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CYCLIZATION[1] OF POLYENES XIII. INTRAMOLECULAR ACYLATION OF GERANIC AND FARNESIC ACID CHLORIDES

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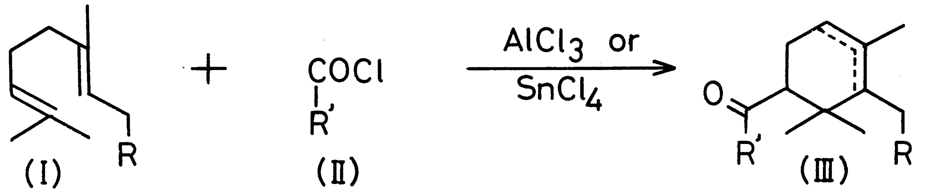
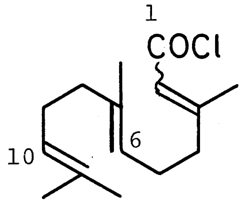
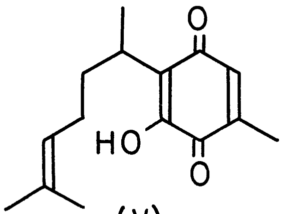
Intramolecular acylation reaction took place easily when geranic and farnesic acid chlorides (IV and VII) were treated with $AlCl_3$ or $SnCl_4$, affording the cyclohexenone derivatives in fairly good yields. These as well as our previous results promise the usefulness of the acylation reaction of polyenes for the construction of some kinds of terpenoid skeleton.

In a previous paper[2] we described the reaction of polyenes (I) with several kinds of acid chlorides (II) in the presence of $AlCl_3$ or $SnCl_4$, where the acylation occurred selectively at the terminal double bond accompanying simultaneous ring closure, and the yield of the products (III) is usually fairly good enough to apply the reaction for the construction of complex organic molecules.





(IV)



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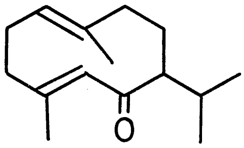


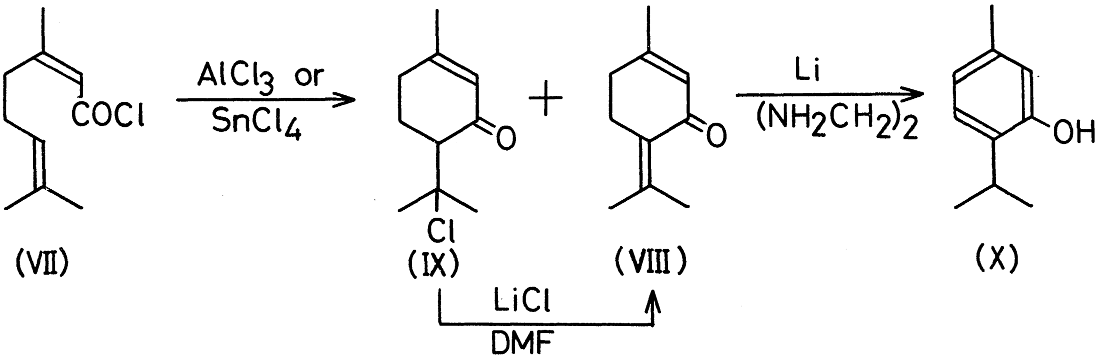
(VI)

It is of particular interest to examine the applicability of our method to the intramolecular acylation of farnesic acid chloride (IV) since bonding between C_1

and C_6 leads to the formation of bisabolane skeleton exemplified by perezone (V)[3], while connection of C_1 with the terminal double bond (C_{10}) results in the construction of germacrane types. Acoragermacrone (VI)[4] is a good example of the latter sesquiterpenoids. Assuming that the fashion of these bond formations is the key step in the biogeneses of these natural products, we studied the intramolecular acylation, first using geranic acid chloride as a model experiment and then farnesic acid chlorides.

Cyclization of geranic acid chlorides

When cis geranic acid chloride (VII)[5] was treated with $SnCl_4$ (or $AlCl_3$) at -78° in CH_2Cl_2, piperitenone (VIII)[7] and its chlorinated derivative (IX) were isolated in 77 and 11% yields, respectively. By treatment with LiCl in DMF, the latter was easily converted to the former, which was in turn isomerized to the known thymol (X) by Li-ethylenediamine.[8] The 2,3-trans isomer of VII was then submitted to the same reaction conditions, resulting in the predominant polymerization probably due to the intermolecular acylation.

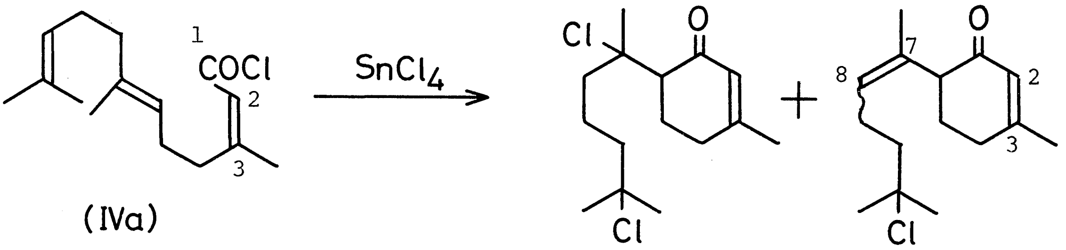


Cyclization of farnesic acid chlorides

By the reaction of 2,3-cis farnesic acid chloride (IVa) under the same conditions as applied in the model experiment, the chloride was converted in 70% yield to a mixture of XI and monochloro compounds, (XII) and (XIII) in the ratio of 1:3:1, respectively, which was separated by column and thin layer chromatographies on SiO_2. The structure of these products was confirmed as follows. On treatment with LiCl at room temperature, XI was transformed into a 3:4 mixture of cross conjugated dienones, (XIV) and (XV), in high yield. After separated with preparative TLC of silica gel (n-hexane: AcOEt=20:1), each isomer was further dehydrochlorinated with LiCl (100°, 3 hr), affording XVI (3:1 mixture of a and b) from XIV, and XVII (a and b) from XV, respectively. On the other hand, each of the monochlorinated products, XII and XIII, was transformed into a mixture of XVI (a and b) (36%) and XVII (a and

b) (30%) by treatments with LiCl (110°, 3 hr). The double bond isomers, a and b, of XVI and XVII, in which a is formed predominantly, were separated by high pressure liquid liquid chromatography.[9] Finally, XVIa, which was contaminated with 20% of XVIb, was converted to the known phenolic isomer (XVIII)[10] in 50% yield by the action of Li-ethylenediamine. NMR spectra of these derivatives, summarized in table 1, are compatible with the assigned structures and the stereochemistry of C$_7$-C$_8$ of XII and XIII was tentatively assigned based on the comparison of the chemical shifts[11] of C$_6$- and C$_8$-protons, and C$_7$-Me, respectively, while geometrical isomers of each pair, i. e., XIV and XV, and XVI and XVII, all of which absorbed at 243 and 286 nm in UV spectra, were determined by comparison of the chemical shift of C$_7$-methyls with those of piperitenone (VIII), where cisoid and transoid methyls appeared at 2.05 and 1.83 ppm, respectively.

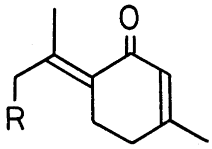
It was thus found that bisabolane skeleton was formed by simple operation in a fairly good yield and this transformation means the execution of the biogenetic type cyclization. Cyclization of 2,3-trans isomer will be the subject of future investigation.



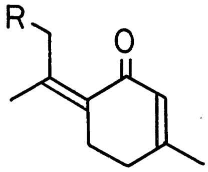
(IVa)

(XI)

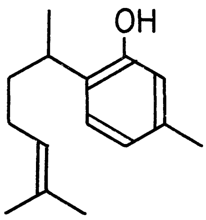
(XII) C$_7$-Me, C$_8$-H cis
(XIII) " " trans



(XV) R=$CH_2CH_2CMe_2Cl$
(XVIIa) R=$CH_2CH{=}CMe_2$
(XVIIb) R=$CH_2CH_2CMe{=}CH_2$



(XIV) R=$CH_2CH_2CMe_2Cl$
(XVIa) R=$CH_2CH{=}CMe_2$
(XVIb) R=$CH_2CH_2CMe{=}CH_2$



(XVIII)

Table 1[12].

	2-H	6-H	8-H	10-H	3-Me	7-Me	11-Me(s),=CH$_2$	
a XI	5.67, (m)				1.92, (bs)	1.83, (s)	1.57, (s)	
b XII	5.73, (q, 1.3)	2.73, (dd, 9.6, 6.0)	5.08, (bt, 7.5)		1.93, (bs)	1.56, (s)		
b XIII	5.77, (m)	3.16, (dd, 11.5, 6.0)	5.27, (bt, 6.5)		1.94, (bs)	1.53, (s)	1.55 (s)	
a XIV	5.77, (q, 1.3)				1.91, (dt, 1.3, 0.6)	1.84, (t, 0.8)	1.57 (s)	
a XV	5.77, (q, 1.3)				1.91, (dt, 1.3, 0.6)	2.02, (t, 1.1)	1.55 (s)	
b XVIa	5.74, (q, 1.4)			5.09, (bt, 7.0)	1.91, (bs)	1.81, (bs)	1.64 (bs)	
b XVIb	5.74, (q, 1.3)				1.91, (bs)	1.81, (bs)	4.61, (m)	1.72, (bs)
a XVIIa	5.77, (m)			5.07, (bt, 6.5)	1.91, (bs)	2.02, (bs)	1.60, (bs)	1.68, (bs)
a XVIII	6.51, (bs)	4-H, 6.65, (bd, 9.0) 5-H, 7.00, (d, 9.0)		5.15, (bt, 6.5)	2.27, (bs)	1.21 (d, 6.5)	1.54, (bs)	1.67, (bs)

a, measured with varian T-60 or A-60 and *b*, with varian HA-100.

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