## Steric Control Based on Alkyl Substituents in the [2,3]Sigmatropic Rearrangement of Nine-membered Allylsulfonium Ylides. A New Entry to the Stereoselective Synthesis of Elemane-type Sesquiterpenoids

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The rhodium(u)-catalysed cyclisation of acyclic  $\alpha$ -diazomalonate **1b** and  $\alpha$ -diazo- $\beta$ -keto esters **1c**, **d** give stereoselectively the highly substituted  $\delta$ -lactone **3b** and cyclohexanones **3c**, **d**, respectively, by [2,3]sigmatropic rearrangement *via* the stereocontrolled nine-membered allylsulfonium ylides **2b–d**.

We have recently reported that the rhodium(II)-catalysed cyclisation of the acyclic  $\alpha$ -diazomalonate 1a possessing a methyl group at the C(5)-position gave a mixture of diastereoisomeric  $\delta$ -lactones **3a** with respect to the C(5)-methyl group by [2,3]sigmatropic rearrangement via a cyclic allylsulfonium ylide.1 This result indicates that in the proposed nine-membered transition state 2a consisted of two fused rings, i.e. a chair-like six-membered ring and a five-membered one, the C(5)-substituent in the former ring does not influence the stereochemistry of cyclisation from the standpoint of a steric effect on the conformational equilibrium. This consideration implies that the  $\alpha$ -diazomalonate **1b** possessing a methyl group at the C(6)-position in place of the C(5)-one generates predominantly, on the sulfonium-ylide formation, the cyclic transition state 2b, in which the methyl group is substituted equatorially in the six-membered part, rather than the other transition state 4 with a severe non-bonded interaction as depicted, thus producing stereoselectively the  $\delta$ -lactone 3b with a trans-arrangement between the methyl and newly formed vinyl groups. In addition, starting with  $\alpha$ -diazo- $\beta$ -keto esters, 1c, d, with an alkyl substituent  $(R^2)$  at the same C(6)position, this methodology may be applicable to the stereoselective synthesis of six-membered carbocycles 3c, d with the stereochemically same arrangement between the alkyl  $(R^2)$ and vinyl groups as above. Here we describe a remarkably stereoselective, good to high yields, and one-step synthesis of



**a** X = O,  $R^1 = R^2 = H$ ,  $R^3 = Me$ ,  $R^4 = Et$  **b** X = O,  $R^1 = R^2 = Me$ ,  $R^3 = H$ ,  $R^4 = Et$  **c**  $X = CH_2$ ,  $R^1 = R^2 = R^4 = Me$ ,  $R^3 = H$ **d**  $X = CH_2$ ,  $R^1 = R^4 = Me$ ,  $R^2 = CMe = CH_2$ ,  $R^3 = H$ 



a highly substituted  $\delta$ -lactone and cyclohexanones along this line.

The  $\alpha$ -diazomalonate **1b** was prepared in a high yield from condensation of the phenylsulfenyl alcohol 5,† readily available from 3,4-dimethyl-2-penten-5-olide by reduction with lithium aluminium hydride followed by the regioselective phenylsulfenylation, with ethyl hydrogen diazomalonate, a diazomalonylation reagent recently developed by us.<sup>2</sup> On preparation of  $\alpha$ -diazo- $\beta$ -keto ester substrates,  $\alpha$ -diazo ester Ic possessing two methyl groups at the C(7)- as well as C(6)positions was first adopted with intention of utilisation of the cyclisation product 3c as a key intermediate for the synthesis of natural products (vide post), and prepared from compound 5 as the common starting material in 59% overall yield via condensation of the aldehyde 6, readily obtainable from 5, with the dianion of methyl acetoacetate, followed by hydrogenation and a diazo transfer reaction.3 When the compounds 1b and 1c were treated in boiling benzene with a catalytic amount of rhodium(11) acetate, freshly prepared from rhodium(III) chloride,4 the [2,3]sigmatropic rearrangement via nine-membered allylsulfonium ylide the proceeded stereoselectively as expected, giving, as the sole isolable product, the cyclisation products 3b and 3c in 80 and 78% yields, respectively. No isomer could be detected in each reaction in spite of a careful inspection of the reaction mixture. The relative stereochemistry of these products was deduced as depicted from the reaction mechanism, and the validity of this assignment was proven by a chemical transformation of the compound 3c into the known cyclohexanone  $8^{5}$  by reductive desulfurisation to give the ester 7 followed by its alkaline decarboxylation.

Next, to examine the utility of our methodology to the asymmetric synthesis, (6S)- $\alpha$ -diazo- $\beta$ -keto ester 1d flanking an isopropenyl group at the C(6)-position was prepared from (+)-limonene as the chiral source by a sequence of conventional reactions via the (5S)-hydroxy ketone 9, and treated with a catalytic amount of rhodium(11) acetate in benzene. The result was in accordance with our expectations, and the cyclisation product 3d obtained in 61% yield as the sole product provided, on removal of both methoxycarbonyl and phenylthio groups by the procedures described above, the



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known (3*S*,4*S*)-4-isopropenyl-3-methyl-3-vinylcyclohexanone **10**,  $[\alpha]_D$  -29.8 (CHCl<sub>3</sub>), [lit.  $[\alpha]_D$  -29.2 (CHCl<sub>3</sub>);<sup>6</sup>  $[\alpha]_D$  -26.2 (CHCl<sub>3</sub>)<sup>7</sup>].

Although the intramolecular carbene insertion reaction starting with parent  $\alpha$ -diazo esters is known as one of important carbocyclic constructions, this method seems to be useful practically for preparation of five-membered rings.8 Not only are the above findings sufficiently favourable to support chemically our proposed reaction mechanism via the cyclic transition state 2, but also it is demonstrated that the present methodology starting with  $\alpha$ -diazo esters with the allyl sulfide function at the terminal position provides effectively six-membered rings as well as five-membered ones.<sup>1</sup> In addition, both cyclohexanones 7 and 10 obtained in this study could serve as promising key intermediates for the synthesis of natural products, *i.e.* the former 7 is synthetically equivalent to a contiguously cis-arranged trimethylcyclohexanone part of ascochlorin,9 an antibiotics isolated from Ascochyta vicae, and the latter 10 is a versatile compound for the synthesis of elemanoids. Since we have succeeded in the synthesis of (+)- $\beta$ -elemenone 11<sup>6,7</sup> and its related elemanolides<sup>6</sup> from (-)- $\beta$ pinene via the (3S, 4S)-cyclohexanone 10, the present synthesis of the compound 10 is an asymmetric synthesis of these natural poducts from (+)-limonene.

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## Footnote

 $\dagger$  All new compounds gave satisfactory spectroscopic and microanalytical data.

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