Synthesis of Heterocycles. Part VII [1]. Synthesis and Antimicrobial Activity of Some 7*H*-*s*-Triazolo[3,4-*b*][1,3,4]thiadiazine and *s*-Triazolo[3,4-*b*][1,3,4]thiadiazole Derivatives

N F. Eweiss [2] and A. A. Bahajaj*

Department of Chemistry, University of Kuwait,
Kuwait

Received January 15, 1987

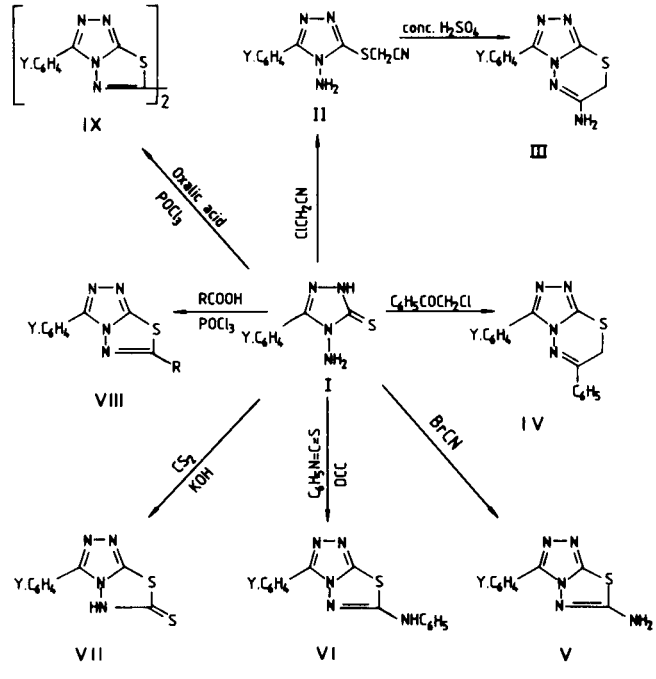
The cyclization of 4-amino-5-aryl-3-cyanomethylthio-1,2,4-triazoles **II** in the presence of concentrated sulfuric acid yields 7*H*-6-amino-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **III**. Cyclization of 4-amino-5-aryl-1,2,4-triazole-3-thiones **I** with phenacyl chloride yields 7*H*-3-aryl-6-phenyl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **IV**. Similarly, compounds **I** condensed with cyanogen bromide, phenyl isothiocyanate and carbon disulfide to give the corresponding cyclized products 6-amino-3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **V**, 3-aryl-6-phenylamino-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VI** and 3-aryl-striazolo[3,4-*b*][1,3,4]thiadiazol-6(5*H*)thiones **VII**, respectively. Also in the presence of phosphoryl chloride, compounds **I** underwent cyclization with monocarboxylic acids and oxalic acid to 3,6-diaryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazole **VIII** and 6,6'-bis(3-aryl-*s*-triazolo-[3,4-*b*][1,3,4]thiadiazoles) **IX**. The above compounds were screened for their antimicrobial activity.

J. Heterocyclic Chem., **24**, 1173 (1987).

Cyclocondensation of 4-amino-5-aryl-1,2,4-triazole-3-thiones **I** with α-chloroacetonitrile [3] and α-halocarbonyl compounds [4-23] constitute an ideal approach to the synthesis of the fused system 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine. Other methods were also reported [24,25]. *s*-Triazolo[3,4-*b*][1,3,4]thiadiazole is another interesting fused system of 1,2,4-triazole ring which was successfully synthesized *via* two routes. The first route involved the cyclocondensation of 4-amino-5-substituted-1,2,4-triazole-3-thiones with cyanogen bromide, carbon disulfide, isothiocyanates, carboxylic acids and acid chlorides [7,8,26-34]. The second route was *via* the ring closure of 5-substituted-2-hydrazino-1,3,4-thiadiazoles with appropriate reagents [35-37]. Other routes were also known [38-40]. These two fused systems were reported to possess antimicrobial activity [16-21, 28, 31, 33, 37]. In continuation of our research in the synthesis of pharmacologically active heterocycles [1,41,42], we wish to describe here the synthesis and antimicrobial activity of some 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine and *s*-triazolo[3,4-*b*][1,3,4]thiadiazole derivatives.

Results and Discussion.

The required 4-amino-5-aryl-1,2,4-triazole-3-thiones **I** and 4-amino-5-aryl-3-cyanomethylthio-1,2,4-triazoles **II** were prepared as previously described [1]. The latter compounds namely 4-amino-5-aryl-3-cyanomethylthio-1,2,4-triazoles underwent cyclization when treated with concentrated sulfuric acid at room temperature to yield 7*H*-6-amino-3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **III** (Scheme I). The structure assigned to compounds **III** was substantiated by their analytical (Table I) and spectral data (Table II). Their ir spectra lacked the C≡N stretching frequency of their precursor **II** and showed two bands in the region 3300-3340 cm^{-1} characteristic of ν N-H [43]. The nmr spectra of compounds **II** showed singlets at δ 3.91 ppm (2H, CH_2) and at δ 7.32-7.61 ppm (2H, NH_2). The cyclization of **II** to **III** involved a nucleophilic addition at the cyano group followed by a proton acquisition, result-

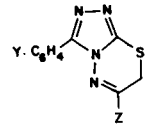


Y=a,H; b,4-Me; c,4-MeO; d,2-Cl; 4-Cl; f,2-Br; g,3-Br; h,4-Br; i,Y.C_6H_4= $C_6H_5CH_2$; j,2-Me

Scheme I

Table I

Analytical Data of 7*H*-3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **III**, **IV**



Compound	Y	Z	MP °C (Lit mp)	Yield %	Molecular formula	C Calcd. (Found)	H Calcd. (Found)	N Calcd. (Found)	S Calcd. (Found)
IIIa	H	NH_2	246-247	60	$C_{10}H_9N_5S$	51.92 (51.90)	3.93 (4.02)	30.29 (30.12)	13.86 (13.77)
IIIb	4-Me	NH_2	255-256	81	$C_{11}H_{11}N_5S$	53.85 (54.01)	4.53 (4.59)	28.55 (28.46)	13.07 (13.02)
IIIh	4-Br	NH_2	257-258	65	$C_{10}H_8BrN_5S$ [a]	38.72 (38.77)	2.60 (2.70)	22.58 (22.46)	10.34 (10.16)
IIIi	[b]	NH_2	160-161	69	$C_{11}H_{11}N_5S$	53.85 (53.80)	4.53 (4.58)	28.55 (28.49)	13.07 (13.00)
IVa	H	C_6H_5	212-213 (214-215) [4]	75	$C_{16}H_{12}N_4S$	65.72 (65.66)	4.15 (4.15)	19.17 (19.15)	10.96 (10.86)
IVb	4-Me	C_6H_5	198-199 (200-201) [21]	78	$C_{17}H_{14}N_4S$	66.63 (66.57)	4.61 (4.59)	18.29 (18.37)	10.47 (10.30)
IVc	4-MeO	C_6H_5	197-198 (200-203) [21]	68	$C_{17}H_{14}N_4OS$	63.33 (63.19)	4.39 (4.29)	17.38 (17.44)	9.94 (9.84)
IVd	2-Cl	C_6H_5	175-176 (172) [8]	70	$C_{16}H_{11}ClN_4S$ [c]	58.80 (58.65)	3.40 (3.27)	17.15 (17.22)	9.80 (9.75)
IVe	4-Cl	C_6H_5	255-256 (260-261) [21]	65	$C_{16}H_{11}ClN_4S$ [d]	58.80 (58.54)	3.40 (3.38)	17.15 (16.89)	9.80 (9.58)
IVf	2-Br	C_6H_5	195-196	89	$C_{16}H_{11}BrN_4S$ [e]	51.76 (51.68)	2.99 (3.03)	15.09 (15.02)	8.64 (8.45)
IVg	3-Br	C_6H_5	224-225	67	$C_{16}H_{11}BrN_4S$ [f]	51.76 (51.63)	2.99 (2.94)	15.09 (15.04)	8.64 (8.60)
IVh	4-Br	C_6H_5	256-257 (258-259) [21]	59	$C_{16}H_{11}BrN_4S$ [g]	51.76 (51.57)	2.99 (2.88)	15.09 (15.03)	8.64 (8.58)
IVi	[b]	C_6H_5	143-144	65	$C_{17}H_{14}N_4S$	66.63 (66.55)	4.61 (4.67)	18.29 (18.28)	10.47 (10.35)
IVj	2-Me	C_6H_5	165-166	64	$C_{17}H_{14}N_4S$	66.63 (66.32)	4.61 (4.58)	18.29 (18.06)	10.47 (10.26)

[a] *Anal.* Calcd: Br, 25.76. Found: Br, 25.73. [b] Y. C_6H_4 = $C_6H_5CH_2$. [c] *Anal.* Calcd: Cl, 10.85. Found: Cl, 10.70. [d] *Anal.* Calcd: Cl, 10.85. Found: Cl, 10.59. [e] *Anal.* Calcd: Br, 21.52. Found: Br, 21.68. [f] *Anal.* Calcd: Br, 21.52. Found: Br, 21.70. [g] *Anal.* Calcd: Br, 21.52. Found: Br, 21.72.

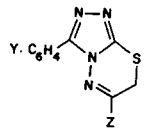
ing in ring closure and the formation of the amino-substituted heterocycles. This cyclization is very similar to the already reported cyclization of aminonitrile to iminopyrrolidines [44].

Reaction with Phenacyl Chloride.

Heating the triazoles **I** in absolute ethanol with phenacyl chloride followed by neutralization with potassium carbonate afforded 7*H*-3-aryl-6-phenyl-*s*-triazolo[3,4-*b*][1,3,4]-thiadiazines **IV** in 60-89% yield. The analytical (Table I) and spectral data (Table II) are in accordance with the structure asigned. The infrared spectra of compounds **IV** were devoid of the characteristic stretching frequencies of the NH_2 and C=O groups. Their nmr spectra revealed a singlet at δ 4.13-4.39 ppm (2H, CH_2) and lacked the signals for both SH and NH_2 protons indicating that cyclization involving both functional groups took place. A recent report [21] suggested that this reaction always yields the cyclized product even under the mildest conditions which is in contrast to the two earlier reports [8,22] which claimed the isolation of the uncyclized products **A** and **B** (Scheme II). George *et al* [8] claimed that the reaction of triazole **I**

Table II

Spectral Data of 7*H*-3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **III** and **IV** [a]



Compound	Y	Z	δ (Dimethylsulfoxide) (Multiplicity, assignment)
IIIa	H	NH_2	8.51-7.92 (m, 5H, aromatic H), 7.48 (s, 2H, NH_2), 3.93 (s, 2H, CH_2)
IIIb	4-Me	NH_2	8.29-7.53 (m, 4H, aromatic H), 7.40 (s, 2H, NH_2), 3.92 (s, 2H, CH_2), 2.41 (s, 3H, CH_3Ar)
IIIh	4-Br	NH_2	8.52-8.08 (m, 4H, aromatic H), 7.60 (s, 2H, NH_2), 3.92 (s, 2H, CH_2)
IIIi	[b]	NH_2	7.49 (s, 5H, aromatic H), 7.28 (s, 2H, NH_2), 4.22 (s, 2H, CH_2Ar), 3.81 (s, 2H, CH_2)
IVa	H	C_6H_5	8.10-7.71 (m, 10H, aromatic H), 4.42 (s, 2H, CH_2)
IVb	4-Me	C_6H_5	8.19-7.74 (m, 9H, aromatic H), 4.30 (s, 2H, CH_2), 2.51 (s, 3H, CH_3Ar)
IVc	4-MeO	C_6H_5	8.21-7.74 (m, 9H, aromatic H) [c], 4.41 (s, 2H, CH_2), 3.87 (s, 3H, CH_3OAr)
IVd	2-Cl	C_6H_5	8.00-7.59 (m, 9H, aromatic H), 4.31 (s, 2H, CH_2)
IVe	4-Cl	C_6H_5	7.92-7.46 (m, 9H, aromatic H), 4.31 (s, 2H, CH_2)
IVf	2-Br	C_6H_5	7.92-7.62 (m, 9H, aromatic H), 4.31 (s, 2H, CH_2)
IVg	3-Br	C_6H_5	8.19-7.72 (m, 9H, aromatic H), 4.31 (s, 2H, CH_2)
IVh	4-Br	C_6H_5	8.00-7.70 (m, 9H, aromatic H), 4.23 (s, 2H, CH_2)
IVi	[b]	C_6H_5	7.93-7.38 (m, 10H, aromatic H), 4.31 (s, 2H, CH_2), 3.92 (s, 2H, CH_2Ar)
IVj	2-Me	C_6H_5	8.11-7.48 (m, 9H, aromatic H), 4.40 (s, 2H, CH_2), 2.51 (s, 3H, CH_3Ar)

[a] The ir spectra of compounds **III** showed two bands in the region 3300-3340 cm^{-1} for ν N-H. [b] Y. C_6H_4 = $C_6H_5CH_2$. [c] Solvent deuterated chloroform.

(R = C_2H_5) with phenacyl bromide in ethanol yields the uncyclized product **A** which then cyclized into **IV** in the presence of sodium ethoxide. On the other hand, El-Shafei *et al* [22] claimed that the reaction of triazole **I** (R = C_6H_5) with phenacyl bromide in ethanolic potassium carbonate gave the uncyclized product **B** which upon treatment with phosphoryl chloride cyclized to **IV**.

Reaction with Cyanogen Bromide.

Cyclocondensation of triazoles **I** with cyanogen bromide was first reported by Potts and Huseby [29]. Refluxing the triazole **I** and cyanogen bromide in aqueous ethanol yielded 6-amino-3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **V**. Their analytical and spectral data (Table III and IV) are in accordance with the structure assigned. Their ir showed two broad bands in the region 3200-3400 cm^{-1} characteristic of ν N-H [43]. The 6-amino group protons resonate further downfield (δ 7.72-8.71 ppm) than the 4-amino group protons of their precursor **I** (δ 5.14-5.87 ppm) [1]. Potts and Huseby [29] suggested that the transformation of triazoles **I** to **V** probably occurs *via* the intermediacy of a thiocyanate. However, a recent report by Sasaki and Ito [30] based on their CNDO/2 calculations of triazole **I** suggested the cyanamide as a preferable intermediate.

Reaction with Phenylisothiocyanate.

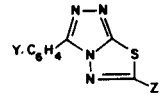
The reaction of triazoles **I** with aryl isothiocyanates and arylisocyanates in dry pyridine was first reported by Rudnicka [45] to afford the corresponding uncyclized substituted thiourea and urea derivatives. Molina [34] recently reported that mixing the triazoles **I** with arylisothiocyanates in dry dimethylformamide at room temperature afforded the uncyclized substituted thiourea which upon refluxing has cyclized into 6-arylamino-3-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VI**. Molina was also able to obtain compounds **VI** by refluxing the triazoles **I** with arylisothiocyanates. In our hands, the reaction between triazoles **I** and phenylisothiocyanate was carried out in refluxing ethanol for four hours where the only product isolated was *O*-ethylphenylthiocarbamate. The structure of this thiocarbamate was inferred from its spectral data and mixed melting point. This indicates that the reaction took place between the solvent and phenylisothiocyanate. When the same reaction was repeated in the presence of cyclohexylcarbodiimide (DCC), 3-aryl-6-phenylamino-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VI** were obtained. Furthermore reacting *O*-ethylphenylthiocarbamate with the triazole **Ii** in DCC yielded 6-phenylamino-3-phenylmethyl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazole **VIi**. The structure of compounds **VI** was based on their analytical (Table III) and spectral data (Table IV). The infrared spectra of compounds **VI** showed two bands at 3240-3280 cm^{-1} characteristic of ν N-H [43] and a band at 1600-1630 cm^{-1} for ν C=N. Their nmr spectra were devoid of the signals for both NH_2 and SH groups and revealed a singlet at δ 10.74-10.81 ppm (1H, NH) and a multiplet at δ 7.41-8.18 ppm (aromatic protons).

Reaction with Carbon Disulfide.

Refluxing the triazoles **I** and carbon disulfide in alcoholic potassium hydroxide as reported by Potts and Huseby [29] afforded 3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazole-6(5*H*)-thiones **VII**. The analytical (Table III) and

Table III

Analytical Data of 3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **V-VI**



Compound	Y	Z	MP °C (Lit mp)	Yield %	Molecular formula	C Calcd. (Found)	H Calcd. (Found)	N Calcd. (Found)	S Calcd. (Found)
Va	H	NH_2	255-256 (256-257) [29]	73	$C_9H_7N_5S$	49.75 (49.68)	3.25 (3.33)	32.24 (32.27)	14.76 (14.91)
Vb	4-Me	NH_2	293-294 (295) [29]	58	$C_{10}H_9N_5S$	51.92 (51.87)	3.93 (4.02)	30.29 (30.21)	13.86 (13.78)
Vc	4-MeO	NH_2	267-268 (268) [29]	51	$C_{10}H_9N_5OS$	48.56 (48.41)	3.68 (3.77)	28.33 (28.13)	12.96 (13.10)
Vd	2-Cl	NH_2	240-242 (243) [29]	75	$C_9H_6ClN_5S$ [a]	42.94 (42.72)	2.41 (2.39)	27.83 (27.93)	12.74 (12.85)
Ve	4-Cl	NH_2	281-282	80	$C_9H_6ClN_5S$ [b]	42.94 (42.83)	2.41 (2.50)	27.83 (27.68)	12.74 (12.62)
Vf	2-Br	NH_2	203-204	70	$C_9H_6BrN_5S$ [c]	36.50 (36.32)	2.05 (2.03)	23.65 (23.76)	10.82 (10.65)
Vg	3-Br	NH_2	278-279	68	$C_9H_6BrN_5S$ [d]	36.50 (36.38)	2.05 (1.96)	23.65 (23.60)	10.82 (10.91)
Vh	4-Br	NH_2	277-279	46	$C_9H_6BrN_5S$ [e]	36.50 (36.48)	2.05 (2.01)	23.65 (23.50)	10.82 (10.98)
Vi	[f]	NH_2	189-190 (190) [29]	79	$C_{10}H_9N_5S$	51.92 (52.02)	3.93 (4.01)	30.28 (30.12)	13.86 (13.78)
VIa	H	C_6H_5NH	307-308	51	$C_{15}H_{11}N_5S$	61.41 (61.33)	3.79 (3.86)	23.88 (23.77)	10.92 (10.87)
VIb	4-Me	C_6H_5NH	305-306	60	$C_{16}H_{13}N_5S$	62.51 (62.37)	4.27 (4.36)	22.79 (22.66)	10.43 (10.31)
VIc	4-MeO	C_6H_5NH	296-297	62	$C_{16}H_{13}N_5OS$	59.42 (59.34)	4.06 (4.09)	21.66 (21.50)	9.91 (9.90)
VId	2-Cl	C_6H_5NH	286-287	59	$C_{15}H_{10}ClN_5S$ [g]	54.96 (54.90)	3.08 (3.12)	21.37 (21.25)	9.78 (9.63)
VIe	4-Cl	C_6H_5NH	310	68	$C_{15}H_{10}ClN_5S$ [h]	54.96 (54.84)	3.08 (3.10)	21.37 (21.21)	9.78 (9.65)
VIg	3-Br	C_6H_5NH	307-308	70	$C_{15}H_{10}BrN_5S$ [i]	48.39 (48.23)	2.71 (2.74)	18.82 (18.66)	8.61 (8.49)
VIh	4-Br	C_6H_5NH	325	72	$C_{15}H_{10}BrN_5S$ [j]	48.39 (48.38)	2.71 (2.78)	10.82 (10.75)	8.61 (8.56)
VIi	[f]	C_6H_5NH	250	76	$C_{16}H_{13}N_5S$	62.51 (62.41)	4.27 (4.30)	22.79 (22.59)	10.43 (10.31)
VIIa	H	SH	212-213 (210) [29]	76	$C_9H_6N_4S_2$	46.13 (46.12)	2.59 (2.50)	23.92 (23.84)	27.36 (27.13)
VIIb	4-Me	SH	227 (227) [29]	51	$C_{10}H_8N_4S_2$	48.36 (48.52)	3.25 (3.28)	22.57 (22.39)	25.82 (25.68)
VIIc	4-MeO	SH	228-229 (225) [29]	45	$C_{10}H_8N_4OS_2$	45.43 (45.34)	3.06 (3.01)	21.20 (21.11)	24.26 (24.33)

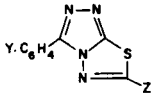
Table III (continued)

Compound	Y	Z	MP °C (Lit mp)	Yield %	Molecular formula	C Calcd. (Found)	H Calcd. (Found)	N Calcd. (Found)	S Calcd. (Found)
VIId	2-Cl	SH	171-172 (128-130) [9]	53	$C_9H_5ClN_4S_2$ [k]	40.22 (40.10)	1.88 (1.75)	20.85 (20.68)	23.86 (23.59)
VIIe	4-Cl	SH	134-135	47	$C_9H_5ClN_4S_2$ [l]	40.22 (40.17)	1.88 (1.92)	20.85 (20.77)	23.86 (23.73)
VIIf	2-Br	SH	166-167	45	$C_9H_5BrN_4S_2$ [m]	34.51 (34.32)	1.61 (1.49)	17.89 (18.01)	20.48 (20.32)
VIIg	3-Br	SH	182-183	60	$C_9H_5BrN_4S_2$ [n]	34.51 (34.70)	1.61 (1.50)	17.89 (17.95)	20.48 (20.56)
VIIh	4-Br	SH	193-194	57	$C_9H_5BrN_4S_2$ [o]	34.51 (34.46)	1.61 (1.56)	17.89 (17.84)	20.48 (20.30)
VIIi	[f]	SH	199-200 (148) [9]	52	$C_{10}H_8N_4S_2$	48.36 (48.31)	3.25 (3.23)	22.57 (22.49)	25.82 (25.96)
VIIj	2-Me	SH	193-194	48	$C_{10}H_8N_4S_2$	48.36 (48.50)	3.25 (3.13)	22.57 (22.73)	25.82 (26.01)

[a] *Anal.* Calcd: Cl, 14.08. Found: Cl, 13.98. [b] *Anal.* Calcd: Cl, 14.08. Found: Cl, 14.18. [c] *Anal.* Calcd: Br, 26.98. Found: Br, 26.83. [d] *Anal.* Calcd: Br, 26.98. Found: Br, 26.95. [e] *Anal.* Calcd: Br, 26.98. Found: Br, 27.05. [f] Y. $C_6H_4 = C_6H_5CH_2$. [g] *Anal.* Calcd: Cl, 10.81. Found: Cl, 11.01. [h] *Anal.* Calcd: Cl, 10.81. Found: Cl, 10.67. [i] *Anal.* Calcd: Br, 21.47. Found: Br, 21.56. [j] *Anal.* Calcd: Br, 21.47. Found: Br, 21.39. [k] *Anal.* Calcd: Cl, 13.19. Found: Cl, 13.35. [l] *Anal.* Calcd: Cl, 13.19. Found: C, 13.27. [m] *Anal.* Calcd: Br, 25.51. Found: Br, 25.52. [n] *Anal.* Calcd: Br, 25.51. Found: Br, 25.56. [o] *Anal.* Calcd: Br, 25.51. Found: Br, 25.23.

Table IV

Spectral Data of 3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **V-VII** [a]

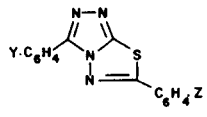


Compound	Y	Z	δ (Dimethylsulfoxide) (Multiplicity, assignment)
Va	H	NH_2	8.51-7.89 (m, 5H, aromatic H), 8.31 (s, 2H, NH_2)
Vb	4-Me	NH_2	8.11-7.34 (m, 4H, aromatic H), 7.92 (s, 2H, NH_2), 2.70 (s, 3H, CH_3Ar)
Vc	4-MeO	NH_2	8.19-7.09 (m, 4H, aromatic H), 7.92 (s, 2H, NH_2), 3.81 (s, 3H, CH_3OAr)
Vd	2-Cl	NH_2	7.72 (s, 2H, NH_2), 7.50 (m, 4H, aromatic H)
Ve	4-Cl	NH_2	8.20-7.61 (m, 4H, aromatic H), 8.00 (s, 2H, NH_2)
Vf	2-Br	NH_2	8.00 (s, 2H, NH_2), 7.71 (m, 4H, aromatic H)
Vg	3-Br	NH_2	8.38-7.71 (m, 4H, aromatic H), 8.20 (s, 2H, NH_2)
Vh	4-Br	NH_2	8.71 (s, 2H, NH_2), 8.52-8.13 (m, 4H, aromatic H)
Vi	[b]	NH_2	7.79 (s, 2H, NH_2), 7.32 (s, 5H, aromatic H), 4.31 (s, 2H, CH_2Ar)
VIa	H	C_6H_5NH	8.12-7.41 (m, 10H, aromatic H) [c]
VIb	4-Me	C_6H_5NH	8.00-7.21 (m, 9H, aromatic H) [c], 2.41 (s, 3H, CH_3Ar)
VIc	4-MeO	C_6H_5NH	8.00-7.12 (m, 9H, aromatic H) [c], 3.81 (s, 3H, CH_3OAr)
VId	2-Cl	C_6H_5NH	8.22-7.51 (m, 9H, aromatic H) [c]
VIe	4-Cl	C_6H_5NH	8.11-7.62 (m, 9H, aromatic H) [c]
VIg	3-Br	C_6H_5NH	8.31-7.49 (m, 9H, aromatic H) [c]
VIh	4-Br	C_6H_5NH	10.83 (s, 1H, NH) [d], 8.23-7.51 (m, 9H, aromatic H)
VIi	[b]	C_6H_5NH	10.74 (s, 1H, NH) [d], 7.41 (s, 5H, aromatic H), 4.28 (s, 2H, CH_2Ar)
VIIa	H	SH	8.27-7.61 (m, 5H, aromatic H), 5.52 (s, 1H, NH)
VIIb	4-Me	SH	8.11-7.42 (m, 4H, aromatic H), 5.42 (s, 1H, NH), 2.31 (s, 3H, CH_3Ar)
VIIc	4-MeO	SH	8.28-7.31 (m, 4H, aromatic H), 5.71 (s, 1H, NH), 3.92 (s, 3H, CH_3OAr)
VIId	2-Cl	SH	8.21-7.51 (m, 4H, aromatic H), 5.32 (s, 1H, NH)
VIIe	4-Cl	SH	8.28-7.61 (m, 4H, aromatic H), 5.51 (s, 1H, NH)
VIIf	2-Br	SH	8.19-7.57 (m, 4H, aromatic H), 5.22 (s, 1H, NH)
VIIg	3-Br	SH	8.00-7.48 (m, 4H, aromatic H), 5.00 (s, 1H, NH)
VIIh	4-Br	SH	8.18-7.82 (m, 4H, aromatic H), 6.16 (s, 1H, NH)
VIIi	[b]	SH	7.43 (s, 5H, aromatic H), 6.18 (s, 1H, NH), 4.39 (s, 2H, CH_2Ar)
VIIj	2-Me	SH	8.13-7.48 (m, 4H, aromatic H), 4.93 (s, 1H, NH), 2.31 (s, 3H, CH_3Ar)

[a] The ir spectra of compounds **V-VII** showed the characteristic stretching frequencies of the NH group. [b] Y. $C_6H_4 = C_6H_5CH_2$. [c] Solvent deuterated trifluoroacetic acid. [d] Board.

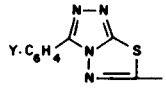
Table V

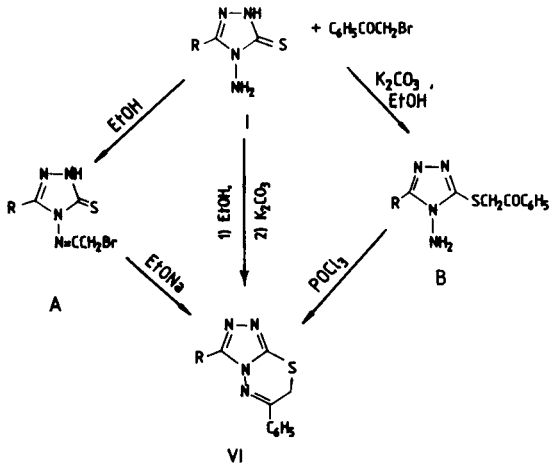
Analytical Data of 3,6-Diaryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VIII** and **IX**



Compound	Y	Z	MP (Lit mp)	Yield %	Molecular Formula	C Calcd. (Found)	H Calcd. (Found)	N Calcd. (Found)	S Calcd. (Found)
VIIIaa [a]	H	H	201-202 (201) [27]	63	$C_{15}H_{10}N_4S$	64.72 (64.35)	3.63 (3.76)	20.13 (19.98)	11.52 (11.48)
VIIIba	4-Me	H	199-200	86	$C_{16}H_{12}N_4S$	65.72 (65.64)	4.15 (4.20)	19.17 (19.05)	10.96 (10.98)
VIIIca	4-MeO	H	188-189	65	$C_{16}H_{12}N_4OS$	62.31 (62.22)	3.93 (4.01)	18.17 (18.00)	10.40 (10.41)
VIIIce	4-MeO	H	186-188	56	$C_{16}H_{11}ClN_4OS$ [b]	56.05 (55.92)	3.24 (3.32)	16.35 (16.19)	9.35 (9.39)
VIIIda	2-Cl	H	176-177 (183) [7]	60	$C_{15}H_9ClN_4S$ [c]	57.59 (57.48)	2.91 (2.92)	17.92 (17.86)	10.25 (10.10)
VIIIce	4-Cl	4-Cl	235-236	60	$C_{15}H_8Cl_2N_4S$ [d]	51.88 (51.74)	2.33 (2.41)	16.14 (16.08)	9.23 (9.15)
VIIIfa	2-Br	H	159-160	95	$C_{15}H_9BrN_4S$ [e]	50.43 (50.33)	2.54 (2.46)	15.69 (15.57)	8.97 (9.08)
VIIIfb	2-Br	4-Me	186	57	$C_{16}H_{11}BrN_4S$ [f]	51.76 (51.63)	2.99 (3.04)	15.09 (15.02)	8.64 (8.45)
VIIIgb	3-Br	4-Me	215-216	65	$C_{16}H_{11}BrN_4S$ [g]	51.76 (51.56)	2.99 (3.07)	15.09 (14.98)	8.64 (8.58)
VIIIha	4-Br	H	228-229	51	$C_{15}H_9BrN_4S$ [h]	50.43 (50.32)	2.54 (2.46)	15.69 (15.52)	8.97 (8.89)
IXa	H	[i]	326-327 (>300) [7]	50	$C_{16}H_{10}N_8S_2$	53.71 (53.59)	2.51 (2.56)	27.85 (27.76)	15.93 (15.96)
IXb	4-Me	[i]	315-316	58	$C_{20}H_{14}N_8S_2$	55.79 (55.63)	3.28 (3.38)	26.03 (25.83)	14.89 (14.78)
IXc	4-MeO	[i]	319-320	62	$C_{20}H_{14}N_8O_2S_2$	51.93 (51.78)	3.06 (2.97)	24.23 (24.09)	13.86 (13.59)
IXe	4-Cl	[i]	328-330	72	$C_{18}H_8Cl_2N_8S_2$ [j]	45.86 (45.73)	1.71 (1.83)	23.78 (23.78)	13.60 (13.55)
IXf	2-Br	[i]	318-320	65	$C_{18}H_8Br_2N_8S_2$ [k]	38.59 (38.66)	1.44 (1.35)	20.01 (19.95)	11.44 (11.42)
IXg	3-Br	[i]	331-332	50	$C_{18}H_8Br_2N_8S_2$ [l]	38.59 (38.61)	1.44 (1.29)	20.01 (20.05)	11.44 (11.39)
IXh	4-Br	[i]	343-344	59	$C_{18}H_8Br_2N_8S_2$ [m]	38.59 (38.73)	1.44 (1.38)	20.01 (19.89)	11.44 (11.34)
IXi	[n]	[i]	309-310	68	$C_{20}H_{14}N_8S_2$	55.79 (55.74)	3.28 (3.21)	26.03 (26.07)	14.89 (14.89)

[a] Two letters after compound number: the first one indicates an aryl substituent in the triazole nucleus at position 3-, and the second one indicates an aryl substituent at other cities. [b] *Anal.* Calcd: Cl, 10.34. Found: Cl, 10.43. [c] *Anal.* Calcd: Cl, 11.33. Found: Cl, 11.44. [d] *Anal.* Calcd: Cl, 20.42. Found: Cl, 20.33. [e] *Anal.* Calcd: Br, 22.37. Found: Br, 22.51. [f] *Anal.* Calcd: Br, 21.52. Found: C, 21.72. [g] *Anal.* Calcd: Br, 21.52. Found: Br, 21.71. [h] *Anal.* Calcd: Br, 22.37. Found: C, 22.24. [i] For compounds of series IX, Z. C_6H_4 = structure below where Y corresponds to the same in the Table. [i] *Anal.* Calcd: Cl, 15.04. Found: Cl, 14.92. [k] *Anal.* Calcd. Br, 28.52. Found: Br, 28.59. [l] *Anal.* Calcd: Br, 28.52. Found: Br, 28.65. [m] *Anal.* Calcd: Br, 28.52. Found: Br, 28.80. [n] Y. C_6H_4 = $C_6H_5CH_2$.





Scheme II

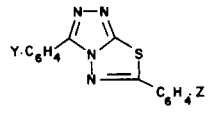
spectral data (Table IV) are in accordance with the structure assigned. Their ir spectra showed a band at 3100-3180 cm^{-1} for ν N-H [43] and their nmr spectra showed a singlet at δ 5.00-6.17 ppm (1H, NH). These spectral data showed that compounds **VII** exist preferably in the thione rather than the thiol form. Similar conclusion for 1,3,4-thiadiazole-3-thiones was supported by ir, uv and LCAO-MO calculation studies [46]. Dash *et al* [9] claimed the novel reaction of triazoles **I** with carbon disulfide in pyridine to afford **VII** and did not refer to the fact that this reaction was previously reported by Potts and Huseby [29] using alcoholic potassium hydroxide. However, when the same reaction was repeated according to the Dash procedure only unchanged starting material was recovered which is in accordance with an earlier report [36]. It was suggested [29] that this ring closure has most likely involved dithiocarbamate intermediate.

Reaction with Monocarboxylic Acid and Oxalic Acid.

The reaction of triazoles **I** with carboxylic acid in the presence of phosphoryl chloride was previously described by Lalezari *et al* [27]. Heating the triazoles **I** with benzoic acid or substituted benzoic acids in the presence of phosphoryl chloride yielded 3,6-diaryl-*s*-triazolo[3,4-*b*][1,3,4]-thiadiazoles **VIII**. On the other hand, when the same reaction was repeated with oxalic acid 6,6'-bis(3-aryl-*s*-triazolo-[3,4-*b*][1,3,4]thiadiazoles **IX** were obtained. The analytical and spectral data of compounds **VIII** and **IX** are given in Tables V and VI respectively, and are in accordance with the structure assigned. Their infrared spectra showed a band at 1600-1620 cm^{-1} for ν C=N. The nmr spectra of compounds of series **VIII** and **IX** lacked the signals for SH and NH_2 protons and revealed the presence of the aromatic and alkyl substitutent protons characteristic of every member of the two series, integrating to the correct number of protons present.

Table VI

Spectral Data of 3,6-Diaryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VIII** and **IX** [a]



Compound	Y	Z	δ (Dimethylsulfoxide) (Multiplicity, assignment)
VIIIaa	H	H	8.31 (m, 10H, aromatic H)
VIIIba	4-Me	H	8.19 (m, 9H, aromatic H), 3.91 (s, 3H, CH_3Ar)
VIIIca	4-MeO	H	8.00 (m, 9H, aromatic H), 4.21 (s, 3H, CH_3OAr)
VIIIce	4-MeO	4-Cl	8.41 (m, 8H, aromatic H), 4.15 (s, 3H, CH_3OAr)
VIIIda	2-Cl	H	8.00 (m, 9H, aromatic H)
VIIIee	4-Cl	4-Cl	8.51 (m, 8H, aromatic H)
VIIIfa	2-Br	H	8.00 (m, 9H, aromatic H)
VIIIfb	2-Br	4-Me	8.41 (m, 8H, aromatic H), 4.00 (s, 3H, CH_3Ar)
VIIIgb	3-Br	4-Me	8.33 (m, 8H, aromatic H), 3.91 (s, 3H, CH_3Ar)
VIIIha	4-Br	H	8.42 (m, 9H, aromatic H)
IXa	H	[b]	8.81-8.32 (m, 10H, aromatic H)
IXb	4-Me	[b]	8.32-7.68 (m, 8H, aromatic H), 3.61 (s, 6H, $2CH_3Ar$)
IXc	4-MeO	[b]	8.39-7.39 (m, 8H, aromatic H), 4.11 (s, 6H, $2CH_3OAr$)
IXe	4-Cl	[b]	8.29-7.81 (m, 8H, aromatic H)
IXf	2-Br	[b]	8.18-7.83 (m, 8H, aromatic H)
IXg	3-Br	[b]	8.29-7.62 (m, 8H, aromatic H)
IXh	4-Br	[b]	8.42-7.51 (m, 8H, aromatic H)
IXi	[c]	[b]	8.18-7.39 (s, 10H, aromatic H), 4.81 (s, 4H, $2CH_2Ar$)

[a] The ir spectra of compounds **VIII** and **IX** showed a band in the region 1620-1600 cm^{-1} for ν C=N. [b] Same as in [i] Table V. [c] Y. C_6H_4 = $C_6H_5CH_2$.

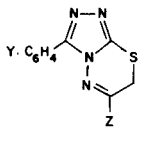
Electronic Spectra of Compounds III-V, VII and VIII.

The ultraviolet absorption spectra of compounds **III-V**, **VII** and **VIII** were determined in ethanol, a summary of the spectral data is listed in Tables VII and VIII. The ultraviolet absorption of the 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine nucleus, as represented by the 3-ethyl-6-methyl product, occurs at λ max 273 nm (log ε 4.15). The introduction of a 6-amino substituent (compounds **III**, Table VII) results in a hypsochromic shift of about 8 nm of the above absorption maximum. On the other hand, the introduction

of a 6-phenyl substituent (compounds **IV**) results in a 10 nm bathochromic shift of the absorption maximum. The introduction of a substituted phenyl group at position 3 of 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine nucleus **III** and **IV** results in the appearance of a second absorption maximum at λ 243-256 nm (log ε 3.95-4.68) and also a 8-10 nm bathochromic shift of the absorption maximum which originally occurs at 273 nm. This red shift is due to the increase in conjugation which results from the aryl group. The ultraviolet absorption of *s*-triazolo[3,4-*b*][1,3,4]thiadiazole nucleus as reported [29] occurs at λ max 251 nm (log ε 3.45). The introduction of a 6-amino substituent (compounds **V**, Table VIII) results in a 9 nm hypsochromic shift of the absorption maximum, whereas the introduction of 6-thione substituent (compounds **VII**) does not affect the maximum absorption of the *s*-triazolo[3,4-*b*][1,3,4]-thiadiazole nucleus. In contrast, Potts and Huseby [29] reported a 13 nm hypsochromic shift for the 6-amino substitutent and a 36 nm bathochromic shift for the 6-thione substituent. The introduction of a 3-aryl substituent gave the expected red shift due to the increase in conjugation. It is worthwhile to notice that the 3-*ortho*-substituted phenyl derivatives does not show such red shift. This is due to steric inhibition of the *ortho* substituted phenyl derivatives to acheive complete coplanarity with the *s*-triazolo-[3,4-*b*][1,3,4]thiadiazole nucleus [29].

Table VII

Ultraviolet Absorption Spectral Data for 7*H*-3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **III-IV**

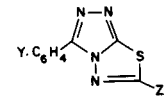


Compound	Y	Z	λ max (Ethanol) nm (log ε)
IIIa	H	NH_2	273 (4.42), 243 (4.16) [a]
IIIb	4-Me	NH_2	276 (4.24), 245 (4.07) [a]
IIIh	4-Br	NH_2	281 (4.44), 245 (4.11) [a]
IIIi	[b]	NH_2	265 (4.33)
IVa	H	C_6H_5	286 (4.28), 248 (4.31)
IVb	4-Me	C_6H_5	280 (4.30), 251 (4.38)
IVc	4-MeO	C_6H_5	286 (4.53), 256 (4.39)
IVd	2-Cl	C_6H_5	282 (4.21), 246 (4.06)
IVe	4-Cl	C_6H_5	286 (4.57), 254 (4.63)
IVf	2-Br	C_6H_5	282 (4.12), 246 (3.95)
IVg	3-Br	C_6H_5	281 (4.08), 251 (4.01)
IVh	4-Br	C_6H_5	282 (4.60), 256 (4.68)
IVi	[b]	C_6H_5	280 (4.22)
IVj	2-Me	C_6H_5	262 (4.25), 248 (4.25)

[a] Shoulder. [b] Y. C_6H_4 = $C_6H_5CH_2$.

Table VIII

Ultraviolet Absorption Spectral Data for 3-Aryl-6-substituted-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **V**, **VII** and **VIII**



Compound	Y	Z	λ max (Ethanol) nm (log ε)
Va	H	NH_2	272 (4.29) [a]
Vb	4-Me	NH_2	272 (4.37) [a], 263 (4.38)
Vc	4-MeO	NH_2	278 (4.43)
Vd	2-Cl	NH_2	250 (4.07)
Ve	4-Cl	NH_2	270 (4.57)
Vf	2-Br	NH_2	260 (4.42)
Vg	3-Br	NH_2	269 (4.50)
Vh	4-Br	NH_2	280 (4.39), 272 (4.40)
Vi	[b]	NH_2	242 (4.32)
VIIa	H	SH	274 (4.09) [a], 251 (4.40), 233 (4.24)
VIIb	4-Me	SH	274 (4.20) [a], 251 (4.47)
VIIc	4-MeO	SH	274 (4.28) [a], 254 (4.46)
VIId	2-Cl	SH	251 (4.30)
VIIe	4-Cl	SH	290 (4.02), 250 (4.40)
VIIf	2-Br	SH	251 (4.31)
VIIg	3-Br	SH	292 (3.91), 251 (4.29)
VIIh	4-Br	SH	290 (4.03), 251 (4.29)
VIIi	[b]	SH	251 (4.33)
VIIj	2-Me	SH	250 (4.03)
VIIIba	H	C_6H_5	263 (4.47)
VIIIca	4-MeO	C_6H_5	264 (4.49)
VIIIda	2-Cl	C_6H_5	268 (4.53)
VIIIfa	2-Br	C_6H_5	268 (4.41)
VIIIha	4-Br	C_6H_5	266 (4.09)

[a] Shoulder. [b] Y. C_6H_4 = $C_6H_5CH_2$.

Antimicrobial Activities of Compounds **III-IX**.

The above synthesized compounds were tested for their antimicrobial activity by the agar dilution technique. The results [42,47] showed that compounds **IIIh**, **VIa-c,g-i**, and **VIIa,b,e,f,h,j** are active against the gram-positive bacteria *S. aureus* and compound **VIIe** is active against the gram-negative bacteria *E. coli*. Compounds **VIa-e,g,h** show an inhibition of growth of the yeast-like *C albicans* and the fungi *A. niger*.

EXPERIMENTAL

All melting points were determined on an electrothermal melting point apparatus, and are uncorrected. Elemental analysis were performed by Prof. Dipl. Ing., Dr. H. Malissa and G. Reuter, West Germany. Spectra were recorded with Perkin-Elmer 580B Infrared spectrophotometer (potassium bromide wafer technique) and Pye-Unicam SP8-100 visible and ultraviolet spectrophotometer (in ethanol). The ^{1}H-nmr spectra were recorded on a varian T-60A spectrometer using tetramethylsilane (TMS) as an internal standard.

7*H*-6-Amino-3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine (**III**).

4-Amino-5-aryl-3-cyanomethylthio-1,2,4-triazole **II** (0.005 mole) [1] was dissolved in 10 ml of concentrated sulfuric acid and left for 3 hours at room temperature. It was then diluted with water and neutralized with 20% ammonium hydroxide. The precipitate was filtered and crystallized from ethanol-water mixture (Table I).

7*H*-3-Aryl-6-phenyl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine (**IV**).

Phenacyl chloride (1.55 g, 0.01 mole) was added portionwise to a stirred solution of the triazole **I** (0.01 mole) in a minimum amount of absolute ethanol (*ca.* 50 ml). The mixture was then refluxed for 5 hours, cooled to room temperature and neutralized with aqueous sodium carbonate solution. The solid product was crystallized from ethanol-water mixture (Table I).

7*H*-3-Ethyl-6-methyl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazine was prepared as above using 4-amino-5-ethyl-1,2,4-triazole-3-thione and chloroacetone, yield 40% mp 97-98° (lit mp 95-97° [24]).

6-Amino-3-aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazole (**V**).

Cyanogen bromide (0.05 mole) and triazole **I** (0.04 mole) were refluxed in 75% aqueous ethanol (50 ml) for 2-3 hours. The reaction mixture was evaporated to one-fourth of its volume and then diluted with a saturated solution of sodium acetate. The precipitated solid was collected and crystallized from ethanol (Table III).

3-Aryl-6-phenylamino-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VI**.

Phenylisothiocyanate (2 ml, 0.015 mole) was added to a solution of triazole **I** (0.01 mole) in absolute ethanol (100-150 ml) and the mixture stirred at room temperature for 3-4 hours. To the stirred solution, dicyclohexylcarbodiimide (DCC) (3.1 g, 0.015 mole) was added and the whole mixture was refluxed for 5-6 hours. Upon cooling a white solid separated, filtered and crystallized from a large volume of ethanol (Table III).

3-Aryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazol-6(5*H*)-thiones **VII**.

The triazole **I** (0.01 mole) and potassium hydroxide (0.6 g, 0.01 mole) were dissolved in methanol (100 ml). To this mixture, carbon disulfide (4 ml) was added and the whole mixture refluxed for 24 hours. The solution was then evaporated to dryness and aqueous hydrochloric acid (50%, 50 ml) was added. The filtered solid was washed with water and crystallized from pyridine-acetate mixture (Table III).

3,6-Diaryl-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **VIII**.

A mixture of triazole **I** (0.01 mole), carboxylic acid (0.01 mole) and phosphoryl chloride (10 ml) was refluxed for about one hour. The reaction mixture was poured onto crushed ice and the solid was filtered and crystallized from acetic acid (Table V).

6,6'-Bis(3-aryl)-*s*-triazolo[3,4-*b*][1,3,4]thiadiazoles **IX**.

A mixture of triazole (0.02 mole), oxalic acid (1.26 g, 0.01 mole) and phosphoryl chloride (15 ml) was refluxed for about one hour. The reaction mixture was poured onto crushed ice and the solid was filtered and crystallized from acetic acid (Table V).

Acknowledgements.

This work is supported by Kuwait University Research Grant SC016. We wish to thank Dr. M. A. Ghannoum (Department of Microbiology, Kuwait University) for performing the anti-microbial activity study. Our thanks are also extended to Prof. A. M. Kiwan for reading the manuscript and for valuable suggestions.

REFERENCES AND NOTES

[1] Part **VI**. N. F. Eweis, A. A. Bahajaj and E. A. Elsherbini, *J. Heterocyclic Chem.*, **23**, 1451 (1986).

[2] Present address: 70 Gameat Ddewal Alarabia, Giza, Egypt.

[3] W. Rudnick and Z. Osmialowska, *Acta. Pol. Pharm.*, **36**, 411 (1979).

[4] E. Hoggarth, *J. Chem. Soc.*, 4811 (1952).

[5] S. V. Sokolov and I. Y. Postovskii, *Zh. Obshch. Khim.*, 1781 (1960); *Chem. Abstr.*, **55**, 7399d (1961).

[6] L. Giammanco, *Atti Accad. Ci., Lett. Arti Palermo, Parte 1.*, **33**, 235 (1973); *Chem. Abstr.*, **83**, 97228e (1975).

[7] V. K. Chadha and G. R. Sharma, *J. Indian Chem. Soc.*, **57**, 112 (1980).

[8] T. George, R. Tahilramani and D. A. Dobholkar, *Indian J. Chem.*, **7**, 959 (1969); *Chem. Abstr.*, **72**, 3470a (1970).

[9] B. Dash, E. K. Dora and C. S. Panda, *Indian J. Chem.*, **20B**, 369 (1981).

[10] W. Guenter and P. Henklein, *Z. Chem.*, **9**, 111 (1969); *Chem. Abstr.*, **70**, 96771W (1969).

[11] K. S. Dhada, J. Mohan, V. K. Chadha and H. K. Pujari, *Indian J. Chem.*, **12**, 287 (1974); *Chem. Abstr.*, **81**, 1366118z (1974).

[12] I. Y. Postovskii, A. D. Sinegibskaya and A. P. Novikova, *Tezisy Dokl. Nauchn. Sess. Khim. Tekhnol. Org. Soedin. Sery Sernistyhk Neftei*, 14th 207 (1975); *Chem. Abstr.*, **88**, 190771q (1978).

[13] V. P. Upadhyaya and V. R. Srinivasan, *Indian J. Chem.*, **16B**, 737 (1978).

[14] V. K. Chadha, *J. Indian Chem. Soc.*, **55**, 817 (1978).

[15] S. Somasekhara, R. K. Thakhar and G. F. Shah, *J. Indian Chem. Soc.*, **49**, 1057 (1972).

[16] S. Bala, R. P. Gupta, M. L. Sachdeva, A. Singh and H. K. Pujari, *Indian J. Chem.*, **16B**, 481 (1978).

[17] W. L. Albrecht, U. S. Patent 3,954,984 (1976); *Chem. Abstr.*, **85**, 78173h (1976).

[18] W. L. Albrecht and W. D. Jones, U. S. Patents 3,954,981 (1976) and 4,230,715, (1980); *Chem. Abstr.*, **85**, 177501V (1976), and *Chem. Abstr.*, **94**, 121552f (1981).

[19] W. L. Albrecht and F. W. Sweet, U. S. Patent 3,954,983 (1976); *Chem. Abstr.*, **85**, 78173h (1976).

[20] J. Mohan, *Indian J. Chem.*, **22B**, 270 (1983).

[21] M. A. El-Dawy, A. M. M. E. Omer, A. M. Ismail and A. A. B. Hazzaa, *J. Pharm. Sci.*, **72**, 45 (1983).

[22] A. K. El-Shafei, A. B. A. G. Ghattas, A. Sultan, H. S. El-Kashef and G. Vernin, *Gazz. Chim. Ital.*, **112**, 345 (1982).

[23] P. Molina and M. J. Vilaplana, *J. Chem. Res. S.*, 70 (1986); *Chem. Abstr.*, **105**, 6495y (1986).

[24] T. Saskai, E. Ito and I. Shimizu, *J. Org. Chem.*, **47**, 2757 (1982).

[25] W. D. Pfeiffer, E. Dilk and E. Bulka, *Z. Chem.*, **17**, 15 (1977).

[26] M. Kanaoka, *J. Pharm. Soc. Japan*, **76**, 113 (1956); *Chem. Abstr.*, **51**, 3579b (1957).

[27] H. Golgolab, I. Lalezari and G. L. Hosseini, *J. Heterocyclic Chem.*, **10**, 387 (1973); A. Shafiee and I. Lalezari, *ibid.*, **14**, 567 (1977).

[28] M. K. Mody, A. K. Prasad, T. Ramalingam and P. B. Sattur, *J. Indian Chem. Soc.*, **59**, 769 (1982).

[29] K. T. Potts and R. M. Huseby, *J. Org. Chem.*, **31**, 3528 (1966).

[30] T. Sasaki and E. Ito, *J. Heterocyclic Chem.*, **18**, 1353 (1981).

[31] H. K. Gakhar, A. Jain and S. B. Supta, *J. Indian Chem. Soc.*, **59**, 900 (1982).

[32] F. Malbec, R. Milcent and G. Barbier, *J. Heterocyclic Chem.*, **21**, 1689 (1984).

[33] A. A. Deshmuke, M. K. Mody, T. Ramalingam and P. B. Sattur, *Indian J. Chem.*, **23B**, 793 (1984).

[34] P. Molina and A. Tarraga, *Synthesis*, 411 (1983).

[35] M. Kanaoka, *Pharm. Bull.*, **5**, 385 (1957); *Chem. Abstr.*, **52**, 5390e

(1958).

[36] M. Kanaoka, T. Okuda and D. Shiho, *Yakugaku Zasshi*, **87**, 119 (1967); *Chem. Abstr.*, **67**, 11458q (1967).

[37] S. Singh, L. D. S. Yadav and H. Singh, *Bokin Bobai.*, **8**, 385 (1980); *Chem. Abstr.*, **94**, 103250b (1981).

[38] T. Resetova, *Zb. Stud. Ved. Obd. Pr.*, 19 (1979); *Chem. Abstr.*, **92**, 128822m (1980).

[39] R. G. Child and A. S. Tomcufcik, *J. Heterocyclic Chem.*, **2**, 302 (1965); *Chem. Abstr.*, **63**, 14850b (1965).

[40] J. Sandtrom, *Acta. Chem. Scand.*, **15**, 1295 (1961); *Chem. Abstr.*, **57**, 12471 (1962).

[41] N. F. Eweiss and A. Osman, *J. Heterocyclic Chem.*, **17**, 1713 (1980); N. R. Eweis, *ibid.*, **19**, 273 (1982).

[42] M. A. Ghanannoum, N. F. Eweiss, A. A. Bahajaj and M. A. Qureshi, *Microbios*, **37**, 151 (1983).

[43] L. P. Bellamy, "The Infrared Spectra of Complex Molecules", 3rd Ed, Chapman and Hall London, 1975, p 205.

[44] A. I. Mayer and J. C. Sircar, "The Chemistry of the Cyano Group", in "The Chemistry of Functional Groups", Z. Rappoport, ed, Interscience Publishers, London, 1970, pp 397-404 and references cited therein.

[45] W. Rudnicka and J. Sawlewicz, *Acta. Pol. Pharm.*, **35**, 135 (1978); *Chem. Abstr.*, **89**, 215308e (1978).

[46] J. Elguero, C. Marzin, A. R. Katritzky and P. Linda, "The Tautomerism of Heterocycles", Supplement I in "Advances in Heterocyclic Chemisray", A. R. Katritzky and A. J. Boulton, eds, Academic Press, New York, 1976, pp 403-412.

[47] M. A. Ghannoum N. F. Eweiss and A. A. Bahajaj, unpublished results.