Cyclopentenones by Internal Acylation of Vinylsilanes. Rapid Construction of Trichothecane-type Carbon Frameworks†

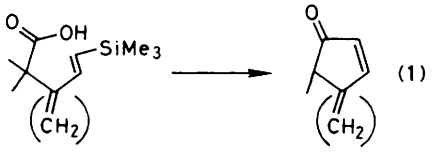
Eiichi Nakamura, Kentaro Fukuzaki, and Isao Kuwajima*

Department of Chemistry, Tokyo Institute of Technology, Meguro, Tokyo 152, Japan

The internal acylation of vinylsilanes has made available new syntheses of cyclopentenones and efficient routes to the intermediates for trichothecane synthesis.

We report here the intramolecular acylation of vinylsilanes as a method for the preparation of cyclopentenones, especially 5-substituted cyclopentenones, equation (1). This reaction also works well for the preparation of 4-methylene derivatives and provides short routes to intermediates for trichothecane synthesis.

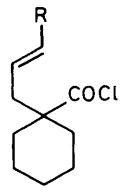
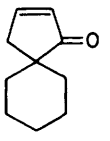
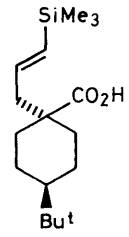
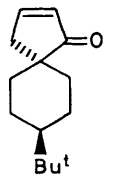
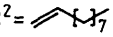
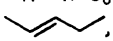
The internal acylation of olefins[1] is not a particularly good synthetic reaction. Thus, the $AlCl_3$-mediated cyclization of (**1**) gives a mixture of the enone (**3**) and a 3-chlorocyclopentanone derivative. The use of a silyl group in this cyclization, however, proved successful; the reaction of (**2**) with $TiCl_4$ gave (**3**) in 65—70% yield. Other examples of this cyclization are shown in Table 1. Since (**4**) is obtained stereoselectively (by the *ca.* 90% equatorial alkylation of methyl 4-t-butylcyclohexanecarboxylate)[2] the method is suitable for the construction of spiro[4.5]decanes of known stereochemistry [Table 1, entry (B)]. The reaction tolerates double bonds in the vicinity of the incipient acyl cation as well as at a remote centre [entries (D)—(F)]. The vinylsilane group effectively competes with the allylic [entry (D)] and the crotyl [entry (E)] groups.

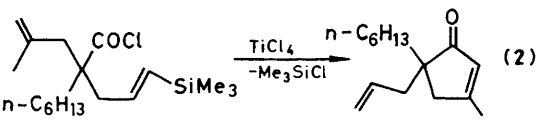


(1)

† Part of this work has been presented in the 45th Annual meeting of the Chemical Society of Japan (April 1982, Tokyo).

Table 1. Internal acylation of vinylsilanes.

Entry	Acids or acid chorides	Enones	Yield (%)
(A)	 (1) R = H (2) R = $SiMe_3$	 (3)	65–70
(B)	 (4)		61
(C)	(5) R^1=H, R^2=n-C_6H_{13}		79
(D)	(6) R^1=H, R^2= 		60
(E)	(7) R^1=  R^2=n-C_6H_{13}		69
(F)	(8) R^1=  R^2=n-C_6H_{13}		70

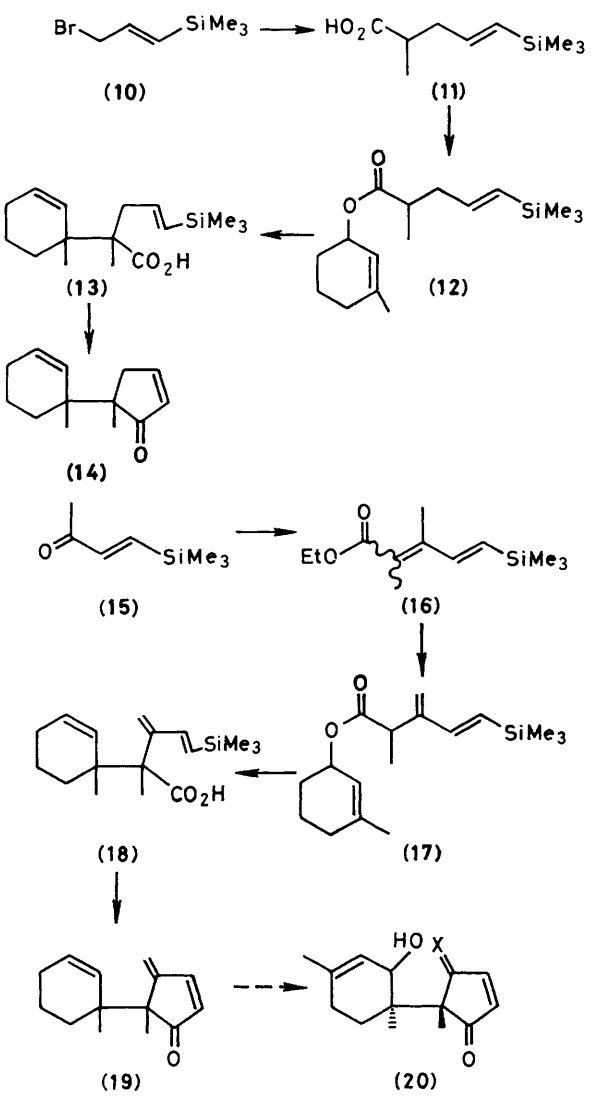

(9) (2)

The participation of the allyl group in the reaction of (**9**) is worth noting [50% yield, equation (2)].

In spite of previous studies on the electrophilic attack on vinylsilanes,[3] the precise electronic effects of the silyl group have remained obscure. The above results indicate that the silyl group, having a slightly electron-withdrawing effect,[4] does not have a powerful activating effect in such an exothermic reaction. The role of the silyl group is thus significant, but should not be overestimated.

In the preparation of the starting materials in Table 1, the required carbon numbers of the substrates were obtained by alkylation of the appropriate ester enolates with (**10**), available from the corresponding alcohol (PBr_3).[5] The acid chloride was prepared *in situ* using oxalyl chloride–cat. *N*,*N*-dimethylformamide–collidine (1 equiv.) and then treated in methylene chloride with 1 equiv. of $TiCl_4$ or $SnCl_4$ at 0—25 °C. $AgBF_4$ also worked in some cases, but did not seem to offer any advantages over the others.

Having established the conditions for the cyclization, we examined the preparation of some intermediates for trichothecane synthesis. Straightforward application of the method provided a route to the enone (**14**) in four steps from the acid (**11**) which is available by the standard malonic ester synthesis. Esterification[6] of (**11**) with 3-methylcyclohex-2-enol


(10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20)

gave (**12**) (94%), which on ester-enolate Claisen rearrangement [lithium di-isopropylamide (LDA) in hexamethylphosphoramide–tetrahydrofuran (THF) at −70—0 °C; Me_3SiCl; THF, reflux 5 h][7] gave (**13**) in 80—90% yield. Cyclization under standard conditions gave (**14**) in 60—70% yield. The reaction was not affected by the presence of either the cyclohexene ring or the two consecutive quaternary centres.

The bicyclic material (**20**), which incorporates the methylene carbon required by another line of approach, has been obtained by the reaction of the dienylsilane (**18**). The enone (**15**) was converted into (**16**) by the action of ethyl 2-trimethylsilylpropionate (LDA in THF at −70 °C, 59%). Hydrolysis of the acid followed by esterification (2-chloropyridine methiodide, 4-dimethylaminopyridine, Et_3N, 94%)[6] gave (**17**) containing a small amount of the conjugated isomer. The Claisen rearrangement as above gave (**18**) in 70—80% yield as a 70:30 mixture of stereoisomers. The cyclization of (**18**) gave the dienone (**19**) in 80% yield [from (**18**) with $SnCl_4$].‡

‡ Representative spectral properties of the key compounds are as follows: cyclopentenones in general: i.r. (neat) 1705 and 1635—1615 cm^{-1}, ^1H n.m.r. (CCl_4) 5.91—6.05 (dt, *J* 2 and 5—6 Hz), and 7.4 ± 0.1 (dt, *J* 2—3 and *ca.* 6 Hz); (**16**) ^1H n.m.r. (CCl_4) 5.79 (d, 0.4 H, *J* 19 Hz), 5.97 (d, 0.6 H, *J* 19 Hz), 6.80 (d, 0.6 H, *J* 19 Hz), and 7.13 (d, 0.4 H, *J* 19 Hz); (**19**) ^1H n.m.r. (CCl_4) 0.76 (s, 2 H), 0.98 (s, 1 H), 1.10 (s, 3 H), 5.09 (s, 1 H), 5.20 (s, 1 H), 5.45—5.6 (m, 2 H), 5.98 (d, *J* 5.5 Hz), 6.00 (d, *J* 5.5 Hz), and 7.45 (d, 1 H, *J* 5.5 Hz).

A dienone of this type is not readily available by conventional methods.

The vinylsilane cyclization has also provided a stereoselective preparation of α-alkylidene cyclopentanones, the results of which are being incorporated in our current project for steroid synthesis.

We acknowledge financial support from the Ministry of Education, Science, and Culture (Grant-in-Aid for Special Project Research).

Received, 7th February 1983; Com. 175

References

1 J. K. Groves, *Chem. Soc. Rev.*, 1972, **1**, 73.
2 A. P. Krapcho and E. A. Dundulis, *J. Org. Chem.*, 1980, **45**, 3236.
3 I. Fleming and A. Pearce, *J. Chem. Soc., Chem. Commun.*, 1975, 633; S. D. Burke, C. W. Murtiashaw, M. S Dike, S. M. S. Strickland, and J. O. Saunders, *J. Org. Chem.*, 1981, **46**, 2400; K. Mikami, N. Kishi, and T. Nakai, *Tetrahedron Lett.*, in the press.
4 H. Bock and H. Alt, *J. Am. Chem. Soc.*, 1970, **92**, 1569; A. J. Smith, W. Adcock, and W. Kitching, *ibid.*, p. 6140.
5 G. Stork, M. E. Jung, E. Colvin, and Y. Noel, *J. Am. Chem. Soc.*, 1974, **96**, 3684.
6 K. Saigo, M. Usui, K. Kikuchi, E. Shimada, and T. Mukaiyama, *Bull. Chem. Soc. Jpn.*, 1977, **50**, 1863.
7 R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Am. Chem. Soc.*, 1976, **98**, 2868.