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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.

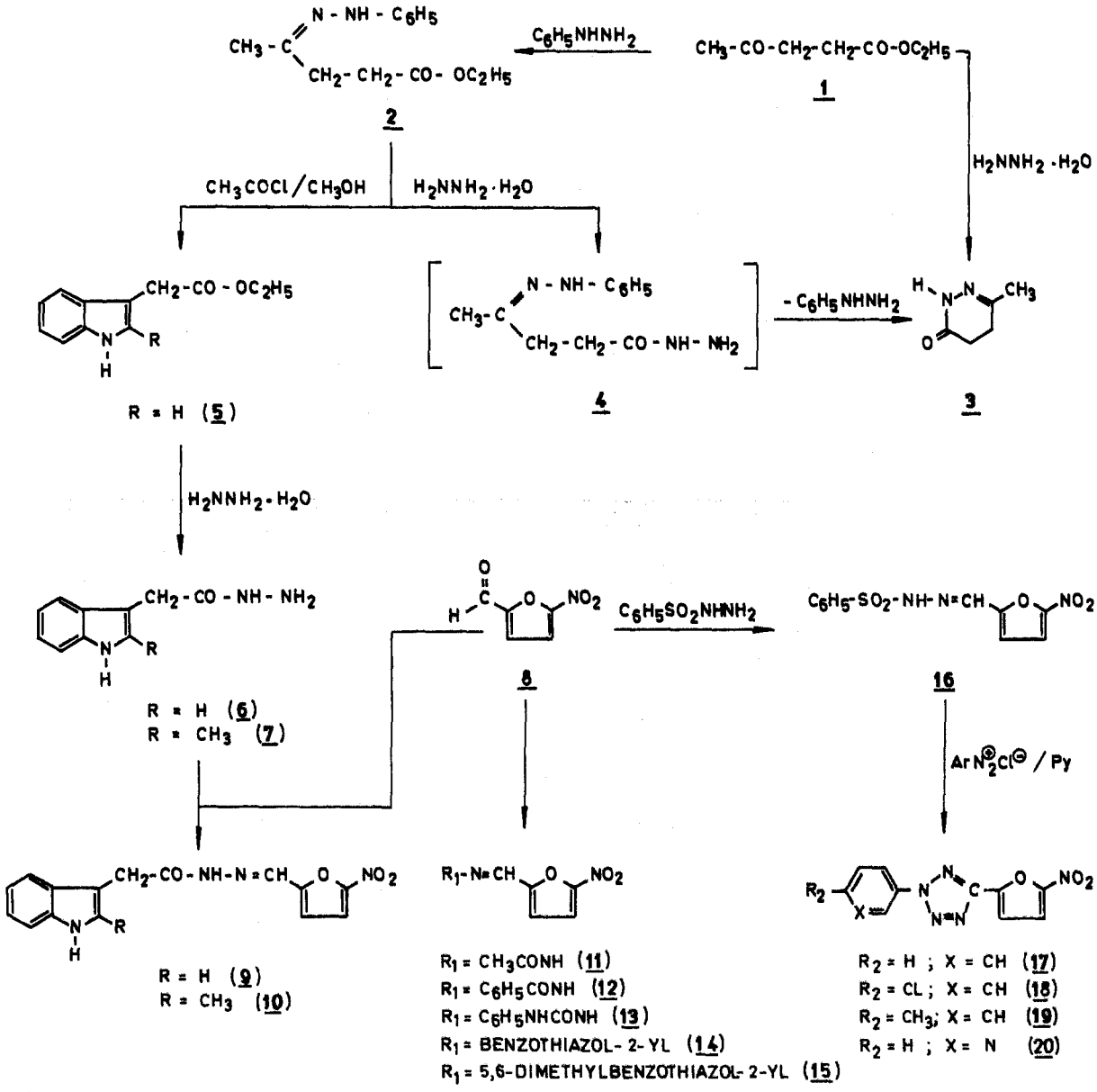
Introduction

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-MAT8230 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. C66.67, H7.69, N11.97; found C66.35, H7.70, N12.09.

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, 3H), 2.10–2.50 (m, *DMSO* and 4H), 3.30 (H_2O), 8.30 (s, 1H). $C_5H_8N_2O$. Calc. C53.56, H7.19, N24.98; found C53.80, H7.22, N25.16.

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 5 min 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 15 min. Isolation of the crude hydrazone **16** was carried out by filtering the cooled reaction mixture. Yield: 86%; m.p. 177°C (*Ph*H).

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 6.4 ml of ice-cooled 18% hydrochloric acid. To the ice-cooled amine hydrochloride solution continuously was added 5 ml 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}): 3 140, 3 090, 2 960–2 850 st, 1 615, 1 590, 1 540, 1 505, 1 480, 1 450 st, 1 375 st, 1 350, 1 335, 1 310, 1 290, 1 240, 1 210, 1 195, 1 080, 1 020, 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}): 3 150, 3 100, 2 960–2 850 st, 1 640, 1 620, 1 590, 1 550, 1 515, 1 485, 1 460 st, 1 415, 1 400, 1 375 st, 1 350, 1 300, 1 245, 1 220, 1 170, 1 145, 1 095, 1 080, 1 015, 1 000, 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}): 3 160, 3 100, 3 030, 2 960–2 850 st, 1 910, 1 820, 1 675, 1 660, 1 620, 1 550, 1 500, 1 460 st, 1 380 st, 1 350, 1 335, 1 310, 1 245, 1 200, 1 180, 1 025, 1 000, 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}): 3 160, 3 100, 2 960–2 850 st, 1 825, 1 675, 1 640, 1 615, 1 590, 1 545, 1 500, 1 480, 1 450 st, 1 430, 1 380 st, 1 350, 1 335, 1 310, 1 245, 1 200, 1 180, 1 025, 1 000, 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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