Eucalyptol: a novel biomass-originated solvent for Pd-catalyzed carbonylative cross coupling reactions

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The transition metal-catalyzed industrially relevant transformations are usually performed in conventional organic solvents e.g. THF, DMF, toluene etc. having high toxicity, high vapor pressure, just to name a few drawbacks. Thus, the replacement of these conventional reaction media by non-toxic and even biomass-originated alternative ones could result in a greener and cleaner alternative chemical process [1].

The Pd-catalyzed carbonylative Sonogashira reactions represent a powerful tool for the synthesis of various α , β -unsaturated functionalized ketones [2], which can be utilized as building blocks of subsequent synthetic schemes, typically in pharmaceutical industry, where the residual solvent traces could result in serious health issues.

It was shown that a natural eucalyptol (1,8-cineole) could be applied as a safer solvent for the carbonylative coupling reactions of iodoaromatic and phenylacetylene compounds leading to the formation of corresponding ketones with high yields (>90%).

$$R^{1} \rightarrow I + R^{2} + CO \xrightarrow{Pd catalyst} R^{2} + R^{2} + R^{2} \xrightarrow{R^{2} + CO} R^{2} \xrightarrow{R^{2} + CO} R^{2} \xrightarrow{R^{2} + CO} R^{2}$$

R¹: H, 4-Cl, 4-F, 4-CH₃, 4-NO₂, 4-tBu, 3-Cl, 4-OMe, 3-F R²: H, 4-OMe, 4-(C=O)-Me

Our contribution will present the determination of temperature dependent vapor pressure and viscosity, the key solvent properties of eucalyptol, optimization of reaction conditions (temperature, pressure, catalyst, bases etc.) as well as the investigation of substrate scope.

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