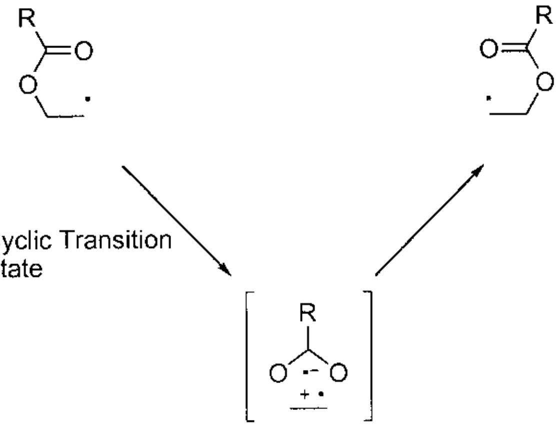
A Novel 1,2-Migration of Acyloxy, Phosphatoxy, and Sulfonyloxy Groups in Allenes: Efficient Synthesis of Tri- and Tetrasubstituted Furans

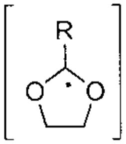
Gevorgyan and Co-workers

Angew. Chem. Int. Ed. **2004**, *43*, 2280

The 1,2-Acyloxy Rearrangement



Cyclic Transition State

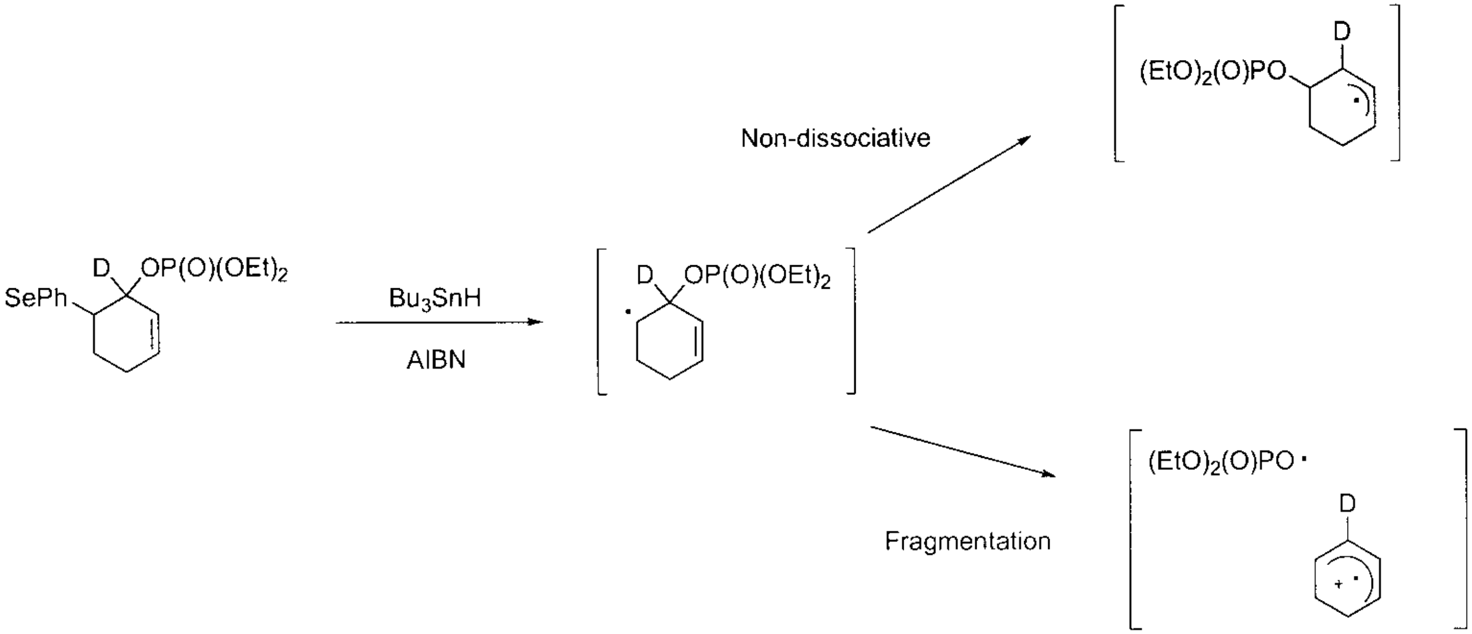


-Intermediate ruled out based on its reactivity (facile ring opening) as well as calculations.

-Reaction acceleration by electron-withdrawing R groups.
-Reaction accelerated by polar solvents including water.

J. Org. Chem. **1988**, 53, 464
J. Am. Chem. Soc. **1982**, *104*, 4399
J. Am. Chem. Soc. **1984**, 106, 1793
Calculations: *J. Am. Chem. Soc.* **1984**, *106*, 5119

Radical Acyloxy Rearrangement Mechanistic Analysis

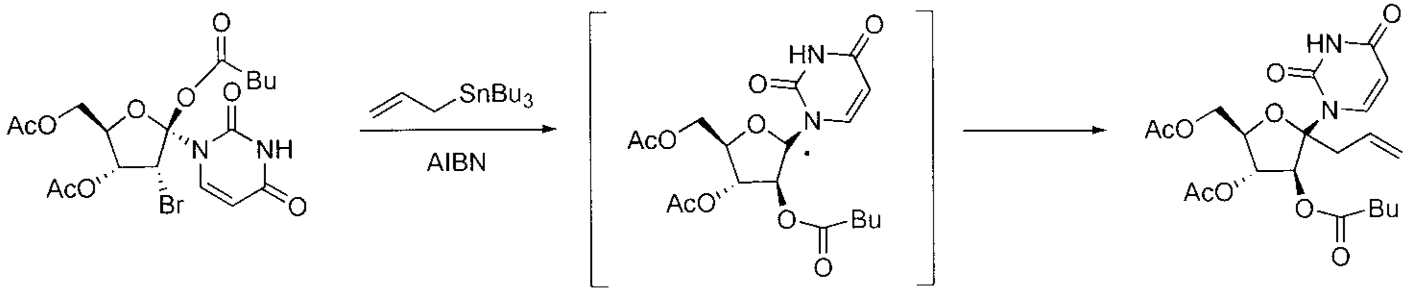


-Fragmentation would result in D scrambline across four carbons, whereas a non dissociative pathway would distribute it across two.

-Labeling experiments suggest a non-dissociative rearrangement.

J. Am. Chem. Soc. **1994**, *116*, 2631

The 1,2-Acyloxy Rearrangement in Carbohydrate Chemistry

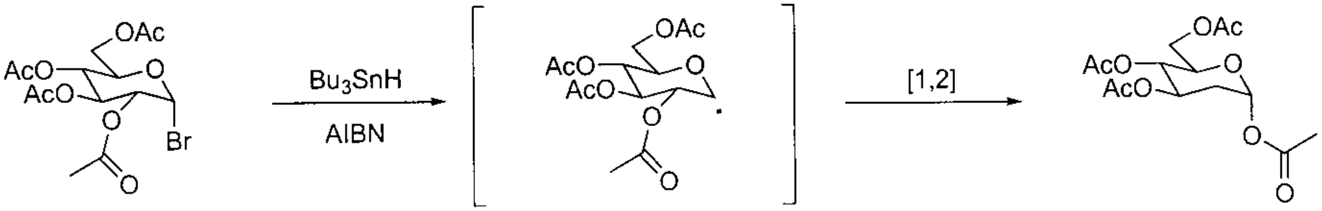


-Reactions can be initiated thermally or photolytically.

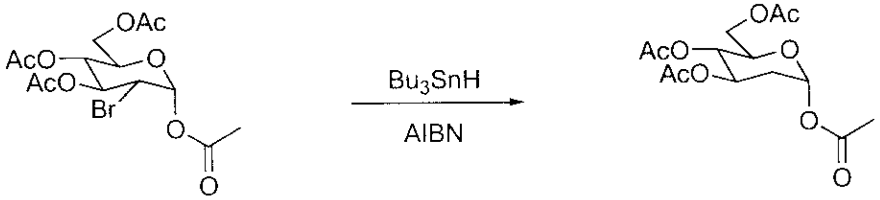
-Yields variable (40-60%) and reduced radical or elimination products are the balance of the products.

Tetrahedron Lett. **1995**, *36*, 3867
J. Org. Chem. **2003**, *68*, 2006

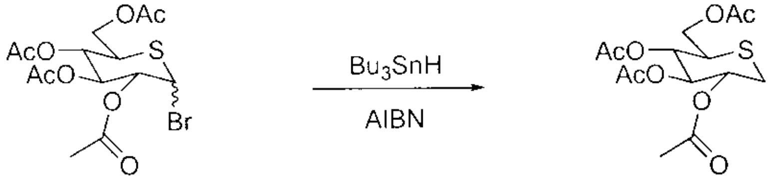
The 1,2-Acyloxy Rearrangement in Carbohydrate Chemistry



-Rearrangment to secondary radical



-Reduction of radical

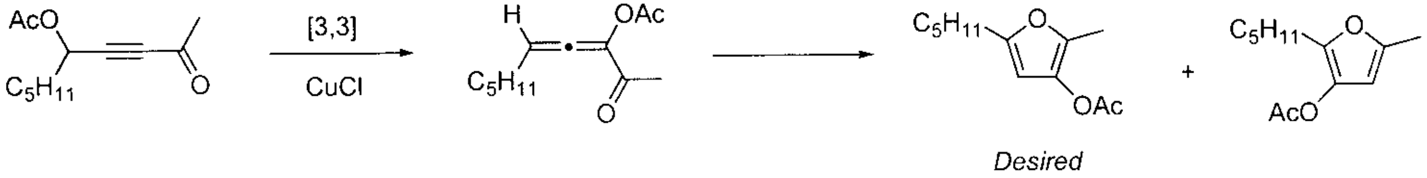


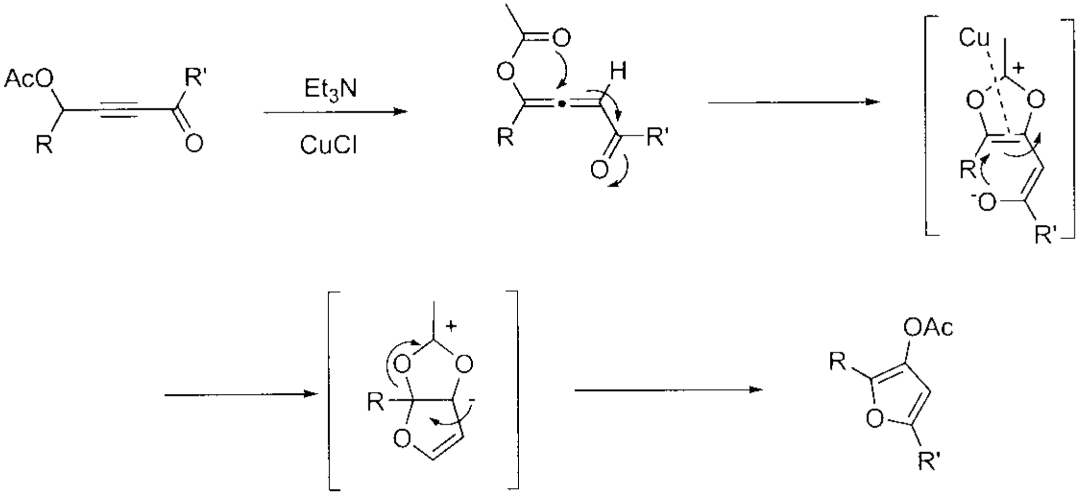
-Sulfur gives only reduced anomeric radical

-The stabilized anomeric radical will undergo rearrangement to the less stable secondary radical. Why? Calculations indicate a net gain in energy (~ 17 kcal/mol) for the molecule if a second C-O bond in made at an oxygen bearing carbon.

J. Org. Chem. **1988**, *53*, 4364
Calculations: *J. Am. Chem. Soc.* **1985**, *107*,6393

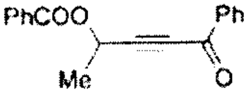
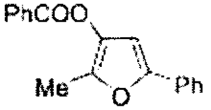
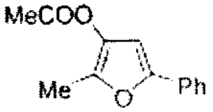
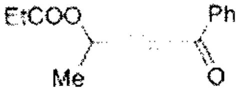
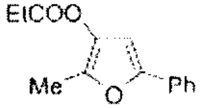
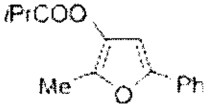
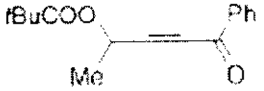
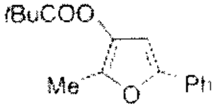
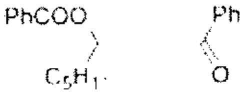
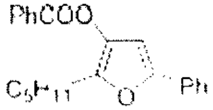
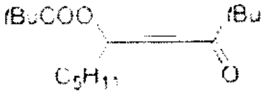
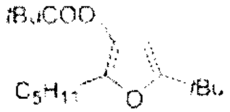
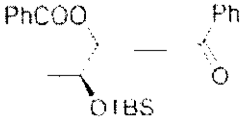
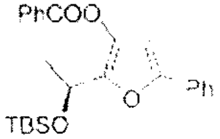
A Unique 1,2 Acyloxy Rearrangement





-A alkynyl-allenyl isomerization, metal-promoted closure of the furanoid ring, and addition-elimination to effect a net 1,2-acyloxy rearrangement.

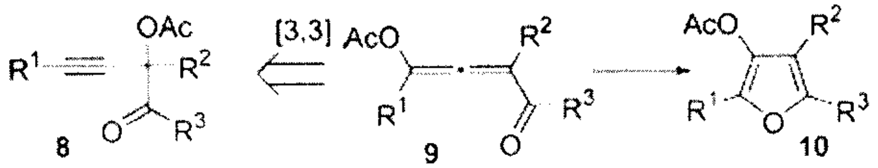
Synthesis of Trisubstituted Furans

Substrate		t [h]	Product		Yield [%][b]
	**5a**	22		**4a**	82[c]
	**5b**	1		**4b**	81
	**5c**	9		**4c**	69
	**5d**	2		**4d**	90
	**5e**	17		**4e**	86
	**5f**	23		**4f**	80
	**5g**	32		**4g**	80
	**5h**	46		**4h**	83[c,d]

[a] All reactions carried out on a 1-mmol scale. [b] Yields of isolated products. [c] Reactions carried out at 80°C. [d] TBS = *tert*-butyldimethylsilyl.

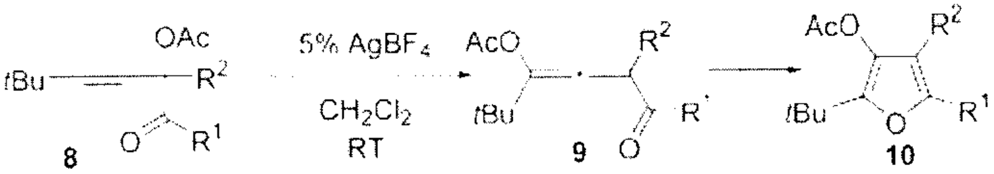
-Selectivities are best with phenyl and t-butyl ketones.
-Reactions carried out at room temperature unless otherwise noted.

Expansion to Tetrasubstituted Furans

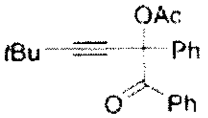
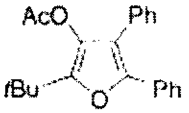
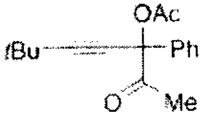
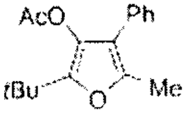
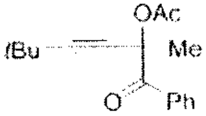
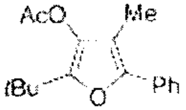
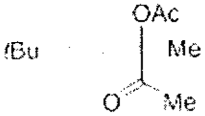
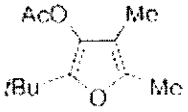
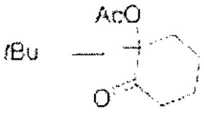
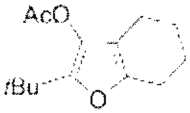


-Acess the allenyl intermediate by a [3,3] rearrangement of an α-acetoxy alkynyl ketone.
-1,2-Acyloxy rearrangement and cycolisomerization should proceed from the allene.

-The result....



The Sythesis of Tetrasubstituted Furans

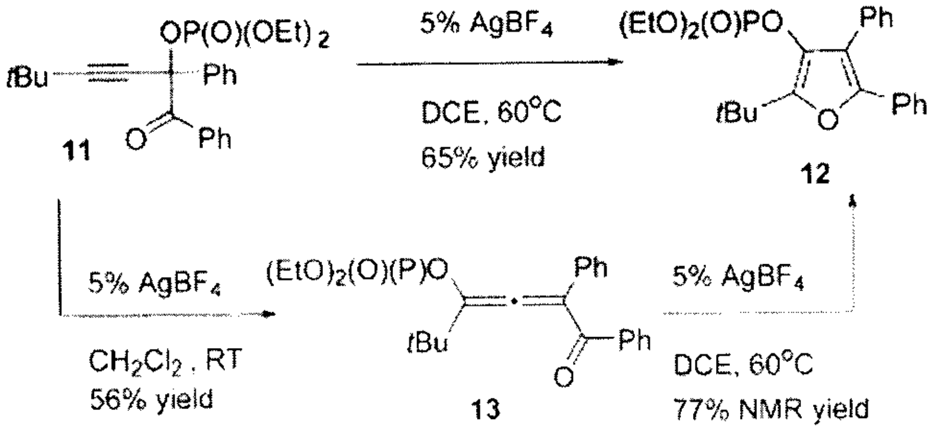
Substrate		t [min]	Product		Yield [%][b]
	**8 a**	2		**10 a**	> 99
	**8 b**	15		**10 b**	73
	**8 c**	15		**10 c**	84
	**8 d**	15		**10 d**	90
	**8 e**	10		**10 e**	86

[a] Reactions carried out on a 1-mmol scale. [b] Yields of isolated products.

-Reactions proceed at room temperature in the presence of 5 mol% $AgBF_4$.

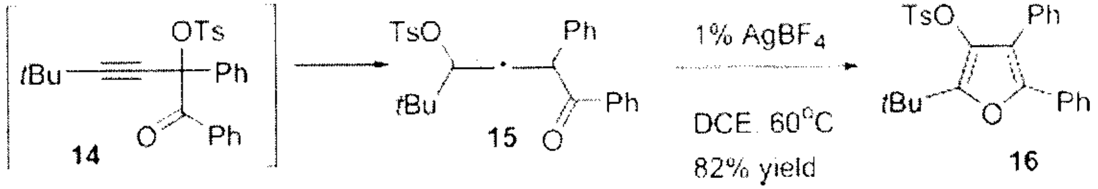
-Reaction still limited at the terminal position of the alkyne.

Heteroatomic Migrating Groups in the Synthesis of Tetrasubstituted Furans



-Phosphorous analogues require heating, but yields of furans are presumable still good.

-Attempted synthesis of 14 gave 15, which underwent furan formation in good yield.



Conclusions

-A new "polar" 1,2 acyloxy rearrangement was discovered with allows access to tri- and tetrasubstituted furans.

-These furans bear oxygenationat the 3-position, but the scope is somewhat limited to phenyl and tert-butyl ketones.

-Further development could render this method quite attractive in the context of natural product synthesis and/or combinatorial library development.