Total Synthesis of Albolic Acid and Ceroplastol II, 5–8–5-Membered Tricyclic Insect Sesterterpenoids, *via* a Lactol-Regulated Silyloxy–Cope Rearrangement

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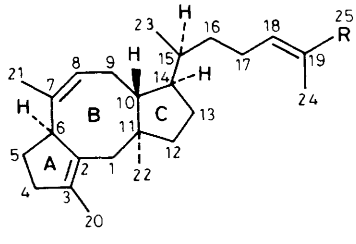
Optically active albolic acid and ceroplastol II, 5–8–5-membered tricyclic sesterterpenoids, were stereoselectively synthesised from two C_{10} synthons (iridoids) *via* $CrCl_2$-condensation, lactol-regulated silyloxy–Cope rearrangement with a normally disfavoured boat transition geometry, $TiCl_2$-ring closure, and C_5-homologation.

Albolic acid (**1**)[1] and ceroplastol II (**2**)[2] are sesterterpenoids isolated from the wax secretion of *Ceroplastes albolineatus*, a scale insect. The total syntheses of (**1**) and (**2**) are described herein.[3]

The carbon framework of (**1**) can be constructed by the $CrCl_2$-condensation of two iridoid synthons,[4—6] a Cope rearrangement, and intramolecular eight-membered ring formation; the required stereochemistry of (**1**) at C-6 and C-14 can be transferred from (3*R*)-irida-1,8-dien-7-al (**3**) and (3*S*,8*R*)-9-benzyloxy-7-chloro-1-iridene (**4**) to the expected condensate (**5**).†

However, the usual silyloxy–Cope rearrangement of compounds like (**5**) is known to give products having the opposite configuration at the C-11 methyl to that required, through a chair transition state.[4] Therefore, it is essential to perform the Cope rearrangement *via* the boat transition state, and this has been achieved by means of a 'lactol-regulated Cope rearrangement'[7] where a lactol formed in the 1,5-diene system precludes formation of the *Z*-type enol ether *via* the chair transition state.

Compound (**5**) was obtained from (**3**) and (**4**) in 88% yield by a $CrCl_2$-condensation in the presence of Pr^{i}OH, the yield of



(**1**) R = CO_2H
(**2**) R = CH_2OH

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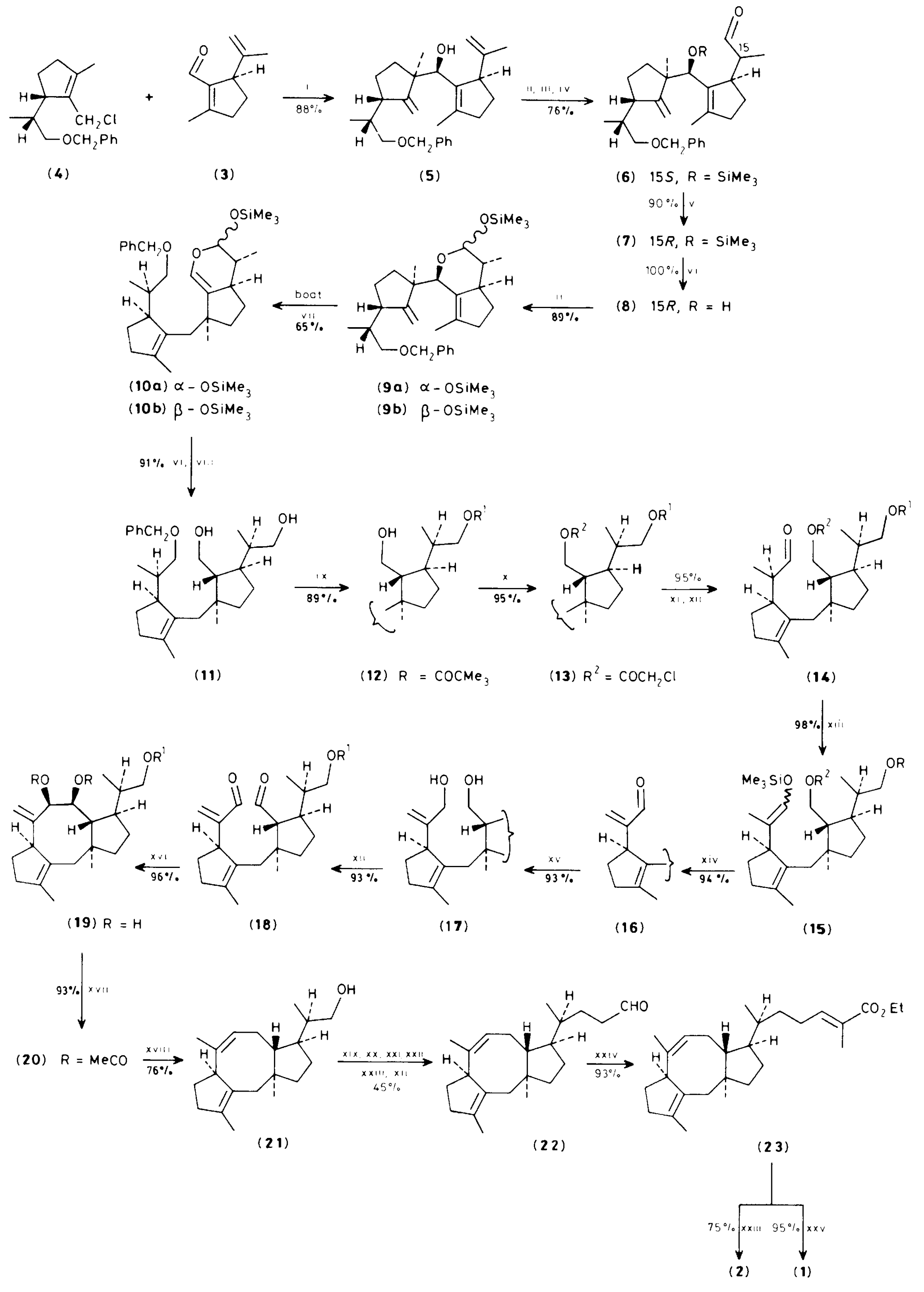
† The new compounds described in this paper showed satisfactory elemental analyses, together with structure-consistent spectroscopic data.



Scheme 1. *Reagents and conditions*: i, $CrCl_2$, tetrahydrofuran (THF), dimethylformamide (DMF), Pr^{i}OH; ii, Me_3SiCl/pyridine (Py); iii, $[Me_2CHCH(Me)]_2BH$, H_2O_2/OH^-; iv, pyridinium chlorochromate/CH_2Cl_2; v, KF–Florisil/MeOH, vi, pyridinium toluene-*p*-sulphonate /aq. THF; vii, 190 °C, C_7H_8; viii, $NaBH_4$/aq. $NaHCO_3$, MeOH; ix, Bu^{t}COCl, Py; x, $ClCH_2COCl$/Py; xi, H_2/Pd/C; xii, $(COCl)_2$/dimethyl sulphoxide (DMSO), Et_3N, CH_2Cl_2; xiii, $CF_3SO_3SiMe_3$, Et_3N, CH_2Cl_2; xiv, $Pd(OAc)_2$/MeCN; xv, $NaBH_4$, $CeCl_3$, MeOH; xvi, $TiCl_4$, Zn/THF; xvii, Ac_2O/Py; xviii, Li/liq. NH_3, EtOH; xix, tosyl chloride/Py; xx, $NaCH(CO_2Me)_2$/DMF; xxi, NaCN/DMSO; xxii, CH_2N_2; xxiii, lithium aluminium hydride/THF; xxiv, $Ph_3P{=}C(Me){-}CO_2Et$/benzene; xxv, 3 M NaOH/MeOH.

the epimeric alcohol was only 3%. Compound (**5**) was regio- and stereo-specifically converted to the silyloxy aldehyde (**6**). The unnatural configuration at C-15[8] was isomerised using KF-on-Florisil to give the aldehyde (**7**) which gave the hydroxy aldehyde (**8**) on further hydrolysis.

Upon heating at 190 °C (**9a**) and (**9b**), derived from (**8**), underwent a Cope rearrangement without cleavage of the lactol ring system to the thermolysates (**10a**) and (**10b**).‡ However, heating the lactol trimethyl silyl (TMS) ethers derived from (**6**) under similar conditions failed; this is thought to be due to a severe steric interaction between the A-ring and the axial C-15-Me. Hydrolysis and subsequent $NaBH_4$-reduction of (**10a**) and (**10b**) produced a single compound (**11**). The ^{13}C n.m.r. data of (**11**) were used to ascertain the correct *C*-ring configuration for (**1**) or (**2**) by comparison with related compounds.[5,7]

Thus, the Cope rearrangement of (**9**) has proceeded *via* a normally disfavoured boat transition geometry to give the desired product. See Scheme 1 for detailed synthesis leading to (**21**).[9—11]

The final step of the synthesis was a conventional C_5-elongation of the side chain; *i.e.*, (**21**) was converted to the aldehyde (**22**) and a Wittig reaction of (**22**) with ethyl (2-triphenylphosphoranylidene)propionate gave (*E*)-(**23**), which corresponds to ethyl albolate, as the major product (93% *vs.* 4% of *Z*-isomer); a portion of (**23**) was saponified to the acid (**1**), and the remainder was reduced to the alcohol (**2**). The ^1H n.m.r. spectra of (**1**) and (**2**) measured in CCl_4 were identical with those reported. In addition, the 3,5-dinitrobenzoate of (**2**) was identical with the sample prepared from the 3,5-dinitrobenzoate of ceroplastol I[12] in every respect.

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3 Major part of the content, the synthesis of (**2**), was presented at 54th National Meeting of Chem. Soc. of Jpn., Tokyo, April 1987, Abstr., No. 1IIIL 45.

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8 Hydroboration of irida-1,8-diene derivatives always occurs stereoselectively to give (3*S**,8*R**)-irid-1-en-9-ols without exception. See S. Yamasaki, T. Hatsui, and H. Takeshita, *Kyushu Daigaku Seisan Kagaku Kenkyusho Hokoku*, 1986, **81**, 7. The chemical shifts of Me adjacent to the α-carbon of the aldehydes, δ 13.0 for (**6**) and 7.4 for (**7**), parallel those for dehydroiridodial (δ 10.7) chrysomelidial (δ 7.8).[6]

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‡ (**10a**) gave another thermolysate in 32% yield which must be a chair transition product judging from the appearance of silylenol ether and an aldehydic proton signals. A 1,3-silyl migration probably occurred prior to Cope rearrangement.