

A NEW SYNTHESIS OF 1,1-DIPHENYL-3-ARYLISOQUINOLIN-4-ONES BY THE NOVEL
CYCLIZATION OF 2-AZABUTA-1,3-DIENES.

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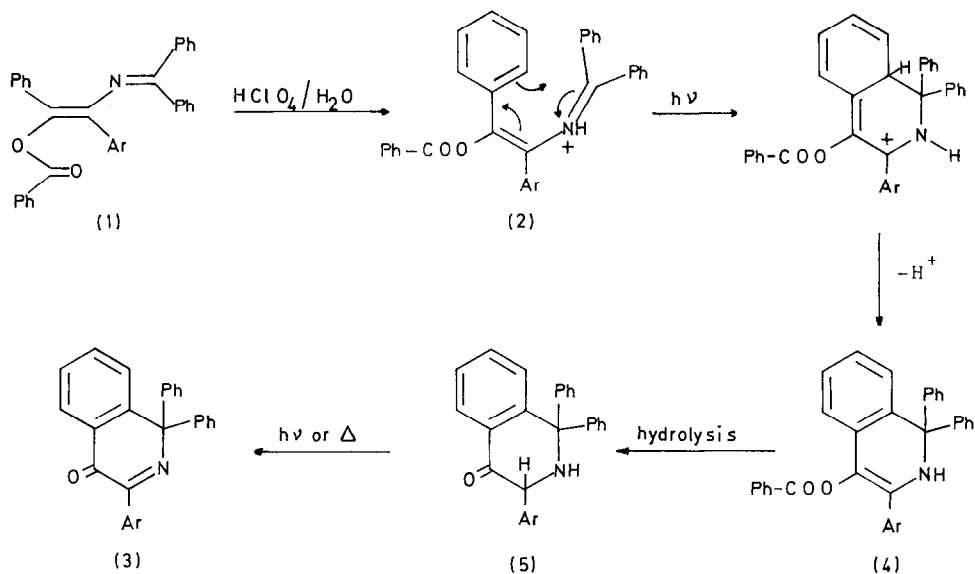
Summary: The facile synthesis of novel 1,1-diphenyl-3-arylisquinolin-4-ones by
the cyclization of protonated 2-azabuta-1,3-dienes is reported.

The synthesis of alkaloids of the pontevedrine type can be approached by
the use of substituted isoquinolin-4-ones^{1,2}. There are only a few routes either
to these intermediates or to the isomeric isoquinolin-3-ones³. We wish to report
a novel approach to the former class of compound.

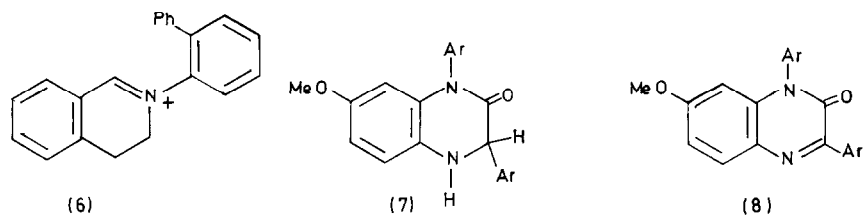
The azadienes (1) required for the synthetic approach are readily obtained
either by the trapping of the anion from (N-diphenylmethyl)-arylmethanimines by
two moles of benzoyl chloride⁴ or by the trapping of the anion of monoimines of
1,2-diketones by one mole of benzoyl chloride⁵. The azadienes (1) so obtained
are readily protonated in the presence of HClO₄ to yield the iminium salts (2)⁶.
The exposure of a solution of the salt (2, Ar=p-MeC₆H₄) in methylene chloride to
light ($\lambda > 300\text{nm}$)⁷ brings about a rapid conversion to yield the azadiene (1, Ar=
p-MeC₆H₄) as a mixture of trans-cis-isomers (27%), benzoic acid (61%) and a new
compound in 64% yield. The mixture is readily separated by chromatography on

silica gel. This new compound is obtained as yellow crystals (m.p. 187-8°C). The product showed in the i.r. that the ester group had been replaced by an aryl keto function (1670 cm^{-1}) and also that a C=N group was present (1590 cm^{-1}). The ^1H n.m.r. (δ 2.33, 3H, s; 7.01-7.05, 15H, m; 7.76 and 7.93, 2H, d; 8.15, 1H, m) and the ^{13}C n.m.r. (δ 21.41, 71.83, 126.98-132.83, 140.43, 145.53, 148.55, 160.32 and 176.25) spectra in conjunction with the mass spectrum and microanalytical results (m/z 387, 270, 241, 239, and 165; Found: C, 86.82; H, 5.42; N, 3.61. $\text{C}_{28}\text{H}_{21}\text{NO}$ requires C, 87.77; H, 5.79; N, 3.35%) identifies the photoproduct as the novel isoquinolin-4-one (3, Ar=p-MeC₆H₄). A similar photocyclization of the salt (2, Ar=Ph) yields the corresponding isoquinolin-4-one (3, Ar=Ph) (m.p. 168-9°C) again in good yield (51%).

The conversion of the iminium salt (2) to the isoquinolin-4-one (3) and benzoic acid can be accounted for by the reaction scheme shown below. The key step in this sequence is the photochemical cyclization of the salt (2). (Dark control reaction clearly demonstrates that this process is photochemical). This step involves the uncommon attack by an iminium carbon atom on the ortho position of an aryl ring⁸. Previously there has been only one other example of such a process in the reported photocyclization⁹ of the iminium salt (6). The cyclization of the protonated azadienes (2) is a departure from the usual photoreaction of the azadienes (1) which efficiently yield 3-oxazolines¹⁰. Following the photocyclization deprotonation affords the intermediate enol ester (4). This is not isolated and presumably undergoes hydrolysis (a thermal reaction) in the presence of $\text{HClO}_4/\text{H}_2\text{O}$ to the ketone (5) and benzoic acid. The resultant ketone (5) is then oxidised¹¹ during the irradiation, by the perchloric acid, or during workup to afford the isolated product (3).



Scheme



The scope and generality of this synthetic approach to these new isoquinolin-4-ones is currently under investigation with the intention of developing new routes to the alkaloids of the type represented by pontevedrine.

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