ORGANIC LETTERS

2009
Vol. 11, No. 21
4962−4965

Dinuclear Gold−Silver Resting States May Explain Silver Effects in Gold(I)-Catalysis

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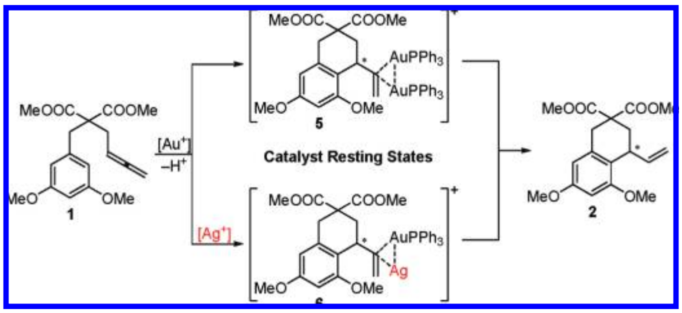
Received September 13, 2009

ABSTRACT



The resting state of the gold(I)-catalyzed hydroarylation of 1 changes in the presence of Ag^+, with silver free catalysts resting at the dinuclear gold structure 5 and Ag^+ containing solutions resting at a heteronuclear species like 6. Adventitious Ag^+ (typically from LAuCl activation) can therefore intercept key organogold intermediates and effect the catalysis even when it does not effect the reaction in Au free control experiments.

Silver salts are commonly used to activate metal halides for catalytic transformations, and this strategy is especially useful in homogeneous gold catalysis.[1] After control experiments demonstrating that the AgX (X = BF_4, OTf, NTf_2, etc.) activator does not catalyze the reaction of interest, the silver salts are often used in excess to ensure quantitative activation of the precatalyst.[2] Despite proving that the silver salts themselves are unreactive, there are examples of gold(I)-catalyzed reactions where Ag^+ effected either activity or selectivity,[3] but models for accommodating such observations are not well appreciated in the gold catalysis community. We report herein observations that point to Ag^+ ions intercepting Au(I) catalytic intermediates and subsequently effecting catalyst speciation and reaction kinetics; a structural model is also suggested.

In a recent investigation of the gold(I)-catalyzed hydroarylation of **1** to **2**,[4] we noted that the catalyst rested at the digold vinyl intermediate **5**,[5] which could additionally be

(1) Selected review articles on gold catalysis: (a) Hashmi, A. S. K. *Gold Bull.* **2004**, *37*, 51. (b) Hashmi, A. S. K.; Hutchings, G. J. *Angew. Chem., Int. Ed.* **2006**, *45*, 7896. (c) Hashmi, A. S. K. *Chem. Rev.* **2007**, *107*, 3180. (d) Hashmi, A. S. K. *Catal. Today* **2007**, *122*, 211. (e) Li, Z.; Brouwer, C.; He, C. *Chem. Rev.* **2008**, *108*, 3239. (f) Widenhoefer, R. A. *Chem.—Eur. J.* **2008**, *14*, 5382. (g) Gorin, D. J.; Sherry, B. D.; Toste, F. D. *Chem. Rev.* **2008**, *108*, 3351. (h) Arcadi, A. *Chem. Rev.* **2008**, *108*, 3266. (i) Jiménez-Núñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326. (j) Bongers, N.; Krause, N. *Angew. Chem., Int. Ed.* **2008**, *47*, 2178. (k) Gorin, D. J.; Toste, F. D. *Nature* **2007**, *446*, 395. (l) Fürstner, A.; Davies, P. W. *Angew. Chem., Int. Ed.* **2007**, *46*, 3410. (m) Hashmi, A. S. K.; Rudolph, M. *Chem. Soc. Rev.* **2008**, *37*, 1766.

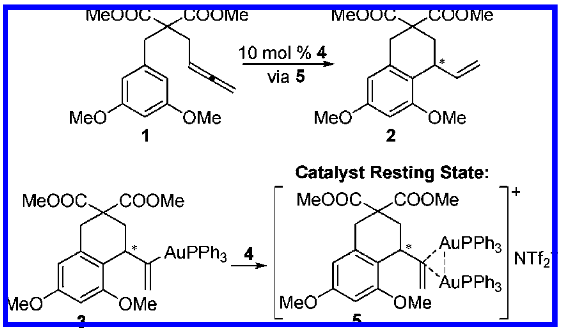
(2) Selected example of a silver and gold catalyzed reaction: (a) Godet, T.; Vaxelaire, C.; Michel, C.; Milet, A.; Belmont, P. *Chem.—Eur. J.* **2007**, *13*, 5632. Selected review articles on silver-catalyzed reactions: (b) Halbes-Letinois, U.; Weibel, J.-M.; Pale, P. *Chem. Soc. Rev.* **2007**, *36*, 759. (c) Weibel, J.-M.; Blanc, A.; Pale, P. *Chem. Rev.* **2008**, *108*, 3149. (d) Naodovic, M.; Yamamoto, H. *Chem. Rev.* **2008**, *108*, 3132. (e) Álvarez-Corral, M.; Muñoz-Dorado, M.; Rodríguez-García, I. *Chem. Rev.* **2008**, *108*, 3174. (f) Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3199. (g) Patil, N. T.; Yamamoto, Y. *Chem. Rev.* **2008**, *108*, 3395.

(3) See for example: (a) Li, H.; Widenhoefer, R. A. *Org. Lett.* **2009**, *11*, 2671. (b) Tarselli, M. A.; Chianese, A. R.; Lee, S. J.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2007**, *46*, 6670.

10.1021/ol902116b CCC: $40.75
Published on Web 10/06/2009

synthesized by the combination of $Ph_3PAuNTf_2$ (**4**) and the monoaurated vinylgold(I)-complex **3** (Scheme 1). Based on

Scheme 1. Catalyst Resting State **5** Was Observed for the Gold(I)-Catalyzed Intramolecular Hydroarylation of **1** to **2**



the doubly aurated aryl compounds of Schmidbaur, **5** was formulated as an out of plane Au−C−Au 3-center-2-electron bond with a stabilizing d^{10} closed shell aurophilic interaction.[6] Motivated by the observation of Ag^+-effects in gold(I)-catalysis and the known examples of auro-argentophilic closed shell interactions in polymetallic complexes, we examined the effect of Ag^+ on the catalyst speciation.[7]

As expected, the catalyst generated *in situ* from Ph_3PAuCl/$AgNTf_2$ (5 mol %/25 mol %) was found to be effective for the conversion of **1** to **2**, while the $AgNTf_2$ activator was much less reactive at RT.[8] Monitoring the reactions by NMR, however, revealed a significantly different behavior from $Ph_3PAuNTf_2$ (**4**) alone.[9] Instead of **5** being observed using **4**, the Ag^+-containing catalyst formulations rested at a new structure with a singlet in the ^{31}P NMR at $\delta = 41$ ppm (Figure 1a) and regenerated **4** at the end of the reaction. This compound, **6**, could be independently synthesized by reacting

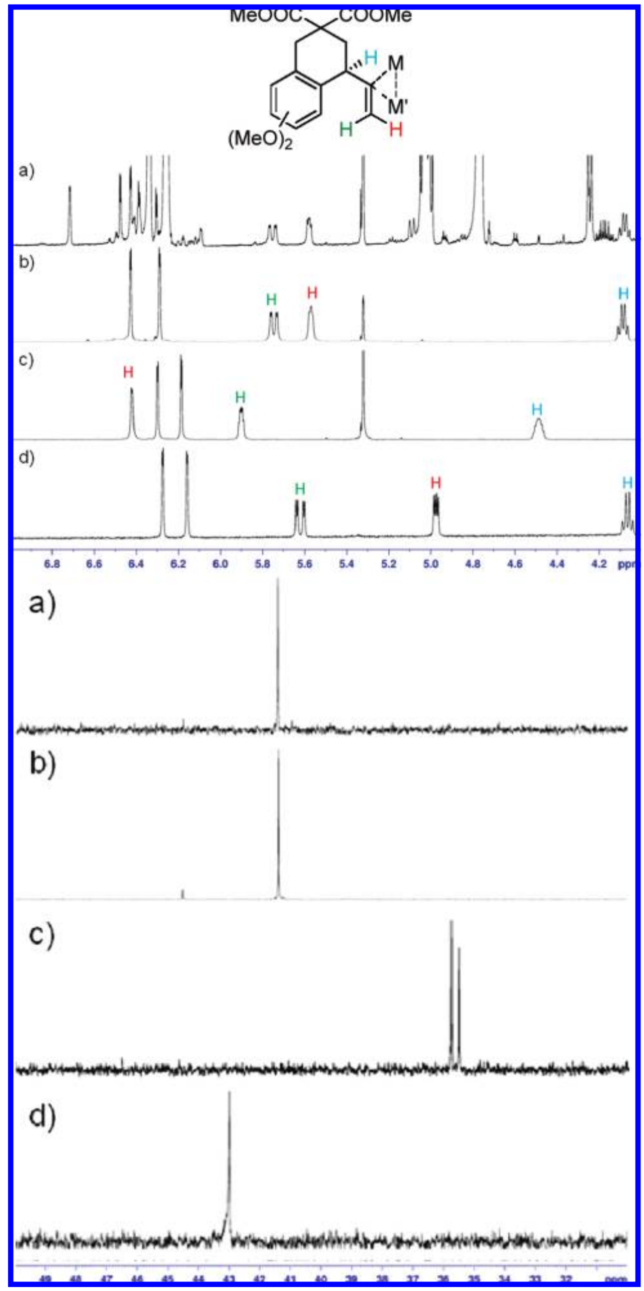


Figure 1. Comparison of ^1H (top) and ^{31}P NMR (bottom) data. (a) Catalysis of **1** with 5 mol % **4** in the presence of 20 mol % $AgNTf_2$ in CD_2Cl_2. (b) Compound **6** trapped with 2,6-di-*tert*-butylpyridine in CD_2Cl_2. (c) Isolated **5** in CD_2Cl_2. (d) Isolated **3** in $CDCl_3$.

a mixture of **4** and $AgNTf_2$ with **1** in the presence of 2,6-di-*tert*-butylpyridine, which acts to arrest protodemetalation.[10] The resonances of this new species (Figure 1b) exactly matched those observed in the ^1H and ^{31}P NMR of the *in situ* monitored catalytic reactions. Figure 1c and d additionally display the corresponding spectra for the isolated intermediates **5** and **3**, respectivley.

Analysis of the ^1H NMR of **6** indicated a complex with a PPh_3 to carbocyclic framework ratio of one. Both vinyl protons additionally were found to couple to one phosphorus nuclei (H_{syn}: $^4J_{PH} = 5$ Hz; H_{anti}: $^4J_{PH} = 14$ Hz), and like **5**

(4) For selected examples of allene activation by Au(I) catalysts, see: (a) Hashmi, A. S. K.; Schwarz, L.; Choi, J.-H.; Frost, T. M. *Angew. Chem., Int. Ed.* **2000**, *39*, 2285. (b) Liu, L.; Xu, B.; Mashuta, M. S.; Hammond, G. B. *J. Am. Chem. Soc.* **2008**, *130*, 17642. (c) Zhang, Z.; Liu, C.; Kinder, R. E.; Han, X.; Qian, H.; Widenhoefer, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 9066. (d) Liu, Z.; Wasmuth, A. S.; Nelson, S. G. *J. Am. Chem. Soc.* **2006**, *128*, 10352. (e) Park, C.; Lee, P. H. *Org. Lett.* **2008**, *10*, 3359. (f) Toups, K. L.; Liu, G. T.; Widenhoefer, R. A. *J. Organomet. Chem.* **2009**, *694*, 571. (g) Gockel, B.; Krause, N. *Org. Lett.* **2006**, *8*, 4485.

(5) Weber, D.; Tarselli, M. A.; Gagné, M. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 5733.

(6) These Au−Au interactions are estimated to be worth ~10 kcal mol^{-1}. (a) Porter, K. A.; Schier, A.; Schmidbaur, H. *Organometallics* **2003**, *22*, 4922. Selected review articles on aurophilicity: (b) Schmidbaur, H.; Schier, A. *Chem. Soc. Rev.* **2008**, *37*, 1931. (c) Schmidbaur, H. *Gold Bull.* **2000**, *1*, 33. (d) Schmidbaur, H. *Chem. Soc. Rev.* **1995**, *24*, 391. See also: (e) Pyykkö, P. *Angew. Chem., Int. Ed.* **2004**, *43*, 4412. (f) Pyykkö, P. *Inorg. Chim. Acta* **2005**, *358*, 4113. (g) Pyykkö, P. *Chem. Soc. Rev.* **2008**, *37*, 1967. (h) Nesmeyanov, A. N.; Perevalova, E. G.; Grandberg, K. I.; Lemenovskii, D. A. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1974**, *5*, 1124.

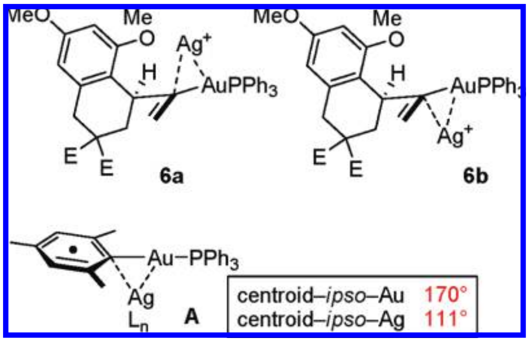
(7) Selected review on auro-metallophilic interactions: (a) Bardaji, M.; Laguna, A. *Eur. J. Inorg. Chem.* **2003**, 3069. See ref 12 for selected examples of auro-argentophilic interactions.

(8) Tarselli, M. A.; Gagné, M. R. *J. Org. Chem.* **2008**, *73*, 2439.

(9) $Ph_3PAuNTf_2$ is a silver-free catalyst: Mézailles, N.; Ricard, L.; Gagosz, F. *Org. Lett.* **2005**, *7*, 4133.

(10) In the presence of $AgNTf_2$, full conversion of **1** to **6** required only 1 equivalent of **4**. In contrast 2 equivalents of **4** were needed for full conversion of **1** to **5** when no silver salt was present, see ref 5. Resin-bound 2,6-di-*tert*-butylpyridine was used for synthetic applications.

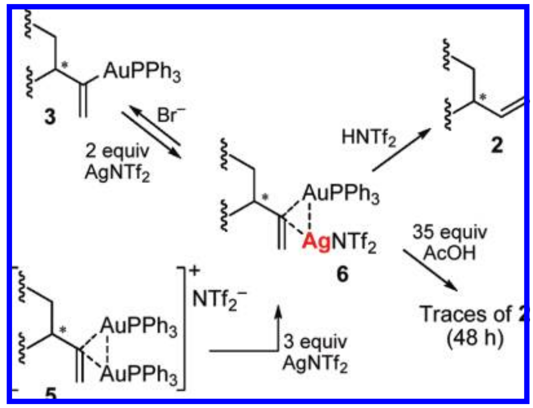
and previously reported multimetalated compounds, the quaternary bimetalated sp^2 carbon showed no signal in the ^{13}C NMR, perhaps a result of the quadrupole moment of gold.[6a] High resolution mass spectrometry showed an *m/z* of 899.1046 (calcd 899.0966) for the $[M-NTf_2]^+$ ion with the isotope pattern expected for a Au−Ag containing compound.



Inspection of X-ray data for numerous simple Au−Ag complexes, e.g. **A**,[12b] suggests that Ag^+ likely binds to the vinyl carbon and the Au ion without significantly perturbing the gold-vinyl structure.[12] In other words, the 3-center-2-electron interaction is not equal and the stronger C−Au bond dominates the structure. Since only a single diastereomer is observed, one of the diastereofaces must be preferentially populated (i.e. **6a** or **6b**).[13]

Since the putative role of **6** is to react with acid to give **2** and regenerate **4** and $AgNTf_2$, the acid stability of **6** was tested. Compound **6** was unchanged in the presence of 5 equivalents of AcOH,[5] but did provide traces of **2** with 35 equivalents over 48 h. One equivalent of the stronger acid $HNTf_2$ (generated *in situ* during catalysis) resulted in a rapid protodeauration to form **2**. When treated with Br^-, precipitation of AgBr drives the conversion of **6** to the monoaurated goldvinyl **3** (Scheme 2).

Scheme 2. Reactions of Intermediate **6**[a]



[a] For experimental details, see the Supporting Information.

The rapid and clean reaction of **3**, a putative reaction intermediate, with 2 equivalents of $AgNTf_2$ to form **6**, suggests that this process may be viable under catalytic conditions, and thus act to trap intermediate Au(I)-compounds. Similarly, the dinuclear gold intermediate **5** reacted with 3 equivalents of $AgNTf_2$ to provide the mixed metal species **6** showing that even preformed digold structures can be driven to the heterometallic structure.[14]

Such a silver-for-gold substitution seems only slightly downhill as it was found in catalytic experiments that the resting state monitonically shifted from **6** to **5** as the Au/Ag ratio was increased. The change in speciation was especially dramatic when gold was added as Ph_3PAuCl, which simul-

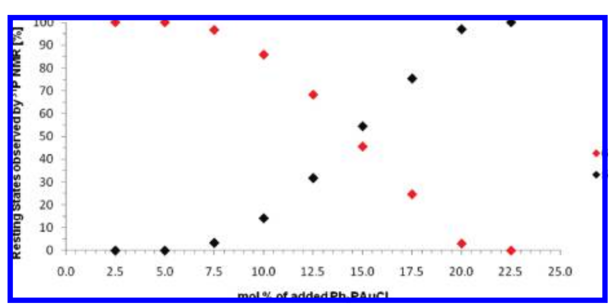


Figure 2. Change in catalyst resting state from **6** (Au−Ag) to **5** (Au−Au) upon additions of Ph_3PAuCl to a solution of 0.1 mmol of **1** and 25 mol % $AgNTf_2$ in CD_2Cl_2.

(11) We presume that Ag^+ is either coordinated by a weak neutral ligand (e.g. substrate) or by NTf_2^-. ^{19}F NMR data was not indicative. X-ray quality crystals have not been forthcoming.

(12) Examples of Au−Ag complexes with a bridging carbon: (a) Contel, M.; Garrido, J.; Gimeno, M. C.; Jones, P. G.; Laguna, A.; Laguna, M. Organometallics **1996**, *15*, 4939. (b) Contel, M.; Jiménez, J.; Jones, P. G.; Laguna, A.; Laguna, M. J. Chem. Soc., Dalton Trans. **1994**, 2515. (c) Fernández, E. J.; Hardacre, C.; Laguna, A.; Lagunas, M. C.; López-de-Luzuriaga, J. M.; Monge, M.; Montiel, M.; Olmos, M. E.; Puelles, R. C.; Sánchez-Forcada, E. Chem.−Eur. J. **2009**, *15*, 6222. (d) Fernández, E. J.; Gimeno, M. C.; Laguna, A.; López-de-Luzuriaga, J. M.; Monge, M.; Pyykkö, P.; Sundholm, D. J. Am. Chem. Soc. **2000**, *122*, 7287. (e) Fernández, E. J.; Laguna, A.; López-de-Luzuriaga, J. M.; Montiel, M.; Olmos, M. E.; Pérez, J.; Puelles, R. C. Organometallics **2006**, *25*, 4307. (f) Fernández, E. J.; Laguna, A.; López-de-Luzuriaga, J. M.; Monge, M.; Montiel, M.; Olmos, M. E.; Rodríguez-Castillo, M. Organometallics **2006**, *25*, 3639. (g) Ruiz, J.; Riera, V.; Vivanco, M.; García-Granda, S.; García-Fernández, A. Organometallics **1992**, *11*, 4077. (h) Vicente, J.; Chicote, M. T.; Alvarez-Falcón, M. M.; Jones, P. G. Organometallics **2005**, *24*, 4666. (i) Schuster, O.; Monkowius, U.; Schmidbaur, H.; Ray, S. S.; Krüger, S.; Rösch, N. Organometallics **2006**, *25*, 1004. (j) Wei, Q.-H.; Zhang, L.-Y.; Yin, G.-Q.; Shi, L.-X.; Chen, Z.-N. J. Am. Chem. Soc. **2004**, *126*, 9940. (k) Xie, Z.-L.; Wei, Q.-H.; Zhang, L.-Y.; Chen, Z.-N. Inorg. Chem. Commun. **2007**, *10*, 1206. (l) Wei, Q.-H.; Yin, G.-Q.; Zhang, L.-Y.; Chen, Z.-N. Organometallics **2006**, *25*, 4941. (m) Hussain, M. S.; Mazhar-Ul-Haque; Abu-Salah, O. M. J. Cluster Sci. **1996**, *7*, 167. (n) Mazhar-Ul-Haque; Horne, W.; Abu-Salah, O. M. J. Crystallogr. Spectrosc. Res. **1992**, *22*, 421. Other examples: (o) Crespo, O.; Gimeno, M. C.; Laguna, A.; Larraz, C.; Villacampa, M. D. *Chem.−Eur. J.* **2007**, *13*, 235. (p) Catalano, V. J.; Moore, A. L. Inorg. Chem. **2005**, *44*, 6558. (q) Catalano, V. J.; Etogo, A. O. Inorg. Chem. **2007**, *46*, 5608. (r) Catalano, V. J.; Etogo, A. O. J. Organomet. Chem. **2005**, *690*, 6041. (s) Vicente, J.; Chicote, M.-T.; Lagunas, M.-C. Inorg. Chem. **1993**, *32*, 3748. (t) Catalano, V. J.; Horner, S. J. Inorg. Chem. **2003**, *42*, 8430. (u) Rawashdeh-Omary, M. A.; Omary, M. A.; Fackler, J. P., Jr. Inorg. Chim. Acta **2002**, *334*, 376. (v) Fernández, E. J.; Laguna, A.; López-de-Luzuriaga, J. M.; Monge, M.; Pyykkö, P.; Runeberg, N. Eur. J. Inorg. Chem. **2002**, 750.

(13) Alternatively the two diastereofaces could be rapidly interconverting through a doubly argented intermediate or transition state. Laguna has recently reported a cluster with just such a bonding model, see refs 12e and 12f.

taneously decreased the Ag^+ concentration by precipitation of AgCl (Figure 2 and 3). Under suitably balanced conditions it is therefore possible to detect both digold and mixed gold/silver resting states.[15]

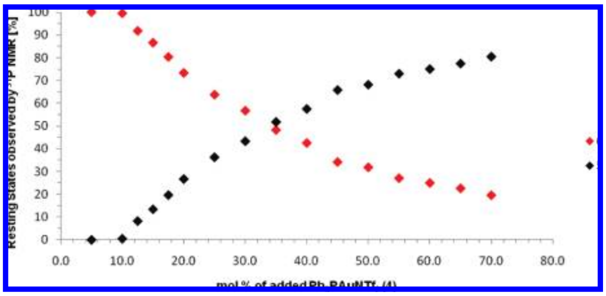


Figure 3. Change in catalyst resting state from **6** (Au−Ag) to **5** (Au−Au) upon additions of **4** to a solution of 0.1 mmol **1** and 15.5 mol % $AgNTf_2$ in CD_2Cl_2.

The effect of excess $AgNTf_2$ on the kinetics of the cyclization was also investigated. At a Au(I) loading of 5 mol %, the rate with a 3-fold excess of Ag^+ was significantly retarded relative to the gold only experiment (Figure 4). Unexpected was the increased rate of **1** consumption as the reaction progressed.

We show herein that even if the reactants are untouched by Ag^+, silver ions can still influence gold-catalyzed reactions by intercepting key organogold intermediates to form dinuclear intermediates with their own unique reactivity. A structural model based on existing Au/Ag cluster chemistry literature is proposed, which may rationalize known Ag^+ effects.

(14) Auro-argentophilic interactions are stronger than Au-Au interactions due to the introduction of a dipolar interaction: Catalano, V. J.; Malwitz, M. A.; Etogo, A. O. *Inorg. Chem*. **2004**, *43*, 5714.
(15) After adding >15 mol % **4** some of it was also observed in the NMR, as was $(Ph_3P)_2AuNTf_2$, see ref 4b.

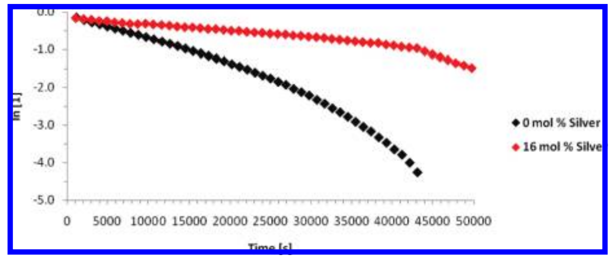


Figure 4. ln [**1**] versus time [s] for the conversion to **2** by ^{1}H NMR; 0.1 mmol **1**, 5 mol % $Ph_3PAuNTf_2$ (**4**), and 0.05 mmol hexamethylbenzene (internal standard) in 0.5 mL CD_2Cl_2; 6.2 mg (16 mol %) $AgNTf_2$ was added as a solid (see Supporting Information for details).

Acknowledgment. We thank J. Jacob Byrne (University of North Carolina at Chapel Hill) for samples of **1**. Financial support is gratefully acknowledged from the Fulbright Foreign Student Program (for D.W.) and the National Institute of General Medicine (GM-60578).

Supporting Information Available: Synthetic procedures, characterization, and additional spectroscopic data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL902116B