DOI 10.5012/bkcs.2011.32.8.3145

Morita–Baylis–Hillman Route to 8,9,9a,10-Tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-ones and 3,4,4a,5-Tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-ones†

Sang-Hyun Ahn, Seung Soon Jang, Yong Hyun Kim, and Kee-Jung Lee*

Department of Chemical Engineering, Hanyang University, Seoul 133-791, Korea
**E-mail: leekj@hanyang.ac.kr*
Received February 23, 2011, Accepted March 22, 2011

Key Words : Tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one, Tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-one, Morita-Baylis-Hillman reaction, 2-Cyclohexen-1-one, Primary amine, S_N2'–S_NAr reaction

1,8-Naphthyridine, tetrahydro-1,8-naphthyridine and its annelated derivatives are present in many natural and synthetic compounds.[1] 1,8-Naphthyridine derivatives show a broad range of interesting physiological activities such as antiinflammatory,[2,3] analgesic,[2] antiaggressive,[3] anticancer,[4] antibacterial,[5] antitumor,[6] antihypertensive,[7] antiallergitic,[8] and antimalarial.[9] Several synthetic approaches have been developed to form the 1,8-naphthyridine derivatives,[10] but due to their great importance, the development of new synthetic methods remain an active research area.

The Morita–Baylis–Hillman (MBH) reaction[11] has attracted the attention of organic chemists in recent years. This reaction provides synthetically useful multi-functional molecules which have been successfully employed in the preparation of various heterocyclic systems.[12] MBH adducts have already been used as substrates for the synthesis of 1,8-naphthyridine skeletons. Basavaiah and Reddy reported an elegant strategy to prepare tri and tetracyclic frameworks containing 1,8-naphthyridine-2-one moiety from the MBH adduct of 2-nitrobenzaldehyde and acrylonitrile.[13] Su used an acetylated MBH adduct derived from 2-chloroquinoline-3-carboxaldehyde with acrylic acid esters as a substrate for the syntheses of benzo[*b*][1,8]naphthyridine-3-carboxylate derivatives.[14] Rao and co-worker have reported synthesis of [1,8]naphthyridine-3-carboxylates from the acetates of MBH adducts, derived from substituted 2-chloropyridine-3-carboxaldehydes, via the reaction with $TsNH_2$ (or NH_4OAc) followed by cyclization or via the treatment with NaN_3 followed by reductive cyclization.[15] Coelho also reported highly diastereoselective access to 3,4-substituted tetrahydro-1,8-naphthyridines from a silylated MBH adduct derived from 2-chloropyridine-3-carboxaldehyde or 2-chloroquinoline-3-carboxaldehyde with acrylic acid esters.[16]

Meanwhile, Kim and co-workers reported[17] a transformation of the MBH acetates, obtained from 2-halobenzaldehyde or 2-chloroquinoline-3-carboxaldehyde with 2-cyclohexen-1-one, with a base into 2-arylmethylphenol or 2-(quinoline-3-yl)methylphenol, respectively. This reaction proceeded by a base assisted elimination of acetic acid and following keto–enol tautomerization and aromatization by 1,5-hydrogen transfer. Although the acetylated MBH adduct between 2-cyclohexen-1-one and 2-chloropyridine-3-carboxaldehyde or 2-chloroquinoline-3-carboxaldehyde are known,[17,18] but the reaction of acetates with primary amines was not studied. In this note we disclose a facile synthesis of 8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-ones and 3,4,4a,5-tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-ones via the successive S_N2'–S_NAr elimination strategy.

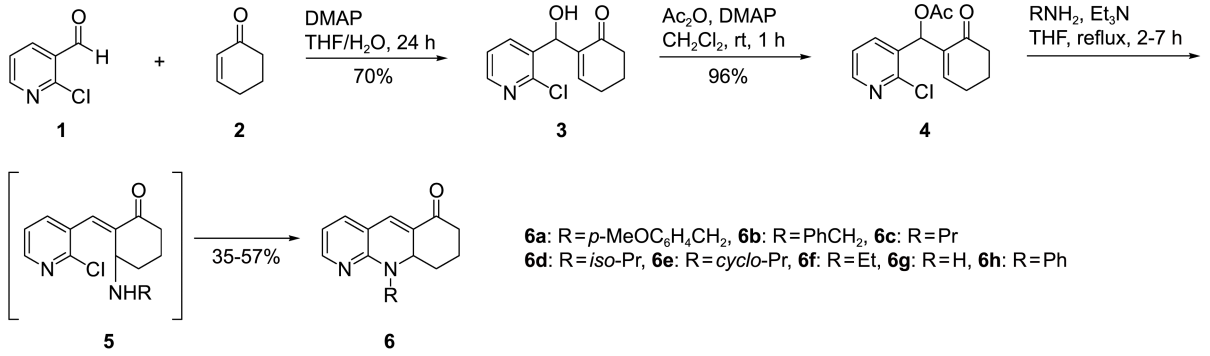
The key starting material MBH adduct **3** was prepared by the reaction of 2-chloropyridine-3-carboxaldehyde (**1**) with 2-cyclohexen-1-one (**2**) in the presence of DMAP in aqueous THF at room temperature in 70% yield following the earlier reported procedure.[18] Acetylation of **3** with Ac_2O/ DMAP gave acetate **4** in 96% yield. The known MBH acetate **7** were prepared in similar manner using 2-chloroquinoline-3-carboxaldehyde.[17] The reaction between MBH acetate **4** and several primary amines or NH_4OAc in THF in the presence of triethylamine at reflux temperature for 2–7 h afforded the desired 8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-ones **6a-g** in 35–57% yields (Table 1, Scheme 1).[19] Also, we examined the same reaction with an aromatic amine, aniline, however, the corresponding naphthyridine **6h** was not formed in any trace amount, only starting acetate **4** was recovered. Under the same reaction conditions the known

Table 1. Synthesis of Tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-ones **6** and Tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-ones **8**[a]

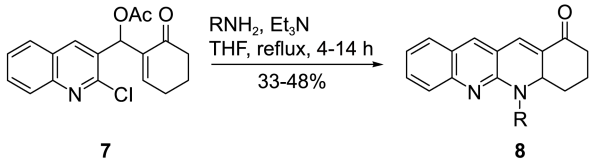
Entry	Acetate	Time (h)	R	Product	Yield (%)[b]
1	4	2	*p*-$MeOC_6H_4CH_2$	**6a**	44
2	4	2	$PhCH_2$	**6b**	41
3	4	2	Pr	**6c**	42
4[c]	4	7	*iso*-Pr	**6d**	35
5[c]	4	5	*cyclo*-Pr	**6e**	37
6[c]	4	6	Et	**6f**	57
7	4	3	H	**6g**	40
8	4	24	Ph	**6h**	-
9	7	5	*p*-$MeOC_6H_4CH_2$	**8a**	48
10	7	4	$PhCH_2$	**8b**	44
11[c]	7	14	Et	**8c**	39
12	7	7	H	**8d**	33

[a]The reaction was performed with acetate (1 mmol), amine (1.5 or 3 mmol), and Et_3N (2.2 mmol) in THF at reflux temperature. [b]Isolated yields. [c]3 mmol of amine was used.

†This paper is dedicated to Professor Eun Lee on the occasion of his honourable retirement.



Scheme 1



Scheme 2

acetate **7** gave 3,4,4a,5-tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-ones **8a-d** in 33–48% yields (Table 1, Scheme 2).[19] It is worth mentioning that the reactions of the acetates **4** and **7** with isopropyl-, cyclopropyl-, and ethyl amines having low boiling points were achieved with adding same amounts of these amines (1.5 equiv) after refluxing for 2 h as shown in entries 4, 5, 6, and 11 of Table 1. With the aid of Et_3N the amine undergoes Michael addition to the exocyclic C=C bond of acetate **4** and subsequent migration of the C=C bond with the simultaneous ejection of the acetic acid to give the allyl amine **5**. The intermediate could not be isolated, and subsequently amine moiety can attack in an S_NAr reaction at C(2) of the pyridine ring followed by elimination of chloride ion to give **6**.

The structures of **6** were elucidated by ^1H and ^{13}C NMR and mass spectral analyses. In a DEPT experiment of **6a**, four CH_2 peaks (δ = 19.7, 30.4, 38.5, 46.7) and seven CH peaks (δ = 58.5, 113.5, 113.9, 128.5, 129.4, 137.0, 150.2) were observed, and we could exclude the possible regioisomeric structure about double bond.

In conclusion, we have successfully elaborated a simple synthetic method for tri and tetracyclic frameworks containing 1,8-naphthyridine moiety from the Morita–Baylis–Hillman acetates and primary amines or NH_4OAc through the tandem S_N2'–S_NAr reaction.

Experimental Section

2-[(2-Chloropyridine-3-yl)(hydroxyl)methyl]cyclohex-2-en-1-one (3). A mixture of 2-chloropyridine-3-carboxaldehyde (**1**, 1.42 g, 10 mmol), and DMAP (0.14 g, 2 mmol) in 10 mL of aqueous THF (1:1) was stirred at rt for 24 h. The reaction mixture was diluted with H_2O (20 mL) and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel eluting with hexane–EtOAc (1:1) to produce **3** (1.66 g, 70%) as a white solid that was recrystallized (Et_2O–PE); mp 87–88 °C; IR (KBr): 3392, 1671, 1567, 1405 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.97–2.06 (m, 2H, CH_2), 2.38–2.53 (m, 4H, 2 × CH_2), 3.91 (br s, 1H, OH), 5.83 (s, 1H, CH), 6.59 (t, *J* = 4.1 Hz, 1H, CH), 7.33 (dd, *J* = 7.6 and 4.7 Hz, 1H, aromatic), 8.02 (dd, *J* = 7.6 and 1.5 Hz, 1H, aromatic), 8.34 (dd, *J* = 4.7 and 1.8 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 22.3, 25.7, 38.4, 68.8, 122.7, 135.5, 137.4, 138.4, 148.5, 148.6, 149.3, 200.6; MS *m/z* 237 (M^+, 1), 236 (3), 203 (14), 202 (100), 184 (18). Anal. Calcd for $C_{12}H_{12}ClNO_2$: C, 60.64; H, 5.09; N, 5.89. Found: C, 60.38; H, 5.25; N, 5.64.

2-[(Acetoxy)(2-chloropyridine-3-yl)methyl]cyclohex-2-en-1-one (4). A mixture of **3** (1.19 g, 5 mmol), acetic anhydride (0.71 mL, 7.5 mmol) and DMAP (0.11 g, 1 mmol) in CH_2Cl_2 (15 mL) was stirred at rt for 1 h. The mixture was neutralized with a saturated aqueous $NaHCO_3$ solution. The resulting mixture was extracted with CH_2Cl_2 (2 × 30 mL) and the organic layers were dried over $MgSO_4$ and concentrated in vacuo. The resulting mixture was chromatographed on silica gel eluting with hexane–EtOAc (1:1) to produce **4** (1.33 g, 96%) as a white solid that was recrystallized (Et_2O–PE); mp 134–135 °C; IR (KBr): 1744, 1676, 1567, 1410, 1370, 1226 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.99–2.07 (m, 2H, CH_2), 2.13 (s, 3H, CH_3), 2.43–2.49 (m, 4H, 2 × CH_2), 6.84–6.86 (m, 2H, 2 × CH), 7.27 (dd, *J* = 4.7 and 2.9 Hz, 1H, aromatic), 7.78 (dd, *J* = 7.6 and 1.8 Hz, 1H, aromatic), 8.34 (dd, *J* = 4.7 and 2.1 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 22.3, 25.9, 38.3, 69.2, 122.3, 132.9, 135.7, 137.4, 148.8, 149.5, 149.8, 169.2, 196.6; MS *m/z* 280 (2), 244 (8), 236 (6), 202 (45), 184 (100), 140 (14), 123 (10). Anal. Calcd for $C_{14}H_{14}ClNO_3$: C, 60.11; H, 5.04; N, 5.01. Found: C, 59.98; H, 4.84; N, 4.86.

8,9,9a,10-Tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-ones (6).

General Procedure: To a stirred solution of MBH acetate **4** (1 mmol) in THF (10 mL) was added either RNH_2 (1.5 mmol) or. NH_4OAc (1.5 mmol) and Et_3N (0.31 mL, 2.2 mmol) at rt. The reaction mixture was heated at reflux temperature for 2–7 h. In the case of isopropyl-, cyclopropyl-, and ethyl amines 1.5 mmol of amines was added again after refluxing for 2 h. The mixture was diluted with H_2O (10 mL)

and extracted with CH_2Cl_2 (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was evaporated under reduced pressure. The resulting mixture was chromatographed on silica gel eluting hexane–EtOAc (2:1) to produced **6** as an oil.

10-(*p*-Methoxybenzyl)-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6a): Reaction time: 2 h; yield: 44%; IR (CH_2Cl_2): 1683, 1610, 1555, 1511 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.84–2.02 (m, 2H, CH_2), 2.22–2.53 (m, 4H, 2 × CH_2), 3.78 (s, 3H, OCH_3), 4.56 and 5.20 (d, *J* = 16.0 Hz, each 1H, CH_2), 4.70–4.76 (m, 1H, CH), 6.47 (dd, *J* = 7.3 and 5.0 Hz, 1H, aromatic), 6.81–6.87 (m, 2H, aromatic), 7.08 (d, *J* = 2.1 Hz, 1H, CH), 7.16–7.20 (m, 3H, aromatic), 7.96 (dd, *J* = 5.0 and 2.1 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 30.4, 38.5, 46.7, 55.2, 58.5, 113.5, 113.9, 114.3, 128.5, 129.4, 130.8, 131.6, 137.0, 150.2, 156.9, 158.5, 198.4; MS *m/z* 278 (26), 277 (100), 199 (46), 183 (12), 170 (13), 152 (10). Anal. Calcd for $C_{20}H_{20}N_2O_2$: C, 74.98; H, 6.29; N, 8.74. Found: C, 74.76; H, 6.01; N, 9.04.

10-Benzyl-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6b): Reaction time: 2 h; yield: 41%; IR (CH_2Cl_2): 1684, 1602, 1556, 1450, 1400 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.90–1.99 (m, 2H, CH_2), 2.28–2.54 (m, 4H, 2 × CH_2), 4.71 and 5.16 (d, *J* = 16.4 Hz, each 1H, CH_2), 4.73–4.79 (m, 1H, CH), 6.48 (dd, *J* = 7.3 and 5.0 Hz, 1H, aromatic), 7.10 (d, *J* = 2.1 Hz, 1H, CH), 7.17–7.20 (m, 2H, aromatic), 7.23–7.32 (m, 4H, aromatic), 7.96 (dd, *J* = 5.0 and 2.1 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.7, 30.6, 38.5, 47.5, 58.8, 113.6, 114.2, 126.8, 127.2, 128.5, 130.8, 131.6, 137.0, 137.6, 150.2, 156.9, 198.4; MS *m/z* 246 (18), 245 (100), 190 (11), 181 (32). Anal. Calcd for $C_{19}H_{18}N_2O$: C, 78.59; H, 6.25; N, 9.65. Found: C, 78.25; H, 6.09; N, 9.84.

10-Propyl-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6c): Reaction time: 2 h; yield: 42%; IR (CH_2Cl_2): 1684, 1618, 1554, 1456 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.95 (t, *J* = 7.3 Hz, 3H, CH_3), 1.66–1.79 (m, 2H, CH_2), 2.03–2.14 (m, 2H, CH_2), 2.35–2.59 (m, 4H, 2 × CH_2), 3.27–3.37 and 3.57–3.67 (m, each 1H, CH_2), 4.77–4.83 (m, 1H, CH), 6.41 (dd, *J* = 7.0 and 5.0 Hz, 1H, aromatic), 7.05 (d, *J* = 2.1 Hz, 1H, CH), 7.10 (dd, *J* = 7.0 and 1.8 Hz, 1H, aromatic), 7.96 (dd, *J* = 5.0 and 1.8 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.4, 19.3, 19.8, 30.8, 38.6, 46.2, 58.7, 112.9, 114.5, 131.2, 131.3, 136.7, 150.2, 156.8, 198.4; MS *m/z* 242 (M^+, 35), 241 (16), 240 (27), 214 (32), 213 (26), 199 (36), 187 (42), 186 (100), 172 (24), 171 (25), 170 (37), 144 (43). Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.56; H, 7.40; N, 11.38.

10-(*iso*-Propyl)-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6d): Reaction time: 7 h; yield: 35%; IR (CH_2Cl_2): 1692, 1629, 1591, 1555 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (d, *J* = 6.7 Hz, 3H, CH_3), 1.41 (d, *J* = 7.0 Hz, 3H, CH_3), 1.89–2.17 (m, 2H, CH_2), 2.27–2.57 (m, 4H, 2 × CH_2), 4.32–4.41 (m, 1H, CH), 4.84–4.90 (m, 1H, CH), 6.34 (dd, *J* = 7.0 and 5.0 Hz, 1H, aromatic), 6.79 (d, *J* = 1.8 Hz, 1H, CH), 6.99–7.02 (m, 1H, aromatic), 7.90 (dd, *J* = 5.0 and 2.1 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 18.7, 19.1, 21.2, 33.7, 38.4, 48.7, 58.0, 112.3, 114.1, 128.8, 133.6, 136.3, 149.5, 155.9, 199.2; MS *m/z* 242 (M^+, 31), 214 (47), 200 (20), 199 (28), 188 (32), 186 (82), 145 (32), 144 (100). Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.35; H, 7.49; N, 11.56. Found: C, 74.16; H, 7.24; N, 11.29.

10-Cyclopropyl-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6e): Reaction time: 5 h; yield: 37%; IR (CH_2Cl_2): 1688, 1628, 1605, 1556 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.60–0.72 (m, 2H, CH_2), 0.84–0.92 (m, 2H, CH_2), 1.11–1.18 (m, 1H, CH), 1.98–2.16 (m, 2H, CH_2), 2.36–2.62 (m, 4H, 2 × CH_2), 4.68–4.73 (m, 1H, CH), 6.49 (dd, *J* = 7.3 and 5.0 Hz, 1H, aromatic), 6.91 (d, *J* = 1.8 Hz, 1H, CH), 7.11 (dd, *J* = 7.3 and 2.1 Hz, 1H, aromatic), 8.04 (dd, *J* = 5.0 and 2.1 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 6.5, 11.8, 19.3, 27.3, 30.3, 38.7, 60.3, 113.6, 115.4, 129.0, 133.9, 136.2, 149.5, 157.1, 199.1; MS *m/z* 240 (M^+, 100), 239 (81), 223 (94), 213 (79), 211 (85), 199 (42), 197 (49), 184 (50), 183 (60), 182 (34), 181 (64), 169 (68), 168 (43). Anal. Calcd for $C_{15}H_{16}N_2O$: C, 74.97; H, 6.71; N, 11.66. Found: C, 74.82; H, 6.64; N, 11.75.

10-Ethyl-8,9,9a,10-tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6f): Reaction time: 6 h; yield: 57%; IR (CH_2Cl_2): 1683, 1602, 1555, 1401 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.10 (t, *J* = 7.0 Hz, 3H, CH_3), 1.96–2.08 (m, 2H, CH_2), 2.29–2.54 (m, 4H, 2 × CH_2), 3.34–3.46 and 3.64–3.76 (m, each 1H, CH_2), 4.70–4.76 (m, 1H, CH), 6.36 (dd, *J* = 7.0 and 5.0 Hz, 1H, aromatic), 7.00 (d, *J* = 2.1 Hz, 1H, aromatic), 7.05 (dd, *J* = 7.3 and 1.8 Hz, 1H, aromatic), 7.91 (dd, *J* = 5.0 and 1.8 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 11.5, 19.8, 30.7, 38.6, 39.0, 58.2, 113.0, 114.8, 131.2, 136.8, 145.4, 150.2, 156.6, 198.4; MS *m/z* 228 (M^+, 100), 227 (88), 226 (34), 213 (18), 211 (28), 201 (40), 199 (94), 197 (27), 181 (31), 169 (22). Anal. Calcd for $C_{14}H_{16}N_2O$: C, 73.66; H, 7.06; N, 12.27. Found: C, 73.41; H, 7.29; N, 12.05.

8,9,9a,10-Tetrahydrobenzo[*b*][1,8]naphthyridine-6(7*H*)-one (6g)[20]: Reaction time: 3 h; yield: 40%; yelleow solid; mp 118–119 °C; IR (KBr): 3221, 1675, 1617, 1575, 1504 cm^{-1} ;^1H NMR (300 MHz, $CDCl_3$) δ 1.74–2.62 (m, 6H, 3 × CH_2), 4.86–4.92 (m, 1H, CH), 5.77 (s, 1H, NH), 6.51 (dd, *J* = 7.3 and 5.0 Hz, 1H, aromatic), 7.13 (d, *J* = 2.1 Hz, 1H, CH), 7.21 (dd, *J* = 7.3 and 1.5 Hz, 1H, aromatic), 7.86 (dd, *J* = 5.0 and 1.5 Hz, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 31.9, 39.0, 53.7, 114.3, 114.8, 131.0, 131.1, 137.0, 149.6, 157.7, 198.0; MS *m/z* 200 (M^+, 38), 199 (44), 198 (67), 197 (11), 171 (41), 170 (99), 169 (53), 145 (43), 144 (100), 143 (28), 130 (25). Anal. Calcd for $C_{12}H_{12}N_2O$: C, 71.98; H, 6.04; N, 13.99. Found: C, 71.72; H, 5.97; N, 13.87.

3,4,4a,5-Tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-ones (8).

General Procedure: To a stirred solution of MBH acetate **7**[17] (1 mmol) in THF (10 mL) was added RNH_2 (1.5 mmol) or NH_4OAc (1.5 mmol) and Et_3N (0.31 mL, 2.2 mmol) at rt. The reaction mixture was heated at reflux temperature for 4–14 h. In the case of ethyl amine 1.5 mmol of amine was added again after refluxing for 2 h. The work–up procedure was the same as described above to give **8** as an oil.

5-(*p*-Methoxybenzyl)-3,4,4a,5-tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-one (8a): Reaction time: 5 h;

yield: 48%; IR (CH_2Cl_2): 1687, 1614, 1557, 1511 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.87–2.03 (m, 2H, CH_2), 2.32–2.58 (m, 4H, 2 × CH_2), 3.78 (s, 3H, OCH_3), 4.63 and 5.54 (d, J = 15.2 Hz, each 1H, CH_2), 4.70–4.74 (m, 1H, CH), 6.81–6.86 (m, 2H, aromatic), 7.11–7.16 (m, 2H, CH and aromatic), 7.26–7.28 (m, 2H, aromatic), 7.41–7.54 (m, 4H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 30.7, 38.8, 46.7, 55.2, 58.8, 113.8, 116.8, 122.6, 124.1, 126.4, 127.6, 128.9, 129.1, 129.9, 130.3, 135.0, 136.4, 149.1, 154.3, 158.5, 198.8; MS *m/z* 339 (4), 325 (4), 281 (14), 265 (32), 249 (47), 210 (56), 208 (100), 193 (10), 191 (16), 163 (14), 146 (16). Anal. Calcd for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56. Found: C, 77.65; H, 6.12; N, 7.39.

5-Benzyl-3,4,4a,5-tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-one (8b): Reaction time: 4 h; yield: 44%; IR (CH_2Cl_2): 1688, 1615, 1558, 1494, 1447 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.83–2.03 (m, 2H, CH_2), 2.31–2.57 (m, 4H, 2 × CH_2), 4.70–4.76 (m, 1H, CH), 4.80 and 5.48 (d, J = 15.8 Hz, each 1H, CH_2), 7.11–7.16 (m, 2H, CH and aromatic), 7.22–7.35 (m, 5H, aromatic), 7.40–7.54 (m, 4H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 30.9, 38.8, 47.6, 59.2, 116.8, 122.6, 124.1, 126.4, 126.9, 127.5, 127.6, 128.5, 129.2, 130.4, 135.0, 136.5, 138.1, 149.1, 154.3, 198.8; MS *m/z* 241 (17), 240 (100), 226 (26), 225 (71), 197 (10), 182 (20), 166 (19), 165 (27), 154 (10), 153 (14). Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.15; H, 5.92; N, 8.23. Found: C, 80.92; H, 5.74; N, 7.96.

5-Ethyl-3,4,4a,5-tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-one (8c): Reaction time: 14 h; yield: 39%; IR (CH_2Cl_2): 1688, 1615, 1594, 1556, 1495 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J = 7.0 Hz, 3H, CH_3), 1.93–2.03 (m, 2H, CH_2), 2.09–2.64 (m, 4H, 2 × CH_2), 3.60–3.71 and 3.81–3.92 (m, each 1H, CH_2), 4.76–4.82 (m, 1H, CH), 7.08–7.13 (m, 2H, CH and aromatic), 7.41–7.55 (m, 4H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 12.1, 19.9, 31.4, 38.9, 39.8, 59.2, 117.1, 122.3, 123.8, 126.4, 127.6, 129.4, 130.2, 134.8, 136.1, 149.4, 153.9, 198.8; MS *m/z* 278 (M^+, 39), 276 (24), 251 (41), 249 (44), 224 (35), 222 (100), 194 (38). Anal. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.48; H, 6.34; N, 9.82.

3,4,4a,5-Tetrahydrodibenzo[*b*,*g*][1,8]naphthyridine-1(2*H*)-one (8d)[20]: Reaction time: 7 h; yield: 33%; yellow solid; mp 189–191 °C; IR (KBr): 3228, 1683, 1626, 1593, 1574 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 2.01–2.68 (m, 6H, 3 × CH_2), 4.90–4.96 (m, 1H, CH), 5.35 (br s, 1H, NH), 7.15–7.21 (m, 1H, aromatic), 7.25 (d, J = 2.4 Hz, 1H, CH), 7.48–7.54 (m, 3H, aromatic), 7.62 (s, 1H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 32.4, 39.3, 54.3, 117.2, 123.0, 124.8, 125.5, 128.1, 129.8, 130.8, 134.3, 136.9, 148.5, 155.3, 198.0; MS *m/z* 251 (94), 249 (100), 221 (9), 208 (14), 207 (19), 193 (14). Anal. Calcd for $C_{16}H_{14}N_2O$: C, 76.78; H, 5.64; N, 11.19. Found: C, 77.04; H, 5.41; N, 11.32.

References

1. (a) For reviews, see: Ivanov, A. S.; Tugusheva, N. Z.; Granik, V. G. *Russ. Chem. Rev.* **2005**, *74*, 915-936. (b) Litvinov, V. P. *Russ. Chem. Rev.* **2004**, *73*, 637-669. (c) Litvinov, V. P.; Roman, S. V.; Dyachenko, V. D. *Russ. Chem. Rev.* **2000**, *69*, 201-220. (d) Allen, C. F. H. *Chem. Rev.* **1950**, *47*, 275-305.
2. Roma, G.; Grossi, G.; Braccio, M. D.; Piras, D.; Ballabeni, V.; Tognolini, M.; Bertoni, S.; Barocelli, E. *Eur. J. Med. Chem.* **2008**, 43, 1665-1680.
3. Roma, G.; Braccio, M. D.; Grossi, G.; Mattioli, F.; Ghia, M. *Eur. J. Med. Chem.* **2000**, *35*, 1021-1035.
4. Atanasova, M.; Ilieva, S.; Galabov, B. *Eur. J. Med. Chem.* **2007**, *42*, 1184-1192.
5. Kuramoto, Y.; Ohshita, Y.; Yoshida, J.; Yazaki, A.; Shiro, M.; Koike, T. *J. Med. Chem.* **2003**, *46*, 1905-1917.
6. Chen, K.; Kuo, S.-C.; Hsieh, M.-C.; Mauger, A.; Lin, C. M.; Hamel, E.; Lee, K.-H. *J. Med. Chem.* **1997**, *40*, 2266-2275.
7. Ferrarini, P. L.; Mori, C.; Badawneh, M.; Calderone, V.; Greco, R.; Manera, C.; Martinelli, A.; Nieri, P.; Saccomanni, G. *Eur. J. Med. Chem.* **2000**, *35*, 815-826.
8. Sherlock, M. H.; Kaminski, J. J.; Tom, W. C.; Lee, J. F.; Wong, S.-C.; Kreutner, W.; Bryant, R. W.; Mcphail, A. T. *J. Med. Chem.* **1988**, *31*, 2108-2121.
9. Barlin, G. B.; Tan, W.-L. *Aust. J. Chem.* **1984**, *37*, 1065-1073.
10. (a) Schramm, O. G.; Oeser, T.; Müller, T. J. J. *J. Org. Chem.* **2006**, *71*, 3494-3500. (b) Zong, R.; Zhou, H.; Thummel, R. P. *J. Org. Chem.* **2008**, *73*, 4334-4337. (c) Litvinov, V. P. In *Advanced Heterocyclic Chemistry*; Elsvier: San Diego, 2006; Vol. 91, pp 189-300. (d) Lahue, B. R.; Lo, S.-M.; Wan, Z.-K.; Woo, G. H. C.; Snyder, J. K. *J. Org. Chem.* **2004**, *69*, 7171-7182.
11. For reviews of the Morita–Baylis–Hillman reaction, see: (a) Drewes, S. E.; Roos, G. H. P. *Tetrahedron* **1988**, *44*, 4653-4670. (b) Basavaiah, D.; Rao, P. D.; Hyma, R. S. *Tetrahedron* **1996**, *52*, 8001-8062. (c) Ciganek, E. *Org. React.* **1997**, *51*, 201-350. (d) Langer, P. *Angew. Chem. Int. Ed.* **2000**, *39*, 3049-3052. (e) Basavaiah, D.; Rao, A. J.; Satyanarayana, T. *Chem. Rev.* **2003**, *103*, 811-891. (f) Kataoka, T.; Kinoshita, H. *Eur. J. Org. Chem.* **2005**, 45-58. (g) Basavaiah, D.; Rao, K. V.; Reddy, R. J. *Chem. Soc. Rev.* **2007**, *36*, 1581-1588. (h) Singh, V.; Batra, S. *Tetrahedron* **2008**, *64*, 4511-4574. (i) Declerck, V.; Martinez, J.; Lamaty, F. *Chem. Rev.* **2009**, *109*, 1-48. (j) Ma, G.-N.; Jiang, J.-J.; Shi, M.; Wei, Y. *Chem. Commun.* **2009**, 5496-5514. (k) Basavaiah, D.; Reddy, B. S.; Badsara, S. S. *Chem. Rev.* **2010**, *110*, 5447-5674.
12. For our recent examples, see: (a) Hong, W. P.; Lim, H. N.; Park, H. W.; Lee, K.-J. *Bull. Korean Chem. Soc.* **2005**, *26*, 655-657. (b) Hong, W. P.; Lee, K.-J. *Synthesis* **2005**, 33-38. (c) Hong, W. P.; Lee, K.-J. *Synthesis* **2006**, 963-968. (d) Song, Y. S.; Lee, K.-J. *J. Heterocycl. Chem.* **2006**, *43*, 1721-1724. (e) Ji, S.-H.; Hong, W. P.; Ko, S. H.; Lee, K.-J. *J. Heterocycl. Chem.* **2006**, *43*, 799-801. (f) Lim, H. N.; Ji, S.-H.; Lee, K.-J. *Synthesis* **2007**, 2454-2460. (g) Song, Y. S.; Lee, K.-J. *Synthesis* **2007**, 3037-3043. (h) Lim, H. N.; Song, Y. S.; Lee, K.-J. *Synthesis* **2007**, 3376-3384. (i) Jeon, K. J.; Lee, K.-J. *J. Heterocycl. Chem.* **2008**, *45*, 615-619. (j) Ahn, S.-H.; Lim, H. N.; Lee, K.-J. *J. Heterocycl. Chem.* **2008**, *45*, 1701-1706. (k) Park, S. P.; Song, Y. S.; Lee, K.-J. *Tetrahedron* **2009**, *65*, 4703-4708. (l) Han, E.-G.; Kim, H. J.; Lee, K.-J. *Tetrahedron* **2009**, *65*, 9616-9625. (m) Park, S. P.; Ahn, S.-H.; Lee, K.-J. *Tetrahedron* **2010**, *66*, 3490-3498. (n) Ahn, S.-H.; Jang, S. S.; Han, E.-G.; Lee, K.-J. *Synthesis* **2011**, 377-386.
13. Basavaiah, D.; Reddy, K. R. *Tetrahedron* **2010**, *66*, 1215-1219.
14. Zhong, W.; Lin, F.; Chen, R.; Su, W. *Synthesis* **2009**, 2333-2340.
15. Narender, P.; Ravinder, M.; Sadhu, P. S.; Raju, B. C.; Ramesh, C.; Rao, V. J. *Helv. Chim. Acta* **2009**, *92*, 959-966.
16. Rodrigues, M. T., Jr.; Gomes, J. C.; Smith, J.; Coelho, F. *Tetrahedron Lett.* **2010**, *51*, 4988-4990.
17. Lee, K. Y.; Na, J. E.; Kim, J. N. *Bull. Korean Chem. Soc.* **2003**, *24*, 409-410.
18. Narender, P.; Srinivas, U.; Ravinder, M.; Rao, B. A.; Ramesh, C.; Harakishore, K.; Gangadasu, B.; Murthy, U. S. N.; Rao, V. J. *Bioorg. Med. Chem.* **2006**, *14*, 4600-4609.
19. Some other intractable, unidentified decomposition products were also formed.
20. Aqueous THF (20%) was used as a solvent.