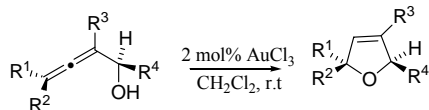


Stereoselective Synthesis of Conjugated Bisallenols as Precursors of Novel Bis(2,5-dihydrofuran) Derivatives

Manojkumar Poonoth and Norbert Krause†

Introduction

By taking advantage of the high reactivity and axial chirality of allenes¹, our group has established an efficient and stereoselective synthesis of 2,5-dihydrofurans by gold-catalyzed cycloisomerization of α -hydroxyallenes².



At this point, the synthesis of conjugated bis(α -allenols) as precursors of bis(2,5-dihydrofurans) seemed to be challenging.

Since 2,5-dihydrofurans can be easily transformed to tetrahydrofuran systems, this protocol assumes importance because the bis(THF) core is present in a family of natural products called Annonaceous acetogenins (ACGs)³ that shows highly diverse biological activities.

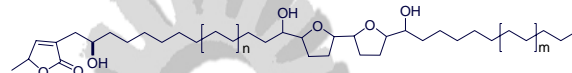
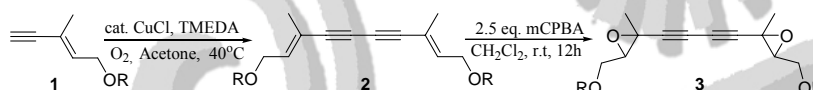


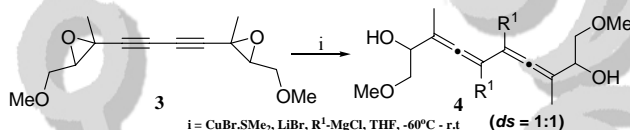
Figure 1 : General structure of acetogenins

Results

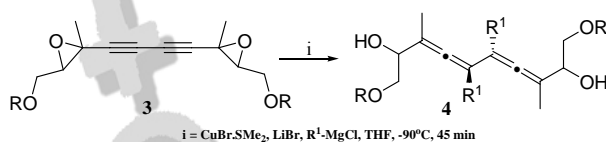
Synthesis of Bis(propargyloxiranes)



Copper-mediated S_N2' -Substitution⁴ of Bis(propargyloxiranes) at -60°C



Temperature-dependent Stereoselective Formation of Bisallenols



X-ray Crystal structure of 4a:

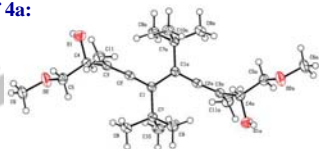
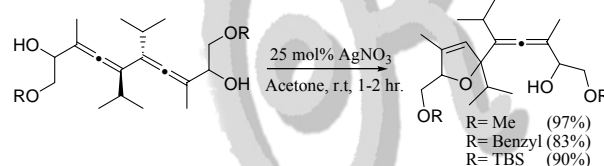


Table 1: Generality of Stereoselective Bisallene Synthesis

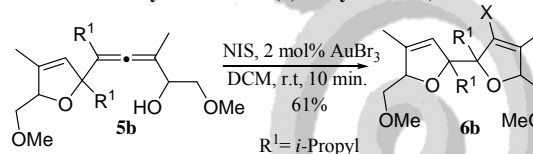
Entry	R	R ¹	Product	Yield(%)
1	Methyl	<i>t</i> -Butyl	4a	60
2	Methyl	<i>i</i> -Propyl	4b	57
3	Methyl	Phenyl	4c	36
4	Benzyl	<i>i</i> -Propyl	4d	50
5	Benzyl	<i>t</i> -Butyl	4e	60
6	TBS	<i>i</i> -Propyl	4f	63
7	TBS	<i>t</i> -Butyl	4g	61
8	TBS	Phenyl*	4h	55
9	TBS	<i>n</i> -Butyl	4i	46

* Highly unstable and decomposes on exposure to air at r.t.

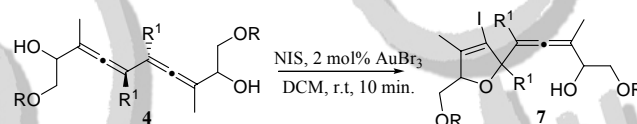
AgNO_3 -catalyzed⁵ Cycloisomerization of Bisallenols: Synthesis of 2-Allenyl-substituted 2,5-Dihydrofurans



NIS-mediated⁶ Gold-catalyzed Cycloisomerization: Synthesis of Bis(2,5-dihydrofuran)



NIS-mediated Gold-catalyzed Cycloisomerization: Synthesis of 2-Allenyl-3-iodo-2,5-dihydrofurans



Entry	R	R ¹	Product	Yield(%)
1	Methyl	<i>t</i> -Butyl	7a	81
2	TBS	<i>t</i> -Butyl	7g	80
3	Benzyl	<i>t</i> -Butyl	7e	69
4	Methyl	<i>i</i> -Propyl	7b	60

Conclusion:

We have developed a convenient method for the synthesis of highly substituted conjugated bis(α -allenols) and thereby providing a successful route to novel bis(2,5-dihydrofurans) and 2-allenyl-2,5-dihydrofuran derivatives. Further studies regarding the synthesis and application of conjugated bis(α -allenols) and their cycloisomerization products are currently under investigation.

References

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