Synthesis K. Sugimoto et al. Special Topic

# Synthesis of Substituted Pyrrolo[2,1-*a*]isoquinolines by Gold-Catalyzed Domino Cyclization of Alkynyl Iminoesters

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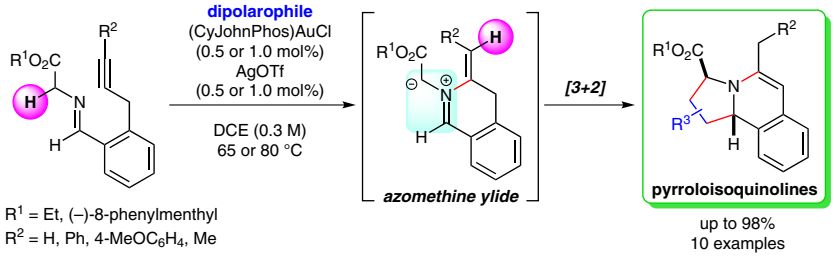


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**Abstract** A novel gold-catalyzed double cyclization leading to a biologically important pyrroloisoquinoline skeleton was established. The reaction sequence involving 6-*exo*-dig cyclization of alkynyl iminoester and [3+2] cycloaddition of azomethine ylide proceeded smoothly in the presence of 0.5–1.0 mol% (CyJohnPhos)AuCl/AgOTf at 65 or 80 °C. This strategy with (–)-phenylmenthol-derived iminoester enables a generation of chiral azomethine ylide in situ to construct an optically active pyrroloisoquinoline in a highly diastereoselective manner. An alkyne and alkenes with electron-withdrawing group could be utilized as dipolarophiles. Iminoesters having terminal and internal alkynes were applied as reaction substrates to afford the corresponding pyrroloisoquinolines.

**Key words** domino reaction, cycloaddition, gold, azomethine ylides, pyrroloisoquinolines

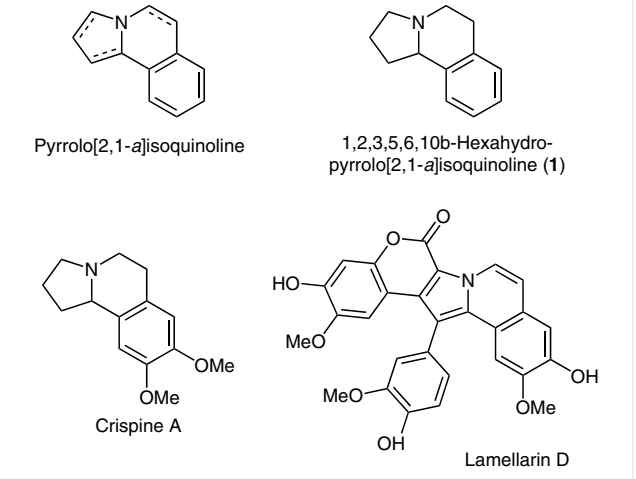


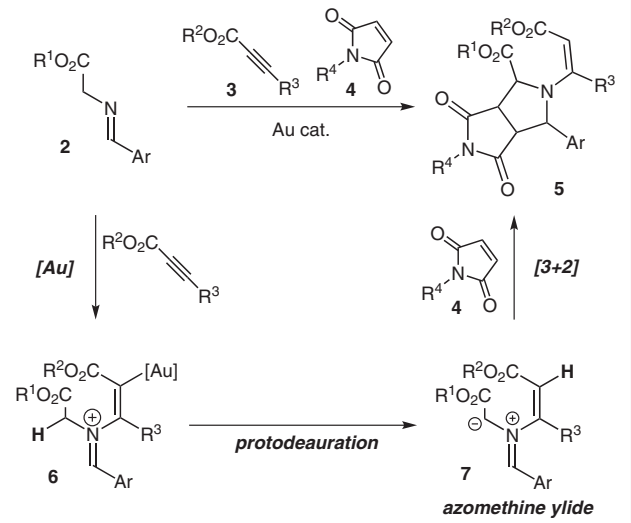

**Figure 1** Pyrrolo[2,1-*a*]isoquinolines

Pyrroloisoquinolines are broadly observed in natural products, which exhibit attractive biological activity as pharmacological leads (Figure 1).[1] For example, unsubstituted 1,2,3,5,6,10b-hexahydropyrrolo[2,1-*a*]isoquinoline (**1**) exhibits an antagonist activity against $\alpha_2$-adrenoreceptor and 5-phenyl congener is reported as a potent antidepressant.[2,3] Furthermore, dimethoxy-substituted analogue crispine A, which was prepared by organic synthesis[4] prior to its isolation from *Carduus crispus*,[5] has antitumor activity. Lamellarin family from marine tunicates also have pyrroloisoquinoline nucleus and shows interesting biological activity.[6] Among the diverse derivatives, lamellarin D possesses several interesting properties, such as cytotoxicity,[7a] inhibition of topoisomerase I,[7a] and targeting of mitochondria.[7b]

Because of the importance of such alkaloids, synthetic chemists have paid attention on the approaches for these pyrroloisoquinoline skeletons for a long time.[8] Though the methods are known since 1950s, various characteristic reactions have been developed until quite recent years.[9] For example, Bischler–Napieralski reaction of 1-(2-phenylethyl)-2-oxopyrrolidine was applied for the construction of pyrroloisoquinoline framework by Boekelheide and coworkers.[8a] Pearson revealed that intramolecular TfOH-mediated Schmidt reaction-reduction sequence of azidoindene gave a mixture of pyrroloisoquinoline and pyrroloquinoline in a ratio of 1:1.[8q] $BF_3$·$OEt_2$-mediated *N*-acyliminium ion cyclization was conducted with hydroxyl lactam derived from L-malic acid and L-tartaric acid to produce an enantiomeric pair of pyrroloisoquinolines.[8m] Recently, to make a distinction with such strong Brønsted or Lewis acid promoted reactions, much attention has focused on the method under milder reaction conditions such as π-acid promoted cyclization through an activation of triple bond. Silver reagent could be utilized for this purpose and was ap-

plied for a construction of the core of crispine A. The Ag-mediated hydroamination-oxidation reaction of propargyl tetrahydroisoquinoline afforded pyrroloisoquinolines under a neutral condition at room temperature.[8z] AgOTf/DTBMP system also catalyzed a reaction cascade including isoquinoline formation, dipolar cycloaddition, and oxidative aromatization to furnish pyrroloisoquinolines.[8aa]

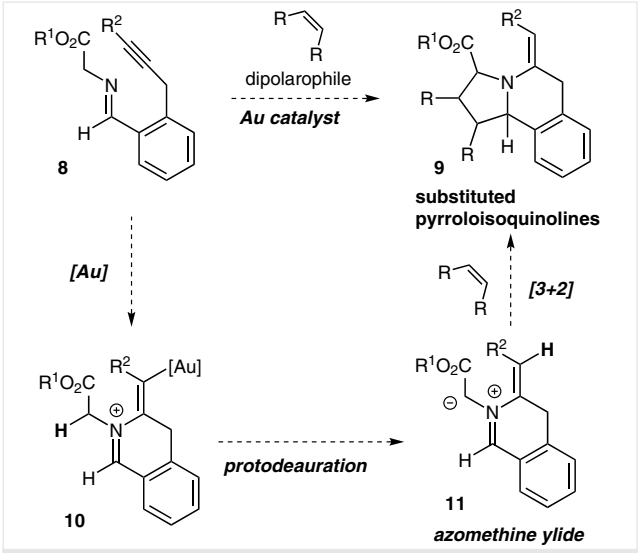
In this context, we focused on our recent work in regard to the gold-catalyzed intermolecular three-component domino reaction via azomethine ylide formation under mild conditions (Scheme 1).[10] The reaction was triggered by a selective activation of triple bond on **3** with gold catalyst. Nucleophilic attack of nitrogen on iminoester **2** onto the activated triple bond produced a vinyl gold complex **6**, from which a gold catalyst was regenerated by protodeauration with the acidic α-proton of the ester **6** and, at this time, reactive azomethine ylide **7** was produced in situ. Finally, a pyrrolidine ring was immediately formed by [3+2] cycloaddition reaction of the ylide **7** with maleimide **4**.




**Scheme 1** Our previous work

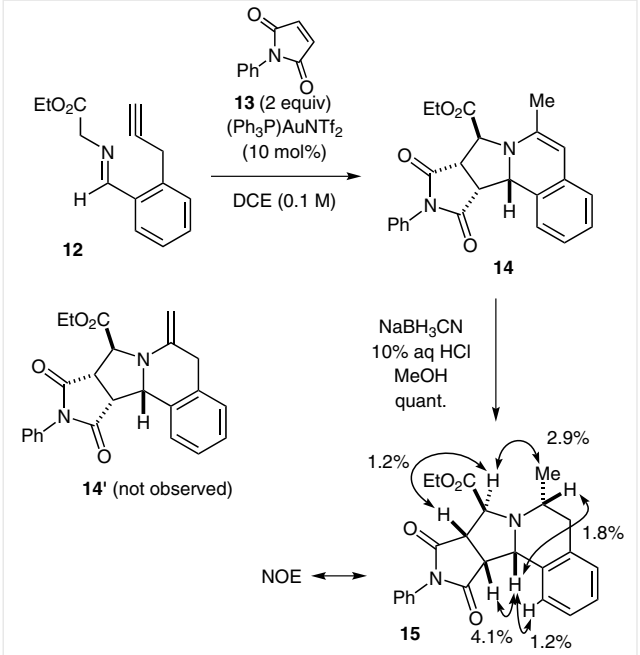
Based on this result, we planned a gold-catalyzed, double cyclization strategy for pyrroloisoquinoline synthesis as depicted in Scheme 2. (2-Propargyl)benzylidene iminoester **8** could be transformed into substituted pyrroloisoquinoline **9** via 6-*exo*-*dig* cyclization of **8**, protodeauration-mediated azomethine ylide formation, and [3+2] cycloaddition of **11**.

Using a known benzylidene iminoester **12** as a substrate, we started the examination of the working hypothesis with *N*-phenylmaleimide (**13**) (2 equiv) and 10 mol% $(Ph_3P)AuNTf_2$ (Gagosz catalyst[11]) in 0.1 M DCE solution (Scheme 3). Through the assumed transformation, pyrroloisoquinoline **14**, which would be caused by the conjugated isomerization of the *exo*-olefin of **14'**, was produced as a




**Scheme 2** Working hypothesis

sole product at room temperature within two hours in 55% yield. The reaction at 50 °C gave a slightly better result (50 min, 61% yield). After several trials at higher reaction temperature, we finally obtained the best result at 65 °C (30 min, 85%). The relative stereochemistries of the cycloadduct **14** were determined after reduction of the enamine moiety by $NaBH_3CN$. The NOE experiments on the resultant tetrahydroisoquinoline suggested the relative stereochemistries as shown in Scheme 3.




**Scheme 3** Trial on the domino cyclization

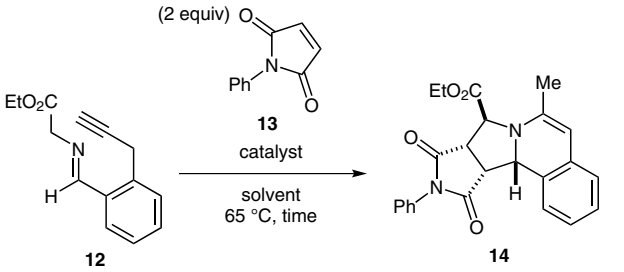
Further optimization of reaction conditions was continued as shown in Table 1. Catalyst loading could be reduced to 1 mol% and finally 0.5 mol% catalyst proved to be enough for the reaction in higher 0.3 M solution (Table 1, entries 1–5). In our cases, Buchwald ligands worked effectively (entries 6–8) and among them, the reaction with (CyJohnPhos)$AuNTf_2$ afforded the pyrroloisoquinoline **14** in 92% yield (entry 7). Counter anion effect was also surveyed (entries 9–11). In the presence of $Cl^-$ or $BF_4^-$, the yields were decreased to 70 and 75%, respectively. On the other hand, $OTf^-$ was quite effective to produce the desired **14** in almost quantitative yield (entry 11). It is noteworthy that the product is completely a single stereoisomer. The reaction could not proceed in the absence of gold catalyst (entry 12). Additionally, none of the other π-philic metals containing AgOTf could catalyze this reaction more effectively than gold(I) complex (entries 13–18). Although the reaction in THF proceeded in comparable yield with in DCE, other solvents were not efficient (entries 19–23).

With optimal conditions in hand, we envisaged an enantioselective synthesis of pyrroloisoquinolines starting with the iminoester **16** equipped with (–)-8-phenylmenthyl group as a chiral auxiliary (Scheme 4). The domino reaction with sterically demanding phenylmenthyl group uneventfully proceeded to give **17** as a sole stereoisomer. For the determination of the configuration of the product, the resultant dihydroisoquinoline was transformed into crystalline solid **18**·HCl by reduction with $NaBH_3CN$ in acidic methanol followed by exposure with HCl in $Et_2O$. The crystal structure of **18**·HCl was determined by the single crystal X-ray analysis.[12] Two crystallographically independent **18**·$H^+$ cations with the same absolute configuration were observed in a unit cell together with two chloride anions and 0.5 EtOAc. In Scheme 4, one of the two ions is disclosed as an ORTEP drawing, and absolute configuration of the salt was unambiguously confirmed as an *endo*-cycloadduct. Consequently, the relative stereochemistry of the pyrroloisoquinoline **14** in Table 1 was also confirmed as *endo*-adduct by the similarity of $^1H$ NMR spectrum for **17**.

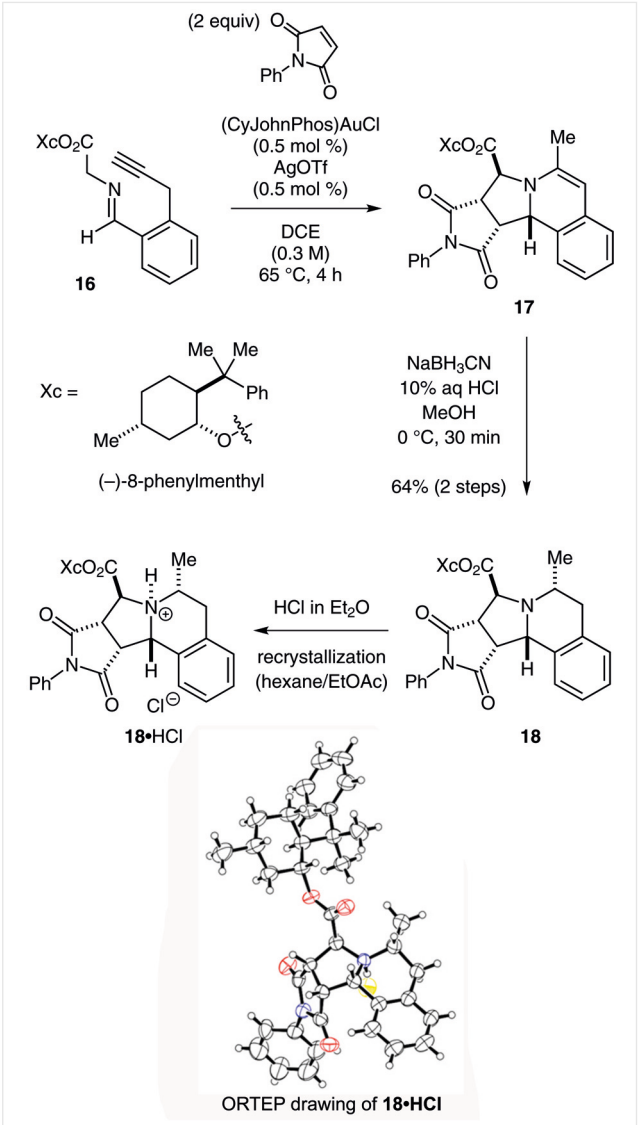
The observed diastereoselectivity could be rationalized as shown in Scheme 5. Chiral induction with 8-phenylmenthyl group in cycloaddition of azomethine ylide would rely on a stabilization of one conformer by π-stacking.[13] In our case, **TS A** would be stabilized more effectively than **TS B** by successful overlapping of isoquinoline ring containing ylide structure with phenyl group on chiral auxiliary. Since one of the diastereofaces of the ylide in **TS A** was blocked by the phenyl ring on the auxiliary, dipolarophile could approach from another side and *endo*-selective cycloaddition proceeded to give the observed isomer in a highly diastereoselective manner.

Next, the scope of the dipolarophile was investigated (Table 2). Whereas olefins having an electron-donating group, such as ethyl vinyl ether or cyclohexene, did not af-

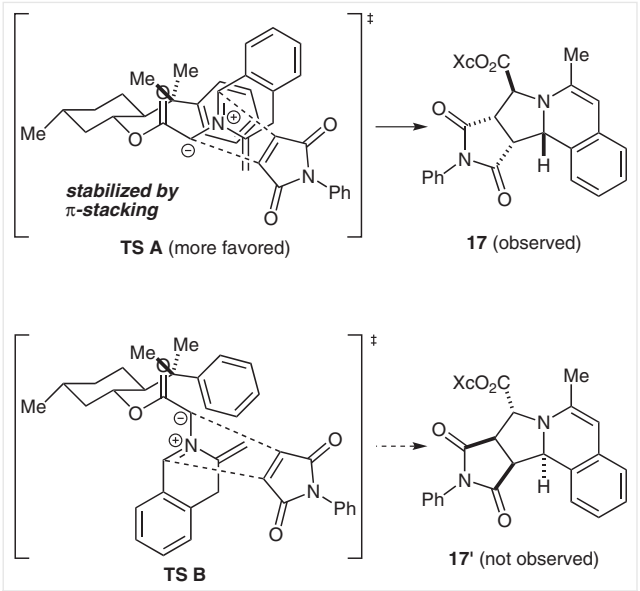
**Table 1** Optimization of Reaction Conditions




| Entry | Catalyst (mol%) | Solvent (M) | Time (h) | Yield (%) |
|---|---|---|---|---|
| 1 | $(Ph_3P)AuNTf_2$ (10) | DCE (0.1) | 30 min | 85 |
| 2 | $(Ph_3P)AuNTf_2$ (5) | DCE (0.1) | 30 min | 88 |
| 3 | $(Ph_3P)AuNTf_2$ (1) | DCE (0.1) | 2 | 86 |
| 4 | $(Ph_3P)AuNTf_2$ (0.5) | DCE (0.1) | 8 | 62 (68) |
| 5 | $(Ph_3P)AuNTf_2$ (0.5) | DCE (0.3) | 4 | 88 |
| 6 | (JohnPhos)$AuNTf_2$ (0.5) | DCE (0.3) | 5 | 82 |
| 7 | (CyJohnPhos)$AuNTf_2$ (0.5) | DCE (0.3) | 5 | 92 |
| 8 | (XPhos)$AuNTf_2$ (0.5) | DCE (0.3) | 4 | 87 |
| 9 | (CyJohnPhos)AuCl (0.5) | DCE (0.3) | 6 | 70 |
| 10 | (CyJohnPhos)AuCl (0.5) $AgBF_4$ (0.5) | DCE (0.3) | 4.5 | 75 |
| 11 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | DCE (0.3) | 4.5 | 98 |
| 12 | None | DCE (0.3) | 19 | – |
| 13 | AgOTf (0.5) | DCE (0.3) | 9 | <51 |
| 14 | $AuCl_3$ (0.5) | DCE (0.3) | 13 | 79 |
| 15 | CuOTf·0.5benzene (0.5) | DCE (0.3) | 10 | 71 |
| 16 | $Cu(OTf)_2$ (0.5) | DCE (0.3) | 6 | 80 |
| 17 | $Pd(OAc)_2$ (0.5) | DCE (0.3) | 4 | <79 |
| 18 | $PtCl_4$ (0.5) | DCE (0.3) | 8 | 41 |
| 19 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | MeCN (0.3) | 4.5 | 78 |
| 20 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | toluene (0.3) | 3.5 | 82 |
| 21 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | EtOAc (0.3) | 4 | 80 |
| 22 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | THF (0.3) | 5 | 88 |
| 23 | (CyJohnPhos)AuCl (0.5) AgOTf (0.5) | 1,4-dioxane (0.3) | 5.5 | 78 |




**Scheme 4** Stereoselective synthesis of pyrrolo[2,1-*a*]isoquinoline using chiral auxiliary




**Scheme 5** Rationale for the observed diastereoselectivity

The relative stereochemistry on **22** was determined by NOE experiments (Figure 2). Relative configuration of the methyl group indicated that the reduction occurred from the less hindered α-face, which was the opposite side of the bulky $SO_2Ph$ group.

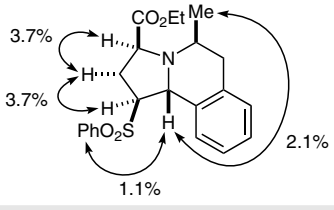


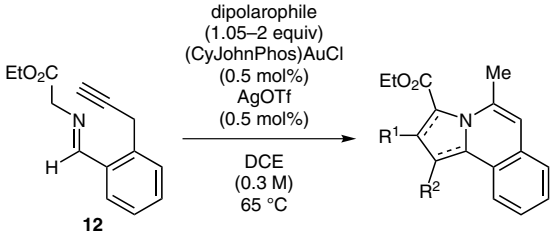

**Figure 2** Selected NOEs for tetrahydropyrroloisoquinoline **22**

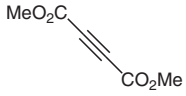
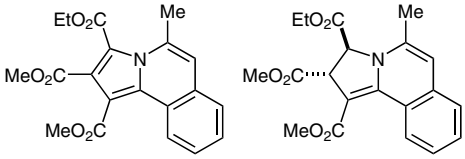
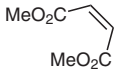
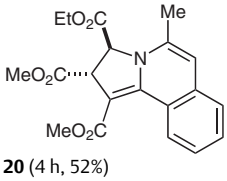
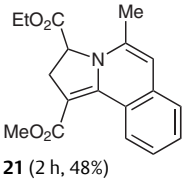
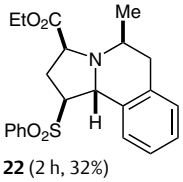
This domino reaction was applicable for internal alkynes (Table 3). Although higher catalyst loading (1.0 mol%) was required than that for terminal alkynes, phenyl- and *p*-methoxyphenyl-substituted alkynes afforded the corresponding isoquinolines in moderate yields (Table 3, entries 1 and 2). An alkyl substituent could also be introduced on the pyrroloisoquinolines by the domino reaction (entry 3).

In summary, we have accomplished a novel, double cyclization method for biologically important pyrroloisoquinoline skeleton based on the Au-catalyzed azomethine ylide formation strategy.[10] This one-pot cyclization system could furnish highly substituted pyrroloisoquinolines and can be applied for the preparation of optically active derivatives under auxiliary-controlled diastereoselective process. Merged with the findings obtained in our three-component

ford desired cycloadduct, an alkyne and alkenes equipped with electron-withdrawing group could work as dipolarophile to afford corresponding pyrroloisoquinoline skeletons. However, since the oxidation of the reaction product was observed in reaction media (or reaction analyses on TLC), purification process on silica gel column, and storage in opened flask, our cycloadducts were found to be prone to the air oxidation (Table 2, entries 1–3). The cycloadduct with phenyl vinyl sulfone was seriously unstable to isolate. However, after reduction with $NaBH_3CN$, the resultant tetrahydroisoquinoline **22** could be partially isolated (entry 4).[14]

**Table 2** Scope of Dipolarophile




| Entry | Dipolarophile (equiv) | Product (time, yield) |
|---|---|---|
| 1 |  (1.05) |  (6 h, **19**: 24%; **20**: 36%) |
| 2 |  (2.0) |  **20** (4 h, 52%) |
| 3 |  (1.1) |  **21** (2 h, 48%) |
| 4[a] |  (1.1) |  **22** (2 h, 32%) |

[a]Pyrroloisoquinoline was isolated after further reduction with $NaBH_3CN$. The yield shown is for two steps.

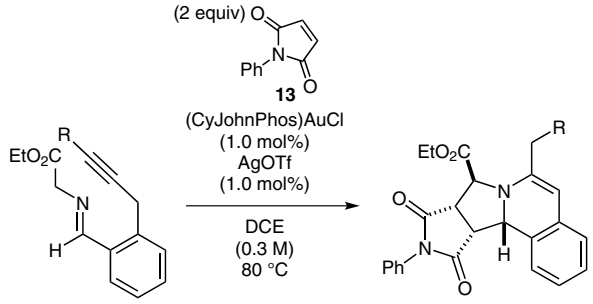
pyrrolizine formation reaction,[10] this novel strategy for pyrroloisoquinolines is now employed for synthetic studies on biologically active polycyclic alkaloids in our laboratory.

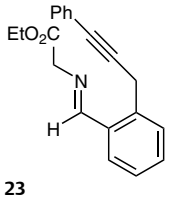
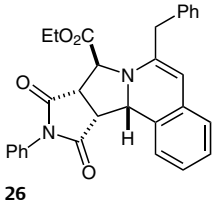
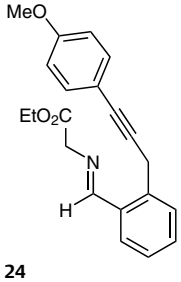
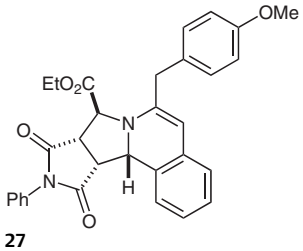
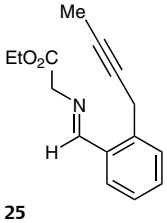
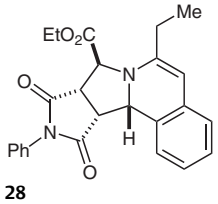
All nonaqueous reactions were carried out under an argon atmosphere. Reagents were purchased from commercial suppliers and used as received. Anhyd solvents were prepared by distillation over $CaH_2$, or purchased from commercial suppliers. $^1H$ and $^{13}C$ NMR spectra were measured on a JEOL ECX 400 or a Varian GEMINI 300 instrument, using TMS (0.00 ppm for $^1H$), $CDCl_3$(77.0 ppm for $^{13}C$), benzene (7.15 ppm for $^1H$), benzene-$d_6$ (128.0 ppm for $^{13}C$) as an internal reference. Mass spectra were measured on a JEOL JMS-GCmate II or a JEOL AX 505 mass spectrometer, and the ionization method was electron impact (EI, 70 eV). IR spectra were recorded on a JASCO FT/IR-460Plus spectrometer. Column chromatography was carried out by employing Cica Silica Gel 60N (spherical, neutral, 40–50 µm or 63–210 µm). Preparative TLC was performed on precoated silica gel 60 $F_{254}$ plates (Merck).

### Iminoesters; General Procedure

A suspension of ethyl glycinate hydrochloride (2.2 equiv) in $CH_2Cl_2$ (0.3 M) was washed with $NH_4OH$. To the separated $CH_2Cl_2$ phase was added $MgSO_4$ (1 g/mmol) and the corresponding aldehyde. The reaction mixture was stirred for several days at r.t. until completion of the reaction (monitored by $^1H$ NMR spectroscopy). After completion of the reaction, the solution was washed with sat. aq $NH_4Cl$. The aqueous phase was extracted with $CH_2Cl_2$ and the combined organic phases were dried ($MgSO_4$), filtered, and concentrated in vacuo. The

**Table 3** Reactions with Internal Alkynes




| Entry | Substrate | Product | Time (h) | Yield (%) |
|---|---|---|---|---|
| 1 |  **23** |  **26** | 3.5 | 69 |
| 2 |  **24** |  **27** | 3 | 48 |
| 3 |  **25** |  **28** | 4 | 58 |

resultant crude iminoester, the purity of which was checked by $^1$H NMR spectroscopy, was conducted to the gold-catalyzed reaction without further purification because of their instability.

### Ethyl 2-[2-(Prop-2-ynyl)benzylideneamino]acetate (12)

According to the general procedure for the preparation of iminoester, treatment of 2-(prop-2′-ynyl)benzaldehyde[15] (353 mg, 2.45 mmol) with ethyl glycinate hydrochloride (752 mg, 5.39 mmol) for 9 days gave the crude iminoester **12** (561 mg, quant) as a yellow oil.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.59 (s, 1 H), 7.83 (dd, *J* = 7.6, 1.4 Hz, 1 H), 7.56 (d, *J* = 7.3 Hz, 1 H), 7.42 (ddd, *J* = 7.6, 7.6, 1.4 Hz, 1 H), 7.33 (dd, *J* = 7.3, 7.3 Hz, 1 H), 4.42 (d, *J* = 1.4 Hz, 2 H), 4.24 (q, *J* = 7.3 Hz, 2 H), 3.92 (d, *J* = 2.8 Hz, 2 H), 2.22 (t, *J* = 2.8 Hz, 1 H), 1.31 (t, *J* = 7. 3 Hz, 3 H).

### Gold-Catalyzed Reaction Leading to Pyrroloisoquinolines; Pyrroloisoquinoline 14; Typical Procedure (Table 1, entry 11)

To a stirred solution of the iminoester **12** (37.4 mg, 0.163 mmol) and *N*-phenylmaleimide (56.5 mg, 0.326 mmol) in DCE (0.4 mL) was added the gold catalyst solution in DCE [0.0058 M, 0.14 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)]. After stirring the mixture for 5 h at 65 °C, the reaction was quenched with $H_2O$. The aqueous phase was extracted with $CH_2Cl_2$, and the combined organic phases were washed with brine, dried ($Na_2SO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: gradient, *n*-hexane/EtOAc = 70:30 to 65:35) to give the pyrroloisoquinoline **14** (64.4 mg, 98%) as a yellow solid; mp 107–114 °C; $R_f$ = 0.48 (*n*-hexane/EtOAc, 60:40).

IR ($CHCl_3$): 3019, 1714, 1499, 1383, 1215, 909, 764, 669 cm$^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 4 H), 7.24 (d, *J* = 7.3 Hz, 1 H), 7.17 (dt, *J* = 7.3, 1.4 Hz, 1 H), 7.10 (dt, *J* = 7.3, 1.4 Hz, 1 H), 7.05–7.02 (m, 2 H), 6.90 (dd, *J* = 7.8, 0.9 Hz, 1 H), 5.26 (s, 1 H), 5.22 (d, *J* = 7.8 Hz, 1 H), 5.17 (s, 1 H), 4.36–4.22 (m, 2 H), 3.96 (d, *J* = 7.8 Hz, 1 H), 3.62 (dd, *J* = 7.8, 7.8 Hz, 1 H), 1.94 (s, 3 H), 1.35 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 176.3, 173.5, 169.6, 139.6, 132.26, 132.25, 131.8, 128.6, 128.5, 127.1, 125.9, 125.1, 124.9, 123.9, 100.6, 64.9, 63.9, 62.3, 50.9, 47.0, 19.3, 14.1.

MS (EI) *m*/*z* = 402 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{22}N_2O_4$: 402.1580; found: 402.1612.

### Pyrroloisoquinoline 15

To a solution of **14** (65.7 mg, 0.16 mmol) in MeOH (1.9 mL) were added $NaBH_3CN$ (21.0 mg, 0.33 mmol) and 10% aq HCl (0.5 mL) at 0 °C. After stirring for 75 min at 0 °C, the reaction was quenched with sat. aq $NaHCO_3$ and the aqueous phase was extracted with $CH_2Cl_2$. The combined organic phases were washed with brine, dried over $Na_2SO_4$, filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/AcOEt, 70:30) to afford **15** quantitatively (65.2 mg) as a pale yellow oil.

$R_f$ = 0.56 (*n*-hexane/EtOAc, 60:40).

IR ($CHCl_3$): 3027, 3012, 2970, 1779, 1714, 1499, 1384, 1231, 1199, 1023, 851, 804, 765, 691 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.43 (d, *J* = 7.8 Hz, 1 H), 7.39–7.29 (m, 3 H), 7.10 (d, *J* = 8.2 Hz, 2 H), 7.05 (d, *J* = 7.3 Hz, 1 H), 4.71 (d, *J* = 7.3 Hz, 1 H), 4.54 (s, 1 H), 4.30–4.21 (m, 2 H), 3.84 (dd, *J* = 7.3, 7.3 Hz, 1 H), 3.77 (d, *J* = 7.3 Hz, 1 H), 3.27 (m, 1 H), 2.72 (dd, *J* = 16.0, 3.2 Hz, 1 H), 2.61 (dd, *J* = 16.0, 10.8 Hz, 1 H), 1.33 (t, *J* = 7.1 Hz, 3 H), 1.31 (d, *J* = 6.0 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 176.9, 174.4, 170.4, 134.6, 131.8, 129.0, 128.5, 128.3, 128.0, 126.8, 126.3, 125.2, 63.1, 62.8, 61.2, 49.5, 47.7, 46.4, 39.2, 20.2, 14.4.

MS (EI): *m*/*z* = 398 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{24}O_4N_2$: 404.1736; found: 404.1744.

### (1*R*,2*S*,5*R*)-5-Methyl-2-(2-phenylpropan-2-yl)cyclohexyl 2-[(*E*)-2-(Prop-2-ynyl)benzylideneamino]acetate (16)

According to the general procedure for the preparation of iminoester, treatment of 2-(prop-2′-ynyl)benzaldehyde[15] (80.0 mg, 0.55 mmol) with (–)-8-phenylmenthan-3-yl glycinate[16] (239 mg, 0.83 mmol) for a day gave the crude iminoester **16** (238 mg, quant) as an orange oil.

$^1$H NMR (400 MHz, $C_6D_6$): δ = 8.09 (s, 1 H), 7.79 (dd, *J* = 7.6, 1.6 Hz, 1 H), 7.50 (d, *J* = 7.8 Hz, 1 H), 7.25–7.19 (m, 6 H), 7.08–6.98 (m, 4 H), 5.04 (dt, *J* = 10.7, 4.4 Hz, 1 H), 3.81 (d, *J* = 2.3 Hz, 2 H), 3.79 (t, *J* = 1.4 Hz, 2 H), 1.94–1.92 (m, 4 H), 1.51 (dt, *J* = 13.6, 1.5 Hz, 2 H), 1.34 (s, 3 H), 1.13 (s, 3 H), 0.95–0.83 (m, 4 H).

### Pyrroloisoquinoline 17

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **16** (51.3 mg, 0.123 mmol) with *N*-phenylmaleimide (42.6 mg, 0.246 mmol, 2 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.11 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] for 4 h gave the pyrroloisoquinoline **17** (26.2 mg, <60%) as a mixture with a slight amount of unidentified byproduct as an orange oil; $R_f$ = 0.31 (*n*-hexane/EtOAc, 80:20); $[\alpha]_D^{23}$ –123 (*c* 1.31, $CHCl_3$).

IR ($CHCl_3$): 3058, 2958, 2925, 1776, 1634, 1599, 1500, 1384, 1267, 1222, 1198, 1179, 828, 733, 701 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.40–7.25 (m, 7 H), 7.20–7.06 (m, 4 H), 7.00 (d, *J* = 7.3 Hz, 2 H), 6.86 (d, *J* = 7.3 Hz, 1 H), 5.21 (s, 1 H), 5.17 (d, *J* = 6.9 Hz, 1 H), 4.88 (dt, *J* = 10.8, 4.4 Hz, 1 H), 4.67 (s, 1 H), 3.64–3.43 (m, 2 H), 2.09 (t, *J* = 10.1 Hz, 1 H), 1.85 (s, 3 H), 1.77–1.64 (m, 1 H), 1.34 (s, 3 H), 1.24 (s, 3 H), 1.23–1.03 (m, 3 H), 0.91–0.87 (m, 6 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 175.9, 173.5, 168.4, 150.6, 139.8, 132.3, 131.9, 129.1, 128.5, 128.1, 127.9, 127.1, 125.9, 125.5, 125.4, 125.3, 125.2, 125.0, 123.8, 100.6, 64.8, 63.9, 51.0, 50.2, 47.2, 41.8, 39.8, 34.4, 31.4, 27.6, 26.7, 26.1, 21.8, 19.7.

MS (EI): *m*/*z* = 588 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{38}H_{40}N_2O_4$: 588.2988; found: 588.2993.

### Pyrroloisoquinoline 18

To a solution of crude **17** (from 58.1 mg of **16**, 0.078 mmol) in MeOH (0.9 mL) were added $NaBH_3CN$ (19.6 mg, 0.31 mmol) and 10% aq HCl (0.5 mL) at 0 °C. After stirring for 75 min at 0 °C, the reaction was quenched with sat. aq $NaHCO_3$ and the aqueous phase was extracted with $CH_2Cl_2$. The combined organic phases were washed with brine, dried ($Na_2SO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc, 85:15) to give **18** (37.6 mg, 64% for 2 steps) as a white amorphous solid; $R_f$ = 0.28 (*n*-hexane/EtOAc, 85:15); $[\alpha]_D^{23}$ –113 (*c* 1.12, $CHCl_3$).

IR ($CH_2Cl_2$): 3054, 2966, 2926, 2304, 1780, 1716, 1498, 1386, 1266, 1201, 737, 703 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.33 (m, 7 H), 7.31–7.27 (m, 1 H), 7.19–7.11 (m, 3 H), 7.06–7.02 (m, 3 H), 4.95 (dt, *J* = 10.7, 4.3 Hz, 1 H), 4.55 (d, *J* = 7.8 Hz, 1 H), 4.09 (s, 1 H), 3.53 (t, *J* = 7.8 Hz, 1 H), 3.32–3.27 (m, 1 H), 2.80 (d, *J* = 7.8 Hz, 1 H), 2.68 (dd, *J* = 15.6, 2.7 Hz, 1 H), 2.55 (dd, *J* = 15.6, 10.5 Hz, 1 H), 2.17 (dt, *J* =11.3, 3.2 Hz, 1 H), 1.87 (d, *J* = 11.9 Hz, 1 H), 1.75 (dd, *J* = 13.6, 3.5 Hz, 1 H), 1.67 (d, *J* = 12.8 Hz, 1 H), 1.37 (s, 3 H), 1.27 (d, *J* = 6.0 Hz, 3 H), 1.23 (s, 3 H), 1.19–0.99 (m, 3 H), 0.96–0.85 (m, 1 H), 0.88 (d, *J* = 6.4 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 176.4, 174.3, 169.2, 151.5, 134.9, 131.9, 131.8, 128.9, 128.33, 128.31, 128.1, 126.7, 125.5, 125.2, 125.0, 62.9, 62.7, 49.8, 49.2, 47.2, 46.6, 42.3, 39.7, 39.1, 34.4, 31.4, 28.5, 26.6.

MS (EI): *m*/*z* = 590 ($M^+$).

### Pyrroloisoquinoline 19 and 20 (Table 2, entry 1)

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **12** (25.4 mg, 0.111 mmol) with dimethyl acetylenedicarboxylate (17 mg, 0.117 mmol, 1.05 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.096 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] for 6 h gave the pyrroloisoquinoline **19** (9.9 mg, 24%) and the pyrroloisoquinoline **20** (14.7 mg, 36%) as yellow solids.

### Pyrroloisoquinoline 19

Mp 79–86 °C; $R_f$ = 0.53 (*n*-hexane/EtOAc, 60:40).

IR ($CHCl_3$): 3027, 2952, 1722, 1468, 1455, 1252, 1228, 1197, 1162, 1126, 773 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 8.40–8.38 (m, 1 H), 7.58–7.55 (m, 1 H), 7.52–7.47 (m, 2 H), 6.84 (s, 1 H), 4.45 (q, *J* = 7.2 Hz, 2 H), 4.01 (s, 3 H), 3.90 (s, 3 H), 2.61 (s, 3 H), 1.43 (t, *J* = 7.2 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 167.0, 164.1, 163.0, 132.7, 130.6, 128.6, 128.1, 127.6, 126.3, 124.0, 123.6, 121.0, 120.1, 115.8, 109.3, 62.5, 52.7, 52.3, 20.2, 13.9.

MS (EI): *m*/*z* = 369 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{19}NO_6$: 369.1212; found: 369.1206.

**Pyrroloisoquinoline 20**

Mp 50–56 °C; $R_f$ = 0.38 (*n*-hexane/EtOAc, 60:40).

IR ($CHCl_3$): 3031, 3007, 2952, 1742, 1671, 1521, 1226, 1200, 1098, 794, 732 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.76 (d, *J* = 8.0 Hz, 1 H), 7.48 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.34 (dd, *J* = 8.0, 8.0 Hz, 1 H), 7.26 (d, *J* = 8.0 Hz, 1 H), 6.13 (s, 1 H), 5.03 (d, *J* = 2.3 Hz, 1 H), 4.30–4.23 (m, 2 H), 4.21 (d, *J* = 2.3 Hz, 1 H), 3.75 (s, 3 H), 3.71 (s, 3 H), 2.17 (s, 3 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 173.2, 169.6, 153.6, 137.3, 136.7, 132.0, 131.1, 125.5, 125.1, 122.5, 107.6, 90.3, 63.8, 62.5, 52.7, 50.7, 50.6, 19.0, 14.1.

MS (EI): *m*/*z* = 371 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{21}NO_6$: 371.1369; found: 371.1375.

**Pyrroloisoquinoline 20 (Table 2, entry 2)**

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **12** (29.4 mg, 0.128 mmol) with dimethyl maleate (36.9 mg, 0.256 mmol, 2 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.11 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] for 4 h gave the pyrroloisoquinoline **20** (24.6 mg, 52%).

**Pyrroloisoquinoline 21 (Table 2, entry 3)**

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **12** (35.1 mg, 0.153 mmol) with methyl acrylate (15 mg, 0.168 mmol, 1.1 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.013 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] for 2 h gave the pyrroloisoquinoline **21** (23.0 mg, 48%) as an orange oil; $R_f$ = 0.54 (*n*-hexane/EtOAc, 70:30).

IR ($CHCl_3$): 3010, 2948, 1741, 1663, 1639, 1528, 1337, 1273, 1200, 1099, 1023 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 9.72 (d, *J* = 8.0 Hz, 1 H), 7.45–7.41 (m, 1 H), 7.31–7.26 (m, 1 H), 7.20 (d, *J* = 8.0 Hz, 1 H), 6.00 (s, 1 H), 4.85 (dd, *J* = 12.8, 3.7 Hz, 1 H), 4.28–4.18 (m, 2 H), 3.71 (s, 3 H), 3.43 (dd, *J* = 15.6, 12.8 Hz, 1 H), 3.14 (dd, *J* = 15.6, 3.7 Hz, 1 H), 2.12 (s, 3 H), 1.28 (t, *J* = 7.1 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 171.4, 152.8, 137.8, 136.6, 131.6, 130.8, 128.3, 125.2, 124.8, 123.0, 106.4, 91.1, 61.9, 60.5, 50.6, 34.4, 19.0, 14.1.

MS (EI): *m*/*z* = 313 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{18}H_{19}NO_4$: 313.1314; found: 313.1309.

**Tetrahydropyrroloisoquinoline 22 (Table 2, entry 4)**

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **12** (33.6 mg, 0.147 mmol) with phenyl vinyl sulfone (27.2 mg, 0.162 mmol, 1.1 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.13 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] for 2.5 h at 65 °C gave the crude intermediate pyrroloisoquinoline as an orange oil. Then to a solution of the crude mixture in MeOH (1.7 mL) was added $NaBH_3CN$ (37 mg, 0.59 mmol) and 10% aq HCl (0.9 mL) at 0 °C. After stirring for 60 min at 0 °C, the reaction was quenched with sat. aq $NaHCO_3$ and the aqueous phase was extracted with $CH_2Cl_2$. The combined organic phases were washed with brine, dried ($Na_2SO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (eluent: gradient, *n*-hexane/EtOAc = 80:20 to 60:40) to afford the pyrroloisoquinoline **22** (19.0 mg, 32% over 2 steps) as a yellow oil; $R_f$ = 0.30 (*n*-hexane/EtOAc, 70:30).

IR ($CHCl_3$): 3032, 3004, 1743, 1448, 1382, 1306, 1225, 1203, 1148, 1087, 790, 732 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.99 (d, *J* = 6.8 Hz, 2 H), 7.67 (t, *J* = 6.8 Hz, 1 H), 7.58 (dd, *J* = 6.8, 6.8 Hz, 2 H), 7.36 (d, *J* = 7.6 Hz, 1 H), 7.22 (dd, *J* = 7.6 Hz, 1 H), 7.15 (dd, *J* = 7.6 Hz, 1 H), 7.02 (d, *J* = 7.6 Hz, 1 H), 5.04 (s, 1 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 3.78 (ddd, *J* = 9.2, 8.1, 3.3 Hz, 1 H), 3.53 (dd, *J* = 9.6, 6.6 Hz, 1 H), 3.35 (quint, *J* = 6.4 Hz, 1 H), 3.11 (dd, *J* = 16.8, 5.6 Hz, 1 H), 2.48 (ddd, *J* = 13.0, 9.7, 8.0 Hz, 1 H), 2.29 (d, *J* = 16.8 Hz, 1 H), 2.19 (ddd, *J* = 13.0, 9.1, 6.7 Hz, 1 H), 1.25 (t, *J* = 7.1 Hz, 3 H), 1.10 (d, *J* = 6.9 Hz, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 171.3, 137.6, 135.3, 133.9, 132.5, 129.7, 129.2, 129.1, 127.0, 126.9, 126.7, 69.6, 61.1, 56.5, 47.2, 30.9, 26.8, 19.0, 14.2.

MS (FAB): *m*/*z* = 400 (M + $H^+$).

HRMS (FAB): *m*/*z* calcd for $C_{22}H_{26}NO_4S$: 400.1583; found: 400.1585.

**Ethyl 2-[2-(3-Phenylprop-2-ynyl)benzylideneamino]acetate (23)**

According to the general procedure for the preparation of iminoester, treatment of 2-(3-phenylprop-2-ynyl)benzaldehyde[15] (71.0 mg, 0.32 mmol) with ethyl glycinate hydrochloride (98.1 mg, 0.71 mmol) for 3 days gave the crude iminoester **23** (97.0 mg, 99%) as a yellow oil.

$^1$H NMR (400 MHz, $C_6D_6$): δ = 8.19 (s, 1 H), 7.83 (d, *J* = 7.3 Hz, 1 H), 7.57 (d, *J* = 7.8 Hz, 1 H), 7.44–7.42 (m, 2 H), 7.10–6.96 (m, 5 H), 4.12 (s, 2 H), 4.02 (s, 2 H), 3.95 (q, *J* = 7.0 Hz, 2 H), 0.93 (t, *J* = 7.0 Hz, 3 H).

**2-{2-[3-(4-Methoxyphenyl)prop-2-ynyl]phenyl}-1,3-dioxolane**

To a solution of 2-[2-(prop-2-ynyl)phenyl]-1,3-dioxolane[15] (173 mg, 0.92 mmol) in anhyd DMF (1.3 mL) were added $Et_3N$ (0.51 mL, 3.68 mmol), *p*-iodoanisole (258 mg, 1.10 mmol), $PdCl_2(PPh_3)_2$ (19 mg, 28 μmol), CuI (11 mg, 55 μmol) at r.t. After stirring for 2 min at 50 °C, the reaction was quenched with sat. aq $NH_4Cl$ and the aqueous phase was extracted with $Et_2O$. The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography (*n*-hexane/EtOAc = 90:10) to afford the title arylacetylene (181 mg, 67%) as a yellow oil; $R_f$ = 0.30 (*n*-hexane/EtOAc, 90:10).

IR ($CHCl_3$): 3039, 3006, 2889, 2838, 2050, 1606, 1509, 1247, 1173, 1109, 1074, 1032, 833, 802, 759 $cm^{-1}$.

$^1$H NMR (400 MHz, $CDCl_3$): δ = 7.64 (d, *J* = 7.8 Hz, 1 H), 7.56 (d, *J* = 7.3 Hz, 1 H), 7.39–7.34 (m, 3 H), 7.29–7.23 (m, 1 H), 6.81 (d, *J* = 7.8 Hz, 2 H), 6.05 (s, 1 H), 4.14–4.00 (m, 4 H), 3.98 (s, 2 H), 3.77 (s, 3 H).

$^{13}$C NMR (100 MHz, $CDCl_3$): δ = 159.1, 135.5, 134.7, 132.9, 129.3, 129.0, 126.6, 126.2, 115.8, 113.8, 101.9, 85.5, 82.8, 65.1, 55.7, 55.2, 22.6.

MS (EI): *m*/*z* = 294 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{19}H_{18}O_3$: 294.1256; found: 294.1273.

**2-[3-(4-Methoxyphenyl)prop-2-ynyl]benzaldehyde**

To a stirred solution of the above dioxolane (179 mg, 0.61 mmol) in a mixture of acetone and $H_2O$ (6.1 mL, 1:1 v/v) was added 10 mol% of *p*-TsOH·$H_2O$ (11.5 mg, 0.061 mmol) at r.t. After stirring for 20 h, the mixture was quenched with sat. aq $NaHCO_3$ and extracted with $Et_2O$. The combined organic phases were washed with brine, dried ($MgSO_4$), filtered, and concentrated in vacuo. The residue was purified by flash column chromatography on silica gel (eluent: *n*-hexane/EtOAc = 90:10) to afford the title aldehyde (109 mg, 72%) as a pale yellow oil; $R_f$ = 0.47 (*n*-hexane/EtOAc, 90:10).

IR ($CHCl_3$): 3072, 3007, 2838, 2743, 2290, 2047, 1695, 1606, 1509, 1290, 1247, 834, 738 $cm^{-1}$.

$^1H$ NMR (300 MHz, $CDCl_3$): δ = 10.28 (s, 1 H), 7.83 (d, *J* = 7.4 Hz, 1 H), 7.79 (d, *J* = 7.7 Hz, 1 H), 7.69–7.58 (m, 1 H), 7.46–7.41 (m, 1 H), 7.38 (d, *J* = 8.5 Hz, 2 H), 6.83 (d, *J* = 8.5 Hz, 2 H), 4.28 (s, 2 H), 3.80 (s, 3 H).

$^{13}C$ NMR (75 MHz, $CDCl_3$): δ = 192.5, 159.1, 138.9, 133.9, 133.2, 133.1, 132.9, 129.8, 127.1, 115.4, 113.8, 85.1, 83.7, 55.6, 23.1.

MS (EI): *m*/*z* = 250 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{17}H_{14}O_2$: 250.0994; found: 250.0965.

**Ethyl 2-{2-[3-(4-Methoxyphenyl)prop-2-ynyl]benzylideneamino}-acetate (24)**

According to the general procedure for the preparation of iminoester, treatment of the above aldehyde (107 mg, 0.43 mmol) with ethyl glycinate hydrochloride (131 mg, 0.94 mmol) for 7 days gave the crude iminoester **24** (144 mg, quant) as a yellow oil.

$^1H$ NMR (300 MHz, $C_6D_6$): δ = 8.24 (s, 1 H), 7.87 (d, *J* = 7.7 Hz, 1 H), 7.59 (d, *J* = 7.7 Hz, 1 H), 7.39 (d, *J* = 8.8 Hz, 2 H), 7.18–7.01 (m, 2 H), 6.58 (d, *J* = 8.8 Hz, 2 H), 4.13 (s, 2 H), 4.04 (s, 2 H), 3.95 (q, *J* = 7.1 Hz, 2 H), 3.16 (s, 3 H), 0.93 (t, *J* = 7.1 Hz, 3 H).

**Ethyl 2-[2-(But-2-ynyl)benzylideneamino]acetate (25)**

According to the general procedure for the preparation of iminoester, treatment of 2-(but-2-ynyl)benzaldehyde[15] (78.0 mg, 0.49 mmol) with ethyl glycinate hydrochloride (151 mg, 1.08 mmol) for 5 days gave the crude iminoester **25** (95.0 mg, 79%) as a yellow oil.

$^1H$ NMR (300 MHz, $C_6D_6$): δ = 8.23 (s, 1 H), 7.93 (d, *J* = 7.7 Hz, 1 H), 7.51 (d, *J* = 7.4 Hz, 1 H), 7.10–7.04 (m, 1 H), 7.04–6.99 (m, 1 H), 4.12 (s, 2 H), 3.95 (q, *J* = 7.1 Hz, 2 H), 3.76 (d, *J* = 2.5 Hz, 2 H), 1.52 (t, *J* = 2.5 Hz, 3 H), 0.93 (t, *J* = 7.1 Hz, 3 H).

**Pyrroloisoquinoline 26 (Table 3, entry 1)**

According to the general procedure for the gold-catalyzed reaction, treatment of iminoester **23** (32.4 mg, 0.106 mmol) with *N*-phenylmaleimide (36.7 mg, 0.212 mmol, 2 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.18 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] at 80 °C for 3.5 h gave the pyrroloisoquinoline **26** (34.8 mg, 69%) as a yellow solid; mp 99–104 °C; $R_f$ = 0.23 (*n*-hexane/EtOAc, 70:30).

IR ($CHCl_3$): 3028, 3012, 2359, 1714, 1632, 1601, 1498, 1384, 1227, 1198, 1176, 1029, 753 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.43–7.33 (m, 4 H), 7.29–7.11 (m, 8 H), 7.05 (d, *J* = 7.3 Hz, 1 H), 6.93, (d, *J* = 6.9 Hz, 1 H), 5.27–5.25 (m, 2 H), 5.13 (s, 1 H), 4.15–4.04 (m, 2 H), 3.90 (d, *J* = 7.8 Hz, 1 H), 3.63 (t, *J* = 7.8 Hz, 1 H), 3.55 (s, 2 H), 1.16 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 176.1, 173.5, 169.5, 142.0, 136.1, 131.8, 129.1, 128.9, 128.56, 128.55, 128.5, 127.2, 126.7, 125.9, 125.4, 125.1, 124.3, 101.8, 64.1, 62.1, 50.6, 46.9, 39.1, 14.0.

MS (EI): *m*/*z* = 478 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{30}H_{26}O_4N_2$: 478.1893; found: 478.1888.

**Pyrroloisoquinoline 27 (Table 3, entry 2)**

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **24** (51.0 mg, 0.144 mmol) with *N*-phenylmaleimide (50 mg, 0.288 mmol, 2 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.25 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] at 80 °C for 3 h gave the pyrroloisoquinoline **27** (35.3 mg, 48%) as a yellow solid; mp 112–118 °C; $R_f$ = 0.40 (*n*-hexane/EtOAc, 70:30).

IR ($CH_2Cl_2$): 3063, 2981, 2936, 2837, 2360, 1715, 1512, 1383, 1248, 1033, 761, 731 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.42–7.32 (m, 3 H), 7.26–7.23 (m, 1 H), 7.18 (dd, *J* = 7.6, 7.6 Hz, 1 H), 7.16–7.06 (m, 3 H), 7.05 (d, *J* = 7.3 Hz, 2 H), 6.92 (d, *J* = 8.2 Hz, 1 H), 6.77 (d, *J* = 8.7 Hz, 2 H), 5.25 (d, *J* = 7.8 Hz, 1 H), 5.23 (s, 1 H), 5.14 (s, 1 H), 4.18–4.07 (m, 2 H), 3.90 (d, *J* = 7.8 Hz, 1 H), 3.75 (s, 3 H), 3.63 (dd, *J* = 7.8, 7.8 Hz, 1 H), 3.48 (s, 2 H), 1.19 (t, *J* = 7.1 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 176.1, 173.5, 169.6, 158.4, 142.4, 132.2, 131.8, 129.9, 129.1, 128.7, 128.5, 127.1, 125.9, 125.3, 125.1, 124.3, 113.9, 101.5, 64.3, 64.1, 62.1, 55.2, 50.6, 46.9, 38.2, 14.2, 14.0.

MS (EI): *m*/*z* = 508 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{31}H_{28}O_5N_2$: 508.1998; found: 508.1968.

**Pyrroloisoquinoline 28 (Table 3, entry 3)**

According to the general procedure for the gold-catalyzed reaction, treatment of the iminoester **25** (32.2 mg, 0.132 mmol) with *N*-phenylmaleimide (45.7 mg, 0.264 mmol, 2 equiv) in the presence of the gold catalyst solution in DCE [0.0058 M, 0.23 mL, prepared from (CyJohnPhos)AuCl (3.4 mg, 0.0058 mmol) and AgOTf (1.5 mg, 0.0058 mmol) in DCE (1 mL)] at 80 °C for 4 h gave the pyrroloisoquinoline **28** (32.0 mg, 58%) as a yellow solid; mp 90–94 °C; $R_f$ = 0.38 (*n*-hexane/EtOAc, 70:30).

IR ($CHCl_3$): 3020, 2980, 2938, 1715, 1499, 1385, 1216, 765, 749, 668 $cm^{-1}$.

$^1H$ NMR (400 MHz, $CDCl_3$): δ = 7.41–7.30 (m, 3 H), 7.23–7.09 (m, 3 H), 7.03 (d, *J* = 5.5 Hz, 2 H), 6.93 (d, *J* = 7.1 Hz, 1 H), 5.29 (s, 1 H), 5.19 (d, *J* = 7.8 Hz, 1 H), 5.18 (s, 1 H), 4.36–4.21 (m, 2 H), 3.96 (d, *J* = 7.8 Hz, 1 H), 3.60 (dd, *J* = 7.8, 7.8 Hz, 1 H), 2.33–2.13 (m, 2 H), 1.34 (t, *J* = 7.1 Hz, 3 H), 1.17 (t, *J* = 7.3 Hz, 3 H).

$^{13}C$ NMR (100 MHz, $CDCl_3$): δ = 176.3, 173.5, 169.7, 145.1, 132.3, 131.8, 129.1, 128.6, 128.5, 127.0, 125.2, 125.0, 124.1, 98.9, 64.7, 64.1, 62.4, 51.1, 47.0, 25.7, 14.1, 12.1.

MS (EI): *m*/*z* = 416 ($M^+$).

HRMS (EI): *m*/*z* calcd for $C_{25}H_{24}O_4N_2$: 416.1736; found: 416.1702.

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## Supporting Information

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