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NEW SYNTHETIC REACTIONS: ON THE REGIOSELECTIVITY AND CHEMOSPECIFICITY OF THE CYCLOPENTANE ANNELATION-CYCLOPENTENONE ANNELATION

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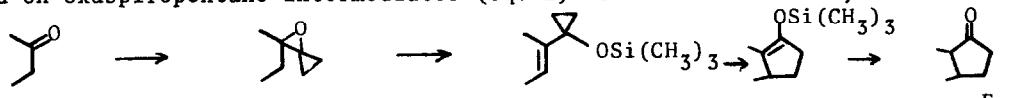
The growing importance of cyclopentane compounds for both biological and theoretical reasons has generated great interest into methods to achieve their formation.[1] The application of the vinylcyclopropane rearrangement[2] has been recognized as a potentially useful approach.[3,4] The uniqueness of the version based on oxaspiropentane intermediates (eq. 1)[4] lies in its ability to

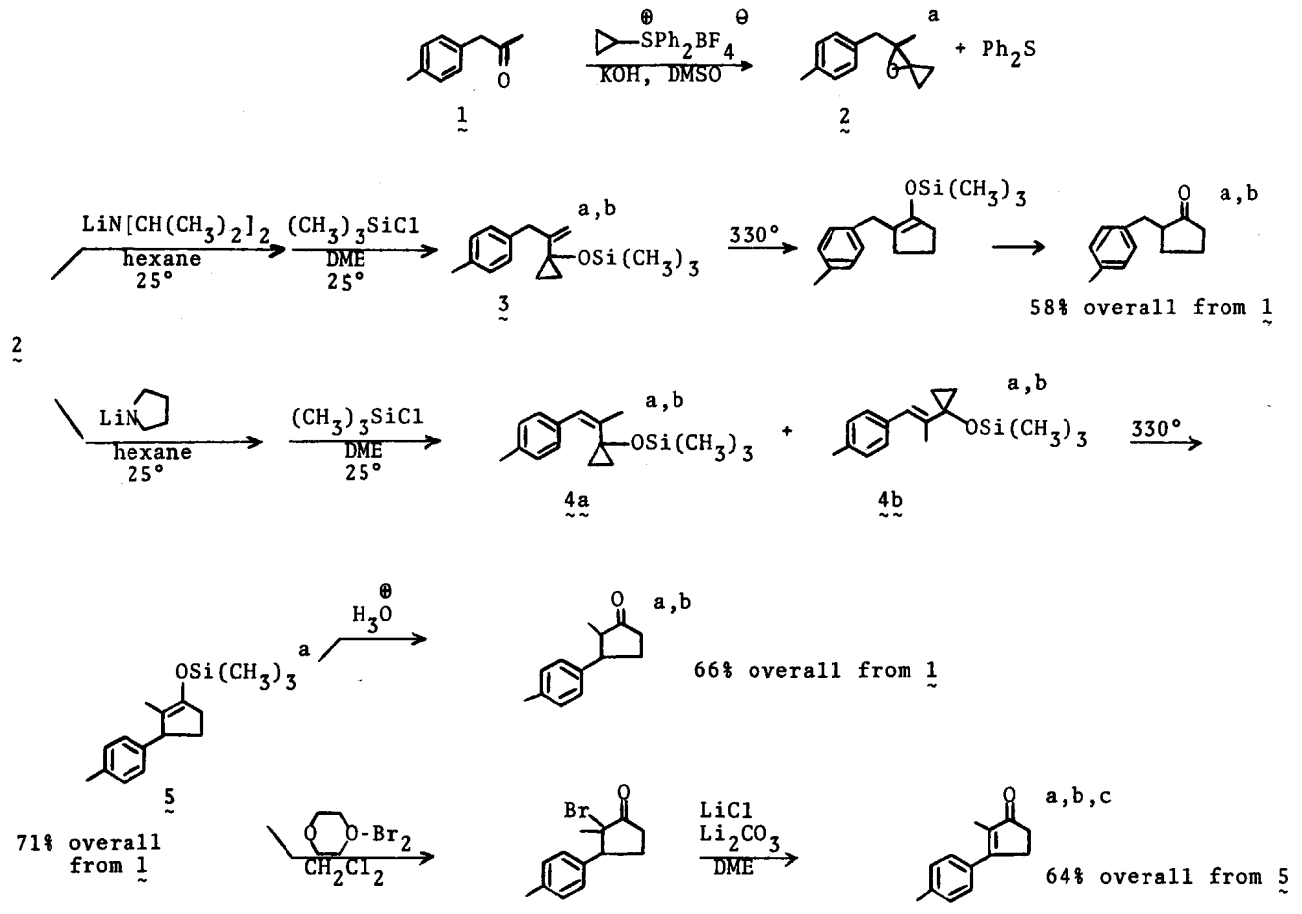


Eq.1

directly anneal a cyclopentanone ring onto a carbonyl compound possessing an adjacent methylene or methyl group. In this letter, we wish to report fascinating observations regarding the factors involved in both the regioselectivity and chemospecificity of the process as well as the extension of the method for cyclopentenone annelation.

The orientational specificity of the annelation depends upon the regioselectivity in the base induced ring opening which generally follows the order benzylic > 1° > 2° >> 3°.[5] In contrast to this reactivity order, we find that the oxaspiropentane 2, available in 85% yield from p-tolylacetone (1), eliminates in either direction depending upon the reaction conditions (see Scheme 1 and Table 1). As the data in Table 1 demonstrates, there is a kinetic preference in hexane solution for abstraction of a proton of the methyl group. However, the initially produced allylbenzene derivative 3 can isomerize to the thermodynamically more stable propenylbenzene 4 under the conditions of the reaction. By use of a sterically hindered base for relatively short times in hydrocarbon solvent compound 3 can be made the almost exclusive product (Table 1, entry 7); by use of a sterically less demanding base for long times in hydrocarbon solvent, compounds 4a and 4b become the exclusive products (Table 1, entry 4). Ether favors formation of only the thermodynamically more stable propenyl isomers 4a and 4b. To our knowledge, this example represents

Scheme 1. Annelations of p-Tolylacetone



a) This compound has been fully characterized by satisfactory spectral properties.
b) Satisfactory elemental composition has been obtained for this compound.
c) Mp 79.0-79.5°.

Table 1. Regioselectivity of Cyclopentane Annelation of 1

Entry	Base	Solvent	Time at R.T.[a]	Products (%) 3	4a	4b
1	lithium pyrrolidide	hexane	15	34	10	56
2	" "	"	30	20	14	66
3	" "	"	50	4	6	90
4	" "	"	120	--	2	98
5	" "	ether	30	--	48	52
6	lithium diethylamide	hexane	30	81	--	19
7	lithium diisopropylamide	hexane	30	99	--	1

a) All reactions were carried out at -78° for 5-10 min then warmed to room temperature at which it was kept for the specified time.

b) Vpc analysis utilizing a 10' x 1/4" 20% DEGS on Chromosorb P column at 180°.

the first case in base induced epoxide ring openings where kinetic versus thermodynamic control determines the orientation. Bromination of the enol derivative 5 followed by dehydrobromination effects an overall regioselective cyclopentenone annelation.[6]

Complementing the regioselectivity is the chemospecificity of the method. Conversion of keto esters 6a and 6b to their oxaspiropentanes 7a and 7b proceeds in 76% and 90% yields, respectively (see Scheme 2). While base induced ring opening of the methyl ester derivative 7a led only to decomposition of the ester, the t-butyl ester derivative 7b undergoes regioselective base-induced ring opening in high yield. Loss of isobutylene accompanies thermal rearrangement to produce the carboxylic acid 8 directly. Hydrolysis of the enol silyl ether yields the annelated cyclopentanone 9. Alternatively, bromination of 8 followed by dehydrobromination produces the cyclopentenone 10 which has been used as a prostaglandin precursor.[7]

The ability to control both the regioselectivity and chemospecificity[8] of this annelation method as well as to make use of the enol silyl ethers for introduction of unsaturation in an orientationally defined manner enhances the utility of the procedure.

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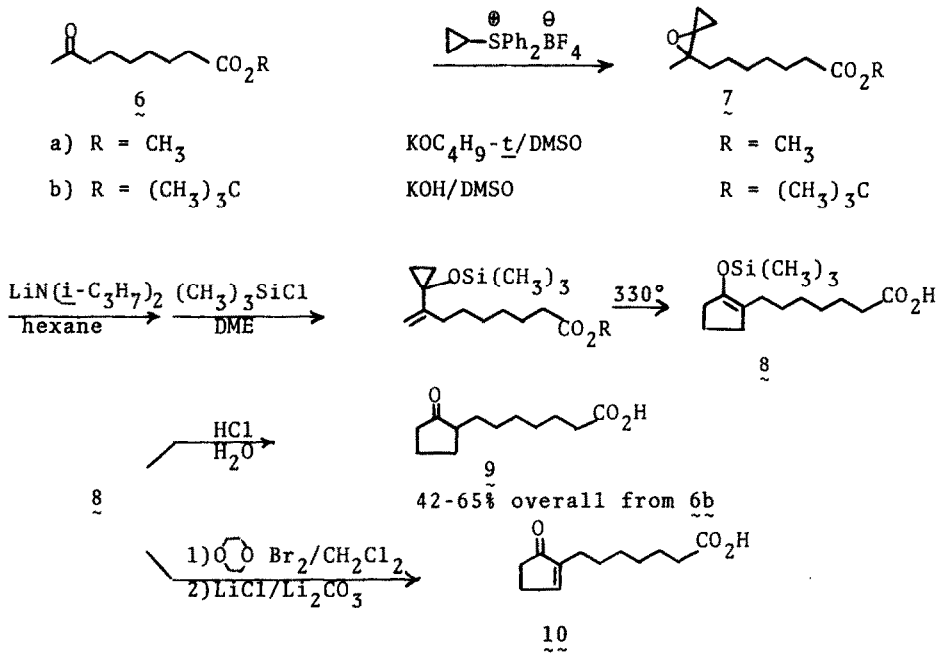
Scheme 2. Chemospecificity of the Annelation[a]



a) All compounds had satisfactory spectral properties.

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