Monatshefte für Chemie 121, 931 – 939 (1990)

Monatshefte für Chemie
Chemical Monthly

The Application of Levulinic Acid and 5-Nitro-2-furylmethylene Diacetate in the Total Synthesis of Some Novel Biologically Active (5-Nitro-2-furyl)azomethines

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Summary. The syntheses and *in vitro* antibacterial and antifungal evaluation of certain (5-nitro-2-furyl)azomethines with different heterocyclic nuclei are described.

Keywords. Pesticide active compounds; (5-Nitro-2-furyl)azomethines; Synthesis and biological evaluation.

Die Anwendung von Lävulinsäure und 5-Nitro-2-furylmethylendiacetat in der Totalsynthese einiger neuer biologisch aktiver (5-Nitro-2-furyl)azomethine

Zusammenfassung. Es wird die Synthese und die *in-vitro*-antibakterielle und antifungale Wirksamkeit für bestimmte (5-Nitro-2-furyl)azomethine mit verschiedenen heterocyclischen Kernen beschrieben.

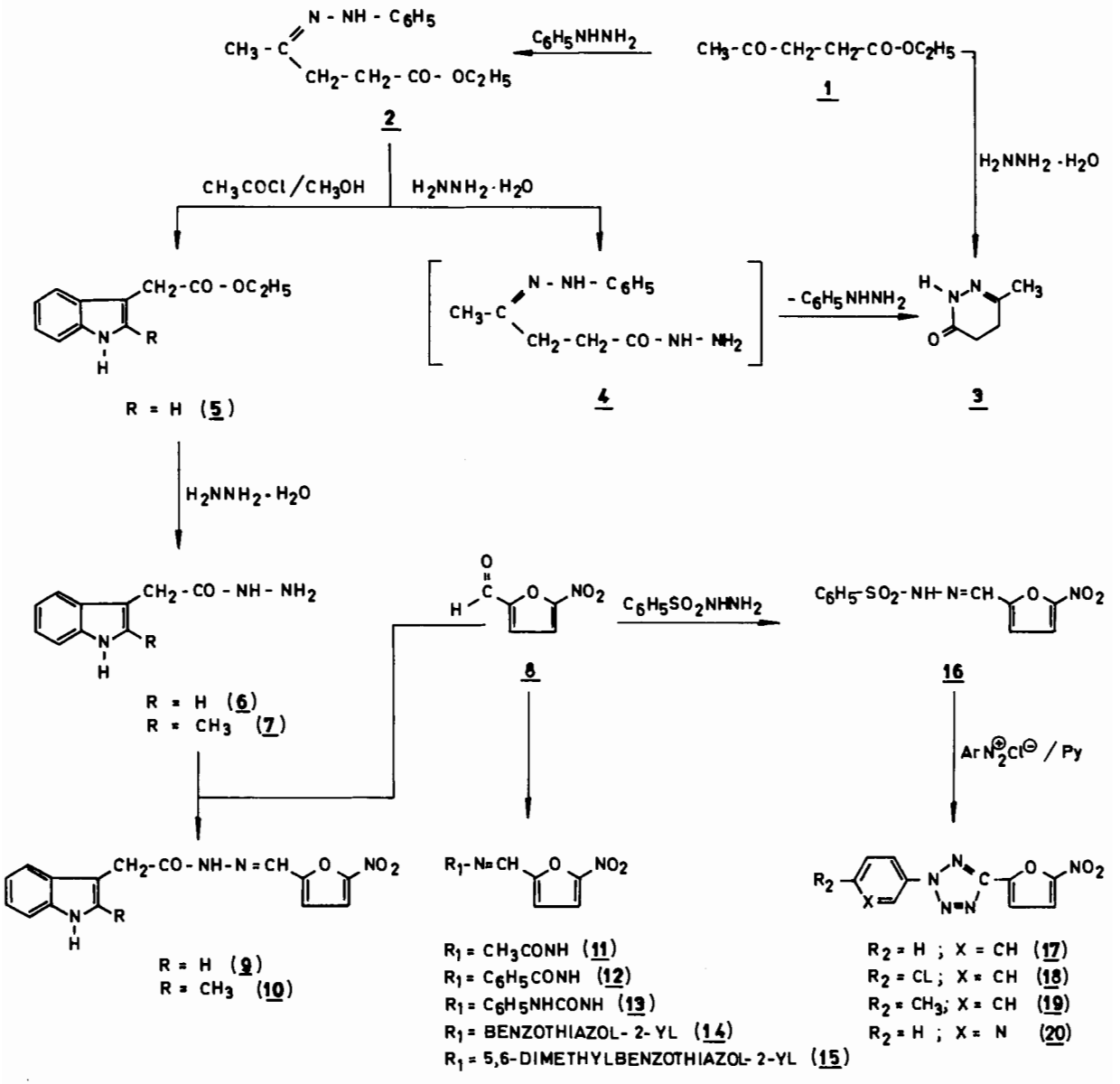
Introduction

In continuation of our interest in the synthesis of various heterocycles linked to the nitrofuran ring [1] and the antimicrobial activities of nitrogen-containing heterocycles we wish to report the synthesis of several types of (5-nitro-2-furyl)azomethines. Nitrofurans have received much attention during the last four decades because of their antibacterial and antitumor activities [2–4]. As a part of an extensive program directed towards the preparation of some novel pesticides certain 5-nitro-2-furyldehyde Schiff bases (**14**, **15**), hydrazones (**9**–**12**) and cyclohydrazones (**17**–**20**) were synthesized from natural raw materials containing pentosans and hexosans (corn cobs, brens, straw grains, oats etc.).

Results and Discussion

Syntheses

5-Nitro-2-furaldehyde (**8**), synthesized by acid hydrolyse of 5-nitro-2-furylmethylene diacetate (referred to in the literature as 5-nitro-2-furaldehyde diacetate) which



was obtained by modified procedure from 2-furaldehyde of 2-furylmethylene diacetate by nitration with acetyl nitrate [1], has been condensed with [(3-indolyl)methylene]-carbonylhydrazine (**6**), [(2-methylindol-3-yl)methylene]-carbonylhydrazine (**7**), acetohydrazide, benzohydrazide, 4-phenylsemicarbazide, 2-aminobenzothiazole, 5,6-dimethyl-2-aminobenzothiazole and benzenesulphonylhydrazide to respective N-(5-nitro-2-furfurylidene)-[(3-indolyl)methylene]-carbonylhydrazine (**9**), N-(5-nitro-2-furfurylidene)-[(2-methylindol-3-yl)methylene]-carbonylhydrazine (**10**), N-(5-nitro-2-furfurylidene)-acetohydrazide (**11**), N-(5-nitro-2-furfurylidene)-benzohydrazide (**12**), 1-(5-nitro-2-furfurylidene)-4-phenylsemicarbazide (**13**), 2-(5-nitro-2-furfurylideneamino)-benzothiazole (**14**), 2-(5-nitro-2-furfurylideneamino)-5,6-dimethylbenzothiazole (**15**), and N-(5-nitro-2-furfurylidene)-benzenesulphonylhydrazine (**16**).

The preparation of 2-aryl-5-(5-nitro-2-furyl)-tetrazoles i.e. 2-phenyl-5-(5-nitro-2-furyl)-tetrazole (**17**), 2-(4-chlorophenyl)-5-(5-nitro-2-furyl)-tetrazole (**18**), 2-(4-methylphenyl)-5-(5-nitro-2-furyl)-tetrazole (**19**), and 2-(3-pyridyl)-5-(5-nitro-2-furyl)-tetrazole (**20**) followed the literature method [5] starting from N-(5-nitro-2-furfurylidene)-benzenesulphonylhydrazine (**16**) and the appropriate diazonium salts.

By condensation of ethyl 4-ketopentanoate (ethyl levulinate) (**1**), which is easily obtained from 4-ketopentanoic acid (levulinic acid), with phenylhydrazine in the atmosphere of nitrogen ethyl 4-phenylhydrazonopentanoate (**2**) has been synthesized and by Fischer cyclization (acetyl chloride in methanol) converted to ethyl 2-methylindole-3-acetate (**5**).

By hydrazinolysis of ethyl levulinate (**1**), ethyl 4-phenylhydrazonopentanoate (**2**), ethyl 2-methylindole-3-acetate (**5**), and commercial ethyl indole-3-acetate the respective 4,5-dihydro-6-methyl-3(2*H*)-pyridazinone (**3**), [(3-indolyl)methylene]-carbonylhydrazine (**6**) and [(2-methylindol-3-yl)methylene]-carbonylhydrazine (**7**) have been synthesized.

Some of (5-nitro-2-furyl)azomethines synthesized in this work have been previously described by the application of various experimental methods: N-(5-nitro-2-furfurylidene)-benzenesulphonylhydrazine(**16**) [5], 2-(5-nitro-2-furfurylideneamino)-benzothiazole (**14**) [6], N-(5-nitro-2-furfurylidene)-acetohydrazide (**11**) [7], and N-(5-nitro-2-furfurylidene)-benzohydrazide (**12**) [8]. For this paper the known nitrofurans **11**, **12**, **14** were synthesized in order to compare them with the antimicrobial activities of some new (5-nitro-2-furyl)azomethines. N-(5-Nitro-2-furfurylidene)-benzenesulphonylhydrazine (**16**) was used as an intermediate in the synthesis of 2-aryl-5-(5-nitro-2-furyl)-tetrazoles **17**–**20**.

1-(5-Nitro-2-furfurylidene)-4-phenylsemicarbazide (**13**), a structural analogue of 5-nitro-2-furaldehyde semicarbazone (in literature well known as nitrofurazone or furacin) [9], was prepared in order to provide a new potential antitumor agent (its *in vitro* activity against A_tB_6 bacteria responsible for appearance and growth of carrot root tumors seems promising for future *in vivo* tests).

2-Methylindole-3-acetate (**5**), a useful synthetic intermediate was previously described [10] but in this work it was synthesized by a different method: in a two-step procedure starting from ethyl levulinate (**1**) via ethyl 4-phenylhydrazonopentanoate (**2**) which was isolated and fully characterized.

2,5-Diaryltetrazoles, e.g. 2-aryl-5-(5-nitro-2-furil)-tetrazoles **17**–**20**, are very important and particularly useful synthetic intermediates. More specifically, 2,5-diaryltetrazoles undergo thermal and/or photo-denitrogenation reactions giving reactive 1,3-dipols for cycloadditions. 2-Aryl-5-(5-nitro-2-furyl)-tetrazoles have not been described in the literature yet and represent relatively rare cyclic disubstituted hydrazones. In comparison with other ones, the 5-nitro-2-furaldehyde hydrazones tetrazoles (**17**–**20**) synthesized in this work are not intensively coloured, do not decompose while heated at melting point temperatures and, unfortunately, show greatly decreased antimicrobial activities (Table 1).

Hydrazinolysis of ethyl levulinate (**1**) and the product of its reaction with phenylhydrazine i.e. ethyl 4-phenylhydrazonopentanoate (**2**) led surprisingly exclusively to the formation of 4,5-dihydro-6-methyl-3(2*H*)-pyridazinone (**3**) which should have been the desired starting material in the synthesis of 4,5-dihydro-6-methyl-4-(5-nitro-2-furfurylidene)-3(2*H*)-pyridazinone. Unfortunately, we were un-

Table 1. *In vitro* antibacterial and antifungal activities of the synthesized (5-nitro-2-furyl)azomethines **9–15** and **17–20**

Compd.	Concentr. (mg/ml)	Bacteria				Fungi
		$A_t B_6$	KF_2	P-2092	V-88	BCP
9	1	+ + +	+ + +	+ + +	+ + +	−
	0.1	+ +	+ +	+ +	+ +	−
	0.01	−	−	−	−	−
10	1	+ + +	+ + +	+ + +	+ + +	+
	0.1	+ +	+ +	+ +	+ +	−
	0.01	+	+	+	+	−
11	1	+ + +	+ + +	+ + +	+ + +	−
	0.1	+ +	+ + +	+ + +	+ +	−
	0.01	+	+ + +	+ +	−	−
12	1	+ + +	+ + +	+ + +	+ + +	−
	0.1	+	+	+	+	−
	0.01	−	−	−	−	−
13	1	+ + +	+ + +	+ + +	+ + +	−
	0.1	+	+	+ + +	+ +	−
	0.01	−	−	+ +	+	−
14	1	+ + +	+ + +	+ + +	+ + +	−
	0.1	+ + +	+ + +	+ +	+	−
	0.01	+	−	−	−	−
15	1	+ + +	+ + +	+ + +	+ + +	+ +
	0.1	+ + +	+ + +	+ +	+ + +	−
	0.01	−	−	−	−	−
17	1	+ + +	+	+ +	+ + +	−
	0.1	−	−	−	−	−
	0.01	−	−	−	−	−
18	1	−	−	−	−	−
	0.1	−	−	−	−	−
	0.01	−	−	−	−	−
19	1	−	+	+	−	−
	0.1	−	−	−	−	−
	0.01	−	−	−	−	−
20	1	−	−	−	−	−
	0.1	−	−	−	−	−
	0.01	−	−	−	−	−

$A_t B_6$ *Agrobacterium radiobacter pv. tumefaciens*
KF_2 *Xanthomonas campestris pv. kampestris*
P-2092 *Xanthomonas campestris pv. Vesicatoria*
V-88 *Pseudomonas sp.*
BCP *Botrytis cinerea, Pers.*

able to prepare the above compound under standard reaction conditions of aldol and/or Perkin condensation of 5-nitro-2-furaldehyde with cyclohydrazone, because its C4 methylene group is not sufficiently reactive to be replaced by the 5-nitro-2-furfurylidene substituent.

Anyway, as a part of a very extensive study on (5-nitro-2-furyl)-azomethines, we have succeeded to synthesize four (**9**, **10**, **13**, **15**) highly active antibacterial and two (**10**, **15**) moderately efficient antifungal compounds (Table 1); their properties for plant protection should be tested *in vivo*.

Antimicrobial Activities of Compounds **9–15** *and* **17–20**

The incorporation of a nitrofuran ring as pharmacophore in the molecule of various compounds is of interest for the synthesis and biological activities of the (5-nitro-2-furyl)azomethines **9–15** and **17–20**. In the expectation that the above compounds display pharmacological activity against different parasities and physiological disorders we have applied whole plate and filter paper disc methods [11–16] for determination of antibacterial and antifungal properties of all 11 compounds (8 are new). The biological activity of the compounds **9–15** and **17–20** has been tested *in vitro* against phytopathogenic strains of bacteria and fungi. Usually the concentrations of the solutions were in the range 0.01–1 mg/ml. Commercial (Fluka) *DMF* was employed for dissolving tested samples.

Experimental

All melting points were determined on an electrothermal melting point apparatus, and are uncorrected. Infrared (IR) spectra were recorded on a Perkin Elmer 1420 spectrometer (Nujol Mull) and on a Pye Unicam 1100 spectrometer (KBr disc). Nuclear magnetic resonance (^{1}H NMR) spectra were recorded on a JEOL GX270 spectrometer and on a Varian FT80A spectrometer using *TMS* as internal standard. Mass (M) spectra were taken with a VG-MS9 spectrometer and with a Finigan-MAT 8230 spectrometer.

Ethyl 4-Phenylhydrazonopentanoate (**2**)

Ethyl levulinate (**1**) (0.1 mol) was heated with phenylhydrazine (0.105 mol) in a stream of nitrogen during 2 h. The crude hydrazone **2** separated on cooling. Yield: 89%; m.p. 109°C (Me_2CO-H_2O).

IR (KBr, ν_{max}, cm^{-1}): 3360, 3050, 3000, 2920, 1720, 1610, 1525, 1505, 1420, 1380, 1360, 1320, 1270, 1230, 1180, 1130, 1080, 1025, 1000, 970, 880, 860, 805, 750, 700, 635. $C_{13}H_{18}N_2O_2$. Calc. C 66.67, H 7.69, N 11.97; found C 66.35, H 7.70, N 12.09.

4,5-Dihydro-6-methyl-3(2H)-pyridazinone (**3**)

1 was condensed with 1 molar excess of hydrazine hydrate in refluxing ethanol during 4 h. Isolation of the cryde hydrazide **3** was carried out by evaporation the reaction mixture. Yield: 90%; m.p. 100°C (*Ph*H-petrol 40/60).

IR (KBr, ν_{max}, cm^{-1}): 3600–3400, 3230, 3150, 2960, 1675, 1650, 1500, 1440, 1350, 1260, 1200, 1175, 1130, 1000, 940, 825, 750, 600. ^{1}H NMR (*DMSO*, δ, ppm): 1.90 (s, 3 H), 2.10–2.50 (m, *DMSO* and 4 H), 3.30 (H_2O), 8.30 (s, 1 H). $C_5H_8N_2O$. Calc. C 53.56, H 7.19, N 24.98; found C 53.80, H 7.22, N 25.16.

Ethyl 2-Methylindole-3-acetate (**5**)

Ethyl 4-phenylhydrazonopentanoate (**2**) (0.05 mol) was dissolved in 100 ml of methanol. To the solution acetyl chloride (0.1 mol) in 25 ml of methanol was added gradually. The reaction mixture was refluxed for 6 h and poured in 500 ml of water. The water solution was extracted with ether, the ethereal solution dried over sodium sulphate, and evaporated. Yield: 60%; b.p. 165°C/0.3 mm Hg.

IR (neat, ν_{max}, cm^{-1}): 3 500–3 300, 3 100, 3 080, 3 010, 2 925, 1 925, 1 880, 1 760, 1 660, 1 625, 1 580, 1 570, 1 485, 1 470, 1 440, 1 420, 1 380, 1 360, 1 310, 1 250, 1 220, 1 180, 1 130, 1 110, 1 080, 1 035, 1 015, 970, 930, 880, 830, 785, 750, 675, 620. ^{1}H NMR ($CDCl_3$, δ, ppm): 1.25 (t, 3 H), 2.16 (s, 2 H), 2.30 (s, 3 H), 2.65 ($CDCl_3$), 3.70 (H_2O), 4.15 (q, 2 H), 7.05–7.60 (m, 4 H), 7.95 (s, 1 H). $C_{13}H_{15}NO_2$. Calc. C 71.89, H 6.91, N 6.45; found C 72.15, H 6.95, N 6.50.

[(3-Indolyl)methylene]-carbonylhydrazines **6** *and* **7**

The appropriate ethyl ester (0.1 mol) was heated with 1 ml of hydrazine hydrate in 10 ml of refluxing ethanol during 4 h. Isolation of the crude hydrazides **6**, **7** was carried out by evaporating the reaction mixtures, followed by adding a small amount of benzene.

6: Yield 80%; m.p. 142°C (*Ph*H). IR (KBr, ν_{max}, cm^{-1}): 3 460, 3 350, 3 120, 3 000, 1 935, 1 710, 1 640, 1 565, 1 490, 1 465, 1 395, 1 370, 1 300, 1 280, 1 260, 1 180, 1 130, 1 090, 1 040, 1 020, 940, 910, 890, 810, 790, 750, 690, 630. ^{1}H NMR (*DMSO*, δ, ppm): 2.50 (*DMSO*), 3.30 (H_2O), 3.45 (s, 2 H), 4.25 (s, 2 H), 6.85–7.15 (m, 6 H), 10.10 (s, 1 H). $C_{10}H_{11}N_3O$. Calc. C 63.48, H 5.86, N 22.21; found C 63.70, H 5.89, N 22.00.

7: Yield 70%; m.p. 153°C (*Ph*H). IR (KBr, ν_{max}, cm^{-1}): 3 350–3 150, 3 050, 2 950, 1 925, 1 875, 1 670, 1 635, 1 590, 1 575, 1 475, 1 425, 1 370, 1 320, 1 270, 1 250, 1 210, 1 160, 1 120, 1 030, 960, 860, 750, 730, 620. ^{1}H NMR (*DMSO*, δ, ppm): 2.45 (s, 3 H), 2.65 (*DMSO*), 3.05 (s, 2 H), 3.70 (H_2O), 4.40 (s, 2 H), 7.60–8.40 (m, 5 H), 10.10 (s, 1 H). $C_{11}H_{13}N_3O$. Calc. C 65.02, H 6.41, N 20.69; found C 65.30, H 6.39, N 20.80.

N-(5-Nitro-2-furfurylidene)-[(3-indolyl)-methylene]-carbonylhydrazines **9** *and* **10**

The appropriate hydrazine (0.005 mol) was condensed with an equimolar amount of 5-nitro-2-furaldehyde (**8**) in refluxing methanol during 1 h. Isolation of the crude hydrazones **9**, **10** was carried out by trituration (water) the reaction mixtures, followed by filtering.

9: Yield 80%; m.p. 229°C (*DMF*-H_2O). IR (KBr, ν_{max}, cm^{-1}): 3 500, 3 370, 3 240, 3 180, 3 050, 1 730, 1 620, 1 540, 1 450, 1 410, 1 380, 1 310, 1 240, 1 220, 1 160, 1 120, 1 080, 1 030, 1 010, 985, 870, 830, 790, 695, 645, 620. ^{1}H NMR (*DMSO*, δ, ppm): 2.50 (*DMSO*), 3.30 (H_2O), 3.70 (s, 2 H), 4.05 (s, 2 H), 6.85–7.45 (m, 4 H), 7.60 (d, 1 H), 7.75 (d, 1 H), 7.90 (s, 1 H), 8.20 (s, 1 H), 10.85 (s, 1 H). M (*m*/e): 313, 312, 173, 157, 144, 130, 129, 128, 103, 102, 101, 77, 76, 51, 44, 30. $C_{15}H_{12}N_4O_4$. Calc. C 57.69, H 3.87, N 17.94; found C 57.44, H 3.90, N 17.80.

10: Yield 85%; m.p. 140°C (*DMF*-H_2O). IR (KBr, ν_{max}, cm^{-1}): 3 420, 3 280, 3 140, 3 060, 2 950, 1 730, 1 675, 1 575, 1 545, 1 490, 1 410, 1 360, 1 330, 1 255, 1 195, 1 150, 1 110, 1 030, 1 010, 980, 960, 940, 890, 820, 740, 660, 610. ^{1}H NMR (*DMSO*, δ, ppm): 2.30 (s, 3 H), 2.50 (*DMSO*), 3.25 (H_2O), 4.90 (s, 2 H), 5.20 (s, 1 H), 6.70–7.40 (m, 4 H), 7.10 (d, 1 H), 7.60 (d, 1 H), 8.10 (s, 1 H), 10.10 (s, 1 H). M (*m*/e): 327, 326, 217, 203, 187, 171, 144, 143, 115, 102, 77, 51, 44. $C_{16}H_{14}N_4O_4$. Calc. C 58.90, H 4.20, N 17.18; found C 59.15, H 4.17, N 17.30.

5-Nitro-2-furaldehyde Hydrazones **11–13**

The appropriate hydrazine (0.01 mol) was condensed with an equimolar amount of **8** in a refluxing inert solvent (e.g. low m.w. alcohol) during 15 min. Isolation of the crude hydrazones was carried out by filtering either the cooled or triturated (water) reaction mixtures.

N-(5-Nitro-2-furfurylidene)-acetohydrazide (**11**)

Yield: 90%; m.p. 254°C (1-*Bu*OH). IR (KBr, ν_{max}, cm^{-1}): 3150, 2900, 2790, 1700, 1650, 1600, 1520, 1480, 1390, 1350, 1260, 1210, 1150, 1030, 980, 940, 840, 820, 780, 740. ^{1}H NMR (*DMSO*, δ, ppm): 2.20 (s, 3H), 2.50 (*DMSO*), 3.30 (H_2O), 7.15 (d, 1H), 7.70 (d, 1H), 7.85 (s, 1H), 11.50 (s, 1H). $C_7H_7N_3O_4$. Calc. C 42.65, H 3.58, N 21.31; found C 42.90, H 3.60, N 21.20.

N-(5-Nitro-2-furfurylidene)-benzohydrazide (**12**)

Yield: 95%; m.p. 218°C (*DMF*-H_2O). IR (KBr, ν_{max}, cm^{-1}): 3640, 3420, 3285, 3170, 3100, 1670, 1610, 1590, 1565, 1530, 1485, 1400, 1360, 1275, 1210, 1150, 1090, 1020, 975, 935, 910, 815, 740, 700. $C_{12}H_9N_3O_4$. Calc. C 54.96, H 4.61, N 16.02; found C 55.19, H 4.63, N 16.20.

1-(5-Nitro-2-furfurylidene)-4-phenylsemicarbazide (**13**)

Yield: 100%; m.p. 206°C (1-*Bu*OH). IR (KBr, ν_{max}, cm^{-1}): 3410, 3240, 3190, 3150, 2960, 1700, 1605, 1550, 1510, 1460, 1365, 1345, 1290, 1210, 1165, 1030, 970, 920, 880, 815, 760, 740, 690, 640. ^{1}H NMR (*DMSO*, δ, ppm): 2.50 (*DMSO*), 3.35 (H_2O), 6.90–7.65 (m, 5H), 7.70 (d, 1H), 7.85 (s, 1H), 11.50 (s, 1H). $C_{12}H_{10}N_4O_4$. Calc. C 52.56, H 3.68, N 20.43; found C 52.30, H 3.65, N 20.60.

2-(5-Nitro-2-furfurylideneamino)-benzothiazoles **14** *and* **15**

The appropriate 2-aminobenzothiazole (0.05 mol) was condensed with 10% excess of **8** in refluxing toluene containing catalytic amount of *p*-toluenesulphonic acid during 2h. At the end of reaction period a large amount of charcoal was added, heating continued for 5min and the hot reaction mixture filtered. Isolation of the crude Schiff bases **14**, **15** was carried out by filtering the cooled reaction mixtures.

14: Yield: 61%; m.p. 205°C (*EtOAc*). IR (KBr, ν_{max}, cm^{-1}): 3140, 1610, 1580, 1540, 1500, 1420, 1350, 1270, 1210, 1040, 975, 920, 830, 780, 740, 670. ^{1}H NMR (*DMSO*, δ, ppm): 2.50 (*DMSO*), 3.20 (H_2O), 7.70 (d, 1H), 7.80 (d, 1H), 7.40–8.10 (m, 4H), 9.15 (s, 1H). $C_{12}H_7N_3O_3S$. Calc. C 52.74, H 2.58, N 15.35; found C 52.90, H 2.60, N 15.20.

2-(5-Nitro-2-furfurylideneamino)-5,6-dimethylbenzothiazole (**15**)

Yield: 44%; m.p. 210°C (*PhMe*). IR (KBr, ν_{max}, cm^{-1}): 3150, 3100, 2940, 1620, 1570, 1535, 1510, 1475, 1410, 1355, 1265, 1170, 1135, 1040, 970, 850, 810, 760, 740. ^{1}H NMR (*DMSO*, δ, ppm): 2.40 (s, 6H), 2.50 (*DMSO*), 3.30 (H_2O), 7.63–7.85 (m, 4H), 9.05 (s, 1H). $C_{14}H_{11}N_3O_3S$. Calcd. C 55.81, H 3.67, N 13.90; found C 56.00, H 3.64, N 13.99.

N-(5-Nitro-2-furfurylidene)-benzenesulphonylhydrazine (**16**)

Benzenesulphonylhydrazine (0.02 mol) was condensed with an equimolar amount of redestilled **8** in refluxing ethanol during 15min. Isolation of the crude hydrazone **16** was carried out by filtering the cooled reaction mixture. Yield: 86%; m.p. 177°C (*PhH*).

IR (KBr, ν_{max}, cm^{-1}): 3205, 3185, 2880, 1570, 1525, 1495, 1450, 1410, 1375, 1360, 1315, 1255, 1185, 1075, 1030, 990, 980, 945, 920, 830, 820, 780, 760, 740, 720, 690. ^{1}H NMR (*DMSO*, δ, ppm): 2.52 (*DMSO*), 3.46 (H_2O), 7.17 (d, 1H), 7.37 (s, 1H), 7.63–7.72 (m, 5H), 7.73 (d, 1H), 7.90 (d, 1H), 12.27 (s, 2H). $C_{11}H_9N_3O_5S$. Calc. C 44.75, H 3.07, N 14.23; found C 44.52, H 3.08, N 14.09.

2-Aryl-5-(5-nitro-2-furyl)-tetrazoles **17–20** [5]

The appropriate aromatic amine was dissolved in 6.4ml of ice-cooled 18% hydrochloric acid. To the ice-cooled amine hydrochloride solution continuously was added 5ml of concentrated sodium

nitrite solution at 0°C and left for 15 min. The obtained diazonium salt solution was added dropwise to a cold solution of N-(5-nitro-2-furfurylidene)-benzenesulphonylhydrazine (**16**) at 0°C during 15 min with continuous stirring. After completion, the reaction mixture was left at 0–5°C for 12 h. Formed crude crystalls of tetrazoles **17–20** were separated by filtration and washed thoroughly with water.

2-Phenyl-5-(5-nitro-2-furyl)-tetrazole (**17**)

Yield: 61%; m.p. 194°C (*Et*OH – H_2O). IR (Nujol, ν_{max}, cm^{-1}): 3140, 3090, 2960–2850 st, 1615, 1590, 1540, 1505, 1480, 1450 st, 1375 st, 1350, 1335, 1310, 1290, 1240, 1210, 1195, 1080, 1020, 995, 965, 910, 835, 805, 760, 750, 730, 700, 680. ^{1}H NMR (*DMSO*, δ, ppm): 2.51 (*DMSO*), 3.36 (H_2O), 7.69–7.73 (m, 5 H), 7.95 (d, 1 H), 8.18 (d, 1 H). M (*m/e*): 257, 229, 91, 77, 64, 63, 51. $C_{11}H_7N_5O_3$. Calc. C 51.37, H 2.74, N 27.23; found C 51.58, H 2.76, N 27.11.

2-(4-Chlorophenyl)-5-(5-nitro-2-furyl)-tetrazole (**18**)

Yield: 32%, m.p. 182°C (*Et*OH). IR (Nujol, ν_{max}, cm^{-1}): 3150, 3100, 2960–2850 st, 1640, 1620, 1590, 1550, 1515, 1485, 1460 st, 1415, 1400, 1375 st, 1350, 1300, 1245, 1220, 1170, 1145, 1095, 1080, 1015, 1000, 970, 920, 820, 810, 750, 735, 680. ^{1}H NMR (*DMSO*, δ, ppm): 2.51 (*DMSO*), 3.41 (H_2O), 7.70 (d, 1 H), 7.78 (d, 2 H), 7.94 (d, 1 H), 8.19 (d, 2 H). M (*m/e*): 292, 291, 265, 263, 127, 126, 125, 111, 90, 89, 75, 64, 63, 51. $C_{11}H_6N_5O_3Cl$. Calc. C 45.30, H 2.07, N 24.01; found C 45.08, H 2.09, N 23.83.

2-(4-Methylphenyl)-5-(5-nitro-2-furyl)-tetrazole (**19**)

Yield: 39%; m.p. 185°C (*Et*OH). IR (Nujol, ν_{max}, cm^{-1}): 3160, 3100, 3030, 2960–2850 st, 1910, 1820, 1675, 1660, 1620, 1550, 1500, 1460 st, 1380 st, 1350, 1335, 1310, 1245, 1200, 1180, 1025, 1000, 965, 950, 915, 835, 815, 750, 735, 695, 650. ^{1}H NMR (*DMSO*, δ, ppm): 2.44 (s, 3 H), 2.51 (*DMSO*), 3.40 (H_2O), 7.52 (d, 2 H), 7.69 (d, 1 H), 7.94 (d, 1 H), 8.06 (d, 2 H). M (*m/e*): 271, 243, 106, 105, 91, 78, 77, 65, 52, 51. $C_{12}H_9N_5O_3$. Calc. C 53.14, H 3.34, N 25.82; found C 53.10, H 3.33, N 25.68.

2-(3-Pyridyl)-5-(5-nitro-2-furyl)-tetrazole (**20**)

Yield: 35%; m.p. 203°C (*Et*OH). IR (Nujol, ν_{max}, cm^{-1}): 3160, 3100, 2960–2850 st, 1825, 1675, 1640, 1615, 1590, 1545, 1500, 1480, 1450 st, 1430, 1380 st, 1350, 1335, 1310, 1245, 1200, 1180, 1025, 1000, 965, 950, 915, 835, 815, 750, 735, 695, 650. ^{1}H NMR (*DMSO*, δ, ppm): 2.51 (*DMSO*), 3.37 (H_2O), 7.76 (d, 1 H), 7.78 (t, 1 H), 7.94 (d, 1 H), 8.58 (d, 1 H), 8.87 (d, 1 H), 9.38 (d, 1 H). M (*m/e*): 259, 258, 231, 230, 93, 92, 78, 66, 65, 64, 51, 38, 28. $C_{10}H_6N_6O_3$. Calc. C 46.52, H 2.34, N 32.54; found C 46.45, H 2.37, N 32.20.

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Received February 23, 1990. Revised April 24, 1990. Accepted May 3, 1990

Printed in Austria