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A CONVENIENT PREPARATION OF MALTOL, ETHYLMALTOL, AND PYROMECONIC ACID FROM 2-ALKYL-6-METHOXY-2H-PYRAN-3(6H)-ONES

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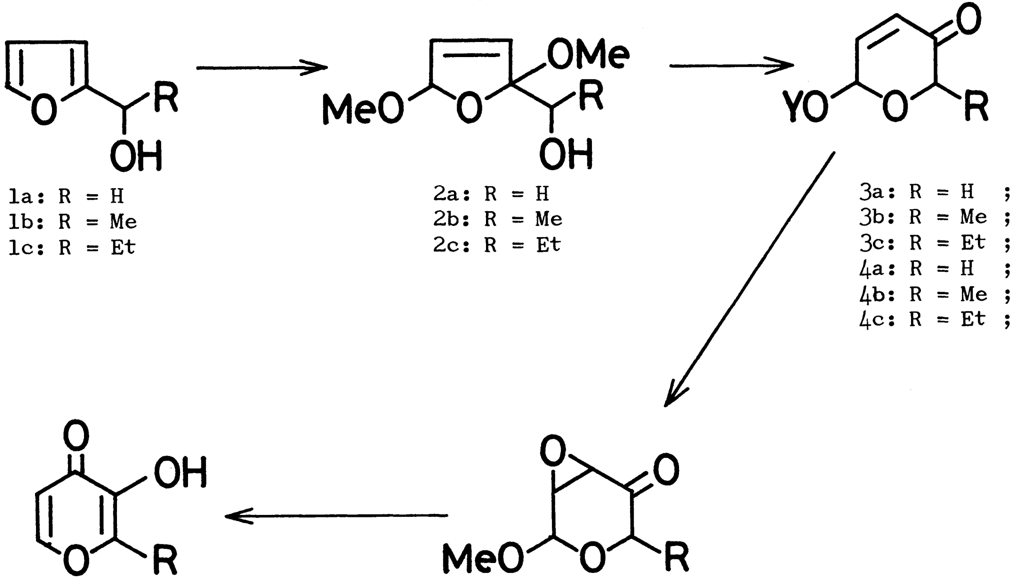
The efficient synthesis of 2-alkyl-3-hydroxy-4H-pyran-4-ones, e. g., pyromeconic acid (6a), maltol (6b), and ethyl maltol (6c), from 2-alkyl-4,5-epoxy-6-methoxytetrahydropyran-3-ones 5 by acid-catalyzed rearrangement is described. The key precursors 5 were obtained by epoxidation of 2-alkyl-6-methoxy-2H-pyran-3(6H)-ones 4, which were synthesized by three steps starting from furfuryl alcohols 1.

Maltol (3-hydroxy-2-methyl-4H-pyran-4-one) (6b) and its related compounds 6a and 6c have been of great interest as the flavoring additives in foods.$^{1)}$ For the synthetic purpose of 3-hydroxy-4H-pyran-4-ones 6, kojic acid,$^{2)}$ meconic acid,$^{3)}$ comenic acid,$^{4)}$ pyromeconic acid,$^{5)}$ rhamnopyranoside,$^{6)}$ 1,1-dimethoxy-3,5-heptanedione,$^{7)}$ and the related compounds$^{8)}$ have been frequently employed as a starting material. Strange enough, attempt to prepare 6 from 2H-pyran-3(6H)-ones 3, which can be easily provided by ring expansion of 2,5-dialkoxy-2-(1-hydroxyalkyl)-2,5-dihydrofurans 2,$^{9)}$ has not yet been reported. We wish to report here a new and efficient synthetic way to 2-alkyl-3-hydroxy-4H-pyran-4-ones 6 via 2H-pyran-3(6H)-ones 4 and tetrahydropyran-3-ones 8, which were obtained by several steps starting from furfuryl alcohols 1.

Ring expansion of 2-(1-hydroxypropyl)-2,5-dimethoxy-2,5-dihydrofuran (2c) in aqueous 50% THF solution containing a few drops of 1 M aqueous perchloric acid$^{10)}$ at room temperature for 10 min afforded 2-ethyl-6-hydroxy-2H-pyran-3(6H)-one (3c) in 98% yield; IR 3330 (OH), 1675 (C=O), 1632 cm^{-1} (C=C). The preparation of the key intermediate 2c from 1c was carried out using electrochemical procedures improved in our laboratory.$^{11)}$ Refluxing the dihydropyran-3-one 3c with methyl orthoformate in the presence of magnesium sulfate$^{12)}$ gave the acetal 4c in 90% yield; IR 1702 (C=O), 1686 (C=O), 1631 cm^{-1} (C=C); PMR δ 3.47, 3.51 (2s, 3H, CH_3O)(see Table 1). Addition of 2 molar amounts of 15% H_2O_2 to a two-phase solution containing 4c in diethyl ether and aqueous 5% sodium carbonate at 5-10 °C provided the epoxy ketone 5c in 88% yield; IR 1726 cm^{-1} (C=O); PMR δ 3.33-3.75 (m, 2H, $\mathrm{H{-}C\underset{O}{\frown}C{-}H}$)(see Table 2). Heating of 5c in dioxane in the presence of sulfuric acid afforded 6c in 91% yield (see Table 3). On the other hand, reaction of the epoxide 5c with 1:20 concentrated hydrochloric acid-ethanol at 75-80 °C for 20 hr afforded the chlorinated product 7c13) (34%); IR 1710 (C=O), 1627 cm^{-1} (C=C); PMR δ 6.98 (d, 1H, HC=C) along with 6c (39%). Refluxing 5c with 1:4:16 hydrochloric acid-water-ethanol gave exclusively 6c in 67% yield.



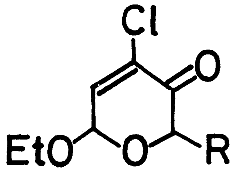
1a: R = H
1b: R = Me
1c: R = Et

2a: R = H
2b: R = Me
2c: R = Et

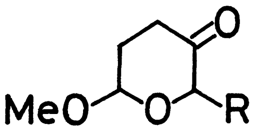
3a: R = H ; Y = H
3b: R = Me ; Y = H
3c: R = Et ; Y = H
4a: R = H ; Y = Me
4b: R = Me ; Y = Me
4c: R = Et ; Y = Me

6a: R = H
6b: R = Me
6c: R = Et

5a: R = H
5b: R = Me
5c: R = Et



7b: R = Me
7c: R = Et



8b: R = Me
8c: R = Et

The alternative way to 6 was accomplished via tetrahydropyran-3-ones 8. Thus, hydrogenation14) of 4c in methanol in the presence of PtO$_2$ gave 8c in 87% yield; IR 1730 cm^{-1} (C=O). Refluxing 8c with selenium dioxide in aq. 60% ethanol afforded 6c in 58% yield.

Studies on the development of the further alternative synthetic ways for maltol synthesis from furfuryl alcohols 1 are currently in progress.

Table 1. Conditions and Results in Acetalization of 3

Compound (g)	$CH(OMe)_3$ ml	$MgSO_4$ g	MeOH ml	Time h	Bp °C/ mmHg	Product	Yield %
3a (1.14)	15	3	0.3	6	68-70/11	4a 9a)	77
3b (1.28)	20	3	----	6	72-74/11	4b 9a)	87
3c (1.42)	25	3	----	20	74/10	4c 16)	90

Table 2. Conditions and Results in Epoxidation of 4

Compound (g)	Solvent (ml)	5% Na_2CO_3 ml	15% H_2O_2 g	Temp °C	Time h	Bp °C/ mmHg	Product	Yield %
4a (2.56)	Ether (40)	10	9.2	5	3	75-78/11	5a 15)	89
4b (2.84)	Ether (40)	10	9.2	10	3	83-86/11	5b 13)	90
4b (2.84)	MeOH (30)	10	4.6	0-3	3	83-86/11	5b 13)	93
4b (2.84)	H_2O (30)	10	14.5*	0-5	3	83-86/11	5b 13)	90
4c (3.12)	Ether (40)	10	9.2	5	3	80-85/5	5c 16)	88

* Aqueous 5% hydrogen peroxide was used.

Table 3. Conditions and Results in Isomerization of Epoxides 5 *

Compound (g)	Solvent (ml)	Catalyst (g)	Time h	Product	Yield %
5a (2.88)	Dioxane (25)	80% H_2SO_4 (3.5)	1	6a 17)	78
5b (3.16)	H_2O (30)	conc H_2SO_4 (3.0)	4	6b 5)	87
5c (3.44)	Dioxane (25)	80% H_2SO_4 (3.5)	1	6c 5)	91

* The reactions were carried out at 95-100 °C.

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10) It has been shown that the isomerization of 2c to 3c was carried out on treatment with 1-2% sulfuric acid for ca. 2 hours: Ref. 9.

11) Electrolytic methoxylation of furfuryl alcohols (1a and 1b) in MeOH using NH_4Br as a supporting electrolyte have been shown to give 2a (66%) and 2b (73%), respectively: see N. Clauson-Kaas, F. Limborg, and P. Dietrich, Acta Chem. Scand., 6, 545 (1952); P. Nedenskov, N. Elming, J. T. Nielsen, and N. Clauson-Kaas, ibid., 9, 17 (1955). However, the improved method in MeOH containing Et_4NClO_4 under a constant current of 0.07-0.01 A/cm^2 (2.02 F/mol) gave 2a (91%), 2b (95%), and 2c (94%), respectively. The details will be published elsewhere.

12) The acetalization of the hemiacetals (3a and 3b) using BF_3-OEt_2 or $SnCl_4$ as catalysts has been shown to give 4a (43%) and 4b (45%), respectively: Ref. 9a.

13) The related chlorinated compound of 7b has been obtained by the reaction of 5b with lithium chloride in THF at 65 °C in 80% yield: H. Paulsen, K. Eberstein, and W. Koebernick, Tetrahedron Lett., 4377 (1974).

14) The hydrogenation of 3b with 5% Pd on charcoal giving 6-hydroxy-2-methyltetrahydropyran-3-one has been reported: Ref. 9b.

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