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Reaction of Camphene with Chloroacetic Acid and the Synthesis of 2-(8-Camphenyl)ethanol[1,2]

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Synopsis. Camphene (**1**) reacts with chloroacetic acid (**2**) or its polymer, polyacetoxamer; α-chloro, ω-carboxy in the presence of potassium bromide at reflux temperature to give the 2,2-dimethyl-*exo*-3-hydroxynorbornane-*endo*-3-propanoic acid lactone and the 2,2-dimethyl-*endo*-3-hydroxynorbornane-*exo*-3-propanoic acid lactone in a 50% yield. The synthesis of 2-(8-camphenyl)ethanol from **1** was simplified by utilizing this reaction.

There are no reports on the reactions of terpenes with halocarboxylic acids and also few reports on the reactions of olefins with halocarboxylic acids. These are reports on the carboxymethylation of olefins making use of iodo- and bromoacetic acids.[3] Specifically, the carboxymethylation of naphthalene[4] in the presence of potassium bromide was carried out using chloroacetic acid or its polymer, polyacetoxamer; α-chloro, ω-carboxy in the title reaction. However, it is of interest to note that the reaction of manganese(III) acetate with olefins in cyanoacetic acid was recently reported by Heiba *et al.*[5] and therefore, γ-lactones can be obtained in a single step.

As a part of the study of the reactions of olefins with halocarboxylic acids, the reaction of camphene (**1**) with chloroacetic acid (**2**) or its polymer, polyacetoxamer; α-chloro, ω-carboxy (**3**) was first investigated in the presence of potassium bromide. As a result, it was found that **1** reacts with **2** or **3** to give γ-lactones, which are useful in the synthesis of 2-(8-camphenyl)ethanol (**7**). Therefore, the structure of the γ-lactones and a simple method for synthesizing **7** from **1** are reported here.

Results and Discussion

The results of the experiments are shown in Table 1. In the presence of potassium bromide (KBr), the treatment of camphene (**1**) with chloroacetic acid (**2**) at reflux temperature gave, after distillation, the maximum yield (50%) of the γ-lactones which was composed of two components, **4A** and **4B**, in a gas chromatogram. These components (**4A** and **4B**) were isolated by redistillation and gas chromatography. Their structures were confirmed by IR and NMR spectroscopy or by a comparison of their physical constants with those reported in the literature. Table 2 shows the properties of **4A** and **4B**. The IR and NMR spectra showed the characteristic absorptions of γ-lactones and the *gem*-dimethyl group. These data indicate a configurational isomer **4A** or **4B** in Fig. 1. Of the two γ-lactones obtained, the melting point for the **4B** isomer agreed precisely with that reported by Bhati.[6] Therefore, the **4B** isomer can be assigned to the 2,2-dimethyl-*endo*-3-hydroxynorbornane-*exo*-3-propanoic acid lactone (**4B**) in Fig. 1. Consequently, the **4A** isomer supported the structure of the 2,2-dimethyl-*exo*-3-hydroxynorbornane-*endo*-3-propanoic acid lactone (**4A**) in Fig. 1. The structure of **4A** was confirmed, moreover, by deriving 2-(8-camphenyl)ethanol (**7**) from a mixture of **4A** and **4B**. The γ-lactone **4A** has not as yet been synthesized.

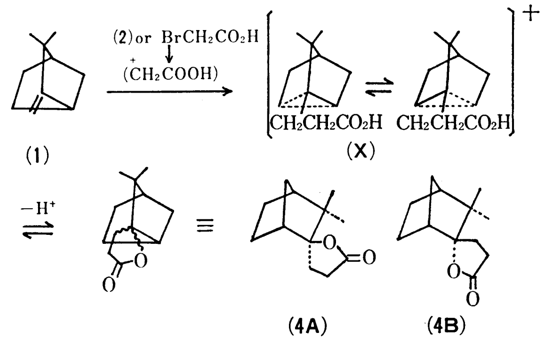

Fig. 1. Lactonization of **1**.

On the other hand, when **1** was treated with **2** in the absence of KBr, the γ-lactone fraction was afforded in only an 8% yield (Table 1). A gas chromatogram of the γ-lactone fraction also showed the two components, **4A** and **4B**. Their structures were confirmed by IR and NMR spectroscopy. In contrast with the reaction in the presence of KBr, the yield of γ-lactones was much lower. This behavior shows that in the presence of KBr, bromoacetic acid may initially be formed. The decomposition of bromoacetic acid can result in the formation of the carbonium ion ($^+CH_2COOH$),[4] which might account for an attack upon the

TABLE 1. THE RESULTS OF EXPERIMENT

Expt No.	Conditions (**1**) g(mol)	(**2**) g(mol)	(**3**) g	KBr g	Temp[a] °C	Time h	Yield[b] %	Lactones Formation (**4A**)	Ratio[c] (**4B**)
1	35.8(0.25)	24.9(0.32)	—	3.0	187	20	20	41	59
2	35.8(0.25)	24.9(0.32)	—	3.0	189	30	38	35	65
3	35.8(0.25)	24.9(0.32)	—	3.0	180	40	50	39	61
4	35.8(0.25)	24.9(0.32)	—	—	178	20	8	42	58
5	10.0(0.07)	— (—)	10.0	1.0	172	20	17	35	65

a) Shows the temperature of the refluxing liquid after completion of stirring. b) Based on **1** used. c) Shows the relative ratio of the γ-lactone from gas chromatographic analysis.

TABLE 2. PROPERTIES OF γ-LACTONES

γ-Lactone	Rt.[a] (min)	Mp (°C)	IR(cm^{-1})[b] OCO		$C(CH_3)_2$		NMR(ppm)[c] $C(CH_3)_2$	$(CH_2)_2CO$
(**4A**)	58.0	99—100	1780, (sh)	1760 (vs)	1385, (w)	1365 (m)	1.01 (br s)	2.13—2.48 (M)
(**4B**)	64.5	103—104[d]	1780, (sh)	1760 (vs)	1386, (w)	1366 (m)	0.99, 1.04 (s) (s)	2.10—2.47 (M)

a) Retention time in gas chromatogram, PEG-20M, 4m, 180 °C. b) vs: very strong, sh: shoulder, w: weak, m: medium. c) s: singlet, br: broad, M: multiplet. d) Value from the literature (mp 103—104 °C[6]).

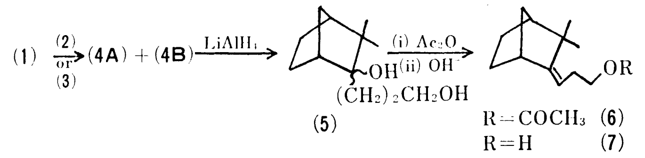

Fig. 2. Synthesis of **7**.

methylene group of **1** to give the γ-lactones (**4A** and **4B**) by lactonization of an intermidiate (**X**), as is shown in Fig. 1.

Next, polyacetoxamer; α-chloro, ω-carboxy (**3**) in the presence of KBr was also allowed to react with **1** to give the γ-lactones which comprised the two components, **4A** and **4B**. However, the γ-lactone yield was only about 17% (Table 1). These components were isolated using gas chromatography and their structures were confirmed by comparisons of their IR and NMR spectra with those of authentic samples. From this method, the lactonization could be explained by assuming the formation of carbonium ions of the type $^+CH_2CO_2(CH_2CO_2)_pCH_2CO_2H$.4)

Lactone **4B** has in general been prepared by the hydration of tricycloekasantalic acid, which was obtained by the oxidation of the higher boiling fraction of East Indian sandalwood oil or α-santalene, as well as by the hydration of bicycloekasantalic acid or isobicycloekasantalic acid.6–8) However, no simple synthesis of the γ-lactones (**4A** and **4B**) from **1** has yet been established. Bhati6) has reported only that **4B** was synthesized *via* a multi-step process starting from **1**, in order to determine whether **4A** or **4B** is the hydration product (70 % yield) of tricycloekasantalic acid. The method described by Bhati is the only route for synthesizing **4B** from **1**, but it is not a method applicable to the synthesis of **7** from **1**. Using the present method, the γ-lactones (**4A** and **4B**) were prepared in a 50% yield in a single step from **1**, which is readily available. The synthesis of **7** was carried out according to known procedures,7) as shown in Fig. 2. The γ-lactones (**4A**/**4B**=39/61) upon reduction with lithium aluminium hydride afforded a crystalline diol (**5**) which was converted to the corresponding unsaturated alcohol **7** by treatment with acetic anhydride, followed by saponification of the resultant acetate (**6**).

Experimental

Material. Camphene (**1**): bp 157—159 °C/760 Torr, mp 51—53.5 °C, purity 95% (in gas chromatogram, contains 5% tricyclene). Potassium bromide: commercial material (Wako Pure Chemical Industries) was used without purification. Polyacetoxamer; α-chloro, ω-carboxy (**3**): this polymer was prepared by the method of Southwick *et al.*4) The resulting black powder was dried under reduced pressure for one day. Mp 115—158 °C (lit,4) mp 118—138 °C)

Measurements. The NMR spectra were recorded on a Hitachi Perkin-Elmer R-24 (60 MHz) instrument. The IR spectra were obtained on a Yanagimoto ISG-25 spectrometer.

*Reaction of **1** with **2**. In the Presence of KBr*: In a flask fitted with a thermometer, stirrer and reflux condenser were placed 24.9 g (0.32 mol) of **2** and 3.0 g of KBr. The mixture was stirred vigorously in a sand bath for one hour at reflux temperature and 35.8 g (0.25 mol) of **1** was added to the solution dropwise for 30 min. The stirring was then continued for 30 h at the reflux temperature. At the end of the heating period, the temperature of the refluxing liquid was 189 °C. After cooling and benzene extraction, the extract was washed with a 10% aqueous solution of sodium carbonate and then water. The benzene extracts were dried over magnesium sulfate. Evaporation of the dried benzene layer followed by distillation gave the γ-lactone fraction (bp 122—125 °C/1 Torr, 18 g, 50% yield based on the amount of **1** used), which was composed of two components, **4A** and **4B**, in a 35 : 65 ratio based on gas chromatographic analysis. The γ-lactone fraction was crystallized from hexane: mp 98—99.5 °C; IR(KBr): 1780, 1760, 1386, and 1365 cm^{-1}.

In the Absence of KBr: A mixture of 24.9 g (0.32 mol) of **2** and 35.8 g (0.25 mol) of **1** was heated with stirring for 20 h at reflux temperature. At the end of the heating period, the temperature of the refluxing liquid was 178 °C. The conventional working-up described above and distillation afforded a mixture of 2.85 g (an 8% yield) of **4A** and **4B** in a 42 : 58 ratio.

*Reaction of **1** with **3** in the Presence of KBr.* The reaction was carried out with the same apparatus as used in the reaction of **1** with **2**. A mixture of 10 g of **3** and 1.0 g of KBr were heated with stirring for one hour at 160±2 °C and then 10.0 g (0.07 mol) of melted **1** was added to the solution dropwise for 30 min. Stirring was then continued for 20 h at reflux temperature. At the end of the heating period, the temperature of the refluxing liquid was 172 °C. The conventional work-up and distillation afforded 1.7 g (17% yield) of a mixture of **4A** and **4B** in a 35 : 65 ratio.

*Synthesis of **7**.* The alcohol was prepared according to the method of Ramaswami *et al.*7) The diol (**5**): yield 85%, mp 99—107 °C, (lit,7) mp 112 °C); IR: 3350, 1380, 1365, 1062, and 1040 cm^{-1}, NMR ($CDCl_3$) δ=0.91, 0.98 (two s, 6, CMe_2), 2.05 (br s, 2, OH, disappeared with D_2O), 3.90—3.75 ppm (m, 2, CH_2O), 2-(8-camphenyl)ethyl acetate (**6**): yield 90%, bp 107—109 °C/1 Torr, d_4^{25}=0.9915, n_D^{25}=1.4775, IR: 1740, 1666, 1380, 1365, and 842 cm^{-1}, NMR ($CDCl_3$) δ=0.98, 1.00 (two s, 6, CMe_2), 2.01 (s, 3, OAc), 3.88—4.11 (t, 2, CH_2O), and 4.69—4.98 ppm (t, 1, =CH–), (lit,8) bp 105—110 °C/0.5 Torr, n_D^{28}=1.4749). 2-(8-Camphenyl)ethanol (**7**): yield 82%, bp 95—97.5 °C/2 Torr, n_D^{25}=1.4970, IR: 3300, 1666, 1383, 1366, and 842 cm^{-1}, NMR ($CDCl_3$) δ=1.02 (br s, 6, CMe_2), 1.86 (br s, 1, OH, disappeared with D_2O), 3.46—3.68 (t, 2, CH_2O), and 4.72—4.68 ppm (m, 1, =CH–), (lit,8) bp 96—98 °C/2 Torr, n_D^{25}=1.4963).

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