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PARTIAL SYNTHESIS OF DIHYDROTHYSANOLACTONE

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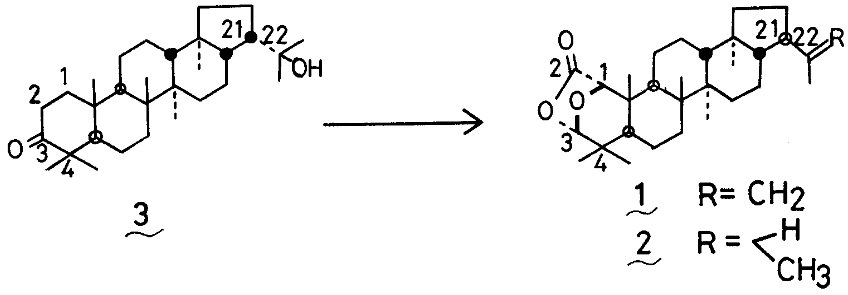
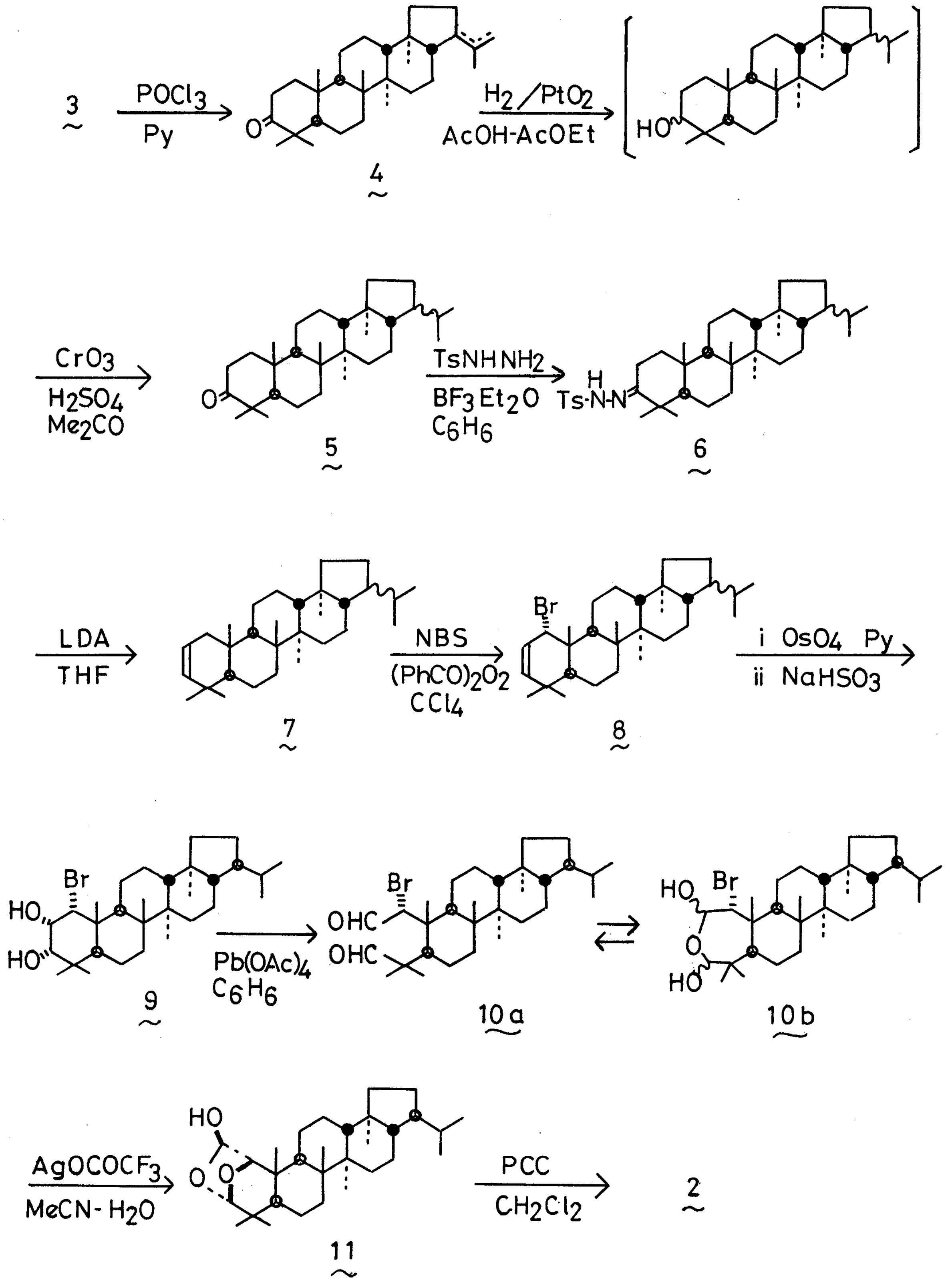
Dihydrothysanolactone (2), the dihydro derivative of a novel triterpene thysanolactone (1), was synthesized from an easily available pentacyclic triterpene, hydroxyhopanone (3).

KEYWORDS ——— triterpene; thysanolactone; dihydrothysanolactone; hydroxyhopanone; *Thysanospermum diffusum* Champ. var. *longitubum* Ohwi; Rubiaceae; chemical transformation; absolute configuration

Thysanolactone (1), the main constituent of the Rubiaceous plant, *Thysanospermum diffusum* Champ. var. *longitubum* Ohwi, was found to be a moretane type triterpene with a novel type A ring.[1] We were interested in the partial synthesis of 1 from hydroxyhopanone (3), which is a possible biogenetic precursor of 1 in the plant and is readily available from a commercial resin.[2] The transformation involves structural changes in three of the main features of the starting material: 1) construction of the A ring of 1 through the oxidative cleavage of the $C_{(2)}$-$C_{(3)}$ bond of the starting material , 2) inversion of the stereochemistry at $C_{(21)}$ and 3) modification of the side chain structure. Here we report the successful accomplishment of the first two requirements, which has enabled us to synthesize dihydrothysanolactone (2).



3 was dehydrated using $POCl_3$ in pyridine to give a mixture of two olefins (4a, 4b) (87% yield), which were then catalytically reduced. The resulting alcohol (88% yield), without further purification, was oxidized to ketone (5), $C_{30}H_{50}O$, mp 177-179°C, in 66% yield, which was found to be an epimeric mixture involving $C_{(21)}$. Tosylhydrazone (6), $C_{37}H_{58}N_2O_2S$, mp 185-192°C (dec.), pre-


3
POCl3
Py
O
4
H2/PtO2
AcOH-AcOEt
HO
CrO3
H2SO4
Me2CO
O
5
TsNHNH2
BF3Et2O
C6H6
H
Ts-N-N
6
LDA
THF
7
NBS
(PhCO)2O2
CCl4
Br
8
i OsO4 Py
ii NaHSO3
Br
HO
HO
9
Pb(OAc)4
C6H6
Br
OHC
OHC
10a
HO
Br
O
HO
10b
AgOCOCF3
MeCN-H2O
HO
O
O
11
PCC
CH2Cl2
2

pared by the action of tosylhydrazine and $BF_3 \cdot Et_2O$ on 5 in a yield of 88%, was treated with LDA in THF[3] to give the desired olefin (7) (86% yield), $C_{30}H_{50}$, mp 190-191°C. The ^{1}H-nuclear magnetic resonance (NMR) spectrum[5] indicated that this product was an epimeric mixture consisting of $C_{(21)}$-αH and $C_{(21)}$-βH derivatives in the approximate ratio of 3 : 1. Bromination at $C_{(1)}$ using NBS gave the allylic bromide (8) as an amorphous powder, δ 4.50 (1H,d, J=5.6Hz, $C_{(1)}$-H), δ 5.79 (1H,dd, J=5.6 and 10.6Hz, $C_{(2)}$-H) and δ 5.37 (1H,d, J=10.6Hz, $C_{(3)}$-H). The OsO_4 oxidation of 8 afforded glycol (9), $C_{30}H_{51}O_2Br$, mp 164-167°C (dec.), δ 4.45 (2H,s-like, $C_{(1)}$-H and $C_{(2)}$-H) and δ 3.84 (1H,br s, $C_{(3)}$-H), as a single isomer after purification with flash column chromatography[6] (SiO_2 230-400 Mesh, AcOEt-C_6H_6 3:17) (42% from 7). The correct stereochemistry at $C_{(21)}$ was demonstrated in the last stage of the conversion by the formation of 2 with the known stereochemistry. Cleavage of the glycol with lead tetraacetate in benzene gave dialdehyde (10) as an amorphous powder. The ^{1}H-NMR spectrum of 10 in $CDCl_3$ showed two aldehyde protons at δ 9.62 (1H,d, J=4Hz) and δ 9.60 (1H,s). On addition of D_2O to the sample solution of the NMR measurement, the intensities of the signals due to the aldehyde protons decreased, while new peaks of the acetal protons appeared at δ 5.10 (1H,d) and δ 5.68 (1H,s) suggesting the formation of an equilibrium between the aldehyde and acetal forms. The dialdehyde (10) was treated with silver trifluoroacetate (1.3 eq) in a mixture of CH_3CN and H_2O under reflux to give the oxide hemiacetal (11), mp 204.5-206°C, in a yield of 37% from 9. The ^{1}H-NMR spectrum revealed three protons on the oxygen-bearing carbons at δ 3.85 (1H,s, $C_{(1)}$-H), δ 5.05 (1H,s, $C_{(3)}$-H) and δ 5.45 (1H,d, J=9Hz, $C_{(2)}$-H; changing to singlet on addition of D_2O). The lack of the vicinal coupling between $C_{(1)}$-H and $C_{(2)}$-H in the ^{1}H-NMR spectrum of 11 indicated β-orientation of the hemiacetal hydroxyl group on $C_{(2)}$. Oxidation of 11 was made using pyridinium chlorochromate (PCC) in CH_2Cl_2 in a yield of 80%. The resulting lactone (2), $C_{30}H_{48}O_3$, mp 254-256°C, $[\alpha]_D$ -22.7° (c=0.2, $CHCl_3$), showed two singlet signals at δ 4.06 and δ 5.31 attributable to $C_{(1)}$-H and $C_{(3)}$-H respectively in the ^{1}H-NMR spectrum. The mixed fusion of this compound with dihydrothysanolactone (2) which had been obtained by hydrogenation of the natural thysanolactone (1)[1] proved their identity. Comparison of the ^{1}H- and ^{13}C-NMR, and infrared (IR) spectra together with optical rotations also proved that both compounds were identical. Thus the partial synthesis of 2 was completed. As an additional outcome of this work, the absolute configuration of thysanolactone (1), which had remained undetermined, was clarified as shown in the figure, since the absolute configuration of 3 has been known through the chemical correlation with a compound with the known absolute configuration.[4a-c]

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3) For a review of the Shapiro reaction, see R.H.Shapiro, "Organic Reactions" Vol. 23, ed. by W.G.Dauben, John Wiley and Sons, Inc., New York, 1976, pp 405 - 507.

4) Hydroxyhopanone (3) has been chemically correlated 4a,4b) with adiantol whose absolute configuration was determined by the X-ray crystallography. 4c)
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