Reactions of Isoquinolinium Ylides: Amine-catalysed Cycloaddition of Aldehydes and Ketones

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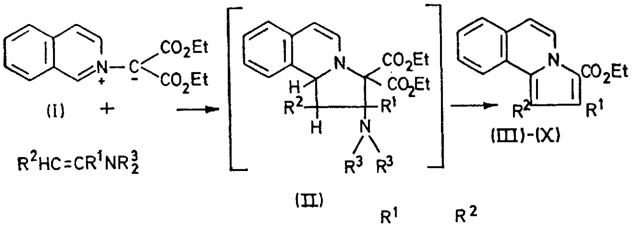
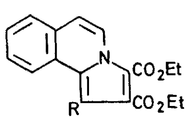
Summary Isoquinolinium diethoxycarbonylmethylide reacts with aldehydes and ketones in the presence of primary and secondary amines to yield 1- and 2-alkylbenzo[*g*]indolizines, thought to result from cycloaddition to the intermediate enamines; some ketones also yield 1-alkyl-2,3-diethoxycarbonylbenzo[*g*]indolizines, resulting from 1,2 ester shifts of the initial adducts.

Nitrones,[1] nitrileimines,[2] nitrile oxides,[2,3] and azides[4] undergo 1,3-cycloaddition reactions with enamines. We now report the formation of the 1- and 2-alkylbenzo[*g*]indolizines (III)—(X) from isoquinolinium diethoxycarbonylmethylide(I) and the enamines formed *in situ* from aldehydes and ketones with primary and secondary amines; the enamines formed from primary amines will exist in equilibrium with the corresponding Schiff's bases.[5]

Acetone and (I) in the presence of various primary and secondary amines give (III) (*ca.* 36%) presumably *via* the enamine and the adduct (II; $R^1 = Me$, $R^2 = H$). Methyl ethyl ketone and (I) give a mixture of (IV) and (V), arising from the two possible enamines. Cyclic ketones react similarly, cyclohexanone and dimedone giving (XI) and (XII), respectively. Compound (XI) is also obtained from *N*-(1-cyclohexenyl)pyrrolidine and (I).

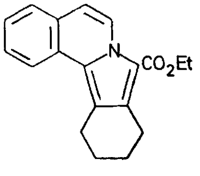


	R^1	R^2
(III)	Me	H
(IV)	Et	H
(V)	Me	Me
(VI)	Pr	H
(VII)	H	Me
(VIII)	H	Et
(IX)	H	Pr
(X)	H	Ph

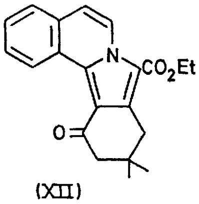


(XV) R = Et
(XVI) R = Pr

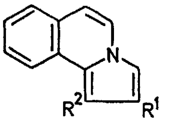
The orientation of addition of aldehydes to (I) is highly specific, propionaldehyde, butyraldehyde, valeraldehyde, and phenylacetaldehyde yielding only the respective 1-substituted benzo[*g*]indolizines (VII)—(X). The u.v. spectra of (VII), (VIII), and (IX) are almost identical and show small but significant changes from those of the corresponding 2-alkylbenzo[*g*]indolizines (III), (IV), and (VI). Structures (III)—(X) are those expected on the basis of the polarisation of the enamines and have been confirmed in the case of the isomeric pair (III) and (VII) by hydrolysis and decarboxylation to (XIII) and (XIV), respectively. In the n.m.r. spectrum of (XIII) 3-H and 1-H give rise to singlets at δ 7·03 and 6·78, whereas the spectrum of (XIV) contains the expected doublets for 3-H and 2-H at 7·17 and 6·57 (J 2·0 Hz).



(XI)



(XII)



(XIII) $R^1 = Me$, $R^2 = H$
(XIV) $R^1 = H$, $R^2 = Me$

The diesters (XV) and (XVI) are obtained as minor products from (I) and methyl ethyl ketone and methyl propyl ketone and must arise by the alternative mode of addition of the enamine to (I), followed by a 1,2 ester shift in the initially formed adduct; similar shifts have been reported.[6]

We have recently isolated initial adducts of type (II) in high yield from the reaction of (I) with various enamines and these are slowly converted into benzo[*g*]indolizines in solution.

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