acid [17], ion exchange resins [18], silica-bonded *N*-propyl sulfamic acid [8], and MCM-41-anchored sulfonic acid [19]) have been employed to catalyze the Biginelli reaction. The majority of these catalysts have disadvantages such as long reaction time, low yield, expensive reagents, formation of toxic by-products, tedious work-up, and strongly acidic conditions.

In this work, we used KF-modified clay as a low-cost eco-friendly heterogeneous catalyst for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones (Scheme 1). We studied the effect of the amount of catalyst, sol-

Scheme 1.



1, **4**, **5**, R = H (**a**), 4-MeO (**b**), 4-Me (**c**), 4-Cl (**d**), 3-O_2N (**e**).

vent, temperature, and aromatic aldehyde nature on the yield of the desired products for both reactions.

The modified clay was characterized by X-ray powder diffraction (XPD) using a Bruker Phaser diffractometer with a copper anticathode bombarded by accelerated electrons, which generated radiation wavelength λα1 = 1.54060 Å and λα2 = 1.54439 Å at a tube voltage of 30 kV and a tube current of 10 mA. The X-ray powder pattern is shown in Fig. 1. According to the obtained data, the modified clay contains two phases: the first phase corresponds to merwinite which is represented by peaks at 2θ = 23.22, 23.59, 29.57, 38.50, 38.86, 39.24, 39.61, 42.64, 45.31, 46.05, 46.69, 47.06, 48.90, of Miller indices (–111), (111), (012), (–411), (013), (411), (020), (213), (–511), (511), (122), (–204), and (222), respectively, in accordance with JCPDS card no. 00-035-0591. The second phase was attributed to silica due to coincidence with the standard JCPDS card no. 01-087-2275. This phase is confirmed by peaks located at 2θ = 16.14, 17.43, 18.81, 20.55, 25.43, 25.89, 26.26, 28.20, 32.24, 33.34, 35.65, 36.93, 37.57, 41.44° and characterized by Miller indices (310), (301), (12–2), (400), (203), (402), (150), (033), (61–1), (450), (153), (253), (07–1), and (154), respectively.

The FTIR spectrum of KF-modified clay (Burker Vertex 70) is shown in Fig. 2. The spectrum indicated the presence of silica which is represented by an in-

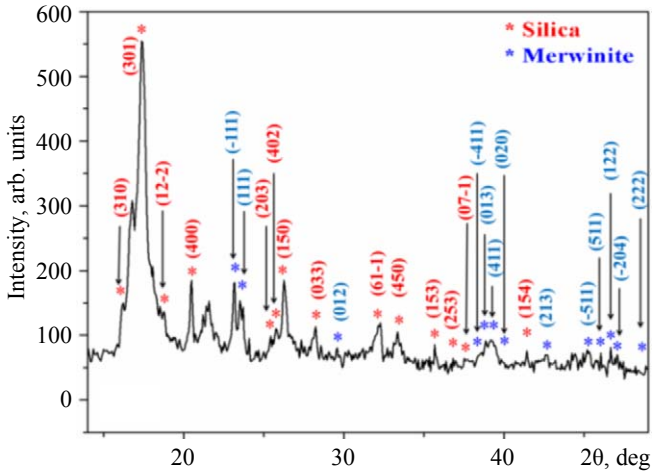


Fig. 1. X-Ray powder pattern of the KF-modified clay.

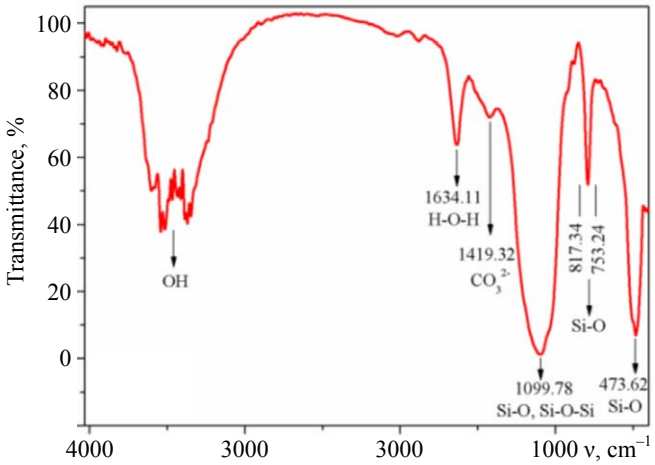


Fig. 2. IR spectrum of the KF-modified clay.

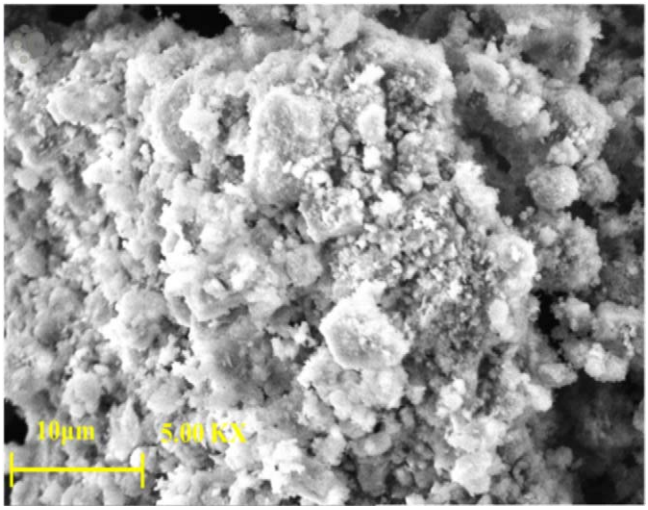


Fig. 3. SEM microphotograph of the KF-modified clay.

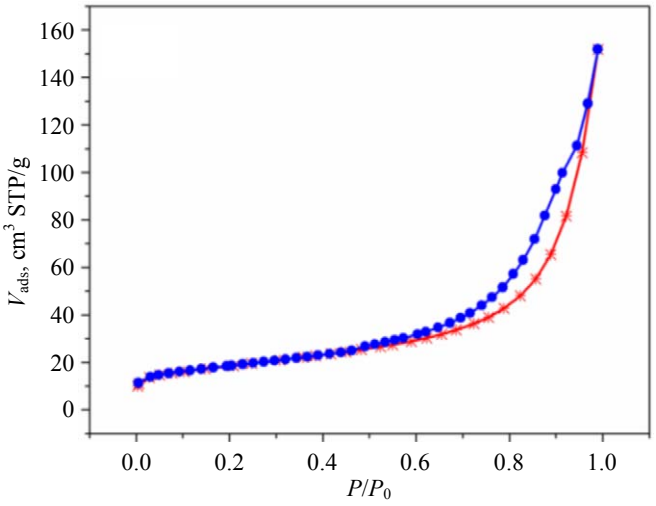


Fig. 4. Nitrogen adsorption–desorption isotherms for the KF-modified clay.

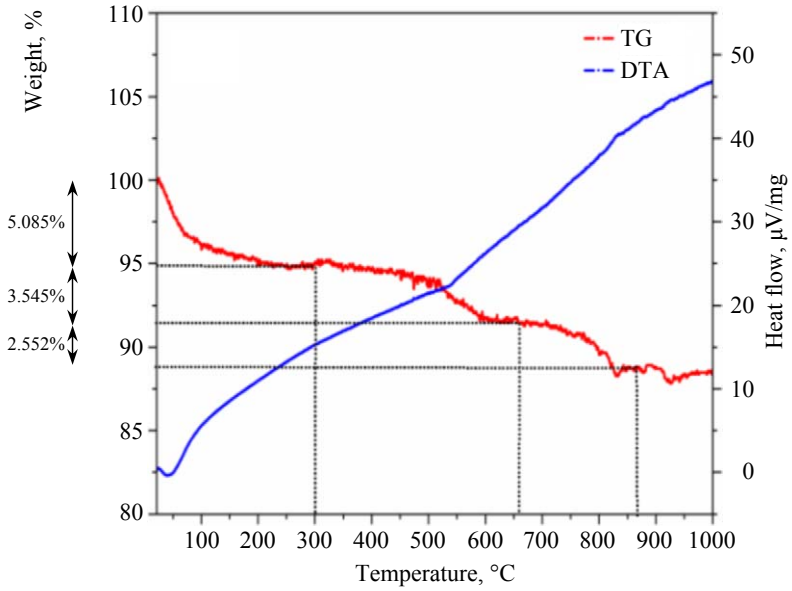


Fig. 5. TG and DTA curves for KF-modified clay.

tense peak at 1099.78 cm^{-1} due to Si–O–Si stretchings and Si–O stretching vibration bands appearing at 817.34–753.24 and 473.62 cm^{-1} [20]. Carbonates are represented by a weak characteristic band of the CO_3^{2-} group located at 1419.32 cm^{-1} [21]. All these bands already exist in the spectrum of the natural untreated clay [22]. The only remarkable difference is the shape of the broad band around 3400 cm^{-1}, probably corresponding to OH vibrations.

The morphology of the modified clay was investigated by scanning electron microscopy with a Supra 40 VP Colonne Gemini Zeiss instrument (Fig. 3). The SEM photograph showed large agglomerates of different shapes with irregular morphologies and dimensions of tens of microns. These agglomerates are formed by aggregation of smaller particles of different sizes (from 1 to 10 μm). Magnification of a part of the SEM image showed that the surface formed by all these particles is characterized by the presence of pores and cavities of heterogeneous shape and morphology (dimensions ranging from 1 to 5 μm). These cavities and pores may be useful for heterogeneous catalysis in organic synthesis.

The nitrogen adsorption–desorption isotherms of the modified clay at 77 K are shown in Fig. 4. The isotherm obtained is of type IV according to the

IUPAC classification [23]. This type of isotherm is characterized by the presence of mesopores [24]. The specific surface area of the clay treated by KF was determined by the Brunauer–Emmett–Teller (BET) method using a Quantachrome AsiQuin automated gas sorption analyzer version 2.02. According to the numerical data deduced from this isotherm, the modified clay has a specific surface of 63.842 m²/g with a pore diameter of 1.69 nm.

Table 1. Effect of the amount of KF-modified clay on the yield of 3,4-dihydropyrimidin-2(1*H*)-ones **4a** and **5a**[a]

Entry no.	Amount of the catalyst, mg	Reaction time, min	Product no. (yield,[b] %)
1	10	90	**4a** (51)
2	20	60	**4a** (75)
3	30	35	**4a** (94)
4	40	35	**4a** (93)
5	50	35	**4a** (80)
6	10	90	**5a** (69)
7	20	60	**5a** (80)
8	30	25	**5a** (98)
9	40	25	**5a** (98)
10	50	25	**5a** (93)

[a] Reaction conditions: benzaldehyde (1 mmol), urea (1.5 mmol), ethyl acetoacetate or ethyl cyanoacetate (1 mmol), temperature 40°C, solvent acetonitrile.
[b] Isolated yield.

Table 2. Influence of solvent on the yield of 3,4-dihydropyrimidin-2(1*H*)-ones **4a** and **5a**[a]

Entry no.	Solvent	Reaction time, min	Product no. (yield,[b] %)
1	MeCN	35	**4a** (94)
2	MeOH	35	**4a** (75)
3	EtOH	35	**4a** (71)
4	$CHCl_3$	35	**4a** (30)
5	H_2O	35	**4a** (21)
6	CH_2Cl_2	35	**4a** (18)
7	MeCN	25	**5a** (98)
8	MeOH	25	**5a** (81)
9	EtOH	25	**5a** (76)
10	$CHCl_3$	25	**5a** (41)
11	H_2O	25	**5a** (25)
12	CH_2Cl_2	25	**5a** (21)

[a] Reaction conditions: benzaldehyde (1 mmol), urea (1.5 mmol), ethyl acetoacetate or ethyl cyanoacetate (1 mmol), temperature 40°C, catalyst amount 30 mg.
[b] Isolated yield.

The thermal analysis of the modified clay was carried out on a Shimadzu D 60 instrument. A 9.381-mg sample of the modified clay was heated from 15.58 to 1100°C under dry air at a heating rate of 10 deg/min. The results obtained are shown in Fig. 5. Three weight losses were observed. The first loss (5.08%, 0.477 mg) between 22 and 300°C corresponds to endothermic removal of surface water and bound water. The second loss (3.545%, 0.332 mg) between 300 and 659°C is likely due to exothermic decomposition of organic matter which can be mixed with the clay or bound to the surface. The third exothermic loss (2.552%, 0.239 mg) is localized between 659 and 867°C, which can be attributed to the crystallization of merwinite [25].

To optimize the condensation conditions, the reaction of benzaldehyde (**1a**, 1 mmol) with urea (**2**, 1.5 mmol) and ethyl acetoacetate (**3a**, 1 mmol), as well as ethyl cyanoacetate (**3b**, 1 mmol), was carried out by varying the amount of the catalyst (Table 1) and solvent (Table 2) at different temperatures (Table 3). As follows from the data in Table 1, the yield of **4a** increased from 51 to 94% (entry nos. 1–3), and the yield of **5a** increased from 69 to 98% (entry nos. 6–9), as the amount of the catalyst was raised from 10 to 30 mg. Thus, 30 mg can be considered the optimal amount of the KF-modified clay for these reactions.

According to Table 2, good yields of **4a** were obtained using acetonitrile (94%), methanol (75%), and ethanol (71%) as solvents (entry nos. 1–3) after 35 min. In the synthesis of **5a**, the yields were 98, 81, and 76% in acetonitrile, methanol, and ethanol, respectively (entry nos. 7–9), after 25 min. The lowest yields were obtained using chloroform, water, and methylene chloride for both reactions. Therefore, acetonitrile was selected as the best solvent for the two condensations. Similar results were reported previously [16, 26].

Raising the temperature from 22 to 40°C improved the yield of **4a** from 57 to 94% (Table 3, entry nos. 1, 2) and the yield of **5a** from 61 to 98% (entry nos. 5, 6). Further raising the temperature to 70°C either had no effect or reduced the yield. This may be explained by increased disagreement between the catalytic sites on the clay surface at elevated temperature, so that the reactants no longer adsorbed on the clay surface.

Having optimized the conditions of both reactions, various aromatic aldehydes **1a**–**1e** bearing electron-donor and electron-withdrawing groups were involved

therein. The results are presented in Table 4. Both reactions were relatively fast and were complete on the average in 30 min, and the products were obtained in excellent yields. No appreciable effect of the substituent in the benzene ring on the reaction rate was observed, but the substituent nature influenced extraction and purification features of the product. Thus, the KF-modified clay tolerates various substrates and thus allows extension of the series of available new products certainly possessing new properties.

To propose a plausible mechanism for the two reactions, we tested three supports, namely raw clay, clay treated with HCl, and KF-modified clay, in the condensation of benzaldehyde (**1a**) with urea (**2**) and ethyl acetoacetate (**3a**) or ethyl cyanoacetate (**3b**). No condensation took place in the presence of HCl-treated clay consisting essentially of silica, aluminum phosphate, and potassium chloride [28]. In the case of the raw clay, which consists of dolomite (major phase) and silica (minor phase) [22], we observed the formation of a small amount of the product which we failed to isolate. In contrast, the KF-modified clay (consisting of silica and merwinite) afforded the desired products with very good yields. Therefore, it was concluded that merwinite is likely to be responsible for the catalytic activity of KF-modified clay in the condensations under study. Scheme 2 outlines a probable two-step mechanism for the formation of 3,4-dihydropyrimidin-2(1*H*)-one **4a**. The first step is the formation of *N*-acylimine intermediate via nucleophilic attack of urea on the aldehyde. In fact, Merwinite calcium plays the role of Lewis acid and makes the carbonyl carbon atom more electron-deficient [29]. This carbon atom is then attacked by the lone electron pair of the urea nitrogen atom, which leads to *N*-(1-hydroxybenzyl)urea. The latter undergoes dehydration to give *N*-acylimine which is activated by coordination of the lone electron pair of the oxygen atom to the vacant orbital of calcium metal [5]. The second step begins with enolization of ethyl acetoacetate, and the enol attacks the imine [29]. The subsequent intramolecular cyclization and dehydration yield the final product.

Scheme 3 shows a probable mechanism of the condensation of benzaldehyde with urea and ethyl cyanoacetate to give pyrimidine **5a**. This mechanism in-

Table 3. Temperature effect on the yield of 3,4-dihydropyrimidin-2(1*H*)-ones **4a** and **5a**[a]

Entry no.	Temperature, °C	Reaction time, min	Product no. (yield,[b] %)
1	22	35	**4a** (57)
2	40	35	**4a** (94)
3	60	35	**4a** (93)
4	70	35	**4a** (89)
5	22	25	**5a** (61)
6	40	25	**5a** (98)
7	60	25	**5a** (98)
8	70	25	**5a** (86)

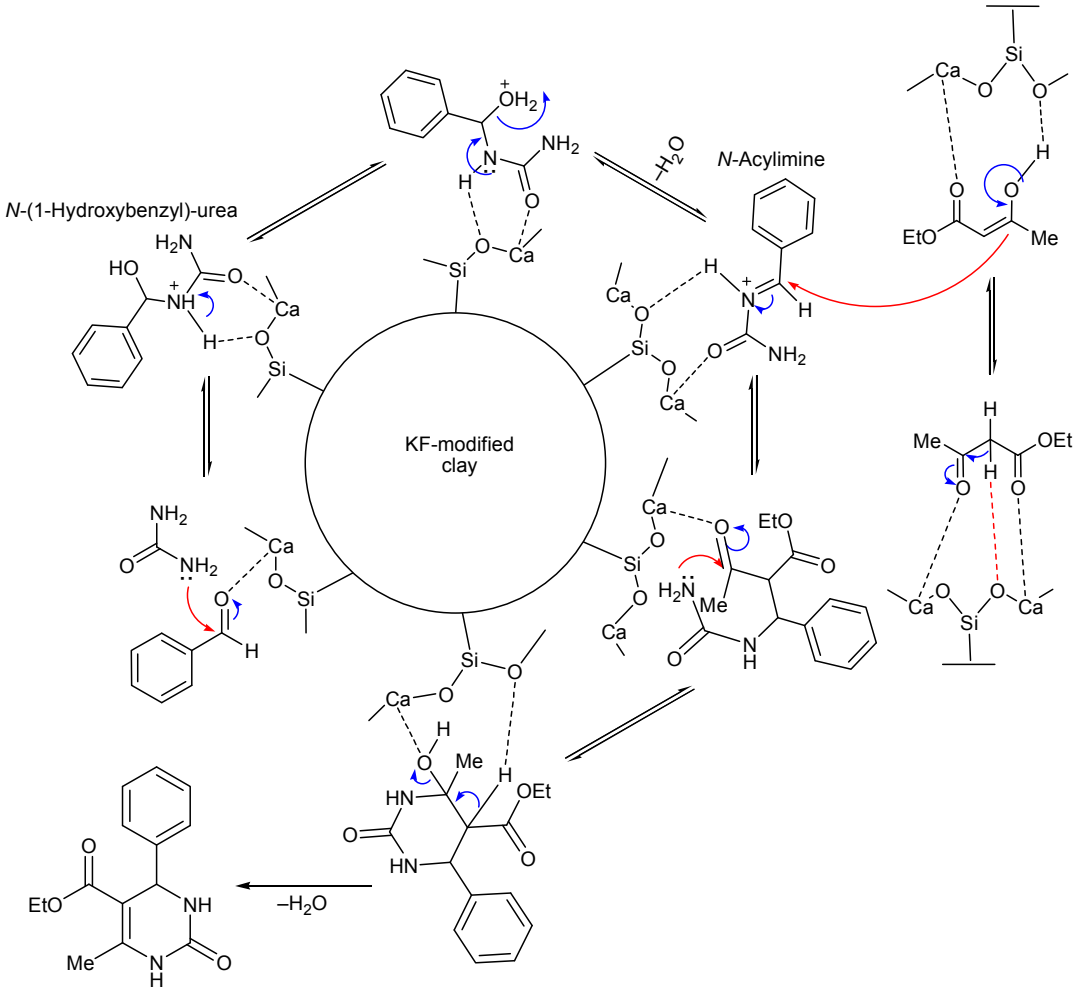
[a] Reaction conditions: benzaldehyde (1 mmol), urea (1.5 mmol), ethyl acetoacetate or ethyl cyanoacetate (1 mmol), catalyst amount 30 mg, solvent acetonitrile.
[b] Isolated yield.

Table 4. Condensation of substituted benzaldehydes with urea and ethyl acetoacetate or ethyl cyanoacetate under the optimized conditions (Scheme 1)[a]

Entry no.	R	Reaction time, min	Product no.	Yield,[b] %	mp, °C	
					this work	published data
1	H	35	**4a**	94	203–205	200–202 [5]
2	4-MeO	40	**4b**	88	206–208	209–210 [27]
3	4-Me	30	**4c**	91	213–215	215.4–216.4 [2]
4	4-Cl	30	**4d**	96	211–213	209.4–211.4 [2]
5	H	25	**5a**	98	55–57	–
6	4-MeO	30	**5b**	91	82–84	–
7	4-Me	25	**5c**	95	98–100	–
8	4-Cl	25	**5d**	97	92–94	–
9	3-O_2N	25	**5e**	91	137–139	–

[a] Reaction conditions: aldehyde (1 mmol), urea (1.5 mmol), ethyl acetoacetate or ethyl cyanoacetate (1 mmol), catalyst amount 30 mg, solvent acetonitrile, temperature 40°C.
[b] Isolated yield.

Scheme 2.

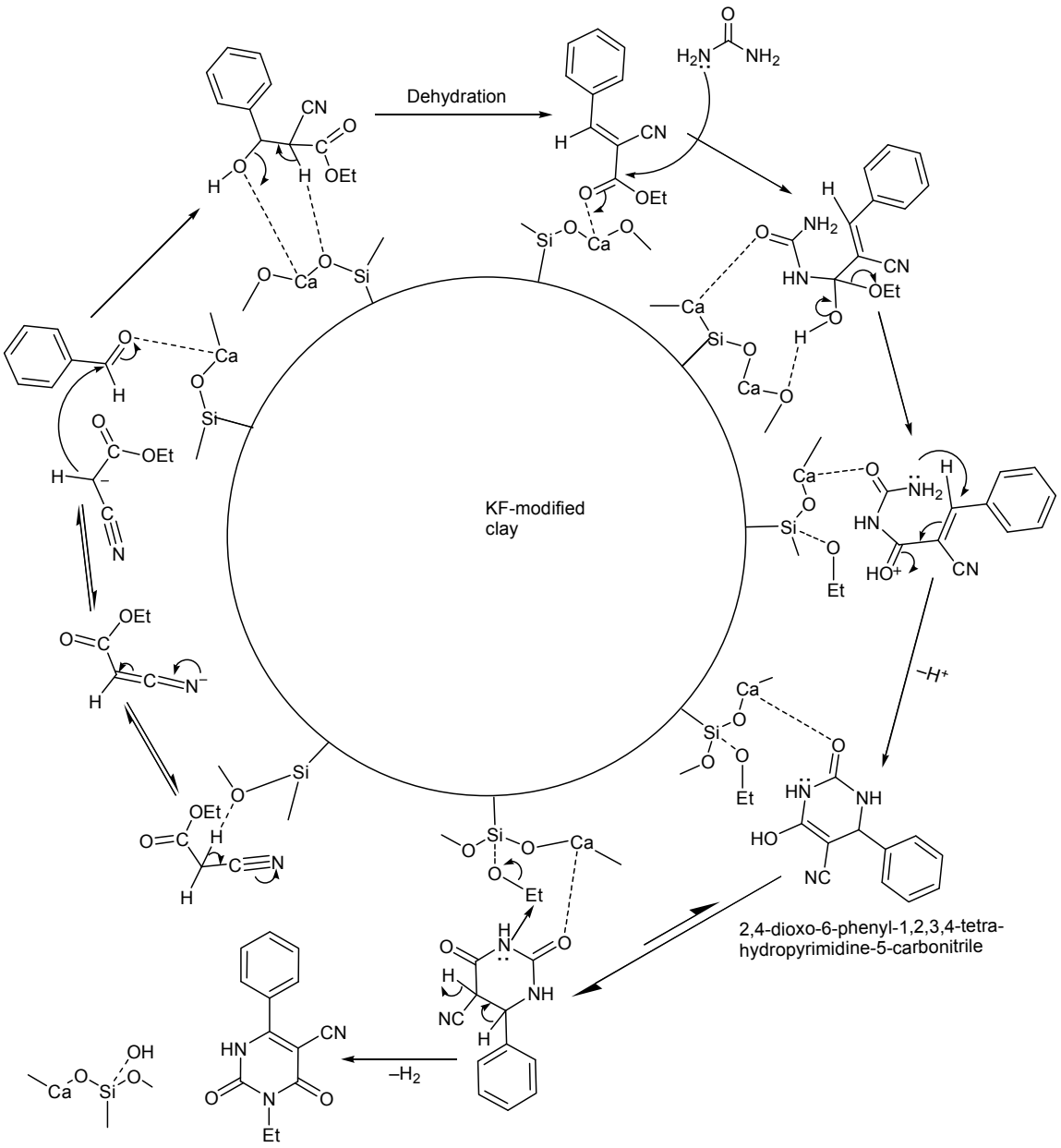


cludes several steps. The first step is Knoevenagel condensation between benzaldehyde and ethyl cyanoacetate, which is preceded by deprotonation of ethyl cyanoacetate by the negatively charged site at the catalyst surface to give a very stable anion due to conjugation with the cyano group. The carbonyl carbon atom of benzaldehyde is activated by the positively charged site on the catalyst surface bonded to carbonyl oxygen. The aldol undergoes dehydration to give substituted alkene [30]. The second step is initiated by nucleophilic attack of the lone electron pair of the urea nitrogen atom on the ester carbonyl function, leading to the departure of the ethoxy group as reported in the case of homogeneous catalysis [31]. Next follows cyclization via intramolecular attack of the second urea nitrogen atom on the previously formed C=C double bond to give the enol form [31] which tautomerizes to the oxo structure. Finally, *in situ* *N*-alkylation affords the final product, dioxopyrimidine **5a**. In keeping with published data, compound **5a** was synthesized by alkylation of preliminarily isolated and purified 2,4-dioxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbonitrile [32, 33].

The possibility of recycling the KF-modified clay was studied in the synthesis of **5a** under the optimal conditions. For this purpose, the catalyst was successively washed with acetone and ether for 30 min and then dried in an oven at 80°C for 8 h after each cycle. The results showed that the KF-modified clay can be recycled five times with no appreciable loss of its catalytic activity (the total loss was equal to 5% after five cycles).

In summary, we have reported the use of KF-modified clay as a heterogeneous catalyst for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones via one-pot three-component condensation of aromatic aldehydes with urea and ethyl acetoacetate or ethyl cyanoacetate. The products attract interest as potential biologically and therapeutically active compounds. The described reactions are complete in a shorter time than those

Scheme 3.



catalyzed by other supports reported in the literature and afford the target products in excellent yields and with high purity under mild conditions.

EXPERIMENTAL

The modified clay was prepared by adding 2 g of KF to 10 g of the natural clay collected from the Agadir region in 30 mL of distilled water. The mixture was stirred at room temperature for 24 h. The resulting material was washed several times with distilled water and then centrifuged, dried in an oven at 70°C, and finally crushed.

Commercial reagents were purchased from Aldrich. All solvents were distilled before used by standard procedures. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance DMX 300 spectrometer at 300 and 75 MHz, respectively; the chemical shifts are given relative to tetramethylsilane. The IR spectra were recorded with a Jasco 4100 spectrometer equipped with an ATR accessory. The progress of reaction was monitored by thin-layer chromatography (TLC) using 20×20-cm silica gel UV 254 plates (0.2 mm thick) (ALBET). Spots were detected using an ultraviolet lamp (λ 254 and 365 nm). The melting points were measured with a Kofler bench (Wagner & Munz).

General procedure for the synthesis of 3,4-dihydropyrimidin-2(1*H*)-ones 4a–4d and 5a–5e. A mixture of 1 mmol of aldehyde **1a**–**1e**, 1 mmol of ethyl acetoacetate (**3a**) or ethyl cyanoacetate (**3b**), 1.5 mmol of urea, and 30 mg of the KF-modified clay in 5 mL of acetonitrile was stirred at 40°C until the reaction was complete (TLC). The catalyst was filtered off, the solvent was removed, the residue was extracted with methylene chloride, the extract was evaporated, and the residue was recrystallized from ethanol.

Ethyl 6-methyl-2-oxo-4-phenyl-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4a). Yield 94%, yellow solid, mp 203–205°C. IR spectrum, ν, cm^{-1}: 3450 (N–H), 3102 (C–H_{arom}), 3018–2886 (C–H_{aliph}), 1634 (C=O), 1450 (C=C_{arom}), 1210 (C–O, ester), 1141, 1057 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.63 s (1H, NH), 7.37 m (5H, H_{arom}), 5.62 s (1H, NH), 5.42 s (1H, CH), 4.1 q (2H, CH_2), 2.39 s (3H, CH_3), 1.19 t (3H, CH_3).

Ethyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4b). Yield 88%, yellow solid, mp 206–208°C. IR spectrum, ν, cm^{-1}: 3435 (N–H), 3095 (C–H_{arom}), 2970–2865 (C–H_{aliph}), 1684 (C=O, ester), 1621 (C^2=O), 1467 (C=C_{arom}), 1210 (C–O, ester), 1044 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.14 d (2H, H_{arom}), 7.1 s (1H, NH), 6.88 d (2H, H_{arom}), 5.41 s (1H, NH), 5.39 s (1H, CH), 4.05 q (2H, CH_2), 3.8 s (3H, CH_3), 2.38 s (3H, CH_3), 1.19 t (3H, CH_3).

Ethyl 6-methyl-4-(4-methylphenyl)-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4c). Yield 92%, yellow solid, mp: 213–215°C. IR spectrum, ν, cm^{-1}: 3484 (N–H), 3095 (C–H_{arom}), 2991–2850 (C–H_{aliph}), 1684 (C=O, ester), 1614 (C^2=O), 1454 (C=C_{arom}), 1259 (C-O_{ester}), 1065 (C-N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.22 d (2H, H_{arom}), 7.18 d (2H, H_{arom}), 7.11 s (1H, NH), 5.39 s (1H, CH), 5.37 s (1H, NH), 4.05 q (2H, CH_2), 2.39 s (3H, CH_3), 1.59 s (3H, CH_3), 1.19 t (3H, CH_3).

Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1,2,3,4-tetrahydropyrimidine-5-carboxylate (4d). Yield 96%, yellow solid, mp 211–213°C. IR spectrum, ν, cm^{-1}: 3331 (N–H), 3102 (C–H_{arom}), 3005–2873 (C–H_{aliph}), 1669 (C=O, ester), 1593 (C^2=O), 1461 (C=C_{arom}), 1412, 1190 (C–O, ester), 1057 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.22 m (4H, H_{arom}), 5.25 s (1H, CH), 4.03 q (2H, CH_2), 3.2 s (1H, NH), 3.2 s (1H, NH), 2.37 s (3H, CH_3), 1.18 t (3H, CH_3).

3-Ethyl-2,4-dioxo-6-phenyl-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (5a). Yield 98%, white solid, mp 55–57°C. IR spectrum, ν, cm^{-1}: 3408 (N–H), 3018–2976 (C–H_{arom}, CH_3), 2879 (CH_2), 2267–2136 (C≡N), 1700 (C=O), 1572 (C=O), 1440 (C=C_{arom}), 1197 (C–N), 1072 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.25 s (1H, NH), 8.02 d (2H, H_{arom}), 7.58 m (3H, H_{arom}), 4.4 q (2H, CH_2), 1.41 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 162.55, 155.53, 133.85, 131.82, 131.26, 129.77, 116.03, 103.08, 62, 39.39, 14.43.

3-Ethyl-6-(4-methoxyphenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (5b). Yield 91%, pale yellow solid, mp 82–84°C. IR spectrum, ν, cm^{-1}: 3498 (N–H), 3088–2893 (C–H_{arom}, C–H_{aliph}), 2191 (C≡N), 1711 (C=O), 1551 (C=O), 1509 (C=C_{arom}) 1204 (C–N), 1155 (C–N), 1009 (C–O, ether). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.19 s (1H, NH), 8.03 d (2H, H_{arom}), 7.02 d (2H, H_{arom}), 4.39 q (2H, CH_2), 3.9 s (3H, CH_3), 1.41 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 164.02, 162.83, 154.89, 133.98, 124.42, 116.69, 115.42, 99.01, 62.53, 56.22, 39.36, 14.48.

3-Ethyl-6-(4-methylphenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (5c). Yield 95%, white solid, mp 98–100°C. IR spectrum, ν, cm^{-1}: 3470 (N–H), 3053–2831 (C–H_{arom}, C–H_{aliph}), 2204 (C≡N), 1704 (C=O), 1544 (C=O), 1447 (C=C_{arom}), 1204 (C–N), 1001 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.21 s (1H, NH), 7.85 d (2H, H_{arom}), 7.35 d (2H, H_{arom}), 4.39 q (2H, CH_2), 2.4 s (3H, CH_3), 1.41 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 162.47, 155.41, 144.88, 131.45, 130.34, 129.17, 116.26, 101.60, 62.73, 39.38, 21.82, 14.46.

6-(4-Chlorophenyl)-3-ethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (5d). Yield 97%, white solid, mp 92–94°C. IR spectrum, ν, cm^{-1}: 3345 (N–H), 3067 (C–H_{arom}), 2970 (CH_3), 2914 (CH_2), 2233 (CN), 1711 (C=O), 1565 (C=O), 1454 (C=C_{arom}), 1182 (C–N), 1050 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.21 s (1H, NH), 7.99 d (2H, H_{arom}), 7.5 d (2H, H_{arom}), 4.4 q (2H, CH_2), 1.41 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 162.10, 154.16, 138.48, 132.92, 130.72, 129.96, 115.89, 103.73, 62.94, 39.38, 14.44.

3-Ethyl-6-(3-nitrophenyl)-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbonitrile (5e). Yield 91%, white solid, mp 137–139°C. IR spectrum, ν, cm^{-1}: 3317 (N–H), 3080 (C–H_{arom}), 3005 (CH_3), 2949 (CH_2), 2204 (C≡N), 1704 (C=O), 1504 (C=O), 1475 (C=C_{arom}), 1204 (C–N), 1072 (C–N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 8.61 s (1H, NH), 8.35 d (2H,

H_{arom}), 8.25 s (1H, H_{arom}), 7.68 t (1H, H_{arom}), 4.35 q (2H, CH_2), 1.35 t (3H, CH_3). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 161.71, 153.28, 148.54, 136.93, 133.34, 131.37, 127.57, 125.41, 115.54, 106.07, 63.14, 39.37, 14.43.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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