***N*-Fmoc-D-Glu α-Amide γ-*tert*-Butyl Ester (D-5b).** *N*-Fmoc-D-Glu γ-*tert*-butyl ester (**18**, 6.47 g produced the α-amide D-**5b**, 5.78 g, 92% yield): ^{13}C NMR ($CDCl_3$) ppm 173.78, 172.89, 156.31, 143.82, 141.37, 127.76, 127.12, 125.10, 120.01, 81.09, 67.09, 54.10, 47.26, 31.75, 28.09; $[\alpha]^{25}_{578}$ +2.5° (*c* 1.3, MeOH).

***N*-Fmoc-D-Glu α-Thioamide γ-*tert*-Butyl Ester (D-6b).** Amide D-**5b** (5.7 g) produced thioamide D-**6b** (5.52 g, 94% yield); $[\alpha]^{25}_{578}$ +2.2° (*c* 1, MeOH).

(*R*)-*N*-Fmoc-(glu)Thz γ-*tert*-Butyl Ester (D-8b). Thioamide D-**6b** (5.42 g) produced thiazole acid D-**8b** (4.93 g, 79% yield): $[\alpha]^{25}_{578}$ +9.6° (*c* 0.8, MeOH).

(*R*)-*N*-Fmoc-(glu)Thz-(gly)Thz γ-*tert*-Butyl Ester, Ethyl Ester (D-10b). Acid D-**8b** (1.0 g) produced bis-thiazole dipeptide diester D-**10b** (1.17 g, 88% yield): $[\alpha]^{25}_{578}$ +8.2° (*c* 1, MeOH).

(*R*)-*N*-Fmoc-(glu)Thz-(gly)Thz Ethyl Ester (D-11b). *tert*-Butyl ester D-**10b** (1.17 g) produced acid D-**11b** (1.07 g, 88% yield); +7.5° (*c* 1, MeOH).

Determination of Optical Purity of (*S*)-8b and (*R*)-8b. The materials were first converted to their methyl esters by treatment with ethereal diazomethane. The residues on evaporation were dissolved in methylene chloride (2 mg/mL) and 5 μL of this solution injected onto a Pirkle-type 10A column (0.46 × 25 cm, Regis Chemical Co.). The materials were eluted with 30% ethyl acetate in *n*-hexane pumped at a flow rate of 1 mL/min and monitoring the peak elution at 265 nm. Under these conditions the *S* isomer eluted in 18.3 min and the *R* isomer in 19.1 min. Peak height measurements show that the particular sample of *S* isomer run had an ee of 56%. We have subsequently learned that the extent of racemization varies in the Hantzsch condensation and can be complete at higher temperatures or in the absence of base to absorb the generated hydrobromic acid.

Registry No. **1**, 80387-90-2; **2**, 25438-22-6; **4a**, 13574-13-5; **4b**, 71989-18-9; **5a**, 18800-73-2; **5b**, 104090-92-8; D-**5b**, 104090-93-9; **6a**, 104090-94-0; **6b**, 104090-95-1; D-**6b**, 104090-96-2; **7**, 1113-59-3; **8a**, 104090-97-3; **8b**, 104090-98-4; D-**8b**, 104090-99-5; **9**, 104091-00-1; **10a**, 104091-01-2; **10b**, 104091-02-3; D-**10b**, 104091-03-4; **11a**, 104091-04-5; **11b**, 104091-05-6; D-**11b**, 104091-06-7; **12**, 104091-07-8; **13**, 104091-08-9; **14**, 45125-00-6; *N*-Fmoc-D-Glu, 104091-09-0; *N*-Fmoc-D-Glu-OCH_2Ph, 104091-10-3; *N*-Fmoc-D-Glu(OCH_2Ph), 104091-11-4; Fmoc-Cl, 28920-43-6; isobutylene, 115-11-7.

Total Synthesis of (±)-3β-Hydroxynagilactone F

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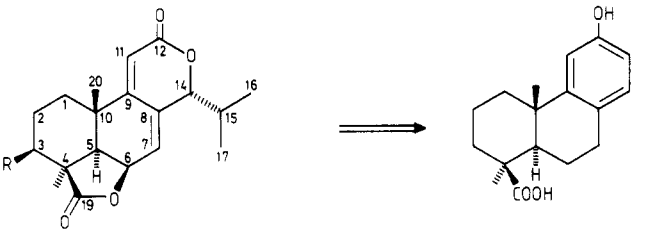
The total synthesis of racemic 3β-hydroxynagilactone F (**3**), a biologically active norditerpenoid dilactone isolated from *Podocarpus nagi* (Thunberg) Pilger, is described. Starting from the trans-fused bicyclic keto ester **5a**, two possible synthetic routes were explored. Annelation of the δ-lactone to **5a** gave the lactone **9** which was transformed to the 7(8),9(11)-dienolide **17a**. Ring closure of **17a** to a γ-lactone followed by demethylation afforded 1 mg of the title compound **3**. The overall yield of **3** from **5a** was 0.2%.

Norditerpenoid dilactones isolated from various species of *Podocarpus* plants have attracted considerable attention[1,2] because of their remarkable biological activity in such areas as plant growth regulation,[3] insect toxicity,[2] and antitumor activity.[2,4] Some studies have appeared which deal with the synthesis of potentially useful intermediates for this type of compound,[5] but until now only one total synthesis of a norditerpenoid dilactone has been reported. In 1982, Hayashi et al.[6] published the synthesis of nagilactone F (**1**), starting from the natural product, podocarpic acid (**2**) (Scheme I). A great number of norditerpene dilactones with interesting biological activity have structures with a functionalized ring A, and these compounds are accessible with difficulty from natural products such as podocarpic acid (**2**). Our aim was to develop a route to these ring-A functionalized dilactones, and initially 3β-hydroxynagilactone F (**3**) was chosen as the target molecule. This compound was isolated from the root bark of *Podocarpus nagi* (Thunberg) Pilger.[7] The 3β-hydroxy

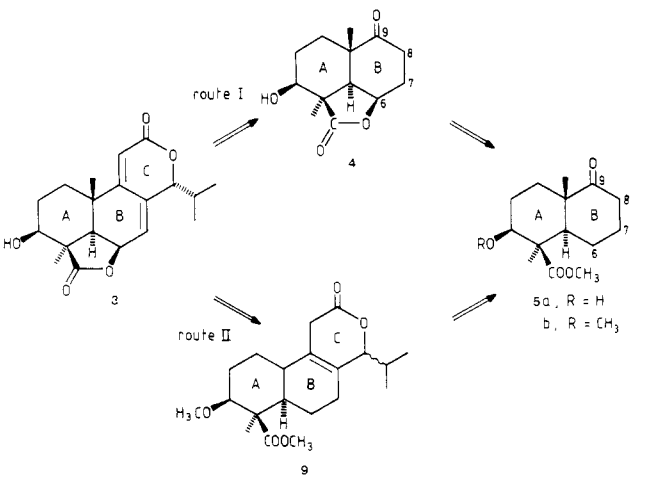
Scheme I



1, R = H
3, R = OH

2

Scheme II



4

3

5a, R = H
b, R = CH₃

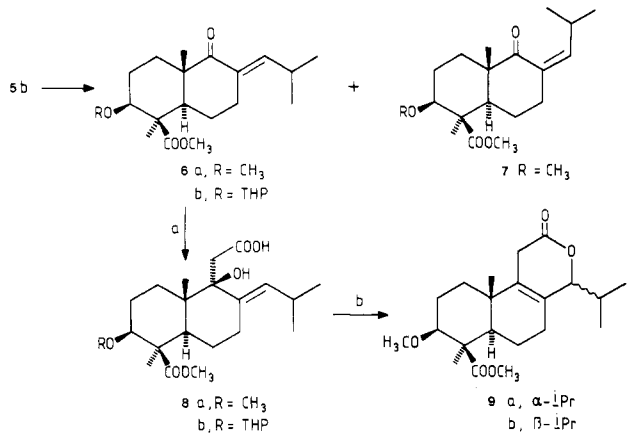
9

keto ester **5a**[8] seemed a convenient starting compound for the synthesis of **3**. The two major synthetic problems in

(1) Itô, S.; Kodama, M. *Heterocycles* **1976**, *4*, 595 and references cited therein.
(2) Hayashi, Y.; Matsumoto, T. *J. Org. Chem.* **1982**, *47*, 3421 and references cited therein.
(3) Hayashi, Y.; Sakan, T. *Proc. 8th Int. Conf. Plant Growth Substances* **1974**, 525.
(4) Cassady, J. M.; Lightner, T. K.; McCloud, T. G.; Hembree, J. A.; Byrn, S. R.; Chang, C.-j. *J. Org. Chem.* **1984**, *49*, 942.
(5) (a) Welch, S. C.; Hagan, C. P.; White, D. H.; Fleming, W. P.; Trotter, J. W. *J. Am. Chem. Soc.* **1977**, *99*, 549. (b) Mangoni, L.; Adinolfi, M.; Laonigro, G.; Caputo, R. *Tetrahedron* **1972**, *28*, 611. (c) Burke, S. D.; Smith Strickland, S. M.; Powner, T. W. *J. Org. Chem.* **1983**, *48*, 454. (d) Burke, S. D.; Powner, T. H. *Tetrahedron Lett.* **1983**, *24*, 4529. (e) van Hijfte, L.; Vandewalle, M. *Synth. Commun.* **1984**, *14*, 1149.
(6) Hayashi, Y.; Matsumoto, T.; Nishizawa, M.; Togami, M.; Hyono, T.; Nishikawa, N.; Uemura, M.; Sakan, T. *J. Org. Chem.* **1982**, *47*, 3428.
(7) Hayashi, Y.; Matsumoto, T.; Sakan, T. *Heterocycles* **1978**, *10*, 123.

0022-3263/86/1951-4594$01.50/0

Scheme III[a]



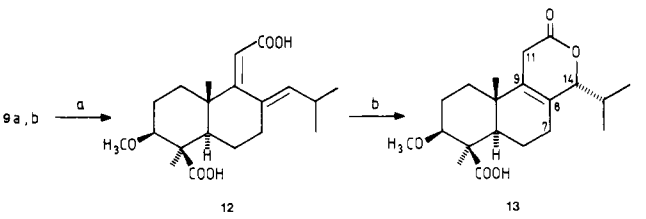
[a] a, $LiCH_2COOLi$, THF, HMPA; b, TsOH, PhH.

this synthesis are the functionalization of C-6, necessary for the construction of the γ-lactone, and the annelation of the δ-lactone. Therefore the two routes indicated in Scheme II were investigated. The transformation of keto ester **5a** into γ-lactone **4** (route I) was reported previously.[9] The annelation of the δ-lactone according to the method developed before[10] (Scheme III) met with difficulties. The isopropylidene side chain at C-8[11] could be introduced in good yield, but the addition of dilithioacetate to the carbonyl function at C-9 failed completely and also failed when the 3β-hydroxyl group was protected as its tetrahydropyranyl ether. Since the addition of dilithioacetate to a similarly protected keto ester **6b** (vide infra) gave good results, the conclusion was drawn that the γ-lactone was responsible for the failure of this approach. Therefore the second route was elaborated, in which the δ-lactone was first annelated to keto ester **5**, and the construction of the γ-lactone was postponed to a later stage in the synthesis (Scheme II, route II).

The δ-lactone annelation has to be performed on a properly protected 3β-hydroxy keto ester **5**. Protection of the 3β-hydroxyl group as the acetate or trimethylsilyl ether gave problems in the aldol condensation and in the addition of dilithioacetate, respectively. Conversion of **5a** into the 3β-methyl ether **5b** proved to be satisfactory, although at this point it was not known whether selective deprotection in one of the last steps of the total synthesis could be achieved. The formation of this 3β-methyl ether **5b** proved rather difficult, but ultimately the procedure according to Kuhn,[12] i.e., barium oxide and barium hydroxide in dimethyl sulfoxide/dimethylformamide and dimethyl sulfate as methylating agent, gave the desired transformation. Now the introduction of the δ-lactone could be achieved as outlined in Scheme III.

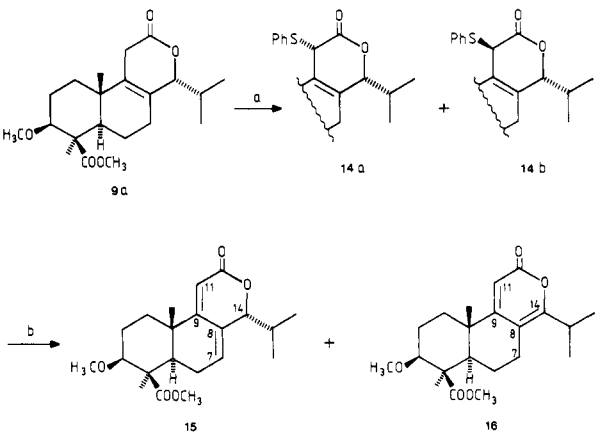
The aldol condensation and subsequent dehydration of the β-ketols resulted in a 8:1 mixture of (*E*)-**6a** and (*Z*)-**7** (84%). These enones were separated, and the addition of dilithioacetate was performed on **6a**, yielding 78% of the 1,2-addition product **8a**.[13] The indicated stereochemistry

Scheme IV[a]



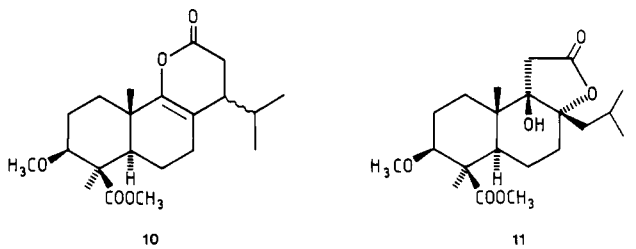
[a] a, *n*-PrSLi, HMPA; b, *hν*, EtOH.

Scheme V[a]



[a] a, LDA, THF, $PhSSO_2Ph$; b, $NaIO_4$, Δ.

of the addition product results from an α attack of the nucleophile.[14] In addition 5% of the 1,4-addition product was obtained, which was not characterized as such but transformed into the δ-lactone **10**. The cyclization of the 1,2 adduct **8a** led to the expected δ-lactones **9a** and **9b** in a 1:1 mixture of the α- and β-C-14 epimers. The yield was 63% since concomitant formation of 20% of the hydroxy γ-lactone **11** occurred. Treatment of the mixture of **9a** and



9b with lithium *n*-propyl mercaptide in HMPA at room temperature afforded the diene dicarboxylic acid **12**, and irradiation of this compound gave stereoselective ring closure to the tricyclic acid **13**[6] (Scheme IV).

For the introduction of the 7(8),9(11)-dienolide moiety, present in **3** and needed for the activation of C-6, a sulfenylation and subsequent oxidative elimination of sulfenic acid was planned.[15] Unfortunately this reaction sequence (Scheme V) applied to the methyl ester **9a**[16] gave the 7(8),9(11)-dienolide **15** and the 8(14),9(11)-dienolide **16** in an unfavorable ratio of 1:3. The attempted hydrolysis of the methyl ester group in **15** with concentrated sulfuric acid[6] was unsuccessful. Therefore, the dehydrogenation

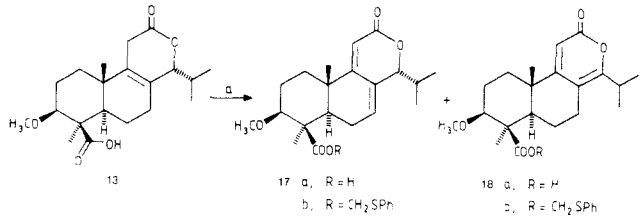
(8) Reuvers, J. T. A.; de Groot, A. *J. Org. Chem.* **1984**, *49*, 1110.
(9) Reuvers, J. T. A.; Wijnberg, J. B. P. A.; de Groot, A. *Recl. Trav. Chim. Pays-Bas* **1985**, *104*, 16.
(10) Reuvers, J. T. A.; de Groot, A. *Synthesis* **1982**, 1105.
(11) In order to avoid confusion the numbering corresponding with that of the diterpenoid dilactones is used throughout the discussion. In the Experimental Section, however, the IUPAC rules are used for the numbering.
(12) Kuhn, R.; Trischmann, H. *Chem. Ber.* **1963**, *96*, 284.
(13) The addition of dilithioacetate to the tetrahydropyranyl-protected keto ester **6b**, performed as described for **8a**, gave the corresponding adduct **8b** in 55% yield.
(14) Welch, S. C.; Prakasa Rao, A. S. C.; Lyon, J. T.; Assercq, J. H. *J. Am. Chem. Soc.* **1983**, *105*, 252.
(15) de Groot, A.; Jansen, B. J. M.; Reuvers, J. T. A.; Tedjo, E. M. *Tetrahedron Lett.* **1981**, *22*, 4137.
(16) This ester **9a** was obtained via a ring opening of the δ-lactones **9a** and **9b** with potassium *tert*-butoxide in dimethyl sulfoxide, followed by irradiation of the resulting dienoic acid.[6]

Table I. ^{13}C NMR Chemical Shifts of Several Compounds Described in This Paper

C atom	5b[a,f]	6a	8a	9a	11	13	14b[d]	15	16	17	3[e]
1	31.3	32.5	30.8	29.0	32.6	32.0	35.8	34.3	36.7	34.8	29.7
2	22.2*	22.3*	22.6*	22.7	21.9	23.6	22.8	22.5	22.7	23.7	28.7
3	87.4	87.7	88.3	87.8	87.7	87.7	87.7	87.3	87.3	86.7	72.4
4	49.8**	50.0	49.9	49.1	49.2	49.0	48.7	49.6	49.6	49.2	
5	53.5	50.1	49.7	52.8	51.0	52.8	52.9	48.4	49.1	49.1	49.5
6	22.4*	21.0*	23.9*	19.7	20.0	19.6	19.9	25.2	19.5	24.5	73.2
7	26.0	26.1	25.7	29.0	39.5	28.9	28.4	130.7	23.7	132.2	121.1
8	37.4	132.4	134.9	125.3	90.6	126.0	132.7	128.1	108.0	127.3	
9	214.5	206.1	78.6	133.8	83.8	132.9	137.4	162.5	168.8	162.0	
10	48.9**	47.3	43.0	37.9	41.3	37.5	38.9	37.5	38.5	37.7	
11			39.3	35.0	40.9	34.6	45.3	109.8	107.0	110.1	111.7
12			175.0	170.6	174.4	170.4	168.4	165.5	164.8	165.4	
14		146.3	131.5	86.7	35.1	83.6	87.8	163.8	83.9	83.7	82.8
15		27.1	26.5	32.2	25.2	29.3	28.8	32.7	29.1	32.9	29.3
16		22.3	23.4	16.7	24.5	18.0	18.5	19.3*	19.7*	19.5	19.6
17		21.6	23.1	14.8	24.5	14.7	14.9	16.1	21.9*	16.2	15.1
18	24.4	24.6	25.2	23.7	24.1	24.2	23.8	24.5	24.4	23.8	23.3
19	174.4	174.4	174.4	174.4	174.5	174.9	174.5	174.0	174.1	174.9	
20	17.0	17.4	12.9	19.4	12.7	19.4	201.7	19.5*	19.4*	21.4	22.1
b	58.3	58.2	58.4	58.6	58.6	57.9	58.7	58.3	58.2	57.9	
c	51.3	51.2	51.2	51.2	51.4		51.2	51.4	51.2		

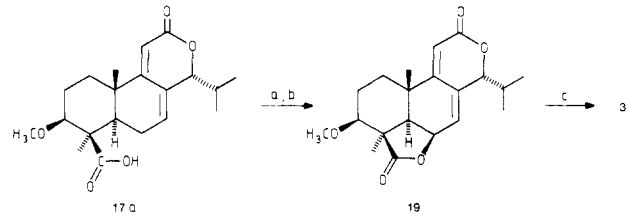
[a] The spectrum of the methyl ether was recorded. [b] The OCH_3 of the ether group. [c] The OCH_3 of the ester group. [d] The SPh group: 135.0 (s)8 133.7 (2d), 128.8 (d). [e] These values correspond with those mentioned in ref 7. The other carbon atoms could not be detected due to the low concentration. [f] *,** these values may be interchanged in one column.

Scheme VI[a]



[a] a, DDQ, MSA, dioxane.

Scheme VII[a]



[a] a, pyr, $HBr{\cdot}Br_2$, HOAc; b, K_2CO_3, DMF; c, BBr_3, CH_2Cl_2.

of **13** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) was investigated as an alternative. Treatment of **13** with DDQ and *p*-toluenesulfonic acid in refluxing dioxane resulted in the formation of a 3:4 mixture of the 7(8),9(11)- and 8(14),9(11)-dienolides **17a** and **18a**. A reaction with DDQ and hydrochloric acid as catalyst at *ambient* temperature failed, although we had hoped to achieve the conversion of **13** exclusively into the desired dienolide **17a**.[17] With DDQ and hydrochloric acid, *reflux* temperature proved necessary to obtain a complete conversion, but again the compounds **17a** and **18a** were both present in the crude reaction mixture, now in a 2:3 ratio. A reaction performed with the bulkier 2-mesitylenesulfonic acid increased the ratio of **17a** and **18a** to 3:2. Separation of the two dienolide carboxylic acids was accomplished after conversion into a mixture of esters, followed by column chromatography and hydrolysis. Reaction of the 3:2 mixture of the potassium salts of acids **17a** and **18a** with (phenylthio)methyl chloride in the presence of 18-crown-6 and sodium iodide[18] (Scheme VI) gave the corresponding esters **17b** and **18b** in 52% and 24% yields, respectively. Cleavage of ester **17b** with trifluoroacetic acid afforded the pure carboxylic acid **17a** in 90% yield. Attempted allylic lactonization by oxidation with lead(IV) acetate[6] failed. Therefore we investigated the γ-lactonization via bromination of the diene moiety followed by a base-induced ring closure,[8] realizing that the regioselectivity of the bromination and the stability of the intermediates might pose problems. The bromination of **17a** with pyridinium bromide perbromide was performed, and after stirring for 24 h 2.8 equiv of anhydrous potassium carbonate was added for the ring closure via elimination and intramolecular substitution (Scheme VII).

A reproducible yield of 10% of the cyclized product **19**, the methyl ether of 3β-hydroxynagilactone F, was obtained via preparative TLC. Finally, demethylation of **19** was achieved with boron tribromide in dichloromethane at −24 °C. Approximately 50% demethylation was obtained in a 48-h treatment, according to ^1H NMR investigation of the crude product. After continuing the reaction with this crude product at 4 °C for 4 days, some decomposition had occurred. After purification by preparative TLC on silica gel, 1 mg (26%) of 3β-hydroxynagilactone F (**3**) was isolated. The product was characterized by ^{13}C NMR, ^1H NMR,[19] IR, mass measurement, and exact mass. The same obsevations described by Hayashi et al.[7] in relation to the stereochemistry of the protons around the dienolide system were made, i.e., the same characteristic couplings and relations in ^1H homospin decoupling experiments were determined. The ^{13}C NMR and IR spectra were in agreement with those of an authentic sample of **3**.

Experimental Section

Melting points are uncorrected. ^1H NMR spectra were recorded on a Varian EM-390 or a Hitachi Perkin-Elmer R-24B spectrometer. The line positions for the ^1H NMR spectra are given in the δ-scale as parts per million (ppm) downfield from the

(17) Sarel, B.; Shalon, Y.; Yamuka, Y. *J. Chem. Soc., Chem. Commun.* **1970**, 81.

(18) (a) Wade, L. G.; Gerdes, J. M.; Wirth, R. P. *Tetrahedron Lett.* **1978**, 731. (b) Ho, T.-L.; Wong, C. M. *J. Chem. Soc., Chem. Commun.* **1973**, 224.

(19) The ^1H NMR spectrum was recorded on a Bruker CXP-300 spectrometer operating at 300.066 MHz.

internal tetramethylsilane in chloroform-*d* as the solvent, unless otherwise stated.

^{13}C NMR spectra were recorded on a Bruker CXP-300 spectrometer operating at 75.460 MHz in the pulse FT mode, using chloroform-*d* as solvent and tetramethylsilane as the internal standard (Table I).

Mass spectral data and exact mass measurements were obtained with an AEI-MS-902 or a VG MM 70-70F instrument. GC analyses were carried out on a Varian 3700 provided with a 2-m glass column packed with 3% SP-2250 on Chromosorb W.

The equipment for all dry reactions performed under a nitrogen atmosphere were dried in an oven at 150 °C for several hours and then allowed to cool in an atmosphere of dry nitrogen. Dry tetrahydrofuran was obtained by distillation of the commercial material from sodium hydride. Dry benzene was obtained by storage of commercial benzene (p.a.) over sodium wire. Other dry solvents were obtained by storage of distilled material over molecular sieves. The solvents for column chromatography were distilled prior to usage. Extracts were dried with anhydrous sodium sulfate prior to filtration and evaporation of the solvent under reduced pressure.

Methyl 5-Oxo-1α,4aβ-dimethyl-2β-methoxy-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene-1β-carboxylate (5b). To a solution of 4.33 g (17 mmol) of **5a**[8] in a mixture of 60 mL of dimethyl sulfoxide and 60 mL of dimethylformamide were added at 0 °C 22.5 g (147 mmol) of barium oxide and 12.3 g (39 mmol) of barium hydroxide octahydrate, and subsequently 44.0 g (350 mmol) of dimethyl sulfate was added dropwise at 0 °C under nitrogen. After stirring for 18 h at ambient temperature under nitrogen, 33 mL of a concentrated aqueous ammonia solution was added dropwise over 0.5 h, and subsequently 35 mL of 4 N hydrochloric acid at 0 °C over 0.5 h. This mixture was poured into water and extracted with ethyl acetate (5 × 100 mL). The organic layer was washed with water and brine and dried. Evaporation of the solvent in vacuo gave the crude product which was purified by column chromatography to afford the methyl ether **5b** (4.01 g, 88%) as a white solid: mp 105.0–106.0 °C; ^1H NMR ($CDCl_3$) δ 1.05 (s, 3 H), 1.35 (s, 3 H), 1.1–2.7 (m, 11 H), 2.73 (dd, *J* = 5, 11 Hz, 1 H), 3.37 (s, 3 H), 3.67 (s, 3 H); mass spectrum (70 eV), *m/e* (relative intensity) 268 (M^+, 3), 236 (46), 110 (33), 95 (26), 71 (100), 58 (40). Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.13; H, 9.02. Found: C, 67.22; H, 8.83.

Methyl 5-Oxo-1α,4aβ-dimethyl-2β-methoxy-6(*E*)-(2-methylpropylidene)-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene-1β-carboxylate (6a) and Methyl 5-Oxo-1α,4aβ-dimethyl-2β-methoxy-6(*Z*)-(2-methylpropylidene)-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene-1β-carboxylate (7). To a stirred solution of 29.5 mmol of *n*-butyllithium in 19.7 mL of hexane at 0 °C was added dropwise over a period of 10 min a solution of 3.25 g (32.2 mmol) of diisopropylamine in 100 mL of dry tetrahydrofuran. After 30 min of stirring at 0 °C, the solution was cooled to −78 °C and then a solution of 7.19 g (26.8 mmol) of methoxy keto ester **5b** in 75 mL of dry tetrahydrofuran was added dropwise over 20 min, and stirring was continued another 0.5 h. Then a solution of 2.88 g (40 mmol) of freshly distilled isobutyraldehyde in 30 mL of dry tetrahydrofuran was added dropwise. Stirring was continued for 1 h, 20 mL of 4 N hydrochloric acid was added at −78 °C, and the mixture was allowed to warm to room temperature. This mixture was poured into 0.5 N hydrochloric acid and extracted with ether (4 × 100 mL). The organic layer was washed with water and brine and dried. Evaporation of the solvent afforded the crude β-hydroxy ketone, which was used immediately without further purification in the dehydration. The crude product was dissolved in 150 mL of dry benzene and a catalytic amount (200 mg) of *p*-toluenesulfonic acid was added. The reaction mixture was refluxed for 2 h in a Dean–Stark apparatus and then poured into saturated sodium bicarbonate solution. The aqueous layer was extracted with ether (2 × 100 mL) and the combined organic layers were washed with brine and dried. The solvent was removed in vacuo, and the residue was purified by column chromatography on silica gel (150 g; eluent diethyl ether/petroleum ether (40–60 °C), 3:7). The first compound eluted was (*Z*)-**7**, a white solid (0.86 g, 10%): mp 104.0–104.5 °C; ^1H NMR ($CDCl_3$) δ 0.89 (d, *J* = 7 Hz, 3 H), 0.98 (s, 3 H), 0.99 (d, *J* = 7 Hz, 3 H), 1.39 (s, 3 H), 1.1–2.8 (m, 10 H), 2.79 (dd, *J* = 5, 10 Hz, 1 H), 3.40 (s, 3 H), 3.67 (s, 3 H), 5.36 (br d, *J* = 10 Hz, 1 H); mass spectrum (70 eV), *m/e* (relative intensity) 322 (M^+, 100), 247 (45), 215 (23), 187 (29), 71 (44). Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 71.00; H, 9.32. The second compound obtained was (*E*)-**6a** as a white solid (6.35 g, 74%): mp 100.0–101.0 °C; ^1H NMR ($CDCl_3$) δ 0.97 (d, *J* = 3 Hz, 3 H), 1.02 (s, 3 H), 1.03 (d, *J* = 3 Hz, 3 H), 1.41 (s, 3 H), 1.3–2.7 (m, 10 H), 2.82 (dd, *J* = 5, 10 Hz, 1 H), 3.40 (s, 3 H), 3.67 (s, 3 H), 6.29 (br d, *J* = 10 Hz, 1 H); mass spectrum (70 eV), *m/e* (relative intensity) 322 (M^+, 17), 290 (37), 247 (19), 121 (37), 71 (100), 55 (27), 41 (35). Anal. Calcd for $C_{19}H_{30}O_4$: C, 70.77; H, 9.38. Found: C, 70.99; H, 9.46.

Methyl 5α-(Carboxymethyl)-1α,4aβ-dimethyl-5β-hydroxy-2β-methoxy-6(*E*)-(2-methylpropylidene)-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene-1β-carboxylate (8a). To a stirred solution of 52.0 mmol of *n*-butyllithium in 34.7 mL of hexane was added dropwise at 0 °C over 10 min a solution of 5.73 g (56.7 mmol) of diisopropylamine in 150 mL of dry tetrahydrofuran. After stirring for 0.5 h at 0 °C, 12.7 g (70.9 mmol) of hexamethylphosphorus triamide was added at once. The solution was cooled to −20 °C and then a solution of 1.42 g (23.6 mmol) of acetic acid in 35 mL of dry tetrahydrofuran was added dropwise over 10 min. This mixture was heated at 50 °C for 3 h and then cooled to −20 °C. A solution of 6.35 g (19.7 mmol) of (*E*)-**6a** in 30 mL of dry tetrahydrofuran was added dropwise, and this mixture was stirred for 16 h under nitrogen during which time it was allowed to warm to room temperature. The mixture was poured into 1 N hydrochloric acid and extracted with chloroform (4 × 100 mL). The organic layer was washed with water and brine and dried. After removal of the solvent in vacuo the residue was chromatographed on silica gel (150 g; eluent diethyl ether), yielding 5.86 g (78%) of the 1,2-addition product **8a** as a white solid: mp 210.0–212.0 °C; ^1H NMR ($CDCl_3$) δ 0.81 (s, 3 H), 0.87 (d, *J* = 6 Hz, 3 H), 0.97 (d, *J* = 6 Hz, 3 H), 1.39 (s, 3 H), 1.1–2.8 (m, 11 H), 2.60 (H_A, J_{AB} = 13 Hz, 1 H), 2.90 (H_B, 1 H), 3.40 (s, 3 H), 3.63 (s, 3 H), 5.23 (d, *J* = 9 Hz, 1 H), 8.1 (br s, 2 H, exchanges with D_2O); mass spectrum (70 eV), *m/e* (relative intensity) 382 (M^+, 20), 364 (6), 350 (5), 338 (9), 323 (24), 311 (18), 293 (29), 237 (39), 180 (41), 85 (59), 71 (100). Anal. Calcd for $C_{21}H_{34}O_6$: C, 65.94; H, 8.96. Found: C, 65.72; H, 8.89. In addition, 0.407 g (5%) of the Michael-type addition product was isolated. This product was not characterized, but ring closure according to the preparation of **9** gave **10**: ^1H NMR ($CDCl_3$) δ 0.93 (m, 6 H), 0.99 (s, 3 H), 1.40 (s, 3 H), 1.2–3.0 (m, 14 H), 3.42 (s, 3 H), 3.65 (s, 3 H); mass spectrum (70 eV), *m/e* (relative intensity) 364 (M^+, 46), 321 (100), 289 (84), 229 (62), 123 (47), 71 (69); calcd for $C_{21}H_{32}O_5$ M^+ 364.2250, found M^+ 364.2238.

Diastereomeric Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4-(1-methylethyl)-1,4,5,6,6aα,7,8,9,10,10a-decahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (9) and Methyl 2-Oxo-6α,9aβ-dimethyl-9bβ-hydroxy-7β-methoxy-3aβ-(2-methylpropyl)-1,2,3a,4,5aα,6,7,8,9,9a,9b-dodecahydronaphtho[2,1-*b*]furan-7β-carboxylate (11). To a solution of 1.03 g (2.68 mmol) of **8a** in 75 mL of dry benzene was added 100 mg of *p*-toluenesulfonic acid, and this mixture was refluxed in a Dean–Stark apparatus for 14 h. After cooling, the reaction mixture was poured into a saturated aqueous sodium bicarbonate solution (75 mL). The aqueous layer was extracted with ether (2 × 75 mL), and the combined organic layers were washed with brine and dried. The solvent was removed under reduced pressure. Chromatography of the crude product on silica gel afforded as first component **9** (0.615 g, 63%) as a solid which consisted of a diastereomeric mixture of the α- and β-epimers at C-14: ^1H NMR ($CDCl_3$) δ 0.80 (d, *J* = 6 Hz, 3 H), (0.89 (s) + 0.90 (s), 3 H), 1.08 (d, *J* = 6 Hz, 3 H), 1.40 (s, 3 H), 1.2–2.5 (m, 10 H), 2.76 (dd, *J* = 5, 11 Hz, 1 H), 2.93 (m, 2 H), 3.40 (s, 3 H), 3.63 (s, 3 H), 4.49 (m, 1 H). The second component eluted was the γ-lactone **11** (0.206 g, 20%) as a white solid: mp 189.0–190.5 °C; ^1H NMR ($CDCl_3$) δ 0.93 (s, 3 H), 0.99 (d, *J* = 6 Hz, 6 H), 1.42 (s, 3 H), 1.2–2.4 (m, 13 H), 2.34 (H_A, J_{AB} = 17.7 Hz, 1 H), 2.94 (H_B, 1 H), 2.73 (dd, *J* = 5, 11 Hz, 1 H), 3.40 (s, 3 H), 3.68 (s, 3 H); mass spectrum (70 eV), *m/e* (relative intensity) 382 (M^+, 4), 323 (8), 293 (11), 237 (17), 180 (25), 85 (41), 71 (100). Anal. Calcd for $C_{21}H_{34}O_6$: C, 65.94; H, 8.96. Found: C, 66.19; H, 9.10.

5(*E*)-(Carboxymethylene)-1α,4aβ-dimethyl-2β-methoxy-6(*E*)-(2-methylpropylidene)-1,2,3,4,4a,5,6,7,8,8aα-decahydronaphthalene-1β-carboxylic Acid (12). 1-Propanethiol

(1.34 g, 17.6 mmol) was added dropwise under nitrogen via a syringe to a suspension of 0.141 g (17.6 mmol) of lithium hydride in 8.0 mL of dry HMPA. This mixture was stirred under nitrogen at room temperature overnight. Then a solution of 0.400 g (1.10 mmol) of the ester lactone **9a,b** in 1 mL of dry HMPA was added dropwise, and the reaction mixture was stirred an additional 24 h. The solution was poured into ice-cold 0.1 N aqueous sodium hydroxide solution and this aqueous layer was washed with dichloromethane (3 × 50 mL). The aqueous layer was acidified to pH 2 with concentrated hydrochloric acid and extracted with dichloromethane (5 × 50 mL). The organic layer was washed with brine and dried. After evaporation of the solvent under reduced pressure, there remained a crude product which contained some HMPA. Column chromatography on silica gel (50 g; eluent diethyl ether) afforded 0.351 g (91%) of the diene dicarboxylic acid **12** as a white solid: mp 180.0–182.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, J = 5 Hz, 3 H), 1.00 (s, 3 H), 1.00 (d, J = 5 Hz, 3 H), 1.42 (s, 3 H), 1.2–3.0 (m, 11 H), 3.52 (s, 3 H), 5.04 (dt, J = 1, 9 Hz, 1 H), 5.45 (s, 1 H), 11 (br s, 2 H, exchanges with D_2O); mass spectrum (70 eV), m/e (relative intensity) 350 (M^+, 5), 307 (100), 289 (19), 229 (19). Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.54; H, 8.63. Found: C, 68.48; H, 8.83.

2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-1,4,5,6,6aα,7,8,9,10,10a-decahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylic Acid (13). A solution of 0.920 g (2.63 mmol) of diene dicarboxylic acid **12** in 95% ethanol (300 mL) was irradiated with a high-pressure mercury lamp at 0 °C for 6 h under nitrogen. After evaporation of the solvent in vacuo at ambient temperature, the residue was purified on silica gel (eluent diethyl ether) to afford lactone **13** in a quantitative yield: ^{1}H NMR ($CDCl_3$) δ 0.80 (d, J = 8 Hz, 3 H), 1.00 (s, 3 H), 1.10 (d, J = 8 Hz, 3 H), 1.43 (s, 3 H), 1.1–2.3 (m, 10 H), 2.90 (m, 3 H), 3.87 (s, 3 H), 4.57 (m, 1 H), 9.5 (br s, 1 H, exchanges with D_2O); mass spectrum (70 eV), m/e (relative intensity) 350 (M^+, 3), 307 (23), 289 (24), 229 (25), 213 (20), 184 (66), 83 (100); calcd for $C_{20}H_{30}O_5$ M^+ 350.2093, found M^+ 350.2096.

Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-1,4,5,6,6aα,7,8,9,10,10a-decahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (9a). The procedure of Hayashi et al.[6] was employed. To a solution of 1.113 g (3.06 mmol) of **9a** and **9b** in dry dimethyl sulfoxide under nitrogen was added at room temperature 0.529 g (4.68 mmol) of potassium *tert*-butoxide. After 4 h of stirring an additional amount of potassium *tert*-butoxide (0.320 g, 2.85 mmol) was added and stirring was continued for 18 h. Then the mixture was poured into 0.5 N hydrochloric acid and extracted with chloroform (4 × 75 mL). The organic layer was washed with brine and dried. After filtration and evaporation of the solvent in vacuo, the residual oil was chromatographed on silica gel (100 g, eluent diethyl ether) to afford the dienoic acid ester (0.780 g, 70%) as a white solid: mp 145.0–147.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.92 (d, J = 5 Hz, 3 H), 0.95 (s, 3 H), 0.98 (d, J = 5 Hz, 3 H), 1.37 (s, 3 H), 1.2–2.7 (m, 10 H), 2.81 (dd, J = 5, 12 Hz, 1 H), 3.43 (s, 3 H), 3.68 (s, 3 H), 5.07 (d, J = 10 Hz, 1 H), 5.50 (s, 1 H), 9.5 (br s, 1 H, exchanges with D_2O); mass spectrum (70 eV), m/e (relative intensity) 364 (M^+, 3), 322 (21), 321 (100), 289 (13), 257 (6), 229 (15). Anal. Calcd for $C_{21}H_{32}O_5$: C, 69.20; H, 8.85. Found: C, 68.89; H, 8.83.

A solution of 0.710 g (1.95 mmol) of this dienoic acid ester in 95% ethanol (300 mL) was irradiated with a high-pressure mercury lamp at 0 °C for 6 h under nitrogen. After evaporation of the solvent in vacuo at ambient temperature, the residue was purified on silica gel (eluent diethyl ether) to afford 0.552 g (78%) of **9a**: ^{1}H NMR ($CDCl_3$) δ 0.80 (d, J = 8 Hz, 3 H), 0.89 (s, 3 H), 1.04 (d, J = 8 Hz, 3 H), 1.40 (s, 3 H), 1.1–2.5 (m, 10 H), 2.78 (dd, J = 5, 11 Hz, 1 H), 2.95 (m, 2 H), 3.41 (s, 3 H), 3.65 (s, 3 H), 4.55 (br q, 1 H); mass spectrum (70 eV), m/e (relative intensity) 364 (M^+, 3), 332 (15), 321 (39), 289 (57), 257 (66), 229 (59), 73 (73), 53 (100); calcd for $C_{21}H_{32}O_5$ M^+ 364.2250, found M^+ 364.2236.

Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-1α-(phenylthio)-1,4,5,6,6aα,7,8,9,10,10a-decahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (14a) and Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-1β-(phenylthio)-1,4,5,6,6aα,7,8,9,10,10a-decahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (14b). To a solution of 1.92 mmol of *n*-butyllithium in 1.3 mL of hexane and 10 mL of dry tetrahydrofuran was added dropwise over a period of 5 min at −10 °C a solution of 209 mg (2.1 mmol) of diisopropylamine in 5 mL of dry tetrahydrofuran under nitrogen. After being stirred for 0.5 h the solution was cooled to −78 °C and then a solution of 574 mg (1.58 mmol) of **9a** in 10 mL of dry tetrahydrofuran was added dropwise over 15 min. The solution turned orange and was stirred for another 0.5 h at −78 °C. This cooled solution was then added dropwise to a solution of 434 mg (1.73 mmol) of benzenesulfenyl thiosulfonate in 10 mL of dry tetrahydrofuran which was cooled (−78 °C). Stirring was continued for 1.5 h. The reaction mixture was quenched with 1 mL of 4 N hydrochloric acid and subsequently poured into 25 mL of 0.5 N hydrochloric acid. This mixture was extracted with dichloromethane (3 × 50 mL). The organic layer was washed with water and brine and dried. Evaporation of the solvent afforded the crude product. Column chromatography on silica gel afforded 0.296 g (63%) of a 7:3 mixture of **14b** and **14a**. After repeated chromatography, 26 mg of **14a** was obtained in pure form: ^{1}H NMR ($CDCl_3$) δ 0.90 (s, 3 H), 1.06 (d, J = 6 Hz, 3 H), 1.13 (d, J = 6 Hz, 3 H), 1.43 (s, 3 H), 1.1–2.5 (m, 10 H), 2.85 (dd, J = 5, 10 Hz, 1 H), 3.43 (s, 3 H), 3.63 (s, 3 H), 4.00 (s, 1 H), 4.20 (br s, 1 H), 7.60 (m, 5 H); mass spectrum (70 eV), m/e (relative intensity) 472 (M^+, 5), 363 (100), 362 (48), 321 (23), 287 (25), 71 (71). In addition, 60 mg of **14b** was obtained in pure form as a white solid: mp >170 °C dec; ^{1}H NMR ($CDCl_3$) δ 0.83 (d, J = 7 Hz, 3 H), 1.16 (d, J = 7 Hz, 3 H), 1.23 (s, 3 H), 1.41 (s, 3 H), 1.1–2.5 (m, 10 H), 2.77 (dd, J = 5, 11 Hz, 1 H), 3.41 (s, 3 H), 3.67 (s, 3 H), 4.28 (s, 1 H), 4.93 (br s, 1 H), 7.4 (m, 5 H); mass spectrum (70 eV), m/e (relative intensity) 472 (M^+, 1), 363 (100), 362 (56), 321 (30), 71 (75). Anal. Calcd for $C_{27}H_{36}O_5S$: C, 68.61; H, 7.68. Found: C, 68.08; H, 7.83.

Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-4,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (15) and Methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4-(1-methylethyl)-5,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (16). To a solution of 170 mg (0.36 mmol) of a 7:3 mixture of **14b** and **14a** in 10 mL of methanol and 1 mL of water was added 470 mg (2.2 mmol) of sodium periodate. This mixture was refluxed for 6 h and then the reaction mixture was poured into water and extracted with dichloromethane (3 × 25 mL). The organic layer was washed with water and brine and dried. Evaporation of the solvent under reduced pressure afforded an oil which was chromatographed on silica gel (35 g, eluent diethyl ether/petroleum ether (40–60 °C), 3:1), affording 17 mg (13%) of **15**: ^{1}H NMR ($CDCl_3$) δ 0.93 (d, J = 7 Hz, 3 H), 1.03 (s, 3 H), 1.06 (d, J = 7 Hz, 3 H), 1.38 (s, 3 H), 1.1–2.6 (m, 8 H), 2.83 (dd, J = 4, 10 Hz, 1 H), 3.40 (s, 3 H), 3.69 (s, 3 H), 4.73 (m, 1 H), 5.73 (br s, 1 H), 6.03 (m, 1 H); mass spectrum (70 eV), m/e (relative intensity) 362 (M^+, 0.3), 287 (5), 227 (3), 85 (89), 83 (100); calcd for $C_{21}H_{30}O_5$ M^+ 362.2093, found M^+ 362.2088. The second compound isolated was **16** (53 mg, 41%): ^{1}H NMR ($CDCl_3$) δ 1.13 (s, 3 H), 1.19 (d, J = 6 Hz, 3 H), 1.21 (d, J = 6 Hz, 3 H), 1.41 (s, 3 H), 1.2–3.2 (m, 11 H), 3.40 (s, 3 H), 3.67 (s, 3 H), 6.04 (s, 1 H); mass spectrum (70 eV), m/e (relative intensity) 362 (M^+, 60), 334 (41), 319 (48), 308 (46), 71 (100), 59 (20), 45 (84), 43 (81); calcd for $C_{21}H_{30}O_5$ M^+ 362.2093, found M^+ 362.2101.

Attempted Hydrolysis of Dienolide Ester 15. The method of Hayashi was employed.[6] The ester **15** (17 mg) was dissolved in 0.3 mL of concentrated sulfuric acid. After 2 h of standing at room temperature crushed ice was added, and this mixture was extracted with chloroform (4 × 25 mL). The organic layer was washed with brine and dried. Evaporation of the solvent gave the starting material in quantitative yield.

2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-4,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylic Acid (17a) and 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4-(1-methylethyl)-5,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylic Acid (18a). To a solution of 0.200 g (0.57 mmol) of **13** in 15 mL of dioxane were added 0.259 g (1.14 mmol) of DDQ and subsequently 0.270 g (1.14 mmol) of 2-mesitylenesulfonic acid. The mixture was refluxed under nitrogen for 5.5 h and, after cooling, concentrated in vacuo in the presence of 5 g of silica gel. The resulting mixture was poured on a column of silica gel (25 g) and eluted with diethyl ether, affording 0.200 g of an oil which solidified on treatment with diethyl ether. The ether was decanted and 0.120 g (60%) of a mixture of **17a** and **18a** in a ratio of 3:2 remained. This

mixture could not be separated and was used as such in the next reaction.

(Phenylthio)methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4α-(1-methylethyl)-4,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho[2,1-*c*]pyran-7β-carboxylate (17b) and (Phenylthio)methyl 2-Oxo-7α,10aβ-dimethyl-8β-methoxy-4-(1-methylethyl)-5,6,6aα,7,8,9,10,10a-octahydro-2*H*-naphtho-[2,1-*c*]pyran-7β-carboxylate (18b). To a suspension of 120 mg (0.34 mmol) of a 3:2 mixture of **17a** and **18a** in 15 mL of dry benzene was added 129 mg (1.15 mmol) of potassium *tert*-butoxide, and this suspension was stirred for 25 min. Then 61 mg (0.23 mmol) of 18-brown-6 was added and stirring was continued for 5 min. Subsequently 34 mg (0.25 mmol) of sodium iodide and a solution of 166 mg (1.15 mmol) of (phenylthio)methyl chloride in 3 mL of dry benzene was added, and this mixture was refluxed for 10 h. After cooling, the reaction mixture was poured into water and extracted with dichloromethane (3 × 25 mL). The organic layer was washed with brine and dried. Evaporation of the solvent afforded a residue which was chromatographed on silica gel (30 g; eluent petroleum ether (40–60 °C)/diethyl ether, 7:3). The first compound eluted was 84 mg (52%) of **17b**: ^{1}H NMR ($CDCl_3$) δ 0.93 (d, J = 7 Hz, 3 H), 1.02 (s, 3 H), 1.05 (d, J = 7 Hz, 3 H), 1.40 (s, 3 H), 1.2–2.6 (m, 8 H), 2.83 (dd, J = 7, 12 Hz, 1 H), 3.40 (s, 3 H), 4.70 (m, 1 H), 5.37 (H_A, J_{AB} = 12.6 Hz, 1 H), 5.65 (H_B, 1 H), 5.68 (s, 1 H), 5.93 (m, 1 H), 7.2–7.6 (m, 5 H); mass spectrum (70 eV), m/e (relative intensity) 470 (M^+, 10), 347 (13), 123 (100); calcd for $C_{27}H_{34}O_5S$ M^+ 470.2127, found M^+ 470.2120. The second compound eluted was 38 mg (24%) of **18b** as a white solid: mp 164.5–166.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.12 (s, 3 H), 1.16 (d, J = 3 Hz, 3 H), 1.23 (d, J = 3 Hz, 3 H), 1.40 (s, 3 H), 1.4–2.8 (m, 10 H), 2.95 (dd, J = 6, 15 Hz, 1 H), 3.42 (s, 3 H), 5.35 (H_A, J_{AB} = 12.1 Hz, 1 H), 5.57 (H_B, 1 H), 6.00 (s, 1 H), 7.2–7.6 (m, 5 H); mass spectrum (70 eV, m/e (relative intensity) 470 (M^+, 43), 331 (100), 303 (12), 271 (26), 123 (27). Anal. Calcd for $C_{27}H_{34}O_5S$: C, 68.90; H, 7.28. Found: C, 68.71; H, 7.39.

Hydrolysis of 17b to 17a with Trifluoroacetic Acid. The phenylthio ester **17b** (0.110 g, 0.23 mmol) was dissolved in 1 mL of trifluoroacetic acid at ambient temperature. After stirring for 15 min the solution was poured into water (50 mL) and extracted with dichloromethane (5 × 20 mL). The organic layer was washed with brine, dried, and filtered, and the solvent was evaporated under reduced pressure. The residual oil was crystallized from methanol–diisopropyl ether to afford 52 mg (64%) of **17a**. The mother liquor was chromatographed on silica gel (10 g; eluent diethyl ether) and afforded an additional 23 mg (28%) product: mp 193.5–194.5 °C; ^{1}H NMR ($CDCl_3$) δ 0.94 (d, J = 7 Hz, 3 H), 1.06 (d, J = 7 Hz, 3 H), 1.10 (s, 3 H), 1.45 (s, 3 H), 1.2–2.7 (m, 8 H), 2.99 (dd, J = 3, 10 Hz, 1 H), 3.58 (s, 3 H), 4.75 (m, 1 H), 5.70 (br s, 1 H), 6.10 (m, 1 H); mass spectrum (70 eV), m/e (relative intensity) 348 (M^+, 5), 346 (10), 330 (11), 287 (100), 227 (86) 37 (38); calcd for $C_{20}H_{28}O_5$ M^+ 348.1937, found M^+ 348.1934.

3aα,10bβ-Dimethyl-3β-methoxy-7α-(1-methylethyl)-1,2,3,3a,5a,7,10b,10cα-octahydro-4*H*,9*H*-furo[2′,3′,4′:4,5]naphtho[2,1-*c*]pyran-4,9-dione (19). To a solution of 81 mg (0.23 mmol) of **17a** in 2 mL of dimethylformamide was added 93 mg of pyridine·HBr·Br_2 (80%) (0.23 mmol), and this mixture was stirred for 17 h at ambient temperature. To this solution was added 90 mg (0.65 mmol) of dry potassium carbonate. After being stirred overnight at room temperature under nitrogen, the reaction mixture was poured into water and extracted with dichloromethane (5 × 20 mL). The organic layer was washed with brine and dried. Evaporation of the solvent afforded an oil, which was purified via preparative TLC eluting twice with diethyl ether. This afforded 8 mg (10%) of **19**: ^{1}H NMR ($CDCl_3$) δ 1.00 (d, J = 6 Hz, 3 H), 1.20 (d, J = 6 Hz, 3 H), 1.30 (s, 3 H), 1.55 (s, 3 H), 1.5–2.4 (m, 6 H), 3.33 (dd, J = 6, 14 Hz, 1 H), 3.55 (s, 3 H), 4.87 (t, J = 2 Hz, 1 H), 5.00 (m, 1 H), 5.77 (br s, 1 H), 6.15 (m, 1 H); mass spectrum (70 eV), m/e (relative intensity) 346 (M^+, 29), 318 (15), 303 (30), 286 (18), 275 (100), 243 (53); calcd for $C_{20}H_{26}O_5$ M^+ 346.1780, found M^+ 346.1774.

3aα,10bβ-Dimethyl-3β-hydroxy-7α-(1-methylethyl)-1,2,3,3a,5a,7,10b,10cα-octahydro-4*H*,9*H*-furo[2′,3′,4′:4,5]naphtho[2,1-*c*]pyran-4,9-dione (3) (3β-Hydroxynagilactone F). To a solution of 4 mg of **19** in 1.0 mL of dry dichloromethane at −40 °C was added under nitrogen 0.5 mL of 1 M boron tribromide solution in dichloromethane. After standing at −24 °C for 48 h the reaction mixture was poured into saturated aqueous sodium bicarbonate, extracted with dichloromethane (3 × 25 mL), and washed with brine and dried. Evaporation of the solvent in vacuo afforded 4 mg of crude product which consisted of a ca. 1:1 mixture of product and starting material. The reaction was repeated on the crude product in the same way as described, but the temperature was raised to 4 °C and the mixture was allowed to stand for 4 days at this temperature. The same workup procedure afforded a crude product, which was purified by preparative TLC, affording 1.0 mg (26%) of the desired product **3**: ^{1}H NMR ($CDCl_3$) δ 0.99 (d, J = 6, 5 Hz, 3 H), 1.21 (d, J = 6.5 Hz, 3 H), 1.24 (s, 3 H), 1.55 (s, 3 H), 1.75–1.91 (m, 2 H), 1.94 (d, J = 4.5 Hz, H_5), 2.14–2.25 (m, 2 H), 2.25–2.39 (m, H_{15}), 3.57–3.80 (m, 2 H^{21}), 4.89 (ddd, J = 2.0, 2.0, 2.0 Hz, H_{14}), 5.11 (ddd, J = 4.0, 4.5, 2.0 Hz, H_6), 5.78 (d, J = 2.0 Hz, H_{11}), 6.18 (ddd, J = 2.0, 2.0, 4.0 Hz, H_7); IR (KBr)[20] 3476, 1769, 1707, 1610 cm^{-1}; mass spectrum (70 eV), m/e (relative intensity) 332 (M^+, 45), 289 (83), 261 (100), 243 (95), 215 (53); calcd for $C_{19}H_{24}O_5$ M^+ 332.1624, found 332.1635.

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Registry No. (±)-**3**, 104833-03-6; (±)-**5a**, 88825-31-4; (±)-**5b**, 104761-89-9; **5b** (β-hydroxy ketone), 104761-90-2; (±)-(*E*)-**6a**, 104761-92-4; (±)-(*Z*)-**7**, 104761-91-3; (±)-**8a**, 104761-93-5; (±)-**8a** (dienoic acid ester), 104761-99-1; (±)-**9a**, 104761-95-7; (±)-**9b**, 104833-02-5; **10**, 104761-94-6; (±)-**11**, 104761-96-8; (±)-**12**, 104761-97-9; (±)-**13**, 104761-98-0; (±)-**14a**, 104870-59-9; (±)-**14b**, 104762-00-7; (±)-**15**, 104762-01-8; (±)-**16**, 104762-02-9; (±)-**17a**, 104762-03-0; (±)-**17b**, 104762-05-2; (±)-**18a**, 104762-04-1; (±)-**19**, 104778-47-4; isobutyraldehyde, 78-84-2; acetic acid, 64-19-7; 1-propanethiol, 107-03-9.

Supplementary Material Available: ^{13}C NMR, ^{1}H NMR, and IR spectra for β-hydroxynagilactone F (**3**) (6 pages). Ordering information is given on any current masthead page.

(20) This IR spectrum was recorded on a Brucker IFS-85 using the diffuse-reflexion technique.

(21) 1 H exchanges with CD_3OD. The remaining H_3 appears as a doublet of doublets with coupling constants of 7 and 11 Hz.