CHEMISTRY LETTERS, pp. 1191-1192, 1976. Published by the Chemical Society of Japan

CYCLIZATION OF POLYENES XXI[1]. SYNTHESIS OF DL-INCENSOLE

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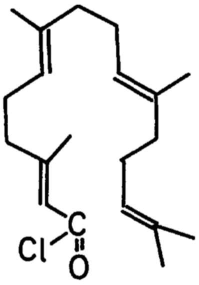
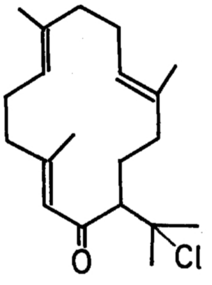
By treatment of dl-mukulol (III) with tetrabromocyclohexadienone (V, TBCO), bromo ether (VI) was obtained. The ether (VI) was converted to dl-incensole (IV) by the sequential reactions of isomerization with BF_3-etherate, replacement of bromine atom of VII with OAc group followed by reduction with $LiAlH_4$.

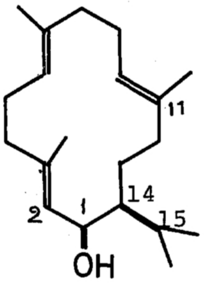
Previously we reported the biogenetic type cyclization of geranyl geranic acid chloride (I) into macrocyclic chloroketone (II) and also transformation of the latter to dl-mukulol (III)[2]. This paper concerns with the synthesis of dl-incensole (IV) and two related diterpenoids, incensole oxide and isoincensole oxide (IX).



(I)



(II)



(III)

Oxygen bridging between C_1 and C_{11} of dl-mukulol (III) was successfully performed in 54% yield when III was treated with recently developed etherification reagent, tetrabromocyclohexadienone (V, TBCO)[3] in CH_2Cl_2, giving bromo ether (VI), mp 91-92°. PMR, 5.21 (C_2-H, d, 11 Hz), 4.98 (C_6-H, m), 4.26 (C_{10}-, and C_1-protons), 1.60 and 1.63 (C_3- and C_7-methyls), 1.13 (C_{11}-Me), and 0.86 (CH$\underline{Me}_2$) ppm. Dreiding model shows that the distance between C_1-OH and C_6=C_7 of III is too far to make ether bonding, thus resulting the predominant formation of VI.

During our study on the synthesis of dl-mukulol, we have observed that 14,15-dehydromukulol was easily dehydrated to give 1(14)-dehydronephthenol by contact with SiO_2[2]. This evidence suggests that the ether linkage might be cleaved at C_1-position under acidic conditions, resulting in the formation of 1(14),2(3)-conjugated diene moiety. As expected, treatment of VI with BF_3-etherate (-15°, 1 hr) and subsequent separation of the reaction mixture with SiO_2 column chromatography afforded the isomeric bromo ether (VII), oil, in 46% yield, presumably formed from the diene intermediate. PMR (VII), 5.05 (bs, C=CH x 2), 3.78 (C$\underline{H}$Br, d, 10 Hz), 1.51 and 1.63

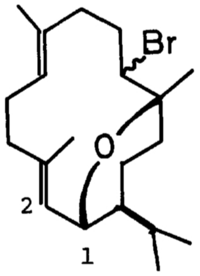
(C=CMe), 1.25 (-OCMe), and 0.91 (CHMe$_2$) ppm.

Replacement of Br atom of VII with OAc group (AgOAc in AcOH, 55°, 2 hrs) followed by reduction with LiAlH$_4$ afforded the corresponding hydroxy ether (IV) in 70% yield from VII. PMR spectrum of IV was identical with that of natural incensole reported by Nicoletti et al[4]. PMR, Acetate (VIII), 5.12 (C=CH x 2, bs), 4.82 (CHOAc, d, 9 Hz), 2.00 (OAc), 1.55 and 1.56 (C=CMe x 2), 1.07 (OCMe), and 0.91 (CHMe$_2$) ppm. dl-Incensole (IV), 5.08 (C=CH x 2, bs), 3.18 (CHOH, d, 9 Hz), 1.50 and 1.60 (C=CMe x 2), 1.03 (OCMe) and 0.91 (CHMe$_2$) ppm[5].

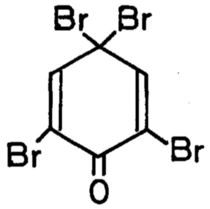
Since each double bond of our starting material (III) has trans geometry, both of the double bonds in dl-incensole (IV) should be trans although Nicoletti and coworkers have described the 2,3-double bond as cis without clarifying any experimental details[6]. Incensole oxide (2,3-oxidoincensole)[7] and isoincensole oxide (IX)[8] have already been derived from natural incensole and hence our present work means the formal synthesis of these oxygenated cembrene type diterpenes, too[9].

References

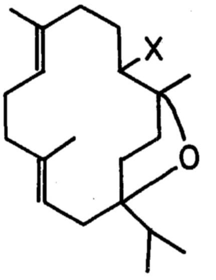
1. Part XX of this series, T. Kato, I. Ichinose, T. Hosogai, and Y. Kitahara, preceding paper.
2. T. Kato, T. Kobayashi, and Y. Kitahara, Tetrahedron Lett., 3299 (1975).
3. Selective bromo etherification of polyene alcohols is published in the preceding paper.
4. S. Corsano and R. Nicoletti, Tetrahedron, 23, 1977 (1967).
5. PMR were measured with PMX-60 in CCl$_4$ with TMS as an internal standard.
6. Trans geometry of two double bonds in dl-incensole was confirmed by detailed comparison of CMR spectra. Details will be published elsewhere.
7. R. Nicoletti and M. L. Forcellese, Tetrahedron, 24, 6519 (1968).
8. M. L. Forcellese, R. Nicoletti, and C. Santarelli, Tetrahedron Lett., 3783 (1973).
9. Numbering is conventionally based on that of mukulol. All the compounds described herein have satisfactory analytical and/or mass spectral data.



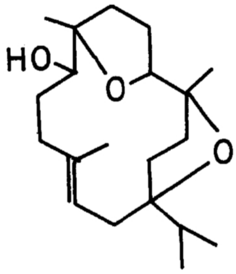
(VI)



(V)



(IV) X=OH
(VII) X=Br
(VIII) X=OAc



(IX)

(Received September 7, 1976)