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Note

Development and assessment of green synthesis of hydrazides[†]

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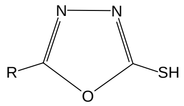
An expeditious, solvent free one pot method for the preparation of hydrazides from corresponding acids directly under microwave irradiation is developed. The method has been assessed using green chemistry measures and found superior to conventional method with higher E(environmental) factor, atom economy, atom efficiency, carbon efficiency, reaction mass efficiency.

Enhancing the efficiency and maneuverability of organic synthesis constitutes one of the most exciting challenges to synthetic chemists. Within the last decade, green chemistry has attained the status of a major scientific discipline[1]. The investigation and application of green chemistry principles[2] has led to the development of cleaner and more benign chemical processes, with many new technologies being developed each year. In today's world, synthetic chemists in both academia and industry are constantly challenged to consider more environmentally benign and sustainable methods for the generation of desired target molecules. Among the twelve principles of green chemistry "design for energy efficiency" is one of the key principles of relevance to synthetic chemists[3]. Much attention has been given to the applications of microwave dielectric heating in organic synthesis since the first reported[4] acceleration of a chemical reaction under the influence of microwaves. It is significantly more energy-efficient than conventional heating[5] with the enhanced reaction rates, simplified manipulation and work-up, and higher purity of final products.

Hydrazides are important intermediates in organic synthesis[6], especially in the preparation of pharmaceuticals and agrochemicals. Their synthesis has attracted significant attention due to their utility as building blocks in many syntheses[7], e.g., 1,2,4-triazoles, 1,3,4-oxadiazoles, 1,3,4-thiadiazoles, 1,2,4,5-tetrazines etc. Hydrazides are also potent bioactive molecules and possess biological activities such as antituberculous agents (Isoniazid), HIV inhibitors, inhibitors of myeloperoxidase, glycogen phosphorylase, pesticides[8]. Maleic hydrazide is an important herbicide[8g]. 5-Substituted-1,3,4-oxadiazoles-2-thiols **1** are potential nitrification inhibitors under development[9]. We were in need of an efficient, fast and high yielding method for preparing hydrazides, intermediate to compound **1**, to fulfill its bulk requirement.



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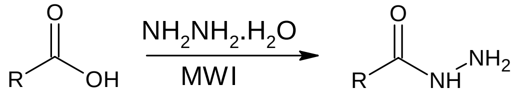
To date, a variety of procedures have been developed to prepare hydrazides. Acyl anhydrides and acid chlorides[10] both react rapidly with hydrazine to give hydrazides. However, acid chlorides and anhydrides are so reactive that it is difficult to stop the reaction short of diacylation. The most widely used method to prepare hydrazides is hydrazinolysis of the corresponding esters[11] with hydrazine monohydrate which has a requirement of preparing esters from corresponding acids. The use of inclusion complexes of hydroquinone and hydrazine[12] as an alternative of hydrazine monohydrate in solid state hydrazinolysis of esters is also reported. Esters seldom produce significant amounts of diacylhydrazine, but less reactive esters may require inconveniently longer reaction times and/or severe reaction conditions.

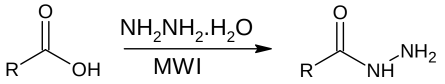
The demands for new bioactive heterocycles such as 1,3,4-oxa/thiadiazoles in the fields of agrochemical research, combined with the pressure to produce these substances expeditiously and in an environmentally benign fashion, pose significant challenges to the synthetic chemical community working for agrochemical development. We, therefore, report herein an efficient method for the preparation of hydrazides from corresponding acids directly under microwave irradiation in the absence of organic solvents and other auxiliary agents such as surfactants and its assessment using green chemistry matrices[13].

[†] Contribution No. - 991



Scheme I

Table I — Physical data of hydrazides (R-CONHNH$_2$)



Compd	R	Reaction time Process		% Yield Method	
		1 (hr)	2 (s)	A	B
1	C_6H_5-	6.0	60	77	90
2	4-ClC_6H_4-	6.5	105	70.5	90
3	2,4-$(Cl)_2C_6H_3$-	7.0	150	65	83
4	2-$CH_3C_6H_4$-	8.5	200	59	82
5	3-$CH_3C_6H_4$-	9.0	160	63	81
6	4-$CH_3C_6H_4$-	7.0	170	68	85
7	4-$CH_3OC_6H_4$-	7.0	100	64	87
8	3,4-$(CH_3O)_2C_6H_3$-	8.0	150	62	88
9	2-HOC_6H_4-	9.0	140	67.5	89
10	4-HO, 3-$CH_3OC_6H_3$-	7.0	170	62	79
11	4-*t*-$C_4H_9C_6H_4$	8.5	120	60.5	82
12	CH_3-	6.0	80	69	86
13	CH_3CH_2-	6.5	90	71	82
14	$CH_3CH_2CH_2$-	7.0	90	72	84
15	$CH_3(CH_2)_5CH_2$-	8.0	100	61	82
16	$CH_3(CH_2)_7CH_2$-	8.5	80	63	81
17	$CH_3(CH_2)_9CH_2$-	8.5	110	61.5	82
18	$CH_3(CH_2)_{14}CH_2$-	8.5	180	65	81
19	2-Furyl	9.0	170	63	80
20	3-Pyridyl	8.5	180	66	82
21	4-Pyridyl	9.0	190	65	80

The hydrazides were synthesized following both conventional[14] (Process 1) and green method (Process 2). In process 1, synthesized esters were hydrazineloysed to yield the hydrazides[14]. In process 2, organic carboxylic acids and hydrazine hydrate were directly irradiated under microwaves (**Scheme I**) without any solvent for 60-200 seconds at 900 Watt at 2.45 GHz. The yield of hydrazides following new process was 79.0-90.0% as compared to 59.0-77.0% from conventional procedure (**Table I**). The total heating time was just 60-200 seconds under microwaves in process 2 as compared to 6-9 hr in process 1.

The processes (1 and 2) were assessed using various green chemistry matrices taking benzoic hydrazide as a representative case (**Table II**). There was 13.0% increase in the yield. The number of steps was also reduced to one as compared to two in process 1. This resulted in the higher energy efficiency and reduction of time, as total heating time was just 60 seconds under microwaves in process 2 as compared to 6 hr in process 1. The reaction time was reduced by 360 times. Consequently there was 400 times decrease in the energy consumption as it is 6 KWh for process 1 and 0.015 KWh for process 2.

Among the various green chemistry matrices, E-factor values for process 1 and 2 were 4.5 and 0.3 kg waste/kg product respectively showing the reduction of 93.3% in the waste produced over the production of one kilogram of the product, benzoic hydrazide. Atom economy was increased by 16.8% as it was 62.3 and 79.1% for process 1 and 2 respectively. Atom efficiency which considers both atom economy and yield parameters, showed an improvement of 23.0 per cent. Carbon efficiency was found to be 77.8 and 100.0% for process 1 and 2 respectively. It was improved by 22.2%. Reaction mass efficiency

Table II — Comparative assessment of processes 1 and 2 using green chemistry measures taking benzoic hydrazide as a case

S. No.	Matrix	Process 1 (Conventional)	Process 2 (Greener)	Improvement
1	Overall yield (%)	77.0	90	13% Increase
2	Number of steps	Two	One	50% Reduction
3	Heating time	6-9 hr	60-200 s	162-360 Less
4	Energy consumption (KWh)	6-9	0.015-0.050	180-400 times less
5	E(environmental) factor (Kg waste / Kg product	4.5	0.3	93.3% Reduction
6	Atom economy (%)	62.3	79.1	16.8% Increase
7	Atom efficiency (%)	48.2	71.2	23% Increase
8	Carbon efficiency (%)	77.8	100	22.2% Increase
9	Reaction mass efficiency (%)	16.0	69.2	53.2% Increase

possessed the values of 31.5 (process 1) and 36.1 (process 2) and an increase of 4.6% was observed.

In conclusion, a useful, fast and green method for the synthesis of hydrazides was developed and assessed for its greenness. In comparison to conventional method, the method has faster reaction rate, higher yield, higher atom economy, higher energy efficiency and ecofriendly reaction conditions.

Experimental Section

Melting points were determined by using electro thermal melting point apparatus and are incorrect. Microwave irradiation was carried out by using Samsung microwave oven model CE118KF operating at 2450 MHZ. A Christ Lypholizer model Alpha 1-2 LD was used for lyophilizing purpose. Nuclear magnetic resonance (NMR) spectra were recorded on a Brucker Abamce, 400 MHz. Infrared (IR) spectra were recorded on a Nicolet Fourier Transform Infrared Spectrophotometer, Model Impact 400 (FTIR) in either nujol mull or KBr disc. Elemental analysis was carried out using EuroVector CHNS analyzer.

Conventional method of synthesis of carboxylic acid hydrazides: General procedure. The hydrazides were synthesized in following two steps conventionally by the reported method[14a].

Synthesis of ester from corresponding carboxylic acid: In a 500 mL round bottomed flask mixture containing 0.0246 mole of acid, 0.25 mole of absolute ethanol and 0.5 g of conc. sulphuric acid were taken and mixture was refluxed for 3-4 hr. Excess alcohol was distilled off on a water bath and allowed to cool. The residue was poured into about 250 mL of water contained in a separatory funnel and flask was rinsed with a few mL of water which was also poured into the separatory funnel. Carbon tetra chloride (10-15 mL) was added and the mixture in the funnel was shaken vigorously. Lower layer was carefully run off, the upper aqueous layer was rejected, ethyl ester was returned to the funnel and shaken with a strong solution of sodium hydrogen carbonate until all the free acid was removed and washed with water, and was dried over magnesium sulphate. Ethyl ester solution was filtered directly into a round bottomed flask and distilled. For example ethyl benzoate (a colourless liquid) at 212-214°C was collected in 86% yield.

Synthesis of carboxylic acid hydrazides from esters: Hydrazine hydrate (0.011 mole) and ethyl ester (0.01 mole) were taken in a flat bottomed flask. A minimum amount of ethyl alcohol was added to make the reaction-mixture a clear solution. The contents were refluxed for 3-5 hr. The progress of the reaction was monitored in thin layer chromatography plate. After completion of the reaction, the ethanol was distilled off under reduced pressure to give the desired product. The hydrazide was recrystallised using alcohol. The hydrazides were characterized on the basis of physical and spectral data.

Green synthetic method for carboxylic acid hydrazides 1-21: General Procedure. Carboxylic acid (0.01 mole) and hydrazine hydrate (0.012 mole) were taken in a 150 mL conical flask. The reaction mixture was irradiated under microwaves for 60-200 s at 900 Watt at 2.45 GHz. The reaction mixture was cooled to -20^{o}C and then it was lypholized at -50^{o}C. The products obtained were recrystallized from methyl alcohol. The hydrazides were characterized on the basis of physical and spectral data which is in agreement with reported literature[10-12, 14]. The physical data are given in **Table I**.

Benzoic hydrazide 1: m.p. (Penciclovir C) 110-13°C (Lit.[14a] 112°C). IR (KBr): 3200, 1670 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.65 (s, 2H, NH_2), 7.44 (dd, 2H, 3,5-Ar-H), 7.51 (m, 1H, 4-Ar-H), 7.95 (dd, 2H, 2,6-Ar-H), 8.75 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 127.1 (2,6-Ar-C), 128.2 (3,5-Ar-C), 131.5 (4-Ar-C), 135.1 (1-Ar-C), 171.1 (C=O); Anal. Calcd. for $C_7H_8N_2O$: C, 61.75; H, 5.92; N, 20.58. Found: C, 61.86; H, 5.98; N, 20.69%.

4-Chloro benzoic hydrazide 2: m.p. 162-63°C (Lit[14a] 63°C) IR (KBr): 3207, 1678 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.81 (s, 2H, NH_2), 7.45 (d, 2H, 2,6-Ar-H), 7.91 (d, 2H, 3,5-Ar-H), 8.89 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 128.78 (2,6-Ar-C), 133.14 (3,5-Ar-C), 133.89 (4-Ar-C), 135.85 (1-Ar-C), 172.1 (CO); Anal. Calcd. for $C_7H_7ClN_2O$: C, 49.28; H, 4.14, N, 16.42. Found: C, 49.24; H, 4.19, N, 16.29%.

2,4-Dichloro benzoic hydrazide 3: m.p. 158-61°C (Lit.[14a] 163-64°C). IR (KBr): 3211, 1672 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.63 (s, 2H, NH_2), 7.32-7.39 (m, 1H, 6-Ar-H), 7.57 (d, 1H, 5-Ar-H), 8.2 (d, 1H, 3-Ar-H), 8.71 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 134.58 (2-Ar-C), 129.20 (3-Ar-C), 138.47 (4-Ar-C), 127.55 (5-Ar-C), 130.02 (6-Ar-C), 139.62 (1-Ar-C), 179.60 (CO); Anal. Calcd. for $C_7H_6Cl_2N_2O$: C, 41.00 H, 2.95, N, 13.66. Found: C, 40.88; H, 2.93, N, 13.59%

2-Methyl benzoic hydrazide 4: m.p. 120-21°C (Lit[14a]) (KBr) 3221, 1678 cm^{-1}; ^{1}H NMR (DMSO-d_6 +

$CDCl_3$): 2.35 (s, 3H,CH_3), 4.63 (s, 2H, NH_2), 7.29-7.32 (m, 1H, 3-Ar-H), 7.46-7.49 (m, 1H, 4-Ar-H), 7.92-8.1 (m, 1H, 5-Ar-H), 8.12-8.31 (m, 1H, 6-Ar-H), 9.11 (brs, 1H, CONH); ^{13}C NMR: (DMSO-d_6 + $CDCl_3$) 21.19 (CH_3), 134.59 (1-Ar-C), 127.71 (2-Ar-C), 129.98 (3-Ar-C), 131.79 (4-Ar-C), 125.4 (5-Ar-C), 136.4 (6-Ar-C), 173.76 (CO); Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65. Found: C, 63.78; H, 6.76; N, 18.76%

3-Methyl benzoic hydrazide 5: m.p. 99-100°C (Lit[14a] 97°C); IR (KBr): 3205, 1682 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 2.43 (s, 3H, CH_3), 4.47 (s, 2H, NH_2), 7.17 (d, 1H, 4-Ar-H), 7.29 (d, 1H, 5-Ar-H), 7.41 (d, 1H, 2-Ar-H), 7.49 (d, 1H, 6-Ar-H), 9.01 (brs, 1H, CONH); ^{13}C NMR: (DMSO-d_6 + $CDCl_3$) 21.19 (CH_3), 134.10 (1-Ar-C), 128.71 (2-Ar-C), 137.98 (3-Ar-C), 132.79 (4-Ar-C), 128.4 (5-Ar-C), 136.4 (6-Ar-C), 177.76 (CO); Anal. Calcd. for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65. Found: C, 63.91; H, 6.83; N, 18.79%.

4-Methyl benzoic hydrazide 6: m.p.) 116-17°C (Lit.[14a] 117°C). IR (KBr) 3300, 3205, 1681 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 2.33 (s, 3H, CH_3), 4.52 (s, 2H, NH_2), 7.39 (d, 2H, 3, 5-Ar-H), 7.73 (d, 2H, 2,6-Ar-H), 8.77 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 21.12 (CH_3), 128.58 (4-Ar-C), 129.33 (2,6-Ar-C), 129.78 (3,5-Ar-C), 143.43 (1-Ar-C), 181.8 (CO); Anal. Calcd.for $C_8H_{10}N_2O$: C, 63.98; H, 6.71; N, 18.65. Found: C, 64.01; H, 6.73; N, 18.51%.

4-Methoxy benzoic hydrazide 7: m.p. 160-64°C (Lit.[12] 163-64°C). IR (KBr): 3207, 1676 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 3.62 (s, 3H, CH_3), 4.52 (s, 2H, NH_2), 7.12 (d, 2H, 2,6-Ar-H), 7.84 (d, 2H, 3,5-Ar-H), 8.77 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 56.31 (OCH_3), 114.45 (3,5-Ar-C), 128.78 (2,6-Ar-C), 141.34 (1-Ar-C), 165.15 (4-Ar-C), 170.8 (CO); Anal. Calcd. for $C_8H_{10}N_2O_2$: C, 57.82; H, 6.07; N, 16.86. Found: C, 57.61; H, 6.01; N, 16.21%.

3,4-Dimethoxy benzoic hydrazide 8: m.p. 151-152°C (Lit.[12] 150-51). IR (KBr) 3208, 1671 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 3.9 (s, 3H, OCH_3), 4.8 (s, 3H, OCH_3), 6.82 (d, 1H, 5-Ar-H), 7.59 (s, 1H, 2-Ar-H), 7.76-7.78 (dd, 6-Ar-H, J=6.81), 4.62 (s, 2H, NH_2), 8.77 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6+ $CDCl_3$): 55.978 (OCH_3), 56.04 (OCH_3), 110.297 (Ar-C), 112.22 (Ar-C), 121.70 (Ar-C), 124.59 (Ar-C), 148.61 (Ar-C), 153.45 (Ar-C), 172.03 (CO); Anal. Calcd. for $C_9H_{12}N_2O_3$: C, 55.09; H, 6.16; N, 14.28. Found: C, 54.71; H, 6.11; N, 13.99%.

2-Hydroxy benzoic hydrazide 9: m.p. 152-54°C (Lit.[14b] 150-51°C). IR (KBr): 3311, 3281, 1655 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.53 (s, 2H, NH_2), 5.2 (s, 1H, OH), 6.75-6.87 (m, 1H, 5-Ar-H), 7.31-7.41 (m, 1H, 4-Ar-H), 7.78 (d, 1H, 6-Ar-H), 7.88 (d, 1H, 3-Ar-H), 9.76 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 115.37 (3-Ar-C), 120.96 (5-Ar-C), 126.16 (6-Ar-C), 131.67 (4-Ar-C), 141.16 (1-Ar-C), 158.20 (2-Ar-C), 172.37 (CO); Anal. Calcd. for $C_7H_8N_2O_2$: C, 55.26; H, 5.30; N, 18.41. Found: C, 54.93; H, 5.33; N, 17.98%.

4-Hydroxy-3-methoxy benzoic hydrazide 10: m.p. 179-81°C (Lit[14c] 178°C). IR (KBr): 3215, 1675 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 3.8 (s, 3H, OCH_3), 4.71 (s, 2H, NH_2), 5.09 (s, 1H, Ar-OH), 6.63 (d, 1H, 2-Ar-H), 6.83-6.99 (m, 1H, 6-Ar-H), 7.03 (d, 1H, 5-Ar-H), 9.13 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 55.87 (CH_3), 127.05 (1-Ar-C), 114.46 (2-Ar-C), 149.03 (3-Ar-C), 151.45 (4-Ar-C), 117.72 (5 ArC), 121.14(4-Ar-C), 171.3 (CO); Anal. Calcd. for $C_8H_{10}N_2O_3$: C, 52.74; H, 5.53; N, 15.38. Found: C, 52.13; H, 5.55; N, 14.97%.

4-*t*-Butyl benzoic hydrazide 11: m.p. 121-23°C (Lit.[11] 118-20°C). IR (KBr): 3201, 1682 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 1.34 (s, 9H, 3×CH_3), 4.51 (s, 2H, NH_2), 7.45 (d, 2H, 3,5-Ar-H), 7.96 (d, 2H, 2,6-Ar-H), 8.83 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 14.3 (Aliph-C), 29.7 (Aliph-C), 31.1 (Aliph-C), 35.2 (Aliph-C), 136.5 (1-Ar-C), 126.3 (2,6-Ar-C), 125.3 (3,5-Ar-C), 140.5 (4-Ar-C), 172.58 (CO), Anal. Calcd. for $C_{11}H_{16}N_2O$: C,68.72; H, 8.39; N, 14.57. Found: C, 67.99; H, 8.48; N, 14.81%.

Acetic hydrazide 12: m.p. 78-79°C (Lit.[14a] 77°C). IR (KBr): 3250, 1650 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 2.1 (s, 3H, CH_3), 4.34 (s, 2H, NH_2), 8.5 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 20.2 (CH_3), 170.1 (CO); Anal. Calcd. for $C_2H_6N_2O$: C, 32.43; H, 8.16; N, 37.81. Found: C, 32.55; H, 8.25; N, 37.91%.

Propanoic hydrazide 13: m.p. 38-40°C (Lit.[14a,] 40°C, IR (KBr): 3201, 1651 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 1.12 (t, 3H, 3-CH_3), 2.13 (q, 2H, 2-CH_2), 4.20 (s, 2H, NH_2), 8.17 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 13.1 (CH_3), 28.8 (CH_2), 173.3 (CO); Anal. Calcd. for $C_3H_8N_2O$ C, 40.90; H, 9.15; N, 31.79. Found: C, 40.62; H, 8.97, N, 31.79%.

Butanoic hydrazide 14: m.p. 42-44°C (Lit.[14a], 44°C). IR (KBr): 3203, 1648 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 0.95 (t, 3H, 4-CH_3), 1.63 (m, 2H, 3-CH_2), 2.21 (t, 2H, 2-CH_2), 4.26 (s, 2H, NH_2), 8.29 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6+ $CDCl_3$): 13.8 (CH_3), 19.1 (CH_2), 38.3 (CH_3), 171.3 (CO); Anal. Calcd. for $C_4H_{10}N_2O$: C, 47.04; H, 9.87; N, 27.43. Found: C, 46.62; H, 8.71; N, 26.79%.

Octanoic hydrazide 15: m.p. 85-87°C (Lit.[10] 87-89°C. IR (KBr): 3225, 1655 cm^{-1}; ^{1}H NMR (DMSO-d_6+ $CDCl_3$): 0.96 (t, 3H, 8-CH_3), 1.28 (m, 8H, 4×CH_2), 1.58 (m, 2H, 3-CH_2), 2.18 (m, 2H, 2-CH_2), 4.15 (s, 2H, NH_2), 8.25 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 14.0 (CH_3), 23.1 (CH_2), 29.6, (CH_2), 29.9 (CH_2), 30.0 (CH_2), 32.1 (CH_2), 32.5 (CH_2), 174.2 (CO); Anal. Calcd. for $C_8H_{18}N_2O$: C, 60.72; H, 11.47; N, 17.7. Found: C, 60.82; H, 11.31; N, 17.61%.

Decanoic hydrazide 16: m.p. 104-106°C (Lit.[10] 102°C; IR (KBr) 3231, 1652 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 0.88 (t, 3H, 10-CH_3), 1.29 (m, 12H, 6×CH_2), 1.61 (m, 2H, 3-CH_2), 2.11 (m, 2H, 2-CH_2), 4.11 (s, 2H, NH_2), 8.19 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 14.2 (CH_3), 23.1 (CH_2), 32.5 (CH_2), 30.0 (CH_2), 30.3 (CH_2), 30.2 (CH_2), 31.2 (CH_2), 26.3 (CH_2), 36.1 (CH_2), 176.4 (CO); Anal. Calcd. for $C_{10}H_{22}N_2O$: C, 64.47; H, 11.90; N, 15.04. Found: C, 64.57; H, 11.94; N, 15.09%.

Dodecanoic hydrazide 17: m.p. 107-108 (Lit.[14a] 105°C IR (KBr) 3245, 1657 cm^{-1}; ^{1}H MR (DMSO-d_6 + $CDCl_3$): 0.86 (t, 3H, 12-CH_3), 1.23 (m, 16H, 8×CH_2), 1.63 (m, 2H, 3-CH_2), 2.09 (m, 2H, 2-CH_2), 4.01 (s, 2H, NH_2), 8.29 (brs, 1H, CONH); ^{13}C MR (DMSO-d_6 + $CDCl_3$): 15.1 (CH_3), 24.1 (CH_2), 30.1 (CH_2), 31.2 (CH_2), 29.5 (CH_2), 31.2 (CH_2), 33.0 (CH_2), 31.2 (CH_2), 30.5 (CH_2), 32.1 (CH_2), 34.1 (CH_2), 176.1 (CO); Anal. Calcd. for $C_{12}H_{26}N_2O$: C, 67.24; H, 12.23; N, 13.07. Found: C, 67.24; H, 12.14; N, 12.99%.

Hexadecanoic hydrazide 18: m.p. 110-12°C (Lit.[14a] 111°C). IR (KBr): 3200, 1637 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 0.86 (t, 3H, 16-CH_3), 1.26-1.61 (m, 24H, 12×CH_2), 2.09 (m, 2H, 3-CH_2), 2.29 (m, 2H, 2-CH_2), 3.91 (s, 2H, NH_2), 8.09 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 15.1 (CH_3), 22.1 (CH_2), 26.1 (CH_2), 29.2 (CH_2), 29.5 (CH_2), 30.2 (7×CH_2), 31.2 (CH_2), 33.0 (CH_2), 34.1 (CH_2), 174.1 (CO); Anal. Calcd. for $C_{16}H_{34}N_2O$: C, 71.06; H, 12.67; N, 10.36;. Found: C, 70.94; H, 12.64; N, 10.29%.

Furoic acid hydrazide 19: m.p. 79-80°C (Lit.[14c] 80°C);. IR (KBr): 3271, 1685 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.79 (s, 2H, NH_2), 6.61 (dd, 1H, 4-Ar-H), 7.23 (d, 1H, 3-Ar-H), 7.73 (d, 1H, 5-Ar-H), 8.45 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6+ $CDCl_3$): 113.6 (3-Ar-C), 117.5 (4-Ar-C), 145.5 (5-Ar-C), 148.2 (2-Ar-C), 167.1 (CO); Anal. Calcd. for $C_6H_7N_3O$: C, 47.62; H, 4.80; N, 22.21. Found: C, 46.96; H, 4.61; N, 21.86%.

Nicotinic acid hydrazide 20: m.p. 160-62°C (Lit.[14b] 159-61°C). IR (KBr): 3207, 1688 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.71 (s, 2H, NH_2), 7.53 (dd, 1H, 5-Ar-H), 8.32 (d, 1H, 4-Ar-H), 8.84 (d, 1H, 6-Ar-H), 9.17 (s, 1H, 2-Ar-H), 9.39 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6 + $CDCl_3$): 125.8 (5-Ar-C), 135.81 (4-Ar-C), 140.1 (3-Ar-C), 149.1 (6-Ar-C), 154.5 (2-Ar-C), 169.1 (CO); Anal. Calcd. for $C_6H_7N_3O$: C, 52.55; H, 5.14; N, 30.64. Found: C, 51.94; H, 4.99; N, 31.09%.

Isonicotinic acid hydrazide 21: m.p. 162-164°C (Lit. [11] 161-163°C). IR (KBr): 3127, 1688 cm^{-1}; ^{1}H NMR (DMSO-d_6 + $CDCl_3$): 4.83 (s, 2H, NH_2), 7.96 (d, 2H, 3&5-Ar-H), 8.86 (d, 2H, 2 & 6-Ar-H), 9.09 (brs, 1H, CONH); ^{13}C NMR (DMSO-d_6+ $CDCl_3$): 150.2 (2 & 6-Ar-C), 122.6 (3 & 5-Ar-C), 142.5 (4-Ar-C), 177.1 (CO); Anal. Calcd. for $C_6H_7N_3O$: C, 52.55; H, 5.14; N, 30.64. Found: C, 52.04; H, 4.91; N, 30.06%.

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