I.A.U. Karaj Branch

Journal of Applied Chemical Research, 9, 2, 7-14 (2015)

Journal of Applied Chemical Research

www.jacr.kiau.ac.ir

Synthesis and Insecticide Activity of Octahydroquinazolinone derivatives

Ali Akbari[1*], Asghar Hosseini-Nia[2]

[1]Department of Chemistry, Faculty of Science, University of Jiroft, Jiroft, Iran.

[2]Department of Plant Protection National Research Station of Ornamental Plants, Mahallat, Iran.

(Received 11 Oct. 2014; Final version received 12 Dect. 2014)

Abstract

A simple method for the synthesis of octahydroquinazolinone derivatives in the presence of $BF_3.SiO_2$ and Insecticide activity of these compounds against *spodoptera litura* was investigated to be comparable to commercial pyrethroid insecticides, Cypermethrin and Cyhalothrin. The structure of the isolated compounds was characterized by ^{1}HNMR and FT-IR spectroscopy.The proposed method had some advantages such as high yield, mild reaction condition, ease of operation and workup, high product purity and green process.

Key words: *Insecticidal activity, $BF_3.SiO_2$, Octahydroquinazolinone.*

Introduction

Octahydroquinazolinone derivatives are an important class of the organic compounds which due to their molecular structure, have important biological activities such as antibacterial activity [1,2] and calcium antagonist activity [3,4].

Several methods have been developed for the preparation of Octahydroquinazolinone derivatives. In general, simple procedures have been employed for the synthesis of dihydropyrimidinones using dimedone, aromatic aldehydes and urea/thiourea, in the present of catalysts such as $Zn(OTf)_2$ [2] Nafion-H [4], TMSCl [5], Conc.H_2SO_4 [6], lanthanum oxide [7], $ZrOCl_2.8H_2O$ [8], silica sulfuric acid [9], ionic liquid [tbmim]Cl_2/$AlCl_3$ [10], Phosphotungstic Acid Nanoclusters [11] and ammonium metavanadate [12].

Silica supported boron trifluoride, $BF_3.SiO_2$, which is easy to prepare, shows unusually high acidity which can be controlled by activation temperature, and exhibits considerable catalytic activity [13], enables

**** Corresponding author:*** *Ali Akbari, Department of Chemistry, Faculty of Science, University of Jiroft, Jiroft, P. O. Box 8767161167, Islamic Republic of Iran. E-mail: a.akbari@ujiroft.ac.ir.*

better accessibility of the reactants to the active sites. The $BF_3.SiO_2$ is used in several organic transformations, such as in *Claisen-Schmidt* condensations [14], in syntheses of 14-aryl or alkyl-14*H*-dibenzo[*a,j*] xanthenes [15], 1,2,4,5-tetrasubstituted imidazoles [16], tetrahydrobenzo[a]xanthenes-11-one [17], in the polymerization of styrene [18], the preparation of polyfunctionalized piperidin-4-ones [19], α-amino phosphonates [20], quinoxalines [21], and 3,4-dihydropyrimidin-2(1*H*)-ones [22].

Spodoptera litura is a serious pest causing enormous losses to many economically important cultivated crops such as cotton, soybean, groundnut, tobacco and vegetables [23]. Sometimes it has been found to cause 26–100% yield loss in the field [24]. Its control has depended mostly on application of various insecticides. As a result, many field populations of this pest have developed multiple resistances and field control failure has been observed very frequently [25-29].

Materials and methods

General

The materials were purchased from Sigma–Aldrich and Merck and were used without any additional purification. Products were characterized by FT-IR, ^{1}H-NMR and comparison of their physical properties with those reported in the literature. FT-IR spectra were run on a Bruker, Eqinox 55 spectrometer. A Bruker (DRX-500 Avanes) NMR was used to record the ^{1}H NMR spectra.

Preparation of $BF_3.SiO_2$

3.7 g of BF_3 (7.0 ml of $BF_3.Et_2O$) was added dropwise to a mixture of 6.3 gr of silicagel and 10 ml of chloroform. The mixture was stirred for 1 h at room temperature. The resulted suspension was filtered. The obtained solid was washed by chloroform and dried in a domestic microwave oven for 20 min in power 100 [30].

General procedure for the synthesis of octahydroquinazolinone derivatives in solvent condition

A mixture of aldehydes (10 mmol), dimedone (10 mmol) and urea/thiourea (15 mmol) with the $BF_3.SiO_2$ (10 mol%) in 1,2-dichloroethanesolvent at the reflux. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was extracted with ethyl acetate and the catalyst was separated by the filtration. The organic layer was then washed by deionized water and dried over anhydrous Na_2SO_4. Organic solvent was evaporated under reduced pressure and solid compound was crystallized from absolute ethanol to afford the pure corresponding octahydroquinazolinone derivatives in excellent yields. All products were identified by comparison of their physical and spectral data with those of authentic samples.

In vitro insecticidal activity

The biological assay was conducted against third-instar larvae of S. *litura* (7 ± 1 day old) using the feeding method and topical treatment [31].

Feeding method

The castor leaf was dipped in a 0.1% solution of synthesized compounds for 2 s and then air-dried. Moist filter paper was placed in glass Petri plates (9 cm diameter) on which treated leaf disks were kept. Larvae of S. *litura* preserved for 4h were released individually into each Petri plates. Thirty replications were kept for each treatment. Solvent was used as control. Mortality was observed after 24h.

Topical treatment

The 0.1% stock solution of various compounds was prepared in dichloromethane. 2 mL of each compound was applied on the ventral side of the S. *litura* larvae. Ten treated larvae were released in glass bottles, and fresh tender castor leaves were given as food. Each treatment was kept in triplicate, and solvent was used as control. Mortality was observed after 24h.

Insect growth regulatory activity (IGR)

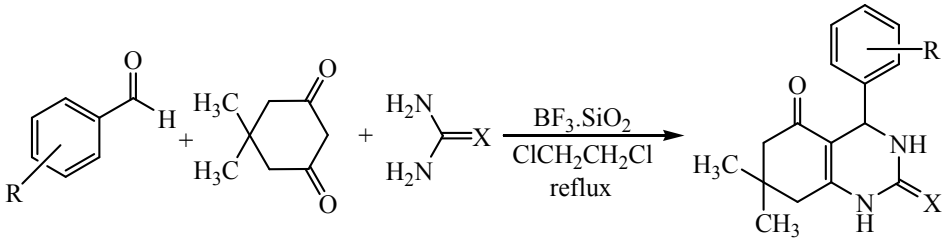
The IGR activity of the above synthesized compounds was evaluated against *S. litura* following the test procedure. Third Instar larvae (*S. litura*) reared on the artificial diet was used for IGR activity. The 0.1% stock solution of test compounds was prepared using appropriate solvent. Newly mold pre-weighed (30-40 mg) 3rd instar larvae were treated through leaf dip method with different concentrations of the compounds. Individual leaves were placed on moistened pieces of filter paper in Petri dishes. The leaves were then sprayed with the test solution and allowed to dry. The dishes were infested with ten third-instar larvae. Each treatment was performed in triplicate. Controls were treated with carrier solvent alone. After 24h, treated larvae were observed for larval weight, larval mortality, percentage pupation, deformed pupae, larval-pupal and pupil-adult intermediates, percentage adult emergence and deformed adults and the same were recorded.

Results and discussion

In our continuing search for insecticidal activity of substances and in connection with our efforts towards the study of synthesis of octahydroquinazolinone, we initiated an investigation on the insecticidal activity of these compound adducts against insecticidal. First, we described an efficient synthetic protocol for the preparation of these compounds that were shown to be active against *Spodoptera litura*.

Initially, we investigated the synthesis of 4-(4-nitro-phenyl)-7,7-Dimethyl-1,2,3,4,5,6, 7, 8-octahydroquinazoline - 2, 5 - dione

using 4-nitrobenzaldehyde (10 mmol, 1.55g), dimedone (10 mmol, 1.50g), urea (15 mmol, 0.9g) and $BF_3.SiO_2$ as the catalyst under various conditions (*Scheme 1, Table 1*). The best conditions were obtained for $BF_3.SiO_2$(10 mol%) in 1,2-dichloroethane solvent at the reflux (Table 1, entry 10).



Scheme 1. Synthesis of octahydroquinazolinone derivatives using $BF_3.SiO_2$.

Next, the synthesis of octahydroquinazolinone derivatives were studied and summarized in *Table 2*. In all cases, the three-component reaction proceeded smoothly to give the corresponding octahydroquinazolinone in moderate to good yields. In brief, in this study$BF_3.SiO_2$ is introduced as an efficient, catalyst for synthesis of octahydroquinazolinone derivatives. All of products were characterized by FT-IR and ^{1}H-NMR.

Table 1. The synthesis of 4-(4-nitro-phenyl)-7,7-Dimethyl-1,2,3,4,5,6,7,8-octahydroquinazoline-2,5-dione.

Entry	Catalyst (mol %)	Solvent	Conditions	Time (min)	Yield[a] %
1	$BF_3.SiO_2$ (10)	Chloroform	r.t.	25	42
2	$BF_3.SiO_2$ (10)	Chloroform	Reflux	25	67
3	$BF_3.SiO_2$ (10)	Ethanol	r.t.	25	28
4	$BF_3.SiO_2$ (10)	Ethanol	Reflux	25	73
5	$BF_3.SiO_2$ (10)	Water	r.t.	25	scarce
6	$BF_3.SiO_2$ (10)	Water	Reflux	25	38
7	$BF_3.SiO_2$ (10)	Solvent-free	r.t.	25	36
8	$BF_3.SiO_2$ (10)	Solvent-free	80°C	25	65
9	$BF_3.SiO_2$ (10)	$ClCH_2CH_2Cl$	r.t.	25	59
10	$BF_3.SiO_2$ (10)	$ClCH_2CH_2Cl$	Reflux	25	97
11	$BF_3.SiO_2$ (10)	$ClCH_2CH_2Cl$	Reflux	15	77
12	$BF_3.SiO_2$ (5)	$ClCH_2CH_2Cl$	Reflux	25	68
13	$BF_3.SiO_2$ (10) 2nd run	$ClCH_2CH_2Cl$	Reflux	15	95
14	$BF_3.SiO_2$ (10) 2nd run	$ClCH_2CH_2Cl$	Reflux	15	94

[a] Isolated yield

Table 2. The synthesis of octahydroquinazolinonederivatives in the presence of $BF_3.SiO_2$.[a]

Entry	R^1	X	Yield (%)[a]	m.p.(°C)	Found
1	4-OHC_6H_4	O	96	292-293	300-302[5]
2	4-$OMeC_6H_4$	O	93	279-281	272-274 [8]
3	4-ClC_6H_4	O	88	318-320	318-320 [7]
4	4-FC_6H_4	O	94	138-140	138-140 [7]
5	4-$NO_2C_6H_4$	O	97	302-304	302–304[12]
6	C_6H_5	O	96	292-295	290–293[12]
7	4-BrC_6H_4	O	93	330-332	324-326 [8]
8	4-OH,3-$OMeC_6H_3$	O	88	192-194	192-194[10]
9	4-$OMeC_6H_4$	S	94	278-280	278-280 [7]
10	4-ClC_6H_4	S	97	288-290	288-290 [7]
11	3-ClC_6H_4	S	96	274-276	275–276 [12]
12	4-$NO_2C_6H_4$	S	97	288-290	288-290 [7]
13	C_6H_5	S	92	286-288	286-288 [7]
14	4-BrC_6H_4	S	97	285-286	286–288 [12]

[a]1,3-Diketone (10 mmol), aldehyde (10 mmol), urea/thiourea (15 mmol), $BF_3.SiO_2$ (10 mol%).

All the octahydroquinazolinone derivatives were also evaluated for insecticide activity as well as insect growth regulatory activity against lepidopteran insect pest namely, *Spodoptera litura* (third instar larvae) at 0.1% dose by both contact and feeding method [30]. The results obtained asinsecticidal activities against *Spodoptera litura* at 0.1% through both contact and feeding technique are presented in Table 3 and IGR (insect growth regulator) activities of octahydroquinazolinone derivatives against *Spodoptera litura* at 0.1%are presented in Table4. Figure 1 shows the insecticide activities of all compounds. In this figure the percent of inhibition of all compounds versus Spodoptera litura at 0.1% through both contact and feeding technique is presented. The contact and stomach Insecticidal activities of compound increase as 2-thioxo replace 2,5-dione and also the insecticidal activities of the compound increase with increasing the number of hydroxyl and methoxy groups in the molecule. For instance, compound 8 shows only moderate activities owing to1-hydroxyl groups and methoxy group in its structure. Figure 2 illustrates IGR (insect growth regulator) activities of all compounds by means of the percent of growth inhibition index of all compounds versus *Spodoptera litura* at 0.1%. The increase of the IGR (insect growth regulator) activities of compounds increase by replacing 2-thioxo with 2,5-dione.

Table 3. Insecticidal activities against *Spodoptera litura* at 0.1% through both contact and feeding technique.

Compound	Insect mortality (*S. litura*)	
	Contact	Stomach
1	65	70
2	66	62
3	51	58
4	47	55
5	47	48
6	39	35
7	53	33
8	78	100
9	90	85
10	83	78
11	73	72
12	55	55
13	47	42
14	58	48
Cypermethrin	93	100
Cyhalothrin	80	100

Table 4. IGR (insect growth regulator) activities of all compounds against *Spodoptera litura* at 0.1%.

Compound	% Mortality	% Abnormal larva/dead larva	% Abnormal pupa/dead pupa	% Normal adult	% Growth inhibition index
1	20	8	12	20	80
2	40	20	20	23	77
3	5	0	5	29	71
4	45	15	30	25	75
5	30	20	10	42	58
6	10	5	5	53	47
7	15	8	7	47	53
8	20	15	5	0	100
9	40	25	15	4	96
10	10	5	5	7	93
11	20	15	5	28	72
12	30	10	20	35	65
13	10	10	0	48	52
14	20	10	10	32	68

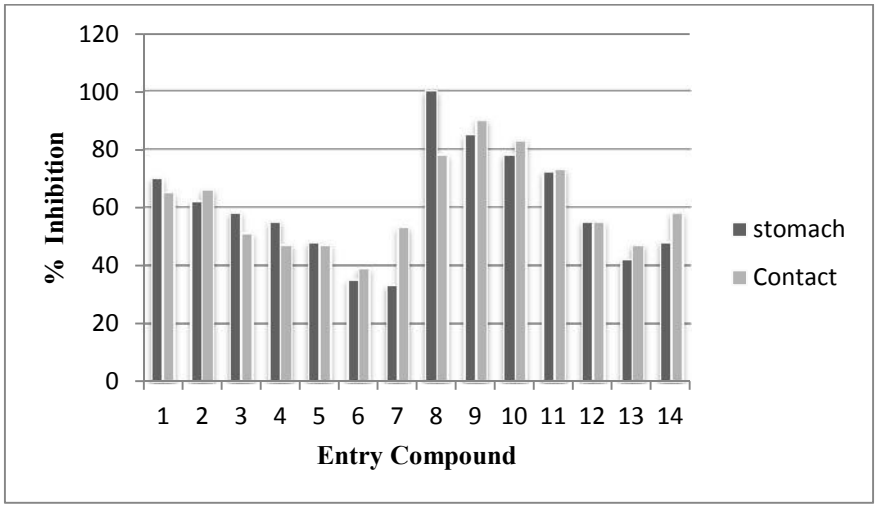


Figure 1. Insecticidal activities of all compounds.

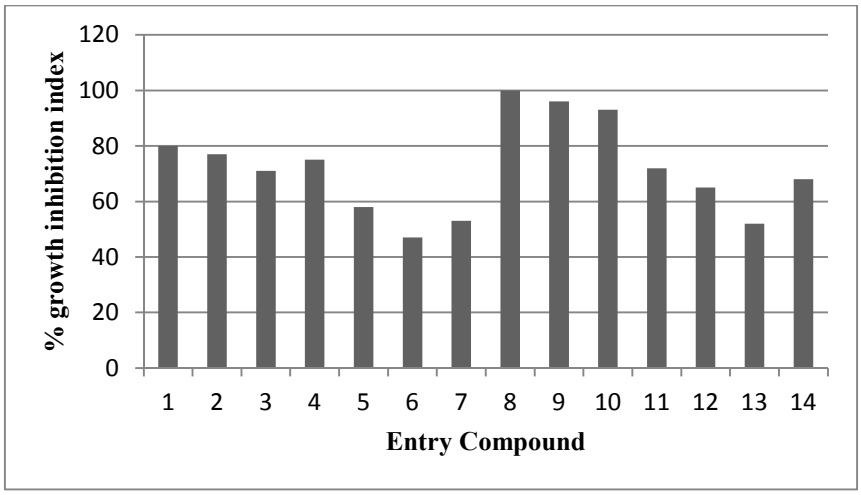


Figure 2. IGR (insect growth regulator) activities of all compounds.

In conclusion, we demonstrated a simple method for the synthesis of octahydroquinazolinone derivatives using $BF_3.SiO_2$, as an eco-friendly, inexpensive and efficient reagent. Short reaction times, high yield and simplicity of operation are the main advantages of the present method.These promising results suggest that the evaluation of insecticidal activity should be extended to other structural types of octahydroquinazolinone derivatives.

Acknowledgements

The Research Council of University of Jiroft is gratefully acknowledged for the financial support for this work.

References

[1] M. Kidwai, S. Saxena, M.K.R. Khan, S.S. Thukral, *Eur. J. Med. Chem*., 40, 816 (2005).

[2] P. Shah, M. Patel, *Med. Chem. Res*., 21, 1188 (2012).

[3] M. Yarım, S. Saraç, F.S. Kılıç, K. Erol, *Il Farmaco.,* 58, 17 (2003).

[4] H. Lin, Q. Zhao, B. Xu, X. Wang, *J. Mol. Catal. A: Chem.*, 268, 221 (2007).

[5] S. Kantevari, R. Bantu, L. Nagarapu, *Arkivoc*., xvi, 136 (2006).

[6] Z. Hassani, M.R. Islami, M. Kalantari, *Bioorg Me. Chem. Lett*., 16, 4479 (2006).

[7] A. Kuraitheerthakumaran, S. Pazhamalai, H. Manikandan, M. Gopalakrishnan, *J. Saudi. Chem. Soc*.,11, 14 (2011).

[8] S. Karami, B. Karami, S. Khodabakhshi, *J. Chin. Chem. Soc*., 60, 22 (2013).

[9] A. Mobinikhaledi, N. Foroughifar, H. Khodaei, *Eur. J. Chem.,* 1, 291 (2010).

[10] J. Khurana, S. Kumar, *Monatsh. Chem*. 141, 561 (2010).

[11] M. Naik, S. Samantaray, B.G. Mishra, *J. Cluster Sci*. 22, 295 (2011).

[12] K.S. Niralwad, B.B. Shingate, M.S.

Shingare, *Tetrahedron Lett*., 51, 3616 (2010).

[13] K. Wilson, J. H. Clark, *Chem. Commun*., 2135 (1998).

[14] B. Sadeghi, B.F. Mirjalili, M.M. Hashemi, *J. Iran Chem. Soc*., 5, 694 (2008).

[15] B.B.F. Mirjalili, A. Bamoniri, A. Akbari, *Tetrahedron Lett*., 49, 6454 (2008).

[16] B. Sadeghi, B.B.F. Mirjalili, M.M. Hashemi, *Tetrahedron Lett*., 49, 2575 (2008).

[17] A. Akbari, A. Hosseini-Nia, *J Saudi Chem Soc*.

[18] K.V.K. Boodhoo, W.A.E. Dunk, M. Vicevic, R.J. Jachuck, V. Sage, D.J. Macquarrie, J.H. Clark, *J. Appl. Polym. Sci.*, 101, 8 (2006).

[19] S. Dindulkar, P. Parthiban, Y. Jeong, *Monats.Chem*.,143, 113 (2012).

[20] M.V. Reddy, S.D. Dindulkar, Y.T. Jeong, *Tetrahedron Lett*., 52, 4764 (2011).

[21] B.B.F. Mirjalili, A. Bamoniri, A. Akbari, *Chem. Heterocycl. Com*., 47, 487 (2011).

[22] B.F. Mirjalili, A. Bamoniri, A. Akbari, *J. Iran Chem. Soc.*, 8, S135 (2011).

[23] H. Qin, Z. Ye, S. Huang, J. Ding, R. Luo, *Chin. J. Eco. Agric*., 12, 40 (2004).

[24] B.C. Dhir, H.K. Mohapatra, B. Senapati, *Indian J. Plant. Protect*., 20, 215 (1992).

[25] M. Ahmad, M. Iqbal Arif, M. Ahmad, *Crop. Protect*., 26, 809 (2007).

[26] M. Ahmad, A.H. Sayyed, N. Crickmore, M.A. Saleem, *Pest. Manag. Sci*., 63, 1002 (2007).

[27] N.J. Armes, J.A. Wightman, D.R. Jadhav, G.V. Ranga Rao, *Pestic. Sci*. 50, 240 (1997).

[28] M. Ahmad, *Crop. Protect*., 28, 264 (2009).

[29] K.R. Kranthi, D.R. Jadhav, R.R. Wanjari, S.S. Ali, D. Russell, *Bull. Entomol. Res*., 91, 37 (2001).

[30] A. Akbari, *Heterocycl Commun*., 19, 425(2013)

[31] N. Aggarwal, R. Kumar, C. Srivastva, P. Dureja, J.M. Khurana, *J. Agric. Food Chem.,* 58, 3056 (2010).