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Reactivity of "Ligand-Free" Au+: C−H and C−C Activation versus π Coordination

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S Supporting Information

ABSTRACT: $[(Me_2S)Au]^+$ cations, generated from (Me_2S)-AuCl and $AgSbF_6$ in dichloromethane at 0−20 °C, serve as sources of solvated Au^+ (alongside unreactive $[Au(SMe_2)_2]^+$), which reacts with the methyl-substituted arenes $C_6Me_{6−n}H_n$ (n = 0−2) with C−H bond cleavage to give the sulfonium salts $[C_6Me_{5−n}H_nCH_2SMe_2]^+$. There was no evidence for arene π coordination to Au^+ or for the formation of σ-bonded Au−benzyl species. Surprisingly, the reaction of Au^+ with CH_2Ar_2 leads to C−C bond cleavage (Ar = $2,4,6\text{-}C_6H_2Me_3$). The reactions are highly selective for benzylic C−H and C−C bonds, whereas metalation of the arene ring is not observed.
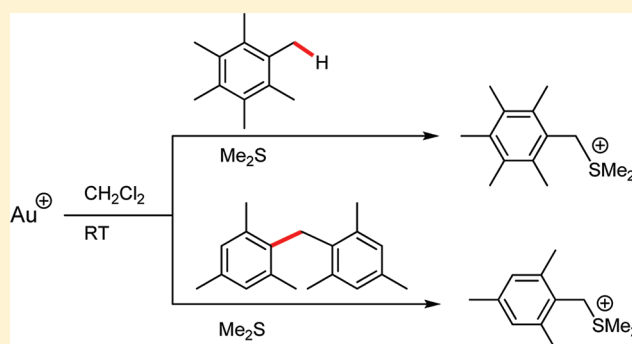
The complexation of arenes by coinage and related heavy metals has a long tradition. For example, benzene coordination to silver ions in aqueous solutions led to the suggestion of half-sandwich (L−Ag+) and inverse sandwich (Ag+−L−Ag+) bonding concepts long before the discovery of metallocenes.[1] Since then, numerous Ag(I) complexes with η^1- and η^2-coordinated arenes have been characterized.[2] Arene coordination to electrophilic zinc[3] and mercury(II)[4] metal centers is also well established. Following our recent isolation of a series of mono-, bis-, and tris-arene complexes of thallium stabilized by very weakly coordinating anions,[5,6] we wished to explore whether the same synthetic strategy, i.e. partnering heavy-metal cations with weakly coordinating anions in nondonor solvents, could be extended to a missing link in this compound family: namely, gold(I).

The coordination chemistry of gold with π ligands such as alkenes, alkynes, and arenes is comparatively unexplored.[7] For example, whereas Stone's synthesis of $Pt(C_2H_4)_3$ and Pt-(COD)$_2$ dates back more than 30 years (COD = 1,5-cyclooctadiene),[8] the analogous homoleptic olefin complexes of Au^+ have only been reported in the past few years.[9] Isolable π-arene complexes of gold are known only if stabilized by strong donor ligands.[10]

Earlier work had shown that the most stable zinc and thallium arene complexes were obtained with methyl-substituted benzenes.[3,5,6] We report here that the interaction of such arenes with "ligand-free"[11] Au^+ ions follows a distinctly different route, where C−H and C−C activations are preferred over arene π coordination.

The reaction of equimolar amounts of $(Me_2S)AuCl$, $AgSbF_6$, and hexamethylbenzene in dichloromethane in the absence of light at room temperature was found to lead cleanly to the functionalization of a benzylic C−H bond, to give $[C_6Me_5CH_2SMe_2][SbF_6]$ (**1**), alongside colloidal gold. The

originally anticipated π-coordination of C_6Me_6 to Au(I) was not observed, and there was no evidence for conventional C−H activation by an electrophilic metal center and formation of an Au−C σ-bond (Scheme 1).

Scheme 1
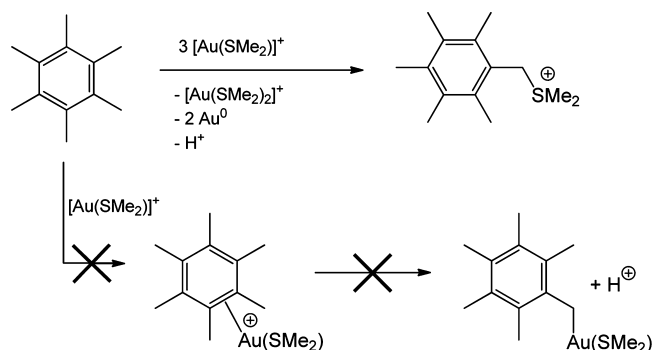
Monitoring the process by ^1H NMR spectroscopy showed that the reaction was accompanied by the formation of $[Au(SMe_2)_2][SbF_6]$ (**2**). In the solid state, **2** contains two independent binuclear cations $[L_2Au\cdots AuL_2]^{2+}$ held together by aurophilic interactions: Au(1)−Au(2) = 3.139(2) Å and Au(3)−Au(3′) = 3.087(2) Å.[12]

There was no reaction with hexamethylbenzene of either $(Me_2S)AuCl$ or $AgSbF_6$ alone. The introduction of 1 equiv or more of free dimethyl sulfide prior to addition of $(Me_2S)AuCl$

and AgSbF$_6$ gave only unreactive [Au(SMe$_2$)$_2$][SbF$_6$] in quantitative yield, without arene ring activation.

Formation of **1** was also observed using AuBr$_3$(SMe$_2$)/3AgSbF$_6$,[13] while (THT)AuCl (THT = tetrahydrothiophene) gives the corresponding THT—sulfonium cation **3** (Table 1).

Table 1. C—H Activation of C$_6$Me$_6$ by Gold Complexes^a

entry	Au complex	activator	product	yield^b
1	(Me$_2$S)AuCl	AgSbF$_6$	[Me$_5$C$_6$CH$_2$SMe$_2$][SbF$_6$] (**1**)	33
2	(Me$_2$S)AuCl			0
3		AgSbF$_6$		0
4	(Me$_2$S)AuBr$_3$	3 AgSbF$_6$	[Me$_5$C$_6$CH$_2$SMe$_2$][SbF$_6$] (**1**)	33
5	(THT)AuCl	AgSbF$_6$	[Me$_5$C$_6$CH$_2$THT][SbF$_6$] (**3**)	30
6	(Me$_2$S)AuCl	AgBF$_4$	[Me$_5$C$_6$CH$_2$SMe$_2$][BF$_4$] (**4**)	33
7	(Me$_2$S)AuCl	AgOTf	[Me$_5$C$_6$CH$_2$SMe$_2$][OTf] (**5**)	32
8	(Me$_2$S)AuCl	^{i}Pr$_3$SiOTf		0

^{a}Reaction conditions: C$_6$Me$_6$ (0.5 mmol), LAuCl (0.5 mmol), AgX (0.5 mmol), CH$_2$Cl$_2$ (15 mL), N$_2$ atmosphere, 20 °C, 1 h. ^{b}Yields (%) determined by ^{1}H NMR spectroscopy, relative to initial C$_6$Me$_6$ concentration.

No reaction occurred with (Ph$_3$P)AuCl, (C$_5$H$_5$N)AuCl, and ligand-free AuCl (presumably due to the last species' insolubility). Thioether ligands are particularly suitable here, since they not only help to solubilize the gold chloride precursors but are also sufficiently labile to undergo the ligand exchange reactions required to generate the active species. On the other hand, using (Bu$^t_2$S)AuCl/AgSbF$_6$ led only to reduction to metallic gold, without C—H activation. The nature of the silver activator is not critical, whereas NaBF$_4$ and ^{i}Pr$_3$SiOTf lead to the formation of gold films.

The reaction follows the stoichiometry given in eq 1.

$$Ar-CH_3 + 3[Au(SR_2)]^+$$
$$\rightarrow [Ar-CH_2SR_2]^+ + [Au(SR_2)_2]^+ + 2Au(0)$$
$$+ H^+ \qquad\qquad (1)$$
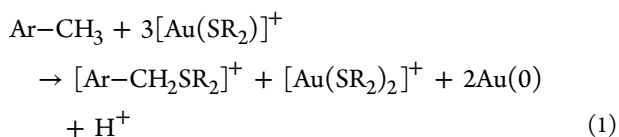
For most arene substrates tested, an arene to gold molar ratio of 1:1 was employed and kept constant for comparison. The maximum achievable conversion of Ar—CH$_3$ was therefore 33% (Table 1). In agreement with eq 1, employing a C$_6$Me$_6$ to Au ratio of 1:3 gave near-quantitative hydrocarbon conversion. There was, however, no reaction between C$_6$Me$_6$ and [Au(SMe$_2$)$_2$][SbF$_6$], confirming that the [Au(SMe$_2$)$_2$]$^+$ ion is an unreactive side product.

Surveying a range of aromatic substrates revealed that the C—H activation is highly selective and *exclusively involves the CH$_3$ groups*, never the C—H bonds of the arene ring (Table 2). This selectivity is in contrast with the reactions of most electrophilic late transition metals, where ring metalation is strongly favored.[14] This selectivity also differs from the reaction of arenes with AuCl$_3$, which readily proceed under ring metalation to give [(aryl)AuCl$_2$]$_2$.[15]

While hexamethylbenzene and 1,2,4,5-tetramethylbenzene (durene) react at 20−30 °C, pentamethylbenzene required cooling to 0 °C for clean C—H activation to take place, giving a mixture of ortho, meta, and para regioisomers in the ratio 51:29:20. No reaction was observed with mesitylene, 1,2,4-trimethylbenzene, o- and p-xylene, or toluene.
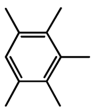
The relative reactivity of methyl-substituted arenes was probed by competition experiments, using equimolar mixtures of (i) hexamethyl- and pentamethylbenzene (0 °C, 2 h) and (ii) hexamethyl- and 1,2,4,5-tetramethylbenzene in dichloromethane (room temperature, 1 h), in the presence of (Me$_2$S)AuCl/AgSbF$_6$. In each case the activation of C$_6$Me$_6$ was strongly favored (29.8% and 1.5% conversion for reaction i and 28.8% and 3.0% for reaction ii); the combined yield was close to the expected value of 33%.

The reaction of dimesitylmethane takes a rather different and unexpected path: exposure to Au$^+$ in the presence of SMe$_2$ led predominantly to C—C bond cleavage (Scheme 2). The major product is [2,4,6-Me$_3$H$_2$C$_6$CH$_2$SMe$_2$][SbF$_6$] (**8**), accompanied by a small amount of a component derived from C—H activation of the methylene bridge (**9**). Signals consistent with the formation of [Au(mesityl)]$_5$[16] were also observed in the ^{1}H NMR spectrum of a reaction conducted at −10 °C over a 5 h period.

The kinetics of reaction 1 can be conveniently monitored by ^{1}H NMR spectroscopy. Since each C—H bond activation is accompanied by formation of H$^+$, the reaction can also be independently monitored by pH measurements (Figure 1); the rate constants obtained by either method are in very close agreement. The kinetic isotope effect, $k_H/k_D \approx 3.5$, is consistent with the breaking of a C—H bond in the rate-limiting step.

There was no evidence for the formation of gold π complexes or benzylgold species. Monitoring the reaction by EPR spectroscopy failed to detect any involvement of radicals. The most plausible reaction path, in our view, is the two-electron oxidation of the arenes to the corresponding resonance-stabilized carbocations, which are then scavenged by thioethers (Scheme 3). The required solvated Au$^+$ cations are generated by the ligand exchange equilibrium 2[LAu]$^+$ ⇌ Au$^+$ + [AuL$_2$]$^+$.[17] This proposal gains some support from the reaction of Au$^+$ ions with benzene in the gas phase, which has been

Table 2. C—H Activation of Methyl-Substituted Arenes^a

Entry	^{Me}ArCH$_3$	[MeArCH$_2$SMe$_2$]$^+$	Yield (%)^b
1^c		[o-C$_6$Me$_4$CH$_2$SMe$_2$]$^+$ **6a**	16.8
		[m-C$_6$Me$_4$CH$_2$SMe$_2$]$^+$ **6b**	9.6
		[p-C$_6$Me$_4$CH$_2$SMe$_2$]$^+$ **6c**	6.7
2		[Me$_3$H$_2$C$_6$CH$_2$SMe$_2$]$^+$ **7**	33

^{a}Reaction conditions: ArCH$_3$ (0.5 mmol), (Me$_2$S)AuCl (0.5 mmol), AgSbF$_6$ (0.5 mmol) in CH$_2$Cl$_2$ (15 mL), 1 h. ^{b}Yields determined by ^{1}H NMR spectroscopy, relative to initial ArCH$_3$. ^{c}Conditions: 0 °C, 3 h.

Scheme 2
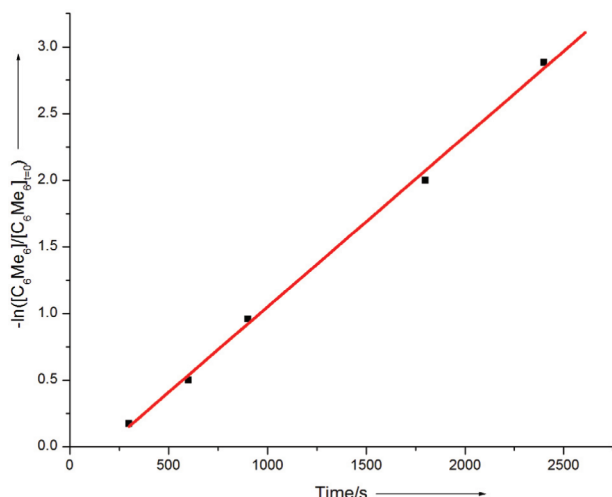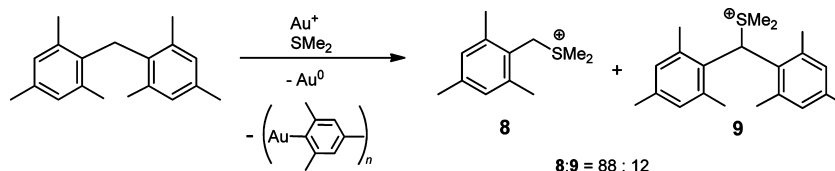
Figure 1. C−H activation of C_6Me_6 (CH_2Cl_2, 30 °C) determined from the pH change: $k = 0.0013$ s^{-1}.

shown to proceed both to Au(η-C_6H_6)$^+$ and to Au^0 + [C_6H_6]$^{•+}$.[18] The oxidation potentials of arenes to their respective radical cations[19] suggest that durene and 1,2,3,5-tetramethylbenzene may be susceptible to oxidative activation by Au$^+$, while p-xylene, mesitylene, and toluene are not, as has been borne out by our observations.[20]

In summary, in situ generated Au$^+$ ions in weakly coordinating solvents react with benzylic C−H and C−C bonds under remarkably mild (0−20 °C), nonacidic, non-aqueous conditions.[21] The reactions proved highly selective for −CH$_3$ rather than ring CH activation. Gold(I) cations differ in this respect from other electrophilic heavy-metal ions such as Ag$^+$, Tl$^+$, and Hg^{2+}, which readily form arene π complexes, and from AuCl$_3$, which metalates arenes to give [(aryl)AuCl$_2$]$_2$.[15] The observations are consistent with the formation of carbocationic intermediates, which are quenched by thioethers. Efforts to convert these stoichiometric reactions into productive catalytic systems are continuing.

ASSOCIATED CONTENT

Ⓢ Supporting Information
Text, tables, figures, and CIF files giving experimental and spectroscopic details and crystal data for **1**−**3**, **8**, and **9**. This material is available free of charge via the Internet at http://pubs.acs.org. CCDC Nos. 818512−818516 also contain the

supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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DEDICATION

This contribution is dedicated to the memory of Gordon Stone, with gratitude for his inspiration and support.

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Scheme 3
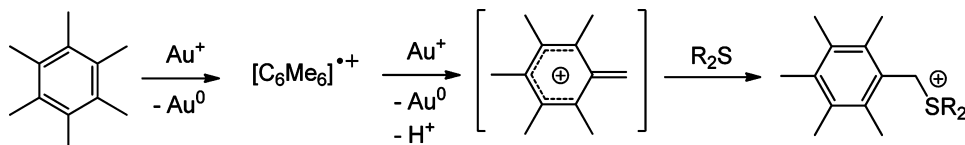
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(11) The term "ligand-free" refers here to ions stabilized only by weak anion interactions and weakly coordinating solvents such as dichloromethane.

(12) For the crystallographic characterization details, see the Supporting Information.

(13) As indicated by the formation of Au(0) in this reaction, Au(III) is reduced under these conditions and therefore exhibits the same reaction pattern as outlined for Au(I) precursors.

(14) For example, in the Pd(IV)-mediated chlorination of methylated arenes, ring-chlorination ≫ benzylic chlorination: McCall, A. S.; Wang, H.; Desper, J. M.; Kraft, S. *J. Am. Chem. Soc.* **2011**, *133*, 1832.

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(17) In principle there is the possibility that Au^+ disproportionates: $3Au^+ \rightarrow 2Au^0 + Au^{3+}$, to give Au^{3+} as the active species. Such an ion would, however, react preferentially with SMe_2 and, as is known for Au(III), lead to ring metalation; none of these products are observed.

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(20) Precise values for the Au^+/Au^0 couple in dichloromethane solvent are lacking. The standard potential for Au^+/Au of +1.83 V (vs standard hydrogen electrode) compares with those of hexamethylbenzene (1.58 V), pentamethylbenzene (1.69 V), and tetramethylated arenes (1.75−1.82 V) in acetonitrile vs the standard calomel electrode (SCE). The SCE/SHE correction is +0.241 V.[19]

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