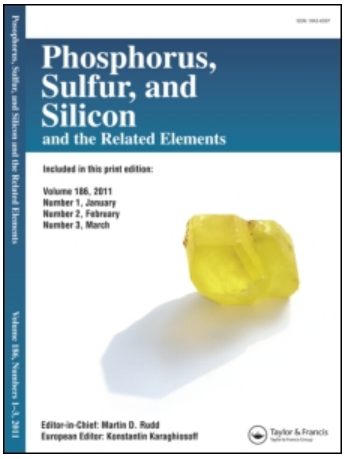


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

A Microwave Assisted Diazo Coupling Reaction: The Synthesis of Alkylazines and Thienopyridazines

Saleh Al-Mousawi[a]; Abdel-Zaher Elassar[a]; Morsy Ahmed El-Apasery[a]
[a] Department of Chemistry, University of Kuwait, Safat, Kuwait

To cite this Article Al-Mousawi, Saleh , Elassar, Abdel-Zaher and El-Apasery, Morsy Ahmed(2006) 'A Microwave Assisted Diazo Coupling Reaction: The Synthesis of Alkylazines and Thienopyridazines', Phosphorus, Sulfur, and Silicon and the Related Elements, 181: 8, 1755 — 1771
To link to this Article: DOI: 10.1080/10426500500536457
URL: http://dx.doi.org/10.1080/10426500500536457

Phosphorus, Sulfur, and Silicon, 181:1755–1771, 2006

ISSN: 1042-6507 print / 1563-5325 online
DOI: 10.1080/10426500500536457

Taylor & Francis
Taylor & Francis Group

A Microwave Assisted Diazo Coupling Reaction: The Synthesis of Alkylazines and Thienopyridazines

Saleh Al-Mousawi
Abdel-Zaher Elassar
Morsy Ahmed El-Apasery
Department of Chemistry, University of Kuwait, Safat, Kuwait

*Heating diazoaminobenzene with active methylene compounds **1–3** in microwave oven in acetic acid, in the presence of hydrochloric acid, afforded the corresponding arylhydrazones **5–7**. These reaction products were condensed with ethyl cyanoacetate in a domestic microwave oven after 1–2 minutes heating to yield the pyridazinones **8–12**. Compounds **8c** and **12** reacted with sulfur in basic DMF solution, in microwave oven using MORE technology to yield the thienopyridazinone **14** and **16** respectively. While **17** was produced when **8b** was treated like wise with sulfur and DMF in the presence of piperidine. Compounds **16** coupled with aromatic diazonium salts to yield arylazo derivatives **21a–c.***

Keywords Aminothiophenes; coupling reactions; Gewald reactions; pyridazines

INTRODUCTION

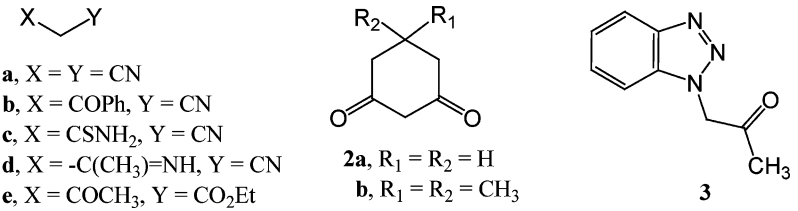
Since 1986, when Gedye et al.[1] and Giguere et al.[2] published their first articles on microwave-assisted synthesis in a household microwave oven, there has been enormous interest in this research filed. Several recent publications[3–10] published in more than one thousand articles have covered technical and synthetic achievements in this area. Almost every reaction type has been conducted in a domestic microwave oven where generally shorter reaction times and better yields were observed. The utility of microwave organic reaction enhancement technology developed by Bose et al.[11] or the dye technologies developed by Varma[12]

Received September 14, 2005; accepted November 20, 2005.
The authors are grateful to the University of Kuwait, Research Administration, for financial support through project SC 02/02. Analytical facilities provided by Science Analysis Facilities (SAF) are highly appreciated. The authors also express deep gratitude to Dr. Balkis Al-Saleh for her valuable supervision, useful discussion, and help.
Address correspondence to Abdel-Zaher Elassar, University of Kuwait, Department of Chemistry, Faculty of Science, P.O. Box 5969, Safat, 13060 Kuwait. E-mail: aelassar@yahoo.com

has substantially added green value to this technology because it saves waist and energy. The synthesis of azo dyes using microwave irradiation has received considerable attention in recent years.[13,14] Thus, treating equimolar amounts of aromatic amine, sodium nitrite, potassium hydroxide, and 2-naphthol or 2-naphthylamine in the presence of a few drops of water as an initiator with microwave irradiation was reported to give an azo product.[13] In addition, irradiation by the microwave of nitroarenes in the presence of bismuth metal and potassium hydroxide could be coupled to give azo dye.[14] In this article, a one-pot diazo coupling reaction under microwave irradiation by using diazoaminobenzene has been investigated. The obtained coupling product was used as building blocks for the synthesis of polyfunctionally substituted heteroaromatics. Since these reactions are two basic steps in the synthesis of our condensed aminothienopyridazines that have in the past been extensively utilized for the synthesis of phthalazenes,[15–18] we decided to develop a way to enable conducting both reactions in a microwave oven. In addition, such heteroaromatic amines as potential intermediates for the preparation of dyes for thermal diffusion printing was reported.[19]

RESULTS AND DISCUSSION

When **1a–e**, **2a,b**, and **3** (Scheme 1) were left at r.t. in acetic acid solution in the presence of hydrochloric acid with an quimolecular amount of diazoaminobenzene **4**, no coupling occurred, while a rearrangement of **4** into p-aminoazobenzene was observed.



1a, X = Y = CN
b, X = COPh, Y = CN
c, X = $CSNH_2$, Y = CN
d, X = -$C(CH_3)$=NH, Y = CN
e, X = $COCH_3$, Y = CO_2Et

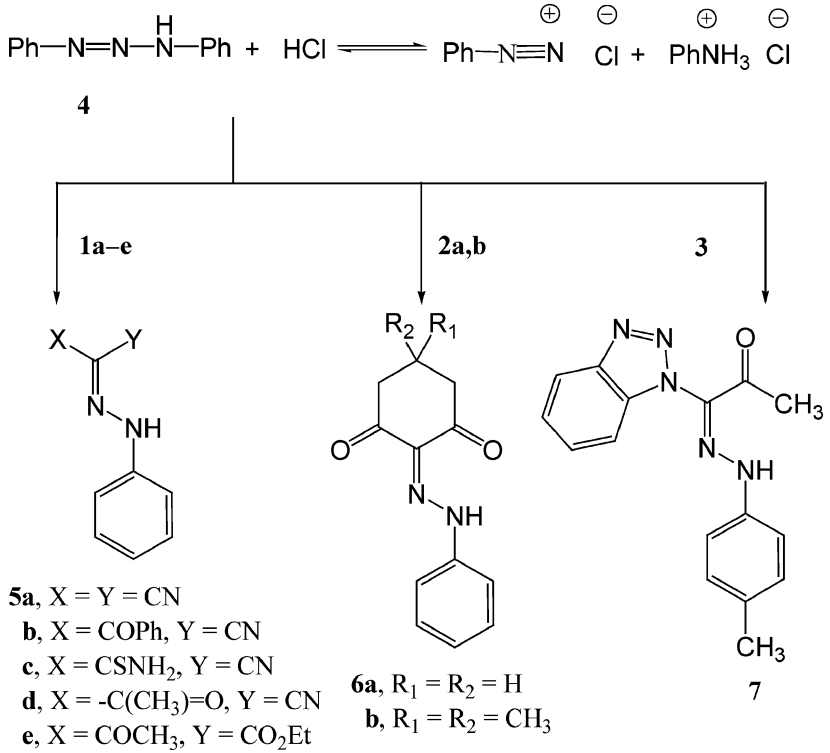
2a, $R_1 = R_2 = H$
b, $R_1 = R_2 = CH_3$

3

SCHEME 1

However, when the reaction mixture was heated in a microwave oven for 150 s in glacial acetic acid and in the presence of hydrochloric acid, arylazo derivatives **5–7** were formed in good yields (Scheme 2). The reaction product was established based on elemental analysis and spectral data. For example, the IR of compound **5a** revealed the presence of the NH and CN group at 3204 and 2223 cm^{-1}, respectively. The ^1H NMR showed aromatic protons at 7.20–7.48 ppm and NH at 13.02 ppm. In addition,^{13}C NMR data agreed with the expected one. Thus, signals

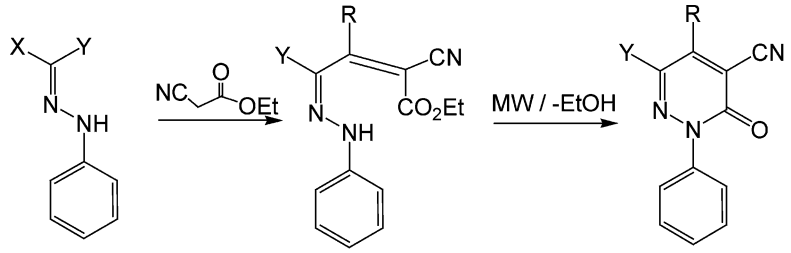
at 142.39, 130.84, 126.89, and 117.55 referred to the aromatic carbon atoms, while signals at 110.97 and 85.54 ppm revealed the presence of cyano and imine carbons. Moreover, MS (EI) showed m/z at 170 (M^+).



SCHEME 2

The arylhydrazones **5b,d,e** condensed with ethyl cyanoacetate in presence of ammonium acetate and acetic acid on heating in a microwave oven for 60 s to yield pyridazinones **8a–c**. It is of value to report that only **5e** condensed with ethyl cyanoacetate on heating in AcOH-$AcONH_4$ in 2 h. Under similar classical reflux conditions, **5b** failed earlier to condense, and **5d** required utilizing to produce **8b** in the absence of an azotropic water separator. The amide **8d** (X = $CONH_2$, R=CH_3) was the only product (Scheme 3). The reaction product was believed to proceed through the condensation of active methylene in ethyl cyanoacetate with the carbonyl group in **5b,d,e** to give an intermediate, which readily cyclized under the reaction condition to give the pyridazinone derivatives **8a–c**. The structure of **8a** was established based on ^{13}C NMR, which showed the carbonyl group at

156.88, in addition to the aromatic, pyridazine, and cyano carbons at 152.04, 140.74, 132.98, 130.96, 130.89, 130.30, 130.28, 129.66, 126.56, 124.02, 114.50, 114.45, and 114.00 ppm. Moreover, the mass spectrum showed m/z of the molecular formula $C_{18}H_{10}N_4O$ at 298 (M^+), which agreed with the postulated structure. Similarly, compounds **8b,c** were established.



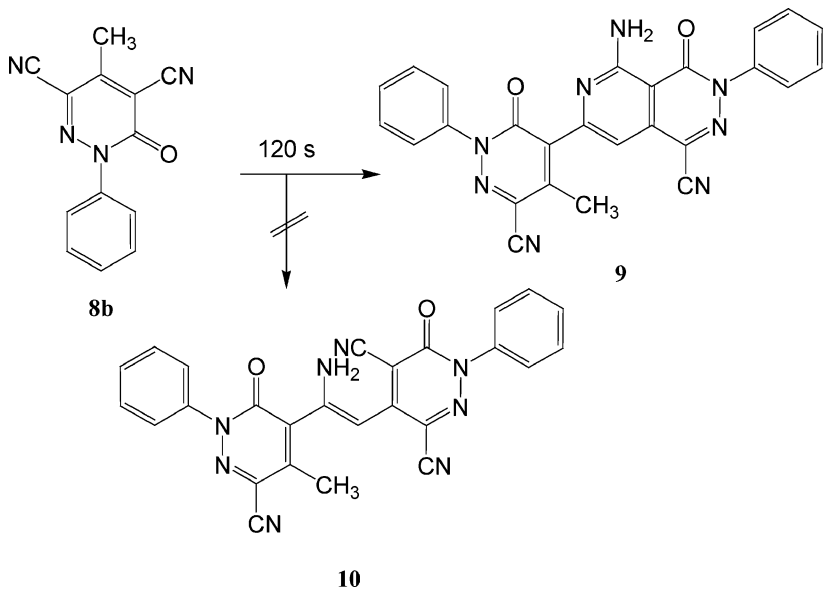
5b, X = COPh, Y = CN
d, X = -C(CH_3)=O, Y = CN
e, X = $COCH_3$, Y = CO_2Et

8a, Y = CN, R = Ph
b, Y = CN, R = CH_3
c, Y = CO_2Et, R = CH_3

SCHEME 3

When **8b** was heated under microwave irradiation for 120 s, a dimeric compound was produced. This was assigned structure **9** rather than **10** based on ^{13}C NMR, which revealed only two cyano carbons, 159.31, 158.59 (2CO), 158.21, 156.98, 152.27, 145.30, 141.83, 141.48, 141.02, 130.50, 130.06, 130.01, 129.77, 128.86, 127.13, 126.77, 102.28, 98.42 (aromatic and azine carbons), 115.62, 114.72 (2CN), and 20.40 ppm (CH_3). In addition,^1H NMR showed a singlet at 2.64 ppm, which represented protons of the methyl group. Signals at 7.64–7.51 ppm represented 10 aromatic protons, a pyridinic proton at 7.75 ppm, and a broad band at 8.51 ppm for the amino group (Scheme 4).

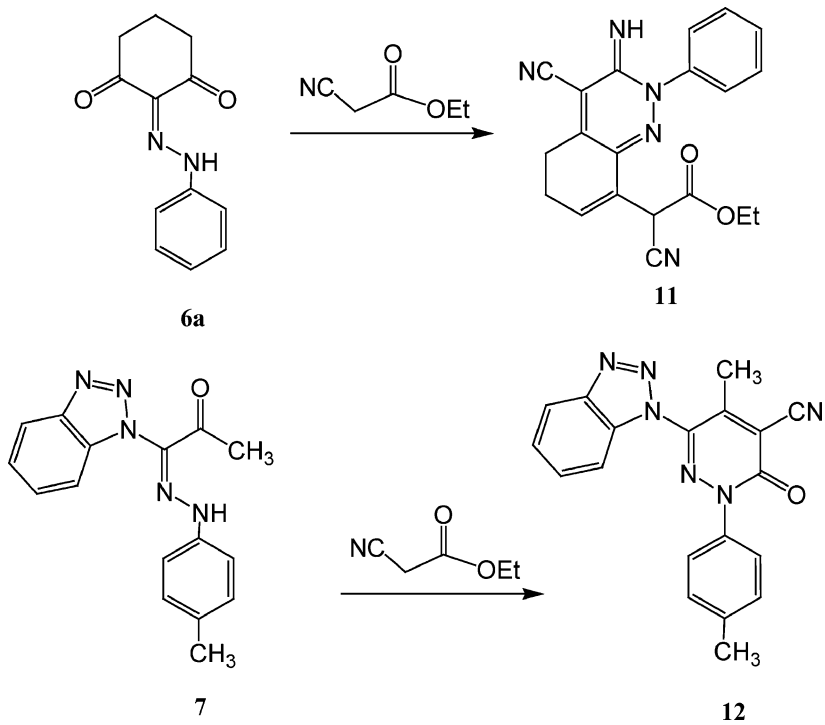
Compounds **6a** and **7** were condensed with ethyl cyanoacetate, ammonium acetate, and acetic acid in a microwave at 840 w for 60 s to yield the pyridazinones **11** and **12**, respectively (Scheme 5). Compound **11** was established based on mass spectrum, which indicated that the reaction happened in a 1:2 ratio (**6a**:ethyl cyanoacetate), where m/z equaled 359 (M^+). ^1H NMR showed the ester group at 1.04 ppm (triplet, methyl) and 4.32 ppm (quartet, methylene) in addition to the other characteristic protons. While compound **12** was considered as a reaction product based on ^1H NMR, which revealed the presence of benzotriazole protons at 7.89 ppm (d, 1H, J = 8 Hz, benzotriazolyl-H), 8.20 ppm (d, 1H, J = 8 Hz, benzotriazol-H). In addition, other 6 aromatic protons at 7.33–7.71 ppm.



SCHEME 4

Alkyl groups attached at activated positions in azines were active toward an electrophilic reagent in acidic and basic media. In a basic medium, the carbanion was stabilized by delocalizing its negative charge on the heteroatom. The presence of the cyano group adjacent to the alkyl group in such system was able to undergo Gewald synthesis to give the thiophene ring, whereas the carbanion formed in a basic medium and reacted with sulfur and cyclized to give the binuclear product. Thus, the target ring system, thienopyridazines **14** and **16**, could be obtained when **8c** or **12** reacted with sulfur in DMF in the presence of piperidine in a microwave oven for 120 s and afforded the thienopyridazinone **14** and **16**. The formation of **14** and **16** was believed to be obtained through the formation of the nonisolated intermediates **13** and **15** that readily cyclized under the reaction condition to give the final isolated products **14** and **16** (Scheme 6). These products were characterized by the presence of the elemental analysis of sulfur in 10.01% and 8.19%, respectively.

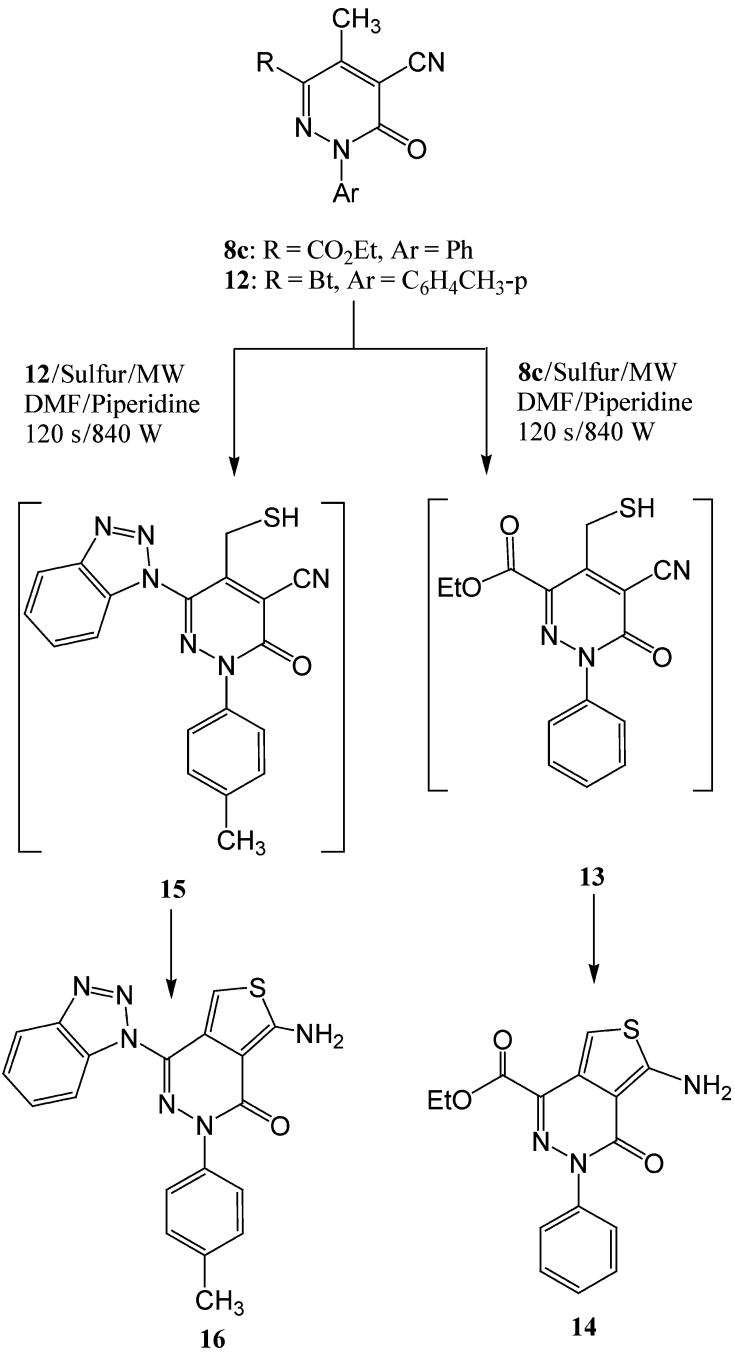
Depicts all possible structures proposed for the reaction of **8b** with sulfur was indicated in Scheme 7. However, among these structures, **17** was assigned to be an isolated product on the basis of elemental analysis and spectral data. For example, mass spectrum, which revealed the formation of a compound **17** with the molecular formula $C_{26}H_{16}N_8O_3S$ and molar mass m/z = 502 (M^+). In addition, the elemental analysis



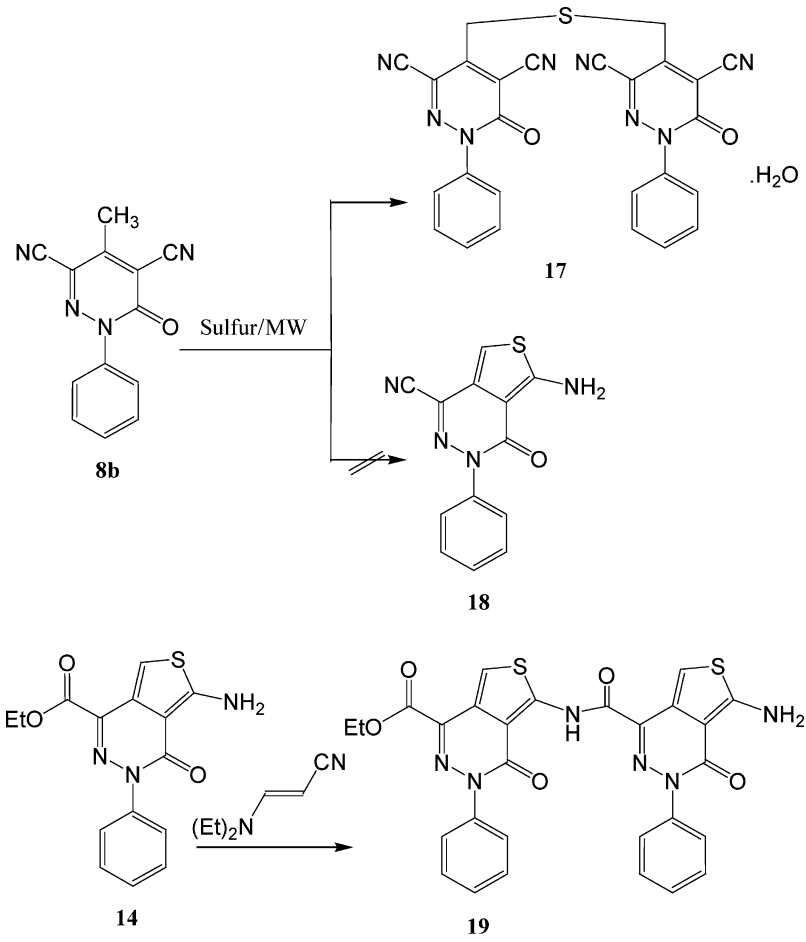
SCHEME 5

of sulfur was found to be 6.00%, which closed to the theoretical value 6.16%. Similar behavior had been reported in previous stadies.[20] It was reported that fused thiophenees added to dienophiles in a Diels-Alder type [4 + 2] according to a suprafacial-suprafacial mode to yield products of addition followed by hydrogen sulfide elimination or thiepen formation.[20–22] When compound **14** underwent investigation as a diene for cycloaddition with the 3-diethylaminoacrylonitrile as a dienophile, in acedic medium the unexpected product **19** was obtained. Compound **19** was established based on mass spectrum, which indicated the formation of a dimer with the molecular formula $C_{28}H_{20}N_6O_5S_2$ with the molar mass m/z = 584 (M^+). In addition, the elemental analysis of sulfur and nitrogen were 10.60% and 14.62%, respectively (Scheme 7).

The Reactivity of aminothienopyridazine toward nitrogen electrophiles, e.g., benzenediazonium chloride, was investigated. The coupling took place at the amino group rather than thienyl-H; this may be attributed to the steric effect due to the presence of bulky group, benzotriazolyl group, at position-4. A similar coupling product has been obtained when benzenediazonium chloride coupled with aniline in the

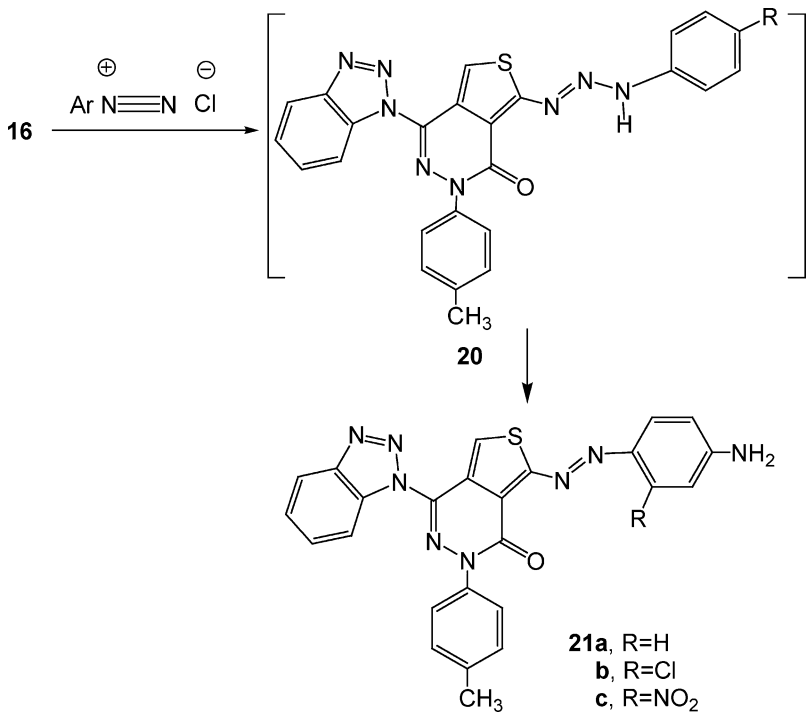


SCHEME 6



SCHEME 7

case of decreasing mineral acids. A rearrangement was expected for these compounds in an acidic medium at 40°C. Thus, compound **16** reacted with benzenediazonium salt in an acidic medium to afford the diazo compound **21**. The obtained compound **21** is believed to be formed through the nonisolated intermediate **20**, which underwent rearrangement to give the final isolated product **21a–c**. Structures **21a–c** were supported by ^{1}H NMR spectra that displayed a singlet at δ_H ca. 7.4 ppm, assigning for thienyl-H with downfield aromatic protons and NH_2 signals (Scheme 8).



SCHEME 8

CONCLUSION

1. Diazo coupling has been obtained in a good yield, short time, and in one step, when active methylene compounds were treated with diazoaminobenzene under microwave irradiation.
2. The target thienopyridazines could be obtained when diazo compounds were treated with ethyl cyanoacetate and then with sulfur in a microwave oven.
3. The reactivity of thienopyridazines toward dienophiles and azonium salt had been studied. Thus, developing a way to enable conducting all reaction steps in a microwave oven had been successful.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Perkin-Elmer System 2000 FTIR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 400, 400MHz superconducting NMR spectrometer in $CDCl_3$ or DMSO-d_6 as a solvent

and TMS as an internal standard; chemical shifts are reported in units (ppm). Mass spectra were measured on a VG Autospec-Q (high resolution, high performance, trisector GC/MS/MS). Microanalyses were performed on a LECO CHNS-932 elemental analyzer. Microwave experiments were conducted in a microwave oven DAEWOO, edition II (KOR-8667).

The General Procedure for the Preparation of Compounds 5–7

A mixture of compounds **1–3** (0.01 mol), diazoaminobenzene **4** (0.01 mol), and glacial acetic acid (20 mL) in the presence of hydrochloric acid (2 mL) was heated in a microwave oven at 560 W for 150 s. The mixture was left to cool at r.t. and then poured onto ice water containing sodium carbonate (2 g). The solid product, so formed, was collected by filtration and crystallized from the proper solvent.

(Phenylhydrazono)malononitrile (5a)

Yellow crystals (70%); m.p. 157–159°C; IR (ν_{max}: 3204 (NH), 2223 cm^{-1} (CN); ^1H NMR: (DMSO-d_6) δ_H 7.20–7.48 (m, 5H, Ar-H), 13.02 ppm (br, ^1H, NH). ^{13}C NMR: (DMSO-d_6) δ_C: 142.39, 130.84, 126.89, 117.55 (aromatic carbon atoms), 110.97 (CN), 85.54 ppm (imine carbon). MS (EI): m/z = 170 (M^+). Anal. calcd. for $C_9H_6N_4$: C, 63.52; H, 3.55; N, 32.92. Found: C, 63.89; H, 3.84; N, 31.37.

3-Oxo-3-phenyl-2-(phenylhydrazono)propionitrile (5b)

Yellow crystals (90%), m.p. 138–140°C; IR (ν_{max}: 3221 (NH); 2217 (CN), 1652 cm^{-1} (CO); ^1H NMR ($CDCl_3$) (δ_H: 7.21–8.04 (m, 10H, Arom-H), 9.41 ppm (br, 1H, NH). ^{13}C NMR: (DMSO-d_6) (δ_C: 188.53 (CO), 143.06, 137.40, 133.34, 130.84, 130.54, 129.11, 126.10, 117.38, 114.16, 112.52 ppm (aromatic, imine, and cyano carbons). MS (EI) m/z = 249 (M^+). Anal. calcd. for $C_{15}H_{11}N_3O$: C, 72.28; H, 4.45; N, 16.86. Found: C, 71.97; H, 4.49; N, 16.91.

2-Cyano-2-(phenylhydrazono)ethanethioamide (5c)

Orange crystals (68%), m.p. 215°C; IR (ν_{max}: 3234 and 3140 (NH_2), 3061 (NH), 2209 cm^{-1} (CN); ^1H NMR (DMSO-d6) δ_H: 7.10–7.74 (m, 5H, Arom-H), 9.34, 9.68 (s, 2H, NH_2); 11.57 ppm (s, 1H, NH). ^{13}C NMR: (DMSO-d_6) (δ_C: 188.94 (CS), 143.11; 130.44, 125.36, 117.50, 113.67; 112.37 ppm (imine, aromatic, and cyano carbons). MS (EI) m/z = 204 (M^+). Anal.

calcd. for $C_9H_8N_4S$: C, 52.93; H, 3.95; N, 27.43; S, 15.70. Found: C, 53.39; H, 4.05; N, 27.39; S, 16.04.

3-Imino-2-(phenylhydrazono)butanenitrile (5d)

Yellow crystals (86%); m.p. 174–176°C; IR (ν_{max}: 3227 (NH); 2213 (CN), 1683 cm^{-1} (CO); ^1H NMR (DMSO-d_6) δ_H: 2.41 (s, 3H, CH_3); 7.16–7.56 (m, 5H, Arom-H), 12.28 ppm (s, 1H, NH). ^{13}C NMR: (DMSO-d_6) (δ_C: 193.76 (CO), 142.99, 130.51, 126.04, 117.26, 114.60, 112.02 (imine, aromatic, and cyano carbons), 25.63 ppm (CH_3). MS (EI) m/z = 187 (M^+). Anal. calcd. for $C_{10}H_9N_3O$: C, 64.16; H, 4.85; N, 22.45. Found: C, 64.16; H, 4.78; N, 22.27.

Ethyl 3-Oxo-2-(phenylhydrazono)butanoate (5e)

Yellow crystals (78%); m.p. 77°C; IR (ν_{max}: 3063 (NH), 1710 cm^{-1} (CO); ^1H NMR (DMSO-d_6) δ_H: 11.68 (br, 1H, NH), 7.44–7.06 (m, 5H, Arom-H), 4.30 (q, 2H, CH_2), 2.47 (s, 3H, CH_3), 1.27 ppm (t, 3H, CH_3). ^{13}C NMR: (DMSO-d_6) δ_C: 194.60 (acetyl carbonyl carbon), 163.64 (ester carbonyl carbon), 143.47, 131.80, 130.45, 126.34, 117.17 (imine and aromatic carbons), 61.45 (CH_2), 26.48, 14.92 ppm ($2CH_3$). MS (EI) m/z = 234 (M^+). Anal. calcd. for $C_{12}H_{14}N_2O_3$: C, 61.53; H, 6.02; N, 11.96. Found: C, 61.52; H, 6.01; N, 12.11.

2-(Phenylhydrazono)cyclohexane-1,3-dione (6a)

Orange crystals (83%), m.p. 144°C; IR (ν_{max}: 3055 (NH), 1676 (CO), 1628 cm^{-1} (CO); ^1H NMR (DMSO-d_6); δ_H: 1.94–2.00 (m, 2H, cyclohexanyl-H); 2.50–2.67 (m, 4H, cyclohexanyl-H), 7.20–7.81 (m, 5H, Arom-H), 14.84 ppm (s, 1H, NH). ^{13}C NMR: (DMSO-d_6) δ_C: 198.63, 194.21 (2CO), 142.50, 132.31, 130.71, 127.41, 118.34 (imine and aromatic carbons), 39.56, 39.88, 18.90 ppm (cyclohexyl-CH_2). MS (EI) m/z = 216 (M^+). Anal. calcd. for $C_{12}H_{12}N_2O_2$: C, 66.65; H, 5.59; N, 12.96. Found: C, 66.46; H, 5.42; N, 13.00.

5,5-Dimethyl-2-(phenylhydrazono)cyclohexane-1,3-dione (6b)

Brown crystals (89%), m.p. 149°C; IR ν_{max}: 3052 (NH), 1673 (CO), 1632 cm^{-1} (CO); ^1H NMR (DMSO-d_6); δ_H: 1.03 (s, 6H, $2CH_3$); 2.50–2.63 (m, 4H, cyclohexanyl-H); 7.24–7.61 (m, 5H, Arom-H), 14.88 ppm (s, 1H, NH). ^{13}C NMR: (DMSO-d_6) δ_C: 197.68, 193.53 (2CO), 142.30, 130.93, 130.54, 127.31, 117.94 (aromatic and imine carbons), 52.77 (cyclohexyl-CH_2), 39.71 (cyclohexyl-t-carbon), 31.14, 28.83 ppm (2 CH_3). MS (EI)

m/z = 244 (M^+). Anal. calcd. for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47. Found: C, 68.84; H, 6.49; N, 11.67.

1-(1H-1,2,3-benzotriazol-1-yl)-1-[(4-methylphenyl)hydrazono] Acetone (7)[23]

Brown crystals (86%), m.p. 186°C; IR ν_{max}: 3186 (NH), 1671 cm^{-1} (CO). ^1H NMR (DMSO-d_6); δ_H: 2.26 (s, 3H, CH_3), 2.63 (s, 3H, $COCH_3$), 7.10–7.53 (m, 6H, Arom-H), 7.89 (d, 1H, J = 8 Hz, benzotriazolyl-H), 8.12 (d, 1H, J = 8Hz, benzotriazolyl-H), 10.96 ppm (br, 1H, NH). MS (EI) m/z = 293 (M^+). Anal. calcd. for $C_{16}H_{15}N_5O$: C, 65.52; H, 5.15; N, 23.88. Found: C, 65.67; H, 5.15; N, 23.86.

The General Procedure for the Preparation of Compounds 8a–c, 9, 11, and 12

A mixture of **5b** or **5d,e**, **6a**, or **7** (0.01 mol); ethyl cyanoacetate (1.13 g, 0.01 mol); ammonium acetate (2 g), and acetic acid (0.6 mol) was heated in a microwave at 840 w for 60 s (120 s needed for compound **9**) and then left to cool and triturated with ethanol. The solid product, so formed, was collected by filtration and crystallized from dioxane.

6-Oxo-1,4-diphenyl-1,6-dihydropyridazine-3,5-dicarbonitrile (8a)

Orange crystals (83%), m.p. 258–259°C; IR ν_{max}: 2245 (CN), 1690 cm^{-1} (CO); ^1H NMR (DMSO-d_6); δ_H: 7.59–7.75 ppm (m, 10H, Arom-H). ^{13}C NMR: (DMSO-d_6) δ_C: 156.88 (CO), 152.04, 140.74, 132.98, 130.96, 130.89, 130.30, 130.28, 129.66, 126.56, 124.02, 114.50, 114.45, 114.00 ppm (aromatic, pyridazine, and cyano carbons). MS:(EI) m/z = 298 (M^+). Anal. calcd. for $C_{18}H_{10}N_4O$: C, 72.48; H, 3.38; N, 18.78. Found: C, 71.98; H, 3.71; N, 18.73.

4-Methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3,5-dicarbonitrile (8b)

Brown crystals (81%), m.p. 182–184°C; IR ν_{max}: 2238 (CN), 1685 cm^{-1} (CO); ^1H NMR (DMSO-d_6); δ_H: 2.60 (s, 3H, CH_3), 7.55–7.57 ppm (m, 5H, Ar-H). ^{13}C NMR: (DMSO-d_6) δ_C: 156.46 (CO), 152.81, 140.66, 130.81, 129.77, 127.12, 126.77, 125.28, 114.64, 113.63 (aromatic, pyridazine, and cyano carbons), 19.46 ppm (CH_3). MS: (EI) m/z = 236 (M^+). Anal.

calcd. for $C_{13}H_8N_4O$: C, 66.10; H, 3.41; N, 23.72. Found: C, 66.11; H, 3.62; N, 23.71.

Ethyl 5-Cyano-4-methyl-6-oxo-1-phenyl-1,6-dihydropyridazine-3-carboxylate (8c)

Green crystals (84%), m.p. 168–170°C; IR ν_{max}: 2234 (CN), 1719 (CO ester), 1676 cm^{-1} (ring CO). ^1H NMR (DMSO-d_6); δ_H 1.30 (t, 3H, CH_3); 2.64 (s, 3H, CH_3); 4.30 (q, 2H, CH_2); 7.20–7.57 ppm (m, 5H, Arom-H). ^{13}C NMR: (DMSO-d_6) δ_C: 162.82, 162.79 (2CO), 160.53, 157.02, 123.12 (pyridazine carbons), 141.17, 136.51, 130.23, 126.81 (aromatic carbons), 114.43 (CN), 62.33 (CH_2), 14.95, 14.90 ppm ($2CH_3$). MS (EI): m/z = 283 (M^+). Anal. calcd. for $C_{15}H_{13}N_3O_3$: C, 63.60; H, 4.63; N, 14.83. Found: C, 63.45; H, 4.63; N, 14.97.

5-Amino-7-(6-cyano-2-phenyl-5-methyl-3-oxo-2,3-dihydropyridazin-4-yl)-4-oxo-3-phenyl-3,4-dihydropyrido[3,4-d]pyridazine-1-carbonitrile (9)

Dark brown crystals (85%), m.p. >300; IR ν_{max}: 3282 and 3162 (NH_2), 2217 (CN), 1652 and 1632 cm^{-1} (2CO). ^1H NMR (DMSO-d_6); δ_H 2.64 (s, 3H, CH_3); 7.64–7.51(m, 10H, Arom-H), 7.75 (s, 1H, pyridine-H), 8.51 ppm (br, 2H, NH_2). ^{13}C NMR (DMSO-d_6); δ_C 159.31, 158.59 (2CO), 158.21, 156.98, 152.27, 145.30, 141.83, 141.48, 141.02, 130.50, 130.06, 130.01, 129.77, 128.86, 127.13, 126.77, 102.28, 98.42 (aromatic and azine carbons), 115.62, 114.72 (2CN), 20.40 ppm (CH_3). MS (EI): m/z = 472 (M^+). Anal. calcd. for $C_{26}H_{16}N_8O_2$: C, 66.10; H, 3.41; N, 23.72. Found: C, 65.62; H, 3.66; N, 23.04.

Ethyl Cyano(4-cyano-3-imino-2-phenyl-2,3-5,6-tetrahydrocinnolin-8-yl)acetate (11)

Dark green crystals (79%), m.p. 206–208°C; IR ν_{max}: 3185 (NH), 2212 (CN), 1632 cm^{-1} (CO); ^1H NMR (DMSO-d_6) δ_H 1.04 (t, 3H, CH_3); 2.50–3.45 (m, 5H, cyclohexenyl and CH); 4.32 (q, 2H, CH_2); 6.51 (t, 1H, CH); 6.69–7.81 ppm (m, 6H, Arom-H and NH). MS (EI): m/z = 359 (M^+). Anal. calcd. for $C_{20}H_{17}N_5O_2$: C, 66.84; H, 4.77; N, 19.49. Found: C, 66.99; H, 4.53; N, 19.74.

6-(1H-1,2,3-benzotraizol-1-yl)-5-methyl-2-(4-methylphenyl)-3-oxo-2,3-dihydropyridazine-4-carbonitrile (12)

Green crystals (91%), m.p. 210°C; IR ν_{max}: 2229 (CN), 1673 cm^{-1} (CO); ^1H NMR (DMSO-d_6); δ_H 2.35 (s, 3H, CH_3); 2.51 (s, 3H, CH_3); 7.33–7.71 (m, 6H, Arom-H); 7.89 (d, 1H, J = 8 Hz, benzotriazolyl-H), 8.20 ppm (d, 1H, J = 8 Hz, benzotriazol-H). ^{13}C NMR (DMSO-d_6) δ_C: 157.00 (CO), 150.07, 145.66, 140.02, 139.00, 138.54, 133.78, 130.58, 130.46, 126.46, 126.34, 120.70, 117.26, 114.39, 112.80 (aromatic, pyridazine, and cyano carbons), 21.78, 18.89 ppm (2 CH_3). MS (EI): m/z = 342 (M^+). Anal. calcd. for $C_{19}H_{14}N_6O$: C, 66.66; H, 4.12; N, 24.55. Found: C, 66.57; H, 4.17; N, 24.26.

The General Procedure for the Preparation of Compounds 14, 16, and 17

A solution of compounds **8b**, **8c**, or **12** (0.01 mol) in dimethyl formamide (5 mL) was treated with sulphur (0.01 mol) and piperidine (0.2 mol). The reaction mixture was heated in a microwave at 840 W for 120 s and then poured onto water. The solid product, so formed, was collected by filtration and crystallized from dioxane/ethanol.

Ethyl 5-Amino-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-d]pyridazine-1-carboxylate (14)

Green crystals (80%), m.p. 191°C, IR ν_{max}: 3301 and 3148 (NH_2), 1701 (CO ester), 1643 cm^{-1} (ring CO); ^1H NMR (DMSO-d_6); δ_H 1.45 (t, 3H, J = 8 Hz, CH_3), 4.42 (q, 2H, J = 8 Hz, CH_2); 7.11(s, 1H, thienyl-H). 7.37–7.52 (m, 5H, Arom-H). 7.64(s, 2H, NH_2). MS (EI): m/z = 315 (M^+). Anal. calcd. for $C_{15}H_{13}N_3O_3S$: C, 57.13; H, 4.16; N, 13.33; S, 10.17. Found: C, 57.16; H, 4.29; N, 13.31; S, 10.01.

7-Amino-4-(1H-1,2,3-benzotriazol-1-yl)-2-(4-methylphenyl)thieno[3,4-d]pyridazin-1(2H)-one (16)

Green crystals (88%), m.p. 220°C, IR ν_{max}: 3277 and 3149 (NH_2), 1641 cm^{-1} (CO). ^1H NMR (DMSO-d_6) δ_H 2.38 (s, 3H, CH_3), 7.31 (d, 2H, J = 8 Hz, Arom-H), 7.37(s, 1H, thienyl-H). 7.53–7.57 (m, 3H, Arom-H). 7.67 (t, 1H, J = 8 Hz, benzotriazolyl-H), 7.77 (s, 2H, NH_2), 8.12 (d, 1H, J = 8 Hz, benzotriazolyl-H), 8.22 (d, 1H, J = 8 Hz, benzotriazolyl-H), ^{13}C NMR (DMSO-d_6) δ_C: 164.52 (CO), 158.93, 145.95, 139.22, 137.50, 136.62, 131.97, 130.44, 130.10, 126.67, 126.63, 123.60, 120.68, 114.63, 105.85, 105.65 (aromatic and thienopyridazine carbons), 21.71 ppm

(CH_3). MS (EI): m/z = 374 (M^+). Anal. calcd. for $C_{19}H_{14}N_6OS$: C, 60.95; H, 3.77; N, 22.45; S, 8.54. Found: C, 61.26; H, 3.82; N, 22.31; S, 8.19.

{Di-4-[(3,5-dicyano-1-phenylpyridazine-6-one)]methylsulphide}monohydrate (17)

Dark brown crystals (75%), m.p. >300°C; IR ν_{max}: 2213 (CN), 1650 cm^{-1} (CO); ^1H NMR (DMSO-d_6) δ_H 2.73 (s, 2H, CH_2); 2.89 (s, 2H, CH_2); 7.08–7.96 (m, 10H, Ar-H). ^{13}C NMR (DMSO-d_6) δ_C: 163.44 (CO), 159.71, 158.73, 140.53, 130.38, 129.53, 127.67, 126.97, 115.92, 106.95 (aromatic, pyridazine, and cyano carbons), 31.80 ppm (CH_2). MS (EI): m/z = 502 (M^+). Anal. calcd. for $C_{26}H_{16}N_8O_3S$: C, 59.99; H, 3.10; N, 21.53; S, 6.16. Found: C, 59.99; H, 3.46; N, 21.17; S, 6.00.

Ethyl 5-[(5-Amino-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-d]pyridazine-1-carbonyl)amino]-4-oxo-3-phenyl-3,4-dihydrothieno[3,4-d]pyridazine-1-carboxylate (19)

A mixture of compound **14** (3.15 g, 10 mmol) and 3-diethylaminoacrylonitrile (1.24 g, 10 mmol) in a mixture of acetic acid (10 mL) and dioxane (20 mL) was refluxed for 10 h and then allowed to cool to r.t. The solvent was removed, and the residue cooled to deposit a solid, which was crystallized from DMF.

Buff crystals (65%), m.p. >300°C; IR ν_{max}: 3424, 3312 (NH_2) and 3168 (NH), 1726 (CO ester), 1679 and 1659 cm^{-1} (ring 2CO); ^1H NMR (DMSO-d_6); δ_H 1.33 (t, 3H, J = 8 Hz, CH_3), 4.36 (q, 2H, J = 8 Hz, CH_2); 6.19 (s, 2H, thienyl-H). 7.21–7.48 (m, 10H, Arom-H). 8.02 (s, 2H, NH_2, D_2O exchangeable), 12.22 (s, 1H, NH_2, D_2O exchangeable). MS (EI): m/z = 584 (M^+). Anal. calcd. for $C_{28}H_{20}N_6O_5S_2$. C, 57.52; H, 3.45; N, 14.38; S, 10.97. Found: C, 57.52; H, 3.75; N, 14.62; S, 10.60.

The Reaction of Compound 16 with Aromatic Diazonium Salts

A solution of aryldiazonium chloride (prepared from the corresponding aromatic amine [0.01 mol] and the appropriate quantities of both hydrochloric acid and sodium nitrite) (10 mmol) at 0°C was added to a solution of **16** (10 mmol) in acetic acid (50 mL) containing sodium acetate (0.60 g). The reaction mixture was stirred at r.t. for 1 h, and the solid product was collected by filtration and crystallized from DMF/ethanol (3:1).

7-(4′-Aminophenylazo)-4-[benzotriazol-1-yl]-2-P-tolyl-2H-thieno[3,4-d] pyridazin-1-one (21a)

Light red crystals (75%), m.p. > 300°C; IR: (max/cm^{-1} 3326 and 3215 (NH_2), 1655 (CO); 1H NMR (DMSO-d_6): δ_H 2.38 (s, 3H, CH_3), 6.49 (d, 2H, J = 8.7 Hz, 4-tolyl-H), 7.16 (d, 2H, J = 8.7 Hz, 4-tolyl-H), 7.30–7.32 (m, 2H, benzotriazolyl-H), 7.38 (s, 1H, thienyl-H), 7.49–7.60 (m, 4H, phenyl-H), 7.76 (br, 2H, NH_2, D_2O exchangeable), 7.90 (d, 1H, J = 8 Hz, benzotriazolyl-H). 8.28 (d, 1H, J = 8 Hz, benzotriazolyl-H). Ms: m/z 478 [M^+]. $C_{25}H_{18}N_8OS$: C, 62.74; H, 3.79; N, 23.41; S, 6.70. Found: C, 62.63; H, 3.79; N, 23.18; S, 6.86.

7-(4′-Amino-2′-chlorophenylazo)-4-[benzotriazol-1-yl]-2-P-tolyl-2H-thieno[3,4-d]pyridazin-1-one (21b)

Red crystals (76%), m.p. >300°C; IR: ν_{max} cm^{-1} 3325 and 3220 (NH_2), 1655 (CO); ^{1}H NMR (DMSO-d_6): δ_H = 2.38 (s, 2H, CH_3), 6.43 (d, 2H, J = 8.8 Hz, 4-tolyl-H), 7.20 (d, 2H, J = 8.8 Hz, 4-tolyl-H), 7.30–7.32 (m, 2H, benzotriazolyl-H), 7.37 (s, 1H, thienyl-H), 7.54 (d, 2H, J = 8.6 Hz, 4-chlorophenyl-H), 7.60 (d, 2H, J = 8.6 Hz, 4-chlorophenyl-H), 7.76 (br, 2H, NH_2, D_2O exchangeable), 7.89 (d, 1H, J = 8 Hz, benzotriazolyl-H), 8.31 (d, 1H, J = 8 Hz, benzotriazolyl-H). Ms: m/z 512 [M^+]. $C_{25}H_{17}N_8OSCl$: C, 58.53; H, 3.34; N, 21.84; S, 6.25. Found: C, 59.10; H, 3.49; N, 21.89; S, 6.32.

7-(4′-Amino-2′-nitrophenylazo)-4-[benzotriazol-1-yl]-2-P-tolyl-2H-thieno[3,4-d]pyridazin-1-one (21c)

Light red crystals (78%), m.p. >300°C; IR: ν_{max}/cm^{-1} 3323 and 3218 (NH_2), 1666 (CO); ^{1}H NMR (DMSO-d_6): δ_H = 2.37 (s, 3H, CH_3), 6.53 (d, 2H, J = 8.8 Hz, 4-tolyl-H), 7.33 (d, 2H, J = 8.8 Hz, 4-tolyl-H), 7.36 (s, 1H, thienyl-H), 7.55–7.62 (m, 5H, benzotriazolyl-H and arom-H), 7.90 (d, 1H, J = 8 Hz, benzotriazolyl-H). 7.96 (br, 2H, NH_2, D_2O exchangeable), 8.38 (d, 1H, J = 8 Hz, benzotriazolyl-H). Ms: m/z 523 [M^+]. $C_{25}H_{17}N_9O_3S$: C, 57.35; H, 3.27; N, 24.07; S, 6.12. Found: C, 57.33; H, 3.36; N, 23.79; S, 5.88.

REFERENCES

[1] R. Gedye, F. Smith, K. Westaway, A. Humera, L. Baldisera, L. Laberge, and J. Rousell, *Tetrahedron Lett.*, **26,** 279 (1986).

[2] R. J. Giguere, T. L. Bray, S. M. Duncan, and G. Majetich, *Tetrahedron Lett.*, **27,** 49451 (1986).

[3] D. Kumar, K. V. G. Sekhar, H. Dhillon, V. S. Rao, and R. S. Varma, *Green Chem.*, **6,** 156 (2004).
[4] V. R. Kurteva and C. A. M. Afonso, *Green Chem.*, **6,** 183 (2004).
[5] A. R. Gholap, K. Venkatesan, T. Daniel, R. J. Lahoti, and K. V. Srinivasan, *Green Chem.*, **6,** 147 (2004).
[6] K. Mogilaiah and G. R. Reddy, *J. Chem. Res*., **7,** 477 (2004).
[7] H. P. Mahana, C. D. P. Mahana, R. Salazar, J. A. Valderrama, E. Saez, and R. A. Maturana, *Synthesis*, **3,** 436 (2004).
[8] B. Kaboudin and A. Rahmani, *OPPI*, **36,** 82 (2004).
[9] Y. Peng G. Song, and L. Liu, *OPPI*, **36,** 151 (2004).
[10] M. Nüchter, B. Ondruschka, W. Bonrath, and A. Gum, *Green Chem.*, **6,** 128 (2004).
[11] A. K. Bose, M. S. Manhas, M. Ghosh, M. Shah, V. S. Raju, S. S. Bari, S. N. Newaz, B. K. Banik, A. G. Chaudhary, and K. J. Barakat, *J. Org. Chem.*, **56,** 6968 (1991).
[12] R. S. Varma, *Green Chem.*, **2,** 43 (1999).
[13] J. Lin, Z. Wen, J. Long, Y. Wang, T. Matsuttra, and J. Meng, *Synth. Commun.*, **30,** 829. (2000).
[14] D. D. Laskar, D. Prajapati, and J. S. Sandhu, *J. Chem. Soc., Perkin Trans.*, **1,** 67 (2000).
[15] M. H. Elnagdi, A. M. Negm, and A. W. Erian, *Liebigs Ann. Chem.*, 1255 (1989).
[16] A. A. El-Bannany, A. A. Elassar, and M. H. Elnagdi, *J. Prakt. Chem.*, **331,** 726 (1989).
[17] S. M. El-Kousy, I. El-Sakka, A. M. El-Torgoman, H. Rashdy, and M. H. Elnagdi, *Collect. Czech. Chem. Commun.*, **55,** 2977 (1990).
[18] M. H. Elnagdi, R. M. Mohareb, F. A. A. El-Aal, and H. A. Mohamed, *Phosph., Sulf., and Silicon*, **82,** 195 (1993).
[19] A. W. Erian, E. A. Z. Hafez, E. S. Darwish, and M. H. Elnagdi, *Can. J. Chem.*, **76,** 1038. (1998).
[20] (a) F. Al-Omran, N. Al-Awadi, A. Elassar, and A. El-Khair, *J. Chem. Res.*, (*S*), 20. *Ibid. (M).* 237 (2000).
[21] E. Nyiondi-Bonguen, E. Sopbue Fondjo, T. Fomum, and D. Döpp, *J. Chem. Soc. Perkin Trans.* **1,** 2191 (1994).
[22] H. Al-Awadi, F. Al-Omran, M. H. Elnagdi, L. Infantes, C. Foces-Foces, N. Iagerovic, and J. Elguero, *Tetrahedron*, **51,** 12745 (1995).
[23] A. Al-Naggar, M. M. Abdelkhalik, and M. H. Elnagdi, *J. Chem. Res. (S)*, 648 (1999); Ibid., (M), 2801 (1999).