Anodic Reaction of 2-Furoic Acids. II. Electrolysis of Methyl 5-Acetyl-2-furoate and Its Homologous in Protic Solvents

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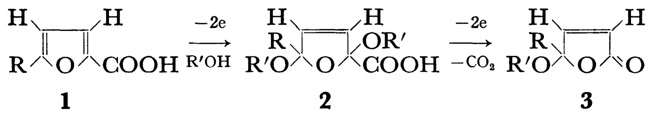
Anodic oxidation of methyl 5-acetyl-2-furoate **4** in methanol leads to ring-opened diesters **8** and **9**, and lactone **10** in addition to methyl 5-acetyl-2,5-dimethoxy-2,5-dihydro-2-furoates **7**. Formation of **8**, **9**, and **10** can be rationalized as arising from **7**. On the other hand, oxidation of methyl 5-methoxy- and 5-bromo-2-furoates, **5** and **6**, also give **9** and **10**. The reactions involve initial production of cationic intermediates **13** and **15**, which are readily solvolized to give **8**, **9**, and **10**. A mechanism of the formation of the intermediates **13** from **5**, **6**, and **7** is discussed.

Recently a review[1] describing an anodic oxidation of 2-acetylfuran in methanol in the presence of sulfuric acid suggested that the corresponding 2,5-dimethoxy-2,5-dihydrofurans was isolated in low yield, but details on isolation and on structural assignment of the reaction products have not been described. Apparently little attention has been paid to the fate of the acetyl group attached to the furan ring under this oxidation conditions.

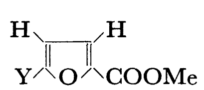
In the previous investigation on anodic oxidation of 5-alkyl-2-furoic acids in protic media,[2] we found that the oxidation of the furan ring and the carboxy group on the anode electrode proceeded stepwise as shown in the following scheme.



1 **2** **3**

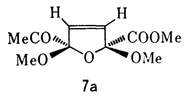
R = Alkyl R' = Me, Ac

Our interest in the anodic reaction of more complex 2-furoic acids led us to investigate the oxidation of methyl 5-acetyl-2-furoate **4**[3] and the related compounds **5** and **6** on the electrode. We wish here to report on studies concerning anodic reaction of **4**, **5**, and **6** as well as detail structures of the products.

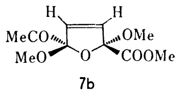


	Y
4	MeCO
5	MeO
6	Br

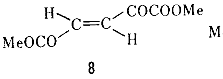
Thus, **4** was electrolyzed in methanol containing concentrated sulfuric acid and lithium perchlorate under constant current using two platinium foil electrodes. Details of the experimental conditions together with results are shown in Table 1. The products were generally a mixture of **7a**, **7b**, **8**, **9a**, and **10**, however in runs 1 and 2 the major product was **9a**. In the experiment 3 an increase of the formation of ketoester **8** and lactone **10** was found to be caused by addition of a small amount of water. In the earlier stage of the reaction as shown in run 4, prominent proportion of **7a** and **7b** among the constituents of the product was observed.



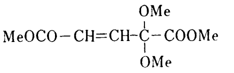
7a



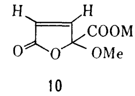
7b



8



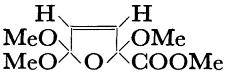
9a *cis*; 9b *trans*



10

The results obtained in run 5 clearly showed that electrolysis of a mixture of **7a** and **7b** separated from the reaction products (run 4) gave **8**, **9**, and **10**, indicating that compounds **7a** and **7b** should be a precursor of the products.

Similar reaction fashions were observed (see Table 2) when methyl 5-bromo- and 5-methoxy-2-furoates, **5**[4] and **6**,[4] were electrolyzed in the almost same conditions as the cases of **4** and **7**, since oxidations of **5** and **6** gave principally **9** and **10**. Analytical specimen of these compounds were isolated by preparative vpc.



11

Electrolytic methoxydation of **6** has been attempted by several groups[5] and they assigned the incorrect structure **11** for the compounds **9**. They visualized the attack of methoxy group to the oxidized furan ring to yield trimethoxy derivative **11**, since anodic methoxydation of furan derivatives are known to afford 2,5-dimethoxy-2,5-dihydrofurans.[2,6] However, the

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[1] N. L. Weinberg and H. R. Weinberg, *Chem. Revs.*, **68**, 464 (1968).

[2] S. Torii, H. Tanaka, H. Ogo, and S. Yamasita, This Bulletin, **44**, 1079 (1971).

[3] R. Ercoli, E. Mantica, G. Claudia, S. Chiozzotto, and E. Santambrogio, *J. Org. Chem.*, **32**, 2917 (1967).

[4] a) R. M. Whitlaker, *Rec. Trav. Chim. Pays-Bas*, **52**, 352 (1933); b) A. L. Mndzhoyan, *J. Gen. Chem. (USSR)*, **16**, 767 (1946); *Chem. Abstr.*, **41**, 2033 (1947); c) R. J. Ptfield and K. D. Amstutz, *J. Org. Chem.*, **19**, 1944 (1954); d) D. G. Manly and E. D. Amstutz, *ibid.*, **21**, 516 (1956).

[5] a) G. P. Sokolov and S. Hillers, *Akad. Nauk Latv. SSR*, **1965**, 163; *Chem. Abstr.*, **63**, 6943 (1965); b) S. Hillers, G. P. Sokolov, and A. Ya, Karmilchik, *Konf. Po. Vysokomolekul. Soedin.*, **1962**, 170; *Chem. Abstr.*, **62**, 6449 (1965); c) Y. Hata, S. Senoo, and M. Murakami, *Nippon Kagaku Zasshi*, **79**, 1447 (1958).

[6] a) A. J. Baggaley and R. Brettle, *J. Chem. Soc., C*, 969 (1968); b) S. D. Ross, M. Finkelstein, and J. J. Uebel, *J. Org. Chem.*, **34**, 1018 (1969).

Table 1. Reaction conditions and results in the cases of the compounds **4** and **7**

Experiment	1	2	3	4	5
Compound	**4**	**4**	**4**	**4**	**7**[a)]
(g)	1	1	1	1	0.045
MeOH (m*l*)	130	130	130	130	130
H_2SO_4 (g)	0.3	0.3	0.3	0.3	0.3
$LiClO_4$ (g)	6	12	6	6	6
H_2O (m*l*)	—	—	13	—	—
Temp (°C)	27—28	20	27—28	20	22—25
Current (A)	0.5	0.5	0.5	0.5	0.5
Terminal voltage (V)	21—65	14—23	21—33	18—22	28—36
Time (hr)	5	5	5	1	1
Product (g)	0.99	0.87	0.70	0.97	0.045
Total conversion (%)	99	99	90	40	—
Products (mol %)					
7a	12	5	15	31	33
7b	6	1	7	12	10
8	—	4	20	—	4
9a	79	73	35	55	18
10	3	17	23	2	35

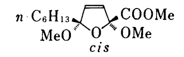
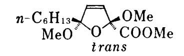
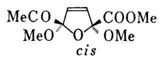
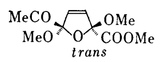
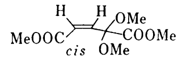
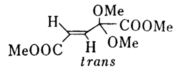
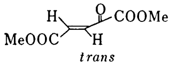
a) The ratio of **7a** to **7b** was 4 to 1.

Table 2. Reaction conditions and results in the cases of the compounds **5** and **6**

Experiment	6	7	8	9	10
Compound	**5**[a]	**5**[b]	**5**[b]	**6**	**6**
(g)	1	0.5	0.2	1	2.5
MeOH (m*l*)	30	20	20	30	9.2
H_2SO_4 (g)	0.1	—	0.03	0.1	0.1
H_2O (m*l*)	—	4	—	—	—
Temp (°C)	15	20	20	15	−13—−10
Current (A)	0.5	0.5	0.5	0.5	0.5
Terminal voltage (V)	11	7	25	6	4—6.5
Time (hr)	1.5	1.5	0.5	5	4
Products	0.97	0.16	0.2	0.91	2.2
Total conversion (%)	70	80	90	99	85
Products (mol %)					
8	—	—	—	—	—
9a	97	68	11	18	45
9b	3	22	4	82	55
10	—	10	85	trace	trace

a) The specimen was a mixture of **5** and **6** in a ratio 4/1. b) This specimen contains 2—3% of **6** elucidated by vpc.

Table 3. Comparison of NMR data of 2,5-dihydrofurans and their related compounds

	Compound	Functional group, τ						
		OMe		COOMe		COMe	>=<H	
19[2)]**a**		6.55 (3H)	6.70 (3H)	6.17 (3H)				3.91 (2H)
19[2)]**b**		6.61 (3H)	6.80 (3H)	6.17 (3H)				3.91 (2H)
7a		6.55 (3H)	6.67 (3H)	6.21 (3H)		7.68 (3H)		3.87 (2H)
7b		6.76 (3H)	6.79 (3H)	6.17 (3H)		7.67 (3H)		3.77 (2H)
9a		6.73 (6H)		6.20 (3H)	6.29 (3H)			3.93 (2H)
9b		6.68 (6H)		6.19 (3H)	6.22 (3H)		3.22 (1H) J_{AB}=15.7 Hz	3.62 (1H)
8				6.07 (3H)	6.15 (3H)		2.37 (1H) J_{AB}=16.5 Hz	3.01 (1H)

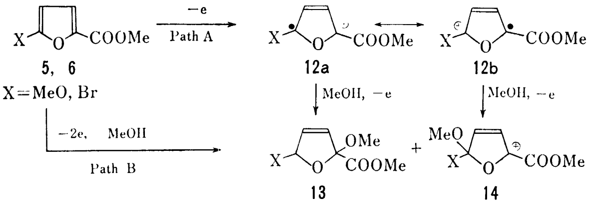
ring opened structures of **8**, **9a**, and **9b** are now distinctly established by NMR spectra as shown in Table 3.

The NMR spectra of **9a** and **9b** had singlet bands at τ 6.73 (6H) and 6.68 (6H), respectively, ascribable to geminal methoxy groups and two bands at τ 6.19—6.29 regions due to the protons (6H) attached to carbomethoxy groups. The structure of **11** instead of **9** should be rejected, since NMR signals due to the methoxy groups of **11** would be expected to be magnetically nonequivalent by the influence of the carbonyl group, being observed upon **19**,[2] but the signals at τ 6.73 can account for the above assignment. The isomer **9b** had a typical AB type signals at τ 3.22 and 3.62 (J_{AB}=15.7 Hz) due to *trans* olefinic protons, in well agreement with the pattern observed in **8**, whereas the *cis* isomer **9a** had a singlet band appearing at τ 3.93 (2H, olefin), in agreement with values observed in 2,5-dihydrofuran derivatives **7** and **19** in Table 3. The carbonyl absorption bands of **9a** and **9b** assigned to the ester groups contiguous to dimethyl acetal carbon atoms were observed at 1762—1763 cm^{-1}.

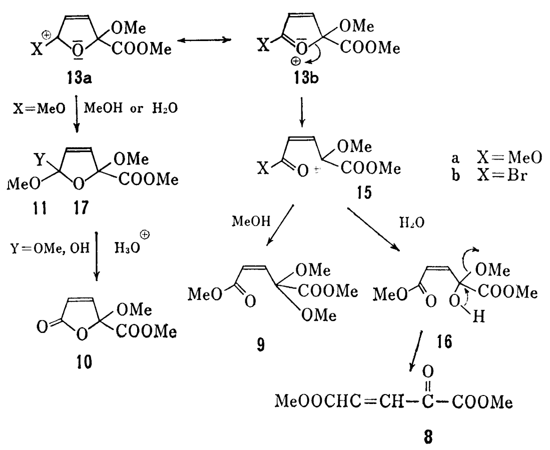
The structure of butenolide **10** was confirmed by its infrared spectrum; 1810, 1785, and 1766 cm^{-1} (unsaturated lactone and ester carbonyls), by its NMR spectrum; τ 2.72 (d, 1H), 3.65 (d, 1H), 6.14 (s, 3H), and 6.54 (s, 3H), and by its microanalyses.

A plausible mechanism for the transformation of **5** and **6** by the anodic oxidation to **9** and **10** *via* intermediates **13** or **14** are shown in Schemes 1, 2, and 3. In fact, the same two electron oxidation, which is considered to involve cation radical or dication intermediates (path A and path B), has been shown by the results from electrolyses of furans and furoic acids.[1,2,6b,7] As shown in Scheme 2, it is possible that the intermediates **13a** and **13b** would be subjected to solvolysis to give **9** and **10** *via* **11** and **15**. However, it must be noted that **13** (X=Br) does not give any appreciable amount of **10** in vpc. This reveals that the intermediate **15b** derived from **13** (X=Br) should be generated more readily in contrast to **15a** (X=MeO).

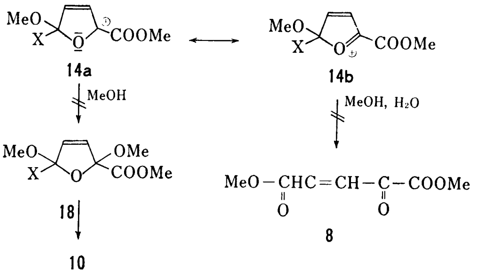
Most of our endeavour to isolate the key intermediates **11** and **17** failed. On the other hand, it must be mentioned that relatively high terminal voltage and presence of water were effective in producing **10**. The precise mechanism of the formation of **10** is not certain, but the most likely explanation for the formation of **10** is that it results from methanolysis or hydrolysis of **13a** *via* **17**, probably in an acid-catalyzed hydrolysis *in situ* or during after treatment.



Scheme 1

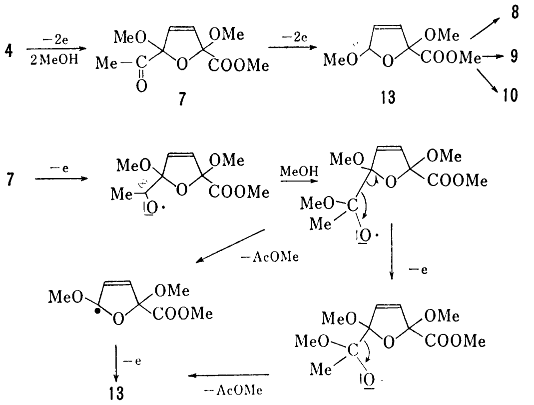


Scheme 2



Scheme 3

As illustrated in Scheme 3, the intermediates **14a** and **14b** (X=Br), if formed, would be expected to afford **8**, **18**, and **10** by the attack of the solvents. The results from the experiments 9 and 10 shown in Table 2 suggest that the absence of **8** and **18** reveals a probability of the presence of **13** rather than **14**.



Scheme 4

In the course of the conversion of **7** to **8**, **9**, and **10**, the intermediate **13** is supposed to play an important role, but it is not easy to elucidate its behavior. A tentative mechanism of the conversion of **7** to **13** is depicted in Scheme 4. Any change could not be observed in its constituent on vpc, when a mixed solution of **7** in methanol in the presence of catalytic

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7) S. Arita, Y. Takahashi, and K. Takeshita, *Kogyo Kagaku Zasshi*, **72**, 2289 (1969); K. Yoshida and T. Fueno, This Bulletin, **42**, 2411 (1969); C. K. Mann and K. K. Barnes, "Electrochemical Reactions in Nonaqueous Systems," Marcel Dekker, Inc., N. Y. (1970), p. 157.

amount of sulfuric acid was stirred for 5 hr without passing electric current. This demonstrates that removal of the acetyl group from **7** would be assisted by electrolysis, however, little is known of anodic oxidation on carbonyl function except for aroyl derivatives[8] and adduct of bisulfite.[9] Concerning the elimination of acetyl group from **7**, a further detailed mechanism could not be discussed on the basis of our present results.

The isomerization of the *cis* isomer **9a** to the *trans* **9b** occurred when the bromide **6** was electrolyzed. Addition of ammonium bromide to the runs 1 and 2 in Table 1 resulted in the production of **9b**. In both cases, liberation of bromine was encountered. This seems to implicate a catalyst of the **9a**→**9b** isomerization in the electrolytic media.

Experimental[10]

Ethyl 5-Acetyl-2-furoate 4.[3] An improved method. To a solution of methyl 2-furoate (50.4 g, 0.4 mol) and acetic anhydride (20.4 g, 0.2 mol) in benzene (188 m*l*), anhydrous stannic chloride (104 g, 0.4 mol) was added at −5—0°C with stirring. The mixture was stirred for 7 hr at room temperature and then treated with 50 m*l* of 20% aqueous hydrochloric acid. The organic layer was extracted with benzene and the extract was shaken with aqueous sodium bicarbonate and aqueous sodium chloride. Distillation of the extract, after removal of the solvent, gave 13.3 g of oily material, bp 90—110°C (1 mmHg). The distillate was once dissolved in benzene and washed with aqueous sodium carbonate followed by aqueous sodium chloride. Evaporation of the solvent gave 10 g of crystalline **4** (yield 45%), mp 99—100°C from methanol (lit,[3]) mp 101—102°C).

Anodic Oxidation of Methyl 5-Acetyl-2-furoate 4. Apparatus: A cell used in this electrolysis is depicted in Fig. 1. The inside beaker (cathode compartment) fitted with a condenser, a cathode, a thermometer, a stirrer, and a drying tube was immersed in an anode vessel. The outside beaker (Anode compartment) fitted with an anode electrode, a thermometer, a stirrer, and a drying tube was immersed in a water bath. Electrodes were two platinium foils (1.5× 2.0 cm^2). Current was controlled manually.

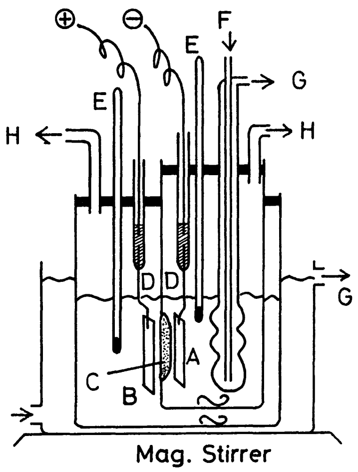

Fig. 1. Electrolysis cell. A: Cathode, B: Anode, C: Glass filter, D: Hg pool, E: Thermometer, F: Cooling water inlet, G: Cooling water outlet, H: $CaCl_2$ Tube

The reaction conditions and results are summarized in Table 1. A typical electrolysis procedure (Exp. 1) is indicated as follows: a solution of lithium perchlorate (6 g) in methanol (130 ml) containing 0.3 g of conc. sulfuric acid was poured into both the compartments. In the anode compartment, **4** (1.0 g) was charged and electrolyzed under a constant current of 0.5 A at 27—28°C for 5 hr with tirring. Then the electrolyzed solution in the anode compartment was concentrated *in vacuo*. The residue was taken up in ether, and the solution was washed with aqueous sodium bicarbonate and sodium chloride, and dried over anhydrous sodium sulfate. Evaporation of the solvent gave 0.99 g of crude liquid product. The yield of the products was estimated by vpc and the results are listed in Tables 1 and 2. Isolation of main constituents was carried out by preparative vpc: **7a** (*cis*): n_{D}^{20} 1.4528, n_{D}^{25} 1.4511. IR (liq. film) 3100 (=C–H), 1755 (ester C=O), 1735 (ketone C=O), 1635, 1440, 1273, 1200, 1090, 1042, 856, and 796 cm^{-1}. NMR (see Table 3).

Found: C, 52.13; H, 6.02%. Calcd for $C_{10}H_{14}O_5$: C, 52.17; H, 6.13%.

7b (trans): n_{D}^{20} 1.4532, n_{D}^{25} 1.4514. IR (liq. film) 3100 (=C–H), 1755 (ester C=O), 1735 (ketone C=O), 1635, 1440, 1275, 1210, 1190, 1130, 1042, 1002, 953, 860, 812, and 790 cm^{-1}. NMR (see Table 3).

Found: C, 51.88; H, 5.88%. Calcd for $C_{10}H_{14}O_5$: C, 52.17; H, 6.13%.

8: IR (nujol) 3070 (=C–H), 1738, 1708 (ester, ketone C=O), 1640 (C=C), 1445, 1312, 1260, 1176, 1078, 996, 950, 928, 778, and 670 cm^{-1}. NMR (see Table 3).

Found: C, 48.68; H, 4.90%. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.66%.

9a: n_{D}^{20} 1.4520, n_{D}^{25} 1.4579. IR (liq. film) 3000 (=C–H), 1763, 1735 (ester C=O), 1645 (C=C), 1440, 1392, 1280, 1220, 1190, 1138, 1100, 1050, 810, and 758 cm^{-1}. NMR (see Table 3).

Found: C, 49.28; H, 6.37%. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47%.

10: n_{D}^{20} 1.4597, n_{D}^{25} 1.4579. IR (liq. film) 3100 (=C–H), 1810, 1776, 1766 (lactone, ester C=O), 1618 (C=C), 1440, 1285, 1232, 1200, 1155, 1103, 1068, 1030, 997, 950, 824, 788, 759, and 690 cm^{-1}. NMR ($CDCl_3$) τ 2.72 (d, 1H, J=5.5 Hz, =C–H), 3.65 (d, 1H, J=5.5 Hz, =C–H), 6.14 (s, 3H, CO–O–CH_3), 6.54 (s, 3H, C–O–CH_3).

Found: C, 48.67; H, 4.63%. Calcd for $C_7H_8O_5$: C, 48.84; H, 4.68%.

Electrolysis of Methyl 5-Acetyl-2,5-dimethoxy-2,5-dihydro-2-furoate 7. Compound **7** (*cis*/*trans* 4/1) isolated by preparative vpc from the product of the experiment 1 was electrolyzed

Table 4. Vpc data of the products

Rt (min)	3.6	3.9	4.3	4.7	5.4	6.3	7.5	8.6	8.8
Compound	**8**	**6**	**5**	**10**	**4**	**9a**	**7a**	**7b**	**9b**

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[8] A. Takeda, S. Torii, and H. Oka, *Tetrahedron Lett.*, **1968**, 1781; L. L. Miller, V. R. Koch, M. E. Larscheid, and J. F. Wolf, *ibid.*, **1971**, 1389.

[9] M. Oyama and M. Ohno, *ibid.*, **1966**, 5201.

[10] All melting and boiling points are uncorrected. Preparative gas chromatography was accomplished with a partially modified Yanagimoto GCG-550T unit, using a column (4ϕ, 3 m long) packed with 10% SE-30 on Celite 545, 80—100 mesh, and H_2 (20 m*l*/min) as a carrier gas at 140°C. The retention times of the products are shown in Table 4. Infrared spectra were determined by a Hitachi EPI-S2 spectrophotometer. NMR spectra were obtained on a Japan Electron Optics Laboratory spectrometer (JNM-C-60) in deuterochloroform with TMS as an internal reference. Microanalyses were carried out by Miss M. Harada of this Laboratory.

in the manner described previously. Vpc analysis of the product showed the presence of **7a**, **7b**, **8**, **9a**, and **10** (Table 1). Structural assignment of each constituents were performed by comparing their IR spectra with those of the corresponding authentic compounds.

*Methyl 5-Bromo-2-furoate **6**.* Methyl 5-bromo-2-furoate **6** was prepared by the method of Amstutz *et al.*,[4d] mp 63—65°C from methanol (lit,[4c] mp 62.5—63.5°C).

*Methyl 5-methoxy-2-furoate **5**.* To a solution of sodium (2 g, 0.087 atom) and sodium iodide (0.1 g) in 100 m*l* of absolute methanol, **6** (7.2 g, 0.035 mol) was added. After refluxing for 4 hr the solvent was removed under diminished pressure. The residue was dissolved in ether and washed with aqueous sodium chloride. Evaporation of the solvent followed by distillation gave 2.5 g of methyl 5-methoxy-2-furoate **5**: bp 78—79°C (1 mmHg) (yield 41%), mp 51—52°C from *n*-hexane (lit,[4c] mp 51—53°C).

*Anodic oxidation of methyl 5-bromo-2-furoate **6**.* Electrolysis was carried out in the same manner described previously.[2] The reaction conditions along with the results are listed in Table 2. The reaction mixture was neutralyzed with methanolic sodium methoxide (Na 0.2 g/MeOH 20 m*l*). After evaporation of the solvent *in vacuo*, the residue was treated in the usual manner to give 0.9 g of crude oil whose constituents were analyzed by vpc and the results are shown in Tables 2 and 4. IR and NMR spectra of **9a** were identical with those of the specimen obtained by the above paragraph. Physical data of **9b** are as follows: n_D^{20} 1.4532, n_D^{25} 1.4513. IR (liq. film) 3000 (=C–H), 1762, 1732 (ester C=O), 1663 (C=C), 1440, 1310, 1260, 1170, 1090, 1050, 1013, 980, 942, 930, 910, 866, and 808 cm^{-1}. NMR (see Table 3).

Found: C, 49.80; H, 6.57%. Calcd for $C_9H_{14}O_6$: C, 49.54; H, 6.47%.

*Electrolysis of Methyl 5-Methoxy-2-furoate **5**.* A solution of **5** (1.0 g) in methanol (30 m*l*) containing conc. sulfuric acid (0.1 g) was electrolyzed in the manner described in preceding paragraph (Table 2). Structural assignment of the products was carried out by vpc analyses and in comparison of their IR spectrum with that of the corresponding authentic specimen.