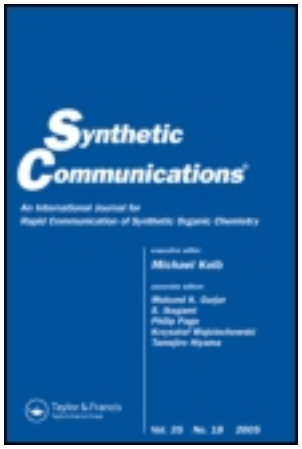


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry
Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Ammonium Chloride-Catalyzed One-Pot Synthesis of 4(3H)-Quinazolinones Under Solvent-Free Conditions

Guoli Huang [a] , Bo Liu [a] , Mingyu Teng [a] & Yegao Chen [a]
[a] School of Chemistry and Chemical Engineering, Yunnan Normal University , Kunming , China
Published online: 14 May 2014.

To cite this article: Guoli Huang , Bo Liu , Mingyu Teng & Yegao Chen (2014) Ammonium Chloride-Catalyzed One-Pot Synthesis of 4(3H)-Quinazolinones Under Solvent-Free Conditions, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 44:12, 1786-1794, DOI: 10.1080/00397911.2013.873467

To link to this article: http://dx.doi.org/10.1080/00397911.2013.873467

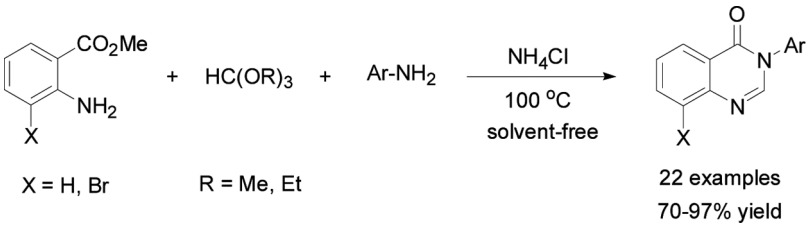
Synthetic Communications®, 44: 1786–1794, 2014

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397911.2013.873467

AMMONIUM CHLORIDE–CATALYZED ONE-POT SYNTHESIS OF 4(3*H*)-QUINAZOLINONES UNDER SOLVENT-FREE CONDITIONS

Guoli Huang, Bo Liu, Mingyu Teng, and Yegao Chen
School of Chemistry and Chemical Engineering, Yunnan Normal University, Kunming, China

GRAPHICAL ABSTRACT



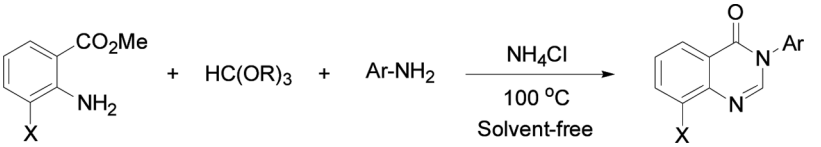
Abstract *Ammonium chloride, which is a very inexpensive and readily available reagent, can efficiently catalyze three-component, one-pot condensation reactions of 2-amino-benzoic acid esters, ortho esters, and aromatic amines to afford the corresponding 4(3*H*)-quinazolinones in good to excellent yields under solvent-free conditions.*

Keywords Ammonium chloride; one-pot condensation; 4(3*H*)-quinazolinones; solvent-free

INTRODUCTION

It is well known that 4(3*H*)-quinazolinones are fused heterocycles and exhibit a wide range of biological activities such as antimalarial, antitumor, anticonvulsant, anti-inflammatory, fungicidal, antimicrobial, antihypertensive, anti-parkinsonism, antihistaminic, and calcilytic activities.[1] In addition, a small number of quinazolinone core units such as 3-aryl-6,8-dichloro-2*H*-1,3-benzoxazine-2,4(3*H*)-diones,[2] 3-arylquinazoline-2,4(1*H*,3*H*)-diones, and quinazolinone derivatives[3] are potent chemotherapeutic agents in the treatment of tuberculosis. Recently, many synthetic methods for the preparation of this class of compounds have been reported. The most direct procedure includes the condensation of anthranilic acid, ortho esters, and amines in the presence of various catalysts such as $Yb(OTf)_3$,[4] SiO_2-$NaHSO_4$ or Amberlyst-15,[5] Yb(III)-resin,[6] $Bi(TFA)_3$-[nbp]$FeCl_4$ ionic liquid,[7]

Received August 1, 2013.
Address correspondence to Guoli Huang, School of Chemistry and Chemical Engineering, Yunnan Normal University, Kunming 650500, China. E-mail: hgli2005@126.com



Scheme 1. Synthesis of 4(3*H*)-quinazolinones catalyzed by NH_4Cl.

$La(NO_3)_3 \cdot 6H_2O$ or *p*-toluenesulfonic acid,[8] SiO_2-$FeCl_3$,[9] Keggin-type heteropolyacid,[10] iodine,[11] $Ce(CH_3SO_3)_3 \cdot 2H_2O$,[12] ceric ammonium nitrate (CAN),[13] $SrCl_2 \cdot 6H_2O$,[14] $Zn(ClO_4)_2$,[15] SiO_2-BF_3,[16] and $Al(NO_3)_3 \cdot 9H_2O$.[17] However, some of these methods are associated with certain drawbacks such as long reaction time (20 h), harmful organic solvent, and use of metal salts. Indeed, anthranilic acid is a precursor chemicals and not readily available. Therefore, the discovery of a new and inexpensive catalyst for the preparation of 4(3*H*)-quinazolinones under neutral and mild conditions is of prime importance. Recently, Vasu reported a novel, efficient, and greener one-pot method for the synthesis of 4(3*H*)-quinazolinones by the reaction of methyl anthranilate, *N,N*-dimethyl formamide dimethyl acetal, and anilines.[18]

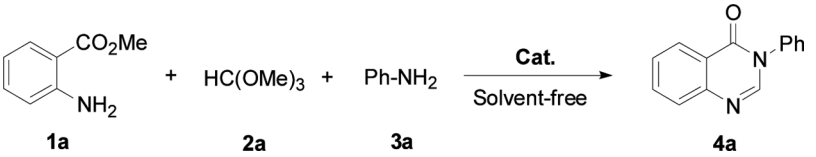
In this regard, ammonium chloride is very inexpensive, easily available, and efficient catalyst in organic synthesis. It can effectively promote reactions such as four-component synthesis of pyrrolo[3,4-*b*]pyridinones,[19] Ugi four-component, five-center reactions,[20] and three-component synthesis of 5-iminooxazoline.[21] Moreover, ammonium chloride was used as an efficient catalyst for reactions such as reduction of nitrophenols under ultrasound,[22] Biginelli synthesis of 3,4-dihydropyrimidinones under solvent-free conditions,[23] one-pot synthesis of diindolylmethanes under solvent-free conditions,[24] and thia-Michael addition reaction of carbon–sulfur bond formation in water.[25]

Herein we report the synthesis of 3-aryl-4(3*H*)-quinazolinones by the three-component condensation of 2-amino-benzoic acid esters, ortho esters, and aromatic amines in the presence of NH_4Cl as a very inexpensive, easily available, and efficient catalyst under solvent-free conditions (Scheme 1).

RESULTS AND DISCUSSION

The one-pot condensation reaction of 2-amino-benzoic acid esters (**1a**), trimethyl orthofomate (**2a**), and aniline (**3a**) was chosen as a model system to determine the optimum reaction conditions, and the results are summarized in Table 1. The initial study was conducted by examining the suitable ammonium salts including organic and inorganic ones in the model reaction. First, the model reaction proceeded in the presence of NH_4OAc and generated the desired product **4a** in 90% yield (entry 1). Further, other ammonium salts, such as $(NH_4)_2(CO_2)_2$, $(NH_4)_2SO_4$, and $(NH_4)_2Fe(SO_4)_2 \cdot 6H_2O$, showed less reactivity than NH_4Cl (entries 2–5), which gave the greatest yield (99%). We investigated the effect of the amount of NH_4Cl on the reaction. Reducing the catalyst loading from 40 to 20 and 10 mol% lowered the conversion from 99 to 85 and 71%, respectively (entries 5–7). In the absence of the catalyst, the trace product was observed after a long reaction time (6 h) (entry 8).

Table 1. Synthesis of 4(3*H*)-quinazolinones under solvent-free conditions[a]



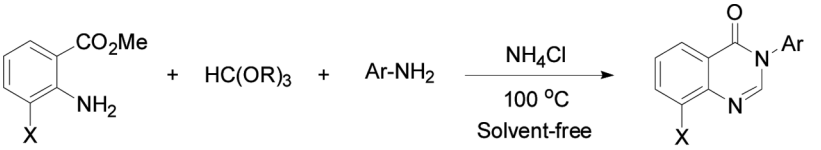
Entry	Catalyst	Amount of catalyst (mol%)	Temperature (°C)	Time (h)	Yield of **4a** (%)[b]
1	NH_4OAc	40	100	2	90
2	$(NH_4)_2(CO_2)_2$	40	100	2	20
3	$(NH_4)_2SO_4$	40	100	2	31
4	$(NH_4)_2Fe(SO_4)_2 \cdot 6H_2O$	40	100	2	10
5	NH_4Cl	40	100	2	99 (81)[c]
6	NH_4Cl	20	100	2	85
7	NH_4Cl	10	100	2	71
8	—	—	100	2	<5
9	NH_4Cl	40	80	2	67
10	NH_4Cl	40	60	2	44
11	NH_4Cl	40	100	1	81
12	NH_4Cl	40	100	0.5	60

[a]Reaction conditions: 2-amino-benzoic acid ester (1.0 mmol), aniline (1.2 mmol), trimethyl orthofomate (1.5 mmol).
[b]Determination from ^1H NMR.
[c]The molar ratio of 2-amino-benzoic acid esters, aniline, and trimethyl orthofomate is 1.0:1.2:1.2.

It is evident that the amount of catalyst has remarkable effect on this reaction. The effect of temperature has also been investigated. The reaction could proceed smoothly at 100 °C. However, lowering the temperature from 100 to 80 and 60 °C significantly reduced the conversion from 99 to 67 and 44% (entries 9 and 10). We have tried to shorten the reaction time from 2 to 1 and 0.5 h, but the conversion was obviously lowered from 99 to 81 and 60%, respectively (entries 11 and 12). Hence, the optimal reaction conditions were 2-amino-benzoic acid esters (1.0 equiv), ortho esters (1.5 equiv), and aromatic amines (1.2 equiv) at 100 °C for 2 h under solvent-free conditions.

After establishing the optimal reaction conditions, a wide range of structurally varied 2-amino-benzoic acid esters, ortho esters, and aromatic amines were examined in the presence of NH_4Cl under solvent-free conditions, and the results are summarized in Table 2. In all cases, the three-component reaction proceeded rapidly to afford the corresponding 4(3*H*)-quinazolinones in excellent yields. In addition to 2-amino-benzoic acid ester (**1a**), 8-bromo-2-amino-benzoic acid ester was subjected to the condensation reactions. The position of substituent groups on the 2-amino-benzoic acid esters did not significantly affect the reaction rates and yields (entries 1 and 7). In addition, equally good results were obtained for trimethyl and triethyl orthoformates, but triethyl orthoformate gave slightly greater yields than trimethyl orthoformate under the optimized conditions (entries 1 vs 2, 3 vs 4, 7 vs 8, 12 vs 13, 18 vs 19). A variety of substituent groups of the aromatic amines were well

Table 2. Synthesis of 4(3*H*)-quinazolinones catalyzed by NH_4Cl under solvent-free conditions[a]



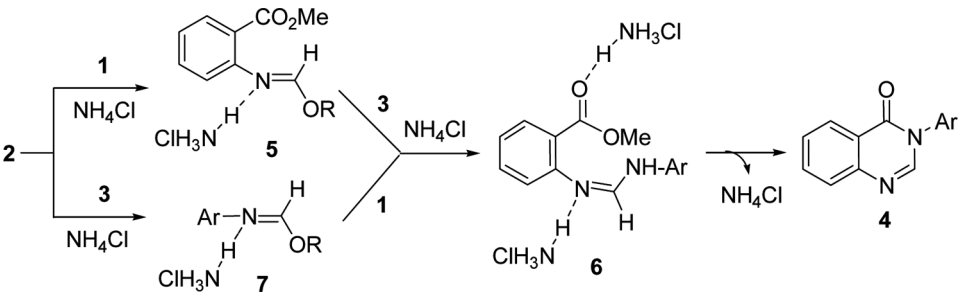
1 2 3 4

Entry	X	R	Ar	Product (yield %)[b]
1	H	Me	Ph	**4a** (92) (99)[c]
2	H	Et	Ph	**4a** (94)
3	H	Me	4-MeC_6H_4	**4b** (95)
4	H	Et	4-MeC_6H_4	**4b** (96)
5	H	Me	1-Naphthyl	**4c** (91)
6	H	Me	2-MeC_6H_4	**4d** (89)
7	Br	Me	Ph	**4e** (93)
8	Br	Et	Ph	**4e** (95)
9	Br	Me	1-Naphthyl	**4f** (95)
10	Br	Me	4-MeC_6H_4	**4g** (97)
11	Br	Me	2-MeC_6H_4	**4h** (91)
12	H	Me	4-$MeOC_6H_4$	**4i** (96)
13	H	Et	4-$MeOC_6H_4$	**4i** (97)
14	H	Me	3,4-$Cl_2C_6H_3$	**4j** (91)
15	H	Me	4-$MeCOC_6H_4$	**4k** (86)
16	H	Me	4-$NO_2C_6H_4$	**4l** (75)
17	H	Me	4-$HO_2CC_6H_4$	**4m** (70)
18	Br	Me	4-$MeOC_6H_4$	**4n** (95)
19	Br	Et	4-$MeOC_6H_4$	**4n** (97)
20	Br	Me	4-$MeCOC_6H_4$	**4o** (90)
21	Br	Me	3,4-$Cl_2C_6H_3$	**4p** (84)
22	Br	Me	2-BrC_6H_4	**4q** (82)

[a]Reaction conditions: 2-amino-benzoic acid esters (1.0 mmol), aromatic amines (1.2 mmol), ortho esters (1.5 mmol).
[b]Isolated yields.
[c]Determination from ^{1}H NMR.

tolerated. In general, reaction substrates with electron-donating groups (such as methoxy and methyl, entries 3, 6, and 12) on the aniline system gave greater yields than those with electron-withdrawing groups (such as chloro, acetyl, nitro, carboxyl and bromo, entries 14–17, and 22), possibly due to the increased electron density of aromatic system. Furthermore, the positions of substituent groups on the aniline system also affected the reaction rates and yields under the optimized conditions. The yield of product with *ortho*-substituted anilines was lower than that with *para* positions (entries 3 vs 6, 10 vs 11).

We propose a mechanism similar to that of Errede[26] and Wang[4] for the reaction (Scheme 2). In the first step of this reaction, NH_4Cl facilitates the reaction of ortho esters **2** with 2-amino-benzoic acid ester **1** or aromatic amines **3** to give imidic ester **5** or **7**, which are very prone to react immediately with amine (**3** or **1**) to form an amidine intermediate **6** that is further activated by NH_4Cl. Subsequently, the



Scheme 2. Possible reaction mechanism for NH_4Cl-catalyzed synthesis of 4(*3H*)-quinazolinones.

reaction proceeds via **6** by an intramolecular attack of the nitrogen nucleophile at carbonyl carbon to produce the corresponding cyclized product **4**.

CONCLUSION

In summary, we have developed an economical and environmentally friendly procedure for the synthesis of 4(*3H*)-quinazolinones via a three-component, one-pot condensation of 2-amino-benzoic acid esters, ortho esters, and aromatic amines in excellent yields. This involves the use of NH_4Cl as a very inexpensive and easily available catalyst, solvent-free conditions, and reduced reaction time.

EXPERIMENTAL

2-Amino-3-bromobenzoic acid methyl ester was synthesized by stirring 2-aminobenzoic acid methyl ester with *N*-bromosuccinimide (NBS) in AcOH (see the supplemental material). The commercially available reagents and solvents were used without further purification unless otherwise noted. Column chromatography was performed with silica gel (200–300 mesh). ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance III 500-MHz spectrometer for solution in $CDCl_3$ or DMSO-d_6. High-resolution mass spectra (HRMS) were obtained from Agilent 6538 UHD accurate-mass Q-TOF. All the products (except **4e–4h** and **4n–4q**) are known compounds,[4,7,8,11–14,18,27] which were characterized by ^1H and ^{13}C NMR spectral data (see the supplemental material).

General Experimental Procedure for the Preparation of Compounds 4a–q

A mixture of 2-amino-benzoic acid esters (1.0 mmol), aromatic amines (1.2 mmol), ortho esters (1.5 mmol), and NH_4Cl (0.021 g, 0.4 mmol) was heated with stirring at 100 °C for 2 h. After cooling, H_2O was added and the product was extracted with EtOAc. The organic layer was dried ($MgSO_4$) and evaporated, and the residue was recrystallized from EtOH–hexane to afford the pure product.

8-Bromo-3-phenyl-4(3*H*)-quinazolinone (4e)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.50$ (s, 1H), 8.13 (s, 1H), 7.88 (d, $J = 8.6$ Hz, 1H), 7.65 (d, $J = 8.6$ Hz, 1H), 7.58–7.50 (m, 3H), 7.42 (d, $J = 7.6$ Hz, 2H). ^{13}C NMR ($CDCl_3$) $\delta = 159.7$, 146.9, 146.8, 137.9, 137.3, 129.9, 129.8, 129.5, 129.4, 127.0, 123.9, 121.4. HRMS (EI): calcd. for $C_{14}H_9BrN_2O$ [MH^+]: 302.1455; found 302.1459.

8-Bromo-3-(1-naphthyl)-4(3*H*)-quinazolinone (4f)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.53$ (d, $J = 1.9$ Hz, 1H), 8.10 (s, 1H), 8.04 (d, $J = 8.3$ Hz, 1H), 7.98 (d, $J = 8.1$ Hz, 1H), 7.93 (dd, $J = 8.7$, 2.1 Hz, 1H), 7.72 (d, $J = 8.7$ Hz, 1H), 7.65–7.47 (m, 5H). ^{13}C NMR ($CDCl_3$) $\delta = 160.0$, 147.3, 147.1, 138.0, 134.5, 133.9, 130.6, 129.9, 129.7, 129.6, 128.8, 128.0, 127.1, 126.0, 125.6, 123.9, 121.9, 121.5. HRMS (EI): calcd. for $C_{18}H_{11}BrN_2O$ [MH^+]: 352.2041; found 352.2044.

8-Bromo-3-(4-methylphenyl)-4(3*H*)-quinazolinone (4g)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.49$ (d, $J = 2.0$ Hz, 1H), 8.11 (s, 1H), 7.87 (dd, $J = 8.6$, 2.1 Hz, 1H), 7.63 (d, $J = 8.6$ Hz, 1H), 7.35 (d, $J = 8.0$ Hz, 2H), 7.29 (d, $J = 8.2$ Hz, 2H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$) $\delta = 159.8$, 146.9, 146.7, 139.6, 137.8, 134.7, 130.4, 129.8, 129.5, 126.7, 123.9, 121.3, 21.3. HRMS (EI): calcd. for $C_{15}H_{11}BrN_2O$ [MH^+]: 316.1720; found 316.1715.

8-Bromo-3-(2-methylphenyl)-4(3*H*)-quinazolinone (4h)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.51$ (s, 1H), 8.00 (s, 1H), 7.90 (dd, $J = 5.4$, 1.8 Hz, 1H), 7.67 (d, $J = 7.1$ Hz, 1H), 7.40 (d, $J = 18.6$ Hz, 3H), 2.20 (s, 3H). ^{13}C NMR ($CDCl_3$) $\delta = 159.4$, 147.1, 146.8, 137.9, 136.4, 135.8, 131.5, 130.0, 129.8, 129.6, 127.8, 127.5, 123.9, 121.4, 17.8. HRMS (EI): calcd. for $C_{15}H_{11}BrN_2O$ [MH^+]: 316.1720; found 316.1726.

8-Bromo-3-(4-methoxyphenyl)-4(3*H*)-quinazolinone (4n)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.48$ (d, $J = 1.8$ Hz, 1H), 8.10 (s, 1H), 7.86 (dd, $J = 8.6$, 2.0 Hz, 1H), 7.63 (d, $J = 8.6$ Hz, 1H), 7.32 (d, $J = 8.8$ Hz, 2H), 7.04 (d, $J = 8.8$ Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 146.9, 146.8, 137.8, 129.9, 129.8, 129.5, 128.2, 123.9, 121.3, 115.0, 55.7. HRMS (EI): calcd. for $C_{15}H_{11}BrN_2O_2$ [MH^+]: 332.1714; found 332.1717.

8-Bromo-3-(4-acetylphenyl)-4(3*H*)-quinazolinone (4o)

Yellow solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.49$ (d, $J = 2.0$ Hz, 1H), 8.15 (d, $J = 8.4$ Hz, 2H), 8.12 (s, 1H), 7.90 (dd, $J = 8.6$, 2.1 Hz, 1H), 7.66 (d, $J = 8.6$ Hz, 1H), 7.55 (d, $J = 8.4$ Hz, 2H), 2.67 (s, 3H). ^{13}C NMR ($CDCl_3$) $\delta = 196.8$, 159.4,

146.7, 145.6, 141.0, 138.2, 137.6, 129.9 (2C), 129.6, 127.2, 123.7, 121.8, 26.9. HRMS (EI): calcd. for $C_{16}H_{11}BrN_2O_2$ [MH^+]: 344.1821; found 344.1824.

8-Bromo-3-(3,4-dichlorophenyl)-4(3*H*)-quinazolinone (4p)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.47$ (s, 1H), 8.06 (s, 1H), 7.95–7.86 (m, 1H), 7.64 (dd, $J = 8.6$, 2.5 Hz, 2H), 7.57 (s, 1H), 7.29 (dd, $J = 8.4$, 1.7 Hz, 1H). ^{13}C NMR ($CDCl_3$) $\delta = 159.4$, 146.6, 145.4, 138.3, 136.3, 134.1, 134.0, 131.5, 129.9, 129.7, 129.2, 126.4, 123.6, 121.9. HRMS (EI): calcd. for $C_{14}H_7BrC_{l2}N_2O$ [NH^+] 371.0356; found 371.0350.

8-Bromo-3-(3-bromophenyl)-4(3*H*)-quinazolinone (3q)

White solid. ^{1}H NMR ($CDCl_3$) $\delta = 8.49$ (d, $J = 2.3$ Hz, 1H), 7.94 (s, 1H), 7.90 (dd, $J = 8.7$, 2.0 Hz, 1H), 7.83–7.77 (m, 1H), 7.67 (d, $J = 8.7$ Hz, 1H), 7.52 (t, $J = 7.4$ Hz, 1H), 7.44–7.20 (m, 2H). ^{13}C NMR ($CDCl_3$) $\delta = 159.1$, 147.0, 146.3, 138.0, 136.5, 134.1, 131.5, 130.0, 129.9, 129.7, 129.0, 124.0, 122.5, 121.5. HRMS (EI): calcd. for $C_{14}H_8Br_2N_2O$ [NH^+] 381.0415; found 381.0410.

FUNDING

We thank the Applied Basic Research Projects of Yunnan Province (No. 2013FZ043, 2014FZ042) and the Scientific Research Fund of Yunnan Education Department (No. 22012Z017, 2013Y431) for the financial support.

SUPPLEMENTAL MATERIAL

Supplemental data for this article can be accessed on the publisher's website.

REFERENCES

1. (a) Jang, C. S.; Fu, F. Y.; Wang, C. Y.; Huang, K. C.; Lu, G.; Thou, T. C. Ch'ang Shan, a Chinese antimalarial herb. *Science* **1946**, *103*, 59; (b) Baker, B. R.; Schaub, R. E.; Joseph, J. P.; McEvoy, F. J.; Williams, J. H. An antimalarial alkaloid from hydrangea, XVIII: Derivatives of 4-pyrimidone. *J. Org. Chem.* **1953**, *18*, 133–137; (c) Bahadur, S.; Saxena, M. Syntheses and biological activities of some new 4(3*H*)-quinazolinones. *Arch. Pharm. (Weinheim)* **1983**, *316*, 964–968; (d) Wolfe, J. F.; Rathman, T. L.; Sleevi, M. C.; Campbell, J. A.; Greenwood, T. D. Synthesis and anticonvulsant activity of some new 2-substituted 3-aryl-4(3*H*)-quinazolinones. *J. Med. Chem.* **1990**, *33*, 161–166; (e) Kurogi, Y.; Inoue, Y.; Tsutsumi, K.; Nakamura, S.; Nagao, K.; Yoshitsugu, H.; Tsuda, Y. Synthesis and hypolipidemic activities of novel 2-[4-[(diethoxyphosphoryl)methyl]phenyl]-quinazolines and 4(3*H*)-quinazolinones. *J. Med. Chem.* **1996**, *39*, 1433–1437; (f) Padia, J. K.; Field, M.; Hinton, J.; Meecham, K.; Pablo, J.; Pinnock, R.; Roth, B. D.; Singh, L.; Suman-Chauhan, N.; Trivedi, B. K.; Webdale, L. Novel nonpeptide CCK-B antagonists: Design and development of quinazolinone derivatives as potent, selective, and orally active CCK-B antagonists1. *J. Med. Chem.* **1998**, *41*, 1042–1049; (g) Liverton, N. J.; Armstrong, D. J.; Claremon, D. A.; Remy, D. C.; Baldvin, J. J.; Lynch, R. J.; Zhang, G.; Gould, R. J. Nonpeptide glycoprotein IIb/IIIa inhibitors: Substituted quinazolinediones and quinazolinones as potent fibrinogen receptor antagonists. *Bioorg. Med. Chem.*

Lett. **1998**, *8*, 483–486; (h) Kamal, A.; Ramana, K. V.; Rao, M. V. Chemoenzymatic synthesis of pyrrolo[2,1-*b*]quinazolinones: Lipase-catalyzed resolution of vasicinone. *J. Org. Chem.* **2001**, *66*, 997–1001; (i) Shcherbakova, I.; Balandrin, M. F.; Fox, J.; Ghatak, A.; Heaton, W. L.; Conklin, R. L. 3*H*-Quinazolin-4-ones as a new calcilytic template for the potential treatment of osteoporosis. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1557–1560; (j) Cao, S.-L.; Feng, Y.-P.; Jiang, Y.-Y.; Liu, S.-Y.; Ding, G.-Y.; Li, R.-T. Synthesis and in vitro antitumor activity of 4(3*H*)-quinazolinone derivatives with dithiocarbamate side chains. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1915–1917.

2. Waisser, K.; Gregor, J.; Dostál, H.; Kuneš, J.; Kubicová, L.; Klimešová, V.; Kaustová, J. Influence of the replacement of the oxo function with the thioxo group on the antimycobacterial activity of 3-aryl-6,8-dichloro-2*H*-1,3-benzoxazine-2,4(3*H*)-diones and 3-arylquinazoline-2,4(1*H*,3*H*)-diones. *Farmaco* **2001**, *56*, 803–807.
3. Kuneš, J.; Bažant, J.; Pour, M.; Waisser, K.; Šlosárek, M.; Janota, J. Quinazoline derivatives with antitubercular activity. *Farmaco* **2000**, *55*, 725–729.
4. Wang, L.; Xia, J.; Qin, F.; Qian, C.; Sun, J. $Yb(OTf)_3$-catalyzed one-pot synthesis of quinazolin-4(3*H*)-ones from anthranilic acid, amines, and ortho esters (or formic acid) in solvent-free conditions. *Synthesis* **2003**, 1241–1247.
5. Das, B.; Banerjee, J. Silica-supported sodium hydrogen sulfate and amberlyst-15: Two efficient heterogeneous catalysts for single-step synthesis of 4(3*H*)-quinazolinones from anthranilic acid, ortho esters, and amines under solvent-free conditions. *Chem. Lett.* **2004**, *33*, 960–961.
6. Jiang, Z.; Chen, R. Synthesis of 3,4-dihydropyrimidine-2(1*H*)-thiones and quinazolin-4(3*H*)-ones over Yb(III)-resin catalyst under solvent-free conditions. *Synth. Commun.* **2005**, *35*, 503–509.
7. Khosropour, A. R.; Mohammadpoor-Baltork, I.; Ghorbankhani, H. $Bi(TFA)_3$-[nbp]$FeCl_4$: A new, efficient, and reusable promoter system for the synthesis of 4(3*H*)-quinazolinone derivatives. *Tetrahedron Lett.* **2006**, *47*, 3561–3564.
8. Narasimhulu, M.; Mahesh, K. C.; Reddy, T. S.; Rajesh, K.; Venkateswarlu, Y. Lanthanum(III) nitrate hexahydrate or p-toluenesulfonic acid–catalyzed one-pot synthesis of 4(3*H*)-quinazolinones under solvent-free conditions. *Tetrahedron Lett.* **2006**, *47*, 4381–4383.
9. Chari, M. A.; Shobha, D.; Mukkanti, K. Silica gel/$FeCl_3$: An efficient and recyclable heterogenous catalyst for one step synthesis of 4(3*H*)-quinazolinones under solvent-free conditions. *Catal. Commun.* **2006**, *7*, 787–788.
10. Ighilahriz, K.; Boutemeur, B.; Chami, F.; Rabia, C.; Hamdi, M.; Hamdi, S. A microwave-assisted and heteropolyacids-catalysed cyclocondensation reaction for the synthesis of 4(3*H*)-quinazolinones. *Molecules* **2008**, *13*, 779–789.
11. Wang, H. S.; Zeng, J. E. Iodine-catalyzed one-pot synthesis of 3,4-dihydroquinazolin-4-ones from anthranilic acids, ortho esters, and amines under solvent-free conditions. *Chin. J. Chem.* **2008**, *26*, 175–178.
12. Wang, M.; Song, Z.-G.; Zhang, T.-T. Synthesis of 3-aryl-4(3*H*)-quinazolinones from anthranilic acid, ortho esters, and anilines using $Ce(CH_3SO_3)_3 \cdot 2H_2O$ as catalyst. *Monatsh. Chem.* **2010**, *141*, 993–996.
13. Wang, M.; Song, Z. G.; Zhang, T. T. Synthesis of 3-substituted 4(3*H*)-quinazolinones catalyzed by ceric ammonium nitrate. *Chem. Heterocycl. Compd.* **2010**, *46*, 581–584.
14. Wang, M.; Song, Z. G.; Zhang, T. T. Strontium chloride–catalyzed one-pot synthesis of 4(3*H*)-quinazolinones under solvent-free conditions. *Chin. Chem. Lett.* **2010**, *21*, 1167–1170.
15. Jing, X.-B.; Li, Z.; Pan, X.; Shi, Y.-C. A novel method for the synthesis of 4(3*H*)-quinazolinones. *J. Chin. Chem. Soc.* **2008**, *55*, 1145–1149.

16. Wu, L. Q.; Ma, W. W.; Yang, L. M.; Yan, F. L. Silica-supported boron trifluoride (BF_3-SiO_2): An efficient, environment friendly, and recyclable catalyst for the one-pot synthesis of 4(3*H*)-quinazolinones. *Asian J. Chem.* **2010**, *22*, 6053–6058.
17. Wang, M.; Song, Z.; Zhang, T. Aluminium nitrate–catalyzed one-pot synthesis of 4(3*H*)-quinazolinones by a three-component coupling of anthranilic acid, amines, and ortho esters. *Synth. Commun.* **2011**, *41*, 385–391.
18. Jalani, H. B.; Pandya, A. N.; Pandya, D. H.; Sharma, J. A.; Sudarsanam, V.; Vasu, K. K. An efficient, greener, and solvent-free one-pot multicomponent synthesis of 3-substituted quinazolin-4(3*H*)ones and thienopyrimidin-4(3*H*)ones. *Tetrahedron Lett.* **2012**, *53*, 4062–4064.
19. Janvier, P.; Sun, X.; Bienaymé, H.; Zhu, J. Ammonium chloride–promoted four-component synthesis of pyrrolo[3,4-*b*]pyridin-5-one. *J. Am. Chem. Soc.* **2002**, *124*, 2560–2567.
20. Bonne, D.; Dekhane, M.; Zhu, J. Ammonium chloride–promoted Ugi four-component, five-center reaction of α-substituted α-isocyano acetic acid: A strong solvent effect. *Org. Lett.* **2004**, *6*, 4771–4774.
21. Pirali, T.; Tron, G. C.; Masson, G.; Zhu, J. Ammonium chloride–promoted three-component synthesis of 5-iminooxazoline and its subsequent transformation to macrocyclodepsipeptide. *Org. Lett.* **2007**, *9*, 5275–5278.
22. Basu, M. K.; Becker, F. F.; Banik, B. K. Ultrasound-promoted highly efficient reduction of aromatic nitro compounds to the aromatic amines by samarium/ammonium chloride. *Tetrahedron Lett.* **2000**, *41*, 5603–5606.
23. Shaabani, A.; Bazgir, A.; Teimouri, F. Ammonium chloride–catalyzed one-pot synthesis of 3,4-dihydropyrimidin-2-(1*H*)-ones under solvent-free conditions. *Tetrahedron Lett.* **2003**, *44*, 857–859.
24. Azizian, J.; Teimouri, F.; Mohammadizadeh, M. R. Ammonium chloride–catalyzed one-pot synthesis of diindolylmethanes under solvent-free conditions. *Catal. Commun.* **2007**, *8*, 1117–1121.
25. Chen, W.; Shi, L. Ammonium chloride–catalyzed carbon–sulfur bond formation in water. *Catal. Commun.* **2008**, *9*, 1079–1081.
26. Errede, L. A.; McBrady, J. J.; Oien, H. T. Acylanthranils, 4: The effect of steric hindrance on selectivity in the reaction of amines with acetylanthranil. *J. Org. Chem.* **1977**, *42*, 656–658.
27. Shi, D.; Rong, L.; Wang, J.; Zhuang, Q.; Wang, X.; Hu, H. Synthesis of quinazolin-4(3*H*)-ones and 1,2-dihydroquinazolin-4(3*H*)-ones with the aid of a low-valent titanium reagent. *Tetrahedron Lett.* **2003**, *44*, 3199–3201.