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SYNTHESIS OF 9,9,9-TRIFLUORO-2-p-MENTHENE-1,8-DIOL.
DETERMINATION OF THE STRUCTURE BY X-RAY ANALYSIS

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The ene reaction product of trifluoroacetone with cyclohexene was oxidized to 4-(1,1,1-trifluoro-2-hydroxy-2-propyl)-2-cyclohexenone, which was converted to the title compound. X-ray analysis of this compound determined the regio- and stereo-chemistries in the ene reaction, oxidation and methylation.

KEYWORDS—menthane; trifluoromethyl; ene reaction; oxidation; methylation; X-ray analysis; p-menthenediol

Previously, we reported the ene reaction of trifluoroacetone with cyclohexene gave 2-(2-cyclohexen-1-yl)-1,1,1-trifluoro-2-propanol (**1**).¹⁾ Now, we report the derivatization of **1** to 9,9,9-trifluoro-2-menthene-1,8-diols (**4** and **5**), trifluoro analogues of menthane derivatives, and the X-ray analysis of **5**.

The procedures are summarized in Chart 1.

Chart 1

The first step might give two diastereoisomers concerning two chiral centers, but we had obtained one isomer, the structure of which had not been determined.¹⁾ Recently, **1** was dehydrated with phosphorus oxychloride and pyridine to 3-(1,1,1-trifluoro-2-propylidene)cyclohexene, whose stereochemistry was tentatively assigned to a Z-form by two dimensional nuclear magnetic resonance.²⁾ Therefore, **1** must have the (R^* , R^*)-configuration. Oxidation of **1** with tert-butyl hydroperoxide in the presence of a catalytic amount of chromium trioxide gave 4-(1,1,1-trifluoro-2-hydroxy-2-propyl)-2-cyclohexenone (**2**) and 3-(1,1,1-trifluoro-2-hydroxy-2-propyl)-2-cyclohexenone (**3**) in a ratio of 2:1. In the formation of the latter, an allylic oxidation was followed by migration of the double bond. If such a migration occurred in the formation of the former, the structure of **2** might be 6-(1,1,1-trifluoro-2-hydroxy-2-propyl)-2-cyclohexenone. Treatment of **2** with methylmagnesium iodide gave 9,9,9-trifluoro-2-menthene-1,8-diols (**4**) and (**5**). To determine the structures of **1** to **5** unambiguously, X ray analysis of **5** was carried out. Crystal data are: Monoclinic; Space group C2/c; $a=19.196(1)$, $b=9.010(1)$, $c=12.414(1)$ Å; $\beta=100.61(1)^\circ$; $Z=8$. The structure was determined as shown in Fig. 1. This result shows that **1** is (R^* , R^*)-isomer, **2** has the structure as shown in Chart 1 and **5** is ($1R^*$, $4R^*$, $8R^*$)-isomer. Thus, **4** is determined to be the ($1S^*$, $4R^*$, $8R^*$)-isomer.

Fig. 1

The stereoselectivity in the ene reaction of trifluoroacetone with cyclohexene assumed to be due to the fact that repulsion between 3- and/or 4-protons and the trifluoromethyl group prevents formation of other isomers. The transition state for formation of **1** is shown in Fig. 2. The fact that hexafluoroacetone hardly reacted with cyclohexene supports the above assumption.

Fig. 2

REFERENCES AND NOTES

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- 3) All new compounds have been characterized by mass, ^1H - and ^{19}F -NMR spectra.

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