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# New Synthetic Approach to 4-*N*-Arylaminoazuleno[2,1-*d*]pyrimides

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**Abstract:** 1-Cyano-2-*N,N*-dimethylformamidinylazulenes as new synthons directed to heterocycle-fused azulenes were obtained by the condensation of 2-amino-1-cyanoazulenes and *N,N*-dimethylformamide dimethyl acetal (DMFDMA). 1-Cyano-2-*N,N*-dimethylformamidinylazulene (**2a**) and 1-bromo-3-cyano-2-*N,N*-dimethylformamidinylazulene (**2b**) reacted with anilines (**3a**–**h**) to give 4-*N*-arylaminoazuleno-[2,1-*d*]pyrimidines in moderate yields. This reaction provides a new procedure for synthesis of pyrimidine-fused azulenes.

**Keywords:** Azulene, azuleno[2,1-*d*]pyrimidines, DMFDMA, synthesis

## INTRODUCTION

Heterocycle-fused azulenes with a variety of chemical properties and physiological activities have been obtained by several synthetic methods.[1–4] In a previous article, we reported that 1-acetyl-2-(bromomethyl)azulene reacted with anilines or thioacetamide to give 2-aryl-3methylazuleno[1,2-*c*]pyrroles[5] or azuleno-[1,2-*c*]thiophenes[6]

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respectively. Of these, pyrimidine-fused azulenes were prepared using different types of starting materials as follows. 2-amino-1-formylazulene reacted with guanidine to convert to 2-aminoazuleno[2,1-*d*]pyrimidine.[7] The reaction of 2-acetylimino-2*H*-cyclohepta[*b*]furan derivatives with active methylene compounds afforded the azuleno[2,1-*d*]pyrimidine derivatives.[8]

In connection with our studies on the synthetic utilities of heterocycle-fused azulenes, this article describes a new synthetic method of 4-*N*-arylaminoazuleno-[2,1-*d*]pyrimidines by the reactions of 1-cyano-2-*N,N*-dimethylformamidinyl azulenes with anilines.

## RESULTS AND DISCUSSION

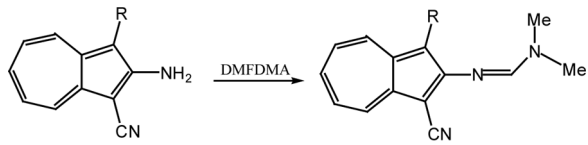
### Synthesis of 1-Cyano-2-*N,N*-dimethylformamidinylazulenes

2-Amino-1-cyanoazulene (**1a**)[9] and 2-amino-3-bromo-1-cyanoazulene (**1b**), which was obtained by bromination of **1a** with *N*-bromosuccinimide, were treated with 3 molar equivalents of *N,N*-dimethylformamide dimethyl acetal (DMFDMA) for 8 h under reflux in toluene to afford 1-cyano-2-*N,N*-dimethylformamidinylazulenes (**2a, 2b**) in 78 and 73% yields respectively (Scheme 1). Because intermediates (**2**) have two reactive functional groups, cyano and *N,N*-dimethylformamidinyl groups, at neighboring positions, they seem to be useful building blocks for heterocycle-fused azulenes.

### Reactions of New Building Blocks (2a, 2b) with Anilines

A solution of 1-cyano-2-*N,N*-dimethylformamidinylazulene (**2a**) and aniline (**3a**) in benzene was stirred for 12 h at 80°C to give 4-*N*-phenylaminoazuleno[2,1-*d*]pyrimidine (**4a**) in 38%. The formula of **4a** was determined to be $C_{18}H_{13}N_3$ from the elemental and spectral data.

To optimize the conditions, we studied the effects of molar ratio, temperature, reaction time, and solvent. In a typical experiment, a mixture

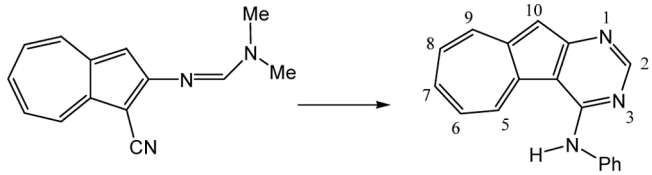



**1 a, b**

a R = H
b R = Br

**2 a, b**

***Scheme 1.*** Synthesis of 1-cyano-2-N,N-dimethylformamidinazulenes.




**2 a** **4 a**

***Scheme 2.*** Synthesis of 4-N-phenylaminoazulen[2,1-d]pyrimidine.

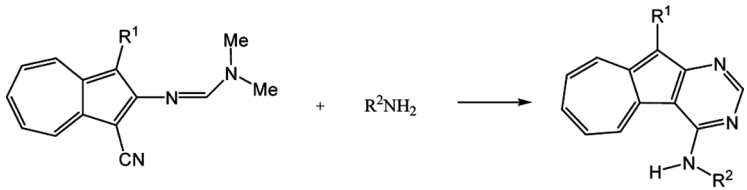
of 1-cyano-2-*N,N*-dimethylformamidinylazulene (**2a**) and aniline (**3a**) was monitored by high-performance liquid chromatography (HPLC) (Scheme 2), and the results are summarized in Table 1. Good results were obtained in the reactions using 2 molar equivalents of aniline in toluene as the solvent at 80°C.

The reactions with methyl, methoxy, chloro, fluoro, and nitro group substitued anilines (**3b**–**g**), 1-naphthylamine (**3h**), and 2-naphthylamine (**3i**) were carried out to give the corresponding 4-*N*-arylaminoazuleno[2,1-*d*]pyrimidines (**4a**–**i**). In a similar manner, 9-bromo-substituted 4-*N*-arylaminoazuleno[2,1-*d*] pyrimidines (**4j**–**m**) were obtained in the reactions of 1-bromo-3-cyano-2-*N,N*-dimethylformamidinylazulene (**2b**) and anilines (**3b, 3g, 3j, 3k**) (Scheme 3). These results are summarized in Table 2.

It was found that 1-cyano-2-*N,N*-dimethylformamidinylazulenes were useful starting materials for syntheses of 4-*N*-arylaminoazuleno[2,1-*d*]pyrimidines. Furthermore, the intermediates are expected to be building blocks for other heterocycle-fused azulene derivatives, and their reactions are now in progress.

## EXPERIMENTAL

All melting points were determined with a Yanaco MP JP-3 apparatus and are uncorrected. The infrared (IR) spectra were measured on a Jasco




**2 a ($R^1$ = H), 2 b ($R^1$ = Br)** **3 a-k** **4 a-m**

***Scheme 3.*** Synthesis of 4-N-arylaminoazuleno[2,1-d]pyrimidines.

**Table 1.** Optimization of reaction conditions and results

| Entry | Molar ratio | Solvent | Temp (°C) | Time (h) | Yield (%) |
|---|---|---|---|---|---|
| 1 | 1:1.5 | Benzene | 25 | 24 | 22 |
| 2 | 1:1.5 | Toluene | 80 | 12 | 40 |
| 3 | 1:1.5 | Toluene | 110 | 8 | 39 |
| 4 | 1:2 | Toluene | 80 | 10 | 49 |
| 5 | 1:2 | $CH_2Cl_2$ | 40 | 24 | 30 |
| 6 | 1:2 | $CHCl_3$ | 60 | 12 | 41 |
| 7 | 1:2 | $CCl_4$ | 75 | 12 | 26 |
| 8 | 1:2 | $CH_2ClCH_2Cl$ | 80 | 8 | 31 |
| 9 | 1:2 | EtOH | 75 | 8 | 29 |
| 10 | 1:2 | AcOH | 80 | 8 | 43 |

A-102 IR spectrophotometer. The NMR spectra were recorded with a Jeol JNM-EX 300 spectrometer (400 MHz for $^1H$). Elemental analysis was carried out using a Heraus CHN rapid analyzer.

## Preparation of 2-Amino-1-bromo-3-cyanoazulene (1b) by Bromination of 2-Amino-1-cyanoazulene (1a) with *N*-Bromosuccinimide

*N*-bromosuccinimide (106 mg, 0.6 mmol) was added to a solution of 2-amino-1-cyanoazulene (**1a**)[9] (0.5 mmol) in benzene (20 mL). After stirring for 1 h at rt, cold water (20 mL) was added to the mixture. The

**Table 2.** Synthesis of 4-*N*-arylaminoazuleno[2,1-*d*]pyrimidines

| Entry | Azulene (**2**) $R^1$ | | Aniline (**3**) $R^2$ | Time (h) | Product **4** | Yield (%) |
|---|---|---|---|---|---|---|
| 1 | H | **a** | $C_6H_5$ | 10 | **a** | 49 |
| 2 | H | **b** | 4-$MeC_6H_4$ | 10 | **b** | 51 |
| 3 | H | **c** | 4-$FC_6H_4$ | 11 | **c** | 29 |
| 4 | H | **d** | 4-$NO_2C_6H_4$ | 16 | **d** | 35 |
| 5 | H | **e** | 3,4-$(Me)_2C_6H_3$ | 10 | **e** | 34 |
| 6 | H | **f** | 3,5-$(Me)_2C_6H_3$ | 10 | **f** | 29 |
| 7 | H | **g** | 3-F-4-$ClC_6H_3$ | 12 | **g** | 52 |
| 8 | H | **h** | 1-Naphthyl | 14 | **h** | 26 |
| 9 | H | **i** | 2-Naphthyl | 12 | **i** | 30 |
| 10 | Br | **b** | 4-$MeC_6H_4$ | 8 | **j** | 32 |
| 11 | Br | **j** | 4-$MeOC_6H_4$ | 8 | **k** | 40 |
| 12 | Br | **g** | 3-F-4-$ClC_6H_3$ | 12 | **l** | 30 |
| 13 | Br | **k** | 2,4,6-$(Me)_3C_6H_2$ | 10 | **m** | 18 |

combined organic layer and extracts were washed with water and dried over sodium sulfate. The evaporation residue was chromatographed on a silica-gel column with benzene as an eluent to afford 2-amino-1-bromo-3-cyanoazulenes (**1b**); yield 110 mg (89%), mp 192–193°C; IR (KBr): $\nu$ 3042, 2951, 2921, 2820, 2209 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 5.29 (s, 2H, $NH_2$), 7.41–7.49 (m, 3H, 5, 6, 7-H), 7.99 (d, 1H, $J = 10.0$ Hz, 4-H), 8.08 (d, 1H, $J = 9.2$ Hz, 8-H). MS: m/z 247 ($M^+$). Anal. calcd. for $C_{11}H_7BrN_2$: C, 53.47; H, 2.86; N, 11.34. Found: C, 53.36; H, 3.06; N, 11.43%.

## 1-Cyano-2-*N,N*-dimethylformamidinylazulenes (2)

### General Procedure

A mixture of 2-amino-1-cyanoazulenes (**1**) (10 mmol) and DMFDMA (2.52 g, 20 mmol) in toluene (100 mL) was heated under reflux for 8 h. The reaction mixture was cooled with ice and extracted with EtOAc. The organic layer was washed with saturated brine and dried over anhydrous sodium sulfate. After filtration, the filtrate was concentrated. The residue was purified by silica-gel column chromatography with benzene as eluent to obtain 1-cyano-2-*N,N*-dimethylform-amidinylazulenes (**2**).

### 1-Cyano-2-*N,N*-dimethylformamidinylazulene (**2a**)

Brown-yellow needles; yield 78%; mp 105–107°C; IR (KBr): $\nu$ 3042, 2951, 2921, 2820, 2205 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.15 (s, 3H, $NCH_3$), 3.19 (s, 3H, $NCH_3$), 6.86 (s, 1H, 3-H), 7.36 (dd, 1H, $J = 9.6$, 10.4 Hz, 5-H), 7.36 (dd, 1H, $J = 9.2$, 9.6 Hz, 7-H), 7.45 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 8.03 (d, 1H, $J = 10.0$ Hz, 4-H), 8.16 (s, 1H, -N=CH-), 8.23 (d, 1H, $J = 9.2$ Hz, 8-H). MS: m/z 223 ($M^+$). Anal. calcd. for $C_{14}H_{13}N_3$: C, 75.31; H, 5.87; N, 18.82. Found: C, 75.26; H, 6.06; N, 18.73%.

### 1-Cyano-3-bromo-2-*N,N*-dimethylformamidinylazulene (**2b**)

Bluish dark needles; yield 73%; mp 126–128°C; IR (KBr): $\nu$ 3045, 2956, 2927, 2810, 2207 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.19 (s, 3H, $NCH_3$), 3.24 (s, 3H, $NCH_3$), 7.43 (dd, 1H, $J = 9.6$, 10.4 Hz, 5-H), 7.45 (dd, 1H, $J = 9.2$, 9.6 Hz, 7-H), 7.52 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 8.18 (d, 1H, $J = 9.6$ Hz, 4-H), 8.20 (d, 1H, $J = 9.6$ Hz, 8-H), 8.36 (s, 1H, -N=CH-). MS: m/z 302 ($M^+$). Anal. calcd. for $C_{14}H_{12}BrN_3$: C, 55.65; H, 4.00; N, 13.91. Found: C, 55.78; H, 4.06; N, 13.75%.

## Reactions of 1-Cyano-2-*N,N*-dimethylformamidinylazulene (2) with Anilines

General Procedure

Anilines (**3**) (1.0 mmol) were added to a solution of 1-cyano-2-*N,N*-dimethylformamidinylazulenes (**2**) (0.5 mmol) in toluene (20 mL). The mixture was heated at 80°C for 8–16 h (tracked with thin-layer chromatography, TLC). After cooling, cold water (50 mL) was added to the mixture. Then the mixture was extracted in ethyl acetate (2 × 20 mL), and the organic layer was washed with water and a solution of saturated aqueous $NaHCO_3$, dried over sodium sulfate, and evaporated in vacuum to afford 4-*N*-arylaminoazuleno[2,1-*d*]pyrimidines (**4a**–**m**). They were purified by chromatography on a silica-gel column with benzene as eluent.

4-*N*-(4-Phenyl)aminoazulen[2,1-*d*]pyrimidine (**4a**)

Brown needle crystals; yield 49%; mp 69–70°C; IR (KBr): $\nu$ 3426, 3228, 2961, 2928, 1612, 1564, 1388 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.28–7.30 (m, 3H, 3′, 4′, 5′-H), 7.41 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.46 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 7.48 (s, 1H, 10-H), 7.61 (dd, 1H, $J = 9.6$, 10.0 Hz, 7-H), 7.72–7.75 (m, 3H, 5, 2′, 6′-H), 8.01 (d, 1H, $J = 10.0$ Hz, 9-H), 8.28 (br s, 1H, NH), 8.92 (s, 1H, 2-H). MS: m/z 271 ($M^+$). Anal. calcd. for $C_{18}H_{13}N_3$: C, 79.68; H, 4.83; N, 15.49. Found: C, 79.70; H, 4.74; N, 15.65%.

4-*N*-(4-Methylphenyl)aminoazulen[2,1-*d*]pyrimidine (**4b**)

Brown needle crystals; yield 51%; mp 174–176°C; IR (KBr): $\nu$ 3455, 3224, 2959, 2926, 1598, 1561, 1384, 813 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.31 (s, 3H, $CH_3$), 7.24 (d, 2H, 3′, 5′-H, $J = 8.4$ Hz), 7.27 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.37 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 7.42 (s, 1H, 10-H), 7.49–7.52 (m, 2H, 5,7-H), 7.55 (d, 2H, $J = 8.4$ Hz, 2′, 6′-H), 8.25 (d, 1H, $J = 10.8$ Hz, 9-H), 8.39 (br s, 1H, NH), 8.85 (s, 1H, 2-H). MS: m/z 285 ($M^+$). Anal. calcd. for $C_{19}H_{15}N_3$: C, 79.97; H, 5.30; N, 14.73. Found: C, 79.82; H, 5.44; N, 14.65%.

4-*N*-(4-Fluorophenyl)aminoazulen[2,1-*d*]pyrimidine (**4c**)

Brown needle crystals; yield 29%; mp 141–143°C; IR (KBr): $\nu$ 3442, 3293, 2955, 2929, 1617, 1560, 1508, 836 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ

(ppm): 7.11–7.15 (d, 2H, 3′, 5′-H), 7.35 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.42 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H ), 7.43 (s, 1H, 10-H), 7.51–7.55 (m, 2H, 5, 7-H), 7.60–7.62 (m, 2H, 2′, 6′-H), 8.28 (d, 1H, $J = 10.8$ Hz, 9-H), 8.36 (br s, 1H, NH), 8.87 (s, 1H, 2-H). MS: m/z 289 ($M^+$). Anal. calcd. for $C_{18}H_{12}FN_3$: C, 74.73; H, 4.18; N, 14.53. Found: C, 74.65; H, 4.24; N, 14.45%.

4-*N*-(4-Nitrophenyl)aminoazulen[2,1-*d*]pyrimidine (**4d**)

Brown needle crystals; yield of 35%; mp 205–208°C; IR (KBr): $\nu$ 3278, 2957, 2921, 1618, 1569, 1506, 849 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.31–7.39 (m, 2H, 6, 8-H), 7.48 (s, 1H, 10-H), 7.52–7.60 (m, 2H, 5, 7-H), 7.88 (d, 2H, $J = 8.8$ Hz, 3′, 5′-H), 8.30 (d, 2H, $J = 8.8$ Hz, 2′, 6′-H), 8.42 (d, 1H, $J = 10.8$ Hz, 9-H), 8.32 (br s, 1H, NH), 8.97 (s, 1H, 2-H). MS: m/z 316 ($M^+$). Anal. calcd. for $C_{18}H_{12}N_4O_2$: C, 68.35; H, 3.82; N, 17.71. Found: C, 68.27; H, 3.93; N, 17.68%.

4-*N*-(3,4-Dimethylphenyl)aminoazulen[2,1-*d*]pyrimidine (**4e**)

Brown needle crystals; yield 34%; mp 245–247°C; IR (KBr): $\nu$ 3430, 3225, 2961, 2925, 1596, 1561, 1447, 815 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.29 (s, 3H, $CH_3$), 2.32 (s, 3H, $CH_3$), 7.21 (s, 1H, 2′-H), 7.29 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.37–7.41 (m, 3H, 6′, 5, 7-H), 7.42 (s, 1H, 10-H), 7.50–7.53 (m, 1H, 5′-H), 7.54 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 8.26 (d, 1H, $J = 10.8$ Hz, 9-H), 8.40 (br s, 1H, NH), 8.85 (s, 1H, 2-H). MS: m/z 299 ($M^+$). Anal. calcd. for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.27; H, 5.54; N, 14.15%.

4-*N*-(3,5-Dimethylphenyl)aminoazulen[2,1-*d*]pyrimidine (**4f**)

Brown needle crystals; yield 29%; mp 203–205°C; IR (KBr): $\nu$ 3342, 3031, 2920, 1609, 1570, 1448, 844, 811 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 2.11 (s, 3H, $CH_3$), 2.40 (s, 3H, $CH_3$), 7.01 (s, 1H, 4′-H), 7.28–7.35 (m, 3H, 5, 6, 7-H), 7.41 (s, 1H, 10-H), 7.42 (s, 2H, 2′, 6′-H), 7.52 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 8.25 (d, 1H, $J = 10.8$ Hz, 9-H), 8.33 (br s, 1H, NH), 8.83 (s, 1H, 2-H). MS: m/z 299 ($M^+$). Anal. calcd. for $C_{20}H_{17}N_3$: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.43; H, 5.54; N, 14.14%.

4-*N*-(3-Fluoro-4-chlorolphenyl)aminoazulen[2,1-*d*]pyrimidine (**4g**)

Brown needle crystals; yield 52%; mp 169–170°C; IR (KBr): $\nu$ 3435, 3045, 2968, 2929, 1617, 1571, 1445, 1106 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.27–7.33

(m, 3H, 5, 6, 7-H), 7.41 (s, 1H, 10-H), 7.42–7.45 (m, 1H, 6′-H), 7.50–7.53 (m, 1H, 5′-H), 8.58 (d, 1H, $J = 9.6$, 9.6 Hz, 8-H), 7.83 (s, 1H, 2′-H), 8.27 (d, 1H, $J = 10.8$ Hz, 9-H), 8.44 (br s, 1H, NH), 8.83 (s, 1H, 2-H). MS: m/z 323 ($M^+$). Anal. calcd. for $C_{18}H_{11}ClFN_3$: C, 66.78; H, 3.42; N, 12.98. Found: C, 66.57; H, 3.54; N, 12.88%.

4-*N*-(1-Naphthyl)aminoazulen[2,1-*d*]pyrimidine (**4h**)

Brown needle crystals; yield 26%; mp 210–212°C; IR (KBr): $\nu$ 3425, 3050, 2926, 1569, 1541, 1384, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.29–7.36 (m, 3H, 5, 6, 7-H), 7.46–7.48 (m, 1H, 8-H), 7.49 (s, 1H, 10-H), 7.51–7.57 (m, 4H, 8, 5′, 6′, 7′-H), 7.54 (d, 1H, $J = 9.6$, 9.6 Hz, 8-H), 7.79 (d, 1H, $J = 8.8$ Hz, 4′-H), 7.84–7.86 (m, 2H, 5′, 8′-H), 7.92 (d, 1H, $J = 8.8$ Hz, 8′-H), 8.09 (d, 1H, $J = 6.8$ Hz, 2′-H), 8.32 (d, 1H, $J = 10.8$ Hz, 9-H), 8.47 (br s, 1H, NH), 8.87 (s, 1H, 2-H). MS: m/z 321 ($M^+$). Anal. calcd. for $C_{22}H_{15}N_3$: C, 82.22; H, 4.70; N, 13.08. Found: C, 82.27; H, 4.64; N, 13.21%.

4-*N*-(2-Naphthyl)aminoazulen[2,1-*d*]pyrimidine (**4i**)

Brown needle crystals; yield 30%; mp 210–212°C; IR (KBr): $\nu$ 3425, 3050, 2926, 1569, 1541, 1384, 775 $cm^{-1}$; $^1H$ NMR ($CDCl_3$): δ 7.29 (d, 1H, $J = 9.6$ Hz, 5-H), 7.38 (dd, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.39 (dd, 1H, $J = 9.6$, 9.6 Hz, 7-H), 7.41–7.43 (m, 1H, 5′-H), 7.44 (s, 1H, 10-H), 7.46–7.48 (m, 2H, 6′, 7′-H), 7.54 (d, 1H, $J = 9.6$, 9.6 Hz, 8-H), 7.79 (d, 1H, $J = 8.8$ Hz, 4′-H), 7.84–7.86 (m, 2H, 5′, 8′-H), 7.90 (d, 1H, $J = 8.8$ Hz, 3′-H), 8.18 (s, 1H, 1′-H), 8.27 (d, 1H, $J = 10.8$ Hz, 9-H), 8.48 (br s, 1H, NH), 8.88 (s, 1H, 2-H). MS: m/z 321 ($M^+$). Anal. calcd. for $C_{22}H_{15}N_3$: C, 82.22; H, 4.70; N, 13.08. Found: C, 82.31; H, 4.62; N, 13.30%.

9-Bromo-4-*N*-(4-methylphenyl)aminoazuleno[2,1-*d*]pyrimidine (**4j**)

Brown needles crystals; yield 32%; mp 254–256°C; IR (KBr): $\nu$ 3199, 2960, 2928, 1568, 1536, 1326, 925 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.34 (s, 3H, $CH_3$), 7.09–7.18 (m, 3H, 5, 6, 8-H), 7.23 (d, 2H, 3′, 5′-H, $J = 8.8$ Hz), 7.31 (d, 2H, $J = 8.8$ Hz, 2′, 6′-H), 7.40–7.43 (m, 2H, 5, 7-H), 8.34 (d, 1H, $J = 10.8$ Hz, 9-H), 8.38 (br s, 1H, NH), 8.94 (s, 1H, 2-H). MS: m/z 364 ($M^+$). Anal. calcd. for $C_{19}H_{14}BrN_3$: C, 62.65; H, 3.87; N, 11.54. Found: C, 62.67; H, 3.74; N, 11.68%.

9-Bromo-4-*N*-(4-Methoxyphenyl)aminoazuleno[2,1-*d*]pyrimidine (**4k**)

Brown needle crystals; yield 40%; mp 240–242°C; IR (KBr): $\nu$ 3242, 3068, 2960, 1607, 1567, 1512, 1247, 1033, 730 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.85 (s, 3H, $OCH_3$), 6.98 (d, 2H, 3′, 5′-H, $J = 7.6$ Hz), 7.40–7.43 (m, 2H, 6, 8-H), 7.52 (d, 2H, $J = 7.6$ Hz, 2′, 6′-H), 7.54–7.58 (m, 2H, 5, 7-H), 8.35 (br s, 1H, NH), 8.39 (d, 1H, $J = 10.4$ Hz, 9-H), 8.94 (s, 1H, 2-H). MS: m/z 380 ($M^+$). Anal. calcd. for $C_{19}H_{14}BrON_3$: C, 60.01; H, 3.71; N, 11.05. Found: C, 60.27; H, 3.84; N, 11.23%.

9-Bromo-4-*N*-(4-fluoro-3-chlorophenyl)aminoazuleno[2,1-*d*]-pyrimidine (**4l**)

Brown needle crystals; yield 30%; mp 255–257°C; IR (KBr): $\nu$ 3296, 3068, 2918, 2850, 1606, 1572, 1535, 1326, 1170, 795, 736 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 7.40–7.46 (m, 2H, 5, 7-H), 7.52–7.55 (m, 1H, 6′-H), 7.61 (d, 1H, $J = 9.6$, 9.6 Hz, 6-H), 7.68 (s, 1H, 2′-H), 7.71–7.74 (m, 1H, 5′-H), 7.84 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 8.33 (br s, 1H, NH), 8.43 (d, 1H, $J = 10.8$ Hz, 9-H), 9.05 (s, 1H, 2-H). MS: m/z 402 ($M^+$). Anal. calcd. for $C_{18}H_{10}BrClFN_3$: C, 53.69; H, 2.50; N, 10.44. Found: C, 53.57; H, 2.64; N, 10.58%.

9-Bromo-4-*N*-(2,4,6-trimethylphenyl)aminoazuleno[2,1-*d*]-pyrimidine (**4m**)

Brown needle crystals; yield 18%; mp > 300°C; IR (KBr): $\nu$ 3294, 2961, 2918, 1560, 1534, 1436, 1323, 923, 742 $cm^{-1}$; $^1H$ NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.22 (s, 6H, $2 \times CH_3$), 2.38 (s, 3H, $CH_3$), 7.01 (s, 2H, 3′, 5′-H), 7.40–7.46 (m, 3H, 5, 6, 7-H), 7.54 (dd, 1H, $J = 9.6$, 9.6 Hz, 8-H), 8.39 (br s, 1H, NH), 8.44 (d, 1H, $J = 10.8$ Hz, 9-H), 8.89 (s, 1H, 2-H). MS: m/z 392 ($M^+$). Anal. calcd. for $C_{21}H_{18}BrN_3$: C, 64.29; H, 4.63; N, 10.71. Found: C, 64.37; H, 4.44; N, 10.68%.

## REFERENCES

1. Morita, T.; Nakadate, T.; Takase, K. A facile method for the synthesis of azuleno[2,1-*b*]furan and azuleno[2,1-*b*]pyrrole derivatives and their some properties. *Heterocycles* **1981**, *15*, 835–838.
2. Fujimori, K.; Fujita, T.; Yamane, K.; Yasunami, M.; Takase, K. Synthesis of azuleno[1,2-*b*]- and azuleno[1,2-*c*]thiophenes by the reactions of 2H-cyclohepta [*b*]furan-2-ones with enamines of 3-oxotetrahydrothiophenes. *Chem. Lett.* **1983**, *12*, 1721–1724.

3. Yamane, K.; Fujimori, K.; Ichikawa, S.; Miyoshi, S.; Hashizume, K. The synthesis and several reactions of 2-methylazuleno[2,1-*d*]thiazole. *Heterocycles* **1983***, 20, 1263–1266.*
4. Fujimori, K.; Fukazawa, H.; Nezu, Y.; Yasunami, K.; Takase, K. Synthesis of azuleno[1,2-*b*]pyrrole and azuleno[1,2-*b*]furan. *Chem. Lett.* **1986**, *15*, 1021–1024.
5. Wang, D. L.; Imafuku, K. New synthetic approach to azuleno[1,2-*c*]pyrroles and conversion to benz[*a*]azulenes. *Heterocycles* **2001**, *54*, 647–665.
6. Wang, D. L.; Imafuku, K. A new synthetic approach to azuleno[1,2-*c*]-thiophenes. *Heterocycles* **2002**, *58*, 405–419.
7. Nozoe, T.; Asao, T.; Kobayashi, M. The synthesis of azulene derivatives condensed with several heterocycles. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 3161–3164.
8. Takase, K.; Nakazawa, T.; Nozoe, T. The formation of azuleno[2,1-*d*]pyrimidine derivatives by the reaction of 2-acetylimino-2*H*-cyclohepta[*b*]furan derivatives with active methylene compounds. *Heterocycles* **1981**, *15*, 839–842.
9. Nozoe, T.; Takase, K.; Nakazawa, T.; Fukuda, S. The formation of azulene derivatives from 2*H*-cyclohepta[*b*]furan-2-one derivatives. *Tetrahedron* **1971**, *27*, 3357–3368.