CHEMISTRY LETTERS, pp. 1495-1498, 1986.

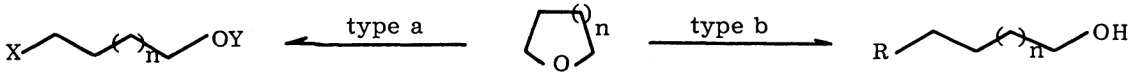
Regioselective Ring-Cleavage Reaction of Tetrahydrofurans and Tetrahydropyrans Accompanied by Carbon-Carbon Bond Formation

Akira OKU,* Yukio HOMOTO, and Toshiro HARADA
Department of Chemistry, Kyoto Institute of Technology,
Matsugasaki, Sakyo-ku, Kyoto 606

Various 2-substituted tetrahydrofurans and tetrahydropyrans were cleaved regioselectively accompanied by a simultaneous carbon-carbon bond formation at the highly substituted α carbon atom by using the reagent system of titanium tetrachloride and ally- (or alkynyl-)silanes.

Ring-cleavage reactions of cyclic ethers such as tetrahydrofurans and tetrahydropyrans have been utilized in the preparation of the functionalized four and five carbon units in organic syntheses.[1] Most of these transformations belong to the cleavage reaction which introduces a hetero atom to the terminal of a carbon chain (Scheme 1, type a); but the cleavage reaction accompanied by a carbon-carbon bond formation (type b) is not common.[2] This makes a marked contrast with the synthetically important ring-cleavage reaction of oxiranes with carbon nucleophiles.[3]

Herein, we wish to report a novel ring-cleavage reaction of tetrahydrofurans and tetrahydropyrans accompanied by a simultaneous carbon-carbon bond formation, which takes place regioselectively by using the reagent system of titanium tetrachloride and allyl- (or alkynyl-)silanes.[4]

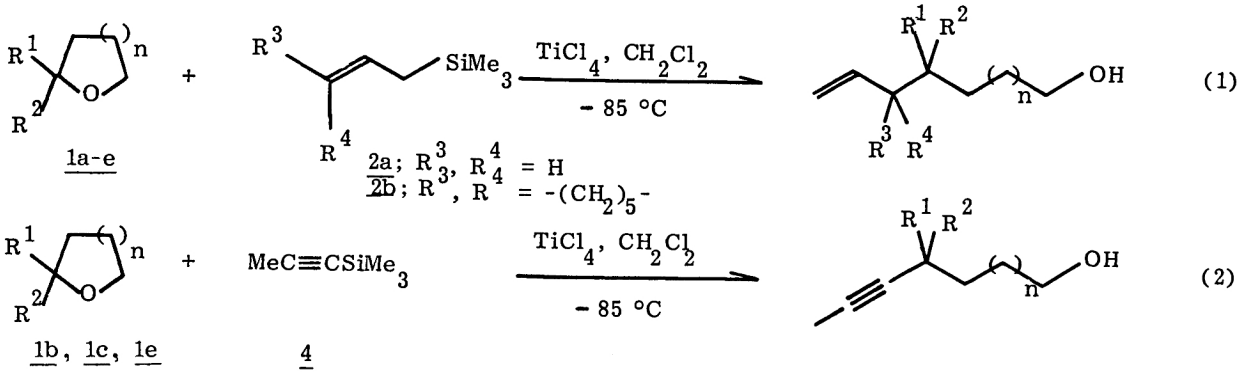


X = halogen, R'O, etc.
n = 1,2

Scheme 1.

The treatment of various 2-substituted cyclic ethers (1a-e) with allylsilanes (2a,b) in the presence of titanium tetrachloride in CH_2Cl_2 gave the corresponding alkenols 3 which were formed by the regioselective introduction of an allylic group at the highly substituted α carbon atom (i.e., C-2) of the starting cyclic ethers (Eq. 1). Similarly, reactions with trimethylsilylpropyne (4) gave the corresponding regioselectively ring-cleaved products 5 in which a propynyl group was introduced (Eq. 2). Results of these reactions are summarized in Table 1. A typical experimental procedure is shown for the reaction of 2-methyl-2-phenyltetrahydrofuran (1b) with 2a as follows. To a solution of 1b

(137.4 mg, 0.847 mmol) and 2a (0.27 mL, 1.70 mmol) in CH_2Cl_2 (4.2 mL) was added titanium tetrachloride (0.11 mL, 1.00 mmol) at -85 °C. After stirring at the same temperature for 9 h, the reaction was quenched by the addition of MeOH (0.5 mL). Extractive work-up (ethyl acetate-brine) followed by the purification by flash column chromatography on silica gel (petroleum ether / ethyl acetate) gave 4-methyl-4-phenyl-6-heptenol (161.9 mg, 87% yield).



While tetrahydrofuran and its 2-monoalkyl derivatives were not reactive under the present reaction conditions, tetrahydrofurans with at least one phenyl group at the 2-position were cleaved efficiently with the introduction of an allyl or alkynyl group (entries 1-6). 2,2-Dialkyl substituted derivative 1d showed a somewhat lower reactivity and the use of 2.1 equiv. of titanium tetrachloride and a longer reaction time (23 h) was necessary for the successful transformation (entries 7 and 8). Tetrahydropyrans have been known to be less reactive than tetrahydrofurans in Lewis acid-promoted ring-cleavage reactions.[5] However, in the present reaction, they underwent efficient cleavage-allylation reactions as well (entries 9, 10, and 11).

2-Vinyltetrahydrofuran (1f) was also cleaved by allylation under the present reaction conditions (Eq. 3). In these reactions, allylation took place regioselectively at the olefinic terminus of 1f with the exclusive formation of an E-double bond. Thus, in the reaction with 2a only 6a (R^3, R^4 = H)[6] was obtained in 50% yield, and in the reaction with 2b a mixture of 6b[6] and 7b (96 : 4) was obtained in 77% yield. It should be noted that the regioselectivity observed here makes a marked contrast to the exclusive α allylation reported in the reaction of acyclic allyl ethers with ethyl 2-trimethylsilyl-3-butenoate.[7,8]

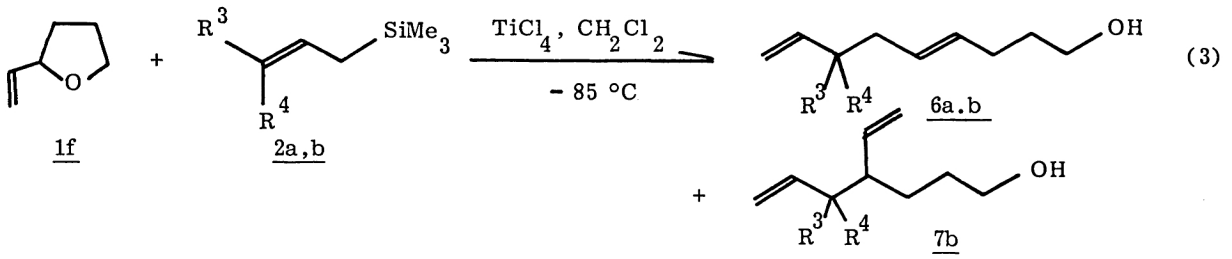
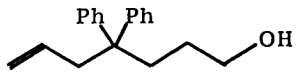
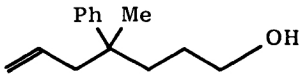
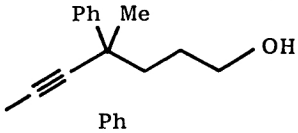
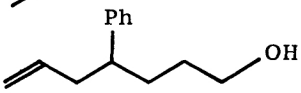
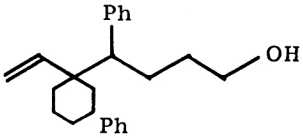
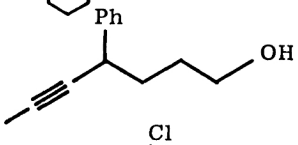
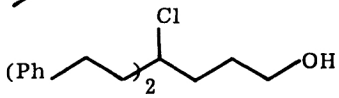
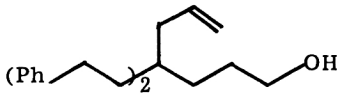
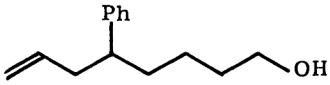
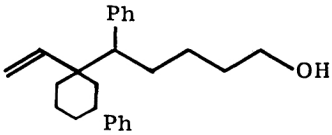
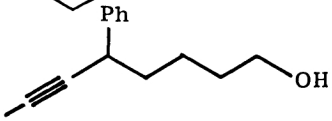


Table 1. Regioselective Ring-Cleavage Reaction of Cyclic Ethers Accompanied by C-C Bond Formation[a)]

Entry	Substrate R^1, R^2	n	Nucleophile	Reaction time / h	Product[b)]	Isolated yield / %
1	1a; Ph, Ph	1	2a	5		100
2	1b; Me, Ph	1	2a	9		94
3	1b		4	18		53
4	1c; Ph, H,	1	2a	4		82
5	1c		2b	5		100
6	1c		4	7		52
7	1d; $PhCH_2CH_2$, $PhCH_2CH_2$	1	2a	5		91
8[c]	1d		2a	23		91
9	1e; Ph, H	2	2a	5		87
10	1e		2b	5		96
11	1e		4	7		39

a) Unless otherwise noted all reactions were performed at -85 °C in CH_2Cl_2 employing 1.2 equiv. of $TiCl_4$ and 2.0 equiv. of 2a,b or 5.0 equiv. of 4. b) All products showed satisfactory spectral (^1H NMR, IR, and mass spectrum) data.
c) 2.1 Equiv. of $TiCl_4$ was used.

Results presented here demonstrate a synthetic potential of the present novel ring-cleavage reaction of cyclic ethers accompanied by a carbon-carbon bond formation. Works are in progress to disclose the full scope of the reaction especially with regard to the reaction with other carbon nucleophiles.

This work was supported by Grant-in-Aid for Special Project Research from the Japan Ministry of Education, Science and Culture (No. 61211019).

References

1) R. L. Burwell, Jr., Chem. Rev., 54, 615 (1954); E. Staude and F. Patat, "The Chemistry of Ether Linkage," ed by S. Patai, Interscience, New York (1967), p. 21; M. V. Bhatt and S. U. Kulkarni, Synthesis, 1983, 249.

2) "Methoden der Organischen Chemie," ed by E. Muller, Thieme, Stuttgart (1965), Vol. 6/3, p. 141.

3) A. H. Haines in "Comprehensive Organic Chemistry," ed by J. F. Stoddart, Pergamon Press, Oxford (1979), p. 866.

4) Z. N. Parnes and G. I. Bolestova, Synthesis, 1984, 991; A. Hosomi and H. Sakurai, Yuki Gosei Kagaku Kyokai Shi, 43, 406 (1985); Allylation of oxiranes and oxetanes under the similar reaction conditions has been reported, I. Fleming and I. Peterson, Synthesis, 1979, 446; S. A. Carr and W. P. Weber, J. Org. Chem., 50, 2782 (1985).

5) D. J. Goldsmith and E. Campbell, J. Org. Chem., 40, 3751 (1975).

6) 6a; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.61 (2H, m), 1.91 - 2.20 (6H, m), 3.63 (2H, t, J = 6.8 Hz), 4.89 - 5.05 (2H, m), 5.39 - 5.48 (2H, m), 5.68 - 5.91 (1H, m); IR (liquid film) 3310 (br), 1000 (m), 975 (s), 920 (s) cm^{-1}; mass spectrum, m/e (relative intensity) 140 (M^+, 0.4), 122 (2.6), 81 (100). 6b; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.12 - 1.72 (10H, m), 1.60 (2H, m), 1.91 - 2.00 (2H, m), 2.00 - 2.12 (2H, m), 3.62 (2H, t, J = 6.6 Hz), 4.89 (1H, dd, J = 1.6 and 17.7 Hz), 5.04 (1H, dd, J = 1.6 and 11.0 Hz), 5.33 - 5.43 (2H, m), 5.64 (1H, dd, J = 11.0 and 17.7 Hz); IR (liquid film) 3340 (br), 1060 (s), 975 (s), 910 (s) cm^{-1}; mass spectrum, m/e (relative intensity) 208 (M^+, 2.4), 91 (16), 79 (26), 67 (82), 42 (100); exact mass calcd for $C_{14}H_{24}O$: 208.1828. Found; 208.1824.

7) Y. Morizawa, S. Kanemoto, K. Oshima, and H. Nozaki, Tetrahedron Lett., 23, 2953 (1982).

8) Allylation of γ-alkenyl-γ-butyrolactones has been reported to proceed with an allylic rearrangement of the substrate. T. Fujisawa, M. Kawashima, and S. Ando, Tetrahedron Lett., 25, 3213 (1984); see also S. Danishefsky and J. F. Kerwin, Jr., J. Org. Chem., 47, 3803 (1982).

(Received June 25, 1986)