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Heterocyclization, Dyeing Applications and Anticancer Evaluations of Benzimidazole Derivatives: Novel Synthesis of Thiophene, Triazole and Pyrimidine Derivatives

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A NUMBER of novel hydrazono benzimidazole, thiophene, triazole and pyrimidine derivatives were prepared and their dyeing properties evaluated. The newly synthesized compounds based on 1-(1*H*-benzimidazol-2-yl)-propan-2-one 3. The reactivity of compound 3 towards different chemical reagents was studied. The structure of the synthesized compounds was established based on elemental analysis and spectral data. Dyes were applied at 1% and 3% depth for disperse dyeing of (nylon 6 + polyester) and polyester fabrics. Their spectral characteristics and fastness properties were measured and evaluated. On the other hand, the anticancer activity of some of the newly synthesized compounds was studied and evaluated. Compounds 5a, 9b, 14b and 17c revealed higher effect when screened *in vitro* against some human cancer cell lines than the reference CHS 828.

Keywords: Benzimidazole, Thiophene, Triazole, Pyrimidine, Dyeing, Textile finishing and Anticancer.

Benzimidazole systems play important role in medical field with so many pharmacological activities such as antimicrobial[1-3], antioxidant[4], antiviral[5,6], anti-inflammatory[7], anti-diabetic[8] and anticancer activity[9-11]. The potency of these clinically useful drugs in treatment of microbial infections and other activities encouraged the development of some more potent and significant compounds. In recent years, attention has increasingly been given to the synthesis of benzimidazole derivatives. The synthesis of novel benzimidazole derivatives remains a main focus of medicinal research[12]. On the other hand, compounds with azo moiety and benzimidazole moiety have been extensively used as dyes, but biological activity is less reported[13]. Hence the goal of the present study was to prepare novel benzimidazole derivatives that incorporated

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different heterocycles of anticancer activity and hydrazono derivatives of fastness properties applications on the dyed fabrics.

Experimental

General

All melting points were determined on an Electrothermal digital melting point apparatus and are uncorrected. Infrared (IR) spectra (KBr discs) were recorded on a FTIR plus 460 or Pye Unicam SP-1000 spectro-photometer. Proton nuclear magnetic resonance (^{1}H NMR) spectra were recorded with Varian Gemini-200 (200 MHz) (Cairo University) instrument in dimethyl sulfoxide (DMSO-d6) as solvent using tetramethylsilane (TMS) as internal standard and chemical shifts are expressed as δ ppm. The mass spectra were recorded with Hewlett Packard 5988 A Gas Chromatograph Mass Spectrometer (GC/MS) system and GCMS-QP 1000 Ex Shimadzu instruments. Analytical data were obtained from the Micro-analytical Data Unit at Cairo University and were performed on Vario EL III Elemental CHNS analyzer. The dyeing operation was carried out using ATAC LAB. DYEHT-HT 10 apparatus. Colour strength (K/S) of the dyed samples was measured by using OPTIMATCH 3100. The colour fastness to washing was determined using Launder-ometer. Colour fastness to rubbing was determined using Crock-Meter Type FD II and colour fastness to perspiration was determined using Perspiration Tester.

Chemistry

Synthesis of 1-(1H-benzimidazol-2-yl)-propan-2-one (3)

Equimolar amounts of ethyl acetoacetate 1 (1.30 g, 0.01 mol) and *o*-phenylenediamine 2 (1.08 g, 0.01 mol) was fused in an oil bath at 120 ^{o}C for about 20 min. The solid product formed upon pouring onto ice/water mixture was collected by filtration, washed with water and crystallized from ethanol.

Offwhite crystals, m.p. 110–113 °C, yield: 1.39 g (80%); Anal. Calcd. for $C_{10}H_{10}N_2O$ (174.20): C, 68.95; H, 5.79; N, 16.08. Found: C, 69.10; H, 5.97; N, 15.76. IR (υ, cm^{-1}): 3372-3136 (NH), 3065-3012 (CH aromatic), 2952-2832 (CH_2, CH_3), 1696 (C=O), 1617, 1477 (C=C); ^{1}H NMR (δ, ppm): 2.50 (s, 3H, CH_3), 3.73(s, 2H, CH_2), 7.02-7.42 (m, 4H, C_6H_4), 10.90 (s, 1H, NH); MS *m/z* (%): 174 [M$^+$] (100.00), 76 [C6H4]$^+$ (7.90).

Synthesis of 1H-benzimidazol-2-yl derivatives (5a-b)(General procedure)

To a solution of compound 3 (1.74 g, 0.01 mol) in ammonium acetate, either malononitrile 4a (0.66 g, 0.01 mol) or ethyl cyanoacetate (4b) (1.13 g, 0.01 mol) was added. The reaction mixture was fused under reflux at 120 ^{o}C for about 15 min. The reaction mixture was then boiled in ethanol (20 ml) for few minutes then cooled by pouring onto ice/water mixture. The solid product formed in each case was collected by filtration and crystallized from ethanol.

2-[2-(1H-Benzimidazol-2-yl)-1-methyl-ethylidene]-malononitrile (5a): Faint offwhite crystals, m.p. over 300 °C, yield: 1.44 g (65%); Anal. Calcd. for

$C_{13}H_{10}N_4$ (222.25): C, 70.26; H, 4.54; N, 25.21. Found: C, 69.81; H, 4.10; N, 24.80. IR (υ, cm^{-1}): 3225-3125 (NH), 3021 (CH aromatic), 2905-2807 (CH_2, CH_3), 2200, 2192 (2CN), 1629, 1480 (C=C); ^{1}H NMR (δ, ppm): 2.53 (s, 3H, CH_3), 3.47 (s, 2H, CH_2), 6.93-6.99 (m, 4H, C_6H_4), 10.60 (s, 1H, NH); MS *m/z* (%): 223 [M^++1] (8.90), 222 [M^+] (4.40), 134 (100.00).

4-(1H-Benzimidazol-2-yl)-2-cyano-3-methyl-but-2-enoic acid ethyl ester (5b): Faint offwhite crystals, m.p. over 300 °C, yield: 1.72 g (64%); Anal. Calcd. for $C_{15}H_{15}N_3O_2$ (269.30): C, 66.90; H, 5.61; N, 15.60. Found: C, 66.50; H, 5.30; N, 15.20. IR (υ, cm^{-1}): 3450-3355 (NH), 3128-3024 (CH aromatic), 2906-2807 (CH_2, CH_3), 2200 (CN), 1736 (C=O), 1633, 1478 (C=C); ^{1}H NMR (δ, ppm): 1.90 (s, 3H, CH_3), 2.50 (t, 3H, CH_3), 3.50 (s, 2H, CH_2), 4.50 (q, 2H, CH_2), 6.91-6.92 (m, 4H, C_6H_4), 10.54 (s, 1H, NH); MS *m/z* (%): 270 [M^++1] (0.04), 269 [M^+] (0.11), 268 [M^+-1] (0.08), 134 (100.00).

Synthesis of 3-(1H-benzimidazol-2-yl)-4-phenyl-pent-3-en-2-one (7)

Equimolar amounts of 3 (1.74 g, 0.01 mol) and acetophenone (6) (1.20 g, 0.01 mol) in ammonium acetate was fused under reflux at 120 ^{o}C for about 1hr. The reaction mixture was then boiled in ethanol (20 ml) for few minutes, poured onto ice/water mixture. The crude product was precipitated, collected by filtration and crystallized from ethanol.

Brown crystals, m.p. 294-296 °C, yield: 1.74 g (63%); Anal. Calcd. for $C_{18}H_{16}N_2O$ (276.33): C, 78.24; H, 5.84; N, 10.14. Found: C, 77.84; H, 5.44; N, 9.80. IR (υ, cm^{-1}): 3349-3124 (NH), 3023 (CH aromatic), 2905-2806 ($2CH_3$), 1735 (C=O), 1634, 1480 (C=C); ^{1}H NMR (δ, ppm): 1.90 (s, 3H, CH_3), 2.50 (s, 3H, CH_3), 6.91-7.41 (m, 9H, C_6H_4, C_6H_5), 10.58 (s, 1H, NH); MS *m/z* (%): 277 [M^++1] (11.25), 276 [M^+] (7.41), 275 [M^+-1] (10.70), 274 [M^+-2] (7.82), 134 (100.00), 77 $[C_6H_5]^+$ (99.73).

Synthesis of 1-(1H-benzimidazol-2-yl)-1-hydrazono-propan-2-one derivatives (9a-d) (General procedure)

To a cold solution (0-5 °C) of 3 (1.74 g, 0.01 mol), in ethanol (20 ml) containing sodium acetate (1.00 g), an equimolar amount of diazotized aniline (8a) (0.93 ml, 0.01 mol), diazotized *p*-chloroaniline (8b) (1.27 ml, 0.01 mol), diazotized *p*-methoxyaniline (8c) (1.23 ml, 0.01 mol) and diazotized *p*-toluidene (8d) (1.07 ml, 0.01 mol) [which was prepared by adding $NaNO_2$ (0.7 g, 0.01 mol) solution to a cold solution of aniline, *p*-chloroaniline, *p*-methoxyaniline and *p*-toluidene in concentrated hydrochloric acid (5 ml)] were gradually added while stirring. The solid products formed upon cooling in an ice-bath were collected by filtration, washed with water and crystallized from ethanol.

1-(1H-Benzimidazol-2-yl)-1-(phenyl-hydrazono)-propan-2-one (9a): Yellow crystals, m.p. 179-182 °C, yield: 1.81 g (65%); Anal. Calcd. for $C_{16}H_{14}N_4O$ (278.31): C, 69.05; H, 5.07; N, 20.13. Found: C, 68.70; H, 5.37; N, 19.80. IR (υ, cm^{-1}): 3370-3179 (2NH), 3067-3015 (CH aromatic), 2955-2821 (CH_3), 1696 (C=O), 1630, 1478 (C=C); ^{1}H NMR (δ, ppm): 2.50 (s, 3H, CH_3), 6.91-7.08 (m, 9H,

C_6H_4, C_6H_5), 10.53 (s, 1H, NH), 10.93 (s, 1H, NH); MS *m/z* (%): 279 [M^++1] (4.24), 278 [M^+] (4.38), 134 (100.00), 77 [C_6H_5]$^+$ (12.71), 76 [C_6H_4]$^+$ (6.28).

1- (1H-Benzimidazol-2-yl)-1- [(4-chloro-phenyl)- hydrazono]- propan-2- one (9b): Faint Orange crystals, m.p. 106-108 °C, yield: 1.88 g (60%); Anal. Calcd. for $C_{16}H_{13}N_4OCl$ (312.75): C, 61.44; H, 4.19; N, 17.91. Found: C, 61.84; H, 4.40; N, 17.60. IR (υ, cm^{-1}): 3430-3134 (2NH), 3068-3017 (CH aromatic), 2904-2823 (CH_3), 1695 (C=O), 1600, 1479 (C=C); ^{1}H NMR (δ, ppm): 2.50 (s, 3H, CH_3), 6.91-7.07 (m, 8H, $2C_6H_4$), 10.58 (s, 1H, NH), 10.97 (s, 1H, NH); MS *m/z* (%): 314 [M^++1] (42.86), 313 [M^+] (50.00), 312 [M^+-1] (50.00), 311 [M^+-2] (60.32), 130 (100.00).

1-(1H-Benzimidazol-2-yl)-1-[(4-methoxy-phenyl)-hydrazono]-propan-2- one (9c): Faint orange crystals, m.p. 137-140 °C, yield: 1.85 g (60%); Anal. Calcd. for $C_{17}H_{16}N_4O_2$ (308.33): C, 66.22; H, 5.23; N, 18.17. Found: C, 66.62; H, 5.56; N, 17.80. IR (υ, cm^{-1}): 3372-3136 (2NH), 3067-3013 (CH aromatic), 2953-2831 (CH_3), 1696 (C=O), 1600, 1477 (C=C); ^{1}H NMR (δ, ppm): 2.50 (s, 3H, CH_3), 3.34 (s, 3H, CH_3), 6.99-7.08 (m, 8H, $2C_6H_4$), 10.50 (s, 1H, NH), 10.97 (s, 1H, NH); MS *m/z* (%): 310 [M^++2] (24.68), 309 [M^++1] (32.90), 308 [M^+] (30.74), 76 [C_6H_4]$^+$ (41.13), 69 (100.00).

1-(1H-Benzimidazol-2-yl)-1-(p-tolyl-hydrazono]-propan-2-one (9d): Orange crystals, m.p. 123-2125 °C, yield: 1.90 g (65%); Anal. Calcd. for $C_{17}H_{16}N_4O$ (292.34): C, 69.85; H, 5.52; N, 19.17. Found: C, 69.45; H, 5.39; N, 18.80. IR (υ, cm^{-1}): 3372-3136 (2NH), 3066-3012 (CH aromatic), 2953-2830 ($2CH_3$), 1696 (C=O), 1610, 1477 (C=C); ^{1}H NMR (δ, ppm): 2.49 (s, 3H, CH_3), 3.29 (s, 3H, CH_3), 6.98-7.08 (m, 8H, $2C_6H_4$), 7.09 (s, 1H, NH), 10.93 (s, 1H, NH); MS *m/z* (%): 294 [M^++2] (18.80), 60 (100.00).

Synthesis of 1-(1H-benzimidazol-2-yl)-3-bromo-propan-2-one (10)

To a solution of compound 3 (1.74 g, 0.01 mol) in acetic acid (30 ml), bromine (0.50 g, 0.01 mol) was added. The reaction mixture was heated at 60 ^{o}C for about 15 min and then cooled by pouring onto ice/water mixture. The solid product formed was collected by filtration and crystallized from acetic acid.

White crystals, m.p. over 300 °C, yield: 1.52 g (60%); Anal. Calcd. for $C_{10}H_9N_2OBr$ (253.10): C, 47.46; H, 3.58; N, 11.07. Found: C, 47.10; H, 3.20; N, 11.40. IR (υ, cm^{-1}): 3420-3176 (NH), 3019 (CH aromatic), 2908-2807 (CH_2), 1746 (C=O), 1580, 1480 (C=C); ^{1}H NMR (δ, ppm): 3.90 (s, 2H, CH_2), 4.70 (s, 2H, CH_2), 6.85-7.22 (m, 4H, C_6H_4), 10.53 (s, 1H, NH); MS *m/z* (%): 253 [M^+] (0.22), 252 [M^+-1] (0.12), 251 [M^+-2] (0.27), 134 (100.00), 76 [C_6H_4]$^+$ (8.23).

Synthesis of 5-(2-1H-benzimidazol-2-yl-acetyl)-2-phenylamino-thiophene-3-carbonitrile derivatives (12a,b) and 1-(4-acetyl-5-phenyl-amino-thiophen-2-yl)-2-(1H-benzimidazol-2-yl)-ethanone derivatives (12c,d)(General procedure)

Equimolar amount of 10 (2.53 g, 0.01 mol) and phenyl isothiocyanate (11) (1.35 g, 0.01 mol) in dimethylformamide (20 ml) and potassium hydroxide were

stirred overnight. Malononitrile (4a) (o.66 g, 0.01 mol), ethyl cyanoacetate (4b) (1.13 g, 0.01 mol), acetylacetone (4c) (1.00 g, 0.01 mol) or ethyl acetoacetate (1) (1.30 g, 0.01 mol) were then added to the reaction mixture while stirring overnight. The solid products formed upon pouring onto ice/water mixture containing few drops of hydrochloric acid were collected by filtration and crystallized from 1,4-dioxane.

4- Amino-5- (2-1H -benzimidazol-2-yl-acetyl) -2- phenylamino- thiophene -3-carbonitrile (12a): Faint brown crystals, m.p. over 300 °C, yield: 2.61 g (70%); Anal. Calcd. for $C_{20}H_{15}N_5OS$ (373.43): C, 64.33; H, 4.05; N, 18.75; S, 8.59. Found: C, 63.93; H, 3.70; N, 18.40; S, 8.20. IR (υ, cm^{-1}): 3427-3169 (NH, NH_2), 3064 (CH aromatic), 2992-2844 (CH_2), 2205 (CN), 1698 (C=O), 1541, 1478 (C=C); ^{1}H NMR (δ, ppm): 3.38 (s, 2H, NH_2), 4.50 (s, 2H, CH_2), 6.85-7.44 (m, 9H, C_6H_4, C_6H_5), 10.77 (s, 1H, NH), 10.92 (s, 1H, NH); MS *m/z* (%): 374 [M^++1] (0.24), 373 [M^+] (0.89), 372 [M^+-1] (0.38), 77 $[C_6H_5]^+$ (58.71), 76 $[C_6H_4]^+$ (92.92), 50 (100.00).

5-(2-1H-Benzimidazol-2-yl-acetyl) -4- hydroxy-2- phenylamino-thiophene -3-carbonitrile (12b): Brown crystals, m.p. over 300 °C, yield: 2.62 g (70%); Anal. Calcd. for $C_{20}H_{14}N_4O_2S$ (374.42): C, 64.16; H, 3.77; N, 14.96; S, 8.56. Found: C, 63.82; H, 3.37; N, 14.60; S, 8.20. IR (υ, cm^{-1}): 3428-3168 (2NH, OH), 3067 (CH aromatic), 2840 (CH_2), 2205 (CN), 1695 (C=O), 1600, 1477 (C=C); ^{1}H NMR (δ, ppm): 4.20 (s, 2H, CH_2), 6.85-7.44 (m, 9H, C_6H_4, C_6H_5), 10.60 (s, 1H, NH), 10.77 (s, 1H, NH), 10.92 (s, 1H, OH); MS *m/z* (%): 376 [M^++1] (1.80), 374 [M^+] (100.00), 373 [M^+-1] (63.96), 77 $[C_6H_5]^+$ (31.53). 76 $[C_6H_4]^+$ (9.91).

1-(4-Acetyl-3- methyl-5-phenylamino-thiophen-2-yl)-2- (1H-benz-imidazol-2-yl)-ethanone (12c): Brown crystals, m.p. over 300 °C, yield: 2.53 g (65%); Anal. Calcd. for $C_{22}H_{19}N_3O_2S$ (389.47): C, 67.84; H, 4.92; N, 10.79; S, 8.23. Found: C, 67.50; H, 4.61; N, 10.43; S, 7.83. IR (υ, cm^{-1}): 3421-3123 (2NH), 3064 (CH aromatic), 2923-2853 (CH_2, $2CH_3$), 1701 (C=O), 1609, 1477 (C=C); ^{1}H NMR (δ, ppm): 1.22 (s, 3H, CH_3), 2.73 (s, 3H, CH_3), 4.00 (s, 2H, CH_2), 6.85-7.48 (m, 9H, C_6H_4, C_6H_5), 10.78 (s, 1H, NH), 10.92 (s, 1H, NH); MS *m/z* (%): 390 [M^++1] (1.46), 389 [M^+] (2.12), 388 [M^+-1] (1.46), 77 $[C_6H_5]^+$ (100.00), 76 $[C_6H_4]^+$ (49.29).

*1-(4-Acetyl-3-hydroxy-5-phenylamino-thiophen-2-yl)-2-(1H-benz-imidazol-2-yl)-ethanone (12d):*Yellowish white crystals, m.p. over 300 °C, yield: 2.54 g (65%); Anal. Calcd. for $C_{21}H_{17}N_3O_3S$ (391.44): C, 64.43; H, 4.38; N, 10.73; S, 8.19. Found: C, 64.11; H, 4.00; N, 10.33; S, 7.84. IR (υ, cm^{-1}): 3418-3171 (2NH, OH), 3012 (CH aromatic), 2900 (CH_2, CH_3), 1744, 1701 (2C=O), 1533, 1477 (C=C); ^{1}H NMR (δ, ppm): 2.60 (s, 3H, CH_3), 4.15 (s, 2H, CH_2), 6.85-7.81 (m, 9H, C_6H_4, C_6H_5), 10.77 (s, 1H, NH), 10.92 (s, 1H, NH), 11.69 (s, 1H, OH); MS *m/z* (%): 393 [M^++2] (7.60), 392 [M^++1] (9.33), 391 [M^+] (10.93), 77 $[C_6H_5]^+$ (26.93), 76 $[C_6H_4]^+$ (10.93), 69 (100.00).

Synthesis of (1H-benzimidazol-2-yl)-acetonitrile (13)

The data of compound 13 has been published earlier [14].

Synthesis of 1H-benzimidazol-2-yl-hydrazono-acetonitrile derivatives (14a-d) (General procedure)

To a cold solution (0-5 °C) of 13 (1.57 g, 0.01 mol), in ethanol (20 ml) containing sodium acetate (1.00 g) an equimolar amount of diazotized aniline (8a) (0.93 ml, 0.01 mol), diazotized *p*-chloroaniline (8b) (1.27 ml, 0.01 mol), diazotized *p*-methoxyaniline (8c) (1.23 ml, 0.01 mol) and diazotized *p*-toluidene (8d) (1.07 ml, 0.01 mol) [which was prepared by adding $NaNO_2$ (0.7 g, 0.01 mol) solution to a cold solution of aniline, *p*-chloroaniline, *p*-methoxyaniline and *p*-toluidene in concentrated hydrochloric acid (5 ml)] were gradually added while stirring. The solid products formed upon cooling in an ice-bath were collected by filtration, washed with water and crystallized from ethanol.

(1H-Benzimidazol-2-yl)-(phenyl-hydrazono)-acetonitrile (14a): Faint orange crystals, m.p. 285-290 °C, yield: 1.96 g (75%); Anal. Calcd. for $C_{15}H_{11}N_5$ (261.28): C, 68.95; H, 4.24; N, 26.80. Found: C, 68.55; H, 3.88; N, 26.40. IR (υ, cm^{-1}): 3407-3229 (2NH), 3050 (CH aromatic), 2219 (CN), 1611, 1480 (C=C), 1540 (=N-NH); ^{1}H NMR (δ, ppm): 7.26-7.72 (m, 9H, C_6H_4, C_6H_5), 10.50 (s, 1H, NH), 12.00 (s, 1H, NH); MS *m/z* (%): 262 [M^++1] (14.65), 261 [M^+] (16.34), 77 $[C_6H_5]^+$ (35.49), 76 $[C_6H_4]^+$ (27.32), 55 (100.00).

(1H- Benzimidazol -2-yl)-[(4- chloro -phenyl)- hydrazono)-acetonitrile (14b): Orange crystals, m.p. over 300 °C, yield: 1.92 g (65%); Anal. Calcd. for $C_{15}H_{10}N_5Cl$ (295.73): C, 60.92; H, 3.41; N, 23.68. Found: C, 60.53; H, 3.01; N, 23.29. IR (υ, cm^{-1}): 3271 (2NH), 3052 (CH aromatic), 2221 (CN), 1596, 1484 (C=C),1546(=N-NH); ^{1}H NMR (δ, ppm): 7.09-7.72 (m, 8H, $2C_6H_4$), 12.70 (s, 1H, NH), 14.63 (s, 1H, NH); MS *m/z* (%): 296 [M^+] (32.47), 295 [M^+-1] (44.33), 80 (100.00), 76 $[C_6H_4]^+$ (31.96).

(1H-Benzimidazol-2-yl)-[(4-methoxy-phenyl)-hydrazono)-acetonitrile (14c):

Deep red crystals, m.p. 237-240 °C, yield: 1.92 g (66%); Anal. Calcd. for $C_{16}H_{13}N_5O$ (291.31): C, 65.97; H, 4.50; N, 24.04. Found: C, 65.58; H, 4.20; N, 23.73. IR (υ, cm^{-1}): 3246 (2NH), 3046 (CH aromatic), 2916-2830 (CH_3), 2219 (CN), 1599, 1478 (C=C), 1556 (=N-NH); ^{1}H NMR (δ, ppm): 3.30 (s, 3H, CH_3), 6.97-7.80 (m, 8H, $2C_6H_4$), 11.69 (s, 1H, NH), 12.70 (s, 1H, NH); MS *m/z* (%): 293 [M^++2] (1.81), 292 [M^++1] (15.60), 291 [M^+] (72.90), 107 (100.00), 76 $[C_6H_4]^+$ (9.48).

(1H-Benzimidazol-2-yl)-(p-tolyl-hydrazono)-acetonitrile (14d): Dark orange crystals, m.p. 237-240 °C, yield: 1.93 g (70%); Anal. Calcd. for $C_{16}H_{13}N_5$ (275.31): C, 69.80; H, 4.76; N, 25.44. Found: C, 69.44; H, 4.37; N, 25.10. IR (υ, cm^{-1}): 3257 (2NH), 3050 (CH aromatic), 2917 (CH_3), 2217 (CN), 1603, 1486 (C=C), 1543 (=N-NH); ^{1}H NMR (δ, ppm): 2.31 (s, 3H, CH_3), 7.17-7.82 (m, 8H, $2C_6H_4$), 11.69 (s, 1H, NH), 12.72 (s, 1H, NH); MS *m/z* (%): 277 [M^++2] (1.17), 276 [M^++1] (8.37), 275 [M^+] (39.65), 274 [M^+-1] (2.69), 91 (100.00), 76 $[C_6H_4]^+$ (5.42).

Synthesis of 5-(1H-benzimidazol-2-yl)-2H-[1,2,3]triazol-4-yl-amine derivatives (16a-d) (General procedure)

To a solution of compounds 14a (2.61 g, 0.01 mol), 14b (2.95 g, 0.01 mol), 14c (2.91 g, 0.01 mol) or 14d (2.75 g, 0.01 mol) in ethanol (25 ml) and dimethylformamide (10 ml), hydrazine hydrate (15) (0.50 g, 0.01 mol) was added. The reaction mixture, in each case, was heated under reflux for 5 hr. The solid product formed, in each case, upon pouring onto ice/water mixture was collected by filtration, and crystallized from ethanol/dimethylformamide mixture.

5- (1H- Benzimidazol -2- yl) -2- phenyl -2H- [1,2,3] triazol -4- ylamine(16a): Yellow crystals, m.p. 295-300 °C, yield: 2.10 g (76%); Anal. Calcd. for $C_{12}H_{12}N_6$ (276.30): C, 65.21; H, 4.38; N, 30.42. Found: C, 64.82; H, 3.98; N, 30.10. IR (υ, cm^{-1}): 3299-3107 (NH, NH_2), 3058 (CH aromatic), 1596, 1482 (C=C); ^{1}H NMR (δ, ppm): 3.50 (s, 2H, NH_2), 7.23-7.85 (m, 9H, C_6H_4, C_6H_5), 11.86 (s, 1H, NH); MS *m/z* (%): 277 [M^++1] (20.50), 276 [M^+] (22.66), 274 [M^+-2] (19.42), 230 (100.00), 77 $[C_6H_5]^+$ (6.12).

5- (1H- Benzimidazol -2- yl) -2- (4- chloro-phenyl) -2H- [1,2,3] triazol -4-ylamine (16b): Yellow crystals, m.p. over 300 °C, yield: 2.36 g (76%); Anal. Calcd. for $C_{15}H_{11}N_6Cl$ (310.74): C, 57.98; H, 3.57; N, 27.05. Found: C, 57.58; H, 3.20; N, 26.70. IR (υ, cm^{-1}): 3400-3276 (NH, NH_2), 3054 (CH aromatic), 1597, 1485 (C=C); ^{1}H NMR (δ, ppm): 3.50 (s, 2H, NH_2), 7.06-7.85 (m, 8H, $2C_6H_4$), 11.75 (s, 1H, NH); MS *m/z* (%): 309 [M^+-2] (0.70), 77 (100.00).

5-(1H- Benzimidazol-2-yl)-2-(4-chloro-phenyl)-2H-[1,2,3]triazol-4-ylamine (16c): Orange crystals, m.p. 275-280 °C, yield: 2.91 g (95%); Anal. Calcd. for $C_{16}H_{14}N_6O$ (306.32): C, 62.74; H, 4.61; N, 27.44. Found: C, 62.35; H, 4.21; N, 27.04. IR (υ, cm^{-1}): 3427-3249 (NH, NH_2), 3050 (CH aromatic), 2913-2831 (CH_3), 1554, 1479 (C=C); ^{1}H NMR (δ, ppm): 3.31 (s, 3H, CH_3), 3.84 (s, 2H, NH_2), 6.97-7.83 (m, 8H, $2C_6H_4$), 11.69 (s, 1H, NH); MS *m/z* (%): 307 [M^++1] (10.84), 306 [M^+] (14.07), 76 $[C_6H_4]^+$ (11.03) 57 (100.00).

5-(1H-Benzimidazol-2-yl)-2-p-tolyl-2H-[1,2,3]triazol-4-ylamine (16d): Faint orange crystals, m.p. 265-270 °C, yield: 2.73 g (94%); Anal. Calcd. for $C_{16}H_{14}N_6$ (290.32): C, 66.19; H, 4.86; N, 28.95. Found: C, 65.87; H, 4.48; N, 28.56. IR (υ, cm^{-1}): 3424-3261 (NH, NH_2), 3026 (CH aromatic), 2913 (CH_3), 1604, 1482 (C=C); ^{1}H NMR (δ, ppm): 1.30 (s, 3H, CH_3), 3.30 (s, 2H, NH_2), 7.19-7.84 (m, 8H, $2C_6H_4$), 11.69 (s, 1H, NH); MS *m/z* (%): 289 [M^+-1] (20.60), 290 [M^+] (12.70), 291 [M^++1] (6.30), 76 $[C_6H_4]^+$ (25.40).

Synthesis of 3-imino-2-phenyl-hydrazono-3,4-dihydro-2H-benzo[4,5]-imidazo [1,2-c] pyrimidine-1-thione derivatives (17a-d)(General procedure)

Equimolar amounts of 14a (2.61 g, 0.01 mol), 14b (2.95 g, 0.01 mol), 14c (2.91 g, 0.01 mol) or 14d (2.75 g, 0.01 mol) containing triethylamine in ethanol (25 ml) and dimethylformamide (10 ml), phenyl isothiocyanate (11) (1.35 g, 0.01

mol) was added. The reaction mixture, in each case, was heated under reflux for 5 hr, then cooled and neutralized by pouring onto ice/water mixture containing few drops of hydrochloric acid. The solid product formed in each case was collected by filtration and crystallized from ethanol/dimethylformamide mixture.

3- Imino -2- phenyl -4- (phenyl - hydrazono) -3,4- dihydro -2H- benzo [4,5]-imidazo[1,2-c]pyrimidine-1-thione (17a): Orange crystals, m.p. 271-276 °C, yield: 3.17 g (80%); Anal. Calcd. for $C_{22}H_{16}N_6S$ (396.47): C, 66.65; H, 4.07; N, 21.20; S, 8.09. Found: C, 66.30; H, 3.70; N, 20.90; S, 7.70. IR (υ, cm^{-1}): 3455-3116 (2NH), 3046 (CH aromatic), 1596, 1493 (C=C), 1546 (=N-NH), 1331, 1289 (C=S); ^{1}H NMR (δ, ppm): 7.06-7.85 (m, 14H, C_6H_4, $2C_6H_5$), 11.03 (s, 1H, NH), 11.75 (s, 1H, NH); MS *m/z* (%): 398 [M^++2] (81.82), 397 [M^++1] (59.09), 396 [M^+] (54.55), 181 (100.00), 77 $[C_6H_5]^+$ (2.73) 76 $[C_6H_4]^+$ (20.91).

4-[(4-Chloro-phenyl)-hydrazono]-3-imino-2-phenyl-3,4-dihydro-2H-benzo [4,5] imidazo [1,2-c]pyrimidine-1-thione (17b): Faint brown crystals, m.p. over 300 °C, yield: 3.02 g (70%); Anal. Calcd. for $C_{22}H_{15}N_6SCl$ (430.91): C, 61.32; H, 3.51; N, 19.50; S, 7.44. Found: C, 60.98; H, 3.11; N, 19.14; S, 7.11. IR (υ, cm^{-1}): 3423-3268 (2NH), 3050 (CH aromatic), 1596, 1480 (C=C), 1545 (=N-NH), 1414, 1283 (C=S); ^{1}H NMR (δ, ppm): 7.13-7.90 (m, 13H, $2C_6H_4$, C_6H_5), 11.02 (s, 1H, NH), 11.83 (s, 1H, NH); MS *m/z* (%): 432 [M^++1] (1.83), 431 [M^+] (9.65), 111 (100.00), 77 $[C_6H_5]^+$ (32.78) 76 $[C_6H_4]^+$ (25.62).

3-Imino-4-[(4-methoxy-phenyl)-hydrazono]-2-phenyl -3,4-dihydro-2H- benzo [4,5]imidazo[1,2-c]pyrimidine-1-thione (17c): Dark yellow crystals, m.p. 252-254 °C, yield: 3.07 g (72%); Anal. Calcd. for $C_{23}H_{18}N_6OS$ (426.49): C, 64.77; H, 4.25; N, 19.70; S, 7.52. Found: C, 64.40; H, 3.90; N, 19.34; S, 7.13. IR (υ, cm^{-1}): 3426-3249 (2NH), 3044 (CH aromatic), 2916-2830 (CH_3), 1599, 1479 (C=C), 1556 (=N-NH), 1304, 1240 (C=S); ^{1}H NMR (δ, ppm): 3.30 (s, 3H, CH_3); 6.96-7.82 (m, 13H, $2C_6H_4$, C_6H_5), 11.68 (s, 1H, NH), 12.70 (s, 1H, NH); MS *m/z* (%): 428 [M^++2] (15.52), 427 [M^++1] (10.92), 426 [M^+] (9.05), 425 [M^+-1] (7.47), 424 [M^+-2] (9.34), 80 (100.00), 77 $[C_6H_5]^+$ (2.16).

3-Imino-2-phenyl-4-(p-tolyl- hydrazono)-3,4-dihydro-2H-benzo[4,5]-imidazo [1,2-c]pyrimidine-1-thione (17d): Faint orange crystals, m.p. 230-235 °C, yield: 3.07 g (72%); Anal. Calcd. for $C_{23}H_{18}N_6S$ (410.49): C, 67.30; H, 4.42; N, 20.47; S, 7.81. Found: C, 66.90; H, 4.10; N, 20.10; S, 7.41. IR (υ, cm^{-1}): 3434-3259 (2NH), 3029 (CH aromatic), 2915 (CH_3), 1604, 1482 (C=C), 1550 (=N-NH), 1294, 1244 (C=S); ^{1}H NMR (δ, ppm): 1.34 (s, 3H, CH_3); 7.14-7.84 (m, 13H, $2C_6H_4$, C_6H_5), 11.02 (s, 1H, NH), 11.69 (s, 1H, NH); MS *m/z* (%): 411 [M^++1] (17.80), 410 [M^+] (50.85), 186 (100.00).

Colour assessment and dyeing properties

Dyeing procedure

Unless otherwise indicated, dyeing was performed using a solution containing 1% and 3% dye (based on weight of sample), 2 g/L dispersing agent

and ammonium per sulphate at 130 °C for 30 min. A material to liquor ratio 1:20 was used. The dye solution was adjusted at pH = 4.5-5 using acetic acid. After the end of dyeing time, the fabric sample was washed in a solution containing 5 g/L detergent for several times until a clear solution was obtained. Finally the fabric sample was rinsed with water and dried at ambient conditions. The colour of the dyes on (nylon 6 + polyester) and polyester fibers is indicated[15] (Table 1).

Colour strength

Colour strength of the dyed samples expressed as (K/S) was measured at λ_{max}= 400 nm (Table 1).

Fastness properties

The colour fastness to washing, rubbing (dry and wet crocking) and perspiration was determined according to the standard method[16]. Data are indicated in Table 1.

Colour fastness to washing

The composite specimens were sewed between two pieces of bleached cotton fabric and then immersed into an aqueous solution containing 5g/L soap non-ionic detergents at liquor ratio 50:1 and 2g/L sodium carbonate. The bath was thermostatically adjusted to 90 °C for 30 min; then samples were removed, rinsed twice with occasional hand squeezing, then dried. Evaluation of the wash fastness was established using the Grey-scale for colour change (Table 1).

Colour fastness to rubbing

The test is designed for determining the degree of colour, which may transfer from the surface of the coloured fabric to another surface, by rubbing.

Dry crocking test: The test specimen was placed flat on the base of the crock-meter. A white testing cloth was mounted. The covered finger was lowered on to the test specimen and caused to slide 20 times back and forth by making ten complete turns at a rate of one turn/sec. The white test sample was then removed for evaluation using the Grey-scale for staining.

Wet crocking test: The white test sample was thoroughly wetted out in water to a 65% and then picked up. The procedure was run as above. The white test samples were air dried before evaluation.

Colour fastness to perspiration

Two artificial perspiration solutions were prepared according to the following:

Acidic solution: L-Histidine monohydrochloride monohydrate (0.5g), sodium chloride (5 g) and sodium dihydrogen phosphate-1-hydrate (2.2g) were dissolved in 1 L distilled water. The pH was adjusted to 5.5 by 0.1N sodium hydroxide solution.

Alkaline solution: L-Histidine monohydrochloride monohydrate (0.5 g), sodium chloride (5 g) and di-sodium hydrogen phosphate-2-hydrate (2.5 g) were

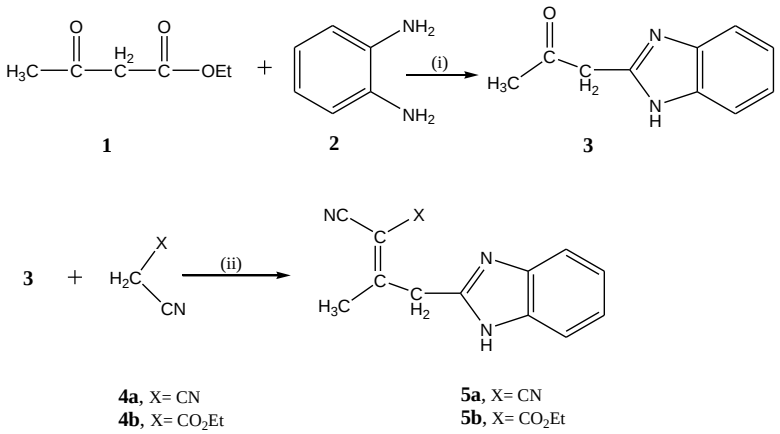
dissolved in 1 L distilled water. The pH was adjusted to 8 by 0.1N sodium hydroxide solution. The coloured specimen was sewed between two pieces of bleached cotton specimen. The composite sample was then immersed for 30 min in the acidic perspiration solution at 37 °C (± 2) with occasional agitation and squeezing to insure complete wetting. The test specimen was placed between two plastic plates under a force of about 5 Kg. The plates containing the composite specimens were left for about 6-8 hr. The same experiment was followed with another composite sample using the alkaline perspiration solution. The effect on the colour of the test specimen was expressed and defined by reference to Grey-scale for colour change.

Results and Discussion

Chemistry

The reaction of ethyl acetoacetate (1) with *o*-phenylenediamine (2) in an oil bath at 120 °C gave the 1-(1*H*-benzimidazol-2-yl)-propan-2-one 3. The structure of compound 3 was established on the basis of analytical and spectral data. Thus, the ^{1}H NMR spectrum which showed singlet at δ 2.50 ppm for CH_3 group, at δ 3.73 ppm for CH_2 group, multiplets at δ 7.02-7.42 for C_6H_4 moiety and singlet at δ 10.90 ppm for NH group.

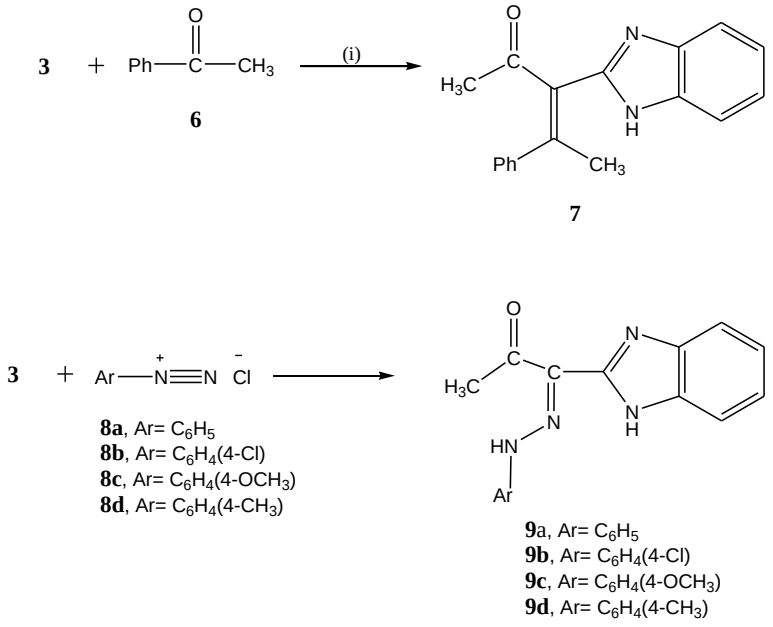
The reactivity of compound 3 towards some chemical reagents was studied. Thus the reaction of compound 3 with either malononitrile (4a) or ethyl cyanoacetate (4b) in ammonium acetate at 120 °C gave the Knoevenagel condensation products 5a and 5b, respectively. The analytical and spectral data are in agreement with the assigned structures (see experimental section). On the other hand, the reaction of compound 3 with acetophenone (6) in sodium acetate at 120 °C gave the condensation product 7.



(i) Fusion 120 °C
(ii) Ammonium acetate/Fusion 120 °C

Scheme 1.

Next we moved towards studying the reactivity of compound 3 with diazonium salts namely benzenediazonium chloride (8a), 4-chlorobenzenediazonium chloride (8b), 4-mehoxybenzenediazonium chloride (8c) and 4-methylbenzenediazonium chloride (8d). The reaction occurred in ethanolic/sodium acetate solution at 0-5 ^{o}C to give the arylhydrazone derivatives 9a, 9b, 9c or 9d, respectively.



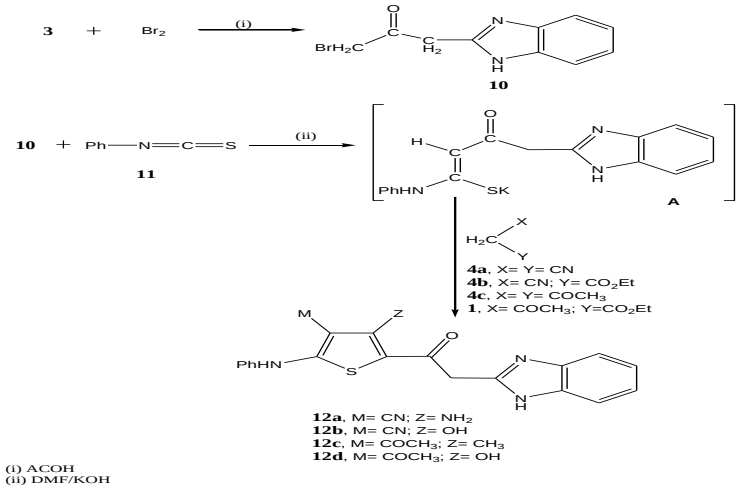
(i) Ammonium acetate/Fusion

Scheme 2.

The reaction of compound 3 with bromine in acetic acid at 60 ^{o}C gave the corresponding α-bromoketone (10). The structure of compound 10 was based on analytical and spectral data. Thus, the ^{1}H NMR spectrum revealed singlet at δ 3.90 ppm for CH_2 group, at δ 4.70 ppm for CH_2, multiplets at δ 6.85-7.22 ppm for C_6H_4 moiety and at δ 10.53 ppm for NH group. The mass spectrum showed [M^+] at *m/z*= 253 corresponding to the molecular formula $C_{10}H_9N_2OBr$.

Recently our research group was involved through a series of reactions through which active methylene reagents react with phenylisothiocyanate (11) in basic dimethylformamide at room temperature to give the non isolable potassium salts (A). The latter reacts with α-halocarbonyl compounds (4a-d) to give either thiophene or thiazole derivatives depending on the nature of the halocarbonyl compound used as well as the conditions of the reactions. The excellent yield of compound 10 encouraged us to use it as the α-bromocarbonyl compound in such

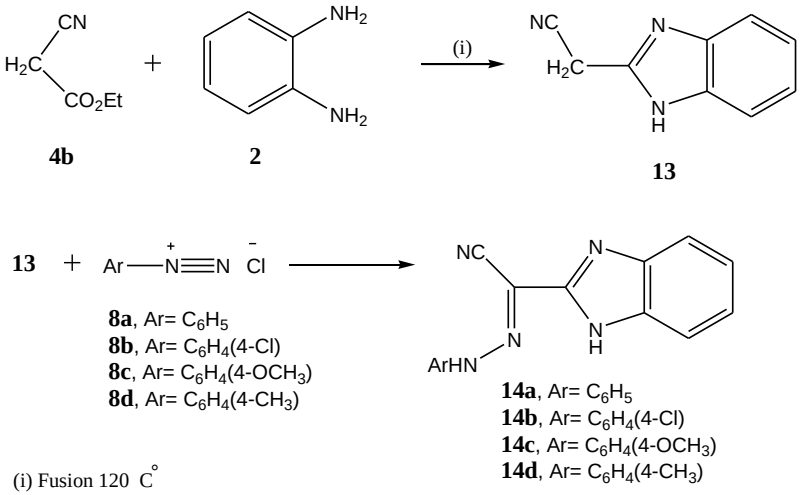
series of reactions. Thus, the reaction of either malononitrile (4a), ethyl cyanoacetate (4b), acetylacetone (4c) or ethyl acetoacetate (1) with phenyisothiocyanate in DMF/KOH solution at room temperature gave the intermediate potassium sulphide salts (A). The latter salts react with compounds (4a-c, 1) to give the thiophene derivatives 12a-d. The structures of the thiophene derivatives were confirmed on the basis of analytical and spectral data. Thus, the ^{1}H NMR spectrum of 12a showed singlet at δ 3.38 ppm for NH_2 group, at δ 4.50 ppm for CH_2 group, multiplets at δ 6.85-7.44 ppm for C_6H_4 and C_6H_5 moieties and two singlet at δ 10.77 ppm and δ 10.92 ppm for two NH group.



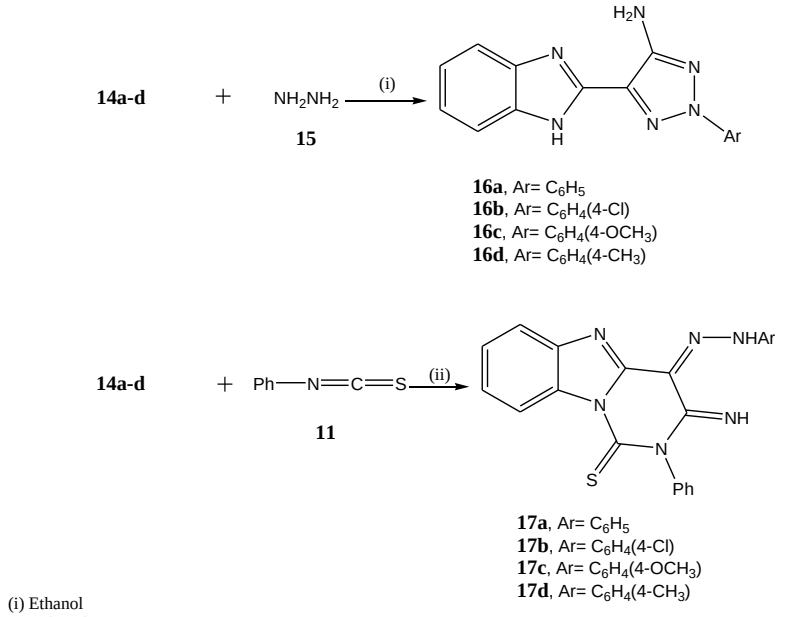
Scheme 3.

Next we moved towards studying the reactions of (1*H*-benzimidazol-2-yl)-acetonitrile 13, the latter was obtained according to the literature procedure (19) via the heating of ethyl cyanoacetate (4b) with *o*-phenylenediamine (2) at 140 ^{o}C for 0.5 hr. Compound 13 reacted with the aryldiazonium salts (8a-d) to give the arylhydrazo derivatives 14a-d, respectively. The analytical and spectral data of the latter products were in consistent with their respective structures (see experimental section).

Compounds 14a-d reacted with hydrazine hydrate (15) to afford the triazole derivatives 16a-d, respectively. On the other hand, the reaction of compounds 14a-d with phenylisothiocyanate (11) in 1,4-dioxan solution and in the presence of triethylamine gave the benzo[*4,5*]imidazo[1,2-c]pyrimidine-1-thione derivatives 17a-d, respectively. The structures of compounds 16a-d and 17a-d were based on the obtained analytical and spectral data (see experimental section).



Scheme 4.



Scheme 5.

Colour assessment and dyeing properties

Data of UV/vis absorption maxima, fastness and optical properties, as well as the colour shades on tested fabrics (nylon 6 + polyester) and polyester) are listed in Table 1.

The novel dyes were applied to (nylon 6 + Polyester) and polyester fabrics at 1% and 3% depth by the high-temperature-pressure technique and gave generally bright, intense canary yellow, mustard yellow, orange, orange yellow, yellowish white, pale orange and buff (Table 2). Due to the good migration properties of these disperse dyes, levelling agents were not required. The dyed fabrics were analyzed on qualitative tests by estimation fastness shades with grey scale, the results were expressed in terms of colour ratings 1-5 (Table 1). In general, the data revealed that wash fastness rating for change in colour as well as staining of adjacent fabrics are very good (4-5). Rubbing fastness of the samples, assessed in terms of dry and wet rubbing indicated also very good fastness to rubbing for both dry and wet (4-5). Perspiration fastness properties (acidic and alkaline) of the dyed samples in terms of ratings for staining of adjacent fabrics and change are very good (4-5). The high ratings for change in colour at both acidic and alkaline conditions indicate that the sensitivity of the dyed samples is not related to pH. This may be due to the stability of the dyes towards degradation under either acidic or basic conditions.

TABLE 1. Fastness properties of disperse dyes on different fabrics.

Dye (Conc. %)	Sample Dyed*	K/S** at λ_{max}= 400 nm	Fastness to Rubbing		Washing fastness at 60 °C		Fastness to Perspiration				λ_{max} nm.
							Acidic		Alkaline		
			Dry	Wet	Alteration	Staining	Alteration	Staining	Alteration	Staining	
9a (1%)	P N&P	0.2551 0.6334	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	741, 340, 225
9a (3%)	P N&P	0.7855 1.0970	4-5 5	4-5 5	4-5 5	4-5 5	4-5 5	4-5 5	4-5 5	4-5 5	
9b (1%)	P N&P	0.2686 0.3723	4 4	4 4	4 4	4 4	4 4	4 4	4 4	4 4	741, 280
9b (3%)	P N&P	0.5175 0.7177	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	
9c (1%)	P N&P	0.4490 0.7755	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5	4 4-5 5	4 4-5	741, 354, 283
9c (3%)	P N&P	0.3545 0.6596	4 4	4 4	4 4	4 4	4 4	4 4	4 4 5	4 4	

TABLE 1. Cont.

Dye (Conc.%)	Sample Dyed*	K/S** at λ_{max}= 400 nm	Fastness to Rubbing		Washing fastness at 60 °C		Fastness to Perspiration				λ_{max} nm.
							Acidic		Alkaline		
			Dry	Wet	Alteration	Staining	Alteration	Staining	Alteration	Staining	
9d (1%)	P	0.3056	4	4	4	4	4	4	4	4	740, 280
	N&P	0.4649	4	4	4	4	4	4	4	4	
9d (3%)	P	0.5915	4	4	4	4	4	4	4	4	
	N&P	0.7774	4-5	4-5	4-5	4-5	4-5	4-5	4-5	4-5	
14a (1%)	P	13.1023	5	5	5	5	5	5	5	5	740, 392, 296
	N&P	11.3356	5	5	5	5	5	5	5	5	
14a (3%)	P	11.4889	5	5	5	5	5	5	5	5	
	N&P	12.6054	5	5	5	5	5	5	5	5	
14b (1%)	P	3.5440	4-5	4-5	5	5	4-5	4-5	4-5	4-5	741, 385 283
	N&P	5.0156	4-5	4-5	5	5	5	5	5	5	
14b (3%)	P	9.5945	5	5	5	5	5	5	5	5	
	N&P	12.3877	5	5	5	5	5	5	5	5	
14c (1%)	P	7.8158	4-5	4-5	4-5	4-5	4-5	4-5	4-5	4-5	741, 399, 293
	N&P	9.0852	5	5	5	5	5	5	5	5	
14c (3%)	P	13.5100	5	5	5	5	5	5	5	5	
	N&P	14.4960	5	5	5	5	5	5	5	5	
14d (1%)	P	6.5746	4-5	4-5	4-5	4-5	4-5	4-5	4-5	4-5	741, 390, 271
	N&P	7.0440	4-5	4-5	4-5	4-5	4-5	4-5	4-5	4-5	
14d (3%)	P	11.1272	5	5	5	5	5	5	5	5	
	N&P	18.4681	5	5	5	5	5	5	5	5	

* P, Polyester; N, Nylon 6. Conc., Concentration

** K/S = (1-R)2/2R.

R: a decimal fraction of reflection of the dyed fabric; K: absorption coefficient; S: scattering coefficient.

TABLE 2. Color shades of the synthesized dyes on (nylon 6 + polyester) and polyester fibers.

Dye. No.	Polyester	Nylon 6 & Polyester	Dye. No	Polyester	Nylon 6 & Polyester
9a (1%)	Pale Canary Yellow	Pale Canary Yellow	9a (3%)	Pale Yellow	Pale Yellow
9b (1%)	Yellowish White	Yellowish White	9b (3%)	Yellowish White	Yellowish White
9c (1%)	Yellowish White	Yellowish White	9c (3%)	Pale Yellow	Pale Yellow
9d (1%)	Pale Buff	Pale Buff	9d (3%)	Pale Buff	Pale Buff
14a (1%)	Bright Yellow	Bright Yellow	14a (3%)	Orange Yellow	Orange Yellow
14b (1%)	Pale Canary Yellow	Pale Canary Yellow	14b (3%)	Pale Yellow	Pale Yellow
14c (1%)	Canary Yellow	Canary Yellow	14c (3%)	Mustard Yellow	Mustard Yellow
14d (1%)	Yellow	Pale Canary Yellow	14d (3%)	Mustard Yellow	Mustard Yellow

In vitro cytotoxic assay

The heterocyclic compounds, prepared in this study, were evaluated according to standard protocols for their in vitro cytotoxicity[17-19] against seven human cancer cell lines including cells derived from human gastric cancer (NUGC and HR), human colon cancer (DLD1), human liver cancer (HA22T and HEPG2), human breast cancer (MCF), nasopharyngeal carcinoma (HONE1) and normal fibroblast cells (WI38). All of IC_{50} values were listed in Table 3. Some heterocyclic compounds were observed with significant cytotoxicity against most of the cancer cell lines tested (IC_{50}=10–1000 nM). Normal fibroblasts cells (WI38) were affected to a much lesser extent (IC_{50}>10.000 nM).

From Table 3 it is clear that:-

- For human gastric cancer cell line (NUGC), compounds 14b, 10 and 17c showed moderate cytotoxic effect than the reference CHS 828.
- For human colon cancer cell line (DLD1), compounds 5a, 9b, 9c, 14b, 14c and 17c indicated higher cytotoxic effect than the reference CHS 828.
- For human liver cancer cell line (HA22T), compounds 5b, 9b, 9c, 14b, 17c and 17d showed higher cytotoxic effect than the reference CHS 828.

- For human liver cancer cell line (HEPG2), compounds 5b, 10 and 12b exhibited no cytotoxic effect, but all the other compounds showed higher effect than the reference CHS 828.
- For nasopharyngeal carcinoma (HONE1), all compounds showed no effect except compounds 5a, 5b and 14b indicated less potent effect.
- For human breast cancer cell line (MCF) compounds 14b, 12b and 17c showed low effect whereas all the other compounds have no effect.
- For normal fibroblast cells (WI38), all compounds indicated no cytotoxic effect except compounds 9a, 9c and 10 showed low potent effect, while compound 17d exhibited optimal cytotoxic effect.

TABLE 3. Cytotoxicity of some newly synthesized compounds against a variety of cancer cell lines [IC_{50} (nM)].

Compound Number	NUGC	DLD1	HA22T	HEPG2	HONE1	MCF	WI38
3	2240	3160	2168	410	2146	1263	NA
5a	210	120	283	359	206	2655	NA
5b	1151	1186	66	2780	180	2227	NA
9a	3277	2369	1336	1120	1268	3849	320
9b	122	90	212	440	1877	436	NA
9c	1280	60	152	320	2280	1663	690
10	33	2670	1374	2693	2227	1438	25
12a	180	2238	2247	425	1168	580	NA
12b	3124	2670	1165	4377	2168	114	NA
14a	1184	893	3269	322	2283	3365	NA
14b	44	70	37	370	244	120	NA
14c	1230	60	3265	365	4423	2539	NA
17c	39	48	29	320	442	66	NA
17d	455	329	120	442	680	1297	1288
CHS 828	25	2315	2067	1245	15	18	NA

NUGC, gastric cancer, DLDI, colon cancer, HA22T, liver cancer, HEPG2, liver cancer; HONEI, nasopharyngeal carcinoma; HR, gastric cancer; MCF, breast cancer; WI38, normal fibroblast cells.

IC_{50}:-The sample concentration produces a 50% reduction in cell growth.

Structure activity relationship

It is obvious that compounds 5a, 9b, 14b and 17c exhibited optimal cytotoxic effect against cancer cell line, with IC50's in the nM range.

Comparing the cytotoxicity of the hydrazono benzimidazole derivatives 9a, 9b and 9c, it is clear that the cytotoicity of 9b is higher than those of 9a and 9c. The presence of the chloro group is responsible for the high potent of 9b. Moreover, for the other hydrazono benzimidazole derivatives 14a-c, it is obvious that also compound 14b showed high cytotoxicity duo to the presence of the chloro group.

On the other hand, for the other series pyrimidine derivatives 17c and 17d, the presence of the OCH_3 group in compound 17c is responsible for the higher cytotoicity than compound 17d which has CH_3 group.

Our results showed that the electronegative Cl and OCH_3 hydrophobic groups in the benzimidazole derivatives might play a very important role in enhancing the cytotoxic effect.

Conclusion

In the present study the objective was to synthesize a series of newly heterocyclic compounds starting from 1-(1*H*-benzimidazol-2-yl)-propan-2-one 3 and (1*H*-benzimidazol-2-yl)-acetonitrile 13. Studying the reactivity of compounds 3 and 13 towards different chemical reagents and establishing the structure of the newly synthesized compounds based on elemental analysis and spectral data. Evaluation and study of the dyeing properties of the newly dyes which applied at 1% and 3% depth for disperse dyeing of (nylon 6 + polyester) and polyester fabrics were done. Their spectral characteristics and fastness properties were measured and evaluated. On the other hand, the anticancer activity of some of the newly synthesized compounds was evaluated. Compounds 5a, 9b, 14b and 17c revealed higher effect when screened *in vitro* against some human cancer cell lines than the reference CHS 828.

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الحولقة غير المتجانسة والتطبيقات الصباغية والتقييم المضاد للسرطان لمشتقات البينزايميدازول: تحضير مبتكر لمشتقات الثيوفين، الترايازول والبيريميدين

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تم تحضير العديد من مشتقات الهيدرازونو بينزايميدازول والثيوفين والترايازول والبيريميدين الجديدة، وتم تقييم الخصائص الصباغية لها. وقد تبين أن المركبات المحضرة تعتمد على المركبان 1-(*H*1- بينزايميدازول-2-ايل) بروبان-2-اون 3 و (*H*1- بينزايميدازول-2-ايل)- اسيتونيتريل 15. وقد تمت دراسة نشاط المركبان 3 و 15 تجاه الكواشف الكيميائية المختلفة. وايضا تم تحديد الشكل البنائى للمركبات الجديدة المحضرة بناء على تحاليل العناصر ونتائج الطيف. بالأضافة إلى ما سبق تم تقييم الأداء الصباغى وخواص الثبات اللوني للصبغات- مجال البحث- وذلك عند تطبيقها على الخامات النسجية (للنايلون 6 + البولي استر) والبولي استر وذلك بعمق صباغة عند 1% و 3%. على الجانب الآخر، تمت دراسة وتقييم النشاط المضاد للسرطان لبعض من المركبات المحضرة حديثا. وقد استخدم فى اختبارات الفحص ست خلايا سرطانية بشرية وهى سرطان المعدة (NUGC)، وسرطان القولون (DLD-1)، وسرطان الكبد (HA22T, HEPG-2)، وسرطان البلعوم (HONE-1)، وسرطان الثدى (MCF-7) والخلايا الليفية العادية (WI-38). وقد أظهر فحص المركبات أن 5a, 9b, 16b, 19c تأثيرا عاليا تجاه بعض الخلايا السرطانية البشرية مقارنة بالنشاط التثبيطي لمركب المرجع CHS 828.