



Synthesis of 1,2,5- and 1,2,3,5-substituted pyrroles from substituted aziridines via Ag(I)-catalyzed intramolecular cyclization

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ABSTRACT

An efficient synthesis of 1,2,5- and 1,2,3,5-substituted pyrroles has been achieved from the sequential reactions including a ring-opening of 1-(aziridin-2-yl)propargylic alcohols by various nucleophiles under mild condition followed by an intramolecular cyclization using Ag(I) catalyst.

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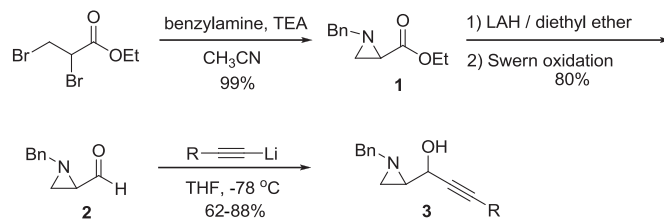
1. Introduction

Pyrroles and substituted pyrroles can be found in various natural products¹ and the importance of pyrrole derivatives is also found in pharmacologically² and biologically³ active substances. In addition, oligopyrroles are widely used in material sciences⁴ and the various synthetic methods have recently been reported.⁵ Therefore, the development of new preparative methods of substituted pyrroles attracts attention from both academia and industry.

Among the various synthetic methods, the notable classical methods are Knorr pyrrole synthesis,⁶ Hantzsch pyrrole synthesis,⁷ and Paal–Knorr synthesis.⁸ However, classical methods suffer from harsh reaction conditions and they are not suitable for the synthesis of functional group incorporated pyrroles. Therefore, milder reaction conditions have been developed using metal catalysts via intramolecular cyclization.⁹ Herein, we report a new strategy for the efficient preparation of 1,2,5- and 1,2,3,5-substituted pyrroles from the sequential reactions including a ring-opening of 1-(aziridin-2-yl)propargylic alcohols by various nucleophiles followed by subsequent metal catalyzed intramolecular cyclization of the nitrogen.

2. Result and discussion

We previously reported the preparation and the elaboration of enantiomerically pure aziridine-2-carboxylates.¹⁰ However, we used racemic aziridine-2-carboxylates in the pyrrole synthesis because we lose all the stereochemical information in the course of reaction. Therefore, we prepared racemic *N*-benzylaziridine-2-carboxaldehyde **2** in a similar manner from readily available starting materials.¹¹ The racemic aldehyde **2** was reacted with various lithium acetylides to provide the corresponding racemic 1-(aziridin-2-yl)propargylic alcohols **3** in high yields (Scheme 1).

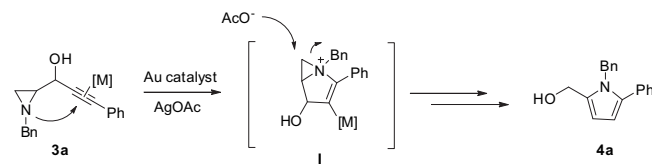


Scheme 1. Preparation of propargylic alcohol **3**.

Since the aziridine nitrogen is quite basic and also nucleophilic, we expected the intramolecular cyclization would be initiated by the activation of the acetylenic bond by Au(I) and AgOAc. When the Au(I) catalyst activates the acetylenic bond by forming a complex,

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the aziridinium intermediate **I** would be formed by the intramolecular cyclization of the nucleophilic aziridine nitrogen. Then, regioselective ring-opening reaction with the cleavage of the aziridine C(3)–N bond would proceed by an acetate, which was liberated from silver acetate to provide 2-hydroxymethyl substituted pyrrole after removing water to form pyrrole and hydrolysis of the acetate (Scheme 2).



Scheme 2. Direct pyrrole forming reaction.

However, the yield of the product was low (15–40%) despite of using a variety of Au catalysts and solvents possibly due to the formation of the highly strained intermediate **I** (Scheme 2 and Table 1, entries 1–5).

Table 1
The results of pyrrole formation

Entry ^a	Catalyst ^b	Solvent	T (°C)	t (h) ^d	Yield (%)
1	AuCl ₃	CH ₃ CN	50	11	40
2	AuCl ₃	THF	80	18	40
3	AuCl ₃	DCE	70	7	15
4	AuCl ₃	MeOH	50	8	33
5	AuCl ₃	DCM	40	8	35
6	AuCl ₃	DCM	rt	1	73
7	(PPh ₃)AuCl	DCM	rt	0.5	85
8	(PPh ₃)AuCl	DCM	rt	1	No reaction
9	CuI	DCM	rt	5	60
10	AgCl	DCM	rt	1	No reaction
11	AgI	DCM	rt	1	No reaction
12	AgOTf ^c	DCM	rt	0.5	47
13	AgOAc	DCM	rt	0.5	89

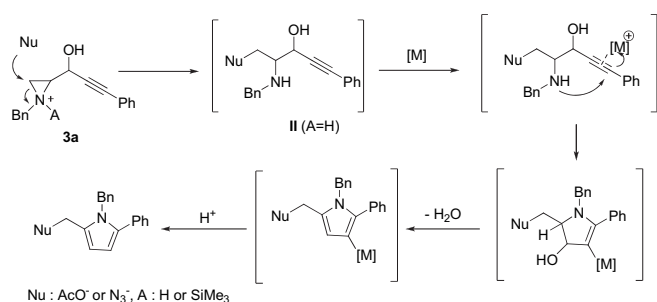
^a Conditions : (1) metal catalyst with 3.0 equiv of AgOAc (entry 1–5), (2) metal catalyst with 5 mol % of AgOAc (entry 6–7), (3) Metal catalyst was added after ring-opening by AcOH (entry 6–13).

^b Metal catalyst (5 mol %).

^c After 3 h, the crude product was decomposed.

^d The cyclization time was monitored by TLC after ring-opening (entry 6–13).

Therefore, we changed the reaction sequence that the aziridine ring-opening reaction was preceded prior to pyrrole formation by the treatment of the substituted aziridine with AcOH. Aziridine ring-opening reaction with AcOH yielded the ring-opening product **II** (A=H, Nu=⁻OAc) and the crude reaction mixture was treated with the Au(I) and AgOAc for the intramolecular cyclization (Scheme 3). This sequence proceeded in milder condition and also provided higher yield of the substituted pyrroles. In search of more



Scheme 3. Proposed mechanism of pyrrole synthesis.

effective conditions, we screened various metal catalysts and solvents. Among them, (PPh₃)AuCl and CH₂Cl₂ gave comparably good result, which produced **4a** in 85% yield in 0.5 h (Table 1, entries 6–9).

Also, we found that the intramolecular cyclization was successfully achieved only with 5 mol % of AgOAc without Au(I) catalyst in high yields (entry 13). Therefore, we screened various silver catalysts to find the optimized condition that provides good yields. As a result, AgOAc and AgOTf turned out to be the best catalyst, which reacted rapidly in 30 min with good chemical yields. However, with AgOTf, the crude product was decomposed after 3 h at room temperature (Table 1, entries 10–13).

Previous articles regarding intramolecular pyrrole ring formation describe that the reactions require both Au(I) and Ag(I) metals and high reaction temperature to make the reaction proceed. When they used only Ag(I) in the cyclization reaction, they obtained either no reaction or only trace amount of the cyclization product.¹² We applied Ag(I) only catalytic system to various propargylic alcohols **3a–i** to compare the results with those of Au(I)/Ag(I) co-catalytic system.

The optimized reaction conditions were applied to various 1-aziridin-2-yl-propargylic alcohols **3a–i**, which were prepared via alkylation of the aziridine-2-carboxaldehyde with various terminal acetylenes in 62–88% yields, to obtain the substituted pyrroles **4a–i**. The reaction provided good yields in all cases even at room temperature whether the substituent was an electron donating group **4b** and **c**, electron withdrawing group **4d** and **e**, as well as aromatic rings **4f–i** (Table 2). Therefore, we concluded that the Ag(I) catalyst system would be also efficient compared with Au(I)/Ag(I) co-catalyst system.

Table 2
Synthesis of 2-hydroxymethyl substituted pyrroles using Au(I)/Ag(I) and Ag(I) catalysts

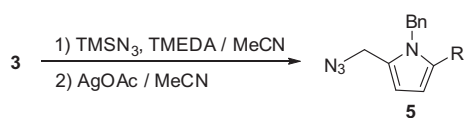
Entry	3	R	Yield of 4 (%)
1	3a	Phenyl	85 ^a , 89 ^b (4a)
2	3b	<i>o</i> -Methoxyphenyl	75 ^a , 81 ^b (4b)
3	3c	<i>o</i> -Tolyl	82 ^a , 70 ^b (4c)
4	3d	<i>p</i> -(Trifluoromethyl)phenyl	80 ^a , 82 ^b (4d)
5	3e	3,5-Difluorophenyl	88 ^a , 75 ^b (4e)
6	3f	Thiophen-3-yl	74 ^a , 75 ^b (4f)
7	3g	Pyridin-2-yl	77 ^a , 69 ^b (4g)
8	3h	1-Methyl-1 <i>H</i> -imidazol-5-yl	60 ^a , 67 ^b (4h)
9	3i	Phenanthren-9-yl	80 ^a , 71 ^b (4i)

^a Using Au(I)/Ag(I) catalyst.

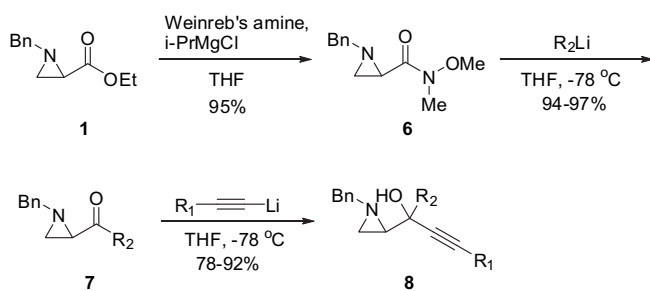
^b Using Ag(I) catalyst only.

We also used TMSN₃ for the aziridine ring-opening reaction to obtain azidomethyl substituted pyrrole precursors. The various substituted propargylic alcohols **3a–f** and **3j** were treated with TMEDA and TMSN₃ as a nucleophile to provide the aziridine ring-opening products¹³ and the ring-opened crude products were directly treated with Ag(I) catalyst for the intramolecular cyclization to provide 2-azidomethyl substituted pyrroles **5a–f** and **5j** in high yields (Table 3).

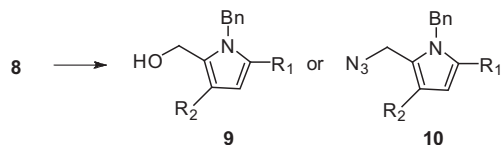
We also prepared various substituted tertiary propargylic alcohols **8** to introduce another substituent at the 3-position of pyrroles. The reaction of **1** with Weinreb's amine hydrochloride and isopropyl magnesium chloride in THF provided the corresponding Weinreb's amide **6** in high yield.¹⁴ Ketone **7** was easily prepared by addition of suitable organometallic reagents (PhLi or *n*-BuLi in Scheme 4) to the Weinreb's amide **6**. Also, propargylic alcohols **8** were prepared by addition of the corresponding acetylides to the ketone **7** (Scheme 4).

Table 3
Synthesis of 2-azidomethyl substituted pyrroles

Entry	3	R	Yield of 5 (%)
1	3a	Phenyl	80 (5a)
2	3b	<i>o</i> -Methoxyphenyl	92 (5b)
3	3c	<i>o</i> -Tolyl	90 (5c)
4	3d	<i>p</i> -(Trifluoromethyl)phenyl	79 (5d)
5	3e	3,5-Difluorophenyl	83 (5e)
6	3f	Thiophen-3-yl	80 (5f)
7	3j	<i>p</i> -Methoxyphenyl	84 (5j)

R₁: aryl, R₂: phenyl or *n*-butyl**Scheme 4.** Preparation of tertiary propargylic alcohol **8**.

As we described above, when the tertiary alcohols were treated with AcOH we did not obtain the corresponding ring-opening product in good yield probably due to the formation of the doubly stable carbocation by benzylic and propargylic, which complicated the reaction. Therefore, the treatment of the crude ring-opening product with AgOAc resulted in low yield of the expected 3-hydroxymethyl substituted pyrroles. On the other hand, when we changed the phenyl with *n*-butyl to form the corresponding propargyl tertiary alcohol, the same ring-opening reaction using AcOH resulted in the complete conversion to the ring-opening product to provide the desired 3-hydroxymethyl pyrrole **9e** after hydrolysis (Table 4) in high yield.

Table 4
Synthesis of 1,2,3,5-substituted pyrrolesR₁: aryl, R₂: phenyl or *n*-butyl

Entry	8	R ₁	R ₂	Yield of 9, 10 (%)
1	8a	Phenyl	Phenyl	60 (9a) 93 (10a)
2	8b	<i>o</i> -Methoxyphenyl	Phenyl	53 (9b) 91 (10b)
3	8c	Pyridin-2-yl	Phenyl	50 (9c) 85 (10c)
4	8d	<i>p</i> -Methoxyphenyl	Phenyl	92 (10d)
5	8e	Phenyl	<i>n</i> -Butyl	84 (9e) 90 (10e)

However, the treatment of the tertiary alcohols with TMSN₃ as the nucleophile in neutral condition provided the ring-opening product in high yield in all cases and the in situ treatment of the crude product with AgOAc gave 1,2,3,5-substituted 2-azidomethyl pyrroles in high yields (Table 4).

3. Conclusion

In conclusion, we developed an efficient methodology for the synthesis of 1,2,5- and 1,2,3,5-substituted pyrroles, which have 2-hydroxymethyl or 2-azidomethyl substituent from various 1-aziridin-2-yl-propargylic alcohols using AgOAc as the catalyst for the intramolecular cyclization. The advantages of this method include facile reaction in one-pot without isolation of the intermediates and the production of variously substituted pyrroles in good yields at low temperature. Also, the reactions use Ag(I) catalyst and we can avoid using Au catalysts. We are currently working on this new metal-catalyzed intramolecular cyclization process and its application for the synthesis of pyrrole containing heterocycles.

4. Experimental section

4.1. General method

All reactions were carried out under an atmosphere of nitrogen in oven-dried glasswares with magnetic stirring. Air sensitive reagents and solutions were transferred via syringe and were introduced to the apparatus through rubber septa. Tetrahydrofuran (THF) and diethyl ether (Et₂O) were distilled from sodium/benzophenone ketyl. Dichloromethane was distilled from calcium hydride. Reactions were monitored by thin layer chromatography (TLC) with 0.25 mm E. Merck pre-coated silica gel plates (60 F₂₅₄). Visualization was accomplished with either UV light, or by immersion in solutions of ninhydrin, *p*-anisaldehyde, or phosphomolybdic acid (PMA) followed by heating on a hot plate for about 10 s. Purification of reaction products was carried out by flash chromatography using Kieselgel 60 Art 9385 (230–400 mesh). ¹H NMR and ¹³C NMR spectra were obtained using a Varian Vnmr-400 (400 MHz for ¹H, and 100 MHz for ¹³C), or a Varian Inova-500 (500 MHz for ¹H, and 125 MHz for ¹³C) spectrometer. Chemical shifts are reported relative to chloroform (δ=7.26) for ¹H NMR and chloroform (δ=77.2) for ¹³C NMR. Data are reported as (br=broad, s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet.) Coupling constants are given in Hertz. Ambiguous assignments were resolved on the basis of standard one dimensional proton decoupling experiments. Elemental analyses were performed by the Organic Chemistry Research Center at Sogang University using a Carlo Erba EA 1180 elemental analyzer. High resolution mass spectra were recorded on a 4.7 T IonSpec ESI-FTMS or a Micromass LCT ESI-TOF mass spectrometer. IR spectra were recorded neat on Nicolet Avatar 330 FT-IR. Melting points were recorded on an Electrothermal-9100 and are uncorrected. All commercially available compounds were used as received unless stated otherwise.

4.2. General procedure for the Ag(I)-catalyzed synthesis of 2-hydroxymethyl pyrrole **4**

To a solution of propargylic alcohol **3** (0.30 mmol) in CH₂Cl₂ (1.0 mL) was added AcOH (0.90 mmol, 50 μL). After stirring for an additional 12 h, the mixture was treated with AgOAc (5.0 mol %, 2.5 mg) and the progress of the reaction was monitored by TLC. After 30 min, the mixture was filtered through a pad of Celite, the solvent was removed under reduced pressure. The crude mixture was treated with KOH (0.60 mmol, 33 mg) in EtOH (1.5 mL). The resulting mixture was stirred for 30 min and then quenched with saturated aqueous ammonium chloride solution. The aqueous layer

was extracted with CH_2Cl_2 (5 mL \times 4). The combined extracts were dried over anhydrous magnesium sulfate and filtered. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using mixture of *n*-hexane and EtOAc as an eluent to give the hydroxymethyl pyrrole products **4**.

4.2.1. (1-Benzyl-5-phenyl-1H-pyrrol-2-yl)methanol (4a). ^1H NMR (500 MHz, CDCl_3): δ 7.36–7.20(m, 8H), 6.91(d, $J=7.5$ Hz, 2H), 6.27(d, $J=3.5$ Hz, 1H), 6.24(d, $J=3.5$ Hz, 1H), 5.31(s, 2H), 4.45(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.3, 137.0, 133.4, 133.2, 129.1, 128.9, 128.6, 127.4, 127.3, 125.7, 109.9, 108.4, 57.5, 47.8; FT-IR: ν 3360 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{18}\text{H}_{17}\text{NO}$ $[\text{M}+\text{Na}]^+$ 286.1208, found 286.1206. TLC R_f (EtOAc/Hexane 3:7)=0.31, yellow oil.

4.2.2. (1-Benzyl-5-(2-methoxyphenyl)-1H-pyrrol-2-yl)methanol (4b). ^1H NMR (500 MHz, CDCl_3): δ 7.36–7.13(m, 5H), 6.92–6.87(m, 4H), 6.28(d, $J=3.0$ Hz, 1H), 6.14(d, $J=3.5$ Hz, 1H), 5.10(s, 2H), 4.45(s, 2H), 3.68(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.5, 139.3, 133.2, 132.9, 132.6, 129.6, 128.6, 127.0, 126.2, 122.5, 120.7, 110.8, 109.7, 108.6, 57.7, 55.4, 48.3; FT-IR: ν 3380 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{19}\text{H}_{19}\text{NO}_2$ $[\text{M}+\text{Na}]^+$ 316.1314, found 286.1312. TLC R_f (EtOAc/Hexane 3:7)=0.13, yellow oil.

4.2.3. (1-Benzyl-5-*o*-tolyl-1H-pyrrol-2-yl)methanol (4c). ^1H NMR (500 MHz, CDCl_3): δ 7.25–7.10(m, 7H), 6.80(d, $J=7.0$ Hz, 2H), 6.28(d, $J=3.5$ Hz, 1H), 6.08(d, $J=3.0$ Hz), 5.05(s, 2H), 4.50(d, $J=4.0$ Hz, 2H), 2.13(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.0, 138.4, 135.4, 133.1, 132.1, 131.4, 130.2, 128.7, 128.3, 127.2, 126.2, 125.6, 109.3, 108.3, 57.6, 47.8, 20.3; FT-IR: ν 3337 cm^{-1} (br, OH); mp 51–53 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{19}\text{H}_{19}\text{NO}$ $[\text{M}+\text{Na}]^+$ 300.1365, found 286.1367. TLC R_f (EtOAc/Hexane 3:7)=0.38, yellow solid.

4.2.4. (1-Benzyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrrol-2-yl)methanol (4d). ^1H NMR (500 MHz, CDCl_3): δ 7.54(d, $J=8.5$ Hz, 2H), 7.39(d, $J=8.0$ Hz, 2H), 7.30–7.21(m, 3H), 6.90(d, $J=7.5$ Hz, 2H), 6.31–6.29(m, 2H), 5.31(s, 2H), 4.46(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.8, 136.82, 136.81, 135.3, 134.3, 129.0, 128.9, 125.61, 125.58, 125.56, 125.53, 110.2, 109.5, 57.3, 47.9; FT-IR: ν 3339 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{19}\text{H}_{16}\text{F}_3\text{NO}$ $[\text{M}+\text{Na}]^+$ 354.1082, found 354.1084. TLC R_f (EtOAc/Hexane 3:7)=0.23, yellow oil.

4.2.5. (1-Benzyl-5-(3,5-difluorophenyl)-1H-pyrrol-2-yl)methanol (4e). ^1H NMR (500 MHz, CDCl_3): δ 7.55–7.45(m, 1H), 7.30–7.21(m, 2H), 6.88(d, $J=7.5$ Hz, 2H), 6.83–6.80(m, 2H), 6.71–6.67(m, 1H), 6.27(s, 2H), 5.33(s, 2H), 4.47(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.0, 163.9, 162.1, 162.0, 138.6, 136.4, 136.34, 136.26, 134.5, 134.4, 134.3, 132.1, 129.4, 129.4, 129.1, 127.6, 125.6, 111.64, 111.59, 111.48, 111.43, 110.1, 109.6, 102.8, 102.6, 102.4, 57.4, 47.9; FT-IR: ν 3395 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{18}\text{H}_{15}\text{F}_2\text{NO}$ $[\text{M}+\text{Na}]^+$ 322.1020, found 322.1022. TLC R_f (EtOAc/Hexane 3:7)=0.33, yellow oil.

4.2.6. (1-Benzyl-5-(thiophen-3-yl)-1H-pyrrol-2-yl)methanol (4f). ^1H NMR (500 MHz, CDCl_3): δ 8.49–8.48(m, 1H), 7.60(td, $J=8$ Hz, 1.5 Hz, 1H), 7.51–7.36(m, 2H), 7.27–7.13(m, 3H), 7.05–7.02(m, 1H), 6.92(d, $J=7.5$ Hz, 2H), 6.55(d, $J=4$ Hz, 1H), 6.26(d, $J=4$ Hz, 1H), 5.94(s, 2H), 4.52(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.7, 148.9, 139.8, 136.6, 135.9, 134.2, 128.6, 126.9, 126.1, 122.3, 120.9, 110.6, 109.9, 57.4, 48.4; FT-IR: ν 3350 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$ $[\text{M}+\text{Na}]^+$ 287.1161, found 287.1160. TLC R_f (EtOAc/Hexane 3:7)=0.33, yellow oil.

4.2.7. (1-Benzyl-5-(pyridin-2-yl)-1H-pyrrol-2-yl)methanol (4g). ^1H NMR (500 MHz, CDCl_3): δ 8.49–8.48(m, 1H), 7.60(td, $J=8$ Hz, 1.5 Hz, 1H), 7.51–7.36(m, 2H), 7.27–7.13(m, 3H), 7.05–7.02(m, 1H), 6.92(d, $J=7.5$ Hz, 2H), 6.55(d, $J=4$ Hz, 1H), 6.26(d, $J=4$ Hz, 1H), 5.94(s, 2H),

4.52(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.7, 148.9, 139.8, 136.6, 135.9, 134.2, 128.6, 126.9, 126.1, 122.3, 120.9, 110.6, 109.9, 57.4, 48.4; FT-IR: ν 3304 cm^{-1} (br, OH); mp 73–75 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{17}\text{H}_{16}\text{N}_2\text{O}$ $[\text{M}+\text{Na}]^+$ 287.1161, found 287.1160. TLC R_f (EtOAc/Hexane 3:7)=0.17, yellow solid.

4.2.8. (1-Benzyl-5-(1-methyl-1H-imidazol-5-yl)-1H-pyrrol-2-yl)methanol (4h). ^1H NMR (500 MHz, CDCl_3): δ 7.36(s, 1H), 7.23–7.16(m, 3H), 6.83(s, 1H), 6.79(d, $J=9.0$ Hz, 2H), 6.27(d, $J=4$ Hz, 1H), 6.19(d, $J=4.0$ Hz, 1H), 5.16(s, 2H), 4.56(s, 2H), 3.19(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.7, 138.4, 134.2, 129.7, 128.7, 127.3, 126.1, 124.6, 122.1, 111.2, 109.2, 56.9, 47.7, 31.7; FT-IR: ν 3336 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{16}\text{H}_{17}\text{N}_3\text{O}$ $[\text{M}+\text{Na}]^+$ 290.1270, found 290.1271. TLC R_f (MeOH/EtOAc 1:9)=0.31, yellow oil.

4.2.9. (1-Benzyl-5-(phenanthren-9-yl)-1H-pyrrol-2-yl)methanol (4i). ^1H NMR (500 MHz, CDCl_3): δ 8.70(d, $J=8.0$ Hz, 1H), 8.65(d, $J=8.5$ Hz, 1H), 7.81(d, $J=8.0$ Hz, 1H), 7.73(d, $J=8.0$ Hz, 1H), 7.65–7.43(m, 5H), 7.14–7.07(m, 3H), 6.77(d, $J=7.5$ Hz, 2H), 6.40(d, $J=3.5$ Hz, 1H), 6.32(d, $J=3.0$ Hz, 1H), 5.21(br, 1H), 4.92(br, 1H), 4.56(br, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.0, 134.2, 132.8, 132.4, 131.4, 130.6, 130.5, 130.3, 129.6, 129.0, 128.7, 127.2, 127.1, 127.0, 126.92, 126.89, 126.76, 126.0, 122.9, 122.6, 109.9, 109.7, 57.6, 48.3; FT-IR: ν 3356 cm^{-1} (br, OH); mp 53–55 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{26}\text{H}_{21}\text{NO}$ $[\text{M}+\text{Na}]^+$ 386.1521, found 386.1522. TLC R_f (EtOAc/Hexane 3:7)=0.31, yellow solid.

4.3. General procedure for the Ag(I)-catalyzed synthesis of 2-azidomethyl pyrroles **5**

To a solution of propargylic alcohol **3** (0.3 mmol) in acetonitrile (1.2 mL) were added azidotrimethylsilane (0.39 mmol, 50 μL) and TMEDA (20 mol %, 9.1 μL). The mixture was stirred at room temperature and the progress of the reaction was monitored by TLC. After consumption of the starting material, the mixture was treated with AgOAc (5 mol %, 2.5 mg). The resulting mixture was stirred for 30 min and then quenched with water. The aqueous layer was extracted with CH_2Cl_2 (5 mL \times 4). The combined extracts were dried over anhydrous magnesium sulfate and filtered. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel using mixture of *n*-hexane and EtOAc as an eluent to give the azidomethyl pyrrole products **5**.

4.3.1. 2-(Azidomethyl)-1-benzyl-5-phenyl-1H-pyrrole (5a). ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.22(m, 8H), 6.91(d, $J=7.5$ Hz, 2H), 6.35(d, $J=3.0$ Hz, 1H), 6.27(d, $J=3.0$ Hz, 1H), 5.23(s, 2H), 4.14(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.7, 133.1, 129.05, 128.98, 128.6, 127.5, 127.4, 127.2, 125.6, 111.4, 108.5, 47.9, 47.4; FT-IR: ν 2102 cm^{-1} (N_3); HRMS m/z calcd for $\text{C}_{18}\text{H}_{16}\text{N}_4$ $[\text{M}+\text{Na}]^+$ 311.1273, found 311.1275. TLC R_f (EtOAc/Hexane 3:7)=0.69, yellow oil.

4.3.2. 2-(Azidomethyl)-1-benzyl-5-(2-methoxyphenyl)-1H-pyrrole (5b). ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.15(m, 5H), 6.94–6.86(m, 4H), 6.35(d, $J=3.5$ Hz, 1H), 6.16(d, $J=3.5$ Hz, 1H), 5.03(s, 2H), 4.15(s, 2H), 3.67(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.5, 138.8, 132.9, 129.8, 128.6, 127.1, 126.6, 126.1, 122.3, 120.8, 111.2, 111.0, 108.7, 55.4, 48.4, 47.5; FT-IR: ν 2097 cm^{-1} (N_3); mp 98–100 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}$ $[\text{M}+\text{Na}]^+$ 341.1379, found 341.1376. TLC R_f (EtOAc/Hexane 3:7)=0.68, white solid.

4.3.3. 2-(Azidomethyl)-1-benzyl-5-*o*-tolyl-1H-pyrrole (5c). ^1H NMR (500 MHz, CDCl_3): δ 7.26–7.10(m, 7H), 6.78(d, $J=7.5$ Hz, 2H), 6.35(d, $J=3.5$ Hz, 1H), 6.11(d, $J=3.5$ Hz, 1H), 4.96(s, 2H), 4.17(s, 2H), 2.14(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.5, 138.4, 136.1, 132.8, 131.4, 130.2, 128.7, 128.5, 127.4, 126.0, 125.9, 125.7, 111.2, 108.4, 47.8, 47.4;

FT-IR: ν 2103 cm^{-1} (N_3); HRMS m/z calcd for $\text{C}_{19}\text{H}_{18}\text{N}_4$ [$\text{M}+\text{Na}$] $^+$ 325.1430, found 325.1430. TLC R_f (EtOAc/Hexane 1:9)=0.52, yellow oil.

4.3.4. 2-(Azidomethyl)-1-benzyl-5-(4-(trifluoromethyl)phenyl)-1H-pyrrole (**5d**). ^1H NMR (500 MHz, CDCl_3): δ 7.57(d, $J=8.0$ Hz, 2H), 7.41(d, $J=8.0$, 2H), 7.33–7.25(m, 3H), 6.90(d, $J=7$ Hz, 2H), 6.38(d, $J=3.5$ Hz, 1H), 6.34(d, $J=3.5$ Hz, 1H), 5.24(s, 2H), 4.17(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.7, 136.36, 135.9, 129.32, 129.0, 128.4, 127.7, 125.7, 125.6, 125.5, 111.7, 109.7, 48.0, 47.2; FT-IR: ν 2105 cm^{-1} (N_3); mp 72–73 $^\circ\text{C}$; Anal. Calcd for $\text{C}_{19}\text{H}_{15}\text{F}_3\text{N}_4$: C 64.04, H 4.24, F 15.99, N 15.72. Found: C 64.16, H 4.34, N 15.54%. TLC R_f (EtOAc/Hexane 2:8)=0.76, yellow solid.

4.3.5. 2-(Azidomethyl)-1-benzyl-5-(3,5-difluorophenyl)-1H-pyrrole (**5e**). ^1H NMR (500 MHz, CDCl_3): δ 7.32–7.24(m, 3H), 6.88–6.80(m, 4H), 6.73–6.69(m, 1H), 6.35(d, $J=3.5$ Hz, 1H), 6.31(d, $J=3.5$ Hz, 1H), 5.25(s, 2H), 4.15(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 164.1, 164.0, 162.1, 162.0, 138.1, 136.2, 136.1, 136.0, 135.0, 129.2, 128.6, 127.8, 125.5, 111.71, 111.67, 111.6, 111.5, 109.8, 103.0, 102.8, 102.6, 48.0, 47.1; FT-IR: ν 2108 cm^{-1} (N_3); mp 74–76 $^\circ\text{C}$; Anal. Calcd for $\text{C}_{18}\text{H}_{14}\text{F}_2\text{N}_4$: C 66.66, H 4.35, F 11.72, N 17.27. Found: C 66.60, H 4.28, N 17.59%. TLC R_f (EtOAc/Hexane 3:7)=0.70, white solid.

4.3.6. 2-(Azidomethyl)-1-benzyl-5-(thiophen-3-yl)-1H-pyrrole (**5f**). ^1H NMR (500 MHz, CDCl_3): δ 7.33–7.23(m, 4H), 7.06–7.03(m, 2H), 6.93(d, $J=7.5$ Hz, 2H), 6.33(d, $J=3.0$ Hz, 1H), 6.30(d, $J=3.0$ Hz, 1H), 5.26(s, 2H), 4.14(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.6, 133.4, 132.2, 129.1, 128.4, 127.5, 126.9, 125.8, 125.6, 121.9, 111.2, 108.4, 47.9, 47.2; FT-IR: ν 2100 cm^{-1} (N_3); Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{N}_4\text{S}$: C 65.28, H 4.79, N 19.03, S 10.89. Found: C 65.30, H 4.71, N 19.24, S 10.76%. TLC R_f (EtOAc/Hexane 3:7)=0.75, yellow oil.

4.3.7. 2-(Azidomethyl)-1-benzyl-5-(4-methoxyphenyl)-1H-pyrrole (**5j**). ^1H NMR (400 MHz, CDCl_3): δ 7.31–7.20(m, 5H), 6.90(d, $J=7.2$ Hz, 2H), 6.85(d, $J=8.4$ Hz, 2H), 6.32(d, $J=3.6$ Hz, 1H), 6.20(d, $J=3.6$ Hz, 1H), 5.19(s, 2H), 4.14(s, 2H), 3.79(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 159.2, 138.8, 137.2, 130.4, 129.0, 127.4, 126.6, 125.6, 114.0, 111.2, 108.0, 55.4, 47.8, 47.4; FT-IR: ν 2101 cm^{-1} (N_3); Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{N}_4\text{O}$: C 71.68, H 5.70, N 17.60, O 5.03. Found: C 71.53, H 5.56, N 17.78%. TLC R_f (EtOAc/Hexane 3:7)=0.68, yellow oil.

4.4. General procedure for the Ag(I)-catalyzed synthesis of 2-hydroxymethyl pyrroles 9

General procedure for the Ag(I)-catalyzed synthesis of 2-hydroxymethyl pyrroles **4** was followed using tertiary propargylic alcohols **8**.

4.4.1. (1-Benzyl-3,5-diphenyl-1H-pyrrol-2-yl)methanol (**9a**). ^1H NMR (500 MHz, CDCl_3): δ 7.53(d, $J=7.5$ Hz, 2H), 7.41–7.27(m, 11H), 6.99(d, $J=7.0$ Hz, 2H), 6.46(s, 1H), 5.35(s, 2H), 4.55(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.2, 136.23, 136.19, 133.0, 129.2, 129.1, 128.8, 128.70, 128.66, 128.4, 127.6, 127.5, 126.3, 126.2, 125.7, 109.0, 55.3, 48.0; FT-IR: ν 3384 cm^{-1} (br, OH); mp 45–47 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{24}\text{H}_{21}\text{NO}$ [$\text{M}+\text{Na}$] $^+$ 362.1521, found 362.1524. TLC R_f (EtOAc/Hexane 3:7)=0.50, yellow solid.

4.4.2. (1-Benzyl-5-(2-methoxyphenyl)-3-phenyl-1H-pyrrol-2-yl)methanol (**9b**). ^1H NMR (500 MHz, CDCl_3): δ 7.55–7.54(m, 2H), 7.39–7.17(m, 8H), 6.97–6.91(m, 4H), 6.38(s, 1H), 5.16(s, 2H), 4.57(d, $J=5.0$ Hz, 2H), 3.71(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.4, 1329.4, 136.5, 133.0, 132.6, 129.8, 128.8, 128.6, 128.4, 128.3, 127.3, 126.2, 126.1, 126.0, 122.1, 120.8, 110.9, 109.3, 55.5, 55.4, 48.5; FT-IR: ν 3435 cm^{-1} (OH); mp 67–69 $^\circ\text{C}$; HRMS m/z calcd for $\text{C}_{25}\text{H}_{23}\text{NO}_2$

[$\text{M}+\text{Na}$] $^+$ 392.1627, found 392.1626. TLC R_f (EtOAc/Hexane 3:7)=0.48, white solid.

4.4.3. (1-Benzyl-3-phenyl-5-(pyridin-2-yl)-1H-pyrrol-2-yl)methanol (**9c**). ^1H NMR (500 MHz, CDCl_3): δ 8.52–8.51(m, 1H), 7.65–7.62(td, $J=7.5$ Hz, 1.5 Hz, 1H), 7.57(d, $J=8.0$ Hz, 1H), 7.52(d, $J=7.0$ Hz, 2H), 7.4(t, $J=7.5$ Hz, 2H), 7.29–7.17(m, 4H), 7.09–7.07(m, 1H), 7.02(d, $J=7.5$ Hz, 2H), 6.75(s, 1H), 6.01(s, 2H), 4.61(d, $J=5.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.5, 149.0, 139.8, 136.7, 136.1, 133.6, 131.5, 128.8, 128.7, 128.5, 127.2, 126.4, 126.3, 126.2, 122.5, 121.2, 111.0, 55.1, 48.5; FT-IR: ν 3346 cm^{-1} (br, OH); HRMS m/z calcd for $\text{C}_{23}\text{H}_{20}\text{N}_2\text{O}$ [$\text{M}+\text{Na}$] $^+$ 363.1474, found 363.1474. TLC R_f (EtOAc/Hexane 3:7)=0.32, yellow oil.

4.4.4. (1-Benzyl-3-butyl-5-phenyl-1H-pyrrol-2-yl)methanol (**9e**). To a solution of the propargylic alcohol (**8e**) (0.47 mmol) in CH_2Cl_2 (1.6 mL) was added AcOH (1.4 mmol, 80 μL). After stirring for an additional 12 h, the mixture was treated with AgOAc (5.0 mol %, 4.0 mg) and the progress of the reaction was monitored by TLC. After 30 min, the mixture was quenched with aqueous sodium bicarbonate solution. The aqueous layer was extracted with CH_2Cl_2 (5 mL \times 4). The combined extracts were dried over anhydrous sodium sulfate and filtered through a pad of Celite and the solvent was removed under reduced pressure. The crude mixture was diluted in CH_2Cl_2 (1.0 mL) was treated with KOH (2.4 mmol, 130 mg) in EtOH (1.0 mL) dropwise. The resulting mixture was stirred for 10 min and then quenched with H_2O . The aqueous layer was extracted with CH_2Cl_2 (5 mL \times 4). The combined extracts were dried over anhydrous sodium sulfate and filtered. The solvent was removed under reduced pressure and the residue was purified using flash column chromatography (0.1 mL TEA/100 mL of *n*-hexane/EtOAc mixture) on silica gel to give the hydroxymethyl pyrrole products (84%).

^1H NMR (400 MHz, CDCl_3): δ 7.31–7.20(m, 8H), 6.93(d, $J=7.2$ Hz, 2H), 6.16(s, 1H), 5.29(s, 2H), 4.45(d, $J=5.6$ Hz, 2H), 2.53(t, $J=8.0$ Hz, 2H), 1.60(m, 2H), 1.40(m, 2H), 1.062(t, $J=5.6$ Hz, 1H), 0.95(t, $J=7.2$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 139.7, 135.7, 133.4, 129.0, 128.97, 128.93, 128.56, 127.3, 127.2, 125.7, 124.8, 109.1, 54.7, 47.8, 34.2, 25.8, 22.8, 14.2; FT-IR: ν 3329 cm^{-1} (br, OH); Anal. Calcd for $\text{C}_{22}\text{H}_{25}\text{NO}$: C 82.72, H 7.89, N 4.38, O 5.01. Found: C 82.83, H 7.72, N 4.34%. TLC R_f (EtOAc/Hexane 2:8)=0.25, colorless oil.

4.5. General procedure for the Ag(I)-catalyzed synthesis of 2-azidomethyl pyrroles 10

General procedure for the Ag(I)-catalyzed synthesis of 2-azidomethyl pyrroles **5** was followed using tertiary propargylic alcohols **8**.

4.5.1. 2-(Azidomethyl)-1-benzyl-3,5-diphenyl-1H-pyrrole (**10a**). ^1H NMR (500 MHz, CDCl_3): δ 7.47–7.23(m, 13H), 6.95(s, 2H), 6.44(s, 1H), 5.29(s, 2H), 4.30(s, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.5, 136.7, 135.9, 132.8, 129.14, 129.05, 128.8, 128.67, 128.66, 127.8, 127.5, 127.4, 126.5, 125.7, 123.6, 109.4, 48.2, 45.6; FT-IR: ν 2108 cm^{-1} (N_3); mp 70–72 $^\circ\text{C}$; Anal. Calcd for $\text{C}_{24}\text{H}_{20}\text{N}_4$: C 79.10, H 5.53, N 15.37. Found: C 79.15, H 5.48, N 15.22%. TLC R_f (EtOAc/Hexane 2:8)=0.61, white solid.

4.5.2. 2-(Azidomethyl)-1-benzyl-5-(2-methoxyphenyl)-3-phenyl-1H-pyrrole (**10b**). ^1H NMR (500 MHz, CDCl_3): δ 7.48(d, $J=7.5$ Hz, 2H), 7.40(t, $J=7.5$ Hz, 2H), 7.33–7.16(m, 6H), 6.96–6.91(m, 4H), 6.35(s, 1H), 5.12(s, 2H), 4.32(s, 2H), 3.69(s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 157.5, 138.6, 136.2, 133.3, 132.9, 129.9, 128.7, 128.6, 127.2, 126.3, 126.1, 123.0, 122.0, 120.8, 111.0, 109.6, 55.5, 48.8, 45.7; Anal. Calcd for $\text{C}_{25}\text{H}_{22}\text{N}_4\text{O}$: C 76.12, H 5.62, N 14.20, O 4.06; FT-IR: ν

2092 cm⁻¹ (N₃); mp 95–96 °C; Found: C 75.92, H 5.45, N 14.13%. TLC R_f(EtOAc/Hexane 1:9)=0.28, white solid.

4.5.3. 2-(5-(Azidomethyl)-1-benzyl-4-phenyl-1H-pyrrol-2-yl)pyridine (**10c**). ¹H NMR (500 MHz, CDCl₃): δ 8.51(d, J=4.0 Hz, 1H), 7.63(td, J=8.0 Hz, 1.5 Hz, 1H), 7.57(d, J=8.0 Hz, 1H), 7.44–7.40(m, 4H), 7.31–7.06(m, 4H), 7.08–7.06(m, 1H), 6.98(d, J=7.5 Hz, 2H), 6.74(s, 1H), 5.97(s, 2H), 4.33(s, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 152.2, 149.0, 139.1, 136.7, 135.7, 134.0, 128.78, 128.77, 128.73, 127.5, 127.1, 126.7, 126.3, 126.1, 122.4, 121.3, 111.2, 48.8, 45.2; FT-IR: ν 2088 cm⁻¹ (N₃); HRMS m/z calcd for C₂₃H₁₉N₅ [M+Na]⁺ 388.1539, found 388.1537. TLC R_f(EtOAc/Hexane 3:7)=0.46, yellow oil.

4.5.4. 2-(Azidomethyl)-1-benzyl-5-(4-methoxyphenyl)-3-phenyl-1H-pyrrole (**10d**). ¹H NMR (500 MHz, CDCl₃): δ 7.47–7.46(m, 2H), 7.43–7.40(m, 2H), 7.33–7.25(m, 6H), 6.96(d, J=6.0 Hz, 2H), 6.88–6.86(m, 2H), 6.38(s, 1H), 5.27(s, 2H), 4.31(s, 2H), 3.80(s, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 159.4, 138.7, 136.5, 136.0, 130.5, 129.1, 128.8, 128.7, 127.5, 127.3, 126.5, 125.7, 125.3, 123.0, 114.1, 108.9, 55.5, 48.1, 45.7; FT-IR: ν 2090 cm⁻¹ (N₃); mp 103–104 °C; Anal. Calcd for C₂₅H₂₂N₄O: C 76.12, H 5.62, N 14.20, O 4.06. Found: C 76.28, H 5.54, N 14.01%. TLC R_f(EtOAc/Hexane 2:8)=0.48, yellow solid.

4.5.5. 2-(Azidomethyl)-1-benzyl-3-butyl-5-phenyl-1H-pyrrole (**10e**). ¹H NMR (400 MHz, CDCl₃): δ 7.31–7.20(m, 8H), 6.90(d, J=7.6 Hz, 2H), 6.18(s, 1H), 5.20(s, 2H), 4.16(s, 2H), 2.53(t, J=7.6 Hz, 2H), 1.61(m, 2H), 1.41(m, 2H), 0.95(t, J=7.2 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 139.1, 136.2, 133.2, 129.0, 128.9, 128.6, 127.34, 127.32, 126.3, 125.6, 123.3, 109.2, 47.9, 44.8, 34.1, 25.9, 22.8, 14.2; FT-IR: ν 2098 cm⁻¹ (N₃); Anal. Calcd for C₂₂H₂₅NO: C 76.71, H 7.02, N 16.27. Found: C 76.76, H 7.07, N 16.33%, TLC R_f(EtOAc/Hexane 0.5:9.5)=0.35, yellow oil.

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References and notes

- (a) Li, Q.; Fan, A.; Lu, Z.; Cui, Y.; Lin, W.; Jia, Y. *Org. Lett.* **2010**, *12*, 4066; (b) Aiello, A.; D'Esposito, M.; Fattorusso, E.; Menna, M.; Müller, W. E. G.; Perovic-Ottstadt, S.; Schröder, H. *C. Bioorg. Med. Chem.* **2006**, *14*, 17; (c) Bellina, F.; Rossi, R. *Tetrahedron* **2006**, *62*, 7213; (d) Balme, G. *Angew. Chem., Int. Ed.* **2004**, *43*, 6238.
- (a) Di Santo, R.; Costi, R.; Artico, M.; Miele, G.; Lavecchia, A.; Novellino, E.; Bergamini, A.; Cancio, R.; Maga, G. *ChemMedChem* **2006**, *1*, 1367; (b) Yin, G.; Wang, Z.; Chen, A.; Gao, M.; Wu, A.; Pan, Y. *J. Org. Chem.* **2008**, *73*, 3377; (c) Rochais, C.; Lisowski, V.; Dallemagne, P.; Rault, S. *Bioorg. Med. Chem.* **2006**, *14*, 8162; (d) Clark, B. R.; Capon, R. J.; Lacey, E.; Tennant, S.; Gill, J. H. *Org. Lett.* **2006**, *8*, 701.
- Fürstner, A. *Angew. Chem., Int. Ed.* **2003**, *42*, 3582.
- (a) Pu, S.; Liu, G.; Shen, L.; Xu, J. *Org. Lett.* **2007**, *9*, 2139; (b) Gabriel, S.; Cécilius, M.; Fleury-Frenette, K.; Cossement, D.; Heccq, M.; Ruth, N.; Jérôme, R.; Jérôme, C. *Chem. Mater.* **2007**, *19*, 2364; (c) López-Pérez, A.; Robles-Machín, R.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2007**, *46*, 9261; (d) Stepień, M.; Donnio, B.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 1431; (e) Dehm, V.; Chen, Z.; Baumeister, U.; Prins, P.; Siebbeles, L. D. A.; Wurthner, F. *Org. Lett.* **2007**, *9*, 1085; (f) West, R.; Panagabko, C.; Atkinson, J. J. *Org. Chem.* **2010**, *75*, 2883.
- (a) Santoso, M.; Somphol, K.; Kumar, N.; Black, D. S. *Tetrahedron* **2009**, *65*, 5977; (b) Setsune, J.-i.; Toda, M.; Watanabe, K.; Panda, P. K.; Yoshida, T. *Tetrahedron Lett.* **2006**, *47*, 7541; (c) Gałęzowski, M.; Jazcwinński, J.; Lewtak, J. P.; Gryko, D. T. *J. Org. Chem.* **2009**, *74*, 5610.
- (a) Magnus, N. A.; Staszak, M. A.; Udodong, U. E.; Wepsiec, J. P. *Org. Process Res. Dev.* **2006**, *10*, 899; (b) Manley, J. M.; Kalman, M. J.; Conway, B. G.; Ball, C. C.; Havens, J. L.; Vaidyanathan, R. J. *Org. Chem.* **2003**, *68*, 6447.
- Wang, Y.-F.; Toh, K. K.; Chiba, S.; Narasaka, K. *Org. Lett.* **2008**, *10*, 5019.
- (a) De, S. K. *Synth. Commun.* **2008**, *38*, 2768; (b) Chen, J.; Wu, H.; Zheng, Z.; Jin, C.; Zhang, X.; Su, W. *Tetrahedron Lett.* **2006**, *47*, 5383.
- (a) Lu, Y.; Fu, X.; Chen, H.; Du, X.; Jia, X.; Liu, Y. *Adv. Synth. Catal.* **2009**, *351*, 129; (b) Peng, H. M.; Zhao, J.; Li, X. *Adv. Synth. Catal.* **2009**, *351*, 1371; (c) Blanc, A.; Alix, A.; Weibel, J. M.; Pale, P. *Eur. J. Org. Chem.* **2010**, *2010*, 1644; (d) Surmont, R.; Verniest, G.; Kimpe, N. D. *Org. Lett.* **2009**, *11*, 2920; (e) Binder, J. T.; Kirsch, S. F. *Org. Lett.* **2006**, *8*, 2151; (f) Davies, P. W.; Martin, N. *Org. Lett.* **2009**, *11*, 2293; (g) Harrison, T. J.; Kozak, J. A.; Corbella-Pané, M.; Dake, G. R. *J. Org. Chem.* **2006**, *71*, 4525; (h) Liu, W.; Jiang, H.; Huang, L. *Org. Lett.* **2010**, *12*, 312; (i) Gorin, D. J.; Davis, N. R.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 11260; (j) Liu, Y.; Song, F.; Song, Z.; Liu, M.; Yan, B. *Org. Lett.* **2005**, *7*, 5409; (k) Istrate, F. M.; Gagosz, F. *Org. Lett.* **2007**, *9*, 3181; (l) Jimenez-Nuñez, E.; Echavarren, A. M. *Chem. Rev.* **2008**, *108*, 3326; (m) Shu, X.-Z.; Liu, X.-Y.; Xiao, H.-Q.; Ji, K.-G.; Guo, L.-N.; Liang, Y.-M. *Adv. Synth. Catal.* **2008**, *350*, 243; (n) Skouta, R.; Li, C.-J. *Tetrahedron* **2008**, *64*, 4917; (o) Chen, D.-D.; Hou, X.-L.; Dai, L.-X. *Tetrahedron Lett.* **2009**, *50*, 6944; (p) Egi, M.; Azechi, K.; Akai, S. *Org. Lett.* **2009**, *11*, 5002; (q) Saito, A.; Konishi, T.; Hanzawa, Y. *Org. Lett.* **2010**, *12*, 372; (r) Zhao, X.; Zhang, E.; Tu, Y.-Q.; Zhang, Y.-Q.; Yuan, D.-Y.; Cao, K.; Fan, C.-A.; Zhang, F.-M. *Org. Lett.* **2009**, *11*, 4002.
- Lee, W. K.; Ha, H.-J. *Aldrichimica Acta* **2003**, *36*, 57.
- Luisi, R.; Capriati, V.; Di Cunto, P.; Florio, S.; Mansueto, R. *Org. Lett.* **2007**, *9*, 3295.
- (a) Du, X.; Xie, X.; Liu, Y. *J. Org. Chem.* **2010**, *75*, 510; (b) Aponick, A.; Li, C.-Y.; Malinge, J.; Marques, E. F. *Org. Lett.* **2009**, *11*, 4624.
- Minakata, S.; Okada, Y.; Oderaotshi, Y.; Komatsu, M. *Org. Lett.* **2005**, *7*, 3509.
- (a) De Jonghe, S.; Lamote, I.; Venkataraman, K.; Boldin, S. A.; Hillaert, U.; Rozenski, J.; Hendrix, C.; Busson, R.; De Keukeleire, D.; Van Calenbergh, S.; Futerma, A. H.; Herdewijn, P. *J. Org. Chem.* **2002**, *67*, 988; (b) Lee, E.; Song, H. Y.; Kang, J. W.; Kim, D.-S.; Jung, C.-K.; Joo, J. M. *J. Am. Chem. Soc.* **2001**, *124*, 384.