Short Articles

Bull. Chem. Soc. Jpn., **74**, 569–570 (2001) 569

Tin(II) Trifluoromethanesulfonate-Catalyzed Highly Selective Synthesis of 2-Substituted 4-Methylenetetrahydropyrans from Trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane and Acetals

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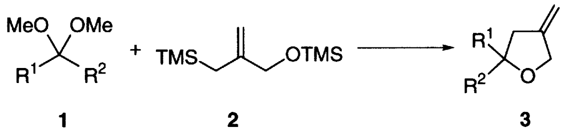
(Received September 18, 2000)

A variety of 2-substituted 4-methylenetetrahydropyrans are easily produced by the reaction of acetals with trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane under the influence of a catalytic amount of tin(II) trifluoromethanesulfonate.

Our previous investigation[1] documented the novel and convenient synthesis of 2-aryl-4-methylenetetrahydrofurans from acetals and trimethyl[2-(trimethylsiloxymethyl)allyl]silane. In this reaction, the acetals **1** and the silane **2** act as geminal dication equivalent and dianion equivalent of 4-atom unit, respectively, to give directly the tetrahydrofurans **3**[2] by a simple one-pot procedure (Scheme 1). As a logical extension, we have envisioned a way to extend our new methodology to the synthesis of 4-methylenetetrahydropyrans by the use of homologous silane, trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane (**4**), in place of trimethyl[2-(trimethylsiloxymethyl)allyl]silane (**2**). On the other hand, Markó et al. reported a trimethylsilyl trifluoromethanesulfonate (TMSOTf)-catalyzed condensation of bis-silylated reagent **4** with carbonyl compounds to give regioisomeric mixtures of dihydropyrans.[3]

Our expectation has been successfully realized, and in this communication, we wish to describe an expedient method for the highly selective synthesis of 2-substituted 4-methylenetetrahydropyrans from various acetals under mild conditions.

The starting homologous silane, trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane (**4**), was prepared from commercially available alcohol, 3-methyl-3-buten-1-ol, by a procedure similar to that for the synthesis of the silane **2**.[4]



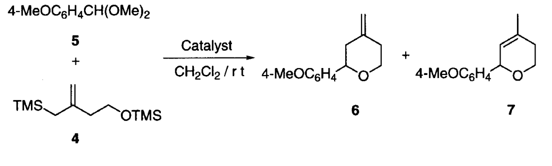
Scheme 1.

First, we undertook to examine the reaction of *p*-anisaldehyde dimethyl acetal (**5**) with trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane (**4**) according to the procedure of 2-aryl-4-methylenetetrahydrofuran synthesis previously reported by us.[1] The desired product, 2-(4-methoxyphenyl)-4-methylenetetrahydropyran (**6**), was obtained in 53% yield (Table 1, Run 2). After a preliminary investigation in search of the optimum catalyst and its molar ratio to the substrates, we have found that tin(II) trifluoromethanesulfonate in a molar ratio between 0.05 to 0.1 to the acetal **5** gave the highest yield of the product **6**. However, a double bond isomer **7** was also obtained in 3/97 to 12/88 molar ratio to **6** (Table 1, Runs 5–8).

The reaction was conducted at room temperature with various dimethyl acetals including those of aromatic aldehydes, aromatic ketones, aliphatic aldehydes, and aliphatic ketones. Representative results are summarized in Table 2. As can be seen, the reaction is successful for all of the acetals of both aldehydes and ketones. The cyclization products are mixtures of double bond positional isomers **9**, **10**, and **11** with a consistent preponderance of exocyclic isomers **9**. Although these exocyclic double bond isomers could not be separated by silica gel chromatography, we have found that this complexity of the product can be conveniently evaded by lowering the reaction temperature. Thus, the reaction performed at –78 °C (Table 2) afforded exclusively the single cyclization products,[5] exocyclic isomers **9**, in good yields without the appearance of double bond isomers.[6]

In conclusion, the present one-step synthesis of 2-substituted 4-methylenetetrahydropyrans from acetals has these advantageous features: 1) experimental convenience, 2) mild reaction conditions, 3) single cyclization product, and 4) starting from acetals, not from carbonyl compounds. Further work on broadening the scope and synthetic applications of this novel methodology is now in progress.

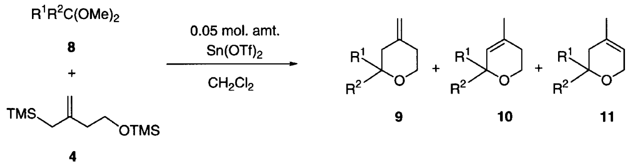
Table 1. The Effect of Catalyst on the Reaction between *p*-Anisaldehyde Dimethyl Acetal and Trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane[a)]



Run	Catalyst (molar amounts)	Time/h	Yield/%	**6** : **7**[b)]
1	SnCl$_2$ (0.05)	1	0	—
2	SnCl$_2$ (0.1)–AcCl (0.1)	4	53	100 : 0
3	SnBr$_2$ (0.05)	1	0	—
4	ZnCl$_2$ (0.05)	1	0	—
5	Sn(OTf)$_2$ (0.05)	0.5	74	96 : 4
6	Sn(OTf)$_2$ (0.05)	4	71	93 : 7
7	Sn(OTf)$_2$ (0.1)	0.5	73	88 : 12
8	Sn(OTf)$_2$ (0.01)	0.5	67	97 : 3

a) Molar ratio of acetal **5** : allylsilane **4** = 1 : 1.2. b) Determined by ^{1}H NMR.

Table 2. Synthesis of Various 4-Methylenetetrahydropyrans from Acetals[a)]



Run	$R^1R^2C(OMe)_2$	Temp	Time/h	Yield of **9** + **10** + **11**/%	**9** : **10** : **11**[b)]
1	4-$MeOC_6H_4CH(OMe)_2$	rt	0.5	74[c)]	96 : 4 : 0
2		−78 °C	4	80	100 : 0 : 0
3	(*E*)-$PhCH{=}CHCH(OMe)_2$	rt	1	65	88 : 3 : 9
4		−78 °C	4	65	100 : 0 : 0
5	$Ph(CH_2)_2CH(OMe)_2$	rt	1	21	63 : 37 : 0
6		−78 °C	4	0	—
7	$PhC(OMe)_2CH_3$	rt	1	85	94 : 3 : 3
8		−78 °C	4	87	100 : 0 : 0
9	(*n*-Pr)$_2C(OMe)_2$	rt	1	83	91 : 5 : 4
10		−78 °C	4	71	100 : 0 : 0
11	[-$(CH_2)_5$-]$C(OMe)_2$	rt	1	86	92 : 8 : 0
12		−78 °C	4	71	100 : 0 : 0

a) Molar ratio of acetal **8** : allylsilane **4** = 1 : 1.2. b) Determined by ^{1}H NMR. c) Reaction was carried out for 0.5 h.

References

1 T. Oriyama, A. Ishiwata, T. Sano, T. Matsuda, M. Takahashi, and G. Koga, *Tetrahedron Lett.*, **36**, 5581 (1995).

2 Markó et al. reported that none of the tetrahydrofuran was formed by the silyl-modified Sakurai reaction of the silane **2** with aldehydes but the *exo*-methylenetetrahydropyran was obtained: I. E. Markó and D. J. Bayston, *Tetrahedron Lett.*, **34**, 6595 (1993).

3 A. Mekhalfia, I. E. Markó, and H. Adams, *Tetrahedron Lett.*, **32**, 4783 (1991).

4 Trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane was obtained in 65% yield from 3-methyl-3-buten-1-ol: B. M. Trost, D. M. T. Chan, and T. N. Nanninga, *Org. Synth.*, **62**, 58 (1984).

5 Typical experimental procedure is as follows: To a suspension of anhydrous tin(II) trifluoromethanesulfonate (5.2 mg, 0.012 mmol) and *p*-anisaldehyde dimethyl acetal (44.5 mg, 0.24 mmol) in dichloromethane (2.0 ml) were added trimethyl{2-[2-(trimethylsiloxy)ethyl]allyl}silane (68.4 mg, 0.30 mmol) in dichloromethane (1.5 ml) at –78 °C under an argon atmosphere. The reaction mixture was stirred for 4 h at –78 °C and quenched with a saturated aqueous sodium hydrogencarbonate. 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-methylenetetrahydropyran (39.9 mg, 80%) was isolated by thin-layer chromatography on silica gel. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 8.8 Hz, 2H), 6.87 (d, J = 8.8 Hz, 2H), 4.79 (dd, J = 6.6, 1.8 Hz, 2H), 4.25–4.18 (m, 2H), 3.79 (s, 3H), 3.54 (td, J = 11.0, 2.6 Hz, 1H), 2.44–2.20 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.0, 134.8, 132.1, 127.2, 119.8, 113.8, 75.4, 66.5, 55.3, 37.6, 22.9.

6 Markó et al. also reported that the TMSOTf-catalyzed condensation of reagent **4** with carbonyl compounds could give the exocyclic isomers selectively by using excess amounts of alkoxytrimethylsilane, such as C_2H_5OTMS: I. E. Markó and A. Mekhalfia, *Tetrahedron Lett.*, **33**, 1799 (1992). I. E. Markó, A. Mekhalfia, D. J. Bayston, and H. Adams, *J. Org. Chem.*, **57**, 2211 (1992).