CHEMISTRY LETTERS, pp. 259-262, 1989.

A Convenient Synthesis of Cyclic Ethers from Siloxy Carbonyl Compounds

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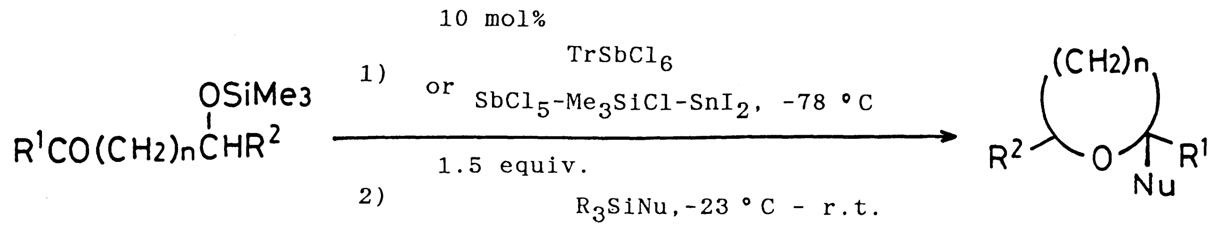
Five — seven membered cyclic ethers are prepared by one-pot procedure in good yields from γ-, δ-, and ε-siloxy carbonyl compounds, respectively, on treatment with silyl nucleophiles (triethylsilane, allyltrimethylsilane, trimethylsilyl cyanide, etc.) in the presence of a catalytic amount of trityl hexachloroantimonate, or a catalyst system of antimony pentachloride, chlorotrimethylsilane and tin (II) iodide.

In previous papers, we have reported that acyclic ethers are synthesized from carbonyl compounds on treatment with alkoxytrialkylsilane and silyl nucleophiles in the presence of $TrClO_4$ or Ph_2BOTf,[1] and that α-mono- and α,α-disubstituted cyclic ethers are synthesized from lactones on treatment with t-butyldimethylsiloxy-1-ethoxyethene and silyl nucleophiles by the promotion of trityl salts such as $TrSbCl_6$, $TrSbF_6$ or $TrClO_4$, or by the catalyst system of $SbCl_5$, Me_3SiCl and SnI_2.[2] Based on the above results, it was assumed that siloxy carbonyl compounds would be employed as the starting materials for the preparation of cyclic ethers. In this communication, we wish to report a convenient synthesis of cyclic ethers according to the following two steps, that is, cyclization of γ-, δ-, and ε-siloxy carbonyl compounds and the following nucleophilic substitution of intermediate silylated cyclic hemiketals by silyl nucleophiles by the promotion of $TrSbCl_6$ or $SbCl_5$ combined with Me_3SiCl and SnI_2.[3]

The results show that the combined use of $SbCl_5$, Me_3SiCl, and SnI_2 is superior to that of $TrSbCl_6$ in terms of yield in every case, and that in the case of preparation of tetrahydropyrans, an axial attack of nucleophiles to the oxonium



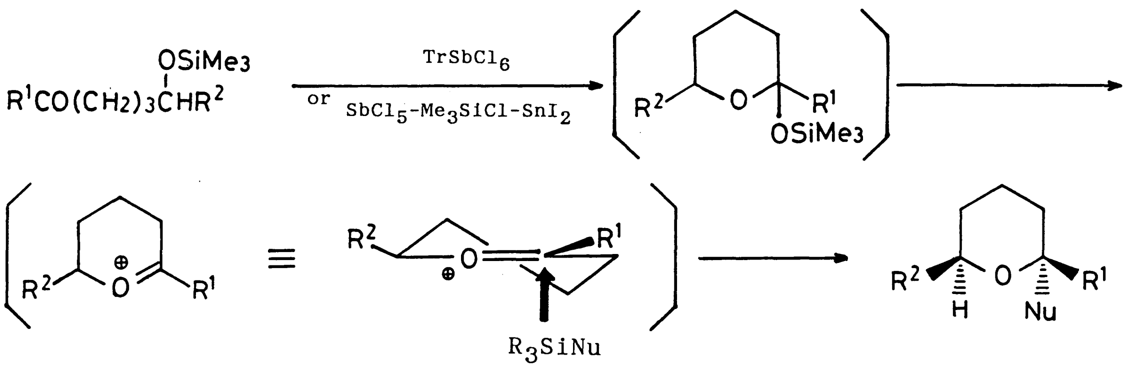
Scheme 1.

Table 1. The Preparation of Cyclic ethers

Entry	n	R^1	R^2	Nucleophile	Yield / %	
					Method A[a)]	Method B[b)]
1	2	Ph	H	Et_3SiH	89	91
2	3	Ph	H	Et_3SiH	90	95
3	3	Ph	Me	Et_3SiH	92[c)] (cis)	96[c)] (cis)
4	3	H	Ph	Et_3SiH	76	90
5	3	H	Ph	$Me_3SiCH_2CH=CH_2$	75[c)] (trans)	83[c)] (trans)
6	3	H	Ph	Me_3SiCN	11 , 19 (cis) (trans)	28 , 53 (cis) (trans)
7	4	Ph	H	Et_3SiH	68	77
8	4	CH_2Ph	H	Et_3SiH	80	95

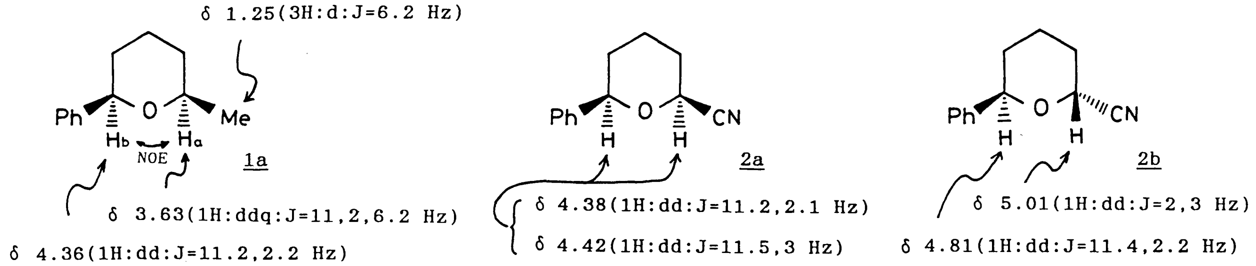
a) $TrSbCl_6$ was used as a catalyst. b) $SbCl_5$ combined with Me_3SiCl and SnI_2 was used as a catalyst. c) No stereoisomer was detected by either ^1H or ^{13}C NMR.

intermediate is preferred to an equatorial attack (entries 3, 5, and 6) due to torsional strain (Scheme 2). Especially, there is a marked tendency toward an axial attack when Et_3SiH or $Me_3SiCH_2CH=CH_2$ was used as silyl nucleophile (entries 3 and 5). This stereoselectivity is similar to that of the reduction of cyclic hemiketals with Et_3SiH in the presence of $BF_3 \cdot Et_2O$ or trifluoroacetic acid, and nucleophilic substitution of lactols with organometallics (Me_2Zn, Me_3Al, $(CH_2CH=CH_2-)_2SnBu_2$, etc.) in the presence of $BF_3 \cdot Et_2O$.[4,5]



Scheme 2.

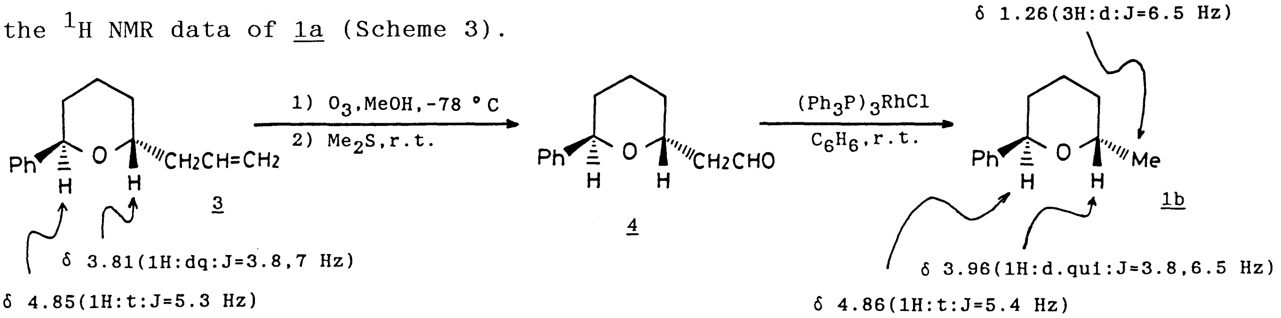
Configuration of cis-2-methyl-6-phenyltetrahydropyran (1a) was assigned by the NOE analysis (400-MHz NMR spectrum) for the ring methine protons. The pyran (1a) showed, upon irradiation of H_a, an enhancement of H_b, which was of the order of 12.6% (Fig. 1). Assignment of stereochemistry for cis- and trans-2-cyano-6-phenyltetrahydropyran (2a,b) was determind by the spin-spin coupling constants for the ring methine protons in the 400-MHz ^{1}H NMR ($CDCl_3$) spectrum (Fig. 1).



d:doublet, dd:double doublet, ddq:double double quartet.

Fig. 1.

The stereochemistry of trans-2-allyl-6-phenyltetrahydropyran (3) was determined by comparison of the ^{1}H NMR data of trans-2-methyl-6-phenyltetrahydropyran (1b), derived from 3 via ozonolysis and then decarbonylation, with the ^{1}H NMR data of 1a (Scheme 3).



d:doublet, t:triplet, dq:double quartet, d.qui:double quintet.

Scheme 3.

A typical procedure is described for the preparation of 2-phenyltetrahydrofuran from 4-trimethylsiloxybutyrophenone using a catalyst system of $SbCl_5$, Me_3SiCl and SnI_2: Under argon atmosphere, a 0.5 molar solution of $SbCl_5$ in CH_2Cl_2 (0.2 ml, 0.1 mmol), a 0.2 molar solution of Me_3SiCl in CH_2Cl_2 (0.5 ml, 0.1 mmol) and SnI_2 (38 mg, 0.1 mol) were added to a solution of 4-trimethylsiloxybutyrophenone (238 mg, 1.0 mmol) in CH_2Cl_2 (3 ml) at -78 °C. After stirring for 5 min, to the mixture was added dropwise a solution of Et_3SiH (172 mg, 1.5 mmol) in CH_2Cl_2 (1.5 ml) at the same temperature. The reaction temperature was raised to -23 °C, and then the reaction mixture was stirred for 2.5 h. Gradually being warmed to room temperature, the reaction was quenched with aqueous saturated $NaHCO_3$. The organic materials were washed with brine, dried over Na_2SO_4 and evaporated in vacuo. The residue was purified by preparative thin layer chromatography on silica gel (12:1 hexane-ethyl acetate as a developing solvent) to give 2-phenyltetrahydrofuran (136 mg, 91%).

Thus, it is noted that five — seven membered cyclic ethers are conveniently prepared from γ-, δ-, or ε-siloxy carbonyl compounds with several silyl nucleophiles using a catalytic amount of $TrSbCl_6$ or $SbCl_5$ combined with Me_3SiCl and SnI_2.

References

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2) T. Mukaiyama, K. Homma, and H. Takenoshita, Chem. Lett., 1988, 1725.

3) Four, eight, and twelve membered cyclic ethers were not synthesized under similar reaction conditions.

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(Received October 25,1988)