Res Chem Intermed
DOI 10.1007/s11164-014-1727-1

Synthesis of bioactive substituted pyrazolylbenzothiazinones

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Received: 10 December 2013 / Accepted: 26 May 2014

Abstract Pyrazolylbenzothiazinones have been synthesized in good yields by the reaction of 2-hydrazinocarbonymethyl-3,4-dihydro-2*H*-1,4-benzothiazin-3-ones with β-diketone in the presence of ethanol. The structures of synthesized pyrazolylbenzothiazinones were confirmed on the basis of their analytical and spectral data. The antimicrobial activities of the synthesized compounds have also been included.

Keywords Pyrazolylbenzothiazinones · Benzothiazinones · 2-aminobenzenethiol · Antibacterial activities

Introduction

Heterocyclic ring systems have played an important role in medicinal chemistry, as most of the heterosystems have served as key templates in the development of numerous important therapeutic agents [1–3]. The design and synthesis of biologically active molecules is one of the main challenges in medicinal chemistry. Potential efforts have been focused on the synthesis of small heterocyclic molecules because of their structural diversity and extensive utility as therapeutic agents. Nitrogen and sulfur-containing heterocycles; thiazine and its derivatives are of synthetic interest because they constitute an important class of natural and synthetic heterocycles, many of which exhibit useful biological and pharmacological activities, and are used as antifungal agents, anticancer, Na/H exchange inhibitors,

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Published online: 13 June 2014

Ca^{2+} channel opener, antagonists, antioxidants, antimicrobial agents, and bactericides [4–15], etc.

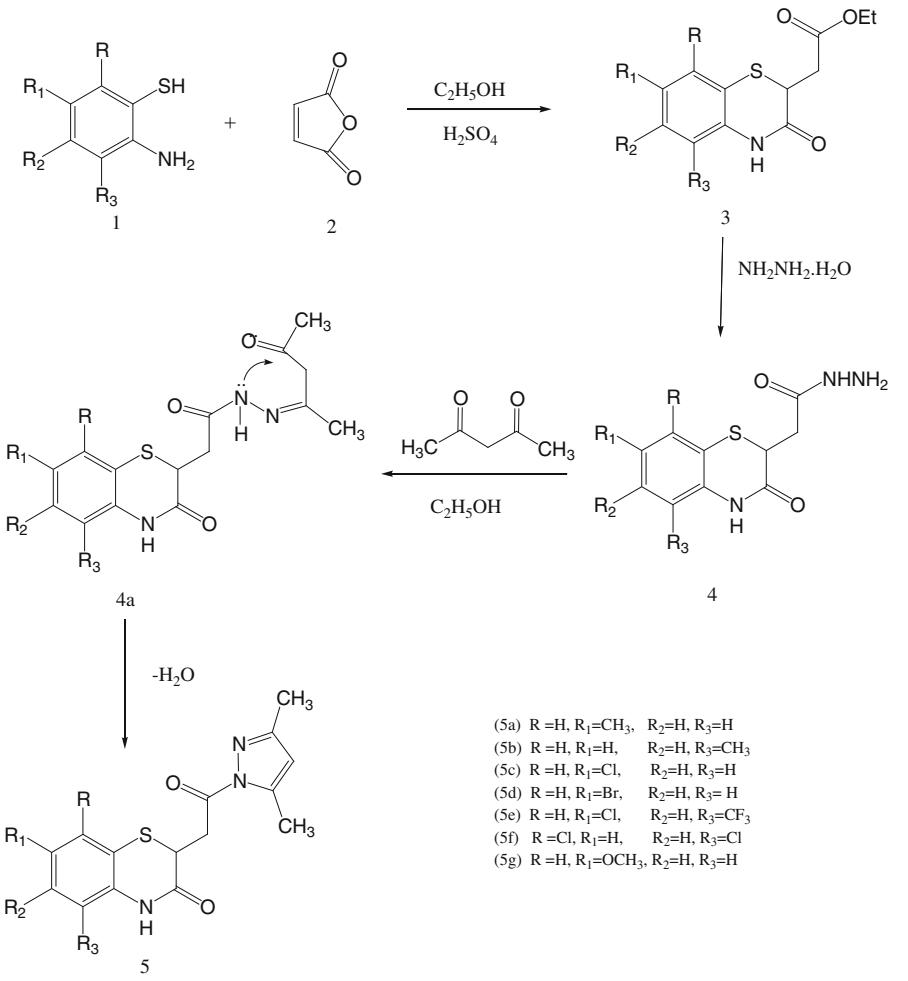
2*H*-1,4-Benzothiazin-3-one derivatives especially attracted the attention of synthetic chemists due to their wide-ranging biological activities [16, 17]. The structural modification in 1,4-benzothiazin-3-ones will lead to the development of a new class of therapeutic agents. Similarly, pyrazole and its derivatives have been identified as active core structures in anti-bacterial, hypotensive, and anti-inflammatory agents, as well as neurotoxicity inhibitors. They have also been reported to exhibit antimicrobial, antifungal, anticancer, and herbicidal activities [18–25]. In addition, pyrazole-fused derivatives have shown a broad spectrum of pharmacological and biological activities. In particular, pyrazole-fused benzothiazines have been reported to exhibit antimalarial activities [26]. The pyrazole derivatives are also used in supramolecular and polymer chemistry, agrochemicals, cosmetic colorings, complexing agents for the synthesis of hydrogenation catalysts, and UV stabilizers [27, 28]. Pyrazole derivatives have also shown liquid crystal properties.

As a consequence of the wide-ranging pharmacological and industrial applications of pyrazoles and benzothiazines and our continuing interest in the synthesis of therapeutically interesting heterocycles, we have designed and synthesized pyrazolylbenzothiazinones, incorporating to medicinally privileged heterosystems attached by ethanone functionality, on the basis of combinatorial synthesis, being practiced in most drug discoveries, with a view to develop multi-target drugs with promising bioactivities.

Results and discussion

The starting 2-aminothiophenols **1a–g** were prepared by the alkaline hydrolysis of 2-aminobenzothiazole, which were synthesized by the brominative cyclization of corresponding phenylthioureas by bromine and chloroform [29–31]. The required intermediates 3,4-dihydro-2-(ethoxycarbonyl)methyl-2*H*-1,4-benzothiazinones **3a–g** were prepared by the reaction of 2-aminothiophenols **1a–g** with maleic anhydride **2** according to literature [32, 33]. Treatment of **3a–g** with hydrazine hydrate in the presence of ethanol provided 2-hydrazinocarbonylmethyl-3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine **4a–g**, which were further reacted with acetyl acetone in ethanol giving pyrazolylbenzothiazine **5a–g** (Scheme 1).

The structures of the synthesized heterocycles have been confirmed by their spectral characteristics. The IR spectra of pyrazolylbenzothiazinones **5a–g** exhibit characteristic absorption bands at 3,375–3,320 cm^{-1}(–NH), 1,730–1,705 cm^{-1} (C=O) and 3,065–3,010 cm^{-1} (Ar, C–H). In compounds **5c**, **5e**, and **5f,** the absorption at 810–805 cm^{-1} is assigned to the C–Cl stretching vibrations. The absorption band at 670 cm^{-1} in compound **5d** is attributed to the C–Br stretching vibrations. In compound **5e**, the absorption at 1,050 cm^{-1} is observed due to C–F stretching vibrations. ^{1}HNMR spectra of all the synthesized pyrazolylbenzothiazinones show a singlet at δ 8.59–8.25 ppm due to NH proton and a multiplet is observed at δ 7.71–6.92 ppm due to the aromatic protons. In all the synthesized



1 2 3 4a 4 5

Scheme 1 Synthesis of substituted pyrazolylbenzothiazinones **5a–g**

pyrazolylbenzothiazinones, a double doublet is observed at δ 4.83–3.90 ppm due to C_2–H proton. In all the synthesized pyrazolylbenzothiazinones, two doublets are observed at δ 3.54–2.83 ppm and at δ 2.85–2.73 ppm due to CH_a and CH_b protons of CH_2 at $C_{1'}$. The formation of pyrazole ring has been confirmed by the fact that all the synthesized pyrazolylbenzothiazine show two singlets at δ 2.58–2.43 ppm and δ 2.46–2.27 ppm due to CH_3 protons at C_3 and C_5 position of pyrazole ring. The formation of pyrazole ring has also been supported by one proton singlet at δ 6.21–5.90 ppm due to pyrazole C_4–H. Compounds **5a** and **5b** show a singlet at δ 2.47 ppm and δ 2.44 ppm due to CH_3 protons at C_7 and C_5, respectively. ^{13}C NMR spectra of the synthesized pyrazolylbenzothiazinone **5e** showed distinct resonance signals in agreement with the structures assigned to the synthesized compounds. In the mass spectrum of compound **5e**, the molecular ion peak at 403 (M^+),

Table 1 Antimicrobial activity of substituted 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro -2*H*-1,4-benzothiazin-3-ones (**5a–g**)

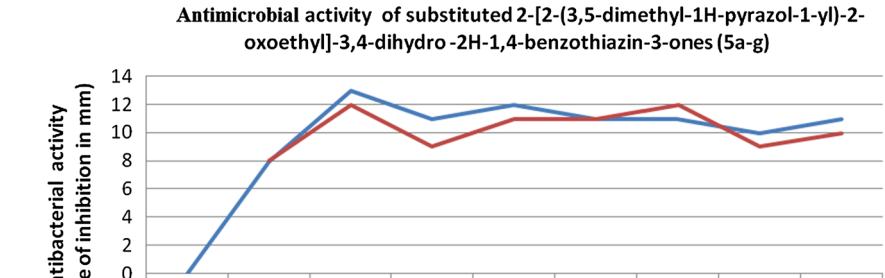
	Compounds				Antibacterial activity (zone of inhibition in mm)	
	R	R_1	R_2	R_3	*E. coli* (A)	*Bacillus cereus* (B)
5a	H	CH_3	H	H	8	8
5b	H	H	H	CH_3	13	12
5c	H	Cl	H	H	11	9
5d	H	Br	H	H	12	11
5e	H	Cl	H	CF_3	11	11
5f	Cl	H	H	Cl	11	12
5g	H	OCH_3	H	H	10	9
Chloramphenicol					11	10

corresponds to the molecular weight of the compound. The base peak at 95 (100 %) (pyrazole ring fragment) supports the formation of pyrazole ring as a result of the reaction of 2-hydrazinocarbonylmethyl-3,4-dihydro-3-oxo-2*H*-1,4-benzothiazine with acetylacetone. The mass fragmentation of the compound **5e** with peaks at (*m/z*, I > 5 %) 91, 107, 136, 147, 175, 191, 267, 281, 341, 371, and 401 is also in accordance with structural fragments of the molecular structure.

All the synthesized compounds were screened for their antimicrobial activity. The data presented in Table 1 indicate that the synthesized compounds are active against two bacterial species; *Escherichia coli* and *Bacillus cereus*. It has been observed that all the synthesized pyrazolylbenzothiazinones **5a–g** show activity against microbes. Compounds **5b**, **5d**, **5e**, and **5f** show better activity against both bacteria, whereas compounds **5c** and **5 g** show moderate activity against *E. coli*, but weak activity was shown by the compound **5c** and **5 g** against *B. cereus*. Compound **5a** shows weak activity against *E. coli* and *B. cereus* as compared to the reference compound. Therefore, it can be concluded that antimicrobial activities of the synthesized compounds are comparable or in some cases more than that of chloramphenicol (Fig. 1). The antimicrobial activity of these compounds may be attributed to the presence of combined structural effect of two privileged heterosystems: pyrazole and 1,4-thiazine. Along with the presence of substituents, especially electron-releasing groups, its orientation also contributes considerably to the activity.

Experimental

Melting points of the synthesized compounds were determined on an electric melting point apparatus and are uncorrected. The IR spectra were recorded on a SHIMADZU 8400 s spectrometer in KBr discs. The ^{1}H NMR and ^{13}CNMR spectra were recorded on a JEOL-300 MHz spectrometer using TMS as an internal standard. The chemical shifts are expressed as δ ppm. Mass spectrum was recorded



		5a	5b	5c	5d	5e	5f	5g	Chloramphinacol
E. Coli	0	8	13	11	12	11	11	10	11
Bacillus Cereus (B)		8	12	9	11	11	12	9	10

Fig. 1 Antimicrobial activity of synthesized pyrazolylbenzothiazinones **5a–g**

on a JEOL SX-102/Da-600 mass spectrometer using Argon/Xenon (6 kV, 10 mA) as the FAB gas.

Preparation of substituted 2-aminobenzenethiols (1)

Substituted 2-aminobenzenethiols(1), required for the synthesis of pyrazolylbenzothiazinones, have been synthesized from substituted anilines by the method described in the literature [34–37].

Synthesis of 3,4-dihydro-2-(ethoxycarbonyl)methyl-2*H*-1,4-benzothiazin-3-ones (3a–g)

A mixture of substituted 2-aminobenzenethiol (0.01 mol), maleic anhydride (0.01 mol), and H_2SO_4 (one or two drops) in ethanol (50 ml) was refluxed for 4–5 h. The excess solvent was distilled off and the residue was poured into cold water and then extracted with $CHCl_3$. The $CHCl_3$ extract was washed with $NaHCO_3$ solution, water, and then dried over anhydrous Na_2SO_4. The solvent was then removed to give a crude solid, which was recrystallized from $CHCl_3$ to hexane to give **3** [38].

Synthesis of 2-hydrazinocarbonylmethyl-3,4-dihydro-2*H*-1,4-benzothiazin-3-ones (4a–g)

A mixture of compound **3** (0.01 mol) and hydrazine hydrate (0.01 mol) was taken in a round-bottomed flask and then refluxed for 15 min. The sufficient quantity of absolute ethanol was added through the condenser to produce a clear solution and refluxed for 2–3 h and then cooled. The resulting solid was dried and crystallized from ethanol [39].

Synthesis of pyrazolylbenzothiazinones (5a–g)

A solution of compound **4** (0.01 mol) and acetylacetone (0.02 mol) in absolute ethanol (50 ml) was refluxed on a boiling water bath for approximately 2 h. After completion of the reaction, the mixture was allowed to stand overnight. The solid residue was filtered and then washed with ethanol to obtain pure sample of pyrazolylbenzothiazine **5**. The following 2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-ones have been synthesized:

(a) 7-methyl-2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 61 % M.P. °C 190; IR (KBr, cm^{-1}): 3,330 (–NH), 1,730 (C=O), 3,015 (Ar, C–H) ^{1}H NMR ($CDCl_3$, δ ppm); 5.90 (s, 1H, pyrazole C_4–H), 8.29 (s,1H,–NH proton), 4.08 (dd, 1H, C_2–H proton), 2.95 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.81 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.47 (s, 3H, CH_3 proton at C_7), 2.52 (s, 3H, CH_3 proton at pyrazole C_3), 2.37 (s, 3H, CH_3 proton at pyrazole C_5), 7.30–7.22 (m, 3H, aromatic protons); Anal. Calcd. for $C_{16}H_{17}N_3O_2S$: C, 60.90, H, 5.43, N, 13.32,. Found: C, 60.86, H, 5.40, N, 13.29.

(b) 5-methyl-2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 58 % M.P. °C 185; IR (KBr): 3,340 (–NH), 1,710 (C=O), 3m010 (Ar, C–H) ^{1}H NMR ($CDCl_3$, δ ppm) 5.95 (s, 1H, pyrazole C_4–H), 8.50 (s,1H,–NH proton), 4.08 (dd, 1H, C_2–H proton), 3.54 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.85 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.44 (s, 3H, CH_3 proton at C_5), 2.54 (s, 3H, CH_3 proton at pyrazole C_3), 2.27 (s, 3H, CH_3 proton at pyrazole C_5),7.32–7.23 (m, 3H, aromatic protons); Anal. Calcd. for $C_{16}H_{17}N_3O_2S$: C, 60.90, H, 5.43, N, 13.32,. Found: C, 60.86, H, 5.40, N, 13.28.

(c) 7-chloro-2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3, 4-dihydro-2*H*-1, 4-benzothiazin-3-one Yield 53 % M.P. °C 200; IR (KBr): 3,320 (–NH), 1,720 (C=O), 3,018 (Ar, C–H), 810 (C–Cl);, ^{1}H NMR ($CDCl_3$, δ ppm); 6.01 (s, 1H, pyrazole C_4–H), 8.59 (s,1H,–NH proton), 3.90 (dd, 1H, C_2–H proton), 2.83 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.68 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.56 (s, 3H, CH_3 proton at pyrazole C_3), 2.31 (s, 3H, CH_3 proton at pyrazole C_5), 7.35–7.21 (m, 3H, aromatic protons); Anal. Calcd. for $C_{15}H_{14}ClN_3O_2S$: C, 53.65, H, 4.20, N, 12.51,. Found: C, 53.61, H, 4.19, N, 12.49.

(d) 7-bromo-2-[2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 63 % M.P. °C 204; IR (KBr): 3,350 (–NH), 1,725 (C=O), 3,055 (Ar, C–H) ^{1}H NMR ($CDCl_3$, δ ppm); 6.21 (s, 1H, pyrazole C_4–H), 8.29 (s,1H,–NH proton), 4.12 (dd, 1H, C_2–H proton), 2.88 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.73 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.48 (s, 3H, CH_3 proton at pyrazole C_3), 2.31 (s, 3H, CH_3 proton at pyrazole C_5), 7.30–6.92 (m, 3H, aromatic protons); Anal. Calcd. for $C_{15}H_{14}BrN_3O_2S$: C, 47.38, H, 3.71, N, 11.05,. Found: C, 47.32, H, 3.65, N, 11.01.

(e) 7-chloro-5-trifluromethyl-2-[2-(3, 5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 58 % M.P. °C 210; IR (KBr): 3,375 (–NH), 1,705 (C=O), 3,065 (Ar, C–H), 810 (C–Cl), 1,050 (C–F); ^{1}H NMR ($CDCl_3$, δ

ppm); 5.92 (s, 1H, pyrazole C_4–H), 8.25 (s,1H,–NH proton), 4.83 (dd, 1H, C_2–H proton), 2.94 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.77 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.58 (s, 3H, CH_3 proton at pyrazole C_3), 2.46 (s, 3H, CH_3 proton at pyrazole C_5), 7.77–7.51 (m, 3H, aromatic protons); ^{13}C NMR ($CDCl_3$, δ ppm); 13.76, 29.91, 64.21, 107.97, 112.21 119.45, 121.76, 122.73, 129.67, 132.81, 143.10, 164.32, 190.11; MS: *m/z*: 403 (M^+), BP: *m/z*: 95; Anal. Calcd. for $C_{16}H_{13}ClF_3N_3O_2S$: C, 47.59, H, 3.24, N, 10.41,. Found: C, 47.54, H, 3.21, N, 10.38.

(f) 5,8-dichloro-2-[2-(3, 5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3,4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 64 % M.P. °C 199; IR (KBr): 3,360 (–NH), 1,710 (C=O), 3,020 (Ar, C–H), 805 (C–Cl); ^{1}H NMR ($CDCl_3$, δ ppm); 6.21 (s, 1H, pyrazole C_4–H), 8.52 (s,1H,–NH proton), 4.18 (dd, 1H, C_2–H proton), 2.92 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.81 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 2.51 (s, 3H, CH_3 proton at pyrazole C_3), 2.29 (s, 3H, CH_3 proton at pyrazole C_5), 7.28–7.02 (m, 3H, aromatic protons); Anal. Calcd. for $C_{15}H_{13}Cl_2N_3O_2S$: C, 48.66, H, 3.54, N, 11.35,. Found: C, 48.61, H, 3.50, N, 11.31.

(g) 7-methoxy-2-[2-(3, 5-dimethyl-1*H*-pyrazol-1-yl)-2-oxoethyl]-3, 4-dihydro-2*H*-1,4-benzothiazin-3-one Yield 69 % M.P. °C 202; IR (KBr): 3,345 (–NH), 1,710 (C=O), 3,012 (Ar, C–H); ^{1}H NMR ($CDCl_3$, δ ppm); 6.21(s, 1H, pyrazole C_4–H), 8.59 (s,1H,–NH proton), 4.03 (dd, 1H, C_2–H proton), 2.91 (d, 1H, CH_a proton of CH_2 at $C_{1'}$), 2.78 (d, 1H, CH_b proton of CH_2 at $C_{1'}$), 3.12 (s, 3H, OCH_3 proton at C_7), 2.43 (s, 3H, CH_3 proton at pyrazole C_3), 2.36 (s, 3H, CH_3 proton at pyrazole C_5), 7.42–7.18 (m, 3H, aromatic protons); Anal. Calcd. for $C_{16}H_{17}N_3O_3S$: C, 57.99, H, 5.17, N, 12.68,. Found: C, 57.95, H, 5.15, N, 12.63.

Antimicrobial activity

All the synthesized compounds were screened for antibacterial activity against *Bacillus cereus* (Gram-positive bacteria) and *E. coli* (Gram-negative bacteria) at a concentration of 30 μg/ml using ethanol as a solvent by well diffusion method [40–44]. After 24 h of incubation at 37 °C, the zone of inhibitions was measured in millimeters. The standard drug chloramphenicol (30 μg/ml) was also screened for antimicrobial activities, which are presented in Table 1.

Acknowledgments The authors are thankful to the Head, Department of Chemistry, University of Rajasthan, Jaipur (India) for providing necessary laboratory facilities as well as instrumentation facilities (IR, and ^{1}HNMR). The Director RSIC, CDRI, Lucknow (India) is acknowledged for providing mass spectra of the synthesized compounds. We express our thanks to University Grant Commission, New Delhi, for providing meritorious student fellowship to one of us (P.K.S.).

References

1. J. Elguero, In *Comprehensive Heterocyclic Chemistry*, vol. 3, ed. by A.R. Katritzky, C.W. Rees, E.V.F. Scriven (Pergamon Press, London, 1996), pp. 1–75
2. S. Zhihua, J. Guan, C. Dennis, Bioorg. Med. Chem. Lett. **10**, 601–604 (2000)
3. T.D. Penning, J.J. Talley, S.R. Bertenshaw, J.S. Carter, J. Med. Chem. **40**, 1347–1365 (1997)

4. R.R. Gupta, *Phenothiazines and 1,4-Benzothiazines Chemical and Biomedical Aspects* (Elsevier, Amsterdam, 1988), pp. 163–269
5. K.G. Nazarenko, N.A. Shtil, M.O. Lozinski, Tetrahedron **63**, 7723–7727 (2007)
6. A. Shah, Y. Natipara, D. Sureja, N. Motohashi, Anticancer Res. **18**, 3001–3004 (1998)
7. R. Fringuelli, F. Schiafella, A. Vecchiarelli, J. Chemother. **13**(1), 9–14 (2001)
8. S. Barriga, P. Fuertes, T. Torroba, J. Org. Chem. **69**, 3672–3682 (2004)
9. T. Yamamoto, M. Hori, I. Watanabe, Chem. Pharm. Bull. **48**, 843–849 (2000)
10. Y. Watanabe, K. Osanai, T. Nishi, Bioorg. Med. Chem. Lett. **6**(16), 1923–1926 (1996)
11. D. Armesine, G. Trapani, V. Arrivo, J. Heterocycl. Chem. **37**, 1611–1616 (2000)
12. V. Calderone, R. Spogli, A. Martelli, J. Med. Chem. **51**(16), 5085–5092 (2008)
13. M. Fujita, K. Yamamoto, Y. Kawashima, H. Yamauchi, J. Med. Chem. **33**, 1898–1905 (1990)
14. S.B. Kale, B.K. Karale, J. Heterocyl. Chem. **44**(2), 289–301 (2007)
15. S. Sabatini, D. Brandini, A. Fravolini, J. Med. Chem. **51**(14), 4321–4330 (2008)
16. G. Campiani, A. Garofalo, I. Fiorini, J. Med. Chem. **38**, 4393–4410 (1995)
17. M.O. Lozinskii, A.M. Demchenko, in *Advanced Methods of Synthesis and Modifications of Heterocycles*, vol. 2 ed. by V.G. Karcev (JBS, Moscow 2003)
18. D. Lednicer, L.A. Mitscher, *Organic Chemistry of Drugs Synthesis A*, vol. 1–3 (Wiley, New York, 1977)
19. G. Turan-Zitouni, P. Chevallet, Eur. J. Med. Chem. **35**, 635–641 (2000)
20. R.N. Comber, R.J. Gray, Carbohydr. Res. **216**, 441–452 (1991)
21. L. Xin-Hua, Bioorg. Med. Chem. **16**, 4075–4082 (2008)
22. Y. Li, J. Liu, J. Agric. Food Chem. **54**, 3636–3640 (2006)
23. M. Manpadi, S. Rogelj, J. Med. Chem. **50**, 5183–5192 (2007)
24. C.B. Vicentini, S. Guccione, J. Agric. Food Chem. **53**, 3848–3855 (2005)
25. R.D. Clark, J. Agric. Food Chem. **44**, 3643–3652 (1996)
26. A. Barazarte, G. Loo, Eur. J. Med. Chem. **44**, 1303–1310 (2009)
27. E. Akbas, I. Berber, Farmaco **60**, 23–26 (2005)
28. A.A. Bekhita, T. Abdel-Aziem, Bioorg. Med. Chem. **12**, 1935–1945 (2004)
29. P.K. Sharma, M. Kumar, V. Mohan, Res. Chem. Intermed. **36**(8), 985–993 (2010)
30. S. Vats, P.K. Sharma, M. Kumar, Med. Chem. Res. **21**, 2072–2078 (2012)
31. M. Kumar, P.K. Sharma, Res. Chem. Intermed. **37**, 1103–1111 (2011)
32. S.K. Mukherji, M. Jain, Ind. J. Chem. **33B**, 990–991 (1994)
33. D.R. Shridhar, B. Ram, Ind. J. Chem. **24 B**, 992–994 (1985)
34. B.S. Rathore, M. Kumar, Bioorg. Med. Chem. **14**, 5678–5682 (2006)
35. A. Fogla, P.K. Sharma, M. Kumar, Res. Chem. Intermed. **35**(1), 35–41 (2009)
36. V. Ankodia, P.K. Sharma, M. Kumar, Heterocycl. Commun. **14**(3), 155–160 (2008)
37. B.K. Sharma, P.K. Sharma, M. Kumar, One-pot. Synth. Commun. **40**(16), 2347–2352 (2010)
38. T. Aotsuka, H. Hosono, Chem. Pharm. Bull. **42**(6), 1264–1271 (1994)
39. K.C. Kim, H.S. Kim, J. Korean Chem. Soc. **46**(6), 585–589 (2002)
40. H. Hussain, V.U. Ahmad, Arkivoc **xiv**, 289–299 (2007)
41. A. Rahman, W.J. Thomsen, *Bioassay Techniques for Drug Development* (Harwood Academic Publishers, The Netherlands, 2001), p. 16
42. M. Serwar, T. Akhtar, Arkivoc **vii**, 210–221(2009)
43. M.I. Choudhary, W.J. Thomsen, *Bioassay Techniques for Drug Development* (Harwood Academic Publishers, The Netherlands, 2001), p. 22
44. V.V. Dabholkar, R.P. Gavande, Indian J. Chem. **51B**(8), 1173–1179 (2012)