Abstract: Upon exposure to singlet oxygen and dimethylsulfide, the addition products between 3-furaldehydes and Grignard reagents undergo an oxidative rearrangement to give 2-substituted 3-furaldehydes, in yields ranging from 26–83%. N-Aryl- and N-tosylpyrroles were similarly obtained if the corresponding nitrogen-containing precursors were used instead, in equally attractive yields (64–92%).

Key words: photochemistry, heterocycles, singlet oxygen, rearrangement, pyrroles, furans

Oxidation reactions are among the most important processes for both life and organic synthesis. The reaction between oxygen and glucose is carefully orchestrated by a series of enzymes, providing the essential form of energy for keeping organisms alive. On the other hand, the uncontrolled version of the process is the combustion reaction, which provides mainly heat and carbon dioxide. In synthesis, oxidations are rarely based on molecular oxygen, and expensive and toxic reagents are routinely used. A notable exception is the photo-oxygenation of alkenes such as 1,2-dienes, which provides mainly heat and carbon dioxide. In contrast, singlet oxygen is a naturally occurring singlet molecule, which can re-close to a triplet state, which can then be used in organic synthesis. A significant amount of research has been devoted to this topic, and a number of reviews have been published.5

Singlet-oxygen-promoted oxidative rearrangement

3-Furfural (1) is a readily available starting material, which reacts with organozinc, organolithium, and Grignard reagents to give alcohols 2, following the work of Walsh et al.6 The oxidative step is induced by N-bromosuccinimide; we report here its photochemical counterpart.

We propose the mechanism as shown in Scheme 3: the furan core of alcohols 2a-i reacts with singlet oxygen according to a very well documented process,7 leading to the endo-peroxides 4. These peroxides are rather unstable, as proton abstraction at the anomeric site is known to give hydroxybutenolides,8 and thus should be reduced to the diols 5 before warming up the mixture. These hydroxyfurans 5 can undergo a ring opening to their enediol forms 6 and 6', which can re-close to 3, along the lines of the mechanism proposed by Walsh. In some cases, particular-
With alkyl R groups, small amounts of alkylidenefuran-2-ones 7 are observed. The formation of this product can be enhanced by the in situ treatment with a sulfonyl chloride (mesyl or tosyl); this is also compatible with a reductive cleavage of the endo-peroxides 4 into 7.

Following this mechanism, the formation of pyrrole derivatives should also be possible if the hydroxyl function of 2 is replaced with an amine. Thus, reductive amination of 1 with aniline gave 8a (94%) and addition of phenylmagnesium bromide to the tosylimine derivative of 1 gave 8b.
We then checked the feasibility of the process, by exposing amines \( 8 \) to the same reaction conditions (Scheme 4), and pyrroles \( 9 \) were obtained in good to excellent yields.

In summary, we reported a photochemical alternative to the halogen-induced rearrangement of 3-hydroxymethylfurans, which is also compatible with the formation of pyrroles. Applications of this chemistry in the green synthesis of industrially relevant compounds are under way.

Typical Procedure for the Oxidation with \( \cdot \text{O}_2 \) Followed by the Rearrangement of 3-(1'-Hydroxyalkyl)furan Derivatives

A 25 mL, two-necked, quartz, cylindrical flask equipped with magnetic stirring bar, was charged with the corresponding 3-(1-hydroxyalkyl)furan (1.15 mmol), methylene blue (5.6 mg, 0.013 mmol), and MeCN (10 mL). The solution was cooled to \(-40 \, ^\circ\text{C} \), and oxygen was bubbled gently through the solution while it was irradiated (Osram Ultra-Vitalux\( ^\circledR \), 300 W) The consumption of 3-hydroxymethylfuran was followed by TLC (CH\(_2\)Cl\(_2\)-MeOH, 98:2). After 90 min, DMS (1 mL, 13.6 mmol) was added at \(-40 \, ^\circ\text{C} \), rapidly followed by PTSA (218 mg, 1.15 mmol). The reaction mixture was allowed to warm to r.t. then stirred for 2 h. Sat. solution of Na\(_2\)CO\(_3\) (30 mL) and CH\(_2\)Cl\(_2\) (50 mL) were added. The layers were separated, the organic layer was dried over anhyd MgSO\(_4\), and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel to afford the desired aldehyde.

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References

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