

SAFROLE AS STARTING MATERIAL FOR THE SYNTHESIS OF  
3-ALKYL MUCONIC ACID MONOMETHYL ESTERS AND  
4,4-DIALKYL BUTENOLIDES

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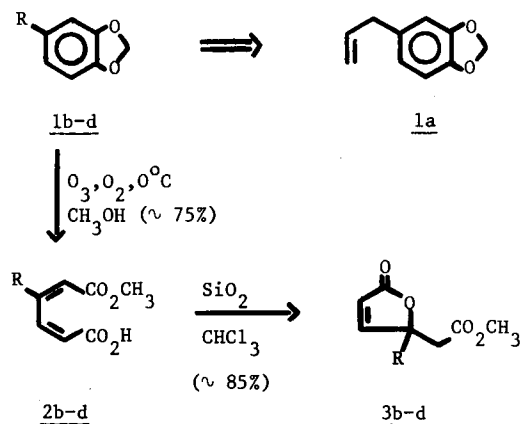
ABSTRACT - Compounds 1b-d, prepared from safrole (1a), were submitted to ozonation in methanol at 0°C furnishing regioespecifically the 3-alkyl muconic acid monomethyl esters (2b-d). These were transformed into the corresponding 4,4-dialkylated butenolides (3b-d).

As part of a program of study of abundant natural products available in Brazil<sup>1</sup> we turned our attention to the transformation of safrole (1a) into aliphatic derivatives. Thus compounds 1b-d were prepared from 1a by usual methods and were submitted to ozonation in methanol at 0°C. Under these conditions acidic products were obtained. After base extraction these products were characterized as the 3-alkyl muconic acid monomethyl esters (2b-d)<sup>2</sup>. While ozonation of veratrolin systems is known in the literature<sup>3</sup>, this paper is, to our knowledge, the first to report about ozonation of aromatic compounds substituted by the dioxolane group<sup>4</sup>. The total control of the stereochemistry of the double bonds and the observed regioselectivity with respect to the position of the ester and acid functions makes these reactions very attractive.<sup>2</sup> The structures of 2b-d were confirmed by their cyclization, catalyzed by silica gel<sup>5</sup>, to the corresponding 4,4-dialkyl butenolides (3b-d).

Since the butenolide moiety is present in many natural products and some of them exhibit interesting biological activities, there is a continuing need for simple and versatile synthetic methods for this class of compounds<sup>6</sup>. With the present approach possible to prepare regioselectively 4,4-dialkylated butenolides starting from safrole derivatives in 63% overall yield.

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- b; R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>  
c; R = CH<sub>2</sub>CH<sub>2</sub>OAc  
d; R = CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OAc

References and notes

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