Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Cross-coupling reactions of unprotected halopurine bases, nucleosides, nucleotides and nucleoside triphosphates with 4-boronophenylalanine in water. Synthesis of (purin-8-yl)- and (purin-6-yl)phenylalanines.

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Electronic Supplementary Information

Starting materials

Starting 4-boronophenylalanine **2** and 6-chloropurines **4a-c** are commercially available. 8-bromoadenine **1c** was prepared by bromination of solid adenine.[1] Compounds **1a**,[2] **1b**,[3] **1d**,[4] **1e**,[5] **1f**[4] and **1g**[6] were prepared by bromination (use of about 1.3 eq. of Br_2) of appropriate adenosines in NaOAc/AcOH buffer (pH 4, 0.5 M) as described for **1a**.[2] Compounds **1a** and **1b** crystallized directly from reaction mixtures.[2] Compound **1d** was isolated from crude reaction mixture by preparative HPLC on C18 column with use of 0.3% AcOH in water to 0.3%AcOH in methanol gradient. Compounds **1e-1g** were isolated after neutralization (NaOH) from crude reaction mixture by preparative HPLC on C18 column with use of 0.1M TEAB in water to 0.1M TEAB in water/methanol (1:1) gradient.

Study on hydrolysis of ATP

The hydrolysis of disodium salt of ATP (0.1 M solution) under microwave (MW) mediated and standard heating in diverse water/organic solvent mixtures with variety of bases (3 equiv.) was studied by analytical HPLC. Ratios of content of starting ATP and the resulting ADP and AMP after 5 min of heating are summarized in table **ESI 1**. Firstly, solution of disodium salt of ATP without any base was heated by microwave irradiation at 100°C and 150°C (Entries 1-2). The same heating in presence of Na_2CO_3 (entries 3-5) indicate slightly higher stability of ATP under basic conditions. Entries 5-8 compare use of diverse bases under MW heating at 150°C. Results show significant influence of base strength on ATP solution stability. Stabilizing effect is growing in line $Li_2CO_3<Na_2CO_3\sim K_3PO_4<Cs_2CO_3$. Entries 9-15 show, that there is no significant influence of co-solvent (with exception of use of water/DMSO which promote hydrolysis slightly more) on the hydrolysis. On the other hand, hydrolysis rate drops significantly, when standard heating is used instead of microwave mediated heating to the same temperature (entry 16).

Table **ESI 1**. Hydrolysis of ATP

Entry	T (°C)[a]	Solvent	Base	ATP (%)	ADP (%)	AMP (%)
1	100 (MW)	water	-	87	3	10
2	150 (MW)	water	-	8	7	85
3	100 (MW)	water	Na_2CO_3	92	7	1
4	125 (MW)	water	Na_2CO_3	53	42	5
5	150 (MW)	water	Na_2CO_3	3	25	72
6	150 (MW)	water	Cs_2CO_3	5	42	53
7	150 (MW)	water	K_3PO_4	1	26	73
8	150 (MW)	water	Li_2CO_3	1	2	97
9	125 (MW)	water	Cs_2CO_3	75	23	2
10	125 (MW)	water/acetonitrile (2:1)	Cs_2CO_3	71	26	3
11	125 (MW)	water/dioxane (2:1)	Cs_2CO_3	66	31	3
12	125 (MW)	water/EtOH (2:1)	Cs_2CO_3	70	27	3
13	125 (MW)	water/acetone (2:1)	Cs_2CO_3	78	20	2
14	125 (MW)	water/DMSO (2:1)	Cs_2CO_3	55	40	5
15	125 (MW)	water/THF (2:1)	Cs_2CO_3	71	26	3
16	125	water	Cs_2CO_3	95	5	0

[a] MW in parenthesis means that reaction was performed under microwave irradiation.

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