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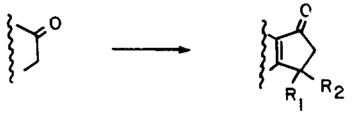
VINYLSILANE MEDIATED REGIOSPECIFIC CYCLOPENTENONE ANNULATION OF KETONES[1]

William E. Fristad,[2a] David S. Dime, Thomas R. Bailey,[2b] and Leo A. Paquette*

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

Summary - The development of a new cyclopentenone annulation sequence of general scope which involves Friedel-Crafts acylation of a vinylsilane with an α,β-unsaturated acid chloride followed by Nazarov cyclization is reported.

The efficient conversion of a ketone to a fused cyclopentenone of type 1 holds considerable promise as a powerful annulation tool. Not only does a new five-membered ring result, but the endocyclic carbon-carbon double bond provides for subsequent control of ring fusion stereochemistry, stereoselective attachment of appendages and/or functional groups, and ring expansion through cleavage (when the starting material is cyclic). Although various methods have been employed to gain access to 1 ($R_1 = R_2 = H$[3] and $R_1 = H$, $R_2 = CH_3$[4]), the lack of a general procedure appears to have impeded the growth of this important area of synthetic methodology.



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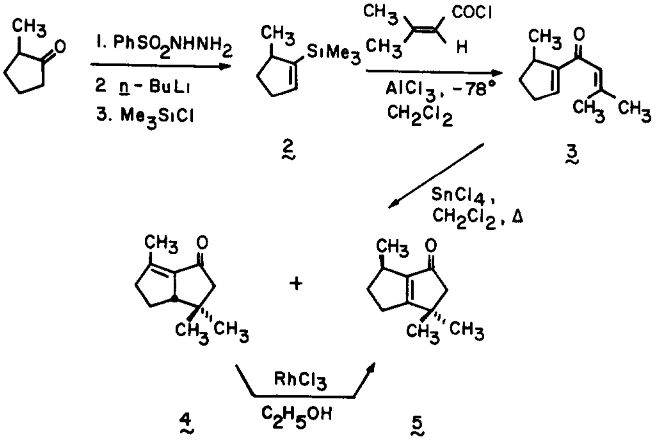
Development of the present widely applicable route was guided by the following five considerations: (a) availability of an excellent procedure for transforming ketone arenesulfonylhydrazones into vinylsilanes in good yield (55-97% in the examples cited herein);[5] (b) the almost universal regiospecificity of this reaction which positions the center of unsaturation between the original carbonyl site and the lesser substituted α position;[6] (c) the powerful activating influence of trialkylsilyl groups on Friedel-Crafts acylation;[7] (d) bonding of such acylium ions directly to the silicon-bearing carbon with subsequent loss of R_3Si;[8] and (e) ultimate electrocyclization of the resulting dienones under acidic conditions.[9]

The overall concept is illustrated for the specific case of 2-methylcyclopentanone and β,β-dimethylacryloyl chloride in Scheme I. Reaction of 2 with 1 equiv each of acid chloride and aluminum chloride in anhydrous dichloromethane at -78° for 5 min effected conversion to 3 which was isolated but not purified. Treatment of 3 with 3 equiv of stannic chloride in refluxing dichloromethane (3 days) followed by preparative layer chromatography produced a mixture of 4 and 5 in isolated yields of 33 and 19%, respectively. Alternatively, prior exposure of these unpurified enones to rhodium(III) chloride trihydrate in hot ethanol[10] gave rise exclusively to 5 (55%).[11] The changeover in Lewis acid catalyst was predicated upon experimental findings which revealed that production of chlorine-containing by-products was minimized

SCHEME I



through use of $AlCl_3$ in the acylation step and that decomposition of the dienones was lessened through use of $SnCl_4$ for electrocyclization. The latter reagent also was not observed to cause methyl migration within the 4,4-dimethylcyclopentenones.[12]

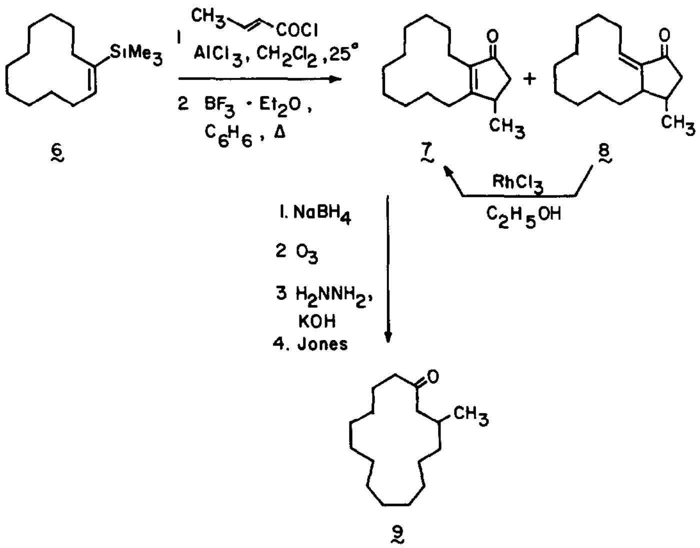
As seen from the examples given in Table I, the relative ease of vinylsilane acylation decreases with lessening of the degree of methyl substitution on the acid halide. Whereas condensation with β,β-dimethylacryloyl chloride was generally complete within several minutes at -78°, crotonyl chloride required 1 hr at room temperature to achieve complete acylation. Reactions with acryloyl chloride were less predictable.

The cyclized products were often obtained as a mixture of double bond isomers. Although the endocyclic/exocyclic ratios expectedly varied from system to system, this phenomenon has presented no complications because subsequent exposure to rhodium(III) chloride promotes isomerization to a single product in most instances.

Utilization of the cyclopentenone double bond for ring expansion is typified by the formal conversion of 1-trimethylsilylcyclododecene (6) to (±)-muscone (9) (Scheme II).[13] Upon condensation of 6 with crotonyl chloride in the presence of $AlCl_3$, the resulting dienone was cyclized with boron trifluoride etherate in hot benzene to give a mixture of 7 and 8 in 48 and 18% isolated yields. Since 8 could be quantitatively isomerized to 7 under conditions of Rh(III) catalysis, this separation becomes unnecessary. Sequential ozonolysis of the derived carbinol, Wolff-Kishner reduction, and oxidation has been shown by Baumann and coworkers[4] to deliver 9.

The methodology outlined above is complementary to a conceptually similar scheme developed by Magnus, et al., which utilizes vinyltrimethylsilane as an ethylene equivalent in intermolecular Friedel-Crafts acylations.[14] We plan to report on further utilitarian developments in this area of vinylsilane chemistry in the near future.[15]

SCHEME II



References and Notes

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(2) (a) The Ohio State University Dissertation Fellow, 1978-1979; (b) Undergraduate research participant, 1976-1978.

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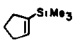
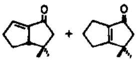
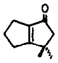
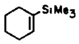
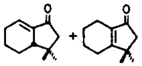
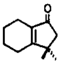
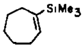
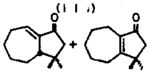
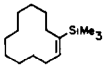
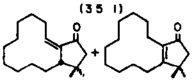
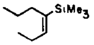
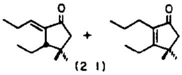
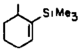
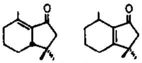
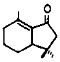
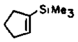
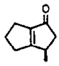
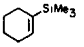
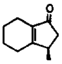
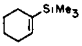
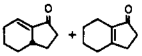
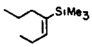
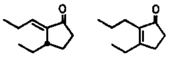
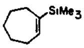
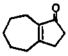
Table I. Cyclopentenone Annulation of Vinylsilanes.

Vinyl-silane	Reaction Conditions	Initial Cyclization Products	Yield %	Rh(III) Catalysis Product	Overall Yield,
A β,β-Dimethylacryloyl Chloride					
	(1) $AlCl_3$, CH_2Cl_2 -78°, 15min (2) $SnCl_4$, CH_2Cl_2, reflux 8-12 hrs	 (1:1.5)	–		62
	as above	 (1:1.[illegible])	–		70
	as above	 (3.5:1)	57		
	1) as above 2) $BF_3 \cdot Et_2O$, C_6H_6, reflux 1-3 days	 (3:2)	43		
	as above	 (2:1)	62		
	as above	 (1:1)	–		60
B Crotonyl Chloride					
	as above		58		
	(1) $AlCl_3$, CH_2Cl_2 RT, 1 hr (2) BF_3 Et_2O, C_6H_6, reflux		44		
C Acryloyl Chloride					
	$AlCl_3$, CH_2Cl_2 RT, 2hr	 (1.25:1)	27		
	as above	 (3.75:1)	24		
	(1) $AlCl_3$, NaOAc CH_2Cl_2, -45° 15 min (2) CF_3COOH, RT, 3hr		10		

(11) Structural assignment to 5 follows also from its lithium/liquid ammonia reduction to 4,4,8-trimethylbicyclo[3.3.0]octan-2-one, which ketone was independently synthesized by lithium dimethylcuprate addition to 4,8-dimethylbicyclo[3.3.0]oct-3-en-2-one [Achmad, S. A.; Cavill, G. W. K. Austr. J. Chem. 1965, 18, 1989].

(12) Agosta, W. C.; Smith, A. B., III J. Am. Chem. Soc. 1971, 93, 5513; Bellamy, A. J. J. Chem. Soc. (B) 1969, 449; Compare Crouse, R. S. J. Org. Chem. 1961, 26, 3525.

(13) For previous dl-muscone syntheses, see footnote 1 in Stork, G.; McDonald, T. L. J. Am. Chem. Soc. 1975, 97, 1264. More recent additions to this list include reference 4 and Taguchi, H.; Yamamoto, H.; Nozaki, H. Tetrahedron Lett. 1976, 2617; Fischli, A.; Branca, Q.; Daly, J. Helv. Chim. Acta 1976, 59, 2443; Ito, Y.; Saegusa, T. J. Org. Chem. 1977, 42, 2326.

(14) Cooke, F.; Schwindeman, J.; Magnus, P. accompanying paper.

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