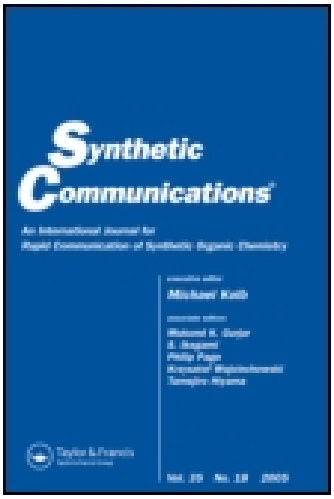


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Facile and One-Pot Synthesis of 1,2-Dihydroquinazolin-4(3H)-ones via Tandem Intramolecular Pinner/Dimroth Rearrangement

Jian-Hong Tang [a] , Da-Xin Shi [a] , Li-Jun Zhang [b] , Qi Zhang [a] & Jia-Rong Li [a]

[a] School of Chemical Engineering and Environment , Beijing Institute of Technology , Beijing, China

[b] School of Chemistry and Chemical Engineering , Tianjin University of Technology , Tianjin, China

Published online: 04 Feb 2010.

To cite this article: Jian-Hong Tang , Da-Xin Shi , Li-Jun Zhang , Qi Zhang & Jia-Rong Li (2010) Facile and One-Pot Synthesis of 1,2-Dihydroquinazolin-4(3H)-ones via Tandem Intramolecular Pinner/Dimroth Rearrangement, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 40:5, 632-641, DOI: 10.1080/00397910902908822

To link to this article: http://dx.doi.org/10.1080/00397910902908822

Synthetic Communications®, 40: 632–641, 2010

ISSN: 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910902908822

Taylor & Francis
Taylor & Francis Group

FACILE AND ONE-POT SYNTHESIS OF 1,2-DIHYDROQUINAZOLIN-4(3*H*)-ONES VIA TANDEM INTRAMOLECULAR PINNER/DIMROTH REARRANGEMENT

Jian-Hong Tang,[1] Da-Xin Shi,[1] Li-Jun Zhang,[2] Qi Zhang,[1] and Jia-Rong Li[1]

[1]*School of Chemical Engineering and Environment, Beijing Institute of Technology, Beijing, China*

[2]*School of Chemistry and Chemical Engineering, Tianjin University of Technology, Tianjin, China*

An efficient synthetic method for the preparation of quinazolin-4-one derivatives was designed. The facile condensation of aromatic o-aminonitriles with aromatic aldehydes catalyzed by Lewis acid give 1,2-dihydroquinazolin-4(3H)-ones in moderate to good yields under refluxing dimethylformamide.

Keywords: Aromatic aldehyde; aromatic *o*-aminonitrile; catalyst; cyclocondensation; one-pot synthesis

INTRODUCTION

1,2-Dihydroquinazolin-4(3*H*)-ones are important and useful nitrogen-containing heterocycles because of their diverse biological activities. They have been widely used as antitumor agents, α_1-adrenoceptors antagonists, plant growth regulators, diuretics, and herbicides.[1] Some dihydroquinazolinones also show potential applications in flat-panel display as electro-luminescence material sandwiched in organic light-emitting devices.[2] The main synthetic approaches to 1,2-dihydroquinazolin-4(3*H*)-ones consist of preliminary amidation of 2-amino-benzonitrile, 2-amino-benzoic acid, or its derivatives followed by oxidative ring closure under basic conditions.[3] Other methods involve cycloaddition of anthranilic acid derivatives with a diverse range of substrates including imidates and iminohalides and the aza–Witting reactions of α-azido-substituted aromatic amides.[4,5] However, some of these methods are associated with drawbacks such as multistep procedures, costly reagents, harsh reaction conditions, and poor yields. Thus, there is still a need to develop efficient methods for the synthesis of dihydroquinazolinones.

Received January 11, 2009.

Address correspondence to Jia-Rong Li, School of Chemical Engineering and Environment, Beijing Institute of Technology, Beijing 100081, China. E-mail: jrli@bit.edu.cn

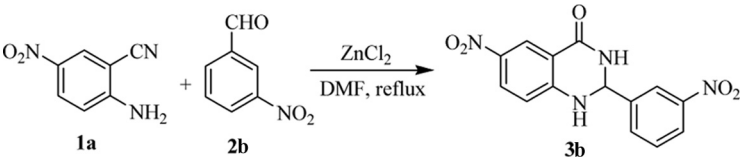
Aromatic *o*-aminonitrile is a versatile synthon for the synthesis of nitrogen-containing fused heterocycles **5**,[6] such as pyrimidine,[7] quinazoline,[8,9] quinazolinone,[10,11] and quin[3,4-a]carbazole.[12] In continuation of our previous work on the synthesis of a variety of nitrogen-containing heterocycles from 2-aminobenzonitriles,[13] we report herein a convenient and one-pot synthesis of 1,2-dihydroquinazolin-4(3*H*)-ones from the cyclocondensation of aromatic *o*-aminonitriles with aromatic aldehydes using anhydrous $ZnCl_2$ as the catalyst.

The reaction of 2-amino-5-nitrobenzonitrile **1a** with 3-nitrobenzoaldehyde **2b** was chosen as a model (Scheme 1). After different conditions were screened, we were delighted to find that the 1,2-dihydroquinazolin-4(3*H*)-one derivative **3b** was obtained from this reaction with $ZnCl_2$ as catalyst in a suitable boiling solvent. After screening solutions, we found dimethylformamide (DMF) was the best solvent and dimethylsulfoxide (DMSO) was also suitable for this annulation, but no product was afforded in nonpolar solvents such as toluene and xylene.

With the optimized reaction conditions in hand, various aldehydes **2**, including aromatic or heteroaromatic aldehydes with either electron-donating or electron-withdrawing substitutents, were subjected to react with **1** to investigate the reaction scope, and the representative results are summarized in Table 1.

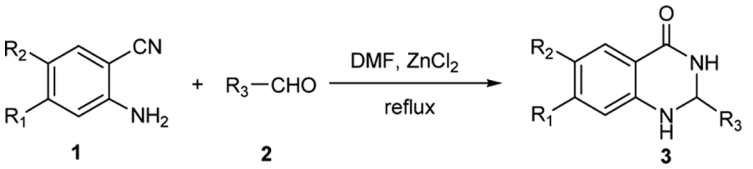
1,2-Dihydroquinazolin-4(3*H*)-one derivatives **3a–n** (Table 1) were formed by the reactions of aromatic *o*-aminonitriles with aldehydes in refluxed DMF in good yields. The position and electronic nature of the substituent on the phenyl ring of arylaldehydes had no relevance to quinazolinone yield. Although nitro- and methoxy- substitutents have different electron effects on benzaldehydes, similar reaction rate and yield were observed. Heteroaromatic aldehydes were also readily cyclized with **1** to afford quinazolinones **3m–n** in 72–77% yield. The new conversion proceeded better when *o*-aminonitriles **1** had electron-withdrawing substituents. The structures of **3** were verified by instrument analysis, and **3l** was also further elucidated by x-ray crystallographic analysis (Fig. 1). Crystal data for **3l**: chemical formula, $C_{14}H_{11}N_3O_3$; formula weight, 269.26; temperature (K), 113(2); crystal system, monoclinic; space group, *Pnma*; and unit cell dimension, $a = 1.09766(13)$ nm, $b = 0.98626(9)$ nm, $c = 1.17636(14)$ nm, $\alpha = 90.00$, $\beta = 109.697(7)^\circ$, $\gamma = 90^\circ$; $V = 1.1990(2)$ nm^3, $Z = 4$, and $D_C = 1.492$ g cm^{-3}.

On the basis of these observations, a possible mechanism was proposed (Scheme 2). Addition of the amino group of the *o*-aminonitrile onto the carbonyl of the aldehyde gave the key intermediate **I**. The hydroxyl group of intermediate **I** then attacked the nitrile group (i.e., Pinner reaction[14]) to afford a benzoxazine **II**, which subsequently rearranged (Dimroth rearrangement[15]) to give the product **3**.



Scheme 1. Condensation of 2-amino-5-nitrobenzonitrile with 3-nitrobenzoaldehyde.

Table 1. Results of the reaction of o-aminonitriles with various aldehydes in DMF[a]



Entry	Product	R_1	R_2	R_3	Time (h)	Yield[b] (%)
1	**3a**	H	NO_2	C_6H_5	1.5	72
2	**3b**	H	NO_2	*m*-$O_2NC_6H_4$	1	80
3	**3c**	H	NO_2	*p*-$CH_3OC_6H_4$	1	82
4	**3d**	H	NO_2	*p*-ClC_6H_4	1	80
5	**3e**	H	NO_2	*p*- $O_2NC_6H_4$	1	77
6	**3f**	Cl	H	*p*- $O_2NC_6H_4$	2	72
7	**3g**	Cl	H	*p*-$CH_3OC_6H_4$	2	74
8	**3h**	H	H	*p*- $O_2NC_6H_4$	2.5	67
9	**3i**	H	H	*o*-HOC_6H_4	2.5	72
10	**3j**	H	H	*p*-$CH_3OC_6H_4$	2.5	73
11	**3k**	H	H	*p*-Cl C_6H_4	2.5	70
12	**3l**	H	H	*m*-$O_2NC_6H_4$	2.5	73
13	**3m**	H	NO_2	furan-2-yl	2.5	72
14	**3n**	H	NO_2	pyridin-4-yl	1	77

[a]All reactions were carried out using **1** (2.5 mmol), **2** (3.0 mmol), $ZnCl_2$(3.0 mmol), and DMF (3 mL).
[b]Isolated yield.

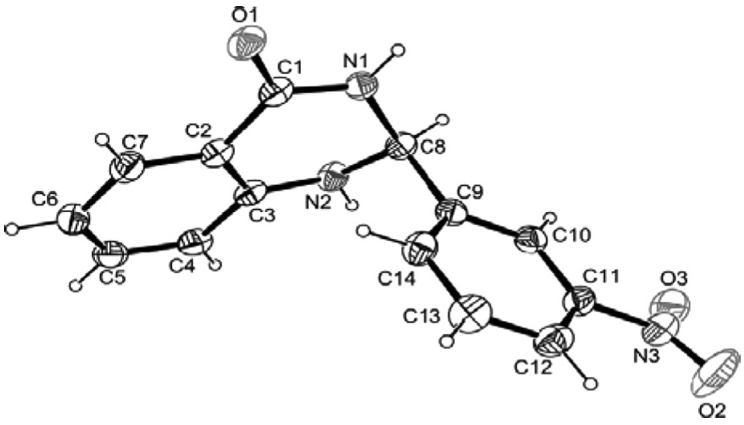
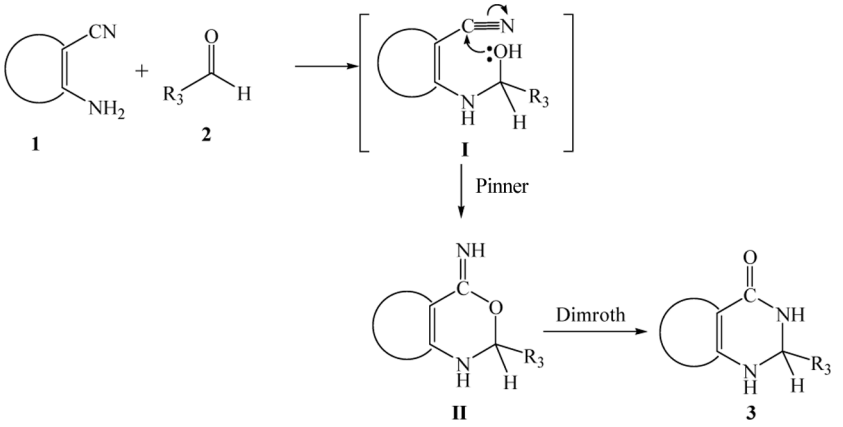


Figure 1. Molecular structure of compound **3l**. Crystal structure: Selected bond length (A°) and bond angles (**3l**): O(1)–C(1) 1.2500(19), O(2)–N(3) 1.237(3), O(3)–N(3) 1.2247(19), N(1)–C(1) 1.346(2), N(1)–C(8) 1.465(2), N(2)–C(3) 1.374(2), N(2)–C(8) 1.456(2), C(1)–C(2) 1.479(2), C(2)–C(3) 1.410(2), C(1)–N(1)–C(8) 123.91(14), C(3)–N(2)–C(8) 119.55(13), O(3)–N(3)–O(2) 123.4(2), N(1)–C(1)–C(2) 116.11(14), C(3)–C(2)–C(1) 119.07(14), N(2)–C(3)–C(2) 119.70(15), N(2)–C(8)–N(1) 108.72(13), N(2)–C(8)–C(9) 112.72(13), N(1)–C(8)–C(9) 112.16(13).

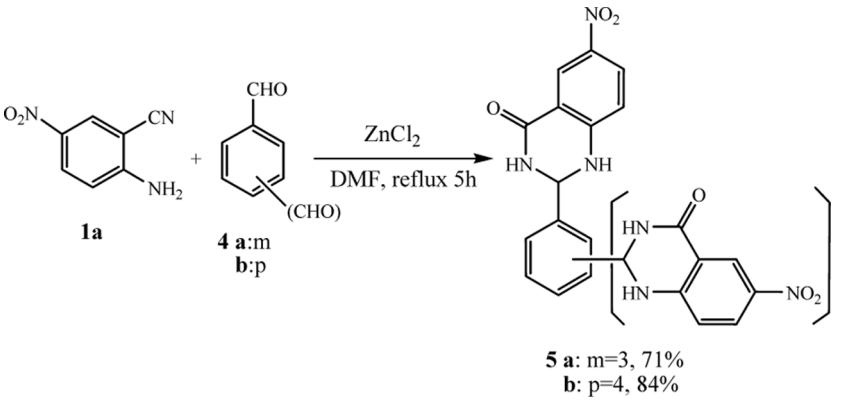


Scheme 2. Reaction of aromatic *o*-aminonitrile with aromatic aldehyde.

As an extension of the research, the reaction of 2-amino-benzonitrile **1a** with terephthalaldehyde **4** in the sealed reactor under the catalyst of $ZnCl_2$ (0.1 mol) at 200°C afforded the expected symmetrical bisquinazolinone derivatives **5** (Scheme 3).

CONCLUSION

Quinazolin-4(3*H*)-one derivatives were conveniently obtained by the cyclization of *o*-aminonitriles with carbonyl compounds using zinc chloride as the catalyst of in DMF. The reaction scope is substantial, and a number of aryl aldehydes could be successfully applied to react with *o*-aminonitriles to give quinazolinone compounds with good yields. Currently work is actively under way to expand this synthetic methodology to other valuable *o*-aminonitrile systems.



Scheme 3. Reaction of 2-amino-5-nitrobenzonitrile with terephthalaldehyde.

EXPERIMENTAL

General Procedure

o-Aminobenzonitrile 1 (2.5 mmol) and aldehydes (2.5 mmol) were added to a solution of DMF (10 mL) and $ZnCl_2$ (3.0 mmol). The mixture was heated at reflux for the specified time (see Table 1). After completion of the reaction as indicated by thin-layer chromatography (TLC; eluent: ethyl acetate), the cooled reaction mixture was quenched with water (10 mL), and the precipitate was separated by filtration. Then the residue was dispersed into water and titrated to pH 12–13 by 20% sodium hydroxide. After filtration, the products **3a–n** were isolated by column chromatography (200- to 300-mesh silica gel, ethyl acetate–petroleum 1:2).

6-Nitro-2-phenyl-1,2-dihydroquinazolin-4(3*H*)-one (3a)

Mp 264–265°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.02 (1H, t, $J = 1.7$ Hz, CH), 6.83 (1H, d, $J = 8.8$ Hz, ArH), 7.39 (1H, t, $J = 7.2$ Hz, ArH), 7.42 (2H, t, $J = 7.2$, 8.0 Hz, ArH), 7.49 (2H, d, $J = 8.0$ Hz, ArH), 8.11 (1H, dd, $J = 2.8$, 8.8 Hz, ArH), 8.44 (1H, d, $J = 2.8$ Hz, ArH), 8.57 (1H, s, NH), 8.75 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 66.30, 112.64, 114.24, 124.18, 126.54 (2C), 128.65 (2C), 128.88, 128.97, 137.12, 141.09, 152.13, 161.28; MS (ESI): m/z (%) = 270.1 (100) $[M + H]^+$. IR (KBr): ν_{max} 3385, 3166, 1690, 1618, 1530, 1329, 1140 cm^{-1}. Anal. calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.28; H, 3.80; N, 15.25.

6-Nitro-(3-nitrophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3b)

Mp 294–296°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.25 (1H, s, CH), 6.89 (1H, d, $J = 8.8$ Hz, ArH), 7.75 (1H, t, $J = 8.0$ Hz, ArH), 7.94 (1H, d, $J = 8.0$ Hz, ArH), 8.14 (1H, dd, $J = 2.8$, 8.8 Hz, ArH), 8.26–8.27 (1H, m, $J = 1.6$ Hz, ArH), 8.35 (1H, t, $J = 1.6$ Hz, ArH), 8.44 (1H, d, $J = 2.8$ Hz, ArH), 8.73 (1H, s, NH), 8.96 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.03, 112.69, 114.55, 121.38, 123.69, 124.16, 129.11, 130.45, 133.02, 137.50, 143.45, 147.80, 151.78, 161.19; MS (ESI): m/z (%) = 315.4 (100) $[M + H]^+$. IR (KBr): ν_{max} 3321, 3191, 1685, 1618, 1532, 1324 cm^{-1}. Anal. calcd. for $C_{14}H_{10}N_4O_5$: C, 53.51; H, 3.21; N, 17.82. Found: C, 53.22; H, 3.27; N, 17.72.

6-Nitro-2-(4-methoxyphenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3c)

Mp 242–243°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 3.75 (3H, s, CH_3), 5.97 (1H, s, CH), 6.82 (1H, d, $J = 8.8$ Hz, ArH), 6.98 (2H, d, $J = 8.4$ Hz, ArH), 7.39 (2H, d, $J = 8.4$ Hz, ArH), 8.11 (1H, dd, $J = 2.8$, 8.8 Hz, ArH), 8.43 (1H, d, $J = 2.8$ Hz, Hz, ArH), 8.50 (1H, s, NH), 8.68 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 55.19, 65.91, 112.62, 113.90 (2C), 114.20, 124.16, 127.94 (2C), 128.93, 132.94, 136.99, 152.19, 159.67, 161.36; MS (ESI): m/z (%) = 300.1 (100) $[M + H]^+$. IR (KBr): ν_{max} 3385, 3162, 1660, 1620, 1512, 1309 cm^{-1}. Anal. calcd. for $C_{15}H_{13}N_3O_4$: C, 60.19; H, 4.38; N, 14.04. Found: C, 60.05; H, 4.40; N, 14.11.

2-(4-Chlorophenyl)-6-nitro-1,2-dihydroquinazolin-4(3*H*)-one (3d)

Mp 263–265°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.06 (1H, s, CH), 6.84 (1H, d, $J = 8.8$ Hz, ArH), 7.50 (4H, s, ArH), 8.13 (1H, dd, $J = 2.8$, 8.8 Hz, ArH), 8.43 (1H, d, $J = 2.8$ Hz, ArH), 8.59 (1H, s, NH), 8.80 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.49, 112.62, 114.32, 124.13, 128.45 (2C), 128.62 (2C), 128.99, 133.40, 137.23, 140.05, 151.96, 161.20; MS (ESI): m/z (%) = 304.4 (100) $[M + H]^+$. IR (KBr): ν_{max} 3366, 3180, 1692, 1615, 1492, 1328 cm^{-1}. Anal. calcd. for $C_{14}H_{10}N_3O_3Cl$: C, 55.37; H, 3.32; N, 13.83. Found: C, 55.59; H, 3.62; N, 13.44.

6-Nitro-2-(4-nitrophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3e)

Mp 263–265°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.21 (1H, s, CH), 6.87 (1H, d, $J = 8.8$ Hz, ArH), 7.73 (2H, d, $J = 8.4$ Hz, ArH), 8.13 (1H, dd, $J = 2.8$, 8.8 Hz, ArH), 8.29 (2H, d, $J = 8.4$ Hz, ArH), 8.43 (1H, d, $J = 2.8$ Hz, ArH), 8.72 (1H, s, NH), 8.96 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.14, 112.63, 114.49, 123.92 (2C), 124.16, 127.80 (2C), 129.11, 137.44, 147.66, 148.29, 151.73, 161.09; MS (ESI): m/z (%) = 315.4 (100) $[M + H]^+$. IR (KBr): ν_{max} 3350, 3084, 1690, 1621, 1522, 1330 cm^{-1}. Anal. calcd. for $C_{14}H_{10}N_4O_5$: C, 53.51; H, 3.21; N, 17.82. Found: C, 53.33; H, 3.31; N, 17.46.

7-Chloro-2-(4-nitrophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3f)

Mp 243–244°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.99 (1H, s, CH), 6.70 (1H, dd, $J = 2.0$, 8.4 Hz, ArH), 6.82 (1H, d, $J = 2.0$ Hz, ArH), 7.60 (2H, d, $J = 8.4$ Hz, Hz, ArH), 7.73 (2H, d, $J = 8.4$ Hz, ArH), 8.26 (1H, s, NH), 8.27 (1H, d, $J = 8.4$ Hz, ArH), 8.66 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.22, 113.59, 113.63, 117.43, 123.72 (2C), 127.95 (2C), 129.43, 138.09, 147.52, 148.20, 148.97, 162.42; MS (ESI): m/z (%) = 304.0 (100) $[M + H]^+$. IR (KBr): ν_{max} 3355, 3282, 1660, 1609, 1521, 1351 cm^{-1}. Anal. calcd. for $C_{14}H_{10}N_3O_3Cl$: C, 55.37; H, 3.32; N, 13.84. Found: C, 55.72; H, 3.39; N, 13.86.

7-Chloro-2-(4-methoxyphenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3g)

Mp 221–223°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 3.75 (3H, s, CH_3), 5.76 (1H, s, CH), 6.69 (1H, dd, $J = 2.0$, 8.4 Hz, ArH), 6.78 (1H, d, $J = 2.0$ Hz, ArH), 6.96 (2H, dd, $J = 1.6$, 6.8 Hz, ArH), 7.29 (1H, s, NH), 7.41 (2H,dd, $J = 1.6$, 6.8 Hz, ArH), 7.60 (1H, d, $J = 8.4$ Hz, ArH), 8.32 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 55.21, 66.23, 113.45, 113.71, 113.76 (2C), 117.01, 128.17 (2C), 129.36, 133.17, 137.79, 148.94, 159.56, 162.84; MS (ESI): m/z (%) = 289.0 (100) $[M + H]^+$. IR (KBr): ν_{max} 3299, 3181, 1653, 1609, 1512 cm^{-1}. Anal. calcd. for $C_{15}H_{13}N_2O_2Cl$: C, 62.40; H, 4.54; N, 9.70. Found: C, 62.00; H, 4.55; N, 9.94.

2-(4-Nitrophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3h)

Mp 198–200°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.91 (1H, s, CH), 6.68 (1H, t, $J = 7.6$ Hz, ArH), 6.76 (1H, d, $J = 8.0$ Hz, ArH), 7.26 (1H, t, $J = 7.6$ Hz,

ArH), 7.33 (1H, s, NH), 7.60 (1H, d, $J = 8.0$ Hz, ArH), 7.73 (2H, d, $J = 8.4$ Hz, ArH), 8.25 (2H, d, $J = 8.4$ Hz, ArH), 8.51 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.76, 115.02, 115.38, 117.92, 124.02 (2C), 127.86, 128.48 (2C), 134.00, 147.68, 147.91, 149.81, 163.71; MS (ESI): m/z (%) = 270.1 (100) $[M + H]^+$. IR (KBr): ν_{max} 3389, 3282, 1647, 1615, 1520, 1349 cm^{-1}. Anal. calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.21; H, 4.51; N, 15.36.

2-(2-Hydroxyphenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3i)

Mp 218∼219°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.79 (1H, s, ArCH), 7.01∼8.73 (8H, m, ArH), 8.36 (1H, s, NH), 8.49 (1H, s, NH), 12.72 (1H, s, OH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 60.85, 111.89, 114.19, 123.90, 124.52, 128.68, 128.85, 130.09, 134.19, 135.00, 137.06, 146.95, 151.39, 165.89; MS (ESI): m/z (%) = 241.2 (100) $[M+H]^+$. IR (KBr): ν_{max} 3428, 3083, 1671, 1611 cm^{-1}. Anal. Calcd. for $C_{14}H_{12}N_2O_2$: C, 69.99; H, 5.03; N, 11.66. found: C, 69.59; H, 5.53; N, 11.03.

2-(4-Methoxyphenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3j)

Mp 255–257°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 3.86 (3H, s, CH_3), 5.67 (1H, s, CH), 6.42 (2H, dd, $J = 2.0$, 7.6 Hz, ArH), 6.89–6.90 (1H, m, $J = 8.0$ Hz, ArH), 7.04 (1H, s, NH), 7.15 (1H, d, $J = 8.0$ Hz, ArH), 7.20–7.21 (1H, m, $J = 8.0$ Hz, Hz, ArH), 7.36 (1H, dd, $J = 8.0$ Hz, ArH), 7.45 (2H, dd, $J = 2.0$, 7.6 Hz, ArH), 8.21 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 55.43, 65.36, 114.45, 114.71, 117.12 (2C), 117.69, 128.31 (2C), 128.75, 132.76, 133.79, 140.59, 147.56, 163.20; MS (ESI): m/z (%) = 255.1 (100) $[M + H]^+$. IR (KBr): ν_{max} 3269, 3171, 1678, 1602 cm^{-1}. Anal. calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 70.88; H, 5.25; N, 10.81.

2-(4-Chlorophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3k)

Mp 227–228°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.78 (1H, s, CH), 6.67 (1H, t, $J = 8.0$ Hz, ArH), 6.75 (1H, d, $J = 8.0$ Hz, ArH), 7.15 (1H, s, NH), 7.25–7.27 (1H, m, $J = 8.0$ Hz, ArH), 7.46–7.47 (2H, m, $J = 2.0$, 6.4 Hz, ArH), 7.52 (2H, dd, $J = 2.0$, 6.4 Hz, ArH), 7.62 (1H, dd, $J = 8.0$ Hz, ArH), 8.34 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 65.79, 114.48, 114.97, 117.30, 127.39, 128.33, 128.34, 128.78 (2C), 132.99, 133.42, 140.70, 147.67, 163.50; MS (ESI): m/z (%) = 259.1 (100) $[M + H]^+$. IR (KBr): ν_{max} 3325, 3188, 1658, 1609, 1483 cm^{-1}. Anal. calcd. for $C_{14}H_{11}N_2OCl$: C, 65.00; H, 4.29; N, 10.83. Found: C, 65.38; H, 4.36; N, 10.88.

2-(4-Chlorophenyl)-1,2-dihydroquinazolin-4(3*H*)-one (3l)

Mp 210–212°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 5.95 (1H, s, CH), 6.70 (1H, t, $J = 7.6$ Hz, ArH), 6.79 (1H, d, $J = 8.0$ Hz, ArH), 7.29 (1H, t, $J = 8.0$ Hz, ArH), 7.35 (1H, s, NH), 7.62 (1H, dd, $J = 7.6$ Hz, ArH), 7.70 (1H, t, $J = 7.6$ Hz, ArH), 7.94 (1H, d, $J = 7.6$ Hz, ArH), 8.21–8.22 (1H, m, $J = 1.4$, 1.4 Hz, ArH), 8.36 (1H, t, $J = 1.8$, 1.8 Hz, ArH), 8.53 (1H, s, NH). ^{13}C NMR (100 MHz, DMSO-d_6)

δ_C: 65.20, 114.61, 114.97, 117.55, 121.59, 123.29, 127.43, 130.06, 133.39, 133.59, 144.32, 147.32, 147.73, 163.36; MS (ESI): m/z (%) = 270.1 (100) $[M+H]^+$; IR (KBr): ν_{max} 3296, 3188, 1653, 1610, 1532, 1353 cm^{-1}. Anal. calcd. for $C_{14}H_{11}N_3O_3$: C, 62.45; H, 4.12; N, 15.61. Found: C, 62.16; H, 4.20; N, 15.24.

2-(Furan-2-yl)-6-nitro-1,2-dihydroquinazolin-4(3H)-one (3m)

Mp 267∼269°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.04 (1H, t, J = 2.8 Hz, CH), 6.37 (1H, d, J = 2.8 Hz, FuH), 6.42–6.43 (1H, m, FuH), 6.86 (1H, d, J = 9.2 Hz, ArH), 7.65 (1H, s, NH), 8.12 (1H, dd, J = 2.8, 9.2 Hz, ArH), 8.44 (1H, d, J = 2.8 Hz, ArH), 8.65 (1H, s, NH), 8.83 (1H, d, J = 1.6 Hz, FuH). ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 60.58, 108.19, 111.17, 113.63, 115.15, 124.75, 129.57, 138.09, 144.05, 152.53, 154.19, 161.99; MS (ESI): m/z (%) = 260.1 (100) $[M+H]^+$; IR (KBr): ν_{max} 3382, 3188, 3072, 1674, 1615, 1530, 1497, 1331, 1299, 1117 cm^{-1}. Anal. Calcd. for $C_{12}H_9N_3O_4$: C, 55.60; H, 3.50; N, 16.21. found: C, 55.74; H, 3.40; N, 16.15.

6-Nitro-2-(pyridin-4-yl)-1,2-dihydroquinazolin-4(3H)-one (3n)

Mp 231∼234°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ_H: 6.38 (1H, t, J = 2.8 Hz, CH), 7.82 (1H, d, J = 8.4 Hz, PyH), 7.95 (1H, s, NH), 8.01–8.04 (2H, m, PyH), 8.38 (1H, dd, J = 2.4, 8.4 Hz, ArH), 8.68–8.71 (3H, ArH, PyH), 8.98 (1H, s, NH); ^{13}C NMR (100 MHz, DMSO-d_6) δ_C: 61.52, 120.30(2C), 122.31, 122.53, 129.19, 130.08, 140.07, 145.89, 153.06(2C), 154.63, 162.15; MS (ESI): m/z (%) = 271.1 (100) $[M+H]^+$; IR (KBr): ν_{max} 3340, 3183, 3072, 1679, 1619, 1567, 1466, 1347, 1143 cm^{-1}; Anal. Calcd. for $C_{13}H_{10}N_4O3$: C, 57.78; H, 3.73; N, 20.73. found: C, 57.98; H, 3.40; N, 20.09.

ACKNOWLEDGMENTS

This work was supported by grants from both Beijing Municipal Commission of Education and Beijing Institute of Technology. We are grateful for analytical help from Beijing University Analysis Center and Institute of Chemistry, Chinese Academy of Sciences.

REFERENCES

1. (a) Jackson, J. R.; Patrick, D. R.; Dar, M. M.; Huang, P. S. Targeted anti-mitotic therapies: Can we improve on tubulin agents? Nature reviews. *Cancer* **2007**, *7*, 107–117; (b) Chen, K.; Al Aowad, A. F.; Adelstein, S. J.; Kassis, A. I. Molecular-docking-guided design, synthesis, and biologic evaluation of radioiodinated quinazolinone prodrugs. *J. Med. Chem.* **2007**, *50* (4), 663–673; (c) Wang, K.; Kirichian, A. M.; Al Aowad, A. F.; Adelstein, S. J.; Kassis, A. I. Evaluation of chemical, physical, and biologic properties of tumor-targeting radioiodinated quinazolinone derivative. *Bioconjugate Chem.* **2007**, *18* (3), 754–764; (d) Blagg, J.; Fray, M. J.; Lewis, M. L.; Mathias, J. P.; Stefaniak, M. H.; Stobie, A. Quinazoline compounds useful therapy. WO PCT Int. Appl. 2,003,076,4279, 2003; (e) Ozaki, K.; Yamada, Y.; Oine, T.; Ishizuka, T.; Iwasawa, Y. Studies on

4(1*H*)-quinazolinones, 5: Synthesis and anti-inflammatory activity of 4(1*H*)-quinazolinone derivatives. *J. Med. Chem.* **1985**, *28* (5), 568–576; (f) Biressi, M. D.; Cantarelli, G.; Carissimi, M.; Cattaneo, A.; Ravenna, F. Derivatives of dihydrobenzothiadiazine and tetrahydro-4-quinazolinone and their hydrogenolysis products: Preliminary study on their diuretic activity. *Farmaco* **1969**, *24*, 199; (g) Bhalla, P. R.; Walworth, B. L. Method to alter or control the development and/or the life cycle of various plant species. US Patent 4,431,440, 1981; (h) Hamel, E.; Lin, C. M.; Plowman, J.; Wang, H. K.; Lee, K. H.; Paull, K. D. Antitumor 2,3-dihydro-2-(aryl)-4 (1*H*)-quinazolinone derivatives: Interactions with tubulin. *Biochem. Pharmacol.* **1996**, *51*, 53–59.

2. Wang, S.; Lou, H.; Liu, Y. Q.; Yu, G.; Lu, P.; Zhu, D. B. Greenish-yellow electroluminescent devices using a novel dihydroquinazolinone derivative as emitting layer. *J. Mater. Chem.* **2001**, *11*, 2971–2973.
3. (a) Bogert, M. T.; Hand, W. F. The synthesis of alkylketodihydroquinazolines from anthranilic nitrile. *J. Am. Chem. Soc.* **1902**, *24*, 1031–1050; (b) Bogert, M. T.; Hand, W. F. 3,5-Bibrom-2-aminobenzoic acid: Its nitrile and the synthesis of quinazolines from the latter. *J. Am. Chem. Soc.* **1903**, *25*, 935–947; (c) Taylor, E. C.; Knopf, R. J.; Borror, A. L. The dimerization of 2-amino-5-nitrobenzonitrile. *J. Am. Chem. Soc.* **1960**, *82*, 3152–3157; (d) Bogert, M. T.; Hand, W. F. The synthesis of alkylketodihydroquinazolines from anthranilic nitrile. *J. Am. Chem. Soc.* **1902**, *24*, 1031–1050; (e) Stephen, H.; Wadge, G. Syntheses in the quinazolone series, part IV: The conversion of *N*-aroylorthanilamides into 2-arylquinazol-4-ones. *J. Chem. Soc.* **1956**, 4420–4421.
4. (a) Kametani, T.; Loc, C. V.; Higa, T.; Koizumi, M.; Ihara, M.; Fukumoto, K. Iminoketene cycloaddition, 2: Total syntheses of arborine, glycosminine, and rutecarpine by condensation of iminoketene with amides. *J. Am. Chem. Soc.* **1977**, *99*, 2306–2309; (b) Majo, V. J.; Perumal, P. T. Dimerization of substituted 2-aminobenzoic acids under Vilsmeier conditions: A novel route to the synthesis of 4-(3*H*)-quinazolinones. *Tetrahedron Lett.* **1996**, *37*, 5015–5018; (c) Fekner, T.; Muller-Bunz, H.; Guiry, P. J. Synthesis and application of quinazoline–oxazoline-containing (quinazox) ligands. *Org. Lett.* **2006**, *8* (22), 5109–5112; (d) Zhichkin, P.; Kesicki, E.; Treiberg, J.; Bourdon, L.; Ronsheim, M.; Ooi, H. C.; White, S.; Judkins, A.; Fairfax, D. A novel highly stereoselective synthesis of 2,3-disubstituted *3H*-quinazoline-4-one derivatives. *Org. Lett.* **2007**, *9* (7), 1415–1418.
5. (a) Takeuchi, H.; Haguvara, S.; Eguchi, S. Use of new phosphonylating and coupling agents in the synthesis of oligodeoxyribonucleotides via the *H*-phosphonate approach. *Tetrahedron Lett.* **1989**, *45*, 6375–6378; (b) Takeuchi, H.; Haguvara, S.; Eguchi, S. Novel ring enlargement of lactams via quinazolinone annelation: A facile route to benzoannelated large-membered cyclic 1,5-diamines. *J. Org. Chem.* **1991**, *56*, 1535–1537.
6. (a) Taylor, E. C.; McKillop, A. *The Chemistry of Cyclic Enaminonitriles and o-Aminonitriles*; Wiley: New York, 1970; (b) Erian, A. W. The chemistry of β-enaminonitriles as versatile reagents in heterocyclic synthesis. *Chem. Rev.* **1993**, *93*, 1991–2005.
7. Abd El-Wahab, A. H. F. Activated nitriles in heterocyclic synthesis: Synthesis of new [1]benzopyrano[3′,4′:5,6]pyrano[2,3-d]pyrimidine and [1]benzopyrano[3′,4′:5,6]pyrano [3,2-e][1]triazolo [1,5-c]pyrimidine derivatives with promising antibacterial activity. *Acta Pharm.* **2002**, *54*, 269–280.
8. (a) Rosowsky, A.; Chen, H. A novel method of synthesis of 2,4-diamino-6-arylmethylquinazolines using palladium(0)-catalyzed organozinc chemistry. *J. Org. Chem.* **2001**, *66*, 7522–7526; (b) Mohareb, R. M.; Al-Omran, F. A. Reaction of 3-cyano-2-amino-4,5,6,7-tetrahydrobenzo[***b***]thiophene with enaminonitriles. *Monatsh. Chem.* **2002**, *133*, 1443–1452; (c) Wiklund, P.; Bergman, J. Ring forming reactions of imines of 2-aminobenzaldehyde and related compounds. *Org. Biomol. Chem.* **2003**, *1*, 367–372.
9. Barreiro, E. J.; Camara, C. A.; Verli, H.; Brazil-Mas, L.; Castro, N. G.; Cintra, W. M.; Aracava, Y.; Rodrigues, C. R.; Fraga, C. A. M. Design, synthesis, and pharmacological

profile of novel fused pyrazolo[4,3-*d*]pyridine and pyrazolo[3,4-*b*][1,8]naphthyridine isosteres: A new class of potent and selective acetylcholinesterase inhibitors. *J. Med. Chem.* **2003**, *46* (7), 1144–1152.

10. (a) Roth, G. A.; Tai, J. J. A new synthesis of aryl substituted quinazolin-4(1*H*)-ones. *J. Heterocycl. Chem.* **1996**, *33*, 2051–2053; (b) Grubs, G. S.; Zhi, L.; Jones, T. K.; Marschke, K. B.; Tegley, C. M. Quinazolinone and benzoxazine derivatives as progesterone receptor modulators. PCT Int. Appl. WO 2,000,066,560, 2000.
11. (a) Mizuno, T.; Okamoto, N.; Ho, T.; Miyata, T. Synthesis of quinazolines using carbon dioxide (or carbon monoxide with sulfur) under mild conditions. *Heteroatom Chem.* **2000**, *11*, 428–433; (b) Mizuno, T. Synthesis of quinazolines by the carbonylation using carbon disulfide under mild conditions. *Kagaku to Kogyo.* **2002**, *76*, 431–434; (c) Mizuno, T.; Iwai, T.; Ishino, Y. The simple solvent-free synthesis of 1*H*-quinazoline-2,4-diones using supercritical carbon dioxide and catalytic amount of base. *Tetrahedron Lett.* **2004**, *45*, 7073–7075.
12. Danish, I. A.; Prasad, K. J. R. An elegant synthesis of quino[2,3-*a*]carbazoles and their antibacterial studies. *Indian J. Chem. Sect. B.* **2004**, *43B*, 1548–1552.
13. (a) Ma, S. L.; Li, J. R.; Sun, Y. J.; Zhao, J. M.; Zhao, X. F.; Yang, X. Q.; Zhang, L. J.; Wang, L. J.; Zhou, Z. M. Synthesis of 1,2-dihydro-4*H*-3,1-benzoxazine derivatives via $ZnCl_2$-catalyzed cyclocondensation. *Tetrahedron* **2006**, *62*, 7999–8005; (b) Li, J. R.; Zhang, L. J.; Shi, D. X.; Li, Q.; Wang, D.; Wang, C. X.; Zhang, Q.; Zhang, L.; Fan, Y. Q. A new conversion of Friedländler reaction and the structure of its product. *Synlett.* **2008**, *2*, 233–236.
14. Roger, R.; Neilson, D. The chemistry of imidates. *Chem. Rev.* **1961**, *61*, 179–211.
15. Rozhkov, V. Y.; Batog, L. V.; Shevtsova, E. K.; Struchkova, M. I. Synthesis and dimroth rearrangement of 3-amino-4-(5-amino-1*H*-1,2,3-triazol-1-yl)-1,2,5-oxadiazoles. *Mendeleev Commun.* **2004**, *14*, 76–77.