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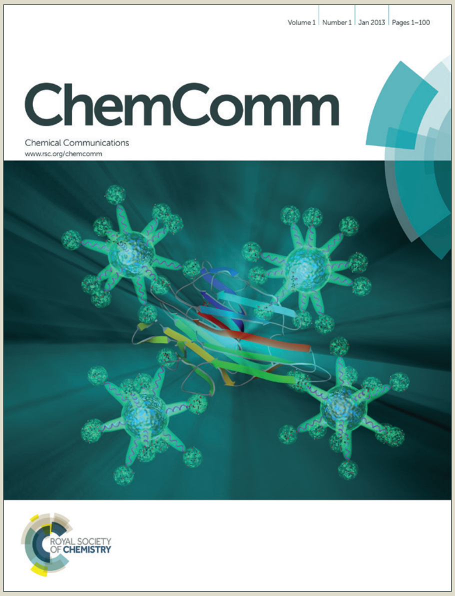

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Potassium Tris(triflyl)methide ($KCTf_3$): A Broadly Applicable Promoter for Cationic Metal Catalysis

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Junbin Han,[a] Zhichao Lu,[a] Weibo Wang,[a] Gerald B. Hammond,[a,]* Bo Xu[b,]*

$KCTf_3$, a commercially available, easily handled neutral salt, enhanced the reaction rates and the chemical yields of a wide spectrum of cationic metal catalyzed reactions, ranging from traditional Lewis acid catalysis to transition metal catalysis

Among the repertoire of cationic metal Lewis acid catalysts, metal triflates (M^+OTf^-) or sometimes metal halides are the most frequently employed for electrophilic activation of organic substrates because they are relatively stable and easier to procure.[1] A recent review by Duñach and coworkers regarded the triflimidate (NTf_2^-) counterion superior to its halide or triflate counterparts because its highly delocalized nature and high steric hindrance results in virtually no nucleophilic behavior and an extremely high positive charge density on the metal cation, thus enhancing its Lewis acid character.[2] Duñach and coworkers also indicated that a tris(triflyl)methide anion (CTf_3^-) would be expected to be even more active than NTf_2^- based on the limited data available using scandium(III), copper(II) and yterbium(III) salts.[3]

Because counterions play an important role in cationic metal catalysis (e.g., gold),[4] we proposed that the laborious preparation of a catalyst containing a CTf_3^- counterion is unnecessary for the purposes of enhancing its reactivity. A similar effect can be achieved by mixing a commercial catalyst (e.g., $M\text{-}OSO_2CF_3$ in Figure 1) with $KCTf_3$.[5] CTf_3^- is a carbon-based soft anion amenable to undergo ion reshuffling with several transition metal catalysts because of their relatively soft metal centers. When a salt like $KCTf_3$ is added to the reaction mixture, the interaction between M and OTf^- may weaken because of the affinity of OTf^- and naked K^+, resulting in partial reshuffling of ions and the generation of a more reactive cationic species *in situ*. In this regard, $KCTf_3$ can be considered a promoter. Being a neutral salt, $KCTf_3$ will not interfere with acidic or basic species in the reaction system.

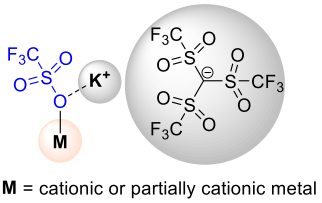

Figure 1. Activation of M-OTf by $KCTf_3$.

We first investigated the feasibility of our *in situ* activation approach using the well-studied gold-catalyzed intermolecular hydroamination of alkynes.[6] We compared $KCTf_3$ with other commercially available salts whose counterions have low coordinating ability, good stability and highly delocalized negative charge, namely, $LiNTf_2$, NaBARF (sodium tetrakis[3,5-bis(trifluoromethyl)phenyl]borate),[7] $Li^+[Al[(CF_3)_3C\text{-}O)]_4]^-$[8,9] (Figure 2). Most of these salts enhanced the kinetics of the reaction, but $KCTf_3$ clearly gave the best result. The reaction inhibition observed with $Li^+[Al[(CF_3)_3C\text{-}O)]_4]^-$ could be explained by the instability of the aluminate anion under the reaction conditions. We also investigated a gold(I)-catalyzed reaction known to experience significant catalyst decay over time: the isomerization of an allenyl carbinol ester (Figure 3).[10] Again, $KCTf_3$ gave the best result. Here we observed that $LiNTf_2$ slowed down the reaction at the beginning but maintained its reactivity over time, probably due to the stabilizing effect of NTf_2^-.[11] NaBARF enhanced the rate of this reaction but only at the beginning. We attributed this time disrupting effect to catalyst deactivation under the reaction conditions.

We proceeded to compare the reactivity of L-Au-OTf/$KCTf_3$ *viz a viz* L-Au-CTf_3 (Figure 4) using the cycloisomerization of 1,6-enyne as model.[12] $KCTf_3$ significantly increased the reactivity of L-Au-OTf in this reaction, and was only slightly less reactive than L-Au-CTf_3 itself (prepared by treating L-Au-Cl with $AgCTf_3$).

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[a] *Department of Chemistry, University of Louisville, Louisville, Kentucky 40292, United States. Email: gb.hammond@louisville.edu*
[b] *College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai 201620, China. Email: bo.xu@dhu.edu.cn*

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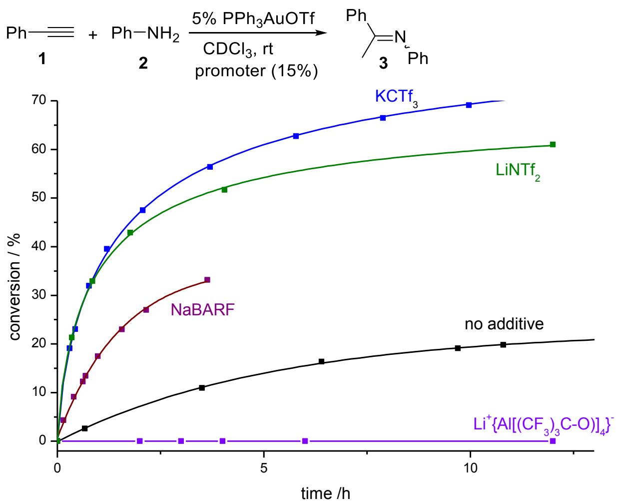


Figure 2. Effect of promoters on hydroamination reaction.

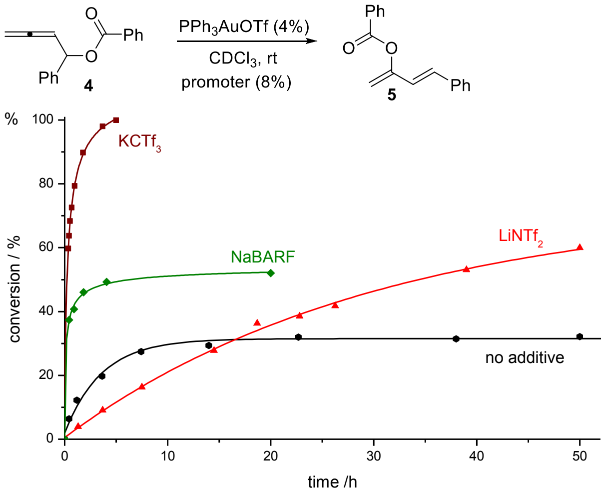


Figure *3*. Effect of promoters in the rearrangement of allenyl ester.

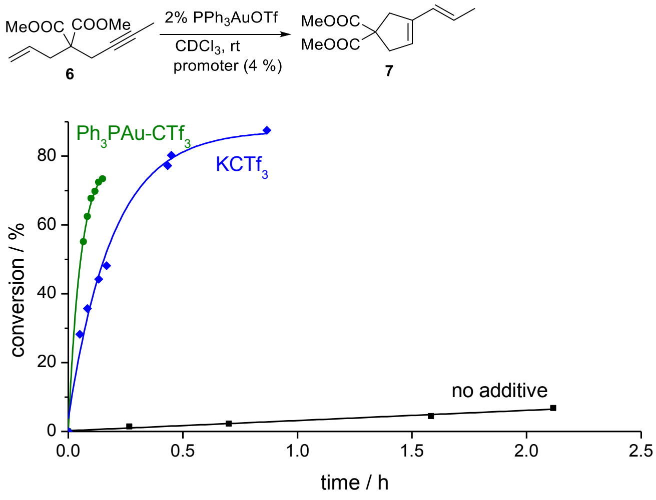
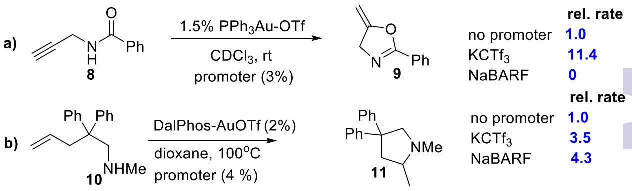


Figure *4*. Effect of promoters in the cycloisomerization of 1,6-enyne **6**.

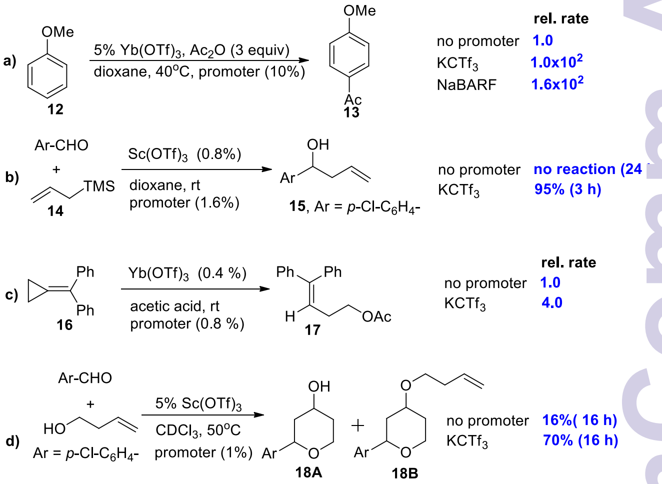
The results of Figure 4 not only demonstrated that CTf_3^- was better than OTf^- as a counterion but also showed that the laborious preparation of a catalyst containing a CTf_3^- counterion for the purpose of enhancing reactivity was unnecessary. Instead, a similar effect was achieved by simply adding $KCTf_3$ as promoter. Surprisingly, the use of NaBARF inhibited this reaction.

We then compared the performances of $KCTf_3$ and NaBARF in other gold-catalyzed reactions, without modifying the original literature conditions (Scheme 1). Because the kinetics of the reactions in Scheme 1 are approximately pseudo-zero order, the relative rate of each reaction served as convenient yardstick. We measured the initial rate, first in the presence, and then in the absence, of a reaction promoter for each reaction. $KCTf_3$ increased the reaction rates of O-H addition to an alkyne and N-H addition to an alkene by 11- and 3.5-fold, respectively (Scheme 1a-b).[13]



Scheme 1. Effect of reaction promoter in cationic gold catalyzed reactions.

We expanded our study to other Lewis acid catalyzed reactions (Scheme 2). Again, we found that $KCTf_3$ increased significantly the rate of these reactions. In the $Yb(OTf)_3$ catalyzed acylation of anisole (Scheme 2a)[14] $KCTf_3$ showed a one-hundred fold increase. In the $Sc(OTf)_3$ catalyzed allylation of aromatic aldehydes[15] (Hosomi-Sakurai Reaction) (Scheme 3b), the addition of $KCTf_3$ (1.6 mol%) led to a 95% yield of product after only 3 h (Scheme 2b). $KCTf_3$ also performed remarkably well in the $Yb(OTf)_3$ catalyzed ring-opening of methylenecyclopropanes (Scheme 2c)[16] and in the Prins cyclization, catalyzed by $Sc(OTf)_3$ (Scheme 2d).[17] NaBARF performed marginally better than $KCTf_3$ in Scheme 1b and Scheme 2a, but inhibited the other reactions (Scheme 1a and Scheme 1c).



Scheme 2. Effect of reaction promoter in various classical Lewis acid catalyzed reactions.

We also investigated reactions catalyzed by silver and rhodium.[18] As shown in Scheme 3a-b, $KCTf_3$ accelerated both reactions. The control reactions were run in our laboratory using the conditions

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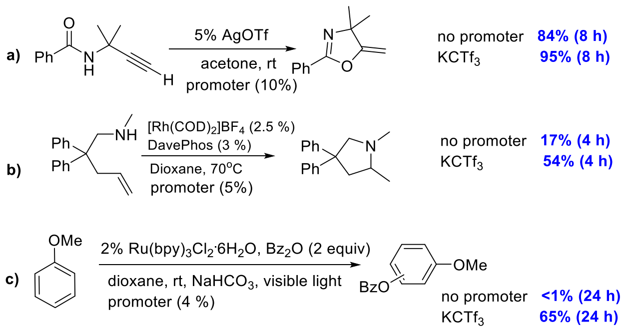
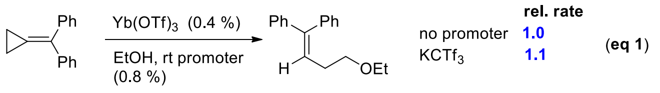
reported in the literature. For example, the Ru catalyzed visible light photoredox reaction[19] (Scheme 3c) gave only trace amounts of product in our hands, but when we added 4% $KCTf_3$ to this reaction we noticed a substantial improvement (65% yield).



Scheme 3. Effect of reaction promoter in silver, rhodium and ruthenium catalyzed ionic reactions.

In some cases (e.g., Scheme 3a), the acceleration effect of $KCTf_3$ was only marginally better than the control. We believed that the effectiveness of a promoter depends on the proximity of ionic species in the reaction system, and here solvents play an important role. The majority of organic reactions are conducted in solvents of relatively low dielectric constant (e.g. DCM, toluene, THF), where cationic metals or their complexes exist as contact ion pairs or even partially covalent in nature (e.g. L-Au-OTf).[20] According to recent studies by Macchioni and others,[21] cationic gold catalysts (e.g., $[LAu^+\text{-alkyne}]BF_4^-$) exist as ion pairs in commonly used low dielectric constant solvents like DCM or chloroform. Thus, counterions are close to the reactive metal center and therefore exert a strong influence on the reaction rate. In these cases, a reaction promoter is expected to play a beneficial role. Most of the reaction examples presented above belong to this category. On the other hand, in reactions conducted in high dielectric constant solvents (e.g., water, methanol or acetone), the majority of ionic species will exist as dissociated ions.[20] In these cases, counterions will be far away from the reaction center and therefore will have minimum influence on the reaction rate. Hence, a reaction promoter will not be useful. This point was demonstrated with the results shown in Scheme 3a, which was conducted in acetone ($\varepsilon = 20.7$), a solvent with a much larger dielectric constant than those used in other reactions (e.g. chloroform, $\varepsilon = 4.8$ or dioxane, $\varepsilon = 2.3$). Another example of the solvent effect discussed above is shown in eq 1. This reaction is similar to the reaction in Scheme 2c, except that it was conducted in EtOH ($\varepsilon = 24.5$) instead of AcOH ($\varepsilon = 6.2$). In this case, the use of $KCTf_3$ led to only a negligible improvement.



Conclusions

We have demonstrated that $KCTf_3$ is a broadly applicable promoter because it enhanced, in consistent and significant manner, the reaction rates and the chemical yields of a wide spectrum of ionic reactions, ranging from traditional Lewis acid catalysis to transition metal catalysis, without modifying the original reaction conditions. Our approach is practical because this salt is commercially available and relatively inexpensive. Further applications are under investigation in our laboratory.

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