

NOVEL OXIDATIVE OPENING OF 2,5-DISUBSTITUTED FURAN RING

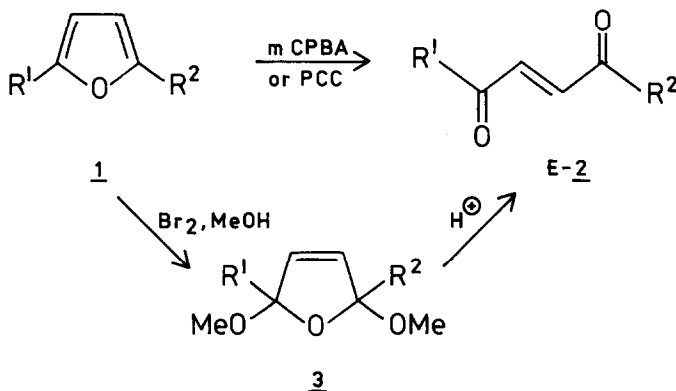
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Abstract: A new reaction of 2,5-disubstituted furans with bromine in an acetone - water solution afforded an efficient and mild method for opening of the furan ring, this leading to the respective enedione system. The reaction was successfully carried out under either basic or acidic conditions.

Recently we have found that furan derivatives can conveniently be used in stereocontrolled synthesis of carbohydrate-like chain compounds.¹ While developing this approach, we faced the problem of efficient transformation of starting furan derivative 1 into the required enedione system E-2 (Scheme 1). This transformation can be performed either directly using pyridinium chlorochromate (PCC)² or *m*-chloroperbenzoic acid (mCPBA),³ or stepwisely via the dihydrodimethoxyfuran intermediate 3.⁴

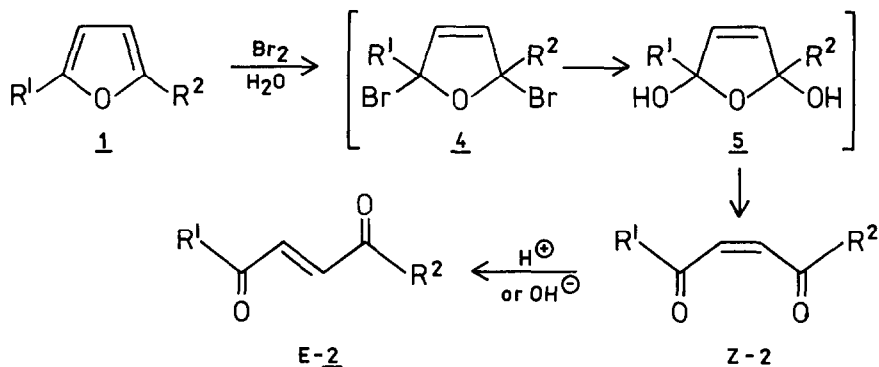


Scheme 1

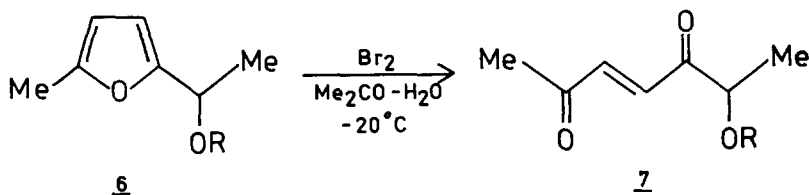
All these methods suffer, however, from certain drawbacks. Oxidation with mCPBA gives exclusively or preferentially Z-2 and its isomerisation to E-2 has to be forced by the action of a strong acid. We have also found that in case of a bulky substituent (R^1 or R^2), a longer reaction time and/or an excess of the peracid are necessary to bring the reaction to completion. On the other hand, PCC failed to oxidize furans with substituents having an α -alkoxy group. The main drawback of the third method is that it calls for two steps: the first requiring mild basic conditions and the second - strongly acidic ones. Thus we decided to search for a more efficient and mild method for furan conversion into enedione, and herein we present our solution of the problem.

The reaction of bromine with a furan derivative, carried out in absolute methanol as solvent, is known as Clauson-Kaas reaction.⁵ It is assumed to proceed through dibromointermediate 4, followed by nucleophilic displacement of bromine atoms by solvent molecules, giving 3 as the reasoned product. We thought that replacement of methanol by water could give bis-hemiacetal 5 which in turn should rearrange to enedione 2, because of an energy gain resulting from formation of a conjugated system (Scheme 2). After many attempts we succeeded in carrying out the reaction under either basic or acidic conditions, using an acetone - water solvent system. Protected compounds of type 6 were chosen as model substrates. Since the applied protective gro-

ups were thought to play a crucial role in the further synthetic steps, it was important to know their stability under the reaction conditions.



Addition of bromine (dissolved in an acetone - water solvent system) to a solution of **6** cooled to -20°C initiated the reaction proceeding very rapidly to completion⁶ which could easily be confirmed by TLC. At this moment there was almost exclusive formation of the *cis*-isomer which after further 1-2 hrs of stirring at room temperature completely isomerised to *trans*-**7**. Usual work-up followed by flash-chromatography afforded the products in very good yields, as presented below.^{7,8}



	A*	Yield (%)	B*
R=CH ₂ Ph	89		87
COPh	88		80
CH ₂ OMe	75		82
Sit-BuMe ₂	73		83
Sit-BuPh ₂	91		88

* Yield of isolated products A - acidic conditions, B - basic conditions.

It can be seen that ethers, silyl ethers, acetals and esters are all stable under either acidic or basic conditions. Therefore, the method presented in this Communication seems to be a very effective route to enedione systems being convenient substrates for stereocontrolled syntheses of polyhydroxylated chain compounds.

Typical Procedures: Basic conditions. To a solution of **6** (1 mmol) and pyridine (4 mmol) in Me₂CO-H₂O (85:15v/v, 10 ml), vigorously stirred and cooled to -20°C , dropwise addition was made of a solution of bromine (1 mmol) in Me₂CO-H₂O (4:1v/v, 1.5 ml). After bromine addition, the cooling bath was removed and the reaction mixture was allowed to warm to room temperature. After subsequent stirring for 2 hrs, TLC showed the presence of pure isomer E. The reaction mixture was then poured into ethyl ether and washed with saturated aqueous NaCl and saturated aqueous CuSO₄. After drying (MgSO₄) and solvent evaporation, the crude product was purified by flash-chromatography. Acidic conditions. The reaction was performed exactly as above, but without pyridine addition. After completion of isomerisation (1 h), solid NaHCO₃ (3 mmol) was added; when gas evolution ceased, the reaction mixture was worked up similarly as under basic conditions, except for the CuSO₄ treatment.

References and Notes

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- To avoid side-reactions, a stoichiometric amount of bromine has to be used.
- The yields concern chromatographically pure compounds.
- Satisfactory analytical and spectral data were obtained for all new compounds described.

(Received in UK 26 February 1985)