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SYNTHETIC STUDIES ON TERPENIC COMPOUNDS—XI[1]

STEREOSPECIFIC TOTAL SYNTHESIS OF PORTULAL[2,3]

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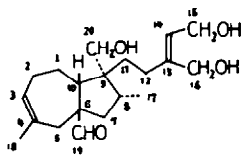
Abstract A stereospecific total synthesis of portulal **1** has been accomplished starting from the Diels–Alder adduct **2** from chloromethylmaleic anhydride and 1-vinylcyclohexene. Firstly **2** was converted by an efficient sequence of reactions to perhydroazulenoid lactone **5**, which possesses the correct relative configuration with respect to three chiral centers out of the four present in **1**. The fourth chiral center at C-6 was introduced stereospecifically together with the one-carbon substituent at C-4 by the ring formation between C-4 and C-6, and its cleavage to give an exomethylene lactone **35**. At this stage the stereochemical validity of the crucial intermediate **35** was confirmed by chemical correlation with the hydroxy lactone **37** which was derived from natural **1** through a systematic degradation. Then **35** was transformed to **37** and the synthesis continued further by using **37** as a relay compound to afford **1**.

Portulal **1** is a diterpene which was isolated from *Portulaca grandiflora* Hook firstly as an inhibitor to the adventitious root formation of *Raphanus* hypocotyl cuttings[5] and later found to show interesting plant growth regulating activities.[6,7] Its structure, disclosed by X-ray crystallographic analysis,[8] has a unique perhydroazulenoid skeleton, closely related to clerodane-type diterpenoid **3**. It is of biosynthetic interest that deep-seated skeletal rearrangement of labdadienol precursor is assumed in the formation of portulal **1**.[8] As a part of the general project toward total syntheses of clerodane diterpenoids,[9] we undertook the synthesis of this attractive target. The starting point was the Diels–Alder product **2** from 1-vinylcyclohexene and chloromethylmaleic anhydride, which had been obtained stereoselectively and proved to possess the correct relative configuration with respect to three chiral centers out of the four present in portulal **1**.[4,10] This report describes the successful stereospecific total synthesis of portulal **1** making use of **2**.



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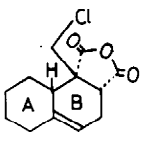

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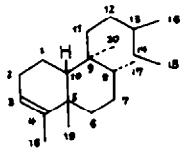

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The strategy we envisaged is outlined in Scheme 1. Firstly the conversion of the chloromethyl and the anhydride groupings in **2** to the spiro-γ-lactone ring at C-9[a] and the Me group at C-8[a] was planned. The formation of the stable spiro-γ-lactone ring would serve as protection of the C-20 OH group during the transformation in other parts of the molecule and at later stage of the synthesis its reaction with an appropriate four carbon anionic synthon to build up the side chain with concurrent liberation of the C-20 OH group. Subsequently the ring juncture in **4** can be rearranged to afford a perhydroazulenoid compound **5** and respective introduction of one-carbon substituents at C-6, stereospecific in this case, and at C-4, appended by the formation of Δ^3-double bond, would afford the key intermediate **6**. Finally, the construction of the side chain would complete the synthesis of portulal **1**.

RESULTS AND DISCUSSION

(i) *Synthesis of perhydroazulenoid lactone* **5**. For conversion of **2** to the first intermediate **4**, substitution of the Cl atom at C-11 by a cyanide anion was examined. Complete recovery of the starting material resulted even when the reactions were conducted in dimethylsulfoxide (DMSO) at elevated temp, the condition which allows cyanation of neopentyl halides.[11,12] Subsequently **2** was reduced with LAH at room temp smoothly to afford the diol **7**, m.p. 136°. Neither **7** nor the derived diacetate **8** underwent the cyanation reaction. The reason for the extreme resistance of **2**, **7** and **8** to the substitution reaction is interpreted in terms of the electrostatic repulsion and the severe steric hindrance due to the presence of the

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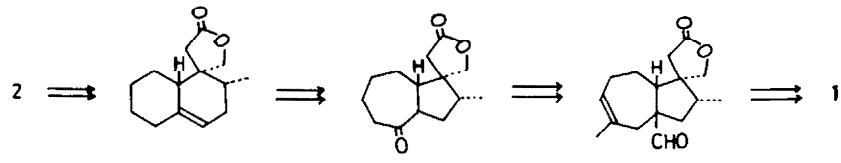
[a]Numbering corresponding to that of the target molecule is used throughout the discussion.



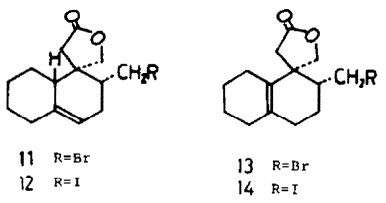
4 5 6

Scheme 1.

dipolar substituents, which would increase their effective bulk by solvation. In this connection, the closure of the 1,4-glycol system in 7 to a tetrahydrofuran could possibly mitigate this unfavorable situation, since by this measure the free rotations of the C-8 and C-9 hydroxymethyl groups would be inhibited and at the same time they would be transformed to a less polar ether grouping. On treatment of **7** with slight excess of one molar equiv of TsCl in pyridine, the cyclic ether **9** was obtained directly in quantitative yield. To our great delight the reaction of **9** with NaCN–NaI in DMSO at 120–125° for 7 hr did afford the crystalline nitrile **10**, m.p. 77.5°, in an excellent yield. This striking effect of the cyclic ether formation to S_N2 reactivity is noteworthy in view of the steric effect exerted by substituents.

Next the cleavage of ether ring, favorably with concomitant hydrolysis of the nitrile group, by acidic reagents was investigated. The experiments in this direction were fruitless due to migration of the double bond in **10** . For instance treatment of **10** with HBr–AcOH, HBr–H_2SO_4 or HI-AcOH did not yield the desired γ-lactones **11** or **12**. Instead the products were the γ-lactones **13** or **14**, which formed with concurrent double bond migration to the more stable position in between ring junctions.[b] Accordingly we decided to precede the ether cleavage-nitrile hydrolysis reaction by the formation of the perhydroazulene ring system.

For this purpose the base-catalyzed rearrangement of the monotosylate **16** of 5β,6β-glycol **15** to the ketone **17** would be an expedient choice.[13] The *cis*-glycol **15** which has the secondary OH group in β-configuration preferred for the rearrangement, represents the product derived from the attack of the oxidizing reagent on **10** from a less-hindered side of the molecule. Moreover, the resulting ketonic group at C-5 in **17** would serve both for the introduction of the angular substituent and the manipulation of the functionalities in the cycloheptane ring. The treatment of **10** with OsO_4 afforded stereospecifically the *cis*-glycol **15** in 84% yield. In the NMR spectrum of **15** the signal due to the cyanomethylene protons appears at the field lower by 0.30 ppm, compared with that of **10**, showing the OH groups in **15** have been introduced from the β-side as expected and the tertiary OH group at C-5 is disposed in 1,3-diaxial relationship to the cyanomethylene group.[4] In consonance with equatorial conformation of the secondary OH group at C-6, the resonance due to C-6 proton appears as a doublet of doublets with coupling constants of 6 and 12 Hz. The inspection of Dreiding models reveals that a non-steroidal conformation is preferred in **15**, since a severe steric interaction would exist between C-2 and C-11 methylene groups in the steroidal conformation.[4] Moreover the B ring is considerably twisted to accommodate the fusion of the tetrahydrofuran ring. Approximate dihedral angles of $H_{6\alpha}$–$H_{7\alpha}$ and $H_{6\alpha}$–$H_{7\beta}$ are 60° and 180°, respectively. For the conversion of **10** to **15**, the use of reagents other than OsO_4 was also investigated for economical reasons. $KMnO_4$ oxidation was a method of choice and produced **15** in yields up to 70% (with 1.4 equiv $KMnO_4$ and 1.15 equiv NaOH in aq t-BuOH or aq pyridine, and the reaction at −8° for a few min). Tosylation of **15** produced the monotosylate **16**, m.p. 181°. Upon treatment of **16** with t-BuOK, the rearrangement occurred smoothly to furnish the perhydroazulene ketone **17**, ν_{max} 1700 cm^{-1} in a high yield.



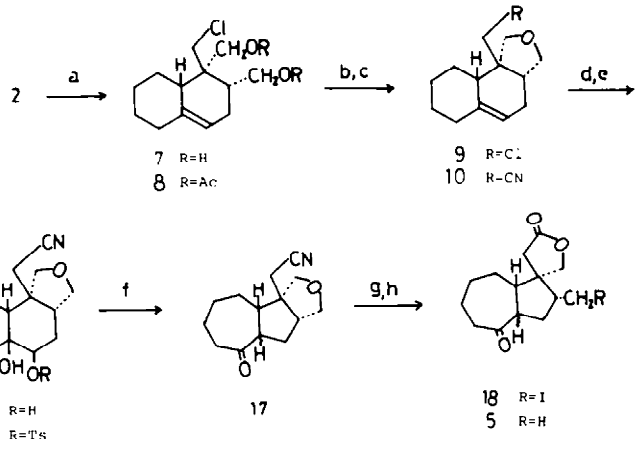
11 R=Br
12 R=I

13 R=Br
14 R=I

The concurrent hydrolysis of the nitrile group and cleavage of the ether ring in **17** was performed via HI-red phosphorus and the reaction at 125–130° afforded the γ-lactone iodide **18** in an excellent yield. Reduction of **18** with Zn–AcOH resulted in the formation of the perhydroazulene intermediate **5**, which represented one of the goals in our initial plan (Scheme 1). The compound **5** was obtained as crystals, m.p. 120°, and the spectroscopic data [ν_{max} 1780, 1700 cm^{-1}, δ 0.80 (3H, d, J = 7 Hz), 2.37 (2H, s), 4.06 ppm (2H, s)] corroborated its formulation. It is remarkable that the synthetic sequence from **2** to **5** is extremely efficient involving steps which proceed almost quantitatively except the permanganate oxidation of **10** and can be used without purification. In this way the conversion of **2** to **5** was achieved in an overall yield exceeding 60%.

(ii) *Introduction of one-carbon substituents at C-6 and C-4: synthesis of exo-methylene lactone* **35.** With the key intermediate **5** in hand, we turned our attention to the construction of the fourth chiral center at C-6. For this aim a functionalized one-carbon substituent had to be introduced stereospecifically at the angular position. Our initial tactics for this problem were the carbene addition to the enol acetate or the enol ether derived from the ketone **5**, followed by cleavage of the cyclopropane ring[14–16] and standard enol alkylation

[b]For the details of the investigation in this line, cf. K. M., D. Sc. dissertation, Osaka City University (1973).



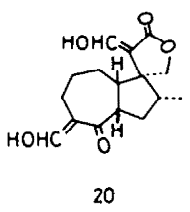
Scheme 2. (a) $LiAlH_4$ (92%), (b) TsCl-pyridine (100%), (c) NaCN-NaI (94%), (d) $KMnO_4$ (70%), (e) TsCl-pyridine (95%), (f) *t*-BuOK-*t*-BuOH (100%), (g) HI-P (94%), (h) Zn-AcOH (100%).

of **5** after blocking of the methylene group at C-4. Both reactions failed due to the obstruction of the reagent attacks from less-hindered convex side (β) by the carboxymethylene groups of the lactone rings in the derivatives concerned. To avoid this steric hindrance, attention was directed to intramolecular methods[17] of alkylation. The process involving the stereospecific introduction of a substituent at C-4β, cyclization to C-6 and subsequent ring cleavage resulted in the introduction of a functionalized one-carbon substituent at C-6β and also the attachment of a one-carbon substituent at C-4. Treatment of perhydroazulenoid ketone **5** with HCO_2Et and MeONa in a mixture of dimethoxyethane (DME) and benzene (3:2) produced the formyl derivative **19**, whereas the reaction of longer time in benzene afforded a mixture of **19** and bis-formylated **20**. The compound **19** was subjected to Michael addition with acrylaldehyde. Treatment of the alkylated product **21** with 10% HCl–EtOH resulted in concomitant deformylation and aldol cyclization, and the tricyclic ketol **22** was obtained in an excellent yield. The inspection of the NMR spectrum indicated that the product **22** represented a single isomer with respect to both configurations of the newly formed ring and the OH group. Moreover the signal due to the proton attached to the C atom bearing the OH group was axial and, namely *exo*-configuration. This result is in conformity with the prediction based on the consideration of the stereochemical requirement in the transition state of addition reaction to a CO group.[18] The required geometry[19] would be more fully satisfied in the transition state leading to the *exo*-product.[c] Since **22a** is very liable to undergo retroaldol reaction by both acid and base, the keto group in **22** was reduced to a methylene before the stereochemistry of the newly formed ring in **22** was examined and subsequent chemical manipulation of the ring C started. After protection of the OH group in **22a** by acetylation, which was successful through the use of isopropenyl acetate and catalytic amount of anhyd TsOH, the derived acetate 23[d] was exposed to the action of 1,2-ethanedithiol and BF_3-etherate. Although the reaction was very sluggish, reflecting the extremely hindered nature of the keto group, the thioketal **24** was obtained in 67% yield by keeping the mixture for several days and recycling the recovered starting material. Treatment of the thioketal **24** with Raney Ni yielded the reduced product **25**.[e] The alkaline hydrolysis of **25** afforded the corresponding tricyclic alcohol **26a**. When the thioketalization was conducted directly with the alcohol **22a** without protection, the ring cleavage product **27** formed in a considerable amount in addition to the monothioketal **28b**. Interestingly the hydrogenation of the latter product **28b** produced an alcohol **26b** different from the tricyclic alcohol **26a** obtained above. Since on oxidation with Jones' reagent both alcohols **26a** and **26b** afforded the same ketone **29**, it was concluded that they are epimers with respect to the configuration of the OH groups. In consonance is the fact that the NMR resonances of the protons attached to the OH-bearing carbon appear as a narrow multiplet ($W_{1/2}$ = 6 Hz) in **26a** and a broad multiplet ($W_{1/2}$ = 20 Hz) in **26b**, indicating the *exo*- and *endo*-configuration of the OH groups respectively. This result means that the configuration of the OH group is inverted during the thioketalization of the alcohol **22a**. Probably the *exo*-alcohol thioketal **28a** is destabilized by the severe electrostatic repulsion existing between 1,3-diaxially standing OH group and the S atom of the

[c]In spite of this propensity, the ring closure leading to the *endo*-alcohol seems to be also possible, *cf* footnote *d*.

[d]The NMR spectrum of the crude product exhibited additional signals at δ 0.97 (d, J = 6 Hz) and 4.88 ppm (m, $W_{1/2}$ = 18 Hz), indicating the contamination of the epimer **23b** (7:4 ratio as estimated from the integral). This fact shows that in the reaction condition above the epimerization of the *exo*-axial alcohol **22a** to the *endo*-equatorial alcohol **22b** is possible to some degree through ring opening and reclosing, and the thermodynamically more stable **23b** forms.

[e]In the NMR spectrum the signal due to the proton attached to the acetoxyl group appeared as a broad multiplet with $W_{1/2}$ = 18 Hz. This fact suggests that in the acetate **24** the conformation of the ring C changes to a boat form, owing to the increased nonbonded interaction of the acetoxyl group with two 1,3-diaxially standing hydrogens. It is interesting that in the free alcohol **26a** the conformation of ring C is chair ($W_{1/2}$ of the signal due to the proton attached to the OH-bearing carbon is 6 Hz), indicating the decreased steric requirement.



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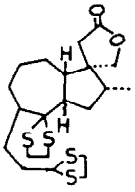

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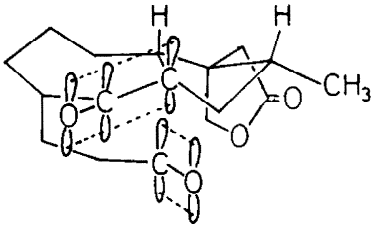
ethylenethioketal group and epimerizes to the *endo*-alcohol thioketal **28b** through ring opening and reclosing process despite that the latter reaction would be kinetically unfavorable. In order to confirm the stereochemical problems associated in the ring C conformation of **22**, lanthanide induced shift (LIS) in the NMR spectra of **26a** and **26b** was investigated (see Experimental). Although the tendency in the shifts of signals due to the carboxy- and hydroxy-methylene protons reverts from **26a** to **26b**, a common feature is that, as compared with these shifts, much smaller LIS values are observed for the secondary Me protons. A large shift observed in the hydroxymethylene signal of the lactone ring may be interpreted solely on the assumption that the lanthanide atoms coordinate to the lactone function in considerable degree other than to the OH group and cause much influence on the shift of the proton signals due to both methylene groups of the lactone ring. The effect of the lanthanide atom coordinating to the OH group would be naturally larger in the *endo*-alcohol **26b** than in the *exo*-alcohol **26a**. In conclusion the relative indifference of the secondary Me shift to the addition of lanthanide reagent provides the evidence for β-configuration of the ring C. The ring formation in this direction to yield **22** is reasonably interpreted also on mechanistic grounds. Michael reaction of **5** would afford the products alkylated from both α- and β-sides, which are in equilibrium in the reaction condition. However the transition state for the cyclization of α-alkylated product (like **30**) would be unfavored due to the severe steric interaction between the aldehyde group and the hydroxymethylene group of the lactone ring and thus only the cyclized product with β-configuration would be obtained.

The next step in the synthesis was the rupture of the ring C to yield the product with the substituents at C-4 and C-6. Formylation of the tricyclic ketone **29** followed by the treatment with H_2O_2 resulted in a poor yield of the dicarboxylic acid **32**. After conversion to the enol acetate **31**, its oxidative cleavage under several conditions was investigated including ozonolysis and Lemieux-von Rudloff[20] reaction, and the best result was obtained by the method shown in the Scheme 3. The dicarboxylic acid **32**, thus obtained was converted to the dimethyl ester **33**, which was partially hydrolyzed to give the half ester **34**. The decarboxylation of **34** by Kochi's procedure[21]



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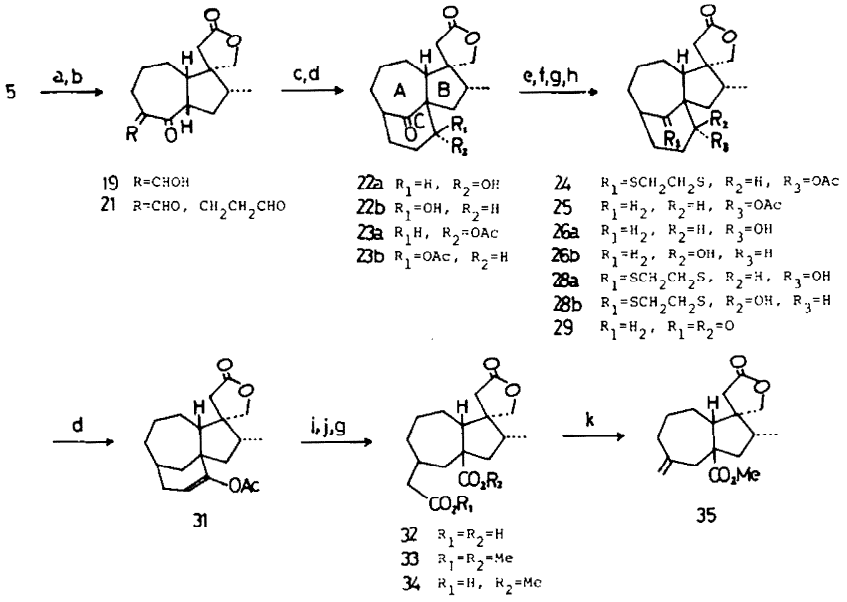
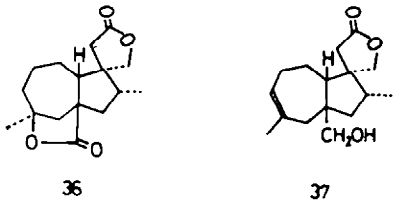


Scheme 3. (a) HCO_2Et-MeONa, (b) CH_2=CHCHO-Et_3N, (c) 10% HCl-EtOH, (d) CH_2=C(OAc)Me—TsOH, (e) CH_2SH-BF_3·Et_2O, CH_2SH (f) Raney Ni, (g) NaOH MeOH, (h) CrO_3-H_2SO_4-acetone, (i) RuO_2-$NaIO_4$, (j) CH_2N_2 (k) $Pb(OAc)_4$ $Cu(OAc)_2$-pyridine-benzene.



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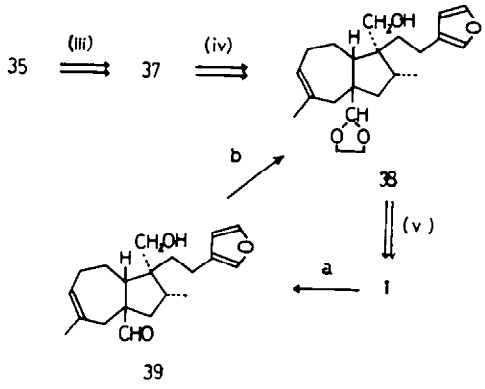
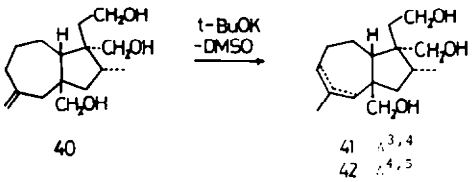


Scheme 4. (a) DDQ-*t*-BuOH, (b) $\begin{matrix}CH_2OH\\CH_2OH\end{matrix}$—TsOH.

proceeded smoothly and thus the synthesis of the crucial intermediate **35**, in which the carbon skeleton of portulal **1** had been completed except the four C atoms in the side chain and the configuration of the four adjacent chiral centers at C-8, C-9, C-10 and C-6 had been secured stereospecifically, was achieved, although the stereochemical validity should be confirmed ultimately. This has been done by chemical correlation. Upon acidic treatment (6N H_2SO_4–EtOH, reflux) the exomethylene compound **35** afforded the crystalline dilactone **36**. The structure of **36** was substantiated by the presence of IR peaks at 1780 and 1760 cm^{-1}, and the appearance of the Me singlet at δ 1.44 ppm in the NMR spectrum. On the other hand the hydroxy lactone **37** derived from natural portulal **1** by stepwise degradation[2b,22] was oxidized with Jones' reagent and then subjected to the same acid treatment as above. The product proved to be identical with the synthetic dilactone **36** with respect to tlc, IR and NMR comparison, although the dilactone **36** obtained from the natural compound shows a higher mp than the synthetic product.

(iii) *Conversion of exomethylene lactone* **35** *to hydroxy lactone* **37**. With the correct stereochemistry of the intermediate **35**, consideration was focussed on the conversion of **35** to portulal **1**. Major transformations to be performed were: (1) isomerization of the *exo*-double bond to the $\Delta^{3,4}$-position, (2) amendment of the angular carbomethoxy function to an aldehyde group and (3) construction of the side chain by the addition of a four-carbon unit. For the achievement of these tasks we (1) used the hydroxy lactone **37**, obtained by the degradation of portulal **1**, as a relay compound and (2) utilized a β-furyl group as the four-carbon synthon. A β-furan compound of type **38** turned out to be the key intermediate in the conversion of the hydroxy lactone **37** to portulal **1**. Therefore the derivation of **38** from natural portulal was also investigated. Of the oxidative methods[23] tried, treatment with 2,3-dichloro-5,6-dicyano-benzoquinone (DDQ) in t-BuOH was found to be most satisfactory. Acetalization of the product **39** afforded **38** in 67% overall yield. Thus our synthetic performance henceforth could be divided into three stages (iii–v) shown in Scheme 4.

Having set up the hydroxy lactone **37** as a goal, this stage of the synthesis entailed two transformations—namely the regioselective isomerization of the *exo*-double bond to the $\Delta^{3,4}$ position and the selective reduction of the angular carbomethoxy group to an OH group. The realization of these processes met with difficulties for several unexpected reasons and needed additional measures for their circumvention. Attempts for the isomerization of the double bond[24] in **35** failed to reveal anything of promise since treatment of **35** with t-BuOK–t-BuOH, $LiNH(CH_2)NH_2$, [25] I_2–benzene[26] or NBS–CCl_4, then Zn–AcOH[27] all led to the formation of complex mixtures. Their NMR inspection revealed weakening or disappearance of the signals due to the Me protons of the ester group and the olefinic proton, which suggested propensity of the interaction between both groups. The feasibility of the isomerization process without this interference was demonstrated when the triol **40**, obtained by LAH reduction of **35** was treated with t-BuOK–DMSO to produce a mixture of the olefins **40**, **41** and **42** in a ratio of 2:7:1. Therefore our tactics changed to attain the selective reduction of the angular carbomethoxy group to a primary OH group first. After failure of the attempts in this direction,[28] the same tactics were pursued on the dicarboxylic acid **32**, the precursor of **35**. The acid-catalyzed esterification of **32** furnished smoothly the monoethyl ester **43**. The selective reduction of the carboxylic group in **43** with diborane[29] was not attained since the lactone ring was unusually vulnerable to the reagent. Next attempts were made to achieve the desired conversion via thiol ester **44**. Treatment of the acid chloride **45** with ethanethiol at the presence of pyridine failed to yield **44**, but the use of stronger bases; e.g. diisopropylethylamine effected nicely this conversion as that of the sterically hindered acid chloride like acetylpodocarpinoyl chloride to the corresponding thiol ester.[30] Reduction of the thiol ester **44** with Raney Ni (W-4) afforded the desired hydroxy ester **46** albeit in low yield (35% from **43**). Alkaline hydrolysis of **46** led to the unexpected formation of the 7-membered lactone **47**. The structure for **47** was sufficiently supported by spectroscopic evidences (*cf* Experimental). The NMR behavior of the signals due to the protons of both methylene group adjacent to the lactone carboxyl would be worthy to mention. At 25° the carboxymethylene and the hydroxymethylene signals appeared as a broad doublet at δ 2.61 ppm and as a collapsed AB quartet centered at δ 3.90 ppm respectively. When the

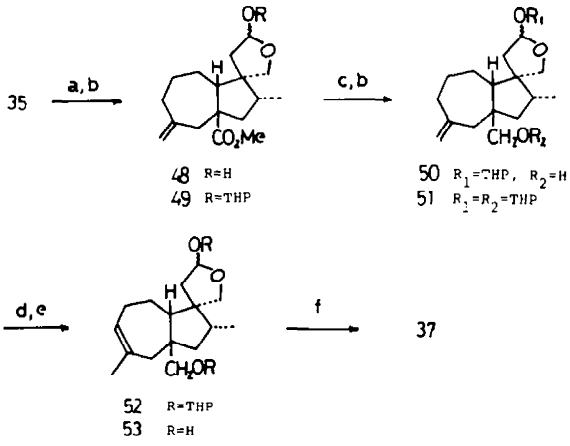


40 41 $\Delta^{3,4}$ 42 $\Delta^{4,5}$

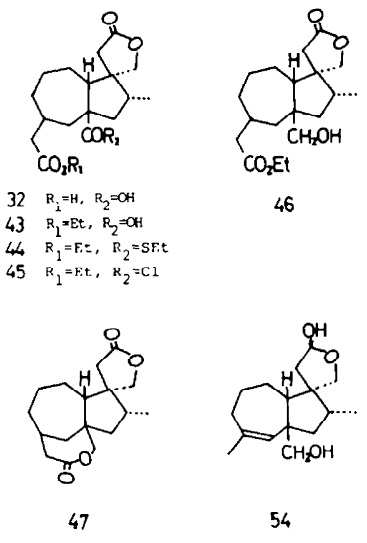
Scheme 5

temperature was raised to 50°, both signals sharpened to almost clear shapes. This observation indicates that at 20° the 7-membered lactone ring in **47** exists in two energetically alike conformation and they are flipping each other at a rate faster than the NMR scale. The unusual stability of the 7-membered ring in **47** is outstanding. When **47** was treated with isopropenyl acetate-TsOH in refluxing benzene or with abs EtOH-conc H_2SO_4 at room temp, the starting material was recovered unchanged. Thus **47** represents a very rare case where a 7-membered lactone ring is stabilized peculiarly by B-strain[31] or steric population control.[32]

The breakthough was attained by the introduction of tactics in which the reactive γ-lactone ring was protected during the transformations. The exom-ethylene lactone **35** was first selectively reduced to the acetal **48** in a good yield (83%) by a modified sodium bis[2-methoxy-ethoxy]aluminum hydride (SMEAH) reagent[33,f] and then **48** was converted to the tetra-hydropyranyl ether **49**. On reduction with LAH **49** afforded the alcohol **50**. Although treatment of **50** with t-BuOK-DMSO at 110° resulted in the formation of complex products, the same reaction of the corresponding dipyranyl ether **51** cleanly effected the isomerization of the double bond and, after removal of the protecting groups, the *endo*-olefin **53** was obtained without appreciable contamination of the undesired $\Delta^{4,5}$ isomer **54**. The exclusive isomerization of the *exo*-double bond to $\Delta^{3,4}$ position is remarkable, but was not unexpected. Thus when the preliminary experiment with the bispyranyl ether **52**, derived from natural **37**, was conducted under similar conditions **53** was obtained as the sole product. Therefore the $\Delta^{3,4}$ olefin was presumed to represent not only a kinetic but also a thermodynamic product. In conjunction with



Scheme 6. (a) SMEAH–EtOH, (b) DHP–TsOH, (c) $LiAlH_4$, (d) *t*-BuOK-DMSO, (e) HCl-acetone, (f) Ag_2O.



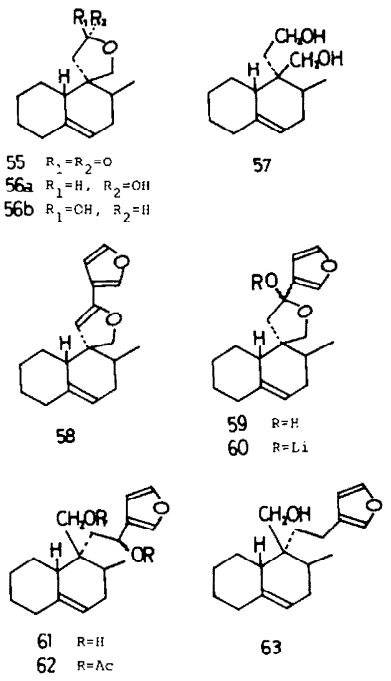
[f]We developed this reagent from economical reason. The use of diisobutylaluminum hydride (DIBAL), a standard reagent for the purpose may equally effective.

[g]The hemiacetal **56** was obtained as a mixture of the epimers **56a** and **56b** in a ratio of 11:5 as revealed by the integration of the NMR signals. The tentative assignment of the configuration to both epimers based on the inspection of the molecular models which indicated the energetical preference of the *exo*-structure **56a** relative to the *endo* **56b**.

the result obtained for the triol **40** (*vide ante*) the presence of a large angular substituent in **51** might serve for the prevention of the kinetic proton removal from the C-5 position. Oxidation of **53** with silver oxide completed the conversion in this section affording the relay compound **37**, which was identified as itself and the crystalline acetate (synthetic, m.p. 116–117°; natural, m.p. 144–145°) by comparison of tlc, IR and NMR data.

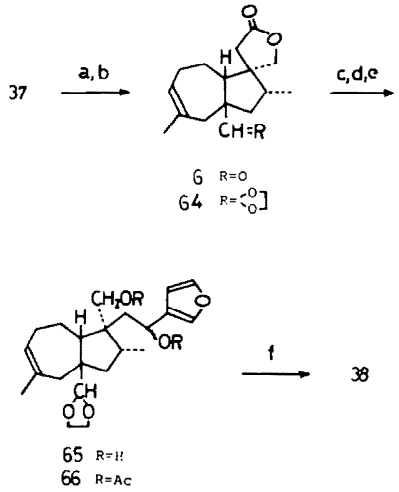
(iv) *Conversion of hydroxy lactone* **37** *to β-furyl compound* **38**. This stage concerned with the extension of the side chain in **37** by four C atoms for which a β-furyl group was selected. The feasibility of the side chain construction from **37** to **38** was first investigated on a model γ-lactone **55**.[4,34] Controlled reduction of **55** with SMEAH at lower temp afforded the hemiacetal **56**,[g] invariably accompanied by consider-able amounts of the diol **57**. However the application of modified SMEAH method[33] produced cleanly **56** in a yield as high as 96%. Curiously treatment of **56** with β-furyl lithium[35] resulted in mere recovery of the starting material, indicating extreme stability of the hemiacetal ring. Next when the γ-lactone **55** was allowed to react with β-furyl lithium, the product obtained after chromatographic purification was the unexpected vinyl ether **58**, which showed a UV maximum at 242 nm and a NMR signal due to a vinyl proton at δ 4.63 ppm. The compound **58** was presumed to form from the intermediary ketal **59**, which would be very liable to dehydrate and be transformed to **58** during work-up including silica gel chromatography. Compound **59** had the unusual propensity for dehydration. To prevent this, the product **60** of the reaction above was reduced *in situ* with SMEAH reagent and then the diol **61** thus obtained was acetylated to furnish, after chromatographic purification, the acetate **62** in 70% overall yield from **55**. Reductive removal of the acetoxyl group allylic to the furan ring in **62** was performed by treatment with Li-liquid NH_3 affording **63** in 46% yield.

In the application of this sequence, the hydroxy lactone **37** was first converted to the acetal **64** by the Collins oxidation to the aldehyde **6**, which represented a key intermediate in our initial plan (Scheme 1), and subsequent protection of the aldehyde group. The reaction of **64** with β-furyl lithium followed by

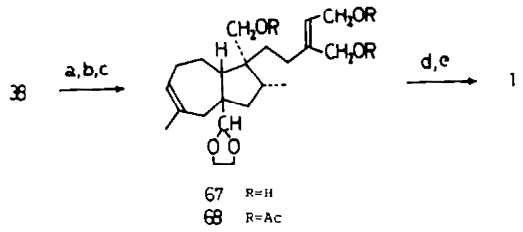


reduction and acetylation furnished smoothly the diacetate **66** in 67% overall yield, which was further converted to the furyl alcohol **38** by metal-NH_3 reduction (44% yield). This product **38** was identical with the compound derived from portulal **1** as mentioned (Scheme 4), confirming the realization of the conversion in this section.

(v) *Conversion of furyl alcohol* **38** *to portulal* **1**. Completion of portulal synthesis required the transformation of the β-furyl group in **38** to the *cis*-1,4-dihydroxy-2-buten-2-yl system and deacetalization. The former called for photosensitized oxygenation of the furan ring. The dye-sensitized photooxygenation of furans[36] is thought to proceed by way of a cyclic peroxide (an ozonide). Reduction with an appropriate



Scheme 7. (a) $CrO_3 \cdot 2C_5H_5N$–CH_2Cl_2, (b) CH_2OH–$TsOH_2$ / CH_2OH, (c)  , (d) SMEAH, (e) Ac_2O-pyridine, (f) Li-liquid NH_3.



Scheme 8. (a) O_2-Rose Bengal-MeOH-hν, (b) SMEAH, (c) Ac_2O-pyridine, (d) HCl-acetone, (e) NaOH–MeOH.

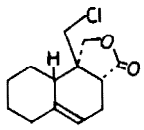
metal hydride should provide a way to *cis*-1,4-dihydroxy-2-butene systems. The furan compound **38** was photooxygenated in the presence of the sensitizer and the peroxide was reduced with SMEAH reagent. In this way portulal ethylene acetal **67** was obtained in 25% yield. The reason for the low yield would be in the most part ascribed to concomitant reduction of the double bond. Nevertheless the present conversion demonstrates photooxygenation of furan derivatives followed by metal hydride reduction could be used as a general entry to *cis*-1,4-dihydroxy-2-butenes. Deacetalization of **67** was not feasible directly since the doubly allylic alcohol system in the side chain was very sensitive to acid treatment. Accordingly **67** was first converted to the triacetate **68** and then subjected to the acid treatment. The triacetate **68** was finally hydrolyzed by alkali.

The product was indistinguishable from natural portulal **1** in every respect (mixed m.p., tlc, IR and NMR). Thus a formal total synthesis of portulal **1** has been accomplished.

EXPERIMENTAL[4]

All m.ps were uncorrected. Merck silica gel was used for column chromatography. IR spectra were recorded, except where noted, as films (liquid) or Nujol mulls (solid) on a JASCO IRA-1 spectrometer. NMR spectra were taken, unless otherwise stated, in $CDCl_3$ on a JEOL PS-100 or, in some cases a JEOL HL-60 spectrometer. Signals are recorded as δ values (ppm) using TMS as an internal standard; multiplicity abbreviations: s, singlet; d, doublet; t, triplet; m, multiplet; br, broad. Microanalyses were carried out at the Microanalytical Laboratory, Faculty of Science, Osaka City University.

LAH reduction of Diels–Alder adduct **2**. A soln of **2** (6.12 g, 24 mmol) in anhyd ether (100 ml) was added dropwise to a soln of LAH (2.8 g, 72 mmol) in anhyd ether (200 ml) and the mixture was stirred overnight at ambient temp. The excess reagent and the reaction complex were destroyed by cautious addition of H_2O and the resulting white ppt was filtered off by the aid of Celite. The ppt was washed thoroughly with ether. The combined two-layer soln was separated and the aq layer was extracted with ether (×2). The organic layers were washed with sat brine, dried over Na_2SO_4 and the solvent was evaporated to afford **7** as a crystalline product (5.4 g, 92% yield), m.p. 134.5 136° (from benzene): IR 3160, 1030, 815 cm^{-1}; NMR ($CDCl_3$–C_5D_5N) 3.48, 4.04 (2H, AB q, J = 11 Hz, $\underset{|}{C}CH_2OH$), 3.70 (2H, s, $-CH_2Cl$), 3.64 (1H, dd, J = 8, 9 Hz, $-\underset{|}{C}HCH_2OH$), 3.84 (1H, dd, J = 4, 8 Hz, $-\underset{|}{C}HCH_2OH$), 5.26 (1H, br s, $-\underset{|}{C}=C\underset{|}{H}CH_2-$), 5.88 (2H, s, OH ×2). (Found: C, 63.84; H, 8.72. $C_{13}H_{21}O_2Cl$ requires: C, 63.78; H, 8.66%). When the reduction was incomplete, the



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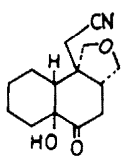

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lactone **69** was obtained as earlier chromatographic fractions: IR 1770 cm^{-1}; NMR 2.64 (1 H, dd, J = 6, 8 Hz, $-CH_2\underline{C}\underline{H}CO_2-$), 3.58, 3.68 (2 H, AB, q, J = 12 Hz, $-CH_2Cl$), 4.00, 4.28 (2 H, AB q, J = 10 Hz, $-CH_2OCO-$), 5.30 (1 H, br s, $\underline{C}=C\underline{H}CH_2-$).

Conversion of diol **7** *into cyclic ether* **9**. After a mixture of the diol **7** (13.6 g, 55.6 mmol), TsCl (13.7 g, 72 mmol, freshly recrystallized from benzene) and anhyd pyridine (125 ml) had been kept overnight at room temp, it was poured onto ice-water and extracted with ether. The extract was washed successively with 2 N HCl, sat $NaHCO_3$ and sat brine, and dried over Na_2SO_4. Evaporation of the solvent left **9** as a colorless viscous oil (12.9 g, 100% yield): IR 1060, 820 cm^{-1}; NMR 3.51, 3.84 (2 H, AB q, J = 9 Hz), $-\underline{C}CH_2O-$), 3.56 (1 H, dd, J = 2, 8 Hz, $-\underline{C}H\underline{C}H_\alpha\underline{H}_\beta O-$), 3.65 (2 H, s, $-CH_2Cl$), 4.03 (1 H, dd, J = 4, 8 Hz, $-\underline{C}H\underline{C}\underline{H}_\alpha H_\beta O-$), 5.36 (1 H, m, $-\underline{C}=C\underline{H}CH_2-$).

Conversion of cyclic ether **9** *into nitrile* **10**. A mixture of **9** (1.4 g, 6.2 mmol), NaCN (dried *in vacuo*, 3.04 g, 62 mmol), NaI (3.26 g, 21.7 mmol) and DMSO (distilled from CaH_2, 30 ml) was heated at 120–125° for 7 hr under N_2. Further amount of NaCN and NaI (0.5 g each) was added and the heating was continued for additional 14 hr. After cooling the mixture was cautiously neutralized with dil H_2SO_4 and the product was extracted with ether. The extract was washed with sat brine, dried and freed from the solvent to furnish a viscous oil (1.3 g) which was chromatographed on a column of SiO_2 (20 g). $CHCl_3$ elution afforded **10** (1.2 g, 94% yield), m.p. 77–77.5° (from n-hexane): IR 2260, 1060, 1055, 890, 840, 830 cm^{-1}; NMR 2.52 (2 H, s, $-CH_2CN$), 3.39, 3.71 (2 H, AB q, J = 8 Hz, $-\underline{C}CH_2O-$), 3.58 (1 H, dd, J = 1.5, 8 Hz, $-\underline{C}H-CH_\alpha\underline{H}_\beta O-$), 3.98 (1 H, dd, J = 4, 8 Hz, $-\underline{C}H\underline{C}\underline{H}_\alpha H_\beta O-$), 5.36 (1 H, m, $-C=\underline{C}H\underline{C}H_2-$). (Found: C, 77.30; H, 8.92; N, 6.41. $C_{14}H_{19}NO$ requires: C, 77.38; H, 8.81; N, 6.45%).

HBr *treatment of nitrile* **10**. A soln of **10** (152 mg, 0.7 mmol) in AcOH (0.45 ml) was treated with aq HBr (47%, 603 mg, 3.5 mmol) at 125–130° for 5 hr. Ice-water was added and the product was extracted with ether. After washing (sat $NaHCO_3$ and sat brine) and drying (Na_2SO_4) the solvent was removed. The residue was chromatographed on a column of SiO_2 to give **13** as an oil (100 mg): IR 1780, 1230, 1210, 1180, 940 cm^{-1}; NMR 2.47, 2.80 (2 H, AB q, J = 17 Hz, $-CH_2CO_2-$), 3.50–4.30 (4 H, m, $-\underline{C}H\underline{C}H_2Br$, $-CO_2CH_2-$).

Oxidation of nitrile **10** *to* cis-*diol* **15**

(a) *With* OsO_4. A soln of OsO_4 (1.33 g, 5.23 mmol) in ether (50 ml) containing pyridine (1 ml) was added in one portion to a stirred soln of **10** (1.35 g, 5.23 mmol) in ether (25 ml). A pale brown ppt separated immediately and the mixture was allowed to react overnight. The complex was destroyed by H_2S gas and the ppt was removed by filtration, then washed thoroughly with THF. Evaporation of the solvents from the combined filtrate and washing furnished the *cis*-diol **15** as a viscous liquid (1.10 g, 84% yield): IR 3440, 2260, 1055, 930 cm^{-1}; NMR 2.64, 3.04 (2 H, AB q, J = 16 Hz, $-CH_2CN$), 3.53 (1 H, dd, J = 7, 9 Hz, $-OCH_\alpha\underline{H}_\beta\underline{C}H-$), 3.54, 3.96 (2 H, AB q, J = 10 Hz, $-OCH_2\underline{C}-$), 3.88 (1 H, dd, J = 6, 12 Hz, $-C\underline{H}OHCH_2-$), 4.06 (1 H, d, J = 9 Hz, $-OC\underline{H}_\alpha H_\beta CH-$).

(b) *With* $KMnO_4$ (*in* aq t-BuOH). A soln of **10** (204 mg, 0.92 mmol) in a mixture of t-BuOH (8.5 ml) and H_2O (6 ml) was rapidly cooled down to −8° in an ice-salt bath under vigorous stirring, then an ice-cooled soln of $KMnO_4$ (200 mg, 1.27 mmol) and NaOH (42.4 mg, 1.06 mmol) in H_2O (6.8 ml) was introduced in one portion. The mixture was stirred for 3 min and then quenched by the addition of $NaHSO_3$. The MnO_2 ppt was filtered off and washed thoroughly with THF. The combined filtrate and washings were concentrated and extracted with $CHCl_3$ (×3). After being washed with sat brine the extract was evaporated to leave an oily residue (222 mg), which was chromatographed (SiO_2, 5 g). Elution with benzene-AcOEt 3:2–2:1) afforded the *cis*-diol **15** (140 mg, 70% yield) with a small amount of a crystalline substance (23 mg) which was identified as **70**, m.p. 157–158°: IR ($CHCl_3$) 3600, 3420, 2255, 1728 cm^{-1}; NMR 2.35, 2.88 (2 H, AB q, J = 16 Hz, $-CH_2CN$), 3.41 (1 H, dd, J = 3.5, 9 Hz, $-CH\underline{C}H_\alpha\underline{H}_\beta O-$), 3.83 (2 H, AB q, J = 10 Hz, $-CH_2O-$), 4.13 (1 H, dd, J = 7, 9 Hz, $-CH\underline{C}\underline{H}_\alpha H_\beta O-$). (Found: C, 67.5; H, 7.63; N, 5.27. $C_{14}H_{19}NO_3$ requires: C, 67.4; H, 7.68; N, 5.62%). This oxidation could be also performed in aq pyridine soln with comparable efficiency and less formation of **70**. Thus a soln of $KMnO_4$ (200 mg, 1.27 mmol) and NaOH (38 mg, 0.95 mmol) in H_2O (20 ml) was added to a soln of **10** (200 mg, 0.98 mmol) in pyridine (10 ml), cooled to −10°, and allowed to react for 3 min. The diol **15**, the product was tosylated as described below without purification to afford **16** in an overall yield of 69.9%.

Tosylation of cis-*diol* **15**. A mixture of **15** (2.58 g, 1.028 mmol), TsCl (4.0 g) and anhyd pyridine (8 ml) was kept overnight in a refrigerator. The crystalline solid (3.88 g, 93% yield) obtained after a usual work-up was recrystallized from EtOH to produce **16** as needles, m.p. 179–181°: IR 3320, 2250, 1590, 1480 cm^{-1}; NMR 2.47 (3 H, s, ArMe), 2.63, 3.13 (2 H, AB q, J = 17 Hz, $-CH_2CN$), 3.52 (1 H, t, J = 8 Hz, $-OCH_\alpha\underline{H}_\beta CH-$), 3.56, 3.95 (2 H, AB q, J = 9 Hz, $-OCH_2-$), 3.78 (1 H, d, J = 8 Hz, $-OC\underline{H}_\alpha H_\beta\underline{C}H-$), 4.82 (1 H, dd, J = 6, 8 Hz, $-C\underline{H}(OTs)CH_2-$). (Found: C, 62.24; H, 6.84; N, 3.55. $C_{21}H_{27}NO_5S$ requires: C, 62.20, H, 6.71; N, 3.45%).

Rearrangement reaction of monotosylate **16**. To a stirred soln of **16** (1.44 g, 3.43 mmol) in dry THF (20 ml) was added a soln of t-BuOK (654 mg, 5.83 mmol) in dry t-BuOH (30 ml) in one portion under N_2. The mixture, heated under refluxing for 50 min, gradually became cloudy. After the addition of ice-water, the product was isolated by $CHCl_3$ extraction (×3) to furnish **17** as a colorless glass in nearly quantitative yield: IR (neat) 2260, 1700, 1255, 1090, 1060, 1040, 930 cm^{-1}.

Conversion of perhydroazulenoid ketone **17** *into perhydroazulenoid lactone* **5**. The ketone **17** (750 mg, 3.2 mmol) dissolved in AcOH (5 ml) was heated at 125–130° with HI (57%, 5 ml) and red P (2 g) for 3 hr. After the removal of red P by filtration, the filtrate was extracted with $CHCl_3$ (×3) and the $CHCl_3$ extract was washed thoroughly with sat $NaHCO_3$, then with sat brine. After drying (Na_2SO_4), the solvent was evaporated to leave **18** as a crystalline mass (1.1 g, 94.4% yield): IR 1780, 1700, 1205, 1175, 1020 cm^{-1}; NMR 2.38, 2.61 (2 H, AB q, J = 18 Hz, $-CH_2CO_2-$), 2.92 (1 H, t, J = 10 Hz, $-CH\underline{C}H_2I$), 3.30 (1 H, dd, J = 5, 10 Hz, $-CH\underline{C}H_2I$), 4.08 (2 H, s, $-CH_2OCO-$). This iodide **18** (4.6 g, 12.7 mmol) dissolved in AcOH (100 ml) was stirred with Zn dust (20 g)

overnight. After the removal of Zn dust by filtration and the concentration of the filtrate, the product was taken up in $CHCl_3$ and the $CHCl_3$ soln was washed with sat $NaHCO_3$. The washings were extracted with $CHCl_3$ and the combined $CHCl_3$ soln was dried over Na_2SO_4. The evaporation of the solvent afforded the **5** as a crystalline mass (3.04 g, 100% yield), m.p. 118–120° (from benzene): IR 1780, 1700, 1183, 1165, 1020 cm^{-1}; NMR 0.80 (3 H, d, J = 7 Hz, $-CH\underline{CH}_3$), 2.37 (2 H, s, $-CH_2CO_2-$), 4.06 (2 H, s, $-CH_2OCO-$). (Found: C, 71.05; H, 8.50. $C_{14}H_{20}O_3$ requires: C, 71.16; H, 8.53%).

Formylation of perhydroazulenoid lactone **5**. A soln of **5** (236 mg, 1.0 mmol) in a mixture of benzene (2 ml) and DME (3 ml) was treated with MeONa (162 mg, 3.0 mmol) and HCO_2Et (222 mg, 3.0 mmol) at room temp for 2 hr. The mixture was poured onto ice-water and acidified with dil H_2SO_4. Extraction with $CHCl_3$ afforded **19** as a crystalline mass (247 mg, 94% yield): IR 1770, 1625, 1570, 1250, 1180, 1150, 1090, 1020 cm^{-1}; NMR 1.01 (3 H, d, J = 7 Hz, $CH\underline{CH}_3$), 2.31, 2.39 (2 H, AB, q, J = 18 Hz, $-CH_2CO_2-$), 4.03 (2 H, s, CO_2CH_2-), 7.26 (1 H, s, $-C{=}C\underline{H}OH$). When this reaction was conducted in benzene soln, **20** was obtained in addition to **19** after chromatography (SiO_2). IR 1710, 1630, 1580, 1400, 1245, 1190, 1110 cm^{-1}; NMR 3.91, 4.05 and 4.00, 4.16 (2 H in total, AB q × 2, J = 10 Hz, $-CO_2CH_2-$), 6.79, 7.79 (each 1 H, s, $=C\underline{H}OH$).

Conversion of formyl derivative **19** *to tricyclic ketol acetate* **23**. To a stirred soln of **19** (250 mg, 0.95 mmol) and acrylaldehyde (280 mg, 5 mmol) in AcOEt (5 ml) were added five drops of 10% AcOEt soln of Et_3N at room temp, after 10 min, a further ten drops of the amine soln and the stirring of the mixture was continued to the completion of the reaction (3–5 hr, tlc monitoring). The mixture was neutralized with AcOH and evaporation of the solvent left **21** as a viscous oil. This product dissolved in EtOH (6 ml) was treated with 10% HCl (3.5 ml) under refluxing for 3 hr. Water was added to the cooled mixture and the product was extracted with $CHCl_3$ (× 3). The $CHCl_3$ extract was washed with sat brine and dried over Na_2SO_4. The yellow oil left after the evaporation of the solvent was chromatographed on a column of SiO_2 to afford **22a** (264 mg, 100% yield) as an oil: IR (liq film) 3440, 1770, 1690, 1010 cm^{-1}; NMR 1.03 (3 H, d, J = 6 Hz, $-CH\underline{CH}_3$), 2.38 (2 H, s, $-CH_2CO_2-$), 3.97 (1 H, br d, $W_{1/2}$ = 7 Hz, $-CH_2C\underline{H}(OH)-$), 4.02 (2 H, s, $-CH_2OCO-$). A soln of **22a** (111 mg, 0.4 mmol) in dry benzene (2 ml) was heated under refluxing with isopropenyl acetate (188 mg, 2 mmol) and a catalytic amount of anhyd TsOH for 6–7 hr. After washing with sat brine, the solvent was evaporated to give **23a** as crystals (130 mg), m.p. 184.5–185.5° (from AcOEt): IR ($CHCl_3$) 1775, 1740, 1705, 1240 cm^{-1}; NMR 1.00 (3 H, d, J = 6 Hz, $CH\underline{CH}_3$), 2.04 (3 H, s, OAc), 2.42 (2 H, s, CH_2CO_2-), 4.04 (2 H, s, $-CO_2CH_2-$), 4.95 (1 H, m, $W_{1/2}$ = 7 Hz, $CH_2C\underline{H}OAc$). (Found: C, 68.19; H, 7.85. $C_{19}H_{26}O_5$ requires: C, 68.24; H, 7.84%).

Tricyclic alcohol **26a**. A mixture of **23** (203 mg, 0.63 mmol), ethanedithiol (446 mg, 4.73 mmol) and AcOH (0.5 ml) was stirred at room temp in the presence of BF_3-etherate (210 mg, 1.48 mmol) for 3–4 days. The mixture was poured onto ice-water and the product was extracted with $CHCl_3$. The $CHCl_3$ layer was washed successively with sat $NaHCO_3$ and sat brine, then dried. Evaporation of solvent left an oily residue, which was chromatographed on SiO_2 column to furnish **24** (149 mg, 60% yield) as earlier fractions followed by some recovery: IR (neat) 1780, 1738, 1240, 1020 cm^{-1}. The thioketal **24** thus obtained (105 mg, 0.27 mmol) was treated with W-2 Raney Ni (from 5 g of the alloy) in EtOH under refluxing for 14 hr. Work-up afforded **25** as crystals, m.p. 189.5–190° (from benzene): IR (neat) 1778, 1732, 1240, 1018 cm^{-1}; NMR 0.91 (3 H, d, J = 7 Hz, $-CH\underline{CH}_3$), 2.05 (3 H, s, –OAc), 2.39, 2.47 (2 H, AB q, J = 18 Hz, $-CH_2CO_2-$), 4.05, 4.25 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$), 4.71 (1 H, m, $W_{1/2}$ = 18 Hz, $-CH_2C\underline{H}(OAc)-$). A soln of **25** (84 mg, 0.27 mmol) in a mixture of MeOH (9 ml) and H_2O (4 ml) was mixed with 2N NaOH (3 ml) and the resulting soln was refluxed for 40 min. Work-up in a usual manner afforded a crystalline product (69 mg) which was purified by SiO_2 chromatography to furnish **26a**: IR ($CHCl_3$) 3630, 3500, 1768, 1018 cm^{-1}; NMR 0.99 (3 H, d, J = 6 Hz, $-CH\underline{CH}_3$), 2.37 (2 H, s, $-CH_2CO_2-$), 3.65 (1 H, m, $W_{1/2}$ = 6 Hz, $-CH_2C\underline{H}(OH)-$), 4.07, 4.49 (2 H, AB q, J = 10 Hz, $-CH_2OCO-$). NMR (molar equiv of added Eu (dpm)$_3$ 0.25, 0.50, 0.75, 1.00) 1.10, 1.30, 1.54, 1.82 ($-CH\underline{CH}_3$), 2.67, 3.31 4.04, 4.92 ($-CH_2CO_2$)[†], 5.89, 10.14, 14.62, 19.24 ($-CH_2C\underline{H}(OH)-$), 4.71, 5.62, 6.61, 7.72 ($-CH_2OCO$)[†].

Tricyclic alcohol **26b**. The ketol **22a** (1.15 g, 4.37 mmol) was dissolved in ethanedithiol (20 ml) and BF_3 etherate (0.1 g) and AcOH (5 drops) were added. The mixture was stirred at room temp overnight and, after addition of further amounts of ethanedithiol (1.0 ml), BF_3-etherate (0.15 ml) and AcOH (15 drops), for a day. Sat Na_2CO_3 was added and the product was isolated by $CHCl_3$ extraction. The chromatographic separation (SiO_2) afforded **28b**: IR (neat) 3460, 1770, 1208, 1015, 755 cm^{-1}; NMR 0.93 (3 H, d, J = 6 Hz, $-CH\underline{CH}_3$), 2.26, 2.52 (2 H, AB q, J = 18 Hz, $-CH_2CO_2-$), 3.14 (4 H, m, SCH_2CH_2S-), 3.80 (1 H, dd, J = 7, 10 Hz, $-CH_2C\underline{H}(OH)-$), 4.18, 4.44 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$) and the bis-thioketal **27**: IR 1775, 1185, 1152, 1020, 755 cm^{-1}; NMR 0.96 (3 H, d, J = 6 Hz, $-CH\underline{CH}_3$), 2.34, 2.42 (2 H, AB q, J = 18 Hz, $-CH_2CO_2-$), 3.20 (8 H, m, $-SCH_2CH_2S$ × 2), 4.02 (2 H, s, $-CO_2CH_2-$), 4.44 (1 H, t, J = 7 Hz, $-CH\langle^{S}_{S}\rangle$). The monothioketal **28b** (55 mg) dissolved in abs EtOH was treated with W-2 Raney Ni under refluxing for 21 hr. Work-up gave **26b** as a glass (38 mg): IR (neat) 3430, 1765, 1175, 1015, 755 cm^{-1}; NMR 0.91 (3 H, d, J = 7 Hz, $-CH\underline{CH}_3$), 2.43 (2 H, s, $-CH_2CO_2-$), 3.53 (1 H, m, $W_{1/2}$ = 20 Hz, $-CH_2C\underline{H}(OH)-$), 4.07, 4.23 (2 H, AB q, J = 10 Hz, $-CH_2OCO-$). NMR (molar equiv of added Eu (dpm)$_3$ 0.25, 0.50, 0.75, 1.00) 1.24, 1.70, 2.20, 2.63 ($CH\underline{CH}_3$), 2.43, 3.13, 4.10, 5.23 ($-CH_2CO_2-$)[†], 7.49, 9.37, 12.60, 15.16 ($-CH_2C\underline{H}(OH)-$), 4.83, 5.80, 6.85, 7.82 ($-CH_2OCO$)[†].

Tricyclic ketone **29**. To an ice-cooled soln of **26a** was added dropwise Jones' reagent (0.1 ml, 0.4 mmol equiv). After the mixture had been stirred at room temp for 1 hr, the excess reagent was decomposed by the addition of MeOH and sat brine was added. $CHCl_3$ extraction afforded **29** as colorless plates, m.p. 148–149°, after the recrystallization from benzene: IR ($CHCl_3$) 1770, 1700 cm^{-1}; NMR 0.95 (3 H, d, J = 6 Hz, $-CO_2CH_3$), 2.40 (2 H, s, $-CH_2CO_2-$), 4.06, 4.17 (2 H, AB q, J = 10 Hz, CO_2CH_2-). (Found: C, 73.57; H, 8.70. $C_{17}H_{24}O_3$ requires: C, 73.88; H, 8.75%).

Conversion of ketone **29** *into enol acetate* **31**. A mixture of **29** (248 mg, 1.0 mmol), isopropenyl acetate (20 ml) and anhyd TsOH (63 mg, 0.37 mmol) was heated under gentle refluxing for 2–3 days. The excess of isopropenyl acetate was slowly distilled off to a small volume and the residue dissolved in ether was washed with sat brine, then dried. The chromatographic purification of the product afforded **31** (303 mg, 100% yield): IR (neat) 1780, 1760, 1690, 1640, 1370, 1210 cm^{-1}; NMR 0.95 (3 H, d, J = 6 Hz, $CH\underline{CH}_3$), 2.15 (3 H, s, –OAc), 2.34 (2 H, s, $-CH_2CO_2-$), 4.20, 4.04 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$), 5.28 (1 H, dd, J = 2.5, 6 Hz, $-CH_2C\underline{H}_2{=}C(OAc)-$).

[†]denote the center of AB quartet.

Dicarboxylic acid monomethyl ester **34** *from enol acetate* **31**. A soln of **31** (670 mg, 2.1 mmol) in a mixture of CCl_4 (20 ml) and AcOH (30 ml) was added to a soln of RuO_4 prepared by stirring overnight a suspension of RuO_2 (422 mg, 3.17 mmol) in CCl_4) (50 ml) with aq $NaIO_4$ soln (1.4 g, 6.5 mmol in 20 ml of H_2O). The mixture was stirred vigorously at room temp while further amounts of $NaIO_4$ (5 g in total) were added occasionally. It took 3–5 days for the completion of the oxidation (tlc monitoring). The excess of the reagent was decomposed by the addition of i-PrOH and the RuO_2 ppt was filtered off with the aid of Celite. Ether was added to the filtrate and the organic layer was separated. The acidic product was extracted as usual with $NaHCO_3$ aq to yield **32** as colorless plates, m.p. 252–253° (from acetone). (Found: C, 63.28; H, 7.56. $C_{17}H_{24}O_6$ requires: C, 62.95; H, 7.46%). The acidic fraction above was treated with CH_2N_2 in ether to give the dimethyl ester **33** as crystals (446 mg, 60% yield from **31**): IR ($CHCl_3$) 1775, 1725, 1080 cm^{-1}; NMR 0.91 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 2.35, 2.53 (2 H, AB q, J = 18 Hz, CH_2CO_2-), 3.62, 3.76 (each 3 H, $-CO_2CH_3 \times 2$), 3.97, 4.13 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$). A soln of **33** (90 mg, 0.24 mmol) in EtOH (10 ml) was mixed with 2N NaOH (3 ml) and the mixture was refluxed overnight. After the mixture had been washed with $CHCl_3$, the aq soln was acidified and extracted with ether. Evaporation of the solvent afforded **34** as an oil: IR 3400–2600, 1780, 1720 cm^{-1}; NMR 0.91 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 2.37, 2.54 (2 H, AB q, J = 18 Hz, $-CH_2CO_2-$), 3.72 (3 H, s, $-CO_2CH_3$), 4.01, 4.15 (2 H, d, J = 10 Hz, $-CO_2CH_2-$).

Exomethylene compound **35**. $Pb(OAc)_4$ (153 mg, 0.34 mmol), $Cu(OAc)_2$ (7 mg) and pyridine (one drop) were added to a soln of **34** (60 mg, 0.18 mmol) in dry benzene and the mixture was refluxed for 6 hr. After the addition of a further amount of $Pb(OAc)_4$ (150 mg), the refluxing was continued overnight. The Pb salt was removed by filtration and the filtrate was washed successively with H_2O, sat $NaHCO_3$ and sat brine. Evaporation of the solvent afforded **35** as colorless plates, m.p. 148° (from ether). IR (CHC_{13}) 1778, 1728, 1640, 908 cm^{-1}; NMR 0.93 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 2.37, 2.45 (2 H, AB q, J = 17 Hz, $-CH_2CO_2-$), 3.62 (3 H, s, $-CO_2CH_3$), 4.01, 4.13 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$), 4.52, 4.63 (each 1 H, m, $-\underset{|}{C}=CH_2$). (Found: C, 69.63; H, 8.16. $C_{17}H_{24}O_4$ requires: C, 69.83; H, 8.27%).

Dilactone **36**

(a) *From the synthetic intermediate* **35**. A mixture of **35** (40 mg, 0.137 mmol), EtOH (6 ml) and 6N H_2SO_4 (2 ml) were refluxed overnight. The product was extracted with $CHCl_3$ and purified by the chromatography on a column of SiO_2. The fractions eluted with benzene–AcOEt (2:1) were recrystallized from benzene to give **36** as colorless plates, m.p. 250–250.5°: IR ($CHCl_3$) 1775, 1730, 1170, 1155, 1020 cm^{-1}; NMR 0.99 (3 H, d, J = 6 Hz, $\underset{|}{C}H\underline{C}H_3$), 1.44 (3 H, s, $-CO_2\underset{|}{C}CH_3$), 2.39 (2 H, s, $-CH_2CO_2-$), 4.02 (2 H, s, $-CO_2\underset{|}{C}H_2-$). (Found: C, 69.05; H, 7.64. $C_{16}H_{22}O_4$ requires: C, 69.04; H, 7.97%).

(b) *From the natural degradation product* **37**. To an ice-cooled soln of **37** (56 mg, 0.21 mmol) in acetone (3 ml) was added Jones' reagent (0.13 ml, 0.52 m equiv) and the mixture was allowed to react for 2 hr. Excess of the reagent was destroyed by addition of MeOH and the product was extracted with $CHCl_3$. The $CHCl_3$ extract was washed with sat brine and the solvent was evaporated to yield the corresponding lactone carboxylic acid: IR ($CHCl_3$) 3600–2300, 1775, 1710 cm^{-1}. This acid dissolved in EtOH (6 ml) was heated with 6N H_2SO_4 (2 ml) under refluxing for 1.5 hr. The crude product (54 mg) was chromatographed on a column of SiO_2 and the eluant (38 mg) with $CHCl_3$–MeOH (33:1) was recrystallized from benzene to furnish colorless needles, m.p. 278–282°, which was identical with the product obtained above in tlc, IR and NMR comparison. (Found: C, 68.77: H, 7.73. $C_{16}H_{22}O_4$ requires: C, 69.04; H, 7.97%).

Isomerization experiment with triol **40**. The *exo*-methylene lactone **35** (37 mg, 0.127 mmol) was reduced with LAH (10 mg, 0.39 mmol) in THF (6 ml) at room temp for 20 hr. After addition of H_2O, the product was isolated with $CHCl_3$ extraction giving the triol **40** as an oil (35 mg): NMR 1.00 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 3.2–3.8 (6 H, m, $-C\underline{H}_2OH \times 3$), 4.71 (2 H, m, $-\underset{|}{C}=CH_2$). This triol **40** was treated with t-BuOK (84 mg) in DMSO (2 ml) at 120° for 8 hr. After cooling ice-water was added and the product was extracted with $CHCl_3$, then purified by SiO_2 chromatography. The elution with EtOAc afforded an olefin mixture: IR ($CHCl_3$) 3400, 1020 cm^{-1}; NMR, signals of vinylic proton region at δ 4.69, 5.27 and 5.48 in a ratio of 2:7:1.

Half ester **43**. A mixture of **32** (290 mg, 0.88 mmol), TsOH (2 mg), abs EtOH (2 ml) and dry benzene (2 ml) was refluxed for 20 hr. A part of the solvents was distilled to remove azeotropically the water formed and then the refluxing was continued for further 5 hr. The isolation of the acidic product afforded **43** as colorless crystals (270 mg, 86% yield): IR (neat) 1780, 1740, 1710 cm^{-1}; NMR 0.96 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.25 (3 H, t, J = 7 Hz, $-CO_2CH_2C\underline{H}_3$), 2.40, 2.56 (2 H, AB q, J = 17 Hz, $-CH_2CO_2-$), 4.06, 4.20 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$), 4.13 (2 H, q, J = 7 Hz, $-CO_2C\underline{H}_2CH_3$). In addition a neutral product (50 mg) of undefined structure was obtained. IR (neat) 1777, 1735, 1696, 1180, 1020 cm^{-1}.

Conversion of half ester **43** *to hydroxy ester* **46**. **43** (60 mg, 0.16 mmol) was converted to the corresponding acid chloride **45** by treatment with an excess of $SOCl_2$ in dry benzene under refluxing (addition of pyridine as catalyst). The acid chloride was stirred with an excess of ethanethiol (~0.2 ml) and diisopropylethylamine (0.12 ml) overnight at ambient temp. The crude product (45 mg) obtained by ether extraction was purified by SiO_2 chromatography giving **44** as an oil (33 mg): IR (neat) 1785, 1735, 1675 cm^{-1}; NMR 0.94 (3 H, d, J = 6.5 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.26 (6 H, t, J = 7 Hz, $-CO_2CH_2C\underline{H}_3$ and $-COSCH_2C\underline{H}_3$), 2.34, 2.52 (2 H, AB q, J = 17.5 Hz, $-CH_2CO_2-$), 2.86 (2 H, q, J = 7 Hz, $-COSC\underline{H}_2CH_3$), 4.01, 4.15 (2 H, AB q, J = 9.5 Hz, $-CO_2CH_2-$), 4.08 (2 H, q, J = 7 Hz, $-CO_2C\underline{H}_2CH_3$). This thiol ester (32 mg) was treated with W-4 Raney Ni (prepared from 2 g of the alloy)[38] in abs EtOH (3 ml) at room temp under stirring overnight. Removal of the catalyst by filtration and evaporation of the solvent from the filtrate afforded **46** as an oil (20 mg, 35% overall yield): IR ($CHCl_3$) 3460, 1770, 1730, 1020 cm^{-1}; NMR 0.97 (3 H, t, J = 7 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.24 (3 H, t, J = 7 Hz, $-CO_2CH_2C\underline{H}_3$), 2.33, 2.43 (2 H, AB q, J = 17 Hz, $-CH_2CO_2-$), 3.28, 3.32 (2 H, AB q, J = 11 Hz, $-CH_2OH$), 4.07 (2 H, q, J = 7 Hz, $-CO_2C\underline{H}_2CH_3$), 4.10, 4.30 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$).

7-Membered lactone **47**. A mixture of **46** (60 mg, 0.18 mmol) in MeOH (15 ml) and 2N NaOH (7 ml) was refluxed overnight. Usual work-up including acidification with dil HCl and ether extraction afforded **47** as an oil (54 mg): IR ($CHCl_3$) 1770, 1730, 1175 cm^{-1}; NMR 0.98 (3 H, d, J = 7 Hz, $-\underset{|}{C}HC\underline{H}_3$), 2.38 (2 H, s, $-CH_2CO_2-$), 2.62 (2 H, collapsed d, J = 6 Hz, $-\underset{|}{C}HCH_2CO_2-$), 3.7–4.0 (2 H, collapsed m, $-CO_2CH_2-$ of the 7-membered lactone ring), 4.01, 4.12 (2 H, AB q, J = 10 Hz, $-CO_2CH_2-$ of the γ-lactone). When the measurement was carried out at 50°, the collapsed signals at δ 2.62 and 3.7–4.0 turned to a doublet (J = 2 Hz) and an AB quartet (δ 3.84, 3.92 with J = 9 Hz).

Reduction of exomethylene lactone **35** *to hemiacetal* **48**. A modified SMEAH soln was prepared by the addition of a mixture of abs EtOH (0.27 ml, 4.6 mmol) and toluene (0.7 ml) to SMEAH soln in benzene ('RDB soln', 3 ml, 0.58 mmol) diluted with toluene (6 ml) under ice-cooling. This soln (8 ml, 4.64 mmol) was added dropwise to an ice-cooled soln of **35** (90 mg, 0.31 mmol) in toluene (4 ml) by means of a syringe. The mixture was allowed to react for 2.5 hr and then the reaction was quenched by the addition of H_2O. Extraction with benzene, washing with sat NaCl and evaporation of the solvent afforded a crude product which was purified by SiO_2 chromatography. Elution with a mixture of benzene–EtOAc (10:1) gave **48** as a mixture of the epimers: IR(CCl_4) 3450, 3090, 1735, 1640, 890 cm^{-1}; NMR(CCl_4) 0.83, 0.99 (3 H in total, each d, J = 7 Hz, $-\underset{|}{C}HCH_3$), 3.56 (3 H, s, $-CO_2CH_3$), 3.40, 3.64 and 3.60, 3.79 (2 H in total, AB quartets, $-CH_2O-$), 4.46, 4.56 (each 1 H, br s, $-\underset{|}{C}=CH_2$), 5.32 (1 H, m, $-CH_2\underset{|}{C}H(OH)O-$).

Conversion of hemiacetal **48** *to bispyranyl ether* **51**. A mixture of **48** (75 mg, 0.255 mmol) in CH_2Cl_2 (3 ml) and dihydropyran (0.04 ml), after addition of catalytic amount of TsOH, was allowed to stand at room temp for 1.5 hr. The reaction quenched by stirring with anhyd K_2CO_3. The filtered soln was evaporated giving **49** as a colorless oil (105 mg): IR (neat) 3100, 1735, 1640 cm^{-1}.

A soln of **49** (105 mg) was added dropwise to an ice-cooled soln of LAH (60 mg, 1.6 mmol) in THF (6 ml) and the mixture was swirled at room temp for 2.5 hr. Small amounts of EtOAc and H_2O were added successively, then anhyd $MgSO_4$ was added. After filtration the filtrate was evaporated affording **50** as a colorless oil (100 mg): IR (neat) 3450, 3095, 1640, 895 cm^{-1}.

The alcohol **50** (35 mg, 0.1 mmol) was converted to **51** in a similar manner. The crude product was chromatographed on a column of SiO_2 and the elution with benzene–EtOAc (30:1) furnished **51** as an oil (50 mg): IR(CCl_4) 3070, 1635, 1120, 1063, 1033, 968, 900, 865 cm^{-1}; NMR 0.83, 0.96 (3 H in total, each d, J = 7 Hz, $-\underset{|}{C}HCH_3$), 4.48 (2 H, m, $-O\underset{|}{C}HCH_2$), 4.66, 4.82 (each 1 H, m, $-\underset{|}{C}=CH_2$), 4.75 (1 H, m, $-O\underset{|}{C}HCH_2$).

Isomerization of bispyranyl ether **51** *to* endo*-olefin* **52**. The ether **51** (50 mg) was dissolved in DMSO (5 ml) and heated with t-BuOK (400 mg, 3.6 mmol) at 110° for 7 hr. The mixture was poured onto ice and the product was isolated by the extraction with $CHCl_3$. After chromatographic purification [SiO_2, elution with benzene-EtOAc (20:1)], the *endo*-olefin **52** was obtained as a yellow-colored oil (25 mg).

Hydroxy hemiacetal **53**

(a) *From bispyranyl ether* **52**. The ether **52** (25 mg) dissolved in a mixture of acetone (3 ml) and H_2O (1 ml) was treated with t-BuOK (400 mg, 3.6 mmol) at 110° for 7 hr. The mixture of sat $NaHCO_3$, the product was extracted with EtOAc and the extract soln was washed with sat NaCl, then dried with anhyd $MgSO_4$. Evaporation of the solvent left **53** as an oil (16 mg, 60% yield from **50**): IR ($CHCl_3$) 3600, 3400, 1620, 1235, 1010, 925 cm^{-1}; NMR 0.88, 1.02 (3 H in total, d, J = 7 Hz, $\underset{|}{C}HCH_3$), 1.72 (3 H, br s, $-\underset{|}{C}=\underset{|}{C}CH_3$), 3.2–4.0 (4 H, m, CH_2O- and $-CH_2OH$), 5.41 (2 H, m, $-OCHCH_2$ and $CH=\underset{|}{C}$).

(b) *From hydroxy-γ-lactone* **37**. The modified SMEAH soln was prepared by the addition of a mixture of abs EtOH (0.27 ml, 0.46 mmol) and toluene (0.7 ml) to a mixture of SMEAH soln in benzene (3 ml, 5.8 mmol). This soln (1.5 ml) was added to a stirred and ice-cooled toluene (2 ml) soln of **37** (46 mg, 0.17 mmol), derived from natural portulal by degradation. After 1 hr, a further amount of the reagent soln (1.0 ml) was added and the reaction was continued for further 50 min, then quenched by the addition of H_2O. The crude product obtained by the extraction with benzene was chromatographed on a column of SiO_2 and eluted with a mixture of benzene–EtOAc (2:1) giving **53** as a colorless oil (27 mg). This product was identical with the material obtained in (a).

Isomerization experiment with bispyranyl ether **52**. Compound **53** (27 mg) was converted to **52** in a similar manner. Chromatography on a column of SiO_2 and elution with benzene afforded **52** (40 mg) as a colorless oil: IR (CCl_4) 1130, 1080, 1035, 970 cm^{-1}; NMR 0.87, 0.98 (3 H in total, d, J = 7 Hz, $\underset{|}{C}HCH_3$), 3.0–3.9 (8 H, m, $-CH_2O-$ × 4), 4.44 (1 H, m, $-O\underset{|}{C}HCH_2-$), 4.80 (1 H, m, $-O\underset{|}{C}HCH_2-$), 5.26 (1 H, m, $-C=C\underset{|}{H}CH_2-$).

The ether **52** (40 mg, 0.092 mmol) was treated with t-BuOK (400 mg) in DMSO (5 ml) at 100° for 4.5 hr under N_2. The oily product (27 mg) was hydrolyzed (HCl-acetone-H_2O) yielding the starting material **52**, uncontaminated with the double bond isomers as revealed by NMR analysis.

Conversion of hydroxyhemiacetal **53** *to hydroxy lactone* **37**. To a soln of Ag_2O, prepared from NaOH (340 mg, 8.5 mmol) in H_2O (5 ml) and $AgNO_3$ (170 mg, 1 mmol) in H_2O (2 ml), was added a soln of **53** (20 mg, 0.75 mmol) in MeOH (3 ml). The mixture was stirred overnight at ambient temp. The mixture was shaken with $CHCl_3$ and aq layer was acidified, then extracted with $CHCl_3$. After the washing with sat NaCl and the drying with anhyd $MgSO_4$, the organic layer was evaporated leaving a residue which was purified by chromatography [SiO_2, elution with benzene–EtOAc (10:1–5:1)]. **37** was obtained as an oil (14 mg, 71% yield), which proved identical with the compound derived from natural portulal **1** by degradation (tlc, IR and NMR comparison). The acetate was prepared from synthetic and degradative products by treatment with Ac_2O and pyridine at room temp overnight. The acetate from the synthetic **37** was obtained as colorless needles, m.p. 116–117° (from n-hexane $CHCl_3$): IR ($CHCl_3$) 1775, 1735, 1240, 1025 cm^{-1}; NMR 0.97 (3 H, d, J = 6 Hz, $\underset{|}{C}HCH_3$), 1.64 (3 H, br s, $-C=\underset{|}{C}CH_3$), 2.05 (3 H, s, —OAc), 2.35, 2.53 (2 H, AB q, J = 17 Hz, $-CH_2CO_2$), 3.91 (2 H, s, $-CH_2OAc$), 4.08, 4.20 (2 H, AB q, J = 9 Hz, CO_2CH_2-), 5.35 (1 H, m, $-C=C\underset{|}{H}CH_2-$). (Found: C, 70.62; H, 8.59. $C_{18}H_{26}O_4$ requires: C, 70.56; H, 8.55%. The acetate derived from **37** crystallized from n-hexane-$CHCl_3$ as needles, m.p. 144–145°. (Found: C, 70.34; H, 8.53%). IR and NMR spectra of this specimen were superimposable with those of the synthetic product above.

Reduction of γ-lactone **55** *to hemiacetal* **56**

(a) *With SMEAH soln*. To a soln of **55** (66 mg, 0.3 mmol) cooled to −65°, was added dropwise a mixture of SMEAH soln (0.05 ml, 0.36 mmol) and THF (0.5 ml) during 10 min. After 1 hr, further amount of SMEAH soln (0.05 ml, 0.36 mmol) and THF (0.5 ml) was added and the mixture was allowed to react a further 20 min. The mixture was quenched by the addition of H_2O and acidified with 1N HCl, then extracted with benzene. The residue, left after the evaporation of the solvent, was chromatographed on a column of SiO_2. Elution with a mixture of benzene EtOAc (20:1 5:1) afforded **56** as prisms, m.p. 102–108.5° (from petroleum benzine, 42 mg, 64% yield): IR (Nujol) 3390, 1262, 1150, 1020, 925, 825, 727 cm^{-1}; NMR **56a**: 1.05 (3 H, d, J = 7 Hz, $-\underset{|}{C}HCH_3$), 3.26 (1 H, d, J = 3 Hz, $-\underset{|}{C}HOH$, disappeared on the addition of D_2O), 3.75 (2 H, s, $-OCH_2-$), 5.35 (1 H, m, $-C=C\underset{|}{H}CH_2-$), 5.58 (1 H, q, J = 4 Hz, $-O\underset{|}{C}H(OH)CH_2-$, turned to a triplet on the addition of D_2O). The observable smaller signals due to the presence of the epimer **56b** were:

0.97 (d, J = 7 Hz, $-\underset{|}{C}HCH_3$), 3.43 (1 H, d, J = 4 Hz, $-\underset{|}{C}HOH$, disappeared on the addition of D_2O), 3.70, 3.90 (AB q, J = 10 Hz, $-OCH_2-$). (Found: C, 74.75; H, 10.77. $C_{14}H_{24}O_2$ requires: C, 74.95; H, 10.78%). Further elution with benzene-EtOAc (1:1) afforded **57** as needles (18 mg, 27% yield), m.p. 141–143° (from benzene): IR (Nujol) 3300, 3210, 1048, 1033, 1018, 805 cm^{-1}; NMR (pyridine-d_5) 1.03 (3 H, d, J = 7 Hz, $-\underset{|}{C}HCH_3$), 3.73 (2 H, s, $-CH_2OH$), 3.83 (2 H, t, J = 7 Hz, $-CH_2CH_2OH$), 5.28 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$). (Found: C, 75.53; H, 9.91. $C_{14}H_{22}O_2$ requires: C, 75.63; H, 9.91).

(b) *With modified SMEAH soln.* This was prepared by mixing a mixture of SMEAH soln (2 ml) and toluene (2 ml) with a mixture of EtOH (0.18 ml) and toluene (1 ml). A part of this soln (0.5 ml) was added to an ice-cooled soln of **55** (25 mg, 0.114 mmol) in toluene (1 ml). After 1 hr further amount of the reagent soln (1.5 ml) was added and the mixture was left for 30 min. Water was added and the product was isolated by benzene extraction. Chromatographic separation (SiO_2) furnished **56** (24 mg, 96% yield) with a small amount of the diol **57** (< 1 mg).

Reaction of γ-lactone **55** *with β-furyl lithium. Formation of diacetate* **62**. An aliquot (3.5 ml) of β-furyl lithium soln, prepared from n-BuLi in hexane (0.5 ml, 1.15 mmol) and β-bromofuran (140 mg, 1 mmol) in abs ether (4 ml), was added dropwise to a soln of **55** (72 mg, 0.33 mmol) in ether (5 ml) cooled at −20° by means of a long hypodermic needles bringing two flasks with serum caps and argon pressure. The mixture was left for 1 hr and then SMEAH soln (0.25 ml, 1.8 mmol) was injected at −10°. A further amount of SMEAH soln (0.1 ml) was added after 30 min and the reaction was continued for another 30 min. The reaction was stopped by the addition of H_2O and the product was extracted with ether. The organic layer was washed with sat NaCl and dried with anhyd $MgSO_4$. The residue left after the evaporation of the solvent was acetylated with Ac_2O (1 ml) and anhyd pyridine (1 ml) overnight at room temp. The crude product obtained was chromatographed on a column of SiO_2. Elution with benzene-EtOAc (40:1) afforded **62** as a colorless oil (87 mg, 70% yield): IR (CCl_4) 1740, 1500, 1235, 1165, 880 cm^{-1}; NMR 1.04 (3 H, d, J = 6 Hz, $-\underset{|}{C}HCH_3$), 1.91, 2.00 (each 3 H, s, OAc), 3.90, 3.99 (2 H, AB q, J = 11 Hz, $-CH_2OAc$), 5.22 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 5.87 (1 H, m, $-CH_2C\underline{H}(OAc)-$), 6.32 (1 H, m, furan), 7.28 (1 H, m, furan), 7.32 (1 H, m, furan). When the mixture between **55** and β-furyl lithium was worked up without subsequent reduction and the crude product was purified by the chromatography on a column of SiO_2 or neutral Al_2O_3 (Woelm, activity II), **58** was obtained almost exclusively (63% yield). IR (CCl_4) 1670, 1300, 1170, 1105, 1055, 965, 870 cm^{-1}; NMR 0.95 (3 H, d, J = 6 Hz, $-\underset{|}{C}HCH_3$), 4.02, 4.14 (2 H, AB q, J = 10 Hz, $-CH_2O-$), 4.63 (1 H, s, $-CH=\underset{|}{C}-O-$), 5.28 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 6.40 (1 H, m, furan), 7.31 (1 H, t, J = 2 Hz, furan), 7.47 (1 H, m, furan).

Conversion of diacetate **62** *to furan derivative* **63**. A soln of **62** (87 mg, 0.23 mmol) in THF (1 ml) was added to Li (30 mg, 4.3 mg atom) dissolved in liquid NH_3 and the mixture was kept at −70 to −50° for 1 hr. After the addition of NH_4Cl, the dry ice-acetone bath was removed and NH_3 was allowed to evaporate. The residue was chromatographed on a column of SiO_2 and eluted with benzene-EtOAc (30:1) giving **63** as a colorless oil (29 mg, 46% yield): IR (CCl_4) 3440, 1500, 1160, 1060, 1025, 870 cm^{-1}; NMR (CCl_4) 0.97 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 3.46, 3.56 (2 H, AB q, $-CH_2OH$), 5.28 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 6.16, 7.12, 7.22 (each 1 H, m, furan).

Conversion of hydroxy lactone **37** *to ethylene acetal* **64**. The lactone **37** (89 mg, 0.34 mmol), dissolved in CH_2Cl_2 (3 ml), was added to a soln of the Collins' reagent prepared *in situ* from CrO_3 (300 mg, 3 mmol), pyridine (0.5 ml) and CH_2Cl_2 (10 ml).[39] The mixture was stirred at room temp for 40 min and then filtered through a column of SiO_2. After evaporation of the solvent, the residue was chromatographed on a column of SiO_2. Elution with benzene-EtOAc (20:1) gave **6** as an oil (61 mg, 69% yield): IR (CCl_4) 2690, 1785, 1730, 1170, 1150, 1015 cm^{-1}; NMR (CCl_4) 0.95 (3 H, d, J = 7.5 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.70 (3 H, br s, $-\underset{|}{C}=\underset{|}{C}CH_3$), 2.30, 2.41 (2 H, AB q, J = 16.5 Hz, $-CH_2CO_2-$), 4.00, 4.13 (2 H, AB q, J = 9.5 Hz, $-CO_2CH_2-$), 5.31 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 9.40 (1 H, s, −CHO). A mixture of **6** (61 mg, 0.23 mmol), ethylene glycol (3 ml), anhyd benzene (6 ml) and catalytic amount of TsOH was heated under refluxing for 4 hr, while the H_2O formed was removed by means of Dean-Stark apparatus. Usual workup gave **64** as a colorless oil (71 mg, 100% yield): IR (CCl_4) 1785, 1180, 1150, 1090, 1025 cm^{-1}; NMR (CCl_4) 0.91 (3 H, d, J = 6 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.63 (3 H, br s, $-\underset{|}{C}=\underset{|}{C}CH_3$), 2.27 (2 H, s, $-CH_2CO_2-$), 3.38 (4 H, m, $-OCH_2CH_2O-$), 3.95, 4.09 (2 H, AB q, J = 9.5 Hz, $-CO_2CH_2-$), 4.75 (1 H, s, $-CH\langle^{O}_{O}\rangle$), 5.25 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$).

Conversion of ethylene acetal **64** *to diacetate* **66**. A soln of β-furyl lithium, prepared from β-bromofuran (140 mg, 1 mmol) and n-BuLi (in hexane, 0.5 ml, 1.15 mmol), was added dropwise to a soln of **64** (71 mg, 0.23 mmol) in ether (5 ml) at −20°. The mixture was allowed to react for 1 hr at this temp and then SMEAH soln (0.5 ml), diluted with ether (1.5 ml), was added. After 1 hr, H_2O was added and the product was extracted with ether. The ether layer was washed with sat NaCl and dried with anhyd $MgSO_4$. Evaporation of the solvent left an oily residue which was acetylated with Ac_2O (1 ml) and pyridine (1 ml) overnight at room temp. The usual work-up followed by chromatographic purification (SiO_2) afforded an epimeric mixture of **66** as a colorless oil (72 mg, 67% yield): IR (CCl_4) 1740, 1260, 870 cm^{-1}; NMR (CCl_4) 0.78, 0.88 (3 H in total, each d, J = 7 Hz, $-\underset{|}{C}HC\underline{H}_3$), 1.62 (3 H, br s, $-CH=\underset{|}{C}C\underline{H}_3$), 1.72, 1.99 (each 3 H, s, -OAc × 2), 3.88 (6 H, m, $-C\underline{H}_2OAc$ and $-OCH_2CH_2O-$), 4.77 (1 H, s, $-CH\langle^{O}_{O}\rangle$), 5.20 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 5.90 (1 H, m, $-CH_2C\underline{H}(OAc)Fr$), 6.35 (1 H, m, furan), 7.26 (2 H, m, furan).

Furan derivative **38**

(a) *From diacetate* **66**. A soln of the diacetate (81 mg, 0.15 mmol) in THF (2 ml) was added to Li (75 mg, 11 mg, atom), dissolved in liquid NH_3 (15 ml) at −70°. The mixture was kept at −70~−50° for 1 hr and then quenched by the addition of NH_4Cl. After evaporation of NH_3, the product was taken up with ether and purified by SiO_2 chromatography giving **38** as a colorless oil (25 mg, 44% yield): IR (CCl_4) 3630, 3400, 1500, 1090, 1030, 870 cm^{-1}; NMR (CCl_4) 0.92 (3 H, d, J = 6.5 Hz, $-\underset{|}{C}HC\underline{H}_3$) 1.63 (3 H, br s, $-\underset{|}{C}=\underset{|}{C}CH_3$), 3.52 (2 H, s, $-CH_2OH$), 3.85 (4 H, m, $-OCH_2CH_2O-$), 4.78 (1 H, s, $-CH\langle^{O}_{O}\rangle$), 5.18 (1 H, m, $-\underset{|}{C}=C\underline{H}CH_2-$), 6.17, 7.12, 7.22 (each 1 H, m, furan).

(b) *From portulal* **1**. A soln of portulal (300 mg, 0.89 mmol) in anhyd t-BuOH (15 ml) was heated with DDQ (270 mg, 1.19 mmol) at 40–50° under N_2 for 4 hr. The mixture was diluted with $CHCl_3$ and washed with sat $NaHCO_3$. The

organic layer was dried with anhyd $MgSO_4$ and evaporated to leave an oily residue which was chromatographed on a column of SiO_2. Elution with benzene–EtOAc (33:1) afforded **39** as a pale yellow oil (262 mg, 93% yield): IR (CCl_4) 3625, 3500, 3035, 2680, 1720, 1495, 1025, 870 cm^{-1}; NMR (CCl_4) 0.93 (3H, d, $J = 6$ Hz, $-CHCH_3$), 1.64 (3H, br s, $-CH=CCH_3$), 3.52 (2H, s, $-CH_2OH$), 5.22 (1H, m, $-C=CHCH_2-$), 6.13, 7.10, 7.20 (each 1H, m, furan), 9.31 (1H, s, CHO). When **39** (262 mg) was treated with ethylene glycol and TsOH in benzene soln in the usual way, the corresponding acetal **38** (216 mg, 72% yield) was obtained.

Conversion of furan derivative **38** *to portulal ethylene acetal* **67**. A soln of **38** (164 mg, 0.46 mmol) and Rose Bengal (1.5 mg) in MeOH (20 ml) was irradiated with fluorescent light (20W × 6), while O_2 was bubbled through a fritted glass inlet. After 30 min's reaction, the solvent was evaporated and the residue was dissolved in anhyd THF (20 ml). To this soln was added SMEAH soln (1.7 ml) under ice-cooling. The mixture was allowed to stand for 1.5 hr and then worked up. The crude product, obtained by the extraction with EtOAc, was chromatographed on a column of SiO_2 and eluted with benzene-EtOAc (1:2–1:4) giving **67** as crystals (43 mg, 25% yield). Recrystallization from benzene–petroleum benzine furnished a pure specimen as prisms, m.p. 127–128°: IR ($CHCl_3$) 3400, 1233, 1085, 1010, 950 cm^{-1} NMR 0.93 (3H, d, $J = 7$ Hz, $CHCH_3$), 1.68 (3H, br s, $-C=CCH_3$), 3.61 (2H, s, $-CH_2OH$), 3.88 (4H, m, OCH_2CH_2O), 4.14 (4H, m, $HOCH_2C=CH$), 4.85 (1H, s, $-CH<$), 5.27 (1H, m, $-C=CHCH_2-$), 5.58 (1H, t, $J = 7$ Hz, $-C=CH$ CH_2OH). (Found: C, 69.15; H, 9.47. $C_{22}H_{36}O_5$ requires: C, 69.44; H, 9.47%).

Conversion of **67** *to portulal* **1**. A mixture of portulal ethylene acetal **67** (14 mg, 0.037 mmol), Ac_2O (0.4 ml) and pyridine (0.4 ml) was kept at room temp for 18 hr. Usual work-up, including EtOAc extraction, afforded the acetylated product (25 mg), which was dissolved in acetone (4 ml) and treated with 6% HCl (0.2 ml) at ambient temp for 2 hr. After the addition of $NaHCO_3$ to neutralize the soln, the solvent was evaporated. The residue was mixed with MeOH (4 ml) and 0.5 N NaOH (4 ml), and the mixture was allowed to react at room temp for 18 hr. Then it was diluted with H_2O and extracted with ether. The ether layer was washed with sat NaCl and dried with anhyd $MgSO_4$. The residue, left after the evaporation of the solvent, was purified by SiO_2 chromatography (EtOAc elution) and crystallization from aq MeOH giving portulal **1** as colorless needles, m.p. 117–118°. The identity with natural portulal **1** was confirmed by mixed m.p. determination and, comparison of tlc behavior and spectroscopic data (IR and NMR).

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