PARTIAL SYNTHESIS OF DIHYDROISOTHYSANOLACTONE, AND ^{13}C-NMR STUDY OF THYSANOLACTONE

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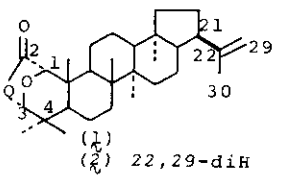
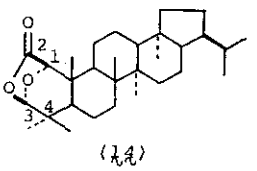
Abstract – Dihydroisothysanolactone (14) which has the diastereomeric construction of the bridged ring system of the A ring of the novel triterpene, thysanolactone (1), has been partially synthesized from an easily available triterpene, hydroxyhopanone (3). ^{13}C-NMR assignment of all carbons of thysanolactone (1) has been made by the help of the reference compounds including the above newly prepared unnatural congener.

The structure of thysanolactone (1) , a novel A-seco-moretane type triterpene found in a Ryukyu plant, Thysanospermum diffusum Champ. var. longitubum Ohwi, was clarified with chemical and X-ray structural analysis methods.[1] From the novelty of the A-ring part structure which has not been encountered in any structural type of triterpene, we have been working on the partial synthesis of this and the related compounds. Already partial syntheses of dihydrothysanolactone (2)[2] and thysanolactone (1)[3] have been reported. In this communication the partial synthesis of an iso-type compound which has the opposite stereochemical arrangement of the lactone ring is reported. Having this stereoisomer in our hands, unambiguous assignments of ^{13}C-NMR signals of thysanolactone (1) and the congeners have been made. These results are also reported.

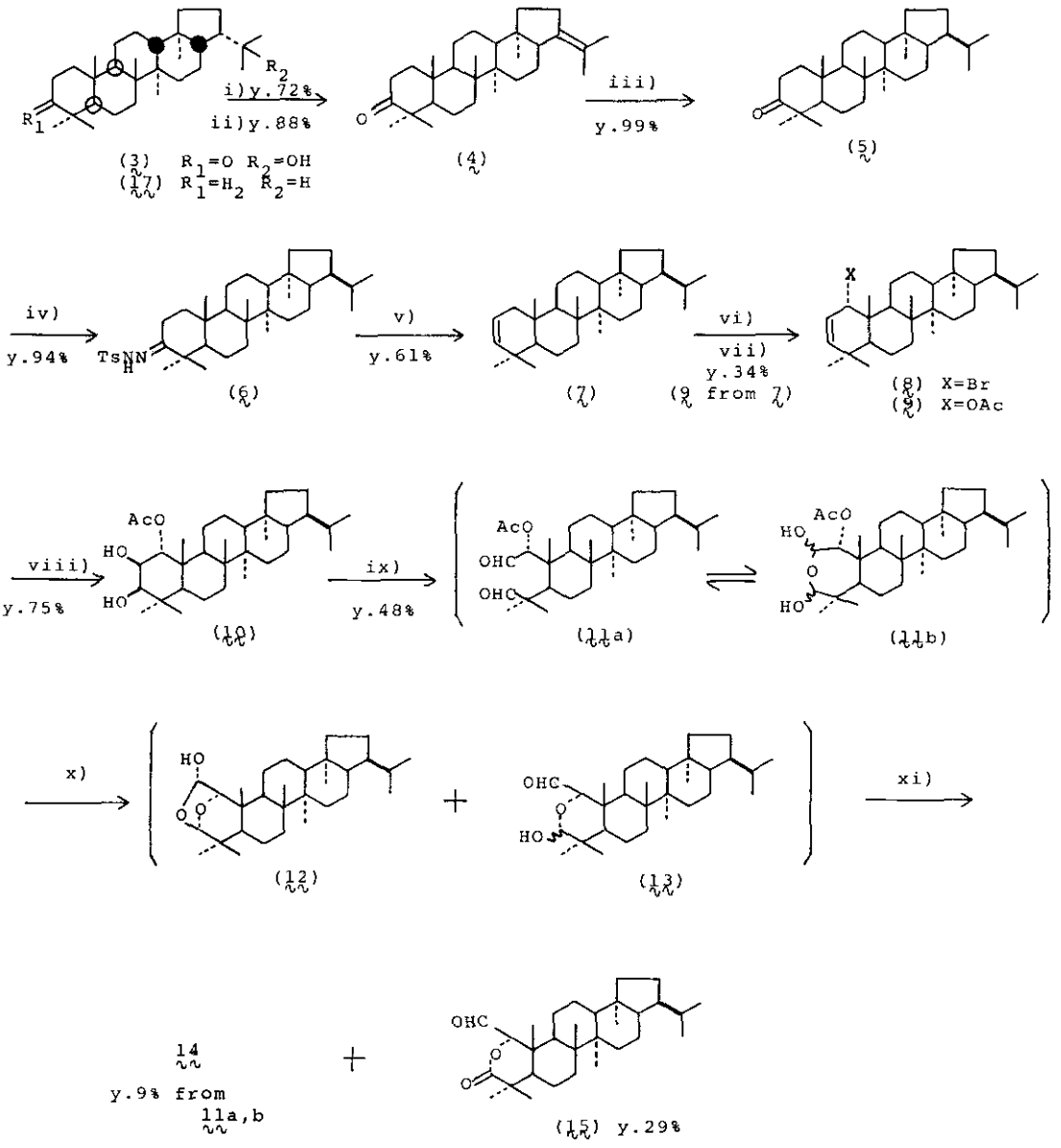


(1)
(2) 22,29-diH



(14)

Chart 1



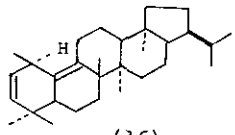
i)$POCl_3$,Py ii)p-TsOH,$CHCl_3$ iii)H_2,PtO_2,THF-AcOH iv)$TsNHNH_2$,BF_3-Et_2O,C_6H_6

v)LDA,THF vi)NBS,$(PhCOO)_2$,CCl_4 vii)AgOAc,AcOH viii)OsO_4,Py

ix)$Pb(OAc)_4$,C_6H_6 x)NaOMe,MeOH xi)PCC,CH_2Cl_2

Chart 2

The whole scheme of the partial synthesis of (14) is shown in Chart 2. Hydrocarbon (7) was prepared from hydroxyhopanone (3) in an essentially same manner as in the partial synthesis of dihydrothysanolactone (2).[2] In our former work, however, (7) was obtained and used for the subsequent steps as an epimeric mixture concerning with the stereochemistry at C-21. Now we isolated hopenone a ($\Delta^{21,22}$) (4) separated from the $\Delta^{22,29}$ isomer, hopenone b, and catalytically reduced it to moretanone (5), $C_{30}H_{50}O$, mp 175-179°C, $[\alpha]_D$ +35° (dioxane).[4] Tosylhydrazone (6), mp 210°C, $[\alpha]_D$ +35.9° ($CHCl_3$), was treated with excess of LDA (12 eq) in THF to yield olefin (7), $C_{30}H_{50}$, mp 182-184°C, $[\alpha]_D$ +41.8° ($CHCl_3$). Allylic bromination of the above olefin (7) with NBS gave 1α-bromo derivative (8) as an unstable amorphous solid, which was then treated with silver acetate without further purification to afford allylic acetate (9), $C_{32}H_{52}O_2$, mp 133-134°C, (δ 4.80(dd, J=3.5,2.0 Hz, H-1), δ 5.60(d, J=3.5 Hz, H-2), δ 5.59(d, J=2.0 Hz, H-3), δ 2.04(3H,s,1-OAc)). The α-configuration of the acetoxyl group at C-1 was not fully evidenced by the spectral data at this stage but the following series of reactions which lead to the objective compound (14) clearly indicated the correctness of this stereochemical assignment. Besides the allylic acetate (9), a hydrocarbon (16), $C_{30}H_{50}$, mp 140-141°C, was obtained as a by-product in the above reaction. The ^{13}C-NMR spectrum of (16) showed four olefinic carbons in which two are singlets (δ 133.8 and δ 134.2) and the other two are doublets (δ 130.6 and δ 136.0). A newly formed doublet methyl proton signal was observed at δ 1.03. These and other evidences suggest the structure of (16) as shown. Allylic acetate (9) was then oxidized with OsO_4 in dry pyridine to give glycol (10), $C_{32}H_{54}O_4$, mp 234-236°C. The β-configuration of the glycol function in (10) was assigned by analogy to the results obtained in our previous works.[3]



(16)

Glycol cleavage was successfully carried out on compound (10) by use of lead tetraacetate. The ^{1}H-NMR spectrum of the resulting dialdehyde (11) demonstrated the co-existance of the aldehyde form (11a) (δ 9.69 (2- or 3-CHO), δ 9.63 (3- or 2-CHO) and δ 5.38 (H-1)) and acetal form (11b) (δ 5.38 (H-1), δ 5.15 (H-2), and δ 5.26 (H-3)) in a ratio of 2.5 : 1.

Treatment of the dialdehyde (11) with NaOMe afforded a mixture of two hemiacetals (12) and (13). Oxidation of the above mixture, without further purification, gave the objective compound (14) after chromatographical separation of the reaction mixture; (14), $C_{30}H_{48}O_3$, mp 203-204°C, $[\alpha]_D$ +114° ($CHCl_3$), mass spectrum

m/z 456 (M^+, 10%) and 191 (base peak), IR ν_{max}^{KBr} 1806 cm^{-1}, ^{1}H-NMR δ 4.20 (s, H-1) and δ 5.39 (s, H-3). The above spectral data definitely proved the structure of dihydroisothysanolactone (14) which has the reversed construction of the bridged ring system to that of dihydrothysanolactone (2). As an accompanying by-product lactone aldehyde (15) was obtained as an amorphous solid.

The ^{13}C-NMR spectra were measured for thysanolactone (1), dihydrothysanolactone (2), and isodihydrothysanolactone (14), and these data were compared with those reported for hopane (17)[5] and the closely related compounds.[6] The functionalized carbons of (1), (2) and (14) showed the expected shift values. Apart from these, C-5 and C-9 of (1) and (2) showed characteristic high field shifts evidently due to α-axially oriented lactone-forming bonds at C-1 and C-3. In (14) also high field shift was observed for C-5 but in a smaller extent. Almost no effect was observed for C-9. These findings will have a strong diagnostic value for elucidation of the structure of the thysanolactone type modified triterpenes.

	1	2	14	17[5]
1	78.7	78.8	77.6	40.2
2	172.2	172.2	172.5	18.6
3	110.9	110.9	110.7	42.0
4	36.4	36.4	36.7	33.0
5	41.1	41.2	46.4	56.0
6	17.6	17.7	17.7	18.6
7	32.5[a]	32.7[a]	32.6[a]	32.9[a]
8	40.0	40.0	39.0	41.6[b]
9	47.9	48.5	50.1	50.4
10	41.9	42.0	43.5	37.2
11	21.7[b]	21.7[b]	21.5[b]	20.8
12	23.2	23.1	23.5	23.8
13	48.5	48.7	48.6	49.2
14	42.8	42.8	42.9	41.8[b]
15	33.2[a]	33.3[a]	33.7[a]	33.5[a]
16	20.8[b]	21.5[b]	22.1[b]	22.5
17	53.8	53.2	53.2	54.5
18	44.2	44.9	44.5	44.2
19	40.1	39.9	39.7	41.5
20	27.3	22.7	22.7	27.5
21	47.5	45.5	45.5	47.8
22	148.1	28.9	28.7	31.9
23	24.3	24.4	28.8	33.2
24	19.4[c]	19.4	18.6	21.4
25	14.7[d]	14.8[c]	14.7[c]	15.6[c]
26	15.0[d]	15.1[c]	14.9[c]	16.4[c]
27	16.8[e]	16.9[d]	17.3[d]	16.5[c]
28	17.5[e]	17.5[d]	17.5[d]	22.7[d]
29	109.5	22.1	22.1	23.7[d]
30	19.7[c]	17.5[d]	17.8[d]	25.7[d]

Table 1 ^{13}C-NMR Chemical Shifts ($CDCl_3$)

a,b,c,d,e: Values with the same superscript may be interchanged in the vertical column.

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