

A SIMPLE ROUTE TO INDOLIZINE-2-CARBOXYLATES. CYCLOADDITION
 REACTIONS OF PYRIDINIUM ARYLSULPHONYLMETHYLIDES.

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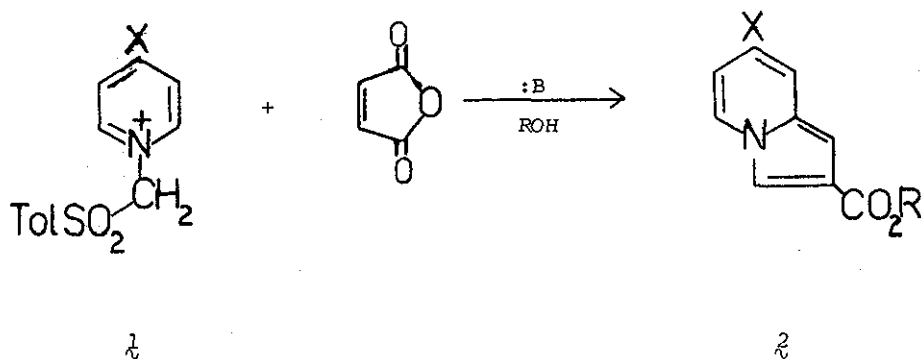
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Pyridinium-p-toluenesulphonylmethylides react with
 maleic anhydride in the presence of alcohols to give
 indolizine-2-carboxylates in a process involving selective
 decarboxylation and aromatization, and with phenyl-
 cyanoacetylene to give 1-cyano-2-phenylindolizines.

The 1,3-dipolar cycloaddition of pyridinium arylsulphonylmethylides
 with dimethyl acetylenedicarboxylate has been described recently¹ and led
 to the formation of 1,2-dimethoxycarbonylindolizines. Reaction with methyl
 propiolate gave the 1-methoxycarbonylindolizine. We now report the synthesis
 of indolizine-2-carboxylates via a novel route.

Reaction of 4-benzoyl-1-p-toluenesulphonylpyridinium trifluoromethane-
 sulphonate (\downarrow ; X=COPh) with maleic anhydride in the presence of triethylamine

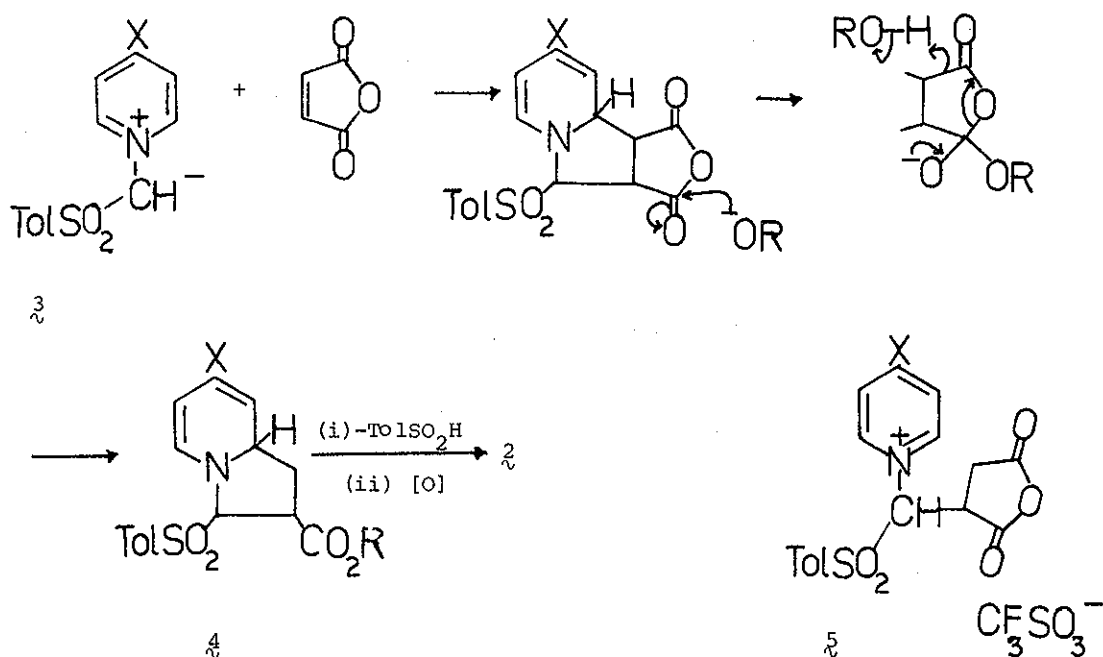
or DBU in chloroform containing ethanol gave 7-benzoyl-2-ethoxycarbonyl-indolizine (2 ; X=COPh, R=Et) (34.4%), m.p. 145-147°. ² A similar reaction carried out in methylene chloride containing methanol gave 2 (X=COPh, R=Me) (60%), m.p. 205°. The orientation of the carboxyl function was established by the hydrolysis of dimethyl 7-benzoylindolizine-1,2-dicarboxylate ¹ with alcoholic KOH to give 7-benzoylindolizine-2-carboxylic acid, m.p. 262° (decomp.), identical with the acid obtained from 2 (X=COPh, R=Et), and was esterified to 2 (X=COPh, R=Me or Et). It is known ³ that carboxyl groups in the 1- and 3-positions of indolizine are labile. The methyl ester was different from the 1-carboxylate obtained previously. ¹ 4-Cyano-1-p-toluene-



sulphonylpyridinium triflate (1 ; X=CN) similarly gave 2 (X=CN, R=Me), m.p. 205° (26%), but the yield of 2 (X=H, R=Et) from 1 (X=H) was very low. It seems as though an electron-withdrawing substituent in the pyridine ring is required to give respectable yields of 2 . The nature of the products formed in the absence of an electron-withdrawing substituent is under investigation.

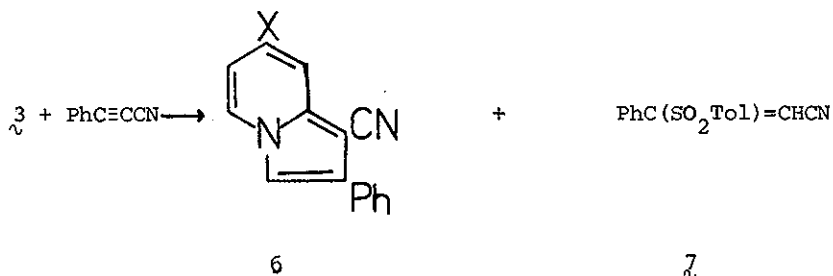
A possible mechanism for the formation of 2 would involve a cycloaddition of maleic anhydride to the ylide (3) to give a tetrahydroindolizine, followed

by attack by the alcohol at the C₂ carbonyl, decarboxylation of the C₁ carboxyl, elimination of toluenesulfinic acid and aromatization.⁴ Alternatively, Michael addition of **3** to the anhydride would give **5** which would



then react with alcohol at the more hindered carbonyl group of the maleic anhydride.⁵ Decarboxylation and cyclization would then give **4**. This stepwise addition and cyclization could account for the observed need for an electron-withdrawing substituent in the pyridine ring.

The ylides (**3**; X=COPh, Me, CN, H and 3,5-Me₂) and phenylcyanoacetylene give 1-cyano-2-phenylindolizines (**6**)² in moderate yields and β-p-toluenesulphonylcinnamionitrile (**7**), m.p. 114°.



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