Synthesis of 1-(2-Indolyl)-2-arylethylene Derivatives

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Summary A convenient route to new 2-substituted indole derivatives (**3a**—**e**) *via* the Wittig reaction has been developed.

RECENTLY the preparation of 1-(2-indolyl)-2-(3-pyridyl)-acrylonitrile (**1**) has been described[1,2] and the potential utility of this compound in new routes to heterocyclic systems and indole alkaloids has been partially realized.[1,3] In view of these results and the lack of methods for chain extension at the 2-position of the indole nucleus,[4] we report on a new preparation of (**3a**) and the analogous compounds (**3b**—**e**) *via* the Wittig reaction: this method may be of some general synthetic interest.

Treatment of (**2**) (prepared from the known 2-dimethylaminomethylindole methiodide[5] and triphenylphosphine in dimethylformamide under reflux) with sodium methoxide in absolute methanol or with 1,5-diazabicyclo[4,3,0]non-5-ene[6] and the selected aromatic aldehydes gave the Wittig products (**3a**—**e**). The reaction could be conveniently followed by the appearance of intense u.v. absorption in

Physical and spectral data of 1-(2-*indolyl*)-2-*arylethylene derivatives*

				N.m.r.[c]			
Compound[a]	Preparation method[b]	% Yield	M.p. (°)	NH[d,e]	Pyridine α-H	Indole β-H[e]	Other
(**3a**)	A	56	194	−0·6	1·3 (m,1H) 1·56 (m,1H)	3·33	2·04 (m,1H, pyridine γ-H) 2·35—3·19 (m,5H, aromatic, pyridine β-H), 2·50 (br d,1H, J 14 Hz) and 2·85 (br d, 1H, J 14 Hz, H^1 and H^2).
(**3b**	B (Tetrahydrofuran)	58	118	not detected	1·05 (m,1H)	3·23	1·97—3·15 (m,7H, aromatic, pyridine β- and γ-H), 3·18 (d,1H, J 14 Hz) and 3·53 (d,1H, J 14 Hz, H^1 and H^2).
(**3c**)	A	59	215—217	−1·5	1·4 (br d,2H)	3·23	2·2—3·03 (m,8H, aromatic, pyridine β-H, H^1, H^2).
(**3d**)	A B(Me$_2$SO)	49 39	210	−0·5		3·31	2·28—3·04 (m,11H, aromatic, H^1, H^2).
(**3e**)	B Tetrahydrofuran)	74	165—166 (decomp.)	−1·9		3·4	1·73 (d,2H, J 9 Hz) and 2·18 (d,2H, J 9 Hz, p-NO$_2$·C$_6H_4$), 2·42—3·14 (m,6H, aromatic, H^1, H^2).

[a] All compounds gave satisfactory analytical data.

[b] Procedure A: A solution of (**2**) in absolute methanol at 75—80° (oil bath) is consecutively treated with sodium methoxide and aldehyde and the mixture is heated under nitrogen for 24 h. The solution is concentrated and the product is isolated by chromatography (silica gel). Procedure B: A mixture of (**2**), 1,5-diazabicyclo[4,3,0]non-5-ene, and aldehyde (1 : 1 : 1) in dry tetrahydrofuran or Me$_2$SO is stirred at room temperature overnight and then heated at 75—80° for 1—4 h. Product isolation: in the case of (**3d**), the mixture is diluted with a large excess of water and the product is collected and recrystallized (EtOH); in cases (**3a**), (**3b**), and (**3e**), the solution is concentrated and thoroughly extracted with ether which, in turn, is concentrated and chromatographed; (**3c**) is best isolated by precipitation of its citrate salt from the ethereal extract. Dissolution of the salt in dilute aqueous sodium carbonate and ether extraction gave reasonably pure material.

[c] Recorded in τ values downfield from internal Me$_4$Si with a Varian HA-100 spectrometer and determined in (CD$_3$)$_2$CO with the exception of (**3c**) and (**3e**) which were run in (CD$_3$)$_2$SO.

[d] Exchanged with D$_2$O.

[e] Broad singlet (br s), 1H.

the 330—415 nm region. The Table shows the conditions for the reaction and some physical data of the products. No attempts have been made to maximize the yields.

trans-Geometry is assigned to compounds (**3a**) and (**3b**) on the basis of vinyl proton coupling constants; in other cases, *trans*-assignment is precluded by the complexity of the n.m.r. spectra but is assumed by analogy and on the basis of previous experience with similar reaction conditions.[6,7]

We have also found that (**2**) undergoes an analogous reaction with saturated heterocyclic ketones (*e.g.* *N*-methyl-4-piperidone),[8] and we are examining the photochemical reactivity of compounds (**3a**—**e**) (see ref. 1).

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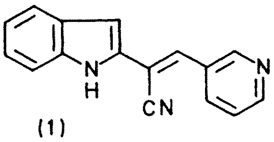
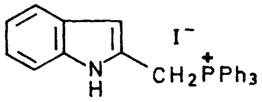


(1)



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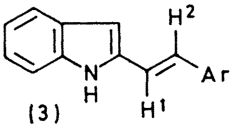

(3)

	Ar
a;	3-pyridyl
b;	2-pyridyl
c;	4-pyridyl
d;	Ph
e;	*p*-$NO_2 \cdot C_6H_4$

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[8] J. A. Eenkhoorn, unpublished data.