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C-C BOND FORMATION ON REDUCTION OF ORGANOMERCURIAL AND ITS APPLICATION TO BIOMIMETIC SYNTHESIS OF STROBANE CARBON SKELETON

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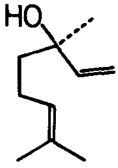
The bicyclic ethers obtained by the oxymercuration-demercuration reaction of linalool was found to be formed in the demercuration step. The facile C-C bond formation is due to the proximity of Hg and the vinyl group in the organomercurial intermediate. Applying this process to epimanool a biomimetic synthesis of strobane carbon skeleton was achieved.

In the previous paper[1)], we have reported the Hg(II)-induced cyclization of terpenic vinyl carbinols, whereby iridanol **2** was formed regio- and stereoselectively (**2a** predominates) from linalool **1** and biomimetic one-step synthesis of cyclonerodiol, a cyclopentanoid sesquiterpene isolated from fungii, was achieved from nerolidol. However, under certain conditions [$Hg(OAc)_2$ in aq. THF or aq. t-BuOH, r.t. 12 h], the hydroxy ethers **3** and **4** were formed in up to 71% yield along with **2** and the ethers **5**[1)]. Further investigation revealed that **4** and **5** as well as **3** were formed via the common intermediate, organomercurial of the type **6**, and that the rearrangement to **4** and the C-C bond formation to **5** took place in the reductive demercuration step. This paper describes the possible mechanism to **4** and **5** and the application of the result to the biomimetic cyclization of 13-epimanool to the strobane carbon skeleton.



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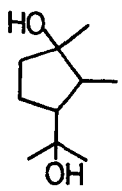

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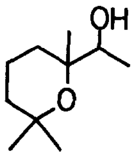
2a: β-OH, β-sec. Me

α-$Me_2C(OH)$-



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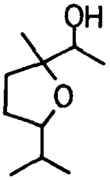

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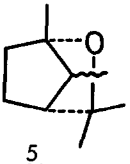


5

5t: β-Me

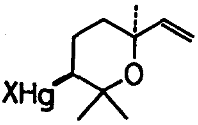
5c: α-Me

The time course experiments of the reaction of **1** [$Hg(OAc)_2$ in aq. THF, r.t.], after reductive demercuration[2)], revealed as shown in Table that 1) the reaction is quite rapid (practically no linalool **1**

Table Time course of $Hg(OAc)_2$-aq. THF reaction (yield %)[2)]

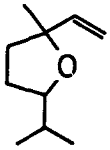
	1	2	3	4	5t	5c	7
1 min	trace	15	1	2	52	16	10
15 min	trace	14	7	11	49	11	4
1 hr	trace	13	17	14	21	7	2
12 hr	trace	19	22	27	7	2	0

was detected after 1 min.), 2) the unsaturated ether 7 was attacked by another mole of Hg(II) to give the hydroxyether 4, 3) iridanols were formed at the early stage and stayed constant during the reaction period, and 4) both bicyclic ethers 5 were formed very rapidly but replaced later by the hydroxyether 3 (and to some extent 4). Since the direct formation of 3 from 5 is unlikely, the organomercurial formed initially was isolated and its reduction was studied in order to establish the reaction pathways to these ethers. The organomercurial acetate was converted to the more stable chloride by addition of NaCl after the reaction for 1 min, and the solvent was replaced by acetone, thereby crystalline chloride 6a, m.p. 144-146°C, was obtained in 25% yield. The structure of 6a was deduced from the spectral analysis [m/e 377, 376, 375, 374, 373, 372, 371 (M^+-CH_3), 153 (M^+-HgCl); ν (Nujol) 1628 cm^{-1}; δ (acetone-d_6), 1.10 (1Me, s), 1.32 (1Me, s), 1.41 (1Me, s), 2.67 (1H , m), 4.96 (1H, dd, J=10.0, 2.0, $\underline{A}BX$), 5.02 (1H, dd, J=17.5, 2.0, $A\underline{B}X$), 5.97 (1H, dd, J=17.5, 10.0, $AB\underline{X}$)]. While planer structure of 6a was established firmly from the spectra, cis relationship of Hg and the vinyl group in 6a was implied from the observed IR frequency which is shifted[3)] from that of rose oxide 8 (ν 1640 cm^{-1})[4)]. Reduction of 6a with alkaline $NaBH_4$ afforded 5t, 5c, 7 and 1 in the ratio of 65:22:9:4, none of 8, the simple demercuration product, being detected. The reduction with $NaBD_4$ yielded 5t-d, 5c-d and 7-d. In the first two products, a deuterium


6

6a: X=Cl

6b: X=OAc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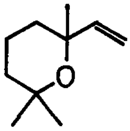
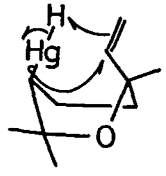

8

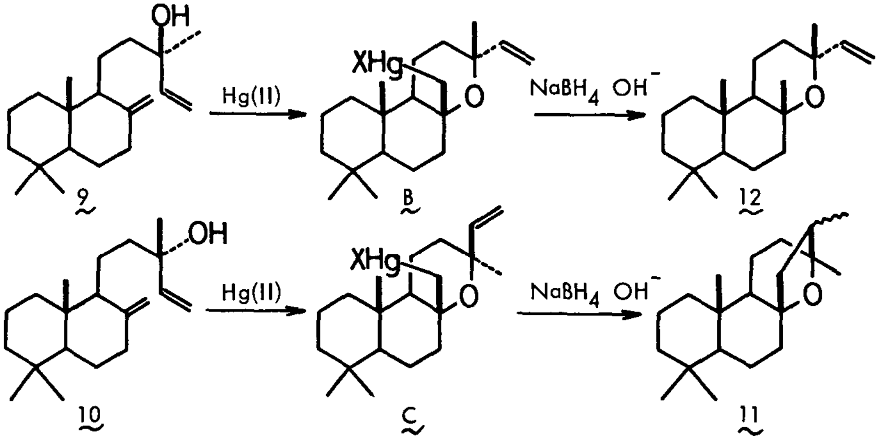
is located exclusively at the secondary methyl group and in the last product at the methine of isopropyl group. These experiments verified that 1) a part of 7 was derived from 6a by a rearrangement at the reduction step and therefore likely from 6b in time course experiment and 2) the C-C bond formation to

5t and 5c occurred from 6a, therefore also from 6b, at the demercuration step. Although similar C-C bond formation was previously observed and explained as non-cage radical process5), the high efficiency of the bond formation in the present sudy is remarkable. This may be caused by the proximity of Hg and vinyl group in the organomercurials 6a and 6b, so that the hydrogen in hydromercurial formed by the reduction is transfered to the vinyl group preferentially (cf. A). The attempted capture of the radical with $O_2$5) was unsuccessful. With the results described in the previous1) and the present papers combined, it is now clear that the iridane carbon skeleton has been produced from linalool by the attack of Hg(II) salts at either double bonds; iridanols 2 via the Markovnikov attack at the vinyl group, and the ethers 5 at the trisubstituted double bond.



A

The proximity of Hg and a vinyl group in a cyclic ether may be realized with 13-epimanool 10 but not with manool 9, and, if it is essential for the reductive C-C bond formation, strobane oxide 11 would be formed from the former, constituting a biomimetic cyclization of the latter carbon skeleton6).



Although manool 9 yielded only manoyl oxide 127,8) through B when subjected to oxymercuration [$Hg(OAc)_2$ in aq. nitromethane]-demercuration reactions, the 1 : 1 mixture of 9 and 10 under the same conditions afforded 11 in 72% yield through C along with 129). 11: m.p. 77-78°C; m/e 290 (M^+), 275, 232, 190, 137 (b.p.), 109; ν^{CCl_4} 1425, 1121, 1100 cm^{-1}; δ^{CCl_4} 0.80 (6H, s), 0.88 (3H, s), 0.95 (3H, d, J=6.8), 1.03 (3H, s). The strobane carbon skeleton in 11 was easily deduced by the presence of secondary methyl group though its configuration is unknown10).

Our deepest gratitude is expressed to Takasago Perfumery Industry Ltd. for their generous gift of linalool and manool.

References and Notes

1) Y. Matsuki, M. Kodama and S. Itô, Tetrahedron Letters, in press.

2) Two equivalents of $Hg(OAc)_2$ were added under vigorous stirring to the solution of **1** at room temperature. After the period indicated, excess of 2N-NaOH and $NaBH_4$ were added consecutively. Normal work up and a short column chromatography gave the product mixture, in which product ratio was determined by GLC (5% Apiezon-L and Carbowax 20M on Chromosorb G-AW-DMCS, 150°C).

3) The shift is probably due to the attractive interaction between Hg and π-electrons. Similar interaction has been observed [H. Hodjat-Kachani, A. Lattes, J.J. Perie and J. Roussel, J. Organometal. Chem., **96**, 175 (1975), E.F. Kjerter, W.L. Waters and D.A. Carson, J. Am. Chem. Soc., **90**, 5127 (1968)].

4) H. Strickler and E. sz. Kovats, Helv. Chim. Acta, **49**, 2055 (1966).

5) R.P. Quirk and R.E. Lea, Tetrahedron Letters, 1925 (1974), Idem, J. Am. Chem. Soc., **98**, 5973 (1976).

6) Although an abietane derivative has been converted to a strobane, the cyclization from a labdane-type compound was not successful [W. Herz and A.L. Hall, J. Org. Chem., **39**, 14 (1974), P. Sundararaman and W. Herz, Ibid., **42**, 806 (1977)].

7) R. Hodges and R.I. Reed, Tetrahedron, **10**, 71 (1960), E. Wenkert, D. Beak and P.K. Grant, Chem. Ind., 1574 (1961).

8) The transformation indicates the tendency for the methylene group becomes axial methyl group with the intramolecular ether formation.

9) **9** and **10** are inseparable and used as the 1 : 1 mixture. The ratio was determined by the interporation of $[\alpha]_D$ values. The yield was based on the epimanool present in the mixture.

10) However, the PMR spectrum of **11** showed no indication of the presence of diastereomers even on addition of LIS reagents.

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