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PHASE TRANSFER CATALYZED SYNTHESIS OF 1-ARYLOXYACETYL-2-SUBSTITUTED-BENZIMIDAZOLE DERIVATIVES

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Abstract: The title compounds (3) were prepared in good to excellent yield via the reaction of aryloxyacetyl chloride with 2-substituted benzimidazole (2) under the condition of solid-liquid phase transfer catalysis using polyethylene glycol-400 as the catalyst.

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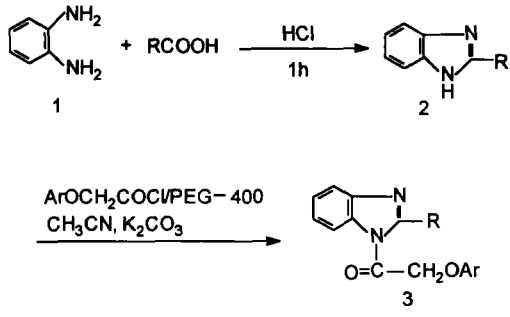

Scheme 1

Aryloxyacetic acids and their derivatives usually possess many important biological activities. Some of them are used as herbicides' and plant-growth regulators[2]. Benzimidazole derivatives are also associated with various kinds of biological activities [3-5]. In view of these observations and in continuation of our earlier work on the synthesis of plant-growth regulators[6-9]. We report herein a facile and convenient procedure for the preparation of 1-aryloxyacetyl-2-substituted benzimidazole derivatives (3) under the condition of solid-liquid phase transfer catalysis using polyethylene glycol-400(PEG-400) as the catalyst.

The reaction sequence leading to the formation of the title compound (3) is shown in scheme 1. 1,2-Phenylenediamine reacted with aryloxyacetic acid and formic acid to give the corresponding benzimidazoles (2). Under solid-liquid phase transfer conditions, using anhydrous potassium carbonate as base and PEG-400 as the catalyst, 2-substituted benzimidazole (2) reacted with aryloxyacetyl chloride in acetonitrile to yield 1-aryloxyacetyl-2-substituted benzimidazole derivatives (3) in good to excellent yield.

A survey of literature revealed that some reports are on record for the synthesis of 1-acylbenzimidazoles [10-15]. However, most of them are patents and detailed experimental procedures are not accessible. Acylation by the Schotten-Baumann procedure results in the formation of diacyl derivatives of the corresponding 1,2-phenylenediamines, due to the cleavage of the imidazole ring; only small amounts of 1-acylbenzimidazole derivatives are formed by this method[10].

Phase transfer catalysis is one of the most attractive techniques in organic synthesis, however, the use of PTC for N-acylation reactions is much less common. Illi has used PTC to acylate indole[16]. Mathias has reported N-acylation reactions under inverse phase transfer catalysis conditon[17]. In recent years, we have focused our attention to PTC N-acylation reactions and obtained good results[6,7]. We have found that solid-liquid phase transfer catalysis offers an attractive alternative for the preparation of the title compounds (3). The advantages are mild reaction conditions, simple operation, short reaction times and high yield.

Experimental

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded in KBr on an Alpha Centauri FT-IR spectrophotometer (ν max in cm^{-1}) and PMR spectra on a FT-80A instrument using $CDCl_3$ as solvent and TMS as internal reference (chemical shifts in ppm). Microanalyses were obtained with PE-2400 CHN instrument.

2-Substituted benzimidazoles were prepared by condensation of 1.2-phenylenediamine with formic acid and aryloxyacetic acid in the presence of hydrochloric acid, according to a previously reported procedure[18]. The known

Table1. Preparation of 1-aryloxyacetyl-2-substituted benzimidazoles (3)

Compd	R	Ar	m.p. ℃	yield %	Mol.formula	Found C	(%) H	(Calc.) N
3a	H	C_6H_5	122-123	84	$C_{15}H_{12}N_2O_2$	71.33	4.58	11.23
						(71.41	4.79	11.11)
3b	H	4-$CH_3C_6H_4$	125-126	85	$C_{16}H_{14}N_2O_2$	72.28	5.21	10.71
						(72.16	5.30	10.52)
3c	H	4-ClC_6H_4	150-151	81	$C_{15}H_{11}ClN_2O_2$	62.59	3.62	9.56
						(62.83	3.87	9.77)
3d	$C_6H_5OCH_2$	C_6H_5	103-104	82	$C_{22}H_{18}N_2O_3$	73.86	5.21	7.75
						(73.72	5.06	7.81)
3e	$C_6H_5OCH_2$	4-ClC_6H_4	117-118	80	$C_{22}H_{17}ClN_2O_3$	67.38	4.52	7.25
						(67.26	4.36	7.13)
3f	2,4-$Cl_2C_6H_3OCH_2$	C_6H_5	164-165	78	$C_{22}H_{16}Cl_2N_2O_3$	61.59	3.85	6.73
						(61.84	3.77	6.56)
3g	2,4-$Cl_2C_6H_3OCH_2$	4-$CH_3C_6H_4$	174-175	85	$C_{23}H_{18}Cl_2N_2O_3$	62.47	4.32	6.14
						(62.60	4.11	6.35)
3h	2.4-$Cl_2C_6H_3OCH_2$	4-ClC_6H_4	153-154	83	$C_{22}H_{15}Cl_3N_2O_3$	57.45	3.38	6.15
						(57.23	3.27	6.07)
3i	2,4,5-$Cl_3C_6H_2OCH_2$	4-$CH_3C_6H_4$	164-165	82	$C_{23}H_{17}Cl_3N_2O_3$	58.21	3.53	5.73
						(58.06	3.60	5.89)
3j	2,4,5-$Cl_3C_6H_2OCH_2$	4-ClC_6H_4	173-174	80	$C_{22}H_{14}Cl_4N_2O_3$	53.38	2.92	5.61
						(53.25	2.84	5.65)

aryloxyacetic acids and aryloxyacetyl chlorides were obtained by the procedure of Wei[6].

General procedure of the preparation of 1-aryloxyacetyl-2-substituted benzimidazole: Powdered anhydrous potassium carbonate (2.76 g, 20 mmol),

Table 2. IR and PMR spectra data of Compounds (3)

Compd.	IR(ν_{max} cm^{-1}) C=O	PMR (δ ,ppm)		
		Ar-H	CH_2	CH_3
3a	1748	6.78-7.58 (m,10H)	5.28(s,2H)	
3b	1736	6.83-7.61 (m,9H)	5.12(s,2H)	2.23(s,3H)
3c	1742	6.72-7.68 (m,9H)	5.25(s,2H)	
3d	1745	6.66-7.88 (m,14H)	5.35(s,2H) 5.56(s,2H)	
3e	1745	6.71-7.86 (m,13H)	5.34(s,2H) 5.55(s,2H)	
3f	1748	6.81-7.89 (m,12H)	5.36(s,2H) 5.58(s,2H)	
3g	1742	6.68-7.85 (m,11H	5.35(s,2H) 5.46(s,2H)	2.33(s,3H)
3h	1743	6.75-7.86 (m,10H)	5.32(s,2H) 5.58(s,2H)	
3i	1745	6.68-7.92 (m,10H)	5.36(s,2H) 5.56(s,2H)	2.31(s,2H)
3j	1747	6.73-7.96 (m,10H)	5.35(s,2H) 5.58(s,2H	

aryloxyacetyl chloride (10 mmol), PEG-400(0.12 g, 0.3 mmol), 2-substituted benzimidazole (10 mmol) and acetonitrile (20 ml) were placed in a dried round-bottomed flask containing a magnetic stirrer bar and stirred at room temperature for 2 h. The precipitate is filtered off, and the filtrate is evaporated under reduced pressure. The 1-aryloxyacetyl-2-substituted benzimidazole (3) thus obtained is recrystallized from pet. ether.

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