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CYCLIZATION OF POLYENES XI[1]

SELECTIVE ACYLATION OF POLYENES ACCOMPANYING THE RING CLOSURE

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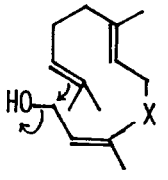
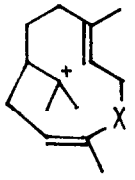
On the biogenetic type synthesis of polycyclic terpenoid from acyclic precursor, there are several reports[2] in which the initiation of ring closure is caused by i) protonation to the terminal double bond, or ii) opening of the terminal epoxide. However, quite few are achieved by iii) C-C bond formation of the terminal double bond with a carbonium ion. A macrocyclic intermediate (II) and a taxane skeleton (III) are the typical examples of iii type initiation which are considered to be derived from the corresponding precursors (I) in terpenoid biogenesis[3]. We are much intrigued to explore an approach of the selective C-C bond formation of polyene in connection with a program directed toward the biogenetic type synthesis of terpenoids.



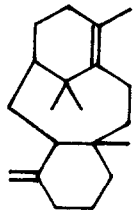
(I)

X = CH_2 (FARNESOL)

X = $CH_2CCH_3{=}CH(CH_2)_2$ (GERANYL GERANIOL)



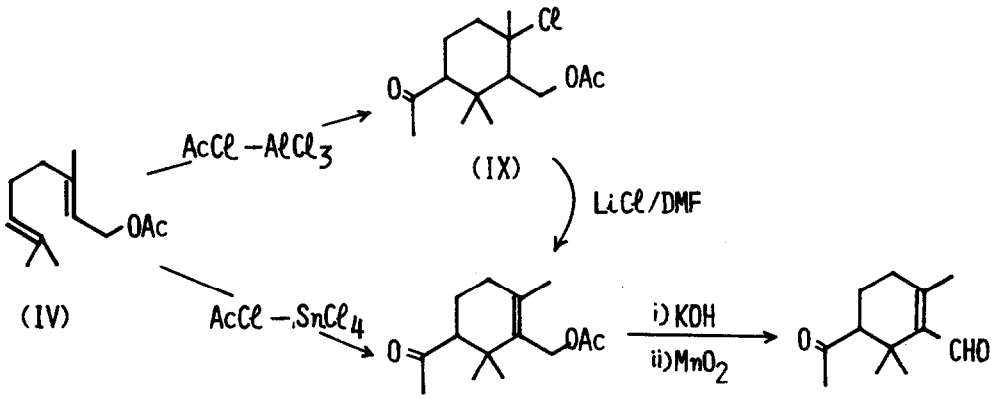
(II)



(III)

As a model experiment for achievement of this sort of C-C bond formation with concomitant ring closure[4], we undertook some preliminary experiments using

geranyl acetate (IV) and its analogues (V, VI, and VII) as polyenes, and acetyl, crotonyl, and 2,6-dimethyl-3-methoxybenzoyl(VIII) chlorides as acylating agents. It was found that the selective acylation had occurred in moderate yields when the polyenes were treated with $SnCl_4$ or $AlCl_3$ complex of these acyl chlorides under ice cooling and that the ring closure was accompanied as expected in the cases of polyenes, IV, V, and VI. The details are described in this communication.



Equimolar mixture of $AlCl_3$ complex of acetyl chloride and geranyl acetate was allowed to react in CH_2Cl_2 under ice cooling for 1 hr and an acylation product (IX) was isolated in 44% yield, while reaction of the $SnCl_4$ complex in CH_3NO_2 under the same conditions afforded the unsaturated product (X) in 31% yield after purification with column chromatography. The former product (IX) was quantitatively converted to the latter (X) when conducted with LiCl in DMF at 90° for 1 hr. The structure of these compounds was confirmed by the following evidence. In addition to the satisfactory physical data of X, i.e., IR 1740 and 1710 cm^{-1}; NMR 1.00 (s) and 1.10 (s) (two gem-methyl groups), 1.70, 2.00, and 2.13 (s, 3H each, methyls of double bond, acetyl and acetoxy groups), and 4.57 (s, 2H, $-\underline{CH}_2OAc$), the compound (X) was converted to the corresponding aldehyde (XI) by alkaline hydrolysis followed by MnO_2 oxidation. When X was submitted to deuterium exchange with D_2O-Na_2CO_3 in MeOH, four deuterium atoms were introduced to the α positions of ketone group. The position of deuterium atoms was determined by mass spectrum of X in which fragment ion corresponding

to $(M\text{-}COCH_3\text{-}HOAc)^+$ appeared as a prominent peak.

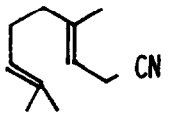
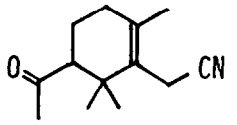
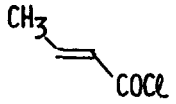
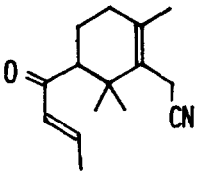
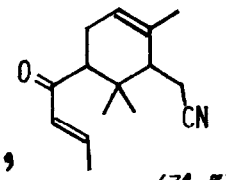
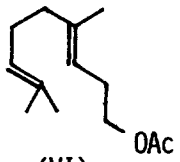
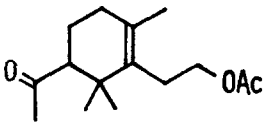
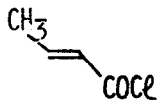
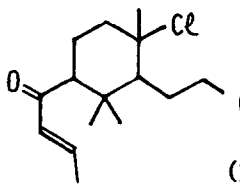
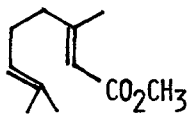
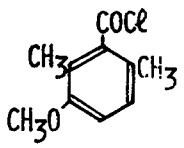
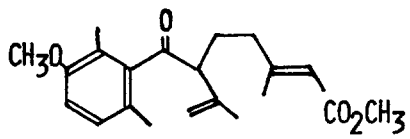
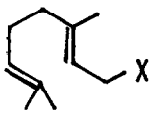
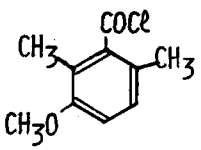
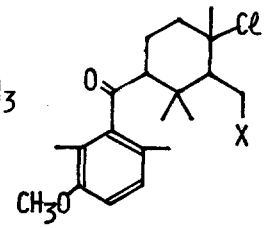
In order to find the generality of this reaction, several polyenes were treated with acyl chlorides under similar conditions to obtain the results shown in the table. It is generally accepted that, when $SnCl_4$ in CH_3NO_2 (method A) was used for the acylation, the unsaturated product is predominantly formed while the corresponding chlorinated compound is the major product when conducted with $AlCl_3$ in CH_2Cl_2 (method B). As an exceptional case, acylation of methyl geranate (VII) did not accompany with the ring closure.

For the construction of a taxane skeleton, the reaction was then extended to the 2,6-dimethyl-3-methoxybenzoyl chloride[6] (VIII) and the acylation reaction with simultaneous ring closure could be demonstrated to have the suitable compounds for this purpose in fairly good yields. The results described here encourage us to extend further approaches on the biogenetic type conversion of I to a macrocyclic compounds (II) as well as to achieve the synthesis of taxane skeleton (III) from the acylation products.

References

* To whom all correspondences should be addressed.

1. Part X of this series, A. Kumanireng, T. Kato, and Y. Kitahara, Chem. Letts., 1045 (1973)
2. For reviews of some extensive investigations see: D. Goldsmith, Forschr. Chem. Organ. Naturstoffe, 29, 363 (1972); W. S. Johnson, Accounts chem. Res., 1, 1 (1968); E. E. van Tamelen, ibid., 1, 111 (1968); T. Kato and Y. Kitahara, J. Syn. Org. Chem. (Japan), 28, 559 (1970)
3. For leading references, G. Rucker, Angew. Chem. Internat. Edit., 12, 793 (1973); R. McCrindle, and K. H. Overton, Adv. in Org. Chem., vol 5, 47 (1965)
4. Although Smit et al reported[5] the selective acylation of polyenes using $AgBF_4$ as catalyst, we could not obtain the same results as Smit et al by $AgBF_4$, maybe owing to the quality of $AgBF_4$ we used.
5. W. A. Smit, A. V. Semenovsky, V. F. Kucherov, T. N. Chernova, M. Z. Krimer, and O. V. Hubinskaya, Tetrahedron Letts., 3101(1971) and references therein.
6. The corresponding acid was easily obtained by NBS oxidation of 2,4-dimethyl-3-carboxycyclohex-2-ene-1-one.[7]
7. D. J. Goldsmith, and J. A. Hartman, J. Org. Chem., 29, 3520 (1964)
8. The ratio of tetra and trisubstituted isomers is 3:2.

Polyenes	Acyl Chlorides	Products (yield)	Method
 (V)	CH_3COCl	 (57 %)	A
(V)		 ,  (71 %)[8]	A
 (VI)	CH_3COCl	 (30 %)	A
(VI)		 (20 %)	B
 (VII)	 (VIII)	 (55 %)	B
	 (VIII)	 (X = CN, 94 %) (X = OAc, 67 %) ($X = CH_2OAc$, 65 %)	B