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

## Tadashi Sato,\* Toshiyuki Watanabe, Toshihiro Hayata, and Tohru Tsukui

Department of Applied Chemistry, Waseda University, Ookubo 3, Shinjuku-ku, Tokyo 160, Japan

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

In our previous paper,<sup>1</sup> we described the versatility of trimethylstannyl-lithium (1) as a synthetic tool. As shown in Scheme 1, the reagent reacted with  $\alpha,\beta$ -enones (2) to produce  $\beta$ -stannyl ketones (3), after trapping the enolates with electrophiles. When treated with Lewis acids, the  $\beta$ -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  $\alpha,\beta$ -enones having substituents at the  $\beta$ -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 stereoselectivity.

Kitching<sup>2</sup> 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<sup>1</sup> that  $\alpha,\beta$ -enones having no substituent at the  $\beta$ -position (R<sup>1</sup> = 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 trifluoromethanesulphonate (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 <sup>13</sup>C n.m.r. spectroscopy,<sup>3</sup> 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.<sup>4</sup>



Scheme 1. <sup>a</sup> LA = Lewis acid.

Table 1. Reaction of  $\beta$ -stannyl ketones with Lewis acids.

Run	Starting enone	Yield of ( <b>8</b> )%	Lewis acid	Temp. /°C	Time /min	Ratio (9): (10)	Total yield/%
1	( <b>7b</b> )	91	TiCl₄	-78	180	41:59	49
2			BF <sub>3</sub> -Et <sub>2</sub> O	room temp.	720	32:68	$\sim 40^{\mathrm{a}}$
3			<b>TMSOTf</b> <sup>c</sup>	-78	180	0:100 <sup>b</sup>	52
4	(7c)	61	TiCl₄	0	15	24:76	64
5			TMSOTf	room temp.	180	5:95	43
6	(7d)	98	TiCl₄	-78	5	14:86	56
7			TMSOTf	0	300	1:99	62
8	(7e)	51	TiCl₄	-78	15	42:58	61
9			BF <sub>3</sub> -Et <sub>2</sub> O	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 trifluoromethane-sulphonate.



Scheme 2. (a):  $R^1 = R^2 = Me$ , (b):  $R^1 = R^2 = H$ , (c):  $R^1 = Me$ ,  $R^2 = -CH_2$ -CH=CH<sub>2</sub>, (d):  $R^1 = Me$ ,  $R^2 = -CH_2$ -C=CH, (e):  $R^1 = Me$ ,  $R^2 = -CH_2$ Ph.



Scheme 3

As an extension of the reaction, we tried to prepare cyclopentanones carrying functionalised substituents. The  $\beta$ -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),<sup>1</sup> 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 <sup>13</sup>C n.m.r. and 400 MHz <sup>1</sup>H 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.

Received, 4th August 1988; Com. 8/03205J

## References

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