Stereoselective Introduction of a Carboxy Group into a Santonin Derivative for Higher Terpene Lactone Synthesis

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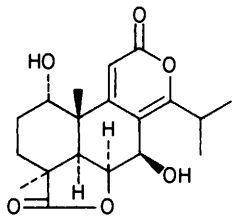
While conjugate addition of potassium cyanide or diethylaluminium cyanide to the enone (**5**) yielded the β-cyano addition product (**6**), reaction of the same substrate with a vinyl Grignard reagent in the presence of copper(I) iodide gave rise to formation of the stereochemically reversed addition product (**10**). The products were transformed to the carboxylic acid (**8a**) and the epimeric acid (**13a**), respectively.

Some higher terpenoids such as nagilactone A[1] (**1**) and nimbolide[2] (**2**) have as a common and characteristic structural unit a γ-lactone ring across two adjacent carbocyclic rings. To provide a new synthetic access to these terpenoids, the enone (**5**) which is readily available from santonin seemed to be a useful chiral starting material if a carboxy group or a latent carboxy group could be introduced at C(4) stereoselectively. We have now found that conjugate additions to (**5**) of potassium cyanide or diethylaluminium cyanide and of vinylmagnesium bromide promoted by a copper(I) salt took place in stereochemically reverse modes, giving β-cyano and α-vinyl addition products (**6**) and (**10**), respectively.

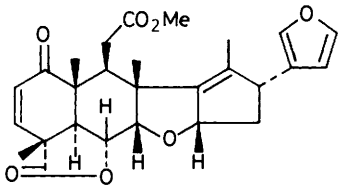
The enone substrate (**5**) was prepared from the bromohydrin (**3**)[3] by Jones oxidation giving the corresponding bromoketone (**4**), followed by dehydrobromination with 1,5-diazabicyclo-[5.4.0]undec-5-ene (Scheme). When (**5**) was treated with potassium cyanide in aqueous *N,N*-dimethylformamide in the presence of ammonium chloride, the cyanoketone (**6**) was produced in moderate yield (66%); the same product was also obtained with diethylaluminium cyanide in toluene in much better yield (87%). On the other hand, copper(I) iodide-promoted addition of vinylmagnesium bromide to the enone (**5**) in tetrahydrofuran provided the vinyl ketone (**10**) (65% yield).

The stereochemistry of the newly introduced quaternary functional groups was elucidated by chemical means. Reduction of (**6**) with sodium borohydride in methanol gave the alcohol (**7a**) in high yield. The ^{1}H NMR spectrum of its acetate (**7b**) showed a one-proton broad signal at δ 5.12, whose relatively narrow half-height width (8 Hz) indicated the acetoxy group to be β-axial.† After hydrolysis of (**7a**) with potassium hydroxide in aqueous ethanol under reflux, treatment of the resulting acid (**8a**) with *N,N'*-dicyclohexylcarbodi-imide afforded the bis-γ-lactone (**9**), whose structure was supported by the sole carbonyl absorption at 1 778 cm^{-1} in the IR spectrum and two lactone γ-protons at δ 4.08 and 4.80 in the ^{1}H NMR spectrum. This outcome demonstrated that the carboxy group of (**8a**) was β-axial and that accordingly the cyano group was introduced from the β-face in the reaction of (**5**) with the abovementioned cyanating agents.

The vinyl ketone (**10**), on the other hand, was quantitatively reduced to give the alcohol (**11a**), which gave the acetate (**11b**) on acetylation. Since attempted configurational assignment of the acetoxy group of (**11b**) from NMR couplings did not give a clear conclusion because of signal overlapping with olefinic protons, (**11b**) was then ozonolysed and the resulting ozonide was reduced with dimethyl sulphide to give the aldehyde (**12**). In (**12**) the proton α to the acetoxy group gave a signal with a half-height width of 8 Hz, which indicated the proton to be equatorial.† Jones oxidation of (**12**) yielded the acid (**13a**),



(**1**)



(**2**)

which was esterified with diazomethane to give the ester (**13b**). The ester (**13b**) and the corresponding acetate (**8b**) obtained from (**8a**) on acetylation showed quite similar but clearly different IR absorptions, mass spectral fragmentation patterns,‡ and ^{13}C NMR signals. This observation strongly suggested these compounds to be epimeric at C(4).

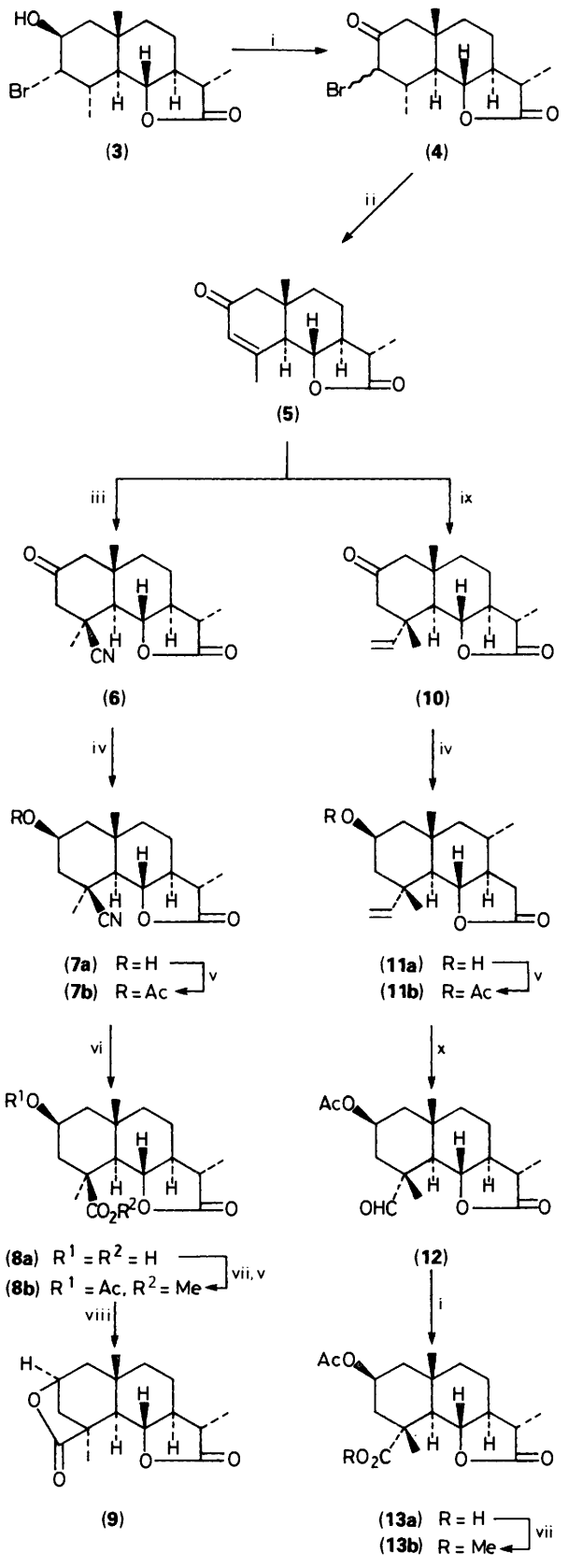
In the conjugate addition to (**5**), the cyanating agents added to the substrate in the stereoelectronically favoured manner to give the β-axial cyano derivative (**6**) as previously observed with a similar substrate;[5] addition of the Grignard reagent was also affected by steric control, probably due to the increased steric effect between the angular methyl of the substrate (**5**) and the bulky solvated Grignard reagent, providing the observed product with the α-equatorial vinyl group (**10**).

To gain further insight into the steric course of this conjugate addition, attempts were made to use other nucleophiles such as lithium 1,3-dithianide[6] and lithium methylsulphinyl(methylthio)methanide.[7] These reagents gave unsatisfactory results in introducing a latent carboxy group however, giving rise to recovery of the substrate or to formation of intractable mixtures under a variety of reaction conditions.

In summary, introduction of the carboxy group to the C(4) position of (**5**) resulted in opposite stereochemical outcomes depending on whether the cyanating agents or the vinyl Grignard reagent was used in the conjugate addition. The resulting β- (**8a**) and α-acids (**13a**) are expected to be convenient chiral starting materials for the synthesis of the abovementioned higher terpene lactones and related natural products.[8]

† As expected, the corresponding axial proton in a similar system shows a signal with a much larger half-height width.[4]

‡ While (**8b**) and (**13b**) gave the same base peak at *m/z* 233 in their mass spectra, (**8b**) showed more intense peaks at *m/z* 324 (M^+ − CO) and 264 (M^+ − CO − CH_3CO_2H) than (**13b**).



Scheme. *Reagents:* i, Jones reagent; ii, 1,5-diazabicyclo[5,4,0]undec-5-ene; iii, KCN, NH_4Cl, or Et_2AlCN; iv, $NaBH_4$; v, Ac_2O, pyridine, 4-(*N*,*N*-dimethylamino)pyridine; vi, aq. KOH; vii, CH_2N_2; viii, *N*,*N*'-dicyclohexylcarbodi-imide; ix, vinylmagnesium bromide, CuI; x, O_3, Me_2S.

Experimental

General.—M.p.s were determined with a Mitamura Riken apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on Jeol FX 90 (90 MHz) and Jeol FX 100 spectrometers, respectively, in deuteriochloroform with tetramethylsilane as internal standard. Chemical shifts and coupling constants (*J*) are given as δ values and in Hz, respectively. IR spectra were recorded on a Jasco A-3 spectrometer in chloroform and absorption maxima are given in wavenumbers (cm^{-1}). Mass spectra were taken on a Jeol JMS-01-SG-2 spectrometer. Optical rotations were measured on a Jasco DIP-181 polarimeter in acetone at 26 °C. Anhydrous magnesium sulphate was used for drying extracts. Kieselgel 60 Art 7734 and Art 7730 were used for column chromatography and preparative TLC, respectively, and solvents for elution are shown in parentheses.

(3S,3aS,5aS,9aS,9bS)-3,5a,9-*Trimethyl*-3a,4,5,5a,9a,9b-*hexahydronaphtho*[1,2-b]*furan*-2(3H),7(6H)-*dione* (**5**).—An excess of Jones reagent (*ca.* 20 ml) was added portionwise to a stirred solution of crude (**3**)[2] (3.4 g) in acetone (100 ml) at 0 °C, while consumption of (**3**) was monitored by TLC. When the substrate was no longer detected, the mixture was diluted with brine and extracted with ether–dichloromethane (5:1). The organic layer was washed with water, aqueous sodium hydrogen carbonate, and brine, and dried. Removal of the solvent left (**4**) as crystals, m.p. 178–179 °C (from benzene–cyclohexane), ν_{max} 1 770 and 1 718; δ 0.95 (3 H, s), 1.23 (3 H, d, *J* 5), 1.27 (3 H, d, *J* 4), 3.8 (1 H, m), and 4.20 (1 H, m) (Found: C, 54.9; H, 6.5. Calc. for $C_{15}H_{21}BrO_3$: C, 54.7; H, 6.4%).

A mixture of crude (**4**) (3.4 g), 1,5-diazabicyclo[5.4.0]undec-5-ene (5 g), and benzene (150 ml) was heated under reflux for 2 h. The mixture was successively washed with water, dilute hydrochloric acid, aqueous sodium hydrogen carbonate, water, and brine, and dried. Removal of the solvent left crystals; recrystallisation from cyclohexane–benzene gave compound (**5**) (1.50 g). Purification of the mother liquor by TLC (10% benzene–acetone) gave additional (**5**) (0.30 g, 68% overall yield), m.p. 132–134 °C (from benzene–cyclohexane) (lit.[9] 130–132 °C, lit.[10] 134–134.5 °C), $[\alpha]_D$ +193.5° (*c* 1.02){lit[9] $[\alpha]_D$ +190° (*c* 2), lit[10] $[\alpha]_D$ +178° (*c* 0.7, $CHCl_3$)}; ν_{max} 1 770 and 1 660; δ 1.01 (s, 3 H), 1.25 (d, 3 H, *J* 6), 2.11 (t, 3 H, *J* 2), 3.98 (t, 1 H, *J* 12), and 5.95 (m, 1 H) (Found: C, 71.95; H, 8.1. $C_{15}H_{20}O_3$ requires C, 72.55; H, 8.1%).

(3S,3aS,5aS,9S,9aR,9bS)-3,5a,9-*Trimethyl*-2,7-*dioxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]*furan*-9-*carbonitrile* (**6**).—*Cyanation with potassium cyanide.* A solution of potassium cyanide (1.08 g, 16.6 mmol) in water (8.8 ml) was added to a stirred mixture of compound (**5**) (2.12 g, 8.55 mmol) and ammonium chloride (700 mg, 13 mmol) in *N*,*N*-dimethylformamide (70 ml). The mixture was stirred at 90 °C for 16 h. After dilution with water, the product was extracted with benzene, and the extract was washed with water and brine, and dried. The crude product obtained on evaporation was purified by column chromatography (5% acetone–benzene, then 10% acetone–benzene) to afford the *cyano compound* (**6**) (1.56 g, 66%) as crystals, m.p. 197–198 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +112.5° (*c* 0.59), ν_{max} 2 240, 1 780, and 1 730; δ 1.22 (d, 3 H, *J* 8), 1.28 (s, 3 H), 1.76 (s, 3 H), and 4.26 (t, 1 H, *J* 12) (Found: C, 69.7; H, 7.75; N, 5.0. $C_{16}H_{21}O_3N$ requires C, 69.8; H, 7.7; N, 5.1%).

Cyanation with diethylaluminium cyanide. To a stirred solution of (**5**) (124 mg, 0.5 mmol) in toluene (2 ml), a toluene solution of diethylaluminium cyanide (1M; 1.5 ml, 1.5 mmol) was added at room temperature. The mixture was stirred at the same temperature for 3 h and then 6M hydrochloric acid was carefully added under cooling with ice–water. Water was added to the

mixture and the product was extracted with ethyl acetate. The extract was washed with brine, aqueous sodium hydrogencarbonate, water, and brine. After drying, the solvent was removed to give a solid, which was purified by column chromatography using dichloromethane–acetone (100:3) as the eluant to afford (**6**) (120 mg, 87% yield). The IR and ^{1}H NMR spectra of the product identical with those of the foregoing authentic compound.

(3S,3aS,5aS,7S,9S,9aR,9bS)-7-*Hydroxy*-3,5a,9-*trimethyl*-2-*oxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]-*furan*-9-*carbonitrile* (**7a**) *and its Acetate* (**7b**).—To a suspension of (**6**) (990 mg, 3.6 mmol) in methanol (25 ml), sodium borohydride (76 mg, 2 mmol) was added portionwise under cooling with ice–water. After the mixture had become homogeneous, the solution was diluted with brine and extracted with benzene. The organic layer was washed with brine, and dried. Removal of the solvent afforded the *hydroxy derivative* (**7a**) in quantitative yield, m.p. 179–181 °C (from ethyl acetate–cyclohexane), $[\alpha]_D$ +70.6° (*c* 0.59); ν_{max} 3 500, 2 250, and 1 780; δ 1.23 (d, 3 H, *J* 8), 1.52 (s, 3 H), 1.60 (s, 3 H), and 4.1–4.3 (m, 2 H) (Found: C, 69.5; H, 8.4; N, 5.0. $C_{16}H_{23}O_3N$ requires C, 69.3; H, 8.4; N, 5.05%).

A mixture of (**7a**) (61 mg, 0.22 mmol), a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine, pyridine (0.15 ml), acetic anhydride (0.15 ml), and dichloromethane (5 ml) was stirred at room temperature for 24 h. The reaction was quenched by adding methanol, and the mixture was diluted with water. After extraction of the product with ethyl acetate, the extract was successively washed with water, aqueous copper(II) sulphate, water, and brine, and dried. Removal of the solvent afforded the *acetate* (**7b**) (69 mg, 98%) as crystals, m.p. 206–207 °C (from ethyl acetate–cyclohexane), $[\alpha]_D$ +39.3° (*c* 0.43); ν_{max} 2 250, 1 780, and 1 735; δ 1.24 (d, 3 H, *J* 8), 1.46 (s, 3 H), 1.60 (s, 3 H), 2.12 (s, 3 H), 4.26 (t, 1 H, *J* 11), and 5.12 (m, 1 H, $W_{\frac{1}{2}}$ 8 Hz) (Found: C, 68.1; H, 7.9; N, 4.4. $C_{18}H_{25}O_4N$ requires C, 67.7; H, 7.9; N, 4.4%).

(3S,3aS,5aS,7S,9S,9aR,9bS)-7-*Hydroxy*-3,5a,9-*trimethyl*-2-*oxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]-*furan*-9-*carboxylic Acid* (**8a**) *and its Acetoxy Ester* (**8b**).—A mixture of (**7a**) (200 mg, 0.72 mmol), potassium hydroxide (2.5 g), water (4 ml), and ethanol (5 ml) was heated under reflux for 48 h, and then acidified with 6M hydrochloric acid. The mixture was extracted with ethyl acetate–dichloromethane (5:1), and the extract was washed with brine, and dried. Compound (**8a**) was obtained as a powder on evaporation of the solvent and characterized as its methyl ester. The powder was dissolved in ethyl acetate and esterified by adding ethereal diazomethane. The residue obtained on evaporation was purified by TLC (50% ethyl acetate–hexane) to afford the *methyl ester* of (**8a**) (175 mg, 78% overall yield) as crystals, m.p. 122.5–123.5 °C (recrystallized from ethyl acetate–cyclohexane); $[\alpha]_D$ +77.6° (*c* 0.47), ν_{max} 3 500, 1 770, and 1 705; δ 1.06 (s, 3 H), 1.12 (d, 3 H, *J* 8), 1.44 (s, 3 H), 3.76 (s, 3 H), 4.10 (m, 1 H), and 4.20 (t, 1 H, *J* 12) (Found: C, 65.85; H, 8.4. $C_{17}H_{26}O_5$ requires C, 65.8; H, 8.4%).

A mixture of the methyl ester of (**8a**) (68 mg, 0.22 mmol), a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine, pyridine (0.3 ml), and acetic anhydride (0.3 ml) was stirred at room temperature for 24 h. After work-up as described for (**7b**), the product was purified by TLC (30% ethyl acetate–hexane) to afford the *acetoxy derivative* (**8b**) (66 mg, 86% yield) as crystals, m.p. 162–163 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +16.1° (*c* 0.61); ν_{max} 1 775 and 1 715; δ 1.04 (s, 3 H), 1.10 (d, 3 H, *J* 8), 1.38 (s, 3 H), 2.00 (s, 3 H), 3.68 (s, 3 H), 4.76 (t, 1 H, *J* 12), and 5.02 (m, 1 H, $W_{\frac{1}{2}}$ 8 Hz); ^{13}C NMR δ 179.4, 176.2, 170.3, 82.0, 68.9, 56.1, 54.4, 51.5, 44.8, 43.2, 42.6, 40.9, 40.0, 36.9, 31.0, 23.1, 21.4, 21.1, 12.5; *m*/*z* 352.1869 (M^+); $C_{19}H_{28}O_6$ requires 352.1886; *m*/*z* 352 (2%), 324 (81), 292 (35), 264 (50), 250 (62), 233 (100), 217 (38), 165 (44), 107 (39), 55 (37), and 43 (76) (Found: C, 64.7; H, 8.05. $C_{19}H_{28}O_6$ requires C, 64.75; H, 8.0%).

(3S,3aS,5aS,7S,9S,9aR,9bS)-3,5a,9-*Trimethyl*-2-*oxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]*furan*-9,7-*carbolactone* (**9**).—A mixture of *N*,*N*′-dicyclohexylcarbodiimide (350 mg, 1.7 mmol), crude (**8a**) obtained from (**7a**) (200 mg) as described above, and tetrahydrofuran (15 ml) was stirred at room temperature for 48 h. After removal of the solvent, the solid obtained was purified by TLC (2% acetone–dichloromethane) to afford the *lactone* (**9**) (126 mg, 63%) as crystals, m.p. 197–198 °C (from ethyl acetate); $[\alpha]_D$ +66.3° (*c* 0.62); ν_{max} 1 778; δ 1.18 (d, 3 H, *J* 8), 1.20 (s, 3 H), 1.38 (s, 3 H), 4.08 (t, 1 H, *J* 12), and 4.80 (t, 1 H, *J* 6) (Found: C, 69.3; H, 8.0. $C_{16}H_{22}O_4$ requires C, 69.0; H, 8.0%).

(3S,3aS,5aS,9S,9aR,9bS)-3,5a,9-*Trimethyl*-9-*vinyl*-3a,4,5,5a,8,9,9a,9b-*octahydronaphtho*[1,2-b]*furan*-2(3H),7(6H)-*dione*(**10**).—A tetrahydrofuran solution of vinylmagnesium bromide (0.8 M; 1 ml, 0.39 mmol) was gradually added to a stirred slurry of copper(I) iodide (75 mg, 0.39 mmol) in dry tetrahydrofuran (3 ml) which had been cooled to −55 °C beforehand. After stirring for an additional 45 min, a solution of (**5**) (62 mg, 0.25 mmol) in tetrahydrofuran (2.5 ml) was added to the above yellowish brown mixture at −40 to −50 °C. After stirring at the same temperature for 2 h, the reaction was quenched by adding aqueous ammonia, and the product was extracted with ethyl acetate. The organic layer was washed with aqueous ammonia, water, and brine, and dried. The crude product obtained on evaporation was purified by TLC (1% acetone–dichloromethane) to afford the *vinyl compound* (**10**) (45 mg, 65% yield) as crystals, m.p. 123–124 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +79.4° (*c* 0.37); ν_{max} 1 775 and 1 710; δ 1.12 (s, 3 H), 1.22 (d, 3 H, *J* 8), 1.22 (s, 3 H), 4.04 (t, 1 H, *J* 12), and 4.8–5.4 (m, 3 H) (Found: C, 73.5; H, 9.0. $C_{17}H_{24}O_3$ requires C, 73.9; H, 8.75%).

(3S,3aS,5aS,9S,9aR,9bS)-7-*Hydroxy*-3,5a,9-*trimethyl*-9-*vinyl*-3a,4,5,5a,6,7,8,9,9a,9b-*decahydronaphtho*[1,2-b]*furan*-2(3H)-*one* (**11a**) *and its Acetate* (**11b**).—To a stirred mixture of (**10**) (242 mg, 0.88 mmol) in methanol (15 ml), sodium borohydride (30 mg, 0.79 mmol) was added portionwise under cooling with ice–water. After dilution with brine, the mixture was extracted with benzene. The organic layer was washed with brine and dried. After removal of the solvent, the crude product was purified by column chromatography (1% acetone–dichloromethane) to give the *hydroxy derivative* (**11a**) as crystals (257 mg), MP 163–164 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +59.5° (*c* 0.42); ν_{max} 3 600 and 1 770; δ 1.20 (d, 3 H, *J* 8), 1.30 (s, 6 H), 3.9–4.2 (m, 2 H), and 4.8–5.2 (m, 3 H) (Found: C, 73.2; H, 9.5. $C_{17}H_{26}O_3$ requires C, 73.3; H, 9.4%).

A mixture of recrystallized (**11a**) (138 mg, 0.5 mmol), a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine, pyridine (2 ml), and acetic anhydride (0.3 ml) was stirred at room temperature for 24 h. The product obtained on work-up as described for (**8b**) was purified by TLC (30% ethyl acetate–hexane) to afford the *acetoxy derivative* (**11b**) (148 mg, 93%) as crystals, m.p. 142–143 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +42.8° (*c* 0.46); ν_{max} 1 775 and 1 730; δ 1.20 (d, 3 H, *J* 8), 1.28 (s, 3 H), 1.29 (s, 3 H), 2.04 (s, 3 H), 4.04 (t, 1 H, *J* 12), and 4.8–5.1 (m, 4 H) (Found: C, 71.5; H, 8.9. $C_{19}H_{28}O_4$ requires C, 71.2; H, 8.8%).

(3S,3aS,5aS,7S,9R,9aR,9bS)-7-*Acetoxy*-3,5a,9-*trimethyl*-2-*oxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]-*furan*-9-*carbaldehyde* (**12**).—Ozone was bubbled through a solution of (**11b**) (117 mg, 0.37 mmol) in dichloromethane (100

ml) at −78 °C until the solution turned slightly blue. The solution was warmed to room temperature, and dimethyl sulphide (1 ml) was added. Stirring was continued for an additional 25 h to complete the reduction. The oil obtained on evaporation was dissolved in ether and washed with water and brine, and dried. The crude product obtained on evaporation was purified by TLC (45% ethyl acetate–hexane) to afford the *aldehyde* (**12**) (106 mg, 91% yield) as crystals, m.p. 128–129 °C (from ethyl acetate–cyclohexane); $[\alpha]_D$ +18.8° (*c* 0.41); ν_{max} 1 778 and 1 718; δ 1.20 (d, 3 H, *J* 8), 1.28 (s, 3 H), 1.46 (s, 3 H), 2.06 (s, 3 H), 4.00 (t, 1 H, *J* 12), 5.20 (m, 1 H, $W_{\frac{1}{2}}$ 8), and 9.40 (s, 1 H) (Found: C, 66.8; H, 8.2. $C_{18}H_{26}O_5$ requires C, 67.1; H, 8.1%).

(3S,3aS,5aS,7S,9R,9aS,9bS)-7-*Acetoxy*-3,5a,9-*trimethyl*-2-*oxo*-2,3,3a,4,5,5a,6,7,8,9,9a,9b-*dodecahydronaphtho*[1,2-b]*furan*-9-*carboxylic Acid* (**13a**) *and its Methyl Ester* (**13b**).—Jones reagent (1 ml) was added to a solution of (**12**) (202 mg, 0.63 mmol) in acetone (8 ml), and the solution was stirred at room temperature overnight. After most of the acetone had been evaporated off, the residue was diluted with water and extracted with ethyl acetate. The organic layer was extracted with aqueous sodium hydrogen carbonate, and the aqueous layer was acidified with 2M hydrochloric acid under cooling with ice–water. The product was extracted with ethyl acetate–dichloromethane (5:1), and the extract was washed with brine, and dried. The residue obtained on evaporation was dissolved in ethyl acetate and esterified by adding ethereal diazomethane. The solvent was removed and the residue was purified by column chromatography (30% ethyl acetate–hexane) to give the *ester* (**13b**) as an oil (150 mg, 68% yield); $[\alpha]_D$ +27.1° (*c* 1.38); ν_{max} 1 778 and 1 730; δ 1.22 (s, 3 H), 1.29 (d, 3 H, *J* 8), 1.49 (s, 3 H), 2.02 (s, 3 H), 3.65 (s, 3 H), 3.99 (t, 1 H, *J* 12), and 5.20 (m, 1 H, $W_{\frac{1}{2}}$ 8); ^{13}C NMR δ 179.2, 177.8, 169.8, 79.2, 68.9, 53.4, 52.3, 50.6, 44.2, 43.5, 43.1, 41.3, 39.3, 35.4, 22.8, 21.6, 21.4, 17.4, and 12.3; *m/z* 352.1866 (M^+); $C_{19}H_{28}O_6$ requires 352.1886; *m/z* 352 (1%), 292 (36), 233 (100), 165 (67), 107 (39), 55 (28), and 43 (60) (Found: C, 64.6; H, 7.9. $C_{19}H_{28}O_6$ requires C, 64.75; H, 8.0%).

References

1 Y. Hayashi, T. Sakan, K. Hirotsu, and A. Shimada, *Chem. Lett.*, 1972, 349; Y. Hayashi, Y. Yuki, and S. Shimada, *Tetrahedron Lett.*, 1977, 2953.
2 D. E. U. Ekong, *Chem. Commun.*, 1967, 808.
3 M. Watanabe and A. Yoshikoshi, *J. Chem. Soc., Perkin Trans. 1*, 1987, 1793.
4 T. Hayashi, T. Handa, M. Ohashi, and H. Kakisawa, *Chem. Commun.*, 1971, 541; T. Anthonsen and G. Bergland, *Acta Chem. Scand.*, 1973, **27**, 1073.
5 W. S. Meyer and K. K. Maheshwar, *Tetrahedron Lett.*, 1964, **32**, 2175.
6 E. J. Corey and D. Crouse, *J. Org. Chem.*, 1968, **33**, 298.
7 K. Ogura, M. Yamashita, and G. Tsuchihashi, *Tetrahedron Lett.*, 1978, 1303.
8 J. R. Hanson, *Nat. Prod. Rep.*, 1984, **1**, 171, 339; 1986, **3**, 307; 1987, **4**, 399.
9 H. Kulkarni, *Chem. Ind. (London)*, 1970, 1498.
10 K. Yamakawa, K. Nishitani, E. Eguchi, S. Kidokoro, and R. Sakaguchi, *Chem. Pharm. Bull.*, 1977, **25**, 385.

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