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Quantitative Kinetic Investigation of Triazole-Gold(I) Complex Catalyzed [3,3]-Rearrangement of Propargyl Ester

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The triazol-gold(I) complex catalyzed [3,3]-rearrangement of propargyl ester has been quantitatively investigated through in situ IR. First order on [Au] and [propargyl ester] suggested that the turnover-limiting step is the associative ligand substitution. The activation enthalpy was also determined to be 7.8 kcal/mol. TA-Au catalysts with different triazole derivatives were also tested, giving a linear free energy relationship with a p value of 0.74.

In 2009, our group introduced a 1,2,3-triazole bound cationic gold(I) complex (TA-Au) as an improved thermally stable catalyst.

Later it was discovered that the TA-Au could preferentially activate alkene over allene in propargyl ester [3,3]- rearrangement, where indene was synthesized using 2 mol% IPrAuCl/AgBF₄. However, in our case, no indene was detected after 12 h using 1 mol% TA-Au. We view this phenomenon as a good opportunity for mechanistic study. The simplified system (over Nolan’s two-step transformation) may allow for the collection of quantitative kinetic information associated with TA-Au. In addition, it is also very important to understand why TA-Au offered the chemoselectivity with excellent stereochemistry control, while other [L-Au] gave rapid racemization at the propargyl position with poor chemoselectivity (activation of both alkene and allene). Herein, we report our quantitative kinetic investigation of TA-Au catalyzed propargyl ester [3,3]-rearrangement using in situ IR spectroscopy from a ‘live’ catalytic reaction.

To acquire meaningful kinetic data for a catalytic reaction, the turnover-limiting step needs to be established. This is a challenge task for LAuCl/AgX system, giving the rapid catalyst decomposition over time. A unique advantage of TA-Au catalyst is the improved stability, which allows relatively steady concentration of the catalyst for the kinetic study. Thus, we set out to evaluate the kinetic dependence of concentration of substrate and TA-Au. The standard reaction was chosen as the model reaction for the detailed investigation (eq. 1).

To avoid the potential influence of acid (formation of HOTf), the concentration of TA-Au was selected. The dependence of the initial rates on the concentration of TA-Au catalyst 4 was studied with varied concentrations from 0.002-0.008 M. The initial rates in different runs were calculated based on the kinetic profiles monitored by in situ IR. A linear relationship is established as depicted in Figure 1. The reaction is therefore first-order dependent on [4], suggesting the involvement of 4 in the turnover-limiting step.

Figure 1. Dependence of the initial rates on catalyst concentrations for rearrangement of I. Reaction conditions: 1 (0.10 M in DCE, 1.2 mL), 4 (0.002-0.008 M in DCE), 30°C.
Subsequent experiment was to determine the kinetic order of [1]. Similarly, the initial rates were plotted against [1] varied from 0.10-0.20 M. Again, a first-order dependence was observed, as shown in Figure 2. Combined with two experiments, we were able to derive the rate law for this reaction: \( r = k_{\text{obs}}[1][4] \). According to the rate law, both the catalyst 4 and substrate 1 were involved, revealing the electronic activation of alkyne (i.e. ligand exchange) as the turnover-limiting step. In situ monitoring of \(^{31}\text{P}\) NMR over the entire course of reaction showed 4 as the resting state further supporting the ligand exchange as the turnover-limiting step.

![Figure 2](image2.png)

**Figure 2.** Dependence of the initial rates on substrate concentrations for rearrangement of 1. Reaction conditions: 1 (0.10-0.20 M in DCE, 1.2 mL), 4 (0.003 M in DCE), 30°C.

With this kinetic data, a tentative proposed mechanism of TA-Au catalyzed propargyl ester [3,3]-rearrangement is shown in Scheme 2. First, the TA-Au undergoes the turnover-limiting ligand exchange with substrate to form cationic gold(I) alkyne π-complex. This complex then rapidly converts the propargyl ester to the corresponding allene. It is clear to see that the ligand exchange step significantly slows the reaction rate compared to the use of free cationic gold(I) (Scheme 1), which is consistent with the fact that the same reaction catalyzed by IPrAu(L)\(^{+}\) (L=Et\(_3\)N, py) was also slower.

![Scheme 2](image3.png)

**Scheme 2.** Proposed Mechanism for TA-Au catalyzed propargyl ester [3,3]-rearrangement

To further probe physical organic nature of this elementary step, a temperature dependent experiment was carried out in order to obtain the activation energy quantitatively. As shown in Figure 3, the reactions were again monitored by in situ IR at different temperatures (295-319 K). The activation enthalpy was determined to be 7.8 kcal/mol through Eyring equation after plotting the ln(k/\(T\)) vs. 1/\(T\). This value reveals that ligand exchange step itself is quite a facile process at room temperature. Similarly, Echavarren reported even lower activation enthalpy values (3.7 and 6.2 kcal/mol) for his studies in the enyne cycloisomerization.

**Figure 3.** Kinetics profile at different temperatures. Reaction conditions: 1 (0.10 M in DCE, 1.2 mL), TA-Au (0.003 M in DCE), at 22, 32, 38, and 46°C.

Assumed that all the catalyst in the reaction remained active throughout the reaction, [4]\(_0\) will be identical to active catalyst concentration. Therefore, activation entropy was determined as -36.6 eu. The negative and relative large value supports the associative ligand substitution through a transient 3-coordinate gold(I) complex. However, the possibility of 3-coordinate gold(I) complex with TA attached as the stable intermediate cannot be ruled out at this point. Further support came from the fact that the reaction was inhibited if additional 1-methyl-benzotriazole (S, 4 equiv. toward TA-Au) was present. Unfortunately, we were unable to determine the exact order of [5] due to the extremely slow reaction rates. But a negative kinetic order of [5] is anticipated, which is consistent with the proposed triazole-alkyne exchange mechanism shown in Scheme 3.

![Scheme 3](image4.png)

**Scheme 3.** Associative ligand substitution through transient 3-coordinate cationic gold(I) complex.

Finally, we prepared various TA-Au catalysts with different substituted groups benzotriazole in order to investigate the impact of the electronic nature of the TA-Au catalysts. The \(^{31}\text{P}\) NMR peaks corresponded to TA-Au catalysts provide direct information regarding the electronic nature of gold center. As expected, more electron-withdrawing group gives more upfield \(^{31}\text{P}\) shift, suggesting the more cationic gold. The reaction kinetics is illustrated in Figure 4.

**Figure 4.** Kinetics profile using various TA-Au catalysts. Reaction conditions: 1 (0.10 M in DCE, 1.2 mL), TA-Au (0.003 M in DCE), 26°C.
Clearly, the more cationic gold(I) led to faster reaction rate. The slowest reaction was observed with 4-methoxyphenyl substituted TA-Au catalyst, however, this reaction is still faster than the reaction catalyzed by 4, suggesting the inherent electron-withdrawing nature of the phenyl group attached to benzo triazole. The linear free energy relationship was established by plotting log(k/k0) vs. \( \alpha_{\text{para}} \) giving a \( \rho \) value of 0.74 (Figure 5).

\[ \log(k/k_0) = \rho \alpha_{\text{para}} \]

\( \rho = 0.74 \)

\( r^2 = 0.994 \)

Figure 5. Hammett plot of substituted TA-Au catalysts.

The positive \( \rho \) value suggested partial positive charge building up during the reaction, which is consistent with the associative ligand substitution being the turnover-limiting step. The more electron-deficient triazole undergoes ligand exchange more rapidly, which is accounted for the faster reaction rate. This result also highlights the tunability of TA-Au catalyst. Based on the different cases, the more electron-deficient TA-Au will give shorter reaction time, while the more electron-rich TA-Au has longer catalyst lifetime.

The chemoselectivity of the TA-Au catalysts (activation of alkyl halides over alkenes) can also be explained by this ligand-substrate exchange mechanism. The DFT calculation revealed the HOMO of propargyl ester \( \text{I} \) is 20 kcal/mol higher than the HOMO of alkenes \( \text{II} \). Thus, the ligand exchange is much slower between allene \( \text{II} \) and TA-Au, which supports the observed selective alkynyl activation.

In summary, the triazole-gold(I) complex (TA-Au) catalyzed propargyl ester [3,3]-rearrangement has been quantitatively investigated. Considering that few physical organic studies have been reported regarding gold catalyzed alkynyl activation due to the poor catalyst stability and complex reaction nature, this work provided direct experimental evidences in understanding the elementary step in the TA-Au catalyzed alkynyl activation. The discovery of associative ligand exchange between TA-Au and alkynyl as the turnover-limiting step provided mechanistic insight, which will benefit future investigations.

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Notes and references


17. The inhibition could be explained by either the formation of 3-coordinate LAu(TA)\(^{\text{2+}}\) type complex or the competition of the external triazole ligand with alkynyl substrate. Unfortunately, our attempts to detect the 3-coordinate gold complex through MS and NMR were unfruitful with no observation of any LAu(TA)\(^{\text{2+}}\) type complexes. Thus, the equilibrium between TA-Au and Au-alkyne π-complex is the likely explanation for the observed decreased reaction.
rate when external TA ligands were used. Detailed derivation of rate law is provided in supporting information.


19 DFT calculation was performed on Gaussian 03 program at the B3LYP/6-311G level of theory.