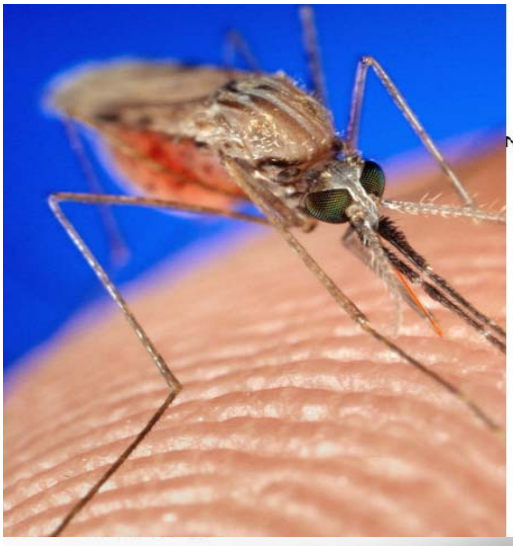
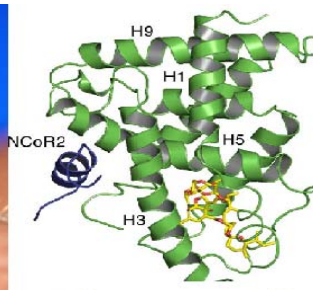
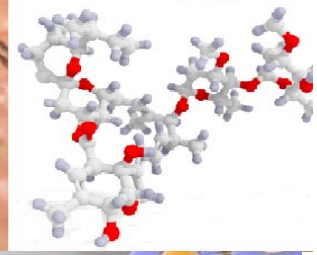
PhytoChem & BioSub Journal

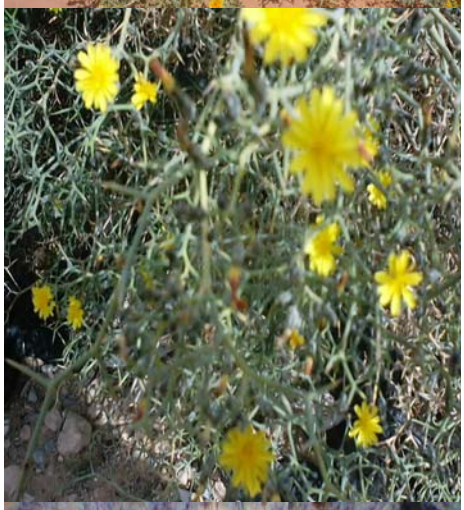
Peer-reviewed research journal on Phytochemistry & Bioactives Substances

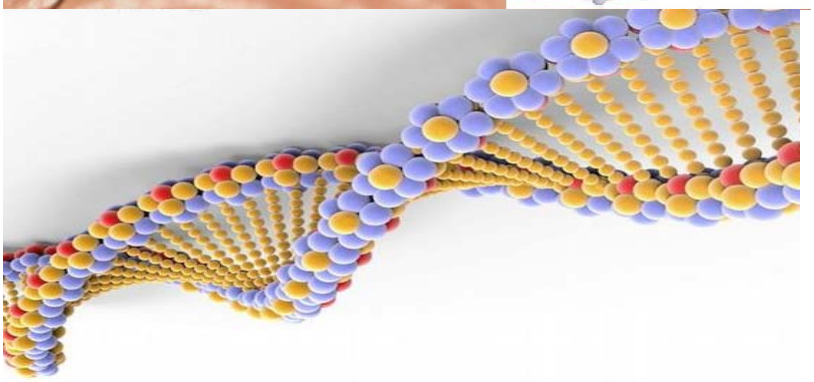
ISSN 2170 - 1768











PCBS Journal

Volume 10 N° 2 **2016**

ISSN 2170-1768

PhytoChem & BioSub Journal

ISSN 2170 – 1768

Peer-reviewed research journal on Phytochemistry & Bioactives Substances

CAS Source Index (CODEN: PBJHB3)

Editor in Chief

Pr *Abdelkrim* CHERITI

Phytochemistry & Organic Synthesis Laboratory

08000, Bechar, Algeria

PhytoChem & BioSub Journal (***PCBS Journal***) is a peer-reviewed research journal published by Phytochemistry & Organic Synthesis Laboratory. The PCBS Journal publishes innovative research papers, reviews, mini-reviews, short communications and technical notes that contribute significantly to further the scientific knowledge related to the field of Phytochemistry & Bioactives Substances (Medicinal Plants, Ethnopharmacology, Pharmacognosy, Phytochemistry, Natural products, Analytical Chemistry, Organic Synthesis, Medicinal Chemistry, Pharmaceutical Chemistry, Biochemistry, Computational Chemistry, Molecular Drug Design, Pharmaceutical Analysis, Pharmacy Practice, Quality Assurance, Microbiology, Bioactivity and Biotechnology of Pharmaceutical Interest). Contributions in all areas at the interface of Chemistry, Pharmacy, Medicine and Biology are welcomed.

Submission of an article to the ***PCBS Journal*** implies that the work described has not been published previously (except in the form of an abstract or as part of a published lecture or academic thesis), that it is not under consideration for publication elsewhere, that its publication is approved by all authors.

The ***PCBS Journal*** reserves the right to submit all received manuscripts to *ad hoc* referees, whose names will be kept confidential, and will have the authority to decide on the pertinence for acceptance. Referees may send back manuscripts to Editor-in-Chief, for transmission to the author(s) with suggestions for necessary alterations, which are to be made in order to conform to the standards and editorial rules of the Journal. All manuscripts should be prepared in MS-Word format, and submitted online to **Phytochem07@yahoo.fr.** Upon receipt of paper submission, the Editor sends an E-mail of confirmation to the corresponding author within 1-4 working days. The Editors reserve the right to edit or otherwise alter all contributions, but authors will receive proofs for approval before publication.

Editorial Board

PhytoChem & BioSub Journal Vol. 10(2) 2016
ISSN 2170-1768
CAS-CODEN:PBJHB3

PCBS Journal
ISSN 2170-1768

PhytoChem & BioSub Journal

2016
Vol.10 No. 2

Microwave-assisted and conventional synthesis of new nitrobenzaldehyde-Schiff base ligands derived from benzothiazolone with potential catalytic properties: A comparative study

Hanane CHABANE, Yasmina ADJEROUD & Messaoud LIACHA*

Laboratory of **S**ynthesis and **O**rganic **B**iocatalysis (LSBO),
Organic Synthesis and Medicinal Chemistry Group,
BADJI Mokhtar University, P.O. Box 12, Annaba 23000, Algeria

Received: June 19, 2016; Accepted: October 17, 2016
Corresponding author Email: m_liacha@yahoo.fr; messaoud.liacha@univ-annaba.dz

DOI:10.163.pcbsj/2016.10.2.73

Abstract. *In the present work, we report the synthesis of a novel series of nitrobenzaldehyde-Schiff base ligands derived from benzothiazolone pharmacophore. The reaction of the appropriate substituted nitrobenzaldehydes (2-nitrobenzaldehyde, 3-nitrobenzaldehyde and 4-nitrobenzaldehyde) with 6-aminobenzothiazolone substrates, under conventional heat and microwave irradiation methods was investigated, in the aim to reduce the time for completion of the reaction and improve the yields for these Schiff base derivatives formation. The new synthesized compounds were characterized through elemental analysis and ^{1}H NMR and ^{13}C NMR spectral data.*

***Key Words*:** *Schiff bases, 2(3H)-benzothiazolone, nitro-substituent effects, green process, catalytic properties*

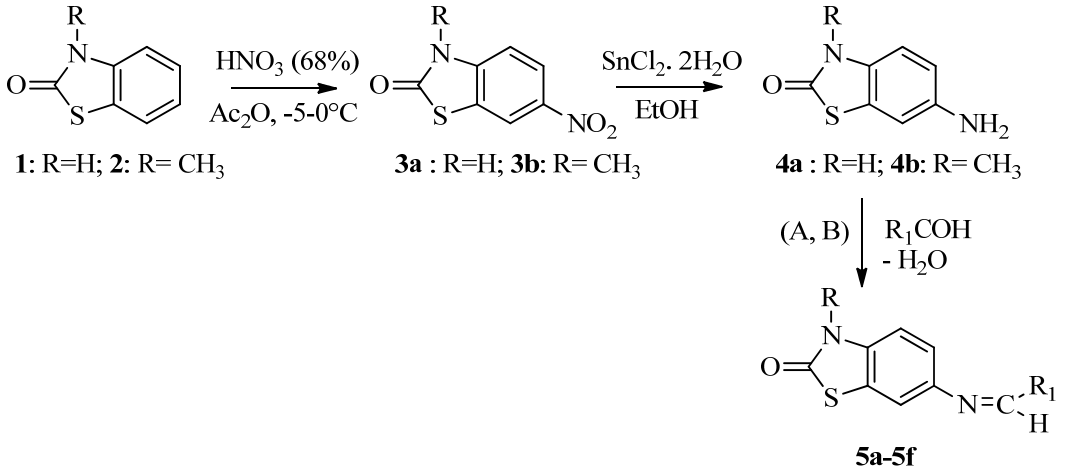
Introduction

Benzothiazolone derivatives constitute an important class of nitrogen and sulphur-containing heterocyclic compounds, extensively studied and used in pharmaceutical chemistry [1, 2]. They have attracted considerable interest due to their broad range of biological and pharmacological activities [3-11]. Some previous study demonstrated that many benzothiazolone derivatives bearing various substituents at position-3 have been reported to exhibit analgesic and anti-inflammatory activity with no observed toxicity [12-13]. Similarly, the nitro group has played an important role in affecting the reactivity and enantioselectivity in asymmetric cyclopropanation and allylic alkylation reactions [14, 15]. Also, the nitrosubstituted benzaldehydes derivatives have been studied, particularly for their Schiff-base compounds in order to investigate their catalytic properties [16-18]. On the other hand, in recent years, the application of microwave irradiation method for the synthesis of organic compounds has opened new perspectives in organic synthesis, and offers advantages over conventional synthetic approach in both isolated yield of the product and required reaction time. This technique has served to support for the development to introduce new methodologies that are efficient and more compatible with the environment [19-25]. As an extension of our reported research studies, on synthetic strategy towards synthesis of pharmaceutically heterocyclic compounds, the present work reveals the comparative aspects of

condensation of some nitro aromatic aldehydes with 6-aminobenzothiazolone derivatives under microwave irradiation and conventional methods. We synthesized a new class of nitrosubstituted 6-(benzylideneamino)benzo[d]thiazol-2(3*H*)-one analogues (**5a-5f**; **Table 1**), and investigated the eventual role of the nitro substituent position effects on the yields and time required for the completion of reaction for the desired Schiff base compounds.

Results and discussion

As a results of present studies related to the development of new heterocyclic compounds, we herein report an easy access to new Schiff bases derived from 2(3*H*)-benzothiazolone and nitrosubstituted benzaldehydes, by the reaction of 6-amino-2(3*H*)-benzothiazolone derivatives with (*o*, *m* and *p*) substituted benzaldehyde, using microwave irradiations as well as conventional synthetic methods. The synthetic route used for the preparation of the novel Schiff base ligands have been realized as shown in scheme 1, and 2(3*H*)-benzothiazolones (**4a-4b)** bearing an amino group in 6-position were used as starting materials to prepare the target compounds (**5a-5f**).
The synthesis of 2(3*H*)-benzothiazolone (**1, R=H**) was carried out by the reaction of *o*-aminothiophenol with urea under heat, that was *N*-methylated with dimethylsulfate in basic medium leading to the formation of the corresponding 3-methy-2(3*H*)-benzothiazolone derivative (**2, R=-CH_3**). Nitration of the aromatic ring of compounds **1** and **2** with nitric acid in acetic anhydride produced the 6-nitro-2(3*H*)-benzothiazolone and 3-methyl-6-nitro-2(3*H*)-benzothiazolone derivatives **3a** and **3b** respectively. Reduction of the nitro group of the nitrobenzothiazolone intermediates was carried out under standard conditions, using tin chloride dihydrate ($SnCl_2$. $2H_2O$) in ethanol to give the corresponding 6-amino-2(3*H*)-benzothiazolone substrates **4a** and **4b** respectively. Finally, the new target compounds (**5a-5f**) were obtained by condensing the appropriate nitrosubstituted benzaldehyde with the corresponding 6-amino-2(3*H*)-benzothiazolone substrates (**4a-4b**) in absolute ethanol, as illustrated in Scheme 1.



Scheme 1. Synthesis of the benzothiazolone Schiff base derivativess (**5a-5f**).
A: method A (Conventional Heat: CH), reflux, ethanol, Glacial acetic acid, 1h
B: method B (Microwave: MW), 100 W, ethanol, 2-6 min.

In the different cases, the obtained results show that the microwave is highest in this reaction under conventional heat conditions. All syntheses of final benzothiazolone benzothiazolone Schiff base derivatives were completed within 60 minutes with yields ranging from 67-91% when

synthesized by conventional method, and in just 2-6 minutes with appreciable yields 76-93% when synthesized by microwave irradiation. The yield and physical data of the synthesized Schiff base compounds are summarized in table 1.

Table 1 Physicochemical data and comparison of microwave and classical heating of the synthesized Schiff base compounds (**5a-5f**).

Entry	Product **5**	R	R'	[a]Mp. (°C)	CH		MW		[d]Mol. F.
					Time (min)	[b]Yield (%)	Time (min)	[c]Yield (%)	
1	**5a**	H	2-NO_2	234-235	60	83	2	88	$C_{14}H_9N_3O_3S$
2	**5b**	CH_3	2-NO_2	157-158	60	91	2	93	$C_{15}H_{11}N_3O_3S$
3	**5c**	H	3-NO_2	275-276	60	75	3	80	$C_{14}H_9N_3O_3S$
4	**5d**	CH_3	3-NO_2	271-272	60	81	3	83	$C_{15}H_{11}N_3O_3S$
5	**5e**	H	4-NO_2	277-278	60	67	3	76	$C_{14}H_9N_3O_3S$
6	**5f**	CH_3	4-NO_2	211-212	60	71	6	80	$C_{15}H_{11}N_3O_3S$

[a]Melting point; [b,c]Isolated yield; [d]Molecular formula.

Based on the results obtained and presented in Table 1, it was found that *ortho* substituted compounds (Table 1, entry **5a** and **5b**) with the electron withdrawing nitro group proved to be more reactive and afford high product yields due to the aldehyde hydrogen bonding. This effect is more pronounced because this *ortho* nitro substituent position has made the carbonyl group more electrophilic due to the strong delocalization of the electron cloud of the sp^2 carbon.

Experimental details

Melting points were determined in open capillary tubes and are uncorrected. The ^{1}H NMR spectra were performed using a Bruker AC 400 spectrometer using dimethylsulfoxide-d_6 with TMS as internal standard, with chemical shifts reported as δ (*ppm*). Reactions were monitored by TLC using silica gel F254 plates and the compounds were visualized by UV light. Compounds **1, 2**, **3a**, **3b**, **4a** and **4b** were previously reported and were prepared as cited in the literature with some minor modifications. Their physical, analytical and spectral properties were in accordance with the literature data [26-30].

General procedure for the preparation of nitro compounds 3a–3b

Nitric acid (68%, 5.30 cm^3, 80 mmol) in 20 cm^3 of acetic anhydride cooled to -0-5°C was added dropwise, a solution of benzothiazolone compounds **1** and **2** (10 mmol) in a minimum of acetic anhydride. The mixture was stirred at -0-5°C for 3 h. The precipitate was filtered, washed with cold water, dried, and recrystallized from suitable solvent to afford the corresponding 6-nitrobenzothiazolones compounds **3a** (56%) and **3b** (68%).

General procedure for the preparation of amino compounds 4a–4b

To a stirring ethanolic solution of 6-nitro-2(3*H*)-benzothiazolone (**4a**) or 3-methyl-6-nitro-2(3*H*)-benzothiazolone (**4b**) (1.0 equiv.) in a 250 cm^3 round bottomed flask, tin chloride dihydrate ($SnCl_2.2H_2O$, 5 equiv.) was added. The reaction mixture was heated at reflux and reaction continued until completion of the reaction (TLC monitoring). After complete reduction, the starting material disappeared, and the solution was allowed to cool down. The p*H* was made slightly basic (p*H* 7–8) by addition of 5% aqueous sodium bicarbonate before extraction with ethyl acetate. The organic phase was washed with brine and dried over magnesium sulfate, and the solvent was removed. The solid 6-aminobenzothiazolone intermediates **4a** (68%) and **4b** (67%), were obtained after being washed with petroleum ether, and used for the next step without further purification.

General procedure for the preparation of Schiff bases derivatives 6 (benzylideneamino) benzo[d]thiazol-2(3*H*)-ones (5a-5f)

Conventional method (method A): Substituted nitrobenzaldehyde derivatives (1 mmol) dissolved in boiling ethanol (10 mL) were mixed with a boiling solution of 6-amino-2(3*H*)-benzothiazolones **(4a-4b)** (1 mmol) in the same solvent (5 mL), and few drops of glacial acetic acid was added. Then the resulting mixture was heated at reflux on a water bath for 1h, and then left to stand overnight at room temperature. The separated solid was filtered, washed repeatedly with water and recrystallized from ethanol to give the desired products **(5a-5f)**.

Microwave method (method B): Compounds **(5a-5f)** were synthesized in the similar manner by treating an equimolar mixture of 6-aminobenzothiazolones **(4a-4b)** with substituted aromatic aldehydes in absolute ethanol in microwave tube. The contents were subjected to microwave irradiation at 100 W for about 2-6 min. Progress of the reaction was monitored by TLC. After the completion of the reaction, solid product was obtained in reaction mixture which was filtered, washed with ethanol, dried, and purified to provide the desired title compounds.

6-(2-Nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5a)
Beige powder; Yield: method A (83%) and method B (88%); M.p. 234-235°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.18 (d, 1H), 7.27 (d, J=10.8Hz, 1H), 7.63 (d, J=2Hz, 1H), 7.75 (t, 1H), 7.85 (t, 1H), 8.09 (d, J=9.2Hz, 1H), 8.16 (d, J=9.6Hz, 1H), 8.91 (s, 1H, N=CH, azomethine), 12.02 (s, 1H, N-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.99 (C=O), 155,34 (N=C), 149.23, 145.44, 13.46, 133.65, 131.75, 129.93, 129.38, 124.47, 124.41, 120.56, 115.47, 112.01 (aromatic carbons). $C_{14}H_9N_3O_3S$ (299.30): Calcd. C 56.18, H 3.03, N 14.04, S 10.71; Found: C 55.89, H 3.00, N 13.71, S 10.42.

3-Methyl-6-(2-nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5b)
Brown powder; Yield: method A (91%) and method B (93%); M.p. 157-158°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.44 (s, 3H, CH_3), 7.39 (d, J=2Hz, 2H), 7.72 (d, J=1.6Hz, 1H), 7.76 (t, 1H), 7.86 (t, 1H), 8.10 (d, J=9.2Hz, 1H), 8.18 (d, J=9.2Hz, 1H), 8.93 (s, 1H, N=CH, azomethine). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 155.76 (C=O), 149.25(N=C), 145.98, 142.87, 136.66, 133.67, 131.82, 129.89, 129.41, 124.49, 122.32, 120.52, 115.61, 111.87 (aromatic carbons) 28.17 (CH_3). $C_{15}H_{11}N_3O_3S$ (313.33): Calcd. C 57.50, H 3.54, N 13.41, S 10.23; Found: C 57.20, H 3.35, N 13.17, S 9.82.

6-(3-Nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5c)
Yellow powder; Yield: method A (75%) and method B (80%); M.p. 275-276°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.17-8.72 (m, 7H, Ar-H), 8.86 (s, 1H, N=CH, azomethine), 11.99 (s, 1H, N-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.92 (C=O), 157.57 (N=C), 148.21, 145.33, 137.59, 135.29 134.47, 130.51, 125.47, 124.31, 122.50, 120.66, 115.45, 111.93 (aromatic carbons). $C_{14}H_9N_3O_3S$ (299.30): Calcd. C 56.18, H 3.03, N 14.04, S 10.71, Found: C 56.15, H 3.01, N 14.00, S 10.60.

3-Methyl-6-(3-nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5d)
Yellow powder; Yield: method A (81%) and method B (83%); M.p. 271-272°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.17 (d, J=8.4Hz, 1H), 7.33 (d, J=10.8Hz, 1H), 7.67 (d, J=2Hz, 1H), 7.80 (t, 1H), 8.33 (m, 2H), 8.72 (s, 1H), 8.86 (s, 1H, N=CH, azomethine), 11.99 (s, 1H, N-H). ^{13}C NMR NMR (100 MHz, DMSO-d_6): δ = 169.92 (C=O), 157.57 (N=C), 148.21, 145.33, 137.59, 135.29, 134.47, 130.51, 125.47, 124.31, 122.50, 120.66, 115.45, 111.93 (aromatic carbons), 29,17 (CH_3).

$C_{15}H_{11}N_3O_3S$ (313.33): Calcd. C 57.50, H 3.54, N 13.41, S 10.23; Found: C 57.10, H 3.01, N 13.81, S 10.60.

6-(4-Nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5e)

Yellow powder; Yield: method A (67%) and method B (76%); M.p. 277-278°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.17 (d, J=8.4Hz, 1H), 7.34 (d, J=10.8Hz, 1H), 7.69 (s, 1H), 8.15 (d, J=10.8, 2H), 8.35 (d, J=8.8Hz, 2H), 8.85 (s, 1H, N=CH, azomethine), 12.00 (s, 1H, N-H). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 169.96 (C=O), 157.49 (N=C), 148.70, 145.28, 141.58, 135.62, 129.44, 124.41, 124.02, 120.89, 115.47, 111.95 (aromatic carbons). $C_{14}H_9N_3O_3S$ (299.30): Calcd. C 56.18, H 3.03, N 14.04, S 10.71; Found: C 56.02, H 3.10, N 14.38, S 10.48.

3-Methyl-6-(4-nitrobenzylideneamino)benzo[d]thiazol-2(3*H*)-one (5f)

Red powder; Yield: method A (71%) and method B (80%); M.p. 211-212°C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.43 (s, 3H, N-CH_3), 7.36 (d, J=8.4Hz, 1H), 7.45 (d, J=10.8Hz, 1H), 7.71 (s, 1H), 8.16 (d, J=8.8 2H), 8.35 (d, J=1.6Hz, 2H), 8.88 (s, 1H, N=CH, azomethine). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 168.61 (C=O), 157.88 (N=C), 148.74, 145.80, 141.53, 136.74, 129.93, 129.49, 124.01, 122.27, 120.78, 115.68, 111.82 (aromatic carbons), 29.18 (CH_3). $C_{15}H_{11}N_3O_3S$ (313.33): Calcd. C 57.50, H 3.54, N 13.41, S 10.23; Found: C 57.11, H 3.10, N 13.43, S 9.83.

Conclusions

In this study, we have developed a simple and efficient synthetic protocol for the preparation of various potentially pharmaceutically useful Schiff base ligands using conventional and microwave heating methodologies. The microwave-assisted method has been compared with the conventional method. This comparative study showed that the microwave technique was excellent method which can be used to prepare benzothiazolinonic Schiff bases in good yields, with a short reaction time, environment friendly and very pure isolated products. Thus, this work opens up new perspectives and will be very useful for further structural activity relationship of potent biologically active benzothiazolone derivatives.

Acknowledgements: This work was supported by Algerian Ministry of Higher Education and Scientific Research (MESRS), (Project number: CNEPRU-E01120140064). Authors are highly thankful to Pr. G. Kirsch, for carrying out spectral ^{1}H-NMR and ^{13}C-NMR and microanalysis for compounds.

References

[1] J. H. Poupaert, P. Carato, E. Colacino and S. Yous, *Curr. Med. Chem.,* 2005, **12**, 877.
[2] P. Carato, S. Yous, D. Sellier, J. H. Poupaert, N. Lebegue and P. Berthelot, *Tetrahedron.,* 2004, **60**, 10321.
[3] T. Takashima, Y. Kadoh and S. Kumada, *Arzneim. Forsch.,* **1992**, *22*, 711.
[4] H. Ucar, K. Van derpoorten, S. Cacciaguerra, S. Spampinato, J. P. Stables, P .Depovere, M. Isa, B. Masereel, J. Delarge and J. H. Poupaert, *J. Med. Chem.,* **1998**, *41*, 1138.
[5] S. H. Ferreira, B. B. Lorenzetti, M. Devissaguet, D. Lesiuer and Y. Tsouderos, *Br. J. Pharmacol.,* 1995, **114**, 303.
[6] S. Yous, J. H. Poupaert, P. Chavatte, J. G. Espiard, D. H. Caignard and D. Lesieur, *Drug Des. Discov.,* 2001, **17**, 331.
[7] K. Van derpoorten, H. Ucar, G. Andrei, R. Snoeck, J. Balzarini and E. De Clercq, *Antivir. Chem. Chemother.,* 1999, **10**, 87.
[8] A. H. Abdelazeem, S. I. Khan, S. W. White, K. J. Sufka and C. R. McCurdy, *Bioog. Med. Chem.,* 2015, **23**, 3248.
[9] O. Petrov, A. Antonova, V. Kalcheva and L. Daleva, *Med. Chem. Res.,* 1995, **5**, 442.

[10] I. Yekini, F. Hammoudi, F. Martin-Nizard, S. Yous, N. Lebegue, P. Berthelot and P. Carato, *Bioorg. Med. Chem.,* 2009, **17**, 7823.
[11] E. Blanc-Delmas, N. Lebegue, V. Wallez, V. Leclerc, C. Carmona, B. Staels, L. Penicaud, L. Casteilla, M. Lonchampt, C. Dacquet, P. Chavatte, P. Berthelot and, D. Lesieur, *Bioorg. Med. Chem.,* 2006, **14**, 7377.
[12] D. S. Doğruer, S. Ünlü, E. Yeşilada and M. F. Şahin, *Il Farmaco.,* 1997, **52**, 745.
[13] D. S. Doğruer, S. Ünlü, M. F. Şahin, E. Yeşilada, *Il Farmaco.,* 1998, **53**, 80.
[14] M. Qiu, G. S. Liu and X. Q. Yao, *Chin. J. Catal.,* 2001, **22**, 77.
[15] Z. Li, Z. Zheng, B. Wan and H. Chen, *J. Mol. Catal. A: Chem.,* 2001, **165**, 67.
[16] W. T. Gao, Z. Zheng, *Molecules* 2003, **8**, 788.
[17] S. L. Renard and T. P. Kee, *J. Organomet. Chem.,* 2002, **643-644**, 516.
[18] I. Karame, M. L. Tommasino, R. Faure, M. Lemaire and *Eur. J. Org. Chem.,* 2003, **7**, 1271.
[19] N. M. Nascimento-Júnior, A. E. Kummerle, E. J. Barreiro and C. A. M. Fraga, *Molecules* 2011, **16**, 9274.
[20] J. A. Seijas, M. P. Vazquez-Tato, M. M. Martinez and J. Rodriguez-Parga, *Green. Chem.,* 2002, **4**, 390.
[21] F. Mavandadi and A. Pilotti, *Drug. Discovery. Today.,* 2006, **11**, 165.
[22] S. K. Upadhyay, R. K. P. Subramanya and S. J. Branko, *Tetrahedron Lett.,* 2010, **51**, 2215.
[23] S. Ravichandran and E. Karthikeyan, *Int. J. Chem. Tech. Res.,* 2011, **3**, 466.
[24] R.S. Oakes, A.A. Clifford and C.M. Rayner, *J. Chem. Soc. Perkin Trans.,* 2001, **1**, 917.
[25] Antonio de la Hoz, Angel Diaz-Ortiz and Andres Moreno, *Chem. Soc. Rev.,* 2005, **34**, 164.
[26] J. J. D'Amico, R. W. Fuhrhop, F. C. Bollinger and W. E. Dahl, *J. Heterocyclic Chem.,* 1986, **23**, 641.
[27] Y. J. Li, C. Y. Li, N. Jin, S. Q. Sun and X. X. Zhou, *Acta. Chim. Sinica.,* 2012, **70**, 151.
[28] O. Diouf, P. Depreux, D. Lesieur, J. H. Poupaert and D. Caignard, *Eur. J. Med. Chem.,* 1995, **30**, 715.
[29] J. J. D'Amico, F. G. Bollinger and J. J. Freeman, *J. Heterocycl. Chem.,* 1988, **25**, 1503.
[30] N. Suzuki, S. Kodoya and R. Donmori, *Chem Pharm Bull.,* 1976, **24**, 1050.

PhytoChem & BioSub Journal

Peer-reviewed research journal on Phytochemistry & Bioactives Substances

ISSN 2170 - 1768

PCBS Journal

ISSN 2170-1768

Edition LPSO - Phytochemistry & Organic Synthesis Laboratory-
http://www.pcbsj.webs.com
https://sites.google.com/site/phytochembsj/
Email: phytochem07@yahoo.fr