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Synthesis and Biological Activities of 3-(2-Furyl)-4-aryl-1, 2, 4-triazole-5-thiones

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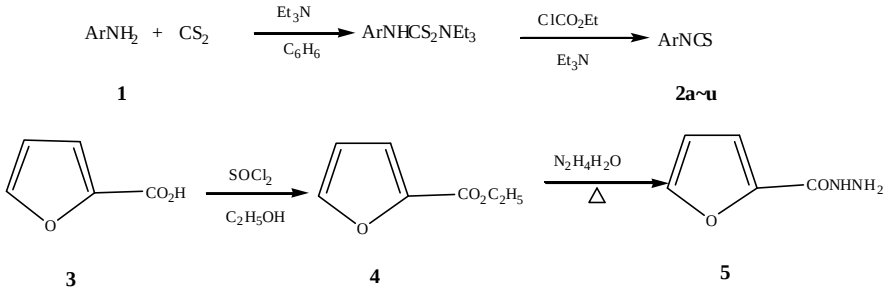
Abstract: A series of novel compounds 3-(2-furyl)-4-aryl-1, 2, 4-triazole-5-thiones have been synthesized. All the compounds were characterized by spectral data and elemental analysis. The preliminary biological test showed that some of them exhibited excellent plant-growth regulative activities.

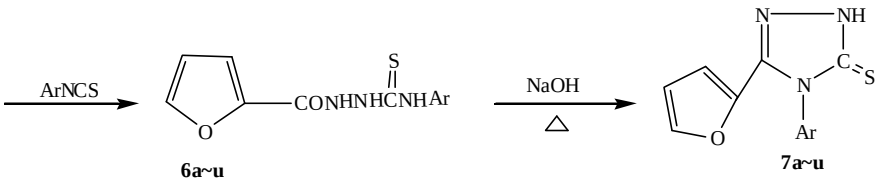
Keywords: 1, 2, 4-Triazoles, synthesis, biological activities.

During these years, a great variety of heterocyclic compounds bearing 1, 2, 4-triazole have been synthesized due to their broad spectrum of biological activities, such as antiviral, antitumor, antifungal and plant-growth regulative activities[1-4]. Some of them have been developed into commercial plant-growth regulative agents including paclobutrazol, uniconazol and triapenthenol. It is obvious that the oxygen atom of furan ring can take part in the formation of hydrogen bond in the species. So furan heterocycle may help to increase the biological activities of triazole derivatives. In this paper, a series of 3-(2-furyl)-4-aryl-1, 2, 4-triazole-5-thiones were synthesized and tested for their biological activities. All of them are new compounds and their structures have been confirmed by IR, ^{1}HNMR and elemental analysis. The preliminary biological test showed some of them exhibited excellent plant-growth regulative activities.

The title compounds **7a~u** were prepared as described in **Scheme 1**, the key intermediates **2a~u** and **5** were prepared according to the literature[5,6] respectively.

Scheme 1





6a~u **7a~u**

Table 1 The substituents Ar- of compounds **7a~u**

Compd.	Ar-	Compd.	Ar-	Comp.	Ar-
7a	4-$CH_3C_6H_4$-	**7h**	4-FC_6H_4-	**7o**	3-$CH_3C_6H_4$-
7b	2,4-$(CH_3)_2C_6H_3$-	**7i**	2-$CH_3C_6H_4$-	**7p**	4-$CH_3OC_6H_4$-
7c	C_6H_5-	**7j**	4-BrC_6H_4-	**7q**	2-$C_4H_3OCH_2$-
7d	$C_6H_5CH_2$-	**7k**	2-ClC_6H_4-	**7r**	2,6-$(CH_3)_2C_6H_3$-
7e	4-ClC_6H_4-	**7l**	2-BrC_6H_4-	**7s**	C_6H_{11}-
7f	3,4-$(CH_3)_2C_6H_3$-	**7m**	2-$C_{10}H_7$-	**7t**	2-Cl-5-$C_5H_3NCH_2$-
7g	3-ClC_6H_4-	**7n**	4-$C_2H_5OC_6H_4$-	**7u**	2-$CH_3OC_6H_4$-

General procedure for preparation of compounds **6a~u**: A solution of equimolar of aryl isothiocyanate **2a~u** and 2-furancarboxylic acid hydrazide **5a~u** in $CHCl_3$ were stirred and refluxed for 2 hours. The white precipitate formed was filtered and recrystallized from N, N-dimethylformamide-ethanol-water (1:10:5) to yield compounds **6a~u**.

Table 2 Physical data of the compounds **7a~u**

Compd.	Molecules	Yield (%)	M.P. (°C)	Elemental analysis (%, Calcd.)		
				C	H	N
7a	$C_{13}H_{11}N_3SO$	79.42	273~274	60.69(60.71)	4.31(4.26)	16.33(16.27)
7b	$C_{14}H_{13}N_3SO$	62.53	250~251	61.98(62.09)	4.83(4.88)	15.49(15.52)
7c	$C_{12}H_9N_3SO$	61.80	150~151	59.25(59.08)	3.72(3.55)	17.27(17.01)
7d	$C_{13}H_{11}N_3SO$	65.80	182~183	60.69(60.51)	4.31(4.31)	16.33(16.51)
7e	$C_{12}H_8N_3SOCl$	73.11	282~283	51.90(51.84)	2.90(2.84)	15.13(15.17)
7f	$C_{14}H_{13}N_3SO$	54.32	231~232	61.98(62.05)	4.83(4.91)	15.49(15.49)
7g	$C_{12}H_8N_3SOCl$	43.82	196~197	51.90(51.93)	2.90(2.71)	15.13(15.13)
7h	$C_{12}H_8N_3SOF$	51.47	260~261	55.17(55.22)	3.09(2.88)	16.09(16.18)
7i	$C_{13}H_{11}N_3SO$	36.43	229~230	60.69(60.65)	4.31(3.97)	16.33(16.37)
7j	$C_{12}H_8N_3SOBr$	45.32	284~285	44.74(44.36)	2.50(2.33)	13.04(13.04)
7k	$C_{12}H_8N_3SOCl$	34.08	271~272	51.90(52.12)	2.90(2.73)	15.13(15.10)
7l	$C_{12}H_8N_3SOBr$	67.00	285~286	44.74(44.36)	2.50(2.42)	13.04(13.26)
7m	$C_{16}H_{11}N_3SO$	54.56	259~260	65.52(65.33)	3.78(3.68)	14.33(14.27)
7n	$C_{14}H_{13}N_3SO_2$	33.05	257~258	58.53(58.38)	4.56(4.61)	14.63(14.59)
7o	$C_{13}H_{11}N_3SO$	44.51	195~196	60.69(60.70)	4.31(4.25)	16.33(16.10)
7p	$C_{13}H_{11}N_3SO_2$	44.12	258~259	57.14(57.13)	4.06(4.02)	15.34(15.40)
7q	$C_{11}H_9N_3SO_2$	46.64	180~181	53.44(53.62)	3.67(3.64)	17.00(17.12)
7r	$C_{14}H_{13}N_3SO$	75.63	267~268	61.98(62.10)	4.83(4.89)	15.49(15.58)
7s	$C_{12}H_{15}N_3SO$	52.90	196~196	57.82(57.58)	6.06(5.98)	16.86(16.70)
7t	$C_{12}H_9N_4SOCl$	39.69	209~210	49.24(48.98)	3.10(3.06)	19.14(18.96)
7u	$C_{13}H_{11}N_3SO_2$	54.23	227~228	57.14(56.96)	4.06(4.00)	15.34(15.31)

Table 3 IR and ^{1}HNMR data of the compounds **7a~u**

NO.	IR (cm^{-1})	^{1}HNMR (δ, ppm)
7a	3400 (m, N-H), 1620(s, C=N), 1320 (s, C=S)	14.14 (s, 1H, NH), 7.83~5.87 (m, 7H, Ph-H & C_4H_3O-H), 2.42 (s, 3H, *p*- CH_3)
7b	3410 (m, N-H), 1620 (s, C=N), 1320 (s, C=S)	14.19 (s, 1H, NH), 7.84~5.74 (m, 6H, Ph-H & C_4H_3O-H), 2.39(3H, s, *o*- CH_3), 1.97 (s, 3H, *p*- CH_3)
7c	3400 (m, N-H), 1620 (m, C=N), 1325 (vs, C=S)	12.11 (s, 1H, NH), 7.64~5.92(m, 8H, Ph-H & C_4H_3O-H)
7d	3400 (s, N-H), 1620 (s, C=N), 1320 (s, C=S)	12.32 (s, 1H, NH), 7.58~6.50 (m, 8H, Ph-H & C_4H_3O-H), 5.57(s, 2H, CH_2)
7e	3400 (m, N-H), 1620 (s, C=N), 1325 (s, C=S), 725 (m, C-Cl)	14.21(s, 1H, NH), 7.83~6.09 (m, 7H, Ph-H & C_4H_3O-H)
7f	3400 (m, N-H), 1620 (s, C=N), 1325 (s, C=S)	12.35 (s, 1H, NH), 7.49 ~ 5.88 (m, 6H, Ph-H & C_4H_3O-H), 2.37 (s, 3H, *m*-CH_3), 2.34 (s, 3H, *p*-CH_3)
7g	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S), 740 (m, C-Cl)	12.01 (s, 1H, NH), 7.61 ~ 6.12 (m, 7H, Ph-H & C_4H_3O-H)
7h	3400 (m, N-H), 1620 (s, C=N), 1322 (s, C=S), 1250(s, C-F)	14.19 (s, 1H, NH), 7.83 ~ 6.00 (m, 7H, Ph-H & C_4H_3O-H)
7i	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S)	12.61(s, 1H, NH), 7.55 ~ 5.75 (m, 7H, Ph-H & C_4H_3O-H), 2.16 (3H, s, *o*- CH_3)
7j	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S), 630 (m, C-Br)	14.20 (s, 1H, NH), 7.83~6.10 (m, 7H, Ph-H & C_4H_3O-H)
7k	3400 (m, N-H), 1620 (s, C=N), 1325 (s, C=S), 742 (m, C-Cl)	14.30 (s, 1H, NH), 7.83~5.98 (m, 7H, Ph-H & C_4H_3O-H)
7l	3400 (m, N-H), 1620 (s C=N), 1320 (s, C=S), 630 (m, C-Br)	14.27 (s, 1H, NH), 7.92 ~ 5.92 (m, 7H, Ph-H & C_4H_3O-H)
7m	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S)	14.37 (s, 1H, NH), 8.23 ~ 5.55 (m, 10H, Ph-H & C_4H_3O-H)
7n	3400 (m, N-H), 1620 (s, C=N), 1325 (s, C=S)	14.11 (s, 1H, NH), 7.83 ~ 5.87 (m, 7H, Ph-H & C_4H_3O-H), 4.15 ~ 4.08 (m, 2H, -OCH_2), 1.40 ~ 1.35 (t, 3H, CH_3)
7o	3400 (m, N-H), 1619 (s, C=N), 1325 (s, C=S)	12.62 (s, 1H, NH), 7.52~5.89 (m, 7H, Ph-H & C_4H_3O-H), 2.37 (s, 3H, *m*-CH_3)
7p	3400 (m, N-H), 1620 (s, C=N), 1340 (s, C=S)	14.13 (s, 1H, NH), 7.84~5.88 (m, 7H, Ph-H & C_4H_3O-H), 3.85 (s, 3H, -OCH_3)
7q	3400 (m, N-H), 1610 (s, C=N), 1320 (s, C=S)	11.98 (s, 1H, NH), 7.65 ~ 6.28 (m, 6H, $(C_4H_3O)_2$-H), 5.55 (s, 2H, CH_2)
7r	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S)	13.03 (s, 1H, NH), 7.51 ~ 5.69 (m, 6H, Ph-H & C_4H_3O-H), 2.12 (s, 6H, *o*-$(CH_3)_2$)
7s	3400 (m, N-H), 1620 (s, C=N), 1350 (s, C=S)	12.46 (s, 1H, NH), 7.66 ~ 6.58 (m, 3H, C_4H_3O-H), 4.80~1.09 (m, 11H, C_6H_{11})
7t	3400 (m, N-H), 1620 (s, C=N), 1320 (s, C=S), 760 (s, C-Cl)	14.27 (s, 1H, NH), 8.37 ~ 6.69 (m, 6H, Py-H & C_4H_3O-H), 5.51 (s, 2H, CH_2)
7u	3400 (m, N-H), 1620 (s, C=N), 1315 (s, C=S)	14.10 (s, 1H, NH), 7.80 ~ 5.92 (m, 7H, Ph-H & C_4H_3O-H), 3.68 (s, 3H, -OCH_3)

The preparation of compounds **7a~u**: Thiosemicarbazide **6a~u** (5 mmol) was added to the aqueous NaOH solution (15 mL, 2 mol/L). The reaction mixture was heated at 76°C for 2 hours, cooled and neutralized with aqueous HCl solution (2 mol/L). The precipitate formed was filtered and recrystallized twice from N, N-dimethylformamide-ethanol (1:10) to yield compounds **7a~u**.

The preliminary plant-growth regulative activities of the title compounds **7a~u** have been determined. Some of them showed excellent promotive function for plant growth.

Table 4 The inhibition percentage of some compounds to rice and cucumber

Compd.	rice				cucumber			
	stalk		root		stalk		root	
	10 ppm	100 ppm	10 ppm	100 ppm	10 ppm	100 ppm	10 ppm	100 ppm
7c	14.66	10.82	10.21	31.71	-31.49	-14.92	-21.49	34.50
7d	14.73	10.86	14.92	51.04	-33.28	11.52	-26.95	23.40
7f	5.70	13.43	-1.71	29.47	-28.98	11.88	-12.23	20.22
7g	-3.35	2.50	1.95	41.53	-22.94	18.14	-20.68	35.10
7i	2.97	6.92	4.77	10.46	-24.08	14.28	-19.44	42.80
CK	-2.13	13.60	-5.55	24.80	7.16	12.17	0.63	29.78

*Negative inhibition percentage shows promotive action for plant growth
*__CK__ is N, N-dimethylpiperinium chloride

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References

1. L. Czollner, G. Szilagyi, J. Lango, J. Janaky, *Arch. Pharm.* (Weinheim, Ger.), **1990**, *323* (4), 225.
2. Jacobson, L. T. Nguyen, *Eur. Pat. Appl.* Ep 338 685; *Chem. Abst*., **1990**, *112*, 178991t.
3. Goswami B. N., *et al.*, *J. Heterocyclic Chem.*, **1984**, *21*, 182.
4. X. M. Feng, R. Chen, Z. Y. Zhang, *Chem. J. Chin. Univ*., **1991**, *12* (10), 1326.
5. D. Q. Wang, L. Z. Li, B. Zhang, *Chin. Sci.* B, **1986**, *5*, 476.
6. W. H. Cheng, Z. X. Si, *Appl. Chem.*, **2000**, *17* (4), 444.

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