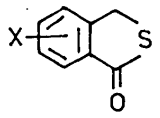
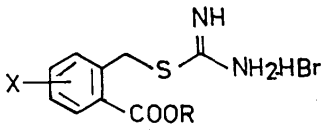
ABSTRACT

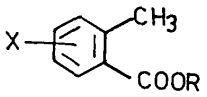
An efficient general method for the preparation of thiophthalides I was developed. It involved a facile one-step sodium bicarbonate assisted transformation of thiouronium salts II to thiophthalides I, the overall yields of I from ortho-toluates III being 45-65%.



I

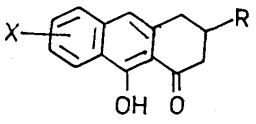


II



III

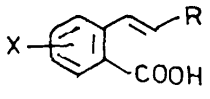
The thiophthalides I were shown for the first time, to undergo successful tandem Michael-Dieckmann cyclisation with 2-cyclohexenones in the presence of ^{t}BuOLi, leading to 3,4-dihydroanthracen-1(2H)-ones IV, the structures featured by aureolic acid group of antibiotics.



IV

R = H
= CH_2OAc

The reaction between thiophthalides I and aldehydes (aliphatic or aromatic) in the presence of ^{t}BuOLi was reported to furnish pure trans isomers of benzoic acids V in respectable yields. A mechanism involving formation of an episulfide

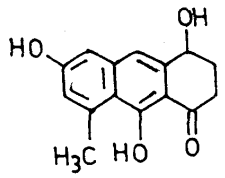


V

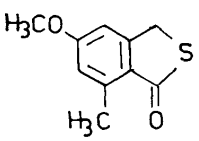
intermediate and elimination of elemental sulfur therefrom, was proposed for the above unusual transformation.

A wide range of electrophilic reagents was treated with the anion of the parent thiophthalide with a view to assess general reactivity profile. It gave 3-phenylthio- thiophthalide with PhSSPh and 9,10-anthraquinone with bromobenzene, and did not react with alkyl halides and Schiff's bases.

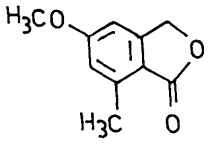
In order to demonstrate the synthetic utility of thiophthalide , an approach to the synthesis of antibiotic okicenone, 4,6-dihydroxy-8-methyl-3,4-dihydroanthracen-1(2H)-one VI was examined. The synthesis involving tandem Michael-Dieckmann reaction as a transform required 5-methoxy-7-methylthiophthalide VII which was prepared in two steps from 5-methoxy-7-methylphthalide VIII. The phthalide VIII obtained through a multistep sequence, was reacted with lithium benzylthiolate to provide 2-benzylthiomethyl-4-methoxyl-6-methyl benzoic acid which on oxalyl chloride promoted cyclisation furnished VII in excellent yield.



VI



VII



VIII