Catalytic Pauson–Khand Reaction in Ethylene Glycol–Toluene: Activity, Selectivity, and Catalyst Recycling

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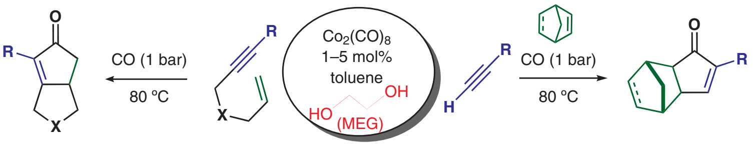

- 11 examples
- enhanced yield and selectivity
- low catalyst loading (as low as 1 mol%)
- intramolecular and intermolecular
- biphasic system: catalyst recycling
- gram-scale synthesis

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Abstract The use of ethylene glycol (15% v/v in toluene) as additive in the catalytic Pauson–Khand reaction (PKR) is reported. In most cases both the yield and selectivity were enhanced compared to standard protocols. Moreover, the immiscibility of ethylene glycol in toluene allowed recycling of the catalyst (which remained mainly in the ethylene glycol). The recycling allowed catalyst loading to be reduced to only 3 mol%. A gram-scale reaction was also performed, allowing the use of only 1 mol% of $Co_2(CO)_8$, the lowest amount reported so far in intermolecular cobalt-catalyzed PKR.

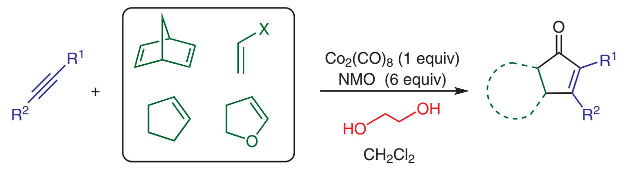
Key words Pauson–Khand Reaction, homogeneous catalysis, cyclization, cobalt, additives, cyclopentenones, cycloaddition, catalyst recycling

The Pauson–Khand reaction (PKR),[1,2] a metal-catalyzed [2+2+1] cycloaddition coupling of an alkyne, an alkene, and CO, is one of the most powerful synthetic tools with which to prepare cyclopentenones.[3,4] The stoichiometric version of the reaction uses large amounts of dicobalt octacarbonyl with the subsequent drawbacks of price, residue disposal, and difficult purification of the final product. In this regard, the development of catalytic methodologies to reduce the amount of metal are required for large-scale preparations. Several catalytic versions of the PKR involving the use of other metals, such as Ti,[5] Ru,[6] Rh,[7] Ni,[8] and Ir[9] or bimetallic species, have been described.[10] However, the use of cobalt complexes is probably the most practical and economical approach. Although the catalytic system can be prepared in situ by reducing $CoBr_2$ with Zn under CO pressure,[11] dicobalt octacarbonyl continues to be the most common catalyst.[12]

Many additives have been described to improve the yields in the cobalt-catalyzed PKR. Ureas such as tetramethylthiourea (TMTU),[13] phosphites,[14] triphenylphosphines,[15] hard Lewis bases,[16] and sulfides[17] are the most relevant. However, the use of large amounts of additives usually hinders the purification of the product.

Catalyst recycling is clearly desirable. Several heterogeneous catalytic systems such as colloidal cobalt nanoparticles (NPs),[18] cobalt on charcoal,[19] or cobalt Raney[20] have been described for the PKR.[21] However, to the best of our knowledge, there are no precedents of catalyst recycling in homogenous systems.

Based on a previous methodology developed by Baran and co-workers,[4a] our group recently reported that, ethylene glycol (ethane-1,2-diol, MEG) can enhance the alkene range in the stoichiometric *N*-oxide promoted intermolecular PKR (Scheme 1).[22] In the present study we report that this additive also has a positive effect on the cobalt-catalyzed PKR, allowing the reaction to be performed with very low catalyst loadings, reducing undesired byproducts, facilitating the purification of the final product, and permitting catalyst recycling by simple liquid–liquid separation.



Scheme 1 Previous work of MEG-assisted intermolecular PKR

We chose three standard enynes **1a–c** to test the intramolecular catalytic PKR (Table 1). As expected the reaction proceeded smoothly in toluene using 5 mol% of $Co_2(CO)_6$ to afford the corresponding bicyclic cyclopentenones **2a–c** in moderate to good yields. The yield of **2c** from the oxygen-containing enyne **1c** was slightly lower than those of **2a** and **2b** from all-carbon **1a** and nitrogen-containing **1b**, respectively. Under the same conditions but using 15% MEG/tolu-