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

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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 arylosulphonylmethylides with dimethyl acetylenedicarboxylate has been described recently \(^1\) 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 trifluoromethanesulphonate (\(L; X=\text{COPh}\)) with maleic anhydride in the presence of triethylamine...
or DBU in chloroform containing ethanol gave 7-benzoyl-2-ethoxycarbonylindolizine \((\mathcal{Z}; X=\text{COPh}, R=\text{Et})\) (34.4%), m.p. 145-147°. A similar reaction carried out in methylene chloride containing methanol gave \(\mathcal{Z} \) \((X=\text{COPh}, R=\text{Me})\) (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 \(\mathcal{Z} \) \((X=\text{COPh}, R=\text{Et})\), and was esterified to \(\mathcal{Z} \) \((X=\text{COPh}, R=\text{Me or Et})\). 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-\(\text{g}\)-toluenesulphonylpyridinium triflate \((\mathcal{Z}; X=\text{CN})\) similarly gave \(\mathcal{Z} \) \((X=\text{CN}, R=\text{Me})\), m.p. 205° (26%), but the yield of \(\mathcal{Z} \) \((X=\text{H}, R=\text{Et})\) from \(\mathcal{Z} \) \((X=\text{H})\) was very low. It seems as though an electron-withdrawing substituent in the pyridine ring is required to give respectable yields of \(\mathcal{Z} \). The nature of the products formed in the absence of an electron-withdrawing substituent is under investigation.

A possible mechanism for the formation of \(\mathcal{Z} \) would involve a cycloaddition of maleic anhydride to the ylide \((\mathcal{Z})\) to give a tetrahydroindolizine, followed

\[
\begin{align*}
\begin{array}{c}
\text{ToS}O_2CH_2 \\
\downarrow
\end{array} + \begin{array}{c}
\begin{array}{c}
\text{ Tol} \\
\downarrow
\end{array}
\end{array} & \xrightarrow{\text{ROH}} \begin{array}{c}
\begin{array}{c}
\text{CO}_2R \\
\text{X}
\end{array}
\end{array}
\end{align*}
\]

\(\mathcal{Z}\)
by attack by the alcohol at the C\textsubscript{2} carbonyl, decarboxylation of the C\textsubscript{1} carboxyl, elimination of toluenesulfinic acid and aromatization.\textsuperscript{4} Alternatively, Michael addition of 3 to the anhydride would give 5 which would

\[ \begin{array}{c}
\text{X} \\
\text{TolSO}_2
\end{array} + \begin{array}{c}
\text{H} \\
\text{O}
\end{array} \rightarrow \begin{array}{c}
\text{X} \\
\text{TolSO}_2
\end{array} \rightarrow \begin{array}{c}
\text{RO}_2H \\
\text{O}
\end{array} \rightarrow \begin{array}{c}
\text{OR} \\
\text{O}
\end{array}
\]

then react with alcohol at the more hindered carbonyl group of the maleic anhydride.\textsuperscript{5} Decarboxylation and cyclization would then give 6. This stepwise addition and cyclization could account for the observed need for an electron-withdrawing substituent in the pyridine ring.

The ylides (\(\text{3; } X=\text{COPh, Me, CN, H and 3,5-Me}_2\)) and phenylcyanoacetylene give 1-cyano-2-phenylindolizines (\(\text{6}\))\textsuperscript{2} in moderate yields and 6-\(p\)-toluenesulphonylcinnamoni trile (\(\text{7}\)), m.p. 114°.

\[ \begin{array}{c}
\text{3} + \text{PhC}=\text{CCN} \rightarrow \begin{array}{c}
\text{X} \\
\text{Ph}
\end{array} \rightleftharpoons \begin{array}{c}
\text{CN} \\
\text{Ph}
\end{array} + \begin{array}{c}
\text{PhC}(\text{SO}_2\text{Tol})=\text{CHCN}
\end{array}
\]

\(\text{6}\) \hspace{1cm} \(\text{7}\)
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REFERENCES

2. All new compounds gave the expected spectral and analytical data.

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