experiment using 2.56 g (14.2 mmol) of **5c** in which the ozonide was allowed to warm to *ca.* 25° the yield of **2** was reduced to 0.87 g (34%). Examination of the ether wash of the basic aqueous solution yielded 0.75 g of a keto alcohol identified as **7**: mp 53–54°; ir (CCl_4) 1745 cm^{-1} (C=O); nmr (CCl_4) δ 1.16 (s, 3, CH_3), 1.33 (s, 3, CH_3COH), and 2.85 ppm (s, 1, OH); mass spectrum (70 eV) *m/e* 154 (M^+).

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.31; H, 9.23.

Registry No.—(±)-**1**, 28117-21-7; **2**, 53166-10-2; **3**, 50459-35-3; **4a**, 53166-11-3; **4b**, 53166-12-4; **4c**, 53166-13-5; **5a**, 53166-14-6; **5b**, 53166-15-7; **5c**, 53166-16-8; **7**, 53166-17-9; methyllithium, 917-54-4; 3-methylcyclopentenone, 2758-18-1; ethylene, 74-85-1; benzaldehyde, 100-52-7; furfural, 98-01-1; acetone, 67-64-1.

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(3) For a review of fragmentation reactions see (a) C. A. Grob and P. W. Schiess, *Angew. Chem., Int. Ed. Engl.,* **6,** 1 (1967); (b) J. A. Marshall and J. L. Belletire, *Tetrahedron Lett.,* 871 (1971).

(4) The conversion, **3** → **2** *via* **4** and **5,** may be viewed as being catalyzed by the carbonyl reagent (benzaldehyde, *etc.*).

(5) Microanalyses were performed by Afred Bernhardt, Microanalytisches Laboratorium, Elbach über Engelskirchen, Mülheim (Ruhr), West Germany.

Synthesis of 2,5-Dihydroxy-2,5-dihydrofurans by Anodic Oxidation of Furans

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During synthetic work on *Lactarius* sesquiterpenes, we needed an efficient method of converting furans into maleic acid derivatives. Hydrolysis of 2,5-dimethoxy-2,5-dihydrofurans[1] followed by Jones oxidation[2] gave only a low yield of anhydride, partly because of the formation of lactones and polymeric material in the hydrolysis step.[3] Direct oxidation of the 2,5-dimethoxy-2,5-dihydrofurans with Jones reagent[2] according to Marei and Raphael[4] gave the desired maleic acid derivative but with significant amounts of γ-methoxy-α, β-unsaturated γ-lactones (up to 35%) and polymeric material.

In order to avoid the hydrolysis step we examined the oxidation of 2,5-dihydroxy-2,5-dihydrofurans to maleic anhydrides. Remarkably, no preparative route to this type of compound has been reported other than a hydroxylation of furan with osmium tetroxide–hydrogen peroxide to 2,5-dihydroxy-2,5-dihydrofuran which was obtained only as the corresponding bis(phenylhydrazone).[5] We now wish to report a preparatively useful route to 2,5-dihydroxy-2,5-dihydrofurans by anodic oxidation of furans. Table I shows the results obtained.

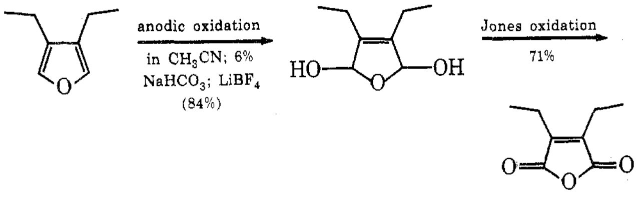
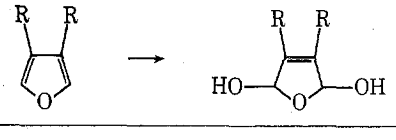
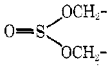
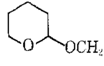


Table I
Anodic Oxidations



Starting material	R	Product	Yield, %	Current yield, %
1[a]	CH_3CH_2-	**8**	84	100
2		**9**	78	87
3[6]	CH_3COOCH_3-	**10**	86	100
4[7]		**11**	77	75
5[8]	Cl-CH_2-	**12**	*ca.* 70[b]	90
6	H-		*c*	
7[6]	CH_3CH_2OOC-		*d*	

[a] Peak potential relative to saturated calomel electrode: E_p = 1.62 V (cyclic voltammetry in MeCN). [b] **12** was unstable and decomposed on SiO_2 chromatography. EtOAc extraction gave a fairly pure crude product: nmr ($CDCl_3$) δ 6.00, 5.74 (s, 2, HO–CH), 4.30 (s, 4, Cl–CH_2). [c] Low yield of undefined material. [d] No reaction.

The electrolysis product (**8**) is conveniently oxidized further to anhydride by standard Jones oxidation.

Experimental Section

3,4-Diethylfuran (1). Methyllithium in ether (0.36 mol) was added to cuprous iodide (14.5 g, 0.165 mol) in ether (100 ml) at 0°. 3,4-Bis(chloromethyl)furan[8] (**5**) (6.9 g, 0.056 mol) in ether (50 ml) was added dropwise at 0° with stirring (continued for 12 hr).[9] Addition of water (300 ml), extraction with ether, drying (Na_2SO_4), and distillation gave 3,4-diethylfuran (**1**) (3.65 g, 70%): bp 39–40° (11 mm); n^{21}D 1.4500; ir (neat) 3160, 1555, 1475, 1060, 887, 805 cm^{-1}; nmr ($CDCl_3$) δ 7.13 (s, 2), 2.36 (q, 4, J = 7.5 Hz), 1.17 (t, 6, J = 7.5 Hz).

Anal. Calcd for $C_8H_{12}O$: C, 77.4; H, 9.7. Found: C, 77.4; H, 9.8.

2-Oxofuro[5,6-*c*]-1,3,2-dioxathiepane (2). 3,4-Bis(hydroxymethyl)furan[8] (25.6 g, 0.2 mol) and triethylamine (40.4 g; 0.4 mol) were dissolved in dry methylene chloride (400 ml). Thionyl chloride (47.2 g, 0.4 mol) in methylene chloride (130 ml) was added dropwise at 0° with stirring (continued for 30 min) (*cf.* ref 10). The reaction mixture was poured into cold water (300 ml) and the methylene chloride phase was separated. Drying (Na_2SO_4), evaporation, and distillation gave 3,4-bis(chloromethyl)furan (**5**)[8] (1.5 g, 5%) and 2-oxofuro[5,6-*c*]-1,3,2-dioxathiepane (**2**) (17.0 g, 49%): bp 56–57° (0.2 mm); n^{23}D 1.5210; ir (neat) 3140, 1565, 1460, 1185, 1053, 885, 813 cm^{-1}; nmr ($CDCl_3$) δ 7.35 (s, 2), 5.72, 4.56 (AB q, 4, J = 14.0 Hz).

Anal. Calcd for $C_6H_6SO_4$: C, 41.4; H, 3.5; S, 18.4. Found: C, 41.5; H, 3.5; S, 18.2.

General Hydroxylation Procedure. The anodic oxidation was performed at constant current (100 mA) in a water-jacketed beaker (100 ml) equipped with magnetic stirrer, Pt anode (120 × 40 × 0.1 mm) and Ni cathode (helical wire, 400 × 1.6 mm). The furan (*ca.* 5 mmol) was dissolved in acetonitrile (50 ml) and saturated sodium bicarbonate solution (3 ml) was added together with lithium tetrafluoroborate (*ca.* 10 mg as supporting electrolyte). After complete oxidation of the furan (tlc: SiO_2/CH_2Cl_2) the reaction mixture was evaporated and the residue chromatographed (35 g SiO_2/EtOAc) to give a mixture of *cis-* and *trans-*2,5-dihydroxy-2,5-dihydrofurans.

3,4-Diethyl-2,5-dihydroxy-2,5-dihydrofuran (8): yield, 84%; n^{21} D 1.4889; ir (neat) 3400 cm^{-1}; nmr ($CDCl_3$) δ 6.05, 5.71 (s, broad, 2, HO–CH), 2.20 (q, broad, 4, J = 8.0 Hz), 1.06 (t, broad, 6, J = 8.0 Hz).

Anal. Calcd for $C_8H_{14}O_3$: C, 60.7; H, 8.9. Found C, 60.9; H, 8.2.

2-Oxo-(2,5-dihydroxy-2,5-dihydrofuro)[5,6-*c*]-1,3,2-dioxathiepane (9): yield, 78%; n^{23}D 1.5180; ir (neat) 3400, 1200 cm^{-1}; nmr (D_2O; sodium 4,4-dimethyl-4-silapentane-1-sulfonate[11]) 6.11, 5.82 (s, 2, HO–CH), 4.45–5.50 (m, 4, CH_2) ppm.

Anal. Calcd for $C_6H_8SO_6$: C, 34.6; H, 3.9. Found: C, 35.0; H, 4.1.

3,4-Bis(acetoxymethyl)-2,5-dihydroxy-2,5-dihydrofuran (10): yield, 86%; n^{27}D 1.4831; ir (neat) 3440, 1740 cm^{-1}; nmr (acetone)d_6) δ 5.60–6.15 (mm 2, HO-CH), 4.96, 4.60 (AB q, broad, 4, J = 13.0 Hz, CH_2), 2.04 (s, 6; CH_3).

Anal. Calcd for $C_{10}H_{14}O_7$: C, 48.8; H, 5.7. Found: C, 49.2; H, 5.7.

3,4-Bis[(2-tetrahydropyranyl)oxymethyl]-2,5-dihydroxy-2,5-dihydrofuran (11): yield, 77%; n^{23}D 1.4938; ir (neat) 3390 cm^{-1}; nmr ($CDCl_3$) δ 6.19, 5.84 (s, 2, HO-CH), 4.73 (s, broad, 4, =C-CH_2-O), 4.40 (t, 2, J = 7.0 Hz; CH_2O-CH-O), 3.25–4.20 (m, 4, O-CH_2), 1.20–2.20 (m, 12, pyranyl-CH_2).

Anal. Calcd for $C_{16}H_{26}O_7$: C, 58.2; H, 7.9. Found: C, 57.9; H, 7.8.

Diethylmaleic Anhydride (13).[12] 3,4-Diethyl-2,5-dihydroxy-2,5-dihydrofuran (217 mg) in acetone (10 ml) was cooled to 0° and Jones reagent[2] (0.6 ml: 10 g CrO_3/8.5 ml concentrated H_2SO_4/30 ml H_2O) was added dropwise (magnetic stirring). After 30 min the reaction mixture was filtered, the filtrate was evaporated, and the residue was partitioned between water and ether. After extraction with ether, drying (Na_2SO_4), and evaporation, the residue was dissolved in dry methylene chloride and treated (4 hr) with molecular sieve (Linde 3 A). Filtration and distillation gave diethylmaleic anhydride (13) (150 mg, 71%): bp 102–104° (10 mm) (lit.[12] bp 115° (13 mm)); n^{21}D 1.4640; ir (neat) 1852, 1773 cm^{-1}; nmr ($CDCl_3$) δ 2.54 (q, 4, J = 7.5 Hz), 1.23 (t, 6, J = 7.5 Hz).

Acknowledgment. We thank Professor Börje Wickberg for stimulating discussions. This work was in part supported by the Swedish Natural Science Research Council.

Registry No.—1, 53059-82-8; **2**, 14496-25-4; **3**, 30614-73-4; **4**, 52618-12-9; **5**, 6372-18-5; *cis*-**8**, 53059-83-9; *trans*-**8**, 53059-84-0; *cis*-**9**, 53059-87-3; *trans*-**9**, 53109-80-1; *cis*-**10**, 53059-85-1; *trans*-**10**, 53059-86-2; **11**, 53059-40-8; *cis*-**12**, 53059-41-9; *trans*-**12**, 53059-42-0; **13**, 28843-39-2; 3,4-bis(hydroxymethyl)furan, 14496-24-3; thionyl chloride, 7719-09-7.

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Assay and Methylation of 2-Methyl-1,2-dihydroisoquinoline

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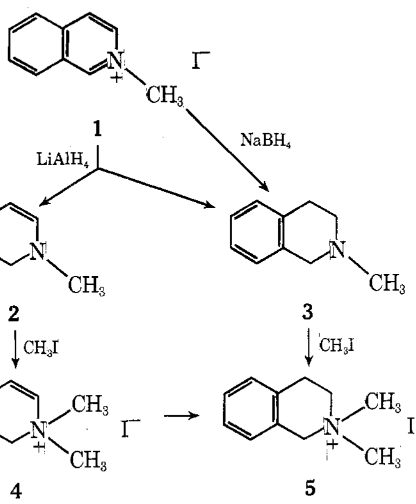
This note describes a procedure for the quantitative determination of 2-methyl-1,2-dihydroisoquinoline (**2**) and the course of its alkylation with methyl iodide. Dihydroisoquinoline **2** was obtained by reducing isoquinolinium methiodide (**1**) with lithium aluminum hydride by an optimization of the Schmid–Karrer method.[1] None of the other preparations tried were satisfactory.[2]

To determine the composition of the routinely distilled product, or more specifically the extent of overreduction to 2-methyl-1,2,3,4-tetrahydroisoquinoline (**3**), we developed a straightforward procedure involving dehydrogenation with excess iodine followed by iodimetric back-titration. Since the dihydroisoquinoline **2** requires 2 equiv of iodine for aromatization while the tetrahydroisoquinoline **3** requires 4 equiv, the amount of iodine absorbed provides a reliable basis for assay. In an exploratory manner, we also investigated a spectroscopic method, which suggested that either or both of the 2-methyl-1,2-dihydroisoquinoline absorption maxima at λ_{max} (absolute C_2H_5OH) 234 and 329 nm[5] might serve as the basis for quantitative analysis. Quantitative gas–liquid chromatography was also tried but was found unreliable.



According to the iodimetric assay, the Schmid–Karrer preparation gives rise to mixtures of di- and tetrahydroisoquinoline (**2** and **3**), with the latter compound comprising as much as 35% of the product. One run that could not be repeated gave an exceptionally low concentration, 2%, of the tetrahydroisoquinoline. Accordingly, the tacit assumption that the Schmid–Karrer product is free of tetrahydro impurity is not warranted.[10] Whether the tetrahydroisoquinoline develops before or during the work-up was not determined. It is pertinent to note, however, that the conditions we employed, which avoided exposure to strong acid and high temperatures,[12] would not be expected to favor disproportionation of the dihydroisoquinoline.

Using starting material whose content of 2-methyl-1,2-dihydroisoquinoline (**2**) had been measured, we examined the reaction with methyl iodide. Only the N-alkylation product **4** was isolated. Hydrogenation of this product furnished 2,2-dimethyl-1,2,3,4-tetrahydroisoquinoline iodide (**5**), the same as the material obtained by methylating 2-methyl-1,2,3,4-tetrahydroisoquinoline (**3**).[11] Our results with the simplest alkyl group and the parent dihydroisoquinoline, therefore, agree with the tendency noted before for eneamine alkylation with alkyl halides to favor nitrogen rather than carbon.[12,13]

Experimental Section

2-Methyl-1,2-dihydroisoquinoline (2). 2-Methylisoquinolinium iodide (8.1 g; 0.030 mol) was added in one portion to a stirred suspension of lithium aluminum hydride (1.2 g; 0.030 mol) in 150 ml of ether protected with a blanket of nitrogen. The mixture was stirred at room temperature for 30 min and then quenched over 200 g of crushed ice layered with 50 ml of ether. The ether layer was separated, the solids in the aqueous phase were washed thoroughly with ether, and the combined ether layers were rinsed with portions of saturated possium chloride solution and dried. Fractional distillation gave yellow oily 2-methyl-1,2-dihydroisoquinoline (**2**), bp 50–60° (0.1–0.2 mm) [lit.[1,4] 60–65° bath temperature (0.03 mm); 69° (0.8 mm)], which decomposed quickly in contact with air and was stored routinely under nitrogen. The product, obtained in 70% yield, contained 65–80% dihydro- and 35–20% tetrahydroisoquinoline **3** by iodimetric analysis. Variations in these directions improved neither the yield nor the content of the desired dihydroisoquinoline.