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Brønsted Acid Catalyzed Cyclization of Hydroxylated Enynes: A Concise Synthesis of Five-Membered Heterocycles

Ke-Gong Ji,[a] Jin Chen,[a] Hai-Tao Zhu,[a] Fang Yang,[a] Ali Shaukat,[a] and Yong-Min Liang*[a, b]

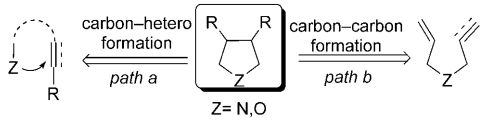
Abstract: A mild and direct pathway for the formation of five-membered heterocyclic compounds from hydroxylated enynes has been developed. In this reaction, hydroxylated enynes were selectively transformed into five-membered heterocyclic compounds **2**, with an allene moiety at the 3-position, in the presence of F_3CSO_3H (0.1 mol%). When R^1, R^2 = Ph, diphenylvinyl-2,3-dihydro-1*H*-pyrrole (**2y**) was obtained. With $HSbF_6$ (5 mol%) as the catalyst, polycyclic skeletons **3** and **4** with adjacent stereocenters were obtained. When R^1 = H and R^2 = styrene, 1,3-dienyl-2,5-dihydro-1*H*-pyrrole (**6as**) was formed. This Brønsted acid catalyzed domino process involves the formation of an allene carbocation intermediate, which can be readily trapped by olefins to give various novel five-membered heterocyclic skeletons.

Keywords: allenes · Brønsted acids · heterocycles · hydroxylated enynes · olefins

Introduction

In recent years, the annulation of heterocycles, especially polyheterocyclic skeletons, has continued to attract the interest of synthetic chemists due to the number of these compounds that are extensively used as synthetic building blocks and also appear as subunits in many natural products that exhibit interesting biological activities.[1] Today, the main challenges that organic chemists face is the production of these architecturally complex molecules in facile and efficient ways.[2] The cycloisomerization of enynes is one such method, for which transition-metal catalysts, such as palladium, platinum, gold, ruthenium, and rhodium, are found to effectively promote the cyclization.[3] However, most of these procedures require high loadings of expensive metal catalysts and ligands. Moreover, the number of accessible heterocyclic skeletons are limited. Therefore, new and effective protocols, involving atom economic, environmentally benign, and mild reaction conditions, for the straightforward synthesis of heterocyclic rings are still of high demand in modern organic synthesis.

Five-membered oxygen- or nitrogenated heterocycles are important intermediates for the synthesis of pharmaceutically and biologically active molecules, such as (−)-domoic acid,[4] isodomoic acid H,[5] kainic acid,[6] conessine,[7] and (+)-intricarene.[8] Some efficient synthetic routes to these skeletons have been reported, of which carbon–hetero formation (through path a) and carbon–carbon formation (through path b) catalyzed by transition metals are more valuable (Scheme 1). In contrast, examples of the cyclization or cycloisomerization reactions of hydroxylated enynes catalyzed by Brønsted acids[9] have rarely been reported.



Scheme 1. Some efficient synthetic routes to heterocyclic skeletons.

In the context of our ongoing efforts to construct various functionalized heterocyclic structures,[10] we found that propargyl carbocation B,[10 e,f,11] in resonance with allene cation C, which can react with nucleophiles (e.g., hydroxy; Scheme 2a), is a perfect intermediate for a domino process.

It is known that an olefin as a nucleophile can also react with a carbocation to form a C–C bond. Thus, we envi-

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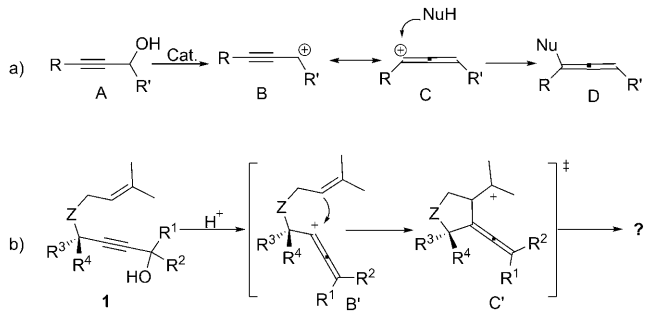


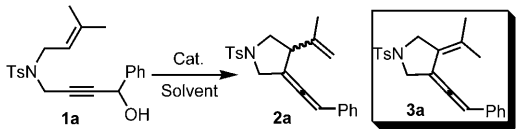
Scheme 2. a) Possible equilibrium. b) Design of the present domino process.

sioned that this type of propargyl alcohol **1** could undergo the isomerization process with trace amounts of Brønsted acid to form putative allene carbocation B′, which can be readily trapped by nucleophiles (olefin in this case; Scheme 2b). Herein, we report a novel C–X (X = C, O) bond formation from 1,6-hydroxylated enynes for the construction of five-membered heterocyclic rings in the presence of Brønsted acids. Note, product **2** is an important structural unit and is easily modified to a natural product, such as kainic acid.[6]

Results and Discussion

Initially, we started by using *N*-(4-*h*ydroxy-4-phenylbut-2-ynyl)-4-methyl-*N*-(3-methylbut-2-enyl)benzenesulfonamide (**1a**; 0.3 mmol) and trifluoromethanesulfonic acid (TfOH; 10 mol%) in CH_2Cl_2 at room temperature, but no desired product was obtained (Table 1, entry 1). Lowering the catalyst loading from 10 to 0.3 mol%, led to decomposition of the starting material **1a** (Table 1, entries 2–4). With an attempt to get the predicted product, the reaction was carried out at 0°C in the presence of 0.3 mol% TfOH. To our delight, the desired product 3-(2-phenylvinylidene)-4-(prop-1-en-2-yl)-1-tosylpyrrolidine (**2a**) was formed in 45% yield after 2 min (Table 1, entry 5). On decreasing the amount of catalyst to 0.1 mol%, a good yield of 81% of **2a** was obtained after 2 min (Table 1, entry 6). Lowering the catalyst loading led to a slow conversion with the decreased yield of **2a** (Table 1, entry 7). Other acids have also been applied to the reaction. It was found that TFA gave the desired product, albeit with a lower yield (Table 1, entry 8). With an attempt to optimize the yield of the product, we further studied the influence of different reaction media (Table 1, entries 12–17). From the results obtained, it can be seen that only DCE and THF were efficient (Table 1, entries 12 and 13). Note, no 3-(2-phenylvinylidene)-4-(propan-2-ylidene)-1-tosylpyrrolidine (**3a**) was observed during this reaction. The reaction conditions were eventually optimized to 0.3 mmol of **1**, 0.1 mol% TfOH as the catalyst, 3 mL of CH_2Cl_2 as the solvent at 0°C (Table 1, entry 6).

Table 1. Optimization of the Brønsted acid catalyzed cascade reaction.[a]



Entry	Catalyst [mol%]	Solvent[b]	T [°C]	t [min]	Yield [%][c]
1	F_3CSO_3H (10)	CH_2Cl_2	RT	5	–[d]
2	F_3CSO_3H (5)	CH_2Cl_2	RT	5	–[d]
3	F_3CSO_3H (1)	CH_2Cl_2	RT	2	–[d]
4	F_3CSO_3H (0.3)	CH_2Cl_2	RT	2	–[d]
5	F_3CSO_3H (0.3)	CH_2Cl_2	0	2	45
6	F_3CSO_3H (0.1)	CH_2Cl_2	0	5	81
7	F_3CSO_3H (0.05)	CH_2Cl_2	0	5	79
8	TFA (0.1)	CH_2Cl_2	0	180	60
9	TsOH (0.1)	CH_2Cl_2	0	180	trace
10	$ClCH_2COOH$ (0.1)	CH_2Cl_2	0	180	0
11	HCl (0.1)	CH_2Cl_2	0	180	0
12	F_3CSO_3H (0.1)	DCE	0	5	80
13	F_3CSO_3H (0.1)	THF	0	30	70
14	F_3CSO_3H (0.1)	toluene	0	30	0
15	F_3CSO_3H (0.1)	DMF	0	30	0
16	F_3CSO_3H (0.1)	acetone	0	30	0
17	F_3CSO_3H (0.1)	CH_3CN	0	30	0

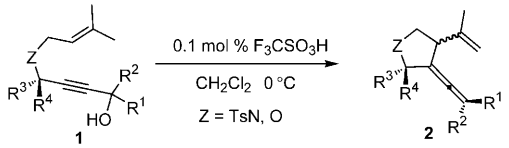
[a] Conditions: **1a** (0.3 mmol) with Brønsted acids in CH_2Cl_2 (3.0 mL). [b] TFA = trifluoroacetic acid, DCE = dichloroethane, Ts = tosyl. [c] Isolated yield. [d] Decomposed.

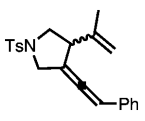
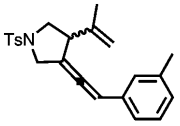
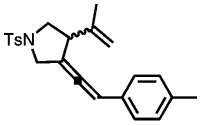
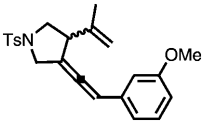
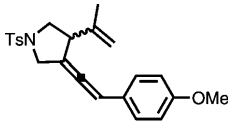
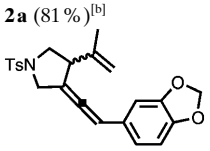
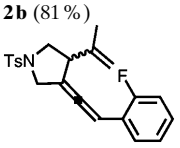
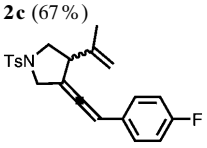
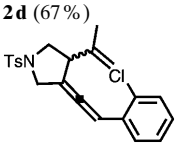
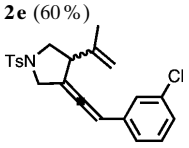
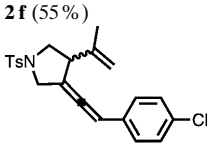
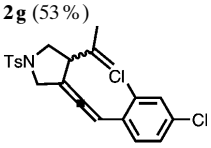
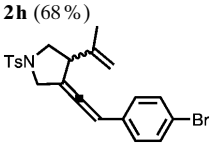
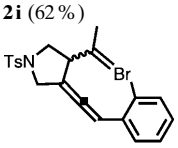
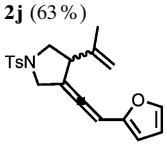
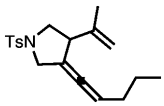
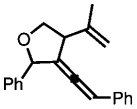
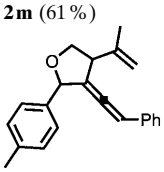
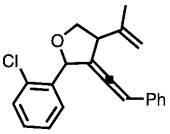
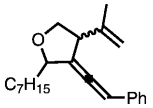
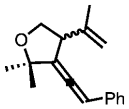
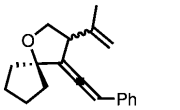
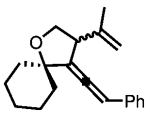
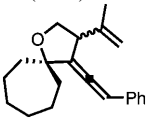
With the optimized conditions in hand, various representative hydroxylated enynes **1a–x** were then subjected to the optimized conditions, as depicted in Table 2. Thus, tandem carbon–oxygen bond cleavage and carbon–carbon bond formation of hydroxylated enynes **1a–x** proceeded smoothly to provide the corresponding allenes in moderate to good yields, except **1p** and **1r**. From these results, it can be seen that this reaction tolerated a variety of functional groups at the *ortho, meta*, and *para* positions of the phenyl moiety in substituted hydroxylated enynes, indicating that the steric effect has little impact on this transformation. Hydroxylated enynes with a heterocyclic ring, such as the furan nucleus, can also afford the desired product (e.g., **2o** in 54% yield). However, the substrate scope cannot be further extended to aliphatic hydroxylated enynes, such as **1p**; this could be ascribed to the fact that the cleavage of C–O bond could not be occur in the presence of F_3CSO_3H (0.1 mol%). Note, some oxygenated hydroxylated enynes can also participate in this reaction. From the results, it can be seen that an electron-donating substituent at the R^2 group hinders product formation (**1r**), whereas an electron-withdrawing group (e.g., Cl) and aliphatic group favors product formation (**1s–x**).

To expand further the scope of the reaction, we also investigated hydroxylated enynes **1y** and **1z**. Surprisingly, heterocyclic diphenylvinyl **2y** and 1, 3-diene **2z** were obtained in 28 and 80% yields, respectively (Scheme 3).

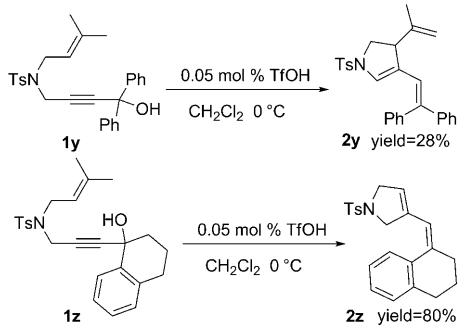
To have more insight of this type of reaction, we investigated hydroxylated enyne **1aa** (Table 3). Fortunately, the desired polycyclic skeletons **3aa** and **4aa** were formed and isolated in a total yield of 36% after 3 h in the presence of TfOH (10 mol%). Other commonly used Brønsted acids,

Table 2. F_3CSO_3H-catalyzed synthesis of heterocyclic allenes **2** from hydroxylated enynes **1**.[a]



Heterocyclic Allenes **2**				
				
2a (81 %)[b]	**2b** (81 %)	**2c** (67 %)	**2d** (67 %)	**2e** (60 %)
				
2f (55 %)	**2g** (53 %)	**2h** (68 %)	**2i** (62 %)	**2j** (63 %)
				
2k (62 %)	**2l** (59 %)	**2m** (61 %)	**2n** (75 %)	**2o** (54 %)
				
2p (0 %)	**2q** (52 %)	**2r** (–)[c]	**2s** (54 %)	**2t** (64 %)
				
2u (64 %)	**2v** (62 %)	**2w** (66 %)	**2x** (60 %)	

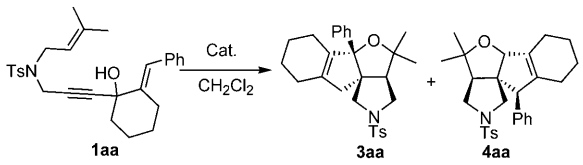
[a] Conditions: **1** (0.3 mmol) with TfOH (0.1 mol %) in CH_2Cl_2 (3.0 mL) at 0 °C. [b] Isolated yield. [c] Decomposed.



Scheme 3.

such as TFA, TsOH, $HNTf_2$, and $HSbF_6$, have also been applied to the reaction. It was found that the strong acid $HSbF_6$ gave the same products as those obtained from TfOH, albeit with a better yield of 86 %. On decreasing the amount of $HSbF_6$ to 5 mol %, a 92 % yield was obtained with a ratio of **3aa**/**4aa** close to 5:4. The reaction conditions were eventually optimized to 0.3 mmol of **1**, 5 mol % of $HSbF_6$ as the catalyst, 3 mL of CH_2Cl_2 as the solvent at room temperature.

Table 3. Optimization of the cascade reaction of hydroxylated enyne **1aa**.[a]

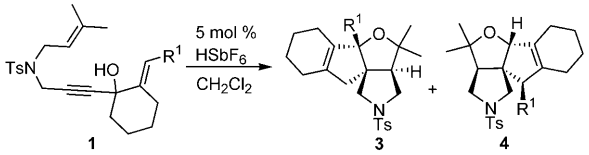


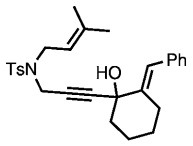
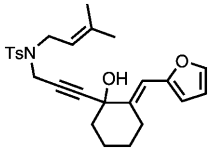
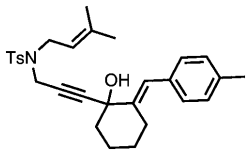
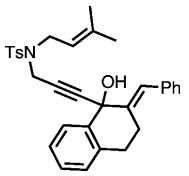
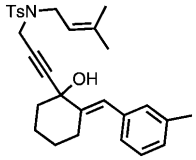
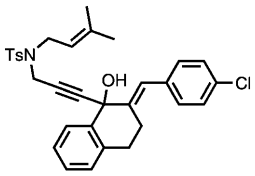
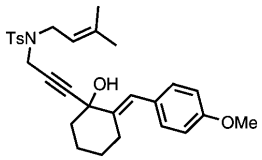
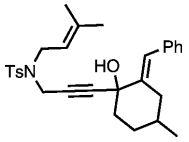
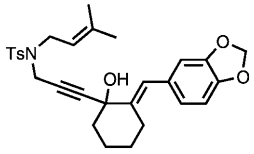
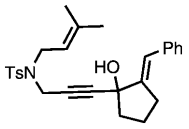
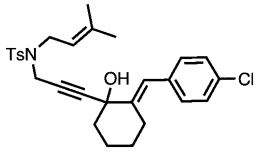
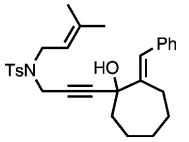
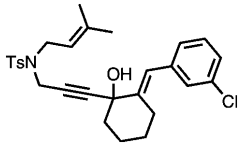
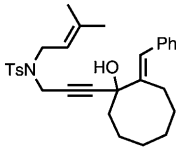
Catalyst ([mol %])	Yield [%][b]	**3aa**/**4aa**
TfOH (10)	36	20:16
TFA (10)	mixture	0
TsOH (10)	0	0
$HNTf_2$ (10)	73	41:32
$HSbF_6$ (10)	86	48:38
$HSbF_6$ (5)	92	52:40

[a] Tf = trifluoromethanesulfonyl. [b] Isolated yield.

With the optimized conditions in hand, various representative hydroxylated enynes **1aa**–**an** were then subjected to the optimized conditions, as depicted in Table 4. Tandem carbon–carbon and carbon–oxygen bond formation of hydroxylated enynes **1aa**–**an** proceeded smoothly to provide the corresponding polycyclic skeletons in moderate to excel-

Table 4. $HSbF_6$-catalyzed synthesis of polycyclic skeletons **3** and **4** from hydroxylated enynes **1**.[a]



Entry	Substrate		3/4	Yield [%][b]	Entry	Substrate		3/4	Yield [%][b]
1		**1aa**	52:40	92	8		**1ah**		–[c]
2		**1ab**	50:40	90	9		**1ai**	36:36	72
3		**1ac**	55:35	90	10		**1aj**	52:18	70
4		**1ad**	44:44	88	11		**1ak**	58:30	88
5		**1ae**	43:43	86	12		**1al**		0
6		**1af**	58:22	80	13		**1am**	65:33	96
7		**1ag**	69:22	91	14		**1an**	61:38	99

[a] Conditions: **1** (0.3 mmol) with $HSbF_6$ (5 mol%) in CH_2Cl_2 (3.0 mL) at room temperature (23–25°C). [b] Isolated yield. [c] Decomposed.

lent yields, except **1ah** and **1al**. From these results, it can be seen that this reaction tolerated a variety of functional groups at the *meta* and *para* positions of the phenyl moiety in the substituted R^1 group. As shown, the position of the substituent on R^1 had only a slight influence on the yield of the products. Both electron-rich aryl groups and electron-withdrawing groups showed good results (Table 4, entries 1–7). Substrate **1ah** with a heteroaromatic R^1 group decomposed, which could be ascribed to the fact that the furan ring was not stable under the reaction conditions (Table 4, entry 8). The steric effect of hydroxylated enynes such as **1ai–ak** was also investigated; this had an impact on this transformation (Table 4, entries 9–11). To confirm the structural assignment of products in the present cascade reaction, the relative configuration of the products **3aj** and **4aj** were unambiguously assigned by X-ray crystallography (Figure 1).[12] Substrates **1al–an**, with 5-, 7-, and 8-membered ring systems, were also applied to the reaction. Substrate **1al** with the 5-membered ring system could not afford the desired product, which might be due to ring strain (Table 4, entry 12). While, substrates **1am** and **1an** with 7- and 8-membered ring systems, respectively, gave an excellent yield of the corresponding products.

Hexahydrofuro[3,4-*c*]furan ring is very important in organic synthesis. Under the optimized conditions, we also investigated a range of oxygen-tethered hydroxylated enynes **1ao–aq**, as shown in Scheme 4. Fortunately, the reactions of **1ao–aq** proceeded smoothly and gave the desired hexahydrofuro[3,4-*c*]furan derivatives in moderate to good yield (65–87%).

When carbon-tethered hydroxylated enyne **1ar** was subjected to the standard conditions, a total yield of 77% of the polycyclic skeletons was isolated after 5 h, with a ratio of **2ar** and **3ar** of 5:1 (Scheme 5).

A deuterium-labeling experiment was performed to rule out a possible 1,4-hydrogen shift in the course of the mechanism. As shown in Scheme 6, hydroxylated enyne [D]**1aa** with $HSbF_6$ (5 mol%) in wet CH_2Cl_2 at room temperature produced the desired polycyclic skeletons [D]**3aa** with a deuterium content of $X=0.27$ D and [D]**4aa** with a deuterium content of $X=0.92$ D. The formation of product [D]**3aa**

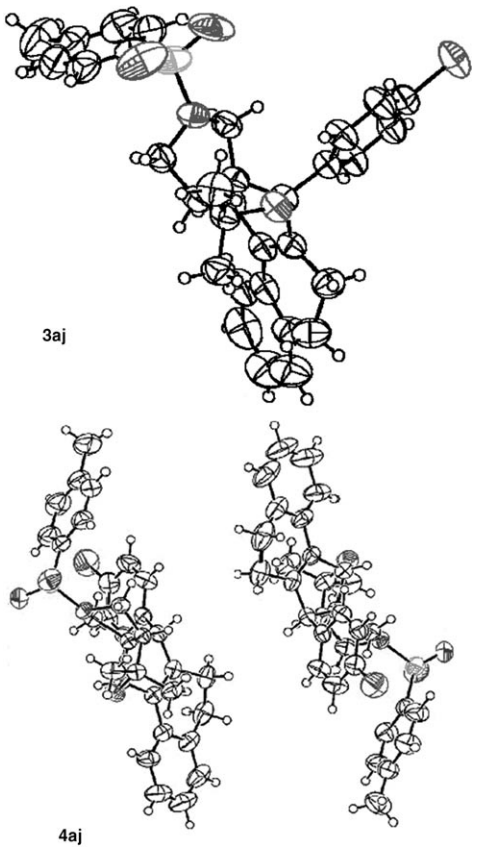
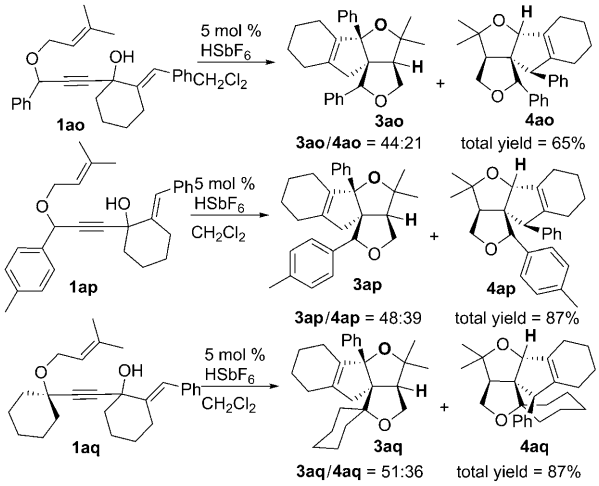
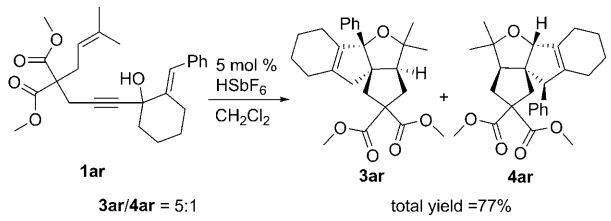


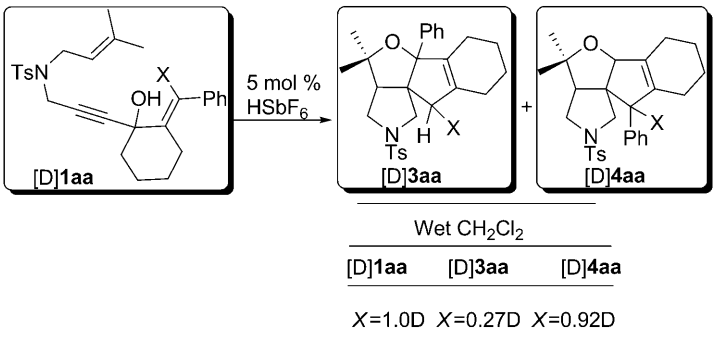
Figure 1. X-ray structures of **3aj** and **4aj**.[13]



Scheme 4. $HSbF_6$-catalyzed hydroxylated enynes **1ao–aq**.



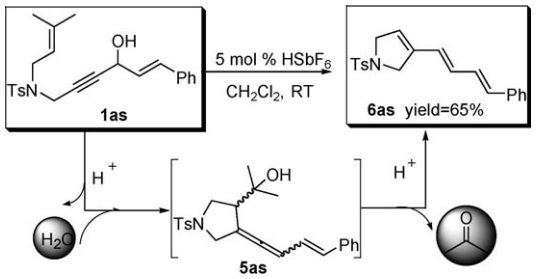
Scheme 5. $HSbF_6$-catalyzed hydroxylated enynes **1ar**.



Scheme 6. Deuterium-labeling experiments.

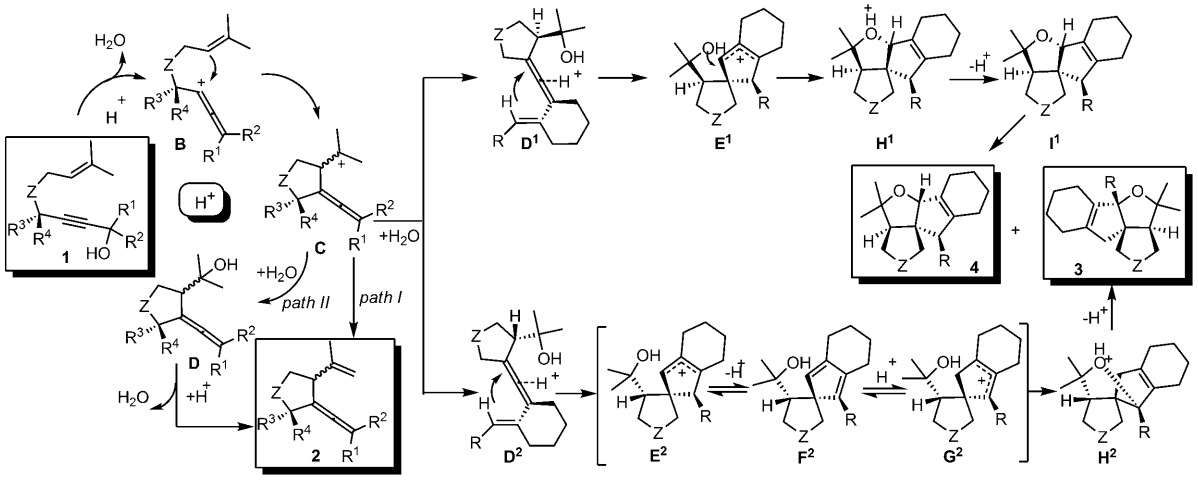
was also confirmed by high-resolution mass spectrometry and NMR spectroscopy.

We also investigated hydroxylated enyne **1as**, and the desired product **6as** was obtained in 65% yield after 8 h. In this reaction, intermediate allene alcohol **5as** was observed, demonstrating the fact that **6as** was formed through a domino carbon–carbon bond cleavage and isomerization in the presence of H^+ (Scheme 7).



Scheme 7. $HSbF_6$-catalyzed domino carbon–carbon bond cleavage for **6as**.

On the basis of the above observations, we propose the following plausible mechanisms for this cascade transformation (Scheme 8). 1) In the presence of trace amounts of H^+, the hydroxyl group of **1** is lost to give the putative allene carbocation intermediate **B**,[13] which can be readily trapped by olefin nucleophile to form carbocation intermediate **C**. 2) Intermediate **C** can lose a proton selectively to give the heterocyclic allene **2** (path I). Alternatively, water as the nucleophile can attack the carbocation intermediate **C** to form intermediate **D**, which loses one molecule of water in the presence of trace amounts of H^+ to give the heterocyclic allene **2** (path II). 3) When R^1 and R^2 are cyclohexylidene substituents, water as the nucleophile attacks the carbocation intermediate **C** to form intermediates $\mathbf{D^1}$ and $\mathbf{D^2}$. 4) Intermediate allene alcohol $\mathbf{D_1}$ follows the domino carbon–carbon bond formation pathway in the presence of H^+ and affords the intermediate cation $\mathbf{E^1}$. 5) The hydroxyl group of intermediate cation $\mathbf{E^1}$ may attack the allyl carbocation to afford $\mathbf{H^1}$, which releases a proton to afford the polycyclic skeleton **4**. 6) The intermediate allene alcohol $\mathbf{D^2}$ also follows the domino carbon–carbon bond formation pathway in



Scheme 8. Proposed mechanism.

the presence of H^+ to afford the intermediate cation $\mathbf{E^2}$. Because of steric effects, the hydroxyl group of intermediate cation $\mathbf{E^2}$ cannot attack the allyl carbocation and intermediate cation $\mathbf{E^2}$ may be in equilibrium with carbocation $\mathbf{G^2}$ via intermediate $\mathbf{F^2}$ in the presence of H^+. Thus, the hydroxyl group of intermediate cation $\mathbf{G^2}$ attacks the allyl cation to give $\mathbf{H^2}$, which loses a proton to afford the polycyclic skeleton **3**.

Conclusion

We have developed an efficient approach to five-membered heterocyclic compounds allenes **2**, diphenylvinyl-2,3-dihydro-1*H*-pyrrole (**2y**), polycyclic skeletons **3** and **4**, and 1,3-dienyl-2,5-dihydro-1*H*-pyrrole (**6as**) by utilizing a Brønsted acid catalyzed tandem cyclization reaction of hydroxylated enynes. This Brønsted acid catalyzed domino process involves the formation of an allene carbocation intermediate, which can be readily trapped by olefins to give various novel five-membered heterocyclic skeletons. Furthermore, the simplest, and least expensive, Brønsted acid shows excellent catalytic activity in the reaction with a low catalyst loading.

Experimental Section

General: Column chromatography was carried out on silica gel. Unless noted, the ^{1}H NMR spectra were recorded at 300 or 400 MHz in $CDCl_3$ and the ^{13}C NMR spectra were recorded at 75 or 100 MHz in $CDCl_3$ with trimethylsilane (TMS) as an internal standard. IR spectra were recorded on a FTIR spectrometer, and only the major peaks are reported (in cm^{-1}). Melting points were determined on a microscopic apparatus and are uncorrected. All new compounds were further characterized by elemental analysis or high-resolution mass spectrometry (HRMS); copies of their ^{1}H and ^{13}C NMR spectra are provided in the Supporting Information. Detailed data of **3aj** and **4aj** and X-ray crystallographic studies of **1aj** are also provided. Commercially available reagents and solvents were used without further purification. THF was distilled immediately before use from Na/benzophenone. All details of instruments that were used for data characterization can be found in the Supporting Information.

General procedure A: **Brønsted acid catalyzed cyclization of hydroxylated enynes toward five-membered heterocyclic allenes 2a–2x**: F_3CSO_3H (0.0003 mmol, 0.1 mol%) was added to a solution of hydroxylated enynes **1** (0.30 mmol) in wet CH_2Cl_2 (3.0 mL) at 0°C. Within minutes, when the reaction was considered to be complete as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (40 mL), washed with water, saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford the corresponding polycyclic skeletons **2a–x**.

*Compound **2a***: Reaction time: 5 min; yield: 81%; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (dd, J = 8.0, 1.6 Hz, 2H), 7.36 (d, J = 8.0 Hz, 2H), 7.29–7.15 (m, 5H), 6.29–6.26 (m, 1H), 4.84–4.77 (m, 2H), 4.12–3.90 (m, 2H), 3.62–3.48 (m, 2H), 3.29–3.18 (m, 1H), 2.46 (s, 3H), 1.68 and 1.66 ppm (2×s, 3H); ^{13}C NMR(100 MHz, $CDCl_3$): δ = 198.0, 197.9, 143.8, 142.5, 142.2, 133.9, 133.7, 133.0, 132.9, 129.8, 129.7, 128.6, 127.9, 127.4, 127.0, 113.2, 105.0, 104.9, 99.4, 99.3, 52.3, 49.8, 49.8, 49.5, 49.0, 21.6, 19.8, 19.5 ppm; IR (neat) 2919, 1597, 1348, 1164, 1092, 1033, 818, 664 cm^{-1}; HRMS (ESI): m/z calcd for $C_{22}H_{23}NO_2S$: 366.1522 [M+H]; found: 366.1520.

General Procedure B: **Brønsted acid catalyzed cyclization of hydroxylated enynes toward five-membered heterocyclic vinylidene 2y**: F_3CSO_3H (0.00015 mmol, 0.05 mol%) was added to a solution of hydroxylated enynes **1y** (0.30 mmol) in wet CH_2Cl_2 (3.0 mL) at 0°C. Within 5 min, when the reaction was considered to be complete, as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (40 mL), washed with water, saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford corresponding vinylidenes **2y** (28%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, J = 8.0 Hz, 2H), 7.42–7.40 (m, 3H), 7.31 (d, J = 8.0 Hz, 2H), 7.26–7.11(m, 7H), 6.31(s, 1H), 5.94 (s, 1H), 4.61 and 4.48 (2×s, 2H), 3.47 (t, J = 10.4 Hz, 1H), 3.30 (dd, J = 10.4, 5.2 Hz, 1H), 3.18 (dd, J = 10.4, 5.6 Hz, 1H), 2.45 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.8, 143.7, 142.1, 141.6, 140.6, 132.7, 130.2, 129.9, 129.6, 128.7, 128.2, 127.7, 127.6, 127.2, 126.8, 123.5, 119.3, 113.3, 51.9, 51.8, 21.6, 18.6 ppm; IR (neat) 2924, 1711, 1596, 1445, 1356, 1165, 1033, 702, 665, 600, 548 cm^{-1}; HRMS (ESI): m/z calcd for $C_{28}H_{27}NO_2S$: 442.1835 [M+H]; found: 442.1833.

General procedure C: **$HSbF_6$-catalyzed tandem C–C and C–O formation toward polycyclic skeletons 3aa–ar and 4aa–ar**: $HSbF_6$ (0.015 mmol, 5 mol%) was added to a solution of hydroxylated enynes **1aa–ar** (0.30 mmol) in wet CH_2Cl_2 (3.0 mL) at room temperature. When the reaction was considered to be complete, as determined by TLC analysis,

the reaction mixture was diluted with ethyl ether (40 mL), washed with water, saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel to afford corresponding polycyclic skeletons **3aa–ar** and **4aa–ar**.

Compound ***3aa***: Reaction time: 2 h; yield: 52%; m.p. 130–132°C; ^{1}H NMR (400 MHz , $CDCl_3$): δ = 7.54 (d, J = 8.4 Hz, 2H), 7.27–7.19 (m, 7H), 3.40 (dd, J = 6.4, 2.4 Hz, 1H), 3.05 (q, J = 10.4 Hz, 1H), 2.79 (d, J = 10.4 Hz, 1H), 2.57 (d, J = 10.4 Hz, 1H), 2.43 (s, 3H), 2.32–2.24 (m, 3H), 2.09–1.95 (m, 3H), 1.68–1.28 (m, 5H), 1.28 (s, 3H), 1.27 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.4, 140.5, 140.5, 135.4, 132.1, 129.4, 128.3, 127.8, 127.0, 125.5, 99.3, 81.7, 64.4, 62.3, 54.6, 50.1, 47.2, 31.1, 26.0, 25.5, 22.7, 22.6, 21.6, 21.5 ppm; IR (neat): 2927, 1446, 1347, 1161, 1093, 1035, 750, 663, 547 cm^{-1}; HRMS (ESI): m/z calcd for $C_{28}H_{33}NO_3S$: 464.2254 [M+H]; found:464.2260.

Compound ***4aa***: Reaction time: 2 h; yield: 40%; m.p. 99–101°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, J = 8.4 Hz, 2H), 7.27–7.21 (m, 5H), 6.75 (dd, J = 7.6, 3.2 Hz, 2H), 4.74 (s, 1H), 3.45 (s, 1H), 3.41 (dd, J = 6.4, 2.0 Hz, 1H), 3.03–2.95 (m, 2H), 2.54 (d, J = 10.4 Hz, 1H), 2.44 (s, 3H), 2.33 (dd, J = 7.2, 1.6 Hz, 1H), 2.26–2.22 (m, 1H), 2.08–2.04 (m, 1H), 1.73–1.49 (m, 7H), 1.24 (s, 3H), 1.18 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.3, 140.0, 139.0, 138.6, 132.0, 129.4, 128.7, 127.9, 127.1, 126.9, 93.6, 83.0, 65.4, 62.7, 61.4, 53.8, 49.5, 31.6, 25.4, 24.8, 23.0, 22.7, 22.6, 21.5 ppm; IR (neat): 2930, 1599, 1451, 1347, 1163, 1040, 817, 737, 665, 551 cm^{-1}; HRMS (ESI): m/z calcd for $C_{28}H_{33}NO_3S$: 464.2254 [M+H]; found:464.2260.

General procedure D: $HSbF_6$-catalyzed tandem C−C and C−O formation toward 6as: $HSbF_6$ (0.015 mmol, 5 mol%) was added to a solution of hydroxylated enynes **1as** (0.30 mmol) in wet CH_2Cl_2 (3.0 mL) at room temperature. When the reaction was considered to be complete, as determined by TLC analysis, the reaction mixture was diluted with ethyl ether (40 mL), washed with water, saturated brine, dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by chromatography on silica gel to afford **6as** as a solid (65% yield). Reaction time: 8 h; m.p. 162–164°C; ^{1}H NMR (400 MHz , CDC_{l3}): δ = 7.75 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 7.2 Hz, 2H), 7.34–7.7.23 (m, 5H), 6.75 (q, J = 15.6 Hz, 1H), 6.60 (d, J = 15.6 Hz, 1H), 6.32 (d, J = 15.6 Hz, 1H), 6.28 (q, J = 15.6 Hz, 1H), 5.61(s, 1H), 4.27 (d, J = 3.6 Hz, 2H), 4.21 (d, J = 2.8 Hz, 2H), 2.42 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 143.5, 137.3, 136.8, 134.2, 134.0, 132.0, 129.8, 128.7, 128.2, 127.9, 127.4, 126.5, 125.2, 123.1, 55.2, 53.7, 21.5 ppm; IR (neat) 3459, 2833, 1595, 1342, 1162, 1107, 989, 811, 753, 669, 544 cm^{-1}; HRMS (ESI): m/z calcd for $C_{21}H_{21}NO_2S$: 352.1366 [M+H]; found: 352.1364.

Acknowledgements

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