

Synthesis of Gold Allyloxysulfonium Complexes and Elimination to form an α,β -Unsaturated Aldehyde

Nana Kim and Ross A. Widenhoefer*

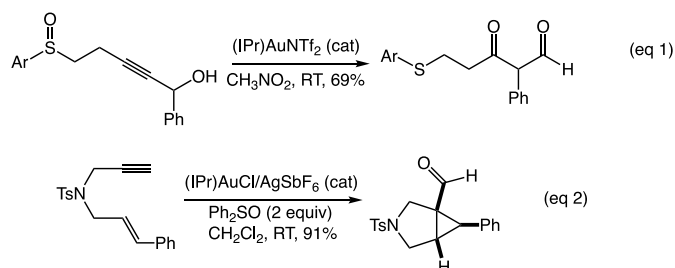
 Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

www.rsc.org/

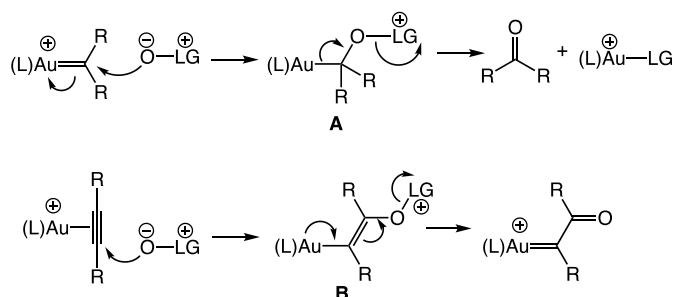
Treatment of the gold vinyl carbene/allylic cation complex (*E*)- $[(\text{IPr})\text{AuC}(\text{H})\text{C}(\text{H})\text{C}(4\text{-C}_6\text{H}_4\text{OMe})_2]^+ \text{OTf}^-$ with sulfoxides at -95°C formed the corresponding gold allyloxysulfonium complexes $[(\text{IPr})\text{AuC}(\text{H})(\text{OSR}_2)\text{C}(\text{H})=\text{C}(4\text{-C}_6\text{H}_4\text{OMe})_2]^+ \text{OTf}^-$ [$\text{R} = \text{Me}, -(\text{CH}_2)_4-, \text{Ph}$] in $\geq 95 \pm 5\%$ NMR yield. Allyloxysulfonium gold complexes underwent elimination at or below room temperature to form 3,3-bis(4-methoxyphenyl)acrylaldehyde in $\geq 72\%$ yield.

Sulfoxides, heterocyclic *N*-oxides, and related nucleophilic oxidants containing an oxygen atom bound to a leaving group (O–LG) have been widely employed as oxygen transfer agents in a variety of gold(I)-catalyzed transformations.^{1–5} Notable examples include the intramolecular oxidation/rearrangement of sulfinyl alkynes to form β -dicarbonyl compounds (eq 1) and the oxidative cycloaddition of enynes to form cyclopropyl carboxaldehydes (eq 2).^{3,4} Two general mechanisms have been invoked for oxygen atom transfer in these transformations involving attack of the nucleophilic oxidant at either the C1 position of a gold carbene complex to generate a gold alkoxy-sulfonium/pyridinium intermediate (**A**) or at the alkyne carbon atom of a gold π -alkyne complex to generate a gold alkenyloxysulfonium/pyridinium intermediate (**B**) (Scheme 1). Heterolytic cleavage of the O–LG bond of **A** or **B** then completes oxygen atom transfer to the substrate, in the latter case to generate a reactive α -oxo carbene complex.^{1,6} However,



^a French Family Science Center, Duke University, Durham, North Carolina, USA

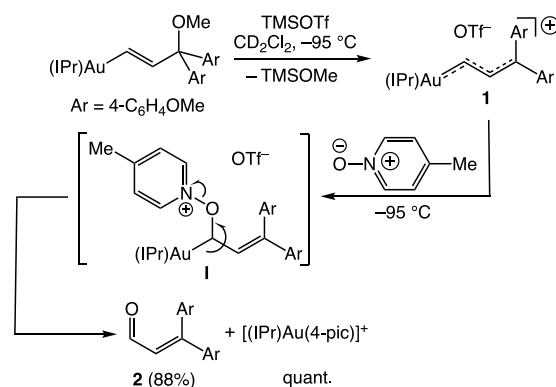
^b Electronic Supplementary Information (ESI) available: For ESI and crystallographic data in CIF see DOI: 10.1039/x0xx00000x.



Scheme 1. Proposed mechanisms for oxygen atom transfer from nucleophilic oxidants (O–LG) to cationic gold carbene (top equation) and π -alkyne complexes (bottom equation).

despite the widespread employment of these oxygen atom transfer reagents in gold(I) catalysis, the key gold oxysulfonium/pyridinium intermediates have never been directly observed. As such, significant gaps remain in our understanding of the structure and reactivity of these intermediates and in the mechanisms of oxygen atom transfer in gold(I)-catalysis.

We have recently reported the synthesis of cationic, two coordinate gold(I) allylic cation/vinyl carbene complex **1**,

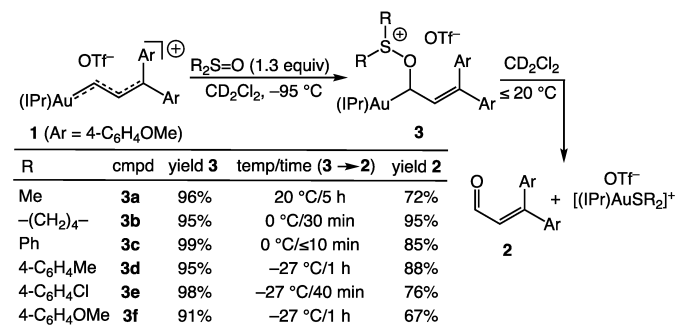


Scheme 2. Synthesis of gold vinyl carbene/allylic cation complex **1** [IPr = 1,3-bis(2,6-bis-(diisopropylphenyl)imidazol-2-ylidene)] and reaction with 4-picoline-*N*-oxide to form aldehyde **2**.

generated via the Lewis acid-mediated ionization of a gold (γ -methoxy) vinyl complex (Scheme 2).⁷ Complex **1** reacted rapidly at -95°C with a range of nucleophiles, preferentially at the C1 carbon atom. Included in this family of transformations was the reaction of **1** with 4-picoline-*N*-oxide to form 3,3-bis(4-methoxyphenyl)acrylaldehyde (**2**), presumably via the unobserved gold allyloxypyridinium intermediate **I** (Scheme 2).^{8,9} Despite the instability of intermediate **I**, we reasoned that reaction of vinyl carbene complex **1** with sulfoxides might lead to formation of detectable gold allyloxysulfonium complexes owing to the stronger S–O bond relative to an N–O bond.¹⁰ Indeed, here we report the direct observation and thermal elimination of gold allyloxysulfonium complexes.

Treatment of a freshly prepared solution of **1** in CD_2Cl_2 with dimethylsulfoxide (DMSO; 1.3 equiv) at -95°C led to immediate disappearance of the bright red/orange color of **1** with formation of the gold allyloxydimethylsulfonium complex **3a** in $96 \pm 5\%$ yield by ^1H NMR spectroscopy (Scheme 3). In a similar manner, treatment of **1** with tetrahydrothiophene sulfoxide (THTSO), diphenylsulfoxide (DPSO), or *p*-substituted diarylsulfoxides ($4\text{-C}_6\text{H}_4\text{R}$)₂S (R = Me, Cl, OMe) at -95°C formed the corresponding gold allyloxysulfonium complexes **3b**–**3f** in $\geq 95 \pm 5\%$ yield (Scheme 3). Complexes **3** were thermally unstable and were characterized in solution by NMR spectroscopy at or below 0°C . For example, selective attack of DMSO at the C1 vinyl carbene carbon atom of **1** was established by a pair of mutually-coupled doublets at δ 3.60 and 5.65 ($J = 11.3\text{ Hz}$) in the ^1H NMR spectrum of **3a** assigned to the aliphatic C1 and vinylic C2 protons, respectively.¹¹ Similarly, the ^{13}C NMR spectrum of the ^{13}C -labelled isotopomer $[(\text{IPr})\text{Au}^{13}\text{C}(\text{H})(\text{OSMe}_2)^{13}\text{C}(\text{H})=\text{C}(4\text{-C}_6\text{H}_4\text{OMe})_2]^+ \text{OTf}^-$ (**3a**- $^{13}\text{C}_2$) displayed a pair of mutually-coupled multiplets at δ 61.6 (dd, $^1J_{\text{CH}} = 139.8$, $^1J_{\text{CC}} = 41.3\text{ Hz}$) and 113.6 (dd, $^1J_{\text{CH}} = 158.0$, $^1J_{\text{CC}} = 42.3\text{ Hz}$) assigned to the aliphatic C1 and vinylic C2 carbon atoms, respectively.

When a solution of **3a** in CD_2Cl_2 was warmed at 20°C for $\sim 5\text{ h}$, **3a** was completely consumed to form aldehyde **2** in 72% yield along with $[(\text{IPr})\text{Au}(\text{SMe}_2)]^+ \text{OTf}^-$ (Scheme 3).¹¹ In a similar manner, complex **3b** underwent elimination at 0°C over the course of 30 min to form **2** in quantitative yield while complexes **3c**–**3f** underwent elimination at or below 0°C to form **2** in 67–88% yield (Scheme 3). To quantify the reactivity differences between complexes **3a**–**3c** with respect to elimination, we analysed the kinetics of the disappearance of **3a**, **3b**, and **3c** in



Scheme 3. Synthesis of gold allyloxysulfonium complexes **3** and thermal elimination to form **2**.

Table 1. First-order rate constants for the conversion of gold allyloxysulfonium complexes **3** (17 mM) to aldehyde **2** in CD_2Cl_2 .

entry	compd	temp ($^\circ\text{C}$)	$k (10^4 \text{ s}^{-1})^a$	entry	compd	temp ($^\circ\text{C}$)	$k (10^4 \text{ s}^{-1})^a$
1	3a	33	11.7 ± 0.6	10	3b	−9	7.97 ± 0.12
2	3b	−16	2.14 ± 0.02	11	3b	−3	12.5 ± 0.2
3	3b	−16	2.33 ± 0.10	12	3b	−3	15.2 ± 0.34
4	3b	−16	2.41 ± 0.06	13	3b	−20	1.33 ± 0.37
5	3c	−28	9.7 ± 0.22	14	3b	−21	1.11 ± 0.01
6	3d	−27	3.71 ± 0.05	15	3b	−28	0.315 ± 0.022
7	3e	−27	15.8 ± 0.4	16 ^b	3b	−16	2.12 ± 0.05
8	3f	−27	4.05 ± 0.17	17 ^c	3a	33	9.6 ± 0.4
9	3b	−9	7.62 ± 0.11	18 ^d	3a	33	1.48 ± 0.09

^aFirst-order decay was observed in all cases. ^bReaction mixture contained THTSO (51 mM). ^cReaction mixture contained DMSO- d_6 (0.45 M). ^dReaction mixture contained DMSO- d_6 (3.0 M).

CD_2Cl_2 at 33, -16 , and -28°C , respectively, employing ^1H NMR spectroscopy. In each case, disappearance of **3** obeyed first-order kinetics (Table 1, entries 1–5) with activation energies that decreased in the order **3a** ($\Delta G^\ddagger_{306\text{K}} = 22.0\text{ kcal/mol}$) > **3b** ($\Delta G^\ddagger_{257\text{K}} = 19.2\text{ kcal/mol}$) > **3c** ($\Delta G^\ddagger_{234\text{K}} = 17.6\text{ kcal/mol}$). To quantify the effect of the electron donor ability of the R_2S moiety on the rate of elimination from complexes **3**, we analysed the kinetics of the disappearance of complexes **3d**–**3f** at -27°C (Table 1, entries 5–8). A plot of $\log k$ versus $\Sigma\sigma$ gave acceptable fit ($R^2 = 0.90$) with a slope of $\rho = 1.0 \pm 0.2$ (Figure 1),¹¹ which established that the electron density on sulfur increased in the transition state for elimination relative to the ground state.

The relative stabilities of complexes **3a**–**3c** with respect to elimination tracked with the relative stabilities of these complexes with respect to sulfoxide displacement. For example, treatment of the allyloxydiphenylsulfonium complex **3c** with THTSO (1 equiv) at -32°C led to rapid (15 min) and quantitative displacement of DPSO to form the allyloxytetramethylenesulfonium complex **3b** (Scheme 4). Similarly, treatment of **3b** with DMSO (1 equiv) at -24°C for 1 h led to quantitative displacement of THTO to form the allyloxydimethylsulfonium complex **3a**.

Additional kinetic experiments were performed to gain insight into the mechanism of the conversion of complexes **3** to **2**. To determine the activation parameters for elimination, the rate of conversion of **3b** to **2** was determined as a function of temperature from -28 to -3°C (Table 1, entries 2–4, 9–15); an Eyring plot of these data provided the activation parameters $\Delta H^\ddagger = 20.4 \pm 0.6\text{ kcal/mol}$ and $\Delta S^\ddagger = 1.1 \pm 0.5\text{ eu}$ (Figure 1). We likewise evaluated the effect of exogenous sulfoxide on the rate

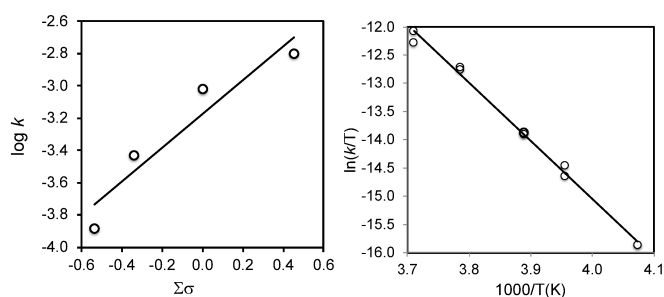
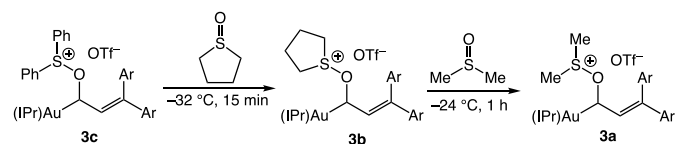
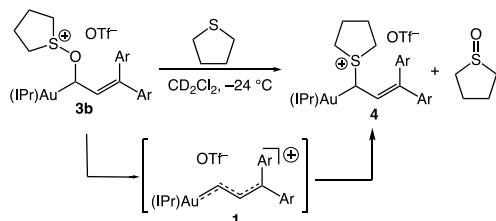


Figure 1. Hammett plot of the elimination of complexes **3c**–**3f**, where $\rho = 1.0 \pm 0.2$ (left plot). Eyring plot of the elimination of **3b** over the temperature range from -28 to -3°C , where $\ln(k/T) = (-10300 \pm 280)/T + (26 \pm 1)$ (right plot).



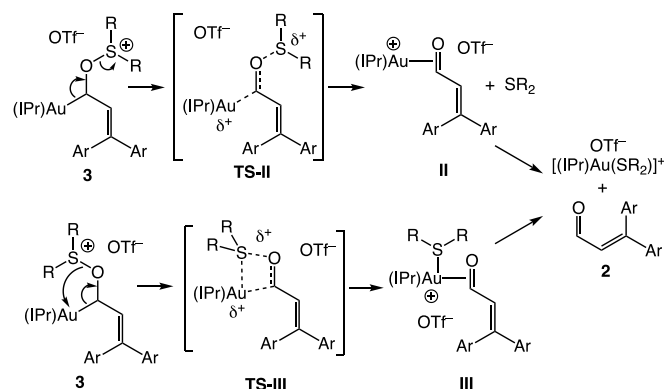
Scheme 4. Sulfoxide exchange experiments involving complexes **3a** - **3c**.



Scheme 5. Reaction of **3b** with THT to form **4**.

of elimination. For example, the rate of elimination of **3b** (17 mM) decreased nominally (<10%) in the presence of three equivalents of THTSO (51 mM; Table 1, entries 2-4, 16). In comparison, the rate of elimination of **3a** in CD_2Cl_2 decreased by a factor of eight as the $\text{DMSO}-d_6$ concentration increased from 0 to 3.0 M (Table 1, entries 1, 17, 18), which we attribute to increasing solvent polarity.^{¶¶¶} Evaluation of the effect of free THT on the rate of elimination of **3b** was precluded by the rapid substitution of THTSO with THT to form the α -sulfonium carbenoid complex **4** (Scheme 5). Specifically, conversion of an equimolar mixture of **3b** and THT to **4** at -24°C ($k = 7.22 \pm 0.01 \times 10^{-4} \text{ s}^{-1}$) was an order of magnitude faster than was decomposition of **3b** and displayed first-order kinetics to ≥ 3 half-lives, which points to a dissociative mechanism involving rate-limiting formation of free **1** followed by rapid trapping by THT (Scheme 5).

We considered two mechanisms for the conversion of gold allyloxysulfonium complexes **3** to aldehyde **2** involving either (1) dissociative elimination via an *anti*-periplanar transition state (**TS-II**) to form π -aldehyde intermediate **II** and free sulfide followed by ligand exchange to form **2** and $[(\text{L})\text{AuSR}_2]^+$ (Scheme 6, top) or (2) non-dissociative elimination via a *syn*-periplanar transition state (**TS-III**) to form the three-coordinate gold π -aldehyde sulfide intermediate **III** followed by dissociation of **2** (Scheme 6, bottom).¹²



Scheme 6. Potential dissociative (top path) and non-dissociative (bottom path) elimination pathways for the conversion of complexes **3** to aldehyde **2**.

Both pathways depicted in Scheme 6 are consistent with the observed first-order dependence of the rate of elimination on [**3**], the zero-order dependence of the rate of elimination of **3b** on [THTSO], and the decreasing rate of elimination of **3a** with increasing solvent polarity, which points to increased delocalization of positive charge in the transition state for elimination relative to the ground state. However, the small positive entropy of activation ($\Delta S^\ddagger = 1.1$) determined for the elimination of **3b** appears inconsistent with a dissociative elimination pathway and points to a non-dissociative pathway for elimination of **3** (Scheme 6, bottom pathway). Indeed, the entropy of activation determined for the elimination of **3b** is similar to values determined for β -hydride and β -alkyl elimination from transition metal alkyl complexes.¹³ Likewise, the Hammett reaction constant determined for the elimination of gold allyloxylarylsulfonium complexes **3c** - **3f** ($\rho = 1.0 \pm 0.2$) appears too small to account for the release of free sulfide in the transition state for elimination, pointing to a non-dissociative pathway for elimination where sulfide remains tricoordinated throughout elimination. As points of comparison, Hammett reaction constants for the oxidation of alkyl aryl sulfides with electrophilic halogen sources involving rate-limiting formation of RArSX^+ range from $\rho = -3.20$ to -4.25 .¹⁴

Although β -hydride elimination from gold(I) complexes is rare,¹⁵ the *syn*-migratory insertion of alkynes into Au(I) -heteroatom bonds is known.¹⁶⁻¹⁸ Notable among these examples is the *syn*-insertion of dimethyl acetylenedicarboxylate into the Au-P bond of gold phosphine complexes of the form $\text{Au(SAr)(PAr}_3)$ to form gold alkenylphosphonium complexes.¹⁸

In summary, we have generated thermally unstable gold allyloxysulfonium complexes **3** via the reaction of gold vinyl carbene/allylic cation complex **1** with sulfoxides and we have demonstrated the thermal elimination of complexes **3** to form aldehyde **2** and a gold sulfide complex. Kinetic analysis of the elimination of complexes **3**, in particular the small positive entropy of activation and modest Hammett reaction constant determined for the elimination of gold allyloxylarylsulfonium complexes **3c** - **3f**, points to a mechanism involving non-dissociative β -elimination through a *syn*-periplanar transition state. Unfortunately, experiments that would unambiguously distinguish between dissociative and non-dissociative mechanisms for elimination from complexes **3**, such as sulfide labelling experiments, were precluded by rapid exchange of free sulfide with the C1 sulfoxide group of complexes **3**.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We thank the NSF (CHE-1800273) for support of this research.

Notes and references

- ¶ The large H1-H2 vicinal coupling constants observed for complexes **3** was likewise observed for the analogous α -ammonium carbenoid complex $[(\text{IPr})\text{AuC(H)(py)C(H)=C(4-}$

- $\text{C}_6\text{H}_4\text{OMe}_2\text{]}^+ \text{OTf}^-$ and was attributed to the large H1–C1–C2–H2 dihedral angle of 160° estimated from X-ray analysis.⁷
- ¶¶** ^1H NMR analysis of the reaction mixture upon complete consumption of **3** was fully consistent with the formation of the corresponding gold sulfide complexes $[(\text{IPr})\text{AuSR}_2]^+ \text{OTf}^-$. However, given the limited dispersion of resonances in the ^1H NMR spectrum, it was not possible to distinguish between bound and free sulfide.
- ¶¶¶** Dielectric constants for CH_2Cl_2 and $\text{DMSO}-d_6$ (3.0 M) in CD_2Cl_2 are $\epsilon = 8.93$ and 15.3 , respectively.^{19,20}
- For reviews on gold α -oxo carbenoid complexes see: (a) Z. Zheng, Z. Wang, Y. Wang and L. Zhang, *Chem. Soc. Rev.*, 2016, **45**, 4448–4458; (b) Y. Wang and L. Zhang, *Synthesis*, 2015, **47**, A–Q; (c) L. Zhang, *Acc. Chem. Res.*, 2014, **47**, 877–888; (d) H.-S. Yeom and S. Shin, *Acc. Chem. Res.*, 2014, **47**, 966–977; (e) J. Xiao and X. Li, *Angew. Chem., Int. Ed.*, 2011, **50**, 7226; (f) M. C. B. Jaimes and A. S. K. Hashmi, in *Modern Gold Catalyzed Synthesis*, ed. A. S. K. Hashmi and F. D. Toste, Wiley-VCH, Weinheim, 2012, pp. 273–296.
 - For the gold-catalyzed ring opening/oxidative trapping of cyclopropenes see: (a) J. T. Bauer, M. S. Hadfield and A.-L. Lee, *Chem. Commun.*, 2008, 6405–6407; (b) M. S. Hadfield, J. T. Bauer, P. E. Glen and A.-L. Lee, *Org. Biomol. Chem.*, 2010, **8**, 4090–4095.
 - G. Li and L. Zhang, *Angew. Chem. Int. Ed.*, 2007, **46**, 5156 – 5159.
 - C. A. Witham, P. Mauleón, N. D. Shapiro, B. D. Sherry and F. D. Toste, *J. Am. Chem. Soc.*, 2007, **129**, 5838–5839.
 - For additional examples of gold(I)-catalyzed oxidative cyclization of 1,*n*-enynes see: (a) B. P. Taduri, S. M. Abu Sohail, H.-M. Cheng, G.-Y. Lin and R.-S. Liu, *Chem. Commun.*, 2007, 2530–2532; (b) D. Vasu, H.-H. Hung, S. Bhunia, S. A. Gawade, A. Das and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2011, **50**, 6911–6914; (c) S. Bhunia, S. Ghorpade, D. B. Huplé and R.-S. Liu, *Angew. Chem., Int. Ed.*, 2012, **51**, 2939–2942; (d) S. Ghorpade, M.-D. Su and R.-S. Liu, *Angew. Chem. Int. Ed.*, 2013, **52**, 4229–4234; (e) D. Qian and J. Zhang, *Chem. Commun.*, 2011, **47**, 11152–11154; (f) W. Wang, J. Yang, F. Wang and M. Shi, *Organometallics*, 2011, **30**, 3859–3869; (g) K. Ji and L. Zhang, *Org. Chem. Front.*, 2014, **1**, 34–38.
 - Base-mediated elimination of alkoxysulfonium ions is common in a range of DMSO-based alcohol oxidation processes: (a) T. T. Tidwell, *Synthesis*, 1990, 857–870; (b) T. T. Tidwell, *Org. React.*, 2004, 39.
 - N. Kim and R. A. Widenhoefer, *Chem. Sci.*, 2019, **10**, 6149–6156.
 - For additional examples of oxygen atom transfer to well defined gold carbene complexes see: (a) R. J. Harris and R. A. Widenhoefer, *Angew. Chem. Int. Ed.*, 2014, **53**, 9369–9371; (b) C. García-Morales, X.-L. Pei, J. M. Sarria Toro and A. M. Echavarren, *Angew. Chem. Int. Ed.*, 2019, **58**, 3957–3961.
 - For examples of oxidative trapping of carbenium ions with sulfoxides see: (a) Y. Ashikari, T. Nokami and J.-i. Yoshida, *Org. Lett.*, 2012, **14**, 938–941; (b) Y. Ashikari, T. Nokami and J.-i. Yoshida, *Org. Biomol. Chem.*, 2013, **11**, 3322–3331; (c) Y. Ashikari, T. Nokami and J.-i. Yoshida, *J. Am. Chem. Soc.*, 2011, **133**, 11840–11843.
 - (a) R. T. Sanderson, *Polar Covalence*, Elsevier, 1983; (b) R. T. Sanderson, *Chemical Bonds and Bond Energy*, Academic Press, 1976.
 - For validation of the additivity of Hammett σ values see: (a) P. Beltrame, P. L. Beltrame and L. Bellotti, *J. Chem. Soc., B*, 1969, 932–934; (b) P. Beltrame, P. L. Beltrame, M. L. Cereda and G. Lazzerini, *J. Chem. Soc., B*, 1969, 1100–1102; (c) J. E. Baldwin and J. A. Kapecki, *J. Am. Chem. Soc.*, 1970, **92**, 4868–4873; (d) D. J. McLennan and R. J. Wong, *J. Chem. Soc., Perkin Trans 2*, 1972, 279–285; (e) P. Beltrame, P. L. Beltrame, O. Sighinolfi and M. Simonetta, *J. Chem. Soc., B*, 1967, 1103–1108; (f) P. Beltrame, D. Pitea, and M. Simonet *J. Chem. Soc., B*, 1967, 1108–1111.
 - For computational analysis of the conversion of σ - to π -bound ligands at gold(I) centers see: L. N. dos Santos Comprido, J. E. M. N. Klein, G. Knizia, J. Kästner and A. S. K. Hashmi, *Chem. Eur. J.*, 2017, **23**, 10901–10905.
 - (a) M. Brookhart, A. F. Volpe, D. M. Lincoln, I. T. Hovath and J. M. Millar, *J. Am. Chem. Soc.*, 1990, **112**, 5634–5636; (b) L. Wang and T. C. Flood, *J. Am. Chem. Soc.*, 1992, **114**, 3169–3170; (c) S. P. Ermer, G. E. Struck, S. P. Bitler, R. Richards, R. Bau and T. C. Flood, *Organometallics*, 1993, **12**, 2634–2643; (d) N. M. Doherty and J. E. Bercaw, *J. Am. Chem. Soc.*, 1985, **107**, 2670–2682; (e) B. J. Burger, B. D. Santarsiero, M. S. Trimmer and J. E. Bercaw, *J. Am. Chem. Soc.*, 1988, **110**, 3134–3146.
 - (a) D. Thenraja, P. Subramaniam and C. Srinivasan, *J. Chem. Soc., Perkin Trans. 2*, 2002, 2125–2129; (b) U. Miotti, G. Modena and L. Seda, *J. Chem. Soc., B*, 1970, 802–805; (c) F. Ruff and A. Kucsman, *J. Chem. Soc., Perkin Trans. 2*, 1975, 509–519.
 - (a) C.-M. Ting, Y.-L. Hsu and R.-S. Liu, *Chem. Commun.*, 2012, **48**, 6577–6579; (b) M. C. Reis, C. S. López, E. Kraka, D. Cremer and O. N. Faza, *Inorg. Chem.*, 2016, **55**, 8636–8645.
 - M. Joost, L. Estevez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *J. Am. Chem. Soc.*, 2014, **136**, 10373–10382.
 - (a) T. Tamai, K. Fujiwara, S. Higashimae, A. Nomoto and A. Ogawa, *Org. Lett.*, 2016, **18**, 2114–2117; (b) X. Zhang and K. T. Wang, *RSC Adv.*, 2015, **5**, 34439–34446.
 - H. Kuniyasu, T. Nakajima, T. Tamaki, T. Iwasaki and N. Kambe, *Organometallics*, 2015, **34**, 1373–1376.
 - A. Jouyban and S. Soltanpour, *J. Chem. Eng. Data*, 2010, **55**, 2951–2963.
 - A. A. Maryott and E. R. Smith, *Table of dielectric constants of pure liquids*, Circular of the National Bureau of Standards, 514; Washington, D.C.; U. S. Gov. Print. Office, 1951.