



Phosphomolybdic acid: a highly efficient solid acid catalyst for the synthesis of *trans*-4,5-disubstituted cyclopentenones

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ABSTRACT

The furan-2-yl(phenyl)methanol undergoes smooth aza-Piancatelli rearrangement with aryl amines in the presence of 0.03 mol % phosphomolybdic acid in acetonitrile under reflux conditions to afford the corresponding *trans*-4,5-disubstituted cyclopentenone derivatives in good yields with high selectivity in short reaction time.

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The cyclopentenone structural units are present in various natural products such as jasmonoids, cyclopentanoid antibiotics and prostaglandins (Fig. 1).^{1–4} They are also useful building blocks for the synthesis of biologically active molecules⁵ such as cepalotaxine, stemonamine, helichlorine, histrionicotoxin, and carbocycles.⁶ Consequently, several methods, for example, Nazarov cyclization, Pauson-Khand reaction have been developed for the synthesis of cyclopentenone derivatives.⁷ Of these, Piancatelli rearrangement is a simple and direct method for the synthesis of cyclopentenone derivatives.⁸ In particular, a few processes have been reported for the synthesis of 4-aminocyclopentenones via multi-step sequence.⁹ Recently, an elegant method has been reported for the synthesis of 4-aminocyclopentenone derivatives by means of aza-Piancatelli rearrangement using lanthanide triflates.¹⁰ However, the use of cost-effective solid acids would make the process more practical in view of environmental perception. Therefore, the development of novel and efficient reagents for the synthesis of amino cyclopentenone derivatives would expand the scope of aza-Piancatelli rearrangement in drug discovery process.

Recently, the use of heteropoly acids (HPAs) has received substantial attention in organic synthesis,¹¹ because of their economic viability, high catalytic activity, and ease of handling. They are non-toxic and allow cleaner reactions in comparison to conventional catalysts, hence, are regarded as greener catalysts.¹² Also, heteropoly acids are potent solid acids and act as bifunctional catalysts in homogeneous as well as in heterogeneous conditions. They are

most attractive, because of their unique properties such as well-defined structure, Bronsted acidity, ability to modify their acid–base, and redox properties by changing their chemical composition (substituted HPAs), ability to accept and release electron and high proton mobility.¹³ Among various heteropoly acids, phosphomolybdic acid (PMA, H₃PMO₁₂O₄₀) is one of the less expensive and a commercially available solid acid catalyst.¹⁴ However, there are no reports on the use of phosphomolybdic acid for the synthesis of *trans*-4,5-disubstituted cyclopentenones via aza-Piancatelli rearrangement.

Following our interest on the catalytic application of solid acid catalysts,¹⁵ we herein report, a simple and efficient method for the

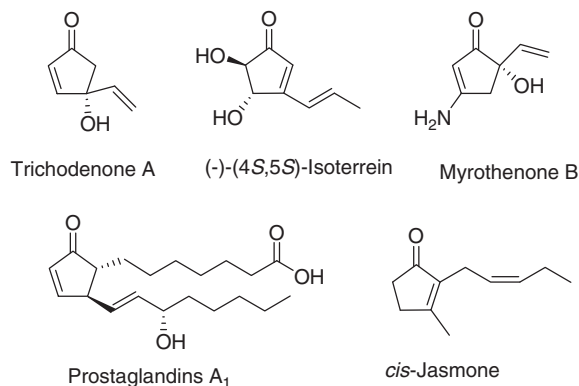
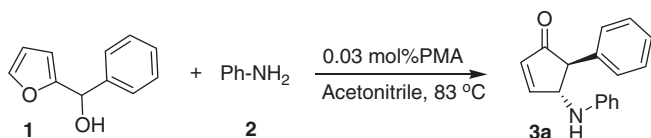


Figure 1. Representative examples of cyclopentenone containing natural products.

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Scheme 1. Reaction of furan-2-yl(phenyl)methanol with aniline.

synthesis of disubstituted cyclopentenones from aryl amines and furan-2-yl(phenyl)methanol using heteropoly acid as a catalyst. Initially, we attempted the reaction of furan-2-yl(phenyl)methanol (1) with aniline (2) in the presence of 0.03 mol % phosphomolybdic acid. Interestingly, the reaction proceeded smoothly in acetonitrile at 83 °C and the desired product 3a was obtained in an 80% yield (Scheme 1, Table 1).

The stereochemistry of 3a was found to be *trans* which was assigned on the basis of coupling constants of the ring protons in the ¹H NMR spectrum and also by comparison with authentic samples.¹⁰ The excellent catalytic activity of heteropoly acid in aza-Piancatelli rearrangement prompted us to investigate its use in the condensation of furan-2-yl(phenyl)methanol with various aryl amines. Interestingly, a variety of aryl amines such as 4-fluoro-

4-chloro-, 2-bromo-, 4-methoxy-, and 2-methyl anilines underwent smooth coupling with furan-2-yl(phenyl)methanol to afford the corresponding *trans*-4,5-disubstituted cyclopentenone derivatives in good yields. Both electron-rich as well as electron-deficient aromatic amines participated well in this reaction. The scope and generality of this process is illustrated with respect to various aryl amines and furan-2-yl(phenyl)methanol and the results are presented in Table 1.¹⁶ As seen from Table 1, halogen substituted aromatic amines gave comparatively higher yields than methoxy- and methyl-substituted aromatic amines. Furthermore, *ortho*-substituted aromatic amines also gave the respective cyclopentenone derivatives in good yields. However, 2,6-disubstituted aromatic amines gave S_N2 substituted product instead of aza-Piancatelli rearranged product under similar conditions. Furthermore, the reaction did not proceed with aliphatic amines like benzyl amine and phenylethyl amine under similar conditions.

Mechanistically, the reaction is assumed to proceed by the activation of furan-2-yl(phenyl)methanol by the heteropoly acid. Subsequent nucleophilic attack of the aryl amine on oxocarbenium ion (B) generates cyclic aminol (C). Acid catalyzed rearrangement of C followed by the electrocyclicization of E would give the desired product as shown in Scheme 2.

Table 1
PMA-catalyzed synthesis of 4,5-disubstituted cyclopentenones

Entry	Substrate (1)	Arylamine (2)	Product ^a (3)	Time (min)	Yield ^b (%)
a				55	80
b				52	85
c				60	81
d				50	85
e				45	89
f				55	83
g				45	90

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