Europe PMC Funders Group
Author Manuscript
Chemistry. Author manuscript; available in PMC 2014 November 20.

Published in final edited form as:
Chemistry. 2014 April 1; 20(14): 3917–3921. doi:10.1002/chem.201400407.

Merging Gold and Organocatalysis: A Facile Asymmetric Synthesis of Annulated Pyrroles

Daniel Hack, **Dr. Charles C. J. Loh**, **Jan M. Hartmann**, **Prof. Dr. Gerhard Raabe**, and **Prof. Dr. Dieter Enders***
Institute of Organic Chemistry, RWTH Aachen University Landoltweg 1, 52074 Aachen (Germany)

Abstract

The combination of cinchona-alkaloid-derived primary amine and Au^{I}–phosphine catalysts allowed the selective C–H functionalization of two adjacent carbon atoms of pyrroles under mild reaction conditions. This sequential dual activation provides seven-membered-ring-annulated pyrrole derivatives in excellent yields and enantioselectivities.

Keywords

annulation; gold catalysis; organocatalysis; primary-amine catalysis; pyrroles

Although gold catalysis and organocatalysis have rapidly grown since the turn of the millennium and emerged as powerful tools in the general field of catalysis, examples of the combination of gold and organocatalysis in sequential and cooperative tandem reactions exploiting complementary activation modes are still scarce.[1-3] Recently, we reported the asymmetric synthesis of tetracyclic indole derivatives containing seven-membered rings by the merger of a thioamide-based organocatalyst with a Au^{I} catalyst to effect two consecutive Friedel–Crafts-type reactions on unsubstituted indole substrates (Scheme 1a).[4]

Due to the immense importance of the indole core, major emphasis has been given to the development of asymmetric Friedel–Crafts reactions involving indole derivatives. Pyrrole is another electron-rich heteroaromatic compound, core of which is found in many natural products.[5,6] One attractive aspect of pyrrole chemistry that is unseen in indole substrates is the inherent nucleophilicity on the C2 position, which stands in contrast to indoles having a classical C3 nucleophilic site. Because Michael-type reactions of pyrroles usually gives 2,5-dialkylated products, it is difficult to monofunctionalize pyrrole substrates (Scheme 1c).[7] To avoid this problem, we wanted to selectively functionalize two adjacent sites on the pyrrolic heterocycle by using two different catalytic modes of activation to generate new

© 2014 The Authors.
This is an open access article under the terms of the Creative Commons Attribution Non-Commercial License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited and is not used for commercial purposes.

*Fax: (+ 49)241-809-2127, enders@rwth-aachen.de.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201400407.

Europe PMC Funders Author Manuscripts
Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

annulated pyrrole derivatives in a one-pot reaction, which is quite difficult to achieve by using conventional methods.

Therefore, we report a new asymmetric one-pot dual catalytic protocol that uses primary amine and Au^{I} catalysis to access 2,3-annulated pyrroles containing a seven-membered ring (Scheme 1b). This method is intriguing, because medium-sized rings are difficult to synthesize by conventional organocatalytic methods.[8] Moreover, a publication documenting a Au^{I}-catalyzed 7-*endo*-dig cyclization mode on pyrrole substrates is not known to date. Such cyclization modes have only been known to occur when platinum or Au^{III} catalysis was utilized.[9] To the best of our knowledge, the method described herein is the first known example of an asymmetric one-pot operation, in which pyrroles act as a double nucleophile, hence augmenting the operational efficiency of this protocol.

To achieve the annulated pyrrole targets, we first focused on the optimization of the Friedel–Crafts-Michael-type reaction. For the 1,4-addition of pyrrole to enone **2a**, primary amines **4**–**6** derived from amino acids and cinchona-alkaloid-derived amines **7**–**10** together with trifluoroacetic acid (TFA) as additive were employed (Scheme 2).[10,11] The primary amines **4**–**6** showed poor to good conversions with good enantioselectivity values, whereas the reactions with the primary amines **7**–**10** were finished within one day and provided comparable or better enantioselectivity values.

The catalyst **10** gave the highest enantioselectivity value, and further optimization was carried out by screening different solvents (Table 1). It turned out that the choice of the solvent did not have any crucial influence on the yield or the observed enantioselectivity values. However, we were able to obtain better yields and slightly improved enantioselectivities at higher dilution and lower temperature. Under these conditions, the amount of dialkylated pyrrole was low, and no other by-products could be observed. This fact is remarkable, because most known methods on 1,4-additions of pyrroles mainly give dialkylated products.[5] We did not investigate the influence of different acids or different amounts of acid, because no beneficial effect was observed in related pyrrole 1,4-additions.[12]

After having optimized the Michael addition, we directed our focus on the cyclization step by screening various gold(I) complexes (Figure 1). We observed that all gold catalysts promoted the cyclization reaction of the Friedel–Crafts product **3** in toluene, generally within 30 min and in excellent yields (Table 2). Only the triazole–gold complex **16** showed lower reactivity due to its higher stability and the strong coordination of the triazole ligand to the gold center (Table 2, entry 6).[13] Although there was no huge difference in terms of yields, using the Echavarren-type catalysts **12**–**14** resulted in a cleaner isomerization without the formation of unwanted by-products (Table 2, Entry 2-4).[14]

It is known from the literature that amines might deactivate gold(I) complexes by coordination to the vacant binding site.[3e-g,k,15] However, the active catalyst can be regenerated upon addition of acidic additives. As was expected, we did not observe any conversion of **3** under the reported conditions when only organocatalyst **10** was present (Table 2, entry 12). On the contrary, the reaction was completed within 30 min, if 30 mol%

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

TFA was also present, and the product **17a** was obtained in excellent yields (Table 2, entry 13).

Thus, it was not necessary to add any further additives, because the same amount of TFA had to be already added in the Michael addition. In an additional control experiment, we could show that TFA does not catalyze the cycloisomerization, because no product could be observed after 24 h (Table 2, entry 11). In addition, other metal catalysts containing platinum or copper also failed to promote this reaction, although those metals are strongly associated with the activation of alkynes (Table 2, entries 8–10).

With the optimized conditions in hand, a variety of substituted enones and pyrroles were used to demonstrate the flexibility of the reported method (Scheme 3). To our delight, we obtained good to excellent yields and enantioselectivity values for all enones tested, tolerating electron-withdrawing, as well as electron-donating, groups (EWG and EDG, respectively; **17a**–**f**). Likewise, 2-aryl-pyrroles can also be used for this reaction, albeit with slightly lower yields and enantioselectivity values (**17g**–**l**). Apparently, the increased steric bulk introduced by the additional aryl group on pyrrole seems to hamper the transition state in the enantioselective step. In addition, we observed that the products are less stable to acid and heat than the products, which are derived from unsubstituted pyrrole, thus leading to lower yields. Further, we investigated if the method could be extended to enones with terminal alkynes and trimethylsilyl (TMS) protected alkynes. Although both substrates reacted smoothly in the Michael addition, no desired product could be isolated after the gold-catalyzed cycloisomerization.[16]

The absolute configuration was assigned by X-ray crystal-structure analysis of (*R*)-**17b** (Figure 2).[17] The absolute configuration of the other products was assigned assuming a uniform reaction pathway. To demonstrate the practicability of this protocol, we conducted the asymmetric synthesis of **17b** on a larger scale with slightly lower yields, but improved enantioselectivity (Scheme 4). The product was converted to the corresponding alcohol by reduction with sodium borohydride at −78°C to give a mixture of two diastereomers **18** in good yield (Scheme 4).

Although we still lack further information on the mechanism, a plausible reaction pathway is depicted in Scheme 5. The organocatalytic reaction is driven by the formation of the iminium ion by condensation of the TFA salt of the primary amine **10** and the enone **2a**. This LUMO activation of the substrate facilitates the nucleophilic attack of pyrrole. The observed stereoselectivity can be attributed to the covalent bonding between the enone and the primary amine, as well as hydrogen bonding between pyrrole and the quinuclidine backbone of the catalyst with trifluoroacetate as mediator.[12]

After hydrolysis, the intermediate **3** can enter the gold-catalyzed cycle. In consent with the reported literature, we believe that the mechanism for the gold-catalyzed step can be rationalized by an initiating 6-*endo*-dig cyclization of the more nucleophilic C2 position of pyrrole to the internal alkyne.[9,18] The alkyne is activated by coordination via the π-acidic Au^{I} complex **20** to form a non-aromatic spirocyclic intermediate **21**, which undergoes fast rearrangement to the seven-membered ring **22** followed by rearomatization and

Europe PMC Funders Author Manuscripts

protodeauration. Thus, the final products **17** seem to be derived from a 7-*endo*-dig cyclization.

In summary, we have developed a convenient one-pot asymmetric synthesis of annulated pyrroles based on a rare 7-*endo*-dig cyclization, thus functionalizing two adjacent carbon atoms on pyrrole by direct C–H functionalization. The combination of a cinchona-alkaloid-derived primary amine and a Au^{I}–phosphine catalyst gave excellent yields and enantioselectivity values, which are rarely achieved in pyrrole chemistry.

Experimental Section

Typical procedure

Freshly distilled pyrrole (69 μL, 1.00 mmol) was added to a solution of 9-amino(9-deoxy)*epi* cinchonine (**10**; 29 mg, 0.20 mmol), TFA (16 μL, 0.15 mmol), and enone (0.5 mmol) in toluene (3 mL) at 0°C. The reaction mixture was stirred at 0°C, and the progress of the reaction was monitored by TLC analysis. After completion, a suspension of $AgNTf_2$ (10 mg, 0.10 mmol) and catalyst **13** (13 mg, 0.10 mmol) in toluene (1 mL) was added to the reaction mixture at room temperature. After complete conversion, the crude product was directly subjected to flash chromatography (silica, *n*-pentane/diethyl ether).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

D.H. thanks the DFG (International Research Training Group “Selectivity in Chemo- and Biocatalysis”—Seleca) and D.E. thanks the European Research Council (ERC Advanced Grant “DOMINOCAT”) for financial support.

References

[1]. For selected general reviews on gold catalysis, see: Hashmi ASK, Hutchings GJ. Angew. Chem. 2006; 118:8064. Angew. Chem. Int. Ed. 2006; 45:7896. Hashmi ASK. Chem. Rev. 2007; 107:3180. [PubMed: 17580975] Fürstner A, Davies PW. Angew. Chem. 2007; 119:3478. Angew. Chem. Int. Ed. 2007; 46:3410. Gorin DJ, Toste FD. Nature. 2007; 446:395. [PubMed: 17377576] Muzart J. Tetrahedron. 2008; 64:5815. Li Z, Brouwer C, He C. Chem. Rev. 2008; 108:3239. [PubMed: 18613729] Arcadi A. Chem. Rev. 2008; 108:3266. [PubMed: 18651778] Jiménez-Nún?ez E, Echavarren AM. Chem. Rev. 2008; 108:3326. [PubMed: 18636778] Gorin DJ, Sherry BD, Toste FD. Chem. Rev. 2008; 108:3351. [PubMed: 18652511] Skouta R, Li C-J. Tetrahedron. 2008; 64:4917. Widenhoefer RA. Chem. Eur. J. 2008; 14:5382. [PubMed: 18442031] Kirsch SF. Synthesis. 2008; 3183 Bongers N, Krause N. Angew. Chem. 2008; 120:2208. Angew. Chem. Int. Ed. 2008; 47:2178. Fürstner A. Chem. Soc. Rev. 2009; 38:3208. [PubMed: 19847352] Shapiro N, Toste FD. Synlett. 2010:675. [PubMed: 21135915] Sengupta S, Shi X. ChemCatChem. 2010; 2:609. Hashmi ASK. Angew. Chem. 2010; 122:5360. Angew. Chem. Int. Ed. 2010; 49:5232. Bandini M. Chem. Soc. Rev. 2011; 40:1358. [PubMed: 21103507] Krause N, Winter C. Chem. Rev. 2011; 111:1994. [PubMed: 21314182] Pradal A, Toullec PY, Michelet V. Synthesis. 2011:1501. Corma A, Leyva-Pérez A, Sabater MJ. Chem. Rev. 2011; 111:1657. [PubMed: 21391565] Rudolph M, Hashmi ASK. Chem. Commun. 2011; 47:6536. Rudolph M, Hashmi ASK. Chem. Soc. Rev. 2012; 41:2448. [PubMed: 22182942]

[2]. For selected reviews on organocatalysis, see: Berkessel A, Grçger H. Asymmetric Organocatalysis. 2005Wiley-VCHWeinheim Dalko PI. Enantioselective Organocatalysis.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

2007Wiley-VCHWeinheim c) Special issue on organocatalysis: List B. Chem. Rev. 2007; 107:5413. Pellissier H. Tetrahedron. 2007; 63:9267. de Figueiredo RM, Christmann M. Eur. J. Org. Chem. 2007:2575. Enders D, Grondal C, Hüttl MMR. Angew. Chem. 2007; 119:1590. Angew. Chem. Int. Ed. 2007; 46:1570. Dondoni A, Massi A. Angew. Chem. 2008; 120:4716. Angew. Chem. Int. Ed. 2008; 47:4638. MacMillan DWC. Nature. 2008; 455:304. [PubMed: 18800128] Barbas CF. Angew. Chem. 2008; 120:44. Angew. Chem. Int. Ed. 2008; 47:42. Enders D, Narine AA. J. Org. Chem. 2008; 73:7857. [PubMed: 18778100] Melchiorre P, Marigo M, Carlone A, Bartoli G. Angew. Chem. 2008; 120:6232. Angew. Chem. Int. Ed. 2008; 47:6138. Jørgensen KA, Bertelsen S. Chem. Soc. Rev. 2009; 38:2178. [PubMed: 19623342] Bella M, Gasperi T. Synthesis. 2009:1583. Pellissier H. Recent Developments in Asymmetric Organocatalysis. 2010RCS PublishingCambridge Maruoka K, List B, Yamamoto H, Gong L-Z. Chem. Commun. 2012; 48:10703. Pellissier H. Adv. Synth. Catal. 2012; 354:237. List B, Maruoka K. Asymmetric Organocatalysis (in Science of Synthesis). 2012ThiemeStuttgart Dalko PI. Comprehensive Enantioselective Organocatalysis: Catalysts, Reactions and Applications. 2013Wiley-VCHWeinheim

[3]. Loh CCJ, Enders D. Chem. Eur. J. 2012; 18:10212. [PubMed: 22696311] For recent examples, see: Binder JT, Crone B, Haug TT, Menz H, Kirsch SF. Org. Lett. 2008; 10:1025. [PubMed: 18232707] Han Z-Y, Xiao H, Chen X-H, Gong L-Z. J. Am. Chem. Soc. 2009; 131:9182. [PubMed: 19518048] Liu X-Y, Che C-M. Org. Lett. 2009; 11:4204. [PubMed: 19678678] Muratore ME, Holloway CA, Pilling AW, Storer RI, Trevitt G, Dixon DJ. J. Am. Chem. Soc. 2009; 131:10796. [PubMed: 19606900] Belot S, Vogt K, Besnard C, Krause N, Alexakis A. Angew. Chem. 2009; 121:9085. Zweifel T, Hollmann D, Prüger B, Nielsen M, Jørgensen KA. Tetrahedron: Asymmetry. 2010; 21:1624. Jensen KL, Franke PT, Arróniz C, Kobbelgaard S, Jørgensen KA. Chem. Eur. J. 2010; 16:1750. [PubMed: 20077548] Wang C, Han Z-Y, Luo H-W, Gong L-Z. Org. Lett. 2010; 12:2266. [PubMed: 20405953] Monge D, Jensen KL, Franke PT, Lykke L, Jørgensen KA. Chem. Eur. J. 2010; 16:9478. [PubMed: 20602371] Barber DM, Sanganee HJ, Dixon DJ. Org. Lett. 2012; 14:5290. [PubMed: 23039069] Chiarucci M, di Lillo M, Romaniello A, Cozzi PG, Cera G, Bandini M. Chem. Sci. 2012; 3:2859. Patil NT, Raut VS, Tella RB. Chem. Commun. 2013; 49:570. Wu H, He Y-P, Gong L-Z. Org. Lett. 2013; 15:460. [PubMed: 23312017] Gregory AW, Jakubec P, Turner P, Dixon DJ. Org. Lett. 2013; 15:4330. [PubMed: 23985045]

[4]. Loh CCJ, Badorrek J, Raabe G, Enders D. Chem. Eur. J. 2011; 17:13409. [PubMed: 22025408]

[5]. For selected asymmetric Michael additions of pyrroles, see: Paras NA, MacMillan DWC. J. Am. Chem. Soc. 2001; 123:4370. [PubMed: 11457218] Cao C-L, Zhou Y-Y, Sun X-L, Tang Y. Tetrahedron. 2008; 64:10676. Trost BM, Müller C. J. Am. Chem. Soc. 2008; 130:2438. [PubMed: 18237176] Sheng Y-F, Gu Q, Zhang A-J, You S-L. J. Org. Chem. 2009; 74:6899. [PubMed: 19639942] Yokoyama N, Arai T. Chem. Commun. 2009:3285. Hong L, Sun W, Liu C, Wang L, Wong K, Wang R. Chem. Eur. J. 2009; 15:11105. [PubMed: 19757430] Singh PK, Singh VK. Org. Lett. 2010; 12:80. [PubMed: 19947623] Huang Y, Suzuki S, Liu G, Tokunaga E, Shiro M, Shibata N. New J. Chem. 2011; 35:2614. Liu L, Ma H, Xiao Y, Du F, Qin Z, Li N, Fu B. Chem. Commun. 2012; 48:9281. Chauhan P, Chimni SS. RSC Adv. 2012; 2:6117.

[6]. Fürstner A. Angew. Chem. 2003; 115:3706. Angew. Chem. Int. Ed. 2003; 42:3582. Hoffmann H, Lindl T. Synthesis. 2003:1753. Balme G. Angew. Chem. 2004; 116:6396. Angew. Chem. Int. Ed. 2004; 43:6238. Jolicoeur B, Chapman EE, Thompson A, Lubell WD. Tetrahedron. 2006; 62:11531. Walsh CT, Garneau-Tsodikova S, Howard-Jones AR. Nat. Prod. Rep. 2006; 23:517. [PubMed: 16874387] Gupton JT. Heterocyclic Antitumor Antibiotics. 2006:53.SpringerHeidelberg

[7]. a) Jorapur YR, Lee CH, Chi DY. Org. Lett. 2005; 7:1231. [PubMed: 15787474] b) Blay G, Fernández I, Mun?oz MC, Pedro JR, Recuenco A, Vila C. J. Org. Chem. 2011; 76:6286. [PubMed: 21682323]

[8]. Nguyen TV, Hartmann JM, Enders D. Synthesis. 2012; 44:845.

[9]. a) Borsini E, Broggini G, Fasana A, Baldassarri C, Manzo AM, Perboni AD. Beilstein J. Org. Chem. 2011; 7:1468. [PubMed: 22238519] b) Modha SG, Kumar A, Vachhani DD, Sharma SK, Parmar VS, Van der Eycken EV. Chem. Commun. 2012; 48:10916.c) Kumar A, Vachhani DD, Modha SG, Sharma SK, Parmar VS, Van der Eycken EV. Eur. J. Org. Chem. 2013; 2013:2288.

[10]. Yang Y-Q, Zhao G. Chem. Eur. J. 2008; 14:10888. [PubMed: 19003833]

Europe PMC Funders Author Manuscripts

[11]. For selected reviews and protocols on cinchona-derived amines, see: Xu L-W, Luo J, Lu Y. Chem. Commun. 2009:1807. Marcelli T, Hiemstra H. Synthesis. 2010:1229. Cassani C, Martín-Rapún R, Arceo E, Bravo F, Melchiorre P. Nat. Protoc. 2013; 8:325. [PubMed: 23329005] Melchiorre P. Angew. Chem. Int. Ed. 2012; 51:9748. Angew. Chem. 2012; 124:9889.

[12]. Hack D, Enders D. Synthesis. 2013; 45:2904.

[13]. Duan H, Sengupta S, Petersen JL, Akhmedov NG, Shi X. J. Am. Chem. Soc. 2009; 131:12100. [PubMed: 19655739]

[14]. Nieto-Oberhuber C, López S, Echavarren AM. J. Am. Chem. Soc. 2005; 127:6178. [PubMed: 15853316]

[15]. Young PC, Green SLJ, Rosair GM, Lee A-L. Dalton Trans. 2013; 42:9645. [PubMed: 23676926]

[16]. From our observation, the TMS-protected product decomposed rapidly, whereas the terminal alkyne underwent a complicated rearrangement with loss of the stereocenter to an unidentified product.

[17]. CCDC-977585 (**17b**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[18]. England DB, Padwa A. Org. Lett. 2008; 10:3631. [PubMed: 18627172]

Europe PMC Funders Author Manuscripts

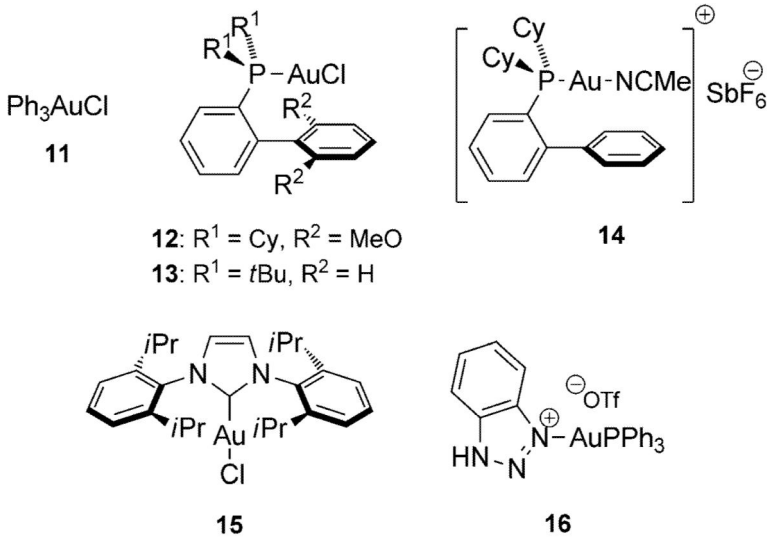


Figure 1.
Au^{I} catalysts employed for the cyclization.

Europe PMC Funders Author Manuscripts
Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

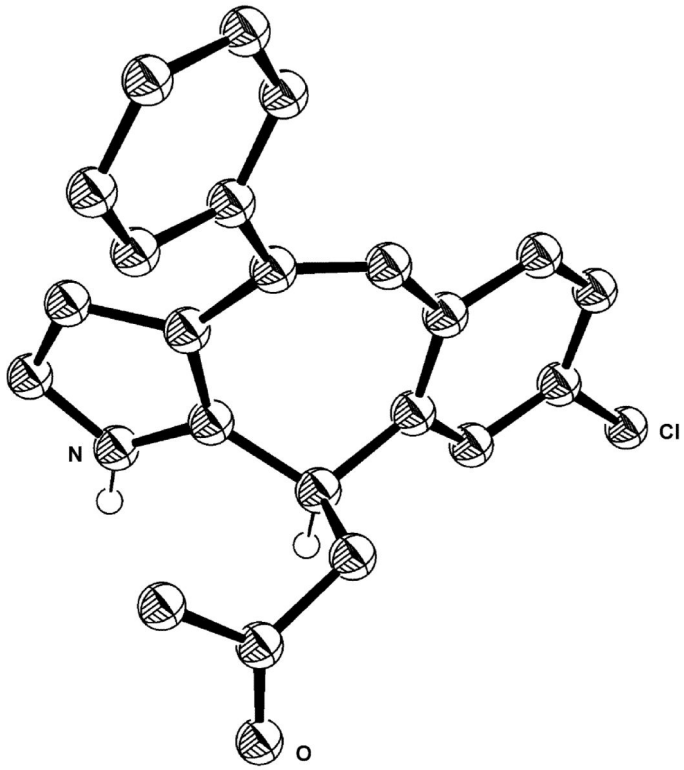
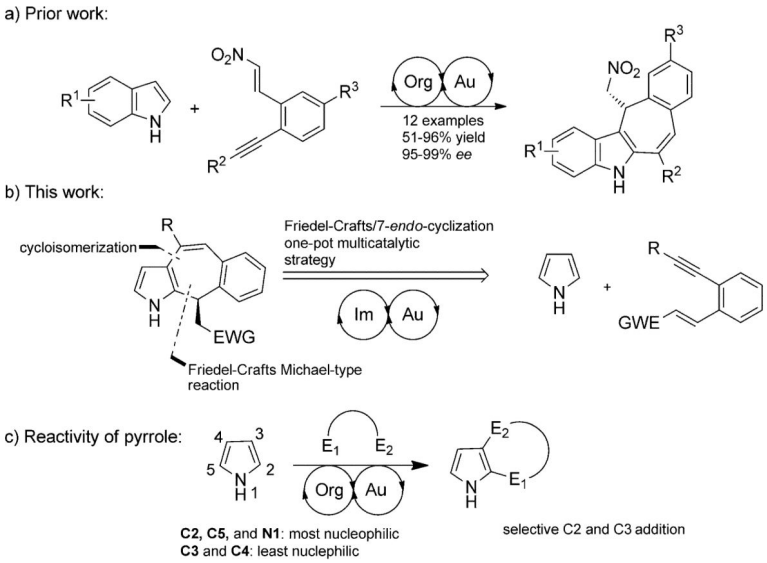


Figure 2.
X-ray crystal structure of (*R*)-**17 b**.

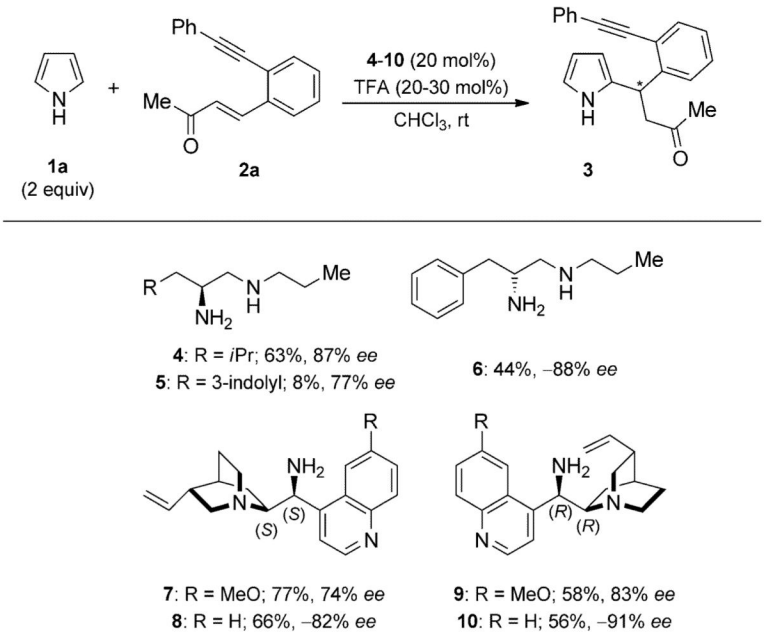


Scheme 1.

Strategy comparison between current work and our recently reported annulations of indoles.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

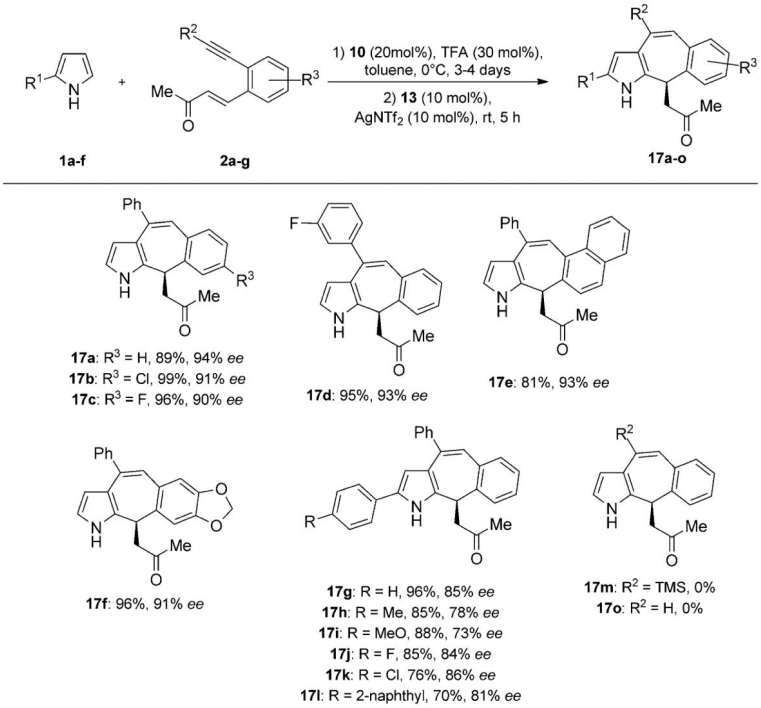


Scheme 2.

Catalyst screening for the Friedel–Crafts Michael-type reaction.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

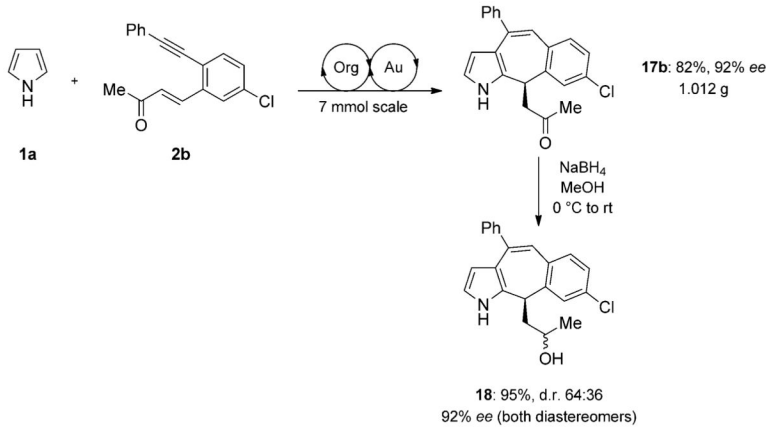


Scheme 3.

Scope of the sequential Michael addition/cyclization reaction.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

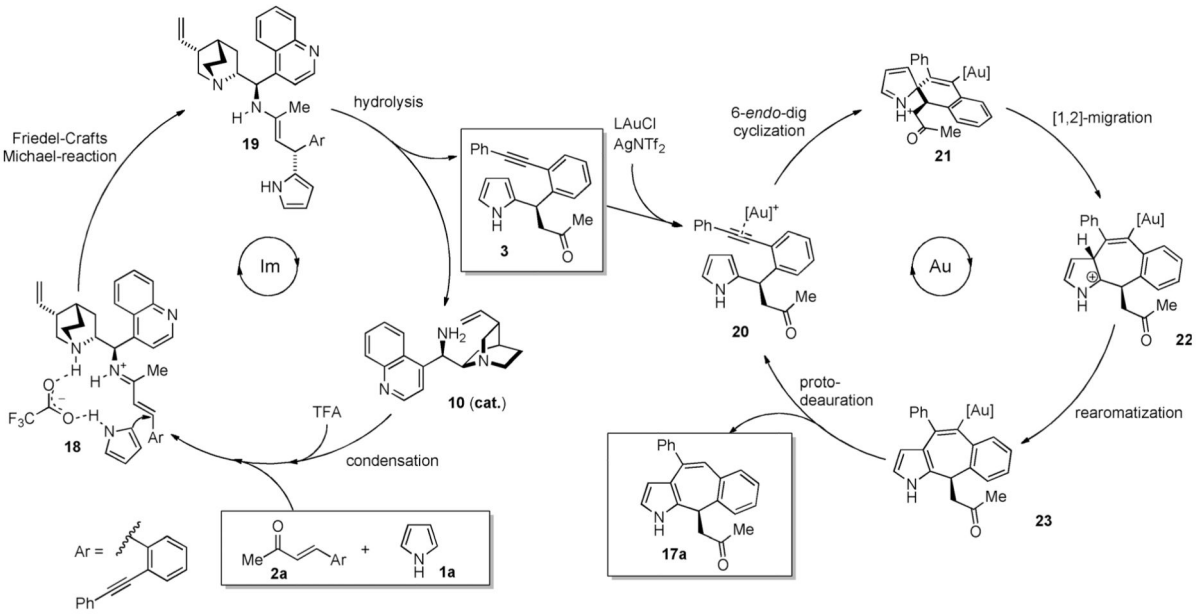


Scheme 4.

Large-scale synthesis of compound **17b** followed by reduction to the alcohol **18**.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts



Scheme 5.
Plausible reaction mechanism.

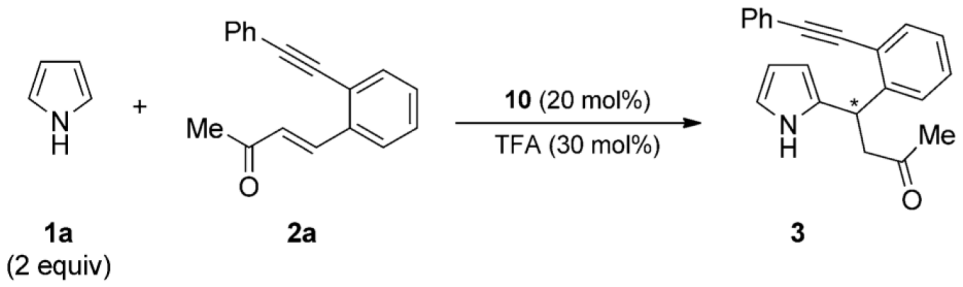
Europe PMC Funders Author Manuscripts
Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Table 1

Optimization of the reaction conditions for the Friedel–Crafts Michael-type reaction.[a]



Entry	Solvent [mL]	*t* [h]	Yield [%][b]	*ee* [%][c]
1	$CHCl_3$ (1.5)	16	56	91
2	CH_2Cl_2 (1.5)	15	59	87
3	toluene (1.5)	21	60	88
4	PhCl (1.5)	21	61	87
5	toluene (3.0)	21	70	91
6	CH_2Cl_2(3.0)	24	68	91
7[d]	$CHCl_3$ (3.0)	65	89	93
8[d]	toluene (3.0)	65	95	93

[a] General reaction conditions: **2a** (0.5 mmol), pyrrole **1a** (1.0 mmol), **10** (20 mol %), TFA (30 mol%), rt.

[b] Yield of isolated **3**.

[c] Determined by HPLC analysis on a chiral stationary phase.

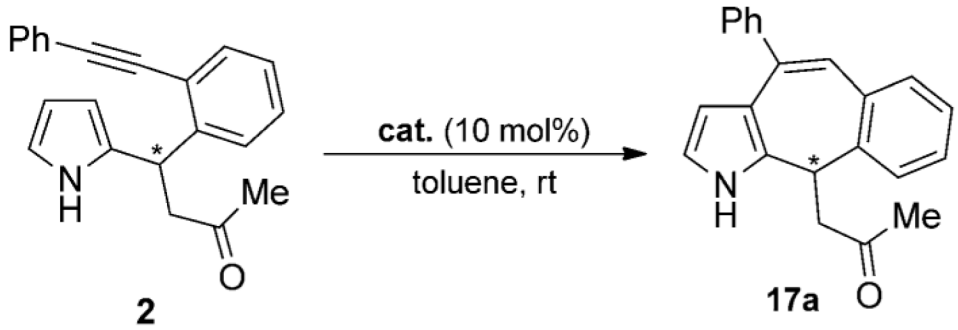
[d] The reaction was performed at 0 °C.

Europe PMC Funders Author Manuscripts

Europe PMC Funders Author Manuscripts

Table 2

Optimization studies for the gold-catalyzed cyclization.[a]



Entry	Catalyst	Additive	*t* [h]	Yield [%][b]
1	**11**/$AgNTf_2$	–	0.5	89
2	**12**/$AgNTf_2$	–	0.5	89
3	**13**/$AgNTf_2$	–	0.5	99
4	**14**	–	0.5	92
5	**15**/$AgNTf_2$	–	0.5	96
6	**16**	–	30	76
7	$AgNTf_2$	–	> 24	–
8	CuI	–	> 24	–
9	$Cu(OTf)_2$	–	> 24	–
10	$PtCl_2$	–	> 24	–
11	–	30 mol % TFA	> 24	–
12	**13**/$AgNTf_2$	20 mol % 10	> 24	–
13	**13**/$AgNTf_2$	20 mol % 10, 30 mol % TFA	0.5	96

[a]General reaction conditions: **2** (0.3 mmol), $AgNTf_2$ (10 mol%), toluene (1.7 mL), rt.

[b]Yield of isolated **17a**.