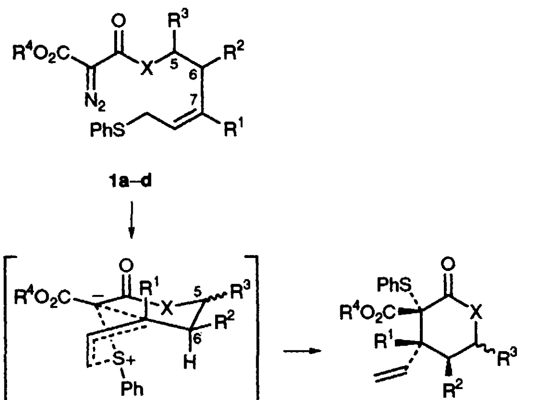
Steric Control Based on Alkyl Substituents in the [2,3]Sigmatropic Rearrangement of Nine-membered Allylsulfonium Ylides. A New Entry to the Stereoselective Synthesis of Elemane-type Sesquiterpenoids

Fusao Kido,* Kazuo Yamaji, Subhash C. Sinha, the late Akira Yoshikoshi and Michiharu Kato*

Institute for Chemical Reaction Science, Tohoku University, Katahira, Aoba-ku, Sendai 980, Japan

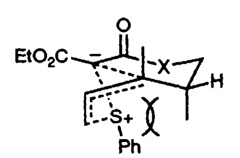
The rhodium(II)-catalysed cyclisation of acyclic α-diazomalonate 1b and α-diazo-β-keto esters 1c, d give stereoselectively the highly substituted δ-lactone 3b and cyclohexanones 3c, d, respectively, by [2,3]sigmatropic rearrangement *via* the stereocontrolled nine-membered allylsulfonium ylides 2b–d.

We have recently reported that the rhodium(II)-catalysed cyclisation of the acyclic α-diazomalonate **1a** possessing a methyl group at the C(5)-position gave a mixture of diastereoisomeric δ-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 α-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 δ-lactone **3b** with a *trans*-arrangement between the methyl and newly formed vinyl groups. In addition, starting with α-diazo-β-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 highly substituted δ-lactone and cyclohexanones along this line.



1a–d → **2a–d** → **3a–d**

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, $R^1 = R^4 = Me$, $R^2 = CMe{=}CH_2$, $R^3 = H$



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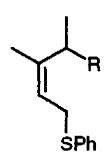
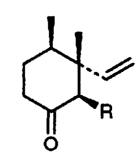
The α-diazomalonate **1b** was prepared in a high yield from condensation of the phenylsulfenyl alcohol **5**,† readily available from 3,4-dimethyl-2-penten-5-olide by reduction with lithium aluminium hydride followed by the regioselective phenylsulfenylation, with ethyl hydrogen diazomalonate, a diazomalonylation reagent recently developed by us.[2] On preparation of α-diazo-β-keto ester substrates, α-diazo ester **1c** 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(II) acetate, freshly prepared from rhodium(III) chloride,[4] the [2,3]sigmatropic rearrangement *via* the nine-membered allylsulfonium ylide 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.

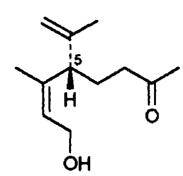
Next, to examine the utility of our methodology to the asymmetric synthesis, (6*S*)-α-diazo-β-keto ester **1d** flanking an isopropenyl group at the C(6)-position was prepared from (+)-limonene as the chiral source by a sequence of conventional reactions *via* the (5*S*)-hydroxy ketone **9**, and treated with a catalytic amount of rhodium(II) 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



5 R = CH_2OH
6 R = CHO



7 R = CO_2Me
8 R = H



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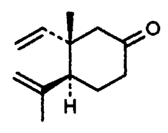

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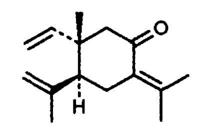

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known (3*S*,4*S*)-4-isopropenyl-3-methyl-3-vinylcyclohexanone **10**, $[\alpha]_D$ −29.8 ($CHCl_3$), [lit. $[\alpha]_D$ −29.2 ($CHCl_3$);[6] $[\alpha]_D$ −26.2 ($CHCl_3$)[7]].

Although the intramolecular carbene insertion reaction starting with parent α-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 α-diazo esters with the allyl sulfide function at the terminal position provides effectively six-membered rings as well as five-membered ones.[1] 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 (+)-β-elemenone **11**[6,7] and its related elemanolides[6] from (−)-β-pinene *via* the (3*S*, 4*S*)-cyclohexanone **10**, the present synthesis of the compound **10** is an asymmetric synthesis of these natural poducts from (+)-limonene.

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Footnote

† All new compounds gave satisfactory spectroscopic and microanalytical data.

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