DOI: 10.1002/cjoc.201100112

Synthesis and *in vitro* Antibacterial Activities of 5-(2,3,4,5-Tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione Derivatives

Cheng, Qingfang*[,a,b](程青芳) Wang, Qifa[b](王启发) Tan, Ting[a](谈婷)
Wang, Mingxiao[a](王明逍) Chen, Na[a](陈娜)

[a] *Department of Chemical Technology, Huaihai Institute of Technology, Lianyungang, Jiangsu 222005, China*
[b] *Jiangsu Key Laboratory of Marine Biotechnology, Huaihai Institute of Technology, Lianyungang, Jiangsu 222005, China*

A series of novel 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione derivatives have been synthesized from substituted salicylaldehydes and barbituric acid or 2-thiobarbituric acid in water catalyzed by phase transfer catalysis of triethylbenzyl ammonium chloride (TEBA). Elemental analysis, IR, ^{1}HNMR, and ^{13}C NMR elucidated the structures of all the newly synthesized compounds. *In vitro* antimicrobial activities of synthesized compounds have been investigated against *Escherichia coli*, *Bacillus subtilis*, *Staphylococcus aureus*, and *Pseudomonas aeruginosa*. These newly synthesized derivatives exhibited significant *in vitro* antibacterial activity.

Keywords 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione, antibacterial activity, phase transfer catalysis, water

Introduction

Chromene and derivatives are an important class of heterocyclic compounds, which are found to possess antiestrogenic activity,[1] and are evaluated for potassium channel opening and hypotensive activies,[2,3] antimicrobial,[4,5] cytotoxicity,[6] antifungal,[7] and molluscidials activies.[8] The primidine group possesses wide range of biological and pharmacological activities.[9,10] Because of intense interest in the biological activity of these compounds, in recent years, several synthetic procedures for preparing of chromene and pyrimidine derivatives have been reported.[6,11] The fusion of chromene to pyrimidine ring is known to increase the biological activity.[5,6]

Water, represents the solvent *par excellence* because of its potential advantages in terms of cost, safety, work-up procedure and environmental concerns, and presents different reactivity and selectivity patterns compared with those observed in common organic solvents. There are a number of chemical transformations that are not only compatible with water but actually benefit from its unique physical and chemical properties, *e.g*., high cohesive energy density, high dielectric constant and internal pressure, and hydrophobic effect.[12] A large number of organic reactions such as Diels-Alder reactions,[13] Claisen rearrangement reactions,[14] and Mannich reactions[15] can be carried out in water with good yields. The concept of reaction "on water" is now well established.[16]

By considering all above aspects, and continuing our studies on the reaction in water,[17-19] we report for the first time an efficient one-pot synthesis of 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione derivatives from substituted salicylaldehydes and barbituric acid or thiobarbituric acid in water catalyzed by phase transfer catalysis.

Results and Discussion

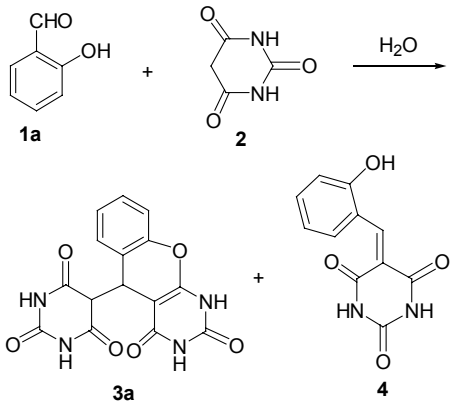
The effects of catalysts were first studied. At the first stage, the reaction of salicylaldehyde with barbituric acid was carried out at 50 ℃ in water without adding any catalyst, the yield is low even though the reaction time prolonged. On the other side, the principal limitation of adding no catalysis at 50 ℃ is the concomitant formation of **3a** and **4** (Scheme 1). In the presence of phase transfer catalysis (PTS), the high yield transformations were carried out without any significant amounts of undesirable side product **4**.

We have not established a detailed mechanism for the formation of **3a**, however, significant amounts of **4** have formed leading us to propose a possible reaction mechanism to explain the formation of **3a**. The formation of products **3a** can be rationalized by initial formation of intermediate **4** via condensation of **1a** and **2**.

* E-mail: cheng_qingfang@yahoo.com.cn
Received July 8, 2011; accepted August 19, 2011; published online January 19, 2012.

CHINESE JOURNAL OF CHEMISTRY

Scheme 1



Subsequent Michael addition of **2** to the intermediate **4** followed by isomerization and dehydration afforded product **3a** (Scheme 1).

The efficiency of various phase transfer catalysts (PTS) has also been compared (Table 1). Two types of phase transfer catalysts including tetramethyl ammonium chloride (TMAC), tetrabutyl ammonium chloride (TBAC), triethylbenzyl ammoium chloride (TEBA), tetrabutyl ammonium bromide (TBAB), and cetyltrimethyl ammonium bromide (CTAB) were selected as the catalyst for this reaction. The results are presented in Table 1.

Table 1 Effect of catalyst on the synthesis of **3a**

Entry	Catalyst	Time/min	Yield/%
1	TMAC	80	75
2	TBAC	90	79
3	TEBA	50	90
4	TBAB	90	80
5	CTAB	90	84

The results showed that the reaction using TEBA as the phase transfer catalyst gave the best result. Thus, TEBA was chosen as the catalyst for all further reactions.

In order to apply this reaction to a library synthesis, we have extended the reaction of substituted salicylaldehydes with barbituric acid or thiobarbituric acid under similar conditions (water/TEBA/50 ℃), furnishing the respective 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]-pyrimidin-5-yl)pyrimidione derivatives (Scheme 2). The optimized results are summarized in Table 2.

The results presented in the Table 2 indicate the scope and generality of the method, which is efficient, not only for urea or thiourea but also for salicylaldehyde as well as substituted salicylaldehydes. In most cases, the reactions proceeded smoothly to produce the corresponding 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione derivatives with good yields.

Scheme 2

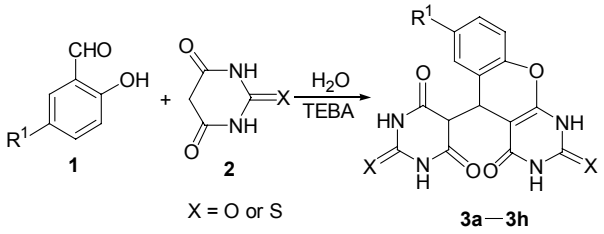


Table 2 Synthesis of 5-(2,3,4,5-tetrahydro-1*H*-chromeno-[2,3-*d*]pyrimidin-5-yl)pyrimidiones **3a—3h**[a]

Product	R^1	X	Time/min	Yield[b]/%	m.p./℃
3a	H	O	45	90	268—270
3b	H	S	50	86	>300
3c	Cl	O	55	87	>300
3d	Cl	S	60	84	252—254
3e	Br	O	55	88	240—242
3f	Br	S	65	86	245—246
3g	NO_2	O	60	81	250—251
3h	NO_2	S	65	84	265—266

[a] Reaction temperature is 50 ℃. [b] Isolated yield.

Antimicrobial screening

In vitro antibacterial activity was screened by considering zone of inhibition of growth. The synthesized compounds **3a**—**3h** were screened with their different concentrations with standard antibiotics such as streptomycin.

The results showed that most of our designed compounds had moderate to good *in vitro* antibacterial activities in between 0.6—5.0 mmol/L concentration as shown in Table 3 with the increase of the concentration of compounds **3a**—**3h**, the antibacterial activity was gradually increasing, but it was not affected so much. Compounds **3a** (R^1=H, X=O), **3g** (R^1=NO_2, X=O) and **3h** (R^1=NO_2, X=S) have the zone of inhibition 14.6, 15.9 and 15.1 mm respectively, comparable to that of the standard streptomycin (15.1 mm) against *Staphylococcus aureus*. Compounds **3e** (R^1=Br, X=O), **3g** (R^1=NO_2, X=O) and **3h** (R^1=NO_2, X=S) have the zone of inhibition 13.8, 14.1 and 13.9 mm, respectively, comparable to that of the standard streptomycin (15.3 mm) against *Bacillus subtilis*. The data indicate that a change in the substituent might also affect the antibacterial activity of the title compounds **3a**—**3h**. Comparison of biological activities among **3a**—**3h** shows functional groups as R^1=NO_2 to be potentially more active against *Staphylococcus aureus*. Also antibacterial potency of compounds among **3a**—**3h** shows that functional groups as R^1=Br/NO_2 are more active against *Bacillus subtilis*. So, these newly synthesized derivatives had the most intense antibacterial activities against Gram positive bacteria such as *Staphylococcus aureu* or *Bacillus subtilis*.

Table 3 The antibacterial activity of the compounds **3a**—**3h**

Product	Concentration/ (mmol•L^{-1})	Diameter inhibition zone/mm			
		E. coli	*B. subtilis*	*S. aureus*	*P. aeruginosa*
3a	0.6	9.9	9.0	11.1	9.7
3a	1.2	10.1	9.3	12.3	9.9
3a	2.5	10.5	10.2	13.8	10.3
3a	5.0	11.8	10.7	14.6	11.2
3b	0.6	9.2	11.3	12.6	9.0
3b	1.2	9.5	11.1	11.4	9.3
3b	2.5	10.1	10.6	10.3	9.8
3b	5.0	10.6	9.9	9.9	10.4
3c	0.6	9.8	10.0	9.7	9.6
3c	1.2	10.1	11.3	10.3	10.2
3c	2.5	10.7	11.6	10.8	10.5
3c	5.0	11.5	12.9	11.3	11.3
3d	0.6	8.9	10.5	9.3	8.7
3d	1.2	9.8	10.9	9.9	9.5
3d	2.5	10.6	11.8	10.3	10.4
3d	5.0	11.1	12.5	10.8	11.2
3e	0.6	9.9	10.6	10.9	9.8
3e	1.2	10.5	11.7	11.3	10.3
3e	2.5	11.0	12.9	12.1	10.9
3e	5.0	11.4	13.8	12.7	11.3
3f	0.6	9.7	10.2	8.7	9.5
3f	1.2	10.3	10.7	9.2	10.1
3f	2.5	10.6	11.9	9.9	10.6
3f	5.0	11.1	13.2	10.5	11.0
3g	0.6	11.2	12.2	13.2	11.1
3g	1.2	11.9	12.8	14.3	12.0
3g	2.5	12.6	13.2	15.0	12.3
3g	5.0	13.2	14.1	15.9	13.1
3h	0.6	10.5	11.8	11.9	10.4
3h	1.2	11.3	12.2	12.7	11.1
3h	2.5	12.3	12.9	13.3	11.9
3h	5.0	12.8	13.9	15.1	12.5
Streptomycin	5.0	16.1	15.3	15.1	15.7

Experimental

Apparatus and materials

All reagents were purchased from commercial sources and used without further purification. The progress of the reactions was monitored by TLC on silica plates. IR spectra were recorded on a Varian F-1000 spectrometer in KBr with absorptions in cm^{-1}. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX 400 MHz spectrometer at 400 and 100 MHz in DMSO-d_6 solution. Elemental analysis was performed on an Elementar Vario EL III analyzer. Melting points were determined on an XT-5A digital melting-points apparatus and are uncorrected.

Biological evaluation procedure

The compounds were diluted in dimethylformamide (DMF) with required concentrations by serial dilution method.[20] Antimicrobial activity was evaluated by screening of the compounds by standard method, *i.e.* agar cup plate method against a panel of human pathogenic microorganisms: two Gram positive (*Bacillus subtilis* CMCC(B) 63501; *Staphylococcus aureu* CMCC(B) 26003), two Gram negative (*Escherichia coli* CMCC(B) 44102; *Pseudomonas aeruginosa* CMCC(B) 10104) were used for the antibacterial studies. Microorganisms were maintained at 37 ℃ on Mueller Hinton (MH) agar slants. The plates containing bacterial organisms were incubated at (37±0.5) ℃ for 24 h. The zone of inhibition was calculated by measuring the diameter zone of inhibition of bacterial growth around the disc. An average of three independent determinations was recorded.

Typical procedure for preparation of products 3a—3h

Preparation of 5-(2,4-dioxo-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (**3a**) is described as an example: To a solution of salicylaldehyde (5 mmol) and barbituric acid (10 mmol), TEBA (5 mg) in 15 mL of water was added under 50 ℃. After the completion of the reaction (monitored by TLC), the crude products collected by filtration were washed respectively with ether and 90 ℃ water and recrystallised from EtOH, to give the product **3a**.

5-(2,4-Dioxo-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3a) m.p. 268—270 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.84 (d, J=4.9 Hz, 1H), 4.70 (d, J=4.9 Hz,1H), 7.01—7.23 (m, 2H), 7.31—7.36 (m, 2H), 11.01 (s, 1H), 11.20 (s, 1H), 11.31 (s, 1H), 12.0 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 34.0, 53.7, 85.6, 116.9, 121.2, 126.0, 128.4, 129.6, 149.5, 149.8, 150.9, 155.8, 163.8, 169.3, 170.0; IR (KBr) v: 3464, 3278, 1701, 1657, 1525, 1493, 1460, 1382, 1280, 1126 cm^{-1}. Anal. calcd for $C_{15}H_{10}N_4O_6$: C 52.63, H 2.94, N 16.37; found C 52.59, H 2.95, N 16.43.

5-(4-Oxo-2-thioxo-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)-2-thioxopyrimidine-4,6(1*H*,5*H*)-dione (3b) m.p.＞300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.12 (s, 1H), 6.83—7.01 (m, 2H), 7.09—7.22 (m, 2H), 11.84 (s, 1H), 12.14 (s, 1H), 12.28 (s, 1H), 12.36 (s, 1H), 13.31 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 26.5, 91.1, 98.3, 116.0, 123.3, 125.5, 128.4, 129.1, 149.3, 155.7, 157.8, 158.7, 161.4, 173.6, 177.5; IR (KBr) *v:* 3460, 3238, 1692, 1657, 1562, 1544, 1485, 1460, 1269, 1132 cm^{-1}. Anal. calcd for $C_{15}H_{10}N_4O_4S_2$: C 48.12, H 2.69, N 14.97; found C 48.16, H 2.64, N

14.94.

5-(2,4-Dioxo-7-chloro-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3c) m.p. > 300 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.91 (d, J=4.8 Hz, 1H), 4.73 (d, J=4.8 Hz, 1H), 7.11—7.36 (m, 2H), 7.62 (s, 1H), 10.87 (s, 1H), 11.16 (s, 1H), 11.25 (s, 1H), 12.15 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 34.6, 54.8, 87.6, 118.2, 127.3, 128.2, 128.7, 130.4, 147.5, 150.2, 151.3, 157.2, 164.8, 169.1, 170.4; IR (KBr) *v:* 3478, 3218, 1691,1640, 1599, 1475, 1436, 1347, 1245, 1137 cm^{-1}. Anal. calcd for $C_{15}H_9N_4O_6Cl$: C 47.82, H 2.41, N 14.88; found C 47.89, H 2.36, N 14.81.

5-(4-Oxo-2-thioxo-7-chloro-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)-2-thioxopyrimidine-4,6(1*H*,5*H*)-dione (3d) m.p. 252—254 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.08 (s, 1H), 7.03—7.28 (m, 2H), 7.53 (s, 1H), 10.21 (s, 1H), 11.84 (s, 1H), 12.25 (s, 1H), 12.39 (s, 1H), 13.38 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 27.1, 90.3, 97.1, 118.2, 126.4, 130.3, 131.1, 131.4, 150.3, 156.2, 158.1, 162.5, 159.2, 172.4, 179.2; IR (KBr) *v*: 3502, 3384, 1657, 1640, 1629, 1580, 1471, 1352, 1258, 1143 cm^{-1}. Anal. calcd for $C_{15}H_9N_4O_4ClS_2$: C 44.06, H 2.22, N 13.71; found C 44.01, H 2.31, N 13.79.

5-(2,4-Dioxo-7-bromo-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3e) m.p. 240—242 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.94 (d, J=4.9 Hz, 1H), 4.71 (d, J=4.9 Hz, 1H), 7.09 (d, J=7.0 Hz, 1H), 7.29 (s, 1H), 7.52 (d, J=7.0 Hz, 1H), 10.94 (s, 1H), 11.11 (s, 1H), 11.23 (s, 1H), 12.08 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 35.2, 54.4, 88.3, 115.9, 118.5, 128.3, 131.4, 133.5, 147.2, 151.2, 151.9, 157.6, 164.7, 169.6, 171.8; IR (KBr) *v:* 3514, 3234, 1674, 1596, 1546, 1427, 1391, 1341, 1299, 1175 cm^{-1}. Anal. calcd for $C_{15}H_9N_4O_6Br$: C 42.77, H 2.15, N 13.31; found C 42.69, H 2.21, N 13.39.

5-(4-Oxo-2-thioxo-7-bromo-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)-2-thioxopyrimidine-4,6(1*H*,5*H*)-dione (3f) m.p. 245—246 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.09 (s, 1H), 6.95 (d, J=7.0 Hz, 1H), 7.22 (s, 1H), 7.39 (d, J=7.0 Hz, 1H), 10.19 (s, 1H), 11.37 (s, 1H), 12.33 (s, 1H), 12.45 (s, 1H), 13.39 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 26.5, 90.8, 97.9, 116.9, 118.3, 130.8, 131.2, 131.5, 148.7, 156.3, 159.7, 161.3, 162.7, 173.7, 177.9; IR (KBr) *v:* 3517, 3234, 1658, 1641, 1624, 1545, 1477, 1369, 1321, 1278 cm^{-1}. Anal. calcd for $C_{15}H_9N_4O_4BrS_2$: C 39.74, H 2.01, N 12.36; found C 39.65, H 2.08, N 12.29.

5-(2,4-Dioxo-7-nitro-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidine-2,4,6(1*H*,3*H*,5*H*)-trione (3g) m.p. 250 — 251 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 3.99 (d, J=4.5 Hz, 1H), 4.86 (d, J=4.5 Hz, 1H), 7.04 (d, J=7.2 Hz, 1H), 7.31 (d, J=7.2 Hz, 1H), 8.02 (s, 1H), 10.98 (s, 1H), 11.32 (s, 1H), 11.47 (s, 1H), 12.23 (s, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 36.8, 55.6, 89.8, 117.8, 123.7, 124.8, 127.4, 141.3, 156.2, 156.8, 161.3, 161.8, 164.2, 171.1, 173.6; IR (KBr) *v:* 3468, 3109, 1738, 1722, 1688, 1658, 1640, 1544, 1384, 1126 cm^{-1}. Anal. calcd for $C_{15}H_9N_5O$: C 46.52, H 2.34, N 18.09; found C 46.45, H 2.39, N 18.16.

5-(4-Oxo-2-thioxo-7-nitro-2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)-2-thioxopyrimidine-4,6(1*H*,5*H*)-dione (3h) m.p. 265—266 ℃; ^{1}H NMR (DMSO-d_6, 400 MHz) δ: 5.95 (s, 1H), 6.85 (d, J=7.2 Hz, 1H), 7.29 (d, J=7.2 Hz, 1H), 7.91 (s, 1H), 10.31 (s, 1H), 11.44 (s, 1H, NH), 11.61 (s, 1H, NH), 12.41 (s, 1H, NH), 12.51 (s, 1H, OH); ^{13}C NMR (DMSO-d_6, 100 MHz) δ: 28.2, 91.1, 97.5, 117.9, 123.8, 124.9, 127.6, 141.5, 156.8, 157.3, 160.2, 161.5, 163.3, 174.2, 178.8; IR (KBr) *v:* 3418, 3241, 1751, 1682, 1647, 1586, 1521, 1436, 1342, 1154 cm^{-1}. Anal. calcd for $C_{15}H_9N_5O_6S_2$: C 42.96, H 2.16, N 16.70; found C 43.04, H 2.17, N 16.65.

Conclusions

In conclusion, we have descried a one-pot and efficient procedure for the preparation of 5-(2,3,4,5-tetrahydro-1*H*-chromeno[2,3-*d*]pyrimidin-5-yl)pyrimidione derivatives from salicylaldehyde or substituted salicylaldehydes with barbituric acid or 2-thiobarbituric acid at 50 ℃ in water using TEBA as phase transfer catalysis. The antimicrobial activities of these new synthesized compounds have been evaluated. All compounds demonstrated potent inhibition against all the strains tested. The importance of such work lies in the possibility that the new compounds might be more efficacious drugs against bacteria, which could be helpful in designing more potent antibacterial agents for therapeutic use.

Acknowledgment

We are grateful to the financial support from the Foundation of Jiangsu Key Laboratory of Marine Biotechnology (No. 2009HS04).

References

[1] Hajela, K.; Kapil, R. S. *Eur. J. Med. Chem.* **1997**, *32*, 135.
[2] Chen, M. J.; Lee, Y. M.; Sheu, J. R.; Hu, C. T.; Yen, M. H. *J. Pharm. Pharmacol.* **1998**, *50*, 83.
[3] Mannhold, R.; Cruciani, G.; Weber, H.; Lemoine, H.; Derix, A.; Weichel, C.; Clementi, M. *J. Med. Chem.* **1999**, *42*, 981.
[4] Kitamura, R. O. S.; Romoff, P.; Young, M. C. M.; Kato, M. J.; Lago, J. H. G. *Phytochemistry* **2006**, *67*, 2398.
[5] Rai, U. S.; Isloor, A. M.; Shetty, P.; Vijesh, A. M.; Prabhu, N.; Isloor, S.; Thiageeswaran, M.; Fun, H. K. *Eur. J. Med. Chem.* **2010**, *45*, 2695.
[6] Sabry, N. M.; Mohamed, H. M.; Khattab, E. S. A. E. H.; Motlaq, S. S.; El-Agrody, A. M. *Eur. J. Med. Chem.* **2011**, *46*, 765.
[7] Tangmouo, J. G.; Meli, A. L.; Komguem, J.; Kuete, V.; Ngounou, F. N.; Lontsi, D.; Beng, V. P.; Choudhary, M. I.; Sondengam, B. L. *Tetrahedron Lett.* **2006**, *47*, 3067.
[8] Abdelrazek, F. M.; Metz, P.; Kataeva, O.; Jäger, A.; El-Mahrouky, S. F. *Arch. Pharm.* **2007**, *340*, 543.
[9] Kappe, C. O.; Fabian, W. M. F.; Semones, M. A. *Tetrahedron* **1997**, *53*, 2803.

[10] Atwal, K. S.; Rovnyak, G. C.; O'Reilly, B. C.; Schwartz, J. *J. Org. Chem*. **1989**, *54*, 5898.
[11] Moafi, L.; Ahadi, S.; Bazgir, A. *Tetrahedron Lett*. **2010**, *51*, 6270.
[12] Li, C. J. *Chem. Rev*. **2005**, *105*, 3095.
[13] Breslow, R.; Maitra, U. *Tetrahedron Lett*. **1984**, *25*, 1239.
[14] Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *J. Am. Chem. Soc*. **1987**, *109*, 1160.
[15] Loh, T. P.; Liung, S. B. K. W.; Tan, K. L.; Wei, L. L. *Tetrahedron* **2000**, *56*, 227.
[16] Chanda, A.; Fokin, V. V. *Chem. Rev*. **2009**, *109*, 725.
[17] Cheng, Q. F.; Xu, X. Y.; Ma, W. X.; Zhang, H.; Liu, L. S; Liu, F.; Yang, X. J. *Chin. J. Org. Chem*. **2008**, *28*, 1767.
[18] Cheng, Q. F.; Xu, X. Y.; Ruan, M. J.; Wen, Y. L.; He, X. J.; Yang, X. J. *Chin. J. Org. Chem*. **2009**, *29*, 1138.
[19] Cheng, Q. F.; Xu, X. Y.; Wang, Q. F.; Liu, L. S.; Liu, W. J.; Lin, Q.; Yang, X. J. *Chin. J. Org. Chem*. **2009**, *29*, 1267.
[20] Cartney, M. M. C. *Practical Medical Microbiology*, Vol. 13, Churchill Livingstone, University of Michigan, **1989**.

(Li, L.)

