SIMPLE CHROMIUM CATALYZED OXIDATIVE SYNTHESIS OF QUINAZOLINONES AND BENZOXAZINONES FROM 2-AMINOBENZAMIDE AND ANTHRANILIC ACID WITH ARYLALDEHYDES

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An easy and efficient protocol for oxidative synthesis of quinazolinones and benzoxazinones using novel catalyst fromed in-situ from chromium trioxide has been developed. Here chromium trioxide acts as an oxidant and its reduction products catalyze the coupling reaction. Newly developed method demonstrates a new alternative to existing method which is a cost effective approach to synthesize important moieties like quinazolinones and benzoxazinones from easily available starting materials in good to excellent yields.

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INTRODUCTION

Nowadays, various heterocyclic compounds have been found with distinguished pharmacological activities in drug design and development.[1] Quinazolinones obtained from natural products form an important skeleton for the synthesis of different therapeutically active drug moieties.[2] Its derivatives are important compounds, and have been widely used in hypnotic,[3] sedative,[4] anticancer,[5-6] anticonvulsant[7] and anti-inflammatory agents.[8] The research interest in the synthesis of 4(3H)-quinazolinone and its derivatives has never faded since the first report of the 4(3H)-quinazolinone.[9] Also, 1-benzoxazin-4-one derivatives are important skeletons due to their proven pharmaceutical activity. For example, some of the drugs which contain 4H-3,1-benzoxazin-4-one as the core structure act as HSV-1 protease inhibitor and human chymase inhibitor[10] along with anti-proliferative activity.[11] Initially, some toxic oxidants like DDQ,[12] $CuCl_2$,[13] MnO_2,[14] $KMnO_4$,[15] $K_2S_2O_8$[16] and $PhI(OAc)_2$[17] were used which yielded the similar quantity of oxidant-derived waste. The use of chromium trioxide as an oxidsant and a catalyst precursor is a promising strategy in organic synthesis which substitutes many expensive transition metal compounds.[18] Especially, the amidation of $C(sp^3)$-H bonds using chromium is very attractive, and it finds the utility in synthesis of a wide range of N and O-heterocycles.[19] Chromium, among transition metals, is particularly attractive in organic synthesis because of its low price.[20] Hence, in continuation to our work,[21-24] we herein tried to report the synthesis of quinazolinones as well as benzoxazinone derivatives using chromium trioxide as the oxidant and catalyst.

MATERIALS AND METHOD

All chemicals and solvents were used from Sigma-aldrich. Melting points were uncorrected and recorded on Optimelt digital melting point apparatus. IR spectra were recorded on Bruker Alpha E FTIR spectrophotometer. ^{1}H NMR was recorded on Varian 300 MHz spectrometer by using TMS as internal standard. Mass spectra were taken with Micromass-QUATTRO-II of WATER mass spectrometer.

General procedure for the synthesis of compound 3a-3m

A mixture of 2-aminobenzamides **1a** (1 mmol), chromium trioxide (20 mol %) and benzaldehyde **2a** (1 mmol) was stirred in dichloroethane (5 mL) and heated at 80 °C for 5 h. After completion of reaction, the resulting solution was cooled to room temperature, and the reaction mixture added to the saturated solution of sodium bisulphate stirred for 10-15 min. Then 10 ml of ethyl acetate was added to the mixture and organic layer was separated, concentrated under vacuum and the resulting residue was purified by column chromatography (hexane /ethyl acetate) to afford the desired product. DCE is very cheap solvents as compared to other solvents, hence we used the same.

Chromium trioxide is explosive with most reactive aldehydes like fluorobenzaldehyde so there is need for precaution.

2-Phenylquinazolin-4(3H)-one (3a)

White solid, mp: 122 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.94 (m, 4H), 8.10 (d, 2H), 12.11 (1H, NH);^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 125.4, 128.6, 130.1, 134.5, 148.5, 154.4, 164.6. Anal. calcd. for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60; Found: C, 75.62; H, 4.5; N, 12.56.

2-(2,4-Dimethoxyphenyl)quinazolin-4(3H)-one (3b)

White solid, mp: 255 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 3.80 (s, 3H), 6.63-6.74 (m, 3H), 7.54 (m, 3H), 7.66-7.91 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.9, 98.4, 106.5, 117.8, 121.8, 124.9, 126.7, 131.8, 134.5, 146.6, 150.7, 160.0, 163.3. Anal. calcd. for$C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; Found: C, 68.11; H, 5.04; N, 9.96.

2-(3-Nitrophenyl)quinazolin-4(3H)-one (3c)

White solid, mp: 147 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.96 (m, 4H), 8.37-8.72 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 124.0, 126.7, 130.8, 134.5, 147.8, 153.1, 163.8. Anal. calcd. for $C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72; Found: C, 62.96; H, 3.43; N, 15.76.

2-(4-Methoxyphenyl)quinazolin-4(3H)-one (3d)

White solid, mp: 298 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 3.78 (s, 3H), 7.54 (m, 3H), 7.66-7.96 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.3, 114.4, 121.3, 126.5, 129.9, 134.5, 148.5, 154.7, 161.3, 164.6. Anal. calcd. for$C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10; Found: C, 71.38; H, 4.75; N, 11.06.

2-(3-Methoxyphenyl)quinazolin-4(3H)-one (3e)

White solid, mp: 198°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm= 3.78 (s, 3H), 7.54 (m, 3H), 7.73 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 55.3, 114.4, 121.3, 126.5, 129.9, 134.5, 148.5, 154.7, 161.3, 164.6. Anal. calcd. for$C_{15}H_{12}N_2O_2$: C, 71.42; H, 4.79; N, 11.10; Found: C, 71.38; H, 4.75; N, 11.06.

2-(4-Nitrophenyl)quinazolin-4(3H)-one (3f)

White solid, mp: 209 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.66-7.94 (m, 4H), 8.25-8.37 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 124.8, 129.2, 134.5, 137.2, 137.2, 149.1, 154.5, 164.6. Anal. calcd. for$C_{14}H_9N_3O_3$: C, 62.92; H, 3.39; N, 15.72; Found: C, 62.96; H, 3.43; N, 15.76.

4-(4-Oxo-3,4-dihydroquinazolin-2-yl)benzonitrile (3g)

White solid, mp: 297 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.54 (m, 3H), 7.65-7.96 (m, 4H), 8.19 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 112.2, 118.5, 121.3, 125.4, 128.73, 133.5, 134.5, 148.5, 154.78, 164.6. Anal. calcd. for$C_{15}H_9N_3O$: C, 72.87; H, 3.67; N, 16.99; Found: C, 72.83; H, 3.63; N, 16.95.

2-(4-Hydroxyphenyl)quinazolin-4(3H)-one (3h)

White solid, mp: 292 °C;^{1}H NMR (400 MHz, DMSO-d_6): δppm= 6.94 (m, 3H), 7.54 (m, 3H), 7.65-7.96 (m, 4H), 8.13 (d, 2H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.8, 121.3, 122.8, 126.5, 130.2, 134.5, 148.5, 151.1, 154.8, 164.6. Anal. calcd. for$C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76; Found: C, 70.62; H, 4.27; N, 11.8.

2-(2,3-Dichlorophenyl)quinazolin-4(3H)-one (3i)

White solid, mp: 299 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.38 (m, 3H), 7.54 (m, 3H), 7.65-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.8, 124.9, 127.7, 131.0, 132.9, 134.5, 146.9, 149.0, 161.5. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62; Found: C, 57.8; H, 2.81; N, 9.66.

2-(2-Phenyl)quinazolin-4(3H)-one (3j)

White solid, mp: 191°C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.04-7.45 (m, 3H), 7.54 (m, 3H), 7.65-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.8, 121.3, 122.8, 126.5, 130.2, 134.5, 148.5, 151.1, 154.8, 164.6. Anal. calcd. for$C_{14}H_{10}N_2O_2$: C, 70.58; H, 4.23; N, 11.76; Found: C, 70.62; H, 4.27; N, 11.8.

2-(2,4-Dichlorophenyl)quinazolin-4(3H)-one (3k)

White solid, mp: 297 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.36 (m, 3H), 7.54 (m, 3H), 7.69-7.94 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.8, 124.9, 127.7, 131.0, 132.9, 134.5, 146.9, 149.0, 161.5. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 57.76; H, 2.77; N, 9.62; Found: C, 57.8; H, 2.81; N, 9.66.

2-(4-Bromophenyl)quinazolin-4(3H)-one (3l)

White solid, mp: 252 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.55 (m, 3H), 7.66-7.96 (m, 4H), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 121.3, 123.9, 126.7, 131.3, 134.5, 148.5, 154.6, 164.6. Anal. calcd. for$C_{14}H_8Cl_2N_2O$: C, 55.84; H, 3.01; N, 9.30; Found: C, 55.8; H, 2.97; N, 9.26.

2-(3-Ethoxy-4-hydroxyphenyl)quinazolin-4(3H)-one (3m)

White solid, mp: 315 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 1.42 (t, 3H, CH_3), 4.14 (q, 2H, CH_2), 5.44 (s, 1H, OH), 6.96 (d, 1H, phenyl ring), 7.46 -7.57 (m, 3H, quinazoline ring), 7.75-7.88 (m, 2H), 7.96 (d, 1H, quinazoline ring), 12.11 (1H, NH); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 14.7, 64.31, 113.5, 121.0, 122.7, 126.7, 134.5, 147.8, 153.8. Anal. calcd. for$C_{16}H_{14}N_2O_3$: C, 68.07; H, 5.00; N, 9.92; Found: C, 68.11; H, 5.04; N, 9.96.

General procedure for the synthesis of compound 6a-6m

An oven dried three necked round bottom flask was loaded with anthranilic acid (**4**) (1 mmol), benzaldehyde (**5**) (1 mmol), chromium trioxide (20 % mol) in dichloroethane (5 mL). Then, the reaction mixture was heated at 80 °C for 16 h. The completion of the reaction was monitored by TLC. After being cooled at room temperature the reaction mixture was poured in the saturated solution of sodium bisulphate stirred for 10-15 min. Then 10 mL of ethyl acetate was added to the mixture and organic layer was separated, concentrated under vacuum and the resulting residue was purified by column chromatography (hexane/ethyl acetate) to afford the desired product.

2-Phenyl-4H-benzo[*d*][1,3]oxazin-4-one (6a)

White solid, mp: 125°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm= 7.49 -7.53 (m, 3H), 7.68-7.87 (m, 4H), 8.04-8.28 (d, 2H), ^{13}C NMR (100 MHz, DMSO-d6): δppm = 116.0, 126.2, 131.4, 132.2, 136.8, 147.0, 156.8, 159.2. Anal. calcd. for$C_{14}H_9NO_2$: C, 75.33; H, 4.06; N, 6.27; Found: C, 75.37; H, 4.10; N, 6.31.

2-(2-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6b)

White solid, mp: 139 °C; ^{1}H NMR (400 MHz, DMSO-d^6): δppm= 7.28-7.53 (m, 3H, quinazoline ring), 7.68-7.99 (m, 4H, phenyl ring), 8.04 (d, 1H, quinazoline ring); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.22; H, 3.09; N, 5.40.

2-(3-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6c)

White solid, mp: 128 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.43-7.69 (m, 5H), 7.87-8.11 (m, 2H), 8.12 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. ^{13}C NMR (100 MHz, DMSO-d6): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.22; H, 3.09; N, 5.40.

2-(4-Chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6d)

White solid, mp: 191°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.40-7.41 (m, 3H), 7.69-7.87 (m, 4H), 8.06 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 116.5, 128.3, 131.9, 132.8, 136.8, 147.2, 156.4, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.30; H, 3.17; N, 5.48.

2-(4-Ethylphenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6e)

White solid, mp: 98°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 1.21 (t, 3H, CH_3), 2.69 (q, 2H, CH_2), 7.42 (d, 2H), 7.68-7.87 (m, 3H), 8.03 (d, 2H), 8.17 (d, 1H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 15.3, 28.6, 116.0, 126.2 128.4, 131.3, 136.8, 147.0, 157.1, 159.2. Anal. calcd. for$C_{16}H_{13}NO_2$: C, 76.48; H, 5.21; N, 5.57; Found: C, 76.44; H, 5.17; N, 5.53.

7-Chloro-2-phenyl-4H-benzo[*d*][1,3]oxazin-4-one (6f)

White solid, mp: 191 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.17 (d, 1H), 7.49-7.87 (m, 5H), 8.19-8.20 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 113.8, 124.8, 129.8, 131.4, 132.3, 137.9, 147.3, 157.1, 159.5. Anal. calcd. for$C_{14}H_8ClNO_2$: C, 65.26; H, 3.13; N, 5.44; Found: C, 65.30; H, 3.17; N, 5.48.

7-Chloro-2-(3-fluorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6g)

White solid, mp: 121°C; ^{1}H NMR (400 MHz, DMSO-d6): δppm==7.43 (d, 1H), 7.60-7.87 (m, 4H), 8.04-8.19 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d6): δppm = 113.8, 115.9, 118.8, 126.3, 129.1, 130.6, 132.8, 137.9, 147.3, 155.6, 159.4, 164.4. Anal. calcd. for$C_{14}H_7ClFNO_2$: C, 61.00; H, 2.56; N, 5.08; Found: C, 61.04; H, 2.6; N, 5.12.

7-Chloro-2-(4-chlorophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6h)

White solid, mp: 141 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm=7.41 (d, 1H), 7.70-7.87 (m, 4H), 8.07-8.20 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 113.8, 124.8, 129.6, 131.7, 138.3, 147.3, 154.5, 159.5. Anal. calcd. for$C_{14}H_7Cl_2NO_2$: C, 57.56; H, 2.42; N, 4.79; Found: C, 57.60; H, 2.46; N, 4.83.

2-(4-Chlorophenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6i)

White solid, mp: 185 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm=7.41 (d, 1H), 7.93 (m, 4H), 8.04-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 127.4, 131.0, 131.7, 138.3, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7ClN_2O_4$: C, 55.56; H, 2.33; N, 9.26; Found: C, 55.52; H, 2.29; N, 9.22.

2-(4-Methoxyphenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6j)

White solid, mp: 177°C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 3.78 (s, 3H, OCH_3), 7.06 (d, 2H), 7.41 (d, 1H), 7.93 (d, 2H), 8.11-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 55.3, 114.2, 118.5, 125.9, 131.0, 145.8, 150.9, 158.9, 163.5. Anal. calcd. for$C_{15}H_{10}N_2O_5$: C, 60.41; H, 3.38; N, 9.39; Found: C, 60.37; H, 3.34; N, 9.35.

6-Nitro-2-(4-nitrophenyl)-4H-benzo[*d*][1,3]oxazin-4-one (6k)

White solid, mp: 185 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.92 (m, 4H), 8.26-8.79 (d, 2H), ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 124.5, 127.4, 130.6, 131.0, 137.4, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7N_3O_6$: C, 53.68; H, 2.25; N, 13.42; Found: C, 53.72; H, 2.29; N, 13.46.

2-(4-Bromophenyl)-6-nitro-4H-benzo[*d*][1,3]oxazin-4-one (6l)

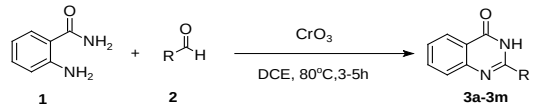
White solid, mp: 150 °C; ^{1}H NMR (400 MHz, DMSO-d$_6$): δppm= 7.70 (d, 1H), 7.93 (m, 4H), 8.02-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d$_6$): δppm = 118.5, 125.9, 127.4, 131.8, 145.8, 150.9, 158.9. Anal. calcd. for$C_{14}H_7BrN_2O_4$: C, 48.44; H, 2.03; N, 8.07; Found: C, 48.40; H, 1.99; N, 8.03.

2-(4-Fluorophenyl)-6-nitro-4H-benzo[d][1,3]oxazin-4-one (6m)

White solid, mp: 230 °C; ^{1}H NMR (400 MHz, DMSO-d_6): δppm= 7.34 (d, 1H),7.93 (m, 4H), 8.09-8.79 (d, 2H); ^{13}C NMR (100 MHz, DMSO-d_6): δppm = 116.2, 118.5, 127.4, 132.2, 145.8, 150.9, 158.9, 166.8. Anal. calcd. for$C_{14}H_7FN_2O_4$: C, 58.75; H, 2.47; N, 9.79; Found: C, 58.79; H, 2.51; N, 9.83.

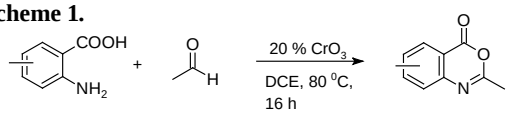
RESULTS AND DISCUSSION

Synthesis of quinazolinones as well as benzoxazinone derivatives using chromium trioxide as the oxidant and catalyst precursor have been performed according to Schemes 1 and 2. The reaction was screened with several copper salts and solvents to enhance the competence of the reactions and the results are summarized in (Table 1).



1 2 3a-3m

Scheme 1.



4 5 6a-6m

Scheme 2.

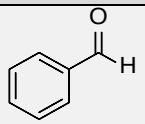
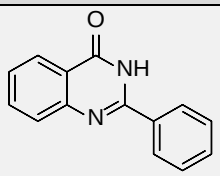
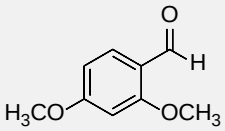
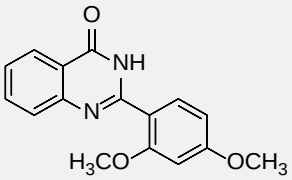
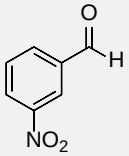
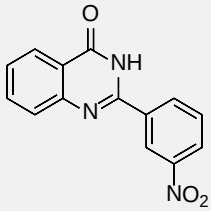
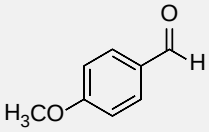
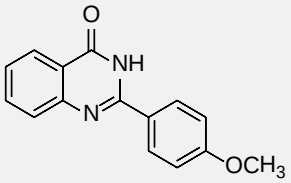
Table 1. Optimization of catalyst and solvent on **3a**

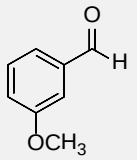
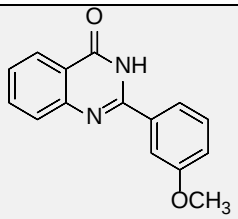
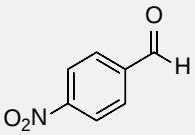
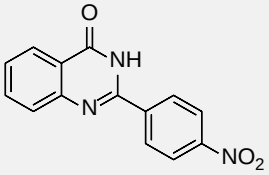
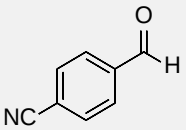
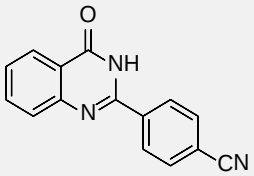
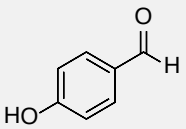
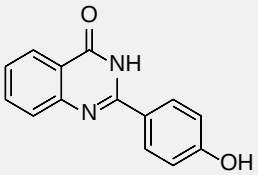
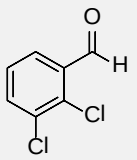
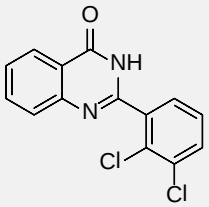
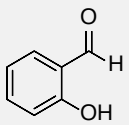
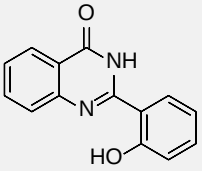
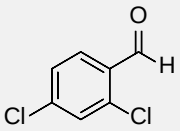
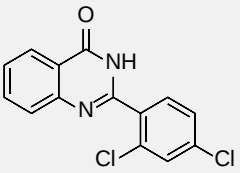
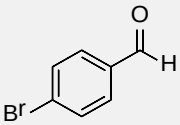
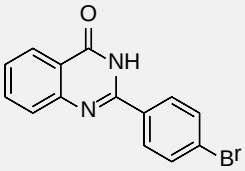
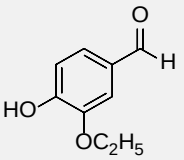
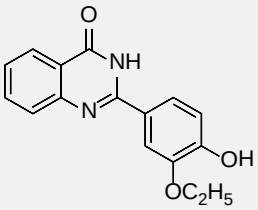
Entry	Catalyst	Solvent	Time, h	Yield,%[a]
1	CuO	DCE	12	10
2	Cu2O	DCE	10	12
3	CuO	DMSO	10	15
4	Cu2O	DMSO	10	21
5	CuO	Dioxane	15	No reaction
6	CuO	DMF	12	26
7	Cu2O	DMF	10	37
8	CrO_3	H_2O	20	No reaction
9	CrO_3	DMF	8	65
10	CrO_3	Toluene	4	80
11	CrO_3	DCE	6	98

It was found that reaction works with each of Cu oxides but there was no reaction with copper(II) oxide in dioxane solvent with reaction time of 15 h (Table 1, Entry 5). Also copper(I) oxide in DMF gave good reaction in 10 h but the yield was considerably low i.e. 37 % (Table 1, Entry 7).

Hence taking into consideration the properties of chromium trioxide, we tried our reactions in the same. Initially we took water as the solvent with chromium trioxide but there was no reaction in 20 h (Table 1, Entry 8). Then we tried taking DMF, toluene and DCE, where DCE turned out to be the best solvent among those examined giving 98% yield (Table 1, Entry 1)

Table 2. Derivatives of quinazolinone compounds **3a-3m**

Entry	R	Product	Yield (%)
3a			90
3b			92
3c			98
3d			97

3e			88
3f			89
3g			80
3h			85
3i			82
3j			81
3k			90
3l			94
3m			88

[a]Isolated yield

This reaction was screened in a number of different Lewis acid catalysts and solvents for its optimization. Using I_2 as a catalyst and DCE as a solvent the obtained yield was 83 % but the reaction time was higher i.e. 16 h (Table 3, Entry 1). Further $AlCl_3$, $ZnCl_2$ and $FeCl_3$ in DCE gave low yield with moderate reaction time (Table 3, Entries 2, 3 and 5). There was no reaction observed with $SnCl_2$ further increasing the reaction time to 20 h (Table 3, Entry 4). Then we choose CrO_3 as the catalyst taking into account our previous quinazolinone reaction. Initially we tried the reaction in

different solvents like toluene, acetonitrile and ethanol but did not observe compatible yields (Table 3, Entries 6-8). Hence, we finally decided to carry out the reaction in DCE as the solvent and got the highest yield of 97 % with the abovementioned combination with comparably less reaction time of 12 h than the other trials (Table 3, Entry 9).

Table 3. Optimization of catalyst and solvent on **6a**

Entry	Catalyst	Solvent	Time, h	Yield, %[a]
1	I_2	DCE	16	83
2	$AlCl_3$	DCE	13	54
3	$ZnCl_2$	DCE	14	12
4	$SnCl_2$	DCE	15	No reaction
5	$FeCl_3$	DCE	12	62
6	CrO_3	Toluene	16	55
7	CrO_3	Acetonitrile	12	26
8	CrO_3	Ethanol	13	46
9	CrO_3	DCE	12	97

[a]Isolated yield

The plausible reaction mechanism of quinazolinone compound is proposed in Fig. 1. Here the aldehyde is reacted with 2-aminobenzamide to give an aminal intermediate. This generated aminal intermediate is oxidized to the corresponding quinazolinone in the presence of $[Cr]^{4+}$ species. Chromium trioxide plays a very important role in the oxidation of aminal intermediate to quinazolinone. $[Cr]^{6+}$ quickly converts to $[Cr]^{4+}$ which forms the most important step in the reaction.

Browsing the literatures related to benzoxazinone synthesis, the following mechanism (Fig. 1) for the oxidative cascade reaction for the synthesis of 2-arylbenzoxazinones using anthranilic acid and benzaldehyde is proposed as an example. First step is the formation of imine **3** from the reaction between anthranilic acid and benzaldehyde catalyzed by chromium trioxide.

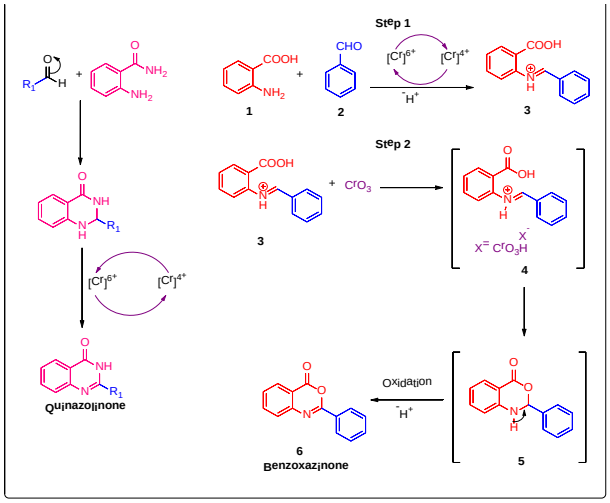


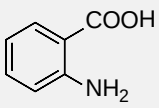
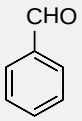
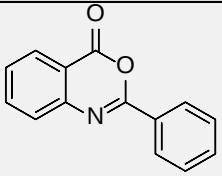
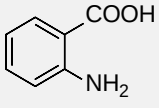
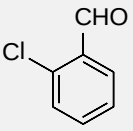
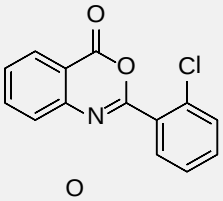
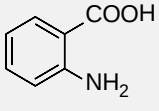
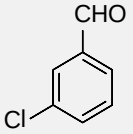
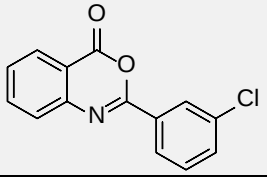
Figure 1. Plausible reaction mechanism for quinazolinone and benzoxazinone compounds

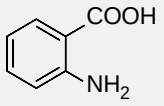
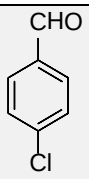
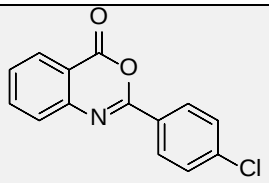
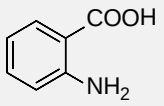
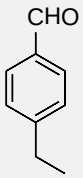
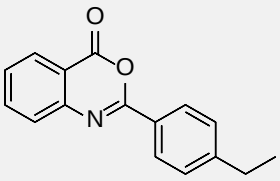
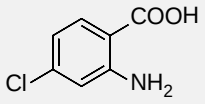
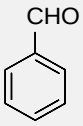
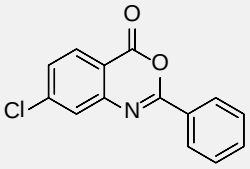
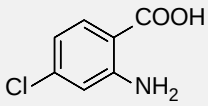
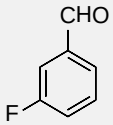
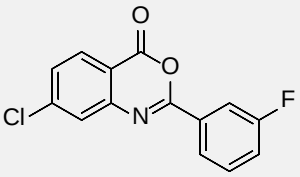
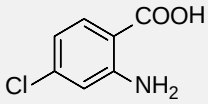
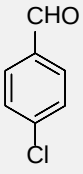
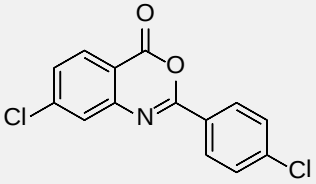
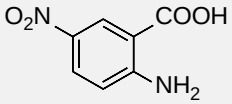
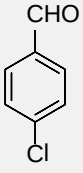
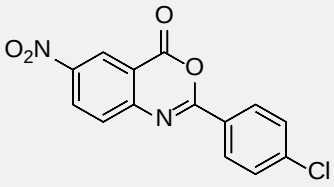
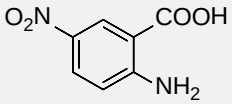
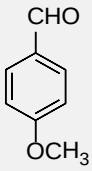
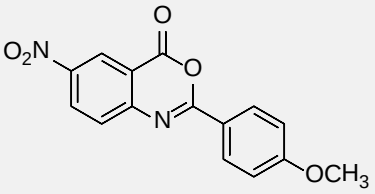
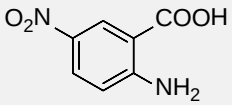
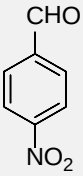
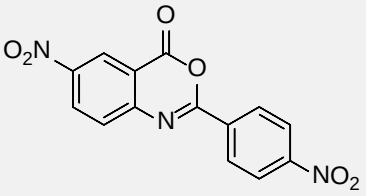
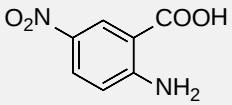
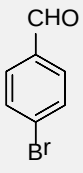
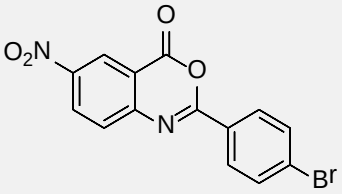
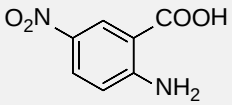
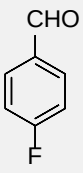
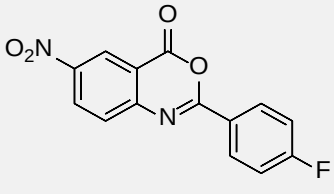
The second step involves the activation of imine group to iminium salt **4** by the active constituent CrO_3H of chromium trioxide (CrO_3). Subsequent cyclization **5** followed by oxidation leads to 2-arylbenzoxazinones **6**.

CONCLUSION

The work illustrates a simple and proficient method for the oxidative synthesis of quinazolinones and benzoxazinones using novel chromium trioxide as the oxidant and catalyst precursor. Also the time required for the completion of reaction is reduced to a great extent. The reaction proceeds very clean and no by-products were observed. Moreover the method is cheap and economical since DCE is used as a solvent. The products were obtained in good to excellent yields.

Table 4. Derivatives of benzoxazinone compounds **6a-6m**

Entry	R1	R_2	Product	Yield(%)
6a				97
6b				87
6c				89

6d				82
6e				86
6f				88
6g				83
6h				92
6i				87
6j				86
6k				89
6l				84
6m				83

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