**Dual-gold(I)-generated trifluoromethylation of terminal alkynes with Togni’s reagent**

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**Abstract**

The interaction of a Au(I) catalyst (JohnPhosAu(I)-MeCN/SbF6) and the Togni’s reagent 1, as a source of electrophilic trifluoromethyl group, has been studied in order to develop gold-catalysed alkyne trifluoromethylation reactions. Alkyne-CF3 products were prepared in moderate yields (up to 46%) by electrophilic trifluoromethylation of terminal arylalkynes with Togni’s reagent 1 in the presence of sub-stoichiometric amounts of gold catalyst (25%). The proposed addition-elimination reaction mechanism proceeds through a Au-Togni Reagent complex with a linear Togni Reagent-O-Au(I)-P-(phorphane) coordination mode (X-ray analysis). Alkyne deprotonation gives rapid formation of protonated Togni Reagent and a σ,π-acetylide dual-Au complex, confirmed by X-ray analysis. It was shown that the σ,π-dual-Aucomplex activates for trifluoromethylation, most likely by transfer of a [LAu]+ fragment to the alkyne substrate. The resulting reactive π-Au+-alkyne intermediate probably undergoes O-/CF3-addition of Togni Reagent, and final elimination of Togni alcohol gives the alkyne-CF3 product.

**Keywords:** Electrophilic trifluoromethylation, CF3-alkynes, Au(I)-Togni Reagent complex, σ,π-alkyne-dual-Au complex, transfer reagent.

1. **Introduction**

Important effects on biological activity have resulted in a dramatic increase in the interest for fluorinated drugs and precursors. Incorporation of fluorine into a molecule is known to give compounds with interesting and beneficial chemical and medicinal properties.[[1](#_ENREF_1)] In particular, trifluoromethyl groups are strongly electron-withdrawing and may increase the lipophilicity and affect the metabolic properties of compounds.[[2](#_ENREF_2)] Electrophilic fluorination is known to proceed by gold(I) catalyst/Selectfluor combinations. On the other hand, Selectfluor can also induce oxidative coupling of substituents on gold.[[3](#_ENREF_3), [4](#_ENREF_4)] Such reactions are proposed to proceed via oxidation of the Au(I) complex by Selectfluor to give an active cationic Au(III)-F species. Final fluorodeauration or reductive elimination allows the formation of monofluorinated products.[[5](#_ENREF_5), [6](#_ENREF_6)] Earlier work on homopropargyl acetals performed in the Fiksdahl group [[7](#_ENREF_7), [8](#_ENREF_8)] demonstrates a one-pot pyrane cyclization-fluorination process, applying a combined Au(I)-Selectfluor system. In analogous ways as above, we envisioned that a trifluoromethyl moiety could be incorporated in relevant substrates by combining gold catalysis with an electrophilic source of trifluoromethyl.

Togni’s trifluoromethylating reagents (Scheme 1) are convenient and stable sources of electrophilic trifluoromethyl groups,[[9](#_ENREF_9)] and are part of a larger group of hypervalent iodine reagents that have been used increasingly in a variety of syntheses.[[10](#_ENREF_10)] Among the many applications of these reagents are *O*-, *N*-, *P*- and *S*-trifluoromethylations and trifluoromethylations of aryl, saturated and unsaturated compounds. The reactions can be acid-, base-, and/or transition metal-catalysed.[[10](#_ENREF_10)] The present investigation of Au-generated electrophilic trifluoromethylation of terminal alkynes was inspired by the fact that, to the best of our knowledge, no reactions applying a Au(I) catalyst-Togni reagent combination has been reported. We wanted to study two possible outcomes for the incorporation of a trifluoromethyl group in alkynes with Togni’s reagent 1 in the presence of gold(I) catalyst. Firstly, gold-catalysed addition of OMe/CF3 to the alkyne bond in MeOH could give the MeO-vinyl-CF3 product **2”** (Scheme 1). Moreover, trifluoromethyl could be incorporated in the terminal alkyne position to give CF3-alkynes **5** (Schemes 2, 3) in the absence of MeOH or other nucleophiles. The studies are reported below.

1. **Results and Discussion**

**2.1 Formation of Au(I) – Togni Reagent complex II**

In order to prepare vinyl-CF3-products (**2”**, **3”** and/or **4”**, Scheme 1a) by alkyne trifluoromethylation in methanol, phenylacetylenes (**1a**,**b**) were subjected to introductory studies at room temperature with JohnPhos-Au(I) catalyst and Togni’s 1, 2 and Umemoto’s [[11](#_ENREF_11), [12](#_ENREF_12)] reagents, respectively. These conditions are related to those presented (methanol/Selectfluor) by Nevado et al. [[6](#_ENREF_6)] for gold-catalysed electrophilic fluorination of alkynes to give corresponding mono-fluoro products **2’**, **3’** and **4’**. The attempted trifluoromethylation reactions were monitored by GLC (see Supplementary Data). The reactions did not give the trifluoromethylated products (**2”**, **3”**, **4”**), and only the non-trifluoromethylated products **2**, **3** and **4** were observed from the addition of methanol over the triple bond, both in the absence and presence of trifluoromethylating agents (Scheme 1b). However, it became apparent that the presence of Togni 1 reagent (Scheme 1b, ii) slowed down the reaction significantly, compared to the full conversion observed in the reference reaction with no electrophile added (Scheme 1b, i). Also, quantitative conversions into products **2**, **3** and **4** were obtained in the reactions with Togni 2 and Umemoto’s reagents (Scheme 1b, iii, iv). The Togni 1 reagent reaction (ii) gave only 17% conversion into products **2**, **3** and **4** after 26 h at room temperature. However, upon heating at 70 °C for 2 h, the reaction rate increased dramatically and 75% conversion was obtained, indicating that the catalyst is reversibly deactivated or that a new catalytically active Au complex is formed at higher temperatures.



**Scheme 1**. a) AuI)-catalysed electrophilic addition to phenylalkynes. b) Au(I)-catalysed conversion of alkyne **1b** at r.t. into products **2b**, **3b** and **4b** in MeOH in the absence (i) or presence (ii-iv) of trifluoromethylating agents (GLC). \*) Reaction ii) was heated at 70 °C for 2 h at after 26 h at r.t.

Investigation of the interactions between the Au catalyst and Togni 1 reagent (“Togni Reagent”) were carried out by a series of experiments studied by NMR, which indicated that an acetonitrile ligand displacement and Au(I) coordination of Togni Reagent took place immediately. The Au-Togni Reagent interaction was observed by 1H and 19F NMR by preparation of a 1:1 mixture of these compounds in CDCl3 (Figure 1a and b). It was seen that the 1H NMR signal for the Au(I)-MeCN ligand (2.42 ppm, Fig 1a, ii)) shifted to a broader signal at 2.20 ppm (Fig 1a iii)), in the 1:1 mixture. This indicates ligand exchange to give the non-ligated “free” acetonitrile. Furthermore, the observed shift of the 19F NMR CF3-Togni Reagent signal from −40.1 ppm to −31.2 ppm (Fig 1b, i, ii)) indicated an interaction between the Au catalyst and Togni Reagent. Minor 1H NMR shifts of the methyl groups in the Togni Reagent (1.48 ppm to 1.50 ppm; Fig 1a, i) and iii)) and the *t*‑butyl groups of the gold ligand (1.42 ppm to 1.43 ppm) were also seen. This led us to believe that a new Au-Togni Reagent complex was formed by MeCN/Togni Reagent ligand replacement.

A similar, but weaker interaction, was observed for Togni 2 reagent, probably due to the lower electron density of the ester oxygen than the alkoxy-oxygen in Togni 1 reagent. No interaction was observed in the case of Umemoto’s reagent. The observed Au-Togni Reagent interaction provides an explanation for the difference in the rates of reaction seen in Scheme 1b, as a Au-Togni Reagent complex would be less catalytically active than the original catalyst. It was also observed that a weakly coordinating counterion, such as SbF6, in the gold catalyst was important, as mixtures of JohnPhosAuCl or (Ph3P)AuCl with Togni Reagent did not show any coordination.



−40.1; CF3

1.48; C(CH3)2

b) 19F NMR

a) 1 H NMR

i)

ii)

iii)

i)

ii)



2.42; Au-ligated MeCN

1.42 (d); *t*-Bu

1.43 (d); *t*-Bu

1:1 JohnPhosAu(I)MeCN:Togni Reagent (Au-Togni Reagent complex **II**)

−31.2; CF3

1.50; C(CH3)2

1:1 JohnPhosAu(I)MeCN:Togni Reagent (Au-Togni Reagent complex **II**)

2.20; "free" MeCN

**Figure 1**. a) 1H NMR of i) Togni Reagent; ii) JohnPhosAu(I)-MeCN; iii) formation of Au-Togni Reagent complex **II**, registered 15 min after preparation of the 1:1 Au-Togni Reagent mixture;.b) 19F NMR of i) Togni Reagent; ii) formation of Au-Togni Reagent complex **II** (after 15 min).

X-ray analysis of crystalline Au(I)-Togni Reagent complex **II**, obtained from an equimolar mixture of JohnPhos-Au(I)-MeCN **I** and Togni Reagent from DCM/diethyl ether (Fig. 2a), revealed for the first time O-binding of Togni Reagent to the Au(I) centre (Fig. 2b). The linear Togni Reagent-*O-Au(I)-P*-(phosphane) coordination mode is clearly verified. NMR spectra of the crystalline complex **II** were identical to NMR of 1:1 mixtures of gold(I)-Togni Reagent in solution, discussed above (Fig 1a iii) and 1b ii)). To the best of our knowledge, previous evidence of metal coordination with Togni reagents is limited to Zn interactions.[[9](#_ENREF_9), [13](#_ENREF_13)]

**Figure 2**. Au(I)-Togni Reagent complex **II**; a) formation from JohnPhos-Au(I)-MeCN **I** and Togni Reagent; b) X-ray structure analysis.

It has previously been proposed [[10](#_ENREF_10)] that O-protonation of Togni Reagent reagent weakens, lengthens and polarises the iodine-oxygen bond and activates the CF3 moiety. Thus, a coordination site on the iodine atom may become accessible, allowing nucleophilic addition of a heteroatom X to the iodine atom. Subsequent reductive elimination would give the X-CF3 product and the “Togni alcohol” (**7**,Scheme 4). The interaction of Togni Reagent with JohnPhosAu(I) catalyst **I** is most likely more complex than activation with simple Brönsted acids, but some conclusions can be drawn from comparison of the crystal structure data of the Au-Togni Reagent complex **II** to that of protonated reagent. Table 1 shows the I-O and I-CF3 bond lengths in the Togni Reagent (a), the protonated Togni Reagent (b) and the Au-Togni Reagent complex **II** (c). Activation of Togni Reagent by protonation has been explored with a strong acid (BArF24-acid) and a crystal structure for protonated Togni Reagent is reported,[[10](#_ENREF_10)] showing that protonation does indeed weaken and lengthen the I-O bond (from 2.118 Å to 2.440 Å; Table 1a,b) and shortens the I-CF3 bond (from 2.267 Å to 2.214 Å), compared with data of the Togni Reagent.[[14](#_ENREF_14)] Data for the Au(I)-Togni Reagent complex **II** (c) shows similarly that Togni Reagent coordination to the gold centre also shortens the I-CF3 bond. The lengthening of the O-I bond length is less than by protonation. In accordance, 19F NMR shift values indicate that the Togni Reagent-CF3 group becomes less shielded by complexation, although this effect is less significant for the Au(I)-Togni Reagent complex **II** (c) than by protonation (b).

**Table 1.** Relationships between Togni Reagent I-O and I-CF3 bond lengths (X-ray) and CF3 shift values (19F NMR).

|  |  |  |  |
| --- | --- | --- | --- |
|  | **I-O** bond length | **I-CF3** bond length | **19F NMR, CF3** |
| a) Togni 1 Reagent [[14](#_ENREF_14)] | 2.118 Å | 2.267 Å | −40.1 ppm |
| b) Protonated Togni 1 Reagent [[10](#_ENREF_10)] | 2.440 Å | 2.214 Å | −20 ppm |
| c) Au-Togni Reagent complex **II** | 2.281 Å | 2.219 Å | −31.2 ppm |

Overall, JohnPhosAu(I)-MeCN **I** and Togni Reagent form a relatively stable Au(I)-Togni Reagent complex **II**, which is less active than the original Au(I) catalyst, thus, retarding the addition of MeOH over the alkyne triple bond (Scheme 1b ii).

**2.2. Trifluoromethylation of terminal alkynes**

As X-ray and NMR studies pointed to a CF3 activating effect by Au(I) complexation of Togni, attempts on Au-catalysed activation of Togni Reagent for addition of CF3/Nu to alkynes **1c** were carried out in aprotic reaction conditions (LiI in acetone-*d*6). However, no CF3/I-incorporation took place, as shown by 1H and 19F NMR monitoring over several days. Nevertheless, minor amounts of alkyne-CF3 **5c** (Scheme 2) was formed, also in the absence of LiI. Neither addition of an organic base nor water affected the reaction. In contrast to Cu-catalysed electrophilic trifluoromethylation of terminal alkynes with Togni Reagent [[15](#_ENREF_15)], corresponding reactions with alkyne and Togni Reagent in the presence of a Au(I) catalyst have, to the best of our knowledge, not previously been described. Based on these initial results of Au generated electrophilic trifluoromethylation of terminal alkyne, quantification and optimization experiments were carried out with alkyne **1c**, JohnPhosAu(MeCN) and Togni Reagent (Scheme 2). The relative amounts of gold, alkyne and Togni Reagent were varied, as well as catalyst counterion, reaction temperature, time and concentration (entries 1-30). Also, the addition of acids or organic bases was tested (entries 31, 32). The alkyne-CF3 **5c** was formed as the main product, but also the alkyne-alkene-CF3 product **6** and small amounts of the -CF3-ketone product **3c** were observed. Ketone **3c** [[16](#_ENREF_16)] may be formed by Au- or acid-catalysed hydration of the alkyne-CF3 product **5c**.[[17](#_ENREF_17), [18](#_ENREF_18)] The presence of water is caused by elimination of the “Togni alcohol” (**7**, Scheme 4) which is produced in the trifluoromethylation reaction, affording “Togni-alkene” **8**. Reactions being allowed to run for longer time after maximum yields had been achieved (at r.t. or 50 °C), showed that the alkyne-CF3 product **5c** was converted into ketone-CF3 **3c**. The formation of the alkyne-alkene-CF3 product **6** may be explained by Au-catalysed addition of alkyne **1c** over the alkyne-CF3 **5c** triple bond. The *cis* configuration of alkene **6** is assigned from the absence of NOE 1H NMR correlations between the vinyl proton and the vinyl-aromatic protons. The formation of the trifluoromethylated products **5c**, **3c** and **6** was analysed by 1H and 19F NMR.

By initial variation of the amount of Au catalyst, it was observed that, relative to a 1:1:1 mixture of Au:Togni Reagent:alkyne **1c**, which gave 16% alkyne-CF3 **5c** (Scheme 2, entry 2), the yields increased by reducing the amount of Au catalyst. Maximum yields were obtained with 0.5:1:1 or 0.25:1:1 mixtures of Au:Togni Reagent:alkyne (up to 29% alkyne-CF3 **5c** and 32% total yield of **5c**, **6** and **3c** in 16-24 h; entries 3, 5). Two eq of Au catalyst (entry 1) gave no CF3-products, as immediate generation of the dual gold complex **III** took place (Section 2.3 below), thereby deactivating for the desired transformation by trapping the alkyne substrate **1c**. The fully protonated Togni Reagent was also observed (19F NMR), as discussed below (Scheme 4). Activation of Togni Reagent by addition of HSbF6 (1 eq generated in situ from *tert*-BuCl and AgSbF6, entry 4) gave no increase in the yield. Based on the most efficient Au:Togni Reagent:alkyne (0.5:1:1) reaction conditions (entry 3), the amount of Togni Reagent was increased. The use of 2-3 eq of Togni Reagent speeded up the reaction and slightly increased the yields (up to 33% alkyne-CF3 **5c** and 36% total yield in 8 h; entries 6, 7). No increase in yields was obtained by varying the reaction temperature. Lower temperature gave no reaction (0 °C, 24 h, entry 8), while reaction at 50 °C reduced the reaction time significantly (32% of **5c** in 2 h, entry 9). Further heating to 80 °C, conducted in a sealed vessel, gave lower yield (21% of **5c** in 2 h, entry 10). The non-MeCN-ligated catalyst (entry 11) gave similar results to the original JohnPhosAuSbF6-MeCN catalyst (entry 9).The nature of the counter-ion is essential for Au(I) catalyst activity and selectivity. By varying the Au(I) catalyst counter-ion in reactions at 50 °C (as in entry 9), a negative effect was observed for the more weakly coordinating anions, as only 13-15% of product **5c** was obtained with JohnPhosAuNTf2 and AuBArF (entries 12, 13), afforded by treatment of JohnPhosAuCl with, respectively, AgNTf2. and NaBArF, followed by filtration into the reaction tube. The addition of base (DBU, 1.6 eq, entry 14) was thought to assist the reaction by alkyne deprotonation, but might rather have neutralised the activated Togni Reagent, as the reaction gave no products (GLC). Based on the reaction conditions in entry 9, it was shown that changing the amount of Togni Reagent (1 and 3 eq, entries 15, 16) did not affect the outcome of the reaction. However decreasing the amount of gold (0.25 - 0.05 eq, entries 17, 18) gave a corresponding decrease in total yields of CF3 products. Henceit seemed like the Au complex was consumed stoichiometrically.

**Scheme 2.** Studies on alkyne trifluoromethylation.a

|  |  |  |  |
| --- | --- | --- | --- |
|  | Amounts of reactants (eq) | Conditions | Yield [%]a |
| Entry | Au | Togni Reagent  | **1c** | T(° C) | time(h) |  [alkyne](approx.. mM) | **5c** | **6** | **3c** | Total |
| 1 | 2 | 1 | **1** | r.t. | 120 | 26 | 0 | 0 | 0 | 0b |
| 2 | 1 | 1 | **1** | r.t. | 16 | 26 | 16 | 1 | 1 | 18 |
| 3 | 0.5 | 1 | **1** | r.t. | 16 | 26 | 29 | 3 | 0 | 32 |
| 4 | 0.5 | 1 | **1** | r.t. | 24 | 25 | 24 | 4 | 3 | 31c |
| 5 | 0.25 | 1 | **1** | r.t. | 24 | 26 | 24 | 3 | 1 | 29 |
| 6 | 0.5 | 2 | **1** | r.t. | 8 | 26 | 33 | 3 | 1 | 36 |
| 7 | 0.5 | 3 | **1** | r.t. | 16 | 25 | 31 | 2 | 0 | 34 |
| 8 | 0.5 | 2 | **1** | 0 | 24 | 25 | 0 | 0 | 0 | 0 |
| 9 | 0.5 | 2 | **1** | 50 | 2 | 26 | 32 | 3 | 3 | 38 |
| 10 | 0.5 | 2 | **1** | 80 | 2 | 26 | 21 | 5 | -d | 26 |
| 11 | 0.5e | 2 | **1** | 50 | 2 | 26 | 32 | 3 | -d | 35e |
| 12 | 0.5f | 2 | **1** | 50 | 2 | 26 | 15 | 3 | -d | 18f |
| 13 | 0.5g | 2 | **1** | 50 | 2 | 26 | 13 | 3 | 2 | 18g |
| 14 | 0.5h | 2 | **1** | 50 | 2 | 21 | 0 | 0 | 0 | 0h |
| 15 | 0.5 | 1 | **1** | 50 | 2 | 26 | 26 | 3 | -d | 30 |
| 16 | 0.5 | 3 | **1** | 50 | 2 | 26 | 28 | 4 | -d | 32 |
| 17 | 0.05 | 2 | **1** | 50 | 2 | 26 | 0 | 5 | -d | 5 |
| 18 | 0.25 | 2 | **1** | 50 | 2 | 26 | 23 | 4 | -d | 27 |
| 19 | 1 | **1** | 4 | 50 | 2 | 52 | 15 | 9 | 6 | 30 |
| 20 | 1 | **2** | 4 | 50 | 2 | 52 | 24 | 7 | 4 | 35 |
| 21 | 1(0.25) | **4**(**1**) | 4(1) | 50 | 2 | 52 | 27 | 5 | 3 | 35 |
| 22 | 1(0.10) | **10**(**1**) | 10(1) | 50 | 2 | 52 | 15 | 7 | 1 | 22 |
| 23 | 0.25 | **1** | 2.5 | 50 | 2 | 134 | 24 | 15 | 2 | 41 |
| 24 | 0.25 | **1** | 2.5 | r.t. | 24 | 115 | 25 | 17 | 3 | 46 |
| 25 | 0.25 | **1** | 5 | 50 | 2 | 70 | 12 | 19 | 3 | 34 |
| 26 | 0.25 | **1** | 10 | 50 | 2 | 187 | 8 | 23 | 2 | 33 |
| 27 | 0.25 | **1** | 1 | r.t. | 16 | 52 | 30 | 5 | 1 | 37 |
| 28 | 0.25 | **1** | 1 | r.t. | 4 | 97 | 36 | 5 | 1 | 42 |
| 29 | 0.25 | **1** | 1 | r.t. | 8 | 222 | 32 | 6 | 1 | 38 |
| 30 | 0.25 | **1** | 1 | 50 | 2 | 119 | 29 | 5 | 3 | 36 |
| 31 | 0.25 | **1** | 0.12+1 | r.t. | 72 | 52 | 11 | 8 | 0 | 19i |
| 32j | 0 | **1** | 1 | r.t. | 2 | 0 | 0 | 0 | 0 | 0 |

a) Reaction conditions; JohnPhosAu(I)(MeCN)SbF6 **I** and Togni Reagent were dissolved in CDCl3 in an NMR tube. Alkyne **1c** and internal standard (4-CF3-toluene) in CDCl3 were added to the NMR tube. The reaction was left at the appropriate temperature and the reaction mixture was analysed by NMR. The reported yields are based on the amounts of the limiting reagent, indicated by bold font; b) Dual gold complex **III** was generated immediately; c) 1 eq HSbF6 was added; d) product **3c** could not be seen by 1H NMR; e) Au = JohnPhosAuSb6; f) Au = JohnPhosAu(NTf2); g) Au = JohnPhosAuBArF; h) 1.6 eq DBU added; i) 0.12 eq DBU+alkyne **1c** was added to the Au-Togni Reagent mixture, then 1 eq alkyne and IS added; j) reactions were carried out in the presence of either acids (HSbF6 or TFA) or bases (DBU or BuLi.; 1 eq); no gold catalyst was added.

In further experiments, the ratio of alkyne relative to Togni Reagent was tested (entries 19-21) and the limiting Togni Reagent was used to calculate product yields. The Au:alkyne ratio was kept at 0.25:1 (1:4 as in entry 18), and the amount of Togni Reagent was varied (1-4 eq,). Highest total yields of CF3-products were obtained with excess Togni Reagent (2-4 eq) relative to Au (entries 20, 21). Most interestingly, the results proved that the Au(I) complex promoted alkyne trifluoromethylation with Togni Reagent in a catalytic manner, as the total yields of CF3 products were higher (up to 35%, entry 21) than the sub-stoichiometric amounts of Au (25% Au). A further decrease in the relative amount of gold (10%, entry 22) gave lower yield with respect to Togni Reagent and alkyne substrates, but showed higher catalytic effect and more than two-fold yield with respect to gold (22% total yield of CF3 products). Based on the reaction conditions in entry 21, it was shown that excess of alkyne (2.5-10 eq, entries 23-26), shifted the selectivity of the reaction away from alkyne-CF3 **5c**, towards the alkyne-alkene-CF3 product **6**. This appears to be rational, given that two units of alkyne are incorporated in product **6**. Nevertheless, the obtained total yields with 25% Au were raised to 46% at room temperature (entry 24). Based on the reactant ratio in entry 21, higher yields were obtained by increasing the reaction concentration (entries 27-30). Highest yield was obtained at 97 mM of alkyne **1c** at room temperature (36% alkyne-CF3 **5c**, total yield 42%, 4 h, entry 28). The potential effect of a base additive was tested (entry 31). The addition of alkyne and DBU (0.12 eq of each) to a mixture of the Au (25%) and Togni Reagent (1eq) caused immediate formation of dual-gold complex **III** (Section 2.3) and non-protonated Togni Reagent (1H and 19F NMR). Interestingly, when the remaining 1 eq alkyne was added, the reaction still generated CF3 products (19% in total), indicating that the dual-Au complex **III** is capable of activating for the trifluoromethylation reaction. Finally, the fact that the alkyne trifluoromethylation reaction was promoted by gold, was supported by the unsuccessful reactions of alkyne and Togni Reagent without Au catalyst, but in the presence of acids or bases (HSbF6, TFA, DBU (1 eq) or BuLi (1 eq), entry 32).

Thus, the screening of reaction conditions showed that highest yields of the alkyne-CF3 target product **5c** were obtained from a 0.25:1:1 mixture of Au:Togni Reagent:alkyne (97 mM) at room temperature (entry 28) or, alternatively, from a 0.5:2:1 mixture of Au:Togni Reagent:alkyne (26 mM) at 50 0C (entry 9). Comparative studies of other aryl-alkyne substrates (**1a,b, 1d-g**) showed that the success of the trifluoromethylation method was highly dependent on the aryl-alkyne **1** electron-density, as only the activated 4-MeO-phenylalkynes **1c** and **1e** were reasonably reactive (Scheme 3).



**Scheme 3.** Au(I)-promoted trifluoromethylation studies on arylalkynes (performed as in Scheme 2, entries 9 or 28).

**2.3. Proposed mechanism**

Attempts to experimentally prove the Au-catalysed trifluoromethylation reaction mechanism with Togni Reagent were made.[[19](#_ENREF_19)] Previous studies of reactions with Togni reagents[[10](#_ENREF_10)] have mainly focused on transformations with Togni reagents, based on different activating reagents and catalysts.A proposed reaction mechanism is presented below and the supporting experimental evidences are discussed (Scheme 4 and Figure 2).

In all the reactions above (Schemes 2 and 3) it seems that the JohnPhosAu catalyst **I** and Togni Reagent immediately generate Au-Togni Reagent complex **II** (Figure 1 and Scheme 4, step i). 19F NMR studies of arylalkyne **1c** support this hypothesis, as 19F NMR shift of Togni Reagent -CF3 (originally at −40.1 ppm, Figure 3a) was seen at −31.2 ppm for Au-Togni Reagent complex **II** (Figure 3a step i). The activated Au-Togni Reagent **II** is stable at r.t. for several days, but gradually decomposes into the original Au catalyst **I** and Togni Reagent by-products over some weeks. A new complex **III** was immediately formed after the addition of alkyne **1c** to the mixtures of JohnPhosAuMeCN-Togni Reagent (Scheme 4, step ii), as shown by 1H NMR (MeO signal shifts from 3.81 to 3.90 ppm; Figure 3b, step ii). The formation of complex **III** also generates the protonated activated “Togni-H” by deprotonation of alkyne **1c**, as shown by the change of 19F NMR shifts for Togni Reagent-CF3 to −37.6 ppm (Figure 3a step ii). As the CF3 of fully protonated “Togni-H”, prepared with excess Au (Table, entry 1), gave 19F NMR shift at −22 ppm (visible in Figure 3a, step v), it is proposed that the NMR shifts at −37.6 ppm arose from partial protonation of Togni Reagent, due to limited amount of acid (0.125 eq) generated from conversion of 0.25 eq JohnPhosAu **I** into dual-Au complex **III** (Scheme 4b, step ii**)**. This is in accordance with results from titration of Togni Reagent with superacid (19F NMR approx. −37 ppm).[[10](#_ENREF_10), [14](#_ENREF_14)] With twice excess of Au **I**, no CF3 products were formed, as only gold complex **III** immediately was generated (Scheme 2, entry 1). Isolation of the crystalline complex allowed full characterization (NMR, HRMS and X-ray) and revealed the structure of the -dual-Au complex **III** (Scheme 4). The complex is relatively stable in solution, but decomposes over time, possibly to gold nanoparticles, when left in the reaction mixture in the presence of the generated HSbF6. It is also significantly less stable when subjected to silica chromatography. This kind of dual-Au complex has previously been reported with phosphine [[20](#_ENREF_20)] or NHC-ligands [[21](#_ENREF_21)], and they are shown to be catalytically active for a limited number of reactions.[[20](#_ENREF_20), [22-24](#_ENREF_22)] It has previously been reported [[20](#_ENREF_20), [21](#_ENREF_21)] that the generation of dual-Au complexes similar to **III**, goes through metal‑π coordination of Au - alkynetriple bond, switching to a metal-σ-coordination of the Au centre. The σ-complex then undergoes metal-π coordination with a second Au unit to give the dual-Au complex **III**.[[21](#_ENREF_21)] The coordination of the second LAu+ fragment to the gold acetylide complex is thermodynamically favoured over a coordination of the same LAu+ fragment to the corresponding non-aurated alkyne.[[25](#_ENREF_25)] These transformations occur very fast, even at sub-zero temperatures. This is in accordance with the lack of observable intermediate complexes in the present investigation. Although the crystal structure of complex **III** showed π,σ-alkyne coordination of the dual-Au complex, 13C NMR studies revealed that the two Au atoms are interchangeable in solution, as both alkyne carbons (118.6 ppm, *J* = 11.5 Hz and 124.6 ppm, 68.5 Hz) appear as triplets, due to coupling to the two equivalent phosphorous atoms, in accordance with earlier reports for dual-Au complexes[[20](#_ENREF_20)] and for related heterobimetallic gold-platinum alkyne complexes.[[26](#_ENREF_26)]

Based on the fact that the dual-Au complex **III** was immediately formed by addition of alkyne **1c**, it seemed likely that the alkyne trifluoromethylation (Scheme 4, steps iii-v) was activated by the dual-Au complex **III**. Previous computational studies have described similar σ,π-dual-(NHC-)gold complexes as a thermodynamic sink for [LAu]+ species, as both [LAu]+ units prefer to be on the same alkyne group. There is a low barrier for the π-bonded [LAu]+ to interact with and transfer to a second alkyne to give a more reactive complex.[[25](#_ENREF_25)] Hence, dual-gold **III** may act as a resting state for the catalyst by transferring the [JohnPhos-Au]+ to another unit of alkyne **1c** to give a reactive [JohnPhos-Au]+-**1c** π-intermediate (Scheme 4, step iii). The present alkyne activation mechanism represents a rare intermolecular case of dual-gold as a transfer reagent. Most reported reactions apply the dual-gold transfer concept in cyclization reactions, involving an almost equal intramolecular interaction of the cationic gold between two alkynes of di-yne substrates. [17] The generation of CF3 products (**5c**, **6**, **3c**) occurred over time, as shown by NMR (Figure 3a,b, step v). The transformation is believed to proceed through an addition-elimination process (Scheme 4, steps iv-v). The O-/CF3-addition to the activated **1c**-Au+ triple bond may take place in a concerted or stepwise manner, including iodine(III)-reduction and de-auration. The resulting CF3-vinyl-ether intermediate undergoes final elimination of the “Togni alcohol” **7** and regains the alkyne triple bond to give the alkyne-CF3 product **5c**.



**Scheme 4.** Proposed mechanism for Au(I)-promoted trifluoromethylation of alkyne **1c**, incl. X-ray structure analysis of dual-Au **III**.

1H and 19F NMR studies of other arylalkynes(**1a,b, 1d-g**, Supplementary Data, Table 3) showed the formation of corresponding dual-Au complexes **III**. Since alkyne-CF3 products were not observed in all cases (Scheme 3), not all dual-Au manage to activate the trifluoromethylation reaction by [LAu]+ transfer, or not all alkynes **1a-g** are able to act as an effective substrate. The proposed complexes **III** from alkynes **1a,b** and **1d-g** were not isolated, but the results indicate that isolation could be possible, e.g. in order to test the reactivity of the different complexes.

In contrast to JohnPhosAuMeCN **I**, the isolated dual-gold complex **III** did not give any coordination or reaction with Togni Reagent (or acid-activated Togni Reagent, 1H and 19F NMR). Hence, it was concluded that the dual Au complex **III** was neither activating Togni Reagent, nor a reactive intermediate towards the CF3 products. It was also observed (Scheme 2, entry 31) that even when the acid generated from the formation of dual-gold **III** was neutralised with DBU, the reaction still took place, albeit slower and with lower total yields. It was thus concluded that the acid assists the conversion, but is not essential for the reaction.

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a) 19F NMR (CF3 region)

b) 1H NMR(OMe region)

δ 3.84; **5c** and **6**

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δ−40.1; Togni Reagent, CF3

δ−37.6; ~12.5% protonated Togni Reagent

δ−34.1; partially protonated Togni Reagent

δ−31.2; Au-Togni Reagent complex **II**

*Step v*) 16 h

 4 h: reaction in progress

*Step ii)* 0 h after addition of alkyne **1c**

*Step i)*

δ 3.82; **6**

δ 3.87

δ 3.89; **3c**

δ 3.90; dual-Au complex **IIIc**

δ 3.81

δ−61.9 (t); **3c**

δ−55.9 (d); **6**

δ−49.4, **5c**

δ−61.2

−62.3; IS

δ−22.4; Togni-H

**Figure 3**. Selected 19F and 1H NMR spectra, following the trifluoromethylation reaction progress (Scheme 4, steps i-v; reaction conditions shown in Scheme 2, entry 24), as shown by respectively CF3 and MeO-alkyne **1c** signal from dual-Au complex **IIIc**, and products **5c**, **6** and **3c**.

Additional mechanistic experiments (Scheme 5), included selective stepwise preparation of dual-Au complex **IIIc** (0.125 eqfrom Togni Reagent, Au(I) **I** and alkyne **1c**, Scheme 4, steps i-ii),followed by addition of alkyne **1e** (0.875 eq, steps iii-v). The reactions showed conversion into only CF3 product **5e** (37%), as this procedure allow selective formation of dual-Au complex **IIIc** and CF3-product **5e**, respectively. Only trace amounts of **1c** and other CF3 products were seen. Similar amounts of CF3 product **5e** (32%) were formed with the original method using only alkyne **1e**. These results show that acetylide (**1c**), incorporated in the initially formed dual-Au **IIIc**, was not converted into CF3 products, but only acted as a transfer agent in trifluoromethylation of the different alkyne **1e** to selectively give CF3 product **5e**. The “real” Au catalytic loading is hence only 14%. In general, the present reaction via intermediate formation of dual-Au complex **IIIc** and Togni-H, does not enable further alkyne **1e** deprotonation, and thus, allow selective triple bond activation of alkyne **1e**, which seems to be crucial for the success of the present trifluoromethylation method.



**Scheme 5.** Selective transformation of alkynes **1c** and **1e** into, respectively, dual-Au **IIIc** and **5e**.

In order to exclude the possibility that a Au-acetylidecomplex was involved in the reaction, the Au-acetylidecomplex **IV** was prepared (from the JohnPhosAuCl and alkyne **1c** in the presence of base) and mixed with non-activated or activated Togni Reagent (TFA, HNTf2, HSbF6 or Au complex **II**). No product was formed in these reactions, indicating that Au-acetylide **IV** was not acting as an acetylide nucleophilic species by attacking the CF3-Togni Reagent to yield the alkyne-CF3 product **5c**.

Another theory included a possible generation of a CF3-Au(III)-acetylide intermediate **V**, which would give the CF3- product by reductive elimination in analogy with the Au-Selectfluor reaction pathways.[[5](#_ENREF_5)]It was hypothesised that a potential gold(III) complex **V** would be observed in experiments at low temperature, where no products were supposed to be formed (Scheme 2, entry 8). As identification of Au(III)-F intermediates, formed in Au-Selectfluor reactions, has previously been made by 19F NMR [[5](#_ENREF_5)], possible Au(III)-CF3 intermediateswould potentially be seen in the Au-Togni Reagent reaction. NMR experiments (1H, 13C, 19F and 31P) were carried out on a 1:4:4 mixture of Au:Togni Reagent:alkyne **1b** at −20 °C. Careful integration and comparison with spectra of relevant compounds (complexes **I**, **II** and **III**, alkyne **1b**, Togni Reagent and Togni-H) confirmed that the reaction mixture only contained dual-Au complex **III**, partially protonated Togni Reagent and alkyne **1c**, which indicated that a possible Au(III)-CF3 complex **V** is not involved in the reaction.

1. **Conclusion**

The interaction of a Au(I) catalyst (JohnPhos-Au(I)-MeCN/SbF6) and the Togni’s reagent 1, as a source of electrophilic trifluoromethyl group, has been studied in order to develop gold-catalysed alkyne trifluoromethylation reactions. 1H, 13C, 19F and 31P NMR studies were essential in this work. We have developed a simple experimental procedure for trifluoromethylation of terminal arylalkynes (1 eq) with Togni Reagent (1 eq) in the presence of sub-stoichiometric amounts of the JohnPhosAuI-MeCN catalyst (25%) to give alkyne-CF3 product (3,3,3-trifluoroprop-1-yn-1-yl)benzene, **5c**). Although the yields are low, the total amounts of CF3-alkyne products (up to 46%) are higher than the Au(I) catalyst loading This indicates that the JohnPhosAu(I) complex promotes alkyne trifluoromethylation with Togni Reagent in a catalytic manner. Future catalyst or substrate optimizations may provide possibilities to increase the yields. The analogous Cu-catalysed method [[15](#_ENREF_15)] requires 20% CuI and 1:1.5:0.4:0.4 alkyne:Togni Reagent:phenantroline:KHCO3 as well as syringe pump addition of alkyne, to give 70-98% yields.

The proposed addition-elimination reaction mechanism is based on immediate generation of Au-Togni Reagent complex **II** from the JohnPhosAu complex **I** and Togni Reagent. Alkyne deprotonation takes place by subsequent addition of alkyne **1c** to give rapid formation of a -dual-Au complex **III** and “Togni-H”. It is believed that the alkyne trifluoromethylation step is activated by [LAu]+ transfer from dual-Au **III** to a new unit of alkyne **1c**. The triple bond activation allows O-/CF3-addition of Togni-H” to the alkyne. This step proceeds through iodine-reduction by cleavage of the I-CF3 and I-O bonds and de-auration. Finally, the CF3-vinyl-ether intermediate regains the alkyne triple bond to give the alkyne-CF3 product **5c** by elimination of “Togni alcohol”.

Three new Au(I) complexes, gold-Togni Reagent complex **II**, dual-gold complex **III** and gold-acetylide complex **IV** were generated and characterised in the course of the studies. The JohnPhosAu-MeCN catalyst **I** and Togni Reagent rapidly interact to form the relatively stable Au-Togni complex **II** by ligand exchange of the acetonitrile ligand with the Togni Reagent molecule. Complex **II** is less active than the original Au(I) catalyst **I**, e.g. retarding the addition of MeOH over alkyne triple bonds. X-ray analysis of the Au-Togni Reagent complex **II** confirmed the linear Togni Reagent-*O-Au(I)-P*-(phosphane) coordination mode by O-binding of the Togni Reagent oxygen to the gold(I) centre. The structure of the dual-gold complex **III**, proposed to be the [LAu]+ transfer reagent in the trifluoromethylation reaction after immediate formation from Au(I) and alkyne **1c**, was confirmed by X-ray analysis.

In summary, the present study on gold-catalysed electrophilic alkyne trifluoromethylation has contributed to the complex picture of gold catalysis and introduced the use of hypervalent iodine reagents into this field.

1. **Experimental**

***4.1. General experimental procedures***

Commercial grade reagents were used as received. Flash chromatography was carried out using silica gel 60 (0.040-0.063 mm) and analysed using thin-layer chromatography (TLC) with silica gel 60 F254 (0.25 mm thickness). Melting points (m.p.) were determined using a Stuart apparatus and are uncorrected. 1H, 13C, 19F and 31P NMR spectra were recorded using 400 MHz or 600 MHz spectrometer. Chemical shifts are reported in ppm (δ) downfield from tetramethylsilane for 1H NMR (0 ppm), CDCl3 for 13C NMR (77.0 ppm), 1-methyl-4-(trifluoromethyl)benzene for 19F NMR (−62.27 ppm)[[27](#_ENREF_27)] and triphenylphosphine for 31P NMR (−6.00 ppm) as internal standards. The PPh3 standard was in a sealed tube to prevent interaction with the compounds, especially the gold complexes. Coupling constants (*J*) are reported in Hertz (Hz). The attributions of the chemical shifts were determined by means of COSY, HSQC, HMBC and NOESY NMR experiments. Accurate mass determination in positive and negative mode was performed on a "Synapt G2-S" Q-TOF instrument from Waters™. Samples were ionized by the use of ASAP probe (APCI) or ESI probe. No chromatographic separation was used previous to the mass analysis. Calculated exact mass and spectra processing was done by Waters™ Software Masslynx V4.1 SCN871. IR spectra were obtained using a Smart Endurance reflection cell. UV spectra were obtained using a Cary 60 UV-Vis spectrophotometer from Agilent Technologies with accompanying fiber optic dip probe accessory. GLC analyses were carried out on a 7890A GC System from Agilent Technologies with a TR-5 column from Thermo Scientific. Single crystal X-ray data was acquired using a Bruker D8 Venture diffractometer with the APEX3 suit, integrated with SAINT V9.32B, solved with XT, and refined with XL using Olex2 as GUI. The cif files were edited with encipher v1.4, and molecular graphics were produced with Diamond v4.0. ORTEP plots are shown in the main document, and all metric data including reflection data are contained in the respective cif files. This data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK. Fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk.

***4.2. General procedure for NMR experiments***

The required amounts of (acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate **I** and Togni Reagent (3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole) were weighed into an NMR tube and dissolved in a small amount of CDCl3. The required amount of alkyne **1** and 1-methyl-4-(trifluoromethyl)benzene (internal standard, IS)[[27](#_ENREF_27)] was dissolved in a small amount of CDCl3 and added to the NMR tube. The NMR tube was then left at the appropriate temperature and the reaction mixtures analysed by NMR at the required times. Sometimes, stock solutions were used when several reactions were run in a short period.

For example, for (Scheme 2, entry 3): A stock solution of 1-ethynyl-4-methoxybenzene (**1c**, 20.9 mg, 0.158 mmol) and 1-methyl-4-(trifluoromethyl)benzene (IS, 23.2 mg, 0.145 mmol) was dissolved in 20 mL CDCl3 using a volumetric flask. (Acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate (**I,** 6.3 mg, 8.16 µmol) and Togni Reagent (5.7 mg, 0.017 mmol) were weighed into an NMR tube and dissolved in 0.2 mL CDCl3, and 0.5 mL of the stock solution was added containing alkyne **1c** (2.09 mg, 0.0158 mmol) and internal standard (2.32 mg, 0.0145 mmol). The reaction mixture was analysed at 2, 4, 8, 16, 24, 36, 48, 60, 72, 96 and 120 h with 1H and 19F NMR, at 400 MHz and 376 MHz respectively.

All the trifluoromethylated alkyne products (**5a-g**) and 3,3,3-trifluoro-1-(4-methoxyphenyl)propan-1-one[[16](#_ENREF_16)] (**3c**) reported in the present work have been reported earlier.[[28-31](#_ENREF_28)] Identification was based on NMR spectra (1H, 19F and/or 13C) and yields reported in Scheme 3 are calculated from a known amount of added IS. Novel compound alkene **6** is characterised below. Analogous alkene compounds for the other substrates were observed in only trace amounts under the reaction conditions used and therefore not isolated and no yields are reported.

***(E)-4,4'-(5,5,5-Trifluoropent-3-en-1-yne-1,3-diyl)bis(methoxybenzene) (alkene-CF3 6*)** was obtained using the general procedure for NMR experiments, with (acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate (**I**, 5.8 mg, 7.5 µmol), Togni Reagent (10.8 mg, 0.0327 mmol) and 1-ethynyl-4-methoxybenzene (**1c**, 38.3 mg, 0.290 mmol) in CDCl3 (0.5 mL). The mixture was heated at 50 °C for 2 h and the solvent was removed *in vacuo.* The crude mixture was purified using pipette chromatography with only pentane (note: not all of the crude mixture was soluble in pentane), giving the desired product, (Z)-4,4'-(5,5,5-trifluoropent-3-en-1-yne-1,3-diyl)bis(methoxybenzene, **6**), as an off-white oil (1.5 mg, 15%): Rf = 0.15 (1:30 EtOAc:pentane); 1H NMR (600 MHz, CDCl3): δ ppm 7.48-7.45 (m, 2H, CHAr), 7.41-7.39 (m, 2H, CHAr), 6.93-6.90 (m, 2H, CHAr), 6.87-6.85 (m, 2H, CHAr), 6.09 (q, 1H, *J* = 8.9 Hz, CHCF3), 3.84 (s, 3H, OCH3), 3.82 (s, 3H, OCH3); 13C NMR (150 MHz, CDCl3): δ ppm 160.34 (COCH3), 160.32 (COCH3), 134.8 (q, *J* = 6.6 Hz, C=CHCF3), 133.4 (2C, CHAr), 129.9 (q, 2C, *J* = 2.0 Hz, CHAr), 127.8 (CAr), 122.7 (q, *J* = 269.9 Hz, CF3), 120.5 (q, *J* = 34.2 Hz, CHCF3), 114.1 (2C, CHAr), 113.6 (2C, CHAr), 113.4 (q, *J* = 13.3 Hz, ≡C-CAr), 94.2 (C≡CCAr), 88.0 (C≡CCAr), 55.33 (OCH3), 55.29 (OCH3); 19F NMR (376 MHz, CDCl3): δ ppm −55.81 (d, 3F, *J* = 8.4 Hz, CF3); IR (film, cm-1) 2953, 2919, 1602, 1509, 1252, 1134, 1033, 833, 555; HRMS (ESI), *m/z*: calcd for C19H16O2F3 [M+H]+ 333.1102, found 333.1106.

***4.3 Mechanistic experiments; stepwise reaction of alkynes 1c and 1e to allow selective formation of dual-Au complex IIIc and CF3-product******5e***

*Exp 1:(Au:Togni* *Reagent:****1c*** *0:25:1:1);*According to the General procedure, using gold catalyst **I** (5.1 mg, 6.6 µmol, 0.25 eq) and Togni Reagent (8.9 mg, 0.027 mmol, 1eq) in 0.2 mL CDCl3, and alkyne **1e** (4.0 mg, 0.027 mmol, 1eq) and IS (2.9 mg, 0.018 mmol) in 0.4 mL CDCl3. The mixture. was monitored at r.t for 120 h with 1H and 19F NMR spectroscopy. Product **5e** was formed in 32% at 48 h. 1H and 19F NMR data were in accordance with previous reports.[[30](#_ENREF_30)]

*Exp 2: (Au:Togni* *Reagent:****1c*** *0:25:1:0.125) + (****1e*** *0.875);* Gold catalyst **I** (11.7 mg, 0.015 mmol) and Togni Reagent (20.3 mg, 0.061 mmol) were dissolved in 0.1 mL CDCl3 in an NMR tube and, after 10 min, alkyne **1b** (1.0 mg, 7.6 µmol) in 0.2 mL CDCl3 was added and the mixture shaken. The mixture was allowed to react at r.t. for ca. 2 min and then alkyne **1e** (7.8 mg, 0.053 mmol) and IS (5.4 mg, 0.034 mmol) in 0.3 mL CDCl3 was added. The mixture was monitored at r.t. with 1H and 19F NMR spectroscopy for 72 h. Product **5e** was formed in 37% (based on alkyne **1e**) at 16 h. Only trace amounts of other CF3-products were observed.

*Exp 3: (Au:Togni Reagent:****1c*** *0:25:0.125:0.125) + (Togni Reagent 0.875) + (****1e*** *0.875);* Gold catalyst **I** (11.9 mg, 0.015 mmol) and Togni Reagent (2.6 mg, 7.88 µmol) were dissolved in 0.1 mL CDCl3 and alkyne **1c** (1.03 mg, 7.79 µmol) in 0.1 mL CDCl3 was added and shaken. The mixture was allowed to react for 10 min and then Togni Reagent (17.6 mg, 0.053 mmol) was added. The mixture was allowed to react for another 10 min and alkyne **1e** (8.7 mg, 0.060 mmol) and IS (5.4 mg, 0.034 mmol) in 0.3 mL CDCl3 was added. The reaction was monitored with 1H and 19F NMR spectroscopy for 72 h. Product **5e** was formed in 37% (based on alkyne **1e**) at 16 h. Only trace amounts of other CF3-products were observed.

***4.4. Procedure for generation and isolation of Au-Togni Reagent complex II***

(Acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate (**I**, 40.7 mg, 0.053 mmol) and Togni Reagent (3,3-dimethyl-1-(trifluoromethyl)-1,2-benziodoxole, 18.9 mg, 0.057 mmol) were weighed into a small vial and dissolved in DCM (400 µL). Crystals, suitable for X-ray diffraction, were obtained by slow diffusion of diethyl ether into this vial at −20 °C, giving the desired Au-Togni Reagent complex (**II**) as colourless needles (40.7 mg, 73%): mp 125.5-127.6 °C; 1H NMR (600 MHz, CDCl3): δ ppm 7.90-7.87 (m, 1H, CHAr), 7.63 (t, 1H, *J* = 7.3 Hz, CHAr), 7.61 (d, 1H, *J* = 8.5 Hz, CHAr), 7.57-7.53 (m,3H, CHAr), 7.47-7.45 (m, 3H, CHAr), 7.29-7.15 (m, 3H, CHAr), 1.51 (s, 6H, 2xOC(CH3)2), 1.44 (d, 18H, *J* = 16.0 Hz); 13C NMR (150 MHz, CDCl3): δ ppm 149.2 (d, *J* = 11.9 Hz, CAr), 148.0 (br s, CCO), 142.7 (d, *J* = 6.7 Hz, CAr), 133.4 (d, *J* = 7.7 Hz, CHAr), 133.2 (d, *J* = 3.8 Hz, CHAr), 131.8 (CHAr), 131.3 (CHAr), 131.2 (d, *J* = 2.3 Hz, CHAr), 129.9 (CHAr), 129.0 (CHAr), 128.7 (CHAr), 128.3 (br s, ICCH), 128.1 (CHAr), 127.2 (d, *J* = 7.4 Hz, CHAr), 123.5 (d, *J* = 49.5 Hz, PCAr), 107.90 (br s, CI), 106.1 (br q, *J* = 380.7 Hz, CF3), 79.0 (CO), 38.3 (d, *J* = 27.6 Hz, PC*t*-Bu), 32.8 (br s, OC(CH3)2), 30.8 (d, *J* = 5.8 Hz, CH3, *t*-Bu); 19F NMR (376 MHz, CDCl3): δ ppm −31.21 (3F, CF3); 31P NMR (162 MHz, CDCl3): δ ppm 56.34 (AuP); IR (film, cm-1) 2960, 2920, 1466, 1159, 1073, 913, 759, 727, 661; HRMS (ESI), *m/z*: calcd for C30H37OF3PIAu [M]+ 825.1244, found 825.1259. X-ray data; CCDC ID: 1508694.

***4.5. Procedure for generation and isolation of dual-Au complex III***

(Acetonitrile)[(2-biphenyl)di-tert-butylphosphine]gold(I) hexafluoroantimonate (**I**, 11.7 mg, 0.015 mmol) and potassium carbonate (2.1 mg, 0.015 mmol, note: base not strictly necessary but used in order to try to absorb the acid that could destroy the product) were weighed into a flask and 1 mL DCM was added. 1-Ethynyl-4-methoxybenzene (**1c**, 5.5 mg, 0.042 mmol) in 1mL DCM was added. The mixture rapidly became dark purple. The solvent was removed *in vacuo* and the residue was purified via pipette chromatography (1:2 acetone:pentane). The fractions containing the desired product were filled to the top with pentane (ca. 1/3 of the vial volume), corked and placed in the freezer. Long needles formed and the solvents were pipetted out and the crystals were washed with pentane to give the product as long colourless needles (5.1 mg, 50%, note: this method also works with or without base to give crystals of X-ray quality): mp decomp. ca. 200 °C; 1H NMR (600 MHz, CDCl3): δ ppm 7.89-7.86 (m, 2H, CHAr), 7.55-7.53 (m, 4H, CHAr), 7.43-7.40 (m, 2H, CHAr, acetylide), 7.37-7.31 (m, 6H, CHAr), 7.26-7.23 (m, 2H, CHAr), 7.10-7.08 (m, 4H, CHAr), 6.97-6.95 (m, 2H, CHAr, acetylide), 3.90 (s, 3H, OCH3), 1.41 (d, 36H, *J* = 15.7 Hz, 6C(CH3)3); 13C NMR (200 MHz, CDCl3): δ ppm 161.2 (1C, COCH3), 149.2 (2C, d, *J* = 14.5 Hz, CAr), 142.6 (2C, d, *J* = 6.8 Hz, CAr), 134.8 (2C, CHAr, acetylide), 133.8 (2C, CHAr), 133.2 (2C, d, *J* = 7.9 Hz, CHAr), 131.1 (2C, CHAr), 129.3 (4C, CHAr), 129.0 (4C, CHAr), 128.0 (2C, CHAr), 127.4 (2C, d, *J* = 6.9 Hz, CHAr), 125.3 (2C, d, *J* = 44.7 Hz, PCAr), 124.6 (1C, t, *J* = 68.5 Hz, AuC≡), 118.6 (1C, t, *J* =11.5 Hz), 114.3 (2C, CHAr, acetylide), 112.4 (1C, ≡CC), 55.6 (1C, OCH3), 37.9 (4C, d, *J* = 23.8 Hz, PC(CH3)3), 30.9 (6C, d, *J* = 7.0 Hz, PC(CH3)3); 31P NMR (162 MHz, CDCl3): δ ppm 62.35 (AuP); IR (film, cm-1) 2954, 2890, 1600, 1504, 1252, 1169, 756, 731, 701, 657; HRMS (ESI) calcd for C49H61OP2Au2 [M]+ 1121.3529, found 1121.3551. X-ray data; CCDC ID: 1508697.

***4.6. Procedure for generation and isolation of Au-acetylide complex IV***

Chloro[(1,1′-biphenyl-2-yl)di-tert-butylphosphine]gold(I) (JohnPhosAuCl, 38.4 mg, 0.072 mmol), 1-ethynyl-4-methoxybenzene (**1c**, 20.3 mg, 0.154 mmol) and *N*-ethyl*-N*-isopropylpropan-2-amine (1.0 mL) were dissolved in dry DCM (3 mL) and NaH (8.9 m, 0.371 mmol) was added. The reaction was stirred at r.t. for 9 h, at which time the reaction was complete. The solvent was evaporated almost to dryness *in vacuo* and a small amount of DCM/pentane was added. Slow evaporation afforded precipitation of the product, which was washed with pentane, giving the Au-acetylide complex **IV** as a white solid (39.1 mg, 86%): mp decomp. ca. 115 °C; 1H NMR (600 MHz, CDCl3): δ ppm 7.88-7.85 (m, 1H, CHAr), 7.56-7.54 (m, 1H, CHAr), 7.52-7.49 (m, 2H, CHAr), 7.48-7.47 (m, 1H, CHAr), 7.47-7.44 (m, 1H, CHAr), 7.41- 7.39 (m, 2H, CHAr), 7.29-7.27 (m, 1H, CHAr), 7.19-7.18 (m, 2H, CHAr), 6.79-6.77 (m, 2H, CHAr, acetylide), 3.79 (s, 3H, OCH3), 1.42 (d, *J* = 15.0 Hz, 18H, C(CH3)2); 13C NMR (200 MHz, CDCl3): δ ppm 157.9 (COCH3), 150.3 (d, *J* = 14.7 Hz, CAr), 142.4 (d, *J* = 5.7 Hz, CAr), 134.3 (CHAr), 133.4 (2C, CHAr, acetylide), 133.1 (d, *J* = 7.5 Hz, CHAr), 132.2 (d, *J* = 132.1 Hz, AuC), 130.1 (d, *J* = 1.8 Hz, CHAr), 129.2 (2C, CHAr), 129.0 (2C, CHAr), 128.0 (CHAr), 127.6 (d, *J* = 39.6 Hz, PCAr), 126.6 (d, *J* = 6.2 Hz, CHAr), 118.5 (d, *J* = 2.4 Hz, AuCCCAr), 102.0 (d, *J* = 23.6 Hz, AuCC), 55.1 (OCH3), 37.4 (d, 2C, *J* = 22.1 Hz, C(CH3)3), 31.0 (d, *J* = 7.0 Hz, 6C, C(CH3)3); 31P NMR (162 MHz, CDCl3): δ ppm 64.06 (AuP); IR (neat, cm-1) 2961, 2852, 1766, 1504, 1461, 1243, 1037, 828, 751, 698; HRMS (ESI) calcd for C29H35OPAu [M+H]+ 627.2091, found 627.2098.

**Appendix. Supplementary data**

Supplementary data associated with this article, including copies of 1H and 13C NMR spectra, can be found in the online version, at version, at <http://dx.doi.org/10.1016/j>. jfluchem.... Crystallographic data of Au-Togni Reagent complex **II** (CCDC 150869) and dual-Au complex **III (**CCDC 1508697)can be obtained free of charge at <http://www.ccdc.cam.ac.uk/conts/retrieving.html> or from the Cambridge Crystallographic Data Centre (CCDC).

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