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## Double catalytic effect of $(\text{PhNH}_3)_2\text{CuCl}_4$ in a novel, highly efficient synthesis of 2-oxo- and thioxo-1,2,3,4-tetrahydropyrimidines

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**Abstract:** An innovative route for the construction of 2-oxo- and thioxo-1,2,3,4-tetrahydropyrimidines was delineated through a multicomponent reaction under Biginelli conditions, starting from different aromatic aldehydes,  $\beta$ -keto esters and urea or thiourea. The proper choice of the copper complex  $(\text{PhNH}_3)_2\text{CuCl}_4$ , as a novel homogeneous catalyst, enabled a facile, efficient, and inexpensive reaction under mild experimental conditions. Moreover, the first application of this complex salts in organic synthesis ever is presented. The obtained products were of high purity, and could be easily isolated from the reaction mixture in good to excellent yields. Moreover, compared to the classical Biginelli reaction conditions, the present method has the advantages of higher yields and experimental and work-up simplicity. To illustrate the joint catalytic action of the  $\text{Cu}^{2+}$  and phenylammonium ions, two key steps of Biginelli reaction were examined using the M06 functional.

**Keywords:** aldehydes; multicomponent reactions; heterocycles; homogeneous catalysis; density functional calculations.

### INTRODUCTION

The 2-oxo- and thioxo-1,2,3,4-tetrahydropyrimidines (3,4-dihydropyrimidine-2(1*H*)-thi(ones)) are a class of compounds that have attracted the enormous interest of the medicinal chemistry community in recent years. Dihydropyrimidinones are very attractive compounds because of the wide range of their biological activities, such as: antihypertensive,<sup>1–4</sup> anti-HIV,<sup>5</sup> antitumor,<sup>6–10</sup> anti-epileptic,<sup>11</sup> antimalarial,<sup>12</sup> anti-inflammatory,<sup>13</sup> antitubercular,<sup>14</sup> antioxidative<sup>15</sup> and anti-HBV (hepatitis B virus).<sup>16</sup> In addition, they act as potassium channel blockers<sup>17,18</sup> and  $\alpha_{1A}$  adrenergic receptor antagonists.<sup>19</sup> Therefore, the pre-

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