Pergamon

Tetrahedron Letters, Vol. 36, No. 31, pp. 5581-5584, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01066-1

A Novel and Convenient Synthesis of 2-Aryl-4-methylenetetrahydrofurans from 2-(Trimethylsiloxymethyl)allyltrimethylsilane and Acetals

Takeshi Oriyama,* Akihiro Ishiwata, Tomohumi Sano, Toshie Matsuda, Masaki Takahashi, and Gen Koga

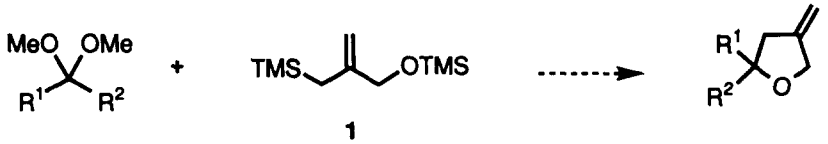
Department of Chemistry, Faculty of Science, Ibaraki University, Bunkyo, Mito 310, Japan

Abstract: The reaction of acetals with 2-(trimethylsiloxymethyl)allyltrimethylsilane under the influence of the combined use of a catalytic amount of tin(II) halide and acetyl halide affords the corresponding 2-aryl-4-methylenetetrahydrofurans in good yields.

Tetrahydrofuran is one of the most common skeletal elements among a wide range of biologically active natural products. While a number of methods have already been documented for the construction of this important ring element,[1] they appear to be only scattered procedures for the efficient synthesis of tetrahydrofurans by a manipulation of carbonyl compounds with relevant three-carbon units. Trost *et al.* reported a palladium-catalyzed cycloaddition of trimethylenemethane to carbonyl compounds to form methylene-tetrahydrofurans.[2] Much more recently, Taddei *et al.* reported a two-step synthesis of methylene-tetrahydrofurans from aldehydes and 2-chloromethyl-3-trimethylsilyl-1-propene via homoallyl alcohols.[3] To the best of our knowledge, however, acetals have never been used in the direct preparation of tetrahydrofurans via a carbon-carbon bond-forming three-carbon manipulation.

Now we wish to report a new and efficient method for the synthesis of methylenetetrahydrofurans from acetals and 2-(trimethylsiloxymethyl)allyltrimethylsilane.[4]

Our previous investigation on the halogenative allylation of acetals with allyltrimethylsilane promoted by SnX_2 / AcX[5] suggested that the reaction of acetals with an allyltrimethylsilane **1** bearing a protected hydroxymethyl group at β-position would provide a simple and efficient route towards the synthesis of 2-substituted-4-methylenetetrahydrofurans (Scheme 1).

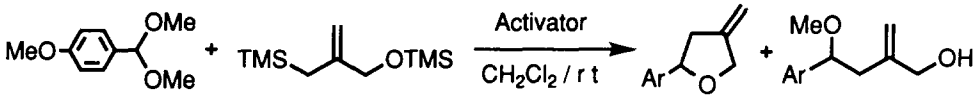


1

Scheme 1

First, we examined the reaction of *p*-anisaldehyde dimethyl acetal (**2**) with 2-(trimethylsiloxymethyl)allyltrimethylsilane (**1**) in the presence of various activator catalysts as shown in Table 1. A stoichiometric amount of a common Lewis acid, $BF_3 \cdot OEt_2$,[6] gave directly 2-substituted-4-methylenetetrahydrofuran (**3**) in 74% yield (Run 5). However, neither reaction with a catalytic amount of $BF_3 \cdot OEt_2$ nor $TiCl_4$ afforded desired cyclization products **3** (Runs 1 and 2). Allylation product **4** was formed predominantly by a catalytic amount of trimethylsilyl trifluoromethanesulfonate (TMSOTf)[7] (Run 4). While the reaction promoted by the combination of $SnCl_2$ and AcCl (5 mol% each to the acetal) afforded the corresponding tetrahydrofuran in 91% yield, a stoichiometric amount of AcCl (1.1 equiv. to the acetal) lowered the yield (Run 7). A catalytic amount of benzoyl halide (BzX) in place of AcCl also gave satisfactory results (Runs 8 and 12). The reagent system, SnX_2 (5 mol%) - AcX (5 mol%)[8] gave better results in terms of both chemical yield and efficiency compared to other activator systems.

Table 1. The Effect of Activator System to the Reaction between *p*-Anisaldehyde Dimethyl Acetal(**2**) and 2-(Trimethylsiloxymethyl)allyltrimethylsilane(**1**).



2 **1** Ar = 4-$MeOC_6H_4$ **3** **4**

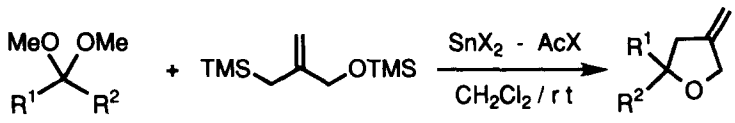
Run	Activator (mol%)[a]	Time / h	Yield[b] of **3** / %	Yield[b] of **4** / %
1	$BF_3 \cdot OEt_2$ (5)	8	0	0
2	$TiCl_4$ (5)	6	0	13
3	$SnCl_4$ (5)	2	65	35
4	TMSOTf (5)	2[c]	6	80
5	$BF_3 \cdot OEt_2$ (120)	2	74	0
6	$SnCl_2$ (5) - AcCl (5)	2	91	0
7	$SnCl_2$ (5) - AcCl (110)	2	57	0
8	$SnCl_2$ (5) - BzCl (5)	2	76	8
9	$SnCl_2$ (5) - TMSCl (5)	30	0	9
10	AcCl (5)	8	0	0
11	$SnBr_2$ (5) - AcBr (5)	1	83	0
12	$SnBr_2$ (5) - BzBr (5)	1.5	83	0
13	$SnBr_2$ (5) - TMSBr (5)	6	17	53
14	$Sn(OTf)_2$ (5)	1	82	0

a) Molar ratio of acetal(**2**) : allylsilane(**1**) = 1 : 1.2 b) Isolated yield of purified product.
c) The reaction was performed at -78°C.

The reaction was conducted with various acetals under the optimum conditions and the results are summarized in Table 2.[9] As can be seen, the reaction is successful for acetals derived from various aromatic aldehydes and ketones. However, in the case of benzaldehyde dimethyl acetal, 2-phenyl-4-methylenetetrahydrofuran was obtained in only 25 % yield.

In this reaction, acetals are used as dication equivalent of one-carbon unit, whereas 2-(trimethylsiloxymethyl)allyltrimethylsilane provides dianion $^-$C-C-C-O$^-$ equivalent as shown in Scheme 2.[10]

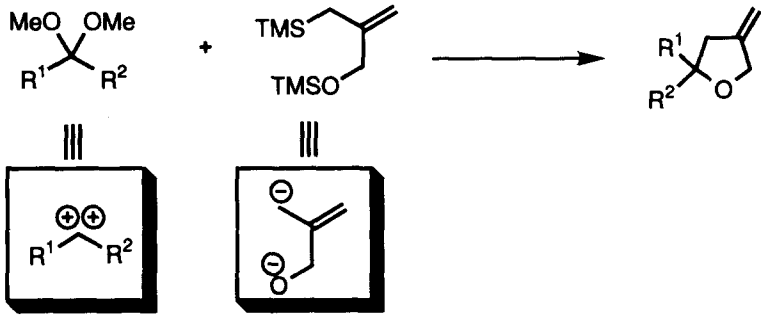
Table 2. Synthesis of Various 4-Methylenetetrahydrofurans from Acetals.[a),b)]



5 1 6

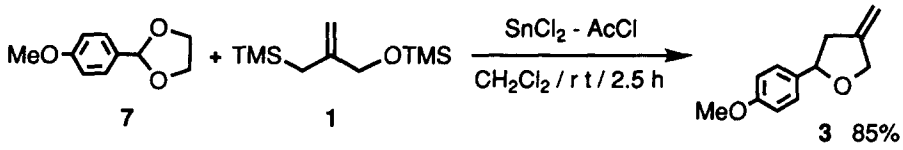
R^1	R^2	X	Time / h	Yield[c)] of **6** / %
Ph	H	Cl	12	25
4-$MeOC_6H_4$	H	Cl	2	91
2-$MeOC_6H_4$	H	Cl	4	97
4-MeC_6H_4	H	Br	24	67
2-Furyl	H	Br[d)]	8	70
(*E*)-PhCH=CH	H	Br	12	64
Ph	Me	Cl	4	66
		Br	2	58
Ph	Et	Cl	6	47
		Br	6	70

a) Each product gave satisfactory ^1H NMR and IR spectra.
b) Molar ratio of acetal : allylsilane : SnX_2 : AcX = 1 : 1.2 : 0.05 - 0.1 : 0.05 - 0.1.
c) Isolated yield of purified product.
d) The reaction was performed at -20°C.



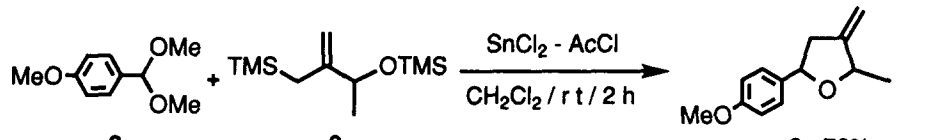
Scheme 2

Next, we examined the reaction of ethylene glycol acetal of *p*-anisaldehyde(**7**) with allylsilane **1**, and the result was also proved to be very successful (Scheme 3).



Scheme 3

This novel methodology was also effective to the synthesis of 2,5-disubstituted-4-methylenetetrahydrofuran **9** from acetal and 2-[1-(trimethylsiloxy)ethyl]allyltrimethylsilane (**8**) as shown in Scheme 4.



Scheme 4

In conclusion, the present one-step reaction of acetals and allylsilane to form methylenetetrahydrofurans has an advantage that features experimental convenience and extremely mild reaction conditions in comparison to the earlier two-step synthesis of methylenetetrahydrofurans. Further work on broadening the scope and synthetic applications of this novel methodology is now in progress.

REFERENCES AND NOTES

1. For example, see: Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.
2. a) Trost, B. M.; Bonk, P. J. *J. Am. Chem. Soc.* **1985**, *107*, 8277. b) Trost, B. M.; King, S. A. *Tetrahedron Lett.* **1986**, *27*, 5971. c) Trost, B. M.; King, S. A.; Schmidt, T. *J. Am. Chem. Soc.* **1989**, *111*, 5902. d) Trost, B. M.; King, S. A. *J. Am. Chem. Soc.* **1990**, *112*, 408.
3. D'Aniello, F.; Mattii, D.; Taddei, M. *Synlett* **1993**, 119.
4. 2-(Trimethylsiloxymethyl)allyltrimethylsilane was prepared according to the procedure reported by Trost: Trost, B. M.; Chan, D. M. T.; Nanninga, T. N. *Org. Synth.* **1984**, *62*, 58.
5. Oriyama, T.; Iwanami, K.; Tsukamoto, K.; Ichimura, Y.; Koga, G. *Bull. Chem. Soc. Jpn.* **1991**, *64*, 1410.
6. Hosomi, A.; Ando, M.; Sakurai, H. *Chem. Lett.* **1986**, 365.
7. Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 71.
8. Other useful reactions promoted by AcX / SnX_2 reagent system, see: Oriyama, T.; Iwanami, K.; Miyauchi, Y.; Koga, G. *Bull. Chem. Soc. Jpn.* **1990**, *63*, 3716.
9. The following experimental procedure is typical: to a suspension of anhydrous tin(II) chloride (2.6 mg, 0.014 mmol) and *p*-anisaldehyde dimethyl acetal (49.5 mg, 0.27 mmol) in dichloromethane (2.0 ml) were added 2-(trimethylsiloxymethyl)allyltrimethylsilane (70.4 mg, 0.33 mmol) in dichloromethane (1.5 ml) and acetyl chloride (1.2 mg, 0.015 mmol) successively at room temperature under an argon atmosphere. The reaction mixture was stirred for 2 h at this temperature and quenched with a saturated aqueous sodium hydrogen carbonate. The organic materials were extracted with dichloromethane and combined extracts were washed with brine and dried over anhydrous sodium sulfate. The solvent was evaporated and 2-(4-methoxyphenyl)-4-methylenetetrahydrofuran (46.9 mg, 91%) was isolated by thin layer chromatography on silica gel. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28 (d, J=8.6 Hz, 2H), 6.87 (d, J=8.6 Hz, 2H), 5.02 (d, J=2.2 Hz, 1H), 4.95 (d, J=2.2 Hz, 1H), 4.89 (dd, J=8.8, 6.2 Hz, 1H), 4.50 (d, J=13.4 Hz, 1H), 4.37 (d, J=13.4 Hz, 1H), 3.79 (s, 3H), 2.89 (dd, J=15.8, 6.2 Hz, 1H), 2.57 (dd, J=15.8, 8.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.1, 148.1, 133.7, 127.3, 113.7, 104.2, 80.8, 71.2, 55.2, 41.0.
10. Concerning the reaction mechanism, allylation product is supposed to be formed first directly from acetal, followed by intramolecular cyclization to give 4-methylenetetrahydrofuran along with a formation of two molar amounts of TMSOMe.

(*Received in Japan* 15 *March* 1995; *revised* 5 *June* 1995; *accepted* 12 *June* 1995)