Gold-Catalyzed Hydroarylation of Alkenes with Dialkylanilines

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Ⓢ *Supporting Information*

ABSTRACT: Anti-Bredt di(amino)carbene supported gold(I) chloride complexes are readily prepared in two steps from the corresponding isocyanide complexes. In the presence of $KB(C_6F_5)_4$ as chloride scavenger, they promote the unprecedented hydroarylation reaction of alkenes with *N,N*-dialkylanilines with high *para*-selectivity. The latter are challenging arenes for Friedel-Craft reactions, due to their high basicity.

Friedel−Crafts reactions[1,2] typically require Lewis acid catalysts and are therefore generally unsuitable for basic substrates. Classical textbooks especially emphasize their incompatibility with amines, which is a major limitation due to the ubiquity of this organic functionality.[3] The intermolecular hydroarylation of alkenes,[4] a powerful atom-economic method for the alkylation of arenes, is no exception. Besides a few examples with the parent aniline $(C_6H_5)NH_2$,[5−7] there are only two reports of hydroarylation of styrene with the more basic *N*-methylaniline; with $Ru_3(CO)_{12}$,[5d] or a rhodium-based catalytic system,[5c] the reaction occurs at 140−150 °C. Under similar conditions, only 17% conversion was observed with the challenging *N,N*-dimethylaniline.[5c] Similarly to hydroarylation reactions, metal-catalyzed hydroaminations[8] are often inhibited by nucleophilic amines, which strongly bind the metal to form inert Werner-complexes.[9] However, our group has demonstrated that cationic gold(I) complexes supported by (alkyl)-(amino)carbenes (CAACs)[10] (Chart 1) can catalyze the
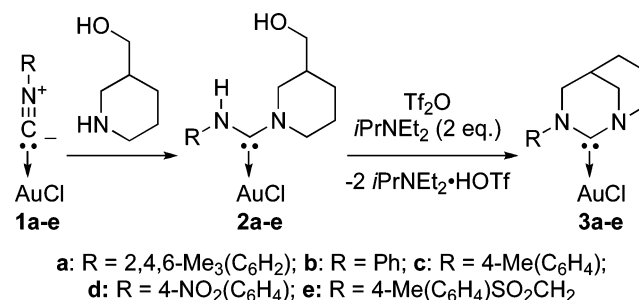
Chart 1
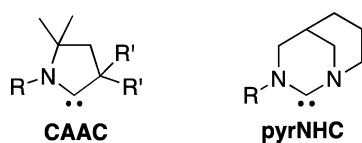
hydroamination of alkynes and allenes with a variety of amines,[11] including ammonia[11b] and hydrazine.[11g] In 2013, we reported that another type of electrophilic carbene, namely the "anti-Bredt NHCs" (pyrNHCs),[12] allows for the gold-catalyzed hydrohydrazination of terminal alkynes at room temperature.[13] This was a significant improvement since CAAC-Au(I) systems typically require temperatures of 70−110 °C for the same transformation.[11g] Here we report that Au(I)/pyrNHC complexes promote the hydroarylation of alkenes with *N,N*-dialkylanilines with high *para*-selectivity.[14]

The scope of the previously reported synthesis of pyrNHC-gold chloride complexes was limited by the scarcity of available precursors, and the instability of free carbenes.[13] Therefore, we considered a new synthetic strategy, in which the ligand is built in the coordination sphere of the metal.[15,16] Isocyanide gold chlorides **1a−e** were reacted with 1 equiv of 3-piperidine methanol, generating the corresponding acyclic di(amino)-carbene gold complexes **2a−e** (Scheme 1). Addition of triflic

Scheme 1. Synthesis of Precatalysts 3a−e

a: R = 2,4,6-Me$_3$(C$_6$H$_2$); **b**: R = Ph; **c**: R = 4-Me(C$_6$H$_4$); **d**: R = 4-NO$_2$(C$_6$H$_4$); **e**: R = 4-Me(C$_6$H$_4$)SO$_2$CH$_2$

anhydride, in the presence of base, triggered the cyclization, and gold chloride complexes **3a−e** were isolated in good yields. These organometallic compounds are air-stable and can be stored for several months with no significant decomposition. They were fully characterized, including by X-ray diffraction analysis for **3a** and **3e** (Figure 1).

In a first experiment, a solution of α-methylstyrene and *N,N*-diethylaniline in benzene was heated in a sealed ampule in the
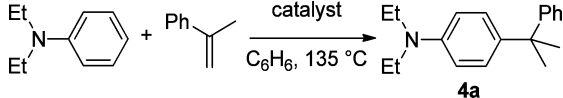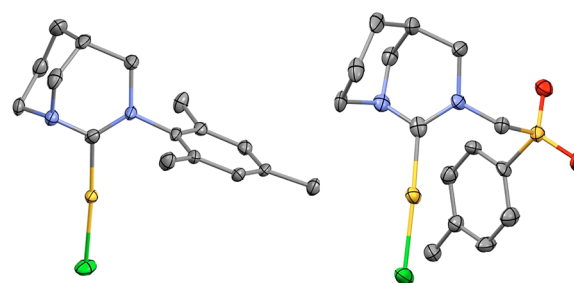

Figure 1. X-ray structure of **3a** (left) and **3e** (right) with thermal ellipsoids drawn at 50% probability level. Hydrogen atoms and solvent molecules are omitted for clarity.

presence of a catalytic amount (5 mol %) of **3a** and KB(C_6F_5)_4. To our delight, we observed the clean formation of the corresponding *para*-hydroarylation adduct **4a** with complete conversion after 24 h at 135 °C (Table 1, entry 1). Under the

Table 1. Hydroarylation of α-Methylstyrene with N,N-Diethylaniline[a]

| entry	catalytic system	conversion (%)
1	[**3a** + KB(C_6F_5)_4] (5 mol %)	97
2	[**3b** + KB(C_6F_5)_4] (5 mol %)	98
3	[**3c** + KB(C_6F_5)_4] (5 mol %)	89
4	[**3d** + KB(C_6F_5)_4] (5 mol %)	69
5	[**3e** + KB(C_6F_5)_4] (5 mol %)	38
6	**3a** (5 mol %)	0
7	[**3a** + AgOSO_2CF_3] (5 mol %)	12
8	[AuCl_3 + 3 AgSbF_6] (5 mol %)	10
9	FeCl_3 (10 mol %)	3
10	BiCl_3 (10 mol %)	4

[a]After 24 h; determined by GC.

same conditions, **3b** and **3c** gave comparable results (entries 2 and 3), whereas a slower rate was observed with the nitro-

substituted pyrNHC **3d** as catalyst (entry 4). In the case of **3e**, the conversion reached a ceiling at 38%, suggesting a decomposition of the catalyst. No reaction was observed with **3a** in the absence of KB(C_6F_5)_4 (entry 6), and even using silver triflate, as an alternative chloride scavenger, led to poor conversion (entry 7). These observations confirm the expected involvement of a cationic gold complex in the catalytic cycle. We also verified that simple systems, such as AuCl_3/AgSbF_6,[17] FeCl_3[18] or BiCl_3,[19] which are recognized as efficient catalysts for the hydroarylation of alkenes, were poorly active for the reaction of *N,N*-diethylaniline with α-methylstyrene (entries 8–10). Not surprisingly, 1 mol % of our catalytic system [**3a** + KB(C_6F_5)_4] promotes the hydroarylation of styrene with anisole, at room temperature, but this reaction is totally inhibited by the presence of *N,N*-diethylaniline. These last observations highlight the powerful deactivating role of anilines (see Supporting Information (SI) for details).

Using **3a** and KB(C_6F_5)_4 as catalytic system, we explored the scope of this unprecedented hydroarylation reaction. We found that *N,N*-dialkylanilines react with a variety of styrenes and norbornene, affording products **4a–q** and **5l,q** in fair to excellent yields (Scheme 2). Not surprisingly, significantly lower temperatures are required for the hydroarylation of 4-methoxystyrene (80–110 °C) than for the less electron-rich styrene and norbornene (145 °C). The high *para*-regioselectivity observed in the reaction leading to **4a–h**, **4j** and **4m–p** is likely the consequence of the steric hindrance of the 1-phenyl-

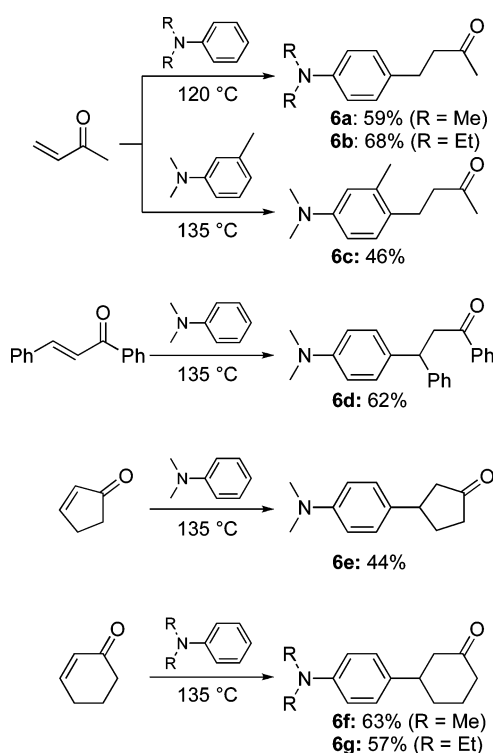### Scheme 2. Hydroarylation of Alkenes with N,N-Dialkylanilines[a]
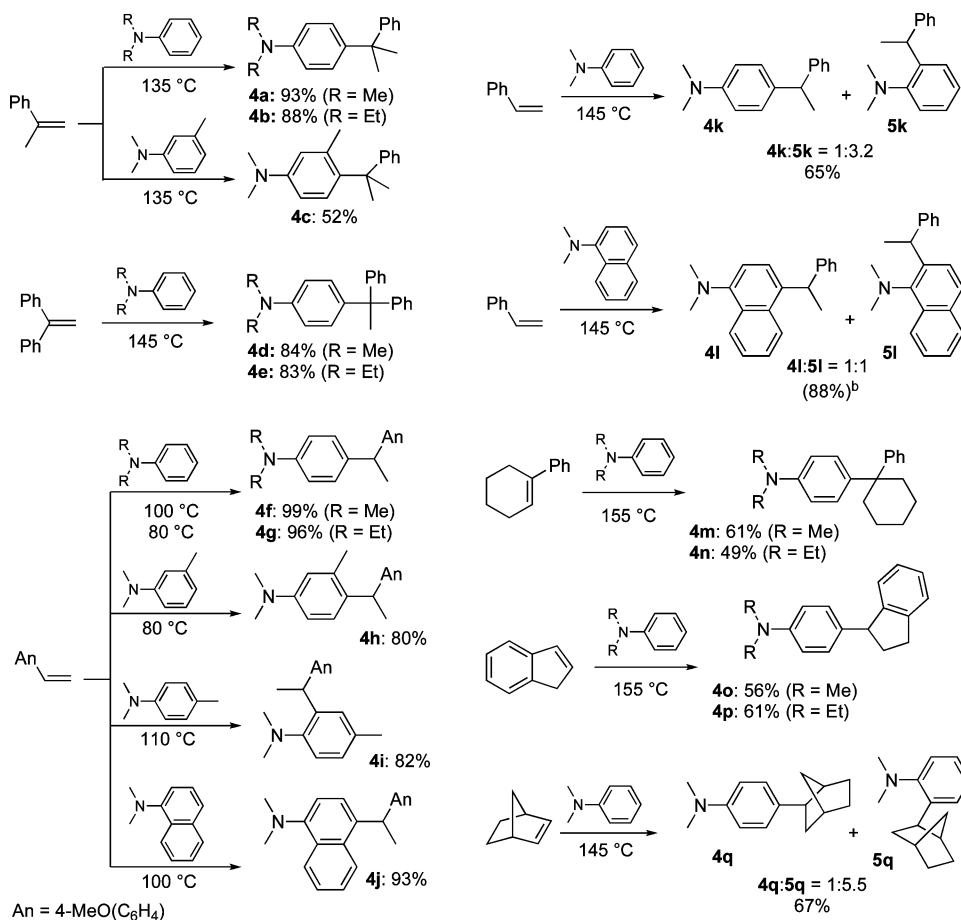
[a]**3a** (5 mol %), KB(C_6F_5)_4 (5 mol %), except for **4m–p** (10 mol %). Solvent: C_6H_6. Isolated yields. See SI for details. [b]GC conversion.

1-(methyl)ethyl and 1,1-diphenylethyl groups. However, electronic effects are also of importance since the *para*-substituted products are selectively formed with 4-methoxystyrene (**4f–j**), but not with styrene (**4k–l** and **5k–l**). Interestingly, the selective formation of **4i** shows that the preference of 4-methoxystyrene for *para*-substitution does not preclude the *ortho*-substitution when the *para*-position is protected. Note that *ortho*-substitution is usually favored by the few systems that are known to promote the hydroarylation of alkenes with the parent aniline.[5,6] Ackermann et al. have even demonstrated that the hydroarylation product results from the rearrangement of the initially formed hydroamination product.[6g]

Although unactivated alkenes, such as 1-octene, 3-octene and tetra(methyl)ethylene do not react with N,N′-dimethylaniline, our catalytic system allowed for the hydroarylation of enones (Scheme 3). This reaction is the atom economic equivalent of a

Scheme 3. Hydroarylation of Enones with N,N-Di(alkyl)anilines[a]

6a: 59% (R = Me)
6b: 68% (R = Et)
6c: 46%
6d: 62%
6e: 44%
6f: 63% (R = Me)
6g: 57% (R = Et)

[a]**3a** (5 mol %), KB(C₆F₅)₄ (5 mol %). Solvent: C₆H₆. Isolated yields. See SI for details.

Michael 1,4-addition. Butanone, chalcone, cyclopentenone and cyclohexenone react with dialkylanilines, the corresponding β-(aryl)ketones being isolated in fair yields and excellent *para*-regioselectivity. Note that although several catalytic systems are known to promote the hydroarylation of electron-poor olefins,[20,21] there are no reports with anilines as substrates.

In conclusion, cationic anti-Bredt di(amino)carbene gold(I) complexes are readily available from the corresponding isocyanide complexes. In the presence of KB(C₆F₅)₄ as chloride scavenger, they promote the hydroarylation of styrenes and norbornene, as well as enones, by dialkylanilines in fair to excellent yields, with very good *para*-selectivity. These results further demonstrate the unique ability of cationic gold(I) complexes, bearing stable electrophilic carbenes as the ancillary ligand, to promote reactions that are usually hampered by nucleophilic substrates.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Full experimental details, ¹H, ¹³C NMR and MS spectra for all new compounds and X-ray crystallographic data for **3a** and **3e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes
The authors declare no competing financial interest.

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