An Efficient Synthesis of 3-Substituted 3*H*-Pyrimidin-4-ones

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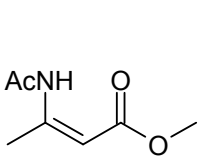
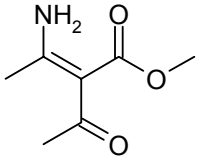
General Experimental. Thomas-Hoover (Uni-Melt) capillary melting point apparatus was used to determine all the melting points (not corrected). Spectra for ^{1}H and ^{13}C NMR were obtained using a Bruker Avance 400 instrument. NMR solvents used were either $CDCl_3$ or DMSO-d6. Infrared spectra were obtained with a Perkin-Elmer Travel-*IR*. Mass spectra was obtained using a LCMS unit incorporating Shimadzu LC pumps, Javelin reversed-phased Aquasil C18 columns, UV and ELS detectors, and Perkin-Elmer Sciex API 150EX mass spectrophotometer with an electrospray ion source in positive ion mode. All reactions were run under nitrogen atmosphere and monitored by use of TLC or LCMS. Flash chromatography was done using pre-packed silica gel columns from Biotage.

Representative procedure for enamide esters 7:

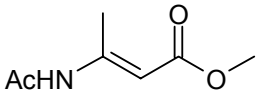
(*Z*)-3-Acetylamino-but-2-enoic acid methyl ester (7a)[1]



7a



7a'



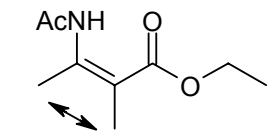
7a(*E*)

To a solution of methyl acetoacetate (0.93 ml, 8.61 mmol) in toluene (17 ml) were added ammonium acetate (3.98 g, 51.67 mmol) and 2 ml of acetic acid at rt. The reaction mixture was heated to reflux for 2 hr. A Dean-Stark trap was placed in between the reaction flask and a reflux condenser. Most of solvents and ammonium acetate were removed through a Dean-Stark trap. The clear resultant residue was cooled down to rt followed by the addition of acetic anhydride (4.5 ml) and acetic acid (1 ml). After heating at 70 ^{o}C for 2 hr, the reaction mixture was cooled down to rt and was quenched with 1N HCl (30 ml), and then extracted with CH_2Cl_2. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine. After drying over $MgSO_4$ and concentration *in vacuo*, the residue was subjected to flash column chromatography on silica gel to

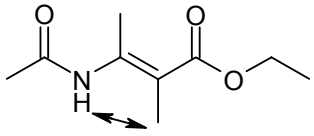
provide three products with a gradient of 5 – 60% EtOAc in hexane as eluent. **7a** (0.93 g, 69%, white crystalline): mp 42-43 ^{o}C (lit.[1a] mp 42-43 ^{o}C); R_f = 0.72 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H), 2.41 (d, 3H, *J* = 1.0 Hz), 3.72 (s, 3H), 4.93 (d, 1H, *J* = 1.0 Hz); ^{13}C NMR ($CDCl_3$) δ 22.4, 25.7, 51.5, 96.4, 155.7, 169.4, 167.0. **7a'** (93 mg, 7 %); Rf = 0.64 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.25 (s, 3H), 2.31 (s, 3H), 3.78 (s, 3H), 5.55 (br s, 1H). **7a**(***E***) (98 mg, 7%); Rf = 0.45 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.14 (s, 3H), 2.38 (s, 3H), 3.70 (s, 3H), 6.63 (br s, 1H), 6.78 (s, 1H).

(Z)-3-Acetylamino-2-methyl-but-2-enoic acid ethyl ester (7b)

Using the same procedure for the preparation of **7a**, 1.66 g (87%, oil) of **7b** was obtained. Rf = 0.60 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.33 (t, 3H, J = 7.1 Hz), 1.85 (s, 3H), 2.13 (d, 3H, *J* = 1.0 Hz), 2.42 (s, 3H), 4.20 (q, 2H, *J* = 7.1 Hz); ^{13}C NMR ($CDCl_3$) δ 12.6, 14.2, 17.3, 25.5, 60.4, 103.1, 150.3, 169.0, 170.2.



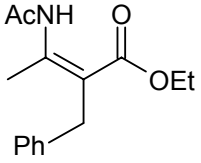
7b



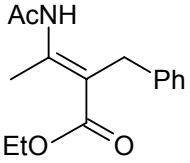
7b(***E***)

7b(***E***) (80 mg, 5%); Rf = 0.06 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 3H, *J* = 7.1 Hz), 1.78 (d, 3H, *J* = 1.5 Hz), 2.04 (s, 3H), 2.34 (d, 3H, *J* = 1.3 Hz), 4.13 (q, 2H, *J* = 7.1 Hz), 6.53 (br s, 1H).

(Z)-3-Acetylamino-2-benzyl-but-2-enoic acid ethyl ester (7c)



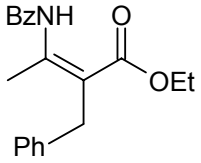
7c



7c(***E***)

Using the same procedure for the preparation of **7a**, 2.10 g (81%) of **7c** was obtained as a white solid: mp 52-53 ^{o}C; R_f = 0.36 (10% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.22 (t, 3H, *J* = 7.1 Hz), 2.17 (s, 3H), 2.48 (s, 3H), 3.72 (s, 2H), 4.14 (q, 2H, *J* = 7.1 Hz), 7.10-7.33 (m, 5H). **7c**(***E***) (50 mg, 2%); R_f = 0.40 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.28 (t, 3H, *J* = 7.1 Hz), 1.94 (s, 3H), 2.53 (s, 3H), 3.73(s, 2H), 4.23 (q, 2H, *J* = 7.1 Hz), 6.79 (br s, 1H), 7.23-7.38 (m, 5H).

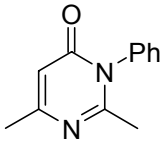
(Z)-2-Benzyl-3-[(1-phenyl-methanoyl)-amino]-but-2-enoic acid ethyl ester (7d)



Using the same procedure for the preparation of **7a**, 2.5 g (81%) of **7d** was obtained as a white solid: mp 79-81 ^{o}C; R_f = 0.32 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.23 (t, 3H, *J* = 7.1 Hz), 2.64 (s, 3H), 3.80 (s, 2H), 4.21 (q, 2H, *J* = 7.1 Hz), 7.20-8.04 (m, 10H).

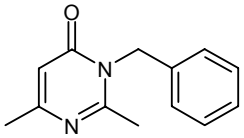
Representative procedure for pyrimidinones 8:

2,6-Dimethyl-3-phenyl-3*H*-pyrimidin-4-one (8a)



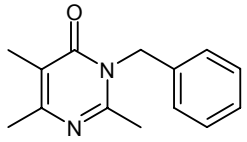
To a solution of aniline (0.14 ml, 1.56 mmol) in dry CH_2Cl_2 (2.5 mL) was slowly added 0.78 ml (1.56 mmol) of a 2.0 M solution of Me_3Al in heptane (Aldrich) at rt under nitrogen. After stirring 20 min at rt, enamide was added. The reaction mixture was stirred for 5h at rt. The reaction was quenched by the slow addition of saturated aqueous NH_4Cl (or 10% (w/w) aq. citric acid) and extracted with CH_2Cl_2. The organic layer was washed with saturated aq. $NaHCO_3$ and brine. After drying over $MgSO_4$ and concentration *in vacuo*, the resultant residue was subjected to flash column chromatography on silica gel to afford the desired pyrimidinone **8a** (87 mg, 84%, white solid): mp 94-95 ^{o}C; R_f = 0.12 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.18 (s, 3H), 2.33 (s, 3H), 6.33 (s, 1H), 7.21-7.58 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 24.2, 24.4, 111.3, 127.9, 129.8, 130.4, 137.7, 158.9, 162.9, 163.5; FT-IR (thin film from $CDCl_3$): **1678**, 1529 cm^{-1} ; LCMS (MH^+): 201.1 (100%).

3-Benzyl-2,6-Dimethyl-3*H*-pyrimidin-4-one (8b)



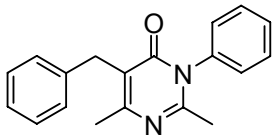
Yield: 116 mg (85%, colorless oily solid); R_f = 0.16 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3H), 2.45 (s, 3H), 5.31 (br s, 2H), 6.32 (s, 1H), 7.19-7.38 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 23.5, 24.1, 47.1, 110.9, 127.0, 128.2, 129.4, 135.7, 159.4, 163.0, 163.2; FT-IR (thin film from $CDCl_3$): **1666**, 1536 cm^{-1}; LCMS (MH^+): 215.1 (100%).

3-Benzyl-2,5,6-trimethyl-3*H*-pyrimidin-4-one (8c)



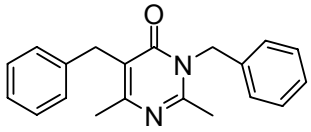
Yield: 110 mg (74%, colorless oil); R_f = 0.31 (50% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.15 (s, 3H), 2.33 (s, 3H), 2.46 (s, 3H), 5.33 (s, 2H), 7.22-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 12.3, 22.0, 23.2, 47.8, 118.3, 127.0, 128.1, 129.3, 136.0, 155.7, 158.3, 163.4; FT-IR (thin film from $CDCl_3$): **1656**, 1546 cm^{-1}; LCMS (MH^+): 229.1 (100%).

5-Benzyl-2,6-dimethyl-3-phenyl-3*H*-pyrimidin-4-one (8d)



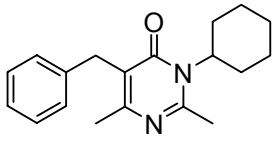
This reaction was quenched by cold 1N aq. HCl solution after the starting material was consumed. Yield: 177 mg (98%, light yellow oil); R_f = 0.21 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.09 (s, 3H), 2.27 (s, 3H), 3.79(s, 2H), 7.09-7.42 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 22.3, 24.2, 32.18, 120.2, 122.2, 124.52, 126.5, 127.9, 128.8, 129, 129.3, 129.7, 130.4, 138.1, 139.9, 156.2, 159.4, 163.3; FT-IR (thin film from $CDCl_3$): **1660**, 1538, 1453cm^{-1}; LCMS (MH^+): 290.4 (100%).

3,5-Dibenzyl-2,6-dimethyl-3*H*-pyrimidin-4-one (8e)



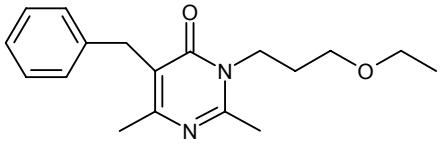
This reaction was quenched by cold 1N aq. HCl solution after the starting material was consumed. Yield: 152 mg (87%, white solid): mp 71-72 ^oC ; R_f = 0.25 (30% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3H), 2.41 (s, 3H), 3.97 (s, 2H), 5.30 (s, 2H), 7.19-7.40 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 22.2, 23.3, 32.3, 47.8, 121.7, 125.5, 126.5, 126.7, 127.1, 128.1, 128.3, 128.7, 128.8, 129.1, 129.3, 135.9, 140.0, 156.7, 159.4, 163.3; FT-IR (thin film from $CDCl_3$): **1656**, 1598, 1537cm^{-1}; LCMS (MH^+): 304.4 (100%).

5-Benzyl-3-cyclohexyl-2,6-dimethyl-3*H*-pyrimidin-4-one (8f)



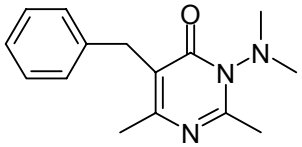
This reaction was quenched by cold 1N aq. HCl solution after the starting material was consumed. Yield: 108 mg (64%, white solid): mp 128-129 ^{o}C ; R_f = 0.28 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.28 (m, 4H), 1.64 (m, 4H), 1.90 (m, 2H), 2.25 (s, 3H), 2.53 (s, 3H), 2.78 (m, 1H), 3.88 (s, 2H), 7.10-7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.8, 24.3, 25.4, 26.8, 28.6, 31.9, 61.9, 122.9, 126.3, 128.7, 128.7, 140.2, 155.9, 158.2, 163.6 ; FT-IR (thin film from $CDCl_3$): **1643**, 1540, 1452, 1402cm^{-1}; LCMS (MH^+): 296.4 (100%).

5-benzyl-3-(3-ethoxy-propyl)-2,6-dimethyl-3-pyrimidin-4-one (8g)



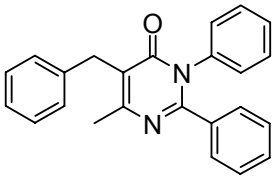
Yield: 121 mg (77%, light yellow oil): R_f = 0.10 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.18-1.22 (m, 3H), 1.98-2.03 (m, 2H), 2.30 (s, 3H), 2.56 (s, 3H), 3.46-3.51 (m, 4H), 3.90 (s, 2H), 4.10-4.13 (m,2H), 7.18-7.28 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 15.17, 21.71, 22.55, 28.41, 31.76, 42.71. 66.29, 67.36, 121.06, 126.01, 128.33, 128.37, 139.70, 155.91, 158.66, 162.61; FT-IR (thin film from DCM) **1656**, 1543 cm^{-1}; LCMS (MH^+): 301.4.

Benzyl-dimethylamino-dimethyl-3-pyrimidin-4-one (8h)



Yield: 86 mg (70%, light yellow solid): mp 62-63 ^{o}C ; R_f = 0.35 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.26 (s, 3H), 2.52 (s,3H), 3.02 (s, 6H), 3.87 (s, 2H), 7.17-7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 22.09, 22.49, 31.77, 43.47, 123.38, 126.42, 128.68, 128.81, 139.98, 158.68, 159.56, 163.11; FT-IR (thin film from DCM): **1657**, 1543 cm^{-1}; LCMS (MH^+): 258.4.

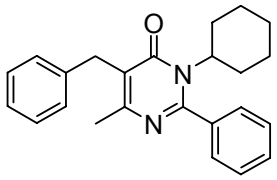
5-Benzyl-6-methyl-2,3-diphenyl-3*H*-pyrimidin-4-one (8i)



This reaction was quenched by cold 1N aq. HCl solution after the starting material was consumed. Yield: 117 mg (72%, white solid): mp 149-151 ^{o}C ; R_f = 0.31 (30% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.40 (s, 3H), 3.89 (s, 2H), 6.98-7.39 (m,

15H); ^{13}C NMR ($CDCl_3$) δ 29.8, 39.7, 130.3, 133.9, 135.7, 136.1, 136.4, 136.6, 137.1, 142.4, 145.1, 147.1, 164.1, 166.8, 170.3; FT-IR (thin film from $CDCl_3$): **1662**, 1620, 1493cm^{-1}; LCMS (MH^+): 352.4 (100%).

5-Benzyl-3-cyclohexyl-6-methyl-2-phenyl-3*H*-pyrimidin-4-one (8j)



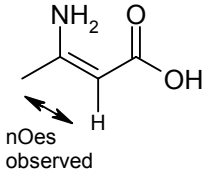
Yield: 102 mg (62%, white solid): mp 117-119 ^{o}C; R_f = 0.26 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 0.79-0.91 (m, 2H), 1.05-1.18 (m, 2H), 1.38-1.42 (m, 2H), 1.55-1.70 (m, 2H), 2.25 (s, 3H), 2.53-2.68 (m, 2H), 3.62-3.73 (m, 1H), 3.84 (s, 2H), 7.09-7.45 (m, 10H); ^{13}C NMR ($CDCl_3$) δ 22.2, 25.2, 26.5, 29.1, 32.0, 33.7, 63.3, 123.8, 126.5, 127.2, 127.6, 128.8, 128.9, 129.2, 130.1, 136.4, 140.1, 158.2, 158.3, 163.5; FT-IR (thin film from $CDCl_3$): **1649**, 1597, 1492, 1452cm^{-1}; LCMS (MH^+): 358.5 (100%).

<u>An experimental procedure for the preparation of 2,6-dimethyl-3-phenyl-3*H*-pyrimidin-4-one (8a) from β-keto ester (6a) without purification of intermediates</u>

To a solution of methyl acetoacetate (0.93 ml, 8.61 mmol) in toluene (17 ml) were added ammonium acetate (3.98 g, 51.67 mmol) and 2 ml of acetic acid at rt. The reaction mixture was heated to reflux for 2 hr. A Dean-Stark trap was placed in between the reaction flask and a reflux condenser. Most of solvents and ammonium acetate were removed through a Dean-Stark trap. The clear resultant residue was cooled down to rt followed by the addition of acetic anhydride (4.5 ml) and acetic acid (1 ml). After heating at 70 ^{o}C for overnight, the reaction mixture was cooled down to rt and was quenched with 1N HCl (30 ml), and then extracted with CH_2Cl_2. The combined organic layer was washed with saturated aqueous $NaHCO_3$ and brine. After drying over $MgSO_4$ and concentration *in vacuo*, half of the crude *E/Z* mixture of the enamide esters **7a**/**7a**(***E***) was carried out for the next reaction. To a solution of aniline (0.91ml, 9.99 mmol) in dry CH_2Cl_2 (10 mL) was slowly added 5.0 ml (9.99 mmol) of a 2.0 M solution of Me_3Al in heptane (Aldrich) at rt under nitrogen. After stirring 20 min at rt, the solution of crude *E/Z* mixture of the enamide esters **7a**/**7a**(***E***) in CH_2Cl_2 (5 mL) was added drpowise to the above solution. The reaction mixture was stirred for 5h at rt. The reaction was quenched by the slow addition of saturated aqueous NH_4Cl

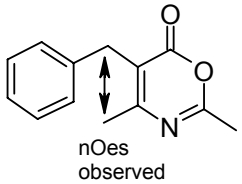
(or 10% (w/w) aq. citric acid) and extracted with CH_2Cl_2 (25 mL x 3). The organic layer was washed with saturated aq. $NaHCO_3$ and brine. After drying over $MgSO_4$ and concentration *in vacuo*, the resultant residue was subjected to flash column chromatography on silica gel to afford the desired pyrimidinone **8a** as a white solid (447 mg, 52% for three steps).

(*Z*)-3-Amino-but-2-enoic acid (9)



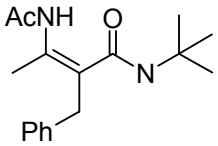
^{1}H NMR ($CDCl_3$) δ 1.84 (s, 3H), 3.58 (s, 3H), 4.46 (s, 1H); R_f = 0.51 (20% EA/Hex).

5-Benzyl-2,4-dimethyl-[1,3]oxazin-6-one (10)



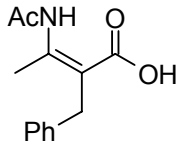
Yield: 45 mg (42%, white solid) from **2c** with *t*-$BuNH_2$ and Me_3Al as shown in Scheme 2 under the standard reaction condition for the preparation of **8a**; mp 120-121 ^oC; R_f = 0.23 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.19 (s, 3H), 2.29 (s, 3H), 3.75 (s, 2H), 7.11-7.29 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 21.3 (two carbons), 31.4, 117.4, 126.6, 128.3, 128.6, 138.2, 160.6, 160.8, 163.7; FT-IR (thin film from $CDCl_3$): **1731**, 1633, 1580, 1272 cm^{-1}; LCMS (MH^+): 216.2, 234.2 (100%).

(*Z*)-3-Acetylamino-2-benzyl-but-2-enoic acid *tert*-butylamide (11)



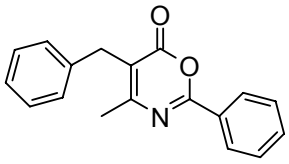
Yield: 8 mg (6%); R_f = 0.15 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 1.09 (s, 9H), 2.07 (s, 3H), 2.38 (s, 3H), 3.52 (s, 2H), 5.26 (br s, 1H), 7.12-7.29 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 17.2, 25.7, 28.5, 33.7, 51.3, 108.4, 127.0, 127.6, 129.1, 138.5, 147.7, 169.4, 169.9; FT-IR (thin film from $CDCl_3$):1680, 1630, 1531, 1445cm^{-1}; LCMS (MH^+): 289.2 (100%).

(*Z*)-3-Acetylamino-2-benzyl-but-2-enoic acid (12)



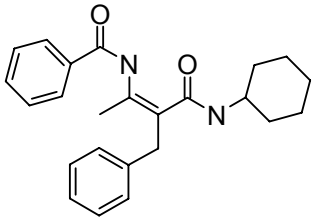
Yield: 15 mg (13%, white solid); R_f = 0.04 (20% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.17 (s, 3H), 2.49 (s, 3H), 3.77 (s, 2H), 7.18-7.33 (m, 5H), 10.50 (br s, 1H), 11.67 (s, 1H); LCMS (MH^+): 234.2 (100%).

5-Benzyl-4-methyl-2-phenyl-[1,3]oxazin-6-one (13)



To a solution of **7d** (100 mg, 0.31 mmol) in dry CH_2Cl_2 (2.0 mL) was slowly added 0.47 ml (0.93 mmol) of a 2.0 M solution of Me_3Al in heptane (Aldrich) at rt under nitrogen. The reaction mixture was stirred at rt under nitrogen overnight. The reaction was quenched by the slow addition 10% (w/w) aq. citric acid and extracted with CH_2Cl_2. The organic layer was washed with saturated aq. $NaHCO_3$ and brine. After drying over $MgSO_4$ and concentration *in vacuo*, the resultant residue was subjected to flash column chromatography on silica gel to afford 74 mg (87%) of the desired product **13** as a white solid: mp 99-101 ^{o}C (lit.[2] mp 99-101 ^{o}C); R_f = 0.68 (30% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 2.29 (s, 3H), 3.80 (s, 2H), 7.08-7.60 (m, 8H), 8.06-8.15 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 20.6, 28.7, 29.1, 30.6, 44.2, 116.8, 125.1, 125.5, 126.3, 127.4, 127.7, 128.8, 131.1, 131.8, 137.2, 139.9, 159.2, 159.6, 160.4, 168.4; FT-IR (thin film from $CDCl_3$): 1737, 1619, 1552, 1450cm^{-1}; LCMS (MH^+): 277.3 (100%).

N-((Z)-2-cyclohexylcarbamoyl-1-methyl-3-phenyl-propenzyl)-benzamide (14)

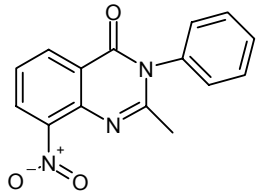


Yield: 20 mg (5%) from the reaction shown in Scheme 3; R_f = 0.45 (30% EA/Hex); ^{1}H NMR ($CDCl_3$) δ 0.82-0.91 (m, 2H), 0.98-1.08 (m, 2H), 1.15-1.29 (m, 2H), 1.35-1.39 (m, 2H),1.55-1.63 (m, 2H) 2.52 (s, 3H), 3.63 (s,2H), 3.71-3.78 (m, 1H), 5.31-5.39 (m, 1H), 7.08-7.50 (m, 8H), 7.91-7.78 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 23.7, 24.4, 28.9, 31.7, 35.3, 47.3, 62.2, 125.8, 126.3, 127.6, 127.7, 131.0, 132.2, 136.9, 165.9, 168.3, 205.7; LCMS (MH^+): 376.5 (100%).

Representative procedure for quinazolinones (3):

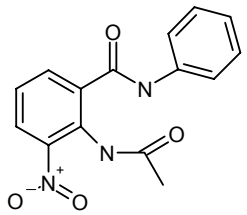
To a solution of *o*-toluidine(0.332 ml, 3.11 mmol) was added a solution of trimethylaluminum in heptane (1.55 ml, 3.11 mmol) and the mixture was stirred for 30 min at room temperature. Methyl-2-acetamido-benzoate (200 mg, 1.04 mmol) was then added to the reaction mixture which was refluxed for 18h. The reaction mixure was then quenched with 10 % (wt/wt) aq. citric acid acid solution, extracted twice with DCM (50 ml), dried over $MgSO_4$, then concentrated *in-vacuo.* Purification on silica gel column afforded the desired quinazolinone **3** (188 mg, 72%, pale white solid): mp 113-114 ^oC (lit.[3] mp 114-115 ^oC); R_f=0.33 (20% EA/Hex); ^1H NMR (DMSO-d6) δ 2.04 (s, 3H), 2.09 (s, 3H), 7.30-8.25 (m, 8H); ^{13}C NMR ($CDCl_3$) δ 17.82, 24.31, 121.15, 127.02, 127.19, 127.55, 128.07, 128.31, 130.01, 131.96, 135.02, 135.76, 137.20, 148.05, 154.75, 162.07; FT-IR (thin film from DCM): **1682** cm^{-1}, 1599 cm^{-1}; LCMS (MH^+): 251.2.

2-Methyl-8-nitro-3-phenyl-3-H-quinazolin-4-one (16);



134 mg (76%) of **16** was obtained as a yellow solid: mp 195-196 ^oC (yellow solid); R_f = 0.38 (20% EA/Hex); ^1H NMR ($CDCl_3$) δ 2.31 (s,3H), 7.26-7.28 (m, 2H), 7.50-7.70 (m, 4H), 8.07 (m, 1H), 8.47 (m, 1H); ^{13}C NMR ($CDCl_3$) 25.29, 122.89, 126.05, 128.10, 128.76, 130.16, 130.67, 131.40, 137.37, 140.36, 146.91, 157.86, 161.11; FT-IR (thin film from DCM): **1692** cm^{-1}, **1672** cm^{-1}, 1583 cm^{-1}; LCMS (MH^+): 282.4

2-Acetylamino-3-nitro-N-phenyl-benzamide (17);



29 mg (15%) of **17** was obtained from the synthesis of **16**; mp 205-206 ^oC (yellow solid); ^1H NMR (DMSO-d6) 2.51 (s, 3H), 7.10-8.10 (m, 8H), 10.16 (s, 1H), 10.54 (s, 1H); ^{13}C NMR (DMSO-d6) 23.20, 120.31, 124.24, 126.40, 126.43,

128.59, 129.04, 133.12, 134.63, 139.35, 146.20, 164.61, 169.12; LCMS (MH^+): 300.4

Synthesis of 2-Methyl-8-nitro-3-phenyl-3-H-quinazolin-4-one (16) from 2-Acetylamino-3-nitro-N-phenyl-benzamide (17); To a solution of **17** (15 mg, 0.05 mmol) in DCM (or DCE) at room temperature was added a solution of Me_3Al in heptane (0.075 ml, 0.150 mmol) and the reaction mixture was refluxed for 20h. Yield of **16** from crude reaction mixture determined from LCMS to be 80%(DCM) and 93%(DCE).

References:

(1) (a) Lubell, W. D.; Kitamura, M; Noyori, R. *Tetrahedron: Asymmetry* **1991**, *2*, 543. (b) Zhu, G.; Chen, Z.; Zhang, X. *J. Org. Chem*. **1999**, *64*, 6907.
(2) Beccalli, E. M.; Benincori, T.; Marchesini, A. *Synthesis* **1988**, 630.
(3) Rathman, T. L.; Sleevi, M. C.; Krafft, M. E.; Wolfe, J. F. *J. Org. Chem*. **1980**, *45*, 2169.