# A One-Pot Synthesis of 2-Aryl-2,3-dihydro-4(1*H*)-quinazolinones by use of Samarium Iodide



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2-Aryl-2,3-dihydro-4(1*H*)-quinazolines have been prepared in a one-pot synthesis by samarium idoide ($SmI_2$) promoted reaction of *o*-nitrobenzamide and aldehydes.

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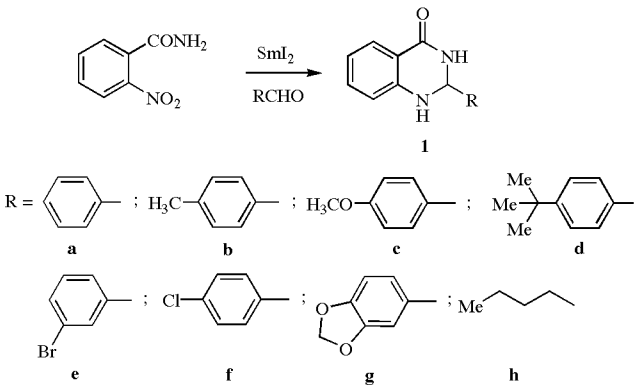
Dihydroquinazolinones have many utilities in agriculture as herbicides and plant hormones [1]. For example, 2-(4-tolyl)-2,3-dihydro-4(1*H*)-quinazolinone and its analogs permit control of Cyperus rotundus, Brassica kaber, Amaranthus retroflexus and other weeds [2]. These compounds are also active inhibitors of Earle cells' growth in suspension [3]. In mammals, dihydroquninazolinones have shown diuretic [4] and anti-cancer activity [5]. Recently, dihydroquinazolinone shows potential application in flat panel display as electroluminescence material sandwiched in organic light emitting device [6].

Dihydroquinazolinones have been previously prepared in two steps from aromatic nitro compounds. The nitro group is reduced to amino group, followed by acid catalyzed condensation of *o*-aminobenzamides with aldehydes or Schiff bases [7,8] or by condensation of *o*-aminobenzamide with benzil followed by base catalyzed hydrolysis [9]. Herein, we report a one-pot synthesis, in which, a stoichiometric amount of $SmI_2$ promotes the reaction of *o*-nitrobenzamide with aldehydes to yield dihydroquinazolinones directly.




$SmI_2$ is a well-known, mild, selective, ether soluble one-electron reductant [10] which easily reduces a variety of nitrogen containing functional groups such as nitro, azo, hydrazone, oxime, imine, azide and hydroxylamine [11]. Clearly, it is worth expanding the use of $SmI_2$ through additional synthetic applications .

Both $^1H$ and $^{13}C$ NMR spectra were obtained on a Bruker 500 AMX spectrometer operating in the FT mode. Five percent w/v solutions in DMSO-$d_6$ were used to obtain NMR spectra, with TMS as an internal standard. $^{13}C$ NMR spectra were acquired with both broad band and off-resonance proton decoupling. The multiplicity observed in the off-resonance $^{13}C$ NMR spectra permits the assignment of particular carbons [12]. Satisfactory elemental analysis data for unknown compounds was obtained by the Analytical Laboratories of Zhejiang University. Sm powder (40 mesh) and aldehydes were purchased and used without further purification. *o*-Nitrobenzamide was prepared from *o*-nitrobenzoic acid [13]. THF was distilled from sodium benzophenone immediately prior to use. IR spectra were recorded on Shimadzu IR-408 in KBr. Hewlett Packard 5989B electron impact Mass Spectrometer with 70 eV ionization potential was used to obtain mass spectra.

General Procedure.

Sm powder (40 mesh) (0.9 g, 6 mmol) was placed a three-neck flask equipped with a reflux condenser and two rubber septa. The outlet of the reflux condenser was connected to a vacuum line. The apparatus was purged with nitrogen three times. THF (40 mL) was injected into the flask. Iodine (1.52 g, 6 mmol) was added. The mixture was stirred at room temperature until the Sm powder had disappeared. The color of the solution was deep ink blue. Nitrogen was bubbled through a methanol (l2 mL)/THF (10 mL) solution of *o*-nitrobenzamide (0.18 g, 1 mmol) for 10 min. The solution was then injected into the flask. It was stirred at room temperature for 3-4 h until the color changed to light yellow. The aldehyde (1.2 mmol) was then added. The reaction mixture was refluxed for 2-3 h. The THF was then removed by evaporation under reduced pressured. Aqueous HCl (0.05 *N*, 15 mL) was added. The mixture was extracted with ethyl acetate (30 mL) three times. The combined extracts were washed with brine three times, dried over anhydrous magnesium sulfate, filtered and the volatiles removed by evaporation under reduced pressure. The residue was recrystallized from ethanol.

2-Phenyl-2,3-dihydro-4-(1*H*)-quinazolinone (1a).

This compound has mp 220-222 °C (Lit. 224-226 °C [3]), and was prepared in 85% yield; $^1H$ NMR: δ 8.32 (s, 1H), 7.64 (d, 1H, J = 8.0 Hz), 7.52 (d, 2H, J = 7.0 Hz), 7.41 (m, 3H), 7.27 (t, 1H, J = 8.0 Hz), 7.15 (s, 1H), 6.77 (d, 1H, J = 8.0 Hz), 6.70 (t, 1H, J = 8.0 Hz), 5.78(s, 1H); $^{13}C$ NMR: δ 163.65 (s), 147.93 (s), 147.71 (s), 136.36 (d), 128.51 (d), 128.38 (d), 127.41 (d), 126.93 (d), 117.17 (d), 115.02 (s), 114.46 (d), 66.62 (d).

2-(4-Tolyl)-2,3-dihydro-4(1*H*)-quinazolinone (1b).

This compound has mp 225-227 °C (Lit. 230-233 °C [3]; 218 °C [14]), and was prepared in 80% yield; $^1$H NMR: δ 8.22 (s, 1H), 7.59 (d, 1H, J = 7.5 Hz), 7.37 (d, 2H J = 7.5 Hz), 7.23 (t, 1H, J = 7.0 Hz), 7.19 (d, 2H, J = 7.5 Hz), 7.05 (s, 1H), 6.73 (d, 1H, J = 8.5 Hz), 6.66 (t, 1H, J = 7.5 Hz), 5.70 (s, 1H), 2.29 (s, 3H); $^{13}$C NMR: δ 163.69, 147.98, 138.74, 137.77, 133.31, 128.87, 127.40, 126.86, 117.12, 115.06, 114.47, 66.43, 20.80.

2(4-Methoxyphenyl)-2,3-dihydro-4(1*H*)-quinazolinone (1c).

This compound has mp 180-182 °C, and was prepared in 85% yield; $^1$H NMR: δ 8.17 (s, 1H, NH), 7.61 (d, 1H, J = 6.5 Hz, ArH), 7.41 (d, 2H, J = 8.0 Hz, ArH), 7.23 (t, 1H, J = 7.5 Hz, ArH), 7.04 (s, 1H, NH), 6.94 (d, 2H, J = 8.0 Hz, ArH), 6.74 (d, 1H, J = 8.5 Hz, ArH), 6.66 (t, 1H, J = 7.5 Hz, ArH), 5.70 (s, 1H, CH), 3.75 (s, 3H, $OCH_3$); $^{13}$C NMR: δ 163.76 (s), 159.50 (s), 148.09 (s), 133.58 (s), 133.29 (d), 128.27 (d), 127.41 (d), 117.12 (d), 115.07 (s), 144.49 (d), 113.70 (d), 66.34 (d), 55.24 (q). IR: ν 1660 cm$^-$; MS found: *m/z*: 119(110.0%), 252(M-2, 77.9%).

*Anal*. Calcd. for $C_{15}H_{14}N_2O_2$: C, 70.85; H, 5.55; N, 11.02. Found: C, 69.87; H, 5.43; N, 11.05.

2-(4-*t*-Butylphenyl)-2,3-dihydro-4(1*H*)-quinazolinone (4d).

This compound has mp 219-220 °C, and was prepared in 75% yield; $^1$H NMR: δ 8.22 (s, 1H, NH), 7.61 (d, 1H, J = 7.5 Hz, ArH), 7.42 (s, 4H, ArH), 7.23 (t, 1H, J = 8.0 Hz, ArH), 7.06 (s, 1H, NH), 6.72 (d, 1H, J = 8.0 Hz, ArH), 6.67 (t, 1H, J = 8.0 Hz, ArH), 5.71 (s, 1H, CH), 1.27 (s, 9H, $3CH_3$); $^{13}$C NMR: δ 163.72, 151.09, 148.04, 138.64, 133.33, 127.43, 126.76, 125.16, 117.12, 115.03, 114.43, 66.53, 34.41, 31.19. IR: ν 1678 cm$^{-1}$; MS found: *m/z*: 119(100.0%), 278(M-2, 82.2%).

*Anal*. Calcd. for $C_{18}H_{20}N_2O$ C, 77.11; H, 7.19; N, 9.99. Found: C, 76.97; H, 7.31; N, 9.99.

2-(3-Bromophenyl)-2,3-dihydro-4(1*H*)-quinazolinone (4e).

This compound has mp 231-233 °C, and was prepared in 75% yield; $^1$H NMR: δ 8.53 (s, 1H, ArH), 8.34 (s, 1H, NH), 8.21 (d, 1H, J = 7.0 Hz, ArH), 7.94 (d, 1H, J = 7.5 Hz, ArH), 7.70 (t, 1H, J = 7.5 Hz, ArH), 7.35 (s, 1H, NH), 7.27 (t, 1H, J = 7.5 Hz, ArH), 6.78 (d, 1H, J = 7.5 Hz, ArH), 6.70 (t, 1H, J = 7.5 Hz, ArH), 5.94 (s, 1H, CH); $^{13}$C NMR: δ 163.40, 147.77, 147.37, 144.36, 133.65, 133.45, 130.13, 127.48, 123.35, 121.63, 117.60, 115.02, 114.66, 65.24; IR: ν 1675 cm$^{-1}$; MS found: *m/z*: 119(100.0%), 300(M-2, 28.4%), 302(29.1%).

*Anal*. Calcd. for $C_{14}H_{11}BrN_2O$ C, 55.47; H, 3.66; N, 9.24. Found: C, 55.35; H, 3.80; N, 9.44.

2-(4-Chlorophenyl)-2,3-dihydro-4(1*H*)-quninazolinone (4f).

This compound has mp 205-206 °C (Lit. 205-208 °C [3]), and was prepared in 84% yield; $^1$H NMR: δ 8.34 (s, 1H), 7.60 (d, 1H, J = 7.5 Hz), 7.50 (d, 2H, J = 8.5 Hz), 7.45 (d, 2H, J = 8.5 Hz), 7.25 (t, 1H, J = 8.0 Hz), 7.15 (s, 1H), 6.74 (d, 1H, J = 7.5 Hz), 6.68 (t, 1H, J = 7.5 Hz), 5.77 (s, 1H); $^{13}$C NMR: δ 163.54 (s), 147.73 (s), 140.76 (s), 133.46 (d), 133.30 (s), 128.82 (d), 128.38 (d), 127.43 (d), 117.34 (d), 115.01 (s), 114.53 (d), 65.82 (d).

2-[3,4-Methylenedioxy]phenyl]-2,3-dihydro-4(1*H*)-quinazolinone (4g).

This compound has mp 199-200 °C (Lit. 202 °C [15]), was prepared in 60 % yield; $^1$H NMR: δ 8.22 (s, 1H), 7.60 (d, 1H, J = 7.5 Hz), 7.24 (t, 1H, J = 8.5 Hz), 7.04 (s, 1H), 7.03 (s, 1H), 6.95 (d, 1H, J = 8.0 Hz), 6.90 (d, 1H, J = 8.0 Hz), 6.73 (d, 1H, J = 8.0 Hz), 6.67 (t, 1H, *J* = 7.5 Hz), 6.01 (s, 2H), 5.67 (s, 1H); $^{13}$C NMR: δ 163.66, 147.91, 147.37, 147.29, 135.64, 133.37, 127.41, 120.50, 117.22, 115.03, 114.50, 107.93, 107.25, 101.19, 66.34.

2-*n*-Butyl-2,3-dihydro-4(1*H*)-quinazolinone, (4h).

This compound has mp 144-146 °C, was prepared in 60% yield; $^1$H NMR: δ 7.88 (s, 1H, NH), 7.57 (d, 1H, J = 7.0 Hz, ArH), 7.22 (t, 1H, J = 8.0 Hz, ArH), 6.72 (d, 1H, J = 8.0 Hz, ArH), 6.65 (t, 1H, J = 8.0 Hz, ArH), 6.57 (s, 1H, NH), 4.68 (t, 1H, J = 5.5 Hz, CH), 1.62 (m, 2H, $CH_2$), 1.39 (m, 2H, $CH_2$), 1.30 (m, 2H, $CH_2$), 0.88 (t, 3H, J = 7.0 Hz, $CH_3$); $^{13}$C NMR: δ 163.97, 148.58, 133.09, 127.41, 116.91, 115.07, 114.43, 64.48, 34.81, 25.49, 22.15, 14.02. IR: ν 1680 cm$^{-1}$; MS found: *m/z*: 119(100.0%), 202(M-2, 53.4%).

*Anal*. Calcd. for $C_{12}H_{16}N_2O$ C, 70.56; H, 7.90; N, 13.71. Found: C, 70.24; H, 7.51; N, 13.54.

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