Chemistry of Heterocyclic Compounds, Vol. 45, No. 12, 2009

SYNTHESIS AND SPECTRAL ANALYSIS OF NOVEL 3-(4,6-DIARYLPYRIMIDIN-2-YL)-2-PHENYLTHIAZOLIDIN-4-ONES

M. Gopalakrishnan[1]*, J. Thanusu[1], V. Kanagarajan[1]

Novel 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones are synthesized by the multicomponent cyclocondensation reaction of the appropriate 2-amino-4,6-diarylpyrimidines, benzaldehyde, and thioglycolic acid catalyzed by dicyclohexylcarbodiimide. The synthesized compounds have been characterized by melting point, elemental analysis, MS, FT-IR, ^{1}H and ^{13}C NMR spectroscopic data.

Keywords: 2-amino-4,6-diarylpyrimidines, dicyclohexylcarbodiimide, 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones, thioglycolic acid, multicomponent cyclocondensation reaction.

In recent years, multicomponent reactions (MCRs) have received considerable attention and emerged as one of the most important protocols in organic synthesis and medicinal chemistry. Various 4-thiazolidinones have attracted substantial attention as they are endowed with a wide range of pharmacological activities. Peptidoglycan is an essential component of the cell wall of both Gram-positive and Gram-negative bacteria. 4-Thiazolidinones have been reported as novel inhibitors of the bacterial enzyme MurB, which is a precursor, acting during the biosynthesis of peptidoglycan [1]. A wide variety of biological properties such as hypolipidemic [2], antidegenerative [3], muscarinic receptor 1 agonist [4], antiproteolytic [5], anti-inflammatory [6], antiviral [7], antifungal [8], antibacterial [9], antitubercular [10], anticonvulsant [11], respiratory [12], and hypnotic [13] activities have been reported for 4-thiazolidinones.

Pyrimidines are the basic heterocycles in nucleic acids and have been associated with a number of biological activities. Substituted aminopyrimidine moiety is common in marketed drugs such as antiatherosclerotic *aronixil*, antihistaminic *thonzylamine*, anxiolytic *buspirone*, antipsoriatic *enazadrem*, and other medicinally relevant compounds. Some notable biological activity of pyrimidine derivatives includes adenosine receptor antagonists [14], kinase inhibitors [15], analgesic [16], anti-inflammatory [16], inhibitors of cyclin-dependent kinases 1 and 2 [17], calcium channel antagonist [18], antihistaminic [19], and antitubercular [20] activities.

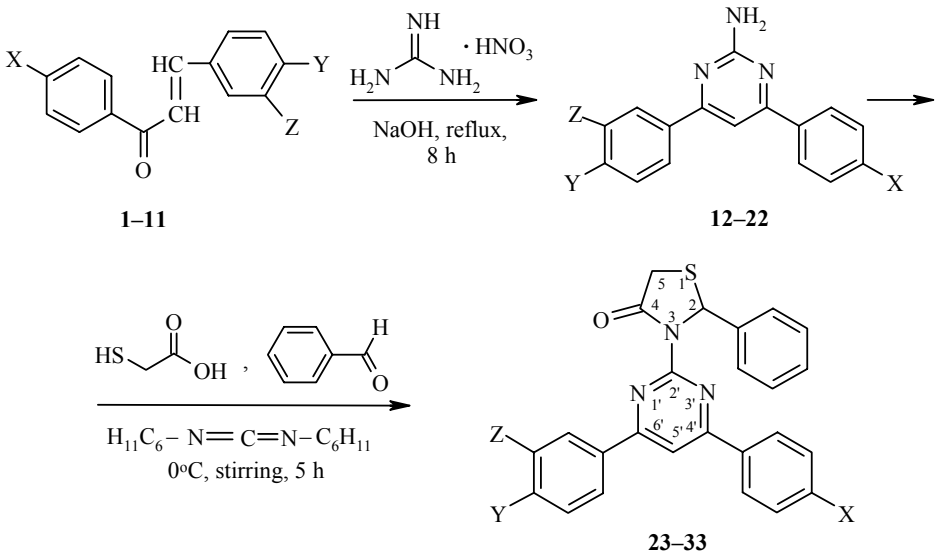
Recently, we synthesized 6-aryl-1,2,4,5-tetrazinane-3-thiones [21] by the multicomponent cyclocondensation reaction of appropriate aromatic aldehydes, thiourea, and ammonium acetate. Some biolabile fused indazoles [22], 2,6-diarylpiperidin-4-one derivatives [23-25] for incorporating various other bioactive

* To whom correspondence should be addressed, e-mail: profmgk@yahoo.co.in.

[1]Synthetic Organic Chemistry Laboratory, Department of Chemistry, Annamalai University, Annamalainagar-608002, Tamil Nadu, India.

Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 12, 1906-1912, December, 2009. Original article received July 29, 2008; revised version received November 11, 2009.

Scheme 1



23, **24** X = Y = H, **23** Z = H, **24** Z = Cl; **25** X = Z = H, Y = Cl; **26–28** X = Y = H, **26** Z = OMe, **27** Z = Me, **28** Z = F; **29**, **30** Y = Z = H, **29** X = Cl, **30** X = OMe; **31-33** X = Cl, Y = H, **31** Z = Me, **32** Z = Cl, **33** Z = F

Scheme 2

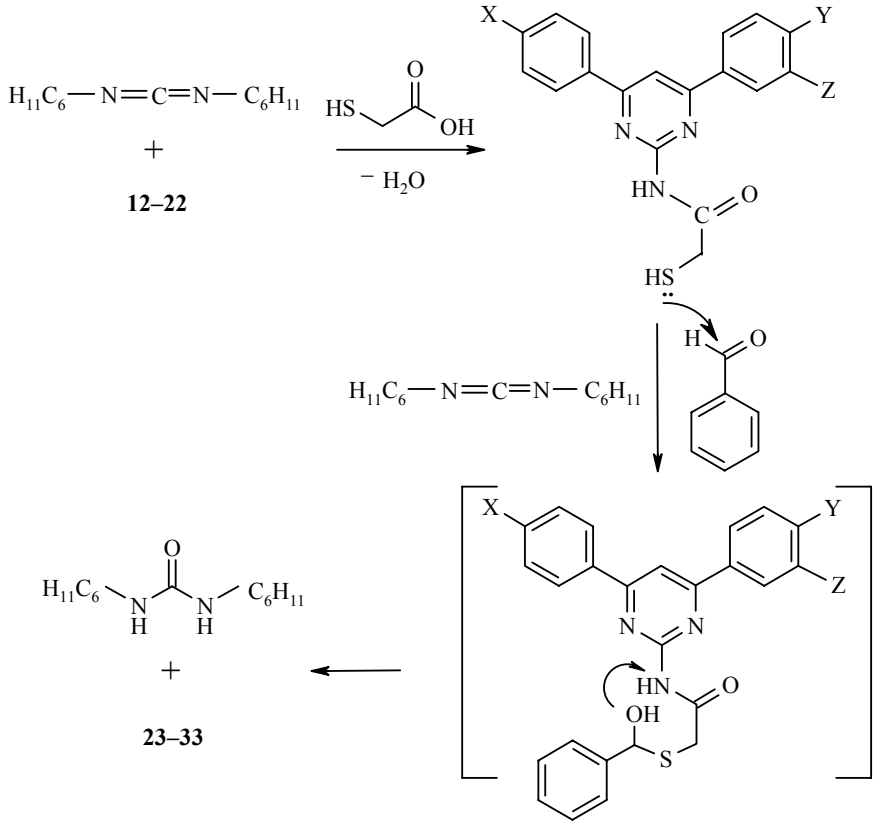


TABLE 1. Physical and analytical data of 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones **23-33**

Compound	Empirical formula	Found, % / Calculated, %			mp,°C	*m/z* $[M+1]^{+\cdot}$	Yield, %
		C	H	N			
23	$C_{25}H_{19}N_3OS$	73.31 / 73.35	4.60 / 4.64	10.23 / 10.26	145	410	65
24	$C_{25}H_{18}Cl\,N_3OS$	67.65 / 67.66	4.04 / 4.06	9.41 / 9.46	162	444	52
25	$C_{25}H_{18}Cl\,N_3OS$	67.62 / 67.66	4.01 / 4.06	9.44 / 9.46	130	444	49
26	$C_{26}H_{21}N_3O_2S$	71.03 / 71.08	4.72 / 4.78	9.51 / 9.56	110	440	60
27	$C_{26}H_{21}N_3OS$	73.72 / 73.76	4.92 / 4.96	9.89 / 9.92	162	424	65
28	$C_{25}H_{18}FN_3OS$	70.23 / 70.27	4.18 / 4.21	9.79 / 9.83	104	428	70
29	$C_{25}H_{18}Cl\,N_3OS$	67.64 / 67.66	4.01 / 4.05	9.41 / 9.46	114	444	65
30	$C_{26}H_{21}N_3O_2S$	71.02 / 71.08	4.72 / 4.78	9.55 / 9.56	137	440	58
31	$C_{26}H_{20}ClN_3OS$	68.17 / 68.21	4.32 / 4.36	9.15 / 9.17	125	458	55
32	$C_{25}H_{17}Cl_2N_3OS$	62.71 / 62.78	3.52 / 3.55	8.76 / 8.78	130	479	60
33	$C_{25}H_{17}ClFN_3OS$	64.98 / 65.02	3.65 / 3.68	9.04 / 9.09	103	462	65

heterocyclic nucleus such as 1,2,3-selenadiazoles and 1,2,3-thiadiazoles, and diazepams intact for evaluation of associated antibacterial and antifungal activities were also prepared in our laboratory. In the interest of the above, we planned to synthesize a system that comprises both 4-thiazolidinones and 2-amino-4,6-diaryl-pyrimidine components together to give a heterocyclic structure like the title 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones.

Initially, a conversion of 2-amino-4,6-diarylpyrimidines **12-22** to 3-(4,6-diarylpyrimidin-2-yl)-2-phenyl-thiazolidin-4-ones **23-33** was tried in the absence of dicyclohexylcarbodiimide (DCC). No yields were achieved. Instead, if DCC was used as a dehydrating agent, the yield of the product was improved significantly (i.e., about 65%) in the stirring mode at about 0ºC. The Claisen–Schmidt condensation of equimolar quantities of various *p*-substituted acetophenones with different *m*- and *p*-substituted benzaldehydes in the presence of sodium hydroxide as a catalyst yields 1,3-diarylprop-2-en-1-ones **1-11**. When compounds **1-11** are treated with guanidine nitrate in the presence of NaOH in refluxing ethanol for 8 h they give 2-amino-4,6-diarylpyrimidines **12-22**. The novel title compounds 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones **23-33** are synthe-sized by the reaction of benzaldehyde and thioglycolic acid with 2-amino-4,6-diphenylpyrimidine in dry dichloromethane at 0°C catalyzed by DCC. The analytical data of compounds **23-33** are given in Table 1. The importance of the title compounds is due to their diverse potential, broad-spectrum biological activity. The structure of the newly synthesized compounds **23-33** is confirmed by elemental analysis, MS, FT-IR, ^{1}H and ^{13}C NMR spectroscopic data. A possible reaction mechanism (Scheme 2) has been proposed for the conversion of 2-amino-4,6-diarylpyrimidines to 3-(4,6-diarylpyrimidin-2-yl)-2-phenylthiazolidin-4-ones catalyzed by DCC.

EXPERIMENTAL

All the reported melting points were taken in open capillaries and were uncorrected. IR spectra were recorded in KBr (pellet forms) on a Nicolet-Avatar–330 FT-IR spectrophotometer and noteworthy absorption

values (cm^{-1}) alone are listed. ^1H and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, on a Bruker AMX 400 NMR spectrometer using DMSO-d_6 as a solvent. The ESI + ve MS spectra were recorded on a Bruker Daltonics LC-MS spectrometer. Satisfactory microanalysis was obtained on a Carlo Erba 1106 CHN analyzer.

By adopting the literature precedent, 1,3-diarylprop-2-en-1-ones **1**–**11** [26] and 2-amino-4,6-diaryl-pyrimidines **12**–**22** [27] were synthesized.

2-Phenyl-3-(4',6'-Diphenylpyrimidin-2'-yl)thiazolidin-4-one (23) (General Method). To an ice-cold stirred solution of 2-amino-4,6-diphenylpyrimidine (2.47 g, 0.01 mol) in dry dichloromethane benzaldehyde (1.06 g, 0.01 mol) was added in drops followed by DCC (2.06 g, 0.0l mol). After 5 min, thioglycolic acid (0.92 g, 0.01 mol) was added and stirring was continued at 0°C for an additional 5 h. Then the reaction mixture was filtered off to remove dicyclohexylurea followed by washing with 5% citric acid, 10% sodium bicarbonate, brine solution, and finally with water, and dried over anhydrous sodium sulfate. After evaporation of the solvent under reduced pressure, a gummy mass was obtained, which solidified on treatment with petroleum ether (bp 40–60°C). Final purification of compound **23** was done by column chromatography using silica gel (100-200 mesh), with ethyl acetate–petroleum ether (bp 40-60°C) in the ratio of 2:8 as an eluent. IR spectrum, ν, cm^{-1}: 3125, 3033, 2927, 2851, 1716, 1627, 1576, 1350, 710, 698, 649. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.21 (1H, d, *J* = 15.4, H-5*a*); 3.38 (1H, d, *J* = 15.4, H-5*e*); 5.25 (1H, s, H-2); 7.19–8.37 (16H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.0 (C-5), 62.5 (C-2), 108.1 (C-5'), 131.4 (C-2'''), 125.9–128.8 (C arom.), 139.1 (C-4''), 139.1 (C-6''), 161.3 (C-4'), 161.3 (C-6'), 163.8 (C-2'), 170.6 (C-4).

Compounds 24-33 were synthesized in a similar way.

3-[6'-(3''-Chlorophenyl)-4'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (24). IR spectrum, ν, cm^{-1}: 3120, 3033, 2927, 2851, 1696, 1627, 1575, 1310, 894, 710, 650, 647. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.22 (1H, d, *J* = 15.4, H-5*a*); 3.39 (1H, d, *J* = 15.3, H-5*e*); 5.27 (1H, s, H-2); 7.31–8.44 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 33.9 (C-5), 62.6 (C-2), 108.8 (C-5'), 127.5–133.1 (C arom.), 131.4 (C-2'''), 135.9 (C-*ipso*), 139.1 (C-4''), 139.7 (C-6''), 164.9 (C-4'), 165.0 (C-6'), 162.9 (C-2'), 170.6 (C-4).

3-[6'-(4''-Chlorophenyl)-4'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (25). IR spectrum, ν, cm^{-1}: 3115, 3033, 2927, 2850, 1714, 1627, 1575, 1344, 894, 767, 690, 648. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.22 (1H, d, *J* = 15.4, H-5*a*); 3.39 (1H, d, *J* = 15.4, H-5*e*); 5.27 (1H, s, H-2); 7.21–8.24 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 33.9 (C-5), 62.4 (C-2), 108.9 (C-5'), 124.6–129.0 (C arom.), 130.6 (C-*ipso*), 131.5 (C-2'''), 139.0 (C-4''), 141.8 (C-6''), 164.9 (C-4'), 165.5 (C-6'), 162.7 (C-2'), 170.6 (C-4).

3-[6'-(3''-Methoxyphenyl)-4'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (26). IR spectrum, ν, cm^{-1}: 3065, 3038, 2927, 2851, 1714, 1627, 1577, 1351, 700, 650, 649. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.23 (1H, d, *J* = 15.35, H-5*a*); 3.39 (1H, d, *J* = 15.3, H-5*e*); 3.84 (3H, s, OCH_3); 5.28 (1H, s, H-2); 7.21-8.21 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.5 (C-5), 54.9 (OCH_3 on aryl ring), 62.5 (C-2), 108.7 (C-5'), 126.0-128.6 (C arom.), 129.1 (C-2'''), 139.1 (C-4''), 141.5 (C-6''), 164.0 (C-4'), 165.0 (C-6'), 162.3 (C-2'), 170.6 (C-4).

3-[6'-(3''-Methylphenyl)-4'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (27). IR spectrum, ν, cm^{-1}: 3060, 3033, 2926, 2852, 1715, 1627, 1579, 1350, 714, 700, 643. ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.32 (3H, s, CH_3), 3.23 (1H, d, *J* = 15.3, H-5*a*); 3.40 (1H, d, *J* = 15.4, H-5*e*); 5.27 (1H, s, H-2); 7.20–8.24 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 24.5 CH_3 on aryl ring, 34.1 (C-5), 62.6 (C-2), 108.4 (C-5'), 126.0–131.4 (C arom.), 133.1 (C-2'''), 135.9 (C-*ipso*), 138.7 (C-4''), 139.1 (C-6''), 164.9 (C-4'), 165.5 (C-6'), 162.6 (C-2), 170.8 (C-4).

3-[6'-(3''-Fluorophenyl)-4'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (28). IR spectrum, ν, cm^{-1}: 3071, 3027, 2928, 2852, 1712, 1626, 1575, 1352, 836, 769, 698. ^1H NMR spectrum, δ, ppm (*J*, Hz): 3.20

(1H, d, *J* = 15.2, H-5*a*); 3.37 (1H, d, *J* = 15.3, H-5*e*); 5.26 (1H, s, H-2); 6.64–8.19 (15H, m, arom.). A singlet for CH proton at position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.5 (C-5), 62.9 (C-2), 108.9 (C-5'), 127.3–143.1 (C arom.), 143.6 (C-2'''), 145.1 (C-4''), 146.1 (C-6''), 166.8 (C-4'), 167.0 (C-6'), 163.9 (C-2'), 171.4 (C-4).

3-[4'-(4''-Chlorophenyl)-6'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (29). IR spectrum, ν, cm^{-1}: 3071, 3027, 2926, 2852, 1721, 1627, 1576, 1398, 782, 730, 693, 582. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.21 (1H, d, *J* = 15.3, H-5*a*); 3.38 (1H, d, *J* = 15.3, H-5*e*); 5.25 (1H, s, H-2); 7.15–7.93 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.1 (C-5), 62.9 (C-2), 108.9 (C-5'), 126.5–128.9 (C arom.); 129.2 (C-2'''), 139.1 (C-4''), 141.9 (C-6''), 164.4 (C-4'), 165.3 (C-6'), 162.5 (C-2'), 170.8 (C-4).

3-[4'-(4''-Methoxyphenyl)-6'-phenylpyrimidin-2'-yl]-2-phenylthiazolidin-4-one (30). IR spectrum, ν, cm^{-1}: 3065, 3033, 2928, 2851, 1715, 1627, 1590, 1370, 835, 770, 699, 656. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.20 (1H, d, *J* = 15.1, H-5*a*); 3.37 (1H, d, *J* = 15.3, H-5*e*); 3.86 (3H, s, OCH_3); 5.26 (1H, s, H-2); 6.97-8.20 (15H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.1 (C-5), 55.2 (OCH_3 on aryl ring), 62.5 (C-2), 108.6 (C-5'), 114.1-129.1 (C arom.), 129.5 (C-2'''), 130.2 (C-*ipso*), 139.2 (C-6''), 146.1 (C-4''), 163.8 (C-4'), 164.4 (C-6'); 161.2 (C-2'), 170.7 (C-4).

3-[4'-(4''-Chlorophenyl)-6'-(3''-methylphenyl)pyrimidin-2'-yl]-2-phenylthiazolidin-4-one (31). IR spectrum, ν, cm^{-1}: 3060, 3027, 2927, 2851, 1721, 1626, 1576, 1398, 781, 728, 694, 650. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.40 (3H, s, CH_3); 3.20 (1H, d, *J* = 15.0, H-5*a*); 3.37 (1H, d, *J* = 15.1, H-5*e*); 5.26 (1H, s, H-2); 7.18–8.33 (14H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 25.2 (CH_3 on aryl ring), 34.5 (C-5), 62.9 (C-2), 108.9 (C-5'), 131.4 (C-2'''), 126.1–130.4 (C arom.), 133.1 (C-*ipso*), 138.7 (C-6''), 139.1 (C-4''), 164.8 (C-4'), 165.0 (C-6'), 161.2 (C-2'), 170.8 (C-4).

3-[4'-(4''-Chlorophenyl)-6'-(3''-chlorophenyl)pyrimidin-2'-yl]-2-phenylthiazolidin-4-one (32). IR spectrum, ν, cm^{-1}: 3060, 3027, 2927, 2852, 1727, 1627, 1575, 1400, 897, 787, 730, 693. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.20 (1H, d, *J* = 15.2, H-5*a*); 3.36 (1H, d, *J* = 15.2, H-5*e*); 5.26 (1H, s, H-2); 7.28–8.20 (14H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.5 (C-5), 62.5 (C-2), 108.7 (C-5'), 129.1 (C-2'''), 126.0–128.6 (C arom.), 139.1 (C-6''). 141.8 (C-4''), 164.1 (C-4'), 161.3 (C-6'), 165.3 (C-2'), 170.9 (C-4).

3-[4'-(4''-Chlorophenyl)-6'-(3''-fluorophenyl)pyrimidin-2'-yl]-2-phenylthiazolidin-4-one (33). IR spectrum, ν, cm^{-1}: 3065, 3027, 2926, 2853, 1719, 1627, 1576, 1394, 897, 833, 776, 728, 695. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 3.18 (1H, d, *J* = 14.9, H-5*a*); 3.35 (1H, d, *J* = 14.9, H-5*e*); 5.26 (1H, s, H-2); 7.18–8.19 (14H, m, arom.). A singlet for CH proton in position 5' of the pyrimidine moiety is merged with aromatic protons. ^{13}C NMR spectrum, δ, ppm: 34.1 (C-5), 62.6 (C-2), 110.1 (C-5'), 133.2 (C-2'''), 127.3–143.1 (C arom.), 145.1 (C-6''), 146.8 (C-4''), 166.8 (C-4'), 167.0 (C-6'), 163.4 (C-2''), 171.8 (C-4).

The authors are thankful to NMR Research Centre, Indian Institute of Science, Bangalore, for recording spectra. One of the authors, V. Kanagarajan, is grateful to the Council of Scientific and Industrial Research (CSIR), New Delhi, Republic of India, for providing financial support in the form of a CSIR-Senior Research Fellowship in Organic Chemistry. J. Thanusu wishes to thank Annamalai University authorities for providing financial support in the form of a Research Fellowship.

REFERENCES

1. C. J. Andres, J. J. Bronson, S. V. D'Andrea, M. S. Deshpande, P. J. Falk, K. A. Grant-Young, W. E. Harte, Hsu-Tso Ho, P. F. Misco, J. G. Robertson, D. Stock, Yaxiong Sun, and A. W. Walsh, *Bioorg. Med. Chem. Lett.*, **10**, 715 (2000).

2. G. K. Nampurath, S. P. Mathew, Vivek Khanna, R. T. Zachariah, Suman Kanji, and Mallikarjuna Rao Chamallamudi, *Chem*. *Biol*. *Interact.*, **171**, 363 (2008).
3. R. Ottanà, R. Maccari, R. Ciurleo, M. G. Vigorita, A. M. Panico, V. Cardile, F. Garufi, and S. Ronsisvalle, *Bioorg*. *Med*. *Chem*., **15**, 7618 (2007).
4. J. N. Narendra Sharath Chandra, Manish Malviya, C. T. Sadashiva, M. N. Subhash, and K. S. Rangappa, *Neurochem*. *Int*., **52**, 376 (2008).
5. V. Kishore, N. K. Narain, S. Kumar, and S. S. Parmar, *Pharmacol*. *Res*. *Commun*., **8**, 43 (1976).
6. B. B. Newbould, *Br*. *J*. *Pharmacol*. *Chemother*., **24**, 632 (1965).
7. P. Schauer, M. Likar, M. Tisler, A. Krbavcic, and A. Pollak, *Pathol*. *Microbiol*., **28**, 382 (1965).
8. V. N. Chaubey and H. Singh, *Bull*. *Chem*. *Soc*. *Jpn*., **43**, 2233 (1970).
9. E. B. Akerblom, *J. Med*. *Chem*., **17**, 609 (1974).
10. M. D. Litvinchuk, *Farmakol*. *Toksikol*., **26**, 725 (1963).
11. A. K. Dimri and S. S. Parmar, *J*. *Heterocycl. Chem*., **15**, 335 (1978).
12. S. S. Parmar, C. Dwivedi, A. Chaudhari, and T. K. Gupta, *J*. *Med*. *Chem*., **15**, 99 (1972).
13. S. P. Singh, S. S. Parmar, Krishna Raman, and V. I. Stenberg, *Chem*. *Rev*., **81**, 175 (1981).
14. P. D. Jacobus, Van Veldhoven, C. W. Lisa, Chang, J. Künzel, T. Mulder-Krieger, R. Struensee-Link, M. W. Beukers, J. Brussee, and I. P. Ijzerman, *Bioorg*. *Med*. *Chem*., **16**, 2741 (2008).
15. T. V. Hughes, S. L. Emanuel, A. K. Beck, S. K. Wetter, P. J. Connolly, Prabha Karnachi, Michael Reuman, Jabed Seraj, AR Fuentes-Pesquera, R. H. Gruninger, S. A. Middleton, Ronghui Lin, J. M. Davis, and D. F. C. Moffat, *Bioorg. Med*. *Chem*. *Lett*., **17**, 3266 (2007).
16. M. T. Chhabria, H. G. Bhatt, H. G. Raval, and P. M. Oza, *Bioorg*. *Med*. *Chem*. *Lett*., **17**, 1022 (2007).
17. K. L. Sayle, J. F. Bentley, T. Boyle, A. H. Calvert, Yuzhu Cheng, N. J. Curtin, J. A. Endicott, B. T. Golding, I. R. Hardcastle, P. Jewsbury, V. Mesguiche, D. R. Newell, M. E. M. Noble, R. J. Parsons, D. J. Pratt, L. Z. Wang, and R. J. Griffin, *Bioorg*. *Med*. *Chem*. *Lett*., **13**, 3079 (2003).
18. A. Pastor, R. Alajarin, J. J. Vaquero, J. Alvarez-Builla, M. Fau de Casa-Juana, C. Sunkel, J. G. Priego, I. Fonseca, and J. Sanz-Aparicio, *Tetrahedron*, **50**, 8085 (1994).
19. M. S. Youssouf, P. Kaiser, G. D. Singh, S. Singh, S. Bani, V. K. Gupta, N. K. Satti, K. A. Suri, and R. K. Johri, *Int*. *Immunopharmacol*., **8**, 1049 (2008).
20. C. Gasse, D. Douguet, V. Huteau, G. Marchal, H. Munier-Lehmann, and S. Poche, *Bioorg*. *Med*. *Chem*., **16**, 6075 (2008).
21. M. Gopalakrishnan, P. Sureshkumar, V. Kanagarajan, and J. Thanusu, *J*. *Sulf*. *Chem*., **28**, 383 (2007).
22. M. Gopalakrishnan, P. Sureshkumar, J. Thanusu, and V. Kanagarajan, *J*. *Enz*. *Inhib*. *Med*. *Chem*., **23**, 974 (2008).
23. M. Gopalakrishnan, P. Sureshkumar, J. Thanusu, and V. Kanagarajan, *J*. *Enz*. *Inhib*. *Med*. *Chem*., **23**, 347 (2008).
24. M. Gopalakrishnan, J. Thanusu, and V. Kanagarajan, *Med. Chem*. *Res*., **16**, 392 (2007).
25. M. Gopalakrishnan, P. Sureshkumar, J. Thanusu, V. Kanagarajan, R. Govindaraju, and G. Jayasri, *J*. *Enz*. *Inhib*. *Med*. *Chem*., **22**, 709 (2007).
26. W. Guthrie and X. P. Wang, *Can*. *J*. *Chem*., **69**, 339 (1991).
27. S. Kothari, M. Singhal, D. Vijayvergia, R. Vyas, and B. L. Verma. *J*. *Indian Chem*. *Soc*., **77**, 329 (2000).