

Balkis Al-Saleh ^a, Mervat Mohammed Abdelkhalik ^b, Morsy Ahmed El-Asasery ^a,
and Mohammed Hilmy Elnagdi ^{*c}

[a] Department of Chemistry, Faculty of Science, University of Kuwait P. O. Box 5969 Safat, 13060 Kuwait

[b] Department of Chemistry, Girls College for Arts, Science and Education, Ain Shams University, P. O. Box
11757 Heliopolis, Cairo, A. R. Egypt

[c] Department of Chemistry, Faculty of Science, Cairo University, Giza, A. R. Egypt

Received June 10, 2002

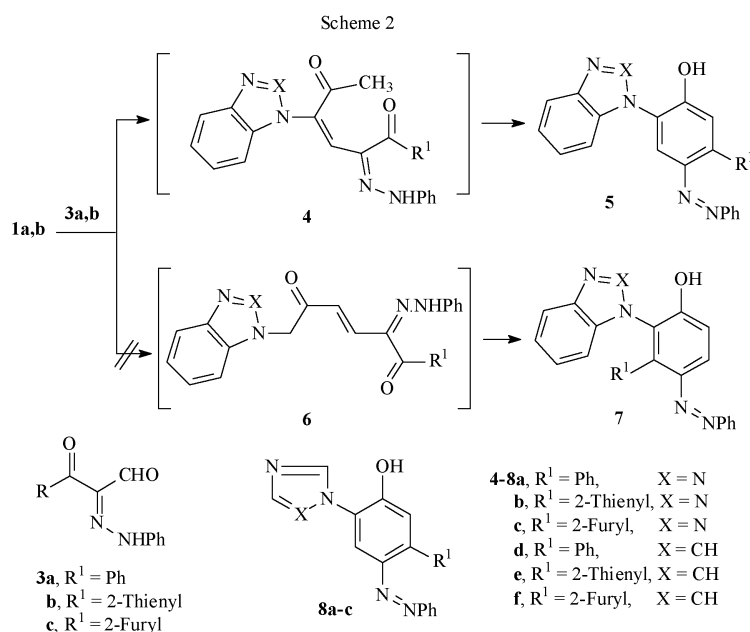
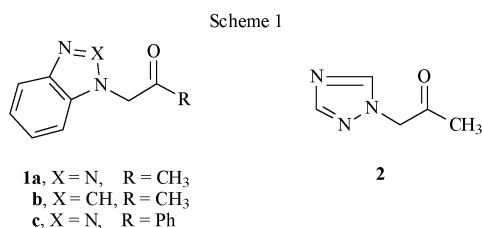
The title compounds **1a-b** and **2** reacted with 2-arylhydrazonopropanals **3a-c** to yield polyfunctionally substituted azolylarylazophenols **5** and **8**. The reaction of **1b** and **2** with phenylisothiocyanate in the presence of α -haloketones afforded the azolylthiophenes **12a,b** and **13a,b**. The reaction of **20** with α -haloketone afforded 5-benzotriazol-1-yl-6-methyl-2-(2-oxopropylsulfanyl)nicotinonitrile **21** that was utilized as building blocks for the synthesis of condensed pyridines. Compound **21** was condensed with dimethylformamide dimethylacetal to yield thieno[2,3-*b*]pyridin-3-yl-*N,N*-dimethylformamidine derivative **22**. This was further cyclized with sodium hydride to 1*H*-thieno[2,3-*b*; 4,5-*b'*]dipyridin-4-one derivative **23**.

J. Heterocyclic Chem., **40**, 171 (2003).

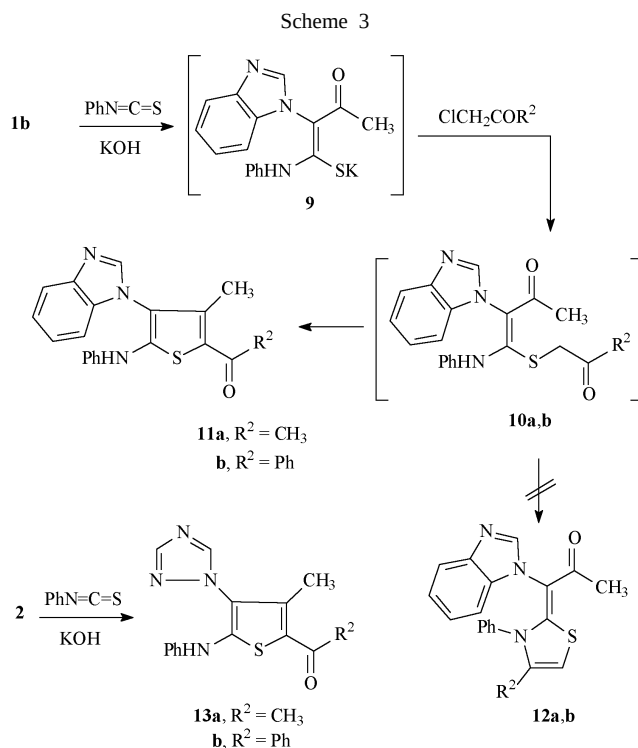
The reactivity of *N*-functionally substituted alkylbenzotriazoles toward electrophiles has been extensively utilized in the last decade by Katritzky *et al.* [1,2] and Elnagdi *et al.* [3-7] in the syntheses of polyfunctionally substituted heterocycles. Recently we have shown that *N*-functionally substituted pyrazolyl [8], *N*-1,2,4-triazolyl and *N*-benzimidazolyl-methyl ketones [9], also furnished carbanions under mild conditions. This enabled ready coupling with aromatic diazonium salts and condensation with dimethylformamide dimethylacetal. In conjunction with this work we report our finding on the reactivity of azolylmethyl ketones of types **1** and **2** (Scheme 1) toward carbon electrophiles in neutral and basic conditions.

Thus, it has been found that **1a,b** and **2** react with 2-arylhydrazonopropanals **3a-c** to yield products of condensation

via elimination of two water molecules. These can thus be formulated as **5** or its positional isomer **7** formed most likely *via* the presumed intermediates **4** and **6** respectively (Scheme 2). Structure **5** has been established based on the ¹H NMR spectra, as it revealed two aryl singlets at $\delta \sim 7.76$ and 8.34 ppm. This excludes completely structure **7** that

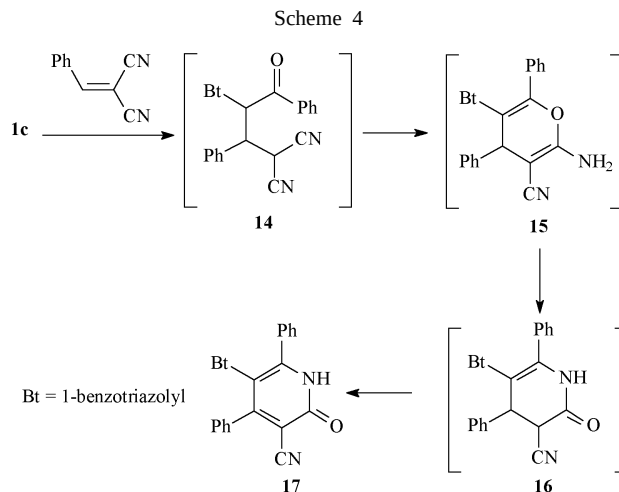


could have resulted, as it should display two doublets in its ^1H NMR spectrum. Similarly, compound **2** reacted with **3a-c** to yield **8a-c**. Similar to the recently reported behavior of **1a** toward phenylisothiocyanate [7], compound **1b** reacted with phenylisothiocyanate and α -haloketones in dimethyl formamide in the presence of potassium hydroxide to yield the azolythiophenes **11a,b** (Scheme 3). These are believed to be formed *via* intermediacy of **9** and **10a,b**. The possible formation of thiazoles **12a,b** was readily excluded based on ^1H NMR which indicated in each case the presence of NH signal at $\delta \sim 9.5$ ppm. Similarly, compound **2** reacted with phenylisothiocyanate and α -haloketones under similar reaction conditions to yield **13a,b**. It is of value to report that in earlier work [7], thiazoles were formed from reaction of **1c** with the same reagents under the same reaction conditions, demonstrating dependency of the final product on the nature of the utilizing ketone.

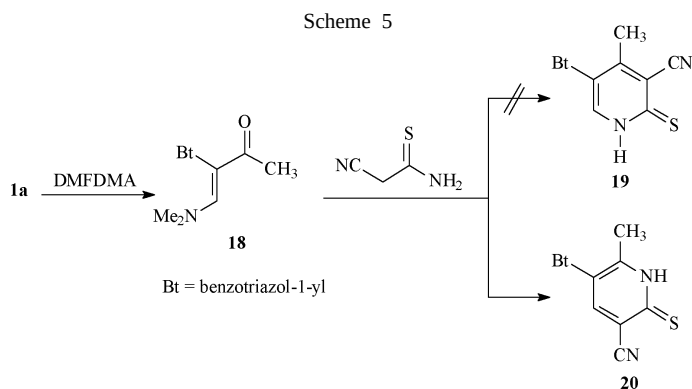


In light of these results, another electrophile was treated under an alkaline condition (Scheme 4). In fact, the reaction of **1c** with benzylidenemalononitrile in ethanolic piperidine has afforded a product of molecular formula $\text{C}_{24}\text{H}_{15}\text{N}_5\text{O}$. This is assumed to be **17**, formed *via* rearrangement of the initially formed *4H*-pyrane **15** into the 1,2,3,4-tetrahydropyridine **16** that auto-oxidized under reaction conditions into the pyridone **17**. Ready oxidation of dihydroazines into azines has been reported earlier under mild conditions [10].

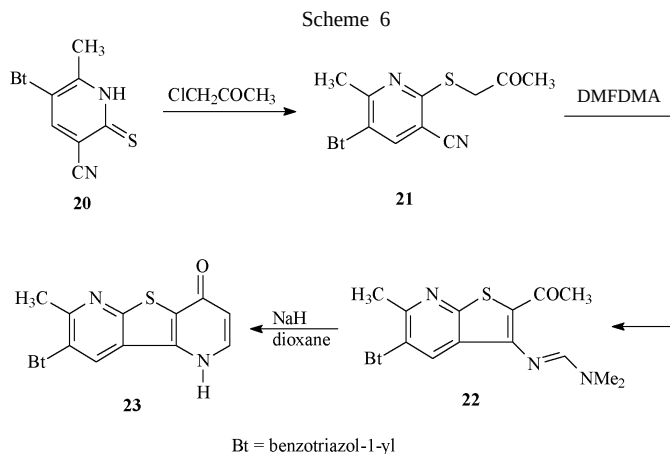
To increase the synthetic scope on the utility of these types of substrates, chemical modification of the synthon



1a was then investigated to access complex heterocyclic systems (Schemes 5 and 6). Accordingly, dimethylformamide dimethylacetal condensed with **1a** yielding the enaminone **18** [7]. Compound **18** reacted with cyanothioacetamide to yield products that were formulated as **20** rather than **19**. ^1H NMR revealed pyridine H_4 proton at $\delta = 8.01$ ppm as singlet. For compound **19**, this proton should appear as a doublet confirming this structural assignment. Compound **20** reacted with chloroacetone to yield 5,6-disubstituted-2-(2-oxopropylsulfanyl)-nicotinonitrile **21**, this is in contrast to the reported direct formation of 1-(3-amino-5-benzotriazol-1-yl-6-methylthieno[2,3-*b*]pyridin-2-yl) derivative on reacting **20** with phenacyl bromide [11]. Compound **21** condensed with dimethylformamide dimethylacetal affording the thieno[2,3-*b*]pyridin-3-yl-*N,N*-dimethylformamidine derivative **22**. This was further cyclized with sodium hydride to thieno[2,3-*b*:4,5-*b'*]dipyridin-4-one derivative **23**. It is of value to report that H_9 in **23** appeared at $\delta = 9.04$ ppm as a singlet, this low field shift is a result of deshielding by the anisotropic effect of the *N*-lone-pair.



One may thus conclude that attaching a methylene ketone to the ring nitrogen in benzotriazole, benzimidazole, triazole and imidazole activate the methylene moiety toward carbon electrophiles. Thus enabling the



synthesis of a variety of polyfunctionally substituted azolyl and azinyl heteroaromatics. This is in contrast with the reported ready elimination of the benzotriazole moiety during reaction of alkyl benzotriazoles with electrophilic reagents, no such elimination has been observed in our systems.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr with a Pye Unicam SP 1100 spectrophotometer. ^1H NMR spectra were recorded on a Varian EM-390 400 MHz spectrometer in deuteriochloroform or $[\text{D}_6]\text{DMSO}$ as solvent and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on MS 30 and MS 9 (AEI) instruments operating at 70 eV. Microanalyses were performed on a LECO CHNS-932. Compounds **1a,b** and **2** were prepared following published procedure [12,13,9].

2-Benzotriazol-1-yl-1-phenylethanone (**1c**).

A mixture of benzotriazole (1.19 g, 10 mmol), and phenacyl bromide (1.99 g, 10 mmol), in DMF (20 ml) and in the presence of sodium hydroxide (0.05 g) was heated under reflux for 2 h. The solvent was reduced under vacuum, poured into water and neutralized with diluted hydrochloric acid solution to deposit a solid, which was crystallized from ethanol. Yield: 1.70 g (72 %); mp 115°. ir (KBr) ν_{max} = 1689 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 237 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 6.11 (s, 2H, CH_2), 7.37-7.41 (m, 2H, arom. H), 7.47-7.57 (m, 3H, arom. H), 7.66-7.70 (m, 1H, arom. H), 8.06-8.11 (m, 3H, arom. H).

Anal. Calcd. for $\text{C}_{14}\text{H}_{11}\text{N}_3\text{O}$ (237.25): C, 70.87; H, 4.67; N, 17.71. Found C, 70.90; H, 4.53; N, 17.69.

General Procedure for the Preparation of Compounds **5a-f**.

To a stirred suspension of each of compound **3a-c** (10 mmol) in ethanol (20 ml) containing potassium hydroxide (0.56 g, 10 mmol), each of compound **1a,b** (10 mmol) was added. The reaction mixture was heated under reflux for 2 h. The solvent was evaporated under reduced pressure and the remaining product was triturated with water and neutralized with hydrochloric acid to deposit a solid, which was crystallized from ethanol/dioxane (3:1).

4-Benzotriazol-1-yl-6-phenylazobiphenyl-3-ol (**5a**).

This compound was obtained in 77% yield (3.01 g); mp. 217°; ir (KBr) ν_{max} = 3432 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 391 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 7.37 (s, 1H, H_2), 7.48-7.56 (m, 7H, arom. H), 7.59-7.64 (m, 4H, arom. H), 7.67-7.69 (m, 2H, arom. H), 7.99 (s, 1H, H_5), 8.19 (d, 1H, J = 8.4 Hz, benzotriazolyl-H), 11.55 (s, 1H, OH); ^{13}C NMR (deuteriochloroform): δ_{C} = 156.01, 152.99, 145.16, 144.07, 143.90, 142.46, 138.44, 135.00, 131.76, 131.37, 130.24, 128.79, 124.20, 124.04, 123.39, 122.97, 120.51, 118.92, 115.64, 111.85.

Anal. Calcd. for $\text{C}_{24}\text{H}_{17}\text{N}_5\text{O}$ (391.42): C, 73.64; H, 4.38; N, 17.89. Found C, 73.64; H, 4.53; N, 17.62.

2-Benzotriazol-1-yl-4-phenylazo-5-thiophen-2-yl-phenol (**5b**).

This compound was obtained in 92% yield (3.65 g); mp. 280°; ir (KBr) ν_{max} = 3422 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 397 [M^+]; ^1H nmr (DMSO): δ_{H} = 7.28 (dd, 1H, J = 4 Hz, thienyl H_4), 7.47-7.51 (m, 1H, thienyl H_3), 7.56 (d, 1H, J = 8.0 Hz, benzotriazolyl-H), 7.59-7.65 (m, 5H, Ph), 7.68 (s, 1H, H_2), 7.86 (dd, 1H, J = 4.6 Hz, thienyl H_5), 7.93 (m, 2H, benzotriazolyl-H), 7.97 (s, 1H, H_5), 8.18 (d, 1H, J = 8.2 Hz, benzotriazolyl H), 11.68 (s, 1H, OH); ^{13}C nmr (DMSO): δ_{C} = 155.68, 153.01, 145.91, 141.17, 138.19, 137.15, 134.37, 132.28, 132.17, 130.42, 129.22, 128.98, 128.35, 125.17, 124.43, 124.11, 120.22, 116.62, 116.32, 112.63.

Anal. Calcd. for $\text{C}_{22}\text{H}_{15}\text{N}_5\text{OS}$ (397.38): C, 66.49; H, 3.80; N, 17.63; S, 8.05. Found C, 66.72; H, 4.08; N, 17.52; S, 7.84.

2-Benzotriazol-1-yl-5-furan-2-yl-4-phenylazo-phenol (**5c**).

This compound was obtained in 91% yield (3.46 g); mp. 260°; ir (KBr) ν_{max} = 3435 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 381 [M^+]; ^1H nmr (DMSO): δ_{H} = 6.76-6.78 (m, 1H, furyl H_4), 7.08 (d, 1H, J = 3.4 Hz, furyl H_3), 7.47-7.51 (m, 1H, furyl H_5), 7.56-7.64 (m, 5H, Ph), 7.76 (s, 1H, H_6), 7.89 (m, 2H, benzotriazolyl H), 7.93 (s, 1H, H_3), 8.01-8.02 (m, 1H, benzotriazolyl-H), 8.17 (d, 1H, J = 8.1 Hz, benzotriazolyl H), 11.54 (s, 1H, OH); ^{13}C nmr (DMSO): δ_{C} = 155.56, 153.08, 149.58, 145.89, 145.22, 140.97, 134.35, 132.57, 132.18, 130.49, 128.95, 125.16, 123.94, 123.71, 120.21, 116.44, 116.38, 114.02, 113.97, 112.65.

Anal. Calcd. for $\text{C}_{22}\text{H}_{15}\text{N}_5\text{O}_2$ (381.38): C, 69.28; H, 3.96; N, 18.36. Found C, 69.18; H, 4.11; N, 18.13.

4-Benzimidazol-1-yl-6-phenylazo-biphenyl-3-ol (**5d**).

This compound was obtained in 80% yield (3.12 g); mp. 288°; ir (KBr) ν_{max} = 3420 cm^{-1} (OH); MS (EI, 70 EV): m/z (%) = 390 [M^+]; ^1H nmr (DMSO): δ_{H} = 7.27 (s, 1H, H_2), 7.29-7.30 (m, 2H, arom. H), 7.38-7.40 (m, 1H, arom. H), 7.46-7.57 (m, 8H, arom. H), 7.64-7.66 (m, 2H, arom. H), 7.77-7.79 (m, 1H, arom. H), 7.90 (s, 1H, H_5), 8.47 (s, 1H, benzimidazolyl H_2), 11.20 (s, 1H, OH).

Anal. Calcd. for $\text{C}_{25}\text{H}_{18}\text{N}_4\text{O}$ (390.43): C, 76.90; H, 4.65; N, 14.35. Found C, 77.09; H, 4.73; N, 14.26.

2-Benzimidazol-1-yl-4-phenylazo-5-thiophen-2-yl-phenol (**5e**).

This compound was obtained in 85% yield (3.36 g); mp. 276°; ir (KBr) ν_{max} = 3439 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 396 [M^+]; ^1H nmr (DMSO): δ_{H} = 7.25-7.31 (m, 3H, arom. H), 7.37-7.40 (m, 1H, thienyl H_4), 7.54 (d, 1H, J = 4.8 Hz, thienyl H_3), 7.62-7.35 (m, 4H, arom. H), 7.76-7.78 (m, 1H, arom. H), 7.84 (d, 1H, J = 4.6 Hz, thienyl H_5), 7.88 (s, 1H, H_3), 7.92 (d, 2H, J = 8.0 Hz, benzimidazolyl H), 8.46 (s, 1H, benzimidazolyl H_2), 11.40 (s, 1H, OH); ^{13}C nmr (DMSO): δ_{C} = 156.46, 153.03, 145.10, 143.82, 141.11,

138.40, 136.16, 134.91, 132.02, 130.40, 128.89, 128.28, 124.26, 124.09, 123.03, 121.96, 120.49, 118.48, 116.49, 115.76, 111.87.

Anal. Calcd. for $C_{23}H_{16}N_4OS$ (396.38): C, 69.69; H, 4.07; N, 14.14; S, 8.07. Found C, 69.63; H, 4.18; N, 13.95; S, 7.83.

2-Benzimidazol-1-yl-5-furan-2-yl-4-phenylazo-phenol (**5f**).

This compound was obtained in 68% yield (2.58 g); mp. 273°; ir (KBr) $\nu_{\max}$ = 3435 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 380 [M^+]; ^1H nmr (DMSO): δ_{H} = 6.75 (t, 1H, J = 3.4 Hz, furyl H_4), 7.03 (d, 1H, J = 3.4 Hz, furyl H_3), 7.28-7.30 (m, 2H, arom. H), 7.36-7.38 (m, 1H, furyl H_5), 7.55-7.63 (m, 3H, arom. H), 7.71 (s, 1H, H-6), 7.76-7.82 (m, 1H, benzimidazolyl H), 7.84-7.87 (m, 3H, benzimidazolyl H), 7.98 (s, 1H, H-3), 8.46 (s, 1H, benzimidazolyl H_2), 11.55 (s, 1H, OH).

Anal. Calcd. for $C_{23}H_{16}N_4O_2$ (380.39): C, 72.62; H, 4.24; N, 14.73. Found C, 72.88; H, 4.25; N, 14.56.

General Procedure for the Preparation of Compounds **8a-c**.

Similar reaction conditions as for compounds **7a-f** using compound **2** (10 mmol) were utilized. The target product **8a-c** was crystallized from ethanol/dioxane (3:1).

6-Phenylazo-4-[1,2,4]-triazol-1-yl-biphenyl-3-ol (**8a**).

This compound was obtained in 88% yield (3.0 g); mp. 230°; ir (KBr) $\nu_{\max}$ = 3415 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 341 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 7.38 (s, 1H, H_2), 7.46-7.51 (m, 6H, arom. H), 7.55-7.57 (m, 2H, arom. H), 7.79-7.81 (m, 2H, arom. H), 8.11 (s, 1H, H_5), 8.27 (s, 1H, triazolyl H_4), 8.89 (s, 1H, triazolyl H_2), 10.61 (s, 1H, OH).

Anal. Calcd. for $C_{20}H_{15}N_5O$ (341.36): C, 70.37; H, 4.43; N, 20.52. Found C, 70.31; H, 4.58; N, 9.87.

4-Phenylazo-5-thiophen-2-yl-2-[1,2,4]-triazol-1-yl-phenol (**8b**).

This compound was obtained in 85% yield (3.0 g); mp. 271°; ir (KBr) $\nu_{\max}$ = 3435 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 396 [M^+]; ^1H nmr (DMSO): δ_{H} = 7.23 (t, 1H, J = 4 Hz, thienyl H_4), 7.54-7.64 (m, 5H, arom. H), 7.82 (d, 1H, J = 4.2 Hz, thienyl H_5), 7.94-7.96 (m, 2H, arom. H), 8.15 (s, 1H, H_3), 8.32 (s, 1H, triazolyl H_4), 9.15 (s, 1H, triazolyl H_2), 11.71 (s, 1H, OH).

Anal. Calcd. for $C_{18}H_{13}N_5OS$ (347.32): C, 62.24; H, 3.78; N, 20.17; S, 9.21. Found C, 62.48; H, 3.99; N, 19.95; S, 9.11.

5-Furan-2-yl-4-phenylazo-2-[1,2,4]-triazol-1-yl-phenol (**8d**).

This compound was obtained in 87% yield (2.85 g); mp. 236°; ir (KBr) $\nu_{\max}$ = 3435 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 380 [M^+]; ^1H nmr (DMSO): δ_{H} = 6.79 (t, 1H, J = 3.6 Hz, furyl H_4), 7.00 (d, 1H, J = 3.6 Hz, furyl H_3), 7.54-7.65 (m, 4H, arom. H), 7.81-7.96 (m, 3H, arom. H), 8.12 (s, 1H, H_3), 8.26 (s, 1H, triazolyl H-4), 9.16 (s, 1H, triazolyl H_2), 11.70 (s, 1H, OH).

Anal. Calcd. for $C_{18}H_{13}N_5O_2$ (331.32): C, 65.25; H, 3.96; N, 21.14. Found C, 65.09; H, 4.07; N, 21.09.

General Procedure for the Preparation of Compounds **11a,b** and **13a,b**.

A stirred suspension of each of compound **1b** and **2** (10 mmol) and phenyl isothiocyanate (1.35 g, 10 mmol) in DMF (20 ml) in the presence of potassium hydroxide (0.06 g); α -haloketone (10 mmol) is added to the stirred solution after 10 h and the reaction mixture is heated under reflux for 4 h. The solvent was removed and the residue was triturated with water and neutralized with hydrochloric acid. The solid product was crystallized from ethanol.

1-(4-Benzimidazol-1-yl-3-methyl-5-phenylaminothiophen-2-yl)ethanone (**11a**).

This compound was obtained in 75% yield (2.60 g); mp. 240°; ir (KBr) $\nu_{\max}$ = 3086 (NH), 1614 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 347 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 2.10 (s, 3H, CH_3), 2.52 (s, 3H, COCH_3), 7.10-7.14 (m, 1H, arom. H), 7.17-7.23 (m, 2H, arom. H), 7.36-7.41 (m, 3H, arom. H), 7.46-7.51 (m, 3H, arom. H), 8.96 (s, 1H, benzimidazolyl-H), 9.57 (br s, 1H, NH); ^{13}C nmr (deuteriochloroform): δ_{C} = 189.9 (CO), 151.8, 143.6, 143.0, 142.4, 141.3, 134.0, 130.0, 124.5, 124.1, 123.7, 120.2, 119.8, 119.2, 115.7, 110.7, 29.5, 14.5.

Anal. Calcd. for $C_{20}H_{17}N_3OS$ (347.36): C, 69.15; H, 4.93; N, 12.10; S, 9.21. Found C, 68.95; H, 5.01; N, 12.08; S, 9.00.

(4-Benzimidazol-1-yl-3-methyl-5-phenylaminothiophen-2-yl)-phenylmethanone (**11b**).

This compound was obtained in 69% yield (2.82 g); mp. 150°; ir (KBr) $\nu_{\max}$ = 3055 (NH), 1606 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 409 [M^+]; ^1H nmr (DMSO): δ_{H} = 1.83 (s, 3H, CH_3), 7.01-7.03 (m, 1H, arom. H), 7.26-7.32 (m, 7H, arom. H), 7.50-7.57 (m, 3H, arom. H), 7.69-7.71 (m, 2H, arom. H), 7.76-7.78 (m, 1H, arom. H), 8.38 (s, 1H, benzimidazolyl H_2), 9.36 (br s, 1H, NH); ^{13}C nmr (DMSO): δ_{C} = 188.3 (CO), 153.3, 145.6, 144.6, 142.5, 141.8, 140.8, 134.6, 132.5, 130.31, 129.4, 128.8, 124.7, 124.3, 123.6, 120.1, 119.8, 118.4, 117.4, 111.5, 15.0.

Anal. Calcd. for $C_{25}H_{19}N_3OS$ (409.43): C, 73.33; H, 4.68; N, 10.26; S, 7.81. Found C, 73.11; H, 4.74; N, 10.39; S, 7.60.

1-(3-Methyl-5-phenylamino-4-[1,2,4]-triazol-1-yl-thiophen-2-yl)ethanone (**13a**).

This compound was obtained in 80% yield (2.40 g); mp. 185°; ir (KBr) $\nu_{\max}$ = 3064 (NH), 1613 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 298 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 2.05 (s, 3H, CH_3), 2.43 (s, 3H, COCH_3), 7.04-7.07 (m, 1H, arom. H), 7.27-7.36 (m, 5H, arom. H), 8.26 (s, 1H, triazolyl H_4), 8.77 (s, 1H, triazolyl H_2), 9.16 (br s, 1H, NH).

Anal. Calcd. for $C_{15}H_{14}N_4OS$ (298.29): C, 60.39; H, 4.73; N, 18.78; S, 10.73. Found C, 60.59; H, 4.79; N, 18.80; S, 10.71.

(3-Methyl-5-phenylamino-4-[1,2,4]-triazol-1-yl)-thiophen-2-ylphenyl-methanone (**13b**).

This compound was obtained in 72% yield (2.60 g); mp. 190°; ir (KBr) $\nu_{\max}$ = 3069 (NH), 1617 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 360.36 [M^+]; ^1H nmr (DMSO): δ_{H} = 1.88 (s, 3H, CH_3), 7.05-7.07 (m, 1H, arom. H), 7.26-7.35 (m, 7H, arom. H), 7.49-7.53 (m, 3H, arom. H), 7.57-7.59 (m, 1H, arom. H), 7.65-7.67 (m, 2H, arom. H), 8.26 (s, 1H, triazolyl H_4), 8.80 (s, 1H, triazolyl H_2), 9.29 (br s, 1H, NH); ^{13}C nmr (DMSO): δ_{C} = 188.47, 153.33, 153.28, 147.62, 144.20, 141.51, 140.71, 132.54, 130.45, 129.44, 128.75, 124.66, 120.12, 119.31, 117.99, 14.87 (CH_3).

Anal. Calcd. for $C_{20}H_{16}N_4OS$ (360.36): C, 66.66; H, 4.48; N, 15.55; S, 8.88. Found C, 67.00; H, 4.48; N, 15.40; S, 9.06.

5-Benzotriazol-1-yl-2-oxo-4,6-diphenyl-1,2-dihydropyridine-3-carbonitrile (**17**).

Benzylidenemalononitrile (1.54 g, 10 mmol) was added to a stirred suspension of compound **1c** (2.37 g, 10 mmol) in ethanol (20 ml) in the presence of sodium hydroxide (0.5 g). The reaction mixture was heated under reflux for 2 h. The solvent was reduced under vacuum; poured onto water and the residue was neutralized

with diluted hydrochloric acid solution to deposit a solid, which was crystallized from dioxane. Yield: 2.40 g (62 %); mp. > 300°; ir (KBr) $\nu_{\max}$ = 3060 (NH), 2229 (CN), 1672 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 389 [M^+]; ^1H nmr (DMSO): δ_{H} = 7.00-7.26 (m, 10H, arom. H), 7.33-7.40 (m, 2H, benzotriazolyl-H), 7.60 (d, 1H, J = 8.6 Hz, benzotriazolyl-H), 7.78 (d, 1H, J = 8.6 Hz, benzotriazolyl-H), 13.46 (br s, 1H, NH).

Anal. Calcd. for $\text{C}_{24}\text{H}_{15}\text{N}_5\text{O}$ (389.40): C, 74.02; H, 3.88; N, 17.99. Found C, 74.27; H, 4.02; N, 18.21.

5-Benzotriazol-1-yl-6-methyl-2-thioxo-1,2-dihydropyridine-3-carbonitrile (**20**).

Cyanothioacetamide (1 g, 10 mmol) was added to a stirred suspension of the enaminone **18** (2.30 g, 10 mmol) in ethanol (20 ml) in the presence of few drops of triethyl amine. The reaction mixture was heated under reflux for 2 h. The solvent was reduced under vacuum; poured onto water and the residue was neutralized with diluted hydrochloric acid solution to deposit a solid, which was crystallized from ethanol. Yield: 1.70 g (64 %); mp. 290°; ir (KBr) $\nu_{\max}$ = 3013 (NH), 2224 (CN) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 267 [M^+]; ^1H nmr (deuteriochloroform): δ = 2.38 (s, 3H, CH_3), 7.36-7.38 (m, 1H, benzotriazolyl-H), 7.52-7.59 (m, 1H, benzotriazolyl-H), 7.62-7.69 (m, 1H, benzotriazolyl-H), 8.01 (s, 1H, pyridyl H_4), 8.18-8.27 (m, 1H, benzotriazolyl-H), 13.65 (br s, 1H, NH).

Anal. Calcd. for $\text{C}_{19}\text{H}_{14}\text{N}_2\text{S}$ (267.24): C, 58.42; H, 3.39; N, 26.21; S, 11.97. Found: C, 58.51; H, 3.54; N, 25.95; S, 11.82.

5-Benzotriazol-1-yl-6-methyl-2-(2-oxopropylsulfanyl)nicotinonitrile (**21**).

Chloroacetone (0.92 g, 10 mmol) was added to a stirred suspension of compound **20** (2.67 g, 10 mmol) in DMF (20 ml) in the presence of potassium hydroxide (0.5 g). The reaction mixture was heated under reflux for 6 h. The solvent was reduced under vacuum; poured onto water and the residue was neutralized with diluted hydrochloric acid solution to deposit a solid, which was crystallized from ethanol/dioxane (1:2). Yield: 2.60 g (80 %); mp. 259°; ir (KBr) $\nu_{\max}$ = 2228 (CN), 1676 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 323 [M^+]; ^1H nmr (deuteriochloroform): δ_{H} = 2.46 (s, 1H, CH_3), 2.48 (s, 1H, COCH_3), 6.79 (s, 2H, CH_2), 7.34 (d, 1H, J = 8.4 Hz, benzotriazolyl-H), 7.50 (t, 1H, J = 8.6 Hz, benzotriazolyl-H), 7.59 (t, 1H, J = 8.6 Hz, benzotriazolyl-H), 8.08 (s, 1H, pyridyl H_4), 8.20 (d, 1H, J = 8.4 Hz, benzotriazolyl-H); ^{13}C nmr (DMSO): δ_{C} = 192.37 (CO), 160.68, 157.78, 148.15, 145.86, 134.42, 131.60, 129.82, 128.79, 125.73, 120.58, 111.62, 106.04, 31.57 (CH_2), 29.89 (CH_3), 22.11 (COCH_3).

Anal. Calcd. for $\text{C}_{16}\text{H}_{13}\text{N}_5\text{OS}$ (323.30): C, 59.44; H, 4.05; N, 21.66; S, 9.90. Found C, 59.64; H, 4.07; N, 21.66; S, 9.68.

N'-(2-Acetyl-5-benzotriazol-1-yl-6-methyl-thieno[2,3-*b*]pyridin-3-yl)-*N,N*-dimethylformamidine (**22**).

To a suspension of compound **20** (3.23 g, 10 mmol) in xylene (20 ml), dimethylformamide dimethylacetal (1.19 g, 10 mmol) was added. The reaction mixture was heated under reflux for 4 h. The solvent was removed and the residue cooled to deposit a solid, which was crystallized from dioxane/ethanol (1:1). Yield: 2.50 g (65 %); mp. 264°; ir (KBr) $\nu_{\max}$ = 1636 (CO) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 378 [M^+]; ^1H nmr (DMSO): δ_{H} = 2.29 (s, 3H, CH_3), 2.55 (s,

3H, COCH_3), 3.01 (s, 6H, NMe_2), 7.53 (t, 1H, J = 8.6 Hz, benzotriazolyl-H), 7.61-7.67 (m, 2H, benzotriazolyl-H), 7.97 (s, 1H, H_4), 8.23 (d, 1H, J = 8.6 Hz, benzotriazolyl-H), 8.42 (s, 1H, amidine-H).

Anal. Calcd. for $\text{C}_{19}\text{H}_{18}\text{N}_6\text{OS}$ (378.38): C, 60.31; H, 4.80; N, 22.21; S, 8.46. Found C, 60.14; H, 4.88; N, 21.98; S, 8.21.

8-Benzotriazol-1-yl-7-methyl-1*H*-thieno[2,3-*b*; 4,5-*b'*]dipyridin-4-one (**23**).

To a suspension of compound **22** (3.78 g, 10 mmol) in dioxane (20 ml), sodium hydride (0.4 g, 60 % dispersion) was added. The reaction mixture was heated under reflux for 6 h. The solvent was reduced under vacuum; poured into water and the residue was neutralized with diluted hydrochloric acid solution to deposit a solid, which was crystallized from dioxane/ethanol (1:3). Yield: 2.0 g (60 %); mp. > 300 °; ir (KBr) $\nu_{\max}$ = 33.92 (OH) cm^{-1} ; MS (EI, 70 EV): m/z (%) = 333 [M^+]; ^1H nmr (DMSO): δ_{H} = 2.48 (s, 3H, CH_3), 3.84 (br s, 1H, NH), 6.62 (d, 1H, J = 8.4 Hz, H_3), 7.57 (t, 1H, J = 8.6 Hz, benzotriazolyl-H), 7.68 (t, 1H, J = 8.6 Hz, benzotriazolyl-H), 7.76 (d, 1H, J = 8.4 Hz, H_2), 8.26-8.30 (m, 2H, benzotriazolyl-H), 9.04 (s, 1H, H_9); ^{13}C nmr (DMSO): δ_{C} = 161.23 (CO), 156.97, 145.92, 142.65, 134.41, 130.62, 129.93, 129.50, 128.45, 127.65, 126.21, 125.82, 124.79, 120.65, 111.97, 111.59, 22.23.

Anal. Calcd. for $\text{C}_{17}\text{H}_{11}\text{N}_5\text{OS}$ (333.38): C, 61.26; H, 3.33; N, 21.01; S, 9.60. Found C, 61.14; H, 3.48; N, 20.92; S, 9.87.

Acknowledgement.

The authors are grateful to the University of Kuwait R. A. for financial support through project Sc 103. Analytical facilities provided by SAF are highly appreciated.

REFERENCES AND NOTES

- [1] A. R. Katritzky, S. A. Henderson and B. Yang, *J. Heterocyclic Chem.*, **35**, 1123 (1998).
- [2] A. R. Katritzky, X. Lan, J. Z. Yang and O. V. Densiko, *Chem. Rev.*, **98**, 409 (1998).
- [3] A. Al-Naggar, M. M. Abdel-khalik and M. H. Elnagdi, *J. Chem. Res. (S)*, 654, (1999).
- [4] H. Behbehani, M. M. Abdel-khalik and M. H. Elnagdi, *Org. Prep. Proced. Int.*, **31**, 551, (1999).
- [5] S. Al-Mousawi, M. M. Abdel-khalik, S. El-Sherbiny, E. John and M. H. Elnagdi, *J. Heterocyclic Chem.*, **38**, 949 (2000).
- [6] F. Al-Omran, N. Al-Awadi, O. Youssef and M. H. Elnagdi, *J. Heterocyclic Chem.*, **37**, 167, (2000).
- [7] B. Al-Saleh, M. M. Abdel-khalik, O. A. Salah and M. H. Elnagdi, *Heteroatom Chemistry*, **13**, 141, (2002).
- [8] M. H. Mohamed, M. M. Abdel-Khalik and M. H. Elnagdi, *J. Heterocyclic Chem.*, **38**, 685, (2001).
- [9] M. Abdel-Megid, M. H. Elnagdi and A. M. Negm, *J. Heterocyclic Chem.*, **39**, 105 (2002).
- [10] M. H. Elnagdi and A. W. Erian, *Bull. Chem. Soc. Jpn.*, **63**, 1854, (1990).
- [11] F. Al-Omran, *J. Heterocyclic Chem.*, **37**, 1219, (2000).
- [12] A. R. Katritzky and J. Wu, *Synthesis*, 597, (1994).
- [13] A. R. Katritzky and J. V. Shcherbakov, *J. Heterocyclic Chem.*, **33**, 2031, (1996).