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A NOVEL METHOD FOR CYCLOPENTANNELATION USING REGIOSELECTIVE ACYLATION OF ALLYLIC SULFIDES VIA α-SILYL INTERMEDIATES

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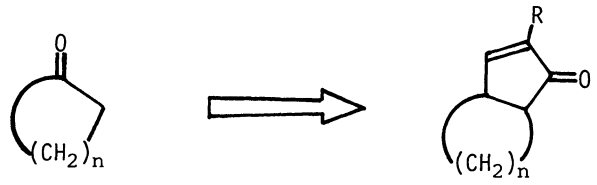
An aluminum chloride-catalyzed reaction of 1-(phenylthiotrimethylsilylmethyl)cyclohexene, readily obtainable from cyclohexanone, with acid chlorides in dichloromethane underwent a regioselective acylation at the γ-position of the allylic system to give γ-acyl enol thioethers in good yields. Heating of these enol thioethers with an equimolar amount of p-toluenesulfonic acid produced 2-cyclopentenone derivatives. This novel method for cyclopentannelation provides a new entry to 2-cyclopentenone ring systems.

Cyclopentane ring systems have received much attention in recent years, from the structural and biological interest on the widespread natural products involving these units,[1] and many methods have been reported for the construction of five-membered ring systems.[2,3]

We wish to communicate herein a novel method for cyclopentannelation of ketones 1 into 2-cyclopentenone derivatives 2, using a regioselective acylation of allylic sulfides via α-silyl intermediates.

Previously we have reported the stereoselective acid-catalyzed acylation of acyclic α-silylallylic sulfides.[4] In our continuous works, we have applied this novel method to cyclic allylic systems for transformation of ketones 1 into 2. A cyclic α-silylallylic system was readily obtainable from a cyclic ketone in the following way. Addition of the α-carbanion (4) of methyl phenyl sulfide to cyclohexanone in the presence of 1,4-diazabicyclo[2.2.2]octane,[5] followed by dehydration of the resulting hydroxy compound 5 under refluxing of benzene with a catalytic amount of p-toluenesulfonic acid produced exclusively 1-phenylthiomethyl-



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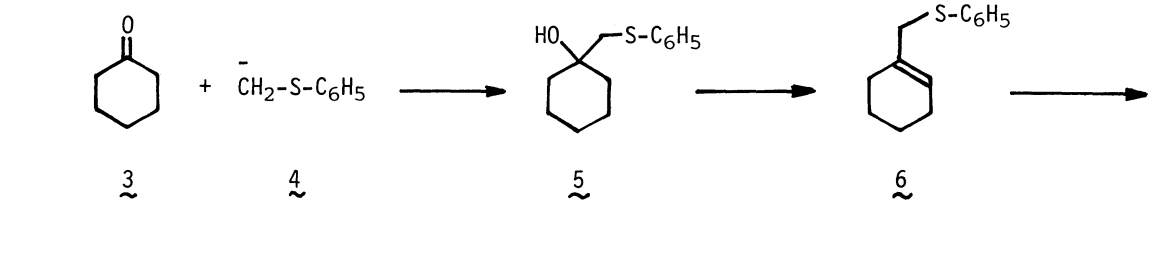
cyclohexene (6) in 95% yield. Reaction of the carbanion of the allylic sulfide 6, generated by treating 6 with lithium diisopropylamide, with trimethylsilyl chloride in tetrahydrofuran at -78 °C for 2 h underwent a regioselective silylation at the α-carbon to give exclusively α-trimethylsilyl sulfide 7 in 98% yield.[6)]

The regioselective acid-catalyzed acylations of 7 with acid chlorides 8a-e (1.2 equiv.) were carried out in dichloromethane at -78 °C for 6 h in the presence of aluminum chloride (1.5 equiv.) to give ketones 9a-e, acylated regioselectively at the γ-position of the allylic part,[4)] in good yields as summarized in Table 1.

These products were calculated to be a 3 : 2 mixture of the geometrical isomers 11a and 11b by the NMR analysis of the olefin protons. The stereochemistry of the olefins was determined by thermal transformation of the Z isomer 11a into the more stable E isomer 11b under refluxing of xylene. Furthermore the structure was unequivocally confirmed by the NMR analysis; the olefin proton in



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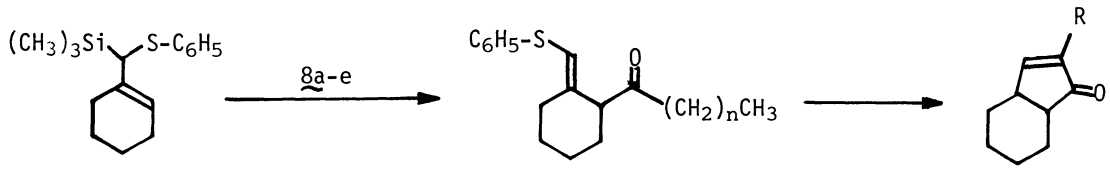

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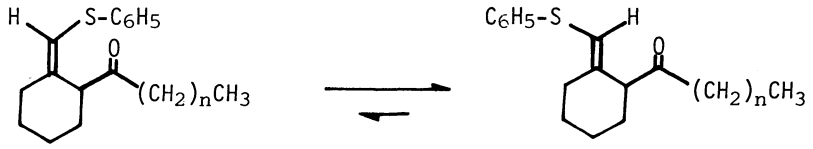
$CH_3(CH_2)_n$-C(=O)-Cl

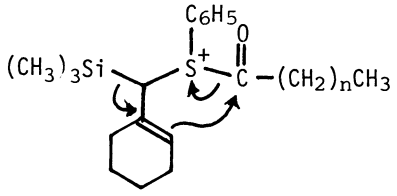
8a n=0
8b =2
8c =3
8d =5
8e =6

9a n=0
9b =2
9c =3
9d =5
9e =6

10a R=H
10b $=CH_2CH_3$
10c $=(CH_2)_2CH_3$
10d $=(CH_2)_4CH_3$
10e $=(CH_2)_5CH_3$



11a 11b



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11b shifted at a little lower field (δ about 6.00, singlet), by the anisotropy of the carbonyl group, than that in 11a (δ about 5.90, singlet).

In the aluminum chloride-catalyzed reaction of 7 with acetyl chloride, phenyl thioacetate was obtained in 61% yield, together with the acylated product 8a (26% yield). The yields of 8a increased by using titanium tetrachloride or tin tetrachloride as an acidic catalyst instead of aluminum chloride[7] and in these cases phenyl thioacetate was also obtained as a by-product in 37 and 32% yields, respectively. In other cases (8b-e), a small amount (about 10% yield) of the corresponding phenyl thioesters was obtained as by-products. These results indicate that the above acid-catalyzed reactions would presumably proceed partially or wholy through an intramolecular acylation via 12.

These γ-acylation products 9a-e would be served as the precursors to synthetically valuable 1,4-dicarbonyl comounds. Accordingly, the construction of cyclopentenone ring systems was attempted by the intramolecular Aldol condensation of these 1,4-dicarbonyl equivalents.

Heating of the ketones 9a-e in refluxing benzene with an equimolar amount of p-toluenesulfonic acid for 2 h underwent an intramolecular condensation to give 2-cyclopentenone derivatives 10a-e in moderate yields (51-59%).
The structure of these products was confirmed by the IR, NMR, and Mass spectral analyses and the stereochemistry of the fused ring system would be deduced to be the more stable cis configuration.

Thus, these procedures led to a smooth conversion of ketones 1 into 2-cyclopentenones 2. Therefore, this novel method for cyclopentannelation provides a new and efficient entry to 2-cyclopentenone derivatives.

Table 1. The Regioselective Acylation of α-Silyl Sulfide 7 under the Acidic Conditions[a)]

Lewis acids	Acid chlorides 8a-e	Products 9a-e	Yields of 9a-e / %
$AlCl_3$	8a	9a	26
$TiCl_4$	8a	9a	44
$SnCl_4$	8a	9a	36
$AlCl_3$	8b	9b	65
$AlCl_3$	8c	9c	80
$AlCl_3$	8d	9d	81
$AlCl_3$	8e	9e	74

a) Reactions of 7 with acid chlorides 8a-e (1.2 equiv.) were carried out in dichloromethane at -78 °C for 6 h in the presence of Lewis acids (1.5 equiv.).

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