

REACTION OF PHENACYLTRIPHENYLARSONIUM BROMIDE WITH AROMATIC PRIMARY AMINES: SYNTHESIS OF 2-ARYLINDOLES AND 2-ARYLBENZINDOLES THROUGH ARSENIC YLIDE *

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Summary

The reaction of phenacyltriphenylarsonium bromide with aromatic primary amines provides a good method for the synthesis of 2-arylindoles and 2-arylbenzindoles through arsenic ylide, and a range of indole and benzindole derivatives have been prepared in good yield.

Introduction

Arsenic ylides have attracted much attention because of their wide applications in synthetic organic chemistry. They have been successfully used in the synthesis of, e.g. olefins [1], cyclopropanes [1,2], isoxazolines [3], pyrones [4], aziridines [2], and a number of other heterocyclics [5]. Studies have been carried out comparing the properties and synthetic utility of arsenic ylides with those of the analogous ylides of other hetero-atoms. Hirose et al. [6] carried out the reaction of *N*-phenacylpyridinium bromide with anilines which led to the formation of 2-phenylindoles. Junjappa [7] extended this reaction to dimethylphenacylsulphonium bromide and prepared several 2-phenylindoles. In these reactions, formation of an ylide intermediate was suggested. As arsenic ylides resemble sulphur ylides in many respects, we studied the reaction of phenacyltriphenylarsonium bromide with a few anilines and reported the synthesis of several 2-phenylindoles in preliminary communication [8]. In contrast to the suggestion by Junjappa [7], our results [8] indicated that the nucleophilic addition of the aniline to the carbonyl group of the salt precedes the formation of the ylide. The latter subsequently undergoes cyclization to furnish the indole.

We now report our full results of the reaction of phenacyl (or substituted

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* Preliminary communication, see ref. 8.

TABLE 1. PHYSICAL CONSTANTS AND ANALYSES FOR THE 2-ARYLBENZINDOLES AND 2-ARYLBENZINDOLES PREPARED

Com- pound	X	R ¹	R ²	M.p. (°C)	Yield (%)	Molecular formulae	Analysis (Found (calcd.)) (%)			IR (cm ⁻¹) ν(N-H) (KBr) [†]	PMR (δ, ppm)
							C	H	N		
IIIa	H	H	H	187 ^a	58	C ₁₄ H ₁₁ N	86.92 (87.01)	5.66 (5.74)	7.02 (7.26)	3405	8.3, b(N-H) 6.95, d(3-H)
IIIb	H	CH ₃	H	117 ^b	63	C ₁₅ H ₁₃ N	86.86 (86.92)	6.30 (6.32)	6.26 (6.76)	3450	8.2, b(N-H) 6.9, d(3-H)
IIIc	H	H	CH ₃	132 ^c	53	C ₁₅ H ₁₃ N	86.92 (86.92)	6.24 (6.32)	6.42 (6.76)	3480	8.2, b(N-H) 6.85, d(3-H)
III d	H	H	Cl	192-194 ^d	51	C ₁₄ H ₁₀ NCl	73.84 (73.55)	4.36 (4.43)	6.02 (6.15)	3410	2.4, s(CH ₃) 7.4, b(N-H)
IIIe	H	NO ₂	H	80	70	C ₁₄ H ₁₀ N ₂ O ₂	70.54 (70.58)	4.22 (4.23)	11.26 (11.76)	3500 (unassociated) 3390 (associated)	6.4, d(3-H) 7.5, q(N-H) 6.3, d(3-H)
III f	H	H	NO ₂	198 ^e	72	C ₁₄ H ₁₀ N ₂ O ₂	70.56 (70.58)	4.16 (4.23)	11.64 (11.76)	3440	7.3, b(N-H) 6.4, d(3-H)
III g	H	Cl	H	112	56	C ₁₄ H ₁₀ NCl	73.92 (73.86)	4.36 (4.43)	6.12 (6.15)	3440	7.4, b(N-H) 6.4, d(3-H)
III h	m-NO ₂	H	H	172 ^f	52	C ₁₄ H ₁₀ N ₂ O ₂	70.56 (70.58)	4.18 (4.23)	11.63 (11.76)	3375	8.3, b(N-H) 6.95, d(3-H)
III i	m-NO ₂	H	Cl	176	60	C ₁₄ H ₉ N ₂ O ₂ Cl	61.62 (61.62)	3.30 (3.30)	10.20 (10.28)	3380	7.4, b(N-H) 6.4, d(3-H)
III j	m-NO ₂	H	NO ₂	180	73	C ₁₄ H ₉ N ₃ O ₄	59.32 (59.37)	3.26 (3.28)	14.71 (14.84)	3380	7.4, b(N-H) 6.35, d(3-H)
III k	m-NO ₂	H	OCH ₃	148	61	C ₁₅ H ₁₂ N ₂ O ₃	67.16 (67.16)	4.47 (4.51)	10.42 (10.44)	3360	8.3, b(N-H) 6.9, d(3-H)
III l	m-NO ₂	NO ₂	H	101	70	C ₁₄ H ₉ N ₃ O ₄	59.30 (59.37)	3.25 (3.28)	14.72 (14.84)	3505 (unassociated) 3380 (associated)	7.6, q(N-H) 6.3, d(3-H)

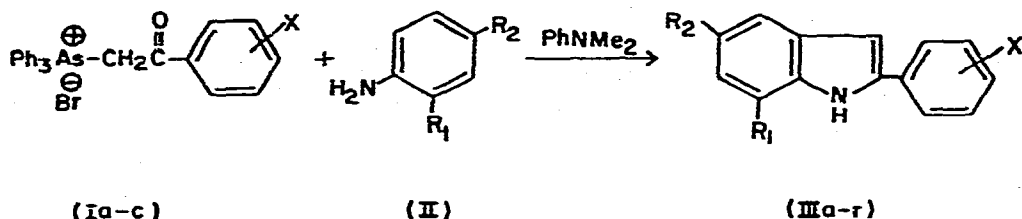
III _m	<i>m</i> -NO ₂	Cl	H	114	58	C ₁₄ H ₉ N ₂ O ₂ Cl	61.62 (61.62)	3.30 (3.30)	10.26 (10.28)	3385	8.2, b(N-H) 6.85, d(3-H)
III _n	<i>p</i> -CH ₃	H	H	219 ^g	63	C ₁₅ H ₁₃ N	86.04 (86.02)	6.26 (6.32)	6.71 (6.76)	3450	8.2, b(N-H) 6.9, d(3-H) 2.4, s(CH ₃)
III _o	<i>p</i> -CH ₃	H	Cl	184	66	C ₁₅ H ₁₂ NCl	74.52 (74.53)	4.91 (5.00)	5.72 (5.79)	3440	8.3, b(N-H) 6.95, q(3-H) 2.5, s(CH ₃)
III _p	<i>p</i> -CH ₃	H	NO ₂	214	69	C ₁₅ H ₁₂ N ₂ O ₂	71.40 (71.42)	4.75 (4.79)	11.09 (11.10)	3410	8.25, b(N-H) 6.85, d(3-H) 2.4, s(CH ₃)
III _q	<i>p</i> -CH ₃	Cl	H	124	52	C ₁₅ H ₁₂ NCl	74.49 (74.53)	4.94 (5.00)	5.76 (5.79)	3400	8.3, b(N-H) 6.95, d(3-H) 2.5, s(CH ₃)
III _r	<i>p</i> -CH ₃	H	CH ₃	142	56	C ₁₆ H ₁₅ N	86.10 (86.12)	7.15 (7.18)	6.66 (6.70)	3410	8.15, b(N-H) 6.85, d(3-H) 2.4, s(CH ₃)
V _a	H	—	—	164 ^h	65	C ₁₈ H ₁₃ N	88.81 (88.86)	5.22 (5.39)	5.70 (5.76)	3410	8.05, q(N-H) 6.55, d(3-H) 8.2, q(N-H)
V _b	<i>m</i> -NO ₂	—	—	196	53	C ₁₈ H ₁₂ N ₂ O ₂	74.98 (74.99)	4.18 (4.20)	6.72 (6.88)	3395	8.2, q(N-H) 6.6, d(3-H) 7.9, q(N-H)
V _c	<i>p</i> -CH ₃	—	—	178 ⁱ	58	C ₁₉ H ₁₅ N	88.70 (88.68)	5.79 (5.88)	5.38 (5.44)	3450	6.65, d(3-H) 2.3, s(CH ₃)
VII _a	H	—	—	132 ^j	61	C ₁₈ H ₁₃ N	88.85 (88.86)	5.20 (5.39)	5.72 (5.76)	3405	7.87, q(N-H) 6.65, d(1-H)
VII _b	<i>m</i> -NO ₂	—	—	217	60	C ₁₈ H ₁₂ N ₂ O ₂	74.98 (74.99)	4.16 (4.20)	6.70 (6.88)	3385	7.8, q(N-H) 6.7, d(1-H)
VII _c	<i>p</i> -CH ₃	—	—	168 ^k	55	C ₁₉ H ₁₅ N	88.72 (88.68)	5.81 (5.88)	5.41 (5.44)	3440	8.15, q(N-H) 6.75, d(1-H) 2.15, s(CH ₃)

^a Lit. [12] 186–188°C, ^b Lit. [6] 118°C, ^c Lit. [6] 195°C, ^d Lit. [6] 194°C, ^e Lit. [13] 201°C, ^f Lit. [14] 173°C, ^g Lit. [15] 221°C, ^h Lit. [16] 166°C, ⁱ Lit. [17] 180°C, ^j Lit. [16] 133°C, ^k Lit. [17] 173°C, ^l b = broad peak; d = doublet; q = quartet; s = singlet.

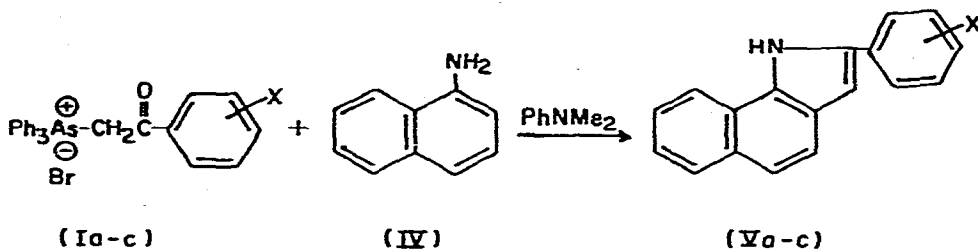
phenacyl) triphenylarsonium bromide with anilines, leading to the formation of 2-arylindoles. Reactions with naphthylamines have also been carried out, and give 2-arylbenzindoles.

Results and discussion

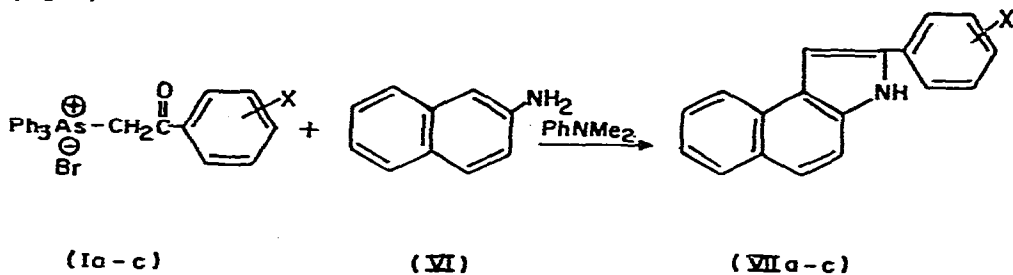
Treating phenacyl (or substituted phenacyl) triphenylarsonium bromide (Ia–c) with various substituted anilines (II) in refluxing *N,N*-dimethylaniline gave corresponding 2-arylindoles (IIIa–IIIr) (eq. 1).



Similar reaction of the arsonium salt (Ia–Ic) with 1-naphthylamine (IV) afforded the corresponding 2-aryl-1*H*-benz[*g*]indole (Va–Vc) (eq. 2).



The reaction of the arsonium salt Ia–Ic with 2-naphthylamine (VI) was also studied. In this case during cyclization the proton could be lost from either the 1- or the 3- position, leading to 2-aryl-3*H*-benz[*e*]indole and 2-aryl-1*H*-benz[*f*]indole, but 2-aryl-3*H*-benz[*e*]indole was the sole product. This is in accordance with the fact that α -proton is more labile than β -proton in naphthylamine (eq. 3).



All the products were characterized on the basis of the elemental analysis, colour test, IR and PMR spectra. All the indoles gave a dark red or violet colour with *p*-(dimethylamino)benzaldehyde and perchloric acid in alcoholic solution,

a characteristic test for the indoles having 3-position unsubstituted [9]. The benzindole derivatives, however, did not give any colour. In IR spectra a sharp peak was usually found in the region $3505\text{--}3360\text{ cm}^{-1}$ which is attributed to N—H stretching frequency [10]. In PMR spectra either a broad unresolved peak or a pair of doublets is observed in the region $\delta\ 7.4\text{--}8.3$ ppm which corresponds to the N-H proton. A doublet centred at $\delta\ 6.3\text{--}7.0$ ppm is attributable to 3-H proton of 2-arylindoles and 2-aryl-1*H*-benz[*g*]indole and 1-H proton of 2-aryl-3*H*-benz[*e*]indole [11].

In this connection mention may be made of 7-nitro-2-phenylindole (IIIe) and 7-nitro-2-(*m*-nitrophenyl)indole (III), which exhibit some unusual properties. The melting points of these compounds (Table 1) are unusually low. In IR, two peaks are observed at 3505 and 3480 cm^{-1} . In PMR spectrum also two sharp peaks of almost equal intensity appear at $\delta\ 7.65$ and 7.5 ppm. All these facts can easily be explained on the basis of intramolecular hydrogen bonding.

Physical data for the 2-arylindoles (IIIa—r) and 2-arylbenzindoles (Va—Vc, VIIa—VIIc) are summarized in Table 1.

Experimental

Melting points are uncorrected. The compounds were purified by recrystallization from an appropriate solvent and their purities checked by thin layer chromatography on silica gel G (solvent, benzene/ethylacetate 1/1; spray reagent 2% ceric sulphate in $2\text{ N H}_2\text{SO}_4$). The IR spectra were recorded on Perkin—Elmer 337 grating IR spectrophotometer in KBr pellet. The PMR spectra were run on Perkin—Elmer RB-12 spectrometer using tetramethylsilane as an internal standard. The spectra of the compounds containing methyl group were recorded in CDCl_3 while the other spectra were determined in Me_2CO .

All the amines were purified either by distillation or by recrystallization. The *N,N*-dimethylamine (B.D.H.), used in the reactions was distilled before use. The arsonium salts were prepared by the method of Johnson et al. [18] as given below.

Preparation of phenacyl (or substituted phenacyl)triphenylarsonium bromide. A mixture of triphenylarsine (20 mmol) and phenacylbromide (or substituted phenacyl bromide) (22 mmol) was refluxed in dry benzene (30 ml) for 4 h. The precipitate of the phenacyltriphenylarsonium bromide was filtered off, washed with benzene, and dried.

Phenacyltriphenylarsonium bromide (Ia), m.p. $183\text{--}184^\circ\text{C}$ (lit. [18] 185°C), $\nu(\text{CO})$ (KBr) 1660 cm^{-1} ; (*m*-nitrophenacyl)triphenylarsonium bromide (Ib), m.p. 196°C , $\nu(\text{CO})$ (KBr) 1670 cm^{-1} ; (*p*-methylphenacyl)triphenylarsonium bromide (Ic), m.p. 165°C , $\nu(\text{CO})$ (KBr) 1660 cm^{-1} .

Reaction of arsonium salt with aromatic primary amine. The following procedure was used throughout. A mixture of arsonium salt (10 mmol) and aromatic primary amine (30 mmol) was refluxed in 50 ml *N,N*-dimethylaniline for 4 h. The mixture was cooled, neutralized with 20% HCl, and extracted with ether. The ether extract was washed with water, dried over anhydrous Na_2SO_4 , and evaporated to give the crude product, which was crystallized from an appropriate solvent to yield the indole.

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