Synthesis of allenes through triazole gold(III) catalysed rearrangement of propargyl vinyl ethers

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An efficient and simple method to the synthesis of allene derivatives was developed through pyridyltriazole gold(III) catalysed rearrangement of propargyl vinyl ethers with moderate to good yields. It was found that the pyridyltriazole gold(III) complex is a good chemoselective catalyst in selective activation of alkynes and allenes. Compared to gold(I) catalysts, the pyridyltriazole gold(III) shows much better substrate tolerance and much higher air and moisture stability.

Keywords: pyridyltriazole, allene, propargyl vinyl ethers, rearrangement, alkynes

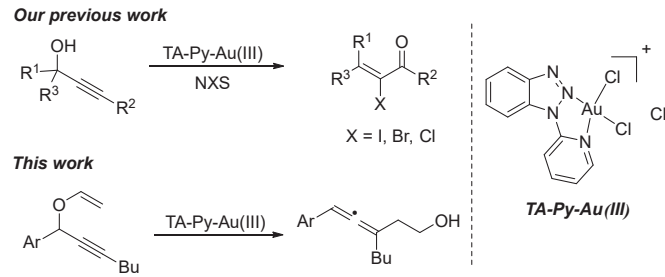
The efficient preparation and reactions of valuable heterocyclic architectures containing diversification sites constitute major challenges in organic chemistry.[1] For example, 3,4-fused tricyclic indole skeletons, 1,2-oxathiane 2,2-dioxides, pyrrolin-2-one skeletons and pyran structures are featured in plenty of natural products and biologically active drug candidates. Some of these skeletons or heterocycles have significant pharmaceutical activities and exhibit a wide range of biological activities such as antidiabetic, inhibitory, and antiviral activities.[2–5] The synthesis of these functional molecules from allenes is an important strategy.[6] However, it is not easy to obtain these allenes; indeed, it is a very challenging task. Among the possibilities, gold(I)-catalysed rearrangement of alkynes is an interesting and useful method for allene synthesis. However, gold usually activates allenes further and it is difficult to retain the products at the allene stage.[7,8] Toste *et al.* reported that $[(Ph_3PAu)_3O)]BF_4$ catalysed propargyl Claisen rearrangements in the synthesis of allenes with good yields.[9–11] The Nolan group showed that [(IPr)Au(pyr)][BF_4] was an effective catalyst for allene synthesis.[12] Shi *et al.* found that triazole-gold TA-Au(I) complexes are very effective chemoselective catalysts in promoting propargyl ester/ether 3,3-rearrangements and resulted in chirality transfer without racemisation over a long period of time, affording enantioenriched allenes with excellent stereoselectivity.[13–18] Later, Shi *et al.* developed a highly efficient synthesis of substituted conjugated dienals *via* triazole–gold-catalysed propargyl vinyl ether rearrangement and an amine catalysed allene–aldehyde tautomerisation.[19] They described intermolecular propargyl alcohol addition to alkynes as a general approach for the synthesis of substituted allenones using triazole-gold(I) (TA-Au) conditions.[20] Substituted bicyclic [4.4.0]dihydronaphthalene compounds were also synthesised through gold-catalysed rearrangement of propargyl esters followed by allene–ene cyclisation.[21] Hiersemann *et al.* reported the Gosteli–Claisen rearrangement of 2-alkoxycarbonyl-substituted propargyl vinyl ethers to afford γ-allenyl-α-keto esters, substituted furans and cyclopentenes.[22] Liu and Cheng described the gold(I)-catalysed propargyl Claisen rearrangement/6-*endo-trig* cyclisation of propargyl vinyl ethers in preparation of bicyclic furopyran derivatives.[23] They reported a gold(I)-catalysed nucleophile-mediated method for stereoselective synthesis of bicyclic furan and pyran derivatives with moderate to good yields.[24]

Recently, we developed a pyridyltriazole gold(III) complex (TA-Py-Au) as an effective catalyst for α-haloenone synthesis with good *E-/Z*-selectivity.[25] However, this gold(III) complex is not well studied and some other transformations need further exploration. In this paper, we report the TA-Py-Au(III) catalysed rearrangement of propargyl vinyl ethers in synthesis of allenes with moderate to good yields (Scheme 1). This is a good example of gold(III) catalysed rearrangement of propargyl vinyl ethers.

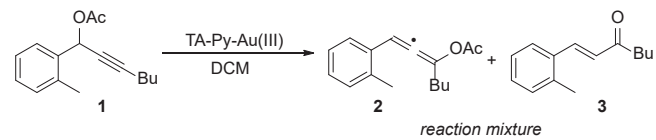
Results and discussion

In light of the above considerations, we initially investigated the rearrangement of propargylic esters in the synthesis of allenes. The substrates, propargylic ester **1**, which were easily prepared in high yields, was chosen as a reaction model to test reaction with 2 mol% TA-Py-Au(III) (Scheme 2). However, only a mixture of compounds **2** and **3** were obtained, even with a range of solvents such as CH_2Cl_2, CH_3CN, 1,4-dioxane, acetone, toluene, THF and MeOH. This revealed that TA-Py-Au(III) is not suitable for allene synthesis using propargyl esters.

To our delight, employing a propargyl vinyl ether **4a** allowed the clean formation of **5a** with enhanced yield. Impressively, **5a** was obtained in good yield when dry dichloromethane was used (Table 1, entry 8). When the reaction was performed in the absence of catalyst (entry 10) no product was observed thus demonstrating the necessity of the gold catalyst. It should be noted the reaction did not happen with $AuCl_3$ as a catalyst (Table 1, entry 9).



Scheme 1 TA-Py-Au(III) catalysed reactions.



Scheme 2 The rearrangement of propargyl esters.

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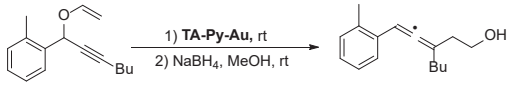
Table 1 Optimisation of reaction conditions[a]



4a **5a**

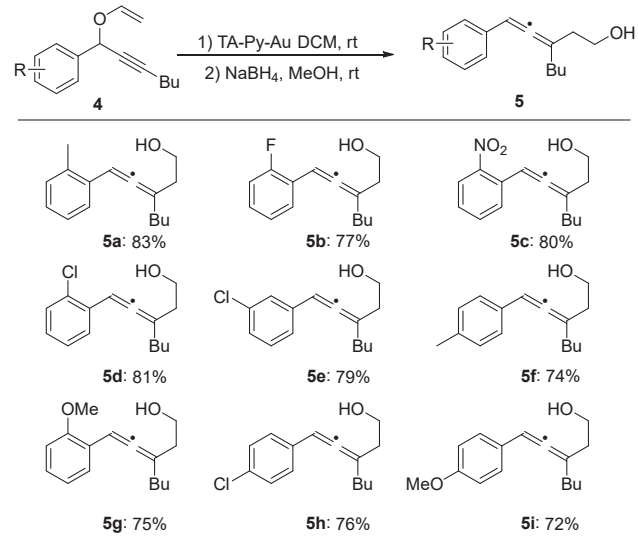
Entry	Solvent	Conversion	Yield of **5a**/%[b]
1	MeCN	5	3
2	1,4-dioxane	13	-
3	acetone	21	7
4	MeOH	7	-
5	DCM	83	72
6	toluene	5	4
7	THF	<5	-
8	DCM(dry)	>95	83
9	DCM(dry)	<5	-[c]
10	DCM(dry)	<5	-[d]
11	DCM(dry)	>95	81[e]
12	DCM(dry)	92	78[f]

[a]Conditions: TA-Py-Au(III) (2 mol%), **4a** (1.0 mmol), solvent (4 mL), 4 h.
[b]Isolated yields based on **4a**, "-" means "no product was observed".
[c]$AuCl_3$ was used.
[d]No catalyst.
[e]TA-Py-Au(III) (1 mol%).
[f]TA-Py-Au(III) (0.5 mol%), 12 h.

With the optimised conditions in hand, the substrate scope of this TA-Py-Au(III) catalysed propargyl vinyl ethers rearrangement was further investigated, the results are summarised in Table 2. We set out to examine the effect of substituents on the aryl moiety in the reaction. The results showed that substrates bearing electron-donating or electron-withdrawing groups have little influence on the reaction outcome. For example, the reactions proceeded smoothly to afford the corresponding allene **5** in moderate to good yields, when the R group of propargyl vinyl ethers **4** was the electron-donating methyl substituent or the electron-deficient 5-fluoro and 5-chlorosubstituents groups. It also should be noted that the presence of a substituent at the *ortho-, meta-* or *para*-positions did not affect the reaction. Compared to the earlier method with TA-Au(I) as a catalyst,[13] this methodology has much better substrate tolerance. Substrates with the substituents NO_2, OMe, Cl and F could be converted into allene products smoothly without increasing catalyst loading, while some other substrates needed enhanced catalyst loading.[13] It should be noted that quite a good yield was obtained even with a reduced catalyst loading (Table 1, entries 11–12). Another point is that the complex TA-Py-Au(III) has much higher air and moisture stability, which means this transformation could take place in the air without yields decreasing. This might be attributed to the better stability of the TA-Py-Au(III) complex, which is stabilised by both the triazole and pyridine units. Thus no reduction in the catalytic activity of the gold complex was observed. All the data indicates that TA-Py-Au(III) is a good choice for the preparation of allenes and is therefore a better chemoselective catalyst.

In summary, the TA-Py-Au(III) catalysed rearrangement of propargyl vinyl ethers was developed to synthesise allenes in moderate to good yields. It was found there was effective activation of the alkyne without affecting the reactivity of the allene ester intermediates and the desired 3,3-rearrangement products were obtained in good yields. This provides an alternative methodology for synthesis of allene derivatives.[11,13]

Table 2 Substrate experiments of propargylic ethers[a,b]



[a]Conditions: **4** (1.0 mmol), TA-Py-Au(III) (2 mol%), dry CH_2Cl_2 (4 mL), r.t., 3–5 h.
[b]Isolated yields based on **4**.

Experimental

Synthesis of allenes (**5a-i**); *general procedure*

To a solution of the appropriate propargyl vinyl ether **4** (1 mmol) in dry CH_2Cl_2 (4.0 mL, 0.25 M), was added TA-Py-Au(III) (2 mol%) at RT. The reaction mixture was kept at room temperature and monitored by TLC. After the reaction was completed (3–5 h), $NaBH_4$ (1.5 mmol) and MeOH (0.5 mL) was added to the mixture. After the reaction was finished (monitored by TLC), the solvent was removed under reduced pressure and purification of the crude product by column chromatography on silica-gel (petroleum ether/ethyl acetate, 80:1) afforded compound **5**.

3-[2-(o-Tolyl)vinylidene]heptan-1-ol (**5a**)[13]: Colourless oil; yield 83%; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 (d, *J* = 7.2 Hz, 1H), 7.18–7.07 (m, 3H), 6.40–6.37 (m, 1H), 3.80 (dd, *J* = 10.8, 5.2 Hz, 2H), 2.45–2.30 (m, 5H), 2.19–2.06 (m, 2H), 1.65–1.30 (m, 5H), 0.91 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.6, 134.8, 133.4, 130.6, 126.7, 126.6, 126.2, 104.7, 93.2, 61.0, 35.9, 32.8, 29.8, 22.5, 19.8, 13.9.

3-[2-(2-Fluorophenyl)vinylidene]heptan-1-ol (**5b**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (td, *J* = 7.2, 1.2 Hz, 1H), 7.18–7.10 (m, 1H), 7.10–6.98 (m, 2H), 6.45–6.37 (m, 1H), 3.78 (t, *J* = 6.4 Hz, 2H), 2.41–2.32 (m, 2H), 2.16–2.05 (m, 2H), 1.63 (s, 1H), 1.53–1.30 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.8 (d, *J* = 2.0 Hz), 161.0 (d, *J* = 249.8 Hz), 128.0 (d, *J* = 8.2 Hz), 127.9 (d, *J* = 3.6 Hz), 124.2 (d, *J* = 3.5 Hz), 122.9 (d, *J* = 11.8 Hz), 115.8 (d, *J* = 21.6 Hz), 105.5, 88.5 (d, *J* = 6.4 Hz), 60.8, 35.9, 32.6, 29.7, 22.4, 13.9.

3-[2-(2-Nitrophenyl)vinylidene]heptan-1-ol (**5c**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.60 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.48 (td, *J* = 7.2, 1.2 Hz, 1H), 7.34–7.26 (m, 1H), 6.86–6.80 (m, 1H), 3.80 (t, *J* = 6.0 Hz, 2H), 2.44–2.35 (m, 2H), 2.20–2.10 (m, 2H), 1.65 (s, 1H), 1.53–1.32 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 204.5, 147.4, 132.7, 130.5, 129.1, 127.1, 124.8, 106.6, 91.0, 60.7, 35.6, 32.3, 29.6, 22.4, 13.9.

3-[2-(2-Chlorophenyl)vinylidene]heptan-1-ol (**5d**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.34 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.10 (td, *J* = 7.6, 1.2 Hz, 1H), 6.70–6.60 (m, 1H), 3.78 (t, *J* = 6.0 Hz, 2H), 2.45–2.30 (m, 2H), 2.20–2.08 (m, 2H), 1.72 (d, *J* = 22.0 Hz, 1H), 1.55 – 1.43 (m, 2H), 1.42–1.33 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 203.1, 133.0, 132.0, 129.8, 127.8, 127.7, 126.8, 105.9, 92.3, 60.8, 35.8, 32.6, 29.7, 22.5, 13.9.

3-[2-(2-Chlorophenyl)vinylidene]heptan-1-ol (**5e**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.23 (m, 1H), 7.24–7.18 (m, 1H), 7.17–7.10 (m, 2H), 6.18–6.10 (m, 1H), 3.78 (t, *J* = 5.6 Hz, 2H), 2.43–2.29 (m, 2H), 2.16–2.08 (m, 2H), 1.58 (s, 1H), 1.51–1.41 (m, 2H), 1.40–1.31 (m, 2H),

0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.3, 137.6, 134.6, 129.8, 126.7, 126.3, 124.6, 106.4, 95.1, 60.9, 35.8, 32.6, 29.7, 22.4, 13.9.

*3-[2-(*p*-Tolyl)vinylidene]heptan-1-ol* (**5f**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, *J* = 7.6 Hz, 2H), 7.12 (d, *J* = 7.6 Hz, 2H), 6.22–6.15 (m, 1H), 3.78 (t, *J* = 6.0 Hz, 2H), 2.39–2.30 (m, 5H), 2.16–2.07 (m, 2H), 1.73 (d, *J* = 12.8 Hz, 1H), 1.54–1.43 (m, 2H), 1.42–1.33 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.5, 136.5, 132.4, 129.4, 126.3, 105.7, 96.0, 61.0, 36.0, 32.8, 30.0, 22.5, 21.2, 13.9.

3-[2-(2-Methoxyphenyl)vinylidene]heptan-1-ol (**5g**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33 (dd, *J* = 7.2, 1.2 Hz, 1H), 7.21–7.13 (m, 1H), 6.97–6.82 (m, 2H), 6.60–6.51 (m, 1H), 3.85 (s, 3H), 3.78 (s, 2H), 2.34 (td, *J* = 6.0, 2.8 Hz, 2H), 2.14–2.06 (m, 2H), 2.02 (s, 1H), 1.53–1.43 (m, 2H), 1.42–1.31 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.4, 156.1, 127.8, 127.6, 123.7, 120.9, 111.1, 104.3, 90.3, 60.8, 55.6, 36.0, 32.8, 29.8, 22.5, 13.9.

3-[2-(2-Chlorophenyl)vinylidene]heptan-1-ol (**5h**)[13]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.78–7.25 (m, 1H), 7.24–7.18 (m, 1H), 7.17–7.11 (m, 2H), 6.18–6.10 (m, 1H), 3.78 (t, *J* = 5.6 Hz, 2H), 2.43–2.29 (m, 2H), 2.16–2.08 (m, 2H), 1.58 (s, 1H), 1.51–1.41 (m, 2H), 1.41–1.31 (m, 2H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.3, 137.6, 134.6, 129.8, 126.7, 126.3, 124.6, 106.4, 95.1, 60.9, 35.8, 32.6, 29.7, 22.4, 13.9.

3-[2-(2-Methoxyphenyl)vinylidene]heptan-1-ol (**5i**)[11]: ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24–7.18 (m, 2H), 6.88–6.81 (m, 2H), 6.21–6.13 (m, 1H), 3.82–3.74 (m, 5H), 2.43–2.25 (m, 2H), 2.15–2.05 (m, 2H), 1.73 (s, 1H), 1.52–1.29 (m, 4H), 0.90 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.1, 158.7, 127.7, 127.5, 114.2, 105.7, 95.6, 61.0, 55.3, 36.0, 32.9, 29.8, 22.5, 13.9.

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