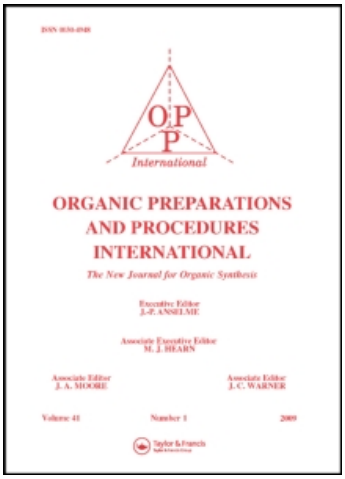

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Minas P. Georgiadis[a]; Kim E. Albizati[b]; Taxiarchis M. Georgiadis[c]
[a] Chemical Laboratories, Agricultural University of Athens, Athens, Greece [b] Department of Chemistry, Wayne State University, Detroit, MI [c] Department of Chemistry, Columbia University, New York, NY

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Minas P. Georgiadis*
Chemical Laboratories
Agricultural University of Athens
75 Iera Odos, Athens 118 55, GREECE

Kim F. Albizati
Department of Chemistry
Wayne State University, Detroit, MI 48202

Taxiarchis M. Georgiadis
Department of Chemistry
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Department of Chemistry
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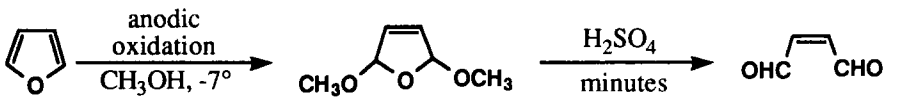
INTRODUCTION

The oxidative rearrangement of 2-furylcarbinols produces 2H-pyran-3(6H)-ones which have been used for a variety of purposes. This review presents the historic evolution of the oxidative rearrangement of 2-furylcarbinols to useful synthons for the production of a large number of compounds such as sugars, pheromones, and medicinally interesting compounds. Brief reviews are given of the main synthetic methodologies in this area as well as typical examples for preparing these valuable synthons.

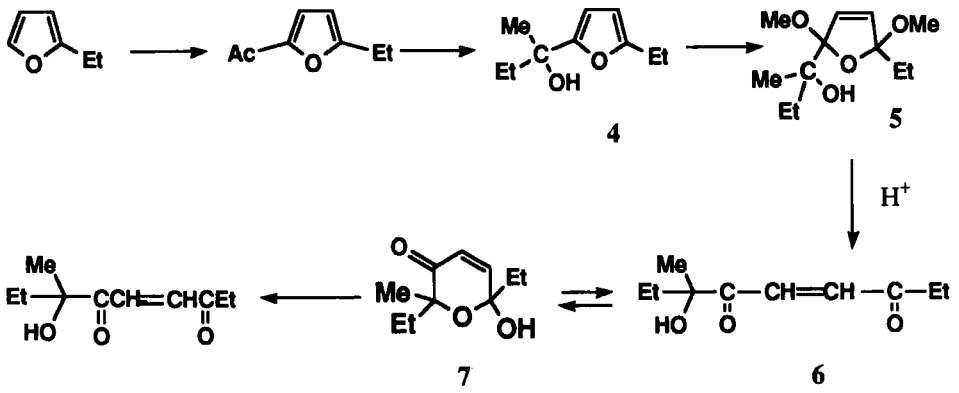
The possibilities of 1,4-addition to furans has been exploited by organic chemists for a variety of purposes, many of which are given in organic chemistry textbooks. The number of publications involving 1,4-oxidative addition to furans and, more specifically, oxidative rearrangement of 2-furylcarbinols have increased enormously in the last decade because of the vast synthetic potential of the highly functionalized 2H-pyran-3(6H)-ones produced by such oxidations.

The first oxidative addition to a furan was reported by Clauson-Kaas[1] who described the synthesis of buten-1,4-dialdehyde (**3**) from furan itself.



1 **2** **3**

Several oxidative additions to furan derivatives and subsequent hydrolyses of the resulting 2,5-dialkoxy-2,5-dihydrofurans were reported[2] before the disclosure[3a] of the first synthesis of 2H-pyran-3(6H)-one. In 1969, Cavill and coworkers[4] described the an oxidative bromination of furfuryl alcohol derivative **4** in methanol and its subsequent hydrolysis of the 2,5-dimethoxy-2,5-dihydrofurfuryl alcohol **5** resulting in the formation of 2H-pyran-3(6H)-one (**7**) as an intermediate in their juvenile hormone synthesis (Scheme 1).

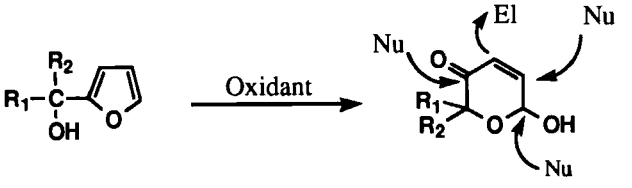


Scheme 1

The synthesis of a great number of 6-hydroxy-2H-pyran-3(6H)-ones by oxidative rearrangement of 2-furylcarbinols was later described independently by Canadian[5] and Polish[6] chemists. Lefebvre reported[5] the oxidative rearrangement of 2-furylcarbinols by peracids to 2H-pyran-3(6H)-ones, a large number of which were prepared for pharmacological screening. Achmatowicz[6] and his coworkers have prepared a variety of compounds with the basic 2H-pyran-3(6H)-one ring system by oxidative addition of bromine to the appropriate 2-furylcarbinols and subsequent acidic hydrolysis. The Polish chemists studied the conformational equilibrium of these compounds and used 2H-pyran-3(6H)-ones as intermediates in the synthesis of various sugars.[6,9] It should be noted that the interest in synthesizing carbohydrates *via* 2H-pyran-3(6H)-ones continues to date.[9]

I. 2H-PYRAN-3(6H)-ONES AND A NEW ERA OF FURAN CHEMISTRY

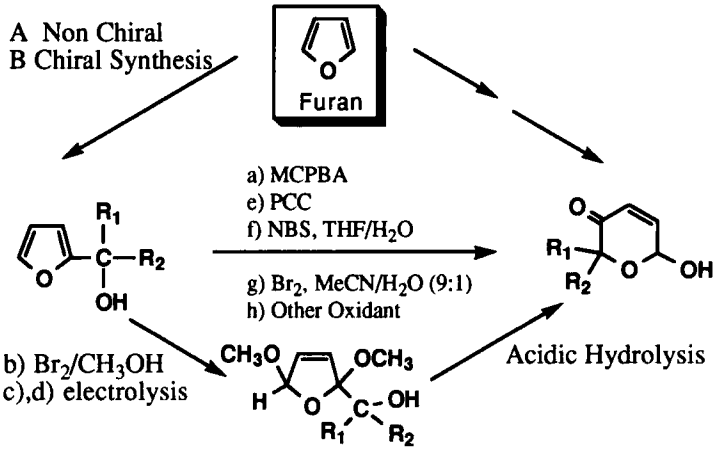
A new era has emerged in furan chemistry with the synthesis of 2H-pyran-3(6H)-ones,[5,6] molecules admirably endowed with different functionality suitable for further elaboration by reaction with selected nucleophiles and electrophiles (Scheme 2).



Scheme 2

Initially, the products of the oxidative rearrangement of 2-furylcarbinols attracted the interest of chemists for their use as precursors to carbohydrates,[6,9] antimicrobial, and anticoccidial compounds.[7] As time passed, however, it was discovered that pyran moieties were constituents of a large number of biologically important, naturally occurring compounds including polyether antibiotics and spiroketal pheromones which were challenging synthetic targets for organic chemists. Thus, in the last decade the number of publications involving furan oxidations and, more specifically, the oxidative rearrangement of 2-furylcarbinols have increased enormously. The chemistry of 2H-pyran-3(6H)-ones up to 1982 has been presented in an outstanding review by Holder.[10] Further leading references[11] can be found on the syntheses of medicinally interesting compounds[12] and representative examples in the use of furans as key intermediates in the preparation of natural products.[13,14] The recent chemistry of 2H-pyran-3-ones and their use in synthesis will be the subject of a forthcoming review to appear in this Journal.

A variety of reagents have been used for the oxidative transformation of 2-furylcarbinols to 2H-pyran-3(6H)-ones such as *m*-chloroperbenzoic acid,[3a,5,7] peracetic acid,[3a] bromine in methanol,[6] anodic oxidation,[15,16] pyridinium chlorochromate,[11d] NBS,[11j] and bromine in acetonitrile in the presence of a small amount of water[17] (see Scheme 3). The NBS method is rapid, convenient, relatively inexpensive and selectively oxidizes 2-furylcarbinols without affecting thioether substituents.



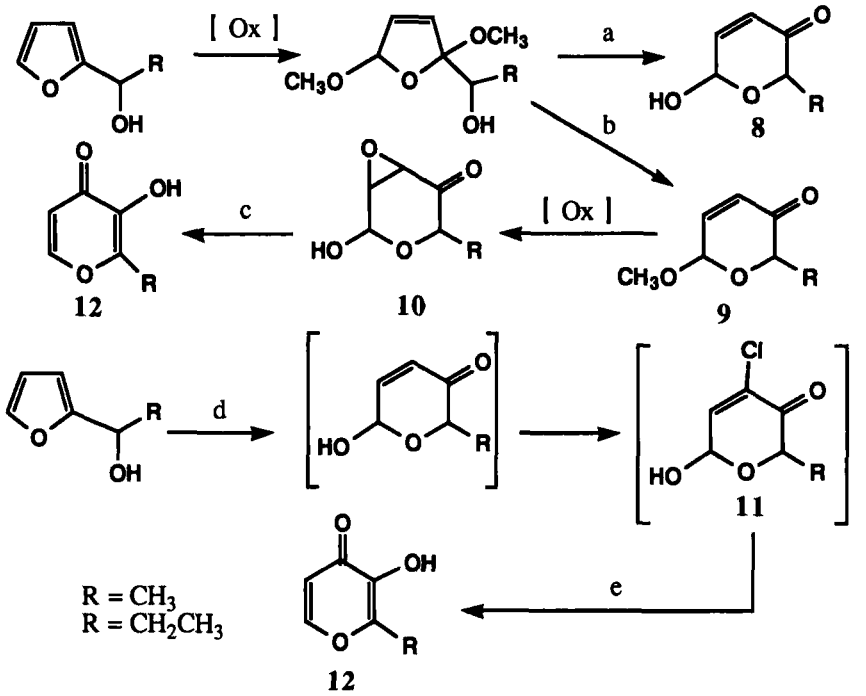
a) see ref. 3.5; b) see ref. 6; c),d) see ref. 15, 16; e) see ref. 11d
f) see ref. 11j; g) see ref. 17; h) see ref. 19d,e.

Scheme 3

Oxidative rearrangement of monosubstituted 2-furylcarbinols using Cl_2 in CH_3OH may yield the corresponding 2-mono-substituted 2H-pyran-3(6H)-ones **8**, which, by subsequent heating results in a one pot synthesis of maltol **12** (R = CH_3) or ethyl maltol (R = CH_2CH_3) (see Scheme 4).[11e]

Regardless of the reagent used in the preparation of 2H-pyran-3(6H)-ones, a common mechanism has been proposed[18] for their formation *via* oxidative rearrangement of 2-furylcarbinols which

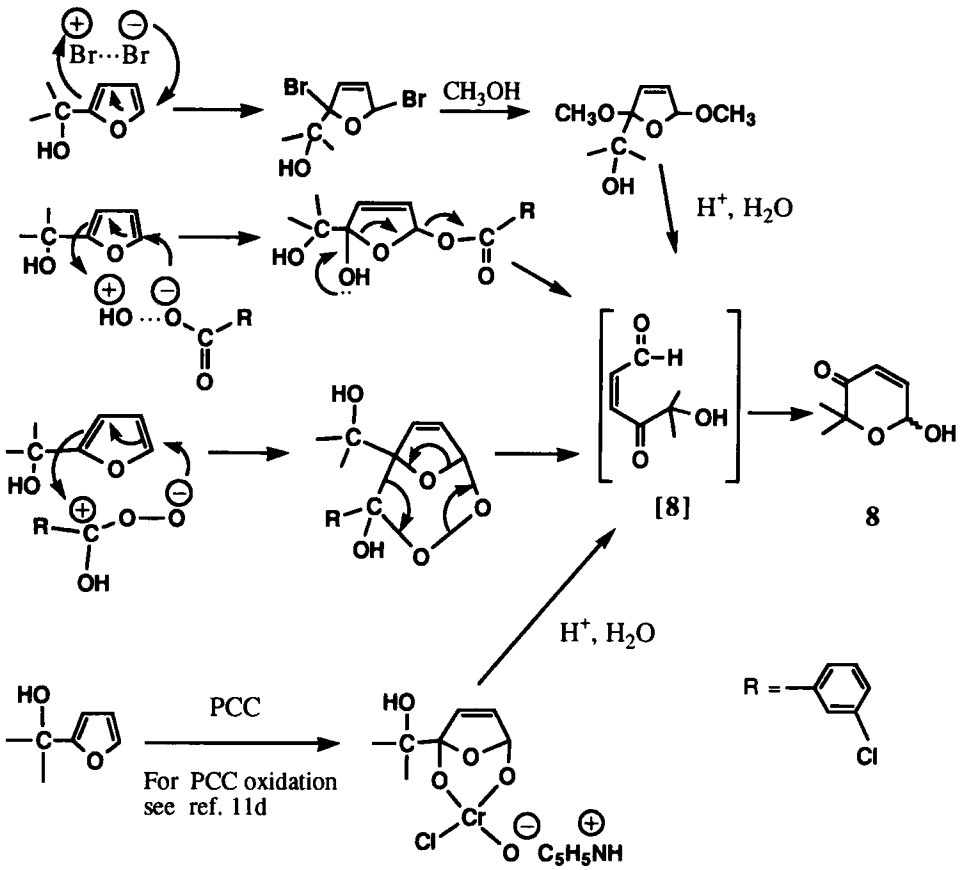
is shown in Scheme 5.



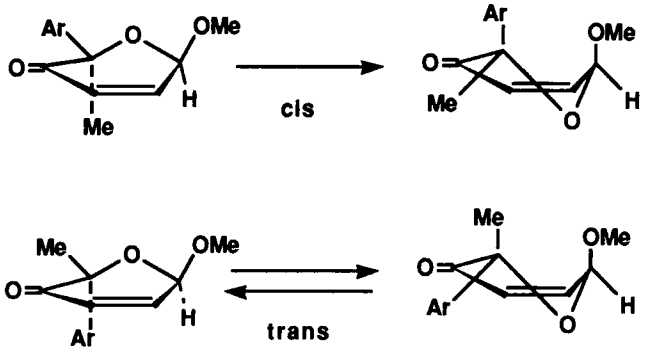
a) H^+ / H_2O; b) H^+, heat; d) $2Cl_2$, MeOH / H_2O, 0°C; e) heat, H_2O

Scheme 4

^1H NMR was found to be quite useful for the characterization of the *cis*- and *trans*-6-hydroxy-2H-pyran-3(6H)-ones. The two *vicinal* olefinic protons together with the H-6 allylic proton gives a characteristic AMX pattern. Achmatowicz[6,11c] and coworkers consider their 2-equatorially monosubstituted-2H-pyran-3(6H)-ones as deformed sugars, and assigned the isomers having a *trans* configuration for which the α conformation prevails, in accord with the Garbisch equation, by their relatively larger vicinal coupling constant and smaller allylic coupling constant. On the other hand, isomers with relatively smaller vicinal coupling constant and larger allylic coupling constant were assigned the *cis* configuration. Georgiadis and coworkers[11g] have reported that for 2-aryl-2-methyl-2H-pyran-3(6H)-ones, the vicinal and allylic *J* values reported by Achmatowicz cannot be utilized for a qualitative structural assignment of these compounds. They have reported that the nature and number of substituents at C-2 determine the configuration of the predominant diastereomer and that the Garbisch equation cannot be applied to their molecules because of the axially-oriented aryl group. It was concluded that a direct configurational assignment of 2-aryl-2-methyl-2H-pyran-3(6H)-ones is possible from the quotient $J_{5,6}/J_{4,6}$ of the vicinal/allylic coupling constants. More specifically, $J_{5,6}/J_{4,6} \approx 1$ is indicative of a *trans* isomer while $J_{5,6}/J_{4,6} \approx 2$ is indicative of a *cis* isomer (see Scheme 6).



Scheme 5



Scheme 6: Molecular Structure and Conformational Equilibrium of *cis* and *trans* 2-Ar-methyl-6-methoxy-2H-pyran-3(6H)-ones. For Conformational Equilibrium Studies (see ref. 6 and 11 c).

The optical purity of 2-furylcarbinols used as starting material is a key factor for preparing

optically pure 2H-pyran-3(6H)-ones by oxidative rearrangement. Thus, a variety of reagents and methodologies have been used for preparing optically active 2-furyl carbinols including chiral-based asymmetric syntheses,[13b-n,19a,b,21] kinetic resolution using the Sharpless epoxidation procedure[19c,d,e,f,11k] and enzyme-catalyzed reductions and saponifications with lipases and esterases[19g] including enantioselective hydrolysis of phenylacetic esters and amides of 2-furylcarbinols by penicillin acylase.[19h] Optically pure 2H-pyran-3(6H)-ones had earlier been prepared from glycals,[20,10] and more recently, they were prepared in two steps after isolation of chiral 2-furyl carbinols from glycals.[21] However, the "chiron approach" using sugars provides limited possibilities for introducing substituents at C-2 in contrast to the numerous possibilities for introducing substituents using the oxidative rearrangement of furyl carbinols.

In the preparation of 6-hydroxy-2H-pyran-3(6H)-ones, it must be kept in mind that one anomer is predominantly formed[11j,19e,24] due to the anomeric effect. A variety of methods for derivatizing[6,11j,19e,24] as well as for removing[23] the anomeric hydroxy group have been reported. When the anomeric hydroxyl is converted to a methyl ether, the diastereoisomers may be separated by column chromatography. Protection, however, of the anomeric hydroxy function with a bulky group such as a *tert*-butyldimethylsilyl ether yields exclusively the formation of only one anomer.[19e] Additionally, it was reported that racemic mixtures may be resolved[22] after derivatization with L-alanine using a DCC coupling method.

II. PRACTICAL CONSIDERATIONS

When oxidative rearrangements of 2-furylcarbinols are to be performed, it must be borne in mind that not only the methodology but also the work-up details play critical roles in obtaining the rather sensitive 2H-pyran-3(6H)-ones. For example, Achmatowicz and coworkers have reported a 73% yield (tlc one spot) for the preparation of the water soluble parent compound, 6-hydroxy-2H-pyran-3(6H)-one by Br_2 - methanol treatment of furfuryl alcohol and subsequent acidic hydrolysis.[6] Kolb and Hoffmann,[13s] however, following the same technique reported only 49% while Georgiadis and coworkers[12f] using a different methodology have prepared the same compound analytically pure in 88-90% yield. The stability as well as the water solubility of these compounds, which have a carbonyl as well as an allylic hemiacetal hydroxy group is affected to a great extent by the number and nature of substituents at C-2 (pyran numbering). For example, the 6-hydroxy-2-methyl-2-phenyl (or biphenyl)-2H-pyran-3(6H)-one is more stable than 6-hydroxy-2-methyl-2H-pyran-3(6H)-one (monosubstituted at C-2) and the unsubstituted 6-hydroxy-2H-pyran-3(6H)-one is water soluble and the least stable. In general, the C-2 disubstituted 6-hydroxy-2H-pyran-3(6H)-ones are stable in moderately acidic or basic media while the monosubstituted compounds are more susceptible to base. The unsubstituted 6-hydroxy-2H-pyran-3(6H)-one is the least stable of all and can be handled only in slightly acidic media (pH $\approx$ 4), but may be stored in pure form (crystalline) at refrigerator temperatures for a year. This appears to be generally true of these compounds as a class. However, all

of them appear to be more sensitive to base.

In conclusion, the proper temperature, oxidant and pH play an important role for making a 2H-pyran-3(6H)-one as well as of obtaining a good yield *via* the oxidative rearrangement of a 2-furylcarbinol. However, practical yields depend also on the handling or work up of the reaction mixture. In other words, one spot on tlc does not mean a quantitative yield in the preparative sense because the actual yield depends on the recovery of a pH sensitive product from the reaction medium.

III. METHODOLOGY

Regardless of the reagent used for oxidative rearrangement, the starting material must be freshly prepared or distilled since 2-furylcarbinols decompose or polymerize on standing. *m*-Chloroperbenzoic (MCPA) is a convenient reagent for the oxidative rearrangement of a 2-furylcarbinol. It gives the desired product in one step, in contrast to the bromine-methanol reagent which requires a subsequent acid hydrolysis step. The preferred solvent for the MCPA method is methylene chloride, the minimum amount of which is used to dissolve the oxidant, which is added portion-wise. The optimum temperature of mixing the reagents is 10-15°. The reaction is monitored by tlc and when complete, the excess of the oxidant is destroyed and the *m*-chlorobenzoic acid produced is removed usually by extraction with bicarbonate solution. Extensive washings with bicarbonate solution may not completely remove the *m*-chlorobenzoic acid from the reaction mixture. In fact, the bicarbonate treatment may be harmful. For example, in the case of 6-hydroxy-2H-pyran-3(6H)-one bicarbonate washing is not applicable since the product is water soluble and is decomposed by the bicarbonate solution (basic pH). Thus, in order to remove the *m*-chloroperbenzoic as well as the m-chlorobenzoic acid the mixture is cooled to -20° for 2-3 hours and filtered. The filtrate is concentrated under reduced pressure to one-third of the original volume, cooled overnight at -10° and again filtered. This may be the method of choice for preparing delicate or unstable 2H-pyran-3(6H)-ones. Treatment of the filtrate with small amount of hexane with or without further concentration yields the desired product in crystalline form. Thus, the above cooling technique for removing the *m*-chlorobenzoic acid used in combination with the bicarbonate solution washing, when applicable, gives optimum yields. The Br_2/CH_3OH method which was followed by Achmatowicz and coworkers extensively is a rather tedious method for obtaining an oxidative rearrangement product from 2-furylcarbinols because it requires two steps and careful handling.

The NBS process of Georgiadis and Couladouros[11j] is a rapid and relatively inexpensive method which selectively oxidizes furfuryl alcohols without affecting thioether substituents. The following conditions, however, are critical if the NBS procedure is to give quantitative results. The furfuryl alcohol derivative must be dissolved in a mixture of an organic solvent such as THF or CH_3CN and water. The temperature should be kept at 0-5°. The NBS must be added as a solid, portion-wise, so that the subsequently liberated bromine is consumed immediately. The excess NBS

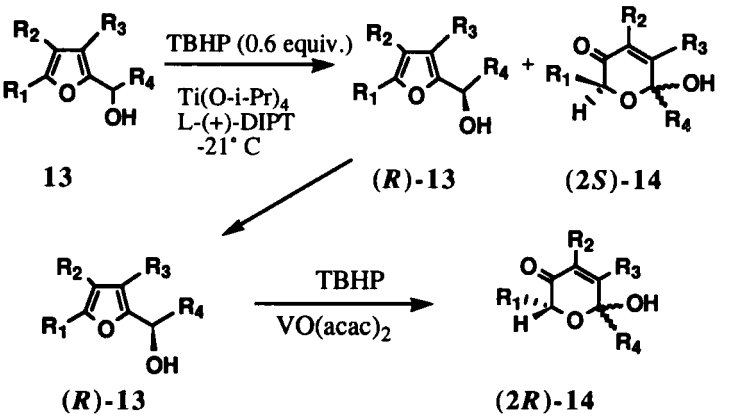
is destroyed together with the HBr formed before the evaporation of the organic solvent. The NBS procedure for the oxidative rearrangment of furylcarbinols may be the most convenient since it allows for the synthesis as well as for the oxidation of furylcarbinol in a one-pot procedure. The furylcarbinol is prepared by the treatment of a ketone or aldehyde with furyllithium in THF followed by the addition of water or water-NH_4Cl. If the pH of the reaction mixture is adjusted to neutrality, then only one equivalent of NBS is required for the *in situ* oxidation as in the two-step procedure, i.e., the isolation of the furylcarbinol and subsequent oxidation. However, if after the furyllithium treatment of a carbonyl compound only water is added without any adjustment of the pH of the reaction mixture, then two equivalents of NBS are required for a rapid oxidation. The temperature for the oxidative rearrangement is very critical and must be kept at or below 0° during the addtion of NBS.

The NBS procedure has been used for the synthesis of spiroketal 2H-pyran-3(6H)-ones by Albizati and coworkers[14d] who replaced NBS as an oxidant in several cases by 5,5-dimethyl-N,N-dibromohydantoin with equal or better results in obtaining these sensitive molecules. A modification of bromine/methanol oxidation introduced by Weeks,[11e] oxidizes the 2-furylcarbinol and subsequently, at elevated temperatures, further oxidizes the resulting unsubstituted or 2-monosubstituted-2H-pyran-3(6H)-one to maltol. This is a remarkable one-pot synthesis of both maltol or ethylmaltol in approximately 75% yield. A variation of bromine oxidation using CH_3CN-H_2O (9:1) as solvent at 0° has shown that it is possible to replace the NBS by bromine as an oxidant when an organic solvent containing a small amount of water is used as the reaction medium.

Although the use of pyridinium chlorochromate (PCC) for the oxidative rearrangement of 2-furylcarbinols has been disclosed,[11d] no experimental details using PCC as an oxidant for preparing 2H-pyran-3(6H)-ones have been published so far. The PCC method is the least used for preparing the title compounds. The use of tert-butylhydroperoxide (TBHP) catalyzed by a transition metal[11h] to provide racemic 2H-pyran-3(6H)-ones has been reported.[19e]

As was mentioned earlier, a prerequisite in preparing an optically active 6-hydroxy-2H-pyran-3(6H)-one is the optical activity of the 2-furylcarbinol. Thus, much effort has been directed to the preparation of optically active 2-furylcarbinols.[19] Sato and co-workers[19d,e] have used the Sharpless reagent for the kinetic resolution[19i,j] of racemic furyl carbinols (see also ref. 11k) leading to optically active 2H-pyran-3(6H)-ones. More specifically, enantioselective oxidation of racemic **13** using TBHP and asymmetric tartrate complex (L-(+) DIPT) provides access to optically active (*S*)-2H-pyran-3(6H)-one **14** which may be separated by column chromatography. However, if access is desired to optically active 2-furylcarbinols, this may be conveniently accomplished by treating the mixture with base (NaOH in Et_2O/H_2O). Under these conditions the base sensitive **14** is converted to an unidentified polar product which may be removed by small column filtration.

It is reasonable to assume that the Sharpless reagent, which is specific for kinetic resolution of allylic alcohols, in the case of 2-furylcarbinols epoxidizes not the allylic double bond, but attacks the 2,5-position on the furan ring yielding the unstable intermediate which hydrolyses to a chiral 2H-pyran-3(6H)-one. This assumption is in accord with the postulated prerequisite 2,5-attack on furan



Scheme 7

TABLE 1. Kinetic Resolution of 1 Using TBHP, Ti(O-*i*-Pr) and L-(+)-DIPT

	Substrate **13**				Slow-reacting, Enantiomer *(R)*-**13**			
	R^1	R^2	R^3	R^4	Method	time (hrs)	yield (%)	ee (%)
a	H	H	H	Me	A	12	33	>95
b	H	H	H	*n*-Am	A	14	38	>95
					B	25	42	>95
c	H	H	H	*È*-Pr	B	25	39	>95
d	H	H	H	*t*-Bu	B	40	41	6
e	H	H	H	Ph	A	48	38	>99
f	Me	H	H	*n*-Am	A	6	40	>95
g	H	H	Me	*n*-Am	B	4	39	>95
h			H	Me	A	45	43	>99
i	H	H	H	$HC{=}CH_2$	B	24	38	>95
j	H	H	H	$CH_2CH{=}CH$	B	36	42	>95
k	H	H	H	$C{\equiv}CSiMe_3$	B	20	38	88
l	H	H	H	CH_2CO_2Et	A	22	40	>95

moiety for the oxidative rearrangement of 2-furylcarbinols regardless of the oxidant used.[18] Noteworthy also is the fact that, although 2-furylcarbinols **13i**, **13j** and **13k** have another site for accepting an oxygen atom, the kinetic resolution occurs instead via oxidation of the furan ring. Hence, the rate of oxidation of the furan ring is far faster than that of olefins.[19e]

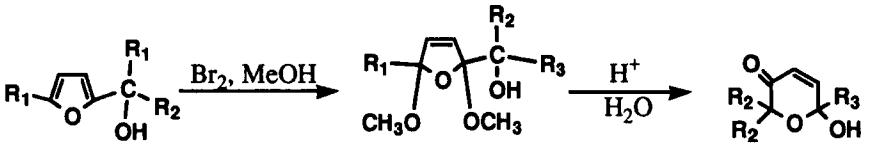
IV SCOPE AND LIMITATIONS

In nearly every case, the goal of an oxidative rearrangement of a 2-furylcarbinol is to produce a starting material or synthon for further elaboration. Thus, when a 2-furylcarbinol bears a thioether substituent, MCPA cannot be used as an oxidant and NBS is preferred. When the targeted compound is sensitive to base and is water soluble, then the reaction mixture cannot be treated with base, and neither can the oxidation product be extracted from water. When chirality is desired at C-2 on the 2H-pyran-3(6H)-one, a modified Sharpless reagent or a chiral furylcarbinol should be used as a substrate. In the latter case, it is obvious that one of a variety of oxidants may be used. Thus, the number and nature of substituents at C-2 of the targeted 2H-pyran-3(6H)-one and the requirement for chirality at the same carbon together with the goals and personal preference of the investigators determine the choice of a procedure in the oxidative rearrangement of furylcarbinol. Representative examples of experimental procedure of oxidizing 2-furylcarbinols are given in the next section.

V. EXPERIMENTAL PROCEDURES

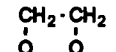
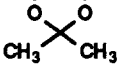
1. Bromine or NBS as an Oxidant

a. *The Bromine-Methanol Procedure*[6]



15 16 17

Scheme 8

Compound	R_1	R_2	R_3	Yield (%)	Reference
16a	H	H	H	73	6
b	H	H	CH_3	92	6
c	H	CH_3	CH_3	97	6
d	H	CO_2Et	CO_2Et	47	6
e	H	H	CO_2Bu	73	6
f	H	$AcOCH_2$	$AcOCH_2$	64	6
g	$PhCH_2O$		H	86	11c
h	H		H	76	6

2-[2.5-Dimethoxy-2,5-dihydrofuryl)]propan-2-ol (16c).- To a solution of **15c** (1.26 g, 10 mmol) in a mixture of anhydrous ether (20 ml) and absolute MeOH (60 ml) stirred at -35°, a solution of bromine (1.92 g, 12 mmol) in 10 ml MeOH was added dropwise. The mixture was neutralized with gaseous ammonia, allowed to warm up and evaporated. Benzene was added to the residue, and NH_4Br was removed by filtration. The filtrate washed with water and dried over $MgSO_4$. Evaporation of the solvent afforded **16c** (1.86 g, 97%), bp. 57-64°/1.3 torr; IR: 3500 (OH), 1630 (C=C), 1100, 1030 (C-O) cm^{-1}; ^1H NMR: δ 1.19, 1.28 (CH_3), 2.25 (OH), 3.19, 3.26, 3.60 (OMe_3), 5.54 (H-5 *cis*), 5.81 (H-5 *trans*), 6.40 (CH=CH); mass *m/e* (% of the base peak): 187 (1) M-1, 157 (9), 141 (7), 129 (100), 125 (7), 115 (22), 101 (29), 99 (35), 98 (53), 83 (29), 71 (16), 59 (42), 55 (10), 43 (36).

Anal. Calcd for $C_9H_{16}O_4$: C, 57.4; H, 8.6. Found: C, 57.2; H, 8.6

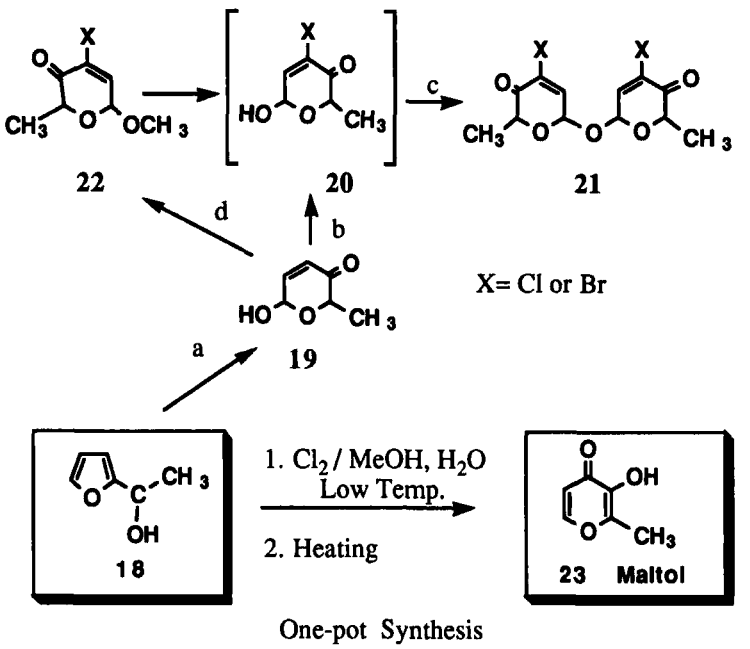
6-Hydroxy-2,2-dimethyl-2H-pyran-3(6H)-one (17c).- Carbinol **16c** (1.69 g, 9 mmol) was dissolved in 1% H_2SO_4 aq (10 ml) and allowed to stand for 2 h at room temperature. The mixture was then adjusted to pH 5 with solid $NaHCO_3$, and the water was evaporated under vacuum below 30°. The residue was triturated with ether, filtered, and dried over $MgSO_4$. Removal of the solvent left **17c** (1.39 g, 98%), bp. 100°/0.5 torr; UV: 207 nm (7200); IR: 3430 (OH), 1690 (α,β-unsaturated ketone), 1630 (C=C), 1100 (C-O) cm^{-1}; mass *m/e* (% of the base peak): 142 (1) M^+, 125 (3), 97 (7), 84 (100), 69 (3), 59 (22), 55 (44), 43 (21).

Anal. Calc. for $C_7H_{10}O_3$: C, 59.1; H, 7.1. Found: C, 59.3; H, 7.3

b. *The Bromine-Methanol-Water Procedure With Subsequent Heating*[11e]

A variety of products may be isolated by the oxidative rearrangement of monosubstituted 2-furylcarbinols using the bromine-MeOH-H_2O method with subsequent heating. The direct one-pot synthesis of maltol is described below in Scheme 9.

Conversion of Furfuryl Alcohol 18 to Maltol 23. One-pot Procedure[11e].- A 500-mL, four-necked vessel equipped with a thermometer, an addition funnel which was modified to add liquid below the liquid level of the reaction, a mechanical stirrer, and a gas inlet/vent assembly was charged with 60 mL of MeOH and 90 mL of H_2O and then cooled to -10°. The addition funnel was charged with 56.0 g (0.50 mol) of methylfurfuryl alcohol dissolved in 40 mL of methanol and 10 mL of water. Chlorine gas (74.6 g, 1.05 mol) was added below the liquid level of the well-stirred reaction mixture, and the furfuryl solution was added at a rapid dropwise fashion. The addition of alcohol and chlorine was controlled such that the alcohol addition was complete after ca. two-thirds of the chlorine had been added, the temperature of the reaction being controlled between -10° and -5° by external cooling. The remainder of the chlorine was then added at -5°. The reaction was then heated to 90°, distilling off a portion of the methanol, and heating was continued at 90-95° for 3-3.5 h. At this point the reaction was cooled to 25° by pulling a vacuum on the system, and the aqueous maltol-rich solution (200 mL) was decanted from the tarlike residue (5.2 g of residue). The aqueous layer was then adjusted to pH 2.2 with 50% NaOH (45 mL) while the temperature was kept below 40°. The well-stirred



One-pot Synthesis

a. Br_2 one eq./H_2O, MeOH -10° to 5° C; b. Br_2 two eq. H_2O/THF -10° to 0° C; c. Adjustment of pH; d. Br_2 2 eq., MeOH/H_2O, -10° C to room temp, 2 h

Scheme 9

solution was then cooled to 5° for 0.5 h to allow maltol granulation. Filtering and air-drying yielded 52.1 g of a first-crop maltol wet cake that assayed 77.4% maltol by UV analysis (40.3 g of assayed maltol, 64% yield). Extraction of the aqueous filtrate with 4 x 25 mL of $CHCl_3$ (or CH_2Cl_2) yielded 5.1 g of second-crop maltol as a semisolid that assayed 50% by UV analysis (2.35 g of assayed maltol, 4% yield). The total yield of assayed maltol, including the 3% maltol found in the reaction residue, was 71%. Analytically pure maltol, mp 159.5-160.5° could be obtained from the first- or second-crop material by methanol recrystallization. The UV assays discussed above were done at 274 nm, using a pure reference sample of maltol for calibration. Maltol can also be assayed by GC, using a 3 ft. x 1/4 in. glass column packed with Porapak P, 80-100 mesh (column temperature 200°, tetradecane internal standard/ maltol retention time 6.5 min, tetradecane retention time 13.6 min).

By the process described above, ethylfurfuryl alcohol (Scheme 4, R = CH_2CH_3) can be converted to ethylmaltol in 67% yield.

6-Hydroxy-2-methyl-2*H*-pyran-3(6*H*)-one (19).- One equivalent (35.7 g) of bromine was added to a solution of 25 g of methylfurfuryl alcohol in 125 mL of tetrahydrofuran and 125 mL of water at 5°. The temperature was maintained at 5° throughout the addition. The solution was adjusted to pH 2.1 with 10% NaOH and extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined,

dried ($MgSO_4$), and concentrated to yield a yellow oil which was purified by chromatography on a silica gel column (3:1 chloroform-ethyl acetate eluant) to give 4.8 g (17%) of pure **19** as a clear oil, which was identical by NMR, IR and TLC comparisons with a sample of made by known methods.[6]

4-Bromo-6-hydroxy-2-methyl-2*H*-pyran-3(6*H*)-one and **6,6'-oxybis[4-bromo-2-methyl-2H-pyran-3(6*H*)-one] (21)**.- To a solution containing 25 mL of water and 15 mL of tetrahydrofuran at 0° was added *via* two addition funnels at equal rates a solution containing 11.2 g (0.10 mol) of methylfurfuryl alcohol in 15 mL of tetrahydrofuran and 5 mL of water and (in the other funnel) bromine (32.0 g, 0.20 mol). The rates of addition were controlled to maintain an almost colorless reaction mixture, at -10° to 0°. After the addition was completed (30 min), the reaction was assayed by TLC (system A) with vanillin spray. This assay showed a clean conversion to the desired 4-bromohydroxy enone (two isomers, R_f 0.40-0.47, intense red-orange spots), along with a trace of the 6-hydroxy enone **19** (R_f 0.25, brown spot) and a trace of the dimeric material **21** (mixture of isomers, three spots, R_f 0.60-0.70, red-orange spots). After 2 h of stirring at 25°, the reaction was adjusted to pH 2.2 with 50% NaOH, and extracted 3 x 50 mL with chloroform. After brine washing and drying ($MgSO_4$), concentration yielded 18.5 g of brown oil, which was chromatographed on a column of 200 g of silica gel (95:5 CH_2Cl_2-EtOAc). In this manner, 4.8 g (24%) of the dimeric material (mixture isomers) was isolated as a white solid which was recrystallized from absolute EtOH, mp 117° (shrinks at 114°); IR: 1724 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.2-7.4 (2H, m), 6.6-6.8 (2 H, m), 4.5-4.9 (2 H, m), 1.4-1.6 (6 H, m).

Anal. Calcd. for $C_2H_{12}Br_2O_5$: C, 36.39; H, 3.05; Br, 40.35. Found: C, 36.40; H, 3.04; Br, 40.64

A later fraction from the column yielded 4.0 g of the 6-hydroxy-4-bromoenone **20** (R = CH_3, X = Br) as a tacky tan solid: IR: 3500, 1710 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.3 (1 H, d, J = 4 Hz), 5.62 (1 H, d, J = 4 Hz), 4.85 (1 H, q, J = 7 Hz), 3.2 (1 H, br s, OH), 1.39 (3 H, t, J = 7 Hz). Attempts to obtain analytically pure samples of this material resulted in dehydration to give the dimer.

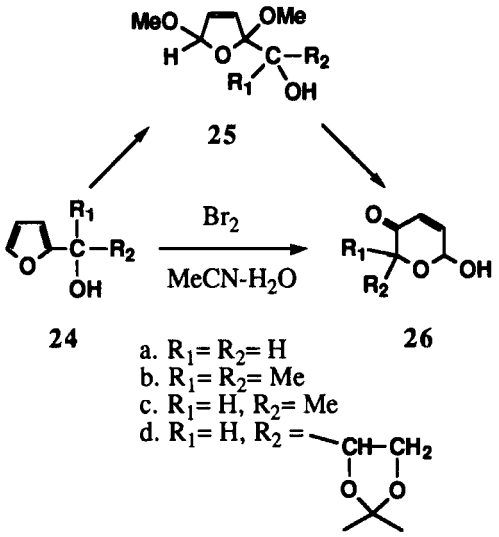
4-Bromo-6-methoxy-2-methyl-2*H*-pyran-3(6*H*)-one (22) from Methylfurfuryl Alcohol.- To a solution containing 25 mL of water and 15 mL of methanol at -10° was added 11.2 g (0.10 mL) of methylfurfuryl alcohol in 5 mL of water and 15 mL of methanol, while bromine (32.0 g, 0.20 mol) was added. A temperature of -10° was maintained throughout the addition. Following this addition (30 min), TLC analysis (see above) showed clean conversion of **18** to the 6-hydroxy-4-bromo enone (**20**). After the mixture was warmed to 25° and stirred for 2 h, most of the hydroxy enone had been converted to two new, less polar compounds which developed as red spots on the TLC system. R_f 0.80 (major) and R_f 0.75 (minor). The reaction was adjusted to pH 2.0 with 50% NaOH and cooled to 5°. A solid precipitated from the solution during the cooling. This material was collected and air-dried to yield 2.7 g. This solid was mainly a mixture of the two less polar compounds by TLC with a minor amount of the 6-hydroxy compound **20** and the dimer **21**. Column chromatography on 100 g of silica gel (90%) hexane-10% acetone eluent) yielded 0.7 g of the pure material of R_f 0.80 and 0.9 g of a mixture of this material together with the compound of R_f 0.75. NMR analysis clearly showed

that the R_f 0.80 material was *trans*-4-bromo-6-methoxy-2-methyl-2*H*-pyran-3(6*H*)-one, which was recrystallized from EtOAc to yield white needles, mp 77-78°: IR: 1710 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.2 (1 H, d, J = 4 Hz), 5.05 (1 H, d, J = 4 Hz), 4.70 (1, H, q, J = 6.5 Hz), 3.55 (3 H, s), 1.5 (3 H, d, J = 6.5 Hz).

NMR analysis of the crude solid isolated from the above reaction showed that the *trans-cis* ratio of was about 4/1. The *cis* isomer was never isolated in pure form, but the second fraction from the above column (mp 57-64°) was enriched in this minor isomer. ^1H NMR ($CDCl_3$): δ 7.5 (1 H, m), 5.15 (1 H, m), 4.50-4.70 (1 H, q, J = 7 Hz), 3.60 (3 H, s), 1.55 (3 H, d, J = 7 Hz).

c. *Bromine-Water [Organic Solvent CH_3CN-H_2O (9:1)]*[17]

Furfuryl alcohol (**24a**) was redistilled commercial reagent. Compounds **25b-d** were prepared through reaction of 2-furyllithium with acetaldehyde, acetone and 2,3-O-isopropylidene-D-glyceraldehyde.[25]

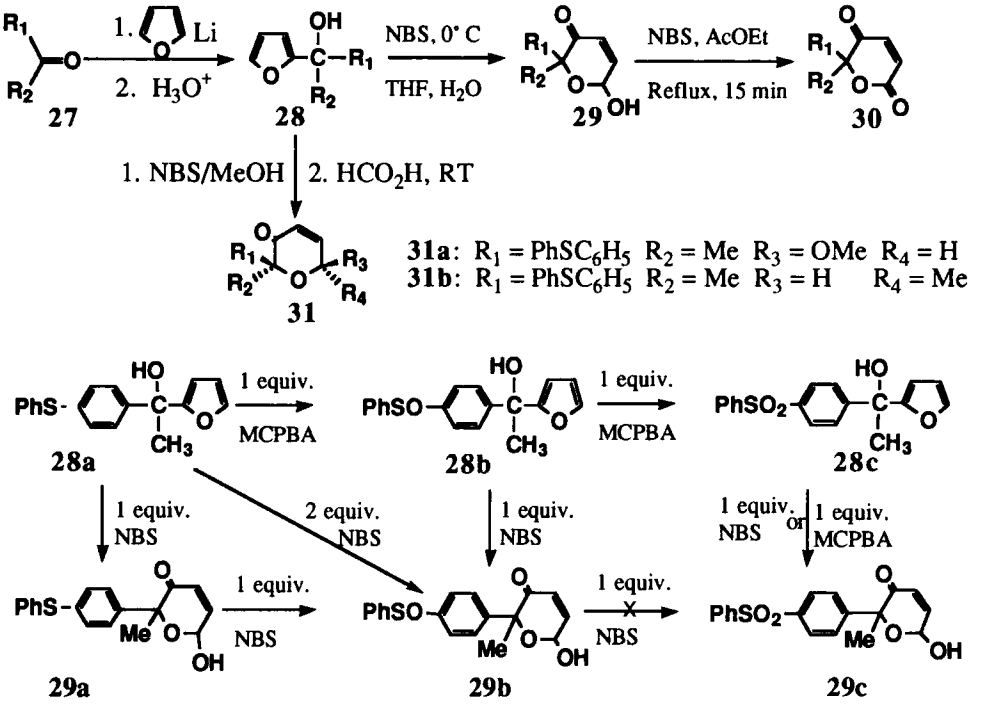


Scheme 10

2*H*-Pyran-3(6*H*)-one (26).- To a solution of **24** (1 mmol) in 10 mL of MeCN-H_2O (10:1 v/v), vigorously stirred and cooled to 0°, bromine (53 μL, 1 mmol) was added dropwise. After 25 min solid $NaHCO_3$ (168 mg, 2 mmol) was added and stirring was continued for further 10 min. TLC analysis at this showed only the presence of pure product **26**. The reaction mixture was then poured into ethyl ether and washed with saturated aqueous NaCl. After drying ($MgSO_4$) and solvent evaporation, the crude product was purified by crystallization (**27a**) or flash-chromatography (**26b-d**) to give **26a**, **26b**, **26c** and **26d** in 86, 78, 82 and 76% yield, respectively. The spectral properties (^1H NMR, IR) of **26a-d** were identical with those reported in the literature.[6,11a,26]

d. *The NBS Method*[11j]

The NBS method is selective for furans over aryl thioethers as shown below.



Scheme 11

TABLE 2. NBS Oxidation of Furfurylalcohols.

Reactant No.	R_1	R_2	Oxidant (equiv)	Product	Yield[a] (%)
28a	CH_3	4-$PhSC_6H_4$	NBS (1)	**29a**	78
28a	CH_3	4-$PhSC_6H_4$	NBS (2)	**29b**	64
28a	CH_3	4-$PhSC_6H_4$	MCPBA (3)	**29c**	72
28b	CH_3	4-$PhSOC_6H_4$	NBS (1)	**29b**	67
28c	CH_3	4-$PhSO_2C_6H_4$	NBS (1)	**29c**	69
28d	CH_3	H	NBS (1)	**29d**	65
28e	H	3,4-methylenedioxyphenyl	NBS (1)	**29e**	77
28f		$(CH_2)_5$	NBS (1)	**29f**	76

a) Total yield for two steps based on the corresponding ketone **27**

Preparation of 6-Hydroxy-2*H*-Pyran-3(6*H*)-ones (29) using NBS.- The appropriate furfuryl alcohol **28** (1 equiv) was dissolved in THF-H_2O (4:1) and cooled to 0°. A stoichiometric amount of

NBS was added portionwise while the temperature was kept to 0°. After the reaction was over (TLC), the reaction mixture was successively washed with KI (10%), $Na_2S_2O_4$ (15%) and $NaHCO_3$ (10%) and the product was extracted with CH_2Cl_2 or ether. The organic layer was separated, washed with water, dried ($MgSO_4$) and evaporated under reduced pressure, yielding the corresponding pyranone **29** as a crude oil. Further purification of the product was achieved by column chromatography.

6-Hydroxy-2-[*p*-(phenylthio)phenyl]-2-methyl-2*H*-pyran-3(6H)-one (29a).- Compund **28a** (14 g, 0.043 mol) in 80 mL of THF and 20 mL of H_2O were reacted with 10 g (0.056 mol) of NBS according to the general procedure. The crude product was chromatographed on silica gel with ether-hexane (40:60) as the eluent. Evaporation of the solvents yielded 13 g of **29a** as a slight yellow oil (yield 78% based on the ketone **27a**): IR (oil): 2940 (CH_3), 3060, 1960, 820, 745 (Ar), 3430 (br d, OH), 1690 (C=O), 1220, 1040 (COC), 750 (CS) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.1 (m, 9 H, Ar), 4.6 (br d, 1 H disappeared on addition of D_2O, OH), 6.6 (dd, 1 H, double bonds, J_{db} = 10 Hz, J_{vic} = 1.7 Hz), 5.9 (dd, 1 H, double bond, J_{db} = 10 Hz, $J_{allylic}$ = 1.4 Hz), 5.3 (dd, 1 H, allylic, J_{vic} = 1.7 Hz, $J_{allylic}$ = 1.4 Hz), 1.6 (s, 3 H, angular methyl). **29a** ($C_{18}H_{16}O_3S$) was analyzed as its methyl carbamate.

Anal. Calcd for $C_{20}H_{19}NO_4S$: C, 65.02; H, 5.18; N, 3.79. Found: C, 64.74; H, 5.08; N, 3.56

6-Hydroxy-2-[*p*-(phenylsulfinyl)phenyl]-2-methyl-2*H*-pyran-3(6*H*)-one (29b) (from 28a).- Compound **28a** (3.5 g, 0.011 mol) and 5.5 g (0.03 mol) of NBS were treated as described above, yielding 2.7 g of pure **29b** (yield 64% based on **27a**).

2-Hydroxy-1-oxaspiro[5.5]undec-3-en-5-one (29f).- **28f** (2.5 g, 0.015 mol) and 4 g (0.02 mol) of NBS were reacted in 40 mL of THF and 10 mL of H_2O according to the described method, yielding 2.1 g (yield 76%) of **29f** as a colorless oil, which was identical by NMR, IR and TLC comparison with a sample of **29f** made by the MCPA method [IR (oil): 3420, 2940, 2880, 1690, 1140, 1030, 1455, 820 cm^{-1}; ^1H NMR ($CDCl_3$): δ 1.5 (br d, 10 H, cyclohexane), 4.4 (br d, 1 H, OH), 6.6 (dd, 1 H, double bond, J_{db} = 10.0 Hz, J_{vic} = 1.7 Hz), 5.8 (dd, 1 H, double bond, $J_{allylic}$ = 0.5 Hz), 5.4 (m, 1 H, allylic)].

6-Methoxy-2-[*p*-(phenylthio)phenyl]-2-methyl-2*H*-pyran-3(6*H*)-one (31).- Compound **28a** (3.5 g, 0.01 mol) was dissolved in 30 mL of CH_3OH (95%) and cooled to 0°. NBS (1.8 g, 0.01 mol) was added portionwise. After the reaction was over (TLC), 0.4 mL of 98% formic acid was added and the reaction was stirred at room temperature for 20 min. The reaction mixture was neutralized and extracted with ether and the combined organic layers were dried ($MgSO_4$), and evaporated under reduced pressure to give a yellow liquid. Column chromatography with silica gel and ether-hexane (80:20) as the eluent gave two products. The one with the higher R_f value, **31a** (white oil, 2.7 g, yield 74%), was identified by NMR[17] to be the trans isomer of **31** and the other one, **31b** (recrystallized from ether, white crystals, 0.7 g, yield 19%), the *cis* isomer of **31.**

31a: IR (oil): 3070, 01590, 1940, 690 (Ar), 2840 (OMe), 1690 (conj. ketone), 1210, 1110 (COC), 2995, 2960 (angular methyl) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.5 (dd, 1 H, double bond, $J_{allylic}$ = 1.0 Hz), 4.8 (t, 1 H, allylic), 1.5 (s, 3 H, angular methyl).

31b: mp 86-87°; IR (KBr): 3080, 3060, 1585, 790 (Ar), 2835 (OMe), 1680 (conj. ketone),

1210, 1010 (COC), 740 (CS) cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.2 (s, 9 H, Ar); 3.3 (s, 3 H, OMe), 6.7 (dd, 1 H, double bond, J_{db} = 10 Hz, J_{vic} = 2.5 Hz), 6.0 (dd, 1 H, double bond, $J_{allylic}$ = 1.2 Hz), 5.3 (dd, 1 H, allylic), 1.6 (s, 3 H, angular methyl).

2-[*p*-(Phenylsulfonyl)phenyl]-2-methyl-2*H*-pyran-3,5-dione (30).- NBS (0.6 g, 0.003 mol) was added to a solution of 0.95 g (0.0027 mol) of **29c** in 10 mL of AcOEt. The reaction mixture is refluxed for 15 min. After workup in the conventional manner and two recrystallizations from AcOEt, we obtained 0.8 g (yield 81%) of **30** as a pale yellow crystal solid, mp 110-112°: IR: 1735 (conj. ester), 1692 (conj. ketone), 750 (CS), 1220, 1040 (COC), 2940 (CH_3), 3060, 1960, 820, 745 (Ar) cm^{-1}; ^1H NMR: δ 7.8 (m) and 7.3 (m, 9 H, Ar), 1.8 (s, 3 H, angular methyl), 6.6 (q, 2 H, double bonds, AB system, J_{A+B} = 9.6 Hz).

2. *Peracids[5,7,12c-f] and Kinetic Resolution of Furylcarbinols[19d-f]*

6-Hydroxy-2-(p-methoxyphenyl)-2-methyl-2H-pyran-3(6H)-one[23a].- To a solution of furan (50 ml) in anhydrous ether (500 ml) cooled to 0°, butyllithium (170 ml, 2.2 N in hexane) was added under nitrogen. The reaction mixture was stirred for 1 hour at room temperature. Then it was cooled to 0° and *p*-methoxyacetophenone [50 g (0.33 mol), melted] was added at such a rate that the temperature was maintained between 5-10°. The mixture was stirred for 3 hours, then water was added slowly. The organic layer was washed, dried and evaporated under reduced pressure to yield α-*p*-methoxyphenyl-α-methylfurfuryl alcohol as a yellowish oil. IR (Nujol): 3580, 3460, 2830, 1240, 1168, 1662, 1600, 1575, 1502, 1000, 828 cm^{-1}. The crude α-(*p*-methoxyphenyl)-α-methylfurfuryl alcohol was dissolved in methylene chloride (950 ml) and the solution was cooled to 5°. *m*-Chloroperbenzoic acid (75 g, 85%) was then added portionwise with stirring. The reaction mixture was stirred for 2.5 hrs. At that time tlc (ether-hexane, 6:4) showed that the reaction was complete. The mixture was cooled and filtered to remove the *m*-chlorobenzoic acid. The filtrate was washed with solutions of potassium iodide, sodium thiosulfate, sodium bicarbonate and dried with magnesium sulfate. Upon evaporation of the solvent in vacuum to a small volume and addition of ether and cooling, the title product was obtained. Crystallization from ether yielded pure material (mp 128-130°, 50 g). Mother liquors were pooled, evaporated and chromatographed on a silica gel column, yielding a second crop of 14 g to give a total yield ~82%. IR (Nujol): 3390 cm^{-1} (OH), 1688 (conj. ketone), 1262, 1175 (-OCH_3), 1089 (C-O-C); ^1H NMR (perdeuterioacetone) 60 MHz: δ 1.50 (3 H, s, angular -CH_3), 3.73 (3 H, s, -OCH_3), 5.33 (1 H, m, H-6), 6.10 (1 H, dd, $J_{4,5}$ = 10 Hz, $J_{4,6}$ = 1.5 Hz, H-4), 6.03 (1 H, broad s, OH), 6.84 (1 H, dd, $J_{4,5}$ = 10 Hz, $J_{5,6} \cong$ 1.5 Hz, H-5), 6.9 (2 H, d, J = 9 Hz, Ar), 7.24 (2 H, d, J = 9 Hz, Ar).

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.65; H, 6.02. Found: C, 66.54; H, 6.10

For the use of MCPA as an oxidant, see also ref. 5, 7, 12c.

6-Hydroxy-2H-pyran-3(6H)-one.[12f] To a solution of freshly distilled furfuryl alcohol, 60 g (0.61 mol) in methylene chloride (1200 ml) cooled to 5°, 120 g of *m*-chloroperbenzoic acid (0.70 mol) was

added portionwise. After approximately two hours, the furfuryl alcohol spot on tlc (developed as a dark violet spot on tlc (hexane-ethyl-acetate 7:3)) disappeared indicating that the reaction was complete. The mixture was cooled for a while at -10° and filtered. The solid precipitate of the acids was washed with a small amount of cold methylene chloride and the washing liquids were combined with the filtrate, evaporated to one third of the original volume (400 ml), cooled at -10° for 4 hours and filtered again. At this point, the total removal of the acid from the solution was checked. Then a small amount of hexane was added with or without further concentration yielding 6-hydroxy-2H-pyran-3(6H)-one (61 g, 88%), mp 58°.[6] IR: 3400 cm^{-1} (OH), 1685 (conj. ketone), 1625 (>C=C<), 1155, 1050 (-C-O-C-); ^1H NMR 60 MHz: δ 4.10 (1 H, d, J = 6.5 Hz), 4.15 (1 H_{5e}, d, $J_{5e,5a}$ = 16 Hz), 4.55 (1 $H_{5a,d}$, $J_{5a,5e}$ = 16 Hz), 5.50 (1H, d, $J_{1,2}$ ~3 Hz, $J_{1,3}$ = 0 Hz), 6.05 (1 H, d, $J_{2,3}$ = 10 Hz), 6.80 (1 H dd, $J_{1,2}$ = 3 Hz, $J_{2,3}$ = 10 Hz).

General Procedure for the Kinetic Resolution of Furylcarbinols and their Subsequent Oxidation by TBHP-VO(acac)$_2$.[19e]

Method A. Kinetic Resolution with a Catalytic Amount of Ti(O-i-Pr)$_4$/L-(+)-DIPT.- The preparation of (*R*)-1-(-2-furyl)-hexan-1-ol (**13b**) (see Scheme 7, Table 1) is described as an illustrative case.[19e] To a mixture of crushed 4Å molecular sieves (5 g) and 0.2 equiv of Ti(O-i-Pr)$_4$ (7.35 mL, 24.7 mmol) in CH_2Cl_2 (100 mL) was added 0.24 equiv of L-(+)-DIPT (6.23 mL, 29.6 mmol) at -21°. The mixture was stirred for 10 min at -21° and cooled to -30°. Racemic **13b** (20.7 g, 123 mmol) dissolved in CH_2Cl_2 (20 mL) was added and the mixture was stirred between -30° and -20° for 30 min. The mixture was again cooled to -30° and 0.6 equiv of TBHP (17.0 mL, 74.0 mmol, 4.35 M in CH_2Cl_2) was slowly added. After stirring for 14 h at -21°, Me_2S (5.43 mL, 74.0 mmol) was slowly added and the mixture was stirred for 30 min at -21°. To this mixture were added 10% aqueous tartaric acid (5 mL), Et_2O (100 mL), and NaF (30 g), and the resulting mixture was vigorously stirred for 2 h at room temperature. The white precipitate was filtered off through a pad of Celite with ether (100 mL). The filtrate was concentrated to give an oil, which was dissolved in ether (200 mL) and treated with NaOH (3 N, 100 mL) for 30 min at 0° with vigorous stirring. The organic layer was washed with brine, dried ($MgSO_4$) and concentrated to give an oil, which was passed through a short silica gel column to afford (*R*)-**13b** (7.94 g, 38%, >95% ee determined by ^1H NMR analysis of the derived MTPA ester): $[\alpha]_D^{25}$ = + 13.8° (c 1.07, $CHCl_3$); IR (neat) 3350, 1140, 1005, 725 cm^{-1}; ^1H NMR (CCl_4, D_2O): δ 0.7-1.9 (m, 11 H), 4.45 (t, J = 7.3 Hz, 1 H), 6.05 (d, J = 3.6 Hz, 1 H), 6.16 (dd, J = 1.8, 3.6 Hz, 1 H), 7.19 (br s, 1 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.71

Method B. Kinetic Resolution with a Stoichiometric Amount of Ti(O-i-Pr)$_4$/L-(+)-DIPT. The preparation of (*R*)-1-(2-furyl)-2-methylpropan-1-ol (**13c**) (See Scheme 7, Table 1) is described as an illustrative case. To a solution of Ti(O-i-Pr)$_4$ (4.04 mL, 13.6 mmol) in CH_2Cl_2 (60 mL) was added L-(+)-DIPT (3.42 mL, 16.3 mmol) at -21°. After 10 min, the solution was cooled to -30° and racemic

13c (1.90 g, 13.6 mmol) dissolved in CH_2Cl_2 (3 mL) was slowly added. After 30 min, TBHP (2.18 mL, 8.13 mmol, 3.73 M in CH_2Cl_2) was added and the solution was stirred for 25 h at -21°. Workup as described above afforded **(R)-13c** (743 mg, 39%, >95% ee determined by ^1H NMR analysis of the derived MTPA ester): $[\alpha]_D^{25}$ = +18.1° (c 1.04, $CHCl_3$); IR (neat): 3360, 1000, 720 cm^{-1}; ^1H NMR (CCl_4, D_2O): δ 0.76 and 0.88 (2 d, *J* = 6.6 Hz, 6 H), 1.70-2.15 (m, 1 H), 4.17 (d, *J* = 7.0 Hz, 1 H), 6.05 (d, *J* = 3.6 Hz, 1 H), 6.16 (dd, *J* = 1.8 Hz, 3.6 Hz, 1 H), 7.20 (br s, 1H).

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.08; H, 8.85

Oxidation by TBHP-VO (acac)$_2$. The Synthesis of (2*R*)-2H-Pyran-3(6H)-one 2R-14 from (*R*)-13 (Scheme 7). This reaction was carried out by using the reported[11h] procedure with a slight modification.[19e] The synthesis of **(2*R*)–14b** (Table 1) is described as an illustrative case. To a solution of **(*R*)-13b** (545 mg, 3.24 mmol) in CH_2Cl_2 (10 mL) were added TBHP (1.30 mL, 4.87 mmol, 3.73 M in CH_2Cl_2) and VO (acac)$_2$ (8.6 mg, 0.032 mmol) at 0°. The solution was stirred for 14 h at 0° and Me_2S (0.36 mL, 4.9 mmol) was added at 0°. After stirring for 30 min at 0°, saturated aqueous $NaHCO_3$ (10 mL) was added. The organic layer was separated and the aqueous layer was extracted with ether (2 x 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford **(2R)-14b** (Table 1 and Scheme 7) as an inseparable mixture (ca 3:1) of α- and β-anomers (535 mg, 90%); IR (neat): 3370, 1670 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O) δ 0.6-1.9 (m, 11 H), 3.81-4.00 (m, 0.24 H), 4.38 (dd, *J* = 4.8 Hz, 6.9 Hz, 0.76 H), 5.45 (d, *J* = 3.6 Hz, 1 H), 5.93 (d, *J* = 9.9 Hz, 0.76 H), 5.97 (dd, *J* = 2.1, 9.9 Hz, 0.24 H), 6.75 (dd, *J* = 3.6 Hz, 10.5 Hz, 1 H).

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.39; H, 8.71

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