S U P P O R T I N G I N F O R M A T I O N

High-Throughput Synthesis of *N*3-Acylated Dihydropyrimidines Combining Microwave-Assisted Synthesis and Scavenging Techniques

Doris Dallinger, Nikolay Yu. Gorobets and C. Oliver Kappe*

Institute of Chemistry, Karl-Franzens-University Graz, Heinrichstrasse 28, A-8010 Graz, Austria.

EXPERIMENTAL PROCEDURES

General Methods. Dihydropyrimidines **1A-J** were prepared according to our recently reported microwave-assisted method (ref. 6). The following types of diamine scavenger resins were used: **4,** PS-DVB (1%), 3.26 mmol N/g, Aldrich 47,209-3; and **5**, Si, 3.02 mmol N/g, Aldrich 53,791-8). Anhydrides were obtained from commercial sources and used without further purification. TLC analysis was performed on Merck precoated 60 F_{254} plates. Melting points were obtained on a Gallenkamp melting point apparatus, Model MFB-595 in open capillary tubes. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AMX360 instrument in $CDCl_3$ or DMSO-d_6, operating at 360 and 90 MHz, respectively. IR spectra were taken on a Perkin-Elmer 298 spectrophotometer in KBr pellets. Mass spectra were taken on a Hewlett-Packard LC/MSD 1100 series instrument in the atmospheric pressure chemical ionization (negative or positive APCI) mode.

HPLC Analysis. For reaction monitoring, kinetic investigations, and quality (purity) control of the synthesized library compounds a Shimadzu LC-10 system, that included LC10-AT(VP) pumps, an autosampler (S-10AXL), and a dual wavelength UV detector set at 215 and 280 nm was used. The separations were carried out using a C18 reversed phase analytical column, LiChrospher 100 (E. Merck, 100 x 3 mm, particle size 5 µm) at 25 °C and a mobile phase from (A) 0.1% TFA in 90:10 water/MeCN and (B) 0.1% TFA acid in MeCN (all solvents were HPLC grade, Acros; TFA was analytical reagent grade, Aldrich). The following gradients were applied at a flow rate of 0.5 mL/min: linear increase from solution 30 % B to 100% solution B in 7 min, hold at 100% solution B for 1 min. Sample preparation was done by diluting approximately 5 µL of the MeCN solution with 0.5 mL of MeCN. 5 µL of the solutions were injected onto the HPLC system.

Microwave Irradiation Experiments. All microwave irradiation experiments were carried out using the Emrys™ Synthesizer from PersonalChemistry AB (Uppsala), including proprietary Workflow Manager software (version 2.1). All experiments were carried out in sealed microwave process vials utilizing the standard absorbance level (300 W maximum power). Reaction times under microwave conditions reflect total irradiation times rather than actual reaction times at a given temperature. A detailed description of this single-mode microwave reactor with integrated robotics was recently published (ref. 6).

Synthesis of N3-Acetylated DHPM 2Aa. A mixture of 1.00 mmol (260 mg) of DHPM **1A**, 2.5 mmol (255 mg, 236 µL, 2.5 equiv) of acetic anhydride, 2.5 mmol (348 µL, 2.5 equiv) of TEA, 0.2 mmol DMAP (24 mg, 0.2 equiv) and 2.0 mL of anhydrous MeCN was

irradiated under microwave conditions at 130°C for 10 min in a 5 mL (large) micowave process vial. To the clear solution 200 μL of H_2O was added, and the reaction mixture was subsequently irradiated for an additional 5 min at 100 °C. The solution was filtered through a short plug (1 cm) of silica with an additional mount of 5 mL of MeCN. The filtrate was evaporated and the remaining solid product treated with Et_2O to give 254 mg (84 % yield) of >98 % purity (HPLC) product, mp 169-170 °C (ref. mp 175-176 °C, Kappe, C. O.; Roschger, P. *J. Heterocycl. Chem.* **1989,** *26***,** 55-64). ^{1}H NMR (DMSO-d_6): δ 1.17 (t, *J* = 7.0 Hz, 3H), 2.30 (s, 3H), 2.43 (s, 3H), 4.08-4.14 (m, 2H), 6.46 (s, 1H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.25-7.34 (m, 3H), 10.20 (br s, 1H); MS (pos. APCI): m/z 303 (M+1).

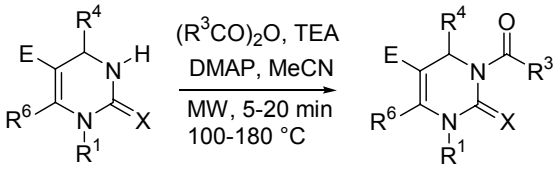
Synthesis of N3-Benzoylated DHPM 2Ab. A mixture of 1.00 mmol (260 mg) of DHPM **1A**, 2.5 mmol (564 mg, 2.5 equiv) of benzoic anhydride, 2.5 mmol (348 μL, 2.5 equiv) of TEA, 0.2 mmol DMAP (24 mg, 0.2 equiv) and 2.0 mL of anhydrous MeCN was irradiated under microwave conditions at 180°C for 15 min in a 5 mL (large) micowave process vial. To the formed yellow solution 200 μL of H_2O was added and the solution was irradiated for an additional 5 min at 100 °C. After cooling, 5 mL of 5 % aq K_2CO_3 solution was added to the stirred, ice-cold solution. After 1 h at 0°C, the formed precipitate was separated by filtration, washed with H_2O and finally twice with 0.5 mL of Et_2O, to give 290 mg (81% yield) of >98 % purity (HPLC) product, mp =155-156°C. ^{1}H NMR (DMSO-d_6): δ 1.20 (t, *J* = 7.0 Hz, 3H), 2.37 (s, 3H), 4.15 (q, *J* = 7.0 Hz, 2H), 6.22 (s, 1H), 7.25-7.47 (m, 7H), 7.47-7.65 (m, 3H), 10.27 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 14.6, 17.7, 55.0, 60.5, 105.1, 126.7, 128.2, 128.4, 129.1, 131.8, 136.2, 140.5, 148.0, 151.4, 165.4, 171.1; MS (pos. APCI) m/z 365 (M+1); IR (KBr, ν, cm^{-1}) 1385, 1630, 1680, 1700, 2945, 3105, 3215.

Synthesis of 1,3-Dibenzoyl-DHPM 3Ab. A mixture of 0.50 mmol (182 mg) of 3-benzoyl-DHPM **2Ab**, 1.0 mmol (116 μL, 2.0 equiv) of benzoyl chloride, 1.25 mmol (174 μL, 2.5 equiv) of TEA, 0.1 mmol of DMAP (12 mg, 0.2 equiv) and 1.0 mL of anhydrous MeCN was irradiated at 100°C for 15 min in a 2.5 mL (small) micowave process vial. After cooling a heavy white precipitate was formed, that was filtered after 1h at 0°C, washed with EtOH and dried to give 121 mg of DHPM **3Ab** (52 % yield, 97 % purity by HPLC), mp = 188-190°C. ^{1}H NMR ($CDCl_3$): δ 1.34 (t, *J*= 6.9 Hz, 3H), 2.53 (s, 3H), 4.33 (q, *J* = 6.9 Hz, 2H), 6.59 (s, 1H), 7.10-7.31 (m, 3H), 7.31-7.57 (m, 10H), 7.57-7.70 (m, 2H); ^{13}C NMR (DMSO-d_6): δ 14.5, 17.2, 54.8, 61.4, 111.5, 127.0, 128.6, 128.9, 129.5, 129.6, 130.6, 132.4, 133.2, 135.2, 135.7, 139.3, 146.1, 151.1, 164.9, 170.7, 171.3; MS (pos. APCI) m/z 469 (M+1): IR (KBr, ν, cm^{-1}) 1220, 1287, 1373, 1648, 1677, 1696.

General Procedure for the Preparation of *N*3-Acylated Dihydropyrimidines in High-Throughput Format (Scheme 2). A mixture of 0.25 mmol of the corresponding DHPM **1A-J** , 0.625 mmol (2.5 equiv) of the corresponding anhydride (**b:** R^3 = Ph; **c**: R^3 = *n*-Bu), 0.625 mmol (2.5 equiv, 63 mg, 87 μL) of TEA, 0.05 mmol (0.2 equiv, 6.1 mg) of DMAP and 0.5 mL of anhydrous MeCN (HPLC Gradient Grade, dried over 3Å molecular sieves) is irradiated in a dry septum-capped 2.5 mL (small) microwave process vial with magnetic stirring in the microwave synthesizer for 5-20 min at 100-180 °C (Table S1). After compressed gas-jet cooling to ca 35 °C (ca 2 min) the vial is moved out of the cavity by the gripper and 2.5 mmol (45 mg, 45 μL) of water are added via syringe through the septum. The mixture is subsequently heated for an additional 5 min at 100 °C in the microwave cavity. After compressed gas-jet cooling to 35 °C (ca 2 min) the solution is filtered through a standard 60 x 12 mm polypropylene frit. The SPE cartridge was prepared by filling the frit successively from the bottom with a 5 mm layer of silica gel 60, followed by a 5 mm pad of activated carbon and finally a 15 mm layer of a basic Al_2O_3/K_2CO_3 mixture (2:1). The desired

*N*3-acylated DHPMs were eluted from the SPE cartridge with EtOAc (5 mL) applying either a mild vacuum or pressure. Evaporation of the clear solution provided products as solids/oils in 47-99 % yield and 84-98 % purity (Table S1). The chemical identity of all compounds was confirmed by ^{1}H NMR and MS measurements (see below).

Table S1. Yields and Purities for N3-Acylated Dihydropyrimidines



1A-J **2Ab, 2Ac.... ....2Jb, 2Jc**

compd	R^1	X	R^4	E	R^6	R^3	time (min)	temp (°C)	yield (%)[a]	purity (%)[b]
2Ab	H	O	Ph	CO_2Et	Me	Ph	10	180	85	>98
2Ac	H	O	Ph	CO_2Et	Me	n-Bu	10	130	97	>98
2Bb	H	O	3,4$(MeO)_2$Ph	CO_2Et	Me	Ph	10	180	90	96
2Bc	H	O	3,4$(MeO)_2$Ph	CO_2Et	Me	n-Bu	10	130	97	>98
2Cb	H	O	3,4$(F)_2$Ph	CO_2Et	Me	Ph	10	180	74	94
2Cc	H	O	3,4$(F)_2$Ph	CO_2Et	Me	n-Bu	10	130	99	>98
2Db	H	O	2,3$(Cl)_2$Ph	CO_2Me	Et	Ph	10	180	n.d.[c]	52
2Dc	H	O	2,3$(Cl)_2$Ph	CO_2Me	Et	n-Bu	10	180	n.d.[c]	86
2Eb	Me	O	3(NO_2)Ph	CO_2allyl	Me	Ph	10	180	98	95
2Ec	Me	O	3(NO_2)Ph	CO_2allyl	Me	n-Bu	10	130	99	95
2Fb	allyl	O	3(NO_2)Ph	CO_2iPr	Me	Ph	20	180	79	96
2Fc	allyl	O	3(NO_2)Ph	CO_2iPr	Me	n-Bu	10	130	99	95
2Gb	H	O	4(Br)Ph	$CONEt_2$	Me	Ph	10	180	75	84
2Gc	H	O	4(Br)Ph	$CONEt_2$	Me	n-Bu	10	130	91	96
2Hb	H	O	3(Me)Ph	COMe	Me	Ph	10	180	47	>98
2Hc	H	O	3(Me)Ph	COMe	Me	n-Bu	10	130	89	>98
2Ib	H	O	Me	CO_2Et	Me	Ph	10	180	79	94
2Ic	H	O	Me	CO_2Et	Me	n-Bu	10	180	98	>98
2Jb	H	S	Ph	CO_2Et	Me	Ph	10	100	50[d]	97
2Jc	H	S	Ph	CO_2Et	Me	n-Bu	5	100	89[e]	93

[a] Yields refer to isolated yields
[b] Purities were established by HPLC analysis at 215 nm. In most cases no additional peaks in addition to the product signals were seen in the ^{1}H NMR (360 MHz).
[c] For these sterically hindered examples with R^4 = 2,3$(Cl)_2$Ph, conversions after 10 min at 180 °C were 52 % (R^3 = Ph) and 86 % (R^3 = n-Bu). For R^3 = Ph the conversion could be increased to 74 % after 20 min of irradiation. Isolated yields were not determined, however.
[d] Isolated by recrystallization of the crude product from from 2-propanol/hexanes.
[e] Isolated by silica gel flash chromatography (hexanes/EtOAc 2:1) of the reaction mixture instead of SPE

2Ab: ^{1}H NMR (DMSO-d_6): δ 1.20 (t, *J* = 7.0 Hz, 3H), 2.37 (s, 3H), 4.15 (q, *J* = 7.0 Hz, 2H), 6.22 (s, 1H), 7.25-7.47 (m, 7H), 7.47-7.65 (m, 3H), 10.27 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 14.6, 17.7, 55.0, 60.5, 105.1, 126.7, 128.2, 128.4, 129.1, 131.8, 136.2, 140.5, 148.0, 151.4, 165.4, 71.1; MS (pos. APCI): m/z 365 (M+1).

2Ac: ^{1}H NMR (DMSO-d_6): δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.25-1.31 (m, 2H), 1.43-1.62 (m, 2H), 2.30 (s, 3H), 2.69-2.78 and 2.90-2.98 (2 m, 2H), 4.09-4.15 (m, 2H), 6.47 (s, 1H), 7.18 (d, *J* = 7.2 Hz, 2H), 7.26-7.34 (m, 3H), 10.15 (br s, 1H); MS (pos. APCI): m/z 345 (M+1).

2Bb: ^{1}H NMR (DMSO-d_6): δ 1.21 (t, *J* = 7.0 Hz, 3H), 2.38 (s, 3H), 3.72 (s, 3H), 3.73 (s, 3H), 4.15 (q, *J* = 7.0 Hz, 2H), 6.17 (s, 1H), 6.80 (m, 1H), 6.86-7.98 (m, 2H), 7.33-7.46 (m, 2H), 7.46-7.60 (m, 3H), 10.19 (s, 1H); MS (pos. APCI): m/z 425 (M+1).

2Bc: ^{1}H NMR (DMSO-d_6): δ 0.85 (t, *J* = 7.3 Hz, 3H), 1.18 (t, *J* = 7.0 Hz, 3H), 1.25-1.31 (m, 2H), 1.42-1.63 (m, 2H), 2.30 (s, 3H), 2.66-2.74 and 2.88-2.92 (2 m, 2H), 3.67 (s, 3H), 3.70 (s, 3H), 4.08-4.13 (m, 2H), 6.41(s, 1H), 6.67 (d, *J* = 8.3 Hz, 1H), 6.76 (s, 1H), 6.88 (d, *J* = 8.4 Hz, 1H), 10.14 (br s, 1H); MS (pos. APCI): m/z 405 (M+1)

2Cb: ^{1}H NMR (DMSO-d_6): δ 1.18 (t, *J* = 7.0 Hz, 3H), 2.39 (s, 3H), 4.14 (q, *J* = 7.0 Hz, 2H), 6.16 (s, 1H), 7.18 (m, 1H), 7.32 (m, 1H), 7.35-7.60 (m, 6H), 10.35 (s, 1H); MS (pos. APCI): m/z 401 (M+1).

2Cc: ^{1}H NMR (DMSO-d_6): δ 0.85 (t, *J* = 7.3 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H), 1.24-1.30 (m, 2H), 1.43-1.60 (m, 2H), 2.31(s, 3H), 2.68-2.77 and 2.89-2.98 (2 m, 2H), 4.06-4.15 (m, 2H), 6.40 (s, 1H), 7.02-7.04 (m, 1H), 7.11-7.17 (m, 1H), 7.40 (q, *J* = 8.6 Hz, 1H), 10.22 (br s, 1H); MS (pos. APCI): m/z 381 (M+1).

2Eb: ^{1}H NMR (DMSO-d_6): δ 2.64 (s, 3H), 3.12 (s, 3H), 4.67 (m, 2H), 5.20 (m, 2H), 5.94 (m, 1H), 6.34 (s, 1H), 7.36-7.77 (m, 7H), 8.10-8.30 (m, 2H); MS (pos. APCI): m/z 436 (M+1).

2Ec: ^{1}H NMR (DMSO-d_6): δ 0.86 (t, *J* = 7.3 Hz, 3H), 1.28-1.32 (m, 2H), 1.46-1.67 (m, 2H), 2.56 (s, 3H), 2.65-2.74 and 2.93-3.02 (2 m, 2H), 3.13 (s, 3H), 4.66 (s, 2H), 5.16-5.22 (m, 2H), 5.86-5.96 (m, 1H), 6.62 (s, 1H), 7.58-7.67 (m, 2H), 7.95 (s, 1H), 8.15 (d, *J* = 7.8 Hz, 1H); MS (pos. APCI): m/z 416 (M+1).

2Fb: ^{1}H NMR (DMSO-d_6): δ 1.20 and 1.26 (2 d, *J*= 5.6 Hz, 6H), 2.58 (s, 3H), 4.30 (m, 1H), 4.94 (m, 2H), 4.98-5.12 (m, 2H), 5.69 (m, 1H), 6.28 (s, 1H), 7.35-7.77 (m, 7H), 8.12 (s, 1H), 8.20 (m, 1H); MS (pos. APCI): m/z 464 (M+1).

2Fc: ^{1}H NMR ($CDCl_3$): δ 0.93 (t, *J* = 7.3 Hz, 3H), 1.21 and 1.30 (2 d, *J* = 6.2 Hz, 6H), 1.34-1.43 (m, 2H), 1.57-1.80 (m, 2H), 2.59 (s, 3H), 2.69-2.78 and 3.03-3.12 (2 m, 2H), 4.23-4.29 and 4.50-4.56 (2 m, 2H), 5.02-5.19 (m, 3H), 5.71-5.79 (m, 1H), 6.67 (s, 1H), 7.48 (t, *J* = 7.9 Hz, 1H), 7.62 (d, *J* = 7.8 Hz, 1H), 8.11-8.14 (m, 2H); MS (pos. APCI): m/z 444 (M+1).

2Gb: ^{1}H NMR (DMSO-d_6): δ 0.60-1.20 (m, 6H), 1.85 (s, 3H), 3.10-3.35 (m, 4H), 5.72 (s, 1H), 7.32 (d, *J* = 8.2, 2H), 7.38-7.46 (m, 2H), 7.48-7.55 (m, 3H), 7.59 (d, *J*= 8.2, 2H), 9.83 (s, 1H); MS (pos. APCI): m/z 470 (M+1).

2Gc: ^{1}H NMR ($CDCl_3$): δ 0.86-1.35 (m, 11H), 1.51-1.67 (m, 2H), 1.86 (s, 3H), 2.77-2.86 and 2.96-3.05 (2 m, 2H), 3.11-3.38 (m, 4H), 6.12 (s, 1H), 7.23 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.4 Hz, 2H), 8.46 (br s, 1H); MS (pos. APCI): m/z 450 (M+1)

2Hb: ^{1}H NMR (DMSO-d_6): δ 2.28 (s, 3H), 2.34 (s, 3H), 2.41 (s, 3H), 6.31 (s, 1H), 7.00-7.60 (m, 9H), 10.15 (s, 1H); MS (pos. APCI): m/z 349 (M+1).

2Hc: ^{1}H NMR (DMSO-d_6): δ 0.86 (t, *J* = 7.3 Hz, 3H), 1.25-1.32 (m, 2H), 1.45-1.63 (m, 2H), 2.24 (s, 3H), 2.28 (s, 3H), 2.33 (s, 3H), 2.67-2.76 and 2.89-2.98 (2 m, 2H), 6.56 (s, 1H), 6.92-6.95 (m, 2H), 7.06 (d, *J* = 7.5 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 10.09 (br s, 1H); MS (pos. APCI): m/z 329 (M+1).

2Ib: ^{1}H NMR (DMSO-d_6): δ 1.18-1.32 (m, 6H), 2.29 (s, 3H), 4.15 (q, *J* = 7.0 Hz, 2H), 5.07 (d, *J* = 6.5 Hz, 1H), 7.36-7.45 (m, 2H), 7.45-7.54 (m, 3H); MS (pos. APCI): m/z 303 (M+1).

2Ic: ^{1}H NMR (DMSO-d_6): δ 0.85 (t, *J* = 7.3 Hz, 3H), 1.07 (d, *J* = 6.5 Hz, 3H), 1.15-1.30 (m, 5H), 1.45-1.59 (m, 2H), 2.21 (s, 3H), 2.68-2.72 and 2.84-2.93 (2 m, 2H), 4.09-4.14 (m, 2H), 5.25-5.32 (m, 1H), 10.00 (br s, 1H); MS (pos. APCI): m/z 283 (M+1).

2Jb: ^{1}H NMR (DMSO-d_6): δ 1.21 (t, *J* = 7.0 Hz, 3H), 2.43 (s, 3H), 4.16 (q, *J* = 7.0 Hz, 2H), 6.05 (s, 1H), 7.27-7.46 (m, 7H), 7.46-7.66 (m, 3H), 1.50 (s, 1H); ^{13}C NMR (DMSO-d_6): δ 14.6, 17.4, 56.2, 60.8, 107.6, 126.8, 128.4, 128.8, 129.0, 129.1, 132.3, 136.0, 140.0, 146.1, 165.4, 173.0, 178.4; MS (pos. APCI): m/z 381 (M+1); IR (KBr, ν, cm^{-1}) 1387, 1498, 1659, 1692, 3300; mp = 152-154°C.

2Jc: ^{1}H NMR (DMSO-d_6): δ 0.85 (t, *J* = 7.2 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H), 1.29 (q, *J* = 7.3 Hz, 2H), 1.46-1.73 (m, 2H), 2.34 (s, 3H), 2.88-2.97 and 3.23-3.32 (2 m, 2H), 4.12-4.20 (m, 2H), 6.35 (s, 1H), 7.17 (d, *J* = 7.4 Hz, 2H), 7.27-7.35 (m, 3H), 11.65 (br s, 1H); MS (pos. APCI): m/z 361 (M+1).

Scavenging Kinetics (Figures 1 and 2). A mixture of 0.25 mmol of DHPM **1A**, 0.625 mmol (2.5 equiv, 141 mg) of Bz_2O, 0.625 mmol (2.5 equiv, 63 mg, 87 μL) of TEA, 0.05 mmol (6.1 mg) of DMAP and 0.5 mL of anhydrous MeCN (HPLC Gradient Grade, dried over 3Å molecular sieves) was irradiated in a dry septum-capped 2.5 mL microwave process vial with magnetic stirring in the microwave synthesizer for 10 min at 180 °C. After cooling to rt the vial was opened and 3.0 equiv of the corresponding supported amine scavenger (**4**: 230 mg; **5**: 248 mg) or 10 equiv of water (2.5 mmol, 45 μL), respectively added (in the case of polystyrene resin **4** an additional amount of 0.1 mL of MeCN was added to allow complete swelling of the resin). For room temperature kinetics (Figure 1) 5 μL aliquots were taken at regular intervalls and diluted with 0.5 mL of MeCN, followed by directl HPLC injection for determination of unscavenged Bz_2O and **3Ab** concentration. In case of microwave scavenging experiments (Figure 2) the vials were resealed after addition of the scavengers, and irradiated 4 times for 150 s each to 80 or 100 °C (Figure 2). 5 μL samples for HPLC measurements were taken after each irradiation cycle to determine the concentration of unscavenged Bz_2O and **3Ab**.

Stability of *N*3-Acylated DHPMs 2Aa and 2Ab towards Scavenger Reagents. In order to establish the stability of the desired *N*3-acylated DHPM products toward the scavenging conditions a series of experiments was performed where isolated, pure samples of DHPMs **2Aa** and **2Ab** were subjected to diamine scavengers **4**, **5**, and water. While **2Aa** and **2Ab** proved totally stable toward those nucleophiles under rt conditions (24 h exposure), trace amounts of hydrolyzed DHPM **1A** were detected by HPLC when samples of **2Aa** or **2Ab** were exposed to 10 equiv of water at 100 °C for 3 min (microwave irradiation) in MeCN in the presence of DMAP/TEA (identical concentrations as in the synthesis step). Increasing the reaction time to 10 min at 100 °C a 2-3 % concentration of DHPM **1A** was detected. Employing the polymer-bound diamine scavengers **4** and **5** (3.0 equiv) the decomposition was more pronounced furnishing significant amounts of DHPM **1A** after 10 min at 100 °C (20-30 %). It has to be noted however, that under the actual synthesis conditions (i.e. in the presence of bis-acylated products, excess anhydrides/acids) this hydrolysis was not observed to a significant extent.

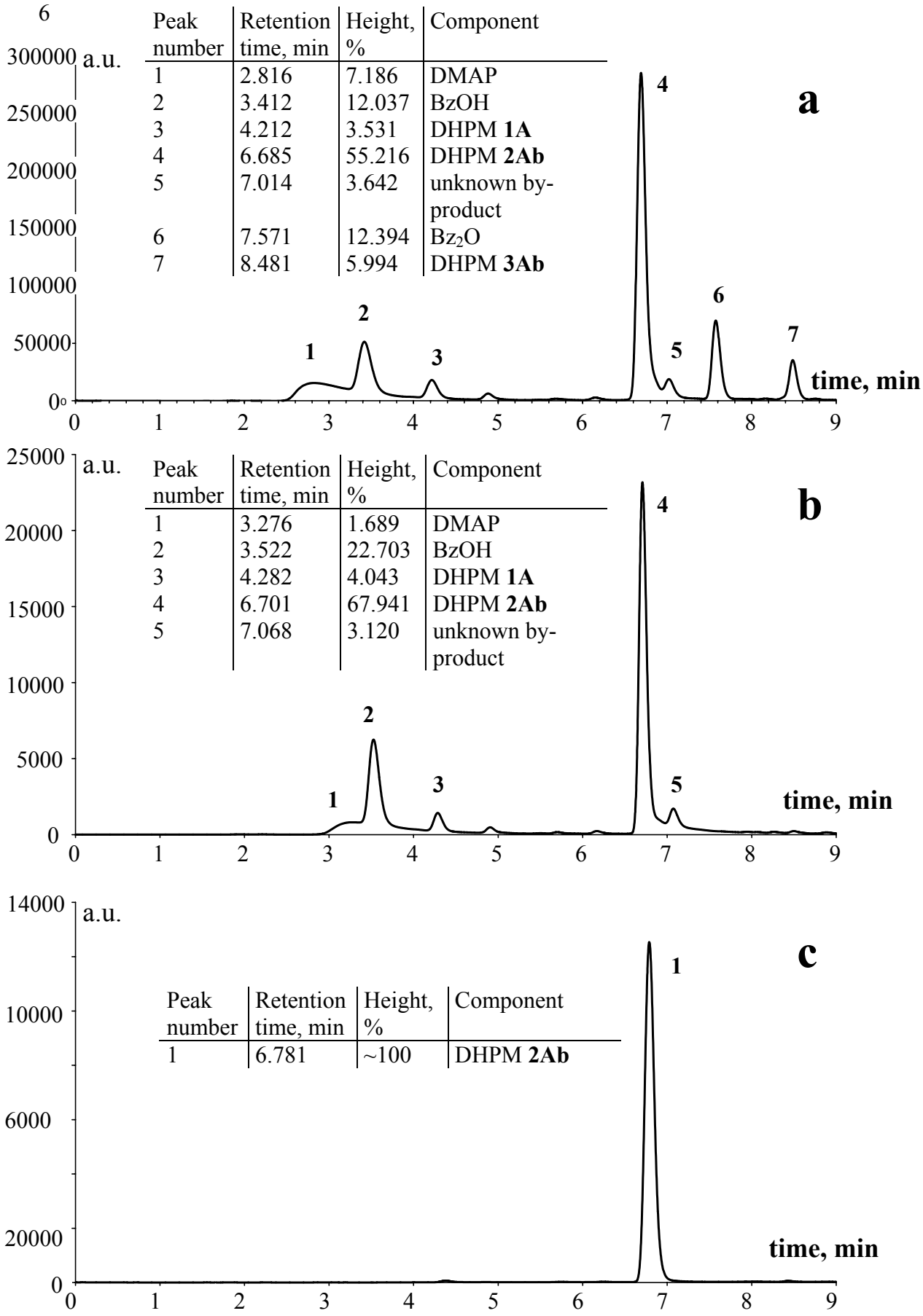


Figure S1. HPLC analysis (280 nm) of the acylation of DHPM **1A** with Bz_2O (Scheme 1): **a**) reaction mixture after MW irradiation at 180°C for 10 min; **b**) after water scavenging (MW irradiation at 100°C for 5 min); and **c**) after SPE column purification.