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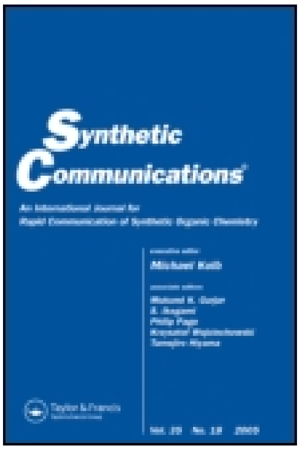

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N-ALKYLATION OF 2,4,5-TRIPHENYL IMIDAZOLE DERIVATIVES USING A NEW PHASE TRANSFER REAGENT UNDER PTC CONDITIONS

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N-ALKYLATION OF 2,4,5-TRIPHENYL IMIDAZOLE DERIVATIVES USING A NEW PHASE TRANSFER REAGENT UNDER PTC CONDITIONS

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ABSTRACT

The phase transfer catalyzed *N*-alkylation of 2,4,5-triphenyl imidazole derivatives using a new phase transfer reagent namely, 2-benzilidine-N,N,N,N′,N′,N′-hexaethyl propane-1,3-diammonium dibromide have been described. The structures of all the 14 compounds have been established by spectroscopic means.

Phase transfer catalysis (PTC) is presently well recognized as a general methodology for promoting reactions between water-soluble reagents and water-insoluble organic substrates.[1–3] The advances of the same in the recent years have made a remarkable impact in organic synthesis and are being enormously employed in a multitude of organic transformations. The primary advantages of PTC in organic syntheses are high product yield,

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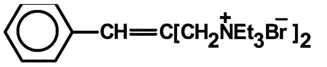
*Corresponding author.

large reaction rates, and high selectivity of the desired products. The main principle in PTC involves the continuous formation of a lipophilic ion-pair of an anionic reactant with a lipophilic cation such a tetraalkyl-ammonium ion and the transport of the anionic reactant from the aqueous phase into the organic phase where it effectively reacts with a second reactant.

N-alkylation of aromatic compounds involving nitrogen heterocycles are important reactions in organic syntheses. Conventional procedures insist the use of polar aprotic solvents under strictly anhydrous conditions.[4] *N*-alkylation of nitrogen heterocycles namely, indole and pyrrole can also be achieved by using various bases such as sodium amide, potassium, sodium hydroxide in hexamethylphosphoric triamide, KOH in DMSO and thallium(I) ethoxide.[5–9] Makosza[10] synthesised *N*-alkylindoles and *N*-butylcarbazole under PTC conditions. The advantages of performing *N*-alkylation under base-catalyzed PTC conditions coupled with the importance of *N*-alkylation in pharmaceuticals, agricultural, chemical, and other products have led *N*-alkylation to be among the most widely used applications of PTC.

We have synthesized and characterized a novel phase transfer reagent, namely, 2-benzilidine-N,N,N,N′,N′,N′-hexaethylpropane-1,3-diammonium dibromide (Dq–Br) and studied its utility in simple dichlorocarbene addition to olefins[11] and in the synthesis of 2-mercaptobenzimidazole derivatives.[12]



Dq-Br

Acetophenone, when reacted with excess aqueous formaldehyde in the presence of CaO at 60°C gave 1-phenyl-2,4,8,10-tetraoxaspiro[5.5] undecane (1). The spiro compound 1 was brominated by refluxing with hydrobromic acid (48% solution) resulting in the formation of dibromocompound 2. The compound 2 was quaternised with excess triethylamine using dry acetonitrile as a solvent under reflux to yield the desired Diquat, Dq–Br. It was found to be highly hygroscopic. The structures were confirmed by spectroscopic means. A detailed procedure for the synthesis of the Diquat, Dq–Br is reported elsewhere.[11]

Control experiments of dichlorocarbene addition to olefins in the absence of the catalyst resulted in 1% conversion in 3 h. Preliminary studies[17,18] on the catalytic abilities of the new Diquat, Dq–Br, revealed its synthetic utility under PTC/OH^- conditions. Control experiments in the preparation of 2-mercaptobenzimidazole derivatives in the absence of the catalyst under specified conditions proceed with low conversions. High yields of products were obtained using the new Diquat, Dq–Br.

In continuation of our studies related to the utility of a new phase transfer reagent, we report *N*-alkylation of 2,4,5-triphenyl imidazole derivatives using the new phase transfer reagent (Dq–Br) under PTC conditions.

EXPERIMENTAL

General: ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a BRUKER-AM-400 NMR spectrometer with TMS as an internal standard. Mass spectra were obtained on a JEOL JMS-100 mass spectrometer at ionization potential, 12 eV. The infrared spectra were measured on a PERKIN-ELMER model 983 IR spectrometer. Liquid chromatography was carried out using Shimadzu LC-9A instrument.

General Procedure for the *N*-Alkylation of 2,4,5-Triphenyl Imidazole Derivatives

A 150 ml cm^3 three-necked round bottomed flask fitted with double walled condenser was charged with 100 mg of 2,4,5-triphenyl imidazole derivative (the different imidazole derivatives were prepared according to the reported procedures) dissolved in 20 cm^3 dichloromethane, 45 cm^3 w/w NaOH and 10 mol% Dq–Br (based on the substrate amount). The contents were conditioned for 10 min with thermostat maintained at 50°C. Alkyl halide (*n*-butyl bromide/ethyl bromide/allyl bromide = 10 mL) was added to the reaction vessel and stirred for 5 h at 500 rpm. Samples were withdrawn from the organic layer at regular intervals of time and were analyzed using HPLC model LC 9A (Shimadzu) having an absorbance detector (254 nm, SPD-6A) and column, Merck RP-8 (5 μm). The eluent was acetonitrile/water = 50 : 50 with flow rate 1.2 ml/min. To the cold reaction, ether (30 mL) was added, washed repeatedly with deionized water and dried over anhydrous magnesium sulfate. The excess, low boiling alkyl bromides were also removed. The compound was purified using silica gel column chromatography. The spectral properties were in agreement with the expected products.

SPECTRAL DATA

1-Butyl-2-(4′-methoxyphenyl)-4,5-diphenyl Imidazole (1)

^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 7.8–7.0$ (m, 14H, Aromatic), 3.85 (s, 3H, -OCH$_3$), 3.8 (t, 2H, -NCH$_2$), 1.3–1.2 (m, 2H, -CH$_2$), 0.98–0.94

Table 1. *N*-Alkylations of Triphenyl Imidazole Derivatives under PTC Conditions

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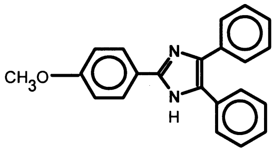
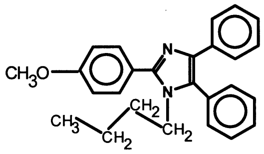
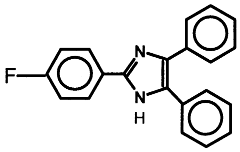
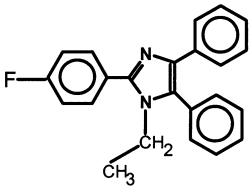
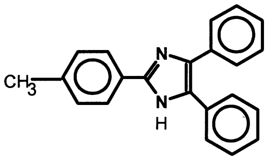
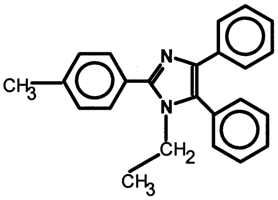
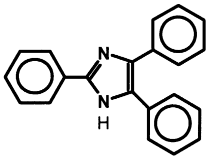
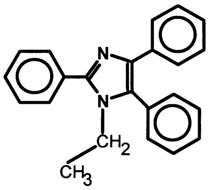
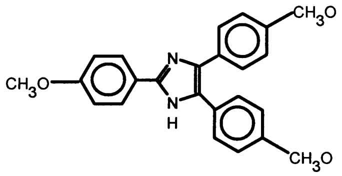
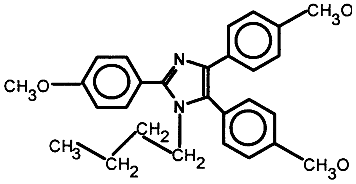
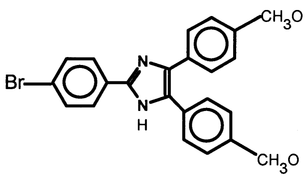
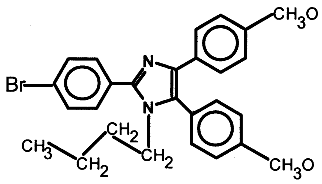
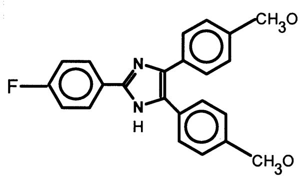
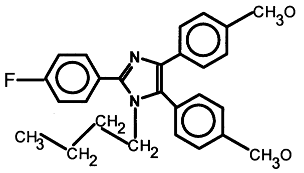
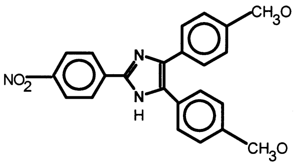
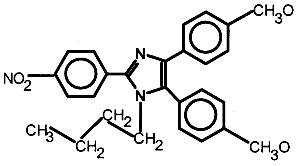
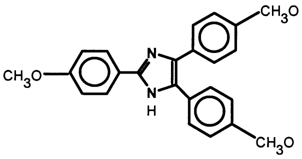
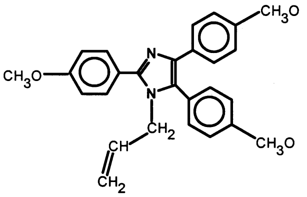
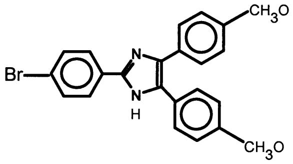
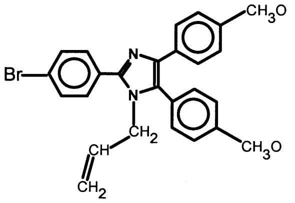
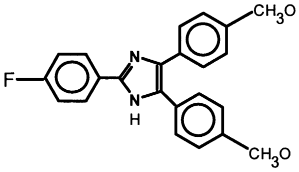
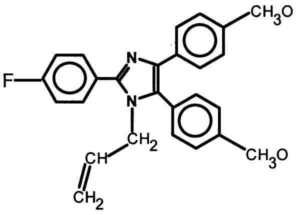
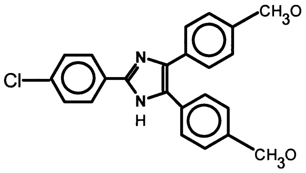
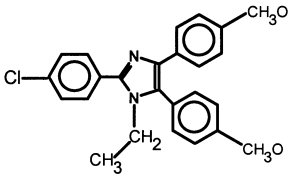
1			87
2			90
3			89
4			88
5			77
6			80

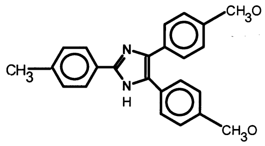
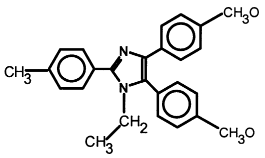
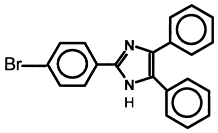
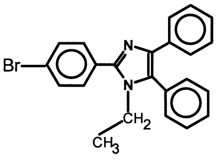
(*continued*)

Table 1. Continued

S. No.	Substrate	Product	% Conv.[a]
7			82
8			79
9			78
10			80
11			85
12			83

(*continued*)

Table 1. Continued

S. No.	Substrate	Product	% Conv.[a]
13			80
14			87

[a]% conversion by HPLC.

(m, 2H, -CH_2), 0.6 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2950, 1612, 1475, 1250, 1188, 1038, 838. MS (m/z): 384 (M^+, 45), 383 (100), 382 (77), 381 (8), 353 (13), 105 (9). HRMS: m/z, Calculated: 382.5055, Found: 382.5039.

1-Ethyl-2-(4′-fluorophenyl)-4,5-diphenyl Imidazole (2)

^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.8$–7.1 (m, 14H, Aromatic), 3.9 (q, 2H, -CH_2), 1.0 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2981, 1728, 1653, 1480, 1270, 1118, 647. MS (m/z): 371 (M^+, 17), 344 (43), 343 (100), 342 (100), 342 (66), 341 (13), 313 (6), 165 (8), 104 (6). HRMS: m/z, Calculated: 370.4695, Found: 370.4087.

1-Ethyl-2-(4′-methylphenyl)-4,5-diphenyl Imidazole (3)

^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.8$–7.0 (m, 14H, Aromatic), 3.9 (q, 2H, -CH_2), 2.4 (s, 3H, -CH_3), 1.0 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2990, 1600, 1480, 1381, 1070, 960, 829. MS (m/z): 367 (M^+, 4), 340 (26), 339 (100), 338 (100), 338 (48), 337 (10), 309 (4), 165 (7), 118 (4), 104 (5), 91 (4), 77 (4). HRMS: m/z, Calculated: 367.5085, Found: 367.4982.

1-Ethyl-2,4,5-triphenyl Imidazole (4)

^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.8$–7.0 (m, 15H, Aromatic), 4.0 (q, 2H, -CH_2), 1.0 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2974, 1891, 1600, 1444, 1272, 1072, 849, 741. MS (*m*/*z*): 326 (M^+, 24), 325 (100), 324 (44), 323 (8), 295 (4), 178 (3), 104 (8), 89 (3). HRMS: *m*/*z*, Calculated: 324.4253, Found: 324.4171.

1-Butyl-2,4,5-*tris*(*p*-methoxyphenyl) Imidazole (5)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.8$–6.9 (m, 12H, Aromatic), 3.85 (s, 3H, -OCH_3), 3.83 (s, 3H, -OCH_3), 3.80 (t, 2H, -CH_2), 3.70 (s, 3H, -OCH_3), 1.3 (m, 2H, -CH_2), 1.0 (m, 2H, -CH_2), 0.6 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2980, 1887, 1725, 1612, 1450, 1225, 1025, 825. MS (*m*/*z*): 444 (M^+, 34), 443 (100), 442 (75), 44 (9), 413 (6), 386 (5), 135 (12), 134 (15), 105 (6), 57 (9). HRMS: *m*/*z*, Calculated: 442.5585, Found: 442.5310.

1-Butyl-2-(4′-bromophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (6)

^{1}H NMR (400 MHz, $CDCl_3$): 7.9–6.8 (m, 12H, Aromatic), 3.86 (s, 3H, -OCH_3), 3.81 (t, 2H, -CH_2), 3.75 (s, 3H, -OCH_3), 1.3 (m, 2H, -CH_2), 0.91 (m, 2H, -CH_2), 0.6 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2985, 1700, 1600, 1475, 1237, 1012, 825. MS (*m*/*z*): 494 (M^+, 27), 493 (98), 492 (74), 491 (74), 491 (100), 490 (49), 443 (8), 184 (8), 154 (32), 137 (15), 135 (65), 107 (11), 105 (12), 77 (12), 57 (8). HRMS: *m*/*z*, Calculated: 491.4281, Found: 491.4111.

1-Butyl-2-(4′-fluorophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (7)

^{1}H NMR (400 MHz, $CDCl_3$): 7.8–6.8 (m, 12H, Aromatic), 3.9 (s, 3H, -OCH_3), 3.80 (t, 2H, -CH_2), 3.75 (s, 3H, -OCH_3), 1.30 (m, 2H, -CH_2), 0.9 (m, 2H, -CH_2), 0.6 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2990, 1737, 1612, 1462, 1250, 1162, 1050, 838. MS (*m*/*z*): 432 (M^+, 27), 431 (100), 430 (74), 401 (4), 374 (5), 135 (23), 122 (9). HRMS: *m*/*z*, Calculated: 430.5225, Found: 430.5089.

1-Butyl-2-(4′-nitrophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (8)

^{1}H NMR (400 MHz, $CDCl_3$): 8.2–6.8 (m, 12H, Aromatic), 3.95 (t, 2H, -CH_2), 3.90 (s, 3H, -OCH_3), 3.73 (s, 3H, -OCH_3), 1.3 (m, 2H, -CH_2), 1.0 (m, 2H, -CH_2), 0.6 (t, 3H, -CH_3). ν_{max}/cm^{-1}: 2992, 1712, 1612, 1275, 1150, 1037,

812. MS (m/z): 459 (M^+, 29), 458 (100), 457 (71), 442 (14), 412 (10), 356 (5), 135 (13), 77 (5), 57 (12). HRMS: m/z, Calculated: 457.5300, Found: 457.5079.

1-Allyl-2,4,5-*tris*(*p*-methoxyphenyl) Imidazole (9)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.0$–6.8 (m, 12H, Aromatic), 5.15–4.90 (m, 3H, $-CH{=}CH_2$), 3.84 (m, 2H, $-CH_2$), 3.82 (s, 3H, $-OCH_3$), 3.79 (s, 3H, $-OCH_3$), 3.70 (s, 3H, $-OCH_3$). ν_{max}/cm^{-1}: 2995, 1725, 1615, 1512, 1262, 1038, 850. MS (m/z): 427 (M^+, 36), 386 (27), 293 (7), 192 (5), 136 (13), 135 (100), 105 (11), 91 (11), 81 (10), 57 (28), 41 (35). HRMS: m/z, Calculated: 426.5157, Found: 426.4991.

1-Allyl-2-(4′-bromophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (10)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.0$–6.6 (m, 12H, Aromatic), 5.21–4.89 (m, 3H, $-CH{=}CH_2$), 3.81 (s, 3H, $-OCH_3$), 3.79 (m, 2H, $-CH_2$), 3.71 (s, 3H, $-OCH_3$). ν_{max}/cm^{-1}: 2992, 1712, 1600, 1512, 1263, 1025, 825. MS (m/z): 475 (M^+, 77), 435 (23), 280 (5), 183 (19), 135 (100), 115 (10), 105 (16), 91 (12), 77 (19), 41 (36). HRMS: m/z, Calculated: 475.3853, Found: 475.3096.

1-Allyl-2-(4′-fluorophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (11)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.2$–6.71 (m, 12H, Aromatic), 5.27–4.79 (m, 3H, $-CH{=}CH_2$), 3.84 (s, 3H, $-OCH_3$), 3.80 (m, 2H, $-CH_2$), 3.77 (s, 3H, $-OCH_3$). ν_{max}/cm^{-1}: 2995, 1737, 1612, 1512, 1262, 1050, 837. MS (m/z): 416 (M^+, 31), 415 (100), 414 (58), 375 (19), 374 (45), 373 (16), 359 (9), 281 (9), 135 (68), 123 (46), 105 (15), 77 (13), 41 (28). HRMS: m/z, Calculated: 414.4797, Found: 414.4675.

1-Ethyl-2-(4′-chlorophenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (12)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.0$–6.9 (m, 12H, Aromatic), 3.85 (s, 3H, $-OCH_3$), 3.84 (s, 3H, $-OCH_3$), 3.72 (q, 2H, $-CH_2$), 1.0 (t, 3H, $-CH_3$). ν_{max}/cm^{-1}: 2838, 1722, 1656, 1599, 1225, 1017, 832. MS (m/z): 418 (M^+, 60), 415 (100), 389 (5), 299 (13), 271 (18), 162 (12), 135 (79). HRMS: *m*/*z*, Calculated: 418.9230, Found: 418.9012.

1-Ethyl-2-(4′-methylphenyl)-4,5-*bis*(*p*-methoxyphenyl) Imidazole (13)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.55$–6.71 (m, 12H, Aromatic), 3.87 (s, 3H, $-OCH_3$), 3.83 (q, 2H, $-CH_2$), 3.71 (s, 3H, $-OCH_3$), 2.38 (s, 3H, $-CH_3$), 0.97 (t, 3H, $-CH_3$). ν_{max}/cm^{-1}: 2987, 1738, 1612, 1487, 1250, 1100, 825. MS (*m*/*z*): 400 (M^+, 28), 399 (100), 398 (68), 369 (5), 134 (6), 91 (5), 69 (6), 57 (8). HRMS: *m*/*z*, Calculated: 398.5015, Found: 398.4989.

1-Ethyl-2-(4′-bromophenyl)-4,5-diphenyl Imidazole (14)

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.90$–7.28 (m, 14H, Aromatic), 3.87 (q, 2H, $-CH_2$), 1.1 (t, 3H, $-CH_3$). ν_{max}/cm^{-1}: 2977, 1731, 1676, 1476, 1238, 1179, 1072, 833. MS (*m*/*z*): 431 (M^+, 34), 403 (100), 325 (14), 211 (13), 178 (7), 165 (19), 105 (40), 77 (15), 57 (8). HRMS: *m*/*z*, Calculated: 431.3751, Found: 431.3114.

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