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SYNTHESIS OF 4-BENZYLIDEN-2-OXAZOLIDINONE DERIVATIVES *VIA* GOLD-CATALYZED INTRAMOLECULAR HYDROAMINATION

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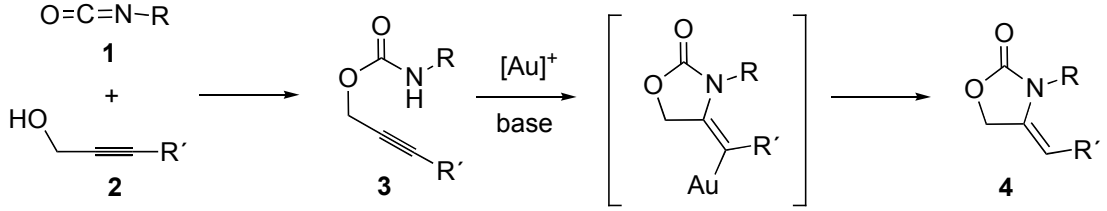
Dedicated to Prof. E. Winterfeldt on the occasion of his 75th birthday

Abstract – AuCl-catalyzed intramolecular hydroamination of *N*-aryl-*O*-propargyl carbamates (**3**) efficiently affords (*Z*)-*N*-aryl-4-benzyliden-2-oxazolidinones (**4**) *via* a 5-*exo dig* cyclization. The reaction proceeds in acetonitrile at 60 °C and requires *t*BuOK or KOH as a base co-catalyst. It tolerates the presence of multiple substituted aryl units with electron donating methoxy groups. The method opens a convenient, flexible and operationally simple access to a new class of twisted molecules with potentially interesting biological properties.

INTRODUCTION

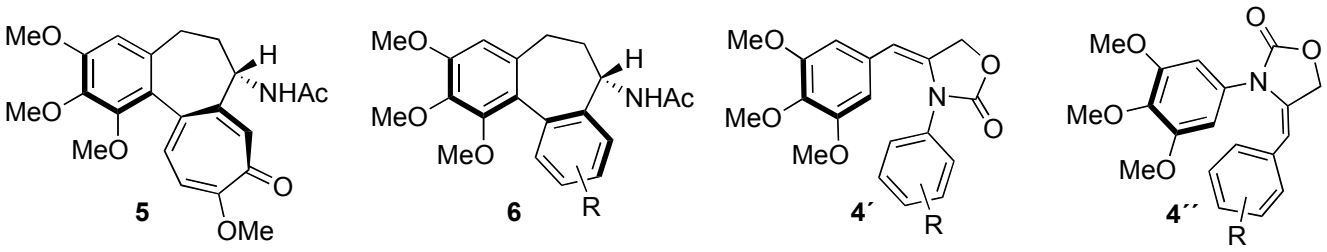
Catalytic nucleophilic addition of N-H bonds across a C-C multiple bond (hydroamination) has become an important tool in the synthesis of nitrogen-containing heterocycles.[1] As they occur in many biologically active natural products and pharmaceuticals, these substructures are synthetic targets of high relevance.[2-4] Belonging to the group of late transition metals, Au(I) is well known to act as a soft Lewis acid, coordinating to alkynes and thereby activating them towards nucleophilic attack.[5] This has led to frequent application of gold catalysis in the field of hydroamination reactions.[6]

We have recently reported that, on treatment with catalytic amounts of gold(I) chloride and a base co-catalyst, *O*-propargyl carbamates of type **3** smoothly undergo a 5-*exo dig* cyclization at moderate temperatures to stereoselectively afford substituted (*Z*)-configurated 2-oxazolidinones of type **4** in high yield.[7] However, in terms of sterical demand and electronical properties, only simple substituents were probed so far (R = Ts, Ph, R´ = H, Me, Ph).



Scheme 1. Gold-catalyzed synthesis of 2-oxazolidinones from *O*-propargyl-carbamates

Influenced by our recent work on the total synthesis of colchicine (**5**)[8] and structurally related molecules such as allocolchicines of type **6**, we reasoned that the gold-catalyzed process described above could eventually be applied in the synthesis of molecules of type **4´** or **4´´**, which also should adapt a twisted conformation. The trimethoxyaryl unit, which frequently occurs in bioactive natural products[9] can either be positioned at the nitrogen (**4´´**) or part of the benzylidene substructure (**4´**).



Scheme 2. Bioactive molecules with a trimethoxyaryl unit adopting a twisted conformation

Herein, we report the synthesis and characterization of seven prototypic compounds of type **4´** and **4´´**, respectively. Thereby, we demonstrate the rather general applicability of the gold-catalyzed process under optimized conditions.

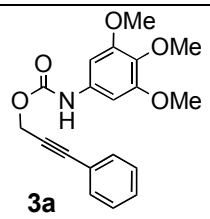
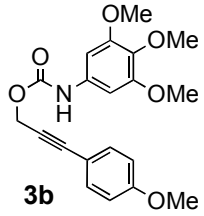
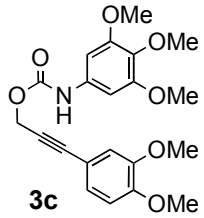
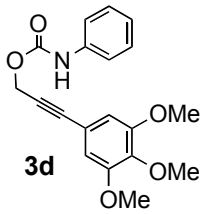
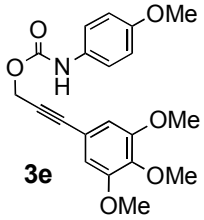
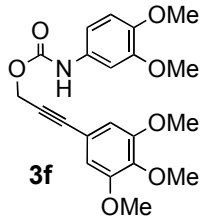
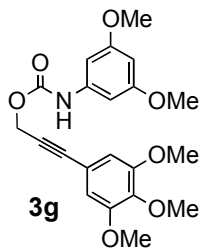
RESULTS AND DISCUSSION

The *O*-propargyl carbamates (**3**), required as substrates for the synthesis of compounds of type **4** via the gold(I) catalyzed 5-*exo dig* cyclization, were prepared from differently substituted isocyanates (**1**) and the corresponding propargylic alcohols (**2**) (Scheme 1).

Using commercialy available 3,4,5-trimethoxyphenylisocyanate as a starting material, the three carbamates **3a**, **3b** and **3c** were obtained in good yield by treatment with the respective propargylic alcohols in THF in the presence of Et_3N (2 equiv.) and DMAP (0.2 equiv.) as a nucleophilic catalyst.[10]

The carbamates **3d**, **3e**, **3f** and **3g** (with R´ = 3,4,5-trimethoxyphenyl) were prepared in a similar manner. In these cases, the required isocyanates were synthesized by treatment of the corresponding anilines with a 20% solution of phosgene in toluene and subsequent removal of all volatiles. This way, the pure cyclization precursors (**3a**-**g**) shown in Table 1 were all obtained in 70 to 87% yield as colourless solids exhibiting the expected spectroscopic data (IR, MS, ^{1}H NMR, ^{13}C NMR). Most characteristic parameters are the IR signals of the carbamate unit ($\tilde{\upsilon}_{C=O}$ = 1730 ±3 cm^{-1}, $\tilde{\upsilon}_{N-H}$ = 3321±10 cm^{-1}) and the ^{1}H NMR signals of the CH_2O group (ca. 5.0 ppm in $CDCl_3$). The NH protons usually appeared between 6.6 and 7.1 ppm but were not visible in the case of **3e** and **3g**.

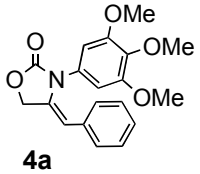
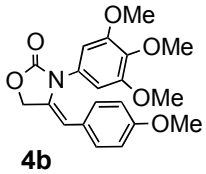
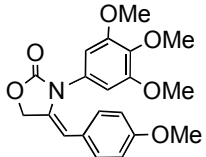
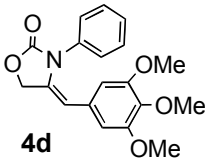
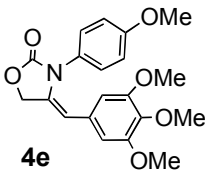
Table 1. Synthesized carbamate precursors for the cyclization reaction (compare Scheme1)

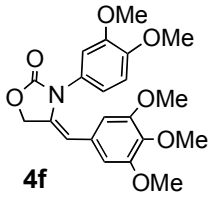
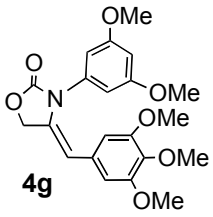
Entry	Structure	Yield	mp [°C]	$\tilde{\upsilon}_{N\text{-}H}$ [cm^{-1}]	$\tilde{\upsilon}_{C=O}$ [cm^{-1}]	δ (CH_2O) [ppm]
1	 **3a**	73%	120 °C	3318	1733	4.99
2	 **3b**	78%	160 °C	3317	1730	4.97
3	 **3c**	70%	143 °C	3323	1733	4.97
4	 **3d**	83%	88 °C	3312	1731	4.98
5	 **3e**	87%	110 °C	3330	1732	4.97
6	 **3f**	82%	128 °C	3326	1728	4.96
7	 **3g**	80%	87 °C	3331	1730	5.22

Next, we investigated the cyclization reactions, the results of which are summarized in Table 2. When the *N*-3,4,5-trimethoxyphenyl substituted carbamates (**3a**-**c**) were treated under the established conditions (A) with 5 mol% of AuCl in acetonitrile at 60 °C in the presence of 5 mol% of *t*BuOK (or KOH) the expected products **4a**-**c** were obtained in reasonable yields within 4-8 hours. Remarkably, carbamates **3d**-**g** only gave marginal conversion under these conditions. However, a dramatic rate enhancement was observed when the amount of base was increased. Thus, using 40 mol% of base (conditions B) full conversion of the carbamate occured within 6-12 hours and the pure *Z*-products (**4d**-**g**) were obtained in 60-80% yield after crystallization from EtOAc.

In all cases, the (*Z*)-configuration of the products (**4**) was secured by NOE measurements irradiating either into the olefinic H or the ring CH_2 group. The *Z*/*E* selectivity, as determined by ^{1}H NMR and GC-MS from the crude product mixtures, was only 7:1 for **4a** but >97:3 in all other cases.

Table 2. Synthesized 4-benzylidene-2-oxazolidinones according to Scheme 1

Entry	Substrate	Method	Product	Isolated yield	*Z*:*E*-Selectivity (crude)
1	**3a**	A	 **4a**	67%	*Z*:*E* = 7:1
2	**3b**	A	 **4b**	54%	*Z*:*E* >99:1
3	**3c**	A	 **4c**	65%	*Z*:*E* >99:1
4	**3d**	B	 **4d**	75%	*Z*:*E* = 97:3
5	**3e**	B	 **4e**	60%	*Z*:*E* = 97:3

6	**3f**	B	 **4f**	80%	*Z*:*E* = 97:3
7	**3g**	B	 **4g**	77%	*Z*:*E* = 97:3

Method A: Acetonitrile, AuCl (5mol%), *t*BuOK or KOH (5mol%), 60 °C, 4-8h.

Method B:Acetonitrile, AuCl (5mol%), *t*BuOK or KOH (40mol%), 60 °C, 4-8h.

In conclusion, we have proven the applicability of the gold(I) catalyzed cyclization of *O*-propargyl carbamates to prepare a set of methoxy-substituted (*Z*)-4-benzylidene-2-oxazolidinones. Under optimized conditions, even unreactive substrates with 3,4,5-trimethoxyphenyl-substituents at the alkyne, could be employed. Due to the modular concept, operational simplicity and functional group tolerance of the method, we are confident that this work paves the way for the future synthesis of compound libraries containing members with interesting biological activity.

EXPERIMENTAL

All solvents were redistilled. Reactions were carried out under an argon atmosphere and in dry glassware and were monitored by TLC (SiO_2) and GC-MS (Agilent, HP 6890, Optima-1-MS). Melting points were taken on a *Büchi* B-545 and are uncorrected. All ^{1}H NMR, ^{13}C NMR and 2D NMR spectra were obtained on a *Bruker* AC 250 (250 MHz) or a *Bruker* DPX 300 (300 MHz) spectrometer using $CDCl_3$ as solvent. IR spectra were recorded on a *Perkin-Elmer* Paragon 100 FT-IR ATR mode (ZnSe discs). MS spectra were obtained on a *Finnigan* MAT Incos 50 Galaxy System (EI) or a MAT 900 (HRMS). Microanalysis for C, H, and N were recorded on a Elementar Vario EL.

General procedure for the preparation of isocyanates from the corresponding anilines (2d-g):

CAUTION: This procedure must be performed in a well ventilated hood. A commercial 20% solution of phosgene in toluene (3.9 mL, 7.8 mmol; 6 equiv.) was dilluted with 6 mL of toluene and cooled to 0 °C followed by the dropwise addition of the aniline (1.3 mmol; 1 equiv.) in 4 mL of toluene. The reaction mixture was refluxed for 1.5 h until it turned clear. After cooling the solution to 0 °C, the remaining phosgene was removed under reduced pressure (oil pump). It was collected in a cooling trap and destroyed by addition of an aqueous ammonia solution. Remaining solvent was then removed under

reduced pressure at rt. All products were used in the carbamate synthesis without further purification.

General procedure for the preparation of carbamates 3a-g:

The aryl isocyanate was dissolved in 4 mL of THF and DMAP (24 mg; 0.2 mmol; 0.2 equiv.) and Et_3N (0.28 mL; 2.0 mmol; 2 equiv.) were added before the reaction mixture was cooled to 0 °C. Then the propargylic alcohol (1 mmol; 1 equiv.) dissolved in 2 mL of THF was added dropwise. The reaction mixture was stirred at rt for 20 h and quenched with saturated aqueous NH_4Cl-solution. After extraction with EtOAc, the combined organic phases were dried over Na_2SO_4 and the solvent was removed under reduced pressure. Recrystallization from EtOAc or flash column chromatography (cyclohexane:EtOAc = 1:1 or 1:2) afforded the desired products **3a-g**.

3-Phenylprop-2-ynyl 3,4,5-trimethoxyphenylcarbamate (3a):

Yield: 73%; R_f = 0.56 (cyclohexane/EtOAc - 1:1); mp 120 °C (EtOAc). MS (EI, 70 eV): m/z (%): 341 (17, $[M]^+$), 209 (62), 194 (68), 182 (41), 166 (44), 151 (28), 136 (30), 115 (100), 104 (20), 89 (12), 80 (29), 69 (11), 65 (14), 63 (21), 52 (20). HRMS (EI, 70 eV): calcd for $[M]^+$: 341.1263; found: 341.1263. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 3318 (m), 2996 (w), 2937 (w), 2837 (w), 2241 (w), 1733 (s, CO), 1605 (s), 1542 (s), 1506 (s), 1489 (m), 1451 (s), 1431 (s), 1365 (m), 1297 (m), 1217 (s), 1124 (s), 1073 (s), 1036 (m), 985 (m), 965 (m), 912 (w), 829 (m), 782 (w), 756 (s), 730 (m), 690 (m). ^1H NMR (250 MHz, $CDCl_3$): δ [ppm] = 3.79 (*s*; 3H, OMe), 3.81 (*s*; 6H, 2xOMe), 4.99 (*s*; 2H), 6.67 (*s*; 2H), 6.73 (br, N-H, 1H) 7.28-7.31 (*m*; 2H), 7.42-7.46 (*m*; 2H). ^{13}C NMR (62.5 MHz, $CDCl_3$): δ [ppm] = 53.6, 56.1, 61.0, 82.9, 86.7, 103.6, 120.6, 122.1, 128.3, 128.8, 131.9, 133.6, 152.7, 153.5.

3-(4-Methoxyphenyl)prop-2-ynyl 3,4,5-trimethoxyphenylcarbamate (3b):

Yield: 78%; R_f = 0.35 (cyclohexane/EtOAc - 2:1); mp 160 °C (EtOAc). MS (EI, 70 eV): m/z (%): 371 (6, $[M]^+$), 209 (8), 194 (11), 182 (9), 145 (100), 102 (12). HRMS (EI, 70 eV): calcd for $[M]^+$: 371.1369; found: 371.1370. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 3317 (m), 2936 (m), 2837 (w), 1730 (m, CO), 1604 (s), 1547 (m), 1507 (s), 1453 (m), 1413 (m), 1365 (w), 1217 (s), 1162 (m), 1126 (s), 1073 (s), 1032 (m), 1001 (w), 965 (m), 830 (m), 731 (m). ^1H NMR (250 MHz, $CDCl_3$): δ [ppm] = 3.79 (*s*; 6H, 2xOMe), 3.82 (*s*; 6H, 2xOMe), 4.97 (*s*; 2H), 6.61 (br, N-H, 1H), 6.62 (*s*; 2H), 6.82 (*d*; ^3J =8.7 Hz, 2H), 6.88 (*d*; ^3J = 8.7 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 53.8, 55.3, 56.1, 61.0, 81.6, 86.8, 96.5, 96.6, 114.0, 133.5, 133.7, 153.5, 153.9, 160.0.

3-(3,4-Dimethoxyphenyl)prop-2-ynyl 3,4,5-trimethoxyphenylcarbamate (3c):

Yield: 70%; R_f = 0.76 (cyclohexane/EtOAc - 1:2); mp 143 °C (cyclohexane). (EI, 70 eV): m/z (%) = 401

(4, $[M]^+$), 209 (27), 194(38), 175 (100), 161 (21), 151 (14), 131 (16), 103 (5), 91 (15), 77 (16). HRMS (EI, 70 eV): calcd for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 3323 (w), 2937 (w), 2834 (w), 1733 (m, CO), 1604 (m), 1539 (m), 1507 (s), 1451 (m), 1412 (m), 1321 (w), 1296 (m), 1267 (m), 1218 (ss), 1173 (m), 1005 (m), 970 (m), 912 (w), 809 (w), 762 (m), 729 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.78 (*s*; 3H, OMe), 3.80 (*s*; 6H, 2xOMe), 3.83 (*s*; 3H, OMe), 3.85 (*s*; 3H, OMe), 4.97 (*s*; 2H), 6.67 (*s*; 2H), 6.76 (br, 1H), 6.78 (*d*; ^{3}J = 8.4 Hz, 1H), 6.94 (*d*; ^{4}J = 1.8 Hz, 1H), 7.04 (*dd*; ^{3}J = 8.4 Hz, ^{4}J = 1.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 53.7, 55.9, 56.1, 61.0, 81.6, 86.8, 96.5, 97.9, 111.0, 114.2, 114.6, 125.4, 133.7, 147.8, 149.9, 152.8, 153.5.

3-(3,4,5-Trimethoxyphenyl)prop-2-ynyl phenylcarbamate (3d):

Yield: 83%; R_f = 0.65 (cyclohexane/EtOAc - 1:1); mp 88 °C (EtOAc). MS (EI, 70 eV) m/z (%) = 341 (18, $[M]^+$), 222 (10, $[M\text{-}C_7H_5NO]^+$), 205 (100), 172 (16), 119 (10, $[M\text{-}C_{12}H_{13}OH]$), 93 (10), 77 (7), 65 (15), 51 (4). HRMS (EI, 70 eV): calcd for $[M]^+$: 341.1236; found: 341.1236. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 3312 (w), 2935 (w), 1731 (s, CO), 1599 (m), 1576 (m), 1539 (s), 1501 (s), 1444 (s), 1409 (m), 1341 (m), 1312 (m), 1215 (s), 1126 (s), 1063 (s), 1028 (m), 996 (m), 909 (w), 836 (m), 752 (m), 692 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.8 (*s*; 6H), 3.83 (*s*; 3H), 4.98 (*s*; 2H), 6.67 (*s*; 2H), 6.88 (*br*; 1H), 7.05 (*t*; ^{3}J = 7.2 Hz, 1H), 7.28 (*m*; 2H), 7.37 (*m*; 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 53.5, 56.1, 60.9, 82.2, 86.6, 109.1, 117.0, 118.7, 123.7, 129.0, 137.5, 139.1, 152.6, 152.9.

3-(3,4,5-Trimethoxyphenyl)prop-2-ynyl 4-methoxyphenylcarbamate (3e):

Yield: 87%; mp 110 °C (cyclohexane). MS (EI, 70 eV): m/z (%): 371 (7, $[M]^+$), 222 (10, $[M\text{-}C_8H_8NO_2]^+$), 205 (100), 172 (13), 149 (9), 134 (7), 122 (12), 106 (6), 95 (5), 78 (5), 63 (5), 52 (4). HRMS (EI, 70 eV): calcd for $[M]^+$: 371.1369; found: 371.1369. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 3330 (w), 2937 (w), 2832 (w), 1732 (m, CO), 1576 (m), 1504 (s), 1462 (m), 1411 (m), 1341 (m), 1296 (m), 1216 (s), 1179 (m), 1126 (s), 1065 (s), 1031 (m), 1002 (w), 828 (m), 764 (m). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.76 (*s*; 3H), 3.81 (*s*; 6H), 3.83 (*s*; 3H), 4.97 (*s*; 2H), 6.69 (*s*; 2H), 6.83 (*d*; ^{3}J = 9.0 Hz, 2H), 7.28 (*d*; ^{3}J = 9.0 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 53.3, 55.4, 56.0, 60.8, 82.3, 86.4, 109.1, 114.2, 117.0, 120.7, 130.5, 139.1, 152.9, 156.0.

3-(3,4,5-Trimethoxyphenyl)prop-2-ynyl 3,4-dimethoxyphenylcarbamate (3f):

Yield: 82%; R_f = 0.30 (cyclohexane/EtOAc - 1:1); mp 128 °C (cyclohexane). MS (EI, 70 eV): m/z (%) = 401 (7, $[M]^+$), 357 (5), 222 (7, $[M\text{-}C_9H_9NO_3]^+$), 205 (100), 179 (7, $[M\text{-}C_{12}H_{13}OH]^+$), 172 (14), 152 (10), 136 (7), 125 (5), 110 (5), 93 (6), 76 (5), 65 (6), 53 (5). HRMS (EI, 70 eV): calcd for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 3326 (w), 2938 (w), 2833 (w), 1728 (m; CO), 1602 (s), 1575 (s),

1501 (s), 1448 (s), 1408 (s), 1340 (s), 1219 (s), 1164 (s), 1123 (s), 1064 (s), 1024 (s), 995 (s), 949 (m), 833 (s), 804 (s), 764 (s) 631 (m), 619 (m), 614 (m), 609 (m).^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.79 (*s*; 6H), 3.80 (*s*; 3H), 3.81 (*s*; 3H), 3.82 (*s*; 3H), 4.96 (*s*; 2H), 6.66 (*s*; 2H), 6.75-6.76 (*m*; 2H), 6.80 (*br*; 1H), 7.14 (*br*; 1H, H-N). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 53.1, 55.6, 55.9, 60.7, 82.3, 86.2, 108.9, 110.7, 111.3, 116.9, 131.1, 132.5, 138.9, 145.2, 148.9, 152.8.

3-(3,4,5-Trimethoxyphenyl)prop-2-ynyl 3,5-dimethoxyphenylcarbamate (3g):

Yield: 80%; R_f = 0.63 (cyclohexane/EtOAc - 1:1); mp. 87 °C. MS (EI, 70 eV): m/z (%): 401 (10, $[M]^+$), 222 (35, $[M\text{-}C_9H_9NO_3]^+$), 205 (100), 179 (48, $[M\text{-}C_{12}H_{13}OH]^+$), 150 (22), 136 (16), 119 (15), 106 (7), 91 (16), 77 (12), 65 (11), 53 (8). HRMS (EI, 70 eV): calculated for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 3331 (w), 2936 (w), 2832 (w), 2245 (w), 1730 (m; CO), 1600 (s), 1577 (m), 1555 (m), 1503 (s), 1454 (s), 1411 (m), 1340 (m), 1202 (s), 1152 (s), 1125 (s), 1041 (s), 966 (m), 907 (s), 832 (s), 765 (m), 726 (s), 681 (m), 647 (m), 630 (m). ^{1}H-NMR: (300 MHz, $CDCl_3$): δ [ppm] = 3.99 (*s*; 6H), 4.06 (*s*; 6H), 4.09 (*s*; 3H), 5.22 (*s*; 2H), 6.43 (*t*; ^{4}J = 1.8 Hz, 1H), 6.88 (*d*; ^{4}J = 1.8 Hz, 2H), 6.93 (*s*; 2H). ^{13}C-NMR: (75 MHz, $CDCl_3$): δ [ppm] = 53.1, 55.2, 56.0, 60.8, 82.1, 86.5, 95.9, 97.0, 109.0, 116.9, 139.1, 139.3, 152.5, 152.9, 161.0.

General procedure for the AuCl-catalyzed cyclization of *O*-propargyl carbamates 4a-c (Method A):

To a solution of 0.5 mmol of an *O*-propargyl carbamate (**3a-c**) and a base co-catalyst (0.025 mmol; 5mol%; *t*BuOK or KOH) in 2 mL of MeCN was added AuCl (0.025 mmol; 5 mol%). The mixture was stirred at 60 °C for 4-8 h. Conversion was monitored by TLC and/or GC-MS analysis. The reaction mixture was filtered through a small pad of Celite® (elution with CH_2Cl_2). Removal of the solvent under reduced pressure and purification of the residue by flash chromatography on SiO_2 (2:1 cyclohexane:EtOAc or 1:1 cyclohexane:EtOAc) afforded the products as clear oil (**4a**) or colourless solids (**4b, 4c**).

General procedure for the AuCl-catalyzed cyclization of *O*-propargyl carbamates 4d-g (Method B):

To a solution of 0.5 mmol of an *O*-propargyl carbamate (**3d-g**) and a base (0.2 mmol; 40 mol%; *t*BuOK or KOH) in 2 mL of MeCN was added AuCl (0.025 mol; 5 mol%). The mixture was stirred at 60 °C for 6-12 h. Conversion was monitored by TLC and/or GC-MS analysis. The reaction mixture was filtered through a small pad of Celite® (elution with CH_2Cl_2). Removal of the solvent under reduced pressure and purification of the residue by flash chromatography on SiO_2 (2:1 cyclohexane:EtOAc or 1:1 cyclohexane:EtOAc) afforded the products (**4d-g**) as white solids.

(*Z*)-4-Benzylidene-3-(3,4,5-trimethoxyphenyl)oxazolidin-2-one (4a):

Yield: 67%; R_f = 0.51 (cyclohexane/EtOAc - 1:1); MS (EI, 70 eV): m/z (%): 341 (100, $[M]^+$), 326 (7, $[M\text{-}CH_3]^+$), 282 (16), 266 (12), 193 (42), 178 (35), 150 (8), 135 (11), 115 (12), 104 (13). HRMS (EI, 70 eV): calcd for $[M]^+$: 341.1263; found: 341.1263. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 2938 (w), 2831 (w), 1768 (ss, CO), 1676 (s), 1596 (s), 1504 (s), 1461 (m), 1417 (s), 1361 (m), 1337 (m), 1268 (s), 1229 (s), 1168 (s), 1147 (m), 1122 (ss), 1077 (m), 1064 (m), 1031 (m), 999 (m), 909 (s), 853 (w), 829 (m), 756 (m), 724 (ss), 697 (ss), 643 (s). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.55 (*s*; 6H, 2xOMe), 3.68 (*s*; 3H, OMe), 5.09 (*d*; ^{4}J= 2.1 Hz, 2H), 5.61 (*t*; ^{4}J = 2.1 Hz, 1H), 6.22 (*s*; 2H), 6.64-6.67 (*m*; 2H), 6.90-6.92 (*m*; 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 56.0, 60.9, 68.1, 99.9, 104.4, 126.2, 127.1, 128.1, 130.1, 131.7, 132.6, 137.3, 152.9, 157.0.

(*Z*)-4-(4-Methoxyphenyl)-3-(3,4,5-trimethoxyphenyl)oxazolidin-2-one (4b):

Yield: 54%; R_f = 0.42 (cyclohexane/EtOAc - 2:1); MS (EI, 70 eV): m/z (%): 371 (98, $[M]^+$), 312 (9), 296 (20), 265 (8), 193 (7), 178 (10), 148 (7), 134 (100), 119 (17), 91 (12). HRMS (EI, 70 eV): calcd for $[M]^+$: 371.1369; found: 371.137. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 2938 (m), 2833 (w), 1768 (ss, CO), 1675 (s), 1596 (s), 1506 (ss), 1457 (s), 1418 (s), 1361 (m), 1337 (m), 1272 (s), 1242 (s), 1170 (s), 1120 (s), 1066 (s), 1030 (m), 912 (m), 860 (m), 846 (m), 757 (m), 738 (s), 714 (s), 687 (m), 646 (m). ^{1}H NMR (250 MHz, $CDCl_3$): δ [ppm] = 3.58 (*s*; 6H, 2xOMe), 3.63 (*s*; 3H, OMe), 3.71 (*s*; 3H, OMe), 5.09 (*d*; ^{4}J = 2.3 Hz, 2H), 5.62 (*t*; ^{4}J = 2.3 Hz, 1H), 6.25 (*s*; 2H), 6.46 (*d*; ^{3}J =8.8 Hz, 2H), 6.59 (*d*; ^{3}J = 8.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 55.3, 56.0, 60.9, 68.2, 99.8, 104.3, 112.6, 125.7, 129.3, 130.2, 131.4, 137.3, 152.8, 157.9.

(*Z*)-4-(3,4-Dimethoxyphenyl)-3-(3,4,5 trimethoxyphenyl)oxazolidin-2-one (4c):

Yield: 65%; R_f = 0.4 (cyclohexane/EtOAc - 1:1); mp 147 °C (cyclohexane). (EI, 70 eV): m/z (%) = 401 (100, $[M]^+$), 386 (8, $[M\text{-}CH_3]^+$), 342 (9), 326 (12), 295 (8), 164 (61), 149 (16), 121 (6), 103 (5), 91 (7), 77 (8). HRMS (EI, 70 eV): calcd for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 2937 (w), 2832 (w), 1769 (ss; CO), 1675 (s), 1596 (s), 1506 (s), 1462 (s), 1417 (s), 1362 (m), 1337 (m), 1316 (m), 1267 (s), 1230 (ss), 1171 (s), 1122 (s), 1067 (m), 1025 (m), 912 (m), 861 (m), 846 (m), 817 (m), 757 (m), 725 (s), 694 (m), 645 (m).^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.56 (*s*; 3H, OMe), 3.58 (*s*; 6H, 2xOMe), 3.69 (*s*; 3H, OMe), 3.72 (*s*; 3H, OMe), 5.08 (*d*; ^{4}J = 1.8 Hz, 2H), 5.62 (*t*; ^{4}J= 1.8 Hz, 1H), 6.16 (*d*; ^{4}J = 1.2 Hz, 1H), 6.29 (*s*; 1H), 6.32 (*dd*; ^{3}J = 8.1 Hz, ^{4}J = 1.2 Hz, 1H), 6.49 (*d*; ^{3}J = 8.1 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 55.4, 56.0, 60.8, 68.1, 100.0, 104.1, 110.3, 112.0, 120.9, 126.2, 130.3, 131.3, 147.6, 147.8, 152.8, 157.0.

(*Z*)-4-(3,4,5-Trimethoxyphenyl)-3-phenyloxazolidin-2-one (4d):

Yield: 75%; R_f = 0.38 (cyclohexane/EtOAc - 1:1); mp 165 °C (EtOAc). *Anal.* Calcd for $C_{19}H_{19}NO_5$: C 66.85; H 5.61; N 4.10. Found: C 66.51; H 5.78; N 3.96. MS (EI, 70 eV): m/z (%): 341 (100, $[M]^+$), 326 (63, $[M\text{-}CH_3]^+$), 207 (18), 179 (44), 151 (25), 136 (17), 119 (13), 103 (10), 91 (20), 77 (40), 65 (13), 51 (15). HRMS (EI, 70 eV): calcd for $[M]^+$: 341.1263; found: 341.126. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 2935 (w), 2832 (w), 1771 (s), 1681 (m), 1579 (m), 1504 (m), 1450 (m), 1417 (m), 1333 (s), 1236 (m), 1201 (m), 1164 (m), 1123 (s), 1079 (m), 1063 (m), 1004 (m), 959 (w), 845 (w), 766 (m), 741 (w), 695 (m), 645 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.55 (*s*; 6H, 2xOMe), 3.67 (*s*; 3H, OMe), 5.10 (*d*; ^{4}J = 2.1 Hz, 2H,), 5.63 (*t*; ^{4}J = 2.1 Hz, 1H), 5.88 (*s*; 2H), 7.01-7.10 (*m*; 5H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 55.7, 60.7, 68.0, 100.1, 105.9, 125.5, 127.2, 128.2, 128.6, 131.9, 134.8, 136.4, 152.0, 156.9.

(*Z*)-4-(3,4,5-Trimethoxyphenyl)-3-(3-methoxyphenyl)oxazolidin-2-one (4e):

Yield: 60%; R_f = 0.60 (cyclohexane/EtOAc - 1:1); mp 143 °C (cyclohexane). *Anal.* Calcd for $C_{20}H_{21}NO_6$: C 64.68; H 5.70; N 3.77. Found: C 64.38; H 5.91; N 3.80. MS (EI, 70 eV): m/z (%): 371 (100, $[M]^+$), 356 (63, $[M\text{-}CH_3]^+$), 296 (7), 237 (6), 207 (9), 194 (15), 179 (55), 151 (25), 136 (17), 121 (17), 108 (10), 91 (20), 77 (24), 65 (17), 51 (8). HRMS (EI, 70 eV): calcd for $[M]^+$: 371.1369; found: 371.1369. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}] = 2920 (m), 2846 (w), 1771 (s), 1682 (m), 1579 (m), 1511 (s), 1463 (m), 1417 (m), 1335 (s), 1296 (w), 1247 (s), 1202 (m), 1170 (m), 1124 (s), 1067 (m), 1030 (w), 1004 (w), 960 (w), 832 (m), 758 (w), 718 (w), 671 (w). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.57 (*s*; 6H, 2xOMe), 3.64 (*s*; 3H, OMe), 3.67 (*s*; 3H, OMe), 5.06 (*d*; ^{4}J = 2.7 Hz, 2H), 5.58 (*t*; ^{4}J = 2.7 Hz, 1H), 5.88 (*s*; 2H), 6.59 (*d*; ^{3}J = 10.8 Hz, 2H), 6.92 (*d*; ^{3}J = 10.8 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 55.3, 55.6, 60.7, 67.9, 99.4, 106.1, 113.4, 126.9, 127.6, 128.6, 132.4, 136.33, 151.9, 157.1, 158.4.

(*Z*)-4-(3,4,5-Trimethoxyphenyl)-3-(3,4-dimethoxyphenyl)oxazolidin-2-one (4f):

Yield: 80%; R_f = 0.63 (cyclohexane/EtOAc - 1:1); mp 41 °C (cyclohexane). MS (EI, 70 eV): m/z (%) = 401 (100, $[M]^+$), 386 (50, $[M\text{-}CH_3]^+$), 326 (7), 295 (8), 280 (87), 268 (7), 207 (9), 194 (30), 179 (65, $[M\text{-}C_{12}H_{13}OH]^+$), 163 (17), 151 (28), 136 (18), 119 (15), 107 (8), 91 (23), 77 (22), 65 (18), 51 (11). HRMS (EI, 70 eV): calcd for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 2934 (w), 2832 (w), 1772 (s; CO), 1683 (m), 1578(m), 1514 (s), 1448 (m), 1335 (s), 1250 (s), 1172 (m), 1124 (s), 1067 (m), 1026 (m), 641 (m).^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 3.54 (*s*; 3H, OMe), 3.57 (*s*; 6H, 2xOMe), 3.67 (*s*; 3H, OMe), 3.75 (*s*; 3H, OMe), 5.07 (*d*; ^{4}J = 1.8 Hz, 2H), 5.60 (*t*; ^{4}J = 1.8 Hz, 1H), 5.92 (*s*; 2H), 6.42 (*d*; ^{4}J = 2.1 Hz, 1H), 6.64 (*d*; ^{3}J = 8.7 Hz, 1H), 6.73 (*dd*; ^{3}J = 8.7 Hz, ^{4}J = 2.1 Hz, 1H).^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 55.5, 55.7, 56.0, 60.7, 67.9, 99.5, 106.1, 109.7, 110.5, 118.4, 127.8, 128.8, 132.5, 136.5, 148.1, 148.5, 152.0, 157.1.

(*Z*)-4-(3,4,5 Trimethoxyphenyl)-3-(3,5-dimethoxyphenyl)oxazolidin-2-one (4g):

Yield: 77%; R_f = 0.13 (cyclohexane/EtOAc - 2:1); mp. 43 °C. *Anal*. Calcd for $C_{21}H_{23}NO_7$: C 62.83; H 5.78; N 3.49. Found: C 62.62; H 6.07; N 3.42. MS (EI, 70 eV): m/z (%): 401 (100, $[M]^+$), 386 (68, $[M\text{-}CH_3]^+$), 207 (13), 194 (10), 179 (53, $[M\text{-}C_{12}H_{13}OH]^+$), 163 (13), 151 (25), 136 (18), 119 (15), 107 (8), 91 (20), 77 (19), 65 (14), 51 (8). HRMS (EI, 70 eV): calculated for $[M]^+$: 401.1474; found: 401.1474. IR (ATR): $\tilde{\upsilon}$ [cm^{-1}]: 2938 (w), 2834 (w), 1771 (s; CO), 1679 (m), 1595 (s), 1505 (m), 1450 (s), 1333 (s), 1264 (s), 1235 (s), 1204 (s), 1174 (S), 1155 (s), 1123 (s), 1072 (s), 1007 (m), 839 (m), 756 (w), 708 (m), 686 (m). ^{1}H-NMR: (300 MHz, $CDCl_3$): δ [ppm] = 3.55 (*s*; 6H, 2xOMe), 3.60 (*s*; 6H, 2xOMe), 3.69 (*s*; 3H, OMe), 5.07 (*d*; ^{4}J = 2.1 Hz, 2H), 5.62 (*t*; ^{4}J = 2.1 Hz, 1H), 5.95 (*s*; 2H), 6.17 (*t*; ^{4}J = 2.1 Hz, 1H,), 6.20 (*d*; ^{4}J = 2.1 Hz, 2H). ^{13}C-NMR: (75 MHz, $CDCl_3$): δ [ppm] = 55.2, 55.6, 60.6, 67.9, 99.7, 100.1, 104.7, 105.7, 129.0, 132.1, 136.2, 136.4, 152.1, 156.6, 160.3.

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REFERENCES

1. For selected reviews, see: a) T. E. Müller, M. Beller and *Chem. Rev.,* 1998, **98**, 675. b)M. Beller, J. Seayad, A. Tillack and H. Jiao, *Angew. Chem. Int. Ed.,* 2004, **43**, 3368. c) S. Hong and T. J. Marks, *Acc. Chem. Res.,* 2004, **37**, 673. d)F. Pohlki and S. Doye, *Chem. Soc. Rev.,* 2003, **32**, 104.
2. F. Reck, F. Zhou, M. Girardot, G. Kern, C. J. Eyermann, N. J. Hales, R. R. Ramsay and M. B. Gravestock, *J. Med. Chem.*, 2005, **48**, 499.
3. M. R. Barbachyn and C. W. Ford, *Angew. Chem. Int. Ed.,* 2003, **42**, 2010.
4. H. Kakeya, M. Morishita, H. Koshino, T. Morita, K. Kobayashi and H. Osada, *J. Org. Chem.,* 1999, **64**, 1052.
5. For recent reviews, see: a) A. S. K. Hashmi, *Gold Bull.*, 2004, **37**, 51. b) A. Hoffmann-Röder and N. Krause, *Org. Biomol. Chem.*, 2005, **3**, 387. c) D. J. Gorin and F. D. Toste, *Nature*, 2007, **446**, 395. d) A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem.,* 2006, **118**, 8064.
6. For recent examples of gold-catalyzed hydroamination, see: a) E. Mizushima, T. Hayashi and M. Tanaka, *Org. Lett.,* 2003, **5**, 3349. b) M. Alfonsi, A. Arcadi, M. Aschi, G. Bianchi and F. Marinelli, *J. Org. Chem.,* 2005, **70**, 2265. c) D. J. Davis and D. Toste, *J. Am. Chem. Soc.,* 2005, **127**, 11260. d) X.-Y. Liu, C.-H. Li and C.-M. Che, *Org. Lett.*, 2006, **8**, 2707. e) D. Kadzimirsz, D. Hildebrandt, K. Merz and G. Dyker, *Chem. Comm.,* 2006, 661. f) A. S. K. Hashmi, M. Rudolph, S. Schymura, J. Visus and W. Frey, *Eur, J. Org. Chem.*, 2006, 4905. g) J. Zhang, C.-G. Yang and C. He, *J. Am.*

Chem. Soc., 2006, **128**, 1798.

7. S. Ritter, Y. Horino and H.-G. Schmalz, *Synlett*, 2006, **19**, 3309.
8. a) T. Graening, W. Friedrichsen, J. Lex and H.-G. Schmalz, *Angew. Chem. Int. Ed.,* 2002, **41**, 1524. b) T. Graening and H.-G. Schmalz, *Angew. Chem. Int. Ed.*, 2004, **43**, 3230. c)T. Graening, V. Bette, J. Neudörfl, J. Lex and H.-G. Schmalz, *Org. Lett.,* 2005, **7**, 4317.
9. a) D. J. Chaplin, G. R. Pettit and S. A. Hill, *Anticancer Res.,* 1999, **19**, 189. b) M. C. Bibby, *Drugs Future,* 2002, **27**, 475. c) D. L. Sackett, *Pharmacol. Ther.*, 1993, **59**, 163. d) J. Chang, J. Reiner and J. Xie, *Chem. Rev,.* 2005, **105**, 4581.
10. W. Steglich and G. Höfle, *Angew. Chem. Int. Ed. Engl.,* 1969, **8**, 981.