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NbCl₅ Functionalized Perlite: A Potent and Recyclable Catalyst for Synthesis of Pyrans

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Abstract: Niobium pentachloride functionalised perlite was prepared via a solid state dispersion technique, which was utilized as an efficient heterogeneous catalyst for the synthesis of pyrans. The immobilisation of NbCl₅ over perlite was examined by Fourier-transform infrared (FT-IR) spectroscopy, X-ray diffraction (XRD), Thermogravimetric analysis (TGA), scanning electron microscope (SEM) with energy dispersive spectra (EDS), and Brunauer, Emmett and Teller (BET) surface area measurements. The wt% of NbCl₅-loaded perlite was optimized based on the adequacy with respect to the yield of the pyrans in various solvents. The recyclability of the catalyst was validated in synthesizing pyrans and the results marked its efficiency up to five runs. The efficacy of the NbCl₅/perlite catalyst was found to be comparable and better with respect to the other heterogeneous catalysts reported. The structures of pyrans were confirmed by FT-IR, ¹H and ¹³C NMR spectral techniques. The proposed recyclable heterogeneous NbCl₅/perlite catalyst simplifies the protocol, and has minimal chemical waste, a lower reaction time and a high-yield.

Keywords: perlite; NbCl₅; heterogeneous catalyst; multi component reactions (MCRs); pyrans



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1. Introduction

Catalysis is an essential mechanism for feasible chemical reactions and processes, and it is the principal backbone of green science. Lately, there has been growing concern in the field of chemical processes, due to the impact of their contaminating side products on the environment; thus, designing new methodology as per the principles of green chemistry is inescapable [1–5]. Therefore, it is necessary to succeed environmentally hazardous and corrosive chemicals with an effective, reusable and less toxic catalyst. This can be successfully accomplished by exploiting a new era of heterogeneous catalysts, which have been evidenced to be more beneficial than homogeneous catalysts. The incorporation of heterogeneous catalysts into synthetic processes in order to prepare novel compounds is, indeed, a cost-effective and environmentally sustainable approach. They are also recognized for their simple and easy handling, their low cost and for generating organic compounds with a better yield [6–10]. Heterogeneous catalysts lead the basis of manufacturing primarily due to their reusability and stability. There are several reports available in the literature that are related to heterogeneous catalyst-assisted synthetic organic transformations with regio and stereo selectivity [11,12]. Generally, this process is involved in a different phase to the reactants. The most common form is seen in solid-based materials and acts as an efficient catalyst in the organic transformation reactions in which the reactants (liquid or gas) adsorb the surface of the catalysts.

Currently, Lewis acid-based heterogeneous catalysts are popular due to their innocuous and economic nature, and their compelling ability to proceed the heterocyclic compound synthesis [11–14]. The Lewis acids are known to be a better candidate for incorporation into a solid support; they have excellent polarisability and a good coordinating capacity [15]. Although they are associated with limited availability, a high cost and toxicity, in most cases, precious metal catalysts are used. In light of this, plentiful inexpensive and non-toxic transition metal-based catalysts have been employed in the current field of research. In this sense, a NbCl_5 -mediated catalyst has been used significantly in the synthesis of various organic compounds [16,17]. Nevertheless, it suffers from disadvantages, including a corrosive nature, toxicity, difficulty in separation and reusability. Therefore, it is appropriate to immobilize Lewis acids over an efficient solid support.

Perlite is an amorphous and volcanic eruption rock that possesses silica as its most abundant constituent, has a considerable amount of oxides of Al, Fe, Mg, Ca, K, Na and has a 3–5% moisture content [18]. Its features, which include chemical inertness, better expansion capabilities and an appreciable surface area, have extended its applications in fields such as dye removal [19], sorption studies [20], catalysis [21], and heavy metal removal [22], etc. The porous nature of perlite makes it a remarkable solid support for Lewis acids. Pharmacologically active pyran and its derivatives have received increasing attention as a result of its application in anti-biotic [23], anti-inflammatory [24], anti-microbial agent [25], anticancer [26,27], and antitubercular pharmaceuticals [28], among others. The catalytic efficiencies of most of the developed new heterogeneous catalysts are generally compared with this specially made catalyst [29]. Furthermore, this catalyst is very cheap and available in large quantities for organic transformation reactions. Hence, this framework takes advantage of the above-mentioned properties of perlite and is a continuation of our efforts to investigate the applications of solid acid in synthetic organic transformations [30]. We had reported BiCl_3 -modified perlite as an effective catalyst for selective organic transformation reactions [30], in which quinoxalines and dihydropyrimidinones were synthesized. Consequently, the inclusion of BiCl_3 in the perlite enhances the acidity of the material and facilitates the acid-catalyzed reactions.

The growth of an environmentally friendly heterogeneous catalyst is absolutely critical for the construction of valuable synthetic targets. Laura Ferrand et al. [16] reported Nb (III)/(V)-based catalytic systems for C–O and C–N bond formations. They reported an efficient method for the intramolecular hydrofunctionalization of alkenes with high yields and selectiveness, and that the Nb-based materials were efficient catalysts for the synthesis of pyran, furan, pyrrolidine, piperidine, lactone, and lactam derivatives, as well as of spirocyclic compounds in high yields. Shu-Tao Ga et al. [17] reported NbCl_5 as an efficient catalyst for the synthesis of 1,5-benzodiazepine derivatives from *o*-phenylenediamine (*o*-PD) and ketones. The reaction was performed under mild conditions (50 °C) in *n*-hexane medium. The authors used a series of symmetrical and unsymmetrical ketones with *o*-PD and in all the cases, the corresponding 1,5-benzodiazepines were produced with good yields (85–96%). Henceforth, this study focuses on the synthesis of a NbCl_5 -impregnated perlite catalyst and on testing its catalytic efficiency in the synthesis of pyrans. This perlite-supported NbCl_5 avoids the problems caused by a homogeneous catalyst, which is an apparent environmentally benign catalyst with fascinating activity and reusability.

2. Experimental

2.1. Materials and Methods

Perlite, NbCl_5 and the other reagents were procured from Merck. The reagents and solvents were utilized as purchased without any further purification. The prepared NbCl_5 /perlite was characterized by various spectral techniques, namely, BET, TGA, SEM-EDS, XRD and FT-IR. The synthesized pyrans were validated by NMR and IR spectral methods. Brunauer–Emmett–Teller (BET) analysis of the catalysts was carried out using Quantachrome Instruments to perform a surface area analysis, and TG-DTA analysis was performed within a range of 0–1000 °C using a NETZSCH STA 449F3 STA449F3A-0929-

M instrument. Carl ZEISS Scanning Electron Microscopy (SEM) attached to an Energy-Dispersive X-ray Spectrometer (EDS) was employed for obtaining SEM images. X-ray diffraction patterns were obtained using an Empyrean X-ray diffractometer with Cu K α irradiation ($\lambda = 1.5416 \text{ \AA}$) working at 20 kv. The structure of the compounds synthesized were characterized by the infrared spectrum using a SCHIMADZU FT-IR spectrometer, and ^1H and ^{13}C NMR spectra were acquired from a BRUCKER 500 MHz spectrometer with DMSO as solvent.

2.2. Preparation of NbCl_5 Loaded Perlite

The catalyst was obtained via a simple dispersion procedure. Then, 1 g of pre-treated perlite [29,30] and 0.1 g NbCl_5 were suspended in 10 mL of 2-propanol separately. NbCl_5 suspension was added in drops to a perlite–propanol suspension and stirred vigorously for 4 h at an ambient temperature. Then, the solvent was evaporated, dried at 120 °C for 2 h and calcinated at 250 °C for 2 h to obtain 10 wt% NbCl_5 -loaded perlite. The other wt% of the NbCl_5 -loaded perlites were prepared with respective amounts of NbCl_5 .

2.3. General Method for Preparation of Diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate

An ethanolic solution of ethyl acetoacetate (EAA, 4 mmol) and substituted aldehydes (2 mmol) was refluxed at 80 °C in the presence of NbCl_5 /perlite (0.15 g) for 15–30 min. The progress of the reaction was monitored by thin-layer chromatography (TLC). Then, the catalyst was removed by filtration, the excess solvent was evaporated and the crude product was recrystallized from ethanol. The formed pyrans were confirmed using IR and NMR spectral technique. The corresponding ^1H and ^{13}C NMR spectra are given as Supplementary information (Figures S1–S16).

Diethyl-2,6-dimethyl-4-phenyl-4H-pyran-3,5-dicarboxylate (**1a**)

IR ν (cm^{-1}) = 2976.81, 2329.46, 1707.26, 1630.58, 1455.86, 1377.93, 1214.52, 1097.62, 1033.51; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.3–7.7 (m, Ar-H), 4.86 (s, $^1\text{H}, \text{H-4}$), 4.14–4.11 (q, 4H, CH_2 -ester), 2.26 (s, 6H, CH_3), 1.14–1.12 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 68.75 (C=O), 167.42 (C-2,6), 145.86–128.30 (Ar-C), 102.27 (C-3,5), 59.44 (CH_2 -ester), C-4 merged with DMSO region, 18.68 (CH_3), 14.64 (ester CH_3).

Diethyl-4-(2-chlorophenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1b**)

IR ν (cm^{-1}) = 2939.02, 1691.57, 1626.74, 1465.90, 1224.80, 1083.99, 837.11, 744.52; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.19–7.16 (m, Ar-H), 3.98–3.95 (q, 4H, CH_2 -ester), 3.69 (s, $^1\text{H}, \text{H-4}$), 2.24 (s, 6H, CH_3), 1.15–1.13 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.32 (C=O), 146.68 (C-2,6), 145.83–127.62 (Ar-C), 102.22 (C-3,5), 61.48 (CH_2 -ester), 37.20 (C-4), 18.53 (CH_3), 14.63–14.47 (ester CH_3).

Diethyl-4-(4-chlorophenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1c**)

IR ν (cm^{-1}) = 2972.31, 2818.00, 2810.28, 1687.71, 1578.38, 1224.80, 1209.37 1055.06, 806.25; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.95–7.54 (m, Ar-H), 4.27–4.24 (q, 4H, CH_2 -ester), 4.08 (s, $^1\text{H}, \text{H-4}$), 2.44 (s, 6H, CH_3), 1.26–1.24 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.30 (C=O), 161.44 (C-2,6), 140.47–131.58 (Ar-C), 103.26 (C-3,5), C-4 merged with DMSO region, 56.50 (CH_2 -ester), 18.99 (CH_3), 14.18 (ester CH_3).

Diethyl-4-(4-bromophenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1d**)

IR ν (cm^{-1}) = 3051.39, 2956.87, 2831.50, 1689.64, 1579.61, 1392.61, 1271.09, 1209.37, 1037.70, 804.32; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.86–7.84 (m, Ar-H), 4.25–4.22 (q, 4H, CH_2 -ester), 4.09 (s, $^1\text{H}, \text{H-4}$), 2.44 (s, 6H, CH_3), 1.19–1.17 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.08 (C=O), 162.04 (C-2,6), 140.62–132.53 (Ar-C), 104.61 (C-3,5), 61.84 (CH_2 -ester), C-4 merged with DMSO region, 26.50 (CH_3), 14.44 (ester CH_3).

Diethyl-4-(4-fluorophenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1e**)

IR ν (cm^{-1}) = 2960.73, 2347.37, 1693.50, 1647.52, 1473.62, 1212.23, 1099.43, 1070.49, 812.03; ^1H NMR (500 MHz, DMSO): δ ppm: 7.29–7.00 (m, Ar-H), 4.85 (s, 1H, H-4), 4.00–3.97 (q, 4H, CH_2 ester), 2.26 (s, 6H, CH_3), 1.15–1.13 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ ppm: 167.49 (C=O), 165.72, 167.31 (C-2,6), 144.90–129.56 (Ar-C), 102.23 (C-3,5), 59.48 (CH_2 -ester), 38.75 (C-4), 18.61 (CH_3), 14.61 (ester CH_3).

Diethyl-4-(3,4,5-trimethoxyphenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1f**)

IR ν (cm^{-1}) = 2962.66, 2837.29, 1695.43, 1587.42, 1460.11, 1421.54, 1336.67, 1313.52, 1226.73, 114.86, 999.13, 833.25, 717.52; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.24 (s, Ar-H), 4.25–4.22 (q, 4H, CH_2 -ester), 4.08 (s, 1H, H-4), 3.86 (s, 6H, Ar- m - OCH_3), 3.76 (s, 3H, Ar- p - OCH_3), 2.29 (s, 6H, CH_3), 1.23–1.21 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.88 (C=O), 153.78 (C-2,6), 153.39–132.11 (Ar-H), 107.15 (C-3,5), 61.74 (CH_2 -ester), 60.64–56.30 (Ar- OCH_3), C-4 merged with DMSO region, 26.30 (CH_3), 14.42 (ester CH_3).

Diethyl-4-(3,4-dimethylphenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1g**)

IR ν (cm^{-1}) = 2939.52, 2339.65, 1697.36, 1624.30, 1377.17, 1234.44, 1087.85, 804.32; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.8–7.6 (m, Ar-H), 3.98–3.95 (q, 4H, CH_2 -ester), 3.88 (s, 1H, H-4), 2.42–2.25 (m, 12H, Ar- CH_3 and CH_3), 1.20–1.18 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.77 (C=O), 152.12 (C-2,6), 142.12–128.99 (Ar-C), 109.64 (C-3,5), 58.24 (CH_2 -ester), C-4 merged with DMSO region, 19.90–19.73 (Ar- CH_3), 19.66 (CH_3), 14.75 (ester CH_3).

Diethyl-4-(4-methylphenyl)-2,6-dimethyl-4H-pyran-3,5-dicarboxylate (**1h**)

IR ν (cm^{-1}) = 2961.73, 2533.04, 2342.03, 1687.15, 1403.07, 1254.94, 1211.30, 1087.56, 950.91, 819.83; ^1H NMR (500 MHz, DMSO- d_6) δ (ppm): 7.84–7.45 (m, Ar-H), 4.81 (s, 1H, H-4), 4.15–4.12 (q, 4H, CH_2 ester), 2.36 (s, 3H, Ar- CH_3), 2.20 (s, 6H, CH_3), 1.19–1.17 (t, 6H, ester CH_3); ^{13}C NMR (500 MHz, DMSO- d_6) δ (ppm): 167.77 (C=O), 163.49 (C-2,6), 145.59–130.13 (Ar-C), 102.44 (C-3,5), C-4 merged with DMSO region, 61.22 (CH_2 -ester), 21.59 (Ar- CH_3), 18.67 (CH_3), 14.65 (ester CH_3).

3. Results and Discussion

Perlite, an inexpensive volcanic mineral consisting mainly of alumina and silica has been used as a solid support in the fabrication of the heterogeneous catalyst NbCl_5 /perlite. NbCl_5 /perlite was prepared via a simple dispersion method. The novel NbCl_5 /perlite catalyst was validated using FT-IR, SEM-EDS, XRD, TGA and BET techniques. The results acquired from these methods supported the formation of NbCl_5 /perlite successfully.

3.1. Characterisation of NbCl_5 /Perlite

The NbCl_5 -impregnated solid acid catalyst loading over the surface of perlite was examined by FT-IR studies. The FT-IR spectra of pure perlite, NbCl_5 and NbCl_5 /perlite are shown in Figure 1. FT-IR spectra of pure perlite and NbCl_5 /perlite show absorption bands between 1030 and 1100 cm^{-1} , which were assigned to Si–O stretching vibrations of the O–Si–O group. Furthermore, an O–Si–O bending vibration was observed between 400 and 500 cm^{-1} . The stretching and bending modes of the OH groups on the surface of perlite (mainly Si–OH groups and surface-adsorbed water molecules) were depicted between 3500–3630 cm^{-1} and 1510–1630 cm^{-1} , respectively. When comparing the spectrum of NbCl_5 (Figure 1c) with NbCl_5 /perlite, the additional band at 686 cm^{-1} in NbCl_5 /perlite (Figure 1d) corresponds to Nb compound [31].

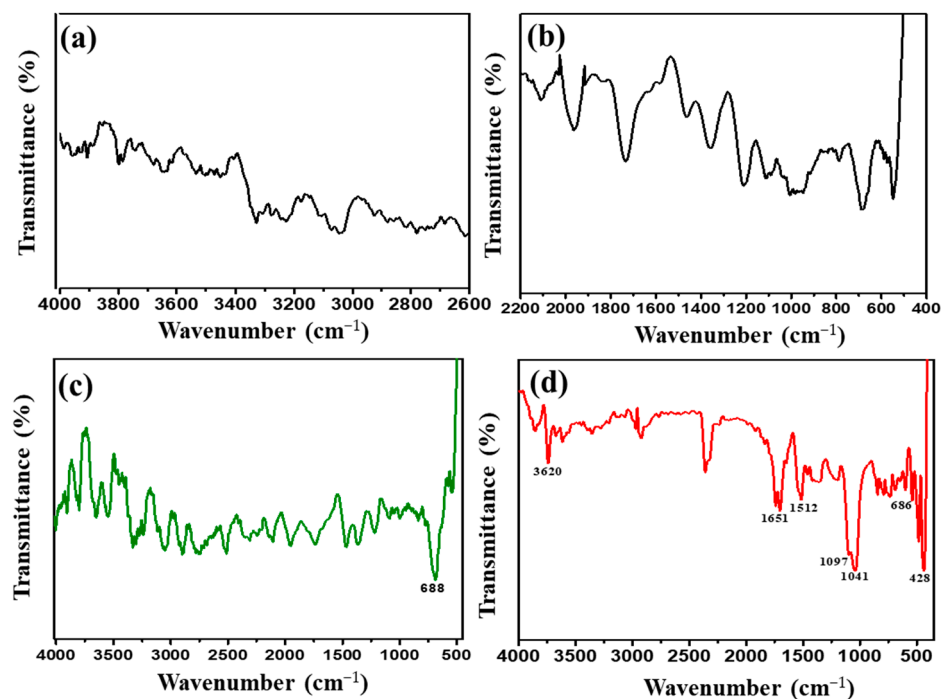


Figure 1. FT-IR Spectra of perlite (a,b), NbCl₅ (c) and NbCl₅/perlite (d).

In order to investigate the crystalline nature of the modified perlite, the X-ray diffraction pattern of NbCl₅/perlite is given Figure 2b, along with pure perlite (Figure 2a) for comparison. The broad peak at the 2θ value of 26° indicated the amorphous nature of perlite (Figure 2). The XRD pattern of NbCl₅/perlite (Figure 2b) is almost comparable with pure perlite, and the additional peaks at the 2θ values of 8.9°, 18.1°, 31.7°, 45.5° and 56.5° that are attributed to Nb [32,33] (partial oxidation of NbCl₅ into its oxides form) reveal the successful immobilization of NbCl₅ onto the perlite surface.

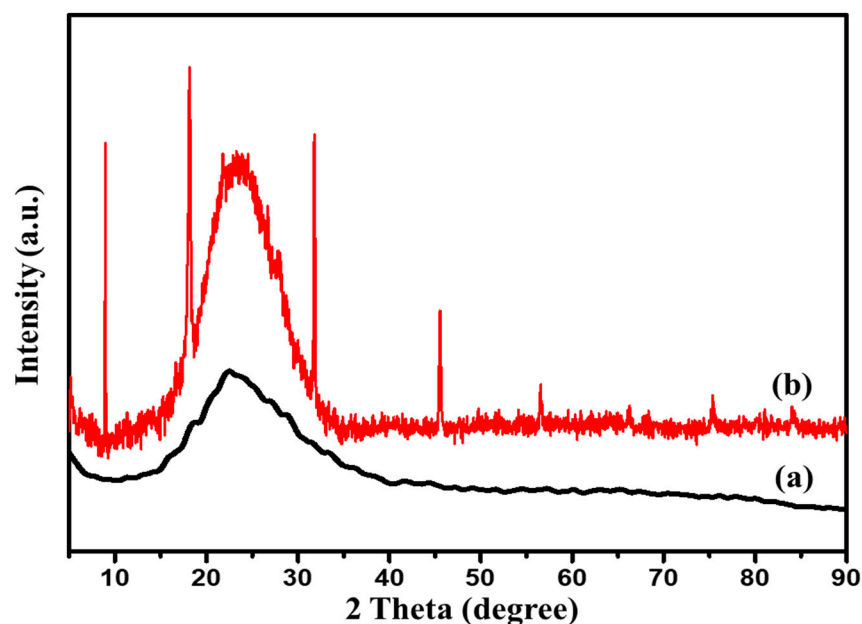


Figure 2. XRD patterns of perlite (a) and NbCl₅/perlite (b).

The surface morphology of the catalyst prepared was examined by SEM technique. Figure 3 depicts the SEM images in different magnifications signifying the irregular shape,

layer-like arrangement and surface roughness of NbCl₅/perlite. The energy-dispersive spectra (EDS) of perlite [30] and NbCl₅/perlite are given in the supporting information (Figure S17). The energy-dispersive spectrum of NbCl₅/perlite implies the existence of Fe, Na Si, Al, O, K, and Ca, as in case of pure perlite, with further peaks at 2.1 and 2.2 KeV for Nb. The elemental percentage composition of NbCl₅/perlite is given in Table 1. From the table, approximately 9.59% of Nb is loaded in pure perlite and the effective loading of NbCl₅ on perlite is confirmed.

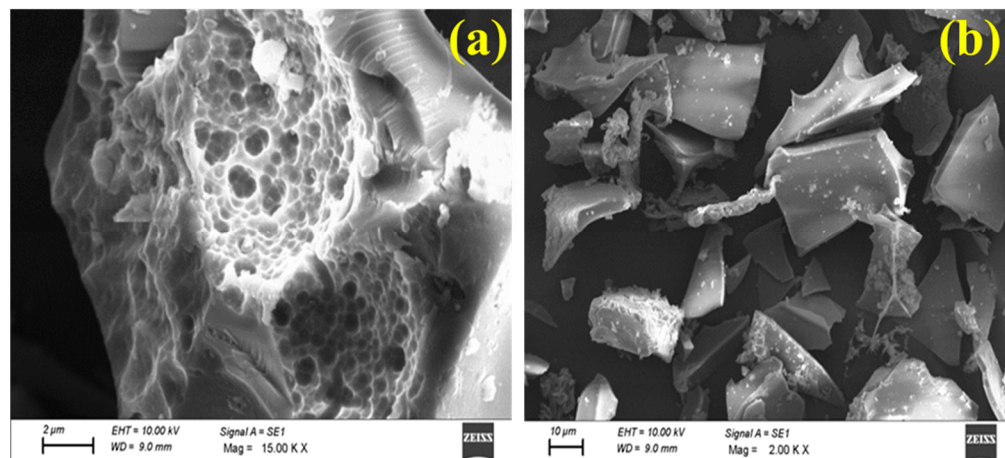


Figure 3. SEM images of NbCl₅/perlite 2 μm (a) and 10 μm (b).

Table 1. Percentage composition of elements in NbCl₅/perlite.

Sample	O	Fe	Na	Al	Si	K	Ca	Nb
Perlite	20.28	1.04	3.09	11.05	60.24	4.33	0.82	-
NbCl ₅ /Perlite	41.29	0.96	2.28	6.48	35.53	3.46	0.97	9.59

The thermal stability of the catalyst was examined by the Thermogravimetric analysis (TGA). The TGA of perlite and NbCl₅/perlite are shown in Figure 4a,b, respectively. For bare perlite, there was no significant mass loss observed until 600 °C, with the initial mass loss observed (about 0.28%) corresponding to the removal of adsorbed water molecules. From Figure 4b, an initial steady mass loss of 3.1% until 200 °C corresponded to the removal of water molecules; then, from 200–550 °C, there is a gradual loss of approximately 6% NbCl₅ from the solid surface, followed by a reliable mass loss of 6.4% from 550–590 °C, which is owing to the rapid removal of NbCl₅ [32]. An additional mass loss above 590 °C might be a result of the dehydroxylation of perlite, as anticipated (Figure S18) [33]. However, NbCl₅/perlite was synthesized at 250 °C, and no significant loss of NbCl₅ occurred. In addition, the partial oxidation of NbCl₅ was evidenced by XRD measurements. The surface analysis of the prepared catalyst was studied using BET analysis. Surface area, pore volume and diameter were analyzed from BET results and were found to be significantly lower than pure perlite, possibly due to the loading of NbCl₅ over perlite (Table 2).

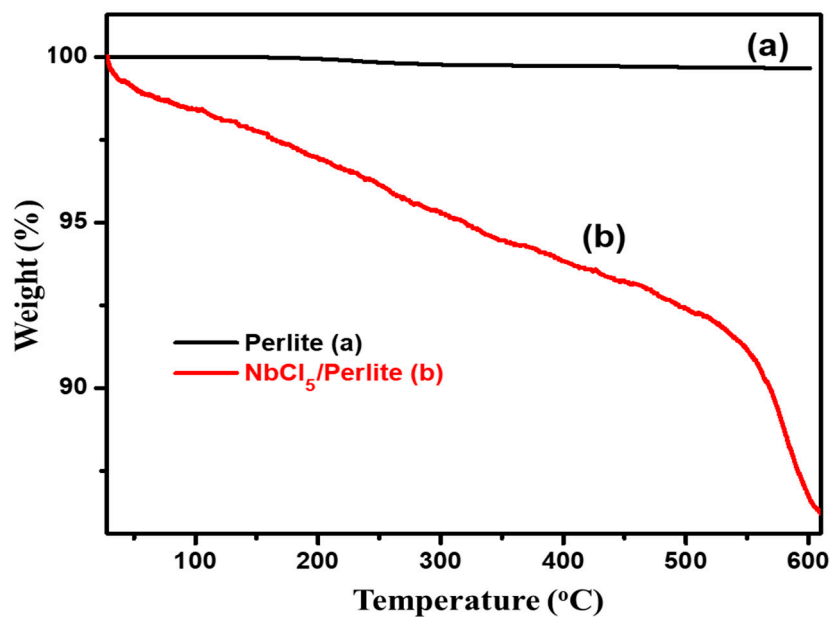


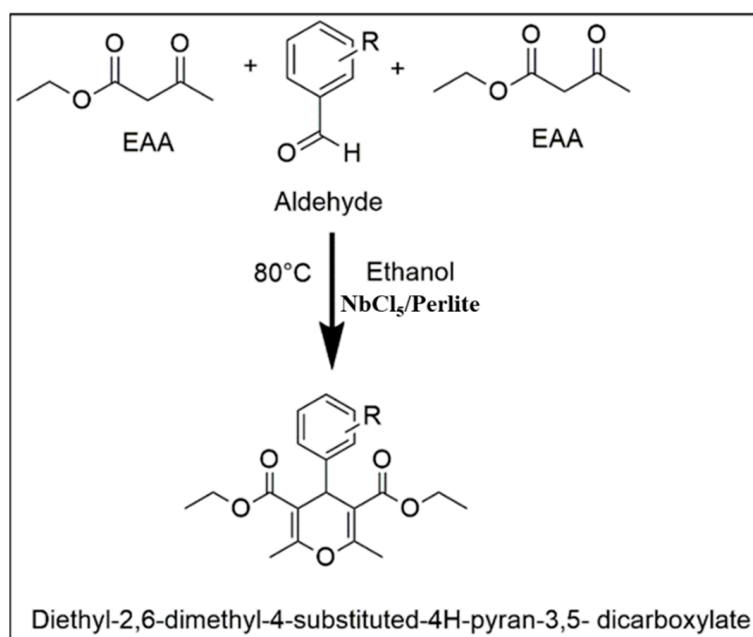
Figure 4. TGA spectra of perlite (a) and NbCl₅/perlite (b).

Table 2. Surface parameters of perlite and NbCl₅/perlite.

Catalyst	Surface Area (m ² /g)	Pore Volume (cm ³ /g)	Pore Diameter (Å ^o)
Perlite	1.874	2.899×10^{-3}	3.910
NbCl ₅ /Perlite	1.217	1.461×10^{-2}	3.473

3.2. Synthesis of Diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate and Optimization Process

Pyrans establish an important class of ring oxygen containing heterocycles, and they are important biologically active compounds with good antibacterial, antitumor and antibiotic effects [24,25]. The viability of the NbCl₅/perlite catalyst was studied by preparing 4-substituted pyrans from EAA (Ethyl acetoacetate) and aromatic aldehydes in its presence (Scheme 1).



Scheme 1. Synthesis of Pyrans.

The optimization of pyran synthesis was originally carried out using EAA and benzaldehyde in order to yield diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate in the presence of NbCl₅/perlite. To study the effectiveness of different wt % of NbCl₅/perlite, 5–25 wt% of NbCl₅/perlite was prepared and tested in the synthesis of pyrans (Figure 5) and the efficiency of the loading was validated. The yields obtained with various wt% catalysts were compared. The wt% NbCl₅ increased from 5 to 10%, and the percentage of yield also increased from 89 to 95. Further, with the increase in the wt% of NbCl₅ over perlite, the yield was slightly decreased (beyond 10 wt%). The best yield was obtained with 10 wt % NbCl₅-loaded perlite. It has been noted that only a 7% enhancement in the yield was observed from 5 wt% to 10 wt% of NbCl₅/perlite. The 7% enhancement in the yield is not the subject of negotiation, and even 1% of the impurity will affect the purity of the synthesized compounds. Therefore, we determine that the 10 wt% NbCl₅ is the optimum concentration over perlite for this reaction. Under the same conditions, the reaction was performed with pure NbCl₅ and gave a 78% yield. Henceforth, the preparation of substituted pyrans was carried out with 10 wt% NbCl₅/perlite.

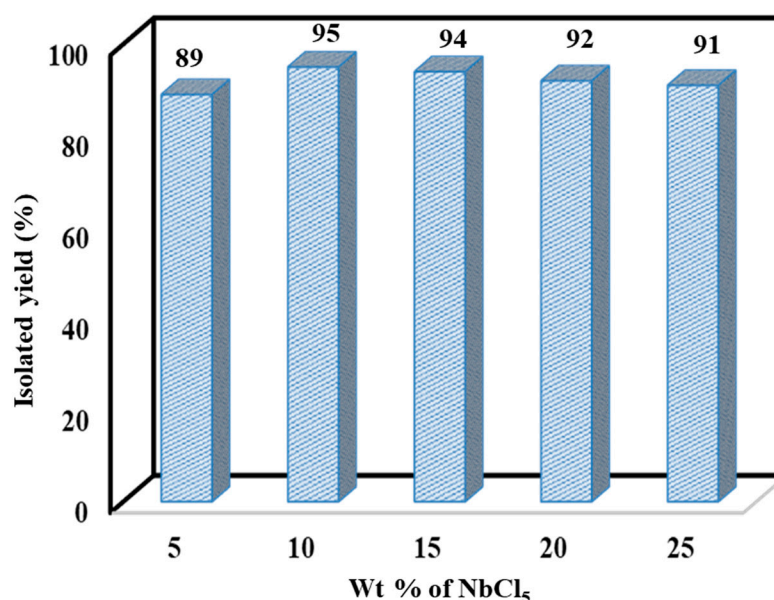


Figure 5. Optimization of NbCl₅ on perlite for the synthesis of diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate.

The condensation reaction of benzaldehyde (2 mmol) and ethyl acetoacetate (4 mmol), catalyzed by NbCl₅/perlite, was performed as a representative reaction for the pyrans preparation with varying amounts of catalyst, from 0.01 to 0.20 g (Table 3). There was no formation of the product observed when the reaction was performed without catalyst. When the concentration of the catalyst was increased from 0.01 to 0.15 g, the formation of the diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate increased from 87 to 95% (Table 3). This may be due to an increase in the number of NbCl₅/perlite particles. When the catalyst was above 0.15 g, a slight decrease in the yield was observed (0.2 g, 93%). The reaction carried out with 0.15 g of catalyst produced a significant yield. The optimum catalyst loading was found to be 0.15 g for the formation of diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate.

Table 3. Effect of catalyst loading in the synthesis of diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate.

S.No.	Catalyst	Catalyst Amount (g)	^b Yield %
1.	-	-	None
2.	NbCl ₅ /perlite	0.01	87
3.	NbCl ₅ /perlite	0.05	89
4.	NbCl ₅ /perlite	0.1	92
5.	NbCl ₅ /perlite	0.15	95
6.	NbCl ₅ /perlite	0.2	93

Reaction Conditions: Benzaldehyde (2 mmol), EAA (4 mmol), Solvent = ethanol (\approx 5–10 mL), Time = 15 min at 80 °C; ^b Isolated Yield.

The reaction temperature of the catalytic activity of the NbCl₅/perlite catalyst was studied at temperature levels from 60 to 120 °C (Table 4). This study was performed to determine the effect of temperature on the diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate formation with a standardized catalytic amount. The formation of the product was found to be a little low, at 60 °C (Table 4, entry 1, 72%). The product formation enhanced with an increase in the reaction temperature from 60 to 80 °C (Table 4, entry 3, 95%). However, on increasing the reaction temperature further to 120 °C, no significant variation in the yield was observed (Table 4, entries 4–7). Hence, 80 °C is the optimum temperature for this reaction. Thus, the temperature was maintained at 80 °C and the analogous reaction was carried out using different solvents, namely dichloromethane (DCM), ethanol (EtOH), acetonitrile (CH₃CN) and water (H₂O), under the same conditions in order to study the effect of the solvent (Table 5). In the solvent ethanol, the reaction produced a quantitative yield (Table 5, entry 2, 95%) of product within 15 min. It was found that the reaction in water required a longer time (12 h) to give a 65% (Table 5, entry 4) yield of product. DCM and CH₃CN gave moderate yields, and also required a longer time.

Table 4. Effect of temperature in the synthesis of diethyl-2,6-dimethyl-4-substituted -4H-pyran-3,5-dicarboxylate.

S.No.	Temperature (°C)	^b Yield %
1.	60	72
2.	70	86
3.	80	95
4.	90	95
5.	100	95
6.	110	95
7.	120	95

Reaction Conditions: Benzaldehyde (2 mmol), EAA (4 mmol), Solvent = ethanol (\approx 5–10 mL), Time = 15 min; ^b Isolated Yield.

Table 5. Effect of solvent in the synthesis of diethyl 2,6- dimethyl-4-substituted-4H-pyran-3,5- dicarboxylate.

S.No.	Solvents Used	^b Yield%	Time
1.	Dichloromethane	80	10 h
2.	Ethanol	95	15 min
3.	CH ₃ CN	70	8 h
4.	Water	65	12 h

Reaction Conditions: Benzaldehyde (2 mmol), EAA (4 mmol), Time = 15 min; ^b Isolated yield.

The reaction carried out in ethanolic medium produced a high yield within 15 min; therefore, ethanol was chosen as the solvent for the further reactions. Thence, the pyran synthesis in the presence of 0.15 g of the catalyst at 80 °C and using ethanol as a solvent was found to be in good agreement. Owing to the plausible outcomes, an identical reaction

was performed on several aromatic aldehydes in order to examine the fluctuation in the time and yield of the substituted pyrans with different substituents (Table 6).

Table 6. Preparation of diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate using NbCl_5 /perlite.

Product	R	Product Structure	Yield (%)	Time (min)	Melting Point ($^{\circ}\text{C}$)	Ref. M.Pt ($^{\circ}\text{C}$)
1a	H		95	15	70–71	72–73 [34]
1b	2-Cl		91	10	60–61	62–64 [35]
1c	4-Cl		93	10	62–64	61–63 [34]
1d	4-Br		94	10	82–84	81–83 [34]
1e	4-F		92	10	80–82	81–83 [36]
1f	3,4,5-(OCH_3) ₃		91	15	85–86	86–87 [37]
1g	3,4-(CH_3) ₂		89	25	80–82	-
1h	4-(CH_3)		85	20	75–76	79 [35]

It is evident from Table 6 that the proposed scheme is applicable for a variety of aldehydes. All the reactions with substituted aldehydes and using ethanol as a solvent proceeded very cleanly at 80 °C, and no undesirable side-reactions were observed; however, the yields were slightly influenced by the substituents. Table 6 shows that electron-withdrawing groups, such as chloro, bromo and fluoro, favored the formation of the product (Table 6, products 1b–1e). In contrast, electron-donating groups (Table 6, products 1f–1h) gave a slightly lower yield.

The efficiency of the prepared catalyst was correlated with the available results (Table 7). Our results are comparable with other methods, and our method gave high yields with a shorter reaction time. The catalyst used in the reaction was removed by simple filtration, and the catalyst's ability to be reused for the reaction of pyrans from benzaldehyde has been estimated. The catalyst was separated by simple filtration. The product was washed with hot ethanol, dried and reused for further reaction. The reusability of the catalyst was remarkable up to five runs without abating its activity (Table 8). The Lewis acidity of the catalyst plays an important role in the reaction mechanism [38]; this is a plausible mechanism that involves Knoevenagel condensation, Michael addition, and then the intermolecular ring closure that causes the formation of substituted-4H-pyran derivatives catalyzed by NbCl₅/perlite [35]. It is probable that a Knoevenagel condensation reaction occurred between aromatic aldehyde with the first equivalent of EAA and formed a benzylidene derivative; due to the keto-enol tautomerism in the ester, the aromatic aldehyde predominantly attacked the carbon, and it is believed that complexation occurred between NbCl₅/perlite and the aromatic aldehydes. Due to this interaction, the carbonyl carbon of the aromatic aldehyde becomes more electrophilic, and the electron-deficient carbonyl carbon can easily be attacked by the keto-enol tautomerism of the ester. The formed intermediate reacts with the second equivalent of the ester (Michael addition), and is followed by the ring closing to obtain pyran derivatives.

Table 7. Effectiveness of NbCl₅/perlite compared with other reported catalysts in the synthesis of 4-substituted pyrans.

S.No.	Catalyst ^a	Catalyst Amount	Conditions	Time	Yield %	References
1.	PPA-SiO ₂	0.1 g	100 °C	10 min	90	[36]
2.	SM-550	25 mg	Reflux	80 min	61	[39]
3.	TUD	10 mol%	70 °C	30 min	90	[40]
4.	SiO ₂ -Pr-SO ₃ H	0.03 g	Reflux	35 min	85	[37]
5.	NbCl ₅	1 mol%	RT	72 h	76	[35]
6.	NbCl ₅ /Perlite	0.15 g	80 °C	15 min	95	Our work

Catalyst ^a PPA-SiO₂ = silica gel-supported polyphosphoric acid; SM-550 = Sulfated MCM-41 nanoparticles prepared at 550 °C; TUD = Thiourea dioxide organic catalyst; SiO₂-Pr-SO₃H = Sulfonic acid functionalized silica.

Table 8. The reusability of the NbCl₅/perlite in the synthesis of diethyl 2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate.

Run	1	2	3	4	5
Yield (%)	95	95	93	91	91

4. Conclusions

In conclusion, an effective solid acid catalyst, NbCl₅/perlite, was introduced for the synthesis of diethyl-2,6-dimethyl-4-substituted-4H-pyran-3,5-dicarboxylate. The yields obtained with various wt% of catalyst were compared, and it was found that the best yield was obtained with 10 wt% of NbCl₅-loaded perlite. For the present reaction, the optimum catalyst loading was found to be 0.15 g. The reaction carried out in ethanolic (EtOH) medium produced a high yield within 15 min when compared with dichloromethane, CH₃CN and H₂O. The notable features of the proposed scheme are that the catalyzed reaction tends to proceed in less time, that it has a remarkable yield and that the catalysts

are easily separated at the end of the reaction. It was found that the catalyst had the ability to be used in several reaction cycles and that it could undergo five runs without any notable change in the activity. Thence, we have demonstrated that the catalyst NbCl₅/perlite is benign and acts as a better activator for the transformation of pyran and its analogues.

Supplementary Materials: The following supporting information can be downloaded at: <https://www.mdpi.com/article/10.3390/su15043678/s1>, The data that support the findings of this study are available. Spectral data of the compounds Figure S1. ¹H NMR spectrum of **1a**, Figure S2. ¹³C NMR spectrum of **1a**, Figure S3. ¹H NMR spectrum of **1b**, Figure S4. ¹³C NMR spectrum of **1b**, Figure S5. ¹H NMR spectrum of **1c**, Figure S6. ¹³C NMR spectrum of **1c**, Figure S7. ¹H NMR spectrum of **1d**, Figure S8. ¹³C NMR spectrum of **1d**, Figure S9. ¹H NMR spectrum of **1e**, Figure S10. ¹³C NMR spectrum of **1e**, Figure S11. ¹H NMR spectrum of **1f**, Figure S12. ¹³C NMR spectrum of **1f**, Figure S13. ¹H NMR spectrum of **1g**, Figure S14. ¹³C NMR spectrum of **1g**, Figure S15. ¹H NMR spectrum of **1h**, Figure S16. ¹³C NMR spectrum of **1h**, Figure S17. Energy dispersive spectra of perlite (a) and NbCl₅/perlite (b) and Figure S18. TGA spectrum of NbCl₅/perlite up to 1200 °C.

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