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Microwave assisted synthesis of indole and furan derivatives possessing good anti-inflammatory and analgesic activity

Sham M Sondhi[a,]*, Shubhi Jain[a], Reshma Rani[a] & Ashok Kumar[b]

[a]Department of Chemistry, Indian Institute of Technology Roorkee, Roorkee 247667, India
[b]Department of Pharmacology, L.L.R.M. Medical College, Meerut 250001, India
E-mail: sondifcy@iitr.ernet.in

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Indole-2-carboxylic acid on condensation with benzene sulfonyl hydrazide and *p*-toluene sulfonyl hydrazide gives condensation products **1a** and **1b**. 1*H*-Tetrazole-5-acetic acid, hydantoin-5-acetic acid, orotic acid, 5-bromo nicotinic acid and indole 2-carboxylic acid have been condensed with furfuryl amine to give corresponding condensation products **2a-e** whereas condensation of succinic acid and adipic acid with furfuryl amine gives products **3a** and **3b** respectively. 3,5-Pyrazole dicarboxlic acid, 4,5-imidazole dicarboxylic acid and 3-carboxy-1,4-dimethyl pyrole-2-acetic acid on condensation with furfuryl amine give compounds **4, 5** and **6**. All these compounds *i.e*. **1a,b**, **2a-e**, **3a,b**, **4**, **5** and **6** have been characterized by spectroscopic means and have been screened for anti-inflammatory and analgesic activity. Compounds **2a**, and **5** exhibit good anti-inflammatory and **2a**, **2c** and **5** exhibit good analgesic activity.

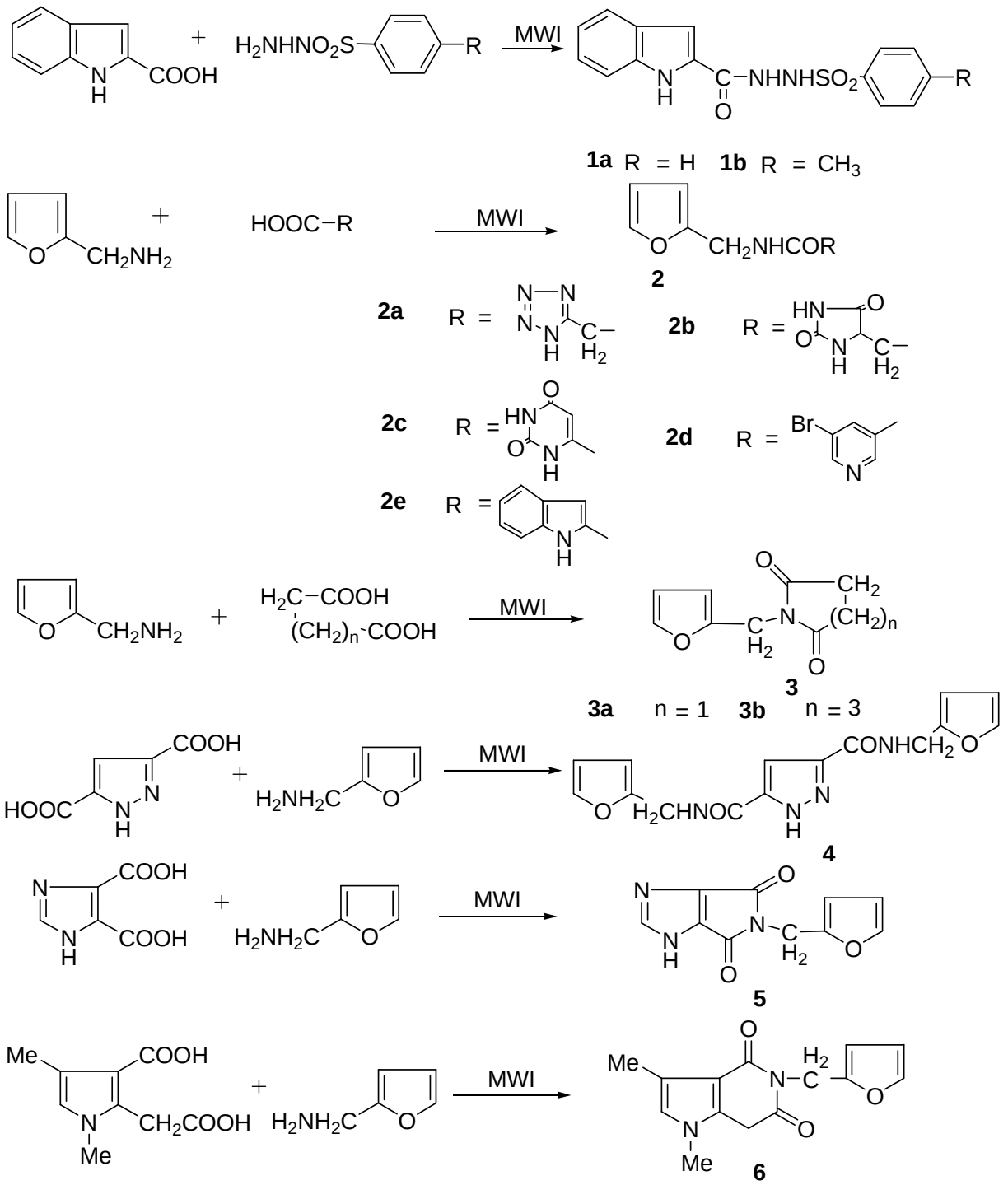
Keywords: Microwave, indole, furan, anti-inflammatory, analgesic

The importance of furan and indole derivatives is quite evident from the number of papers, patents, *etc*. published every year. Furan derivatives exhibiting anti-inflammatory[1], antituberculosis[2], anticancer[3], antimicrobial[4], antifungal[5], and indole derivatives possessing antimicrobial[6], antifungal[7], antibacterial[8] and antidepressant[9] activity have been reported in literature. Above mentioned few references indicate versatile nature of furan and indole derivatives from biological activity point of view. Use of microwave irradiation for synthesis of various organic compounds is also reported in literature[10,11]. In continuation of the efforts[12,13] in search of bioactive molecules, a number of indole and furan derivatives have been synthesized using microwave irradiation and evaluated them for anti-inflammatory and analgesic activity which is being reported in this paper.

Results and Discussion

Chemistry

Indole-2-carboxylic acid and benzene sulfonyl hydrazide were taken together in a petri dish and mixed thoroughly. This reaction mixture was then subjected to microwave irradiation at 600 W (power level) for 2.0 min and the progress of the reaction was monitored by TLC. This process was repeated three times when one of the starting materials disappeared. The crude product so obtained was washed with ethyl acetate: diethyl ether (5:1) and the product so obtained was recrystallized from methanol to give pure condensed product **1a** (**Scheme I**). Spectral characterization data of **1a** shown in **Table I** fully support the structure assigned to it. Similarly, condensation of indole 2-carboxylic acid with *p*-toluene sulfonyl hydrazide gave product **1b** (**Scheme I**). Spectral characterization data of **1b** shown in **Table I** is in complete agreement with the structure assigned to it. 1*H*-Tetrazole-5-acetic acid and furfuryl amine were mixed together to form a paste and this paste was irradiated in the microwave oven for 2.0 min at a power level of 300 W. The progress of the reaction was monitored by TLC after every 2.0 min of irradiation. The reaction was complete after 12.0 min. The crude product so obtained was subjected to column chromatography over silica gel. Elution with ethyl acetate gave the pure product **2a** (**Scheme I**) which was found to be a liquid. The spectral characterization data of **2a** shown in **Table I** fully support the structure assigned to it. Similarly, hydantion-5-acetic acid, orotic acid, 5-bromo nicotinic acid and indole-2-carboxlic acid were condensed with fufuryl amine to give condensation products **2b**, **2c**, **2d** and **2e**, respectively. Spectral



Scheme I

characterization data of **2b-e** shown in **Table I** fully support the structures assigned to them. After gaining enough experience to couple mono acids with primary amine, *i.e.*, furfuryl amine, the work was extended and various diacids were coupled with furfuryl amine. Various types of reaction products were obtained depending on the positions of the two carboxylic acid groups present in the starting material. Condensation of succinic acid with furfuryl amine was carried out by irradiating a mixture of succinic acid and furfuryl amine for 15.0 min in a microwave oven having a power level of 300 W. The crude reaction product

Table I — Physical and spectral characterization data of compounds **1a,b**, **2a-e**, **3a,b** and **4-6**

Compd	Solvent of crystallization/Elution*	m.p. °C	Yield%	Spectral data
1a	MeOH	180	80	^{1}H NMR (DMSO-d_6 + D_2O): δ 7.02-7.05 (t, *J*= 4.5 and 15 Hz , 3H, Ar), 7.19-7.22 (t, *J*= 7.5 and 15 Hz, 2H, Ar), 7.35- 7.36 (t, *J*=3 and 6 Hz, 1H, Ar), 7.42 -7.43 (d, *J*= 8 Hz, 2H, Ar), 7.60-7.64 (d, *J*= 8 Hz, 2H, Ar); GCMS: *m/z* (%) 315(M^+ 35.48).
1b	MeOH	120		^{1}H NMR (DMSO-d_6 + D_2O): δ 2.32 (s , 3H, CH_3), 7.02-7.05(t, *J*=7.5 and 15 Hz, 1H, Ar), 7.07(s, 1H, Ar), 7.19- 7.22 (t, *J*= 7.5 and 15 Hz, 1H, Ar), 7.35 -7.36 (d, *J*= 8, Hz, 2H, Ar), 7.41-7.42 (d, *J*= 8Hz, 1H, Ar), 7.60-7.63 (t, *J*=7.5 and 15 Hz, 3H, Ar); GCMS: *m/z* (%) 329(M^+ 0.56), 155($C_7H_7O_2S^+$ 22.96), 144 ($C_9H_6NO^+$ 2.16), 139 (155-CH_4 100), 91($C_7H_7^+$ 84.52).
2a	Ethyl acetate	Liq	70	^{1}H NMR (DMSO-d_6): δ 3.65 (s, 2H, -CH_2-), 4.03 (s, 2H, -CH_2-), 6.47-6.48 (q, *J*= 3 and 7 Hz, 2H, Ar), 7.68 (s, 1H, Ar), –NH- signal was not detected; GCMS: *m/z* (%) 207 (M^+ 28.37).
2b	MeOH	125	90	^{1}H NMR (DMSO-d_6 + D_2O): δ 2.28-2.33 (dd, *J*= 6 and 1 6.0 Hz, 2H, —CH$_2$-CH—), 2.45 (s, 2H, -CH_2-), 4.12-4.13 (d, *J*= 6 Hz, 1H, —CH—), 6.45-6.47 (d, 2H, *J*= 12 Hz, Ar), 7.62 (s, 1H, Ar); GCMS: *m/z* (%) 237 (M^+ 11.60), 236 (M^+-H 5.85), 209 M^+- CO 3.28), 96($C_5H_6NO^+$ 7.53), 67($C_4H_3O^+$ 5.73), 58(($CH_2N_2O^+$, 3.8), 56 (58- H_2 6.48).
2c	H_2O: MeOH	260	85	^{1}H NMR (DMSO-d_6): δ 4.10 (s, 2H, -CH_2-), 5.72 (s, 1H, =CH-), 6.50-6.53 (d, *J*=15.5, Hz, 2H, Ar), 7.73 (s, 1H, Ar), 8.48 (bs, 2H, 2× NH, exch.), 10.91 (bs, 1H, NH).
2d	MeOH	130	91	^{1}H NMR (DMSO-d_6): δ 4.06 (s, 2H, -CH_2-), 6.45-6.49 (t, *J*=3 and 18Hz, 2H, Ar), 7.67 (s, 1H, Ar), 8.25 (s, 1H, Ar), 8.920-8.922 (d, *J*= 1 Hz, 1H, Ar), 8.668- 8.672 (d, *J*=2 Hz, 1H, Ar), NH- signal was not detected; GCMS: *m/z* (%) 281 (M^+ 4.76).
2e	MeOH	140	85	^{1}H NMR (DMSO-d_6): δ 3.95 (s, 2H, -CH_2-), 5.83 (bs, 1H, NH,exch.), 6.41-6.43(d, *J*=7 Hz, 2H, Ar), 6.83 (s, 1H, Ar), 6.96-6.99 (t , *J*= 7. 5 and 15 Hz, 1H, Ar), 7.11-7.14 (t, *J*=7. 5 and 15 Hz, 1H, Ar), 7.38-7.40 (d, *J*=8 Hz, 1H, Ar), 7.55- 7.56 (d, *J*=8 Hz, 1H, Ar), 7.63 (s, 1H, Ar), 11.34 (bs, 1H, NH, exch.); GCMS: *m/z* (%) 240 (M^+,21.3), 173 ($C_{10}H_9N_2O^+$ 21.00), 159($C_9H_7N_2O^+$ 5.7), 67 ($C_4H_3O^+$ 25.79).
3a	MeOH	110	65	^{1}H NMR (DMSO-d_6): δ 2.32(s, 4H, 2× CH_2), 3.97 (s, 2H, -CH_2-N), 6.43-6.46 (d, *J*= 11 Hz, 2H, Ar), 7.68 (s, 1H, Ar); GCMS: *m/z* (%) 179 (M^+ 2.08)
3b	MeOH	120	61	^{1}H NMR (DMSO-d_6 + D_2O); δ 1.41(s, 4H, 2 × -CH_2-),2.05 (s, 4H, 2× –CH_2CO-),3.94 (s, 2H, - CH_2-N), 6.42-6.44 (d, *J*= 8 Hz, 2H, Ar), 7.58 (s, 1H, Ar); GCMS: *m/z* (%) 207(M^+, 47.83), 85 ($C_5H_9O^+$ 27.60), 81($C_5H_5O^+$ 14.8), 71 ($C_4H_7O^+$ 49.90), 69($C_4H_5O^+$ 47.79).
4	MeOH	260	88	^{1}H NMR (DMSO-d_6): δ 3.96 (s, 4H, 2× – CH_2-), 6.42-6.43 (d, *J*= 5. 5 Hz, 4H, furan Ar), 6.66 (s, 1H, pyrazole Ar), 7.63 (s, 2H, furan Ar), -NH- signal was not detected; GCMS: *m/z* (%) 21.3), (M^+ 68.28), 313 (M^+-H 100), 285 ($C_{14}H_{11}N_3O_4^{+\cdot}$ 23.36),124 ($C_6H_6NO_2^+$ 8.22).
5	MeOH	180	90	^{1}H NMR (DMSO-d_6): δ 4.11(s, 2H, -CH_2N-),6.48- 6.50 (d, *J*=12 Hz, 2H, Ar), 7.58 (s, 1H, Ar), 7.72 (s, 1H, ), 8.55 (bs, 1H, NH exch.); GCMS: *m/z* (%) 217 (M^+,12.07), 216 (M^+-H 4.15).
6	MeOH	185	85	^{1}H NMR (DMSO-d_6 + D_2O): δ 2.069 (s, 3H, -CH_3), 3.15 (s, 3H, H_3C–N<), 3.40 (s, 2H, -CH_2-CO-), 4.00 (s, 2H, —H_2C–N—), 6.37 (s, 1H, Ar), 6.43-6.47 (d, *J*= 9 Hz, 2H, Ar), 7.57 (s, 1H, Ar); GCMS: *m/z* (%) 258 (M^+ 0..90).

All the compounds reported in this table gave satisfactory IR spectral data and elemental analysis for C,H, and N

was washed with ethyl acetate:diethyl ether (2:1) and then recrystallized from methanol to give pure product **3a** (**Scheme I**). Spectral characterization data of **3a** shown in **Table I** is in complete agreement with the structure assigned to it. ^{1}H NMR spectrum of **3a** exhibited a singlet for four protons, *i.e.*, at δ 2.32 (s, 4H, -CH_2- + –CH_2-). This is due to equivalence of all the four protons and this type of observation is also

reported in literature[14,15]. Similarly, condensation of adipic acid with furfuryl amine gave product **3b** (**Scheme I**). Spectral characterization data of **3b** reported in **Table I** fully support the structure assigned to it. 3,5-Pyrazole dicarboxylic acid monohydrate and furfuryl amine were taken in the ratio of 1:3 mole equivalent and were mixed together thoroughly to form a paste. This paste was irradiated for 6.0 min at 600 W power level in a microwave oven. The crude product so obtained was washed with ethyl acetate:diethyl ether (2:1) and then recrystallized from methanol to give pure product **4**, *i.e.*, N^3,N^5-bis(furan-2-yl methyl)-1*H*-pyrazole-3,5-dicarboxamide. Spectral characterization data of **4** shown in **Table I** fully support the structure assigned to it. 4,5-Imidazole dicarboxylic acid and 3-carboxy-1,4-dimethyl pyrole-2-acetic acid on condensation with furfuryl amine by microwave irradiation for 10.0 min at 450 and 600 W power levels respectively after usual workup gave bicyclic products **5** and **6** respectively. Spectral characterization data of **5** and **6** shown in **Table I** fully support the structures assigned to them. A look at the formation of products **3a**, **3b**, **4**, **5** and **6** (**Scheme I**) indicates that wherever possible, cyclic products were obtained, *i.e.*, **3a**, **3b**, **5** and **6** and in those cases where the two carboxylic groups are far away from each other and can not form cyclic product, bis amide was formed.

Biological Studies

Compounds **1a** and **1b** at 100 mg/kg p.o. and compounds **2a-e**, **3a, b**, **4**, **5** and **6** at 50 mg/kg p.o. were tested for anti-inflammatory activity in the carrageenin induced paw edema model[16] and the results are summarized in **Table II**. Compounds **1a**, **1b** at 100 mg/kg p.o. and **1a**, **2a-e**, **3a,b**, **4**, **5** and **6** at 50 mg/kg p.o. were screened for analgesic activity using phenylquinone writhing assay[17] and the results are reported in **Table II**. A look at activity data reported in **Table II** indicates that compounds **2a** and **5** exhibited promising anti-inflammatory activity whereas compounds **2a, 2c** and **5** exhibited promising analgesic activity. Out of all the compounds reported in **Table II**, compound **5** possess very good anti-inflammatory and analgesic activity.

Experimental Section

Domestic microwave oven model M197DL (Samsung) was used for microwave irradiation. Melting points (m.p.) were determined on a JSGW apparatus and are uncorrected. IR spectra were recorded using a Perkin Elmer 1600 FT spectrometer. ^{1}H NMR spectra were measured on a Bruker WH-500 MHz spectrometer at a *ca*. 5-15% solution in DMSO-d_6 or $CDCl_3$ (TMS as internal standard). GCMS was recorded on Perkin Elmer Clarus 500 mass spectrometer. Elemental analysis was carried out on Vario ELIII Elementor. Thin layer chromatography (TLC) was performed on silica gel G for TLC (Merck) and spots were visualized by iodine vapour or by irradiation with ultraviolet light (254 nm). Column chromatography was performed over Qualigens silica gel for column chromatography (60-120 mesh). Physical constants and spectral characterization data of all the compounds reported in this paper are summarized in **Table I**

Table II — Anti-inflammatory and analgesic activity evaluation of **1a,b**, **2a-e**, **3a,b** and **4-6**.

Compd	Dose mg/kg p.o	Anti-inflammatory activity %	Dose mg/kg p.o	Analgesic activity
1a	100	0.0	1 00	50
			50	25
1b	100	0.0	100	50
2a	50	34.8	50	60
2b	50	22.1	50	20
2c	50	16.8	50	50
2d	50	19.5	50	20
2e	50	10.2	50	25
3a	50	11.3	50	10
3b	50	26.4	50	40
4	50	24.9	50	50
5	50	41.6	50	80
6	50	15.7	50	20
Phenyl	100	58.4	100	58
Butazone	50	36.4	50	40

p.o.= from latin word *per os* (means by mouth)

Synthesis of N'-(phenylsulfonyl)-1*H*-indole-2-carbohydrazide, 1a

Indole-2-carboxylic acid (322 mg, 2 mmol) and benzene sulfonyl hydrazide (344 mg, 2 mmol) were mixed thoroughly. This mixture was subjected to microwave irradiation (by keeping inside a microwave oven) for 2.0 min at 600 W power level and reaction progress was monitored by TLC. This process was repeated three times when one of the starting materials disappeared. Crude product was washed with ethyl acetate:diethyl ether (5:1) (10 mL) and the product so obtained was further purified by recrystallization from methanol to give pure product **1a**. Yield 500 mg (80%). m.p. 180°C.

Synthesis of N'-tosyl-1*H*-indole-2-carbohydrazide, 1b

Indole-2-carboxylic acid (322 mg, 2 mmol) and *p*-toluenesulfonyl hydrazide (372 mg, 2 mmol) were mixed together and subjected to microwave irradiation for 5.0 min at 850 W power level. The crude product was recrystallized from methanol to give pure product **1b**. Yield 560 mg (85%), m.p. 120°C.

Synthesis of N-(furan-2-yl methyl)-2-(1*H*-tetrazol-5-yl) acetamide, 2a

1*H*-Tetrazole-5-acetic acid (256 mg, 2 mmol) and furfuryl amine (0.4 mL, 4 mmol) were mixed together to form a paste. This paste was irradiated for 2.0 min by keeping in a microwave oven, at power level 300 W. Progress of the reaction was monitored by TLC after every 2.0 min of irradiation. The reaction was complete in 12.0 min. The crude product so obtained was purified by column chromatography over silica gel. Elution with ethyl acetate gave pure product **2a**. Yield 290 mg (70%).

Synthesis of 2-(2, 5-dioxoimidazolidin-4-yl)-N-(furan-2yl-methyl)acetamide, 2b

Hydantoin-5-acetic acid (316 mg, 2 mmol) and furfuryl amine (0.40 mL, 4 mmol) were mixed together to form a paste. This paste was subjected to microwave irradiation for 10.0 min at power level 300 W. The crude product so obtained was washed with ethyl acetate:diethyl ether (5:1) (20 mL) and then recrystallized from methanol to give pure product **2b**. Yield 420 mg (90%). m.p. 125°C.

Synthesis of N-(furan-2-yl methyl)-2, 6-dioxo-1, 2, 3, 6-tetrahydro pyrimidine-4-carboxamide, 2c

Orotic acid (312 mg, 2 mmol) and furfuryl amine (0.40 mL, 4 mmol) were mixed together to form a paste and then subjected to microwave irradiation for 5.0 min at 600 W power level and reaction progress was monitored by TLC. Reaction contents were once again irradiated for 5.0 min and then crude product so obtained was washed with ethyl acetate and then recrystallized from methanol/water to give pure product **2c**. Yield 400 mg (85%). m.p. 260°C.

Synthesis of 5-bromo-N-(furan-2yl methyl)-nicotinamide, 2d

5-Bromonicotinic acid (202 mg, 1 mmol) and furfuryl amine (0.20 mL, 2 mmol) were mixed together to form a paste. This paste was subjected to microwave irradiation for 4.0 min at 450 W power level and progress of the reaction was monitored by TLC. The irradiation process was repeated three times and the crude product so obtained was washed with ethyl acetate and then recrystallized from MeOH to give pure product **2d**. Yield 255 mg (91%). m.p. 130°C.

Synthesis of N-(furan-2-yl methyl)-1*H*-indole-2-carboxamide, 2e

Indole-2-carboxylic acid (160 mg, 1 mmol) and furfuryl amine (0.20 mL) were mixed together to give a paste. This paste was irradiated for 5.0 min at 600 W power level. Reaction contents were washed with ethyl acetate:diethyl ether (5:1) (10 mL) and the crude product so obtained was recrystallized from methanol to give pure product **2c**. Yield 200 mg (85%) m.p. 140°C.

Synthesis of 1-(furan-2-yl methyl)-pyrrolidine-2,5-dione, 3a

Furfuryl amine (0.3 mL, 3 mmol) and succinic acid (236 mg, 2 mmol) were mixed together to form a paste. This paste was subjected to microwave irradiation for 15.0 min at a power level of 300 W. Crude product was washed with ethyl acetate:diethyl ether (2:1) and then recrystallized from methanol to give pure product **3a**. Yield 232 mg (65%). m.p. 110°C.

Synthesis of 1-(furan-2-yl methyl)-azepane-2,7-dione, 3b

Adipic acid (292 mg, 2 mmol) and furfuryl amine (0.30 mL, 3 mmol) were mixed together and this

mixture was subjected to microwave irradiation for 15.0 min at 300 W power level. The crude product so formed was washed with ethyl acetate and then recrystallized from methanol to give pure product **3b**. Yield 252 mg (61%) m.p. 120°C.

Synthesis of N^3,N^5-bis(furan-2-yl methyl)-1*H*-pyrazole-3,5-dicarboxamide, 4

3,5-Pyrazole dicarboxylic acid monohydrate (348 mg, 2 mmol) and furfuryl amine (0.60 mL, 6 mmol) were mixed together to form a paste. This paste was subjected to microwave irradiation for 6.0 min at 600 W power level. The crude product so formed was washed with ethyl acetate:diethyl ether (2:1) (20 mL) and then recrystallized from methanol to give pure product **4**. Yield 550 mg (88%), m.p. 260°C.

Synthesis of 5-(furan-2-yl methyl)-pyrrolo [3,4-d] imidazole-4,6(1*H*, 5*H*) dione, 5

4,5-Imidazole dicarboxylic acid (312 mg, 2 mmol) and furfuryl amine (0.30 mL, 3 mmol) were mixed together and this mixture was subjected to microwave irradiation at 450 W power level for 10.0 min. The product so formed was washed with ethyl acetate and recrystallized from methanol to give pure product **5**. Yield 390 mg (90%). m.p. 180°C.

Synthesis of 5-(furan-2-yl methyl)-1, 3-dimethyl-1*H*-pyrrolo[3,2-c] pyridine-4,6(5*H*, 7*H*)-dione, 6

3-Carboxy-1,4-dimethyl pyrole-2-acetic acid (396 mg, 2 mmol) and furfuryl amine (0.30 mL, 3 mmol) were mixed together. This mixture was subjected to microwave irradiation for 10.0 min at 600 W power level. The product so obtained was washed with diethyl ether:methanol (5:1) (20 mL) and then recrystallized from methanol to give pure product **6**. Yield 438 mg (85%). m.p. 185°C.

Anti-inflammatory activity evaluation

Antiinflammatory activity evaluation[16] was carried out using carrageenin induced paw oedema in albino rats. Oedema in one of the hind paws was induced by injection of carrageenin solution (0.1 mL of 1%) into planter apponeurosis. The volume of the paw was measured plethysmographically immediately after and 3.0 hr after the injection of the irritant. The difference in volume gave the amount of oedema developed. Percent inhibition of the oedema between the control group and compound treated groups was calculated and compared with the group receiving a standard drug. Anti-inflammatory activity of compounds **1a,b**, **2a-e**, **3a,b**, **4**, **5** and **6** screened are reported in results and discussion part.

Analgesic activity evaluation

Analgesia was measured by the writhing assay[17] using Swiss mice (15-20 g). Female mice were screened for writhing on day-1 by injecting intraperitonially 0.2 mL of 0.02% aqueous solution of phenylquinone. They were kept on flat surface and the number of writhes of each mouse was recorded for 20 min. The mice showing significant writhes (> 10) were sorted out and used for analgesic assay on the following day. The mice consisting of 5 in each group and showing significant writhing were given orally a 50 or 100 mg/kg p.o. dose of the test compounds 15 min prior to phenylquinone challenge. Writhing was again recorded for each mouse in a group and a percentage protection was calculated using following formula:

Protection = 100 – [{No. of writhings for treated mice)/(No. of writhings for untreated mice)} × 100]

This was taken as a percent of analgesic response and was averaged in each group of mice. Percent of animals exhibiting analgesia was determined with each dose. Compounds **1a,b**, **2a-e**, **3a,b**, **4**, **5** and **6** were screened for analgesic activity and results are reported in results and discussion part.

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References

1 Khairatkar-Joshi N, Balasubramanian G & Gharat L A, *PCT Int Appl WO* 2006051390; *Chem Abstr* 144, **2006**, 488509.

2 Tangallapally R P, Lee R E B, Lenaerts A J M & Lee R E, *Bioorg Med Chem Lett*, 16, **2006**, 2584.

3 Srivastava V, Negi A S, Kumar J K, Faridi U, Sisodia B S, Darokar M P, Luqman S & Khanuja S P S, *Bioorg Med Chem Lett*, 16, **2006**, 911.

4 Nagaraja G K, Kumaraswamy M N, Vaidya V P & Mahadevan K M, *ARKIVOC* (Gainesville, FL, United States), 10, **2006,** 1.

5 Shehata I A, *Saudi Pharmaceutical Journal*, 11, **2003,** 87; *Chem Abstr* 140, **2004,** 357263.

6 Saundane A R, Sharma P M V & Badiger J, *Indian J Heterocyclic Chem*, 14**, 2005**, 307.

7 Agarwal A, Agarwal S K, Shukla P K & Khan Z K, *Indian IN 183635*; *Chem Abstr* 141, **2004,** 260731.

8 Palluotto F, Campagna F, Carotti A, Ferappi M, Rosato A & Vitali C, *Farmaco***,** 57**, 2002,** 63.

9 Stack G P, Tran M & Bravo B A, *PCT Int Appl WO 2002088146*; *Chem Abstr* 137, **2002,** 353044.

10 Varughese D J, Manhas M S & Bose A K, *Tetrahedron Lett*, 47, **2006**, 6795.

11 Bose A K, Ganguly S N, Manhas M S, Guha A & Pombo-Villars E, *Tetrahedron Lett*, 47, **2006**, 4605.

12 Sondhi S M, Dinodia M & Kumar A, *Bioorg Med Chem*, 14, **2006**, 4657.

13 Sondhi S M, Dinodia M, Singh J & Rani R, *Current Bioactive Compounds* 3, **2007**, 91.

14 Charles J P & Jacqlynn B, *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, 1, **1993**, 1299A.

15 Charles J P & Jacqlynn B, *The Aldrich Library of ^{13}C and ^{1}H FT NMR Spectra*, 1, **1993**, 770B.

16 Winter C A, Risley E A & Nuss G W, *Proc Soc Exp Biol Med*, 111, **1962,** 544.

17 Singh P P, Junnarkar A V, Seshagiri Rao C, Verma R K & Shridhar D R, *Meth and Find Exptl Clini Pharmacol*, 5, **1983**, 601.