ISSN: 0975-8585

Research Journal of Pharmaceutical, Biological and Chemical Sciences

Synthesis of spiro [indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine] diones by using reusable Nano copper ferrite catalyst in water.

Ravi Kumar Ganata[1]*, Rambabu T[1], China Satyanarayana Ch[2], Bhavani A[1], Manohari J[1], Hariprasad S[1], and Venkateswara Rao B[1].

[1]Departmaent of Engg. Chemistry, A.U College of Engineering (A), Andhra University, 530003, Andhra Pradesh, India.
[2]Dept of Chemistry, SKBR college, Amalapuram, East Godavari (Dist), Andhra Pradesh, India.

ABSTRACT

Efficient multicomponent one pot green synthesis of spiro[indoline-3,4-pyrazolo[3,4-e] [1,4] thiazepine]dione s using Isatin, 2-mercaptoacetic acid and 3-methyl-1-phenyl-1H-pyrazol-5-amine in water by using magnetically reusable 20 mol% nano copper ferrite ($CuFe_2O_4$) catalyst at 100^0C. This method was simple, it involves easy workup, simple purification of products, and easy separation of magnetically recyclable catalyst. The green synthesis of compounds 4a-4j were synthesized in good yields by this method.

Keywords: Spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine]dione, Green synthesis, Nano copper ferrite catalyst, Reusable catalyst.

Corresponding author

ISSN: 0975-8585

INTRODUCTION

Multi component reactions (MCR) are having important strategy in organic synthesis and medicinal chemistry. Multi component reactions have several advantages that are efficient construction of complex molecules in single step, no intermediate isolation and saving both solvents and reagents [1]. Thiazepine are sulpher and nitrogen containing seven member cyclic compounds.1, 4 thiazepine containing heterocyclic comounds are important targets in synthetic and medicinal chemistry because it is a key moiety in wide range of natural and synthetic biological activity agents [2]. Various thiazepine derivatives exhibit angiotensin-converting enzyme inhibition [3] which was important for the development of the drug Temocapril,[4] used for the treatment of hypertension.

The spirooxindole system is one of the prominent heterocycles found in numerous natural and synthetic products, with useful pharmaceutical activities [5-7]. For example, spirotryprostatin A, a natural alkaloid isolated from the fermentation both of Aspergillus fumigatus, has been identified as a novel inhibitor of microtubule assembly,[8] and pteropodine and isopteropodine have been shown to modulate the function of muscarinic serotonin receptors[9]. They have been shown to exhibit local anesthetic properties. The unique structural array and the highly pronounced pharmacological activity displayed by the class of spirooxindoles have made them attractive synthetic targets. Thia-azaheterocycles gained prominence because of their extensive biological and pharmacological activities [10-11]. Several methods have been reported for the preparation of spirooxindole derivatives connecting the thioacid synthon [12-14]. Recently Shi et al., reported novel heptacyclic spirooxindole derivatives by using p-TSA as a catalyst [15]. Despite the importance of these reported protocols many suffer from drawbacks such as use of expensive reagents, harsh reaction conditions, prolonged reaction times, cumbersome product isolation procedures, and low yields as well as more than stoichiometric amount of catalyst. Hence, to explore a mild, efficient and environmentally benign recyclable synthetic protocol for the Spiro [indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine] diones is highly desirable. We report a green, simple multicomponent on pot synthesis of spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine] dione derivatives from substituted isatins, 2-mercaptoacetic acid and 3-methyl-1-phenyl-1H-pyrazol-5-amine in water by using nano copper ferrite catalyst ($CuFe_2O_4$). The synthesized compounds were characterized by IR, H^1 NMR, C^{13} NMR, and Mass spectral data.

MATERIAL AND METHODS

All chemicals and reagents were obtained from Aldrich (Sigma-Aldrich), St. Louis, MO, USA), Lancaster (Alfa Aeser, Johnson Matthey Company, Ward Hill, MA, USA), and Spectrochem Pvt. Ltd. (Mumbai, India) and were used without further purification. Reactions were performed by TLC supported on silica gel glass plate containing 60 GF-254, and visualization was achieved by UV light or iodine indicator. ^1H and ^{13}C NMR spectra were determined in $CDCl_3$ by using Varian and Avance instruments (300 MHz). Chemical shifts are expressed in parts per million (δ in ppm) downfield from TMS (internal reference) signal and coupling constants are expressed in Hz. ^1H NMR spectroscopic data are reported in the following order: multiplicity (s, singlet; brs, broad singlet; d, doublet; dd, doublet of doublets; t, triplet; m, multiplet), coupling constants in Hz, number of protons. ESI mass spectra were recorded on a Micro mass Quattro LC using ESI+ software with capillary voltage 3.98 kV and an ESI mode positive ion trap detector.

Experimental

Procedure for the synthesis of spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine]dione

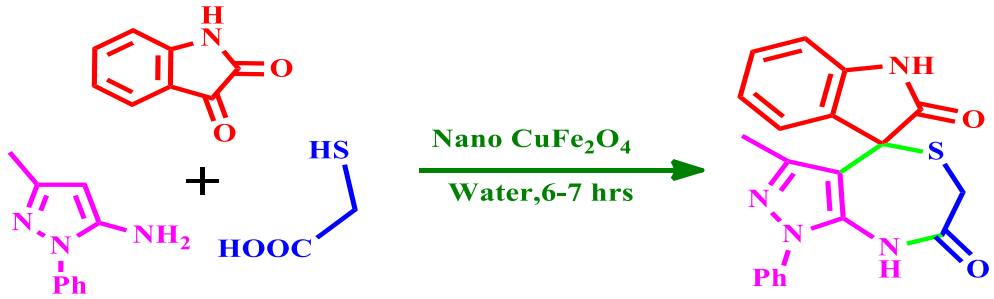
Isatin (1mmol), 2-mercaptoacetic acid (1mmol), and 3-methyl-1-phenyl-1H-pyrazol-5-amine (1mmol), 20 mol% of nano copper ferrite as catalyst and water as solvent were taken in round bottomed flask. The reaction mixture was stirred under reflux at 100°c for 7 hours and monitored by Thin Layer chromatography. After the completion of the reaction, catalyst was separated by using external magnet and compounds were purified by column chromatography. Structures of compounds were confirmed by IR, H^1, C^{13} NMR and Mass spectral analysis.

ISSN: 0975-8585

RESULTS AND DISCUSSION

Initially a model reaction (scheme-2) was conducted using Isatin, 2-mercaptoacetic acid and 3-methyl-1-phenyl-1H-pyrazol-5-amine without any catalyst under various conditions. It was observed that the reaction did not proceed even after 12h (Table 1, entry 1-2).Whereas the same reaction was executed in the presence of 10 mol% of CuFeNPs in water at room temperature and traces of the product were found (less than 10%)(Table 1, entry 3-6). Later, this reaction was carried out with different solvents under reflux conditions and the desired transformation was observed furnishing the product in good yield (Table 1, entry 7-12). Reaction optimization studies were conducted using 10, 15 and 20 mole % of the catalyst and were monitored for 6-8 hours. It was observed that 20 mol% of the catalyst loading provided maximum yield (80 %) in 7 hour (Figure 1: Table 1, entry 13). An additional increase of the catalyst loading to 25% did not improve the yield.

Scheme-1. Optimization reaction



Model reaction

Table-1: Optimization of reaction conditions

Entry	Solvent	Temperature (°C)	Catalyst (mol %)	Time (h)	Yield[a] (%)
1	--	RT	--	12	--
2	--	RT	5	12	--
3	CH_3CN	RT	10	12	<10
4	Methanol	RT	10	12	<10
5	Ethanol	RT	10	12	<10
6	Water	RT	10	12	<10
7	--	80	15	12	32
8	CH_3CN	80	15	6	42
9	Methanol	80	15	6	60
10	Ethanol	80	15	6	62
11	Water	100	10	7	69
12	Water	100	15	7	71
13	Water	100	20	7	80
14	Water	100	25	8	80

With the optimized conditions in hand, the reaction was performed with different isatins (scheme-2) to explore the scope and generality of the present protocol and the results of these observations are summarized in Table 2. From the results, it can be concluded that the isatin with electron donating substituents react well providing excellent to very good yields of the corresponding products(Table 2, entry **4e** & **4f**). The isatin with electron negative groups such as a -Cl and -F substituents (Table 2, entry **4i-4j**) reacted smoothly providing moderate yields.

ISSN: 0975-8585

Scheme-2. $CuFe_2O_4$ catalysed synthesis of spiro[indoline-3,4-pyrazolo[3,4 e][1,4] thiazepine] diones

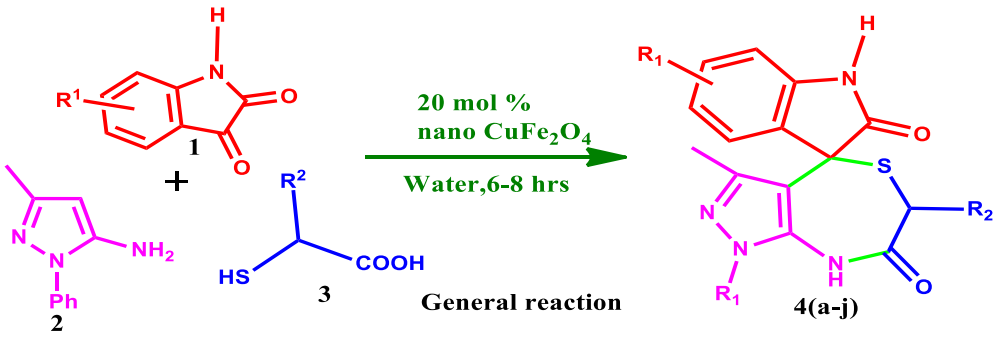


Table-2 $CuFe_2O_4$catalysed synthesis of spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine]diones

S. no	R^1	R^2	Time(hrs)	Yield (%)
4a	5-H	H	6.30	80
4b	5-H	CH_3	7	82
4c	5-CH_3	H	6	89
4d	5-CH_3	CH_3	7.30	91
4e	5-OCH_3	H	8	93
4f	5-OCH_3	CH_3	7.30	96
4g	5-Br	H	6	78
4h	5-Br	CH_3	6	74
4i	5-Cl	H	6.30	71
4j	5-Cl	CH_3	7	69

Reusability of the catalyst

The reusability of CuFeNPs is one of the most important advantages of this protocol that makes it useful for practical commercial applications. We have examined the recyclability of CuFeNPs catalyst for the model reaction. Interestingly, the recovered catalyst could be reused for up to six cycles under optimized reaction conditions without leaching of the Cu and Fe metals which is evident from Table 3. The catalyst was separated by using a external magnet after completion of the reaction, washed with water followed by chloroform, dried in oven and reused for the next cycle.

Table 3 Yields of the product with various cycles of the catalyst

Entry	Reaction Cycle	Yield (%)
1	1^{st} cycle (Fresh run)	80
2	2^{nd} cycle	79
3	3^{rd} cycle	78
4	4^{th} cycle	72
5	5^{th} cycle	69
6	6^{th} cycle	62

Spectral Data

3'-methyl-1'-phenyl-6',8' dihydrospiro[indoline-3,4'-pyrazolo[3,4 e][1,4]thiazepine]-2,7'(1'H)-dione (4a)

^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=11.61 (s, 1H), 8.26 (s, 1H), 7.49-7..59 (m, 4H), 7.29-7.35 (m, 1H), 7.27 (t, *J* = 8.3 Hz, 1H), 7.15 (d, *J* = 8.3 Hz, 1H), 6.83-6.93 (m, 2H), 3.91 (d, *J* = 15.8 Hz, 1H), 2.99 (d, *J* = 15.8 Hz,

1H), 1.29 (s, 3H). ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 169.7, 161.1, 141.6, 139.0, 136.9, 136.4, 131.5, 127.9, 127.8, 127.3, 125.7, 123.7, 111.1, 110.9, 103.5, 39.1, 31..8, 21.7ppm. ESI-MS: 377 $(M+H)^{+;}$ $C_{20}H_{17}N_4O_2S$.

3',6'-dimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)-dione (4b)

^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=9.87 (s, 1H), 8.72 (s, 1H), 7.64 (d, *J* = 7.9 Hz, 2H), 7.61 (t, *J* = 7.4 Hz, 2H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.19 (t, *J* = 7.9 Hz, 1H), 6.99 (d, *J* = 7.4 Hz, 1H), 6.84 (t, *J* = 7.9 Hz, 2H), 4.12 (q, *J* = 7.0 Hz, 1H), 1.36 (s, 3H), 1.31 (d, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 187.9, 169.1, 143.9, 139.5, 137.8, 129.9, 129.6, 129.1, 129.0, 126.1, 124.9, 124.7, 117.6, 107.3, 101.3, 39.6, 29.5, 21.1, 16.7ppm. ESI-MS: 391 $(M+H)^{+;}$ $C_{21}H_{19}N_4O_2S$.

3',5-dimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)-dione (4c)

IR (KBr) 3346, 3021, 2912, 1756, 1693, 1295 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=9.83 (s, 1H), 8.27 (s, 1H), 7.23-7.43 (m, 5H), 7.09 (d, *J* = 7.9 Hz, 1H), 6.99 (s, 1H), 6.57 (d, *J* = 7.9 Hz, 1H), 4.34 (d, *J* = 14.9 Hz, 1H), 2.99 (d, *J* = 14.9 Hz, 1H), 2.46 (s, 3H), 1.36 (s, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 181.8, 169.9, 149.8, 139.7, 138.9, 132.9, 129.9, 129.7, 128.0, 127.9, 125.7, 124.9, 121.9, 110.9, 101.9, 39.2, 31.8, 22.7& 19.8. ESI-MS: 391 $(M+H)^{+;}$ $C_{21}H_{19}N_4O_2S$.

3',5,6'-trimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)- dione (4d)

IR (KBr) 3315, 2899, 2777, 1736, 1689, 1236 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=10.75 (s, 1H), 8.98 (s, 1H), 7.89 (s, 1H), 7.47-7.51 (m, 3H), 7.19 (d, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.88-6.97 (m, 1H), 5.98 (d, *J* = 8.0 Hz, 1H), 4.63 (q, *J* = 7.0 Hz, 1H), 1.99 (s, 3H), 1.63 (s, 3H), 1.13 (d, *J* = 7.0 Hz, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 189.7, 181.3, 154.7, 143.9, 141.1, 139.2, 139.1, 130.9, 130.7, 130.1, 127.0, 125.3, 125.1, 98.4, 50.3, 42.9, 31.9, 20.7, 19.3 ppm. ESI-MS: 405 $(M+H)^{+;}$ $C_{22}H_{21}N_4O_2S$.

5-methoxy-3'-methyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine] -2,7'(1'H)-dione (4e)

IR (KBr) 3344, 3021, 2965, 1747, 1689, 1307 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$, TMS) δ=9.43 (s, 1H), 7.82 (s, 1H), 7.11-7.23 (m, 5H), 6.90-7.05 (m, 3H), 4.45 (d, *J* = 15.0 Hz, 1H), 3.32 (s, 3H), 3.17 (d, *J* = 15.0 Hz, 1H), 1.09 (s, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$, TMS) δ 182.4, 181.9, 164.6, 158.2, 146.9, 142.9, 140.2, 136.9, 130.5, 129.4, 119.6, 114.6, 109.9, 109.1, 99.6, 51.5, 39.4, 25.4, 19.7 ppm. ESI-MS: 407 $(M+H)^{+;}$ $C_{21}H_{19}N_4O_3S$.

5-methoxy-3',6'-dimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazep ine]-2,7'(1'H)-dione (4f)

IR (KBr) 3209, 2924, 2850, 1710, 1660, 1340 cm^{-1}; ^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ= 10.42 (s, 1H), 10.12 (s, 1H), 7.43-7.60 (m, 5H), 7.23-7.28 (m, 1H), 6.96 (d, *J* = 8.4 Hz, 1H), 6.12-6.25 (m, 1H), 4.16 (q, *J* = 7.1 Hz, 1H), 2.98 (s, 3H), 1.58 (s, 3H), 1.21 (d, *J* = 7.1 Hz, 3H), ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 181.9, 180.2, 163.2, 155.7, 143.9, 135.0, 132.4, 130.9, 128.5, 126.5, 124.9, 119.7, 112.5, 109.9, 109.3, 66.5, 53.2, 29.0, 21.3, 12.6 ppm. ESI-MS: 421 $(M+H)^{+;}$ $C_{22}H_{21}N_4O_3S$.

5-bromo-3'-methyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)-dione (4g)

^{1}H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=9.62 (s, 1H), 9.23 (s, 1H), 7.42-7.69 (m, 4H), 7.30-7.39 (m, 2H), 7.27 (s, 1H), 6.87 (d, *J* = 8.4 Hz, 1H), 4.34 (d, *J* = 14.8 Hz, 1H), 3.11 (d, *J* = 14.8 Hz, 1H), 1.54 (s, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 182.7, 179.2, 142.6, 139.3, 137.9, 134.6, 131.3, 129.9, 127.9, 127.4, 125.1, 119.7, 112.9, 112.1, 105.1, 59.5, 29.7, 13.4 ppm. ESI-MS: 457 $(M+H)^{+;}$ $C_{20}H_{16}BrN_4O_2S$.

5-bromo-3',6'-dimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4e][1,4]thiazep ine]-2,7'(1'H)-dione (4h)

IR (KBr) 3335, 3114, 3012, 1745, 1678, 1313 cm^{-1}; ^1H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ=10.23 (s, 1H), 10.01(s, 1H), 7.39-7.45 (m, 3H), 7.33-7.36 (m, 3H), 7.26 (s, 1H), 7.01 (d, *J* = 8.4 Hz, 1H), 4.70 (q, *J* = 7.1 Hz, 1H), 3.22 (s, 3H), 1.58 (s, 3H), 1.29 (d, *J* = 7.1 Hz, 3H), ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 186.7, 182.9, 160.1, 150.1, 136.9, 136.1, 135.1, 130.7, 129.6, 128.3, 124.9, 124.8, 120.8, 109.7, 109.4, 48.9, 33.7, 13.9, 11.7 ppm. ESI-MS: 471 $(M+H)^{+;}$ $C_{21}H_{18}BrN_4O_2S$.

5-chloro-3'-methyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)-dione (4i)

^1H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ= 9.23 (s, 1H), 8.01 (s, 1H), 7.29-7.35 (m, 5H), 7.24 (t, *J* = 6.9 Hz, 2H), 6.93 (d, *J* = 8.9 Hz, 1H), 4.74 (d, *J* = 14.8 Hz, 1H), 3.45 (d, *J* = 14.8 Hz, 1H), 1.62 (s, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 183.7, 181.9, 152.9, 140.1, 138.1, 130.2, 129.6, 129.3, 128.1, 127.3, 126.1, 125.3, 124.9, 109.1, 108.3, 56.9, 29.6, 13.6 ppm. ESI-MS: 411 $(M+H)^{+;}$ $C_{20}H_{16}ClN_4O_2S$

5-chloro-3',6'-dimethyl-1'-phenyl-6',8'-dihydrospiro[indoline-3,4'-pyrazolo[3,4-e][1,4]thiazepine]-2,7'(1'H)-dione (4j)

^1H NMR (300MHz, $CDCl_3$+DMSO-d_6, TMS) δ= 9.01 (s, 1H), 7.98 (s, 1H), 7.37-7.44 (m, 4H), 7.11-7.23 (m, 3H), 7.01 (d, *J* = 7.9 Hz, 1H), 4.34 (q, *J* = 7.1 Hz, 1H), 1.43 (s, 3H), 1.39 (d, *J* = 7.1 Hz, 3H) ppm. ^{13}C NMR (75MHz, $CDCl_3$+DMSO-d_6, TMS) δ 182.5, 180.1, 153.0, 140.1, 140.0, 139.3, 130.1, 129.3, 128.6, 127.4, 125.7, 125.2, 124.3, 109.1, 103.1, 45.6, 32.1, 19.7, 13.7 ppm. ESI-MS: 425 $(M+H)^{+;}$ $C_{21}H_{18}ClN_4O_2S$.

CONCLUSION

In conclusion, we have described a novel, efficient, three component one pot green synthetic method for the preparation of spiro[indoline-3,4-pyrazolo[3,4-e][1,4]thiazepine]dione derivatives in water by using nano copper ferrite catalyst. The novelty and synthetic utility of this method was demonstrated in the efficient synthesis of spiro[indoline-3,4-pyrazolo[3,4-e][1,4] thiazepine]diones. The advantages of this method include its simplicity of operation, cleaner reaction, and good yields. Further, the purification of the product is simple involving filtration. The catalyst is easily separated by using external magnet and is reusable up to six cycles.

ACKNOWLEDGEMENT

The authors are grateful to CSIR, New Delhi for supporting through fellowship (JRF&SRF), and Department of Engineering chemistry, AUCE (A), Andhra University, Visakhapatnam. The corresponding author is also grateful to Prof. B. Venkateswara Rao for his constant support.

REFERENCES

[1] Terrett, N. K. Combinatorial Chemistry; Oxford University: New York, NY, 1998.

[2] (a) Skiles, J. W.; Suh, J. T.; Williams, B. E.; Menard, P. R.; Barton, J. N.; Love, B.; Jones, H.; Neiss, E. S.; Schwab, A.; Mann, W. S. J. Med. Chem. 1986, 29, 784-796; (b) Crescenza, A.; Botta, M.; Corelli, F.; Santini, A.; Tafi, A. J. Org. Chem. 1999, 64,3019-3025;

[3] H. Yanagisawa, S. Ishihara, A. Ando, T. Kanazaki, S. Miyamoto, H.Koike,Y. Iijima, K. Oizumi,Y.Matsushita andT. Hatat, J. Med. Chem., 1987, 30, 1984.

[4] (a) G. M. Pieper and W. Siebeneich, Eur. J. Pharmacol., 2000, 403, 129; (b) M. Arakawa, M. Sasaki, M. Ohmori, K. Harada and A. Fujimura, Eur. J. Clin. Pharmacol., 2001, 56, 775.

[5] (a) Abdel-Rahman, A. H.; Keshk, E. M.; Hanna, M. A.; El-Bady, S. M. Bioorg. Med. Chem. 2004, 12, 2483–2488; (b) Dandia, A.; Singh, R.; Khaturia, S.; Merienne, C.; Morgant, G.; Loupy, A. Bioorg. Med. Chem. 2006, 14, 2409–2417.

[6] (a) Ding, K.; Lu, Y. P.; Nikolovska Coleska, Z.; Wang, G. P.; Qiu, S.; Shangary, S.; Gao, W.; Qin, D.G.; Stuckey, J.; Krajewski, K.; Roller, P. P.; Wang, S. M. J. Med. Chem. 2006, 49,3432–3435; (b) Galliford, C. V.; Scheidt, K. A. Angew. Chem., Int. Ed. 2007, 46,8748–8758;

[7] (a) Badillo, J. J.; Hanhan, N. V.; Franz, A. K. Curr. Opin. DrugDiscovery Dev. 2010, 13, 758–776; (b) Antonchick, A. P.; Gerding-Reimers, C.;Catarinella, M.; Schurmann, M.; Preut, H.; Ziegler, S.; Rauh, D.; Waldmann, H. Nat. Chem. 2010, 2, 735–740.

[8] (a) Khafagy, M. M.; El-Wahas, A. H. F. A.; Eid, F. A.; El-Agrody, A. M. Farmaco 2002, 57, 715; (b) Sebahar, P. R.; Williams, R. M. J. Am. Chem. Soc. 2000, 122,5666.

[9] Kang, T. H.; Matsumoto, K.; Murakami, Y.; Takayama, H.; Kitajima, M.; Aimi, N.; Watanabe, H. Eur. J. Pharmacol. 2002, 444, 39.

[10] Reifschneider, W.; Bisabari-Ershadi, B.; Dripps, J. E.; Bonron, J. B. U.S. Patent 5,075,293, 1991; Chem. Abstr. 1991, 116, 129249.

[11] (a) Rovnyak, G. C.; Narayanan, V. L.; Haugwitz, R. D. U.S. Patent 4,053,613, 1975; Chem. Abstr. 1978, 88, 22892.; (b) Ali, S.; Alam, M. Arch. Pharmacol Res. 1994, 17, 131–133.

[12] (a) Rajopadhye, M.; Popp, F. D. J. Heterocycl. Chem. 1984, 21, 289–291; (b) Rajopadhye, M.; Popp, F. D. J. Heterocycl. Chem. 1985, 22, 93–96; (c) Popp, F. D.; Rajopadhye, M.; Brown, D. S.; Waddington, D.; Uff, B. C. J. Heterocycl. Chem. 1987, 24, 261–265; (d) Rajopadhye, M.; Popp, F. D. J. Heterocycl. Chem. 1987, 24, 1637–1642;

[13] (a) Azizian, J.; Morady, A. V.; Jadidi, K.; Mehrdad, M.; Sarrafi, Y. Synth. Commun. 2000, 30, 537–542; (b) Jain, S. C.; Sinha, J.; Bhagat, S.; Errington, W.; Olsen, C. E. Synth. Commun. 2003, 33, 563–577; (c) Dandia, A.; Singh, R.; Arya, K. Org. Prep. Proced. Int. 2003, 35, 401–408; (c) Dandia, A.; Arya, K.; Sati, M.; Gautam, S. Tetrahedron 2004, 60, 5253–5258;

[14] (a) Jain, M.; Khanna, P.; Saxena, A.; Bhagat, S.; Olsen, C. E.; Jain, S. C. Synth. Commun. 2006, 36(1863), e1872; (b) Mashelkar, U. C.; Rane, D. M.; Kenny, R. S. J. Heterocycl. Chem. 2008, 45, 865–872; (c) Pandey, M.; Raghuvanshi, D. S.; Singh, K. N. J. Heterocycl. Chem. 2009, 46, 49–53.

[15] Chen, H.; Shi, D. Tetrahedron 2011, 67, 5686–5692.