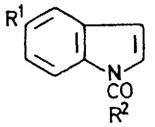
Photoaddition of Olefins to Indoles: Synthesis of Tetrahydro-1*H*-cyclobut[*b*]indoles

By DAVID R. JULIAN* and ROBERT FOSTER

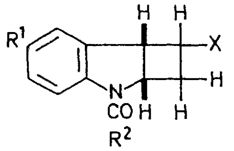
(*Imperial Chemical Industries Limited, Pharmaceuticals Division, Mereside, Alderley Park, Macclesfield, Cheshire* SK10 4TG)

Summary Irradiation of *N*-acylindoles in the presence of olefins produces cyclobutanes by cycloaddition of the olefin to the indole 2,3-double bond.

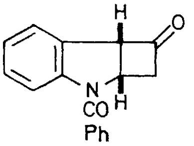
WE have previously described[1] photoadditions of ketones to *N*-acylindoles yielding oxetans, in which the indole is rendered photoreactive by using an electron-withdrawing protecting group on nitrogen. Although little mechanistic evidence on these cycloadditions was available, the results were consistent with excited ketone adding to ground state indole. The feasibility of adding olefins to *N*-acylindoles with sensitised irradiation[2] was therefore considered.



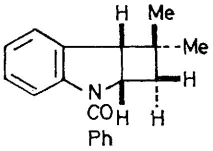
(1) $R^1 = H, R^2 = p\text{-ClPh}$
(4) $R^1 = MeO, R^2 = p\text{-ClPh}$
(9) $R^1 = H, R^2 = Ph$



exo-X	*endo*-X	
(2)	(3)	$R^1 = H, R^2 = p\text{-ClPh}, X = CO_2Me$
(5)	(6)	$R^1 = MeO, R^2 = p\text{-ClPh}, X = CO_2Me$
(7)		$R^1 = H, R^2 = p\text{-ClPh}, X = CO_2H$
(8)		$R^1 = H, R^2 = p\text{-ClPh}, X = Ac$
(10)	(11)	$R^1 = H, R^2 = Ph, X = OAc$
(12)	(13)	$R^1 = H, R^2 = Ph, X = OH$



(14)



(15)

In the event, irradiation of *N*-*p*-chlorobenzoylindole (**1**) and methyl acrylate in acetonitrile using acetophenone sensitiser yielded the *exo*- and *endo*-adducts[3] (**2**),† 40%, m.p. 126—127°, and (**3**),† 5%, m.p. 180—181°. However, direct irradiation of (**1**) and methyl acrylate in benzene gave similar results, based on chemical yields. No reaction was observed when methyl acrylate was irradiated with indole or *N*-methylindole in benzene either directly (Corex filter) or acetophenone sensitised, therefore the *N*-acyl protecting group is critical. Irradiation of the methoxylated indole (**4**) produced (**5**), 50%, m.p. 152—153°, and (**6**), 7%, m.p. 179—180°. Acrylonitrile, acrylamide, and ethyl vinyl ether also added‡ to (**1**) yielding the corresponding *exo*- and *endo*-adducts.§ However, in reactions with acrylic acid and methyl vinyl ketone, only the *exo*-adducts (**7**), m.p. 205—206°, and (**8**), m.p. 146—147°, respectively, have been isolated. Vinyl acetate added to (**9**) yielding a mixture of acetates (**10**) and (**11**) which was resolved as the alcohols (**12**), m.p. 167—169°, and (**13**), m.p. 186—187°. Chromic oxide–pyridine oxidation of each of these isomeric alcohols resulted in the same ketone (**14**), characterised as the semicarbazone, m.p. 214—216°. Irradiation of (**9**) in the presence of isobutene gave (**15**), m.p. 119—120°.†

In a competitive reaction between ethyl vinyl ether and acrylonitrile, (**1**) added almost entirely to the nitrile as measured by t.l.c. and n.m.r. We conclude that the photoaddition is more efficient with electron-deficient olefins. The observations that similar reactions occur on both direct and triplet-sensitised irradiation, and that added naphthalene quenches the cycloadditions, suggest that triplet indole is involved. Transformations of these novel photoadducts into indole derivatives of potential pharmacological activity are in hand.

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† Structure assignment supported by elemental analysis and i.r., u.v., m.s. and n.m.r. data.

‡ Irradiated directly in benzene or acetonitrile using a medium-pressure mercury-vapour lamp through Pyrex glass.

§ *N*-Acetylindole also undergoes these cycloadditions.

[1] D. R. Julian and G. D. Tringham, *J.C.S. Chem. Comm.*, **1973**, **13**.
[2] J. J. McCullough and C. W. Huang, *Canad. J. Chem.*, **1969**, **47**, 757.
[3] M. S. Lin and V. Snieckus, *J. Org. Chem.*, **1971**, **36**, 645; F. Fried, J. B. Taylor, and R. Westwood, *Chem. Comm.*, **1971**, **1226**.