A Mild and Efficient Method for *N*-Arylnucleobase Synthesis *via* the Cross-Coupling Reactions of Nucleobases with Arylboronic Acids Catalyzed by Simple Copper Salts

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A simple and efficient copper-salt catalyzed *N*-arylation of nucleobases is reported. In a mixed solvent of MeOH and H_2O, the coupling products were obtained in moderate to excellent yields at room temperature within a short time. A variety of substituted *N*-aryl nucleobases can be prepared through this procedure.

Introduction. – Because of the significant pharmaceutical, biological, and chemical activities, there has been a growing interest in the modification of nucleobases in recent years. Among these methods, *N*-arylation is a convenient way to prepare *N*-aryl nucleobases. The classical method for the preparation of 9-aryl purines was based on heterocyclization [1][2], and there was only one reported method for the synthesis of *N*-arylpyrimidine by diphenyliodonium salts [3]. Both above routes were not satisfactory because of their numerous steps or low yields.

In 1998, *Chan et al.* [4], *Lam et al.* [5], and *Evans et al.* [6] reported the copper-mediated carbon–heteroatom cross-coupling reactions of boronic acids using a wide range of different nucleophiles (N–H containing substrates). And then, a Cu-mediated *N*-arylation under very mild conditions employing arylboronic acids was developed [7–12] and used for *N*-arylation of nucleobases [13–16].

Schultz and co-workers [13] reported the reaction of 2,6-dichloro-9*H*-purine with boronic acids in the presence of cupric acetate and NEt_3. The reaction resulted in the desired N^9-aryl product, however, the reaction could only be monitored by LC/MS because of difficulties in isolation. Two years later, *Gundersen* and *Bakkestuen* [14] accomplished the regioselective N^9-arylation of various purine derivatives with arylboronic acids, but the *N*-arylation of adenine was not successful under their anhydrous reaction conditions. To improve the solubility of the substrate and to prevent diarylation or triarylation, *Gothelf* and co-workers [16] used readily available protected or masked nucleobases in the Cu-mediated *N*-arylation and *N*-alkenylation with boronic acids. Nevertheless, it was not a general process because too many steps were involved.

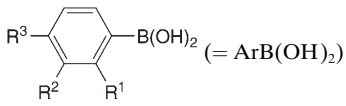
We have developed an efficient, facile, and mild method for the synthesis of *N*-arylnucleobases in our previous work [17]. In this paper, the reactions of nucleobases

(including cytosine, adenine, uracil, and thymine) were performed with arylboronic acids in the presence of cupric acetate, base, and air. The reactions with guanine were unsuccessful due to the poor solubility.

Results and Discussion. – Initial reactions were carried out with cytosine as *N*-nucleophile and phenylboronic acid as the aryl donor. The effect of reaction solvent, bases, ligands, and reaction temperature were investigated in this work, and the results were consistent with our previous work [17].

Generally, the coupling reactions of *N*-heterocycles with arylboronic acids were performed under anhydrous conditions [18]. However, we found, that when a small quantity of H_2O ($MeOH/H_2O$ 8:1) was added, the coupling yield was increased to 44%. When we increased the amount of H_2O to a 4:1 ratio of $MeOH/H_2O$, the yield was up to 90%. Further increasing the amount of H_2O led to the decrease of the yield. Thus, the mixed solvent with a 4:1 ratio of $MeOH/H_2O$ was the optimum solvent for the coupling of cytosine with arylboronic acid [17]. TMEDA was found to be a suitable base for the reaction, and room temperature was found to be the best reaction temperature. The result of the reaction catalyzed by $Cu(OAc)_2$ was slightly better than that catalyzed by other copper salts. The equivalent of phenylboronic acid also affected the result. The reaction with an equimolar ratio of nucleobase and $PhB(OH)_2$ gave only 67% yield. Increasing the amount of phenylboronic acid led to high yields of required product [17].

Table. *Coupling Reaction of Nucleobases with Various Substituted Phenylboronic Acids*

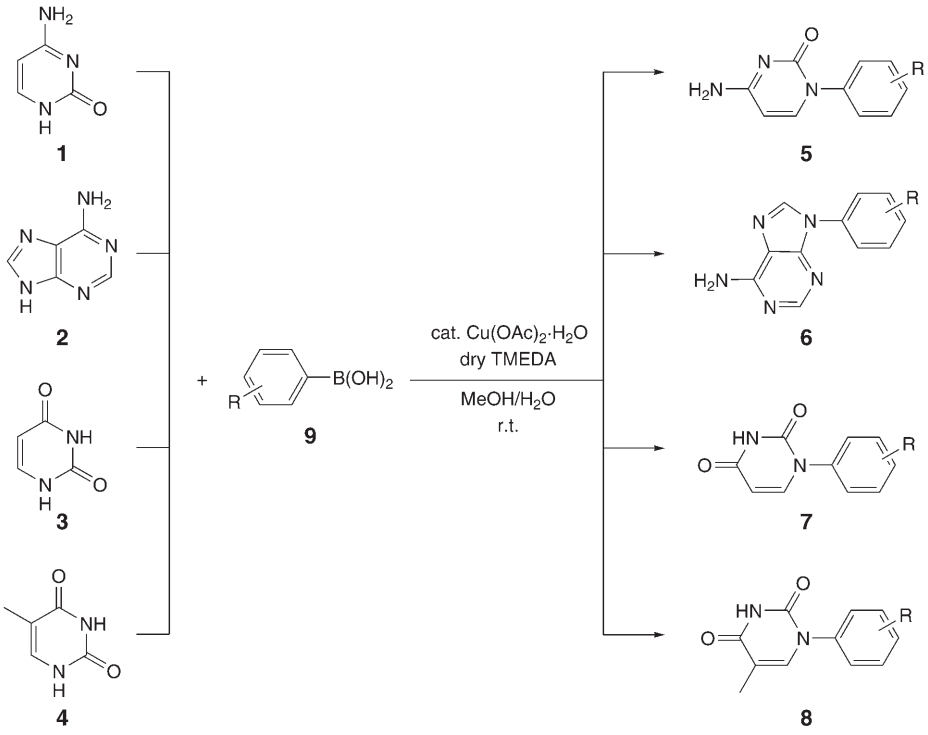
Entry	 (= $ArB(OH)_2$)			Product (yield [%])			
	R^1	R^2	R^3	Ar–C	Ar–A	Ar–U	Ar–T
1	H	H	H	**5a** (90)[a])	**6a** (85)[a])	**7a** (63)	**8a** (59)
2	Me	H	H	**5b** (83)[a])	**6b** (28)	**7b** (40)	**8b** (33)
3	MeO	H	Me	**5c** (48)	**6c** (25)	**7c** (43)	**8c** (35)
4	H	MeO	H	**5d** (53)[a])	**6d** (61)	**7d** (66)	**8d** (51)
5	H	Br	H	**5e** (74)[a])	**6e** (52)	**7e** (54)	**8e** (46)
6	H	H	Me	**5f** (85)[a])	**6f** (55)	**7f** (61)	**8f** (52)
7	H	H	MeO	**5g** (82)[a])	**6g** (66)[a])	**7g** (56)	**8g** (53)
8	H	H	Br	**5h** (68)[a])	**6h** (60)[a])	**7h** (53)	**8h** (52)

[a]) Data taken from [17].

Several substituted arylboronic acids and some other nucleobases were applied to the reaction under optimized conditions (*Scheme 1*), the results are shown in the *Table*. The results did not reveal any obvious trends for either electron-rich or electron-poor aryl boronic acids. The lower yields afforded by the *ortho*-substituted arylboronic acids compared to *para*-substituted or unsubstituted phenylboronic acids might be attributed to the steric hindrance at the reaction center.

Cytosine is superior to uracil and thymine as nucleobase in the coupling reaction, and the reactions involving cytosine were complete within 45 min. Longer reaction

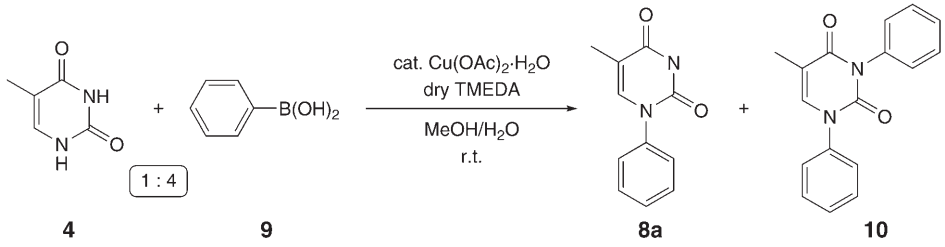
Scheme 1. *Preparation of Cross-Coupling Products*



times were needed when uracil and thymine were employed in this catalytic coupling. Stirring overnight at room temperature might be a good choice for these substrates. Since the *N*-arylated purines could serve as ligands and coordinate to Cu^{II} [19–22], the yields of the reactions involving adenine were moderate. It has been reported that arylboronic acids could be oxidized by Cu^{II} in the presence of H_2O to form the corresponding phenols [23], which could be subsequently converted into quinone-type derivatives [24]. Moreover, arylboronic acids could undergo deboronation in the presence of H_2O. These factors, together with a long reaction time resulted in diminished yields. Increase of the mole amount of arylboronic acid might lead to the appearance of di-arylated products, and the yield of the desired product did not increase. For example, by using a 4:1 mole ratio of arylboronic acid/thymine, after stirring overnight, two products could be separated by column chromatography (*Scheme 2*), the structure of product **10** was characterized by ^{1}H-NMR and ESI-MS.

Conclusions. – In summary, we have developed a mild and efficient approach for the direct *N*-arylation of nucleobases with arylboronic acids catalyzed by simple copper salts. This reaction is cost-effective, easy to handle, and does not need an inert atmosphere. This methodology should be tolerant to many sensitive functional groups and gives the corresponding coupling products in moderate to excellent yields.

Scheme 2



Experimental Part

General. Unless otherwise indicated, all reagents and solvents were obtained from commercial suppliers and used without further purification. Anh. Et_2O was dried and purified under N_2 with K/benzophenone and distilled immediately before use. TMEDA and TEA were distilled before use. IR: *Shimadzu FT-IR-4200* spectrometer; KBr pellets or thin films on KBr plates; in cm^{-1}. ^{1}H-NMR: *Varian INOVA-400* spectrometer; δ in ppm, referenced to residual solvent peaks or internal tetramethylsilane (TMS); J in Hz. ESI-MS: *Finnigan LCQ^{DECA}* mass spectrometer; J in m/z. HR-MS: *Bruker Daltonics Bio TOF*; J in m/z.

General Procedure for the Cross-Coupling Reaction. **1** (0.0556 g, 0.5 mmol), **9** (1 mmol), $Cu(OAc)_2 \cdot H_2O$ (0.099 g, 0.5 mmol), TMEDA (150 µl, 1 mmol), MeOH (40 ml), and H_2O (10 ml) were placed in a 100 ml flask. The mixture was vigorously stirred under an atmosphere of air at r.t. for 45 min. The solvents were evaporated, and the product purified by flash column chromatography (CC) on SiO_2 (CH_2Cl_2/MeOH, 5 : 1) to give the desired *N*-arylcytosine. For a mole ratio of arylboronic acid/thymine 4 : 1, after stirring 24 h at r.t., the side product could be separated by CC.

The following compounds were prepared according to the *General Procedure* except for the reaction time (for cytosine and adenine, 45 min; for uracil and thymine, over night).

1-Phenylcytosine (**5a**; data from [17], for comparison): White powder. M.p. 300°. IR (neat): 3334, 3066, 1638, 1486, 1372, 1294, 1174, 1128, 784, 698. ^{1}H-NMR (400 MHz, (D_6)DMSO): 5.79 (*d*, J = 8.0, CH); 7.24 (*s*, NH); 7.32 (*s*, NH); 7.34 – 7.38 (*m*, 3 arom. H); 7.45 (*t*, J = 7.6, 2 arom. H); 7.63 (*d*, J = 8.0, CH). ^{13}C-NMR (200 MHz, (D_6)DMSO): 94.26; 126.75; 127.50; 128.99; 141.46; 146.03; 154.93; 166.21. ESI-MS: 188.3 ($[M+H]^+$). HR-ESI-MS: 188.0822 ($[M+H]^+$, $C_{10}H_{10}N_3O^+$; calc. 188.0818).

1-(2-Methylphenyl)cytosine (**5b**): IR (neat): 3324, 3092, 1632, 1478, 1372, 1294, 1134, 992, 786, 726, 690. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.07 (*s*, Me); 5.77 (*d*, J = 8.0, CH); 7.14 – 7.18 (*m*, NH_2); 7.25 – 7.33 (*m*, 4 arom. H); 7.47 (*d*, J = 8.0, CH). ESI-MS: 202.1 ($[M+H]^+$).

1-(2-Methoxy-4-methylphenyl)cytosine (**5c**): IR (neat): 3318, 3085, 1647, 1450, 1369, 1301, 1130, 1034, 784, 731. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.25 (*s*, Me); 3.70 (*s*, Me); 5.71 (*d*, J = 8.0, CH); 6.97 – 7.37 (*m*, NH_2, 3 arom. H); 7.41 (*d*, J = 8.0, CH). ESI-MS: 232.9 ($[M+H]^+$).

1-(3-Methoxyphenyl)cytosine (**5d**): IR (neat): 3342, 3094, 1636, 1484, 1374, 1296, 1216, 800, 698. ^{1}H-NMR (400 MHz, (D_6)DMSO): 3.77 (*s*, Me); 5.78 (*d*, J = 5.2, CH); 6.89 – 6.95 (*m*, 3 arom. H); 7.24 (*s*, NH); 7.30 (*s*, NH); 7.35 (*t*, J = 7.8, 1 arom. H); 7.61 (*d*, J = 7.2, CH). ESI-MS: 218.0 ($[M+H]^+$).

1-(3-Bromophenyl)cytosine (**5e**): IR (neat): 3338, 3094, 1636, 1584, 1476, 1374, 1298, 1136, 1088, 798, 692. ^{1}H-NMR (400 MHz, (D_6)DMSO): 5.79 (*d*, J = 7.2, CH); 7.30 – 7.43 (*m*, 4 H); 7.55 – 7.62 (*m*, 2 arom. H); 7.65 (*d*, J = 7.8, CH). ESI-MS: 267.9 ($[M+H]^+$).

1-(4-Methylphenyl)cytosine (**5f**): IR (neat): 3346, 3110, 1636, 1484, 1372, 1294, 1130, 798, 716. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.33 (*s*, Me); 5.77 (*d*, J = 7.6, CH); 7.19 – 7.25 (*m*, 6 H); 7.58 (*d*, J = 7.2, CH). ESI-MS: 202.3 ($[M+H]^+$).

1-(4-Methoxyphenyl)cytosine (**5g**): IR (neat): 3341, 3094, 1628, 1478, 1372, 1296, 1246, 1182, 1132, 1028, 992, 838, 786, 726. ^{1}H-NMR (400 MHz, (D_6)DMSO): 3.78 (*s*, Me); 5.76 (*d*, J = 5.2, CH); 6.97 – 7.00 (*m*, NH_2); 7.15 – 7.32 (*m*, 4 arom. H); 7.58 (*d*, J = 7.2, CH). ESI-MS: 218.3 ($[M+H]^+$).

1-(4-Bromophenyl)cytosine (**5h**): IR (neat): 3354, 3068, 1634, 1484, 1376, 1298, 1132, 1068, 994, 798, 714. ^{1}H-NMR (400 MHz, (D_6)DMSO): 5.80 (*d*, *J* = 7.6, CH); 7.29–7.37 (*m*, 4 H); 7.62–7.66 (*m*, 3 arom. H). ESI-MS: 266.2 ($[M+H]^+$).

9-Phenyladenine (**6a**): IR (neat): 3297, 3126, 1672, 1600, 1510, 1416, 1374, 1306, 1264, 1186, 1102, 964, 756. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.43–7.47 (*m*, 3 H); 7.60 (*t*, *J* = 7.8, 2 arom. H); 7.91 (*d*, *J* = 7.6, 2 arom. H); 8.22 (*s*, CH); 8.60 (*s*, CH). ESI-MS: 212.2 ($[M+H]^+$).

9-(2-Methylphenyl)adenine (**6b**): IR (neat): 3370, 3275, 3044, 2918, 2850, 1702, 1612, 1514, 1474, 1377, 762, 736. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.15 (*s*, Me); 5.77 (*s*, NH_2); 7.14–7.51 (*m*, 4 arom. H); 7.87 (*s*, CH); 8.36 (*s*, CH). ESI-MS: 226.1 ($[M+H]^+$).

9-(2-Methoxy-4-methylphenyl)adenine (**6c**): IR (neat): 3312, 3147, 2948, 2923, 2845, 1667, 1601, 1523, 1463, 776, 639. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.31 (*s*, Me); 3.73 (*s*, Me); 7.17 (*d*, *J* = 9.2, 1 arom. H); 7.27 (*s*, NH_2); 7.30 (*t*, *J* = 2.4, 2 arom. H); 8.10 (*s*, CH); 8.19 (*s*, CH). ESI-MS: 256.8 ($[M+H]^+$).

9-(3-Methoxyphenyl)adenine (**6d**): IR (neat): 3299, 3145, 3027, 2924, 2854, 1669, 1607, 1518, 1463, 957, 815, 672. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.38 (*s*, Me); 7.37–7.39 (*m*, NH_2, 2 arom. H); 7.76 (*d*, *J* = 8.4, 2 arom. H); 8.10 (*s*, CH); 8.19 (*s*, CH). ESI-MS: 226.0 ($[M+H]^+$).

9-(3-Bromophenyl)adenine (**6e**): IR (neat): 3308, 3152, 2910, 1671, 1597, 1509, 1482, 1299, 1186, 763, 685. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.40 (*s*, NH_2); 7.59–7.61 (*m*, 2 arom. H); 7.90 (*d*, *J* = 9.2, 2 arom. H); 8.21 (*s*, CH); 8.59 (*s*, CH). ESI-MS: 291.8 ($[M+H]^+$).

9-(4-Methylphenyl)adenine (**6f**): IR (neat): 3306, 3150, 2967, 2850, 1672, 1605, 1509, 1491, 1370, 983, 828, 678. ^{1}H-NMR (400 MHz, (D_6)DMSO): 2.51 (*s*, Me); 7.39 (*s*, NH_2); 7.46–7.52 (*m*, 4 arom. H); 8.21 (*s*, CH); 8.62 (*s*, CH). ESI-MS: 226.1 ($[M+H]^+$).

9-(4-Methoxyphenyl)adenine (**6g**): IR (neat): 3307, 3128, 1683, 1615, 1504, 1483, 1420, 1341, 1298, 1235, 1182, 1014, 961, 835. ^{1}H-NMR (400 MHz, (D_6)DMSO): 3.83 (*s*, Me); 7.13 (*d*, *J* = 7.6, 2 arom. H); 7.36 (*s*, NH_2); 7.76 (*d*, *J* = 7.2, 2 arom. H); 8.18 (*s*, CH); 8.48 (*s*, CH). ESI-MS: 242.1 ($[M+H]^+$).

9-(4-Bromophenyl)adenine (**6h**): IR (neat): 3294, 3124, 1682, 1604, 1524, 1474, 1418, 1382, 1338, 1302, 1248, 1176, 1104, 1032, 964, 832, 794, 736. ^{1}H-NMR (400 MHz, (D_6)DMSO): 7.43 (*s*, NH_2); 7.78–7.81 (*m*, 2 arom. H); 7.90–7.93 (*m*, 2 arom. H); 8.22 (*s*, CH); 8.62 (*s*, CH). ESI-MS: 291.1 ($[M+H]^+$).

1-Phenyluracil (**7a**): IR (neat): 3446, 3227, 3175, 3091, 2964, 1740, 1627, 1488, 1416, 1188, 826, 761, 696. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.84 (*d*, *J* = 7.6, CH); 7.11 (*d*, *J* = 4.4, 1 arom. H); 7.13 (*d*, *J* = 7.6, 1 arom. H); 7.24 (*t*, *J* = 9.4, 1 arom. H); 7.46 (*t*, *J* = 7.2, 1 arom. H); 7.52 (*t*, *J* = 7.4, 1 arom. H); 7.64 (*t*, *J* = 7.2, CH); 10.11 (*s*, NH). HR-ESI-MS: 211.0472 ($[M+Na]^+$, $C_{10}H_8N_2NaO_2^+$; calc. 211.0478).

1-(2-Methylphenyl)uracil (**7b**): IR (neat): 3421, 3178, 3074, 2961, 1702, 1681, 1437, 1385, 1281, 835, 704. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.25 (*s*, Me); 5.82 (*d*, *J* = 7.6, CH); 7.18 (*d*, *J* = 8, CH); 7.31–7.41 (*m*, 4 arom. H); 8.52 (*s*, NH). ESI-MS: 201.7 ($[M-H]^-$).

1-(2-Methoxy-4-methylphenyl)uracil (**7c**): IR (neat): 3426, 3150, 3043, 2924, 2840, 1700, 1623, 1513, 1455, 1378, 1300, 1241, 806, 763. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.32 (*s*, Me); 3.81 (*s*, Me); 5.75 (*d*, *J* = 7.6, CH); 6.92 (*d*, *J* = 8.4, 1 arom. H); 7.08 (*s*, 1 arom. H); 7.14 (*d*, *J* = 8, 1 arom. H); 7.21 (*d*, *J* = 8, CH); 8.73 (*s*, NH). ESI-MS: 233.0 ($[M+H]^+$).

1-(3-Methoxyphenyl)uracil (**7d**): IR (neat): 3433, 3265, 3140, 3095, 2968, 2840, 1731, 1640, 1488, 1421, 1320, 1232, 1193, 790, 692. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.82 (*s*, Me); 5.86 (*d*, *J* = 9.2, CH); 6.78 (*s*, 1 arom. H); 6.83 (*d*, *J* = 9.6, 1 arom. H); 6.98–7.01 (*m*, 1 arom. H); 7.16–7.20 (*m*, 1 arom. H); 7.42 (*t*, *J* = 8.2, CH); 9.68 (*s*, NH). ESI-MS: 219.7 ($[M+H]^+$).

1-(3-Bromophenyl)uracil (**7e**): IR (neat): 3365, 3203, 3195, 3099, 2964, 1730, 1669, 1472, 1416, 1381, 1247, 1182, 803, 764, 688. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.84 (*d*, *J* = 9.2, CH); 7.11–7.27 (*m*, 2 arom. H); 7.41 (*d*, *J* = 4.8, 1 arom. H); 7.50–7.60 (*m*, 1 arom. H, 1 CH); 10.11 (*s*, NH). ESI-MS: 266.7 ($[M+H]^+$).

1-(4-Methylphenyl)uracil (**7f**): IR (neat): 3375, 3233, 3171, 3081, 2970, 2915, 1741, 1637, 1418, 1388, 1187, 819, 761, 713. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.41 (*s*, Me); 5.84 (*d*, *J* = 9.2, CH); 7.12 (*d*, *J* = 8.4, 1 CH, 1 arom. H); 7.15 (*d*, *J* = 7.6, CH); 7.32 (*d*, *J* = 8, 2 arom. H); 10.04 (*s*, NH). ESI-MS: 203.8 ($[M+H]^+$).

1-(4-Methoxyphenyl)uracil (**7g**): IR (neat): 3438, 3255, 3191, 3115, 2966, 1742, 1638, 1517, 1420, 1109, 936, 807. ^{1}H-NMR (400 MHz, $CDCl_3$): 3.84 (*s*, Me); 5.86 (*d*, *J* = 9.2, CH); 7.02 (*d*, *J* = 6.4, 2 arom. H); 7.14–7.19 (*m*, 2 arom. H, 1 CH); 9.68 (*s*, NH). ESI-MS: 218.9 ($[M+H]^+$).

1-(4-Bromophenyl)uracil (**7h**): IR (neat): 3446, 3234, 3169, 3091, 2966, 1741, 1627, 1589, 1417, 1386, 1069, 827, 760. ^{1}H-NMR (400 MHz, $CDCl_3$): 5.87 (*d*, $J = 8$, CH); 7.13 (*d*, $J = 8.4$, 2 arom. H); 7.18 (*d*, $J =$ 7.6, CH); 7.64 (*d*, $J = 8.4$, 2 arom. H); 9.91 (*s*, NH). ESI-MS: 266.7 ($[M-H]^-$).

1-Phenylthymine (**8a**): IR (neat): 3430, 3292, 3175, 3065, 2925, 1704, 1651, 1491, 1422, 1216, 768, 698. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.93 (*s*, Me); 7.01–7.12 (*m*, 3 arom. H); 7.26 (*s*, CH); 7.63 (*d*, $J = 8.4$, 2 arom. H); 9.76 (*s*, NH). ESI-HR-MS: 225.0642 ($[M+Na]^+$, $C_{11}H_{10}N_2NaO_2^+$; calc. 225.0634).

1-(2-Methylphenyl)thymine (**8b**): IR (neat): 3411, 3276, 3066, 2926, 2838, 1688, 1654, 1459, 1385, 1297, 765, 711. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.94 (*s*, Me); 2.25 (*s*, Me); 7.02 (*s*, CH); 7.19 (*d*, $J = 8$, 1 arom. H); 7.31–7.37 (*m*, 3 arom. H); 8.51 (*s*, NH). ESI-MS: 216.8 ($[M-H]^-$).

1-(2-Methoxy-4-methylphenyl)thymine (**8c**): IR (neat): 3421, 3164, 3035, 2921, 2830, 1716, 1664, 1516, 1464, 1302, 1288, 812. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.94 (*s*, Me); 2.31 (*s*, Me); 3.81 (*s*, Me); 6.91 (*d*, $J =$ 10.8, 1 arom. H); 6.98 (*s*, 1 arom. H); 7.06 (*s*, CH); 7.19 (*d*, $J = 8$, 1 arom. H); 8.65 (*s*, NH). ESI-MS: 247.0 ($[M+H]^+$).

1-(3-Methoxyphenyl)thymine (**8d**): IR (neat): 3446, 3218, 3075, 2948, 1719, 1647, 1494, 1431, 1292, 1231, 1196, 810, 765, 695. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.94 (*s*, Me); 3.81 (*s*, Me); 6.76 (*s*, 1 arom. H); 6.82 (*d*, $J = 7.6$, 1 arom. H); 6.97 (*d*, $J = 5.6$, 1 arom. H); 7.04 (*s*, CH); 7.41 (*t*, $J = 8.2$, 1 arom. H); 9.53 (*s*, NH). ESI-MS: 231.8 ($[M-H]^-$).

1-(3-Bromophenyl)thymine (**8e**): IR (neat): 3441, 3245, 3185, 3100, 2925, 1719, 1654, 1474, 1425, 1221, 1139, 768, 685. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.92 (*s*, Me); 6.99 (*s*, 1 arom. H); 7.18 (*d*, $J = 6$, 1 arom. H); 7.40 (*s*, CH); 7.50 (*t*, $J = 11.4$, 1 arom. H); 10.03 (*s*, NH). ESI-MS: 280.8 ($[M-H]^-$).

1-(4-Methylphenyl)thymine (**8f**): IR (neat): 3334, 3208, 3065, 2925, 1703, 1650, 1428, 1230, 815, 763. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.91 (*s*, Me); 2.39 (*s*, Me); 6.97 (*d*, $J = 6.8$, 1 arom. H); 7.10 (*d*, $J = 10.4$, 2 arom. H); 7.29 (*s*, 1 arom. H); 7.31 (*s*, CH); 10.13 (*s*, NH). ESI-MS: 215.9 ($[M-H]^-$).

1-(4-Methoxyphenyl)thymine (**8g**): IR (neat): 3446, 3208, 3163, 3103, 2922, 2838, 1707, 1646, 1512, 1435, 1247, 834, 769. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.92 (*s*, Me); 3.84 (*s*, Me); 7.00–7.02 (*m*, 2 arom. H, 1 CH); 7.14 (*d*, $J = 8.4$, 2 arom. H); 9.90 (*s*, NH). ESI-MS: 255.1 ($[M+Na]^+$).

1-(4-Bromophenyl)thymine (**8h**): IR (neat): 3398, 3289, 3234, 3135, 3067, 2983, 1735, 1652, 1589, 1420, 1353, 1231, 1066, 829, 767. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.93 (*s*, Me); 7.01 (*d*, $J = 6.8$, 1 arom. H); 7.11 (*d*, $J = 8.8$, 2 arom. H); 7.62–7.65 (*m*, 1 arom. H, 1 CH); 9.91 (*s*, NH). ESI-MS: 280.8 ($[M-H]^-$).

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