Tetrahedron Letters, Vol.27, No.6, pp 719-722, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

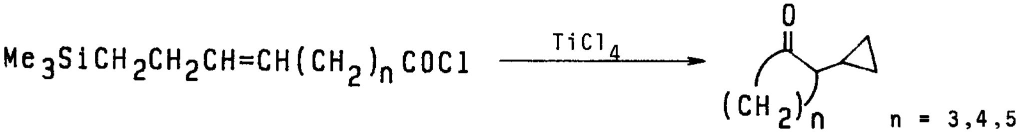
AN INTRAMOLECULAR ACYLATION OF OLEFINS DIRECTED BY TRIMETHYLSILYL GROUP. SYNTHESIS OF 2-CYCLOPROPYLCYCLOALKANONES

Yasuo Hatanaka and Isao Kuwajima*
Department of Chemistry, Tokyo Institute of Technology, Meguro,
Tokyo 152, Japan

Summary: An intramolecular acylation of ω-trimethysilylacyl chlorides bearing C=C bonds at their appropriate positions takes place regioselectively to give the corresponding 2-cyclopropylcycloalkanones in the presence of $TiCl_4$.

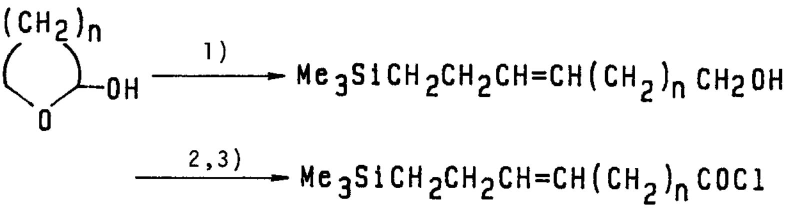
For the construction of carbocyclic systems found in naturally occurring compounds, the ring closure of readily available acyclic precursors has often been employed in organic synthesis, and various procedures have been devised to effect this type of transformation. A Friedel-Crafts like cyclization between acyl chlorides and olefinic moieties is one of the most fundamental methodologies for this purposes, but a serious problem sometimes arises due to the regiochemical ambiguity on direction of ring closure.[1] Introduction of a silyl group at an appropriate position has brought about a remarkable progress to secure the regiochemical outcome of cyclization, and intramolecular acylation of vinylsilanes[2,3] or alkylsilanes[4] has provided an efficient solution for such purposes.

It was reported the intermolecular reaction of acyl chlorides with homoallylsilanes usually accompanies the formation of three types of products including cyclopropyl ketones as major components. Extension to intramolecular version bearing homoallylsilane moieties at appropriate position has disclosed several interesting and synthetically useful features.



(Scheme 1)

The starting materials are readily prepared by the standard procedures as shown in Scheme 2.



(Scheme 2)

1) $Me_3Si(CH_2)_3PPh_3Br$, NaH, DMSO 2) CrO_3-Pyridine
3) $(COCl)_2$

Typical procedures are as follows. To a solution of 9-(trimethylsilyl)-6-nonenoyl chloride (0.2 mmol) in dry dichloromethane (1.5 ml) was slowly added titanium tetrachloride (1.5 eq) at -78°C and the reaction mixture was stirred for 1.5 hr at the same temperature. After usual workup of the reaction mixture and extraction with dichloromethane, removal of the solvent followed by separation on column chromatography afforded 2-cyclopropylcyclohexanone in 71% yield.[4]

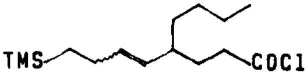
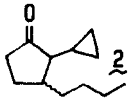
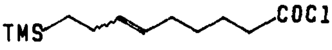
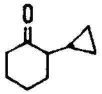
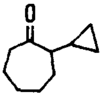
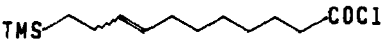
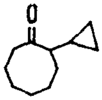
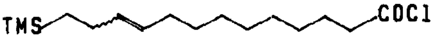
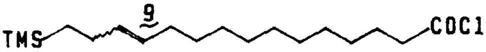
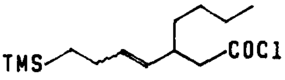
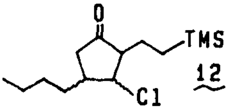
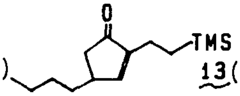
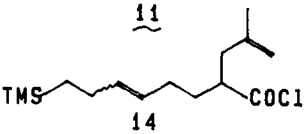
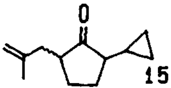
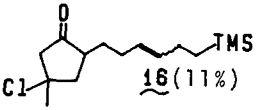
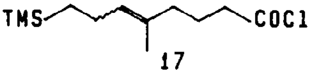
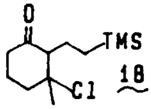
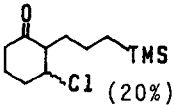
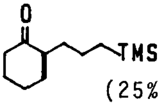
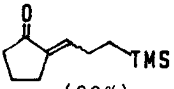
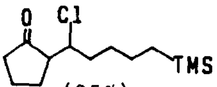
From results shown in the Table, the following characteristic features may be derived.

(1) This intramolecular acylation is highly regio-controlled by silyl group on cyclization to five-, six-, and even seven-membered ring systems. In each case, the corresponding 2-cyclopropyl ketone was isolated as the sole product without any formation of side-products observed on the intermolecular reaction (compare runs 1, 2, and 3). However, for construction of ring systems larger than seven, efficacy is greatly reduced (compare runs 4, 5, and 6).

(2) In contrast to the similar cyclization with vinylsilanes,[2c] cyclobutanone formation is greatly disfavored and the corresponding five-membered products **12** and **13** were formed exclusively against the directing effect of silyl group (run 7). Further, on competitive intramolecular acylation between homoallylsilane and methallyl moieties, the reaction on the former site predominates over that on the latter (run 8), which has made another good contrast to the acylation at vinyl-[2b] or alkylsilanes.[4] However, on the reaction of a substrate as **17**, cyclization is controlled by a greater stability of the intermediary formed tert-carbonium cation rather than the effect of a silyl group.

(3) As proposed by Sakurai and Hosomi,[4] the high degree of regioselectivity may be attributable to the stabilizing effect of silyl group, but such effect appears to be restricted to the three membered system, and silyl group more far from a olefinic part has little effect on the course of cyclization

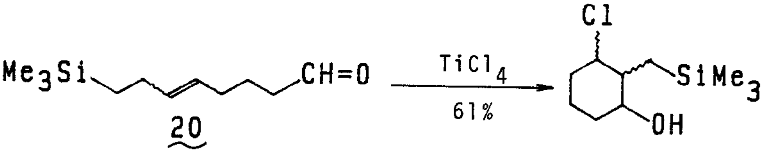
Table

Run	Substrate	Product (Yield %)$^{a)}$
1.	 **1**	 **2** (62%)
2.	 **3**	 **4** (71%)
3.	 **5**	 **6** (65%)
4.	 **7**	 **8** (12%)
5.	 **9**	recovered as the acid
6.	 **10**	recovered as the acid
7.	 **11**	 **12** (53%)  **13** (12%)
8.	 **14**	 **15** (56%)  **16** (11%)
9.	 **17**	 **18** (73%)
10.	 **19**	 (20%)  (25%)  (23%)  (25%)

TMS = Me_3Si

a) Isolated yield.

(see run 10). Further, it is quite interesting that such directing effect based on silyl group was not observed on the Prince-like reaction. For example, cyclization to 6-membered ring took place predominantly on treating the unsaturated aldehyde **20** under standard conditions.



In conclusion, irrespective of some limitations, the present procedure has provided an efficient methodology for preparation of cyclic ketones of 5, 6, and 7-membered rings bearing a 2-cyclopropyl substituent, considering that an introduction of cyclopropyl group is almost impossible by using enolate alkylation or other methods.

References

(1) For example, treatment of 5-undecenoyl chloride with titanium tetrachloride gave an approximately 1:1 mixture of the corresponding cyclopentanone and cyclohexanone.

(2) Intramolecular acylation of vinylsilanes: a) S. D. Burke, C. W. Murtiasshaw, M. S. Dike, S. M. S. Strickland, and J. O. Saunders, J. Org. Chem., **46**, 2400 (1981). b) E. Nakamura, K. Fukuzaki, and I. Kuwajima, J. Chem. Soc., Chem. Commun., 499 (1983). c) K. Mikami, N. Kishi, and T. Nakai, Tetrahedron Lett., **24**, 795 (1983).

(3) Their synthetic application to hydrindanone skeletons: (a) S. E. Denmark and J. P. Germanas, Tetrahedron Lett., **25**, 1231 (1984). (b) K. Fukuzaki, E. Nakamura, and I. Kuwajima, ibid., **25**, 3591 (1984).

(4) Intramolecular acylation of alkylsilanes: H. Urabe and I. Kuwajima, J. Org. Chem., **49**, 1140 (1984).

(5) H. Sakurai, T. Imai, and A. Hosomi, Tetrahedron Lett., 4045 (1977).

(Received in Japan 21 November 1985)