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PMA/SiO_2 as efficient, cost-effective and recyclable catalytic system for the synthesis of highly substituted pyrroles

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Abstract

A mild and efficient method for the synthesis of highly substituted pyrroles is described using phosphomolybdic acid supported on silica gel as a reusable catalyst. The use of PMA supported on silica gel makes it quite simple, more convenient and environmentally benign. This method offers several advantages such as high conversions, short reaction times, cleaner reaction profiles and the use of inexpensive and readily available catalyst.

Keywords: Three-component reaction; Pyrroles; Heteropoly acid; Heterogeneous catalysis

1. Introduction

The pyrrole nucleus is found in various biologically active molecules including the blockbuster drug atorvastatin as well as important anti-inflammatants, antitumor agents and immunosuppressants [1–5], and as structural components in polymers [6–8], and as intermediates in organic synthesis [9]. Therefore, considerable attention has been paid to develop efficient methods for the synthesis of pyrroles. Consequently, a large number of methods have been developed for their synthesis, which include Knorr [10], Paal–Knorr [11], and Hantzsch syntheses [12]. These methodologies typically require the preparation of the precursors prior to cyclization, which can complicate both the synthesis and structural modification of the substituted pyrroles. This has stimulated significant interest in the design of new synthetic routes to pyrroles, including several efficient multi-component reactions [13–16] and metal-catalyzed routes [17–24]. In addition, the three-component reaction of aldehyde, amine and nitroalkene has been reported previously using $Sm(Oi\text{-}Pr)_3$ and $InCl_3/SiO_2$ to synthesize substituted pyrroles [25–28]. In spite of a large number of methods reported for the synthesis of pyrroles, there is always considerable demand in exploring more milder, convenient, practical and benign reagents for their synthesis. Therefore, the developments of simple, convenient and practical procedures for the synthesis of pyrroles continue to be a challenging endeavor in synthetic organic chemistry. Recently, a great attention has been focused on the use of phosphomolybdic acid as environmentally friendly catalyst in organic synthesis. In addition to its abundance, economical and safety reasons, phosphomolybdic acid has naturally become as a substitute and an alternative environmentally benign catalyst. Phosphomolybdic acid (PMA) belongs to the class of heteropoly acids (HPA). Catalysis using HPAs and related polyoxometalate compounds is a field of growing importance [29,30]. HPAs are commercially cheap and environmentally friendly catalysts. They exhibit high activities and selectivities and allow cleaner processes than conventional catalysts. HPAs are promising solid acid bifunctional catalysts under homogeneous as well as in heterogeneous conditions. HPAs are very strong acids, approaching the super acid region, with a Bronsted acidity greatly exceeding that of ordinary mineral acids and solid acid catalysts. HPAs are several times more active than H_2SO_4, TsOH, $BF_3{\cdot}OEt_2$ and $ZnCl_2$ [31]. It has been shown that in organic media, the molar catalytic activity of HPAs is often 100–1000 times higher than that of H_2SO_4 [32,33]. This makes it possible to carry out a catalytic process at low concentrations and at lower temperatures. Supported HPAs are more active than typical solid acids. Acidic or neutral substances such as silica gel [31], active carbon [34,35] or an acidic ion-exchange resin [36] are suitable supports, the more commonly used being silica gel [31]. Synthetically, various

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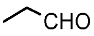
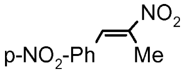
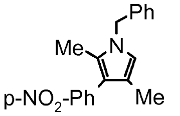
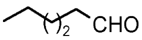
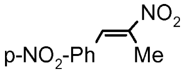
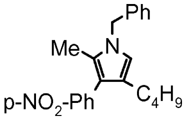
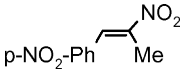
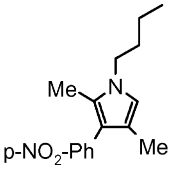
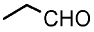
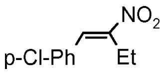
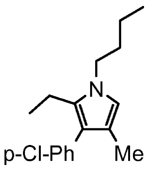
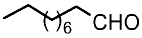
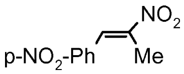
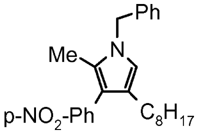
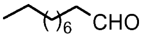
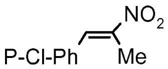
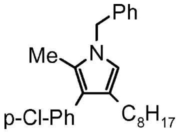
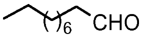
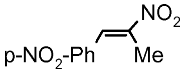
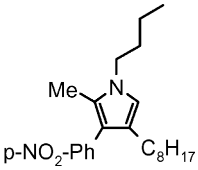
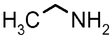
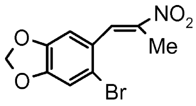
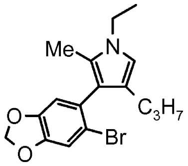
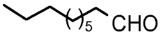
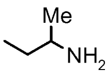
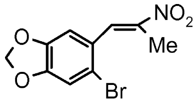
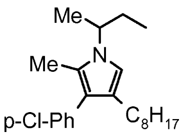
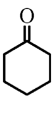
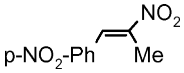
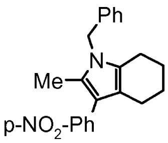
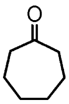
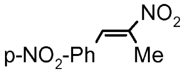
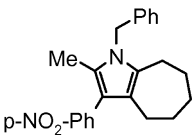
Table 1
PMA/SiO_2 catalyzed synthesis of alkyl pyrroles *via* a three-component reaction

Entry	Carbonyl compound (**1**)	Amine (**2**)	Nitroalkene (**3**)	Product[a] (**4**)	Time (h)	Yield (%)[b]
a					1.5	92 [25]
b					1.5	86
c		*n*-Bu-NH_2			1.5	90
d		*n*-Bu-NH_2			2.0	88
e					1.5	90
f					1.5	90 [25]
g		*n*-Bu-NH_2			1.5	86 [25]
h					2.0	85
i					2.0	78
j					1.5	90
k					1.5	89