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THE COUPLING REACTIONS OF 3-ACYLINDOLES AND PROOF OF STRUCTURE OF THE PALLADIUM (II)ACETATE MEDIATED CYCLISATION REACTION PRODUCT OF 3-BENZOYL-1-METHYLINDOLE.

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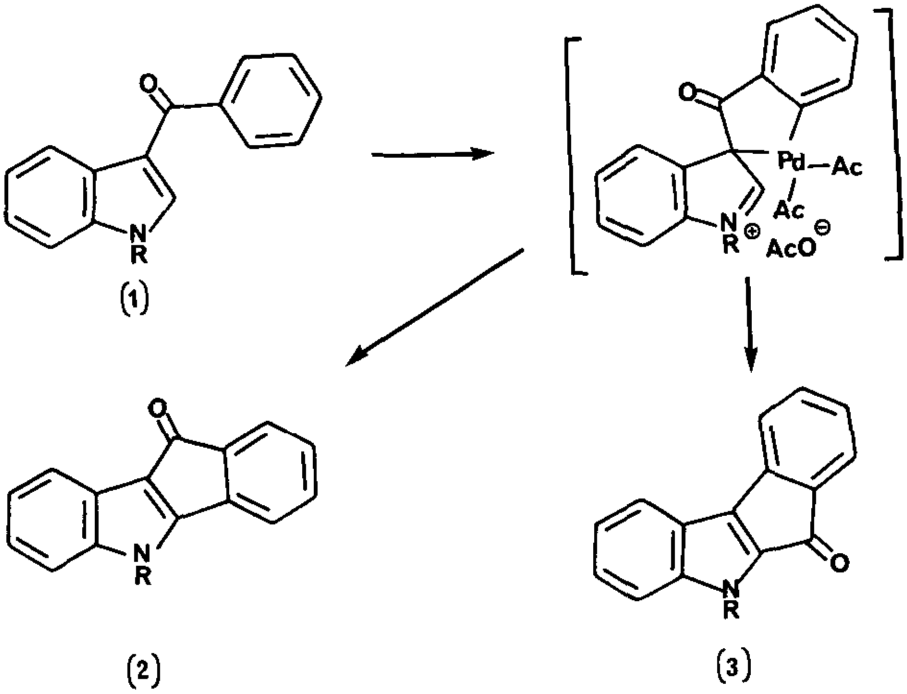
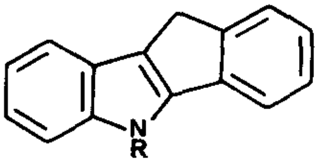
Abstract - The structure previously proposed for the oxidative cyclisation of 3-benzoyl-1-methylindole in the presence of palladium(II)acetate has been confirmed. Attempts to form homologues of the product by similar reactions fail.

Itahara[1] has proposed that the product of the palladium(II)acetate oxidative cyclisation of 3-benzoyl-1-methylindole (**1**, R=H) is 5-methylindeno[1,2-*b*]indol-10-one (**2**, R=Me). Unfortunately, the data presented by this author do not rule out the alternative structure (**3**, R=Me) which could arise through coupling within a palladated intermediate first to the β-position of the indolic nucleus, followed by a β ⟶ α shift of the acyl bond.



We have carried out differential ^{1}H n.m.r. n.O.e. enhancement studies at 400 MHz upon Itahara's compound in order to clarify this uncertainity, but since the majority of the aryl proton resonances occur as an unresolved complex of signals at δ ($CDCl_3$) 7.22 - 7.11 a definitive answer is not possible using this technique.

One might suppose that a chemical solution to the problem is at hand since both of the indenoindoles (4, R=H) and (5, R=H) are available through Fischer indolisation reactions upon 1- and 2-indanones respectively. N-Methylation and oxidation of these compounds should afford the two structures in question. In practice, however, the N-methylated products give complex mixtures on oxidation, probably because the preferred site of attack is at the β-position of the indole rather than at the bridging methylene unit. Eisch and Abraham[2] have experienced similar difficulties in effecting the oxidation of the desmethyl compound (4, R=H), to indeno[1,2-b]indol-10(5H)one (2, R=H), but eventually they succeeded by forming the corresponding anion and exposing it to oxygen and benzophenone. In the case of N-methyl derivatives (4, R=Me) and (5, R=Me) the appropriate anions are not easily formed and, in our hands, we could not bring about the required interconversions.



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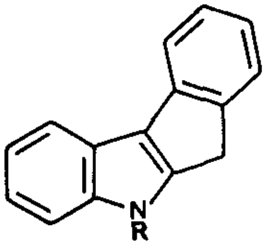

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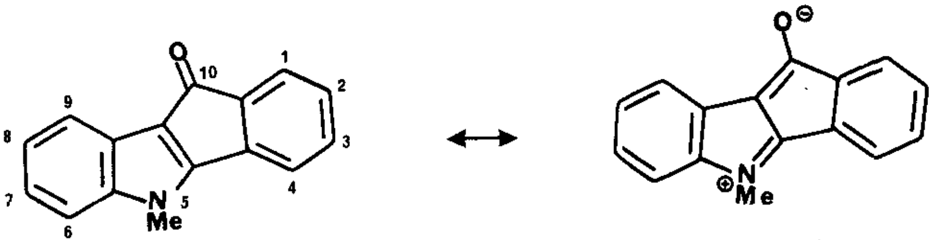
Curruthers and Evans[3] have also prepared indeno[1,2-b]indol-10(5H)-one (2, R=H), by a photochemical cyclisation of 3-(2-iodobenzoyl)indole. Proof of structure was achieved in this case by reduction of the product with lithium aluminium hydride to give 5H,10H-indeno[1,2b]indole (4, R=H). Efforts by us to reduce Itahara's compound to either (4, R=Me) or (5, R=Me) under similar conditions failed since the reduction proceeded only as far as the intermediate alcohol. We were also unable to selectively N-methylate indeno[1,2-b]indol-10(5H)-one (2, R=H) but we did note that the electronic spectrum of this compound is simlar to that of Itahara's product (λ_{max} 219, 229, 223, 267, 276, 289, 302, 349, 439.5 nm and λ_{max} 216, 228, 233, 242, 268, 278, 303, 317, 459 nm respectively) suggesting that Itahara's structural assignment (6) is correct, and this conclusion we have now confirmed by a single crystal X-ray analysis. This data are summarized in Table 1 and it is noteworthy that the C-O bond length in this structure is comparable with that of typical aryl-aryl ketones indicating only a modest contribution from the zwitterionic structure (7). Undoubtedly this property is shared with the N-desmethyl analogues (2, R=H), for the two compounds have the similar infra-red carbonyl stretching frequencies (approximately 1675 cm^{-1}).

We had hoped to cyclise a number of other 3-substituted indoles under Itahara's conditions;

for example, the acyl compounds of the type (8, X=O) but in this we failed. It might be argued that such amides exist as the Z-forms (9) in which the aryl ring of the 3-substituent is remote from the 2-position of the indole nucleus. However, this thesis may not be tenable because we were equally unsuccessful in effecting the ring closure of the 3-aralkylindoles (8, X=CH_2) where such geometrical constraints to coupling no longer apply.



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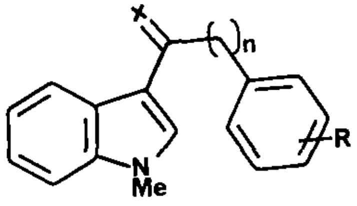

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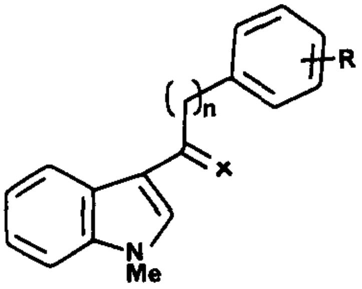

(9)

Crystal data - C H NO, M = 233.3, orthorhombic, space group $P2_12_12_1$, a = 5.4794(3), b= 13.076(1), c = 15.984(2), U = 1145.24 $Å^3$, D_c = 1.36 g cm^{-3}, Z = 4, λ = 1.5418 Å.

X-ray diffraction data were collected with an Enraf-Nonius CAD-4 diffractometer and *using Cu-K_α radiation. Reflections were measured for θ ≤ 76°, 1402 reflections were scanned and* of these 546 had I ≥ 3(θ)I and were used in the refinement. The structure was readily solved using the direct methods MULTAN-80 programme, and then refined with the CRYSTALS package. Refinement proceeded routinely using firstly isotropic and then anisotropic thermal parameters. At a late stage in the refinement all the hydrogen atoms were detected in a difference map. The aromatic hydrogen atoms were then located in their calculated positions, while those of the N-methyl group were placed in their found positions. Further refinement (the hydrogen atoms were not *refined) then gave a final* R *value 4.38%.*

TABLE 1

5-Methylindeno[1,2-*b*]indol-10-one, bond lengths (Å) estimated deviations all 0.01 Å, bond angles (°); estimated deviations in parentheses.

Bond Lengths	N(5) - C(5a)	1.39	C(9b) - C(10)	1.44
	N(5) - C(4b)	1.36	C(10) - O(10)	1.22
	N(5) - C(Me)	1.46	C(10) - C(10a)	1.53
	C(5a)- C(6)	1.38	C(10a)- C(1)	1.37
	C(6) - C(7)	1.39	C(1) - C(2)	1.39
	C(7) - C(8)	1.40	C(2) - C(3)	1.38
	C(8) - C(9)	1.39	C(3) - C(4)	1.41
	C(9) - C(9a)	1.40	C(4) - C(4a)	1.38
	C(9a)- C(5a)	1.40	C(4a) - C(10a)	1.41
	C(9a)- C(9b)	1.44	C(4a) - C(4b)	1.49
	C(9b)- C(4b)	1.37		

Bond Angles	C(4a) - N(5) - C(Me)	127.7(7)	C(9b) - C(10) - O(10)	131.2(8)
	C(Me) - N(5) - C(5a)	125.3(6)	C(9b) - C(10) - C(10a)	103.6(6)
	C(4b) - N(5) - C(4b)	107.0(6)	O(10) - C(10) - C(10a)	125.2(7)
	N(5) - C(4b) - C(6)	127.6(7)	C(10) - C(10a)- C(4a)	11.6(7)
	N(5) - C(4b) - C(9a)	109.3(6)	C(10) - C(10a)- C(1)	128.8(7)
	C(9a) - C(4b) - C(6)	123.1(7)	C(4a) - C(10a)- C(1)	119.6(8)
	C(4b) - C(6) - C(7)	116.4(7)	C(10a)- C(1) - C(2)	120.0(8)
	C(6) - C(7) - C(8)	122.0(8)	C(1) - C(2) - C(3)	119.9(8)
	C(7) - C(8) - C(9)	120.7(8)	C(2) - C(3) - C(4)	121.5(8)
	C(8) - C(9) - C(9a)	118.5(7)	C(3) - C(4) - C(4a)	117.4(7)
	C(9) - C(9a) - C(5a)	119.3(7)	C(4) - C(4a) - C(10a)	121.5(8)
	C(9) - C(9a) - C(9b)	135.2(7)	C(4) - C(4a) - C(4b)	136.4(7)
	C(5a) - C(9a) - C(9b)	105.5(7)	C(10a)- C(4a) - C(4b)	102.2(7)
	C(9a) - C(9b) - C(4b)	106.8(6)	C(4a) - C(4b) - N(5)	135.6(7)
	C(9a) - C(9b) - C(10)	143.5(7)	C(4a) - C(4b) - C(9b)	113.0(6)
	C(4b) - C(9b) - C(10)	109.7(7)	C(9b) - C(4b) - N(5)	111.4(7)

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