Gold-Catalyzed Regioselective Hydration of Homopropargyl Alcohols Followed by Diastereoselective Reduction: An Easy Access to *cis* 2,5-Disubstituted Tetrahydrofurans

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Abstract: A gold (III)-catalyzed hydration of homopropargyl alcohols led to the corresponding γ-hydroxy ketones, which were directly reduced by Ph_3SiH in the presence of a Lewis acid, to afford the expected 2,5-disubstituted tetrahydrofurans as a diastereomeric mixture. NMR analysis of the compounds so obtained allowed us to confirm that the *cis* isomers were the major isomers that can be used for the preparation of new products.

Keywords: Regioselective hydration, diastereoselective reduction, natural products, cascade reactions.

INTRODUCTION

2,5-Disubstituted tetrahydrofurans are found in many natural products, as well as in pharmacologically active products [1]. Access to this class of compounds has been reviewed [2] and recently we have published the diastereoselective preparation of *trans* 2,5-disubstituted tetrahydrofurans based on a highly diastereoselective *C*-glycosylation of lactol acetates with titanium enolates of achiral *N*-acetyl oxazolidin-2-thiones [3].

Gold catalysts are nowadays used as powerful Lewis acids for the activation of carbon-carbon triple bonds toward various nucleophiles [4]. Indeed, H_2O/alcohols [5], alkynes [6], azides [7], carbonyl groups [8], have been successfully used. Gold catalysts present several advantages when compared to other noble metals (Pd, Pt, Ir, etc…): i) gold is more abundant that other noble metals, ii) metallic gold is biocompatible, iii) Au (III) has been reported to be possess antiproliferative properties against human tumor cell lines [9].

This publication reports on highly regioselective Au (III) catalyzed hydration of homopropargyl alcohols, easily accessible from the coupling reaction of epoxides and alkynes, followed by the Ph_3SiH diastereoselective reduction of the γ-hydroxy ketones so obtained, to afford the major *cis* 2,5-disubstituted tetrahydrofurans. These results show furthermore, that Au (III) can also be used in the reductive step, acting as a very efficient Lewis acid.

RESULTS AND DISCUSSION

Recently we have shown that highly functionalized homopropargyl alcohols could be regioselectively hydrated in the presence of $PdCl_2(CH_3CN)_2$ to afford the expected γ-hydroxy ketones [10]. We thus decided to hydrate under palladium catalysis alcohol **3a** (obtained by Yamaguchi coupling reaction [11] between racemic allyl gycidol **1a** and hexyne **2a**) and to directly reduce the γ-hydroxy ketone intermediate, which is in equilibrium with the cyclic hemiketal, with Et_3SiH-$BF_3.OEt_2$[12] (Scheme **1**). Unexpectedly the corresponding 2,5-disubstituted THF **4a** was obtained as a 60:40 *cis*/*trans* diastereomeric mixture in low yield and as the free alcohol since the allyl protecting group was also removed. We thus decided to study the Au (III) catalyzed hydration of alcohol **3a** [13], followed by the direct reduction of the γ-hydroxyketone intermediate (Scheme **2**).

When compound **3a** was treated by 5 mol% of $NaAuCl_4.2H_2O$ in a mixture of CH_2Cl_2/H_2O (9:1) at room temperature for 30 min, starting material **3a** was consumed and a complex mixture of the γ-hydroxy ketone and the *cis* and *trans* cyclic hemiketal intermediates was obtained. The solvent was then evaporated under vacuum, then CH_2Cl_2 was added, and the temperature brought to –78°C. $BF_3.OEt_2$ (1 equiv) was then added followed by either Et_3SiH or Ph_3SiH (2.5 equiv) [14]. After 3 hours, the expected 2,5-disubstituted THF **4a** was obtained in good isolated yields (75 and 83%, respectively) and with d.r. = 55:45 and 70:30, respectively. Unfortunately, isomers could not be easily separated by flash chromatography on silica gel, however GC/MS allowed us to determine the diastereomeric ratios. The major isomer was determined to be the *cis* isomer based on NMR studies and on mechanistic considerations (see below). It is important to note that the allyl-protecting group was stable under these reaction conditions, whereas it was removed when palladium (II) was used as a catalyst. Furthermore, Ph_3SiH reduction was more diastereoselective than Et_3SiH reduction (70:30 *vs* 55:45). Generalization of this method was then studied. Thus alcohols **3b-f** (obtained in 43-82 % yield by Yamaguchi coupling reactions between the required racemic glycidol derivatives and the desired alkynes, see Experimental Part) were treated under the

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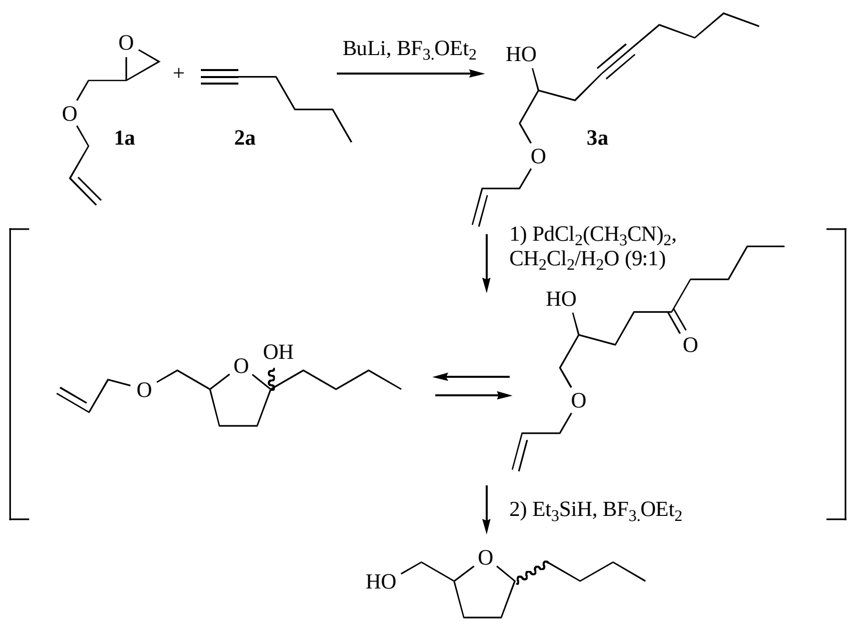
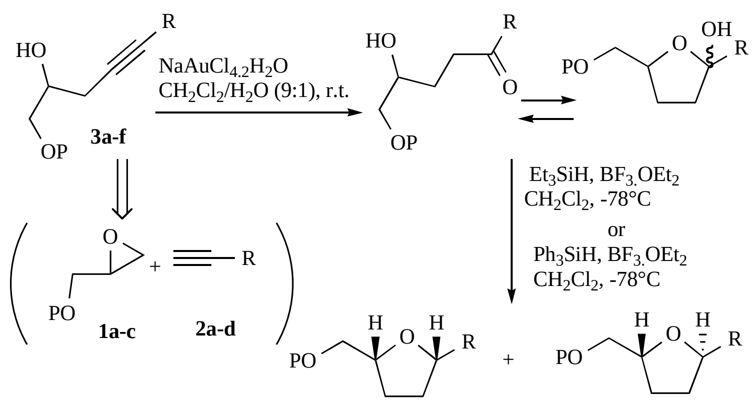


4a : 13%, d.r. = 60:40

Scheme 1. Pallado-catalyzed approach.



major *cis* **4a-f** minor *trans* **4a-f**

Scheme 2. Gold-catalyzed approach.

reaction conditions designed above (5 mol% $NaAuCl_4.2H_2O$, CH_2Cl_2/H_2O (9:1), r.t., 30 min) followed by Ph_3SiH-$BF_3.OEt_2$ reduction. The results are summarized in Table **1** (see Scheme **2** and Table **1**).

It is interesting to note that the expected THF **4a-e** are obtained in moderate to excellent yields (39-98 %), and with a moderate to good diastereoselectivity. However **3f** could not be hydrated under these reaction conditions even when temperature and solvent were changed (reflux and either MeOH, EtOH, CH_3CN). In the case of compound **4e**, it is important to note that the THP protecting group was also removed under these reaction conditions (probably due to the slightly acidic conditions of $NaAuCl_4$ in the presence of water[5a]). Nevertheless, it is noteworthy that allyl ethers, pivalate and *p*-toluylsulfonate groups were stable under these conditions.

In the case of compound **4d**, we were satisfied to separate the major and minor isomers by flash chromatography on silica gel. NOESY spectra of both isomers were slightly different, such as in the major *cis* isomer **4d** a noe was observed between the carbinol protons at δ 4.90 and 4.34 ppm, whereas in the minor *trans* **4d** no noe was observed between the two corresponding protons at δ 5.01 and 4.45 ppm (Fig. **1**).

Based on these findings, and on the mechanism of the reaction (see below), we then assumed that all major isomers **4a-e** were the *cis* THFs.

Then we decided to study the one-pot reaction conditions for this new preparation of *cis* 2,5-disubstituted THF (Scheme **3**). Alcohol **3a** was poured into CH_2Cl_2 and 5 mol% of $NaAuCl_4.2H_2O$ was added followed by H_2O (*1 equiv*). After 1h, Ph_3SiH (2.5 equiv) was added at room temperature and the reaction was stopped when no modification was observed by TLC (3 h). After purification, compound **4a** was thus obtained in 53 % yield and with a d.r. = 75:25. It is interesting to note that the diastereoselectivity is slightly

Table 1. $NaAuCl_4.2H_2O$ Catalyzed Hydration, Followed by $Ph_3SiH-BF_3.OEt_2$ Reduction of 3a-f

P of Alcohols 3	R of Alcohols 3	THF Products 4	Yield (%)[a]	d.r.[b]
CH_2=$CHCH_2$	*n*-Bu	**4a**	83	70:30
p$CH_3C_6H_4SO_2$	*n*-Bu	**4b**	62	73:27
*t*BuCO	*n*-Bu	**4c**	56	80:20
*t*BuCO	*m*ClC_6H_4	**4d**	39	70:30
CH_2=$CHCH_2$	$THPO(CH_2)_{14}$	**4e**	98[c]	80:20
CH_2=$CHCH_2$	$Si(CH_3)_3$	**4f**	0	-

[a]isolated yields after 2 steps for the mixture of *cis* and *trans* **4a-f**; [b]determined by GC/MS; [c]with removal of the THP protecting group.

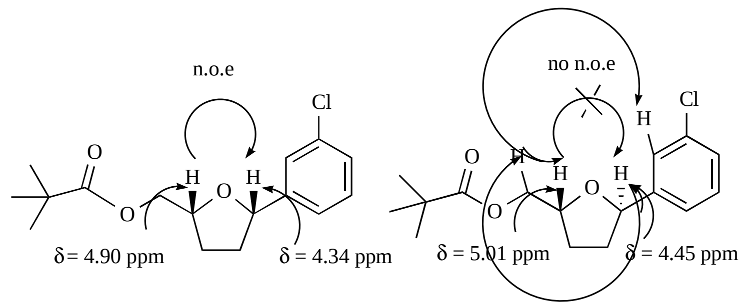
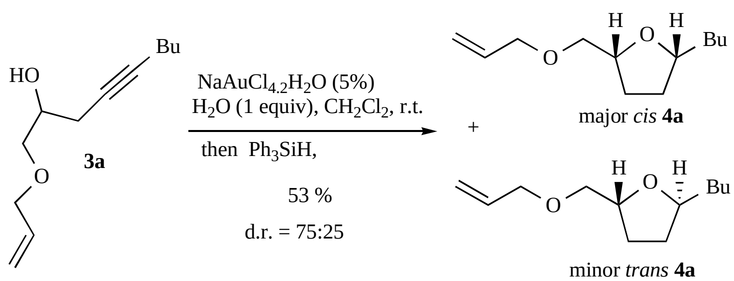


Fig. (1). Noe observed for compound **4d**.



Scheme 3. One pot gold-catalyzed hydration followed by reduction of compound **3**[a].

better than when $Ph_3SiH-BF_3.OEt_2$ was used (see Table **1**, entry 1).

From a mechanistic point of view, Au (III) catalyst may activate the triple bond that will lead to a dihydofuran gold species, through a 5-*endo dig* cyclization, and then to the cyclic hemiketal by hydrolysis. The corresponding hemiketal, by Au (III) Lewis acid activation will then lead to the cyclic oxonium species that will be reduced by the bulky Ph_3SiH reagent on the less sterically demanding face (pathway "a") (Fig. **2**). It is noteworthy that diastereomeric ratios observed in these reactions are typically what is expected for nucleophilic additions on 3,4-nonsubstituted cyclic oxoniums [15].

Then platelet aggregation factor from Uriach Pharma **6** was formally synthesized through this procedure as depicted in Scheme **4** [16]. Butyllithium was added to heptadecyne **2e** at low temperature in THF followed by racemic allyl glycidol **1a** in the presence of $BF_3.OEt_2$ to give the homopropargyl alcohol **3g** in 70 % yield. Then alcohol **3g** was treated by 5 mol% of $NaAuCl_4.2H_2O$ and H_2O (*1 equiv*) in CH_2Cl_2 at room temperature. After 1h, Ph_3SiH (2.5 equiv) was added at room temperature to afford, after 3h of stirring and work-up and purification, the diastereomeric mixture of *cis* and *trans* THF **4g** (d.r. = 85:15) in 60 % yield. Removal of the allyl protecting group was then efficiently performed by treatment of this unseparable mixture of diastereomers **4g** by Et_3SiH in the presence of 5 mol% $PdCl_2(CH_3CN)_2$ in CH_2Cl_2 to give the free primary alcohols. Then treatment of the latter as described in ref [1c] would lead to the target bioactive compound **6**.

CONCLUSION

In conclusion, this study shows that the very simple Au (III) catalyst, $NaAuCl_4.2H_2O$, can be advantageously used as a soft Lewis acid for two domino transformations, namely the regioselective hydration of non-terminal homopropargyl alcohols and the diastereoselective reduction of cyclic hemiketals to afford in good yield and high diastereoselectivity the corresponding *cis* 2,5-disubstituted THF. Furthermore, we showed that in the palladium

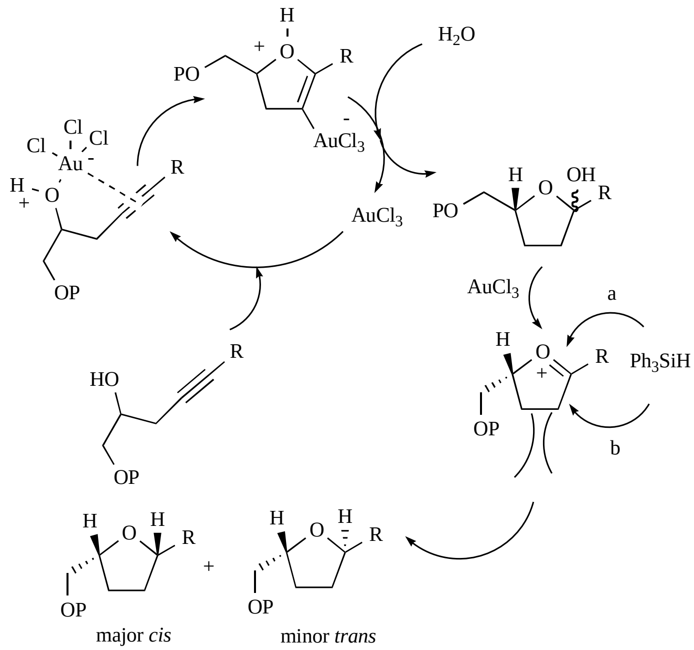
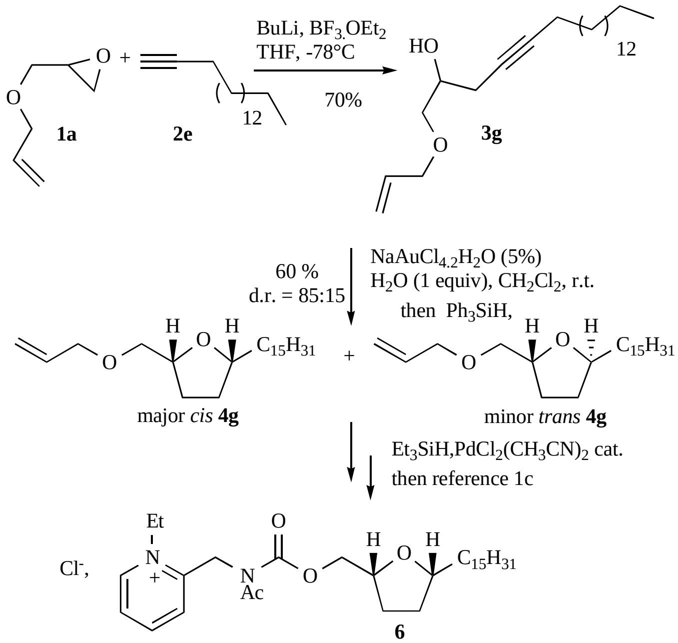


Fig. (2). Proposed mechanism.



Scheme 4. Formal synthesis of compound **6**.

catalyzed removal reaction of allyl protecting group, Bu_3SnH [17] can be efficiently replaced by the less toxic Et_3SiH reagent.

MATERIALS AND METHODS

Solvents were purified according to the procedures described. ^{1}H- and ^{13}C-NMR spectra were recorded at 200 MHz or 400 MHz, and 50 or 100 MHz, respectively. Chemical shifts (δ) were expressed in ppm with the protonated solvent as reference. Patterns were described according to Hoye *et al.* [18], and coupling constants (*J*) were given in hertz (Hz). Flash chromatography was performed with silica gel 60 (9385 Merck), silica gel S (31607 Riedel-de-Haën), and silica gel 60H (7736 Merck). TLC was performed on plates coated with silica gel $60F_{254}$ (554 Merck). Plates were visualised by spraying with Dragendorff's reagent or with 50% H_2SO_4 and then heating.

1-Allyloxynon-4-yn-2-ol (3a)

To a solution of alkyne **2a-e** (15 mmol, 1.5 equiv) in anhydrous THF (30 mL) was added at -78°C butyllithium (16 mmol, 1.6 equiv). After 1 h, protected glycidol **1a-c** (10 mmol, 1 equiv) in THF (5 mL) was added followed by BF_3.THF (15 mmol, 1.5 equiv). After 2 h of stirring, a $NaHCO_3$ saturated aqueous solution (5 mL) was added, and extracted three times with ethyl acetate (3 x 30 mL). The combined organic layers were dried over $MgSO_4$ then filtered and concentrated *in vacuo*. The products were then purified by flash chromatography with a mixture of dichloromethane and ethyl acetate (95: 5) to give clear yellow oil. Yield: 72% (1.42 g). ^{1}H NMR (400 MHz): δ 0.90 (t, *J*= 7.2 Hz, 3H), 1.39 (m, 2H), 1.46 (m, 2H), 2.15 (m, 2H), 2.41 (m, 2H), 3.44 (dd, *J*= 9.6, 6.8 Hz, 1H), 3.56 (dd, *J*= 9.6, 4.0 Hz, 1H), 3.89 (m, 1H), 4.03 (d, *J*= 5.6 Hz, 2H), 5.20 (d, *J*= 10.4 Hz, 1H), 5.28 (dd, *J*= 17.2, 1.6 Hz, 1H), 5.91 (tdd, *J*= 5.6, 10.4, 17.2 Hz, 1H). ^{13}C NMR (75 MHz): δ 13.4, 18.2, 21.7, 23.7, 30.8, 69.0, 72.1, 72.9, 75.4, 82.5, 116.9, 134.4. IR (cm^{-1}): ν 3440, 2930, 2865, 2035, 2020, 1740, 1430, 1240, 1090. ESI-MS *m/z* : 219 (M+Na).

2-hydroxylnon-4-yn-1-yl *p*-toluylsulfonate (3b)

Yield: 60%. ^{1}H NMR (300 MHz): δ 0.89 (t, *J*= 6.9 Hz, 3H), 1.39 (m, 4H), 1.97 (brs, OH), 2.10 (m, 1H), 2.40 (m, 2H), 2.44 (s, 3H), 3.94 (qd, *J*= 6.3, 4.2 Hz, 1H), 4.02 (dd, *J*= 10.2, 6.3 Hz, 1H), 4.13 (dd, *J*= 10.2, 4.2 Hz, 1H), 7.35 (d, *J*= 8.4 Hz, 2H), 7.80 (d, *J*= 8.4 Hz, 2H). ^{13}C NMR (50 MHz): δ 13.5, 18.3, 21.6, 21.9, 23.6, 30.8, 68.0, 72.1, 73.8, 84.0, 128.0, 129.9, 132.9, 145.0. IR (cm^{-1}): ν 3440, 2935, 1600, 1455, 1360, 1190, 1175, 1095. ESI-MS *m/z* : 311 (M+H).

2-hydroxylnon-4-yn-1-yl 2,2-dimethylpropanoate (3c)

Yield: 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.89 (t, *J*= 7.6 Hz, 3H), 1.21 (s, 9H), 1.37 (m, 2H), 1.46 (m, 2H), 2.15 (t, *J*= 6.8 Hz, 2H), 2.42 (m, 2H), 3.94 (quint, *J*= 6.0 Hz, 1H), 4.14 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.5, 18.4, 21.9, 24.2, 27.1, 30.9, 38.8, 67.0, 68.6, 74.6, 83.6, 178.6. IR (liquid phase in CH_2Cl_2, cm^{-1}): ν 2960, 1730, 1282, 1155, 916, 733. ESI-MS *m/z* : 263 (M+Na).

1-(3-chlorophenyl)-4-hydroxypent-4-yn-1-yl 2,2-dimethyl-propanoate (3d)

Yield: 43%. ^{1}H NMR (400MHz, $CDCl_3$): δ 1.23 (s, 9H), 2.45 (brs, OH), 2.68 (d, *J*= 6.0 Hz, 2H), 4.09 (quint, *J*= 4.8 Hz, 1H), 4.20 (dd, *J*= 6.0, 11.2 Hz, 1H), 4.27 (dd, *J*= 4.0, 11.2 Hz, 1H), 7.24 (m, 3H), 7.39 (brs, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.7, 27.2, 38.9, 67.1, 68.6, 81.8, 86.2, 124.8, 128.3, 129.5, 129.8, 131.6, 134.1, 178.7. IR (liquid phase in CH_2Cl_2, cm^{-1}): ν 3470, 2970, 1730, 1590, 1560, 1475, 1400, 1285, 1155, 1095, 1035, 785. ESI-MS *m/z*; 295 (M+H), 297(M+H).

1-Allyloxy-14-tetrahydropyranyloxynonadec-4-yn-2-ol (3e)

Yield: 56%. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.25 (s, 20H), 1.54 (m, 9H), 1.65-1.80 (m, 2H), 2.14 (tt, *J*= 6.9, 2.7 Hz, 2H), 2.41 (m, 2H), 3.36 (dt, *J*= 9.6, 6.6 Hz, 1H), 3.44 (dd, *J*= 9.6, 6.6 Hz, 1H), 3.50 (m, 1H), 3.57 (dd, *J*= 9.6 , 3.9 Hz, 1H), 3.72 (dt, *J*= 9.6, 6.6 Hz, 1H), 3.88 (m, 2H), 4.03 (dt, *J*= 5.4, 1.2 Hz, 2H), 4.57 (t, *J*= 2.7 Hz, 1H), 5.20 (dd, *J*= 1.2, 10.5 Hz, 1H), 5.30 (dd, *J*= 1.2, 17.1 Hz, 1H), 5.91 m, 1H). IR (liquid phase in CH_2Cl_2, cm^{-1}): ν 2925, 2855, 1465, 1120, 1075, 1025, 920. ESI-MS *m/z* : 459 (M+Na).

1-Allyloxy-5-trimethylsilanylpent-4-yn-2-ol (3f)

Yield: 63%. ^{1}H NMR (300 MHz): δ 0.14 (s, 9H), 2.39 (d, *J*= 4.8 Hz, 1H), 2.45 (dd, *J*= 6.0, 2.7 Hz, 2H), 3.44 (dd, *J*= 9.6, 6.6 Hz, 1H), 3.55 (dd, *J*= 9.6, 3.9 Hz, 1H), 3.91 (m, 1H), 4.02 (dt, *J*= 1.2, 5.4 Hz, 2H), 5.20 (dq, *J*= 10.5, 1.2 Hz, 1H), 5.30 (dq, *J*= 17.4, 1.2 Hz, 1H), 5.9 (tdd, *J*= 5.4, 10.5, 17.4 Hz, 1H). ^{13}C NMR (75 MHz): δ 0.02, 25.0, 68.8, 72.3, 72.7, 87.3, 102.5, 117.3, 134.4. IR (cm^{-1}): ν 2180, 1250, 1095, 940. ESI-MS *m/z* : 213 (M+H).

1-Allyloxyicos-4-yn-2-ol (3g)

Yield: 70%. ^{1}H NMR (300 MHz): δ 0.88 (t, *J*= 5.4 Hz, 3H), 1.25 (brs, 26H), 1.47 (m, 2H), 2.15 (t, *J*= 6.3 Hz, 2H), 2.41 (m, 2H), 3.44 (ddd, *J*= 6.9, 9.6, 0.9 Hz, 1H), 3.56 (ddd, *J*= 9.6, 3.9, 0.9 Hz, 1H), 3.89 (m, 1H), 4.03 (dd, *J*= 5.6, 1.2 Hz, 1H), 5.19 (dd, *J*= 10.2, 1.2 Hz, 1H), 5.28 (dt, *J*= 17.4, 1.2 Hz, 1H), 5.90 (tdd, *J*= 5.6, 10.2, 17.4 Hz, 1H). ^{13}C NMR (75 MHz): δ 14.1, 18.7, 22.7, 23.9, 28.9, 29.0, 29.2, 29.3, 29.6, 29.7, 31.9, 69.1, 72.3, 73.0, 75.4, 83.0, 117.2, 134.5. IR (cm^{-1}): ν 2920, 2855, 2355, 1465, 1090, 925. ESI-MS *m/z* : 351 (M+H).

2-Allyloxymethyl-5-butyltetrahydrofuran (4a)

To a solution of homopropargyl alcohol **3a-f** (0.25 mmol, 1 equiv) in a 9:1 mixture of CH_2Cl_2/H_2O (2 mL), $NaAuCl_4.2H_2O$ (0.05 equiv) was added at r.t.. After 30 min of stirring, the reaction mixture was extracted with EtOAc (3 x 2 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The crude products were dissolved in CH_2Cl_2 (5 mL) and $BF_3.OEt_2$ (1 equiv) was added at –78°C followed by either Et_3SiH or Ph_3SiH (2.5 equiv). After 3 to 5 h of stirring (see in Table **1**) a $NaHCO_3$ saturated aqueous solution (5 mL) was added, and extracted three times with ethyl acetate (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The purification by flash chromatography on silica gel of the expected products (CH_2Cl_2/cyclohexane 9:1) led to **4a-e** (for yields and d.r., see in the text). ^{1}H NMR (400 MHz) *cis* and *trans* mixture : δ 0.89 (t, *J*= 6.8 Hz, 3H), 1.32 (m, 4H), 1.45 (m, 2H), 1.62 (m, 2H), 1.93 (m, *0.70x*2H), 2.01 (m, *0.30x*2H), 3.44 (m, 2H), 3.83 (m, *0.70x*1H), 3.94 (m, *0.30x*1H), 4.04 (m, *0.70x*1H and 2H), 4.16 (m, *0.30x*1H), 5.15 (dd, *J*= 1.2, 10.4 Hz, 1H), 5.27 (dd, *J*= 1.2, 17.2 Hz, 1H), 5.91 (tdd, *J*= 5.6, 10.4, 17.2 Hz, 1H). ^{13}C NMR (75 MHz): δ 14.0, 22.8, 28.2, 28.3, 28.4, 28.7, 30.8, 31.7, 35.5, 35.6, 72.4, 73.1, 73.2, 77.3, 77.8, 79.5, 80.1, 116.8, 134.9. IR (cm^{-1}): ν 2925, 2860, 1465, 1380, 1085. ESI-MS *m/z* : 221 (M+Na).

2,5-epoxynonan -1-yl *p*-toluylsulfonate (4b)

^{1}H NMR (400 MHz) *cis* and *trans* mixture : δ 0.87 (t, *J*= 6.8 Hz, 3H), 1.28 (m, 4H), 1.46 (m, 3H), 1.68 (m, 1H), 1.91 (m, 2H), 2.44 (s, 3H), 3.81 (m, 1H), 3.98 (m, 2H), 4.06 (m, *0.73x*1H), 4.16 (m, *0.27x*1H), 7.33 (d, *J*= 8.0 Hz, 2H), 7.80 (d, *J*= 8.0 Hz, 2H). ^{13}C NMR (100 MHz): δ 14.0, 21.6, 22.7, 27.9, 28.2, 28.3, 30.8, 35.2, 35.4, 71.8, 75.4, 75.7, 79.9, 80.6, 128.0, 129.8, 133.0, 144.7. IR (cm^{-1}): ν 2925, 2860, 1460, 1365, 1190, 1175, 1095, 965.

2,5-epoxynonan-1-yl 2,2-dimethylpropanoate (4c)

^{1}H NMR (400 MHz) *cis* and *trans* mixture : δ 0.88 (t, *J*= 6.8 Hz, 3H), 1.20 (s, 9H), 1.31 (m, 4H), 1.55-1.70 (m, 4H), 1.93 (m, 2H), 3.84 (q, *J*= 6.0 Hz, *0.80x*1H), 3.93 (q, *J*= 6.0 Hz, *0.20x*1H), 4.05 (m, *0.80x*1H and 2H), 4.20 (m, *0.20x*1H). ^{13}C NMR (100 MHz): δ 14.0, 22.8, 27.2, 27.9, 28.3, 30.9, 35.6, 38.8, 66.4, 75.9, 76.3, 79.6, 80.2, 178.5. IR (cm^{-1}): ν 2960, 1730, 1480, 1395, 1285, 1155, 1100, 1035. ESI-MS *m/z* : 265 (M+Na).

5-(*m*chlorophenyl)-2,5-epoxypentan-1-yl 2,2-dimethyl-propanoate *cis* 4d

^{1}H (400MHz, $CDCl_3$) δ 1.23 (s, 9H), 1.85 (m, 2H), 2.12 (m, 1H), 2.31 (m, 1H), 4.22 (m, 2H), 4.32 (m, 1H), 4.90 (t, *J*= 7.6 Hz, 1H), 7.23 (m, 3H), 7.37 (brs, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 178.5, 145.0, 134.3, 129.5, 127.4, 125.7, 123.8, 80.7, 77.3, 66.1, 38.8, 34.6, 28.0, 27.2; ESI-MS *m/z*; 319 (M+Na), 321 (M+Na); IR cm^{-1}: ν 1725, 1480, 1280, 1150, 1080, 1035, 880; ESI-HRMS Calcd for $[M+Na]^+$ $C_{16}H_{21}O_3ClNa$: 319.1077 and 321.1047 Found: 319.1071 and 321.1062.

5-(*m*chlorophenyl)-2,5-epoxypentan-1-yl 2,2-dimethyl-propanoate *trans* 4d

^{1}H (400MHz, $CDCl_3$) δ 1.24 (s, 9H), 1.85 (m, 2H), 2.13 (m, 1H), 2.40 (m, 1H), 4.18 (m, 2H), 4.45 (m, 1H), 5.01 (t, *J*= 6.8 Hz, 1H), 7.23 (m, 3H), 7.33 (brs, 1H); ^{13}C (100 MHz, $CDCl_3$) δ 178.4, 145.2, 134.3, 129.5, 127.3, 125.6, 123.6, 80.2, 77.3, 66.2, 34.9, 28.4, 27.2; EI-MS (70 eV) *m/z* (%); 296 (6), 211 (12), 194 (36), 181 (100), 163 (28), 139 (82), 125 (62), 77 (30); IR cm^{-1}: ν 1725, 1480, 1280, 1150, 1080, 1035, 880.

1-Allyloxy-2,5-epoxynonandecan-19-ol (4e)

^{1}H NMR (400 MHz) *cis* and *trans* mixture : δ 1.25 (brs, 22H), 1.60 (m, 7H), 1.93 (m, *0.80x*2H), 2.01 (m, 0.20x2H), 3.43 (m, 2H), 3.64 (t, *J*= 6.4 Hz, 2H), 3.82 (q, *J*= 6.0 Hz, *0.80x*1H), 3.96 (q, *J*= 6.0 Hz, *0.20x*1H), 4.03 (m, 2H and *0.80x*1H), 4.16 (q, *J*= 6.0 Hz, *0.20x*1H), 5.17 (d, *J*= 10.4 Hz, 1H), 5.27 (d, *J*= 17.5 Hz, 1H), 5.91 (tdd, *J*= 5.7, 10.4, 17.5 Hz, 1H). ^{13}C NMR (100 MHz): δ 25.7, 26.2, 28.2, 28.7, 29.4, 29.5, 29.6, 29.7, 30.7, 31.7, 32.8, 35.8, 35.9, 63.1, 72.4, 73.0, 73.2, 77.8, 79.5, 80.1, 116.9, 134.9. IR (cm^{-1}): ν 3435, 2920, 2850, 1470, 1350, 1100, 1060, 925. ESI-MS *m/z* : 355 (M+H).

1-Allyloxy-2,5-epoxyicosane (4g)

To a solution of homopropargyl alcohol **3g** (0.25 mmol, 1 equiv) in CH_2Cl_2 (2 mL), H_2O (4.4 µL, 1 equiv) was added followed by $NaAuCl_4.2H_2O$ (0.05 equiv). After 1 h of stirring at r.t., Ph_3SiH (2.5 equiv) was added. After 3 h of stirring a $NaHCO_3$ saturated aqueous solution (5 mL) was added, and extracted three times with ethyl acetate (3 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum. The purification by flash chromatography on silica gel of the expected products (CH_2Cl_2/cyclohexane 9:1) led to **4g** as a cis/trans mixture (85:15) in 60 % yield : ^{1}H NMR (400 MHz) *cis* and *trans* mixture : δ 0.89 (t, *J*= 6.4 Hz, 3H), 1.25 (m, 13H), 1.42 (m, 3H), 1.64 (m, 2H), 1.93 (m, *0.85x*2H), 2.01 (m, *0.15x*2H), 3.43 (m, 2H), 3.82 (m, *0.85x*1H), 3.94 (m, *0.15x*1H), 4.03 (m, *0.80x*1H and 2H), 4.14 (m, *0.15x*1H), 5.16 (d, *J*= 10.4 Hz, 1H), 5.27 (dd, *J*= 0.8, 17.6 Hz, 1H), 5.91 (tdd, *J*= 5.6, 10.4, 17.6 Hz, 1H). ^{13}C NMR (100 MHz): δ 14.1, 14.2, 22.7, 26.1, 26.2, 28.2, 28.7, 29.3, 29.6, 29.7, 29.8, 30.8, 31.7, 31.9, 35.8, 35.9, 72.4, 73.1, 73.2, 77.8, 79.5, 80.1, 116.8, 134.9. IR (cm^{-1}): ν 2925, 2860, 1465, 1380, 1085. ESI-MS *m/z* : 375 (M+Na).

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