Photoaddition of Ketones to Indoles: Synthesis of Oxeto[2,3-*b*]indoles

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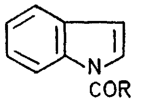
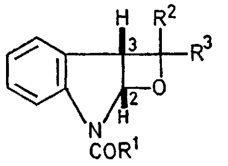
Summary Irradiation of certain ketones in the presence of *N*-acylindoles produced oxetans by cycloaddition of the ketone to the indole 2,3-double bond.

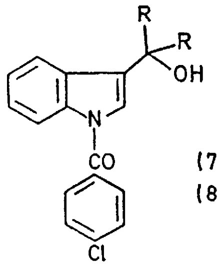
FURANS[1,2] and 2,5-dimethylthiophen[3] are the only reported examples of aromatic heterocycles which form oxetans[2] on irradiation in the presence of benzophenone. Thiophen, pyrrole, oxazole, and isoxazole do not undergo such cycloadditions.[4] This lack of reactivity may be caused by greater resonance energy in the heterocyclic π-system† or a quenching effect on the excited ketone by the non-bonded electrons on the hetero-atom.[5] In either event, such aromatic heterocycles might be rendered more reactive by capturing the non-bonded electron donation with an electron-withdrawing protecting group. We report here our success using this approach with the indole nucleus.



(1) R = p-ClC$_6$H$_4$
(3) R = Me



(2) R^1 = p-ClC$_6$H$_4$, R^2 = R^3 = Ph
(3) R^1 = Me, R^2 = R^3 = Ph
(5) R^1 = p-ClC$_6$H$_4$, R^2 = Ph, R^3 = CONH$_2$
(6) R^1 = p-ClC$_6$H$_4$, R^2 = Ph, R^3 = CO$_2$Me



(7) R^1 = Ph, R^2 = CO$_2$Me
(8) R^1 = Me, R^2 = CO$_2$Me

Indole did not react with benzophenone on irradiation‡ behind Pyrex. However, irradiation of benzophenone in the presence of *N*-*p*-chlorobenzoylindole§ (**1**) gave the

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† The resonance energy of furan is *ca.* 8 kcal mol^{-1} less than that of thiophen and pyrrole.

‡ All irradiations were carried out in benzene using a medium-pressure mercury-vapour lamp with a Pyrex filter.

§ Prepared from indole and *p*-chlorobenzoyl chloride using sodium hydride, m.p. 111—112°.

tetrahydro-oxeto[2,3-*b*]indole (**2**), 83%,¶ m.p. 230—232°, ν_{max} (KBr) 1655, 1590, 1380, 930, 915, 750 cm^{-1}; λ_{max} 265 (log ϵ 3·98) nm; δ (CD_3SO) 8·0—6·7 (18H, m, Ar*H*), 6·20 (d, 2-H), 5·05 (d, $J_{2,3}$ 5 Hz, 3-H); *m/e* 437 ($M^+ < 1\%$), 255 (17), 182 (17), 139 (100). *N*-Acetylindole** (**3**) gave the oxetan (**4**). If indole is also present in the reaction medium, no oxetans are formed, thus suggesting that a quenching effect by the unprotected indole on excited benzophenone, either by triplet–triplet transfer, or *via* an electron transfer involving the non-bonded electrons on nitrogen takes place.

Using (**1**) as a standard substrate, no oxetan formation was observed on irradiation of acetophenone, benzaldehyde, acetone, or propionaldehyde. However, benzoylformamide and methyl benzoyl formate gave the oxetans (**5**), 13%, m.p. 174—177°; and (**6**), 73%, m.p. 166—168°, respectively, characterised by spectral data. It may be significant that only ketones with $n\pi^*$ triplet energies[6] of less than about 68 kcal mol^{-1} add to (**1**). This suggests that the triplet energy of (**1**) is of this order and that with ketones of higher triplet energies, quenching by ground state indole occurs. Although the *N*-acylindole absorbs a major proportion of the incident light (98% of incident light at 308 nm and 90% at 330 nm) excited indole presumably transfers energy to ground state ketone[7] which is also excited directly.

An additional product of the reaction of (**1**) with methyl benzoyl formate was the alcohol (**7**), 6%, m.p. 165—167°, ν_{max} ($CHCl_3$) 3550, 1735, 1690 cm^{-1}; λ_{max} 214, 252, 304 nm; δ($CDCl_3$) 8·2—7·0 (14H, m, Ar*H*), 4·20 (s, O*H*), 3·75 (3H, s, O*Me*); *m/e* 419 (M^+ 56%), 360 (100), 139 (100). Indeed, methyl pyruvate gave the alcohol (**8**), 24%, m.p. 143—145°, as the only isolable product. Presumably the corresponding oxetan is an intermediate[8] and undergoes further ring cleavage. Oxetan (**6**) is unstable in solution, but does not seem to be decomposed by light either directly or with sensitisation from the benzoylformic acid derivatives or added benzophenone.

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¶ All compounds gave satisfactory elemental analyses.

** No reaction was obtained with *N*-tosylindole in this reaction.

[1] G. O. Schenck, W. Hartmann, and R. Steinmetz, *Chem. Ber.*, 1963, **96**, 498.
[2] D. R. Arnold, *Adv. Photochem.*, 1968, **6**, 301.
[3] C. Rivas, M. Vélez, and O. Crescente, *Chem. Comm.*, 1970, 1474.
[4] G. R. Evanega and E. B. Whipple, *Tetrahedron Letters*, 1967, 2163.
[5] S. G. Cohen and A. D. Litt, *Tetrahedron Letters*, 1970, 837.
[6] Measured in hydrocarbon media, D. R. Arnold, *Adv. Photochem.*, 1968, **6**, 328.
[7] For an example where ground state ketone is involved in oxetan formation see C. De Boer, *Tetrahedron Letters*, 1971, 4977.
[8] T. Matsuura, A. Banba, and K. Ogura, *Tetrahedron*, 1971, **27**, 1211.