N-Azolylmethyl Ketones as Building Blocks in Heterocyclic Synthesis: Synthesis of New Polyfunctionally Substituted Azolylarylazophenols, Azolylpyridones and Azolylthiophenes

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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.

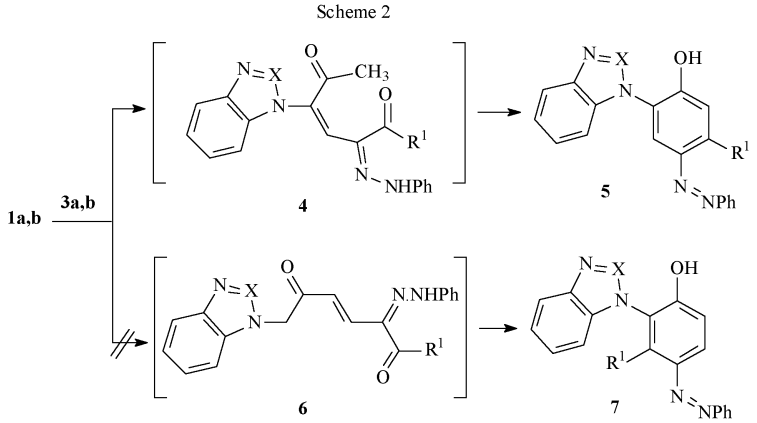
Thus, it has been found that **1a,b** and **2** react with 2-arylhydrazonopropanals **3a-c** to yield products of condensation *via* elimination of two water molecules. These can thus be formulated as **5** or its positional isomer **7** formed most likely *via* the presumed intermediates **4** and **6** respectively (Scheme 2). Structure **5** has been established based on the ^{1}H NMR spectra, as it revealed two aryl singlets at δ ~ 7.76 and 8.34 ppm. This excludes completely structure **7** that

Scheme 1

1a, X = N, R = CH_3
b, X = CH, R = CH_3
c, X = N, R = Ph

2

Scheme 2



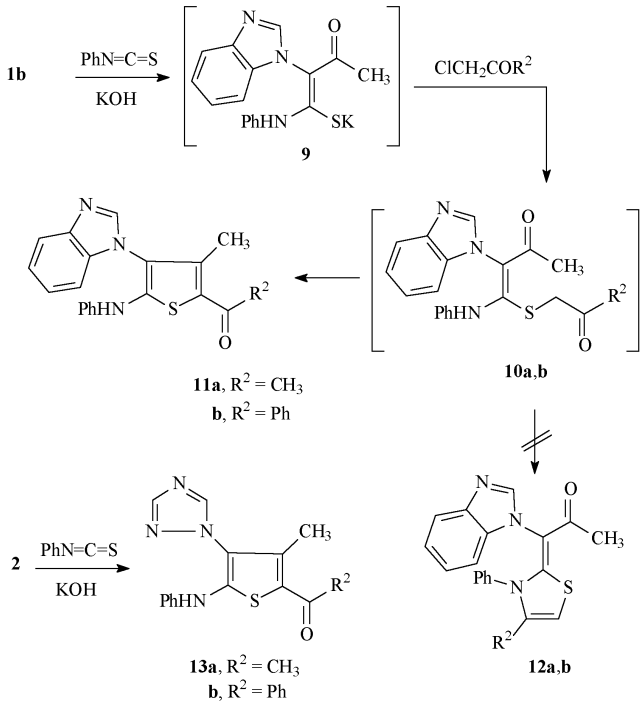
3a, R^1 = Ph
b, R^1 = 2-Thienyl
c, R^1 = 2-Furyl

8a-c

4-8a, R^1 = Ph, X = N
b, R^1 = 2-Thienyl, X = N
c, R^1 = 2-Furyl, X = N
d, R^1 = Ph, X = CH
e, R^1 = 2-Thienyl, X = CH
f, R^1 = 2-Furyl, X = CH

could have resulted, as it should display two doublets in its ^{1}H 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 azolylthiophenes **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 ^{1}H NMR which indicated in each case the presence of NH signal at δ ~ 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.

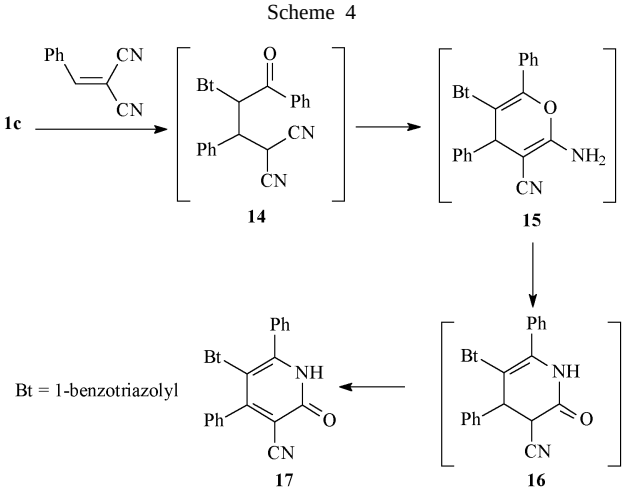
Scheme 3



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 $C_{24}H_{15}N_5O$. This is assumed to be **17,** formed *via* rearrangement of the initially formed 4*H*-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].

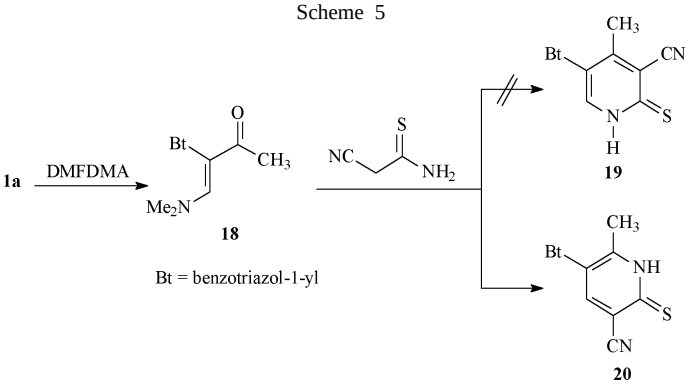
To increase the synthetic scope on the utility of these types of substrates, chemical modification of the synthon

Scheme 4



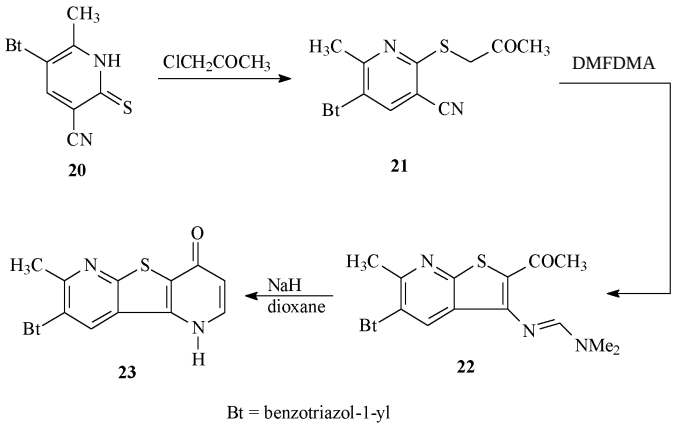
1a was then investigated to access complex heterocyclic systems (Schemes 5 and 6). Accordingly, dimethylformamide dimethylacetal condensed with **1a** yielding the enaminone **18** [7]. Compound **18** reacted with cyanothioacetamide to yield products that were formulated as **20** rather than **19**. ^{1}H NMR revealed pyridine H_4 proton at δ = 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 δ = 9.04 ppm as a singlet, this low field shift is a result of deshielding by the anisotropic effect of the *N*-lone-pair.

Scheme 5



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

Scheme 6



Bt = benzotriazol-1-yl

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. ^{1}H NMR spectra were recorded on a Varian EM-390 400 MHz spectrometer in deuteriochloroform or [$^2H_6$] 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$^+$]; ^{1}H 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 $C_{14}H_{11}N_3O$ (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$^+$]; ^{1}H 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 $C_{24}H_{17}N_5O$ (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$^+$]; ^{1}H 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 $C_{22}H_{15}N_5OS$ (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$^+$]; ^{1}H 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 $C_{22}H_{15}N_5O_2$ (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$^+$]; ^{1}H 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 $C_{25}H_{18}N_4O$ (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$^+$]; ^{1}H 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) ν_{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, benzoimidazolyl H), 7.84-7.87 (m, 3H, benzoimidazolyl H), 7.98 (s, 1H, H-3), 8.46 (s, 1H, benzoimidazolyl H_2), 11.55 (s, 1H, OH).

Anal. Calcd. for $C_{23}H_{16}N4O_2$ (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) ν_{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) ν_{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) ν_{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) ν_{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 (deutereochloroform): 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) ν_{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) ν_{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-yl)phenyl-methanone (**13b**).

This compound was obtained in 72% yield (2.60 g); mp. 190°; ir (KBr) ν_{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) ν_{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 $C_{24}H_{15}N_5O$ (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) ν_{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 $C_{19}H_{14}N_2S$ (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) ν_{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 $C_{16}H_{13}N_5OS$ (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) ν_{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 $C_{19}H_{18}N_6OS$ (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) ν_{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 $C_{17}H_{11}N5OS$ (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.

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