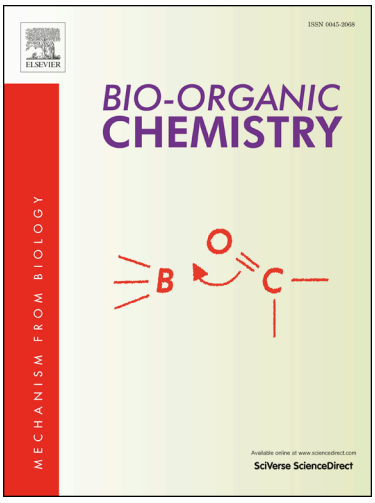


Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold as insecticidal/acaricidal agents

Min Lv, Guangci Liu, Minghong Jia, Hui Xu

PII: S0045-2068(18)30369-9
DOI: https://doi.org/10.1016/j.bioorg.2018.07.034
Reference: YBIOO 2453

To appear in: *Bioorganic Chemistry*

Received Date: 17 April 2018
Revised Date: 18 July 2018
Accepted Date: 31 July 2018

Please cite this article as: M. Lv, G. Liu, M. Jia, H. Xu, Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold as insecticidal/acaricidal agents, *Bioorganic Chemistry* (2018), doi: https://doi.org/10.1016/j.bioorg.2018.07.034

Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold as insecticidal/acaricidal agents

Min Lv[a,1], Guangci Liu[a,1], Minghong Jia[b], Hui Xu[a,b,*]

[a]Research Institute of Pesticidal Design & Synthesis, College of Crop Protection/ Chemistry and Pharmacy, Northwest A&F University, Yangling Shaanxi 712100, China

[b]Beijing Key Laboratory of Agricultural Product Detection and Control for Spoilage Organisms and Pesticides, College of Food Science and Engineering, Beijing University of Agriculture, Beijing 102206, China

*Corresponding author at: Research Institute of Pesticidal Design & Synthesis, Northwest A&F University, Yangling 712100, Shaanxi Province, China. E-mail address: orgxuhui@nwsuaf.edu.cn (H. Xu). Tel: +86-29-87091952; Fax: +86-29-87091952].

[1]These authors contributed equally to this work.

Abstract:

In continuation of our program aimed at the development of natural product-based pesticidal agents, a series of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold were prepared, and their insecticidal and acaricidal activities were evaluated against *Mythimna separata* and *Tetranychus cinnabarinus*. Some compounds exhibited potent insecticidal and acaricidal activities. It suggested that R^1 as a nitro group and R^2 as a fluorine atom, were important for the insecticidal activity; R^1 as the electron-donating groups and R^2 as the methyl group, were necessary for the acaricidal activity.

Keywords: Matrine; 1,3,4-Thiadiazole; Natural product-based; Insecticidal activity; Acaricidal activity

1. Introduction

Mythimna separata Walker (oriental armyworm) and *Tetranychus cinnabarinus* Boisduval (spider mite) are two typical and threatening pests of a wide range of crops [1,2]. In recent years, lots of synthetic agrochemicals have been introduced to protect crops from pests and enhance crop yields. However, extensive and unreasonable applications of these agrochemicals have resulted in resistance in pest populations and negative impacts on human health and environment [3]. Due to the advantages of botanical pesticides, nowadays discovery and development of the potential alternatives from plant-based natural products has attracted considerable interest [4-12].

Matrine (**1**, Fig. 1) is a quinolizidine alkaloid isolated from the roots of *Sophora flavescens* (Kushen), *Sophora tonkinensis*, and *Sophora alopecuroides* (Kudouzi) [13]. Compound **1** and its analogs showed a variety of biological properties such as anticancer activity, anti-inflammatory activity, insecticidal activity, antimicrobial activity, antiviral activity, etc [13-17]. Additionally, many molecules containing 1,3,4-thiadiazole scaffold (Fig. 1) exhibited some interesting biological activities such as antioxidant activity, antitubercular activity, antimicrobial activity, acaricidal activity, insecticidal activity, anticancer activity, etc [18-25]. Recently, we have prepared a series of 14-formyl-15-aryloxy/methoxymatrines (**2**, Fig. 1) and 14-aryloxymethylylidenylmatrines (**3**, Fig. 1) by structural modification of matrine on its lactam ring, and found that some compounds showed more promising pesticidal activities than matrine against *Mythimna separata* and *Plutella xylostella* [26]. Based

upon the above results, and in continuation of our program aimed at the development of new natural-product-based pesticidal agents [27-29], therefore, in this paper we wanted to further investigate necessary of lactam ring by opening it, followed by introduction of the 1,3,4-thiadiazole fragment. Their insecticidal and acaricidal activities were evaluated against *Mythimna separata* and *Tetranychus cinnabarinus*.

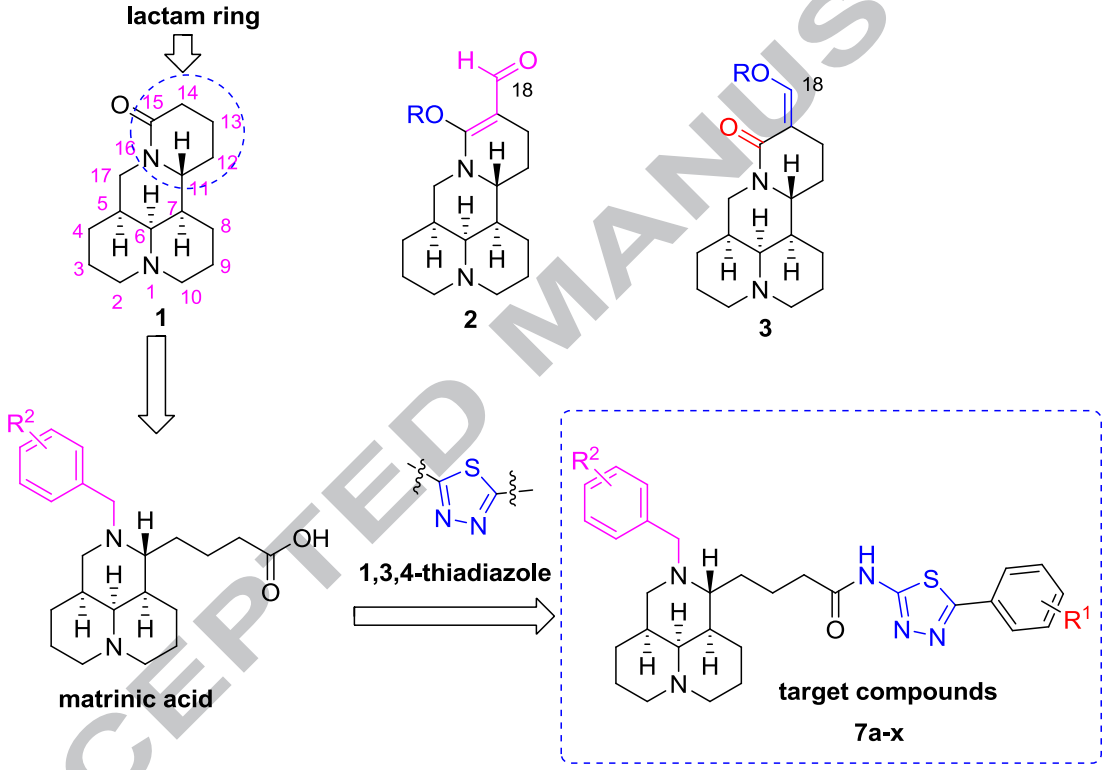


Fig. 1. The chemical structures of matrine (**1**), its derivatives (**2** and **3**), matrinic acid, 1,3,4-thiadiazole, and matrinic amides containing 1,3,4-thiadiazole scaffold (**7a**–**x**).

2. Experimental section

General procedure for synthesis of compounds **7a**–**x**.

A mixture of 1,3,4-thiadiazoles (**4a-i**, 0.28 mmol), *N*, *N'*-dicyclohexylcarbodiimide (DCC, 0.2 mmol), 4-dimethylaminopyridine (DMAP, 0.04 mmol), and matrinic acids (**6a-c**, 0.2 mmol) in dry DCM (10 mL) was stirred at room temperature. When the

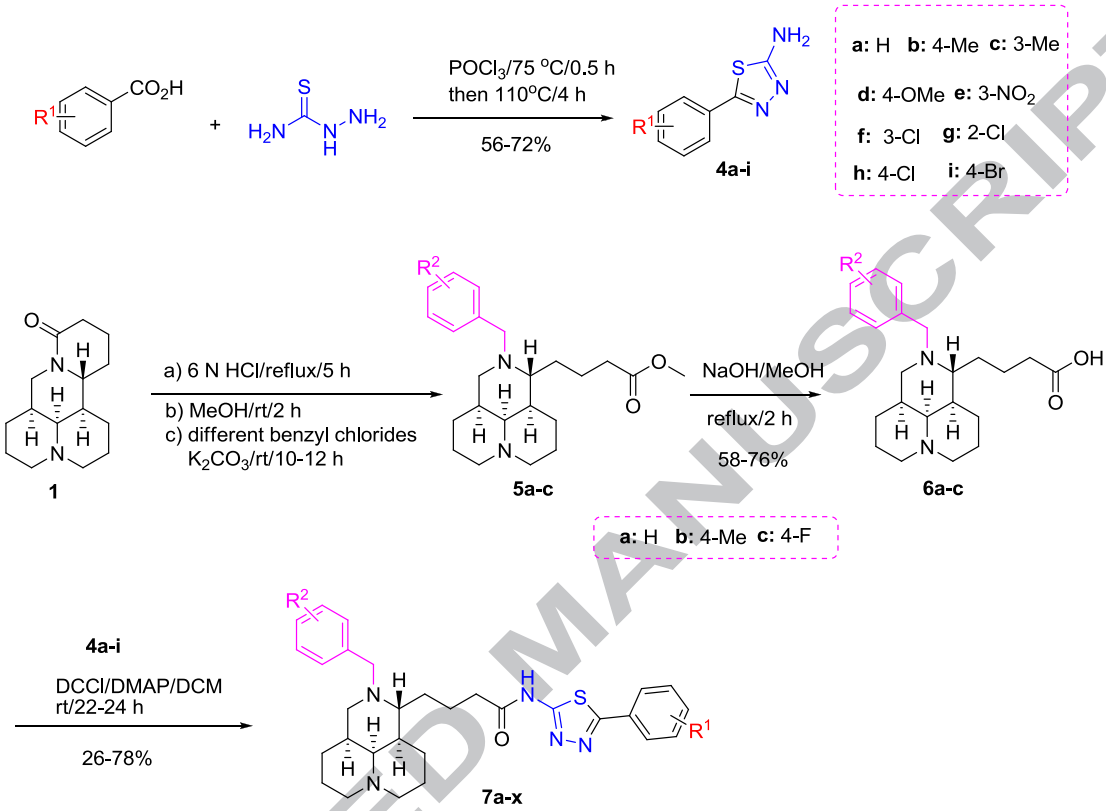
reaction was complete according to TLC analysis, the mixture was diluted by DCM (40 mL), washed by water (20 mL), 0.1 mol/L aq. HCl (20 mL), saturated aq. $NaHCO_3$ (20 mL) and brine (20 mL), dried over anhydrous Na_2SO_4, concentrated *in vacuo*, and purified by preparative thin-layer chromatography (PTLC) to give compounds **7a**–**x** in 26-78% yields. Exemplary data for compounds **7a** and **7b** are as follows:

Data for **7a**: Isolated yield = 54%, white solid, m.p. 206-208 ^{o}C; [α] $^{20}_{D}$ = 3 (*c* 2.2 mg/mL, $CHCl_3$); IR cm^{-1} (KBr): 3027, 2931, 1697, 1560, 1444, 1304, 755; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.87 (d, *J* = 7.0 Hz, 2H, Ar-H), 7.41-7.46 (m, 3H, Ar-H), 7.15-7.21 (m, 5H, Ar-H), 4.08 (d, *J* = 13.0 Hz, 1H), 3.05 (d, *J* = 13.0 Hz, 1H), 2.96 (d, *J* = 10.5 Hz , 1H), 2.73-2.82 (m, 4H), 2.62 (t, *J* = 12.0 Hz, 1H), 2.34 (dd, *J* = 12.0, 3.5 Hz, 1H), 1.99-2.04 (m, 2H), 1.83-1.92 (m, 5H), 1.75-1.77 (m, 3H), 1.63-1.68 (m, 2H), 1.31-1.33 (m, 5H). HRMS (ESI): Calcd for $C_{30}H_{38}ON_5S$ ($[M+H]^+$), 516.2792; Found, 516.2790.

Data for **7b**: Isolated yield = 59%, white solid, m.p. 212-214 ^{o}C; [α] $^{20}_{D}$ = -3 (*c* 2.5 mg/mL, $CHCl_3$); IR cm^{-1} (KBr): 3028, 2931, 1696, 1559, 1444, 1302, 739; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.68 (d, *J* = 10.0 Hz, 2H, Ar-H), 7.32 (t, *J* = 7.5 Hz, 1H, Ar-H), 7.27 (s, 1H, Ar-H), 7.13-7.19 (m, 5H, Ar-H), 4.09 (d, *J* = 13.5 Hz, 1H), 3.02 (d, *J* = 13.5 Hz, 1H), 2.93 (d, *J* = 10.5 Hz, 1H), 2.72-2.83 (m, 4H), 2.59 (t, *J* = 12.0 Hz, 1H), 2.40 (s, 3H, Ar-CH_3), 2.32 (dd, *J* = 11.5, 4.0 Hz, 1H), 2.00 (s, 2H), 1.81-1.94 (m, 5H), 1.75-1.77 (m, 3H), 1.62-1.68 (m, 2H), 1.30-1.33 (m, 5H). HRMS (ESI): Calcd for $C_{31}H_{40}ON_5S$ ($[M+H]^+$), 530.2948; Found, 530.2954

3. Results and discussion

3.1. Chemistry



Scheme 1. Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold (**7a**–**x**).

As shown in Scheme 1, first, a series of aromatic carboxylic acids were condensed with thiosemicarbazide to give 1,3,4-thiadiazoles (**4a**–**i**) [18]. Then opening the lactam ring of compound **1** in the presence of 6 N aq. HCl, followed by introduction of the different benzyl groups on the N-16 afforded compounds **5a**–**c**. Subsequently, hydrolysis of compounds **5a**–**c** in the presence of NaOH produced *N*-benzylmatrinic acids (**6a**–**c**) [30,31]. Finally, by reaction of *N*-benzylmatrinic acids (**6a**–**c**) with 1,3,4-thiadiazoles (**4a**–**i**) in the presence of

N,*N'*-dicyclohexylcarbodiimide (DCC) and 4-dimethylaminopyridine (DMAP), matrinic amide derivatives (**7a**–**x**) were obtained in 26-78% isolated yields [32]. Their structures were well characterized by ^{1}H NMR, IR, optical rotation, HRMS and mp (see Supplementary data).

3.2. Pesticidal activity

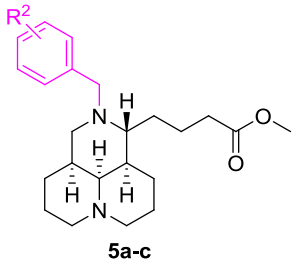
The insecticidal activity of compounds **1**, **5a**–**c**, **6a**–**c** and **7a**–**x** against the pre-third-instar larvae of *Mythimna separata* was tested by leaf-dipping method [32]. Toosendanin was used as a positive control. Leaves treated with acetone alone were used as a blank control group. The symptoms of the treated *M. separata* during three periods such as the larval stage, the pupation stage and the adult stage, were observed in the same way as in our previous papers [29,32].

As shown in Table 1, among all derivatives, compounds **5c**, **6c**, **7e**, **7h**, **7n**, **7q**, **7w** and **7x** exhibited the insecticidal activity equal to or higher than that of the positive control toosendanin. Especially compound **7w** exhibited the most potent pesticidal activity with the final mortality rate (FMR) of 65.5%; whereas the FMR of their precusor (compound **1**) was only 27.6%. To compounds **5a**–**c** and **6a**–**c**, when R^2 was a fluorine atom, the corresponding compounds **5c** and **6c** exhibited more potent insecticidal activity than those containing other substituents (e.g., **5a**,**b** and **6a**,**b**). For instance, the FMRs of **5c** and **6c** were 51.7% and 51.7%, respectively; whereas the FMRs of **5a**, **5b**, **6a** and **6b** were 41.4%, 34.5%, 44.8% and 41.4%, respectively. To compounds **7a**–**x**, generally, when R^1 was a nitro group, the corresponding compounds showed more promising insecticidal activity

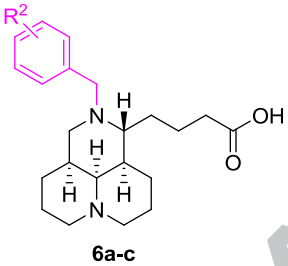
than those containing other substituents (e.g, **7e** vs **7a–b** and **7f–i**; **7n** vs **7j–m** and **7o–r**; **7w** vs **7s–v** and **7x**). All in all, it was noteworthy that when R^1 was a nitro group, and R^2 was a fluorine atom, among all derivatives, the corresponding compound **7w** showed the most potent insecticidal activity.

Table 1

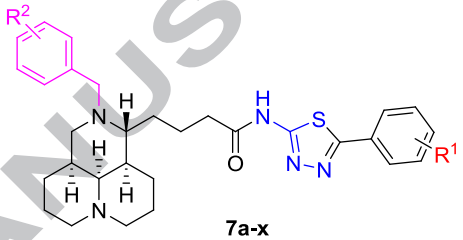
Insecticidal activity of compounds **1**, **5a–c**, **6a–c** and **7a–x** against *M. separata* on leaves treated at a concentration of 1 mg/mL.



5a-c



6a-c



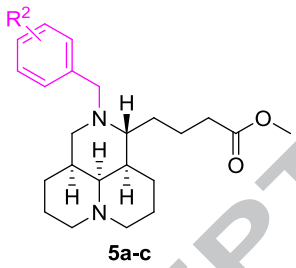
7a-x

Compound	R^1	R^2	Corrected mortality rate (% ± SD)		
			10 days	20 days	35 days
1	/	/	6.7 ± 3.3	13.8 ± 3.3	27.6 ± 0
5a	/	H	10.0 ± 5.8	20.7 ± 3.3	41.4 ± 3.3
5b	/	4-Me	0 ± 0	10.4 ± 3.3	34.5 ± 6.7
5c	/	4-F	16.7 ± 3.3	27.6 ± 5.8	51.7 ± 3.3
6a	/	H	16.7 ± 6.7	24.2 ± 3.3	44.8 ± 3.3
6b	/	4-Me	23.3 ± 6.7	24.2 ± 3.3	41.4 ± 3.3
6c	/	4-F	30.0 ± 0	31.1 ± 3.3	51.7 ± 3.3
7a	H	H	6.7 ± 3.3	17.3 ± 0	27.6 ± 5.8
7b	4-Me	H	13.3 ± 3.3	17.3 ± 5.8	27.6 ± 5.8
7c	3-Me	H	16.7 ± 3.3	20.7 ± 3.3	31.1 ± 3.3
7d	4-OMe	H	13.3 ± 6.7	20.7 ± 3.3	41.4 ± 6.7
7e	3-NO_2	H	23.3 ± 3.3	44.8 ± 3.3	58.6 ± 5.8
7f	3-Cl	H	30.0 ± 0	27.6 ± 0	44.8 ± 3.3
7g	2-Cl	H	13.3 ± 3.3	27.6 ± 5.8	44.8 ± 6.7
7h	4-Cl	H	23.3 ± 3.3	34.5 ± 3.3	51.7 ± 3.3
7i	4-Br	H	13.3 ± 3.3	17.3 ± 5.8	38.0 ± 5.8
7j	H	4-Me	10.0 ± 0	17.3 ± 0	31.1 ± 3.3
7k	4-Me	4-Me	13.3 ± 3.3	13.8 ± 6.7	24.2 ± 3.3
7l	3-Me	4-Me	13.3 ± 3.3	10.4 ± 3.3	27.6 ± 5.8

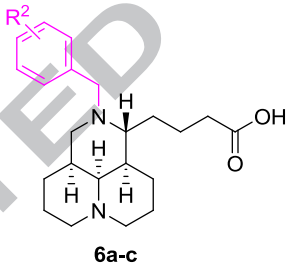
7m	4-OMe	4-Me	16.7 ± 6.7	17.3 ± 5.8	31.1 ± 5.8
7n	3-NO_2	4-Me	16.7 ± 3.3	31.1 ± 3.3	51.7 ± 3.3
7o	3-Cl	4-Me	13.3 ± 6.7	17.3 ± 0	34.5 ± 6.7
7p	2-Cl	4-Me	16.7 ± 3.3	17.3 ± 0	34.5 ± 3.3
7q	4-Cl	4-Me	13.3 ± 3.3	27.6 ± 5.8	48.3 ± 5.8
7r	4-Br	4-Me	13.3 ± 3.3	20.7 ± 3.3	38.0 ± 5.8
7s	H	4-F	13.3 ± 6.7	17.3 ± 5.8	34.5 ± 3.3
7t	4-Me	4-F	20.0 ± 5.8	24.2 ± 3.3	41.4 ± 3.3
7u	3-Me	4-F	23.3 ± 3.3	34.5 ± 3.3	44.8 ± 3.3
7v	4-OMe	4-F	13.3 ± 3.3	24.2 ± 3.3	38.0 ± 5.8
7w	3-NO_2	4-F	23.3 ± 3.3	38.0 ± 5.8	65.5 ± 3.3
7x	4-Br	4-F	16.7 ± 3.3	27.6 ± 5.8	48.3 ± 5.8
toosendanin	/	/	10.0 ± 5.8	27.6 ± 5.8	48.3 ± 5.8

Table 2

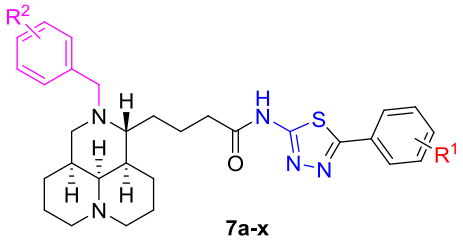
Acaricidal activity of compounds **1**, **5a–c**, **6a–c** and **7a–x** against the female adults of *T. cinnabarinus* at a concentration of 0.5 mg/mL.



5a-c



6a-c



7a-x

Compound	R^1	R^2	Corrected mortality rate (% ± SD)	
			48 hours	72 hours
1	/	/	10.4 ± 2.6	23.4 ± 2.7
5a	/	H	14.1 ± 3.1	34.1 ± 2.7
5b	/	4-Me	17.4 ± 1.4	38.5 ± 5.1
5c	/	4-F	13.2 ± 0.6	25.1 ± 1.3
6a	/	H	24.0 ± 3.0	52.2 ± 1.5
6b	/	4-Me	31.0 ± 0.7	61.0 ± 2.1
6c	/	4-F	19.0 ± 0.4	49.8 ± 3.2
7a	H	H	10.2 ± 3.2	27.7 ± 1.8
7b	4-Me	H	9.7 ± 0.6	34.9 ± 2.9
7c	3-Me	H	13.3 ± 2.2	32.6 ± 3.4
7d	4-OMe	H	18.5 ± 3.5	39.6 ± 3.4
7e	3-NO_2	H	10.2 ± 1.1	19.9 ± 1.5

7f	3-Cl	H	11.2 ± 4.1	24.5 ± 3.0
7g	2-Cl	H	12.6 ± 2.3	27.2 ± 2.8
7h	4-Cl	H	17.5 ± 2.0	30.7 ± 2.6
7i	4-Br	H	11.2 ± 1.5	35.3 ± 1.8
7j	H	4-Me	11.2 ± 1.7	22.3 ± 2.6
7k	4-Me	4-Me	17.0 ± 1.4	42.4 ± 3.3
7l	3-Me	4-Me	17.1 ± 2.9	41.0 ± 2.2
7m	4-OMe	4-Me	16.8 ± 4.3	46.9 ± 2.8
7n	3-NO_2	4-Me	12.7 ± 1.6	26.4 ± 1.3
7o	3-Cl	4-Me	8.4 ± 2.5	33.2 ± 2.7
7p	2-Cl	4-Me	12.3 ± 2.3	32.8 ± 2.4
7q	4-Cl	4-Me	14.2 ± 0.4	28.6 ± 1.4
7r	4-Br	4-Me	13.2 ± 3.1	26.5 ± 2.6
7s	H	4-F	9.5 ± 3.0	21.9 ± 2.3
7t	4-Me	4-F	13.4 ± 0.5	30.2 ± 1.8
7u	3-Me	4-F	17.5 ± 3.4	29.3 ± 3.3
7v	4-OMe	4-F	14.1 ± 2.2	36.1 ± 6.4
7w	3-NO_2	4-F	9.6 ± 1.7	27.2 ± 4.3
7x	4-Br	4-F	11.7 ± 0.3	23.2 ± 2.5
spirodiclofen	/	/	47.7 ± 2.8	73.5 ± 1.0

The acaricidal activity of compounds **1**, **5a**–**c**, **6a**–**c** and **7a**–**x** against the female adults of *Tetranychus cinnabarinus* was tested by slide-dipping method [7,33]. Spirodiclofen was used as a positive control. As shown in Table 2, the mortality rate (MR) at 72 h of compound **1** was 23.4%; whereas its lactam ring was opened, the MRs at 72 h of its derivatives were increased. Especially three *N*-benzylmatrinic acids (**6a**–**c**) showed the most potent acaricidal activity; for example, the MRs at 72 h of compounds **6a**–**c** were 52.2%, 61.0% and 49.8%, respectively. To compounds **5a**–**c** and **6a**–**c**, generally, when R^2 was the methyl group, the corresponding compounds **5b** and **6b** exhibited more potent acaricidal activity than those containing other substituents (e.g., **5b** vs **5a** and **5c**; **6b** vs **6a** and **6c**). To compounds **7a**–**x** (except **7i**), in general, when R^1 were the electron-donating groups such as 4-methyl, 3-methyl

and 4-methoxy, the corresponding compounds displayed more promising acaricidal activity than those containing others (e.g, **7b–d** vs **7a** and **7e–h**; **7k–m** vs **7j** and **7n–r**; **7t–v** vs **7s**, **7w** and **7x**). To compounds **7b–d**, **7k–m**, and **7t–v**, as mentioned above, especially when R^2 was the methyl group, the corresponding compounds **7k–m** exhibited more potent acaricidal activity than compounds **7b–d** and **7t–v**. Therefore, it demonstrated that when R^1 were the electron-donating groups, and R^2 was the methyl group, the corresponding compounds could show potent acaricidal activity. This results were different with those of 3,19-diarylarbonyloxy andrographolides (the derivatives containing the electron-withdrawing groups on the phenyl showed potent acaricidal activity) [34].

4. Conclusion

In summary, a series of matrinic amide derivatives containing 1,3,4-thiadiazole fragment (**7a**–**x**) were prepared, and evaluated for their pesticidal activities against *Mythimna separata* and *Tetranychus cinnabarinus*. Among all derivatives, compound **7w** exhibited the most potent insecticidal activity; compounds **7k**–**m** showed promising acaricidal activity. It demonstrated that R^1 as a nitro group and R^2 as a fluorine atom, were important for the insecticidal activity; R^1 as the electron-donating groups and R^2 as the methyl group, were necessary for the acaricidal activity. Furthermore, three intermediates **6a**–**c** displayed the most potent acaricidal activity. These will pave the way for further structural modifications of matrine as potentially botanical acaricidal and insecticidal agents in crop protection.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

The present research was partly supported by Key R&D Program of Shaanxi Province (No. 2018NY-153), and Beijing Key Laboratory of Agricultural Product Detection and Control for Spoilage Organisms and Pesticides, Beijing University of Agriculture (No. 1086016009).

Appendix A. Supplementary data

Supplementary data (spectral data, and the protocol used for insecticidal and acaricidal studies) associated with this article can be found, in the online version.

References

[1] X.F. Jiang, L. Zhang, H.X. Yang, T. W. Sappington, Y. X. Cheng, L. Z. Luo, Sci. Rep. 6 (2016) 26873.

[2] Z.Q. Sun, M. Lv, X. Yu, H. Xu, ACS Sust. Chem. Eng. 5 (2017) 3945.

[3] L.J. Guillette Jr., T. Iguchi, Science 337 (2012) 1614.

[4] L. Lin, N. Mulholland, Q.Y. Wu, D. Beattie, S.W. Huang, D. Irwin, J. Clough, Y.C. Gu, G.F. Yang, J. Agric. Food Chem. 60 (2012) 4480.

[5] F.E. Dayan, C.L. Cantrell, S.O. Duke, Bioorg. Med. Chem. 17 (2009) 4022.

[6] R. Sharma, L. Yadav, J. Lal, P.K. Jaiswal, M. Mathur, A.K. Swami, S. Chaudhary, Bioorg. Med. Chem. Lett. 27 (2017) 4393.

[7] X.B. Huang, B.C. Zhang, H. Xu, Bioorg. Med. Chem. Lett. 27 (2017) 4336.

[8] Z.H. Gao, P.T. Yuan , D.H. Wang , Z.P. Xu, Z. Li, X.S. Shao, Bioorg. Med. Chem. Lett. 27 (2017) 2528.

[9] T. Drobnjakovic, D. Marcic, M. Prijovic, P. Peric, S. Milenkovic, J. Boskovic, Biocontrol Sci. Technol. 28 (2018) 1.

[10] S. Roy, G. Handique, F.R. Bora, A.J. Rahman, Environ. Biol. 39 (2018) 1.

[11] R. Yang, X. Huang, Z. Che, Y. Zhang, H. Xu, Ind. Crop Prod. 107 (2017) 45.

[12] L.A. Mendes, G.F. Martins, W.R. Valbon, T.D. de Souza, L. Menini, A. Ferreira, M.F. da Silva Ferreira, Ind. Crop Prod. 108 (2017) 684.

[13] J. Huang, H. Xu, Curr. Top. Med. Chem. 16 (2016) 3365.

[14] Y. Liu, Y. Xu, W.D. Ji, X.Y. Li, B. Sun, Q.G. Gao, C.Q. Su, Tumor Biol. 35 (2014) 5111.

[15] L.M. Gao, Y.X. Han, Y.P. Wang, Y.H. Li, Y.Q. Shan, X. Li, Z.G. Peng, C.W. Bi, T.A. Zhang, N.N. Du, J. Med. Chem. 54 (2011) 869.

[16] L.S. Wang, Y.J. You, S.Q. Wang, X. Liu, B.M. Liu, J.N. Wang, X. Lin, M.S. Chen, G. Liang, H. Yang, Bioorg. Med. Chem. Lett. 22 (2012) 4100.

[17] O.Z. Zanardi, L.D. Ribeiro, T.F. Ansante, M.S. Santos, G.P. Bordini, P.T. Yamamoto, J.D. Vendramim, Crop Prot. 67 (2015) 160.

[18] M.R. Mahmoud, M.M. El-Shahawi, F.S. Abu El-Azm, M. Abdeen, J. Heter. Chem. 54 (2017) 2352.

[19] S.M. Gomha, N.A. Kheder, M.R. Abdelaziz, Y.N. Mabkhot, A.M. Alhajoj, Chem. Cent. J. 11 (2017) 25.

[20] H. Dai, G. Li, J. Chen, Y.J. Shi, S.S. Ge, C.G. Fan, H.B. He, Bioorg. Med. Chem. Lett. 26 (2016) 3818.

[21] G. Seelolla, V. Ponneri, J. Heter. Chem. 53 (2016) 929.

[22] T.T. Liu, Y.C. Wan, H. Fang, Chin. J. Org. Chem. 36 (2016) 417.

[23] M.S. Sallam, M.A. El-Hashash, D.B. Guirguis, Med. Chem. Res. 25 (2016) 369.

[24] J. Ramprasad, N. Nayak, U. Dalimba, P. Yogeeswari, D. Sriram, MedChemComm 7 (2016) 338.

[25] J. Ramprasad, N. Nayak, U. Dalimba, P. Yogeeswari, D. Sriram, Bioorg. Med. Chem. Lett. 25 (2015) 4169.

[26] J.L. Huang, M. Lv, H. Xu RSC Adv. 7 (2017) 15997.

[27] X. Yu, Z. Che, H. Xu, Chem. Eur. J. 23 (2017) 4467.

[28] Y.Y. Zhang, H. Xu, RSC Adv. 7 (2017) 35191.

[29] J.L. Huang, M. Xu, S.C. Li, J. He, H. Xu, Bioorg. Med. Chem. Lett. 27 (2017) 511.

[30] C.W. Bi, C.X. Zhang, Y.H. Li, S. Tang, H.B. Deng, W.L. Zhao, Z. Wang, R.G. Shao, D.Q. Song, Eur. J. Med. Chem. 81 (2014) 95.

[31] L.Q. He, J. Liu, D.K. Yin, Y.H. Zhang, X.S. Wang, Chin. Chem. Lett. 21 (2010) 381.

[32] Z.P. Che, X. Yu, X.Y. Zhi, L.L. Fan, H. Xu, J. Agric. Food Chem. 61 (2013) 8148.

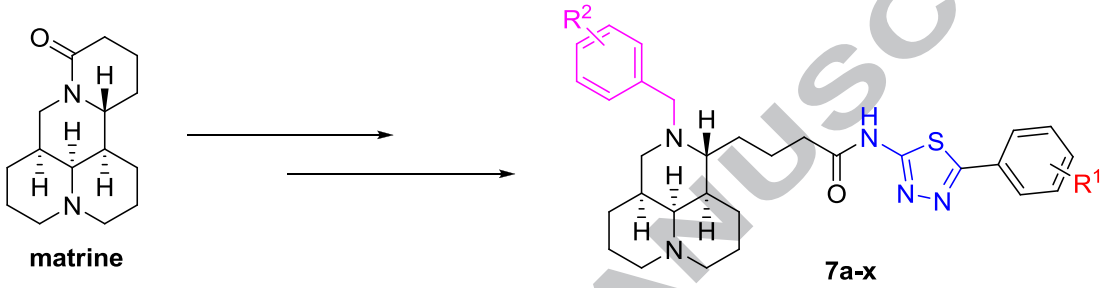
[33] K.M. Chang, C.O. Knowles, J. Agric. Food Chem. 25 (1977) 493.

[34] X.B. Huang, B.C. Zhang, H. Xu, Bioorg. Med. Chem. Lett. 28 (2018) 360.

Graphic abstract

Synthesis of matrinic amide derivatives containing 1,3,4-thiadiazole scaffold as insecticidal/acaricidal agents

Min Lv, Guangci Liu, Minghong Jia, and Hui Xu*



Research highlights

► A series of matrinic amides containing 1,3,4-thiadiazole scaffold were prepared.

► Some compounds potent insecticidal and acaricidal activities.► Their structure-activity relationships were observed.