A Convenient Route for the Synthesis of Pyrazolo[3,4-*d*]pyrimidine, Pyrazolo[3,4-*b*][1,6]naphthyridine and Pyrazolo[3,4-*b*]quinoline Derivatives

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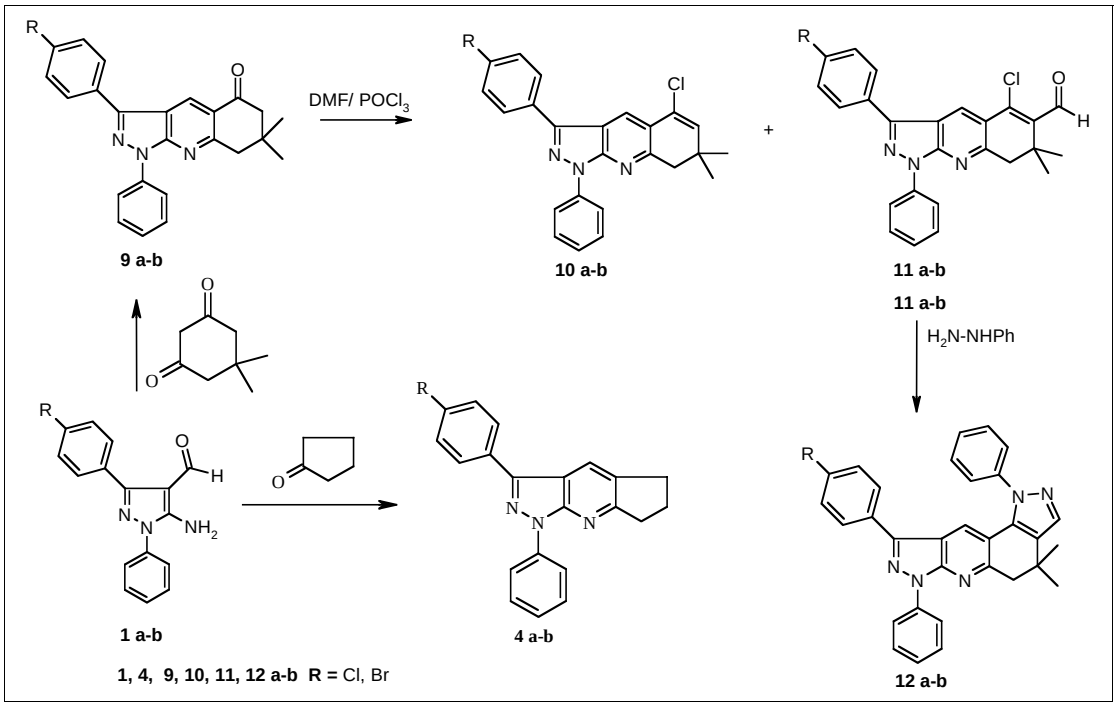

Friedländer condensation of 5-aminopyrazole-4-carbaldehydes **1** with formamide **2a** or benzamide **2b** gave pyrazolo[3,4-*d*]pyrimidine derivatives **3**. Cyclocondensation of **1** with cyclopentanone, *N*-benzyl-4-piperidone and 6-methoxy-1-tetralone yielded cyclopenta[*b*]pyrazolo[4,3-*e*]pyridines **4**, pyrazolo[3,4-*b*]-[1,6]naphthyridines **5** and benzo[*h*]pyrazolo[3,4-*b*]quinolines **6**, respectively. Analogous condensation of cyclohexanone **7a** or 2-methyl-1-cyclohexanone **7b** with **1** afforded pyrazolo[3,4-*b*]quinoline derivatives **8a-d**. Heating **1** with dimedone furnished pyrazolo[3,4-*b*]quinolinone derivatives **9**. Vilsmeier-Haack formylation of **9** yielded a mixture of two compounds **10** and **11**. Further bispyrazolo[3,4-*b*:4,3-*f*]-quinolines **12a**, **b** were obtained on cyclocondensation of **11a**, **b** with phenyl hydrazine.

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Heterocyclic ring systems that containing the pyrazole ring fused to pyrimidine, quinoline or benzoquinoline rings are interesting classes of compounds both chem.-ically and biologically. For example, pyrazolopyrimidines display significant chemical properties [1-7], whereas pyrazoloquinolines and pyrazolobenzoquinolines exhibit a wide range of biological properties [8-15]. Our ongoing interest in this area encouraged us to report the synthesis of title compounds.

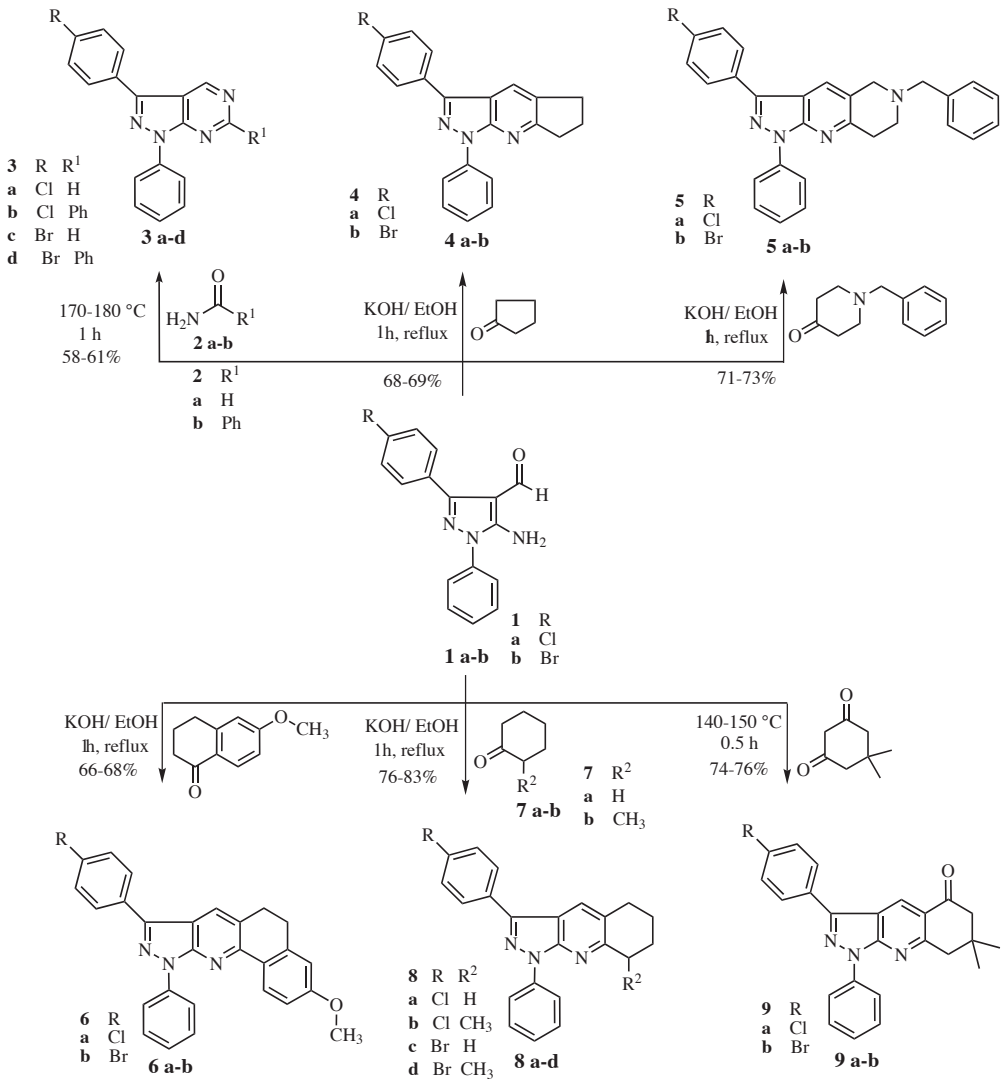
In a recent paper [16], we have reported the synthesis of pyrazolo fused pyridines using orthoaminoaldehyde **1** as a starting material. In this paper we extended this work towards the synthesis of several pyrazolo[3,4-*d*]pyrimidine, pyrazolo[3,4-*b*]quinolines and pyrzolo[3,4-*b*]benzoquinolines from **1**. Compound **1** was synthesized by the method reported in our previous communication [16]. The Friedlander condensation of *ortho*-aminoaldehyde **1** with amides was performed without catalyst or solvent. Thus a mixture of **1a** or **1b** and the corresponding formamide **2a** or benzamide **2b** was heated at 170-180°C to afford pyrazolo[3,4-*d*]pyrimidines **3a-d** in 56-61% yield. However, similar condensation of **1a**, or **1b** with cyclic ketones was unsuccessful.

According to our previous protocol [16], a mixture of **1a** or **1b** and cyclic ketones such as cylopetanone or *N*-benzyl-1-piperidone, on refluxing in ethanolic potassium

hydroxide furnished cylopenta[*b*]pyrazolo[4,3-*e*]pyridine **4** and pyrazolo[3,4-*b*][1-6]napthyridine **5** in 68-73% yield. The cyclocondensation of 6-methoxy-1-tetralone, cyclohexanone **7a** or 2-methyl-1-cyclohexanone **7b** with **1**, under similar reaction conditions smoothly yielded benzo[*h*]pyrazolo[3,4-*b*]quinoline **6**, pyrazolo[3,4-*b*]-quinoline **8** respectively. However, reaction of **1a** or **1b** with dimedone was unsuccessful in ethanolic KOH, hence this condensation was achieved by heating at 140-150°C, which offered 3-(4-chloro/bromopheny)-7,7-dimethyl-1-phenyl-1,6,7,8-terahydro-5*H*-pyrazolo[3,4-*b*]quinoline **9** (Scheme 1). Compounds **3**, **4**, **5**, **6**, **8** and **9** were characterized by IR, ^{1}H and ^{13}C, nmr; *e.g.*, the IR spectrum of **9a** showed carbonyl stretching bands at 1728 cm^{-1}, the ^{1}H nmr spectrum showed a singlet at δ 1.19, for 6 methyl protons, singlets at δ 2.69 and δ 3.24 due to the 4 methylene protons and a down field singlet at δ 9.09 corresponding to C_4-H. The ^{13}C nmr spectrum of this compound exhibits peaks at δ 28, 32, 47, 52, for gemdimethyl and C_7, C_6, C_8 carbons respectively, aromatic carbon resonances appear between δ 76-162 and carbonyl carbon resonances appears at δ 197. The elemental analysis obtained is in agreement with the molecular formula. The mass spectral analysis showed an ion with m/z 401 (M+), which supports the proposed structure **9a**.

Pyrazolo[3,4-*b*]quinolines **9** with α-methylene group are useful compounds for further synthetic transformations. Thus, Vilsemeier Haack formylation of **9** with excess of *N*,*N*-dimethylforamide and phosphorous oxychloride afforded a mixture of two compounds **10** and **11** in 1:2 ratio respectively. This mixture was separated by column chromatography using toluene/hexane as the eluent. The structural assignment of **10a** and **11a** was

Scheme 1



accomplished by spectral and analytical data. Compound **10a** showed a sharp singlet at δ 6.13 for C_6-H, while in **11a** this peak was not present and another singlet at δ 10.48 was observed corresponding to the aldehyde proton. All other signals of **10a** and **11a** are nearly identical. The ^{13}C nmr of **10a** showed a peak at δ 138 for C_6, for **11a** this peak is observed further down field at δ 155. Also, for **11a**, a C=O peak is observed at δ 192, which is absent in the spectrum of **10a**. A stretching vibration in the IR spectrum of **11a** is observed at 2745 cm^{-1}, which further supports the aldehyde function group at C_5. The mass spectrum of **10a** exhibited an ion with m/z 419.10, and that of **11a** exhibited an ion with m/z 447.09. Thus, compound **10a** was assigned as 5-chloro-3-(4-chlorophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline and **11a** was assigned as 5-chloro-3-(4-chlorophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline-6-carbaldehyde.

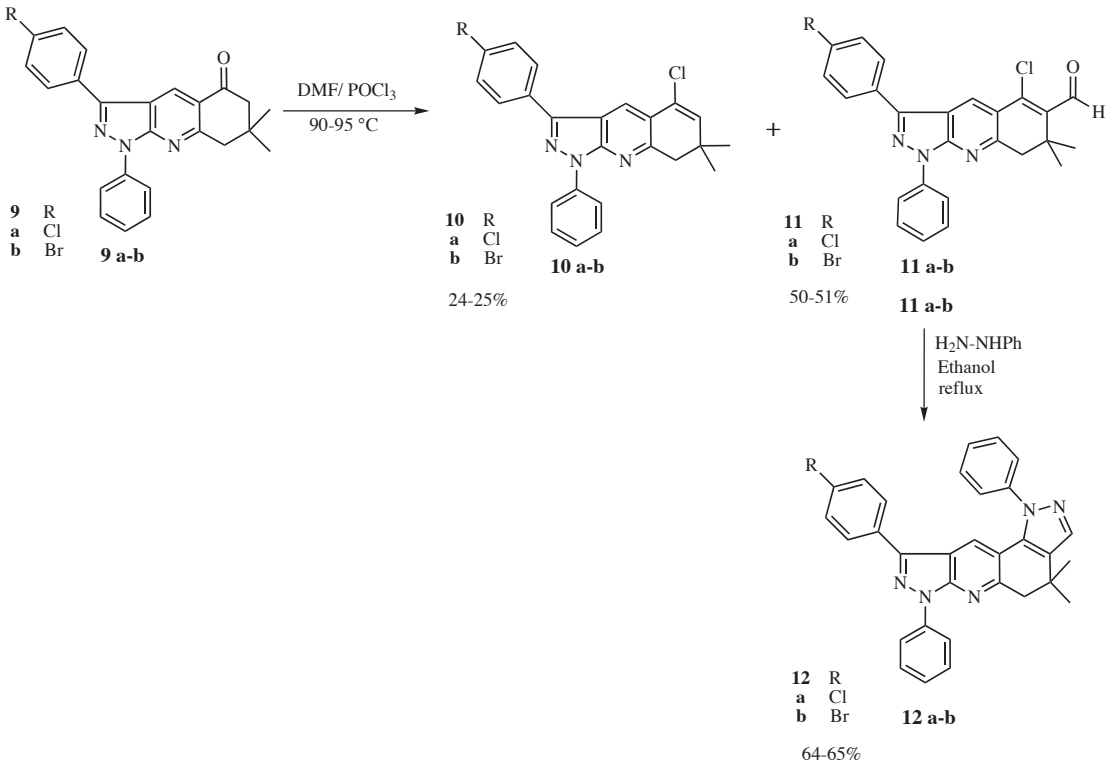
The structure of bromoderivatives **10b** and **11b** were established similarly. Chloro and chloroformyl products like that of **10** and **11**, formed through the Vilsmeier Haack reaction, are not common in the literature. Pyrazolo[3,4-*b*]quinolines **11** are bifunctional compounds and hence interesting to extend bispyrazolo[3,4-*b:*4,3-*f*]-quinoline libraries, *e.g.*, bispyrazolo[3,4-*b*:4,3-*f*]quinoline derivatives **12**, were obtained by cyclocondensation of **11** with phenyl hydrazine in refluxing ethanol. The IR and ^{1}H nmr spectra of compounds **12** clearly show that the aldehyde functional group is no longer present, and in the ^{13}C-nmr spectra of these compounds a peak at δ 192 for C=O was not observed and new a peak at δ 139 was observed corresponding to C_3. The elemental analyses are in agreement with proposed structures (Scheme 2).

The reactions reported here represent new synthetic methods towards novel fused aza heterocyles, with high yields, simple workup, and clean products.

EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting Point Apparatus in open capillary tubes and are uncorrected. The ^{1}H and ^{13}C nmr spectra were recorded on a Varian XL-300 spectrometer (300 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. The solvent for NMR spectra was deuteriochloroform. Infrared spectra were taken on a Shimadzu IR-408 in potassium bromide pellets unless otherwise stated. The mass spectrum was recorded on QP-2010s. Elemental analyses were performed on a Hosli CH-Analyzer and are within ± 0.4 of the theoretical percentages. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using uv light (254 and 366 nm) for detection. Column chromatography was carried out on silica gel (SD Fine Chemicals, 60-80 mesh).

Scheme 2



Common reagent grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

3-(4-Chlorophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**3a**).

A mixture of **1a** (0.60 g, 2 mmol) and formamide (**2a**) (0.39mL, 10 mmol) was heated at 170-180 °C for 1 hour. The solid obtained on cooling was collected by filtration, washed with cold ethanol (5 mL), dried and recrystallized from ethyl acetate to yield colorless prisms, 0.37 g (61%), mp 186-187 °C ; ir: 2678, 1595, 1559 cm^{-1}; ^1H nmr: δ 7.40-7.64 (m, 5H, Ph), 8.04 (d, J =8.4 Hz, 2H, Ar), 8.32 (d, J = 8.4 Hz, 2H, Ar), 9.19 (s,1H C_6-H), 9.53 (s, 1H C_4-H); ^{13}C nmr: δ 105.7, 124.9, 125.5, 127.3, 128.9, 134.2, 137.7, 139.5, 142.1, 150.2, 151.6, 154.4 (17 ArC); ms: 308(M+2), 306(M^+), 271, 243, 217, 195.

Anal. Calcd. for $C_{17}H_{11}ClN_4$: C, 66.56; H, 3.61; N, 18.26. Found: C, 66.82; H, 3.56; N, 18.98.

3-(4-Chlorophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**3b**).

This compound was obtained from **1b** (0.60 g, 2 mmol) and benzamide (**2b**) (1.21 g, 10 mmol) using the method described for **3a**; yield 0.45 g (59%), colorless prisms, mp 198-199 °C (ethyl acetate); ir: 2675, 1593, 1552 cm^{-1}; ^1H nmr: δ 7.38-7.72 (m, 5H, Ph), 7.86(m, 3H, Ph),7.96 (d, J = 8.4 Hz, 2H, ArH), 8.42 (d, J = 8.4 Hz, 2H, Ar), 8.60 (m, 2H, Ph), 9.51(s,1H,C_4-H); ^{13}C nmr: δ 106.3, 120.5, 124.7, 125.4, 127.2, 127.3, 128.5, 128.5, 129.2, 131.4, 134.6, 137.6, 139.8, 142.3, 150.4, 159.7 (23 ArC); ms: (m/z), 384 (M+2), 382(M+1), 304, 269, 241, 193.

Anal. Calcd. for $C_{23}H_{15}ClN_4$: C, 72.16; H, 3.95; N; 14.63. Found: C, 72.36; H, 4.18; N, 14.72.

3-(4-Bromophenyl)-1-phenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**3c**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and formamide (**2a**) (0.39 mL, 10 mmol) using the method described for **3a**; yield 0.42 g (60%), colorless prisms, mp 191-192 °C (ethyl acetate); ir: 2664, 1592, 1555 cm^{-1}; ^1H NMR: δ 7.36-7.71 (m, 5H, Ph), 7.93 (d, J = 8.4 Hz, 2H, Ar), 8.27 (d, J = 8.4 Hz, 2H, Ar), 9.14 (s, 1H, C_6-H), 9.49 (s, 1H, C_4-H); ^{13}C nmr :δ 105.8, 120.9, 124.9, 125.6, 127.5, 128.9, 134.4, 137.9, 139.6, 142.2, 150.3, 151.3, 151.7, 154.5, 917 ArC); ms: m/z, 352 (M+2), 350(M^+), 315, 287, 261, 239.

Anal. Calcd. for $C_{17}H_{11}BrN_4$: C, 58.14; H, 3.16; N; 15.95. Found: C, 58.26; H, 3.35; N, 16.12.

3-(4-Bromophenyl)-1,6-diphenyl-1*H*-pyrazolo[3,4-*d*]pyrimidine (**3d**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and benzamide (**2b**) (1.21 g, 10 mmol) using the method described for **3a**; the yield was 0.50 g (58%) colorless prisms, mp 208-209 °C (ethyl acetate); ir: 2668, 1596, 1557 cm^{-1}; ^1H nmr: δ 7.25-7.47 (m, 5H, Ph), 7.58-7.68 (m, 3H, Ph), 7.69(d, J=8.4Hz, 2H, ArH), 8.01(d, 8.4 Hz, 2H, ArH) 8.44 (m 2H, ArH), 9.51 (s, 1H, C_6H); ^{13}Cnmr: δ 106.4, 120.7, 124.8, 125.5, 127.4, 127.5, 128.6, 128.9, 129.3, 131.5, 134.7, 137.8, 142.5, 150.6, 153.4, 159.9 (23 ArC); ms: (m/z), 426, (M^+), 348, 313, 285.

Anal. Calcd. for $C_{23}H_{15}BrN_4$: C, 64.65; H, 3.54; N; 13.11. Found: C, 64.38; H, 3.65; N, 13.32.

3-(4-Chlorophenyl)-1-phenyl-1,5, 6, 7-tetrahydrocyclopenta[*b*]-pyrazolo[4,3-*e*]pyridine (**4a**).

A solution of **1a** (0.60 g, 2 mmol) and cyclopentanone (0.16 mL, 2 mmol) in ethanolic potassium hydroxide (10 mL, 2%) was reflux for one hour. The mixture was then cooled to room temperature, the solid obtained was collected by suction filtered, washed with ethanol and recystallized from ethyl acetate to yield 0.48 g (69%) of **4a** as colorless prisms, mp 174-175°; ir: 2718, 1592, 1556 cm^{-1}; ^1H nmr: δ 2.21 (q, J=7.2 Hz, 2H, CH_2), 3.03 (t, J=7.2 Hz, 2H, CH_2), 3.11 (t, J=7.2 Hz, 2H, CH_2), 7.27-7.55 (m, 5H, Ph) 7.94 (d, J = 8.4 Hz, 2H, Ar), 8.06 (s, 1H, C_4-H), 8.32 (d, J =7.8 Hz, 2H, Ar); ^{13}C nmr δ: 25.8, 34.3, 35.8, 114.4, 120.6, 124.8, 125.7, 127.5, 128.3, 128.9, 131.4, 134.6, 137.8, 139.4, 142.2, 149.2, 163.2 (18 ArC): ms: (m/z): 345 (M^+), 303, 226.

Anal. Calcd. for $C_{21}H_{16}ClN_3$: C, 72.93; H, 4.66; N, 12.15. Found: C, 72.82; H, 4.56; N, 12.28.

3-(4-Bromophenyl)-1-phenyl-1,5,6,7-tetrahydrocyclopenta[*b*]-pyrazolo[4,3-*e*]pyridine (**4b**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and cyclopentanone (0.16 mL, 2 mmol) using the method described for **4a**; yield 0.53 g (68%), colorless prisms, mp 186-187 °C (ethyl acetate); ir: 2716, 1593, 1556 cm^{-1}; ^1H nmr: δ 2.20 (q, J=7.2 Hz, 2H, CH_2), 2.95 (t, J= 7.2 Hz, 2H, CH_2), 3.05 (t,J= 7.2 Hz, 2H, CH_2), 7.26-7.65 (m, 5H, Ph), 7.95(d, J=8.4Hz, 2H, ArH), 8.30(d, J=8.4Hz, 2H, ArH), 8.06 (s, 1H C_4-H); ^{13}C nmr: δ 25.9, 34.5, 35.9, 114.5, 120.8, 124.9, 125.8, 127.6, 128.5, 128.9, 131.6, 134.7, 137.9,142.3, 149.5, 163.5 (18 ArC); ms: (m/z),389 (M^+), 347, 270.

Anal. Calcd. for $C_{21}H_{16}BrN_3$: C, 64.63; H, 4.13; N; 10.77. Found: C, 64.76; H, 4.34; N, 10.79.

6-Benzyl-3-(4-chlorophenyl)-1-phenyl-5,6,7,8-tetrahydro-1*H*-pyrazolo[3,4-*b*][1,6]-naphthyridine (**5a**).

A solution of **1a** (0.60 g, 2 mmol) and *N*-benzyl-1-piperidone (0.37 mL, 2 mmol) in ethanolic potassium hydroxide solution (10 mL, 2%) was reflux for one hour. The mixture was cooled to room temperature, the solid product that precipitated was collected by suction filtration and washed with ethanol and recrystallized from ethyl acetate to yield 0.66 g (73%) of **5a** as colorless prisms, mp 212-213 °C; ir: 2289, 1596, 1556 cm^{-1}; ^1H nmr: δ 2.99 (m, 2H, CH_2), 3.26 (s, 2H, CH_2), 3.26 (s, 2H, CH_2), 3.82(s, 2H, CH_2Ph), 7.52 (s, 1H, C_4H), 7.31-7.62(m, 10H, 2Ph), 7.95(d, J=8.4Hz, 2H, ArH), 8.34(d, J=8.4Hz, 2H, ArH); ^{13}H nmr: δ 33.3, 50.8, 55.6, 62.6, 113.4, 120.7, 124.9, 125.5, 127.3, 127.5, 128.1, 128.3, 128.9, 129.0, 131.3, 134.2, 137.7, 139.5, 142.1, 150.2, 153.9 (24 ArC); ms (m/z), 450 (M+), 372, 358, 331.

Anal. Calcd. for $C_{28}H_{23}ClN_4$: C, 74.57; H, 5.14; N, 12.42. Found: C, 74.62; H, 5.24; N,12.58.

6-Benzyl-3-(4-bromophenyl)-1-phenyl-5,6,7,8-tetrahydro-1*H*-pyrazolo[3,4-*b*][1,6]-naphthyridine (**5b**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and *N*-benzyl-1-piperidone (0.37 g, 2 mmol) using the method described for **5a**; yield 0.70 g (71%) colorless prisms, mp 234-235 °C (ethyl acetate); ir: 2290, 1594, 1554 cm^{-1}; ^1H nmr δ 2.97 (m, 2H, CH_2), 3.10 (m, 2H, CH_2), 3.30(s, 2H, CH_2), 3.87(s, 2H, CH_2Ph), 7.29-7.57 (m, 10H, 2Ph), 7.62 (s, 1H, C_4-H), 7.96 (d, J=8.4 Hz, 2H, ArH), 8.37 (d, J = 7.8 Hz, 2H, ArH); ^{13}C nmr: δ 33.4, 50.9, 55.8, 62.7, 105.9, 120.8, 124.9, 124.7, 127.5, 127.5, 128.4, 128.9, 129.2,

131.534.3, 137.8, 139.6, 142.3, 150.3, 153.4, (24 ArC); ms: (m/z), 494 (M+), 416, 402, 297.

Anal. Calcd. for $C_{28}H_{23}BrN_4$: C, 67.88; H, 4.68; N; 11.31. Found: C, 67.96; H, 4.85; N, 11.52.

3-(4-Chlorophenyl)-8-methoxy-1-phenyl-5,6,7,8-tetrahydro-1*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline (**6a**).

A solution of **1a** (0.60 g, 2 mmol) and 6-methoxy-1-tetralone (0.35 g, 2 mmol) in ethanolic potassium hydroxide (10 mL, 2%) was heated at reflux temperature for one hour. The mixture was cooled to room temperature, and the solid obtained was collected by suction filtration and washed with ethanol. The yield was 0.60 g (68%), colorless prisms, mp 194-195° (ethyl acetate); ir: 2339, 1597, 1550 cm^{-1}; ^{1}H nmr: δ 2.97 (t, J=7Hz, 2H, CH_2), 3.06 (t, J=7Hz, 2H, CH_2), 3.87 (s, 3H, OCH_3), 6.77 (d, J = 8.4 Hz, 1H, C_7H), 6.96(dd, J = 8.4 , 1 Hz, 1H, C_9H), 7.15-7.48(m, 5H, Ph), 7.82 (dd, J=8.4, 0.9Hz,1H, C_{10}H), 7.95 (d, J = 8.4 Hz, 2H, ArH), 8.01(s, 1H, C_4H), 8.53 (d, J=8.4Hz, 2H, ArH), ^{13}C nmr: δ 29.8, 30.2, 52.8, 114.6, 120.4, 121.7, 122.4, 124.6, 125.6, 126.4, 127.3, 127.7, 128.4, 128.6, 129.4, 131.3, 134.2, 137.7, 142.5, 148.4, 154.6, 159.2, (24 ArC); ms (m/z), 437 (M+), 422, 255, 218, 179.

Anal. Calcd. for $C_{27}H_{20}ClN_3O$: C, 74.05; H, 4.60; N, 9.60. Found: C, 74.24; H, 4.72; N, 9.76.

3-(4-Bromophenyl)-8-methoxy-1-phenyl-5,6,7,8-tetrahydro-1*H*-benzo[*h*]pyrazolo[3,4-*b*]quinoline (**6b**).

A mixture of **1b** (0.68 g, 2 mmol) and 6-methoxy-1-tetralone (0.35 g, 2 mmol) was reacted by the method described for **6a**; yield 0.64 g (66%), colorless prisms, mp 198-199 °C (ethyl acetate); ir: 2341, 1595, 1551 cm^{-1}; ^{1}H nmr: δ 2.99 (t, J=7Hz, 2H, CH_2), 3.15 (t, J=7Hz, 2H, CH_2), 3.88 (s, 3H, OCH_3), 6.78 (d, J = 8.4 Hz, 1H, C_7H), 6.97 (dd, J=8.4, 0.9Hz, 1H, C_9H), 7.15-7.48 (m, 5H, Ph), 7.83 (dd, J = 8.4, 0.9 Hz, 1H, C_{10}-H), 7.99 (d, J = 8.4 Hz, 2H, ArH), 8.02 (s, 1H, C_4H), 8.46 (d, J=8.4Hz, 2H, ArH). ^{13}C nmr: δ 29.9, 30.4, 52.9, 114.7, 120.5, 121.9, 122.6, 124.7, 125.4, 125.7, 126.5, 127.4, 127.9, 128.6, 128.7, 129.5, 131.4, 134.4, 137.9, 142.5, 148.7, 154.7, 159.4 (24 ArC); ms: (m/z), 481 (M+), 466, 299, 262, 223.

Anal. Calcd. for $C_{27}H_{20}BrN_3O$: C, 67.23; H, 4.18; N; 8.71. Found: C, 67.36; H, 4.38; N, 8.92.

3-(4-Chlorophenyl)-1-phenyl-5,6,7,8-tetrahydro-1*H*-pyrazolo-[3,4-*b*]quinoline (**8a**).

A solution of **1a** (0.60 g, 2 mmol) and cyclohexanone (**7a**) (0.21 g, 2 mmol) in ethanolic potassium hydroxide (10 mL, 2%) was reflux for one hour. The mixture was then cooled to room temperature and the solid obtained was collected by filtration and washed with ethanol. The yield was 0.56 g (78%), colorless prisms, mp 160-161° (ethyl acetate); ir: 1742, 1605, 1510 cm^{-1}; ^{1}H nmr: δ 1.65 (t, J=7Hz, 2H, CH_2), 1.85 (m, 2H, CH_2), 1.99 (m, 2H, CH_2), 2.96 (t, J=7H, 2H, CH_2), 7.27-7.54 (m, 5H, Ph) 7.96 (d, J = 8.4 Hz, 2H, ArH), 7.99 (s, 1H, C_4-H), 8.46(d, J=8.4 Hz, 2H, ArH). ^{13}C nmr: δ 29.8, 31.6, 31.9, 113.4, 120.2, 125.1, 126.7, 128.1, 128.8, 129.2, 131.4, 134.0, 139.6, 141.7, 150.1, 162.2 (18 ArC); ms: (m/z), 359 (M^+), 341, 326.

Anal. Calcd. for $C_{22}H_{18}ClN_3$: C, 73.63; H, 5.04; N, 11.68. Found: C, 73.87; H, 5.28; N, 11.84.

3-(4-Chlorophenyl)-8-methyl-1-phenyl-5,6,7,8-tetrahydro-1*H*-pyrazolo [3,4-*b*]quinoline (**8b**).

This compound was obtained from pyrazolecarbaldehyde **1a** (0.60 g, 2 mmol) and methyl-1-cyclohexanone (**7b**) (0.24 mL, 2 mmol) using the method described for **8a**; the yield was 0.62 g (83%) colorless prisms, mp 126-127 °C (ethyl acetate); ir: 1739, 1598, 1552 cm^{-1}; ^{1}H nmr: δ 1.55 (d, J=7.2Hz, 3H, CH_3), 1.99 (m, 2H, CH_2), 2.15 (m, 2H, CH_2), 2.96 (t, 2H, J = 7.8 Hz, CH_2), 3.11 (q, J =7.2 Hz, 1H, C_8-H), 7.27-7.54 (m, 5H, Ph) 7.96 (d, J = 8.4 Hz, 2H, ArH), 7.99 (s, 1H, C_4-H), 8.46 (d, J = 8.4 Hz, 2H, Ar);^{13}C nmr :δ, 21.3, 29.8, 30.0, 31.6, 36.9, 113.5, 120.3, 125.2, 126.9, 128.2, 128.7, 128.9, 129.3, 131.6, 134.1, 139.8, 141.8, 150.1, 162.1 (18 ArC); ms: (m/z) 373 (M+), 352, 337.

Anal. Calcd. for $C_{23}H_{20}ClN_3$: C, 73.89; H, 5.39; N; 11.24. Found: C, 73.96; H, 5.58; N, 11.52.

3-(4-Bromophenyl)-1-phenyl-5,6,7,8-tetrahydro-1*H*-pyrazolo-[3,4-*b*]quinoline (**8c**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and cyclohexanone (**7a**) (0.21 mL, 2 mmol) using the method described for **8a**; yield 0.46 g (76%), colorless prisms, mp 168-169 °C (ethyl acetate); ir: 1741, 1596, 1551 cm^{-1}; ^{1}H nmr: δ 1.63 (t, J=7Hz, 2H, CH_2), 1.83 (m, 2H, CH_2), 1.95 (m, 2H, CH_2), 2.8 (t, J=7Hz, 2H, CH_2), 7.25-7.52 (m, 5H, Ph) 7.93 (d, J = 8.4 Hz, 2H, ArH), 7.96 (s, 1H, C_4-H), 8.45 (d, J = 8.4 Hz, 2H, ArH); ^{13}C nmr: δ 29.9, 31.8, 31.9, 113.5, 120.4, 125.2, 126.6, 128.1, 128.6, 128.9, 129.3, 131.5, 134.2, 139.7, 141.8, 150.3, 162.3 (18 ArC); ms: (m/z) 403 (M+), 385, 370.

Anal. Calcd. for $C_{22}H_{18}BrN_3$: C, 65.36; H, 4.49; N; 10.39. Found: C, 65.56; H, 4.86; N, 10.26.

3-(4-Bromophenyl)-8-methyl-1-phenyl-5, 6, 7, 8-tetrahydro-1*H*-pyrazolo[3,4-*b*]quinoline (**8d**).

This compound was obtained from **1b** (0.68 g, 2 mmol) and 2-methyl-1-cyclohexanone (**7b**) (0.24 mL, 2 mmol) using the method described for **8a**; yield 0.67 g, (82%); colorless prisms; mp 131-132 °C (ethyl acetate); ir: 1740, 1597, 1552 cm^{-1}; ^{1}H nmr: δ 1.60 (d, J=7Hz, 3H, CH_3), 1.66 (m, 2H, CH_2), 1.85 (m, 2H, CH_2), 1.97 (t, J = 6.9 Hz, 2H, CH_2), 3.09 (q, J = 6.9 Hz, 1H, C_8-H), 7.24-7.63 (m, 5H, Ph) 7.89 (d, J = 8.4 Hz, 2H, ArH), 7.96 (s, 1H, C_4-H), 8.46 (d, J = 8.4 Hz, 2H, ArH); ^{13}C nmr : δ 21.4, 29.9, 30.2, 31.7, 36.9, 113.7, 120.5, 126.9, 128.8, 128.9, 129.4, 131.7, 134.3, 139.9, 141.9, 150.2, 162.3 (18 ArC); ms: (m/z) 417 (M+), 396, 381.

Anal. Calcd. for $C_{23}H_{20}BrN_3$: C, 66.04; H, 4.82; N; 10.04. Found: C, 66.16; H, 4.95; N, 10.12.

3-(4-Chlorophenyl)-7,7-dimethyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (**9a**).

A mixture of **1a** (0.60 g, 2 mmol) and dimedone (0.28 g, 2 mmol) was heated at 140-150 °C for half an hour. The solid obtained on cooling was stirred in ethanol (2 mL) for 10 minutes. The solid obtained was collected by filtration and washed with cold ethanol (5 mL). Yield 0.61 g (76%), colorless prisms, mp 197-198 °C (ethyl acetate); ir: 1728, 1592, 1556 cm^{-1}; ^{1}H nmr: δ 1.19 (s, 6H, $2CH_3$), 2.69 (s, 2H, CH_2), 3.24 (s, 2H, CH_2), 7.39-7.62 (m, 5H, Ph) 8.06 (d, J = 8.4 Hz, 2H, ArH), 8.40 (d, J=8.4 Hz, 2H, ArH), 9.06 (s, 1H, C_4-H). ^{13}C nmr :δ, 28.3, 32.9, 47.4, 52.3, 114.5, 121.2, 122.8, 126.3, 128.3, 129.1, 130.3, 130.7, 137.7, 138.8, 162.4, (18 Ar C), 197.0 (C=O); ms: (m/z) 401 (M+), 345, 282.

Anal. Calcd. for $C_{24}H_{20}ClN_3O$: C, 71.73; H, 5.02; N, 10.46. Found: C, 71.82; H, 5.23; N, 10.68.

3-(4-Bromophenyl)-7,7-dimethyl-1-phenyl-1,6,7,8-tetrahydro-5*H*-pyrazolo[3,4-*b*]quinolin-5-one (**9b**).

This compound was obtained from pyrazolecarbaldehyde **1b** (0.68 g, 2 mmol) and dimedone (0.28 g, 2 mmol) using the method described for **9a**; yield 0.66 g (74%) colorless prisms, mp 214-215 °C (ethyl acetate); ir: 1726 , 1597, 1554 cm^{-1}; ^1H nmr: δ 1.18 (s, 6H, $2CH_3$), 2.67 (s, 2H, CH_2), 3.23 (s, 2H, CH_2), 7.29-7.73 (m, 5H, Ph), 7.99 (d, J = 8.4 Hz, 2H, ArH), 8.21 (d, J = 7.8 Hz, 2H, ArH), 9.07 (s, 1H, C_4-H); ^{13}C nmr: δ 28.5, 32.8, 47.6, 52.4, 114.7, 121.4, 122.9, 126.5, 128.4, 128.9, 129.3, 130.4, 130.8, 135.2, 137.9, 138.9, 162.7, (18 ArC), 197.3 (C=O); ms: (m/z) 445 (M+), 389, 326.

Anal. Calcd. for $C_{24}H_{20}BrN_3O$: C, 64.58; H, 4.52; N; 9.41. Found: C, 64.76; H, 4.68; N, 9.74.

General Procedure for the Preparation of 5-Chloro-3-(4-halophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo-[3,4-*b*]quinoline **10** and **11**.

To a solution of compound **9** (2 mmol) in dimethylformamide (0.77 mL, 10 mmol), phosphorous oxychloride (0.56 mL, 6 mmol) was added in small portions at 10-15 °C with stirring, further this reaction mixture was stirred at 80-90 °C for 6 hours and then poured into ice cold water (50 mL). The precipitated product was collected by suction filtration, washed with water and dried. The tlc of this solid showed spots corresponding to two compounds (R_f values: 0.78 and 0.63 in toluene) which were separated by column chromatography (18 x 300 mm, eluent toluene/hexane 5:100, elution volume for **10**: 220-240 mL, for **11**: 380-410 mL), detection by tlc analysis (254 nm).

5-Chloro-3-(4-chlorophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline (**10a**).

This compound was obtained from Vilsmeier-Haack formylation of compound **9a** (0.80 g, 2 mmole) The yield was 0.20 g (24%), colorless prisms, mp 170-171 °C (ethyl acetate); ir: 2287, 1592, 1556 cm^{-1}; ^1H nmr: δ 1.22 (s, 6H, $2CH_3$), 3.13 (s, 2H, CH_2), 6.13 (s, 1H, C_6H), 7.36-7.60 (m, 5H, Ph) 8.02 (d, J = 8.4 Hz, 2H, ArH), 8.40 (d, J = 8.4 Hz, 2H, Ar), 8.44 (s, 1H, C_4H); ^{13}C nmr: δ 27.9, 34.6, 46.5, 113.8, 122.9, 124.8, 126.0, 127.4, 128.4, 128.9, 129.1, 131.0, 134.5, 136.6, 139.2, 143.5, 157.5, (20 ArC); ms: (m/z) 419 (M+), 318, 345.

Anal. Calcd. for $C_{24}H_{19}Cl_2N_3$: C, 68.58; H, 4.56; N, 10.00. Found: C, 68.72; H, 4.68; N, 10.28.

5-Chloro-3-(4-bromophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline (**10b**).

This compound was obtained from Vilsmeier-Haack formylation of compound **9b** (0.89 g, 2 mmole). The yield was 0.23 g (25%) colorless prisms, mp 178-179 °C (ethyl acetate); ir: 2289, 1594, 1555 cm^{-1}; ^1H nmr: δ 1.21 (s, 6H, $2CH_3$), 3.11 (s, 2H, CH_2), 6.14 (s, 1H, C_6H), 7.26-7.65 (m, 5H, Ph) 8.03 (d, J = 8.4 Hz, 2H, ArH), 8.41 (d, J = 8.4 Hz, 2H, ArH), 8.45 (s, 1H, C_4-H).

^{13}C nmr: δ, 27.8, 34.7, 46.8, 113.9, 121.4, 122.9, 124.9, 126.2, 127.5, 128.6, 128.8, 129.3, 131.2, 134.6, 136.8, 139.3, 143.6, 157.6 (20 ArC); ms: (m/z) 464 (M+), 426, 390.

Anal. Calcd. for $C_{24}H_{19}BrClN_3$: C, 62.02; H, 4.12; N; 9.04. Found: C, 62.26; H, 4.35; N, 9.32.

5-Chloro-3-(4-chlorophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline-6-carbaldehyde (**11a**).

This compound was obtained from Vilsmeier-Haack formylation of compound **9a** (0.80 g, 2 mmole) The yield was 0.45 g (50%), colorless prisms, mp 159-160 °C (ethyl acetate); ir: 2745, 1685, 1592, 1556 cm^{-1}; ^1H nmr: δ 1.36 (s, 6H, $2CH_3$), 3.18 (s, 2H, CH_2), 7.37-7.62 (m, 5H, Ph), 8.02 (d, J = 8.4 Hz, 2H, ArH), 8.39 (d, J = 8.4 Hz, 2H, ArH), 8.77 (s, 1H, C_4H), 10.48 (s, 1H, CHO); ^{13}C nmr: δ 26.2, 36.8, 48.1, 114.2, 121.3, 122.4, 126.5, 127.7, 128.4, 129.0, 129.3, 130.6, 135.0, 138.7, 143.2, 150.9, 157.8, (20 ArC), 191.5 C=O; ms: (m/z) 447 (M+), 432, 404, 369.

Anal. Calcd. for $C_{25}H_{19}Cl_2N_3O$: C, 66.97; H, 4.27; N, 9.37. Found: C, 67.18; H, 4.56; N, 9.58.

5-Chloro-3-(4-bromophenyl)-7,7-dimethyl-1-phenyl-7,8-dihydro-1*H*-pyrazolo[3,4-*b*]quinoline-6-carbaldehyde (**11b**).

This compound was obtained from Vilsmeier-Haack formylation of compound **9b** (0.89 g,

2 mmole), the yield was 0.50 g (51%) colorless prisms, mp 168-169 °C (ethyl acetate); ir: 2748, 1687, 1593, 1554 cm^{-1}; ^1H nmr: δ 1.35 (s, 6H, $2CH_3$), 3.16 (s, 2H, CH_2), 7.27-7.63 (m, 5H, Ph), 7.99(d, J = 8.4 Hz, 2H, ArH), 8.40(d, J = 8.4 Hz, 2H, ArH), 8.57 (s, 1H, C_4H)), 10.48 (s, 1H, CHO); ^{13}C nmr: δ 26.4, 36.9, 48.3, 114.3, 121.4, 122.3, 126.4, 127.5, 127.7, 128.6, 129.1, 129.4, 130.7, 135.2, 138.8, 143.6, 144.4, 150.8, 157.9 (20 ArC), 191.7 C=O; ms: (m/z) 477 (M+), 448, 414.

Anal. Calcd. for $C_{25}H_{19}BrClN_3O$: C, 60.93; H, 3.89; N; 8.53. Found: C, 61.21; H, 3.96; N, 8.76.

9-(4-Chlorophenyl)-4,4-dimethyl-1,7-diphenyl-1,4,5,7-tetrahydro-dipyrazolo[3,4-*b*:4,3-*f*]quinoline (**12a**).

A solution of compound **11a** (0.45 g, 1 mmol) and phenylhydrazine (0.20 mL, 2 mmol) in ethanol (10 mL) was heated at reflux temperature for one hour. The mixture was cooled to room temperature, the solid that precipitated was collected by filtration and washed with ethanol. The yield was 0.32 g (64%), colorless prisms, mp 206-207° (ethyl acetate); ir: 2128, 1594, 1553 cm^{-1}; ^1H nmr: δ 1.54 (s, 6H, $2CH_3$), 3.10 (s, 2H, CH_2), 6.93-7.40 (m, 10H, Ph), 8.11 (d, J=8.4Hz, 2H, ArH), 8.18 (s, 1H, $C_{10}H$), 8.45 (d, J=8.4Hz, 2H, ArH), 8.55(s, 1H, C_3H); ^{13}C nmr: δ 27.6, 37.4, 48.9, 112.7, 114.2, 120.4, 121.2, 125.0, 126.1, 128.4, 128.9, 129.1, 128.3, 131.1, 134.6, 135.4, 138.3, 139.2, 143.9, 156.8, (27 ArC); ms: (m/z) 501 (M^+), 486, 444, 394, 243.

Anal. Calcd. for $C_{31}H_{24}ClN_5$: C, 74.17; H, 4.82; N, 13.95. Found: C, 74.32; H, 4.96; N, 14.17

9-(4-Bromophenyl)-4,4-dimethyl-1,7-diphenyl-1,4,5,7-tetrahydro-dipyrazolo[3,4-*b*:4,3-*f*]quinoline (**12b**).

This compound was obtained from compound **11b** (0.20 mL, 2 mmol) and phenylhydrazine (0.28 g, 2 mmol) using the method described for **12a**; The yield was 0.35 g (65%), colorless prisms, mp 214-215° (ethyl acetate); ir: 2127, 1596, 1558 cm^{-1}; ^1H nmr: δ 1.52 (s, 6H, $2CH_3$), 3.09 (s, 2H, CH_2), 6.90-7.39 (m, 10H, Ph), 8.08 (d, J=8.4Hz, 2H, ArH), 8.15 (s, 1H, $C_{10}H$), 8.43 (d, J=8.4Hz, 2H, ArH), 8.49 (s, 1H, C_3H); ^{13}C nmr: δ 27.4, 37.2, 48.6, 112.6, 114.3, 120.6, 121.4, 125.2, 126.3, 128.5, 128.9, 129.3, 131.4, 134.8, 135.5, 138.6, 139.3, 143.8, 156.9, (27 ArC); ms: (m/z) 545 (M+), 530, 488, 438, 286.

Anal. Calcd. for $C_{31}H_{24}BrN_5$: C, 68.14; H, 4.43; N, 12.82. Found: C, 68.36; H, 4.64; N, 12.95.

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