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# A facile synthesis of β-allenyl furanimines via Pd-catalyzed cyclization of 2,3-allenamides with propargylic carbonates

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ABSTRACT

The $Pd(OAc)_2$/TFP-catalyzed cyclization reaction of 2,3-allenamides in the presence of propargylic carbonates provides an efficient route to β-allenyl furanimine derivatives. Preliminary mechanistic study showed that this reaction was probably initiated by Pd(0) species.



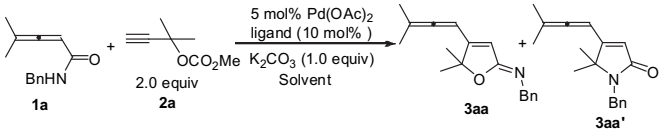
## 1. Introduction

Allenes are a class of unique and powerful compounds in organic synthesis, and therefore the synthesis of differently substituted allenes from readily available starting material is of current interest.[1,2] On the other hand, as we know, it is easy to generate the allenylic/propargylic palladium species via the oxidative addition of Pd(0) with the corresponding esters of propargylic alcohols or propargylic halides.[3] Based on this many allenes have been prepared.[4] Recently, we have reported the reaction of propargylic carbonates with 2,3-allenoic acids to form the β-allenyl butenolide.[5] We have noticed that the cyclization of 2,3-allenamides usually involves the issue of *N*-attack or *O*-attack.[6] Herein, we wish to report an efficient and highly selective route to synthesize β-allenyl furanimines via Pd-catalyzed coupling cyclization of 2,3-allenamides with propargylic carbonates exclusively via *O*-attack.

## 2. Results and discussion

Initially, we used *N*-benzyl 4-methylpenta-2,3-dienamide **1a** and methyl 2-methylbut-3-yn-2-yl carbonate **2a** as the starting materials to try the reaction. At first, we tried the reaction under the catalysis of 5 mol% of $Pd(OAc)_2$ and 10 mol% of TFP with 1.0 equiv of $K_2CO_3$ in DMSO at 38 °C. Fortunately, the corresponding *O*-attacked product **3aa** was formed as the only product with *Z*-configuration in 70% NMR yield (entry 1, Table 1). Interestingly, the *N*-attacked product **3aa′** was not observed. Some of other typical results under different conditions are summarized in Table 1. After screening some other solvents, such as dioxane,

**Table 1**
Optimization of reaction conditions[a]




| Entry | Ligand | Solvent | Temp (°C) | Time (h) | Yield of **3aa** | Recovery of **1a** |
|---|---|---|---|---|---|---|
| 1 | **TFP** | **DMSO** | **38** | **15** | **70** | **0** |
| 2 | TFP | Dioxane | 38 | 15 | 8 | 37 |
| 3 | TFP | MeCN | 38 | 15 | 5 | 60 |
| 4 | TFP | DMF | 38 | 15 | 43 | 32 |
| 5 | TFP | DMA | 38 | 15 | 27 | 43 |
| 6 | TFP | DMSO | 50 | 11 | 52 | 0 |
| 7 | dppe | DMSO | 38 | 23 | 12 | 80 |
| 8 | Sphos | DMSO | 38 | 23 | 2 | 75 |
| 9 | TFP | 1.0 | DMSO | 38 | 15 | 58 |
| 10 | TFP | 1.5 | DMSO | 38 | 15 | 72 |
| 11 | TFP | 2.5 | DMSO | 38 | 15 | 70 |

Bold values represents best condition.

[a] The reaction was carried out using 0.2 mmol of **1a**, 0.4 mmol of **2a**, and 0.2 mmol of $K_2CO_3$ in the presence of 5 mol% of $Pd(OAc)_2$ and 10 mol% of ligand under $N_2$ atmosphere. The yields were determined by $^1H$ NMR analysis with mesitylene as the internal standard.

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MeCN, DMF, DMA, no better results were obtained (entries 2–5, Table 1). When the reaction was conducted at 50 °C, **3aa** was afforded in 52% NMR yield with the reaction time being shortened to 11 h (entry 6, Table 1). Compared with other phosphine ligands, tri(furan-2-yl)phosphine (TFP) was the best (entries 1, 7, and 8, Table 1). When 1.0 and 1.5 equiv of compound **2a** were used, **1a** was recovered in 11% or 1% (entries 9 and 10, Table 1); the yield of **3aa** was not improved further when 2.5 equiv of **2a** were used (entry 11, Table 1).

With the established reaction conditions in hand, the scope of the reaction was explored with some typical results summarized in Table 2. In most cases, the reaction was conducted at 50 °C for consuming the starting material more efficiently. For the terminal propargylic carbonates, the substituent $R^6$ or $R^7$ on propargylic carbonates can be alkyl group and phenyl group, such as **2a**–**d** (entries 1–4, Table 2). With substituted non-terminal propargylic carbonates (the substituent $R^5$ was *n*-butyl or phenyl) **2e** and **2f**, the corresponding products **3ae** and **3af** were afforded in higher yields (entries 5 and 6, Table 2). It should be mentioned that the reaction was complicated using secondary propargylic alcohol carbonate while no reaction occurred with the simple propargyl alcohol carbonate (Scheme 1). The substituent $R^1$ or $R^2$ at 4-position of allenamides **1** can be an alkyl group, such as methyl or ethyl. The substituent $R^4$ can be benzyl, *n*-butyl, *tert*-butyl group (entries 7–10, Table 2); 2,4,4-trisubstituted 2,3-allenamide **1e** gave the products **3ea**–**ef** in good to excellent yields (entries 11–14, Table 2). The structure of products **3** was further confirmed by the X-ray diffraction study of **3cf** (Fig. 1).[7]

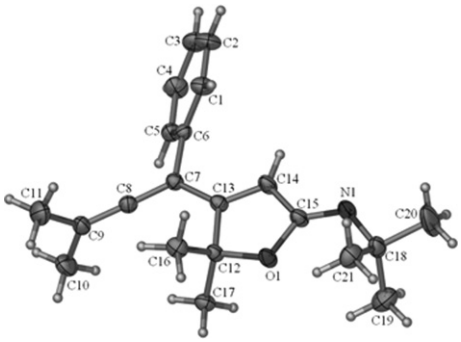
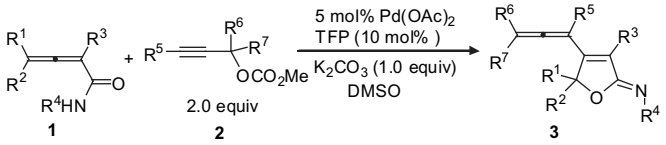



**Fig. 1.** ORTEP Representation of **3cf**.

There are two mechanisms for this reaction, which are depicted in Scheme 2. The first one is the Pd(0)-initiated mechanism: the propargylic carbonate **2** would form the allenylic palladium intermediate **M1** or **M1′** in the presence of the in-situ formed Pd(0). Then the intermediate **M1** or **M1′** underwent intermolecular carbopalladation with the allenamides **1** to form the π-allylic palladium intermediate **M2** via either *N*-attack or *O*-attack. Due to the high steric hindrance at the 4-position, *O*-attack-type product furanimines **3** was afforded.[6] The *Z*-selectivity referring to the C=N bond may be explained by the steric interaction between $R^3$ and $R^4$ in the *E*-products. An alternative is the Pd(II)-initiated mechanism: the intermediate **M3** would form from 2,3-allenamide **1** through oxypalladation, which then would undergo *syn*-carbopalladation with propargylic carbonate **2** to form the intermediate **M4**. The final product **3** was afforded from **M4** through β-$OCO_2Me$ elimination. Since no racemization process occurred with this mechanism, the central chirality in propargylic carbonate **2** would completely transform to axial chirality in the final product **3**.

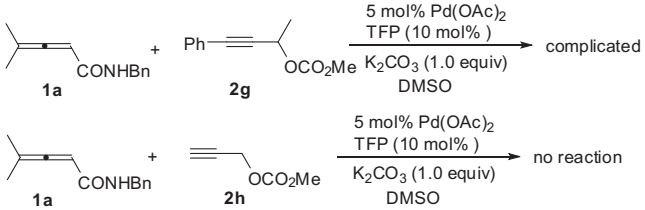
Thus, in order to study mechanism, the optically active methyl 2-phenylbut-3-yn-2-yl carbonate (+)-**2d** (95% ee)[8] was applied under the standard reaction conditions (Scheme 3). Complete racemization was observed in this reaction, which indicated that the Pd(0)-initiated mechanism may be operative here.

**Table 2**
Pd-catalyzed coupling reaction of allenamides **1** with propargylic carbonates **2**[a]

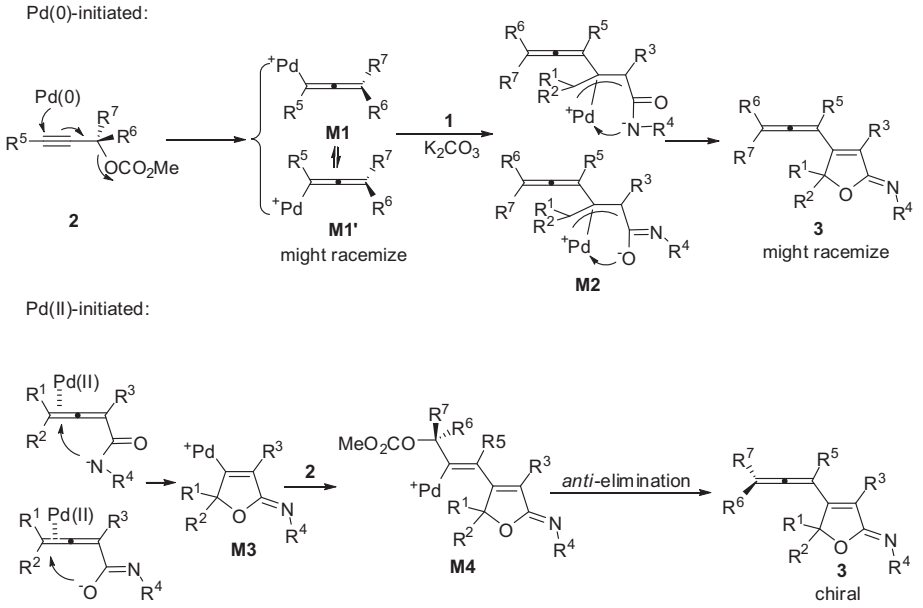



| Entry | 1 | | | | 2 | | | Temp (°C) | Time (h) | Yield of 3[b] (%) |
|---|---|---|---|---|---|---|---|---|---|---|
| | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ | $R^6$ | $R^7$ | | | |
| 1 | Me | Me | H | Bn (**1a**) | H | Me | Me (**2a**) | 38 | 15 | 70 (54) (**3aa**) |
| 2 | **1a** | | | | H | Et | Et (**2b**) | 38 | 13 | 58 (42) (**3ab**) |
| 3 | **1a** | | | | H | $-(CH_2)_5-$ (**2c**) | | 38 | 14 | 74 (56) (**3ac**) |
| 4 | **1a** | | | | H | Me | Ph (**2d**) | 50 | 11 | 61 (57) (**3ad**) |
| 5 | **1a** | | | | *n*-Bu | Me | Me (**2e**) | 50 | 19 | 77 (70) (**3ae**) |
| 6 | **1a** | | | | Ph | Me | Me (**2f**) | 50 | 15 | 88 (72) (**3af**) |
| 7 | Me | Me | H | *n*-Bu (**1b**) | **2e** | | | 50 | 18 | 73 (53) (**3be**) |
| 8 | Me | Me | H | *t*-Bu (**1c**) | **2e** | | | 50 | 17 | 79 (68) (**3ce**) |
| 9 | **1c** | | | | **2f** | | | 50 | 17 | 95 (93) (**3cf**) |
| 10 | Me | Et | H | Bn (**1d**) | **2e** | | | 50 | 14 | 59 (51) (**3de**) |
| 11 | Me | Me | Me | Bn (**1e**) | **2a** | | | 50 | 15 | 98 (89) (**3ea**) |
| 12 | **1e** | | | | **2c** | | | 50 | 23 | 93 (91) (**3ec**) |
| 13 | **1e** | | | | **2d** | | | 50 | 14 | 77 (73) (**3ed**) |
| 14 | **1e** | | | | **2f** | | | 50 | 14 | 100 (93) (**3ef**) |

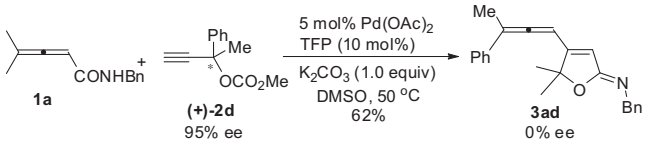
[a] The reaction was carried out using 0.2 mmol of **1**, 0.4 mmol of **2**, and 0.2 mmol of $K_2CO_3$ in the presence of 5 mol % of $Pd(OAc)_2$ and 10 mol % of TFP in 2 mL of DMSO.
[b] Yields were determined by $^1H$ NMR analysis with mesitylene as the internal standard; yields of the isolated products are given in parentheses.




**Scheme 1.**




**Scheme 2.** Mechanistic pathways.




**Scheme 3.**

## 3. Conclusions

We have developed a $Pd(OAc)_2$/TFP-catalyzed cyclization reaction of 2,3-allenamides in the presence of propargylic carbonates, which provides an efficient route to β-allenyl furanimine derivatives. Two different mechanisms were discussed, and Pd(0)-initiated mechanism was considered to be more reasonable based on the results using optically active (+)-**2d** as the probe. As a result of usefulness of the products, the reaction may have potentials in organic synthesis. Further studies in this area are being pursued in our laboratory.

## 4. Experimental

### 4.1. Synthesis of starting materials 2,3-allenamide

Compounds **1a**, **1b**, **1d**, **1e**, and new compound **1c** were prepared following the known procedure.[6c]

*4.1.1. N-(tert-Butyl)4-methylpenta-2,3-dienamide (**1c**).* A stainless steel autoclave fitted with a glass reactor with a stirring bar inside was charged with 1-bromo-3-methylbuta-1,2-diene (2.0333 g, 13.83 mmol), THF (15 mL), $Et_3N$ (2.4 mL, $d$=0.725 g/mL, 1.7400 g, 17.23 mmol), $t$-$BuNH_2$ (1.2102 g, 16.58 mmol), and $Pd(PPh_3)_4$ (0.2012 g, 0.17 mmol) sequentially. The autoclave was charged with CO with a pressure of 25 atm. After the mixture was stirred for 1.5 h at rt, CO was released gently. The reaction was quenched with 10 mL of water followed by the addition of 20 mL of $CH_2Cl_2$. After separation, the organic phase was washed sequentially with dilute HCl and brine, and dried over anhydrous $Na_2SO_4$. After filtration and evaporation, the residue was purified by flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate=10/1 to 1/1) to afford allenamide **1c**. This product was further purified by recrystallization ($n$-hexane/$CH_2Cl_2$) to afford pure **1c** (1.0913 g, 47%) as a white solid, mp: 161.5–162.0 °C ($n$-hexane/$CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.52 (br s, 1H), 5.35–5.26 (m, 1H), 1.78 (d, $J$=3.0 Hz, 6H), 1.34 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 204.8, 165.1, 101.1, 90.5, 51.0, 28.8, 19.7; MS ($m/z$): 168 ($M^+$+1, 8.50), 167 ($M^+$, 76.81), 57 (100); IR (KBr, $cm^{-1}$): 3269, 3076, 2988, 2969, 2946, 2911, 2866, 1968, 1634, 1558, 1484, 1455, 1407, 1391, 1362, 1297, 1231, 1202. Anal. Calcd for $C_{10}H_{17}NO$: C 71.81, H 10.25, N 8.37. Found: C 71.78, H 10.37, N 8.36.

### 4.2. Reactions of 2,3-allenamides with propargylic carbonates

*4.2.1. (Z)-N-Benzyl 5,5-dimethyl-4-(3′-methylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3aa**). General procedure*: To the Schlenk tube containing $K_2CO_3$ (27.0 mg, 0.20 mmol) were charged $Pd(OAc)_2$ (2.3 mg, 0.010 mmol), tri-(2-furanyl)phosphine (4.5 mg, 0.019 mmol), **1a** (41.4 mg, 0.21 mmol), **2a** (58.0 mg, 0.41 mmol), and 2 mL of DMSO sequentially under $N_2$ atmosphere. The resulting mixture was heated at 38 °C (oil bath) with stirring. After 15 h the reaction was completed as monitored by TLC, the reaction was quenched with 10 mL of $H_2O$, extracted with ether (15 mL×3), washed with brine, and dried over anhydrous $Na_2SO_4$. After filtration and evaporation, the NMR yield of **3aa** was 70% as determined by $^1H$ NMR analysis using mesitylene as the internal standard (27 μL, 0.2 mmol). Chromatography on silica gel (eluent: petroleum ether (30–60 °C)/ethyl acetate=7/1) of the crude product afforded pure **3aa** (29.5 mg, 54%) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 7.40–7.15 (m, 5H), 5.97–5.89 (m, 1H), 5.88 (s, 1H), 4.53 (s, 2H), 1.78 (d, $J$=3.0 Hz, 6H), 1.47 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): $\delta$ 206.5, 162.8, 158.3, 141.3, 128.2, 127.9, 126.2, 118.0, 98.5, 89.3, 84.8, 51.2, 26.0, 19.8; MS ($m/z$): 268 ($M^+$+1, 18.65), 267 ($M^+$, 89.46), 162 (100); IR (neat, $cm^{-1}$): 3028, 2979, 2931, 2866, 1951, 1679, 1606, 1582, 1495, 1453, 1380, 1362, 1274, 1222, 1194, 1155, 1110, 1076, 1030, 1001; HRMS calcd for $C_{18}H_{21}NO$ ($M^+$): 267.1623. Found: 267.1618.

*4.2.2. (Z)-N-Benzyl 5,5-dimethyl-4-(3′-ethylpenta-1′,2′-dienyl)furan-2(5H)-imine (**3ab**).* The reaction of 39.8 mg (0.20 mmol) of **1a**, 68.5 mg (0.40 mmol) of **2b**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.5 mg (0.019 mmol) of TFP, and 27.7 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 24.6 mg (42%, 58% by NMR) of **3ab** (eluent: petroleum ether/ethyl acetate=7/1 to 5/1) as a liquid. $^1H$ NMR

(300 MHz, $CDCl_3$): δ 7.41–7.26 (m, 4H), 7.25–7.16 (m, 1H), 6.15–6.06 (m, 1H), 5.89 (s, 1H), 4.53 (s, 2H), 2.20–1.95 (m, 4H), 1.49 (s, 6H), 1.04 (t, *J*=7.5 Hz, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 205.0, 162.9, 158.6, 141.3, 128.2, 127.9, 126.2, 117.7, 110.9, 89.3, 88.2, 51.2, 26.3, 25.3, 11.9; MS (*m*/*z*): 296 ($M^+$+1, 21.64), 295 ($M^+$, 100); IR (neat, $cm^{-1}$): 2970, 2933, 2871, 1941, 1678, 1606, 1495, 1453, 1379, 1361, 1325, 1270, 1193, 1161, 1111, 1031; HRMS calcd for $C_{20}H_{25}NO$ ($M^+$): 295.1936. Found: 295.1947.

*4.2.3. (Z)-N-Benzyl 4-(3′,3′-pentamethylenepropa-1′,2′-dienyl)-5,5-dimethylfuran-2(5H)-imine (**3ac**).* The reaction of 40.7 mg (0.20 mmol) of **1a**, 73.0 mg (0.40 mmol) of **2c**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 28.1 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 34.9 mg (56%, 74% by NMR) of **3ac** (eluent: petroleum ether/ethyl acetate=7/1 to 5/1 to 3/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.42–7.25 (m, 4H), 7.24–7.15 (m, 1H), 5.97–5.89 (m, 1H), 5.87 (s, 1H), 4.53 (s, 2H), 2.30–2.12 (m, 4H), 1.77–1.53 (m, 6H), 1.50 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 203.2, 162.9, 158.5, 141.3, 128.2, 127.9, 126.2, 117.7, 104.9, 89.3, 84.6, 51.2, 30.7, 26.6, 26.1, 25.7; MS (*m*/*z*): 308 ($M^+$+1, 18.55), 307 ($M^+$, 80.56), 91 (100); IR (neat, $cm^{-1}$): 2985, 2929, 2855, 1948, 1681, 1609, 1584, 1549, 1495, 1447, 1374, 1361, 1259, 1236, 1191, 1155, 1111, 1074, 1026; HRMS calcd for $C_{21}H_{25}NO$ ($M^+$): 307.1936. Found: 307.1935.

*4.2.4. (Z)-N-Benzyl 5,5-dimethyl-4-(3′-phenylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3ad**).* The reaction of 40.1 mg (0.20 mmol) of **1a**, 83.1 mg (0.41 mmol) of **2d**, 2.3 mg (0.010 mmol) of $Pd(OAc)_2$, 4.6 mg (0.020 mmol) of TFP, and 27.7 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 37.4 mg (57%, 61% by NMR) of **3ad** (eluent: petroleum ether/ethyl acetate=7/1 to 5/1 to 3/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.45–7.18 (m, 10H), 6.43 (q, *J*=3.0 Hz, 1H), 6.04 (s, 1H), 4.55 (s, 2H), 2.22 (d, *J*=3.0 Hz, 3H), 1.51 (s, 3H), 1.40 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 209.6, 162.8, 157.3, 141.0, 134.4, 128.6, 128.2, 127.9, 127.6, 126.3, 125.8, 119.2, 103.8, 89.4, 88.7, 51.2, 26.1, 26.0, 16.5; MS (*m*/*z*): 330 ($M^+$+1, 16.64), 329 ($M^+$, 65.43), 91 (100); IR (neat, $cm^{-1}$): 3087, 3061, 3028, 2980, 2930, 2865, 1930, 1674, 1605, 1494, 1453, 1362, 1347, 1280, 1184, 1160, 1110, 1066, 1027; HRMS calcd for $C_{23}H_{23}NO$ ($M^+$): 329.1780. Found: 329.1790.

*4.2.5. (Z)-N-Benzyl 5,5-dimethyl-4-(2′-methylocta-2′,3′-dien-4′-yl)furan-2(5H)-imine (**3ae**).* The reaction of 39.5 mg (0.20 mmol) of **1a**, 80.5 mg (0.41 mmol) of **2e**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 27.8 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 44.6 mg (70%, 77% by NMR) of **3ae** (eluent: petroleum ether/ethyl acetate=7/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.42–7.26 (m, 4H), 7.25–7.15 (m, 1H), 5.90 (s, 1H), 4.53 (s, 2H), 2.17 (t, *J*=7.2 Hz, 2H), 1.77 (s, 6H), 1.47 (s, 6H), 1.45–1.27 (m, 4H), 0.90 (t, *J*=6.9 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 204.5, 163.0, 160.6, 141.3, 128.2, 127.8, 126.2, 116.2, 98.0, 96.9, 90.0, 51.1, 30.5, 29.7, 26.3, 22.2, 20.0, 13.9; MS (*m*/*z*): 324 ($M^+$+1, 20.81), 323 ($M^+$, 85.37), 175 (100); IR (neat, $cm^{-1}$): 2961, 2930, 2860, 1947, 1678, 1598, 1495, 1452, 1379, 1361, 1282, 1194, 1125, 1028; HRMS calcd for $C_{22}H_{29}NO$ ($M^+$): 323.2249. Found: 323.2245.

*4.2.6. (Z)-N-Benzyl 5,5-dimethyl-4-(3′-methyl-1′-phenylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3af**).* The reaction of 40.6 mg (0.20 mmol) of **1a**, 86.3 mg (0.40 mmol) of **2f**, 2.3 mg (0.010 mmol) of $Pd(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 27.8 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 49.8 mg (72%, 88% by NMR) of **3ae** (eluent: petroleum ether/ethyl acetate=5/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.42–7.17 (m, 10H), 5.85 (s, 1H), 4.54 (s, 2H), 1.86 (s, 6H), 1.59 (s, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 205.7, 162.6, 159.3, 141.2, 136.7, 128.7, 128.3, 128.2, 127.8, 127.5, 126.2, 119.5, 100.6, 98.6, 90.1, 51.2, 26.3, 20.1; MS (*m*/*z*): 344 ($M^+$+1, 12.65), 343 ($M^+$, 46.82), 91 (100); IR (neat, $cm^{-1}$): 3060, 3027, 2978, 2930, 2856, 1943, 1676, 1598, 1548, 1494, 1452, 1402, 1379, 1361, 1273, 1195, 1153, 1105, 1076, 1014; HRMS calcd for $C_{24}H_{25}NO$ ($M^+$): 343.1936. Found: 343.1938.

*4.2.7. (Z)-N-(n-Butyl)5,5-dimethyl-4-(2′-methylocta-2′,3′-dien-4′-yl)furan-2(5H)-imine (**3be**).* The reaction of 33.2 mg (0.20 mmol) of **1a**, 80.0 mg (0.41 mmol) of **2e**, 2.3 mg (0.010 mmol) of $Pd(OAc)_2$, 4.8 mg (0.021 mmol) of TFP, and 27.8 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 30.2 mg (53%, 73% by NMR) of **3be** (eluent: petroleum ether/ethyl acetate=7/1 to 5/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 5.81 (s, 1H), 3.28 (t, *J*=7.1 Hz, 2H), 2.13 (t, *J*=7.2 Hz, 2H), 1.74 (s, 6H), 1.61–1.47 (m, 2H), 1.46–1.25 (m, 6H), 1.41 (s, 6H), 0.95–0.82 (m, 6H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 204.4, 162.4, 160.1, 116.3, 97.9, 96.9, 89.6, 46.6, 33.3, 30.5, 29.7, 26.3, 22.2, 20.6, 20.0, 14.0, 13.9; MS (*m*/*z*): 290 ($M^+$+1, 12.96), 289 ($M^+$, 55.29), 246 (100); IR (neat, $cm^{-1}$): 2957, 2930, 2861, 1948, 1679, 1599, 1460, 1377, 1361, 1279, 1194, 1126; HRMS calcd for $C_{19}H_{31}NO$ ($M^+$): 289.2406. Found: 289.2414.

*4.2.8. (Z)-N-(tert-Butyl)5,5-dimethyl-4-(2′-methylocta-2′,3′-dien-4′-yl)furan-2(5H)-imine (**3ce**).* The reaction of 33.8 mg (0.20 mmol) of **1c**, 80.2 mg (0.41 mmol) of **2e**, 2.3 mg (0.010 mmol) of $Pd(OAc)_2$, 4.6 mg (0.020 mmol) of TFP, and 27.6 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 39.6 mg (68%, 79% by NMR) of **3ce** (eluent: petroleum ether/ethyl acetate=4/1 to 3/1 to 1/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 5.81 (s, 1H), 2.12 (t, *J*=7.2 Hz, 2H), 1.74 (s, 6H), 1.45–1.23 (m, 4H), 1.41 (s, 6H), 1.29 (s, 9H), 0.87 (t, *J*=7.2 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 204.4, 160.7, 159.2, 117.9, 97.8, 96.8, 90.2, 53.0, 30.6, 29.8, 26.2, 22.3, 20.1, 13.9; MS (*m*/*z*): 289 ($M^+$, 3.05), 274 (100); IR (neat, $cm^{-1}$): 2963, 2930, 2862, 1948, 1681, 1601, 1458, 1385, 1360, 1273, 1218, 1195, 1123; HRMS calcd for $C_{19}H_{31}NO$ ($M^+$): 289.2406. Found: 289.2409.

*4.2.9. (Z)-N-(tert-Butyl)5,5-dimethyl-4-(3′-methyl-1′-phenylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3cf**).* The reaction of 34.0 mg (0.20 mmol) of **1c**, 89.2 mg (0.41 mmol) of **2f**, 2.2 mg (0.010 mmol) of Pd $(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 27.7 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 58.5 mg (93%, 95% by NMR) of **3cf** (eluent: petroleum ether/ethyl acetate=5/1 to 1/1.5) as a solid, mp: 91.5–92.8 °C (*n*-hexane/$CH_2Cl_2$). $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.30–7.12 (m, 5H), 5.69 (s, 1H), 1.76 (s, 6H), 1.46 (s, 6H), 1.23 (s, 9H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 205.5, 160.1, 157.8, 136.7, 128.7, 128.2, 127.4, 121.3, 100.5, 98.4, 90.2, 53.0, 29.7, 26.1, 20.1; MS (*m*/*z*): 309 ($M^+$, 1.39), 294 (100); IR (neat, $cm^{-1}$): 2967, 1940, 1682, 1594, 1492, 1446, 1380, 1360, 1271, 1218, 1191, 1149, 1098, 1020. Anal. Calcd for $C_{21}H_{27}NO$: C 81.51, H 8.79, N 4.53. Found: C 81.46, H 8.62, N 4.47.

*4.2.10. (Z)-N-Benzyl 5-ethyl-5-methyl-4-(2′-methylocta-2′,3′-dien-4′-yl)furan-2(5H)-imine (**3de**).* The reaction of 43.0 mg (0.20 mmol) of **1d**, 80.2 mg (0.41 mmol) of **2e**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 27.7 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 34.2 mg (51%, 59% by NMR) of **3de** (eluent: petroleum ether/ethyl acetate=8/1) as a liquid. $^1H$ NMR (300 MHz, $CDCl_3$): δ 7.42–7.27 (m, 4H), 7.24–7.16 (m, 1H), 5.96 (s, 1H), 4.53 (d, *J*=1.2 Hz, 2H), 2.17 (t, *J*=7.2 Hz, 2H), 1.84–1.70 (m, 8H), 1.48–1.24 (m, 1H), 1.44 (s, 6H), 0.90 (t, *J*=7.2 Hz, 3H), 0.70 (t, *J*=7.4 Hz, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 204.2, 163.6, 158.6, 141.3, 128.2, 127.9, 126.2, 117.7, 97.9, 97.0, 92.7, 51.1, 31.2, 30.6, 29.8, 25.7, 22.3, 20.1, 20.0, 13.9, 7.5; MS (*m*/*z*): 338 ($M^+$+1, 26.93), 337 ($M^+$, 100); IR (neat, $cm^{-1}$): 2967, 2931, 2872, 1947, 1677, 1598, 1495, 1452, 1377, 1350, 1305, 1248, 1129, 1028; HRMS calcd for $C_{23}H_{31}NO$ ($M^+$): 337.2406. Found: 337.2426.

*4.2.11. (Z)-N-Benzyl 3,5,5-trimethyl-4-(3′-methylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3ea**).* The reaction of 43.5 mg (0.20 mmol) of **1e**, 58.1 mg (0.41 mmol) of **2a**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.6 mg (0.020 mmol) of TFP, and 27.6 mg (0.20 mmol) of $K_2CO_3$ in

2 mL of DMSO afforded 50.5 mg (89%, 98% by NMR) of **3ea** (eluent: petroleum ether/ethyl acetate=7/1) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.44–7.36 (m, 2H), 7.35–7.25 (m, 2H), 7.24–7.16 (m, 1H), 6.00–5.90 (m, 1H), 4.59 (s, 2H), 1.88 (s, 3H), 1.79 (d, $J$=3.0 Hz, 6H), 1.43 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 206.0, 163.8, 149.9, 141.5, 128.1, 127.7, 126.1, 124.7, 98.0, 87.7, 83.4, 50.8, 26.1, 20.0, 9.0; MS ($m/z$): 282 ($M^+$+1, 6.09), 281 ($M^+$, 28.47), 91 (100); IR (neat, $cm^{-1}$): 2979, 2929, 2859, 1949, 1751, 1678, 1636, 1495, 1452, 1376, 1361, 1309, 1229, 1192, 1146, 1084, 1047; HRMS calcd for $C_{19}H_{23}NO$ ($M^+$): 281.1780. Found: 281.1780.

*4.2.12. (Z)-N-Benzyl 4-(3′,3′-pentamethylenepropa-1′,2′-dienyl)-3,5,5-trimethylfuran-2(5H)-imine (**3ec**).* The reaction of 42.3 mg (0.20 mmol) of **1e**, 73.7 mg (0.40 mmol) of **2c**, 2.3 mg (0.010 mmol) of Pd $(OAc)_2$, 4.8 mg (0.021 mmol) of TFP, and 27.7 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 57.2 mg (91%, 93% by NMR) of **3ec** (eluent: petroleum ether/ethyl acetate=10/1) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.43–7.35 (m, 2H), 7.34–7.26 (m, 2H), 7.24–7.16 (m, 1H), 6.00–5.92 (m, 1H), 4.59 (s, 2H), 2.27–2.15 (m, 4H), 1.89 (s, 3H), 1.78–1.50 (m, 6H), 1.45 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 202.7, 163.8, 150.1, 141.5, 128.1, 127.7, 126.1, 124.4, 104.5, 87.7, 83.3, 50.8, 30.9, 26.6, 26.2, 25.7, 9.0; MS ($m/z$): 322 ($M^+$+1, 23.29), 321 ($M^+$, 100); IR (neat, $cm^{-1}$): 2977, 2929, 2855, 1946, 1678, 1605, 1495, 1448, 1348, 1309, 1262, 1239, 1190, 1138, 1084, 1047; HRMS calcd for $C_{22}H_{27}NO$ ($M^+$): 321.2093. Found: 321.2092.

*4.2.13. (Z)-N-Benzyl 3,5,5-trimethyl-4-(3′-phenylbuta-1′,2′-dienyl) furan-2(5H)-imine (**3ed**).* The reaction of 42.7 mg (0.20 mmol) of **1e**, 80.9 mg (0.40 mmol) of **2d**, 2.2 mg (0.010 mmol) of $Pd(OAc)_2$, 4.8 mg (0.021 mmol) of TFP, and 28.1 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 49.6 mg (73%, 77% by NMR) of **3ed** (eluent: petroleum ether/ethyl acetate=10/1) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.44–7.35 (m, 5H), 7.34–7.16 (m, 5H), 6.45 (q, $J$=3.0 Hz, 1H), 4.59 (s, 2H), 2.20 (q, $J$=3.0 Hz, 3H), 1.96 (s, 3H), 1.45 (s, 3H), 1.34 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 209.2, 163.5, 148.9, 141.4, 134.9, 128.6, 128.1, 127.7, 127.4, 126.1, 125.8, 103.4, 87.7, 87.4, 50.9, 26.2, 26.1, 16.7, 9.3; MS ($m/z$): 344 ($M^+$+1, 1.18), 343 ($M^+$, 6.48), 209 (100); IR (neat, $cm^{-1}$): 3061, 3028, 2979, 2928, 2859, 1929, 1676, 1604, 1494, 1452, 1361, 1309, 1260, 1190, 1139, 1084, 1047, 1027; HRMS calcd for $C_{24}H_{25}NO$ ($M^+$): 343.1936. Found: 343.1938.

*4.2.14. (Z)-N-Benzyl 3,5,5-trimethyl-4-(3′-methyl-1′-phenylbuta-1′,2′-dienyl)furan-2(5H)-imine (**3ef**).* The reaction of 42.9 mg (0.20 mmol) of **1e**, 88.4 mg (0.41 mmol) of **2f**, 2.3 mg (0.010 mmol) of Pd $(OAc)_2$, 4.7 mg (0.020 mmol) of TFP, and 27.6 mg (0.20 mmol) of $K_2CO_3$ in 2 mL of DMSO afforded 66.1 mg (93%, 100% by NMR) of **3ed** (eluent: petroleum ether/ethyl acetate=20/1) as a liquid. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.50–7.38 (m, 2H), 7.37–7.27 (m, 4H), 7.27–7.17 (m, 4H), 4.62 (s, 2H), 1.84 (s, 6H), 1.66 (s, 3H), 1.43 (s, 6H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 203.0, 163.8, 151.4, 141.4, 136.1, 128.4, 128.1, 127.8, 127.6, 126.90, 126.87, 126.1, 98.8, 98.7, 89.0, 50.9, 26.3, 20.1, 10.6; MS ($m/z$): 357 ($M^+$, 0.75), 342 (100); IR (neat, $cm^{-1}$): 3060, 3027, 2978, 2928, 2859, 1954, 1756, 1682, 1597, 1491, 1451, 1377, 1361, 1291, 1190, 1126, 1084, 1071, 1012; HRMS calcd for $C_{25}H_{27}NO$ ($M^+$): 357.2093. Found: 357.2098.

### 4.3. Mechanistic study

*4.3.1. Synthesis of optically active methyl 2-phenylbut-3-yn-2-yl carbonate ((+)-**2d**).* To a suspension of NaH (60% in oil, 90.2 mg, 2.25 mmol) and THF (2 mL) was slowly added dropwise a solution of (+)-2-phenylbut-3-yn-2-ol, which was prepared by preparative HPLC separation of racemic 2-phenylbut-3-yn-2-ol (305.3 mg, 2.09 mmol, 95% ee, $[\alpha]_D^{20}$ +2.9 ($c$ 1.11, $CHCl_3$)) in THF (1 mL) at rt with stirring under a nitrogen atmosphere. After being stirred for 1 h, the resulting solution was cooled in an ice bath, and then a solution of methyl chloroformate (222.5 mg, 2.35 mmol) in THF (1 mL) was added dropwise. After being stirred at rt for an additional 16 h, the mixture was quenched with $H_2O$, extracted with ether (15 mL×3), washed with brine, and dried over anhydrous $Na_2SO_4$. After filtration and evaporation, chromatography on silica gel (eluent: petroleum ether/ethyl acetate=60/1 to 40/1) of the crude product afforded (+)-**2d** (345.6 mg, 81%) as liquid, 95% ee, GC conditions: column: CP-Chirasil-Dex-CB (30 m×0.25 mm×0.25 μm); carrier: $N_2$, 10.0 psi; injector: 250 °C; detector (FID): 300 °C; oven temperature: 130 °C (30 min), $t_R$ 13.7 (major), 14.0 (minor). $[\alpha]_D^{20}$ +43.8 ($c$ 1.02, $CHCl_3$). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.66–7.58 (m, 2H), 7.44–7.28 (m, 3H), 3.73 (s, 3H), 2.87 (s, 1H), 1.93 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ 153.2, 141.3, 128.4, 128.3, 124.9, 82.3, 77.6, 76.1, 54.6, 32.1; MS ($m/z$): 204 ($M^+$, 71.51), 115 (100); IR (neat, $cm^{-1}$): 3283, 2995, 2957, 2124, 1761, 1492, 1441, 1373, 1266, 1230, 1181, 1081, 1056, 1029; HRMS calcd for $C_{12}H_{12}O_3$ ($M^+$): 204.0786. Found: 204.0790.

*4.3.2. Cyclization of N-benzyl 4-methylpenta-2,3-dienamide (**1a**) in the presence of (+)-methyl 2-phenylbut-3-yn-2-yl carbonate ((+)-**2d**).* The reaction of 20.3 mg (0.10 mmol) of **1a**, 40.2 mg (0.20 mmol) of (+)-**2d**, 1.2 mg (0.005 mmol) of $Pd(OAc)_2$, 2.4 mg (0.010 mmol) of TFP, and 14.0 mg (0.10 mmol) of $K_2CO_3$ in 1 mL of DMSO afforded 20.7 mg (62%) of **3ad** (eluent: petroleum ether/ethyl acetate=4/1 to 3/1) as a liquid. The enantiomer excess of the product **3ad** was determined by HPLC as 0%. HPLC condition: Chiralpak AD-H, rate: 0.8 mL/min, $\lambda$=254 nm, $n$-hexane/$i$-PrOH=90/10, $t_R$ 16.5 min, 18.4 min. $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ 7.45–7.18 (m, 10H), 6.50–6.39 (m, 1H), 6.01 (s, 1H), 4.54 (s, 2H), 2.21 (d, $J$=3.2 Hz, 3H), 1.50 (s, 3H), 1.39 (s, 3H).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## Supplementary data

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2011.01.041.

## References and notes


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7. Crystal data for compound **3cf**: $C_{21}H_{27}NO$, MW=309.44, Orthorhombic, space group *P*bca, final *R* indices [$I>2\sigma(I)$], $R1$=0.0521, $wR2$=0.1468, *R* indices (all data) $R1$=0.0618, $wR2$=0.1575, $a$=9.4358 (6) Å, $b$=11.1669 (7) Å, $c$=36.887 (2) Å, $\alpha=90^\circ$, $\beta=90^\circ$, $\gamma=90^\circ$, $V$=3886.7 (4) Å$^3$, $T$=296 (2) K, $Z$=8, reflections collected/unique 41372/3423 ($R_{int}$=0.0368), number of observations [$I>2\sigma(I)$] 2875, parameters: 208. Supplementary crystallographic data have been deposited at the Cambridge Crystallographic Data Center. CCDC 800853.
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