Chemo- and Stereo-selective Preparation of Cyclopentanone Derivatives from Cyclohexenones using Trimethylstannyl-lithium as a Key Reagent

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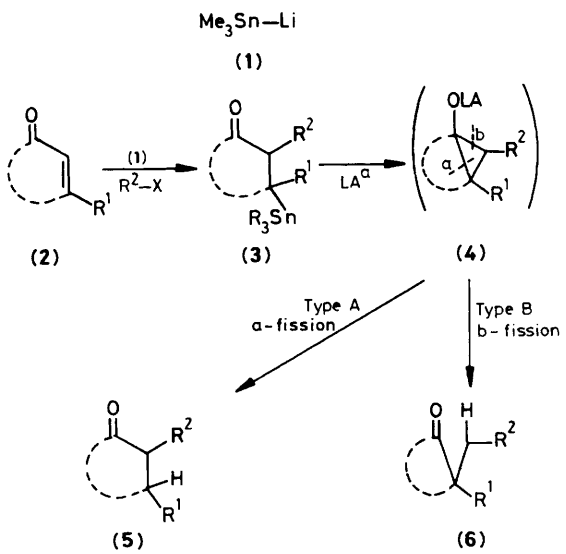
Upon treatment with trimethylsilyl trifluoromethane-sulphonate, β-stannylcyclohexanones afforded cyclopentanones chemo- and stereo-selectively.

In our previous paper,[1] we described the versatility of trimethylstannyl-lithium (**1**) as a synthetic tool. As shown in Scheme 1, the reagent reacted with α,β-enones (**2**) to produce β-stannyl ketones (**3**), after trapping the enolates with electrophiles. When treated with Lewis acids, the β-stannyl ketones underwent two types of reaction producing ketones (**5**) and (**6**), presumably through the ring cleavage of the intermediate cyclopropanols (**4**). It was found that the bond fission occurred predominantly on the bond to the less-substituted carbon, thus affording the Type B products (**6**) as sole products from α,β-enones having substituents at the β-position.

In view of the unique carbon-skeleton rearrangement, the Type B reaction is promising as a method for synthesis of cyclopentanone derivatives, and we investigated the reaction in more detail, particularly regarding its chemo- and stereo-selectivity.

Kitching[2] reported that the conjugate addition of (**1**) to 5-methylcyclohex-2-enone (**7b**) afforded *cis* and *trans* adducts, with the *trans* isomer as the major product (Scheme 2). We monitored the reaction and separated the *trans* isomer (**8b**) in pure state. Treatment of the compound with titanium(IV) chloride gave a mixture of Type A product (**9b**) and Type B product (**10b**) in a ratio of 41 : 59 (Table 1, run 1). The result was in accord with our previous observations[1] that α,β-enones having no substituent at the β-position (R^1 = H) gave both products with low selectivity. With a view to improve the selectivity, we then carried out the reaction using several kinds of Lewis acids, and found that trimethylsilyl trifluoromethane-sulphonate (TMSOTf) gave the best results, producing (**10b**) exclusively as shown in run 3. Comparison of the product with a commercial sample (*cis* : *trans* = 3 : 1) using g.l.c. (with capillary column) and ^{13}C n.m.r. spectroscopy,[3] revealed that the product was mainly the *trans* isomer (*cis* : *trans* 1 : 28). Upon standing at room temperature, the *trans*-dominant product changed into a *cis*-dominant mixture. Evidently, the reaction proceeded under kinetic control, affording the less stable product. The reaction could be rationalised as shown in Scheme 3, proceeding with inversion at the tin-bearing carbon, in accord with earlier observations.[4]

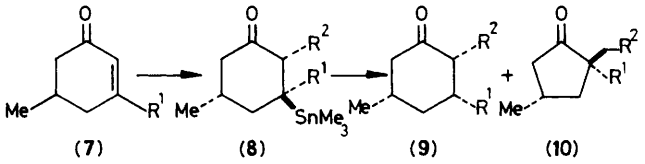


Scheme 1. [a] LA = Lewis acid.

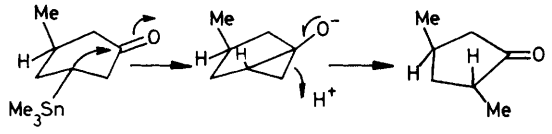
Table 1. Reaction of β-stannyl ketones with Lewis acids.

Run	Starting enone	Yield of (**8**)%	Lewis acid	Temp. /°C	Time /min	Ratio (**9**) : (**10**)	Total yield/%
1	(**7b**)	91	$TiCl_4$	−78	180	41 : 59	49
2			BF_3–Et_2O	room temp.	720	32 : 68	~40[a]
3			TMSOTf[c]	−78	180	0 : 100[b]	52
4	(**7c**)	61	$TiCl_4$	0	15	24 : 76	64
5			TMSOTf	room temp.	180	5 : 95	43
6	(**7d**)	98	$TiCl_4$	−78	5	14 : 86	56
7			TMSOTf	0	300	1 : 99	62
8	(**7e**)	51	$TiCl_4$	−78	15	42 : 58	61
9			BF_3–Et_2O	room temp.	720	24 : 76	56
10			TMSOTf	room temp.	30	4 : 96	66

[a] (**8b**) was recovered (~40%) as a mixture *trans/cis* = 1/16. [b] As a mixture *trans/cis* = 28/1. [c] Trimethylsilyl trifluoromethanesulphonate.



Scheme 2. (**a**): $R^1 = R^2 = Me$, (**b**): $R^1 = R^2 = H$, (**c**): $R^1 = Me$, $R^2 = -CH_2-CH=CH_2$, (**d**): $R^1 = Me$, $R^2 = -CH_2-C\equiv CH$, (**e**): $R^1 = Me$, $R^2 = -CH_2Ph$.



Scheme 3

As an extension of the reaction, we tried to prepare cyclopentanones carrying functionalised substituents. The β-stannyl ketones (**8c**)—(**8e**) were obtained by the reaction of (**1**) with 3,5-dimethylcyclohex-2-enone followed by quenching with allyl bromide, prop-2-ynyl bromide, and benzyl bromide, respectively. In contrast to the case of (**8a**),[1] the Type B selectivity was poor when titanium(IV) chloride or boron fluoride was used as a Lewis acid. However, upon treatment with TMSOTf, these stannyl ketones afforded the corresponding cyclopentanone derivatives with high chemoselectivity (runs 5, 7, 10).† Analyses by g.l.c. as well as ^{13}C n.m.r. and 400 MHz ^1H n.m.r. spectroscopy showed that all the products are stereochemically pure. Since optically active 5-methylcyclohex-2-enone is easily accessible, we expect that this reaction could be developed into a general method for the preparation of useful chiral synthons.

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References

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† The cyclopentanone structure was unambiguously determined in view of the presence of quaternary carbons and complete proton assignment by 400 MHz ^1H n.m.r. spectra of (**10c**)—(**10e**).