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Silver-Catalyzed Cyclization of Sulfonyl Allenes to Dihydrofurans

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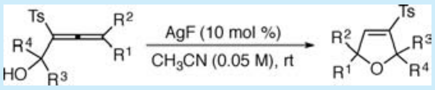
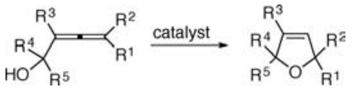
S *Supporting Information*

ABSTRACT: Treatment of α-hydroxy allenic sulfones with 10 mol % of silver fluoride in acetonitrile at ambient temperature furnished the corresponding 3-tosyl 2,5-dihydrofurans in excellent yields via a 5-*endo-trig* cyclization. The starting α-hydroxy allenic sulfones were prepared by lithiation of allenic sulfones and trapping with carbonyl compounds.

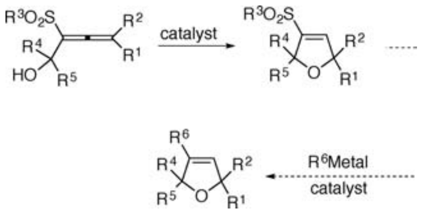


Furans and 2,5-dihydrofurans are very important structural motifs in many biologically active natural products.[1] Among the many approaches to 2,5-dihydrofurans, the metal-catalyzed cyclization of allenols is one that is generally convenient and stereoselective, provided the allene can be easily prepared (Scheme 1).[2] Over the years, the cyclization of α-allenyl alcohols with transition metals (as cations) including Ag,[3] Au,[4] Pd,[5] Pt,[6] Cu,[7] and Hg,[8] as well as protons[9] and base,[10] has been investigated. Given our discovery of a facile synthesis of allenic sulfones,[11] we became interested in their chemistry.[12] In the context of the contents of this paper, we wondered about the effect of an electron-withdrawing sulfone substituent on the rate of cyclization of allenols as well as the potential for further coupling of the vinyl sulfone contained in the product, a reaction that has been known for quite a while but has not been investigated extensively (Scheme 2).[13]

Scheme 1. Cyclization of Allenols

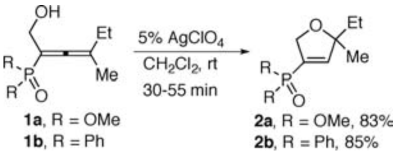


Scheme 2. Cyclization of Sulfonylallenols



Allenes bearing more complex substituents, particularly electron-withdrawing groups, have not been studied to any great extent in the context of metal ion-catalyzed cyclization to heterocycles. Wang studied allenyl silanes,[14] and Lee examined allenyl esters in the context of gold- and copper-catalyzed cyclizations.[15] It was only in 2015 that a silver-catalyzed cyclization of allenes bearing a group 15 electron-withdrawing group was published. Thus, Christov reported that the reaction of phosphonate **1a** and phosphine oxide **1b** with 5 mol % of $AgClO_4$ in CH_2Cl_2 at room temperature afforded dihydrofurans **2a** and **2b** in 83% and 85% yields, respectively, in under 1 h (Scheme 3).[16]

Scheme 3. Silver-Catalyzed Cyclization of Phosphorus(V)-Substituted Allenes



It is worth noting that Mukai developed the cyclization of allenyl alcohols possessing an electron-withdrawing group (including sulfonyl and phosphonate groups) at the C-1 position to produce various oxacycles using potassium *tert*-butoxide.[17] Our study achieves a different outcome in which the hydroxyl group of the allenyl alcohol attacks the terminal sp^2-hybridized carbon, giving stable, substituted dihydrofuran products through a 5-*endo-trig* cyclization under silver catalysis.

Our work began with attempts to oxidize **3j** to the corresponding ketone. When **3j** was treated with Fetizon's reagent (Ag_2CO_3 on Celite),[18] the corresponding dihydrofuran was obtained in 64% yield. While not surprised by this result, we realized that allenes bearing electron-withdrawing groups had not been well studied in this type of cyclization, and we therefore decided to conduct a preliminary investigation into the process, focusing primarily, but not exclusively, on silver catalysts.

We began by examining various catalysts for the cyclization of **3j**. We initially looked at the cyclization with gold catalysts. Treatment of **3j** with 10 mol % of $AuCl_3$ produced **4j** in only 31% yield and **5j** in 10% yield (Table 1, entry 2). The combination of 5 mol % of $AuCl_3$ and 5 mol %

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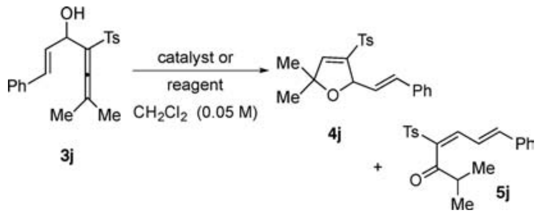
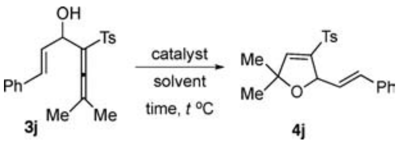
Table 1. Catalyst Optimization in the Cyclization of 3j to 4j



entry	catalyst	equiv	time	yield of **4j** (%)
1	Fetizon's	5.0	2 h	64
2	$AuCl_3$	0.1	8 h	31[b]
3	$AuCl_3$/AgOTf	0.1	18 h	36[b]
4	PPh_3AuCl/AgOTf	0.1	12 h	54[b]
5	$AgSbF_6$	0.1	10 min	81
6	$AgNO_3$	1.1	22 h	92
7	$AgClO_4$	0.1	3 h	62
8	AgOTf	0.1	20 min	70
9	AgOAc	0.1	17 h	74
10	Ag_3PO_4	0.1	48 h	NR
11	Ag_2SO_4	0.1	48 h	NR
12	AgF	0.1	6 h	80
13	AgBr	0.1	48 h	NR
14	AgI	0.1	48 h	NR
15	$CuCl_2$[a]	0.1	15 min	72
16	CuCl[a]	0.1	15 min	43
17	CuBr[a]	0.1	40 min	57
18	CuI[a]	0.1	40 min	54

[a] Reaction conditions: All gold- and silver-catalyzed reactions were carried out in CH_2Cl_2 at room temperature. All copper-catalyzed reactions (entries 15−18) were carried out in DMF (0.3 M) at 110 °C. [b] Product **5j** was also formed in 10% yield.

Table 2. Effect of Solvents on the Cyclization of 3j to 4j



entry	catalyst	equiv	solvent	temp (°C)	time	yield (%)
1	$AgNO_3$	1.1	CH_2Cl_2	40	10 h	78
2	$AgNO_3$	1.1	toluene	110	10 min	64
3	$AgNO_3$	1.1	acetone	60	5 min	76
4	$AgNO_3$	0.1	acetone	rt	1 h	76
5	$AgNO_3$	0.1	acetone	60	40 min	54
6	$AgNO_3$	0.1	H_2O/THF	rt	20 min	70
7	$AgNO_3$	0.1	MeOH	rt	5 h	75
8	AgOTf	0.1	acetone	rt	9 h	68
9	AgF	0.1	MeCN[a]	rt	1 h	92
10	AgF	0.1	MeCN[b]	rt	6 h	86
11	AgF	0.1	MeCN[c]	rt	1 h	96
12	AgF	0.1	MeCN	85	10 min	72
13	AgI	0.1	acetone	rt	48 h	NR

[a] 0.1 M. [b] 0.3 M. [c] 0.05 M.

of AgOTf conditions gave a 36% yield of **4j** along with a 15% yield of **5j** (Table 1, entry 3). The oxophilic nature of Au (III) (d^8 configuration, hard Lewis acid) favors coordination to oxygen,[19] disfavoring cyclization and permitting some oxidation. In contrast, the use of an Au(I) catalyst such as PPh_3AuOTf produced the desired cyclized product **4j** in a moderate 54% yield and **5j** in 10% yield (Table 1, entry 4).

We then examined various silver salts. Treatment of **3j** with $AgSbF_6$ selectively afforded only intramolecular hydroalkoxylation product **4j** in very good yield (Table 1, entry 5). The use of $AgNO_3$ gave a much better yield (92%), but to complete the conversion of the starting material, we had to use 1.1 equiv of the reagent and even then the process required 22 h. $AgClO_4$, AgOTf, and AgOAc also selectively provided **4j** in 62%, 70%, and 74% yield, respectively (Table 1, entries 7−9). The catalysts Ag_3PO_4 and Ag_2SO_4, however, showed no reaction even after 2 days. AgF produced the desired product **2j** with an 80% yield, but AgBr and AgI showed no reaction. Finally, various copper salts were screened at a higher temperature of 110 °C in DMF. $CuCl_2$ gave a better result than Cu(I) salts such as CuCl, CuBr, and CuI but not as good a result as AgF (Table 1, entries 15−18).

Selected catalysts were chosen for solvent optimization studies. The results are summarized in Table 2. We were particularly interested in silver fluoride as a catalyst, as we conjectured that the fluoride ion would hydrogen bond with the hydroxy group of **3j**, increasing its nucleophilicity and hence the rate of the cyclization reaction. One of the best sets of reaction conditions for the process involved treatment of a 0.1 M solution of **3j** with 10 mol % of silver fluoride. This afforded **4j** in 92% yield after 1 h (Table 2, entry 9). The high solubility of silver fluoride may have played a role in this outcome.[20] Interestingly, running the reaction at higher concentration appeared to slow the rate of the cyclization process. At a concentration of 0.05 M, **4j** was obtained in 96% yield after 1 h (Table 2, entry 11). The origin of the concentration effect is not presently known. The reaction was compatible with higher temperatures, but yields were lower compared to reactions run at room temperature (Table 2, entries 2, 3, 5, and 12).

With the optimized conditions in hand, we examined the cyclization of a number of substrates all derived from the same sulfonylallene (**6**). The results are summarized in Table 3. The substrates were easily prepared via deprotonation of **6** followed by trapping with an aldehyde or ketone (Scheme 4; see the Supporting Information).[21]

Allenols derived from aliphatic aldehydes cyclized in excellent yield but relatively slowly, requiring 3−5 h for reaction completion (Table 3, entries 1−5). Those derived from conjugated aldehydes and benzaldehydes appeared to react more quickly, with completion being achieved in 30 min in one case (Table 3, entries 6−18).

The same trend was observed with allenols derived from ketones, though the effect was decidedly muted, likely due to steric effects (Table 3, entries 19−25). Regardless, like all other examples, the cyclization process is reasonably rapid and high yielding.

The mechanism of the cyclization of α-hydroxy allenes to dihydrofurans has been proposed for silver as well as other catalysts.[4b,7] In our case, coordination of the silver ion to the more electron-rich double bond of **3** activates the latter for nucleophilic attack, affording **8**. The cyclization produces the intermediate **9**, which undergoes a proton transfer to produce the final product **4** (Scheme 5). It might be possible to trap the organosilver intermediate, but to the best of our knowledge, this has not been reported.

In a simple approach to accomplish this task, we treated a 0.05 M solution of **3j** in a 1:1 mixture of acetonitrile and D_2O

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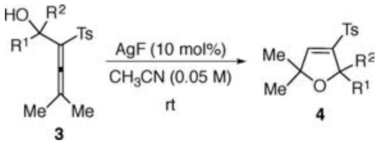
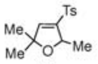
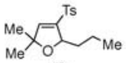
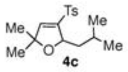
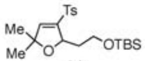
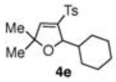
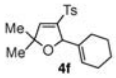
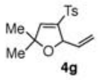
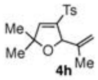
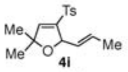
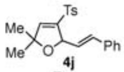
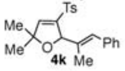
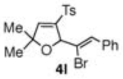
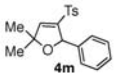
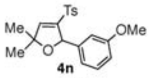
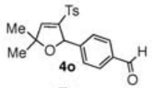
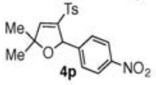
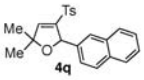
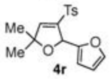
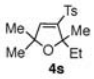
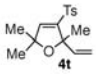
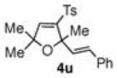
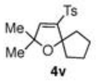
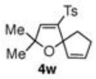
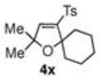
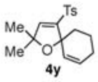
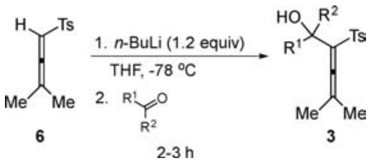
Table 3. AgF-Catalyzed Intramolecular Hydroalkoxylation of Allenols



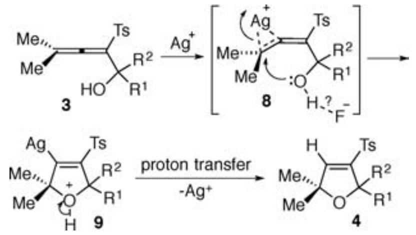
entry	allenol	product	time (h)	yield (%)
1	3a	 4a	2	94
2	3b	 4b	5	94
3	3c	 4c	5	93
4	3d	 4d	4	93
5	3e	 4e	5	90
6	3f	 4f	2.5	99
7	3g	 4g	1.5	99
8	3h	 4h	3	91
9	3i	 4i	1	90
10	3j	 4j	1	96
11	3k	 4k	4	97
12	3l	 4l	0.5	95
13	3m	 4m	1.5	95
14	3n	 4n	0.4	97
15	3o	 4o	2.5	87
16	3p	 4p	7	86
17	3q	 4q	1	95
18	3r	 4r	1	99
19	3s	 4s	5.5	100
20	3t	 4t	3.5	94
21	3u	 4u	4	96
22	3v	 4v	5.5	100
23	3w	 4w	8	90
24	3x	 4x	8	94
25	3y	 4y	8	99

Scheme 4. Lithiation and Subsequent Trapping of an Allenic Sulfone



with silver fluoride. At room temperature, the reaction proceeded over 11 h to produce **4j-d$_1$** with complete deuterium incoporation as assessed by ^{1}H NMR (Scheme 6). We conclude that the putative organosilver intermediate in the cyclization reaction had been trapped formally by D$^+$.

Scheme 5. Likely Mechanism for Silver-Catalyzed Cyclization



In conclusion, we have demonstrated that silver ion catalysis is effective for the cyclization of sulfonylallenols to afford highly substituted dihydrofurans. Further studies of the scope of the

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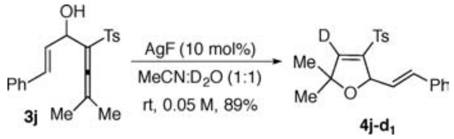
Scheme 6. Deuteration Experiment



process and the chemistry of the products will be reported in due course.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b02917.

Experimental procedures and analytical data for new compounds and products (PDF)

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Notes

The authors declare no competing financial interest.

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