

# SYNLETT Spotlight 412

## PEG 400

Compiled by Udaya Pratap Singh



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Udaya Pratap Singh was born in Allahabad, Uttar Pradesh, India. He received his B. Pharm. and M. Pharm. degree from Allahabad Agricultural Institute, Allahabad, India and Dibrugarh University, India. He was awarded with a scholarship from the Government of Uttar Pradesh and from the Ministry of Human Resource and Development, Government of India. Presently, he is working as an Assistant Professor in Pharmaceutical Chemistry at the Sam Higginbottom Institute of Agriculture, Technology & Sciences (SHIATS) and is pursuing his doctoral studies under the supervision of Dr. Ramendra K. Singh, Nucleic Acids Research Laboratory, University of Allahabad. His research interest is focused on the development of novel heterocyclic scaffolds and their medicinal importance through facile synthetic routes. Recently, he has been awarded with Archimedes Foundation, DoRa5 Scholarship to carry out part of his PhD work under the supervision of Prof. Asko Uri, Institute of Chemistry, University of Tartu, Estonia, on novel protein kinase inhibitors.

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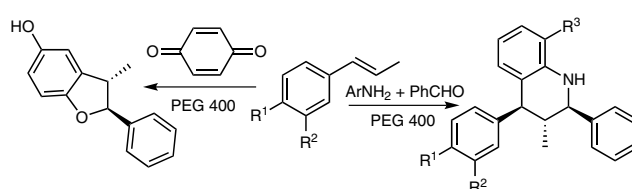
### Introduction

Polyethylene glycol 400 (PEG 400) is a water-soluble and hygroscopic polymer with a molecular weight of 400 Da.<sup>1</sup> At room temperature it exists as colorless viscous liquid. Reactions promoted by PEG 400 have attracted attention due to their ease of workup and inexpensive and eco-friendly nature. It can also act as phase-transfer catalyst.

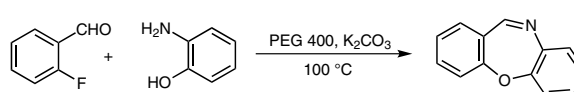
Till date reactions involving PEG 400 have been carried out and investigated, for example, Heck reaction,<sup>2</sup> Lindlar catalytic hydrogenation,<sup>3</sup> asymmetric dihydroxylation,<sup>4</sup> Baylis–Hillman reaction,<sup>5</sup> Biginelli reaction,<sup>6</sup> Suzuki–Miyaura coupling,<sup>7</sup> Stille cross-coupling,<sup>8</sup> Wacker reaction,<sup>9</sup> asymmetric aldol reaction,<sup>10</sup> 3,4-dihydropyrimidones via Biginelli reaction,<sup>11</sup> Strecker reaction,<sup>12</sup> etc.

### Abstracts

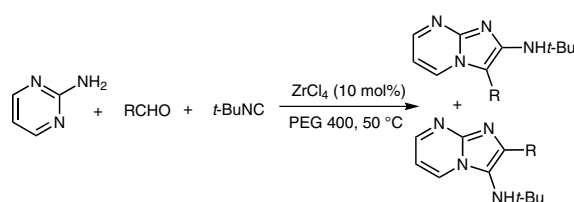
(A) Kouznetsov et al. had developed a simple and efficient one-pot method for the synthesis of novel 2,4-diaryl-1,2,3,4-tetrahydroquinolines using a three-component imino Diels–Alder cycloaddition between *trans*-isoeugenol or *trans*-anethole, anilines, and benzaldehyde in the presence of BF<sub>3</sub>·OEt<sub>2</sub> in PEG 400.<sup>13</sup>



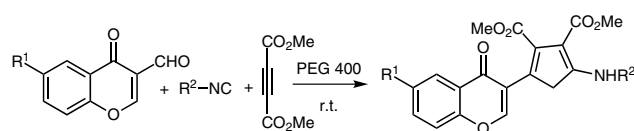
(B) Jorapur et al. reported the synthesis of dibenz[*b,f*]-1,4-oxazepine via intramolecular cyclization and revealed the utility PEG 400 as recyclable reaction medium.<sup>14</sup>



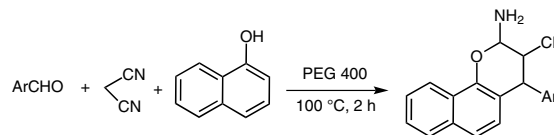
(C) Guchhait and Madaan reported the Ugi-type multicomponent reaction of heterocyclic amidines with aldehydes and isocyanides catalyzed by zirconium(IV) chloride in PEG 400. This protocol offers the rapid, environmentally friendly and regioselective synthesis of medicinally important N-fused 2- and 3-aminoimidazoles in good to high yields.<sup>15</sup>



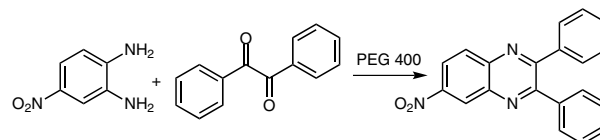
(D) Reddy et al. developed a synthetic route to afford styrylfurans in good yields via 1,3-dipolar cycloaddition between isocyanides, dialkyl acetylenedicarboxylates, and  $\alpha,\beta$ -unsaturated aldehydes in PEG 400.<sup>16</sup>



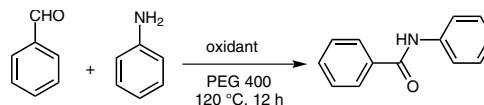
(E) Shitole et al. reported the synthesis of 2-amino-4*H*-chromenes by condensation of aromatic aldehyde, malononitrile, and  $\alpha$ -naphthol.<sup>17</sup>



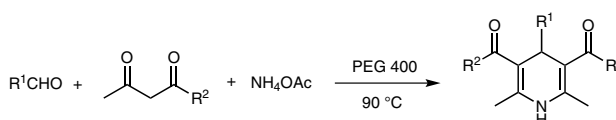
(F) Zhang et al. disclosed the role of PEG 400 as an efficient catalyst to synthesize quinoxalines via condensation of 1,2-diamines with 1,2-dicarbonyl compounds in excellent yields under mild reaction conditions.<sup>18</sup>



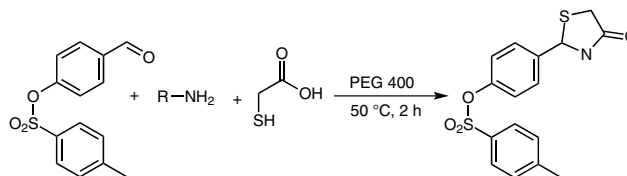
(G) Liang et al. reported a metal-free synthesis of amides by direct oxidative amidation of aldehydes with amines in a PEG 400/oxidant system in good to excellent yields.<sup>19</sup>



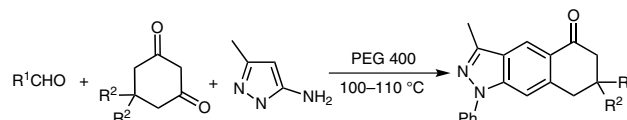
(H) Wang et al. reported a Hantzsch 1,4-dihydropyridines synthesis via a one-pot condensation of aldehydes,  $\beta$ -dicarbonyl compounds, and ammonium acetate in PEG 400. This method has the advantages of good yields, less pollution, and simple reaction conditions.<sup>20</sup>



(I) Bhosle et al. reported an efficient one-pot three-component cyclocondensation of 4-(*p*-tolyl sulfonyl) benzaldehyde, aryl amines, and mercaptoacetic acid in PEG 400 to yield 2,3-disubstituted 4-thiazolidinones.<sup>21</sup>



(J) Karnakar et al. developed a simple, efficient and eco-friendly synthetic protocol for the synthesis of pyrazolo[3,4-*b*]quinolines via a one-pot three-component reaction of aldehydes, amino pyrazole, and 1,3-cyclohexanediones using recyclable PEG 400 as reaction medium.<sup>22</sup>



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