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DIOXIRANE OXIDATION OF BENZOPYRANS, BENZOTHIOPYRANS, AND RELATED COMPOUNDS

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Dioxiranes are shown to be powerful and convenient oxidation agents for benzopyrans, benzothiopyrans, and α,β-unsaturated ketones.

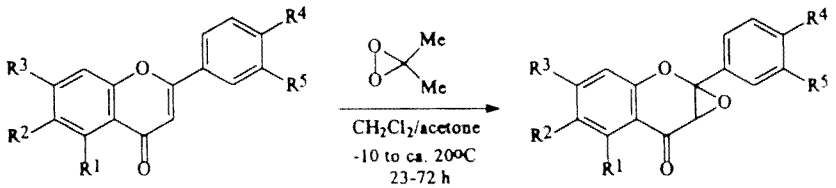
INTRODUCTION

Since the first preparation of the isolated dimethyldioxirane (DMD) as acetone solution in 1985 by Murray and Jeyaraman [1], it has became an important oxidant. Because of its usefulness, a simple procedure for its preparation has been developed [2]. This cyclic peroxide is an efficient oxygen transfer agent, which exhibits high chemo-, regio-, and stereoselectivity. It is mild towards the substrate and oxidized product and reacts under strictly neutral conditions. We have utilized these benefits of DMD for the epoxidation of benzopyrans, benzothiopyrans, and α,β-unsaturated ketones, and report herein our results.

RESULTS AND DISCUSSION

Flavones and isoflavones are well-known natural products widely distributed among many plants. As a consequence of the labile nature of the flavone epoxides towards bases and acids, attempts for their preparation by the classical oxidants failed. By use of the strictly neutral reaction conditions afforded by the acetone solution of the isolated DMD, we managed to convert a variety of flavones **1** at subambient temperature to their previously unknown epoxides **2** in excellent yields (> 95%) (Scheme 1) [3].

Scheme 1



R1, R2, R3, R4, R5 : H, Me, MeO, Cl or NO_2

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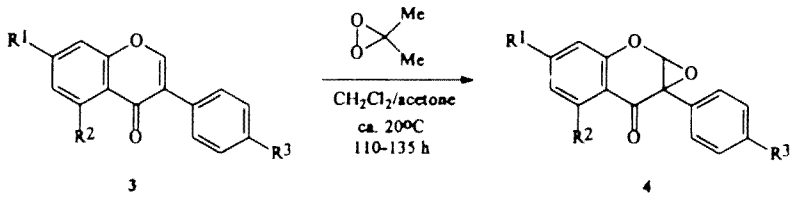
Few isoflavone epoxides **4** have been prepared by the alkaline H_2O_2 epoxidation of isoflavones **3** in moderate yields [4]. We have succeeded in obtaining such epoxides by DMD oxidation of isoflavones **3** in almost quantitative yields [5]. This procedure proved to be advantageous for the synthesis of the formerly unknown isoflavone glycoside epoxides as well (Scheme 2) [6].

Scheme 2

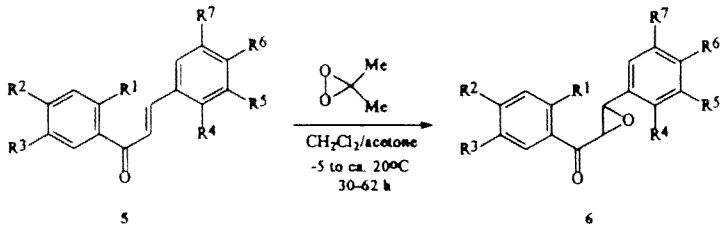


3 4

R^1, R^2, R^3 : H, MeO, OH, MeCOO, Cl or acetylated β-glycosyloxy

Since the DMD operates under mild and neutral conditions, and was shown to epoxidize electron-poor functionalized alkenes such as the chalcones [2], we achieved the direct epoxidation of 2′-hydroxychalcones **5** [7] and chalcone glycoside acetates **5** [6] (Scheme 3). These acid- and base-sensitive epoxides **6** are now available in excellent yields and can be used as building blocks for the synthesis of flavonoid-type compounds, e.g., *trans*-3-hydroxyflavanones **7** [8].

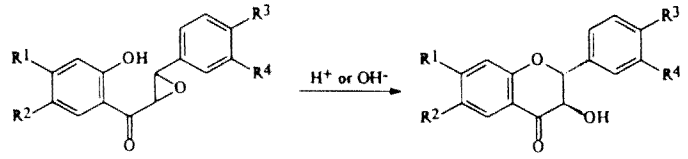
Scheme 3



5 6

R^1 : OH, R^2, R^3, R^4, R^5, R^6, R^7 : H, Me, MeO or Cl

R^1 : H, R^2, R^3, R^4, R^5, R^6, R^7 : H or acetylated β-glycosides



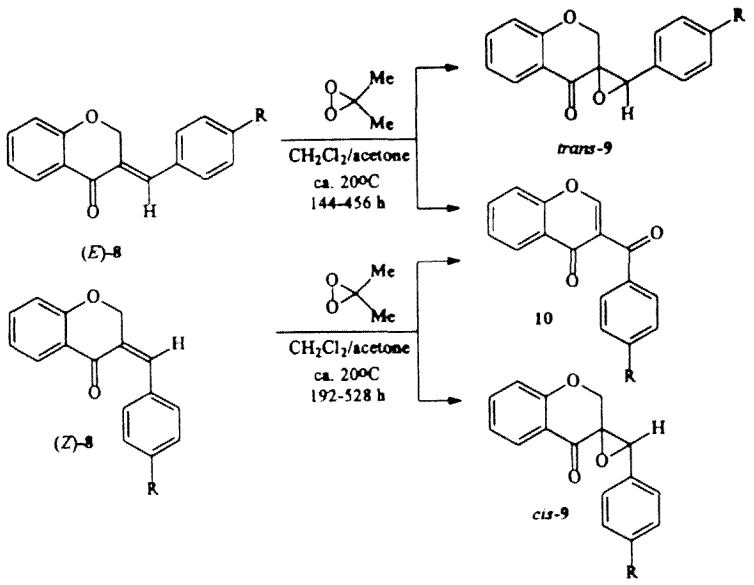
6 7

R^1 : H, Me, R^2 : H, Cl, OMOM, R^3 : H, Me, MeO, F, R^4 : H, R^3, R^4 : $O(CH_2)_2O$

A wide variety of related exocyclic α,β-unsaturated ketones have been oxidized with dioxiranes, viz. DMD and methyl (trifluoromethyl) dioxirane. Thus, 2-arylidenebenzofuran-3-ones (aurones) were subjected to dimethyldioxirane oxidation to afford their epoxides in essentially quantitative yields [5].

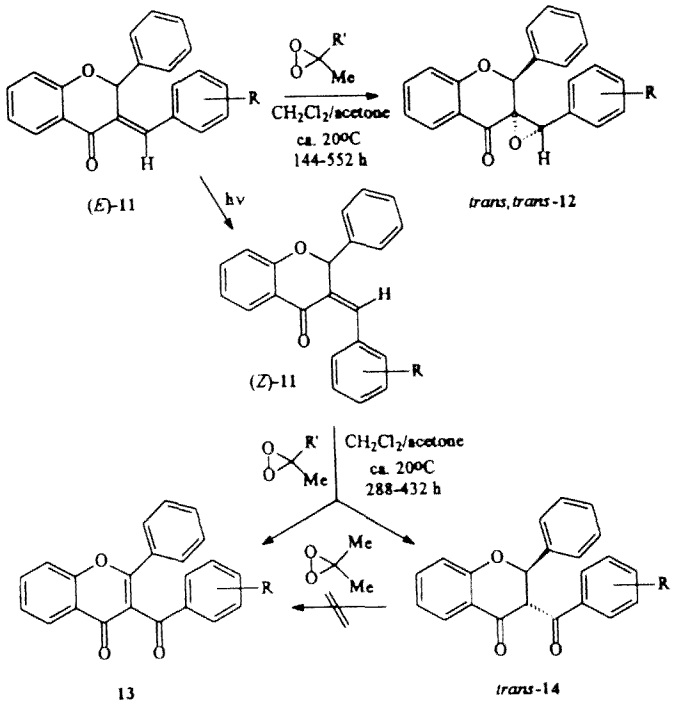
Oxidation of the E- and Z-isomers of the 3-arylidenechromanones **8** by isolated DMD at ambient temperature resulted in the *trans* and *cis* spiroepoxides **9** in moderate yields (23-51%), together with considerable amounts (16-40%) of 3-aroylchromones **10** from both the E- and Z-isomers (Scheme 4) [9]. Nonetheless, despite the moderate yields of the desirable chromanone epoxides, DMD offers a convenient route for the stereoselective formation of these scarcely studied epoxides. Prior to our investigations, *cis* spiroepoxides of 3-arylidenechromanones have not been described in the literature.

Scheme 4



Oxidation of the E-isomers of the 3-arylideneflavanones **11** by isolated dimethyldioxirane or methyl(trifluoromethyl)-dioxirane at ambient temperature led to *trans*, *trans*-**12** spiroepoxides in high yields (≥70%) and completely diastereoselectively. However, attempted epoxidation of the Z-isomers afforded instead the 3-aroylflavones **13** and/or *trans*-3-aroylflavanones **14** (Scheme 5) [10].

Scheme 5

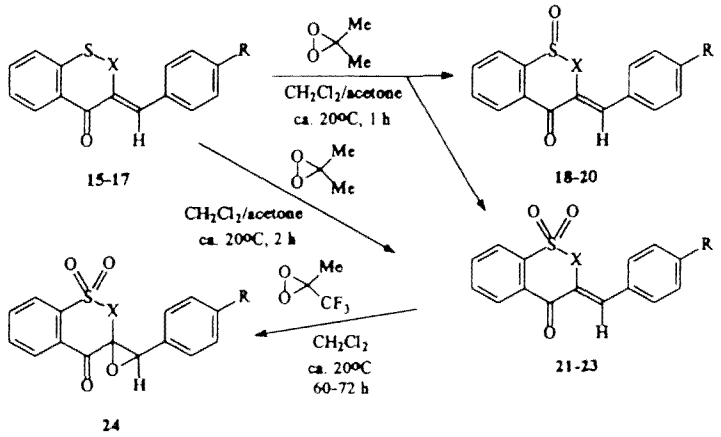


R : H, Me, MeO, EtO, Cl, Br or CN

R' : Me or CF_3

The oxidation of 1-thioaurones (**15**), 3-arylidene-1-thiochromanones (**16**), and 3-arylidene-1-thioflavanones (**17**) with DMD gave the corresponding sulfoxides **18-20** and/or sulfones **21-23** in good yields. Excess dimethyldioxirane afforded the sulfones **21-23** chemoselectively without formation of the epoxides. We managed to epoxidize also the 3-arylidene-1-thiochromanone 1,1-dioxides (**22**) with the much more powerful methyl(trifluoromethyl)dioxirane, but the sulfones of 1-thioaurones (**21**) and 3-arylidene-1-thioflavanones (**23**) could not be epoxidized even under these reaction conditions (Scheme 6) [11].

Scheme 6



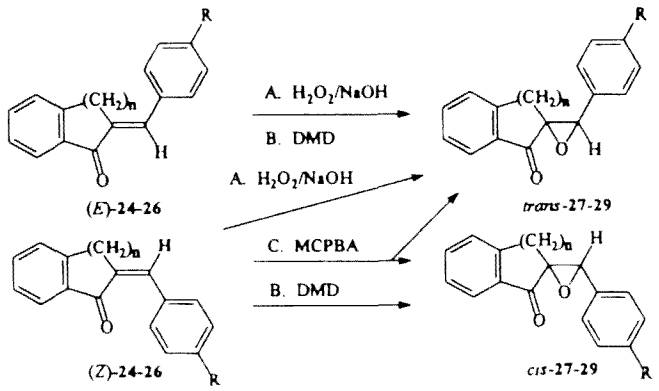
15, 18, 21 : X = bond R : H, Me, Cl

16, 19, 22 : X = CH_2

17, 20, 23 : X = CHPh

We have performed comparative epoxidations on the E- and Z-isomers of 2-arylidene-1-indanones (**24**), -1-tetralones (**25**), and -1-benzosuberones (**26**) by alkaline H_2O_2 (A), DMD (B) and *m*-chloroperoxybenzoic acid (C) as oxygen donors. Their *trans* or *cis* epoxides **27-29** were obtained stereoselectively only when using DMD (Scheme 7) [12].

Scheme 7



24, 27 : n = 1 R = H, Me, OMe, F, Cl, Br, CN

25, 28 : n = 2

26, 29 : n = 3

ACKNOWLEDGMENTS

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