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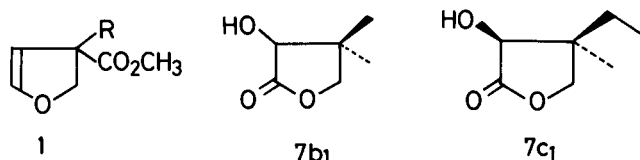
Received October 2, 1990

The title compounds were synthesized from 3-furoic acid *via* the Birch reduction.*J. Heterocyclic Chem.*, **28**, 619 (1991).

The Birch reduction [1] of 3-furoic acid provides a useful entry into the total synthesis of the branched-chain sugars, for example, apiose [2] and dihydrostreptose [3].

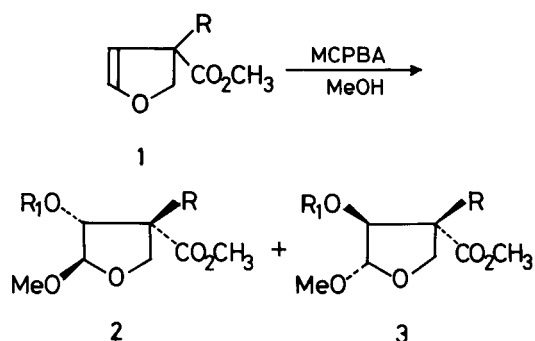
Birch and Slobbe have reported that the reduction of 2-furoic acid with a metal in ammonia by addition of an alkyl halide instead of a proton source gave the reductive alkylation product [4], while the reduction of 3-furoic acid proceeded with β -elimination and ring opening to give the hydroxy lactone in place of the alkylation product [5].

Since the introduction of an alkyl group into the 3-position of 2,3-dihydrofuroic acid is very useful as a synthetic intermediate of 3,3-dialkyl butanolides, we tried alkylation [6] on the 3-position of methyl 2,3-dihydro-3-furoate (**1a**).



Several of the alkylated compounds were successfully converted into natural products. (\pm)-Pantolactone (**7b₁**), a degradation product of pantothenic acid and (\pm)-dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c₁**) [7], a pantolactone homologue isolated from *Marshallia tenuifolia*, were synthesized from **1b** and **1c**, respectively.

Scheme A



R
a H
b CH₃
c CH₂CH₃

R
a₁ H
a₂ H
b₁ CH₃
b₂ CH₃
c₁ CH₂CH₃
c₂ CH₂CH₃
c₃ CH₂CH₃

R₁
H
COC₆H₄NO₂
H
COC₆H₄NO₂
H
COC₆H₄NO₂
SO₂C₆H₄CH₃

Oxidation of **1** with *m*-chloroperbenzoic acid in methanol gave a mixture of *erythro*-**2** and *threo*-**3** in an approximate ratio of 2:1. However, the *p*-nitrobenzoate derivatives were separable by silica gel column chromatography. The peroxy acid oxidation of **1**, *via* the production of unstable 4,5-epoxide, proceeded with ring opening of the epoxide by the attack of methanol as solvent to give a 4-hydroxy-5-methoxy compound. No nmr coupling was observed between H-4 and H-5, indicating that the methoxy group is *anti* with respect to the hydroxy group. As epoxidation of β,γ -unsaturated ester produces predominantly *cis*-epoxide, it is not unreasonable to assume hydrogen bonding [8] of the peroxy acid molecule to the carbonyl oxygen (Scheme A).

The structures of **2** and **3** were elucidated by ¹H nmr (Tables 1, 2 and 3). The larger coupling (*J* = 5.5 Hz) between H-3 and H-4 in *erythro-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-tetrahydrofuran-3-carboxylate (**2a₂**) than in *threo-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-tetrahydrofuran-3-carboxylate (**3a₂**) (*J* = 2.9

Scheme B

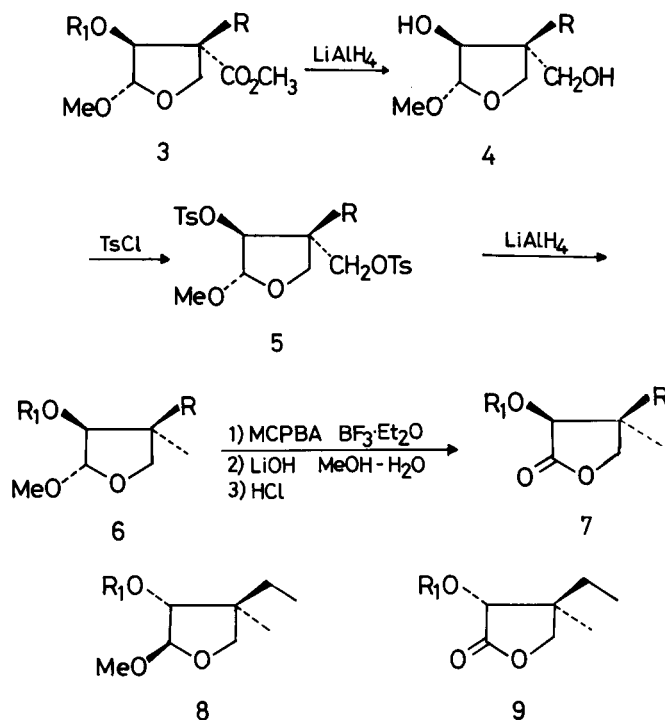


Table 1
¹H NMR (400 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Compounds 2 and 3

Compound No.	H-2/H-2'	H-3	H-4	H-5	OMe	CO ₂ Me	CH ₃	CH ₂ CH ₃	CH ₂ CH ₃	arom
2a ₂	4.21 t 4.51 t	3.66 dt	5.54 d	5.01 s	3.37	3.62				8.12 d 8.27 d
2b ₂	3.87 d 4.72 d		5.28 s	4.98 s	3.39	3.57	1.59			8.11 d 8.26 d
2c ₂	3.94 d 4.67 d		5.29 s	4.93 s	3.35	3.55		0.83 t		8.09 d 8.25 d
3a ₂	4.24 t 4.35 t	3.28 dddd	5.67 d	5.07 s	3.36	3.76				8.21 d 8.30 d
3b ₂	3.81 d 4.55 d		5.73 s	5.00 s	3.34	3.75	1.36			8.19 d 8.28 d
3c ₂	3.90 d 4.70 d		5.78 s	4.93 s	3.31	3.76		0.84 t		8.23 d 8.30 d
No.	J (2,2')	J (2,3)	J (3,4)	J (arom)	J (CH ₂ CH ₃)	J (gem CH ₂)				
2a ₂	8.6	8.6	5.5	8.5						
2b ₂	9.1			8.5						
2c ₂	8.6			8.6	7.3	14.0				
3a ₂	7.3	7.3	2.9	8.6						
3b ₂	8.6			8.6						
3c ₂	8.5			8.5	7.3	14.0				

Table 2
¹³C NMR (25MHz) Chemical Shifts (ppm) of Compounds 2 and 3

Compound No.	C-2	C-3	C-4	C-5	OMe	CO ₂ Me	CH ₃	CH ₂ CH ₃	CO ₂ Me
2a ₂	67.5 t	45.6 d	78.0 d	106.4 d	54.8	52.4			169.4
2b ₂	75.1 t	52.7 s	83.9 d	108.2 d	55.2	52.4	22.9 q		172.3
2c ₂	72.4 t	58.0 s	83.6 d	107.8 d	55.0	52.1	9.8 q	28.6 t	171.4
3a ₂	67.7 t	49.4 d	81.7 d	106.8 d	54.7	52.7			170.4
3b ₂	74.8 t	52.3 s	82.2 d	107.2 d	54.7	52.6	17.2 q		173.4
3c ₂	73.0 t	56.7 s	80.8 d	106.6 d	54.2	52.3	9.9 q	24.8 t	172.4

Table 3
 Physical Data for Compounds 2 and 3

Compound No.	TLC Rf [a]	mp °C	Molecular Formula	Analyses %			IR (cm ⁻¹) nujol
				Calcd./	Found	N	
				C	H		
2a ₂	0.26	98-99	C ₁₄ H ₁₅ NO ₈	51.70	4.65	4.31	1740, 1720, 1610, 1380, 1220, 1105, 1070, 720
				51.80	4.63	4.27	
2b ₂	0.35	106-107	C ₁₅ H ₁₇ NO ₈	53.10	5.05	4.13	1745, 1725, 1608, 1355, 1320, 1280, 1105, 1060, 720
				53.12	5.04	4.09	
2c ₂	0.48	99-100	C ₁₆ H ₁₉ NO ₈	54.39	5.42	3.96	1740, 1720, 1610, 1355, 1270, 1220, 1110, 1070, 720
				54.47	5.43	3.95	
3a ₂	0.20	103-104	C ₁₄ H ₁₅ NO ₈	51.70	4.65	4.31	1740, 1725, 1605, 1350, 1300, 1280, 1110, 1070, 730
				51.76	4.60	4.26	
3b ₂	0.30	75-76	C ₁₅ H ₁₇ NO ₈	53.10	5.05	4.13	1740, 1730, 1610, 1355, 1290, 1115, 1105, 1055, 720
				53.17	5.02	4.08	
3c ₂	0.40	84-85	C ₁₆ H ₁₉ NO ₈	54.39	5.42	3.96	1740, 1730, 1605, 1380, 1350, 1220, 1105, 1065, 720
				54.49	5.30	3.85	

[a] 4:1 Hexame-ethyl acetate.

Table 4
 ^1H NMR (100 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Pantolactone Series (R = CH₃)

Compound No.	H-2/H-2'	H-3	H-4	H-5	OMe	CH ₃	OH	arom	J (2,2)	J (4,5)
4b [a]	3.56 d 3.79 d		3.82 s	4.75 s	3.27	1.06			8.5	0
6b ₁	3.67 d 3.72 d		3.70dd	4.79 d	3.40	1.07 1.08	3.19d [b]		8.5	2.9
6b ₂	3.77 d 3.84 d		5.09 d	4.99 d	3.39	1.10 1.26		8.24 q [c]	8.5	1.3
7b ₁		4.10 s		3.89 s		0.97 1.11	4.05 s			
7b ₂		5.60 s		4.11 s		1.21 1.27		8.26 s		

[a] 3.59 (s, CH₂OH). [b] J_{4,OH} = 5.2 Hz. [c] J_{arom} = 8.5 Hz.

Table 5
 ^{13}C NMR (25MHz) Chemical Shifts (ppm) of Pantolactone Series (R = CH₃)

Compound No.	C-2	C-3	C-4	C-5	OCH ₃	CH ₃	arom				
4b [a]	75.2 t	46.0 s	84.5 d	111.3 d	55.1	20.6					
6b ₁	78.7 t	41.7 s	83.7 d	110.9 d	55.7	19.9 23.7					
6b ₂	79.5 t	42.0 s	86.2 d	109.1 d	55.4	21.4 25.6	123.7	130.9	135.7	150.8	164.0
7b ₁	178.1 s	75.4 d	40.6 s	76.4 t		18.8 22.6					
7b ₂	172.0 s	78.4 d	40.6 s	76.4 t		20.1 23.1	123.8	131.2	135.2	150.8	164.0

[a] 66.9 (t, CH₂OH).

Table 6
 ^1H NMR (100 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Erythro 6 and 7 (R = CH₂CH₃)

Compound No.	H-2/H-2'	H-3	H-4	H-5	OMe	CH ₃	CH ₂ CH ₃	CH ₂ CH ₃	arom	others
6c ₁	3.63 d 3.81 d		3.78	4.80 d	3.39	1.08	0.91 t	1.45 m		2.78 [a]
6c ₂	3.78 d 3.94 d		4.97 s	5.14 s	3.41	1.23	0.90 t	1.55 q	8.15 d 8.28 d	
6c ₃	3.56 d 3.74 d		4.45 d	4.72 d	3.19	1.08	0.82 t	1.44 q	7.35 d 7.87 d	2.45 [b]
7c ₁		4.21 s		3.87 [c] 4.20		1.18	0.91 t	1.47 m		
7c ₂		5.69 s		4.06 [c] 4.32		1.27	1.00 t	1.59 q	8.29 s	
No.	J (2,2')	J (4,5)	J CH ₂ CH ₃	J (arom)						
6c ₁	9.0	2.2	7.8							
6c ₂	8.5	0	7.1	9.0						
6c ₃	8.7	1.2	7.8	8.2						
7c ₁			7.3							
7c ₂			7.3							

[a] OH (d, J_{4,OH} = 5.5 Hz). [b] arom-CH₃. [c] d, J_{5,5'} = 9.3 Hz.

H_z), indicates that the acyloxy group is *syn* to the methoxycarbonyl substituent in **2a**₂, and *anti* in **3a**₂. Comparison of the high-field ^1H nmr spectra of **2** and **3** revealed similarities in structure. The upfield shift of the

carbomethoxyl methyl in **2** and the downfield shift of H-4 in **3** are presumably the result of the anisotropic effect of both the nearby phenyl ring and the methoxycarbonyl group, respectively. The major product was always less

Table 7
 ^{13}C NMR (25 MHz) Chemical Shifts (ppm) of Erythro **6** and **7** (R = CH_2CH_3)

Compound No.	C-2	C-3	C-4	C-5	OMe	CH_3	CH_2CH_3	CH_2CH_3	arom		
6c ₁	76.9 t	44.8 s	83.6 d	111.3 d	55.6	9.0 q	20.8 q	25.0 t			
6c ₂	78.1 t	44.9 s	85.7 d	109.4 d	55.4	9.2 q	21.8 q	26.6 t	123.7	130.9	135.2
6c ₃ [a]	77.0 t	44.8 s	90.7 d	108.6 d	55.5	8.7 q	21.0 q	25.7 t	150.8	164.0	
									128.0	129.8	133.6
									145.0		
7c ₁	178.5 s	75.7 d	43.5 s	73.8 t		8.3 q	20.8 q	24.1 t			
7c ₂	170.6 s	76.3 d	43.4 s	73.6 t		8.3 q	21.2 q	25.7 t	123.7	131.1	134.1
									150.9	163.5	

[a] 21.6 (s, arom- CH_3).

Table 8
 ^1H NMR (100 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Threo **8** and **9** (R = CH_2CH_3)

Compound No.	H-2/H-2'	H-3	H-4	H-5	OMe	CH_3	CH_2CH_3	CH_2CH_3	arom	others	
8c ₁	3.62 d		3.78 s	4.78 [a]	3.38	1.03	0.88 t	1.47 m		4.08 [b]	
	3.72 d										
8c ₂	3.75 d		5.00 s	5.19 s	3.40	1.12	0.93 t	1.65 q	8.21		
	3.91 d								8.33		
8c ₃	3.58 d		4.45 s	4.72 s	3.16	1.02	0.79 t	1.41 m	7.35	2.45 [c]	
	3.71 d								7.82		
9c ₁		4.21 s		3.99 s		1.07	0.96 t	1.55 m			
9c ₂		5.71 S		4.15 s		1.26	0.96 t	1.68 q	8.25		
									8.34		
No.	J (2,2')	J (CH_2CH_3)	J (arom)								
8c ₁	9.0	7.3									
8c ₂	8.6	7.5	8.9								
8c ₃	8.5	7.8	8.1								
9c ₁		7.7									
9c ₂		7.6	9.5								

[a] $J_{4,5} = 3.2$ Hz [b] OH(d, $J_{4,\text{OH}} = 5.5$ Hz). [c] arom- CH_3 (s)

Table 9
 ^{13}C NMR (25 MHz) Chemical Shifts (ppm) of Threo **8** and **9** (R = CH_2CH_3)

Compound No.	C-2	C-3	C-4	C-5	OMe	CH_3	CH_2CH_3	CH_2CH_3	arom		
8c ₁	77.1 t	44.8 s	82.4 d	110.7 d	55.3	8.8 q	16.4 q	29.9 t			
8c ₂	78.1 t	45.8 s	84.8 d	108.9 d	55.2	9.1 q	18.2 q	30.6 t	123.7	130.6	135.2
									150.7	163.9	
8c ₃ [a]	77.2 t	45.5 s	89.9 d	108.2 d	55.3	8.8 d	17.8 q	29.9 t	128.1	129.7	133.5
									145.0		
9c ₁	178.4 s	75.1 d	44.1 s	75.7 t		8.7 q	16.0 q	30.1 t			
9c ₂	171.9 s	75.3 d	43.8 s	75.4 t		8.6 q	17.5 q	30.0 t	123.8	131.2	134.3
									150.2	163.6	

[a] 21.6 (q, arom- CH_3).

polar than the minor isomer. Thus, the less polar component is assigned an *erythro*-configuration **2**, while the polar product should be in a *threo*-configuration **3**.

The 3,3-dimethyltetrahydrofuran derivative **6b**₁ was derived from *threo-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-methyltetrahydrofuran-3-carboxylate (**3b**₂) in

an overall yield of 55% *via* the following sequence of reactions: lithium aluminum hydride (LAH) reduction of **3b**₂ in ether, ditosylate formation of **4b**, and LAH reduction of **5b** in THF. Attempted oxidation [9] of **6b**₁ with *m*-chloroperbenzoic acid and catalytic amounts of boron trifluoride etherate in dry dichloromethane were unsuccessful. How-

Table 10
 Physical Data for Compounds 6,7,8,9

Compound No.	mp °C	Molecular Formula	Analyses %			IR (cm ⁻¹) nujol [a]
			Calcd./Found C	H	N	
6b ₂	92-93	C ₁₄ H ₁₇ NO ₆	56.95	5.80	4.74	3100, 1720, 1605, 1380, 1355, 1290, 1105, 1060, 720
			57.00	5.80	4.74	
6c ₂	93-94	C ₁₅ H ₁₉ NO ₆	58.25	6.19	4.53	3100, 1715, 1605, 1375, 1345, 1280, 1105, 1050, 720
			58.30	6.21	4.53	
7b ₂	137-138	C ₁₃ H ₁₃ NO ₆	55.92	4.69	5.02	3105, 1790, 1725, 1605, 1375, 1340, 1275, 1125, 1000, 720
			56.01	4.66	5.04	
7c ₂	112-113	C ₁₄ H ₁₅ NO ₆	57.34	5.16	4.78	3100, 1790, 1720, 1600, 1375, 1345, 1280, 1120, 1105, 720
			57.23	5.13	4.79	
8c ₁	oil				3430, 1190, 1105, 1020, 1000	
8c ₂	87-88	C ₁₅ H ₁₉ NO ₆	58.25	6.19	4.53	3100, 1720, 1600, 1350, 1280, 1105, 1060, 720
			58.29	6.21	4.54	
8c ₃	viscous oil				1600, 1365, 1190, 1180, 1100, 1060, 1000, 850, 665	
9c ₁	viscous oil				3440, 1770, 1460, 1365, 1280, 1210, 1195, 1160, 1110, 1060	
9c ₂	143-144	C ₁₄ H ₁₅ NO ₆	57.34	5.16	4.78	3100, 1790, 1720, 1605, 1370, 1350, 1280, 1125, 1000, 720
			57.30	5.14	4.76	

[a] Neat for compounds 8c₁, 8c₃ and 9c₁.

ever, treatment of the *p*-nitrobenzoate (**6b₂**) under the same reaction conditions gave the desired γ -lactone (**7b₂**) in 92% yield. Removal of the *p*-nitrobenzoyl group in **7b₂** by hydrolysis with lithium hydroxide in aqueous methanol at room temperature gave (\pm)-pantolactone **7b₁** in 90% yield. The tlc, ir, ¹H nmr and ¹³C nmr spectral data all were identical with natural pantolactone.

By using the same method for the synthesis of **7b₁** from **3b₂**, *threo-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-carboxylate (**3c₂**) and *erythro-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-carboxylate (**2c₂**) were transformed into (\pm)-**7c₁** and its *threo* isomer, respectively. The LAH reduction of ditosylate (**5c**) provided **6c₁** in somewhat poor yield despite prolonged heating; monotosylate (**6c₃**) was obtained in 92% yield. Treatment of **6c₃** with sodium in methanol (Bouveault-Blanc reduction) produced **6c₁** in good yield. The ir, ¹H nmr and ¹³C nmr spectral data of synthetic **7c₁** matched those [7] [10] for the natural compound.

EXPERIMENTAL

Melting points were determined on a micro hot-stage and are uncorrected. Column chromatography was performed with silica gel (Merck NO. 7734; 63-200 μ m), and thin-layer chromatography (tlc) was performed on a glass plate coated with Kieselgel 60 GF₂₅₄ (Merck), followed by heating with anisaldehyde-acetic acid-sulfuric acid (1:100:2). The ir spectra were taken on a JASCO A-102 IR spectrophotometer and were calibrated against the 1600 cm⁻¹ band of polystyrene. The ¹H nmr spectra (400 MHz) were recorded with a JEOL JMN-GX 400 FT NMR spectrometer, and ¹H (100 MHz) and ¹³C (25 MHz) nmr spectra were recorded with a JEOL FX-100 spectrometer for deuteriochloroform solution.

General Procedure for Oxidation with *m*-Chloroperbenzoic Acid of Methyl 2,3-Dihydro-3(*H* or alkyl)furoates **1**.

The methyl 2,3-dihydro-3-furoate (2 mmoles) was dissolved in methanol (2 ml) and treated with *m*-chloroperbenzoic acid (2.2 mmoles) at 0° for 1 hour. The mixture was diluted with 50 ml of dichloromethane and washed successively with 10% aqueous sodium thiosulfate, saturated sodium bicarbonate, and brine. The crude product obtained after drying was acylated with *p*-nitrobenzoyl chloride (2.2 mmoles) in dry pyridine (2 ml) at room temperature overnight. The crude *p*-nitrobenzoate was chromatographed on a column of silica gel (100 g) with a hexane-ethyl acetate (4:1) as eluant.

Threo-4-Hydroxy-5-methoxy-3-methyltetrahydrofuran-3-methanol (**4b**).

To a stirred suspension of lithium aluminum hydride (640 mg, 16.8 mmoles) in dry ether (60 ml) was added a solution of **3b₂** (1.45 g, 4.3 mmoles) in dry ether (5 ml). After refluxing for 3 hours, a small amount of water was added to decompose excess lithium aluminum hydride and the precipitate was filtered off. The residue was chromatographed to give syrupy diol **4b** (610 mg, 88%); ir (neat): 3400, 1100, 1040 cm⁻¹ (Tables 4 and 5).

Ditosylate (**5b**) of *threo*-4-Hydroxy-5-methoxy-3-methyltetrahydrofuran-3-methanol.

Treatment of **4b** (610 mg, 3.8 mmoles) with *p*-toluenesulfonyl chloride (1.5 g, 7.9 mmoles) in dry pyridine (15 ml) at room temperature overnight, gave a syrupy ditosylate **5b** (1.56 g, 89%); ir (neat): 1600, 1365, 1190, 1180, 965, 840 cm⁻¹.

4-Hydroxy-5-methoxy-3,3-dimethyltetrahydrofuran (**6b₁**).

Reduction of the ditosylate **5b** (1.3 g, 2.8 mmoles) with lithium aluminum hydride (600 mg, 15.8 mmoles) in dry tetrahydrofuran (100 ml) and refluxing for 5 hours afforded oily alcohol **6b₁** (280 mg, 69%) after chromatography; ir (neat): 3450, 1200, 1110, 1030, 900 cm⁻¹ (Tables 4 and 5).

p-Nitrobenzoate (**6b₂**) of 4-Hydroxy-5-methoxy-3,3-dimethyltetrahydrofuran (Tables 4, 5 and 10).

This compound was obtained as colorless prisms (hexane-ethyl acetate) in 90% yield from **6b₁**.

Pantolactone *p*-Nitrobenzoate (**7b₂**).

A solution of **6b₂** (150 mg, 0.5 mmole) in 1.5 ml of dry dichloromethane containing catalytic amount (5 drops) of boron trifluoride etherate was treated at room temperature with *m*-chloroperbenzoic acid (100 mg, 0.6 mmole). After 3 hours the reaction mixture was diluted with 50 ml of dichloromethane and washed successively with 10% aqueous sodium thiosulfate, saturated sodium bicarbonate, and brine. The crude product obtained after drying (sodium sulfate) was chromatographed using (2:1) hexane-ethyl acetate giving 130 mg (92%) of pure lactone **7b₂** (Tables 4, 5 and 10).

Pantolactone (**7b₁**).

To a stirred suspension of **7b₂** (100 mg, 0.77 mmole) in methanol (2 ml) was added a solution of lithium hydroxide (45 mg, 1.2 mmoles) in water (2 ml). After stirring for 10 minutes at room temperature, the clear solution of the reaction mixture was acidified with 3*N*-hydrochloric acid, and the precipitate was filtered off and washed with water. The filtrate was evaporated to dryness and the residue was chromatographed using (1:1) hexane-ethyl acetate giving 42 mg (90%) of pure lactone **7b₁**; tlc (Rf 0.48, 1:1 hexane-ethyl acetate); ir (neat): 3450, 1780, 1205, 1120, 1010, 990 cm⁻¹.

The tlc, ir, ¹H nmr and ¹³C nmr spectral data (Tables 4 and 5) all were identical with those of authentic sample of pantolactone.

Threo-4-Hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-methanol (**4c**).

This compound was obtained as a viscous oil in 95% yield from **3c₂**; ir (neat): 3400, 1110, 1040 cm⁻¹.

Ditosylate (**5c**) of *threo*-4-Hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-methanol.

This compound was obtained in 61% yield from **4c** as a viscous oil; ir (neat): 1600, 1365, 1190, 1180, 965, 840 cm⁻¹; ¹H nmr: δ 0.68 (t, 3H, J = 7.8 Hz, CH₂CH₃), 1.42-1.55 (m, 2H, CH₂CH₃), 2.46 (s, 6H, arom-CH₃), 3.11 (s, 3H, OCH₃), 3.67 (d, 1H, J = 9.5 Hz, H-2), 3.73 (d, 1H, J = 9.5 Hz, H-2), 3.99 (s, 2H, CH₂OTs), 4.49 (s, 1H, H-4), 4.76 (s, 1H, H-5), 7.72 (d, 2H, J = 8.5 Hz, arom), 7.81 (d, 2H, J = 8.5 Hz, arom); ¹³C nmr: δ 8.3 (q, CH₂CH₃), 10.1 (t, CH₂CH₃), 21.6 (q, arom-CH₃), 48.8 (s, C-3), 55.1 (q, OCH₃), 69.2 (t, CH₂OTs), 73.0 (t, C-2), 85.2 (d, C-4), 108.2 (d, C-5), 128.0 (d), 129.9 (d), 130.0 (d), 132.3 (s), 132.8 (s), 145.1 (s), 145.5 (s).

erythro-3-Ethyl-4-hydroxy-5-methoxy-3-methyltetrahydrofuran (**6c₁**) and its Tosylate **6c₃** (Tables 6 and 7).

Ditosylate **5c** (830 mg, 1.42 mmoles) was treated as in the preparation of **6b₁** to give, after chromatography, **6c₁** (70 mg, 31%); ir (neat): 3450, 1105, 1040, 1000 cm⁻¹; and **6c₃** (410 mg, 92%); ir (neat): 1595, 1365, 1190, 1180, 1100, 1060, 850, 665 cm⁻¹.

This compound **6c₁** was also obtained from the tosylate **6c₃** on treatment with sodium in methanol in 82% yield.

p-Nitrobenzoate (**6c₂**) of *erythro*-3-Ethyl-4-hydroxy-5-methoxy-3-methyltetrahydrofuran (Tables 6, 7 and 10).

This compound was obtained as colorless prisms (hexane-ethyl acetate) after chromatography in 97% yield from **6c₁**.

p-Nitrobenzoate (**7c₂**) of *erythro*-Dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c₁**) (Tables 6, 7 and 10).

p-Nitrobenzoate **6c₂** (40 mg, 0.13 mmole) was treated as in the preparation of **7b₂** to give, after chromatography, crystalline **7c₂** (35 mg, 90%), mp 112-113°.

erythro-Dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c₁**).

This compound was obtained as a viscous oil in 94% yield from **7c₂**; tlc Rf (0.32, 2:1 hexane-ethyl acetate); ir (neat): 3430, 2950, 1770, 1450, 1380, 1320, 1210, 1190, 1170, 1110, 1000 cm⁻¹.

The tlc, ir, ¹H nmr and ¹³C nmr spectral data (Tables 6 and 7) matched those [7] [10] for the natural compound.

Acknowledgement.

The authors are greatly indebted to Mr. Junichi Goda for the elemental analyses.

REFERENCES AND NOTES

- [1] T. Kinoshita, K. Miyano and T. Miwa, *Bull. Chem. Soc. Japan*, **48**, 1865 (1975).
- [2] T. Kinoshita and T. Miwa, *Carbohydr Res.*, **28**, 175 (1973).
- [3] T. Kinoshita and T. Miwa, *Bull. Chem. Soc. Japan*, **51**, 225 (1978).
- [4] A. J. Birch and J. Slobbe, *Tetrahedron Letters*, 627 (1975).
- [5] J. Slobbe, *Aust. J. Chem.*, **29**, 2553 (1976).
- [6] T. Kinoshita, M. Hirano and N. Yoshida, *Synthesis*, in press (1991).
- [7] W. Herz and M. Bruno, *Phytochemistry*, **26**, 1175 (1987).
- [8a] A. Henbest and R. A. Wilson, *J. Chem. Soc.*, 1957 (1958); [b] P. Kocovsky and I. Stary, *J. Org. Chem.*, **55**, 3236 (1990).
- [9] P. A. Grieco, T. Oguri and Y. Yokoyama, *Tetrahedron Letters*, 419 (1978).
- [10] K. Tadano, S. Kanazawa and S. Ogawa, *J. Org. Chem.*, **53**, 3868 (1988).