Synthesis of Thiazolidinone Related to Pyrroloquinoline Dicarbonitrile

NADIA ALI AHMED ELKANZI^{1,2,*}

¹Chemistry Department, Faculty of Science, Jof University, P.O. Box 2014, Aljof, Saudi Arabia

²Chemistry Department, Faculty of Science, Aswan University, P.O. Box 81528, Aswan, Egypt

*Corresponding author: E-mail: kanzi20@yahoo.com

Received: 15 November 2017;

Accepted: 11 January 2018;

Published online: 28 February 2018;

AJC-18807

Reaction of 5,12-diamino-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (**2**) with different aromatic nitroso compounds (β -nitroso α -naphthol, *p*-nitroso phenol, *p*-nitroso N,N-dimethyl aniline) in presence of ethanol and few drops of piperidine catalyst afford the corresponding Schiff bases (**3a-c**). Also compound **3a** was treated with thioglycolic acid in dry benzene and the water formed after heating the reaction mixture by refluxed for 6 h. removed by Dean-Stark apparatus, then benzene removed by distillation, the solid product formed crystallized from ethanol to give compound **4a**. Similarly, other compounds **4b** and **4c** have been synthesized. The structure of compounds **3a-c** and **4a-c** was demonstrated by elemental analysis, IR, ¹H NMR and ¹³C NMR spectra and mass spectra.

Keywords: Condensation, Thiazolidinones, Treatment, Thioglycolic acid, Synthesis.

INTRODUCTION

Derivatives of thiazolidinones exhibit various activity like diuretic, antiparasitical, tuberculostatic, organoleptic, antileukaemic and antibiotic activity [1,2]. Thiazolidinone derivatives also exhibit analogues as potent anti-HIV agents [3-6]. Heterocycles compounds which have sulfur nucleus possess medical properties [7]. 4-Thiazolidinones provide antimicrobial properties as a part of some different biological activities [8], antifungal [9], antiviral [10], antituberculostatic [11], anti-HIV [12], cardioprotective [13], anticancer [14], anticonvulsant [15], anti-inflammatory [16] and analgesic properties [17].

The compounds which possess quinoid molecules considered very important compound in organic chemistry. The Patai's series the chemistry of functional groups [18] in two volumes contains physical, chemical properties and synthesis of quinones compounds. The reactivity of quinones compounds depends upon the substituents present in rings of quinones and heterocyclic quinones [19]. In addition compounds containing heteroaromatic rings regularly are playing important role as supports of bioactive substances. It is known that the pyridone and its derivatives are among the most popular N-heteroaromatic compounds Integrated into the structures of many pharmaceutical compounds and their structural units occur in several molecules showing diverse biological activities [20-25].

Recently, a series of pyridine derivatives were reported to possess antioxidant, anticancer and angiotensin-I-converting enzyme (ACE-I) inhibitory activity [26-28].

Many of the natural products which named as bio-active natural products contains quinoline molecules and also in several heterocyclic scaffolds [29]. The compounds which contains branched quinolone in their structure aid in the knowledge of drug and possess antimalarial [30] properties as a part of their pharmacological properties, also exhibit activity against protozoal [31], tubercular [32], resistance properties to HIV [33], antimicrobial effect [34], resistant to fungus [35] and anticancer activity [36]. The derivatives of quinoline considered as fluorophores [37]. The quinone was also examined as an organic semiconductors [38].

On the other hand, quinine derivatives possess antipyretic properties [39] as well as being found a many kinds of drugs like the fluoroquinolone antibacterials *viz.* ciprofloxacin [40] and levofloxacin [41].

EXPERIMENTAL

Reagents were purchased from Sigma Aldrich (Bayouni Trading Co. Ltd., Saudi Arabia) and used without further purification. Reaction progress was monitored by thin-layer chromatography on silica gel pre-coated F254Merck plates (Darmstadt, Germany). Spots were visualized by ultraviolet irradiation. Melting points were determined on a Gallenkamp electro thermal melting point apparatus (Weiss-Gallenkamp, Loughborough, UK) and are uncorrected. IR spectra were recorded as potassium bromide disks using Bruker-Vector 22 Fourier transform infrared spectrophotometer (Billerica, MA). The NMR spectra were recorded

with a Varian Mercury VXR-300 NMR spectrometer (Palo Alto, CA) at 300 and 75 MHz for ^1H NMR and ^{13}C NMR spectra, respectively, is using DMSO- d_6 as solvents. Mass spectra were recorded on a Hewlett Packard MS-5988 spectrometer (Palo Alto, CA) at 70 eV. Elemental analyses were carried out at the Micro-analytical Center of Cairo University, Giza, Egypt.

5,12-Diamino-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (2): To a solution of compound **1** [42] (0.01 mol, 3.22 g), chloroacetylchloride (0.01 mol, 1.13 g) were mixed in ethanol 30 mL and triethylamine (0.5 mL) was treated as catalyst. The reaction mixture were heated under reflux for 10 h, then mixture were exposed to evaporation by reduced pressure. Then the precipitate filtered [43], recrystallized from mixture of ethanol and dimethyl formamide to afford the corresponding compound **2**.

This compound was obtained as deep blue crystals. m.p.: $> 300^\circ\text{C}$, Yield: 65 % (EtOH/DMF). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2217 (CN), 1690 (CO), 1675-1640 (CO). ^1H NMR (DMSO- d_6 , δ ppm): 3.12 (s, 4H, 2CH_2), 3.17 (s, 4H, 2CH_2), 4.17 (s, 2H, 2CH), 6.87 (brs, 4H, 2NH_2). ^{13}C NMR (DMSO- d_6 , ppm): δ_{C} : 45.48, 66.53, 70.83, 80.53, 115.89, 113.78, 164.21, 196.77, 206.04; MS (m/z , (%)): 402 (30) [M^+]. Anal. (%) calcd. for $\text{C}_{20}\text{H}_{14}\text{N}_6\text{O}_4$ (402.36): C, 59.70; H, 3.51; N, 20.89; Found: C, 59.73; H, 3.55; N, 20.91.

General procedure for synthesis of compounds 3a-c: To a solution of compound **2** (0.01 mol, 4.02 g) in ethanol 30 mL different aromatic nitroso compounds (β -nitroso α -naphthol, *para*-nitroso phenol, *para*-nitroso N,N-dimethyl aniline (0.01 mol)) and few drops of piperidine (0.5 mL) was added as catalyst, then the mixture was refluxed for 8 h. After the evaporation of solvent, the residue was poured in to ice/water. The precipitate formed was filtered and crystalized from methanol.

(3,10)-5,12-Diamino-3,10-bis[(1-hydroxynaphthalen-2-yl)imino]-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (3a): This compound was obtained as violet red crystals. m.p.: 195°C , Yield: 57 % (MeOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2215 (CN), 1690 (CO), 1675-1640 (CO), 3400-3500 (OH). ^1H NMR (DMSO- d_6 , δ ppm): 3.73 (s, 4H, 2CH_2), 4.2 (s, 2H, 2CH), 6.94 (brs, 4H, 2NH_2), 10.01 (brs, 2H, 2OH), 7.01-8.02 (m, 12H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 61.59, 68.35, 90.23, 115.91, 154.26, 151.81, 205.37, 196.58, 146.74, 155.58, 114.02, 126.72, 128.81, 130.36; MS (m/z , (%)): 712 (25) [M^+]. Anal. (%) calcd. for $\text{C}_{40}\text{H}_{24}\text{N}_8\text{O}_6$ (712.67): C, 67.41; H, 3.39; N, 15.72 Found: C, 67.44; H, 3.41; N, 15.74.

(3,10)-5,12-Diamino-3,10-bis[(4-hydroxyphenyl)imino]-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (3b): This compound was obtained as green crystals. m.p.: 215°C , Yield: 60 % (MeOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2214 (CN), 1690 (CO), 1675-1640 (CO), 3400-3500 (OH). ^1H NMR (DMSO- d_6 , δ ppm): 3.70 (s, 4H, 2CH_2), 4.15 (s, 2H, 2CH), 6.91 (brs, 4H, 2NH_2), 10 (brs, 2H, 2OH), 7.01-8.02 (m, 8H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 61.59, 68.35, 90.23, 115.91, 154.26, 151.81, 205.37, 196.58, 146.74, 155.58, 114.02, 126.72, 128.81, 130.36; MS (m/z , (%)): 612 (50) [M^+].

Anal. (%) calcd. for $\text{C}_{32}\text{H}_{20}\text{N}_8\text{O}_6$ (612.55): C, 62.74; H, 3.29; N, 18.29; Found: C, 62.76; H, 3.32; N, 18.33.

(3,10)-5,12-Diamino-3,10-bis[(4-isopropylphenyl)imino]-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (3c): This compound was obtained as brown crystals. m.p.: 175°C , Yield: 60 % (MeOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2213 (CN), 1690 (CO), 1675-1640 (CO). ^1H NMR (DMSO- d_6 , δ ppm): 3.21 (s, 12H, 4CH_3), 4.09 (s, 4H, 2CH_2), 4.32 (s, 2H, 2CH), 6.91 (brs, 4H, 2NH_2), 7.01-8.02 (m, 8H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 41.48, 61.59, 68.35, 90.23, 115.91, 154.26, 151.81, 205.37, 196.58, 146.74, 155.58, 114.02, 126.72, 128.81, 130.36; MS (m/z , (%)): 666 (30) [M^+]. Anal. (%) calcd. for $\text{C}_{36}\text{H}_{30}\text{N}_{10}\text{O}_4$ (666.69): C, 64.86; H, 4.54; N, 21.01; Found: C, 64.88; H, 4.57; N, 21.03.

Synthesis of spiro thiazolidinone (4a-c): To a solution of compound **3a** in dry benzene (50) mL thioglycolic acid was added and the reaction mixture was heated under reflux for 6 h. Dean-Stark apparatus was used to remove water which formed during the reaction. the reaction was monitored by TLC (benzene-ether was used as eluent). Benzene was removed by distillation after the reaction have been completed, the solid product formed dissolved in methanol (50 mL). The solution formed heated gently and poured with solution of sodium bicarbonate which used to remove excess of acid. the solid product formed was collected by filtration, washed by ether and crystallized from ethanol to afford the corresponding **4a**. Similarly, other compounds **4b** and **4c** have been synthesized.

Spectral data

Compound 4a: Red crystals. m.p.: 250°C , Yield: 65 % (EtOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2216 (CN), 1690 (CO), 1675-1640 (CO), 3400-3500 (OH). ^1H NMR (DMSO- d_6 , δ ppm): 3.88 (s, 4H, 2CH_2), 4.16 (s, 4H, 2CH_2), 4.28 (s, 2H, 2CH), 6.96 (brs, 4H, 2NH_2), 10.01 (brs, 2H, 2OH), 7.01-8.02 (m, 12H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 31.52, 58.21, 70.35, 90.21, 115.91, 154.26, 151.81, 205.37, 196.57, 147.86, 155.58, 114.02, 126.72, 128.81, 130.36, 171.52, 206.24; MS (m/z , (%)): 860 (35) [M^+]. Anal. (%) calcd. for $\text{C}_{44}\text{H}_{28}\text{N}_8\text{O}_8\text{S}_2$ (860.87): C, 61.39; H, 3.28; N, 13.02; S, 7.45; Found: C, 61.42; H, 3.32; N, 13.6; S, 7.48.

Compound 4b: Yellow crystals. m.p.: 275°C , Yield: 70 % (EtOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2215 (CN), 1690 (CO), 1675-1640 (CO), 3400-3500 (OH). ^1H NMR (DMSO- d_6 , δ ppm): 3.86 (s, 4H, 2CH_2), 4.19 (s, 2H, 4CH_2), 4.13 (s, 2H, 2CH), 6.93 (brs, 4H, 2NH_2), 9.97 (brs, 2H, 2OH), 7.01-8.02 (m, 8H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 31.52, 58.21, 70.35, 90.21, 115.91, 154.26, 151.81, 205.37, 196.57, 147.86, 155.58, 114.02, 126.72, 128.81, 130.36, 171.52, 206.24; MS (m/z , (%)): 760 (40) [M^+]. Anal. (%) calcd. for $\text{C}_{36}\text{H}_{24}\text{N}_8\text{O}_8\text{S}_2$ (760.75): C, 56.84; H, 3.18; N, 14.73; S, 8.43; Found: C, 56.86; H, 3.21; N, 14.77; S, 8.45.

Compound 4c: Reddish brown crystals. m.p.: 235°C , Yield: 60 % (MeOH). IR (KBr, ν_{max} , cm^{-1}): 3400-3150 (NH_2), 2214 (CN), 1690 (CO), 1675-1640 (CO). ^1H NMR (DMSO- d_6 , δ ppm): 3.71 (s, 12H, 4CH_3), 3.91 (s, 4H, 2CH_2), 4.21 (s, 4H, 2CH_2), 4.43 (s, 2H, 2CH), 6.91 (brs, 4H, 2NH_2), 7.01-8.02 (m, 8H, Ar protons). ^{13}C NMR (DMSO- d_6 , ppm): 31.52,

58.21, 70.35, 90.21, 115.91, 154.26, 151.81, 205.37, 196.57, 147.86, 155.58, 114.02, 126.72, 128.81, 130.36, 171.52, 206.24; MS (*m/z*, (%)): 814 (40) [M⁺]. Anal. (%) calcd. for C₄₀H₃₄N₁₀O₆S₂ (814.89); C, 58.96; H, 4.21; N, 17.19; S, 7.87; Found: C, 58.99; H, 4.26; N, 17.21; S, 7.90.

RESULTS AND DISCUSSION

The activation of C₃ by cyano group renders the substituted methyl group at the carbon number 2 in compound **1** ready to react with chloro acetyl chloride *via* cyclo condensation reaction afford the corresponding compound **2** (Scheme-I). The spectrum of IR provide a bands at 1690 for ν(CO), 1675-1640 ν(CO). The ¹H NMR spectra revealed the presence of δ 3.12 (s, 4H, 2CH₂), 3.17 (s, 4H, 2CH₂), 4.17 (s, 2H, 2CH), 6.87 (brs, 4H, 2NH₂). The structure of compound **2** was established by ¹H NMR, ¹³C NMR spectra, IR, mass spectra and elemental analysis.

Treatment of 5,12-diamino-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (**2**) with various kinds of compounds for aromatic nitroso (β-nitroso α-naphthol, *para*-nitroso phenol, *para*-nitroso N,N-dimethyl aniline), ethanolic solvent used in presence of piperidine catalyst (5 mL) afford the corresponding Schiff's bases **3a-c** (Scheme-I). The structure of compounds **3a-c** was demonstrated by mass spectra, ¹H NMR, ¹³C NMR spectra, IR and elemental analysis.

On the other hand compound **3a** was treated with mercaptoacetic acid in benzene dried and the water formed after heating the mixture of reactant by heating with reflux to 6 h, removed by Dean-Stark apparatus, then benzene removed by distillation, the solid product formed crystallized from ethanol to give **4a** similarly, other compounds (**4b**, **4c**) have been synthesized (Scheme-II).

The compounds **4a-c** in IR spectra revealed the absorption band in the region 1690-1640 cm⁻¹ this due to The vibration of cyclic carbonyl group (C=O), CN group exhibit absorption band at 2216-2214 cm⁻¹. The NH₂ showed band at 3400-3150 cm⁻¹. The ¹H NMR spectra of compounds **4a-c** afford multiples at δ 7.01-8.02. A singlet due to NH₂ was observed at δ 6.91-6.96.

The OH in both compounds **4a** and **4b** appeared as a broad singlet signals at δ 10.01 and 9.97 respectively.

Conclusion

In this study, application methodology to promote the synthesis of spiro thiazolidinone derivatives by the reaction of 5,12-diamino-2,6,9,13-tetraoxo-1,2,3,6,6a,8,9,10,13,13a-decahydroindolizino[5,6-g]pyrrolo[1,2-a]quinoline-4,11-dicarbonitrile (**2**) and mercapto acetic acid in pure good and satisfied yield. The structure of synthesized compounds were established by IR, ¹H NMR, ¹³C NMR and Mass spectra.

ACKNOWLEDGEMENTS

The financial support from Aswan University, Egypt and Jouf University, Kingdom of Saudi Arabia is gratefully acknowledged.

REFERENCES

1. F.C. Brown, *Chem. Rev.*, **61**, 463 (1961); <https://doi.org/10.1021/cr60213a002>.
2. M.S. Raasch, *J. Heterocycl. Chem.*, **11**, 587 (1974); <https://doi.org/10.1002/jhet.5570110424>.
3. A. Chimirri, S. Grasso, A.M. Monforte, P. Monforte and M. Zappalà, *Farmaco*, **46**, 817 (1991).
4. A. Chimirri, S. Grasso, A.M. Monforte, P. Monforte and M. Zappalà, *Farmaco*, **46**, 925 (1991).
5. A. Chimirri, S. Grasso, C. Molica, A.M. Monforte, P. Monforte and M. Zappalà, *Farmaco*, **51**, 279 (1996).
6. A. Chimirri, S. Grasso, P. Monforte, A. Rao, M. Zappalà, A.M. Monforte, C. Pannecouque, M. Witvrouw, J. Balzarini and E. De Clercq, *Antivir. Chem. Chemother.*, **10**, 211 (1999); <https://doi.org/10.1177/095632029901000405>.
7. K. Lalit, B. Shashi and J. Kamal, *Int. J. Sci.*, **2**, 23 (2012).
8. S.L. Devappa, K.R.V. Reddy, R. Govinda, K.B. Reddy, K.N. Sahana and N.C. Smitha, *Int. J. Chemtech Res.*, **2**, 1220 (2010).
9. A. Srinivas, A. Nagaraj and C.S. Reddy, *Eur. J. Med. Chem.*, **45**, 2353 (2010); <https://doi.org/10.1016/j.ejmech.2010.02.014>.
10. V. Ravichandran, A. Jain, K.S. Kumar, H. Rajak and R.K. Agrawal, *Chem. Biol. Drug Des.*, **78**, 464 (2011); <https://doi.org/10.1111/j.1747-0285.2011.01149.x>.
11. V.V. Vintonyak, K. Warburg, B. Over, K. Hübel, D. Rauh and H. Waldmann, *Tetrahedron*, **67**, 6713 (2011); <https://doi.org/10.1016/j.tet.2011.04.026>.
12. V. Ravichandran, B.R. Prashantha Kumar, S. Sankar and R.K. Agrawal, *Eur. J. Med. Chem.*, **44**, 1180 (2009); <https://doi.org/10.1016/j.ejmech.2008.05.036>.

13. T. Kato, T. Ozaki and N. Ohi, *Tetrahedron Asymm.*, **10**, 3963 (1999); [https://doi.org/10.1016/S0957-4166\(99\)00441-3](https://doi.org/10.1016/S0957-4166(99)00441-3).
14. M.E. Voss, P.H. Carter, A.J. Tebben, P.A. Scherle, L.A. Thompson, G.D. Brown, M. Xu, Y.C. Lo, G. Yang, R.-Q. Liu, P. Strzemienski, J.G. Everlof, J.M. Trzaskos and C.P. Decicco, *Bioorg. Med. Chem. Lett.*, **13**, 533 (2003); [https://doi.org/10.1016/S0960-894X\(02\)00941-1](https://doi.org/10.1016/S0960-894X(02)00941-1).
15. A. Agarwal, S. Lata, K.K. Saxena, V.K. Srivastava and A. Kumar, *Eur. J. Med. Chem.*, **41**, 1223 (2006); <https://doi.org/10.1016/j.ejmech.2006.03.029>.
16. S.K. Bhati and A. Kumar, *Eur. J. Med. Chem.*, **43**, 2323 (2008); <https://doi.org/10.1016/j.ejmech.2007.10.012>.
17. M. Sugumaran, S. Sethuvani and M. Poornima, *J. Pharm. Biomed. Sci.*, **16**, 13 (2012).
18. S. Patai and Z. Rappoport, *The Chemistry of the Quinoid Compounds*, Wiley-Interscience: New York (1988).
19. M. Tisler ed.: A.R. Katritzky, *Heterocyclic Quinones*, In *Advances in Heterocyclic Chemistry*; Academic Press: London, vol. 45, p. 37 (1989).
20. N.M.H. Taha, A.A.A. Boray, N.M. Saleh, S.A. Fouad, *J. Appl. Sci. Res.*, **9**, 3108 (2013).
21. T. Akhtar, S. Hameed, N. Al-Masoudi, R. Loddio and P. Colla, *Acta Pharm.*, **58**, 135 (2008); <https://doi.org/10.2478/v10007-008-0007-2>.
22. A.A. El-Henawy, S. Mohamed, T. Ma, G.A.M. Ibrahim and A. El-Hag, *New York Sci. J.*, **4**, 20 (2011).
23. A. Mohammadi-Farania, N. Heidarianb and A.N. Aliabadi, *Iran. J. Pharm. Res.*, **13**, 487 (2014).
24. A.A. El-Henawya, S.I. Mohamedb, A.A. Hassana, A.H. Halawaa, M.A. Elnassaga and G.A. Elhagea, *New York Sci. J.*, **4**, 19 (2011).
25. W.R. Chegwidan and I.M. Spencer, *Inflammopharmacology*, **3**, 231 (1995); <https://doi.org/10.1007/BF02659120>.
26. M. Miriana, A. Zarghib, S. Sadeghia, P. Tabarakic, M. Tavallaec, O. Dadrassc and H. Sadeghi-Aliabadi, *Iran. J. Pharm. Res.*, **10**, 741 (2011).
27. A. Scozzafava, T. Owa, A. Mastrolorenzo and C.T. Supuran, *Curr. Med. Chem.*, **10**, 925 (2003); <https://doi.org/10.2174/0929867033457647>.
28. Y. Ren, L. Zhang, C.-He. Zhou and R.-X. Geng, *Med. Chem.*, **4**, 640 (2014); <https://doi.org/10.4172/2161-0444.1000207>.
29. (a) R.S. Keri and S.A. Patil, *Biomed. Pharmacother.*, **68**, 1161 (2014); <https://doi.org/10.1016/j.biopha.2014.10.007>.
(b) J.B. Simoes, A. de Fátima, A.A. Sabino, L.C. Almeida Barbosa and S.A. Fernandes, *RSC Advances*, **4**, 18612 (2014); <https://doi.org/10.1039/C4RA02036G>.
(c) H. Li, C. Wang, H. Huang, X. Xu and Y. Li, *Tetrahedron Lett.*, **52**, 1108 (2011); <https://doi.org/10.1016/j.tetlet.2010.12.102>.
30. (a) K. Kaur, M. Jain, R.P. Reddy and R. Jain, *Eur. J. Med. Chem.*, **45**, 3245 (2010); <https://doi.org/10.1016/j.ejmech.2010.04.011>.
(b) R. Sharma, S. Patil and P. Maurya, *Environ. Res.*, **25**, 189 (2014);
(c) D.D. N'Da and P. Smith, *J. Med. Chem. Res.*, **23**, 1214 (2014); <https://doi.org/10.1007/s00044-013-0748-4>.
31. A. Inam, S.M. Siddiqui, T.S. Macedo, D.R.M. Moreira, A.C.L. Leite, M.B.P. Soares and A. Azam, *Eur. J. Med. Chem.*, **75**, 67 (2014); <https://doi.org/10.1016/j.ejmech.2014.01.023>.
32. S.R. Patel, R. Gangwal, A.T. Sangamwar and R. Jain, *Eur. J. Med. Chem.*, **93**, 511 (2015); <https://doi.org/10.1016/j.ejmech.2015.02.034>.
33. (a) R. Musiol, *Curr. Pharm. Des.*, **19**, 1835 (2013); <https://doi.org/10.2174/1381612811319100008>.
(b) L.M. Hu, S. Yan, Z.G. Luo, X. Han, Y.J. Wang, Z.Y. Wang and C.C. Zeng, *Molecules*, **17**, 10652 (2012); <https://doi.org/10.3390/molecules170910652>.
34. (a) V. Krishnakumar, F.R.N. Khan, B.K. Mandal, S. Mitta, R. Dhasamandha and V.N. Govindan, *Res. Chem. Intermed.*, **38**, 1819 (2012); <https://doi.org/10.1007/s11164-012-0505-1>.
(b) L.K. Xia, A. Idhayadhulla, Y.R. Lee, S.H. Kim and Y. Wee, *J. Comb. Sci.*, **16**, 333 (2014); <https://doi.org/10.1021/co500002s>.
(c) J.A. Makawana, C.B. Sangani, S.B. Teraiya and H.L. Zhu, *Med. Chem. Res.*, **23**, 471 (2014); <https://doi.org/10.1007/s00044-013-0655-8>.
35. (a) S. Vandekerckhove, H.G. Tran, T. Desmet and M. D'hooghe, *Bioorg. Med. Chem. Lett.*, **23**, 4641 (2013); <https://doi.org/10.1016/j.bmcl.2013.06.014>.
(b) F.H. Havaladar and S.M. Burudkar, *Indian J. Heterocycl. Chem.*, **22**, 197 (2012).
36. (a) V.R. Solomon and H. Lee, *Curr. Med. Chem.*, **18**, 1488 (2011); <https://doi.org/10.2174/092986711795328382>.
(b) M. Chen, H. Chen, J.W. Ma, X. Liu and S. Zhang, *Bioorg. Med. Chem. Lett.*, **24**, 2867 (2014); <https://doi.org/10.1016/j.bmcl.2014.04.091>.
37. J.P. Bridhkoti, R. Gahlaut, H.C. Joshi and S. Pant, *J. Lumin.*, **131**, 1869 (2011); <https://doi.org/10.1016/j.jlumin.2011.04.038>.
38. A.K. Nedeltchev, H. Han and P.K. Bhowmik, *Tetrahedron*, **66**, 9319 (2010); <https://doi.org/10.1016/j.tet.2010.09.108>.
39. J. Achan, A.O. Talisuna, A. Erhart, A. Yeka, J.K. Tibenderana, F.N. Baliraine, P.J. Rosenthal and U. D'Alessandro, *Malar. J.*, **10**, 144 (2011); <https://doi.org/10.1186/1475-2875-10-144>.
40. D.M. Campoli-Richards, J.P. Monk, A. Price, P. Benfield, P.A. Todd and A. Ward, *Drug*, **35**, 373 (1988); <https://doi.org/10.2165/00003495-198835040-00003>.
41. D.S. North, D.N. Fish and J.J. Redington, *Pharmacotherapy*, **18**, 915 (1998); <https://doi.org/10.1002/j.1875-9114.1998.tb03925.x>.
42. N.A.A. Elkanzi, *Int. J. Org. Chem.*, **2**, 352 (2012); <https://doi.org/10.4236/ijoc.2012.24048>.
43. A.K. Khalafallah, R.M.A. El-Aal and N.A.A.E. Kanzi, *J. Chin. Chem. Soc.*, **49**, 387 (2002); <https://doi.org/10.1002/jccs.200200061>.