The Synthesis of (±)-Glutinosone[1)]

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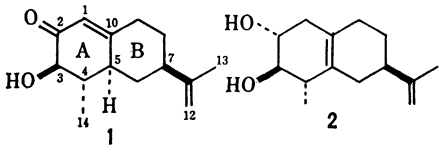
The synthesis of (±)-glutinosone, an antifungal norsesquiterpene from *Nicotiana glutinosa* infected with tobacco mosaic virus, is described. It has been completed by two processes, one being based on the Robinson annelation method and another on a modification of the Dastur procedure.

In the preceding paper[1b)] we reported the structure elucidation of (+)-glutinosone (**1**), a norsesquiterpene isolated from leaves of *Nicotiana glutinosa* infected with tobacco mosaic virus and qualified as a phytoalexin.[2)] The structure and configuration of **1** are characterized by a noreudesmane skeleton with a double bond at an angular position as well as three asymmetric centers in the A ring susceptible to facile aromatization. We now report that the synthesis of (±)-glutinosone [(±)-**1**] has been completed by two independent procedures.

The first synthesis[3)] of (±)-glutinosone was achieved by stereoselective functionalization of the A ring of a *trans*-decalin derivative and subsequent introduction of a double bond at the angular position, as in the case of that[4)] of rishitin (**2**). The Robinson annelation[5)] of dimethyl *trans*-2-oxocyclohexane-1,4-dicarboxylates[6)] (**3**) with 1-diethylamino-3-pentanone methiodide and sodium methoxide produced a 1 : 1 mixture of C-7-epimers of dimethyl 4-methyl-3-oxooctahydronaphthalene-7,10-dicarboxylates[7)] (**4**) in a 52% yield. The octalone mixture (**4**), when hydrogenated over 10% palladium–charcoal in acetic acid, treated with acid ($HClO_4$ in acetic acid) and then with base ($NaOCH_3$ in methanol), and esterified with diazomethane,[5,8)] was converted into a *trans*-decalone (**5**), mp 105—106 °C, showing a single peak by GLPC and TLC, in a 66% yield. The spectral data [*m/e* 282 (M^+); ν_{max} 1735, 1720, and 1169 cm^{-1}; δ 1.08 (3H, d, J=7 Hz, $C\underline{H}_3$ at C-4), 3.06 (1H, do q, J=11, 7, 7, and 7 Hz, 4-H), 3.71 and 3.79 (each 3H, s, $COOC\underline{H}_3$)] were in good accord with the structure (**5**).

Functionalization of the A ring of the *trans*-decalone was commenced by treatment of **5** with isopropenyl acetate and *p*-toluenesulfonic acid (*p*-TsOH) under reflux to give the corresponding enol acetate (**6**) in a 91% yield, in which the location of the double bond at C-2–C-3 was revealed by the NMR spectrum [δ 5.27 (1H, br d, J=6 Hz, 2-H) and 1.04 (3H, d, J=7 Hz, $C\underline{H}_3$ at C-4)]. The compound (**6**), when oxidized with perbenzoic acid, was converted almost quantitatively into 2α,3α-epoxy 3-acetate (**7**), mp 138—139 °C. The α-configuration of the epoxy group was deduced tentatively from attack of the reagent from the less-hindered side (α) and confirmed by the following reactions. Treatment of the epoxy acetate (**7**) with acid (*p*-TsOH in acetic acid, room temp)[10)] effected rearrangement to give 3-oxo 2α-acetate (**8**), mp 142—143 °C, in a 90% yield. Further treatment of **8** with tetramethylammonium acetate in acetone[11)] led to formation of a 1 : 1 equilibrium mixture of the starting 3-oxo 2α-acetate (**8**) and its isomeric 2-oxo 3β-acetate (**9**), mp 131—132 °C, from which the latter (**9**) could be isolated in a 46% yield. The structure and configuration of the two oxo acetates were determined on the basis of the NMR spectra: **8**, δ 1.68 (1H, t, J=13 Hz, 1α-H), 2.59 (1H, do d, J=13 and 6 Hz, 1β-H), and 5.05 (1H, do d, J=13 and 6 Hz, 2β-H); **9**, δ 2.36 and 2.76 (each 1H, ABq, J=14 Hz, 1-H) and 4.86 (1H, d, J=10.5 Hz, 3α-H). The 2-oxo 3β-acetate (**9**) was then derived smoothly to the 3,3-ethylene acetal (**10**), mp 126—128 °C, in an 85% yield by a standard procedure.

Transformation of the methoxycarbonyl group at



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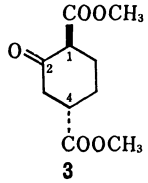

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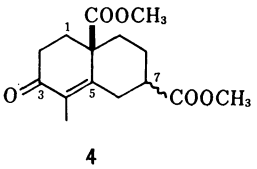

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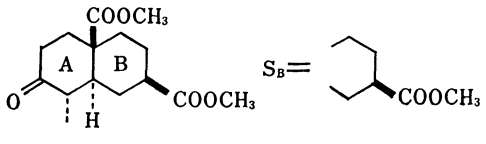

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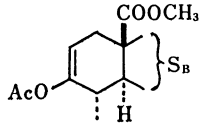

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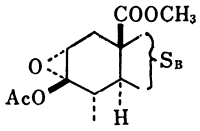

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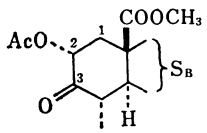

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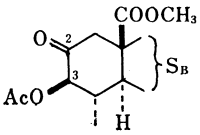

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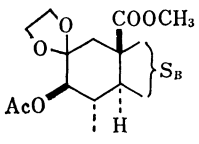

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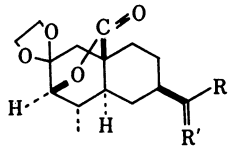
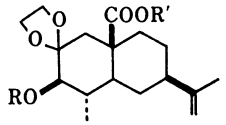
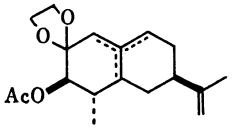
C-7 into an isopropenyl group was carried out by a modification[12] of the Wittig reaction; treatment of **10** with a *large excess* of methylenetriphenylphosphorane in dimethyl sulfoxide (DMSO) at 50 °C for 3 h produced a mixture of δ-lactones, which was separated roughly into two fractions by chromatography. One fraction eluted early afforded isopropenyl δ-lactone (**11**), mp 108—110 °C, in a 22% yield. On the other hand, another fraction eluted later, consisting mainly of acylated phosphorane (**11a**),[12] was hydrolyzed with base (10% KOH in methanol), treated with acetic anhydride and pyridine, and then purified by chromatography to give acetyl δ-lactone (**12**), mp 146—148 °C, in a 50% yield from **10**. The latter (**12**) was again submitted to the Wittig reaction under usual conditions [$(C_6H_5)_3P{=}CH_2$ (3 mol equiv) in DMSO], giving the afore-mentioned δ-lactone (**11**) in an 88% yield. In accordance with the assigned noreudesmane structure, compound **11** displayed following spectra: *m/e* 292 (M^+); ν_{max} 1757 (δ-lactone), 1642 and 895 cm^{-1} (terminal methylene); δ 1.24 (3H, d, J=7 Hz, 14-H), 1.68 (3H, s, 13-H), 1.85 and 2.08 (each 1H, ABq, J=14 Hz, 1-H), 3.97 (4H, br s, W_H=5 Hz, $OC_2\underline{H}_4O$), 4.07 (1H, d, J=3 Hz, 3-H), and 4.68 (2H, br s, W_H=4 Hz, 12-H).



11 R=CH_3, R′=CH_2
11a R=CH=$P(C_6H_5)_3$, R′=O
12 R=CH_3, R′=O



13 R=R′=H
13a R=Ac, R′=H
13b R=Ac, R′=CH_3



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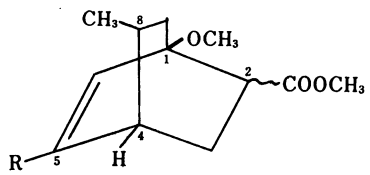
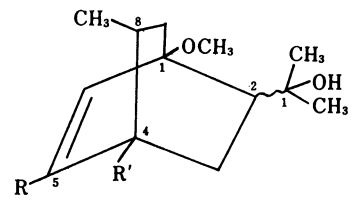
Hydrolysis of the δ-lactone (**11**) with base (10% KOH in methanol) produced hydroxy acid (**13**), mp 201—203 °C, in a 97% yield, which, on treatment with acetyl chloride and pyridine in ethyl acetate, was converted into the corresponding acetate (**13a**), mp 238—241 °C, in an 80% yield without regeneration into the δ-lactone (**11**). The acid was smoothly esterified with diazomethane into the methyl ester (**13b**), mp 139—140 °C. Treatment of the acid (**13a**) with lead(IV) acetate and pyridine in *N,N*-dimethylformamide (DMF) at room temperature[13] resulted in oxidative decarboxylation to give an olefin mixture (**14**) in a 78% yield. The olefins (**14**), when treated with base without further purification and then with triphenylmethyl fluoroborate in dichloromethane at room temperature,[14] were transformed into a mixture containing phenols, from which an α,β-unsaturated ketone, mp 63—65 °C, was obtained as a sole isolable product in a 30% yield. The ketone exhibited the following spectra: *m/e* 220 (M^+), 192, 191, 162, 147, 134, 121, and 94 (base); λ_{max} 234 nm (ε 13400); ν_{max} 3490, 1676, 1621, and 896 cm^{-1}; δ 1.22 (3H, d, J=6 Hz, 14-H), 1.73 (3H, s, 13-H), 3.72 (1H, s, OH), 3.77 (1H, d, J=12 Hz, 3-H), 4.72 (2H, br s, W_H=5 Hz, 12-H), and 5.89 (1H, br s, W_H=4.5 Hz, 1-H). All these spectra were identical with those reported for glutinosone[1b,2] (**1**), establishing a synthesis of (±)-glutinosone [(±)-**1**]. The overall yield amounted to 2.80% from compound **3**.

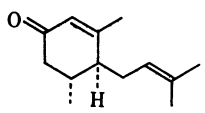
The second, improved synthesis of (±)-glutinosone was completed mostly according to a modification of the Dastur elegant procedure[15] for synthesis of (±)-nootkatone. The Diels-Alder reaction[16] of 3,6-dihydro-3,5-dimethylanisole, prepared by the Birch reduction of 3,5-dimethylanisole, with methyl acrylate at 150 °C in the *absence* of Lewis acids[16] afforded a 1:3 mixture of methyl 1-methoxy-5,8-dimethylbicyclo[2.2.2]oct-5-ene-2-carboxylates (**15a** and **15b**). While the mixture was used for subsequent transformations without further purification, it was separated by chromatography to yield each diastereoisomer (**15a** and **15b**). The spectral data of each isomer [**15a**, δ 0.81 (3H, d, J=6 Hz, $C\underline{H}_3$ at C-8) and 2.66 (1H, do do d, J=11, 5, and 2.5 Hz, 2-H); **15b**, δ 0.83 (3H, d, J=6 Hz) and 2.78 (1H, do d, J=9 and 6 Hz)] and the following reaction indicated that (i) these isomers differed only in the configuration at C-2 and (ii) the methyl group at C-8 would probably be oriented *anti* to the secondary bridge and hence *cis* to the hydrogen atom at C-4; namely, each of these esters (**15a** and **15b**) was converted smoothly into the corresponding tertiary alcohols (**16a** and **16b**) in 90 and 90% yields. The respective alcohols, when treated with acid ($HClO_4$ in acetic acid), produced the same dienone (**17**), showing the following spectra: *m/e* 193 and 192 (M^+); ν_{max} 1670 and 1626 cm^{-1}; δ 1.02 (3H, d, J=6 Hz), 1.64, 1.73, and 1.97 (each 3H, s), 5.11 (1H, br t, J=6 Hz), and 5.76 (1H, br s, W_H=5 Hz).



15a R=CH_3, *exo*-$COOCH_3$
15b R=CH_3, *endo*-$COOCH_3$
18 R=CHO
19 R=CH=CH_2



16a R=CH_3, R′=H, *exo*-$C(CH_3)_2OH$
16b R=CH_3, R′=H, *endo*-$C(CH_3)_2OH$
20 R=CH=CH_2, R′=H
22 R=CH=CH_2, R′=CH_3



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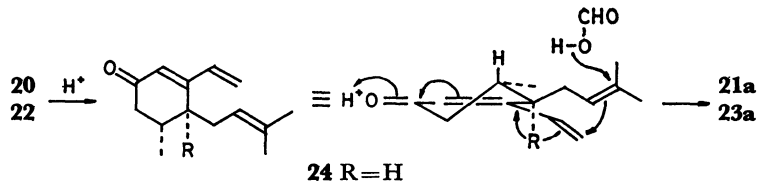
Treatment of the mixture (**15a** and **15b**) with selenium(IV) oxide in dioxane effected selective oxidation of the olefinic methyl group to give α,β-unsaturated

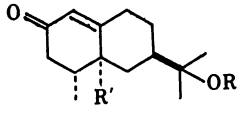


24 R=H
25 R=CH_3

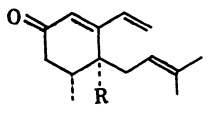
Scheme 1.

aldehydes (**18**) [λ_{max} 233 nm (ε 8700); ν_{max} 2705 and 1680 cm^{-1}; δ 9.40 and 9.46 (total 1H, each s, CHO)] in a 77% yield. The Wittig reaction of aldehydes **18** under usual conditions [$(C_6H_5)_3P=CH_2$ (1.1 mol equiv) in DMSO at room temp] led to formation of dienes (**19**) in a 63% yield with recovery of the starting aldehydes (31%). The dienes (**19**) was then submitted to the Grignard reaction with an excess of methyllithium to yield the corresponding tertiary alcohols (**20**) almost quantitatively. The spectra were consistent with the assigned formulas (Experimental).

Treatment of the alcohols (**20**) with formic acid at room temperature followed by neutralization produced a mixture of bicyclic enones, which were isolated as the tertiary alcohol (**21**) and its formate (**21a**) in 45 and 41% yields, respectively. Naturally the formate (**21a**) was hydrolyzed easily to give the alcohol (**21**) in an 88% yield. This acid transformation of the bicyclooctenes (**20**) into the bicyclic enones (**21** and **21a**) would probably proceed *via* the same process (Scheme 1) as that proposed by Dastur for that of the corresponding 4-methyl derivatives (**22**), in which he emphasized the presence of the relevant methyl group as a factor controlling the configuration of C-7 in the resulting bicyclic enones (**23** and **23a**) (*cf.*, Schemes II and III in Ref. 15). However, the present high yield (86%) formation of the desired bicyclic enones (**21** and **21a**) indicates that, contrary to the Dastur rationalization,[15] the methyl group in question does not an important role in the cyclization of proposed intermediates (**24** and **25**). The structure of the alcohol (**21**) was supported completely by the spectral data: *m/e* 223 (M^++1) and 204; λ_{max} 237 nm (ε 14300); ν_{max} 3440, 1660, and 1624 cm^{-1}; δ 1.09 (3H, d, J=6 Hz, 14-H), 1.20 (6H, s, 12- and 13-H), and 5.81 (1H, br s, W_A=4 Hz, 1-H).

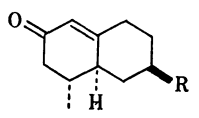


21 R=R'=H
21a R=CHO, R'=H
23 R=H, R'=CH_3
23a R=CHO,R'=CH_3

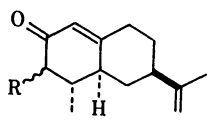


24 R=H
25 R=CH_3

Transformation of the intermediates (**21** and **21a**) into (±)-glutinosone was carried out in usual manners. Treatment of **21** with thionyl chloride in pyridine resulted in dehydration to yield an olefin mixture, which was separated by chromatography over silica gel containing 10% silver nitrate to give isopropenyl (**26**) and isopropylidene bicyclic enones (**27**) in 41 and 20% yields, respectively: **26**, ν_{max} 891 cm^{-1}; δ 1.75 and 4.73 (3H and 2H, each s, 13- and 12-H); **27**, δ 1.70 (6H, br s, 12- and 13-H). Likewise, the formate (**21a**), when treated with aluminium(III) oxide in collidine under reflux, produced a complex mixture, from which compounds **26** and **27** were isolated in 41 and 11% yields, respectively. Oxidation of the isopropenyl bicyclic enone (**26**) with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −70 °C and then with the molybdenum peroxide complex MoO_5·Py·HMPA (MoOPH)[17] effected only hydroxylation at C-3 to afford a mixture of diastereoisomeric hydroxy ketones in a rather good yield (60%), with the starting ketone (**26**) (20%), from which equatorial and axial acetoxy ketones (**28a** and **29a**) were isolated in 33 and 59% yields, respectively, after acetylation and subsequent purification by preparative TLC: **28a**, ν_{max} 1753 cm^{-1}; δ 5.10 (1H, d, J=12 Hz, 3-H): **29a**, ν_{max} 1748 cm^{-1}; δ 5.47 (1H, d, J=5 Hz). These acetoxy ketones (**28a** and **29a**) were hydrolyzed with base (K_2CO_3 in ethanol) to give the corresponding hydroxy ketones (**28** and **29**) in 60 and 55% yields, respectively. The former (**28**), mp 64—66 °C, exhibited the same spectra as synthetic and natural samples of glutinosone, constituting an alternate, more efficient synthesis of (±)-glutinosone [(±)-**1**]. The synthesis involved only nine steps and the overall yield amounted to 3.64% from the bicyclooctanone mixture (**15a** and **15b**).



26 R=−C(=CH_2)CH_3
27 R=−C(CH_3)$_2$



28 [=(±)-**1**] R=β-OH
28a R=β-OAc
29 R=α-OH
29a R=α-OAc

Experimental

All the melting points were uncorrected. The homogeneity of each compound was checked by TLC on silica gel (Wakogel B-5F) with various solvent systems, and the spots were developed with cerium(IV) sulfate in dil sulfuric acid. The UV, IR, and NMR (^{1}H-NMR) spectra were measured in ethanol, chloroform, and chloroform-*d*, respectively, unless otherwise stated. Abbreviations "s, d, t, q, m, br, and do" in the NMR spectra denote "singlet, doublet, triplet, quartet, multiplet,

broad, and double," respectively. The preparative TLC and column chromatography were carried out over silica gel (Wakogel B-5F, 20×20 cm²) and over silica gel (Merck, Kieselgel 60, 70—230 mesh), respectively.

The Robinson Annelation of Dimethyl trans-*2-Oxocyclohexane-1,4-dicarboxylate (3).* Compound **3** (1.08 g) was prepared by addition of an ether solution saturated with diazomethane into the corresponding diacid[6] (0.94 g) in ether (5 ml). The ester (**3**) had mp 99—100 °C (from methanol) (lit,[6] 75—77 °C) and showed the following spectra: MS, *m/e* 214 (M^+), 183, 182, 155, 154, and 123 (base); IR, ν_{max} (Nujol) 1732, 1704, 1201, 1162, and 1031 cm^{-1}; NMR δ 2.70 (1H, m, 4-H), 3.42 (1H, do d, J=9 and 5 Hz, 1-H), 3.74 and 3.78 (each 3H, s, $COOCH_3$). Found: C, 56.19; H, 6.78%. Calcd for $C_{10}H_{14}O_5$: 56.07; H, 6.59%.

To a methanol solution containing sodium methoxide, prepared from sodium (48 mg) and methanol (1 ml), were added **3** (264 mg) in methanol (9.0 ml) and then 1-diethylamino-3-pentanone methiodide in methanol, prepared from 1-diethylamino-3-pentanone (203 mg) and methyl iodide (267 mg) in methanol (1.0 ml). The whole mixture was stirred at room temperature for 17 h and then refluxed for 4.5 h. After being cooled, the mixture was evaporated and shaken with water and ether (6×20 ml). The ether solution was washed with 10% aq sodium carbonate (Na_2CO_3) and water, dried over anhydrous sodium sulfate, and evaporated to leave an oily substance, which was purified by preparative TLC over silica gel with chloroform to yield a 1:1 (by GLPC) mixture of 4-methyl-3-oxooctahydronaphthalene-7,10-dicarboxylates[7] (**4**, 181 mg): MS, *m/e* 280 (M^+), 248, 221, 220, and 161 (base); UV, λ_{max} 246 nm (ε 12400); IR, ν_{max} (neat) 1725, 1664, 1617, and 1175 cm^{-1}; NMR, δ 1.88 and 1.91 (each 1.5H, s, CH_3 at C-4), 3.67 and 3.71 (each 1.5H, s, $COOCH_3$ at C-7), and 3.75 (3H, s, $COOCH_3$ at C-10).

*Dimethyl (4*RS, *5*RS, *7*SR, *10*SR*)-4-Methyl-3-oxo-decahydronaphthalene-7,10-dicarboxylate (5).* Compounds **4** (494 mg) were hydrogenated over 10% palladium-charcoal in acetic acid at room temperature for 15 h. After removal of the catalyst by filtration and subsequent addition of 60% aq $HClO_4$ (one drop), the mixture was again stirred at room temperature for 15 h, diluted with water, and extracted with ether (3×20 ml). The ether extracts were worked up as usual to leave oily residue (480 mg), which was dissolved in methanol (4.0 ml). The methanol solution was added to methanol containing sodium methoxide, prepared from sodium (167 mg) and methanol (6.0 ml), and the whole mixture was refluxed under nitrogen for 40 min. After being cooled, the mixture was evaporated below 30 °C, diluted with water, made acidic with dil sulfuric acid, and extracted with ether (3×20 ml). The ether solution was washed with water, dried and mixed with an ether solution saturated with diazomethane, and evaporated to leave a crystalline substance (**5**, 327 mg), which was so pure as to be used for the next reactions. This was recrystallized from hexane-acetone for analysis and had mp 105—106 °C: MS, *m/e* 282 (M^+), 250, 223, 222, 163, 162, and 145 (base); IR (Nujol) and NMR, in the text. Found: C, 63.75; H, 7.80%. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85%.

*Dimethyl (4*RS, *5*RS, *7*SR, *10*SR*)-3-Acetoxy-4-methyl-1,4,5,-6,7,8,9,10-octahydronaphthalene-7,10-dicarboxylate (6) and Its 2α,-3α-Epoxide (7).* i) A solution of **5** (4.40 g) in isopropenyl acetate (23.0 ml) was evaporated slowly in the presence of *p*-TsOH (416 mg) for 13 h, the acetate (total 13 ml) being added dropwise during the time, when 16 ml of the acetate had been removed. After addition of water, the reaction mixture was mixed with water and extracted with ether (3×50 ml). The ether solution was washed with 5% aq sodium hydrogencarbonate ($NaHCO_3$) and water, dried and evaporated to leave an oily substance, which was purified by chromatography over silica gel. Fractions eluted with benzene–ether (19:1) afforded **6** (4.56 g), showing a single spot on TLC: MS, *m/e* 324 (M^+) and 282 (base); IR, ν_{max} (neat) 1762, 1742, 1734, 1683, 1210, 1180, 1151, and 1123 cm^{-1}; NMR, δ 1.04 (3H, d, J=7 Hz, CH_3 at C-4), 2.10 (3H, s, $OCOCH_3$), 2.64 (1H, do d, J=16 and 6 Hz, 1β-H), 3.69 (6H, s, $COOCH_3$), and 5.27 (1H, br d, J=6 Hz, 2-H). Found: C, 63.10; H, 7.55%. Calcd for $C_{17}H_{24}O_6$: C, 62.95; H, 7.41%.

ii) To a solution of **6** (5.54 g) in chloroform (30 ml) cooled with ice-water was added dropwise perbenzoic acid (purity 94%, 4.77 g) in chloroform (20 ml). The mixture was allowed to stand in a refrigerator for 15 h, and washed with 5% aq sodium hydrogensulfite ($NaHSO_3$), 5% aq $NaHCO_3$ and water, dried and evaporated to leave a crystalline substance (**7**, 5.80 g), mp 138—139 °C; NMR, δ 1.18 (3H, d, J=7 Hz, CH_3 at C-4), 2.05 (3H, s, $OCOCH_3$), 2.84 (1H, do d, J=15 and 6 Hz, 1β-H), 3.43 (1H, d, J=6 Hz, 2-H), 3.69 and 3.77 (each 3H, s, $COOCH_3$). This was used for the next reaction without purification.

*Dimethyl (2*SR,*4*SR,*5*RS,*7*SR,*10*SR*)-2-acetoxy-4-methyl-3-oxodecahydronaphthalene-7,10-dicarboxylate (8), Its 3-Acetoxy-2-oxo Isomer (9), and Its 3,3-Ethylene Acetal (10).* i) Compound **7** (2.5 g) was treated with *p*-TsOH (0.8 g) in acetic acid (100 ml) at room temperature for 14 h under stirring. The mixture, after being worked up as usual, afforded a crystalline substance (**8**, 2.3 g), which was so pure as to be used for the next rearrangement. The sample was recrystallized from hexane–acetone to give an analytical sample, mp 142—143 °C: MS, *m/e* 340 (M^+), 298, 281, 280, 266, 254, 238, and 226 (base); IR, ν_{max} (Nujol) 1762, 1735, 1730, 1237, and 1166 cm^{-1}; NMR, δ 1.09 (3H, d, J=7 Hz, CH_3 at C-4), 1.68 (1H, t, J=13 Hz, 1α-H), 2.14 (3H, s, $OCOCH_3$), 2.30 (1H, do d, J=10 and 2 Hz, 7-H), 2.59 (1H, do d, J=13 and 6 Hz, 1β-H), 3.18 (1H, do q, J=11, 7, 7, and 7 Hz, 4-H), 3.68 and 3.79 (each 3H, s, $COOCH_3$), and 5.05 (1H, do d, J=13 and 6 Hz, 2-H). Found: C, 59.98; H, 7.12%. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11%.

ii) An acetone solution (50 ml) containing **8** (1.16 g) was refluxed with tetramethylammonium acetate (0.72 g) for 16 h. The mixture was evaporated, mixed with water and extracted with ethyl acetate (3×50 ml). The acetate solution was washed with saturated brine, dried and evaporated to leave amorphous residue (1.18 g), which was separated by chromatography over silica gel (60 g) with a 4:3:2 mixture of hexane, ether and diisopropyl ether. Fractions eluted early afforded the starting material (**8**, 0.63 g), while those eluted later gave a crystalline substance (**9**, 0.53 g), which on recrystallization from hexane–acetone had mp 131—132 °C: MS, *m/e* 340 (M^+) and 298 (base); IR, ν_{max} (Nujol) 1735, 1242, 1212, and 1172 cm^{-1}; NMR, δ 1.10 (3H, d, J=7 Hz, CH_3 at C-4), 2.36 and 2.76 (each 1H, ABq, J=14 Hz, 1-H), 3.67 and 3.69 (each 3H, s, $COOCH_3$), and 4.86 (1H, d, J=10.5 Hz, 3-H). Found: C, 60.18; H, 7.12%. Calcd for $C_{17}H_{24}O_7$: C, 59.99; H, 7.11%.

iii) A solution of **9** (390 mg) in benzene (20 ml) was refluxed with ethylene glycol (0.4 ml) in the presence of *p*-TsOH (75 mg) for 20 h, water being removed by a Dean-Stark apparatus. The solution was cooled, evaporated, mixed with water and extracted with ethyl acetate (3×50 ml). The acetate solution was worked up as usual to leave amorphous residue (490 mg), which crystallized on trituration with hexane–acetone, and was collected by filtration and amounted to 130 mg. The filtrate was concentrated and then purified by chromatography over silica gel (9 g) with benzene–ether (6:1) to give an additional crystalline substance (250 mg). Both the crystal-

line substances (**10**, 380 mg) were recrystallized from hexane–acetone to give an analytical sample, mp 126—128 °C: MS, *m/e* 384 (M^+), 352, and 325 (base); IR, ν_{max} (Nujol) 1748, 1736, 1237, 1199, 1181, 1157, 1069, and 1032 cm^{-1}; NMR, δ 0.89 (3H, d, J=7 Hz, CH_3 at C-4), 2.09 (3H, s, $OCOCH_3$), 2.20 (1H, d, J=14 Hz, 1β-H), 3.66 (6H, s, $COOCH_3$), 3.90 (4H, br m, $C_2H_4O_2$), and 4.72 (1H, d, J=11 Hz, 3-H).

*(3RS,4RS,5RS,7SR,10SR)-7-Isopropenyl- (**11**) and (3RS,-4RS,5RS,7SR,10SR)-7- Acetyl-4-methyl-2-oxodecahydronaphthalene 10,3-Carbolactone 3,3-Ethylene Acetal (**12**).* i) To a solution of methyltriphenylphosphonium iodide (1.31 g) in DMSO (8.0 ml) was added a hexane solution (2.16 ml) containing 15% butylithium, and the whole solution was stirred at room temperature for 2 h. To a part (3.16 ml, 1.10 mmol equiv) of the ylide solution was added dropwise **10** (44 mg) in DMSO (1.5 ml). The mixture was stirred at room temperature for 1 h and then at 50 °C for 3 h, and the reaction was ceased by addition of water. The reaction mixture was ceased by addition of water. The reaction mixture was extracted with ethyl acetate (5×50 ml), and the acetate extracts were washed with saturated brine, dried and evaporated to leave resinous material (242 mg), which was submitted to chromatography over silica gel (7 g). Fractions eluted with benzene–ether (7: 1) afforded a crystalline substance (**11**, 7 mg), which was recrystallized from hexane–acetone to give an analytical sample, mp 108—110 °C; MS, *m/e* 292 (M^+, base), 207, 204, 165, 149, and 138; IR, ν_{max} 3100, 1757, 1642, 1192, 1097, and 895 cm^{-1}; NMR, δ 1.24 (3H, d, J=7 Hz, 14-H), 1.68 (3H, s, 13-H), 1.85 and 2.08 (each 1H, ABq, J=14 Hz, 1-H), 3.97 (4H, br s, W_H=5 Hz, $C_2H_4O_2$), 4.07 (1H, d, J=3 Hz, 3-H), and 4.68 (2H, br s, W_H=4 Hz, 12-H). Fractions eluted with methanol were combined and evaporated, and the residue (210 mg) was refluxed with 10% potassium hydroxide (KOH) in methanol (20 ml) for 2 d. The reaction mixture was evaporated, mixed with water, made acidic with 3M hydrochloric acid (HCl), and extracted with ethyl acetate (4× 50 ml). The acetate solution was worked up as usual to leave amorphous residue (540 mg), which was purified by chromatography over silica gel (24 g). Fractions eluted with benzene–ether (5: 1) afforded a crystalline substance (**12**, 17 mg), which was recrystallized from hexane–acetone to give an analytical sample, mp 146—148 °C; MS, *m/e* 294 (M^+), 251, 209, 208, 149, and 99 (base); IR, ν_{max} 1760, 1710, 1176, and 1099 cm^{-1}; NMR, δ 1.29 (3H, d, J=7 Hz, 14-H), 1.89 and 2.15 (each 1H, ABq, J=15 Hz, 1-H), 2.18 (3H, s, $COCH_3$), 4.01 (4H, br s, W_H=4.5 Hz, $C_2H_4O_2$), and 4.12 (1H, d, J=3 Hz, 3-H).

ii) To a solution of methylenetripehnylphosphorane, prepared by addition of 15% butyllithium in hexane (0.22 ml) to methyltriphenylphosphonium iodide (164 mg) in DMSO (1 ml) and stirring at room temperature for 2.5 h, was added **12** (43 mg) in DMSO (1.5 ml). The solution was stirred at room temperature for 1.5 h and then at 50 °C for 5.5 h. The reaction mixture was worked up as described above to leave amorphous residue, which was purified by chromatography over silica gel (10 g) with benzene–ether (7: 1) to give **11** (37 mg), mp 107—110 °C, identical with an authentic sample (IR and NMR).

*(3RS,4RS,5RS,7SR,10SR)-3-Hydroxy-7-isopropenyl-4-methyl-3-oxodecahydronaphthalene-10-carboxylic Acid 3,3-Ethylene Acetal (**13**), Its 3-Acetate (**13a**), and Its Methyl Ester (**13b**).* Compound **11** (62 mg) was refluxed with 10% KOH in methanol (8 ml) for 3 h. After being cooled, the reaction mixture was evaporated, mixed with water, acidified with 3M HCl, and extracted with ethyl acetate (7×30 ml). The acetate extracts were worked up as usual to leave an amorphous substance (**13**, 72 mg), which on trituration with ether crystallized and had mp 201—203 °C: IR, ν_{max} (Nujol) 3325, 1715, 1642, 1180, 1165, 1074, 1039, and 890 cm^{-1}; NMR, δ 1.11 (3H, d, J=7 Hz, 14-H), 1.73 (3H, s, 13-H), 3.21 (1H, d, J=10.5 Hz, 3-H), 4.04 (4H, br s, W_H=7 Hz, $C_2H_4O_2$), and 4.72 (2H, br s, W_H=4 Hz, 12-H).

The crude sample (72 mg) of **13** was stirred with acetyl chloride (0.1 ml) and pyridine (0.2 ml) in ethyl acetate (3 ml) at room temperature for 14 h. The reaction mixture was worked up as usual to leave amorphous residue (96 mg), which was purified by preparative TLC (2 plates) over silica gel, a 20: 1 mixture of benzene and acetic acid being used as a solvent, to give an amorphous substance (**13a**, 60 mg), which on trituration with ether crystallized and had mp 238—241 °C; IR, ν_{max} 2750—2580, 1739, 1711, 1644, 1237, 1036, and 893 cm^{-1}; NMR, δ 0.88 (3H, d, J=7 Hz, 14-H), 1.71 and 2.11 (each 3H, s, 13-H and $OCOCH_3$), 2.50 (1H, d, J=14 Hz, 1β-H), 3.96 (4H, br m, W_H=18 Hz, $C_2H_4O_2$), and 4.71 (2H, s, 12-H), 4.76 (1H, d, J=11 Hz, 3-H), and 6.60 (1H, br s, OH).

The 3-acetate (**13a**) was converted quantitatively into the methyl ester (**13b**), mp 139—140 °C (from hexane–acetone) with diazomethane in ethyl by a standard procedure; MS, *m/e* 366 (M^+), 334, 307, 278, 239, 218, and 183 (base); IR, ν_{max} 1738, 1645, 1240, 1175, 1035, and 897 cm^{-1}; NMR, δ 0.86 (3H, d, J=6 Hz, 14-H), 1.63, 2.07, and 3.63 (each 3H, 13-H, $OCOCH_3$, and $COOCH_3$), 3.79 (4H, br m, W_H=30 Hz, $C_2H_4O_2$), 4.65 (2H, s, 12-H), and 4.70 (1H, d, J=11 Hz, 3-H).

*Transformation of **13a** into (±)-Glutinosone [(±)-**1**].* A solution of **13a** (23.6 mg) in DMF (3 ml) containing pyridine (0.2 ml) was stirred with lead(IV) acetate (123.6 mg) in DMF (3 ml) at room temperature for 3 h. After addition of water, the mixture was made acidic with 3M aq HCl and extracted with ethyl acetate (5×20 ml). The acetate solution was worked up as usual to leave oily residue, which was separated by chromatography over silica gel (20 g). Fractions eluted with benzene–ether (5: 1) afforded an oily olefin mixture (**14**, 18.3 mg); ν_{max} 1737, 1644, 1374, 1244, 1043, and 895 cm^{-1}; NMR, δ 0.95 and 1.13 (total 3H, each d, J=7 Hz, 14-H), 4.93, 4.99, and 5.13 (total 1H, each d, J=11, 10, and 13 Hz, 3-H), 5.54 and 5.90 (total 2/3H, each br s, W_H=9 and 5 Hz, 1- and 9-H).

The olefin mixture (**14**, 18.3 mg) was stirred with 5% KOH in methanol (1.5 ml) at room temperature for 70 min. The reaction mixture was worked up as described before to leave oily material (14.5 mg), which was stirred with triphenylmethyl fluoroborate (28.8 mg) in dichloromethane (2.1 ml) at room temperature for 1 h. The reaction mixture was then stirred with 5% aq $NaHCO_3$ (2 ml) at room temperature for 10 min. The aqueous layer was extracted with chloroform (2×10 ml). The dichloromethane and chloroform solutions were combined, washed with saturated brine, dried and evaporated to leave oily residue (35.8 mg), which was separated by preparative TLC (2 plates) over silica gel with benzene–ether (5: 1) to give an oily substance (3.3 mg, 23% from **13a**), whose spectra (in the text) were completely identical with the reported of natural glutinosone (**1**). The resulting (±)-glutinosone crystallized on standing and had mp 63—65 °C.

The Diels-Alder Reaction of 3,6-Dihydro-3,5-dimethylanisole and Methyl Acrylate. A mixture of the dihydroanisole[16] (47.6 g) and methyl acrylate (100.8 g) was heated at 150—155 °C (bath temp) for 40 h in an autoclave. After being cooled, the mixture was evaporated under reduced pressure, when most of excess of the acrylate and the dihydroanisole (10.6 g) were recovered at room temperature (8 Torr) and at 90—100 °C (8 Torr), respectively. The residue was then distilled to give a *crude* adduct (34.3 g) at 80—100 °C (0.3 Torr), which was used for the next reaction without further purification. A

part (3.9 g) of the crude adduct was separated by chromatography over silica gel, benzene and benzene–ether mixtures being used as solvents. Early fractions eluted with benzene and benzene–ether (50: 1) afforded an oily substance (1.26 g), which was assigned formula **30** [methyl 2-(3,5-dimethylphenyl)propionate] on the basis of the spectral data and the analogous examples:[18] MS, *m/e* 192 (M^+) and 133 ($M^+-COOCH_3$); IR, ν_{max} (neat) 1743, 1605, 1198, 1175, and 1164 cm^{-1}; NMR, δ 1.46 (3H, d, $J=7$ Hz, 3-H), 2.27 (6H, s, CH_3 at C-3′ and C-5′), 3.64 (3H, s, $COOCH_3$), 3.66 (1H, q, $J=7$ Hz, 2-H), and 6.91 (3H, br s, $W_H=4$ Hz, 2′-, 4′-, and 6′-H). Middle fractions eluted with benzene–ether (20: 1) gave an exo-adduct, methyl 1-methoxy-5,8-dimethylbicyclo[2.2.2]oct-5-ene-2-carboxylate (**15a**, 0.21 g), showing a single spot on TLC: MS, *m/e* 224 (M^+), 193, 182, 138, 123 (base); IR, ν_{max} (neat) 1736, 1207, 1167, and 1098 cm^{-1}; NMR, δ 0.81 (3H, d, $J=6$ Hz, CH_3 at C-8), 1.81 (3H, br s, $W_H=4$ Hz, CH_3 at C-5), 2.66 (1H, do do d, $J=11$, 5, and 2.5 Hz, 2-H), 3.37 and 3.71 (each 3H, s, OCH_3 and $COOCH_3$), and 5.97 (1H, br s, $W_H=7$ Hz, 6-H). Next fractions eluted with benzene–ether (20: 1) afforded a 1: 1 (by NMR) mixture (0.72 g) of two adducts (**15a** and **15b**). Final fractions eluted with benzene–ether (20: 1) gave an isomeric endo-adduct (**15b**, 1.21 g), showing a single spot on TLC: MS, *m/e* 224 (M^+), 193, 182, 138, and 123 (base); IR, ν_{max} (neat) 1744, 1203, 1165, and 1103 cm^{-1}; NMR, δ 0.83 (3H, d, $J=6$ Hz, CH_3 at C-8), 1.86 (3H, br s, $W_H=4$ Hz, CH_3 at C-5), 2.78 (1H, do d, $J=10$ and 6 Hz, 2-H), 3.31 and 3.61 (each 3H, s, OCH_3 and $COOCH_3$), and 5.77 (1H, br s, $W_H=6$ Hz, 6-H).

*2-(1-Methoxy-5,8-dimethylbicyclo[2.2.2]oct-5-en-2-yl)-2-propanols (**16a** exo, and **16b** endo), and t-3-dimethyl-r-4-(3-methyl-2-butenyl)-2-cyclohexen-1-one (**17**).* i) A solution of **15a** (165 mg) in ether (3 ml) was stirred with methyllithium (3%) in ether (1 ml) at room temperature for 1 h. After addition of saturated brine under cooling, the mixture was extracted with ether (3×10 ml). The ether extracts were worked up as usual to give **16a** (160 mg), showing a single spot on TLC; MS, *m/e* 224 (M^+), 209, 207, 206, 149, 138, 124, and 123 (base); IR, ν_{max} (neat) 3490, 1391, 1377, 1165, and 1083 cm^{-1}; NMR, δ 0.82 (3H, d, $J=6$ Hz, CH_3 at C-8′), 1.10 and 1.33 (each 3H, s, $C(CH_3)_2OH$], 1.75 (3H, br s, $W_H=4$ Hz, CH_3 at C-3′), 3.34 (3H, s, OCH_3), and 5.98 (1H, br s, $W_H=7$ Hz, 2′-H).

Compound **16a** (127 mg) was stirred with 60% aq $HClO_4$ (one drop) in acetic acid (1 ml) at room temperature for 30 min. The mixture was diluted with water, basified with 6M aq ammonia, and extracted with ether (3×20 ml). The ether extracts were worked up as usual to give oily residue (118 mg), which was purified by chromatography over silica gel (5 g). Fractions eluted with benzene–ether (20: 1) gave an oily substance (**17**, 68 mg), showing a single spot: MS, *m/e* 193, 192 (M^+), 124 and 109 (base); IR, ν_{max} (neat) 1670, 1626, and 1244 cm^{-1}; NMR, δ 1.02 (3H, d, $J=6$ Hz, CH_3 at C-8), 1.64 and 1.73 [each 3H, s, $=C(CH_3)_2$], 1.97 (3H, s, CH_3 at C-3), 5.11 (1H, br t, $J=6$ Hz, 2′-H), and 5.76 (1H, br s, $W_H=5$ Hz, 2-H).

ii) Compound **15b** (251 mg) in ether (4 ml) was stirred with methyllithium (3%) in ether (3 ml) at room temperature for 1 h. The reaction mixture was worked up as described above to give **16b** (243 mg), showing a single spot: MS, *m/e* 224 (M^+), 209, 207, 206, 138, 124, and 123 (base); IR, ν_{max} (neat) 3490, 1391, 1377, 1167, and 1098 cm^{-1}; NMR, δ 0.84 (3H, d, $J=6$ Hz, CH_3 at C-8′), 1.04 [6H, s, $C(CH_3)_2OH$], 1.78 (3H, br s, $W_H=4$ Hz, CH_3 at C-3′), 3.37 (3H, s, OCH_3), and 5.82 (1H, br s, $W_H=7$ Hz, 2′-H).

Compound **16b** (193 mg) was stirred with 60% aq $HClO_4$ (0.06 ml) in acetic acid (1.5 ml) at room temperature for 30 min. The reaction mixture was worked up and purified as described above to give **17** (116 mg), whose spectral data were identical with the afore-mentioned.

*Methyl 5-Formyl-1-methoxy-8-methylbicyclo[2.2.2]oct-5-ene-2-carboxylates (**18**).* i) A solution of a mixture (247 mg) of the Diels-Alder reaction products (**15a** and **15b**), free from methyl phenylacetate (**30**), in dioxane (10 ml) was refluxed with selenium(IV) oxide (123 mg) for 16 h under nitrogen, when precipitates were removed by fitration. The precipitates were washed with ether. The dioxane (filtrate) and ether solutions were combined, dried and evaporated to leave oily residue, which was separated by chromatography over silica gel (10 g). Fractions eluted with benzene–ether (10: 1) gave a mixture (198 mg) of aldehydes (**18**), bp 105—120 °C (bath temp) (0.1 Torr): MS, 238 (M^+), 209, 152, 147, 123, and 99 (base); UV, λ_{max} 233 nm (ε 8700); IR, ν_{max} (neat) 2705, 1742, 1680, 1633, 1206, 1168, and 1106 cm^{-1}; NMR, δ 0.72 (3H, d, $J=7$ Hz, CH_3 at C-8), 3.33 (3H, s, $COOCH_3$), 3.57 and 3.68 (3H, each s, OCH_3), 7.00 and 7.06 (each, 1H, s, 6-H), 9.40 and 9.46 (1H, each s, CHO).

ii) The crude adduct mixture (**15a** and **15b**, 30.0 g) containing **30** (*cf.*, the Diels-Alder reaction described above) in dioxane (390 ml) was refluxed with selenium(IV) oxide (15.0 g) for 16 h under nitrogen. The reaction mixture was worked up as mentioned above to leave oily residue (42 g), which was separated by chromatography over silica gel (1 kg). Fractions eluted with benzene–ether afforded **30** (9.0 g) and those eluted with benzene–ether (10: 1) gave an aldehyde mixture (**18**, 17.0 g), whose spectra were practically the same as those described above.

*Methyl 1-Methoxy-8-methyl-5-vinylbicyclo[2.2.2]oct-5-ene-2-carboxylates (**19**).* A solution of methyltriphenylphosphonium iodide (46.7 g) in DMSO (240 ml) was treated with butyllithium (15%) in hexane (72 ml) at room temperature. A part (260 ml) of the resulting ylide solution was added to a solution of **18** (17.7 g) in DMSO (150 ml), and the whole mixture was stirred at room temperature for 30 min and then at 50 °C for 2 h. After addition of water, the reaction mixture was extracted with ethyl acetate (6×200 ml). The acetate solution was washed with saturated brine, dried and evaporated to leave oily residue (52 g), which was separated by chromatography over silica gel (450 g). Fractions eluted with benzene–ether (20: 1) afforded an oily substance (**19**, 12.9 g): MS, *m/e* 236 (M^+), 177, 161, 150, and 135 (base); UV, λ_{max} 235 nm (ε 18500); IR, ν_{max} (neat) 3090, 1742, 1630, 1593, 1203, 1165, 1107, 989, and 895 cm^{-1}; NMR, δ 0.78 and 0.81 (total 3H, each d, $J=6$ Hz, CH_3 at C-8), 3.38 and 3.44 (total 3H, each s, $COOCH_3$), 3.67 and 3.74 (total 3H, each s, OCH_3), 5.05 and 5.29 (each 1H, br d, $J=10$ and 18 Hz, $CH=CH_2$), and 6.08—6.63 (2H, m, $CH=CH_2$ and 6-H).

*2-(5-Methoxy-8-methyl-5-vinylbicyclo[2.2.2]oct-5-en-2-yl)-2-propanols (**20**).* To compounds **19** (10.0 g) in ether (30 ml) was added dropwise an ether solution (110 ml) containing methyllithium, prepared from methyl iodide (12.0 ml) and lithium (2.7 g), under cooling with an ice–water bath, and the whole mixture was stirred at room temperature for 2 h. After addition of 1M aq ammonium chloride, the mixture was extracted with ether (3×200 ml), and the ether extracts were worked up as usual to leave oily substance (**20**, 9.8 g), which was used for the next reaction: MS, *m/e* 236 (M^+), 221, 219, 218, 203, 150, and 135 (base); UV, λ_{max} 235 nm (18000); IR, ν_{max} (neat) 3495, 3045, 1631, 1591, 1390, 1377, 1208, 1166, 1100, 1077, 989, and 897 cm^{-1}; NMR, δ 0.76 (3H, d, $J=7$ Hz, CH_3 at C-8′), 0.95 and 0.97 [total 6H, each s, $C(CH_3)_2OH$], 3.39 (3H, s, OCH_3), 4.80 (1H, s, OH), 4.99 and 5.23 (each 1H, br s, $J=11$ and 17 Hz, $CH=CH_2$), 6.02—6.58 (2H, m, $CH=CH_2$ and 2′-H).

(4RS,5RS,7SR)-7-(1-Hydroxy-1-methylethyl)-4-methyl-2,3,4,-

5,6,7,8,9-octahydro-2-naphthalenone (21) and Its Formate (21a). Compounds **20** (5.6 g) were dissolved in formic acid (500 ml) and stirred at room temperature for 2 h under nitrogen. The solution was neutralized carefully by addition of 11.5 M aq sodium hydroxide (NaOH) under cooling and extracted with ether (4×500 ml). The ether solution was washed with saturated brine, dried and evaporated to leave oily residue (5.9 g), which was separated into two fractions by chromatography over silica gel (180 g). More mobile fractions eluted with benzene–ether (1: 1) afforded **21a** (2.40 g), showing a single spot on TLC: MS, 251 (M^++1), 234, 210, 204, and 162 (base); UV, λ_{max} 236 nm (ε 14500); IR, ν_{max} (neat) 1724, 1666, 1626, and 1197 cm^{-1}; NMR, δ 1.12 (3H, d, J=6 Hz, 14-H), 1.51 (6H, s, 12- and 13-H), 5.85 (1H, br s, W_H=5 Hz, 1-H), and 8.05 (1H, s, OCHO). Found: C, 71.79; H, 8.84%. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86%. Less mobile fractions eluted with ether–ethyl acetate (9: 1) gave **21** (2.4 g), showing a single spot on TLC: MS, *m/e* 223 (M^++1), 207, 205, 204, 164, 149, 107, and 59 (base); UV, IR, and NMR, in the text. Found: C, 75.48; H, 9.06%. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97%.

A solution of **21a** (102 mg) in *t*-butyl alcohol (3 ml) was stirred with 0.5 M aq NaOH at room temperature for 15 h. The mixture was evaporated to remove the alcohol, mixed with water and extracted with ethyl acetate (3×5 ml). The acetate solution was worked up as usual to leave oily residue (108 mg), which was purified by passing through a silica gel column (5.0 g) to yield **21** (78 mg), whose spectra were identical with those described above.

(4RS,5RS,7SR)-7-Isopropenyl-4-methyl-2,3,4,5,6,7,8,9-octahydro-2-naphthalenone (26) and the Corresponding 7-Isopropylidene Compound (27). i) A solution of **21** (3.56 g) in pyridine (51 ml) was stirred with thionyl chloride (1.5 ml) at 0 °C (bath temp) for 5 min. The reaction mixture was poured into ice–water under stirring, and extracted with ether (4×100 ml). The ether solution was washed with 2 M aq HCl and saturated brine, dried and evaporated to leave oily residue (2.48 g), which was separated by chromatography over a silica gel column (100 g) containing 10% silver nitrate, benzene–ether mixtures being used as solvents. Early fractions eluted with benzene–ether (7: 1) gave **27** (0.42 g), showing a single spot: MS, *m/e* 204 (M^+), 189, and 171 (base); UV, λ_{max} 232 nm (ε 13200); IR, ν_{max} (neat) 1667 and 1622 cm^{-1}; NMR, δ 1.11 (3H, d, J=6 Hz, 14-H), 1.70 (6H, br s, W_H=6 Hz, 12- and 13-H), and 5.84 (1H, br s, W_H=5 Hz, 1-H). Found: C, 82.24; H, 9.96%. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87%. Fractions eluted with benzene–ether (5: 1) afforded **26** (1.32 g), bp 95—105 °C (bath temp) (13 Torr), showing a single spot on TLC: MS, *m/e* 204 (M^+), 189, 176, 162, 147, 134, 121, and 94 (base); UV, λ_{max} 237 nm (ε 15100); IR, ν_{max} (neat) 3080, 1669, 1622, and 891 cm^{-1}; NMR, δ 1.09 (3H, d, J=6 Hz, 14-H), 1.75 and 4.73 (3H and 2H, each s, 13- and 12-H), and 5.82 (1H, br s, W_H=4 Hz, 1-H). Found: C, 82.21; H, 9.96%. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87%.

ii) A solution of **21a** (521 mg) in collidine (35 ml), distilled over calcium hydride, was heated with aluminium(III) oxide [Merck, Aluminiumoxide 90 (Aktivitätsstufe II—III) 70—230 mesh, 275 mg] under reflux for 16 h. The mixture was cooled, mixed with water, neutralized with 2 M aq HCl and extracted with ethyl acetate (4×50 ml). The acetate solution was washed with 2 M aq HCl, and saturated brine, dried and evaporated to leave oily residue (490 mg), which was separated by chromatography over silica gel (15 g). Fractions eluted with benzene–ether (49: 1, 40: 1, 19: 1, and 9: 1) afforded a 4: 1 (by NMR) mixture (281 mg) of **26** and **27**: MS, *m/e* 204 (M^+), 189, 161, 147, 133, 119, 93,, and 91 (base); IR, ν_{max} (neat) 3070, 1722, 1714, 1646, and 889 cm^{-1}; NMR, δ 1.01 and 1.06 (total 3H, each s, 14-H), 1.76 [3.6H, s, =C-(CH_3)$_2$ and -C(CH_3)=CH_2], and 4.74 [1.6H, br s, W_H=5 Hz, -C(CH_3)=CH_2]. Fraction eluted with benzene–ether (3: 1) and only with ether afforded **21a** (37 mg) and **21** (54 mg), respectively.

(±)-Glutinosone [(±)-1=28], Its 3-Epimer (29), and Their Acetates (28a and 29a). i) To a solution of LDA, prepared from diisopropylamine (0.35 ml) and butyllithium (15%) in hexane (1.5 ml) in THF (3 ml) cooled at −70 °C, was added **26** (125 mg) in THF (2 ml) under cooling at the temperature. To the mixture cooled at the temperature for 30 min was added rapidly MoOPH (814 mg), dried over diphosphorus pentaoxide in a desiccator, at −70 °C. The mixture was stirred at the temperature for 80 min, and the reaction was ceased by addition of water at room temperature. The heterogeneous mixture was shaken with ethyl acetate (3×30 ml). The acetate solution was washed with 2 M aq HCl, 5% aq $NaHCO_3$, and saturated brine, dried and evaporated to leave oily residue (189 mg), which was separated by preparative TLC (6 plates) over silica gel with benzene–ether (20: 1). A fraction with large R_f value gave the starting ketone (**26**, 26 mg), while that with small R_f value afforded a mixture (80 mg) of **28** and **29**, which resisted further purification. The mixture (37 mg) was then treated with acetic anhydride (1 ml) and pyridine (2 ml) at room temperature for 38 h under stirring. The reaction products were mixed with water and extracted with ethyl acetate (3×10 ml). The acetate extracts were worked up as usual to leave oily residue (46 mg), which was separated by preparative TLC (3 plates) over silica gel with benzene–ether (20: 1). A more mobile fraction gave a crystalline substance (**29a**, 25 mg), mp 80—85 °C, showing a single spot on TLC: MS, *m/e* 262 (M^+), 234, 220, 202, 201, 121, and 94 (base); IR, ν_{max} 3075, 1748, 1692, 1641, 1631, 1230, and 894 cm^{-1}; NMR, δ 1.04 (3H, d, J=6 Hz, 14-H), 1.73 and 2.17 (each 3H, s, 13-H and OCOCH_3), 4.74 (2H, br, s, 12-H), 5.47 (1H, d, J=5 Hz, 3-H), and 5.81 (1H, br s, W_H=4 Hz, 1-H). A less mobile fraction gave **28a** (16 mg), oily, showing a single spot; MS, *m/e* 262 (M^+), 234, 220, 202, 121, and 94 (base); IR, ν_{max} (neat) 3075, 1753, 1691, 1640, 1627, 1226, and 887 cm^{-1}; NMR, δ 1.08 (3H, d, J=6 Hz, 14-H), 1.72 and 2.19 (each 3H, s, 13-H and OCOCH_3), 4.72 (2H, s, 12-H), 5.10 (1H, d, J=12 Hz, 3-H), and 5.85 (1H, br s, W_H=4 Hz, 1-H).

ii) A solution of **29a** (8.5 ml) in ethanol (1 ml) was stirred with 0.27 M aq K_2CO_3 (0.15 ml) at room temperature for 12 h. After addition of water, the mixture was evaporated to remove ethanol and extracted with ethyl acetate (4×5 ml). The acetate solution was worked up as usual to leave an oily substance (5.8 mg), which was purified by passing through a silica gel column (3 g) with a 10: 1 mixture of benzene and ether to give **29** (3.6 mg), oily; MS, *m/e* 220 (M^+), 192, 177, 162, 147, 121, and 94 (base); UV, λ_{max} 237 nm (ε 12000); IR, ν_{max} 3380, 1677, 1646, 1631, 1090, and 893 cm^{-1}; NMR, δ 0.93 (3H, d, J=6 Hz, 14-H), 1.71 (3H, s, 13-H), 3.53 (1H, s, OH), 4.35 (1H, d, J=5 Hz, 3-H), 4.72 (2H, br s, W_H=7 Hz, 12-H), and 5.83 (1H, br s, W_H=3 Hz, 1-H).

A solution of **28a** (16.0 mg) in ethanol (1.5 ml) was stirred with 0.22 M aq K_2CO_3 (0.3 ml) at room temperature for 12 h under argon. The reaction mixture was worked up as described above to leave oily residue (16 mg), which was separated by preparative TLC (1 plate) over silica gel with benzene–ether (10: 1). While a more mobile fraction afforded the starting acetate (**28a**, 4.6 mg), a less mobile fraction gave **28** [(±)-**1**, 5.7 mg), which crystallized on standing and had mp 64—66 °C: MS, UV, IR, and NMR, in the text.

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