Bulgarian Chemical Communications, Volume 46, Number 4 (pp. 795 – 800) 2014

Synthesis, characterization and biological activities of some novel isatin derivatives

A.M. Amani

Department of Chemistry, Shiraz University of Technology, Shiraz, Iran

Received October 22, 2013; Revised January 4, 2014

A series of novel (arylimino-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N'-(4-aryl-2-yl)-hydrazide derivatives (**5a-g**) were synthesized. The structures of the newly synthesized compounds were characterized by elemental analysis, FT-IR, ^{1}H-, ^{13}C-NMR and mass spectroscopy. The compounds were screened *in vitro* for antibacterial and antifungal activities against some human pathogenic microorganisms by the disc diffusion technique. Some of the compounds showed moderate to good biological activities when compared with commercially available drugs.

Keywords: isatin; 1,3-thiazole; antibacterial, antifungal

INTRODUCTION

A new class of antibacterial and antifungal agents is needed, especially against drug-resistant bacteria and fungi such as gram-positive and gram-negative strains, which are responsible for a number of serious infections in the acute and chronic care units in hospitals. Isatin or 1*H*-indole-2,3-dione is an indole derivative. The compound was first obtained by Erdmann [1] and Laurent [2] in 1841 as a product from the oxidation of indigo dye by nitric acid and chromic acids. The compound is found in many plants, such as *Isatis tinctoria*, *Calanthe discolor* and *Couroupita guianensis* [3]. Schiff bases of isatin are investigated for their pharmaceutical properties [4]. Isatin forms a blue dye (indophenin) when mixed with sulfuric acid and crude benzene. The formation of indophenin was long believed to be a a result of the reaction with benzene. Victor Meyer was able to isolate the substance responsible for this reaction from crude benzene. This new heterocyclic compound was thiophene [5]. Isatin is commercially available. It may be prepared by cyclicizing the condensation product of chloral hydrate, aniline and hydroxylamine in sulfuric acid. This reaction is called the Sandmeyer isonitrosoacetanilide isatin synthesis (**Fig. 1**) and was discovered by Traugott Sandmeyer in 1919 [6,7].

Another classic reaction, the Sandmeyer diphenylurea isatin synthesis (Sandmeyer 1903), starts from diphenylthiourea, potassium cyanide, and lead carbonate [7]. Isatin can be made from the corresponding indole in good yield by a mixture of $InCl_3$ and IBX in an acetonitrile/water solution at 80°C [8]. Literature survey revealed that isatin possesses diverse biological activities such as antibacterial [9], antifungal [10], antiviral [11], antimycobacterial [12], anticancer [13], anti-inflammatory [14] and anticonvulsant [15]

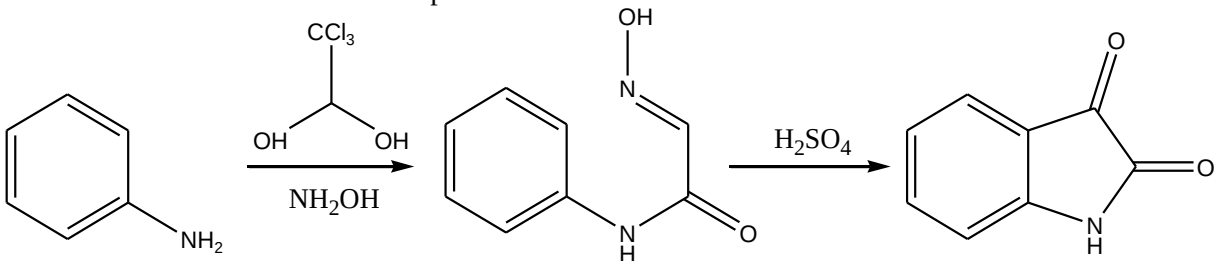
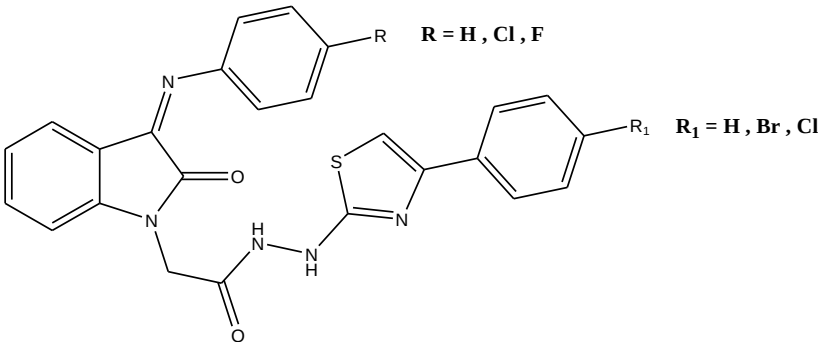


Fig. 1. Isatin synthesis according to Sandmeyer method

.

* To whom all correspondence should be sent:
E-mail: amani@sutech.ac.ir



Compound	R	R_1
5a	H	H
5b	H	Br
5c	Cl	Br
5d	Cl	H
5e	H	Cl
5f	F	H
5g	F	Cl

Fig. 2. Structure of target compounds (**5a-g**)

activities. The thiazole moiety also displays diverse pharmacological activities like anti-microbial [16], anti-inflammatory [17], anti-viral [18], antipsychotic [19], antiarrhythmic and anticoagulant [20] activities. The study of the above pharmacophores reveals that the combination of these two entities may result in increased antimicrobial activity. In view of the biological importance of these two moieties, it was planned to synthesize a new series of isatin containing 1,3-thiazole derivatives and to evaluate the new compounds for their biological activities (**Fig. 2**)

EXPERIMENTAL

Material and Equipments

All chemicals and solvents were obtained from E. Merck and Sigma-Aldrich and used without further purification. All melting points were taken with an Electrothermal melting point apparatus (Electrothermal Eng. Ltd, Essex, UK) and were uncorrected. IR spectra were recorded in KBr on a Shimadzu Dr-8031 instrument. The ^{1}H and ^{13}C-NMR spectra of the synthesized compounds were measured in DMSO-d_6 or $CDCl_3$ solution with TMS as the internal standard using a Varian Mercury 400, 400MHz instrument. All chemical shifts were reported as δ (ppm) values. The mass spectra were recorded on a LCQ ion trap mass spectrometer (Thermo Fisher, San Jose, CA, USA), equipped with an EI source. Elemental analyses were carried out using a Perkin-Elmer, CHN elemental analyzer.

Synthesis of Compounds

The synthetic route of intermediates and target compounds is given in **Fig. 3**.

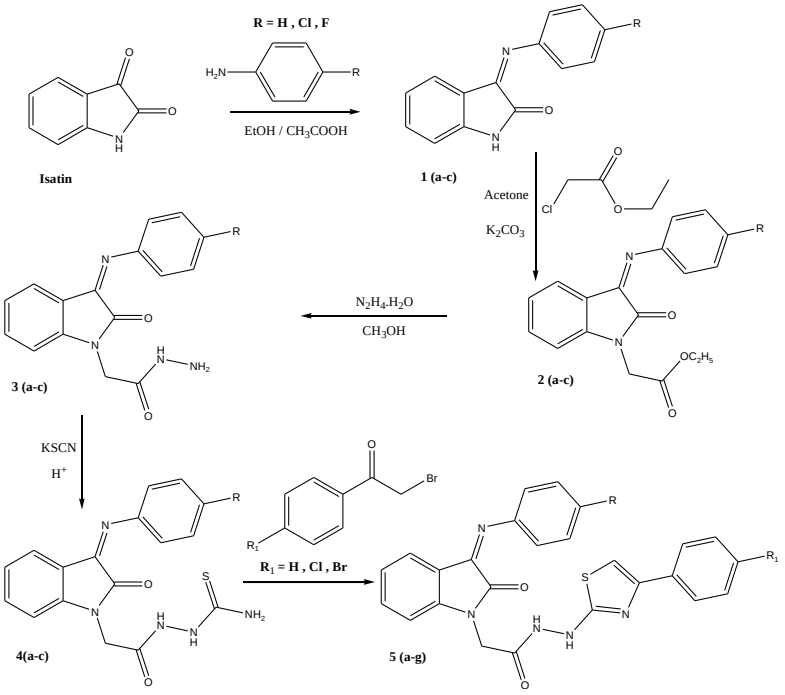


Fig. 3. Schematic synthesis of intermediates and target compounds

General procedure for the preparation of the compounds **1(a-c)**

These intermediates were prepared according to ref. [21] with some modifications.

A mixture of isatin (1.47 g, 0.01 mol) and an appropriate aniline (0.01 mol) in absolute ethanol (20 ml) was refluxed for one hour in the presence of 2-3 drops of glacial acetic acid. Crystals were separated out, filtered and re-crystallized from ethanol to give **1(a-c)**.

General procedure for the preparation of the compounds **2(a-c)**

These intermediates were prepared according to ref. [22] with some modifications.

A mixture of the corresponding 3-phenylimino-1*H*-indol-2,3-dione **1(a-c)** (0.01 mol), ethyl chloroacetate (1.22 ml, 0.01 mol) and potassium carbonate (2.2 g, 0.015 mol) in dry acetone was refluxed for 20 h. The reaction mixture was poured onto crushed ice. The separated solid was filtered, washed with water and re-crystallized from methanol to give **2(a-c)**.

General procedure for the preparation of the compounds **3(a-c)**

These intermediates were prepared according to ref. [23] with some modifications.

A mixture of the corresponding 3-phenylimino-2-oxo-1-indole-ethylacetate **2(a-c)** (0.01 mol) and hydrazine hydrate (99%, 0.5 ml, 0.01 mol) in methanol (20 mL) was refluxed for about 5 h on a steam bath. After completion of the reaction (monitored by TLC), the mixture was cooled and the resulting solid was filtered, dried and re-crystallized from ethanol to give **3(a-c)**.

General procedure for the preparation of the compounds **4(a-c)**

These intermediates were prepared according to ref. [18] with some modifications.

A mixture of the corresponding 3-phenylimino-2-oxo-1-indole-acetylhydrazide **3(a-c)** (0.01 mol) was refluxed with 10 ml of 10% HCl and potassium thiocyanate (0.015 mol) for 4 h. The reaction mixture was allowed to cool to room temperature. The solid formed was collected by filtration, washed with water, dried and re-crystallized from ethanol to give **4(a-c)**.

General procedure for the preparation of the new compounds **5(a-g)**

A mixture of the corresponding 3-phenylimino-2-oxo-1-indole-acetylthiosemicarbazide **4(a-c)** (0.01 mol) and phenacyl bromide (0.01 mol) was refluxed in ethanol (50 mL) for 10 h. The separated solid was filtered off and re-crystallized from DMF to give **5(a-g)**.

(2-Oxo-3-phenylimino-2,3-dihydro-indol-1-yl)-acetic acid N'-(4-phenyl-thiazol-2-yl)-hydrazide **(5a)**

Cream powder; Yield 71 %; m.p. 248-250 ^{o}C; IR (KBr, cm^{-1}): 1052, 1320, 1610, 1658, 2560, 3075 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.3 (s, 2H, N-CH_2), 6.7 (thiazole CH), 7.1-8.00 (m, 14H, Ar-H), 9.62 (s, H, CS-NH), 10.32 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 56, 110.5, 123.5, 134, 152, 155, 159, 165, 170; Anal. Calcd. for $C_{25}H_{19}N_5O_2S$: C, 66.21; H, 4.22; N, 15.44 %. Found: C, 66.11; H, 4.18; N, 15.48 %. MS (m/z, *regulatory intensity*, %): 453 (*100*), 454 (*30*), 131 (*18*), 77 (*22*).

(2-Oxo-3-phenylimino-2,3-dihydro-indol-1-yl)-acetic acid N'-[4-(4-bromo-phenyl)-thiazol-2-yl]-hydrazide **(5b)**

Light reddish powder; Yield 75%; m.p. 256-258 ^{o}C; IR (KBr, cm^{-1}): 670, 1062, 1330, 1622, 1651, 2568, 3100 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.2 (s, 2H, N-CH_2), 6.8 (thiazole CH), 7.3-8.05 (m, 13H, Ar-H), 9.70 (s, H, CS-NH), 10.40 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 58, 111.5,122, 125.5, 133.5, 156, 158, 159.5, 165.5, 171; Anal. Calcd. for $C_{25}H_{18}BrN_5O_2S$: C, 56.40; H, 3.41; N, 13.15 %. Found: C, 56.31; H, 3.45; N, 13.10 %. MS (m/z, *regulatory intensity*, %): 533 (*100*), 531 (*98*), 532 (*18*).

[3-(4-Chloro-phenylimino)-2-oxo-2,3-dihydro-indol-1-yl]-acetic acid N'-[4-(4-bromo-phenyl)-thiazol-2-yl]-hydrazide **(5c)**

Light yellowish powder; Yield 70 %; m.p. 218-220 ^{o}C; IR (KBr, cm^{-1}): 650, 820, 1055, 1328, 1640, 1657, 2582, 3090 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.2 (s, 2H, N-CH_2), 6.8 (thiazole CH), 7.05-7.95 (m, 12H, Ar-H), 9.60 (s, H, CS-NH), 10.25 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 55.5, 113.5, 123.5, 126.5, 131.5, 134.5, 157, 159.5, 160.5, 166, 169; Anal. Calcd. for $C_{25}H_{17}BrClN_5O_2S$: C, 52.97; H, 3.02; N, 12.35 %. Found: C, 53.05; H, 2.96; N, 12.29 %. MS (m/z, *regulatory intensity*, %): 567 (*100*), 565 (*97*), 568 (*38*).

[3-(4-Chloro-phenylimino)-2-oxo-2,3-dihydro-indol-1-yl]-acetic acid N'-(4-phenyl-thiazol-2-yl)-hydrazide **(5d)**

Yellowish powder; Yield 72 %; m.p. 260-262 ^{o}C; IR (KBr, cm^{-1}): 835, 1065, 1328, 1655, 1668, 2575, 2988 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.23 (s, 2H, N-CH_2), 6.75 (thiazole CH), 7.10-8.05 (m, 13H, Ar-H), 9.68 (s, H, CS-NH), 10.40 (s, H, CO-NH); ^{13}C-

NMR (δ, ppm): 54.5, 114.5,122.5, 126, 132.5, 135.5, 158.5, 159, 161.5, 167.5, 170; Anal. Calcd. for $C_{25}H_{18}ClN_5O_2S$: C, 61.54; H, 3.72; N, 14.35 %. Found: C, 61.47; H, 3.66; N, 14.39 %. MS (m/z, *regulatory intensity*, %): 487 (*100*), 488 (*28*), 489 (*36*).

(2-Oxo-3-phenylimino-2,3-dihydro-indol-1-yl)-acetic acid N'-[4-(4-chloro-phenyl)-thiazol-2-yl]-hydrazide **(5e)**

Yellowish powder; Yield 74 %; m.p. 229-231 °C; IR (KBr, cm^{-1}): 830, 1050, 1331, 1642, 1673, 2580, 3000 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.25 (s, 2H, N-CH_2), 6.65 (thiazole CH), 7.10-7.95 (m, 13H, Ar-H), 9.50 (s, H, CS-NH), 10.38 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 52, 111.5,124.5, 128.5, 133.5, 137.5, 159.5, 160, 162.5, 168.5, 171; Anal. Calcd. for $C_{25}H_{18}ClN_5O_2S$: C, 61.54; H, 3.72; N, 14.35 %. Found: C, 61.58; H, 3.76; N, 14.29 %. MS (m/z, *regulatory intensity*, %): 487 (*100*), 488 (*28*), 489 (*36*), 453 (*17*), 398 (*19*), 376 (*18*), 268 (*100*).

[3-(4-Fluoro-phenylimino)-2-oxo-2,3-dihydro-indol-1-yl]-acetic acid N'-(4-phenyl-thiazol-2-yl)-hydrazide **(5f)**

Grayish powder; Yield 69 %; m.p. 225-227 °C; IR (KBr, cm^{-1}): 1060, 1250, 1333, 1653, 1675, 2588, 2950 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.33 (s, 2H, N-CH_2), 6.73 (thiazole CH), 7.15-8.05 (m, 13H, Ar-H), 9.45 (s, H, CS-NH), 10.45 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 53.5, 113.5,126.5, 129.5, 138.5, 158.5, 162, 163.5, 168.5,169, 171; Anal. Calcd. for $C_{25}H_{18}FN_5O_2S$: C, 63.68; H, 3.85; N, 14.85 %. Found: C, 63.61; H, 3.87; N, 14.79 %. MS (m/z, *regulatory intensity*, %): 471 (*100*), 472 (*30*).

[3-(4-Fluoro-phenylimino)-2-oxo-2,3-dihydro-indol-1-yl]-acetic acid N'-[4-(4-chloro-phenyl)-thiazol-2-yl]-hydrazide **(5g)**

Yellowish powder; Yield 68 %; m.p. 239-241 °C; IR (KBr, cm^{-1}): 825, 1065, 1262, 1344, 1659, 1701, 2562, 2985 cm^{-1} ; ^{1}H-NMR (δ, ppm): 4.45 (s, 2H, N-CH_2), 6.69 (thiazole CH), 7.05-8.10 (m, 12H, Ar-H), 9.56 (s, H, CS-NH), 10.48 (s, H, CO-NH); ^{13}C-NMR (δ, ppm): 52.5, 112.5, 128.5, 129, 139.5, 157.5, 163.5, 166.5, 168.5, 169, 170.5; Anal. Calcd. for $C_{25}H_{17}ClFN_5O_2S$: C, 59.35; H, 3.39; N, 13.84 %. Found: C, 59.31; H, 3.32; N, 13.90 %. MS (m/z, *regulatory intensity*, %): 505 (*100*), 506 (*30*), 507 (*36*).

Biological Evaluation

In vitro antibacterial and antifungal activity

All compounds were evaluated for their in vitro anti-bacterial activity against S. aureus, B. subtilis, E. coli, P. vulgaris and antifungal activity against C. albicans, A. niger standard strains using the disc diffusion method [24, 25]. Each disc contained 200 µg/ml of the tested compounds. The paper disc diffusion method was performed using Mueller-Hinton (Hi-Media) agar (antibacterial) and potato dextrose (Hi-Media) agar (antifungal). Suspensions of each microorganism were prepared to contain approximately 10^6 colony forming units (cfu)/ml and applied to plates. The surface of the medium was allowed to dry. The 200 µg/ml (in DMSO) compound-impregnated discs were applied to the surface of the inoculated plates. The petri plates were incubated at 37°C for 18-24 h for antibacterial activity, and at 26°C for approx. 48-72 h for antifungal activity (Table 1) [26].

Minimum Inhibitory Concentration Determination:

The solutions of the newly synthesized compounds and standard drugs were prepared at 500, 250, 125, 62.5, 31.25, 15.63, 7.8, 3.9, 1.95, 0.98, 0.48, 0.24, 0.12 mg/ml concentrations in the wells of micro plates by dilution with the liquid

Table 1: Biological activities of the compounds **5a-g** at a concentration of 200 µg/ml

Compound	Zone of inhibition (mm)					
	Antimicrobial activity (200 µg/ml)				Antifungal activity (200 µg/ml)	
	S. aureus	*B. subtilis*	*E. coli*	*P. vulgaris*	*C. albicans*	*A. niger*
5a	Not Seen	7.5	Not Seen	Not Seen	7.12	Not Seen
5b	Not Seen	7.85	8.9	Not Seen	7.5	7.5
5c	6.85	9.62	9.95	9.1	8.5	8.5
5d	6.72	8.2	10.5	8.5	8.5	7.5
5e	6.85	7.5	8.2	7.5	7.5	8.5
5f	7.1	11.1	11.5	10.5	8.5	7.5
5g	7.6	9.5	12.8	9.5	7.5	7.5
Ampicilin	14.8	8.8	16.5	17.5	-	-
Norfloxacin	8.6	12.5	12.2	12.5	-	-
Fluconazole	-	-	-	-	10.5	12.5

.

Table 2: MIC value of compounds **5a-g**

Compound	Minimum Inhibitory Concentration (μg/ml)					
	S. aureus	*B. subtilis*	*E. coli*	*P. vulgaris*	*C. albicans*	*A. niger*
5a	-	250	-	-	250	-
5b	-	250	125	-	125	250
5c	125	62.5	62.5	125	125	125
5d	125	125	62.5	125	125	125
5e	125	125	125	62.5	250	250
5f	125	62.5	31.25	62.5	125	250
5g	62.5	62.5	31.25	62.5	125	125
Ampicilin	0.48	0.48	3.9	3.9	-	-
Norfloxacin	0.12	0.12	0.12	0.12	-	-
Fluconazole	-	-	-	-	0.98	1.95

double stranded nutrient broth. The bacterial suspensions of 10^5 cfu/ml used for inoculation were prepared by diluting fresh cultures at McFarland 0.5 density (10^7 cfu/ml). Suspensions of the bacteria at 10^5 cfu/ml concentration were inoculated to the two-fold diluted solution of the compounds. There were 10^4 cfu/ml bacteria in the wells after inoculations. Nutrient broth was used for diluting the bacterial suspension and for two-fold dilution of the compound. DMSO, pure microorganisms and pure media were used as control wells. A 10 μl bacterial inoculum was added to each well of the micro dilution trays. The trays were incubated at 37 ^oC in a humid chamber and MIC endpoints were read after 24 h of incubation. For antifungal activity, the same procedure was used. The lowest concentration of the compound that completely inhibits macroscopic growth was determined and the minimum inhibitory concentrations (MICs) were reported (Table 2)

RESULTS AND DISCUSSION

Chemistry

In the present work, nucleophilic addition of 4-substituted aniline to indole-2,3-dione yielded 3-(4-arylimino)-indol-2-one **1(a-c)** which on further treatment with ethyl chloroacetate underwent alkylation reaction in presence of anhydrous K_2CO_3 in dry acetone and yielded 3-(4-arylimino)-2-oxo-1-indole-ethylacetate **2(a-c).** The latter was converted to 3-(4-arylimino)-2-oxo-1-indole-acetylthyrazide **3(a-c)** through reaction with hydrazine hydrate. Further, thiosemicarbazone formation from compounds **3(a-c)** in presence of KSCN and 10 % HCl, yielded 3-phenylimino-2-oxo-1-indole-acetylthiosemicarbazides **4(a-c).** Compounds **4(a-c),** refluxed in ethanol in the presence of phenacyl bromide or substituted phenacyl bromide, yielded (arylimino-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N'-(4-aryl-2-yl)-hydrazide analogues **5(a-g)**. The IR spectrum of the final compounds **5(a-g)** showed isatin carbonyl (C=O str.), 2^o NH str., amide C=O str., C=N str., S-C str., C-X str., which confirmed the formation of the final compound. In the ^{1}H-NMR spectrum of **5(a-g)**, as representative compounds of the series**,** all protons were seen according to the expected chemical shift and integral values. The structure of the compounds **5(a-g)** was confirmed by physical data, elemental analysis, spectral data, IR, ^{1}H-, ^{13}C-NMR and mass spectroscopy.

Biological activities

The compounds **5f**, **5g** with fluoro substitution at the R position were found to be highly active against *S. aureus* and *B. subtilis*. Compounds **5d** with Cl substitution at R and **5e** with Cl substitution at R_1 were found to be moderately active against *S. aureus* and *B. subtilis*.

In the case of gram-negative bacteria *E. coli*, *P. vulgaris*, the compounds **5f** with fluoro substituent at R position and **5g** with fluoro and chloro substituents at R and R_1 position, respectively, were found to be highly active. **5d** was moderately active against *E.coli* and **5e** was moderately active against *P. vulgaris.* All compounds showed moderate activity for *C. albicans* and *A. niger*. All screened compounds showed significant antimicrobial activity.

CONCLUSIONS

In conclusion, the present method may be considered as a practical route for the synthesis of a series of new (arylimino-2-oxo-2,3-dihydro-indol-1-yl)-acetic acid N'-(4-aryl-2-yl)-hydrazide analogues from 3-(4-arylimino)-2-oxo-1-indole-acetylthiosemicarbazide in ethanol in the presence

of phenacyl bromide or substituted phenacyl bromides. The procedure has the advantages of high yield, mild reaction conditions, simple experimental work-up and may be an acceptable method for the preparation of isatin containing 1,3-thiazole derivatives. Our studies clearly demonstrated that the novel synthesized compounds have prospectful pharmaceutical properties and can be used for the development of new drugs in the future.

REFERENCES

1. O.L. Erdmann, *J. Prakt. Chem.*, **19(1),** 321 (1840).
2. A. Laurent, *Annales de Chimie et de Physique*, **3(3),** 393 (1840).
3. J.F.M. da Silva, S.J. Garden, A.C. Pinto, *J. Braz. Chem. Soc.*, **12 (3),** 273 (2001).
4. A.A. Jarrahpour, D. Khalili, *Molbank*, **4,** M437 (2005).
5. W.C. Sumpter, *Chem. Rev.*, **34 (3),** 393 (1944).
6. C.S. Marvel, G.S. Hiers, *Org. Synth.*, **5(71),** 327 **(**1925).
7. T. Sandmeyer, *Helvetica Chimica Acta*, **2(1),** 234 (1919).
8. J.S. Yadav, B.V.S. Reddy, Ch.S. Reddy, A. Krishna, *Synthesis*, **5,** 693 (2007).
9. S.N. Pandeya, D. Sriram, G. Nath, E. De Clercq, *Eur. J. Pharm. Sci.*, **9,** 25 (1999).
10. K. Mirjana, M.M. Saric, M. Morvin, D. Maysinger, *J. Pharm. Sci.*, **68,** 459 (2006).
11. S.N. Pandeya, D. Sriram, G. Nath, E. De Clercq, *Pharm. Acta Helv.*, **74,** 11 (1999).
12. S.K. Sridhar, S.N. Pandeya, S.K. Bajpai, H. Manjula, *Indian Drugs*, **36(6),** 412 (1999).
13. V. SLakshmi, A. Pandeya, S.N. Pandeya, *Indian J. Pharm. Sci.*, **65(3),** 213 (2003).
14. Y.Teitz, ELadizensky, N. Barko, E. Burstein, *Antimicrob. Agents Chem. Ther.*, **37,** 2483 (1993).
15. V. Alagarsamy, S. Meena, S. Vijayakumar, K.V. Ramseshu, Revathi R. *Pharmazie*, **58,** 233 (2003).
16. H. Pajouhesh, R. Parson, F.D. Popp, *J. Pharm. Sci.*, **72(3),** 318 (1983).
17. B.F. Abdel-Wahab, H.A. Abdel-Aziz, E.M. Ahmed. *Eur. J. Med. Chem.*, **44,** 2632 (2009).
18. H.N. Hafez, A.B.A. El-Gazzar, *Bioorg. Med. Chem.*, **18,** 5222 (2009).
19. O. I. el-Sabbagh, M.M. Baraka, S.M. Ibrahim, C. Pannecouque, G. Andrei, R. Snoeck, J. Balzarini, A.A. Rashad, *Eur. J. Med. Chem.*, **44(9),** 3746 (2009).
20. K.V.G. Chandra, V. Rao, R.K. Vyas, M. Murali Krishna Kumar, *Bioorg. Med. Chem. Lett.*, **18,** 6054 (2008).
21. S.B. Bari, A.O. Agrawal, U.K. Patil, *J. Sci. Islamic Rep. Iran.*, **19(3),** 217 (2008).
22. P.V. Frank, K. S. Girish, B. Kalluraya, *J. Chem. Sci.*, **119(1),** 41 (2007).
23. S. George, M.K. Parameshwaran, A.R. Chakraborti, T.K. Ravi, *Acta Pharma.*, **58,** 119 (2008).
24. A.W. Bauer, W.M. Kirby, J.C. Sherris, M. Turck, *Am. J. Clin. Pathol*., 45, 493 (1996).
25. National Committee for Clinical Laboratory Standards. Reference method for broth dilution antifungal susceptibility testing of yeasts; Approved Standard. NCCLS Document M27-A2, 2nd ed. Vol. 22 No. 15; National Committee for Clinical Laboratory Standards: 940 West Valley Road, Suite 1400, Wayne, Pennsylvania 19087-1898 USA (2002).

СИНТЕЗА, ОХАРАКТЕРИЗИРАНЕ И БИОЛОГИЧНА АКТИВНОСТ НА НЯКОИ НОВИ ИЗАТИНОВИ ПРОИЗВОДНИ

А.М. Амани

Департамент по химия, Технологичен университет, Шираз, Иран

Постъпила на 22 октомври, 2013 г.; коригирана на 4 януари, 2014 г.

(Резюме)

Синтезирани са серия от нови производни (арил имино-2-оксо-2,3-дихидро-индол-1-ил)-оцетнакиселина N'-(4-арил-2-ил)-хидразид. Структурите на новосинтезираните съединения са охарактеризирани чрез елементен анализ, FT-IR, ^{1}H-, ^{13}C-NMR и мас-спектроскопия. Съединенията са изследвани *in vitro* за антибактериална и фунгицидна активност спрямо някои патогенни за човека микроорганизми чрез диск-дифузионна техника. Някои от съединенията показват умерена до добра биологична активност в сравнение с търговски достъпните препарати.