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CONCERTED CYCLIZATION OF 4,8-DIMETHYLNONA-3,7-DIENOIC ACID (HOMOGERANIC ACID) TO TRANS-HEXAHYDRO-4,4,7a-TRIMETHYL-2(3H)BENZOFURANONE (TRANS-TETRAHYDROACTINIDIOLIDE)

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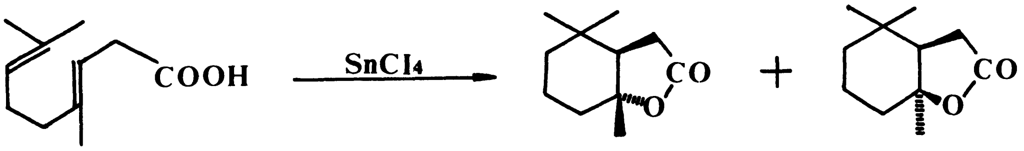
Cyclization of 4,8-dimethylnona-3,7-dienoic acid (homogeranic acid) in the presence of stannic chloride was studied under various conditions. Cyclization product obtained comprises 88 per cent trans- and 12 per cent cis-hexahydro-4,4,7a-trimethyl-2(3H)benzofuranone (trans- and cis-tetrahydroactinidiolide). Other products, such as monocyclic compounds, could not be detected in the reaction mixture. Isomerization of the trans isomer to the cis isomer in the presence of stannic chloride was also observed. It may be concluded that the cyclization reaction proceeds by a concerted mechanism.

It is well known that cis-hexahydrobenzofuranone is more stable than the trans isomer.[1] One of the similar skeletal compounds, hexahydro-4,4,7a-trimethyl-2(3H)benzofuranone (tetrahydroactinidiolide) has been isolated from tobacco[2] and synthesized according to various procedures.[3] Most of them are concerning the cis isomer (3), and the information of the trans isomer (2) is not so enough.[4] In the course of the studies on one step cyclization of 4,8-dimethylnona-3,7-dienoic acid (homogeranic acid)(1), we noticed that (2) is formed in fairly large quantities under some reaction conditions.

Acid, (1), was obtained by bromination of geraniol, followed by nitrilation and hydrolysis. It cyclized in the presence of various quantities of stannic chloride at various temperatures to give both of (2) and (3).



(1) (2) (3)

Identification of (2) and (3) was made by NMR spectrum (trans $\delta^{TMS}_{CDCl_3}$ = 0.95, 0.97, 1.36 ; cis $\delta^{TMS}_{CDCl_3}$ = 0.92, 1.06, 1.54 due to the three methyl groups). These geometrical isomers could not be separated by thin layer or column chromatography.[5)] The ratio of (2) to (3) was measured by gas liquid chromatography (PEG 20M, glass capillary column, ϕ 0.25 mm × 30 m). The results are shown in tables 1 and 2.

Table 1 shows that (2) could be obtained in nearly 90 % ratio of the cyclization product. A rise in temperature and an increase in quantity of stannic chloride increased the proportion of (3) in the cyclization products (Table 1 and 2). Isomerization of (2) to (3) is considered to occur during the reaction.

Table 1 Effect of Temperature

Temperature (°C)	Ratio (%)		Total yield (%)
	trans	cis	
-78	88	12	5
-50	64	36	40
-18	49	51	61
0	40	60	40
20	2	98	84
40	0	100	86

Reaction procedure ; Stannic chloride (0.71 g) was added dropwise to homogeranic acid (0.50 g) in dichloromethane (10 ml) under stirring. The reaction time was 60 min.

Table 2 Effect of Quantity of Stannic Chloride

Mole ratio of stannic chloride to (1)	Ratio (%)		Total yield (%)
	trans	cis	
0.25	83	17	34
0.5	73	27	57
1.0	49	51	61
2.0	42	58	67
4.0	45	55	60

Reaction procedure ; Stannic chloride was added dropwise to homogeranic acid (0.50 g) in dichloromethane (10 ml) under stirring at -18°C. The reaction time was 60 min.

In order to examine this isomerization, stannic chloride was added to the mixture of (2) and (3) ((2):(3) = 78:22) at 23°C. The change of the ratio of the geometrical isomers with the passage of time was observed. The results are shown in table 3.

Table 3 Change of the Ratio of the Geometrical Isomers with the Passage of Time in the Presence of Stannic Chloride

Time (min)	Ratio (%)	
	trans	cis
0	78	22
20	65	35
60	44	56
120	31	69
240	22	78

Reaction procedure ; Stannic chloride (4 mg) was added to the mixture of (2) and (3) ((2):(3) = 78:22) (20 mg) in $CDCl_3$ (0.4 ml) at 23°C. The extent of isomerization was measured with a nuclear magnetic resonance instrument with the passage of time.

Increase of the cis ratio with the passage of time confirmed that (2) isomerized to (3) in the presence of stannic chloride. In this work it was revealed that (2), less stable than (3), can be obtained in high ratio under selected condition, and (2) isomerizes easily to (3) in the presence of stannic chloride and at high temperature. It is possible to consider that first product of cyclization would be the trans structure (2) and at the next step this would isomerize to the cis structure (3). Because of the ease of this isomerization, information about the trans isomer has been little. The production of the unstable isomer (2) mainly suggests that the cyclization would proceed by a concerted mechanism mentioned by Johnson.6) No detection of monocyclic compounds in the reaction mixture supports the mechanism.

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5) We tried to isolate trans isomer according to the method of T. Matsumoto et al., but we could not succeed in the separation.

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