Synthesis of (±)-Pantolactone and (±)-Dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone

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The title compounds were synthesized from 3-furoic acid *via* the Birch reduction.

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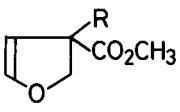
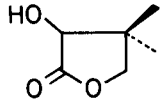
The Birch reduction [1] of 3-furoic acid provides a useful entry into the total synthesis of the branched-chain sugars, for example, apiose [2] and dihydrostreptose [3].

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].

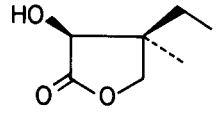
Since the introduction of an alkyl group into the 3-position of 2,3-dihydrofuroic acid is very useful as a synthetic intermediate of 3,3-dialkyl butanolides, we tried alkylation [6] on the 3-position of methyl 2,3-dihydro-3-furoate (**1a**).



1



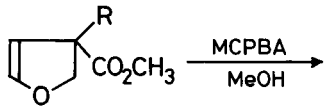
7b$_1$



7c$_1$

Several of the alkylated compounds were successfully converted into natural products. (±)-Pantolactone (**7b**$_1$), a degradation product of pantothenic acid and (±)-dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c**$_1$) [7], a pantolactone homologue isolated from *Marshallia tenuifolia*, were synthesized from **1b** and **1c**, respectively.

Scheme A



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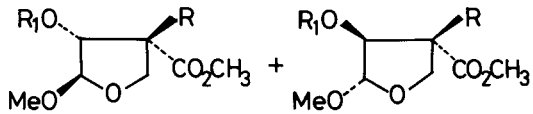


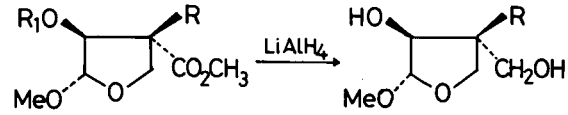
2 3

R			R	R_1
a	H	**a**$_1$	H	H
b	CH_3	**a**$_2$	H	$COC_6H_4NO_2$
c	CH_2CH_3	**b**$_1$	CH_3	H
		b$_2$	CH_3	$COC_6H_4NO_2$
		c$_1$	CH_2CH_3	H
		c$_2$	CH_2CH_3	$COC_6H_4NO_2$
		c$_3$	CH_2CH_3	$SO_2C_6H_4CH_3$

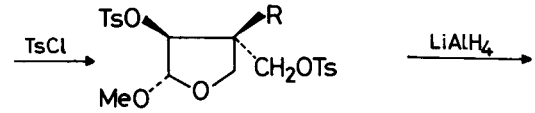
Oxidation of **1** with *m*-chloroperbenzoic acid in methanol gave a mixture of *erythro*-**2** and *threo*-**3** in an approximate ratio of 2:1. However, the *p*-nitrobenzoate derivatives were separable by silica gel column chromatography. The peroxy acid oxidation of **1**, *via* the production of 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 ^{1}H 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 (**2a**$_2$) than in *threo-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-tetrahydrofuran-3-carboxylate (**3a**$_2$) (J = 2.9

Scheme B



3 4



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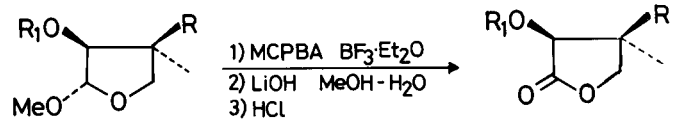

6 7

8 9

Table 1

^{1}H 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_2Me	CH_3	CH_2CH_3	CH_2CH_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	1.77 dq 2.12 dq	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	1.77 dq 1.93 dq	8.23 d 8.30 d

No.	J (2,2′)	J (2,3)	J (3,4)	J (arom)	J (CH_2CH_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

^{13}C NMR (25MHz) Chemical Shifts (ppm) of Compounds 2 and 3

Compound No.	C-2	C-3	C-4	C-5	OMe	CO_2Me	CH_3	CH_2CH_3	CO_2Me
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 % Calcd./Found C	H	N	IR (cm^{-1}) nujol
2a$_2$	0.26	98-99	$C_{14}H_{15}NO_8$	51.70 51.80	4.65 4..63	4.31 4.27	1740, 1720, 1610, 1380, 1220, 1105, 1070, 720
2b$_2$	0.35	106-107	$C_{15}H_{17}NO_8$	53.10 53.12	5.05 5.04	4.13 4.09	1745, 1725, 1608, 1355, 1320, 1280, 1105, 1060, 720
2c$_2$	0.48	99-100	$C_{16}H_{19}NO_8$	54.39 54.47	5.42 5.43	3.96 3.95	1740, 1720, 1610, 1355, 1270, 1220, 1110, 1070, 720
3a$_2$	0.20	103-104	$C_{14}H_{15}NO_8$	51.70 51.76	4.65 4.60	4.31 4.26	1740, 1725, 1605, 1350, 1300, 1280, 1110, 1070, 730
3b$_2$	0.30	75-76	$C_{15}H_{17}NO_8$	53.10 53.17	5.05 5.02	4.13 4.08	1740, 1730, 1610, 1355, 1290, 1115, 1105, 1055, 720
3c$_2$	0.40	84-85	$C_{16}H_{19}NO_8$	54.39 54.49	5.42 5.30	3.96 3.85	1740, 1730, 1605, 1380, 1350, 1220, 1105, 1065, 720

[a] 4:1 Hexame-ethyl acetate.

Table 4

^{1}H NMR (100 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Pantolactone Series (R = CH_3)

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, CH_2OH). [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 = CH_3)

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, CH_2OH).

Table 6

^{1}H NMR (100 MHz) Chemical Shifts (ppm) and Coupling Constants (Hz) of Erythro **6** and **7** (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
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_2CH_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-CH_3. [c] d, $J_{5,5'}$ = 9.3 Hz.

Hz), indicates that the acyloxy group is *syn* to the methoxycarbonyl substituent in **2a$_2$**, and *anti* in **3a$_2$**. Comparison of the high-field ^{1}H 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
									150.8	164.0	
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	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, $J_{4,OH}$ = 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 % Calcd./Found C	H	N	IR (cm^{-1}) nujol [a]
$\mathbf{6b_2}$	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	
$\mathbf{6c_2}$	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	
$\mathbf{7b_2}$	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	
$\mathbf{7c_2}$	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	
$\mathbf{8c_1}$	oil					3430, 1190, 1105, 1020, 1000
$\mathbf{8c_2}$	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	
$\mathbf{8c_3}$	viscous oil					1600, 1365, 1190, 1180, 1100, 1060, 1000, 850, 665
$\mathbf{9c_1}$	viscous oil					3440, 1770, 1460, 1365, 1280, 1210, 1195, 1160, 1110, 1060
$\mathbf{9c_2}$	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 $\mathbf{8c_1}$, $\mathbf{8c_3}$ and $\mathbf{9c_1}$.

ever, treatment of the *p*-nitrobenzoate ($\mathbf{6b_2}$) under the same reaction conditions gave the desired γ-lactone ($\mathbf{7b_2}$) in 92% yield. Removal of the *p*-nitrobenzoyl group in $\mathbf{7b_2}$ by hydrolysis with lithium hydroxide in aqueous methanol at room temperature gave (±)-pantolactone $\mathbf{7b_1}$ in 90% yield. The tlc, ir, ^{1}H nmr and ^{13}C nmr spectral data all were identical with natural pantolactone.

By using the same method for the synthesis of $\mathbf{7b_1}$ from $\mathbf{3b_2}$, *threo-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-carboxylate ($\mathbf{3c_2}$) and *erythro-p*-nitrobenzoate of methyl 4-hydroxy-5-methoxy-3-ethyltetrahydrofuran-3-carboxylate ($\mathbf{2c_2}$) were transformed into (±)-$\mathbf{7c_1}$ and its *threo* isomer, respectively. The LAH reduction of ditosylate (**5c**) provided $\mathbf{6c_1}$ in somewhat poor yield despite prolonged heating; monotosylate ($\mathbf{6c_3}$) was obtained in 92% yield. Treatment of $\mathbf{6c_3}$ with sodium in methanol (Bouveault-Blanc reduction) produced $\mathbf{6c_1}$ in good yield. The ir, ^{1}H nmr and ^{13}C nmr spectral data of synthetic $\mathbf{7c_1}$ 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 μm), and thin-layer chromatography (tlc) was performed on a glass plate coated with Kieselgel 60 GF_{254} (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 ^{1}H nmr spectra (400 MHz) were recorded with a JEOL JMN-GX 400 FT NMR spectrometer, and ^{1}H (100 MHz) and ^{13}C (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 $\mathbf{3b_2}$ (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 ($\mathbf{6b_1}$).

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 $\mathbf{6b_1}$ (280 mg, 69%) after chromatography; ir (neat): 3450, 1200, 1110, 1030, 900 cm^{-1} (Tables 4 and 5).

p-Nitrobenzoate ($\mathbf{6b_2}$) 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 **6b$_1$**.

Pantolactone *p*-Nitrobenzoate (**7b$_2$**).

A solution of **6b$_2$** (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 **7b$_2$** (Tables 4, 5 and 10).

Pantolactone (**7b$_1$**).

To a stirred suspension of **7b$_2$** (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 **7b$_1$**; 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 ^{13}C 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 **3c$_2$**; 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, CH_2CH_3), 1.42-1.55 (m, 2H, CH_2CH_3), 2.46 (s, 6H, arom-CH_3), 3.11 (s, 3H, OCH_3), 3.67 (d, 1H, J = 9.5 Hz, H-2), 3.73 (d, 1H, J = 9.5 Hz, H-2), 3.99 (s, 2H, CH_2OTs), 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); ^{13}C nmr: δ 8.3 (q, CH_2CH_3), 10.1 (t, CH_2CH_3), 21.6 (q, arom-CH_3), 48.8 (s, C-3), 55.1 (q, OCH_3), 69.2 (t, CH_2OTs), 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 (**6c$_1$**) and its Tosylate **6c$_3$** (Tables 6 and 7).

Ditosylate **5c** (830 mg, 1.42 mmoles) was treated as in the preparation of **6b$_1$** to give, after chromatography, **6c$_1$** (70 mg, 31%); ir (neat): 3450, 1105, 1040, 1000 cm^{-1}; and **6c$_3$** (410 mg, 92%); ir (neat): 1595, 1365, 1190, 1180, 1100, 1060, 850, 665 cm^{-1}.

This compound **6c$_1$** was also obtained from the tosylate **6c$_3$** on treatment with sodium in methanol in 82% yield.

p-Nitrobenzoate (**6c$_2$**) 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 **6c$_1$**.

p-Nitrobenzoate (**7c$_2$**) of *erythro*-Dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c$_1$**) (Tables 6, 7 and 10).

p-Nitrobenzoate **6c$_2$** (40 mg, 0.13 mmole) was treated as in the preparation of **7b$_2$** to give, after chromatography, crystalline **7c$_2$** (35 mg, 90%), mp 112-113°.

erythro-Dihydro-4-ethyl-3-hydroxy-4-methyl-2(3*H*)-furanone (**7c$_1$**).

This compound was obtained as a viscous oil in 94% yield from **7c$_2$**; 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 ^{13}C nmr spectral data (Tables 6 and 7) matched those [7] [10] for the natural compound.

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