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Gold-Oxazoline Complex-Catalyzed Cross-Dehydrogenative Coupling of Glycine Derivatives and Alkenes

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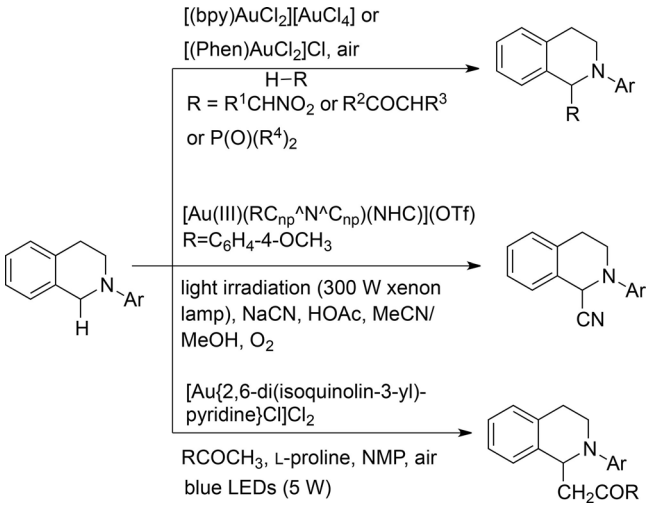
Abstract: A gold-oxazoline complex-catalyzed dehydrogenative Povarov/oxidation tandem reaction for the synthesis of decorated quinolines has been developed from glycine derivatives and alkenes. The reaction performs under mild reaction conditions in the presence of oxygen as the oxidant and features a broad substrate scope and excellent functional group tolerance.

Keywords: C–H activation; cross-coupling; glycine derivatives; gold; oxidation

Introduction

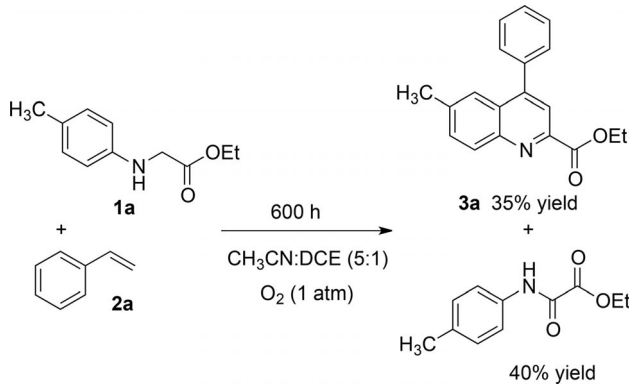
C–C bond forming reactions are especially useful in synthetic chemistry, and have played a vital role in building complicated molecules from simple precursors.[1] Consequently, much effort has been made to establish and improve the methods for constructing new C–C bonds in recent decades.[2] Particularly, C–C bond formation from different C–H bonds under oxidative conditions, termed cross-dehydrogenative coupling (CDC), has attracted much attention. The method greatly increases the overall efficiency and improves the atom economy.[3] Among them, gold-catalyzed cross-dehydrogenative coupling [4] has received special attention, and remarkable progress has been made in recent years. So far, the inert C–H bonds have been directly converted into carbon-carbon and carbon-heteroatom bonds through gold-mediated oxidative cleavage of C–H bonds, hydride shift or C–H insertion. These reactions were mainly catalyzed by gold complexes or salts in combination of oxidants such as TBHP or NBS.[4b,f] Following the principles of green chemistry, here oxygen as an environmentally benign oxidant delivers water as the only by-product, and thus the reaction has gained considerable attention in modern oxidation chemistry.[5] The oxidation of *N*-aryltetrahydroisoquinolines catalyzed by a gold complex has been well developed under aerobic conditions[4c–e,g,h] (Scheme 1). Nevertheless, to the best of our knowledge, no gold-catalyzed oxidative coupling of glycine derivatives with oxygen as an oxidant has been described yet.

The imino Diels–Alder reaction was first discovered by Povarov in the 1960s. Recently, the oxidative dehydrogenative coupling of glycine derivatives has gained significant attention, which relies on the oxidation of the secondary amine substrates.[6] Since the first one-pot Povarov reaction reported by García Mancheño using $FeCl_3$ as the catalyst and a 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) oxoammoni-



Scheme 1. Reported oxidation of *N*-aryltetrahydroisoquinolines catalyzed by gold complex under aerobic conditions.

um salt as the oxidant in 2011,[7] similar catalytic systems have also been developed in other reactions.[8] In 2014, Huo reported the auto-oxidative coupling of glycine (Scheme 2).[8d]



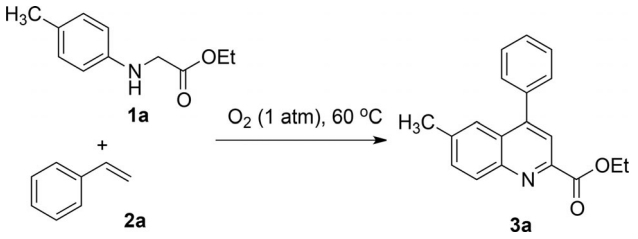
Scheme 2. Reported auto-oxidation reaction of glycine derivatives with styrenes.

However, under these autoxidation conditions, the dehydrogenative Povarov/aromatization tandem reaction of glycine derivatives with alkenes was limited to only highly electron-rich alkenes. The reaction of glycine ester **1a** and styrene **2a** produced only 35% of the desired product **3a**, with 40% of undesired substrate oxidation. The same group also reported that the transformation can be promoted by CBr_4 under an air atmosphere.[8e] Recently, Liu and co-workers also reported a copper(II) triflate-catalyzed aerobic oxidative C–H functionalization of glycine derivatives with olefins.[8i] Quinoline derivatives, arising from these tandem reactions, are very important motifs in a wide array of compounds with activities of relevance to biology or medicinal chemistry.[9] Therefore, there is a continued strong demand for efficient and selective syntheses of these heterocycles. As part of our on-going research interest.[4b,f] herein we report the achievement of the above goal and demonstrate that a gold complex can be used as the catalyst for the oxidative dehydrogenative reaction of glycine derivatives under aerobic conditions.

Results and Discussion

At first, glycine ester **1a** and styrene **2a** were chosen as the model substrates, and the reaction optimization results are summarized in Table 1. A variety of different metal salts (10 mol%) were explored to improve the reaction efficiency under 1 atm of O_2 at 60 °C (Table 1, entries 3–9). While several additives including CuCl, CuOAc, $Fe(ClO_4)_3$ and $Fe(OTf)_2$ proved to be slightly beneficial to improve the efficiency, other salts like $Cu(MeCN)_4PF_6$, $Mg(OTf)_2$ and $Yb(OTf)_3$ in-

Table 1. Optimization of conditions for the O_2 oxidative Povarov/aromatization reaction.[a]



Entry	Catalyst (mol%)	Solvent	*t* [h]	Yield [%][b]
1	–	CH_3CN	600	30
2	–	CH_3CN	12	10
3	CuCl (10)	CH_3CN	12	18
4	CuOAc (10)	CH_3CN	12	27
5	$Cu(MeCN)_4PF_6$ (10)	CH_3CN	12	<5
6	$Fe(ClO_4)_3$ (10)	CH_3CN	12	40
7	$Fe(OTf)_2$ (10)	CH_3CN	12	18
8	$Mg(OTf)_2$ (10)	CH_3CN	12	<5
9	$Yb(OTf)_3$ (10)	CH_3CN	12	<5
10	**4a** (10)	CH_3CN	12	61
11	**4b** (10)	CH_3CN	12	70
12	**5a** (10)	CH_3CN	8	58
13	**5b** (10)	CH_3CN	8	53
14	**6** (10)	CH_3CN	8	61
15	**7** (10)	CH_3CN	8	53
16	**8a** (10)	CH_3CN	3	80
17	**8b** (10)	CH_3CN	3	90
18	**9** (10)	CH_3CN	8	75
19	**10** (10)	CH_3CN	8	73
20	**11a** (10)	CH_3CN	12	42
21	**11b** (10)	CH_3CN	12	50
22	**12** (10)	CH_3CN	12	52
23	$AuCl_3$ (10)	CH_3CN	12	61
24	PPh_3AuCl (10)	CH_3CN	12	20
25	$(PhO)_3PAuCl$ (10)	CH_3CN	12	82
26	$(t\text{-}BuC_6H_4O)_3PAuCl$ (10)	CH_3CN	12	22
27	JohnPhosAuCl (10)	CH_3CN	12	33
28	JohnPhosAuMe (10)	CH_3CN	12	31
29	AuCl (10)	CH_3CN	12	23
30	**8b** (10)	EA	3	83
31	**8b** (10)	xylene	3	85
32	**8b** (10)	EtOH	3	95
33	**8b** (10)	DCE	3	85
34	**8b** (5)	EtOH	3	90
35[c]	**8b** (5)	EtOH	3	24
36[d]	**8b** (5)	EtOH	3	<5
37[e]	**8b** (5)	EtOH	3	93
38[f]	**8b** (5)	EtOH	3	91
39[g]	**8b** (5)	EtOH	3	40

[a] *Reaction conditions:* **1a** (0.5 mmol), **2a** (2 equiv), solvent (2.0 mL), 1.0 atm of O_2, 60 °C.
[b] Isolated yields.
[c] The reaction was performed under an argon atmosphere (1.0 atm).
[d] 1 equiv H_2O_2 (30% aqueous) was used as oxidant.
[e] 1 equiv. TBHP (5.0–6.0 M in decane) was used instead of O_2.
[f] 1 equiv. DTBP was used instead of O_2.
[g] 1 equiv. BPO was used instead of O_2.

hibited the reaction. Gold complexes **4a** and **4b**, which were reported as effective catalyst for the oxidation coupling of *N*-arylisoquinolines,[4] were examined in the reaction of **1a** and **2a**. To our delight, the product **3a** was, respectively produced in 61% and 70% yields in CH_3CN, and no self-oxidation side product was observed (Table 1, entries 10 and 11). Encouraged by this result, the reaction conditions were investigated further in detail. Among the Au(III) catalysts screened (Figure 1), gold-oxazoline complex **8b** showed the best catalytic activity

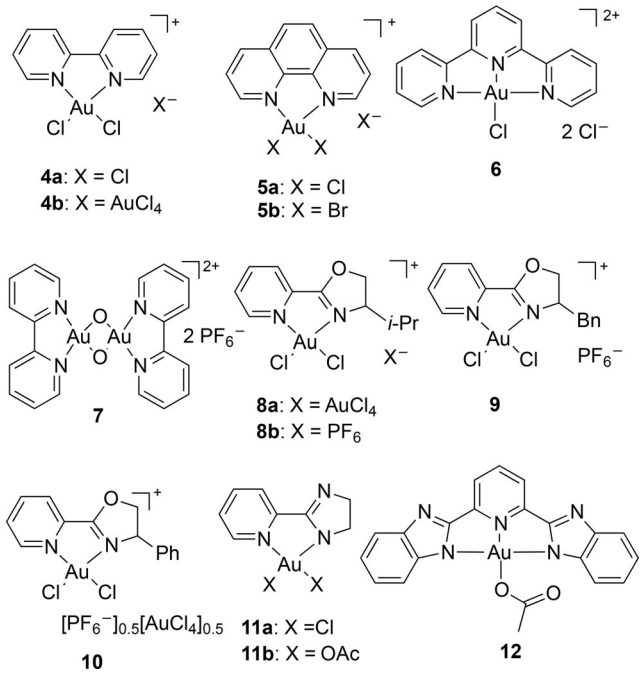


Figure 1. Gold complexes **4**–**12** screened.

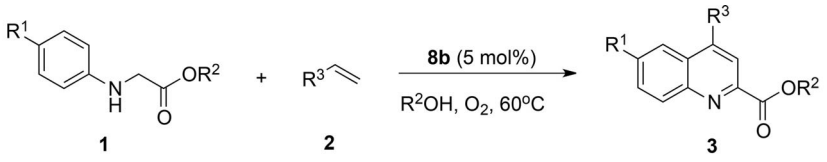
(Table 1, entries 12–23). The utilization of Au(I) (AuCl, PPh_3AuCl, $(t\text{-}BuC_6H_4O)_3PAuCl$, JohnPhosAuCl, JohnPhosAuMe) resulted in the formation of the product with low yields except for $(PhO)_3PAuCl$ (Table 1, entries 24–29). Among the solvents examined, EtOH was the most effective (Table 1, entries 30–34), DCE was not crucial for the reaction yield as reported in auto-oxidation reactions.[8d] Further studies indicated that reducing the catalyst loading of **8b** to 5% had little impact at the reaction outcome (Table 1, entry 34). A control experiment demonstrated that when the aerobic oxidative reaction was carried in an argon atmosphere instead of O_2, a much lower yield was observed (Table 1, entry 35). In order to explore the role of O_2, other oxidants were tested including H_2O_2, TBHP, DTBP, BPO. Targeted **3a** was not obtained with H_2O_2 as oxidant. Similar yields to O_2 were obtained with TBHP and DTBP as oxidants. When BPO was tested, the yield of **3a** dropped to 40% (Table 1, entries 36–39). Consequently, the optimal reaction conditions include as catalyst 5 mol% **8b** at 60 °C in 1 atm of O_2.

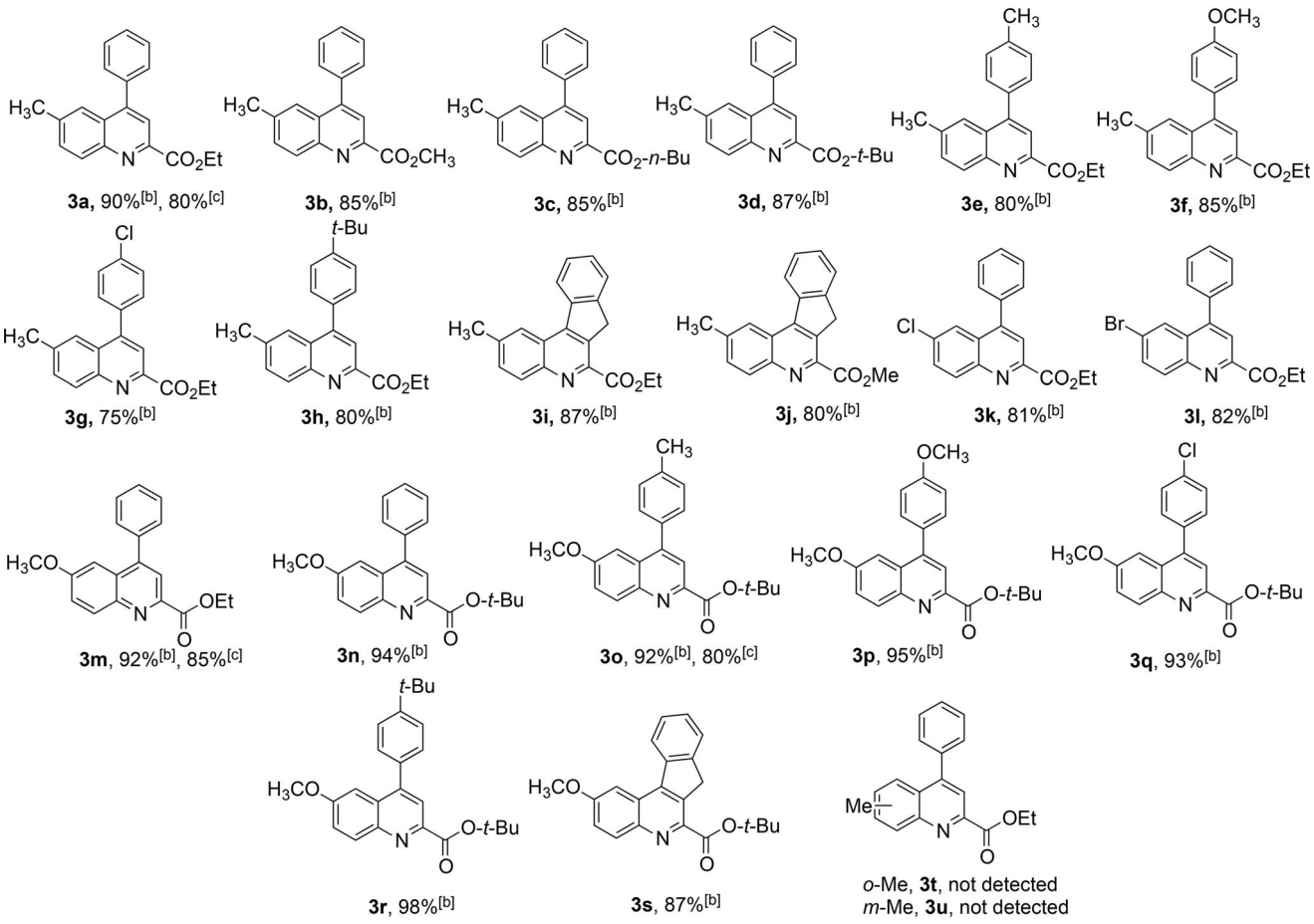
With the optimal reaction conditions in hand, the scope of the coupling reaction of glycine derivatives **1** and alkenes **2** was examined (Table 2 and Table 3). Various glycine esters and glycine amides were smoothly transformed into the desired products. The effect of the substitution of the aniline was also investigated. A wide range of electronically varied anilines **1** with different substituents at the *para* position were compatible with the oxidation system, providing the desired quinolines in good yields. No product was found when *o*-tolyl glycine ester (**1i**) and *m*-tolyl glycine ester (**1j**) were tested to react with styrene (**2a**) under the optimal condition. These results indicated the importance of the *para*-substitution at the aryl moiety. Meanwhile, the scope of this gold-catalyzed CDC reaction was further expanded to a range of substituted alkenes. Reactions with different alkenes including electron-withdrawing and electron-donating groups generally provided the corresponding quinolines in high yields. Alkynes can also serve as dienophiles to participate in this reaction, but yields were lower. When indene was used in this reaction, a complex polycyclic quinoline was obtained.

To gain an insight of the gold-catalyzed oxidative dehydrogenative Povarov/aromatization tandem reaction of glycine derivatives with alkenes, some control experiments were carried out to elucidate the mechanism (Scheme 3). Firstly, the reaction of **1a** in the absence of styrene **2** under the standard reaction conditions was investigated (Scheme 3a). Imine **13a** and its dimer **14a** were obtained in a low yield. The result indicates that the imine would be an important intermediate in the gold-catalyzed process. Gold catalysis might not be absolutely necessary for formation of the imine (Scheme 3a).[10] Secondly, we found that the gold catalyst also played a vital role for a successful cyclization of imine **13a** and styrene **2a** (Scheme 3b). Interestingly, O_2 was indispensable for the synthesis of **3a** as shown in Scheme 3b.

Based on the control experiments, some conclusions could be drawn: (i) imine **13** might be the intermediate in the reaction; (ii) gold catalysis **8b** might be not absolutely necessary for the formation of imine; (iii) O_2 is indispensable for the synthesis of **3a**, not only in the imine formation stage, but also in the nucleophilic addition and aromatization; (iv) the role of gold for activation of the imine is very likely. According to present results and relevant literature,[4,8,13] a possible mechanism was proposed as shown in Scheme 4. Firstly, under the O_2 atmosphere, the glycine ester **1a** was first auto-oxidized to give the hydroperoxide intermediate **17** [11,8d] and imine **13**. In the

Table 2. Gold-oxazoline complex catalyzed O_2 oxidative Povarov/aromatization reaction of glycine esters with alkenes.[a]





[a] *Reaction conditions:* glycine ester (0.5 mmol), alkene (2 equiv.), 5 mol% **8b**, alcohol (2.0 mL), 1.0 atm of O_2, 60 °C.
[b] Isolated yields.
[c] Alkynes were used as dienophiles.

second part, electron-rich styrene **2a** attacked the gold(III)-activated imine intermediate **18**, tetrahydroquinoline **16**[12] was formed and further oxidized and aromatized to afford quinoline **3a**.

Conclusions

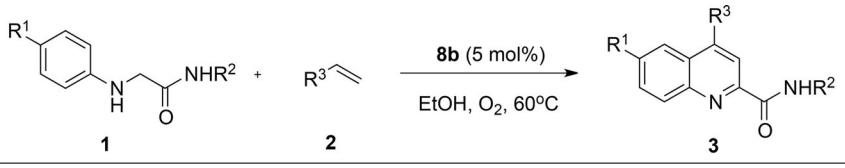
In summary, a gold-oxazoline complex-catalyzed dehydrogenative Povarov/oxidation tandem reaction for the synthesis of decorated quinolines has been developed from glycine derivatives and alkenes. The reaction performs under mild reaction conditions in the presence of O_2 as the oxidant and features a broad substrate scope. This work also represents a new application of the gold complex.

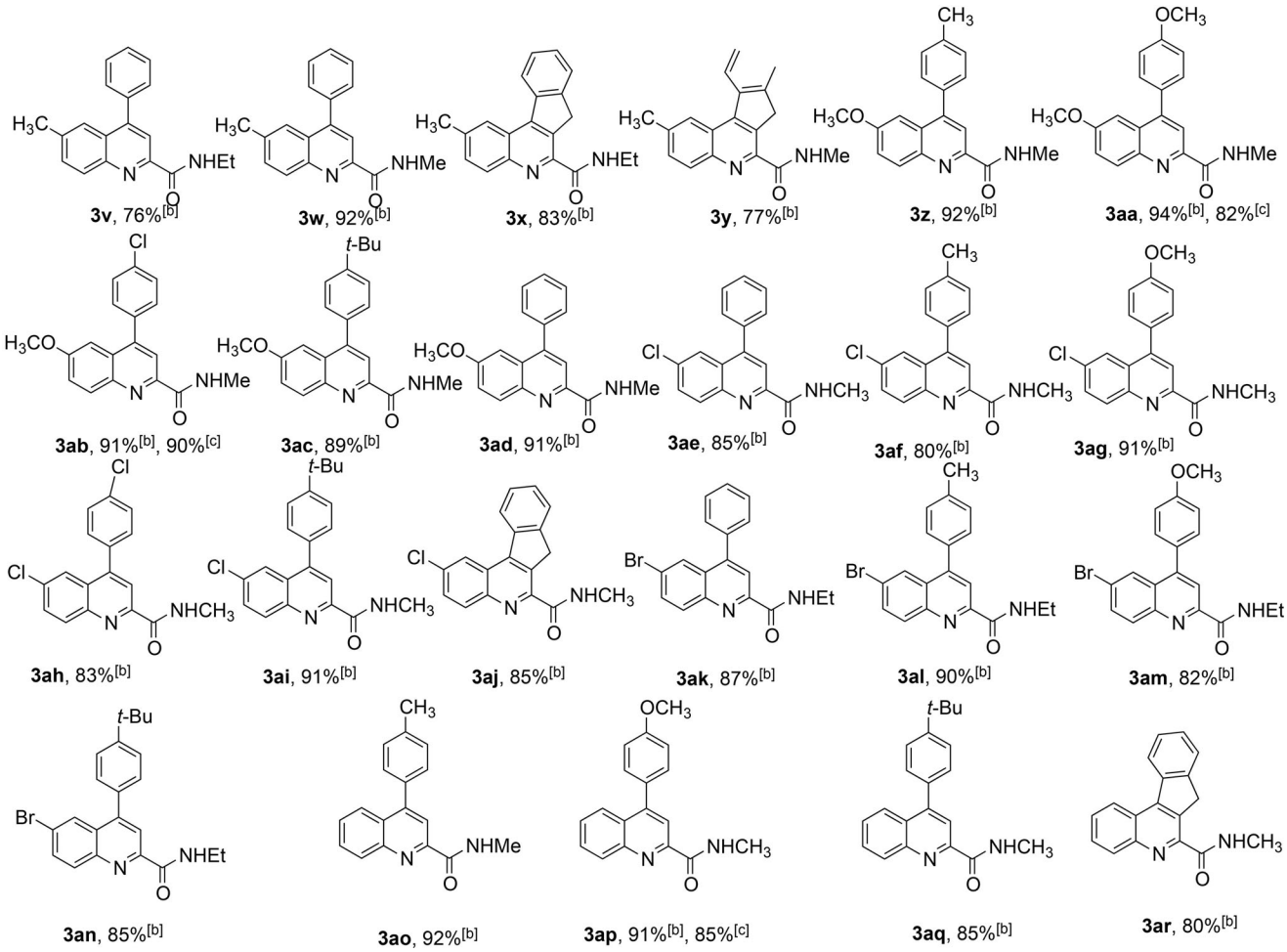
Experimental Section

General Procedure for the O_2 Oxidative Povarov/Aromatization Tandem Reaction of Glycine Derivatives with Alkenes

To a 10-mL vial equipped with an oxygen balloon was added glycine derivative (**1**) (0.5 mmol), alkene (**2**)

Table 3. Gold-oxazoline complex-catalyzed O_2 oxidative Povarov/aromatization reaction of glycine amides with alkenes.[a]





[a] *Reaction conditions:* glycine amide (0.5 mmol), alkene (2 equiv.), 5 mol% **8b**, alcohol (2.0 mL), 1.0 atm of O_2, 60 °C.
[b] Isolated yields.
[c] Alkynes were used as dienophiles.

(2 equiv.), gold catalyst **8b** (5 mol%), and alcohol (2 mL). The mixture was stirred for 3–6 hours at 60 °C. After the reaction was completed as indicated *via* TLC analysis, the reaction mixture was poured into water and extracted with EtOAc. The organic layer was separated and the solvent was evaporated under vacuum. The residue was purified *via* column chromatography over silica gel eluting with EtOAc/PE to give the desired coupling product **3a–3ar**.

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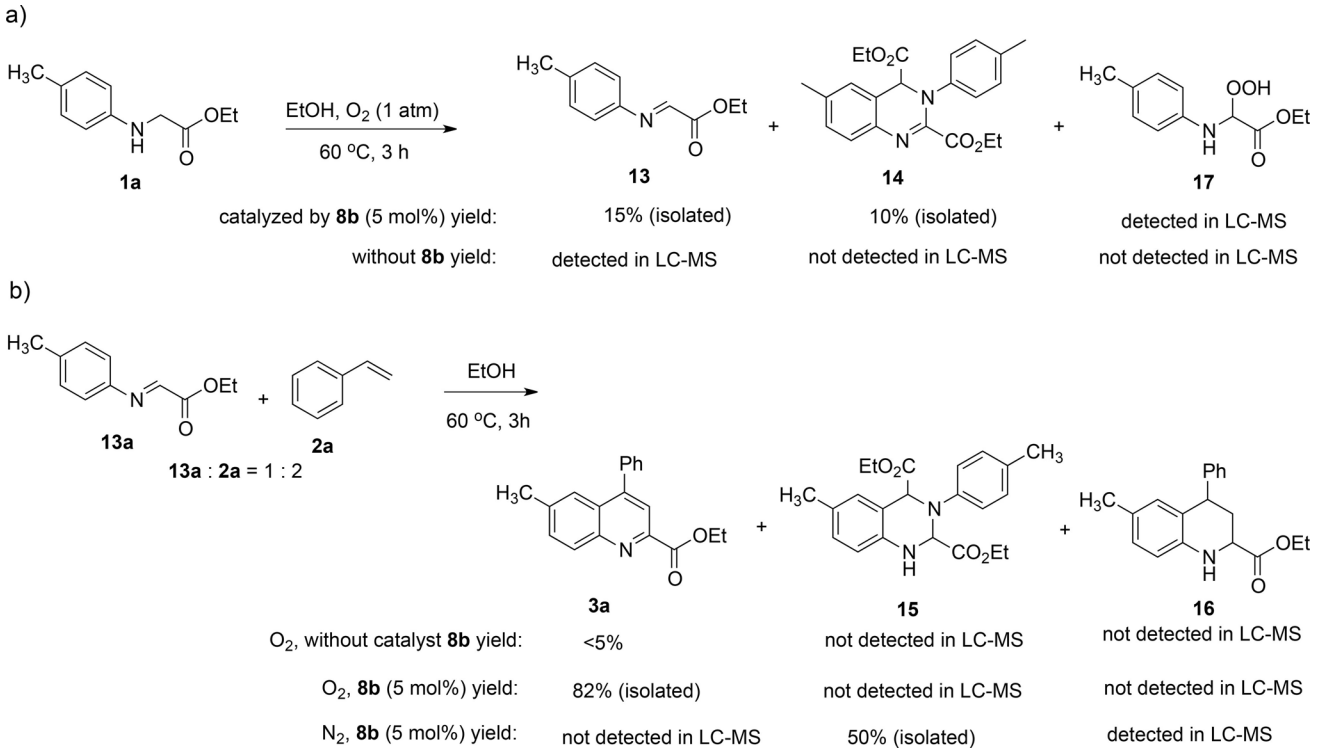
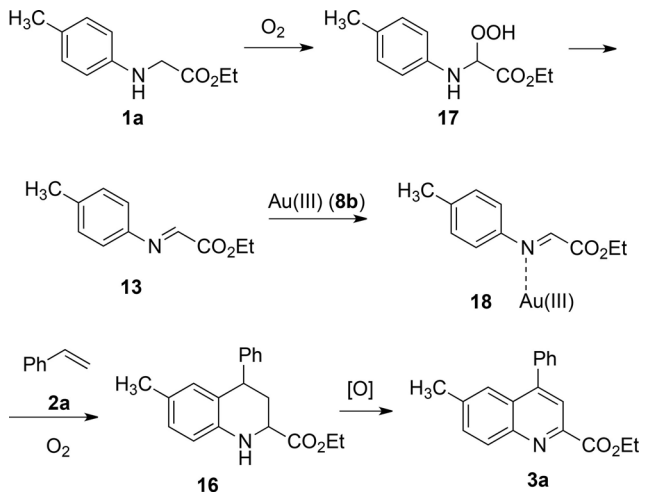


Scheme 3. Control experiments.



Scheme 4. Possible mechanism.

References

[1] For recent reviews, see: a) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem.* **2009**, *121*, 5196–5217; *Angew. Chem. Int. Ed.* **2009**, *48*, 5094–5115; b) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074–1086; c) L. Ackermann, *Chem. Rev.* **2011**, *111*, 1315–1345; d) L. McMurray, F. O'Hara, M. J. Gaunt, *Chem. Soc. Rev.* **2011**, *40*, 1885–1898; e) A. J. Hickman, M. S. Sanford, *Nature* **2012**, *484*, 177–185; f) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651–3678; g) J. Wencel-Delord, F. Glorius, *Nat. Chem.* **2013**, *5*, 369–375.

[2] For recent reviews, see: a) F. Bellina, R. Rossi, *Chem. Rev.* **2010**, *110*, 1082–1146; b) I. A. I. Mkhalid, J. H. Barnard, T. B. Marder, J. M. Murphy, J. F. Hartwig, *Chem. Rev.* **2010**, *110*, 890–931; c) D. Balcells, E. Clot, O. Eisenstein, *Chem. Rev.* **2010**, *110*, 749–823; d) C. Copéret, *Chem. Rev.* **2010**, *110*, 656–680; e) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624–655; f) S. Conejero, M. Paneque, M. L. Poveda, L. L. Santos, E. Carmona, *Acc. Chem. Res.* **2010**, *43*, 572–580; g) M. T. Whited, R. H. Grubbs, *Acc. Chem. Res.* **2009**, *42*, 1607–1616; h) G. Parkin, *Acc. Chem. Res.* **2009**, *42*, 315–325; i) J. C. Lewis, R. G. Bergman, J. A. Ellman, *Acc. Chem. Res.* **2008**, *41*, 1013–1025; j) Y. J. Park, J.-W. Park, C.-H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222–234; k) M. M. Díaz-Requejo, P. J. Pérez, *Chem. Rev.* **2008**, *108*, 3379–3394; l) C. I. Herrerías, X. Yao, Z. Li, C.-J. Li, *Chem. Rev.* **2007**, *107*, 2546–2562; m) C.-L. Sun, B.-J. Li, Z.-J. Shi, *Chem. Rev.* **2011**, *111*, 1293–1314; n) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215–1292; o) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147–1169; p) C. Liu, H. Zhang, W. Shi, A. Lei, *Chem. Rev.* **2011**, *111*, 1780–1824; q) H. L. Davies, J. Du Bois, J. Q. Yu, *Chem. Soc. Rev.* **2011**, *40*, 1855–1856; r) K. M. Engle, T. S. Mei, M. Wasa, J. Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788–802; s) J. Xie, C. J. Zhu, in: *Sustainable C(sp^3)–H Bond Functionalization.* Springer, Heidelberg, **2016**.

[3] a) S. A. Girard, T. Knauber C. J. Li, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 1–32; b) X. J. Zheng, Z. P.

Li, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 55–66; c) C. Darcel, J. B. Sortais, S. Q. Duque, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 67–92; d) G. J. Deng, F. H. Xiao, L. Yang, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 93–113; e) B. DeBoef, A. L. Porter, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 114–132; f) Y. Hamashima, M. Sodeoka, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 133–152; g) H. Ito, K. Ueda, K. Itami, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 153–196; h) O. Baslé, in: *RSC Green Chemistry No. 26: From C–H to C–C Bonds: Cross-Dehydrogenative-Coupling*, (Ed.: C. J. Li), The Royal Society of Chemistry, **2015**, pp 197–218; i) C. Zhang, C. H. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3464–3484; j) M. L. Dinda, C. D. Bose, T. Ghosh, S. Maity, *RSC Adv.* **2015**, *5*, 44928–44932; k) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068–5083; l) A. Dhakshinamoorthy, A. M. Asiri, H. Garcia, *Chem. Soc. Rev.* **2015**, *44*, 1922–1947; m) Z. Z. Shi, C. Zhang, C. H. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381–3430.

[4] a) J. Xie, C. D. Pan, A. Abdukadera, C. J. Zhu, *Chem. Soc. Rev.* **2014**, *43*, 5245–5256; b) Y. Zhang, H. Peng, M. Zhang, Y. Cheng, C. Zhu, *Chem. Commun.* **2011**, *47*, 2354–2356; c) J. Xie, H. Li, J. Zhou, Y. Cheng, C. Zhu, *Angew. Chem.* **2012**, *124*, 1278–1281; *Angew. Chem. Int. Ed.* **2012**, *51*, 1252–1255; d) J. Xie, H. Li, Q. Xue, Y. Cheng, C. Zhu, *Adv. Synth. Catal.* **2012**, *354*, 1646–1650; e) H. Jiang, J. Xie, A. Lin, Y. Cheng, C. Zhu, *RSC Adv.* **2012**, *2*, 10496–10498; f) Y. Zhang, B. Feng, C. Zhu, *Org. Biomol. Chem.* **2012**, *10*, 9137–9141; g) W.-P. To, G. S.-M. Tong, W. Lu, C. Ma, J. Liu, A. L.-F. Chow, C.-M. Che, *Angew. Chem.* **2012**, *124*, 2708–2711; *Angew. Chem. Int. Ed.* **2012**, *51*, 2654–2657; h) Q. Xue, J. Xie, H. Jin, Y. Cheng, C. Zhu, *Org. Biomol. Chem.* **2013**, *11*, 1606–1609.

[5] a) T. Punniyamurthy, S. Velusamy, J. Iqbal, *Chem. Rev.* **2005**, *105*, 2329–2363; b) A.-E. Wendlandt, A.-M. Suess, S.-S. Stahl, *Angew. Chem.* **2011**, *123*, 11256–11283; *Angew. Chem. Int. Ed.* **2011**, *50*, 11062–11087; c) Z. Shi, C. Zhang, C. Tang, N. Jiao, *Chem. Soc. Rev.* **2012**, *41*, 3381–3430; d) W. Wu, H. Jiang, S. Adimurthy, *Acc. Chem. Res.* **2012**, *45*, 1736–1748; e) A. Pintér, A. Sud, D. Sureshkumar, M. Klussmann, *Angew. Chem.* **2010**, *122*, 5124–5128; *Angew. Chem. Int. Ed.* **2010**, *49*, 5004–5007; f) A. Pintér, M. Klussmann, *Adv. Synth. Catal.* **2012**, *354*, 701–711; g) Q. Lu, J. Zhang, F. Wei, Y. Qi, H. Wang, Z. Liu, A. Lei, *Angew. Chem.* **2013**, *125*, 7297–7300; *Angew. Chem. Int. Ed.* **2013**, *52*, 7156–7159; h) Q. Lu, J. Zhang, G. Zhao, Y. Qi, H. Wang, A. Lei, *J. Am. Chem. Soc.* **2013**, *135*, 11481–11484; i) V. Chudasama, R.-J. Fitzmaurice, S. Caddick, *Nat. Chem.* **2010**, *2*, 592–596; j) E.-I. Solomon, P. Chen, M. Metz, S.-K. Lee, A.-E. Palmer, *Angew. Chem.* **2001**, *113*, 4702–4724; *Angew. Chem. Int. Ed.* **2001**, *40*, 4570–4590; k) E. I. Solomon, U. M. Sundaram, T. M. Machonkin, *Chem. Rev.* **1996**, *96*, 2563–2605; l) M. Rolff, J. Schottenheim, H. J. Decker, F. Tuczek, *Chem. Soc. Rev.* **2011**, *40*, 4077–4098; m) C. J. Cramer, W. B. Tolman, *Acc. Chem. Res.* **2007**, *40*, 601–608; n) Z.-Q. Liu, L. Zhao, X. Shang, Z. Cui, *Org. Lett.* **2012**, *14*, 3218–3221.

[6] a) L. S. Povarov, B. M. Mikhailov, *Izv. Akad. Nauk SSSR Otd. Khim. Nauk* **1963**, 953–956; b) L. S. Povarov, V. I. Grigos, B. M. Mikhailov, *Izv. Akad. Nauk SSSR Otd. Khim. Nauk* **1963**, 2039–2041; c) L. S. Povarov, *Russian Chem. Rev.* **1967**, *36*, 656–670; d) S. Murata, M. Miura, M. Nomura, *J. Org. Chem.* **1989**, *54*, 4700–4702; e) S. I. Murahashi, T. Naota, N. Miyaguchi, T. Nakato, *Tetrahedron Lett.* **1992**, *33*, 6991–6994; f) S. Araneo, F. Fontana, F. Minisci, F. Recupero, A. Serri, *Tetrahedron Lett.* **1995**, *36*, 4307–4310; g) L. H. Huang, X. B. Zhang, Y. H. Zhang, *Org. Lett.* **2009**, *11*, 3730–3733; h) M. Nishino, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 6447–6451; i) S. Q. Zhu, A. Das, L. Bui, H. J. Zhou, D. P. Curran, M. Rueping, *J. Am. Chem. Soc.* **2013**, *135*, 1823–1829; j) L. Zhao, O. Baslé, C.-J. Li, *Proc. Natl. Acad. Sci. USA* **2009**, *106*, 4106–4111; k) J. Xie, Z.-Z. Huang, *Angew. Chem.* **2010**, *122*, 10379–10383; *Angew. Chem. Int. Ed.* **2010**, *49*, 10181–10185; l) G. Zhang, Y. Zhang, R. Wang, *Angew. Chem.* **2011**, *123*, 10613–10616; *Angew. Chem. Int. Ed.* **2011**, *50*, 10429–10432; m) Z. Q. Wang, M. Hu, X. C. Huang, L. B. Gong, Y. X. Xie, J. H. Li, *J. Org. Chem.* **2012**, *77*, 8705–8711; n) W. Wei, R. Song, J. Li, *Adv. Synth. Catal.* **2014**, *356*, 1703–1707; o) P. Liu, Y. Li, H. Wang, Z. Wang, X. Hu, *Tetrahedron Lett.* **2012**, *53*, 6654–6656; p) S. Zhu, M. Rueping, *Chem. Commun.* **2012**, *48*, 11960–11962; q) C. Huo, C. Wang, M. Wu, X. Jia, H. Xie, Y. Yuan, *Adv. Synth. Catal.* **2014**, *356*, 411–415; r) C. Huo, C. Wang, C. Sun, X. Jia, X. Wang, W. Chang, M. Wu, *Adv. Synth. Catal.* **2013**, *355*, 1911–1916; s) W.-J. Yoo, A. Tanoue, S. Kobayashi, *Asian. J. Org. Chem.* **2014**, *3*, 1066–1069; t) C. Min, A. Sanchawala, D. Seidel, *Org. Lett.* **2014**, *16*, 2756–2759; u) G. Q. Xu, C. G. Li, M. Q. Liu, J. Cao, Y. C. Luo, P. F. Xu, *Chem. Commun.* **2016**, *52*, 1190–1193.

[7] a) H. Richter, O. García Mancheño, *Org. Lett.* **2011**, *13*, 6066–6069; b) R. Rohlmann, T. Stopka, H. Richter, O. García Mancheño, *J. Org. Chem.* **2013**, *78*, 6050–6064.

[8] a) X. Jia, F. Peng, C. Qing, C. Huo, X. Wang, *Org. Lett.* **2012**, *14*, 4030–4033; b) X. Jia, Y. Wang, F. Peng, C. Huo, L. Yu, J. Liu, X. Wang, *J. Org. Chem.* **2013**, *78*, 9450–9456; c) P. Liu, Z. Wang, J. Lin, X. Hu, *Eur. J. Org. Chem.* **2012**, 1583–1589; d) C. Huo, Y. Yuan, M. Wu, X. Jia, X. Wang, F. Chen, J. Tang, *Angew. Chem.* **2014**, *126*, 13762–13765; *Angew. Chem. Int. Ed.* **2014**, *53*, 13544–13547; e) C. D. Huo, H. S. Xie, M. X. Wu, X. D. Jia, X. C. Wang, F. J. Chen, J. Tang, *Chem. Eur. J.* **2015**, *21*, 5723–5726; f) G. L. Liu, J. R. Qian, J. Hua, F. Cai, X. Li, L. Liu, *Org. Biomol. Chem.* **2016**, *14*, 1147–1152; g) J. Liu, Y. X. Wang, L. L. Yu, C. D. Huo, X. C. Wang, X. D. Jia, *Adv. Synth. Catal.* **2014**, *356*, 3214–3218; h) Y. X. Wang, F. F. Peng, J. Liu, G. D. Huo, X. C.

Wang, X. D. Jia, *J. Org. Chem.* **2015**, *80*, 609–614; i) Z. Y. Xie, J. Jia, X. G. Liu, L. Liu, *Adv. Synth. Catal.* **2016**, *358*, 919–925.

[9] a) V. V. Kouznetsov, *Tetrahedron* **2009**, *65*, 2721–2750; b) R. Musiol, M. Serda, S. Hensel-Bielowka, J. Polanski, *Curr. Med. Chem.* **2010**, *17*, 1960–1973.

[10] See the Supporting Information: **1a** was treated for the same reaction time under the optimized conditions except for the gold catalysis **8b**. Only **1a** was found through TLC (254 nm) analysis after reaction for 3 hours. However, the characteristic peak of **13** could be found in LC-MS. This implies that gold catalysis may be not absolutely necessary for the formation of the imine intermediate.

[11] See the Supporting Information: the characteristic peak of glycine ester hyperoxide **17** (M = 226) was found in LC-MS.

[12] See the Supporting Information: imine **13** and styrene **2a** were catalyted by gold catalyst **8b** under an N_2 atmosphere. The *in situ* LC-MS analysis of the resulting mixture was conducted 3 hours later with gradient elution. **15** (M = 382) and **16** (M = 295, 330 nm in UV) were found in LC-MS. These results imply that under an N_2 atmosphere, self-cyclization of imine had priority. However, under the O_2 atmosphere, the nucleophilic addition of gold-activated imine and styrene occurred exclusively.

[13] See the Supporting Information: 2 equiv. TEMPO were added in the reaction of **1a** and **2a**, no product was obtained and inhibition was also observed in the reaction of **13** and **2a**. The results of TEMPO addition suggest that the present reaction might include a radical process. Oxygen was used as the oxidation reagent in the reaction. In order to explain the TEMPO effect on the control experiment, we refer to some other oxygen-oxidative reactions such as that in: *Angew. Chem. Int. Ed.* **2014**, *53*, 13544. In this reference, auto-oxidative coupling of glycine derivatives was realized with O_2. TEMPO was added and the experiment was inhibited. The reason of the inhibition was that TEMPO restrained the formation of hyperoxide radical anion of glycine derivative oxidized by O_2. In the supporting information, we also found the characteristic peak of hyperoxide in LC-MS. So in our reaction, a similar inhibition might also happen when TEMPO was added.

