PREPARATION OF 1-(2-BENZIMIDAZOLYL)-2-SUBSTITUTED ETHYLENE DERIVATIVES BY THE WITTIG REACTION

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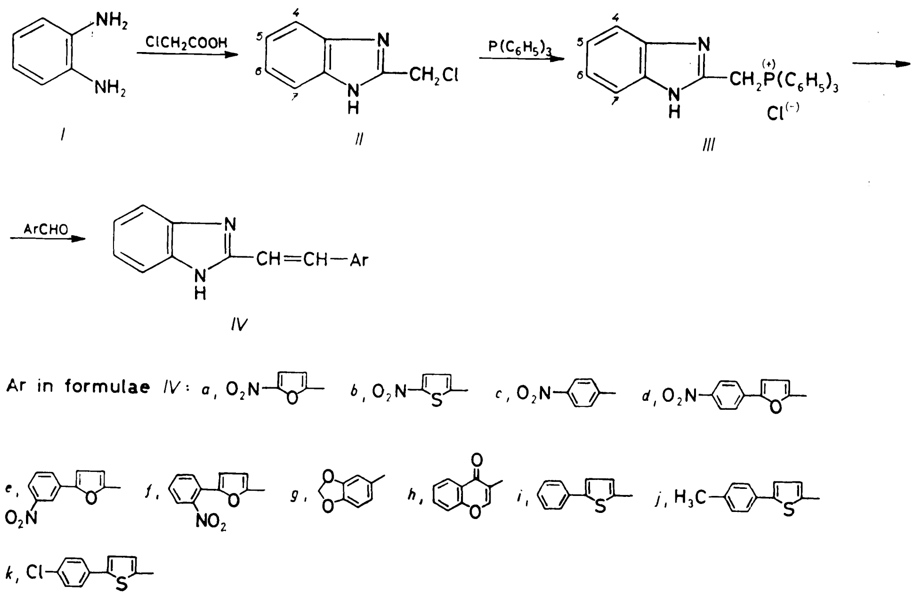
This communication describes the synthesis of new 1-(2-benzimidazolyl)-2-R ethylene derivatives *IVa–IVk* by the Wittig reaction[1], modified according to our previous experience[2,3]. So far, the analogous derivatives were synthesized by condensation reactions of 2-methylbenzimidazole with the corresponding aldehyde[4–7], however, pure products were difficult to obtain. These drawbacks concerning yields as well as the reaction time are removed by our present synthesis.



SCHEME 1

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. ^1H NMR spectra

(300 MHz) (δ, ppm) were taken in FT mode at 28°C with tetramethylsilane as internal standard. IR spectra (cm^{-1}) were measured using the KBr technique. The phosphonium salt *III* was prepared preferably in acetonitrile as solvent. 2-Substituted benzaldehydes (2-NO_2, 2-OH) did not undergo the Wittig reaction even after 2 h in refluxing methanol.

2-Benzimidazolylmethyl Chloride[8] (*II*)

A mixture of *o*-phenylenediamine (*I*) (4·32 g, 0·04 mol), chloroacetic acid (5·67 g, 0·06 mol) and 4M-HCl (40 ml) was refluxed for 3 h. After cooling and neutralization with ammonia, the precipitate was filtered, washed with water and dried. Crystallization from ethanol afforded 6·5 g (97·7%) of compound *II*, m.p. 140—141°C (ref.[8] m.p. 139—140°C). ^1H NMR spectrum (hexadeuteroacetone): 4·94 s, 2 H (CH_2); 7·21 m, 2 H (H_4, H_7); 7·57 m, 2 H (H_5, H_6).

TABLE I
1-(2-Benzimidazolyl)-2-R ethylenic derivatives *IVa*—*IVk*

Compound Yield, %	Formula M.w.	M.p., °C Solvent	Reaction temperature, °C	Calculated/Found		
				% C	% H	% N
IVa	$C_{13}H_9N_3O_3$	272—273	25	61·18	3·55	16·46
80	255·2	ethanol		61·30	3·62	16·58
IVb	$C_{13}H_9N_3SO_2$	193—194	25	57·55	3·34	15·49
32	271·3	ethanml		57·10	3·28	15·36
IVc	$C_{15}H_{11}N_3O_2$	265—266	25	67·91	4·18	15·84
52	265·3	ethanol		68·11	4·23	15·90
IVd	$C_{19}H_{13}N_3O_3$	144—146	40	68·87	3·95	12·68
94	331·3	ethanol		68·66	3·78	12·55
IVe	$C_{19}H_{13}N_3O_3$	212—213	40	68·87	3·95	12·68
67	331·3	ethanol		68·76	3·87	12·60
IVf	$C_{19}H_{13}N_3O_3$	93—95	40	68·87	3·95	12·68
58	331·3	ethanol		68·80	3·90	12·75
IVg	$C_{16}H_{12}N_2O_2$	213—214	40	72·71	4·58	10·60
83	264·3	methanol		72·81	4·67	10·71
IVh	$C_{18}H_{12}N_2O_2$	170—171	25	74·98	4·20	9·72
94	288·3	acetone		75·06	4·30	9·82
IVi	$C_{19}H_{14}N_2S$	226—227	65	75·46	4·66	9·26
60	302·4	methanol		75·52	4·60	9·32
IVj	$C_{20}H_{16}N_2S$	230—231	65	75·91	5·10	8·85
36	316·4	methanol		75·78	5·00	8·76
IVk	$C_{19}H_{13}N_2SCl$	237—238	65	67·74	3·89	8·32
49	336·8	methanol		67·88	3·95	8·43

2-(Triphenylphosphonium Chloride) Benzimidazole (*III*)

A mixture of triphenylphosphine (5·2 g, 0·02 mol), chloride *II* (3·2 g, 0·02 mol) and acetonitrile (25 ml) was refluxed for 3 h. After standing overnight, the reaction mixture deposited a colourless crystalline substance which on crystallization from ethanol (charcoal) afforded 6·5 g (76·5%) of derivative *III*, m.p. 285—287°C. For $C_{26}H_{22}N_2PCl$ (428·9) calculated: 72·81% C, 5·17% H, 6·53% N; found: 72·63% C, 5·12% H, 6·60% N. ^{1}H NMR spectrum (tetradeuteromethanol): 4·90 s, 2 H (CH_2); 7·22 m, 2 H (H_4, H_7); 7·48 bs, 1 H (NH); 7·73 m, 2 H (H_5, H_6); 7·85 m, 5 H (C_6H_5).

Preparation of *IVa*—*IVk*

Methanolic solution of sodium methoxide (0·054 g, 0·001 mol) was added dropwise at 25—65°C (Table I) to a stirred solution of phosphonium salt *III* (0·428 g, 0·001 mol) and the corresponding aldehyde (0·001 mol) (Scheme 1) in dry methanol (3—5 ml) during 1—4 min. After stirring for 10—30 min, the reaction mixture was cooled, the precipitate filtered, washed with cold methanol and dried. Crystallization from ethanol or methanol afforded derivatives *IVa*—*IVk* (Table I). IR spectrum (cm^{-1}) *IVa*: 1 635, 1 572, 1 534, 1 518, 1 507, 1 487, 1 466, 1 412, 1 404, 1 394, 1 359, 1 346, 1 314, 1 279, 1 244, 1 140, 1 018, 961; *IVb*: 1 634, 1 615, 1 587, 1 534, 1 501, 1 422, 1 331, 1 246, 1 229, 1 204, 1 154, 1 119, 1 032, 997; *IVc*: 1 635, 1 597, 1 504, 1 445, 1 416, 1 408, 1 370, 1 341, 1 318, 1 273, 1 231, 1 200, 1 111, 1 022, 976, 957; *IVd*: 1 638, 1 597, 1 537,, 1 510, 1 420, 1 331, 1 277, 1 109, 1 024, 965, 953; *IVe*: 1 640, 1 618, 1 576, 1 526, 1 431, 1 354, 1 315, 1 281, 1 275, 1 263, 1 101, 1 034, 966; *IVf*: 1 638, 1 605, 1 578, 1 524, 1 472, 1 427, 1 360, 1 314, 1 279, 1 236, 1 033, 955; *IVg*: 1 632, 1 624, 1 603, 1 501, 1 485, 1 447, 1 435, 1 350, 1 282, 1 277, 1 256, 1 231, 1 217, 1 096, 1 040, 999, 965; *IVh*: 1 632, 1 601, 1 584, 1 574, 1 539, 1 499, 1 437, 1 393, 1 343, 1 316, 1 285, 1 265, 1 208, 1 138, 1 101, 1 055, 1 030, 990, 945; *IVi*: 1 636; 1 510, 1 456, 1 437, 1 412, 1 379, 1 341, 1 310, 1 275, 1 235, 1 194, 1 115, 1 067, 1 019, 947, 943, *IVj*: 1 636, 1 456, 1 437, 1 412, 1 377, 1 341, 1 310, 1 275, 1 233, 1 192, 1 117, 1 055, 1 013, 955, 951, 943; *IVk*: 1 636, 1 509, 1 487, 1 454, 1 412, 1 377, 1 339, 1 310, 1 277, 1 271, 1 233, 1 190 1 117, 1 100, 1 053, 1 011, 955, 951, 943.

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