The use of phosphonium anhydrides for the synthesis of 2-oxazolines, 2-thiazolines and 2-dihydrooxazine under mild conditions

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Supporting Information

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General procedures

Air sensitive reactions were carried out in flame-dried or oven-dried glassware under an inert atmosphere. CH_2Cl_2 was freshly distilled from calcium hydride and THF was freshly distilled over sodium wire with benzophenone used as indicator. Triflic anhydride was distilled from a small amount of phosphorus pentoxide before use. 1,2-Bis(diphenylphosphinyl)ethane, triphenylphosphine oxide, benzoic acid and all synthesised amides were dried under high vacuum for 48 hours prior to use. All other reagents were purchased from commercial suppliers and used without further purification. Column chromatography was performed using silica gel 60Å (0.040-0.063mm). Analytical thin layer chromatography (TLC) was performed using aluminium plates coated with silica gel 69 F_{254} (0.2 mm). TLC plates were visualized by means of ultra-violet light. Melting points were measured on a GallenKamp Variable Temperature Apparatus by the capillary method and are uncorrected. Infrared (IR) spectra were recorded on a Thermo Nicolet-Nexus FTIR apparatus. Elemental analyses were performed at the University of Tasmania. High resolution mass spectroscopy (HRMS) were performed at Griffith University or at the University of Tasmania. Mass spectra were recorded on a Waters micromass ZQ 4000, using electrospray as the ionization technique. Mass Lynx Version 4 (IBM) software was used to acquire and process data. ^{1}H NMR spectra were obtained at 300 or 400 MHz and chemical shifts are reported in parts per million, using the appropriate signal for solvent protons as a reference. The following are abbreviations used in the assignment of signal multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, ddd = doublet of doublets of doublets, ddq = doublet of doublets of quartets, qq = quartet of quartets, br = broad. The identity of known products was confirmed by ^{1}H NMR, which agreed with those reported in the literature. ^{13}C NMR spectra were recorded at 100 MHz.

2.0 Experimental procedures

2.1 Optimisation of the formation of 2-phenyl-4,5-dihydro-1,3-oxazole (5) starting from benzoic acid and 2-amino-1-ethanol

With 2.0 equivalents of reagent 4. For details see experimental section in the article

2.1.1 With 2.8 equivalents of reagent 4. Triflic anhydride (193 μL, 1.15 mmol) was added slowly to a solution of 1,2-bis(diphenylphosphinyl)ethane (495 mg, 1.15 mmol) in dry CH_2Cl_2 (10 mL) at 0

ºC under a nitrogen atmosphere. A thick white precipitate was formed and left to stir at 0 ºC for 30 minutes. Benzoic acid (50 mg, 0.41 mmol) was added and the mixture was warmed to room temperature and then stirred for 1 hour. 2-Amino-1-ethanol (25 μL, 0.41 mmol) and DIPEA (397 μL, 2.3 mmol) were added simultaneously to the reaction mixture (over 5 minutes). The pale yellow mixture was stirred for 16 hours. The reaction mixture was washed with sodium hydrogen carbonate (5% aqueous solution, 2 x 15 mL), dried (anhydrous Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50). Compound **5**[1,2] (9 mg, 15%) was obtained as a colourless oil. δ_H(300 MHz; $CDCl_3$) 4.07 (2 H, t, *J* 9.5, H-4), 4.44 (2 H, t, *J* 9.5, H-5), 7.38-7.51 (3 H, m, *m*-C_6H_5 and *p*-C_6H_5), 7.94-7.98 (2 H, m, *o*-C_6H_5); *m/z* (ES+) 147.8 ($M + H^+$, 100%), 153.9 ($M + Li^+$, 100%).

2.1.2 With 2.4 equivalents of reagent 4. Triflic anhydride (165 μL, 0.98 mmol), 1,2-bis(diphenylphosphinyl)ethane (362 mg, 0.98 mmol), benzoic acid (50 mg, 0.41 mmol), 2-amino-1-ethanol (25 μL, 0.41 mmol) and DIPEA (340 μL, 1.97 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.1.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50) compound **5**[1,2] (23 mg, 38%) was obtained as a colourless oil.

2.1.3 With 2.4 equivalents of reagent 3. Triflic anhydride (331 μL, 1.97 mmol), triphenylphosphine oxide (1.31 g, 4.72 mmol), benzoic acid (100 mg, 0.82 mmol), 2-amino-1-ethanol (49 μL, 0.82 mmol) and DIPEA (751 μL, 4.30 mmol) were reacted in dry CH_2Cl_2 (20 mL) according to procedure 2.1.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50) compound **5**[1,2] (57 mg, 47%) was obtained as a colourless oil.

2.1.4 With 2.0 equivalents of reagent 3. Triflic anhydride (276 μL, 1.64 mmol), triphenylphosphine oxide (1.09 g, 3.90 mmol), benzoic acid (100 mg, 0.82 mmol), 2-amino-1-ethanol (49 μL, 0.82 mmol) and DIPEA (624 μL, 3.60 mmol) were reacted in dry CH_2Cl_2 (20 mL) according to procedure 2.1.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50) compound **5**[1,2] (65 mg, 54%) was obtained as a colourless oil.

2.2 Formation of 2-phenyl-5,6-dihydro-4*H*-1,3-oxazine (26) starting from benzoic acid and 3-amino-1-propanol

2.2.1 Synthesis of 2-phenyl-5,6-dihydro-4*H*-1,3-oxazine (26) with 2.0 equivalent of reagent 4. Triflic anhydride (275 μL, 1.64 mmol), 1,2-bis(diphenylphosphinyl)ethane (980 mg, 2.46 mmol), benzoic acid (100 mg, 0.82 mmol), 3-amino-1-propanol (62 μL, 0.82 mmol) and DIPEA (426 μL, 2.46 mmol) were reacted in dry CH_2Cl_2 (20 mL) according to procedure 2.1.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50) compound **26**[3,4] (72 mg, 55%) was obtained as a colourless oil. δ_H(400 MHz; $CDCl_3$) 1.97 (2 H, tt, *J* 5.7 and 5.7, H-5), 3.61 (2 H, t, *J* 5.7, H-4), 4.35 (2 H, t, *J* 5.7, H-6), 7.34-7.43 (3 H, m, *m*-C_6H_5 and *p*-C_6H_5), 7.88-7.91 (2 H, m, *o*-C_6H_5); MS (ESI, +ve) *m/z*: 161.8 ($[M+H]^+$, 100%).

2.3 Synthesis of amide 6, 7, 11, 12, 13, 14 and 15

***N*-(2-Hydroxyethyl)benzamide (6).** For details see experimental section in the article.

2.3.1 *N*-(2-Hydroxyethyl)-4-nitrobenzamide (7). 4-Nitrobenzoyl chloride (4.0 g, 21.6 mmol) was added dropwise to 2-amino-1-ethanol (1.3 mL, 21.6 mmol) and TEA (3.0 mL, 21.6 mmol) in dry CH_2Cl_2 (200 mL), and the mixture stirred at room temperature under a nitrogen atmosphere for 16 hours. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/CH_2Cl_2, gradient from 0:100 to 100:0). Compound **7**[5-7](4.49 g, 99%) was obtained as an amorphous pale yellow solid. Mp 131-133 ºC (lit.,[5] mp 132-134 ºC). δ_H(400 MHz; acetone-d_6) 3.54 (2 H, dt, *J* 5.7 and 5.7, H-1), 3.72 (2 H, dt, *J* 5.7 and 5.7, H-2), 3.97 (1 H, t, *J* 5.7, OH), 8.08 (1 H, br s, NH), 8.12-8.16 (2 H, m, *o*-C_6H_5), 8.29-8.33 (2 H, m, *m*-C_6H_5); MS (ESI, +ve) *m/z* 216.9 ($[M+Li]^+$, 100%).

2.3.2 Methyl *N*-benzoylserinate (11). Benzoyl chloride (1.24 mL, 10.7 mmol), D,L-methyl serinate.HCl (1.66 g, 10.7 mmol) and TEA (3.3 mL, 23.5 mmol) were reacted in dry CH_2Cl_2 (150 mL) according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50) compound **11**[8] (2.25 g, 94%) was obtained as a colourless oil. δ_H(400 MHz; $CDCl_3$) 3.73 (3 H, s, CH_3), 3.78 (1 H, br s, OH), 3.96 (1 H, dd, *J* 3.6 and 11.3, CH_2), 4.04 (1 H, dd, *J* 3.6 and 11.3, CH_2), 4.80 (1 H, dt, *J* 3.6 and 7.5, α-CH), 7.36 (2 H, t,

J 7.5, *m*-C_6H_5), 7.47 (1 H, t, *J* 7.5, *p*-C_6H_5) 7.78 (2 H, d, *J* 7.5, *o*-C_6H_5); MS (ESI, +ve) *m/z* 223.9 ($[M+H]^+$, 25%), 245.9 ($[M+Na]^+$, 100%), 229.9 ($[M+Li]^+$, 100%).

2.3.3 *N*-(2-Hydroxypropyl)benzamide (12). Benzoyl chloride (1.24 mL, 10.7 mmol), 1-amino-2-propanol (with approx. 6% of 2-amino-1-propanol present, 836 µL, 10.7 mmol) and TEA (1.5 mL, 10.7 mmol) were reacted in dry CH_2Cl_2 (150 mL) according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/hexane, gradient from 10:90 to 50:50), compound **12**[9] (1.81 g, 95%) was obtained as an amorphous white solid containing approximately 6% of *N*-(2-hydroxy-1-methylethyl)benzamide.[10]

N-(2-Hydroxypropyl)benzamide (**12**): Mp 90-93 ºC* (lit.,[9] mp 89-90 ºC). δ_H(400 MHz; $CDCl_3$) 1.22 (3 H, d, *J* 6.4, CH_3), 3.25-3.32 (2 H, m, CH_2, OH), 3.63 (1 H, m, CH_2), 4.01 (1 H, ddq, *J* 3.2, 7.6 and 12.6, CH), 6.94 (1 H, br s, NH), 7.37-7.41 (2 H, m, *m*-C_6H_5), 7.46-7.50 (1 H, m, *p*-C_6H_5) 7.76-7.79 (2 H, m, *o*-C_6H_5); MS (ESI, +ve) *m/z* 179.9 ($[M+H]^+$, 30%), 201.9 ($[M+Na]^+$, 100%), 186.0 ($[M+Li]^+$, 100%).

N-(2-Hydroxy-1-methylethyl)benzamide: δ_H(400 MHz; $CDCl_3$) 1.26 (3 H, d, *J* 6.8, CH_3), 3.63 (1H, m, CH_2), 3.74 (1 H, dd, *J* 3.8 and 11.0, CH_2), 4.21-4.28 (1 H, m, CH), 6.57 (1 H, br s, NH), 7.37-7.41 (2 H, m, *m*-C_6H_5), 7.46-7.50 (1 H, m, *p*-C_6H_5) 7.76-7.79 (2 H, m, *o*-C_6H_5). OH not observed.

* Melting point of **12** containing 6% of *N*-(2-hydroxy-1-methylethyl)benzamide

2.3.4 *N*-(3-Hydroxypropyl)benzamide (13). Benzoyl chloride (3.28 mL, 28.4 mmol), 3-amino-1-propanol (2.16 mL, 28.4 mmol) and TEA (3.8 mL, 28.4 mmol) were reacted in dry CH_2Cl_2 (200 mL) according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/CH_2Cl_2, 50:50), compound **13**[11,12] (5.08 g, 100%) was obtained as an amorphous white solid. Mp 56-58 ºC (lit.,[11] mp 54-57 ºC). δ_H(400 MHz; CD_3OD) 1.84 (2 H, tt, *J* 6.7 and 6.7, H-2), 3.48 (2 H, t, *J* 6.7, H-1), 3.65 (2 H, t, *J* 6.7, H-3), 7.43-7.47 (2 H, m, *m*-C_6H_5), 7.50-7.54 (1 H, m, *p*-C_6H_5), 7.79-7.82 (2 H, m, *o*-C_6H_5), NH and OH not observed; MS (ESI, +ve) *m/z* 201.9 ($[M+Na]^+$, 100%), 186.0 ($[M+Li]^+$, 100%).

2.3.5 *N*-(4-Hydroxybutyl)benzamide (14). Benzoyl chloride (651 µL, 5.6 mmol), 4-amino-1-butanol (521 µL, 5.6 mmol) and TEA (781 µL, 5.6 mmol) were reacted in dry CH_2Cl_2 (50 mL) according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 100:0), compound **14**[13,14] (875 mg, 81%) was obtained as an amorphous white solid. Mp 71-74 ºC (lit.,[14] mp 71-74 ºC). δ_H(400 MHz; $CDCl_3$) 1.56-1.70 (4 H, m,

H-2, H-3), 3.30 (1 H, s, OH), 3.40-3.43 (2 H, m, H-1), 3.63 (2 H, t, *J* 6.0, H-4), 7.13 (1 H, br s, NH), 7.33-7.37 (2 H, m, *m*-C_6H_5), 7.41-7.45 (1 H, m, *p*-C_6H_5), 7.74-7.76 (2 H, m, *o*-C_6H_5); MS (ESI, +ve) *m/z* 193.9 ($[M+H]^+$, 51%). 215.9 ($[M+Na]^+$, 100%). 200.0 ($[M+Li]^+$, 100%).

2.3.6 *N*-(2-Sulfanylethyl)benzamide (15). Benzoyl chloride (1.65 mL, 14.2 mmol), 2-aminoethanethiol (1.1 g, 14.2 mmol) and TEA (1.98 mL, 14.2 mmol) were reacted in dry CH_2Cl_2 (100 mL) for 4 hours according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0), compound **15**[1,15] (2.43 g, 93%) was obtained as an amorphous white solid. Mp 70-71 ºC (lit.,[15] mp 69-70 ºC). δ_H(400 MHz; CD_3OD) 2.72 (2 H, t, *J* 7.0, H-2), 3.54 (2 H, t, *J* 7.0, H-1), 7.46 (2 H, t, *J* 7.4, *m*-C_6H_5), 7.54 (1 H, t, *J* 7.4, *p*-C_6H_5), 7.82 (2 H, d, *J* 7.4, *o*-C_6H_5), SH not observed; MS (ESI, +ve) *m/z* 187.9 ($[M+Li]^+$, 100%).

2.3.7 Attempted synthesis of methyl *N*-benzoylcysteinate (16) using benzoyl chloride. Benzoyl chloride (826 μL, 7.1 mmol), L-methyl cysteinate.HCl (1.25 g, 7.1 mmol) and TEA (4.4 mL, 31.4 mmol) were reacted in dry CH_2Cl_2 (100 mL) according to procedure 2.3.1. After purification by silica column chromatography (ethyl acetate/hexane, gradient from 5:95 to 50:50), methyl *N*,*S*-dibenzoylcysteinate (**25**) (1.19 g, 98% yield based on benzoyl chloride) was obtained as an amorphous white solid. Compound **16** was not isolated.

Methyl *N*,*S*-dibenzoylcysteinate (**25**): Mp 142-144 ºC; (Found: C, 62.64; H, 5.33; N, 4.03; S, 9.08. Calc. for $C_{18}H_{17}NO_4S$: C, 62.96; H, 4.99; N, 4.08; S, 9.34%); ν_{max}/cm^{-1} 3315, 1744, 1651 and 1238. δ_H(400 MHz; $CDCl_3$) 3.66-3.76 (2 H, m, CH_2), 3.82 (3 H, s, CH_3), 5.08 (1 H, dt, *J* 4.8 and 6.8, α-CH), 7.14 (1 H, br d, *J* 6.8, NH), 7.42-7.53 [5 H, m, *p*-$C_6H_5C(O)N$, *m*-$C_6H_5C(O)N$ and *m*-C_6H_5], 7.58-7.62 (1 H, m, *p*-C_6H_5), 7.80-7.82 [2 H, m, *o*-$C_6H_5C(O)N$], 7.95-7.97 (2 H, m, *o*-C_6H_5); δ_C(100 MHz; $CDCl_3$) 30.7 (CH_2), 52.9 (CH_3), 53.1 (α-CH), 127.2 (*o*-[$C_6H_5C(O)N$), 127.5 (*o*-C_6H_5), 128.6 (*m*-C_6H_5), 128.8 [*m*-$C_6H_5C(O)N$], 131.9 [*p*-$C_6H_5C(O)N$], 133.5 [*i*-$C_6H_5C(O)N$], 133.9 (*p*-C_6H_5), 136.3 (*i*-C_6H_5), 167.1 [C(O)N], 170.7 [C(O)O], 191.9 [C(O)S]. MS (ESI, +ve) *m/z* 344.0 ($[M+H]^+$, 79%), 366.1 ($[M+Na]^+$, 100%), 350.1 ($[M+Li]^+$, 100%). HRMS: calcd for $C_{18}H_{17}NO_4S$ $[M+H]^+$: 343.0878. Found: 343.0879.

2.3.8 Synthesis of methyl *N*-benzoylcysteinate (16) using benzoic anhydride and 5 equivalents of L-cysteine methyl ester. Benzoic anhydride (500 mg, 2.21 mmol) in dry CH_2Cl_2 (50 mL) was added dropwise (over 2 hours) to a vigorously stirred solution of L-cysteine methyl ester.HCl (1.90

g, 11.1 mmol) and TEA (1.54 mL, 11.1 mmol) in dry CH_2Cl_2 (150 mL) at 0 ºC under a nitrogen atmosphere. The reaction mixture was warmed slowly to room temperature and stirred for 16 hours. The mixture was washed with sodium hydroxide (2 M aqueous solution, 2 x 150 mL), dried (anhydrous Na_2SO_4), and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/ hexane, gradient from 5:95 to 50:50). Compound **16**[16] (352 mg, 67%) and compound **25** (113 mg, 30% yield based on benzoic anhydride) was isolated as amorphous white solids.

Methyl *N*-benzoylcysteinate (**16**): Mp 63-65 ºC (lit.,[16] mp 63-65 ºC). δ_H(400 MHz; $CDCl_3$) 1.44 (1 H, t, *J* 8.9, SH), 3.13 (1 H, dd, *J* 3.8 and 3.8, CH_2), 3.15 (1 H, dd, *J* 3.8 and 3.8, CH_2), 3.83 (1 H, s, CH_3), 5.11 (1 H, dt, *J* 3.8 and 6.8, CH), 7.17 (1 H, br d, *J* 6.8, NH), 7.44-7.49 (2 H, m, *m*-C_6H_5), 7.51-7.55 (1 H, m, *p*-C_6H_5), 7.84-7.86 (2 H, m, *o*-C_6H_5), SH not observed; MS (ESI, +ve) *m/z* 239.9 ($[M+H]^+$, 27%), 261.9 ($[M+Na]^+$, 100%), 246.0 ($[M+Li]^+$, 100%).

2.4 Optimisation of the cyclisation of *N*-(2-hydroxyethyl)benzamide (6) to 2-phenyl-4,5-dihydro-1,3-oxazole (5)

Varying the equivalents used of reagent 3 or 4:

With 1.0 equivalent of reagent 4. For details see experimental section in the article.

2.4.1 With 1.2 equivalent of reagent 4. Triflic anhydride (122 µL, 0.73 mmol) was added slowly to a solution of 1,2-bis(diphenylphosphinyl)ethane (350 mg, 0.88 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under a nitrogen atmosphere. A thick white precipitate was formed and the mixture was stirred at 0 ºC for 30 minutes. *N*-(2-Hydroxyethyl)benzamide (**6**) (100 mg, 0.61 mmol) and DIPEA (278 µL, 1.60 mmol) were added to the reaction mixture. The pale yellow mixture was warmed to room temperature and then stirred for 16 hours. The reaction mixture was washed with sodium hydrogen carbonate (5% aqueous solution, 2 x 20 mL), dried (anhydrous Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **5**[1,2] (33 mg, 37%) was obtained as a colourless oil.

2.4.2 With 0.5 equivalent of reagent 3. Triflic anhydride (51 µL, 0.30 mmol), triphenylphosphine oxide (202 mg, 0.73 mmol), *N*-(2-hydroxyethyl)benzamide (**6**) (100 mg, 0.61 mmol) and DIPEA

(115 μL, 0.67 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **5**[1,2] (23%) and amide **6**[11] (41%) were present. Compound 6: δ_H(400 MHz; $CDCl_3$) 3.15 (1 H, br s, OH), 3.60 (2 H, dt, *J* 4.4 and 5.3, H-1), 3.81 (2 H, t, *J* 5.3, H-2), 6.89 (1 H, br s, NH), 7.38-7.42 (2 H, m, *m*-C_6H_5), 7.47-7.51 (1 H, m, *p*-C_6H_5), 7.76-7.79 (2 H, m, *o*-C_6H_5); *m/z* (ES+) 172.1 (M + Li^+, 100%).

2.4.3 With 1.0 equivalent of reagent 3. Triflic anhydride (102 μL, 0.61 mmol), triphenylphosphine oxide (404 mg, 1.45 mmol), *N*-(2-hydroxyethyl)benzamide (**6**) (100 mg, 0.61 mmol) and DIPEA (231 μL, 1.33 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **5** (67%) and amide **6**[11] (23%) were present. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **5**[1,2] (56 mg, 60%) was obtained as a colourless oil.

2.4.4 With 1.2 equivalent of reagent 3. Triflic anhydride (122 μL, 0.73 mmol), triphenylphosphine oxide (489 mg, 1.76 mmol), *N*-(2-hydroxyethyl)benzamide (**6**) (100 mg, 0.61 mmol) and DIPEA (272 μL, 1.57 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **5** (34%) and amide **6**[11] (29%) were present. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **5**[1,2] (29 mg, 33%) was obtained as a colourless oil.

2.4.5 With 2.0 equivalent of reagent 3. Triflic anhydride (204 μL, 1.21 mmol), triphenylphosphine oxide (809 mg, 2.91 mmol), *N*-(2-hydroxyethyl)benzamide (**6**) (100 mg, 0.61 mmol) and DIPEA (461 μL, 2.66 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy showed a complex mixture containing some amount of compound **5**[1,2] (23%). Amide **6** was not observed.

Varying the addition time of *N*-(2-hydroxyethyl)benzamide (6) and DIPEA:

With 5 minutes addition time and 1.0 equivalents of reagent 4. For details see experimental section in the article.

2.4.6 With 4 hours addition time and 1.0 equivalents of reagent 4. Triflic anhydride (306 μL, 1.82 mmol) was added slowly to a solution of 1,2-bis(diphenylphosphinyl)ethane (938 mg, 2.2 mmol) in dry CH_2Cl_2 (30 mL) at 0 ºC under a nitrogen atmosphere. A thick white precipitate was formed and the mixture was stirred at 0 ºC for 30 minutes. *N*-(2-Hydroxyethyl)benzamide (**6**) (300 mg, 1.82 mmol) and DIPEA (692 μL, 4.0 mmol) in dry CH_2Cl_2 were added dropwise (over 4 hours) via a syringe pump to the reaction mixture as a solution in dry CH_2Cl_2 (5 mL). Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **5**[1,2] (52%) and amide **6**[11] (48%) were present.

2.4.7 With 1 hour and 13 minutes addition time and 1.0 equivalents of reagent 4. Triflic anhydride (306 μL, 1.82 mmol) and 1,2-bis(diphenylphosphinyl)ethane (938 mg, 2.2 mmol) were reacted in dry CH_2Cl_2 (30 mL) according to procedure 2.4.6. *N*-(2-Hydroxyethyl)benzamide (**6**) (300 mg, 1.82 mmol) and DIPEA (692 μL, 4.0 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise (over 1 hour and 13 minutes) via a syringe pump to the reaction mixture. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 10:90 to 100:0) compound **5**[1,2] (172 mg, 64%) was obtained as a colourless oil.

2.4.8 With 30 minutes addition time and 1.0 equivalents of reagent 4. Triflic anhydride (306 μL, 1.82 mmol) and 1,2-bis(diphenylphosphinyl)ethane (938 mg, 2.2 mmol) were reacted in dry CH_2Cl_2 (30 mL) according to procedure 2.4.6. *N*-(2-Hydroxyethyl)benzamide (**6**) (300 mg, 1.82 mmol) and DIPEA (692 μL, 4.0 mmol) in dry CH_2Cl_2 (5 mL) was added dropwise (over 30 minutes) via a syringe pump to the reaction mixture. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 10:90 to 100:0) compound **5**[1,2] (194 mg, 72%) was obtained as a colourless oil. Amide **6**[11] (72 mg, 24%) was also recovered.

2.5 Optimisation of the cyclisation of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) to 2-(4-nitrophenyl)-4,5-dihydro-1,3-oxazole (8)

Varying the equivalents used of reagent 3 or 4:

2.5.1 With 2.0 equivalent of reagent 3. Triflic anhydride (160 μL, 0.95 mmol), triphenylphosphine oxide (636 mg, 2.28 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (362 μL, 2.09 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1.

Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (34%) and amide **7**[5] (19%) were present in conjunction with significant amounts of unidentified decomposition products.

2-(4-Nitrophenyl)-4,5-dihydro-1,3-oxazole (**8**): Mp 176-178 ºC (lit.,[5] mp 177-179 ºC). δ_H(400 MHz; $CDCl_3$) 4.13 (2 H, t, *J* 9.6, H-4), 4.51 (2 H, t, *J* 9.6, H-5), 8.12-8.14 (2 H, m, *o*-C_6H_5), 8.27-8.29 (2 H, m, *m*-C_6H_5); MS (ESI, +ve) *m/z*: 192.9 ($[M+H]^+$, 47%).

2.5.2 With 1.5 equivalent of reagent 3. Triflic anhydride (120 μL, 0.71 mmol), triphenylphosphine oxide (477 mg, 1.71 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (272 μL, 1.57 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (52%) and amide **7**[5] (15%) were present. Small amounts of unidentified decomposition products were also present.

2.5.3 With 1.2 equivalent of reagent 3. Triflic anhydride (96 μL, 0.57 mmol), triphenylphosphine oxide (384 mg, 1.38 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (214 μL, 1.24 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (54%) and amide **7**[5] (32%) were present. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **8**[5] (45 mg, 49%) was obtained as an amorphous pale yellow solid. Amide **7**[5] (36 mg, 36%) was also isolated.

2.5.4 With 1.0 equivalent of reagent 3. Triflic anhydride (80 μL, 0.48 mmol), triphenylphosphine oxide (318 mg, 1.14 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (181 μL, 1.05 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (56%) and amide **7**[5] (40%) were present. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **8**[5] (51 mg, 56%) was obtained as an amorphous pale yellow solid. Amide **7**[5] (42 mg, 42%) was also isolated.

2.5.5 With 0.9 equivalent of reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and

DIPEA (91 μL, 0.52 mmol) were reacted in dry CH_2Cl_2 (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (52%) and amide **7**[5] (46%) were present.

2.5.6 With 0.8 equivalent of reagent 3. Triflic anhydride (64 μL, 0.38 mmol), triphenylphosphine oxide (252 mg, 0.90 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (145 μL, 0.84 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (39%) and amide **7**[5] (54%) were present.

2.5.7 With 0.5 equivalent of reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (91 μL, 0.52 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (21%) and amide **7**[5] (63%) were present.

2.5.8 With 1.0 equivalent of reagent 4. Triflic anhydride (80 μL, 0.48 mmol), 1,2-bis(diphenylphosphinyl)ethane (227 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (181 μL, 1.05 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **8**[5] (46 mg, 52%) was obtained as an amorphous pale yellow solid. Amide **7**[5] (47 mg, 47%) was also isolated.

2.5.9 With 1.2 equivalent of reagent 4. Triflic anhydride (96 μL, 0.57 mmol), 1,2-bis(diphenylphosphinyl)ethane (275 mg, 0.69 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (214 μL, 1.24 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **8**[5] (36 mg, 39%) was obtained as an amorphous pale yellow solid. Amide **7**[5] (46 mg, 46%) was also isolated.

Varying the reaction temperature:

2.5.10 At 0 ºC with reagent 3. Triflic anhydride (40 µL, 0.24 mmol) was added slowly to a solution of triphenylphosphine oxide (159 mg, 0.57 mmol) in dry CH_2Cl_2 (5 mL) at 0 ºC under a nitrogen atmosphere. A white precipitate was formed and left to stir at 0 ºC for 30 minutes. *N*-(2-Hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 µL, 0.52 mmol) were added to the reaction mixture. The pale yellow mixture was kept at 0 ºC for 8 hours then slowly warmed to room temperature and stirred for an additional 8 hours. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (27%) and amide **7**[5] (62%) were present.

2.5.11 At 10 ºC with reagent 3. Triflic anhydride (80 µL, 0.48 mmol) was added slowly to a solution of triphenylphosphine oxide (318 mg, 1.14 mmol) in dry CH_2Cl_2 (10 mL) at 0 ºC under a nitrogen atmosphere. A white precipitate was formed and left to stir at 0 ºC for 30 minutes. The reaction mixture was warmed to 10 ºC and *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (181 µL, 1.05 mmol) were added. The pale yellow mixture was stirred at 10 ºC for 16 hours. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (48%) and amide **7**[5] (24%) were present.

At 22 ºC with reagent 3. For result see procedure 2.5.4.

2.5.12 At 40 ºC with reagent 3. Triflic anhydride (40 µL, 0.24 mmol) was added slowly to a solution of triphenylphosphine oxide (159 mg, 0.57 mmol) in dry CH_2Cl_2 (5 mL) at 0 ºC under a nitrogen atmosphere. A white precipitate was formed and left to stir at 0 ºC for 30 minutes. *N*-(2-Hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 µL, 0.52 mmol) were added to the reaction mixture. The pale yellow mixture was heated at reflux for 16 hours. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (43%) and amide **7**[5] (52%) were present.

Varying the solvent used in the reaction:

Using CH_2Cl_2 and 1.0 equivalent of reagent 3. For result see procedure 2.5.4

2.5.13 Using CH_3CN and 1.0 equivalent of reagent 3. Triflic anhydride (40 µL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 µL, 0.52 mmol) were reacted in dry CH_3CN (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (30%) and amide **7**[5] (67%) were present.

2.5.14 Using THF and 1.0 equivalent of reagent 3. Triflic anhydride (40 µL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 µL, 0.52 mmol) were reacted in dry THF (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy showed a complex mixture containing traces (<5%) of compound **8**[5].

Varying the reaction concentration:

2.5.15 With 0.095 mM of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) and reagent 3. The yield of compound 8 is the isolated yield. Triflic anhydride (800 µL, 4.76 mmol), triphenylphosphine oxide (3.18 g, 11.4 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (1.0 g, 4.76 mmol) and DIPEA (1.8 mL, 10.55 mmol) were reacted in dry CH_2Cl_2 (50 mL) according to procedure 2.4.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **8**[5] (420 mg, 46%) was obtained as an amorphous pale yellow solid.

2.5.16 With 0.095 mM of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) and reagent 3. The yield of compound 8 is based on crude analysis. Triflic anhydride (40 µL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 µL, 0.52 mmol) were reacted in dry CH_2Cl_2 (2.5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (42%) and amide **7**[5] (47%) were present.

With 0.048 mM of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) and reagent 3. For result see procedure 2.5.4

2.5.17 With 0.024 mM of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) and reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 μL, 0.52 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (13%) and amide **7**[5] (78%) were present.

2.5.18 With 0.005 mM of *N*-(2-hydroxyethyl)-4-nitrobenzamide (7) and reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (90 μL, 0.52 mmol) were reacted in dry CH_2Cl_2 (50 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (13%) and amide **7**[5] (84%) were present.

Varying the reaction time:

2.5.19 Reaction time of 2 and 24 hours with 1.0 equivalent of reagent 3. Triflic anhydride (160 μL, 0.95 mmol), triphenylphosphine oxide (636 mg, 2.28 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (200 mg, 0.95 mmol) and DIPEA (362 μL, 2.09 mmol) were reacted in dry CH_2Cl_2 (20 mL) according to procedure 2.4.1. After 2 hours an aliquot (10 mL) was removed from the reaction mixture and the solvent removed. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (56%) and amide **7**[5] (40%) were present. After an additional 22 hours the remaining reaction mixture was concentrated and analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (57%) and amide **7**[5] (40%) were present.

Varying the equivalents of DIPEA:

2.5.20 With 4.4 equivalents of DIPEA and reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (181 μL, 1.05 mmol) were reacted in dry CH_2Cl_2 (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that amide **7**[5] (88%) was present. No trace of compound **8**[5] was observed.

2.5.21 With 3.0 equivalents of DIPEA and reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (124 μL, 0.71 mmol) were reacted in dry CH_2Cl_2 (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (19%) and amide **7**[5] (67%) were present

With 2.2 equivalents of DIPEA and reagent 3. For result see procedure 2.5.4

2.5.22 With 1.1 equivalents of DIPEA and reagent 3. Triflic anhydride (40 μL, 0.24 mmol), triphenylphosphine oxide (159 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (50 mg, 0.24 mmol) and DIPEA (45 μL, 0.26 mmol) were reacted in dry CH_2Cl_2 (5 mL) according to procedure 2.4.1. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (47%) and amide **7**[5] (42%) were present

Varying the order of addition:

2.5.23 Synthesis of 2-(4-nitrophenyl)-4,5-dihydro-1,3-oxazole (8) with reverse order of addition using reagent 3. Triflic anhydride (80 μL, 0.48 mmol) was added slowly to a solution of triphenylphosphine oxide (318 mg, 1.14 mmol) in dry CH_2Cl_2 (6 mL) at 0 ºC under a nitrogen atmosphere. A white precipitate was formed. The reaction mixture was stirred at 0 ºC for 30 minutes. The slurry was added dropwise (over 30 minutes) to a mixture of *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (181 μL, 1.05) in dry CH_2Cl_2 (4 mL) at 0 ºC. The mixture was warmed to room temperature and then stirred for 16 hours. The reaction mixture was washed with sodium hydrogen carbonate (5% aqueous solution, 2 x 30 mL), dried (anhydrous Na_2SO_4) and filtered. The solvent was removed under reduced pressure. Analysis of the crude mixture by ^{1}H NMR spectroscopy indicated that compound **8**[5] (25%) and amide **7**[5] (33%) were present.

2.6 Attempted trapping of proposed by-product 1-(4-nitrobenzoyl)aziridine (9)

2.6.1 Attempted synthesis of 4-nitro-*N*-[2-(propylamino)ethyl]benzamide (10). Triflic anhydride (80 μL, 0.48 mmol), 1,2-bis(diphenylphosphinyl)ethane (227 mg, 0.57 mmol), *N*-(2-hydroxyethyl)-4-nitrobenzamide (**7**) (100 mg, 0.48 mmol) and DIPEA (181 μL, 1.05 mmol) were

reacted in dry CH_2Cl_2 (10 mL) according to procedure 2.4.1. The mixture was warmed to room temperature and then stirred for 16 hours. Propylamine (196 μL, 2.4 mmol) was added and the mixture stirred for an additional 16 hours. The reaction mixture was washed with sodium hydrogen carbonate (5% aqueous solution, 2 x 15 mL), dried (anhydrous Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0). Compound **8**[5] (51 mg, 51%) was obtained as a colourless oil and amide **7**[5] (46 mg, 46%) was recovered. Compound **10** was not observed or isolated.

2.7 Synthesis of heterocycles 26, 27 and 30 from the corresponding amides

2.7.1 2-Phenyl-5,6-dihydro-4*H*-1,3-oxazine (26). Triflic anhydride (179 μL, 1.06 mmol) was added slowly to a solution of 1,2-bis(diphenylphosphinyl)ethane (549 mg, 1.28 mmol) in dry CH_2Cl_2 (15 mL) at 0 ºC under a nitrogen atmosphere. *N*-(3-Hydroxypropyl)benzamide (**13**) (191 mg, 1.06 mmol) and DIPEA (405 μL, 2.34 mmol) in dry CH_2Cl_2 (20 mL) were added dropwise (over 5 minutes) to the reaction mixture. The pale yellow mixture was warmed to room temperature and then stirred for 2 hours. The reaction mixture was washed with sodium hydrogen carbonate (5% aqueous solution, 2 x 30 mL), dried (anhydrous Na_2SO_4) and filtered. The solvent was removed under reduced pressure and the residue purified by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0). Compound **26**[3,4] (121 mg, 71%) was obtained as a colourless oil. δ_H(400 MHz; $CDCl_3$) 1.97 (2 H, tt, *J* 5.7 and 5.7, H-5), 3.61 (2 H, t, *J* 5.7, H-4), 4.35 (2 H, t, *J* 5.7, H-6), 7.34-7.43 (3 H, m, *m*-C_6H_5 and *p*-C_6H_5), 7.88-7.91 (2 H, m, *o*-C_6H_5); *m/z* (ES+) 161.8 ($M + H^+$, 100%).

2.7.2 2-Phenyl-4,5,6,7-tetrahydro-1,3-oxazepine (27). Triflic anhydride (97 μL, 0.57 mmol), 1,2-bis(diphenylphosphinyl)ethane (297 mg, 0.69 mmol), *N*-(4-hydroxybutyl)benzamide (**14**) (111 mg, 0.57 mmol) and DIPEA (219 μL, 1.26 mmol) were reacted in dry CH_2Cl_2 (11 mL) according to procedure 2.7.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 25:75 to 100:0) compound **27** (11 mg, 11%) was obtained as a colourless oil. ν_{max}/cm^{-1} 3436, 3052, 2974, 2880, 1626, 1426 and 1266. δ_H(400 MHz; $CDCl_3$) 1.91 (4 H, br s, H-5 and H-6), 3.44 (2 H, br s, H-7), 3.65 (2 H, br s, H-4), 7.38-7.42 (3 H, m, *m*-C_6H_5 and *p*-C_6H_5), 7.50-7.53 (2 H, m, *o*-C_6H_5); δ_C(100 MHz; $CDCl_3$) 24.5 (C-5 or C-6), 26.1 (C-5 or C-6), 46.1 (C-4), 49.6 (C-7), 127.1 (*o*-C_6H_5), 128.2 (*m*-C_6H_5), 129.7 (*p*-C_6H_5), 137.2 (*i*-C_6H_5), 169.7 (C-

2). MS (ESI, +ve) *m/z*: 175.8 ($[M+H]^+$, 100%), 181.9 ($[M+Li]^+$, 100%). HRMS: calcd for $C_{11}H_{13}NO$ $[M+H]^+$: 175.0997. Found: 175.0997.

2.7.3 2-Phenyl-4,5-dihydro-1,3-thiazole (30)

Triflic anhydride (136 μL, 0.81 mmol), 1,2-bis(diphenylphosphinyl)ethane (416 mg, 0.97 mmol), *N*-(2-sulfanylethyl)benzamide (**15**) (146 mg, 0.81 mmol) and DIPEA (307 μL, 1.77 mmol) were reacted in dry CH_2Cl_2 (16 mL) according to procedure 2.7.1. After work-up and purification by silica column chromatography (ethyl acetate/hexane, gradient from 10:90 to 100:0) compound **30**[17-19] (76 mg, 57%) was obtained as a pale yellow oil and disulfide **24**[20,21] (22 mg, 16% yield based on **15**) was isolated as an amorphous white solid. Amide **15**[1,15] (35 mg, 24%) was also recovered.

2-Phenyl-4,5-dihydro-1,3-thiazole (**30**): δ_H(400 MHz; $CDCl_3$) 3.43 (2 H, t, *J* 8.3, H-5), 4.48 (2 H, t, *J* 8.3, H-4), 7.40-7.47 (3 H, m, *m*-C_6H_5 and *p*-C_6H_5), 7.83-7.86 (2 H, m, *o*-C_6H_5); MS (ESI, +ve) *m/z*: 163.9 ($[M+H]^+$, 100%).

N,*N*'-(Disulfanediyldiethane-2,1-diyl)dibenzamide (**24**): Mp 130-132 ºC (lit.,[20] mp 130 ºC). δ_H(400 MHz; $CDCl_3$) 3.01 (4 H, t, *J* 6.2, NHC*H*$_2$), 3.82 (4 H, dt, *J* 6.2 and 6.2, CH_2S), 6.95 (2 H, br s, NH), 7.41-7.46 (4 H, m, *m*-C_6H_5), 7.49-7.54 (2 H, m, *p*-C_6H_5), 7.83-7.85 (4 H, m, *o*-C_6H_5); δ_C(100 MHz; $CDCl_3$) 38.6 (CH_2S), 40.4 (NCH_2), 128.3 (*o*-C_6H_5), 129.5 (*m*-C_6H_5), 132.7 (*p*-C_6H_5), 135.5 (*i*-C_6H_5), 170.3 [C(O)N]. MS (ESI, +ve) *m/z* 361.2 ($[M+H]^+$, 12%), 383.1 ($[M+Na]^+$, 100%), 367.2 ($[M+Li]^+$, 100%). HRMS: calcd for $C_{18}H_{21}N_2O_2S_2$ $[M+H]^+$: 361.79. Found: 361.1040.

2.7.4 Methyl 2-phenyl-4,5-dihydro-1,3-thiazole-4-carboxylate (31).

Triflic anhydride (89 μL, 0.53 mmol), 1,2-bis (diphenylphosphinyl)ethane (257 mg, 0.60 mmol) and *N*-[2-(triphenylmethylsulfanyl)ethyl]benzamide (**23**) (169 mg, 0.35 mmol) were reacted in dry CH_2Cl_2 (10 mL) according to the representative procedure above. Compound **31**[19,22] (68 mg, 88%) was obtained as a pale yellow oil. δ_H(400 MHz; $CDCl_3$) 3.63-3.76 (2 H, m, H-5), 3.84 (3 H, s, CH_3), 5.31 (1 H, t, *J* 9.2, H-4), 7.40-7.44 (2 H, m, *m*-C_6H_5), 7.47-7.51 (1 H, m, *p*-C_6H_5), 7.87-7.90 (2 H, m, *o*-C_6H_5); *m/z* (ES+) 221.9 ($M + H^+$, 71%), 227.9 ($M + Li^+$, 71%).

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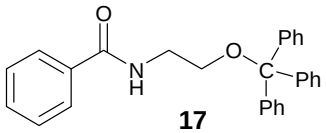
3. ^{1}H NMR spectra of compounds 17-22, 25, 27, and 29



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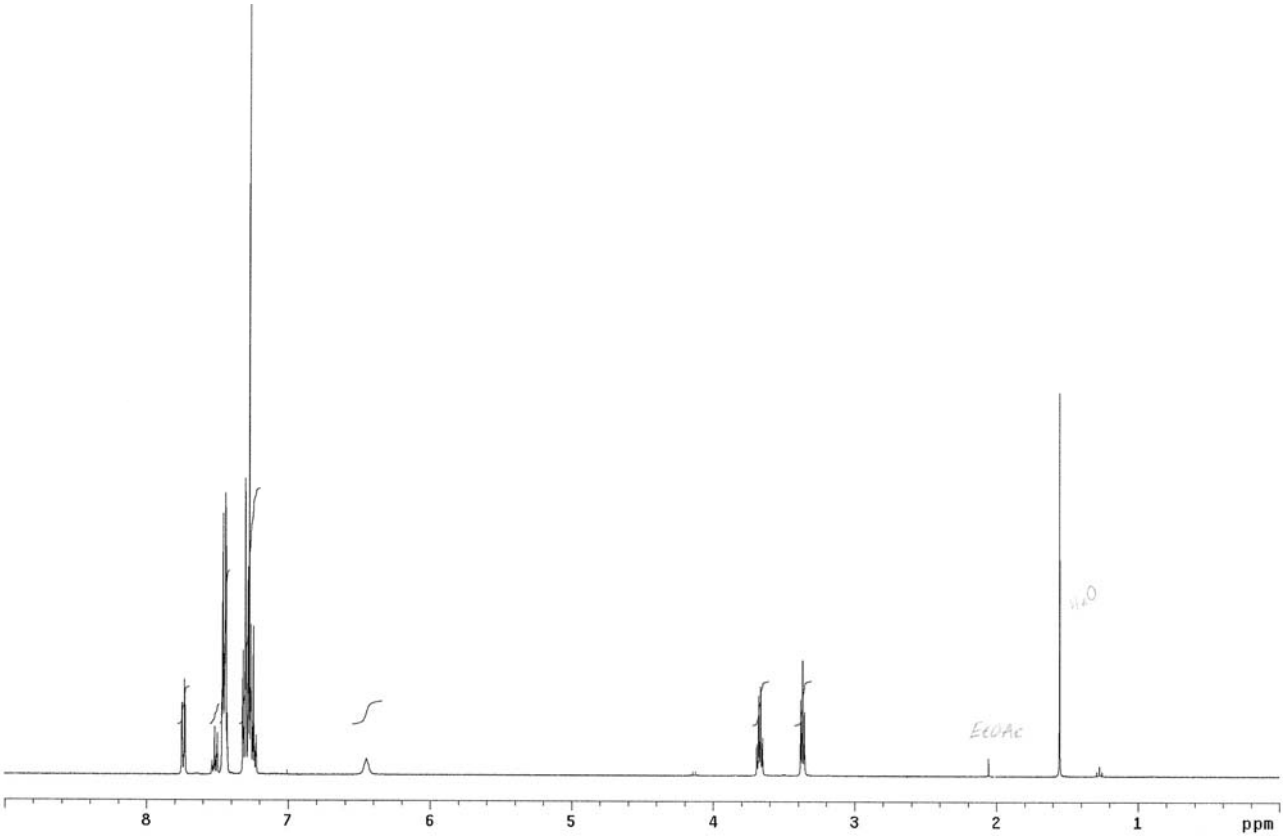

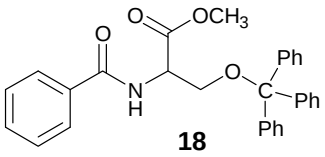

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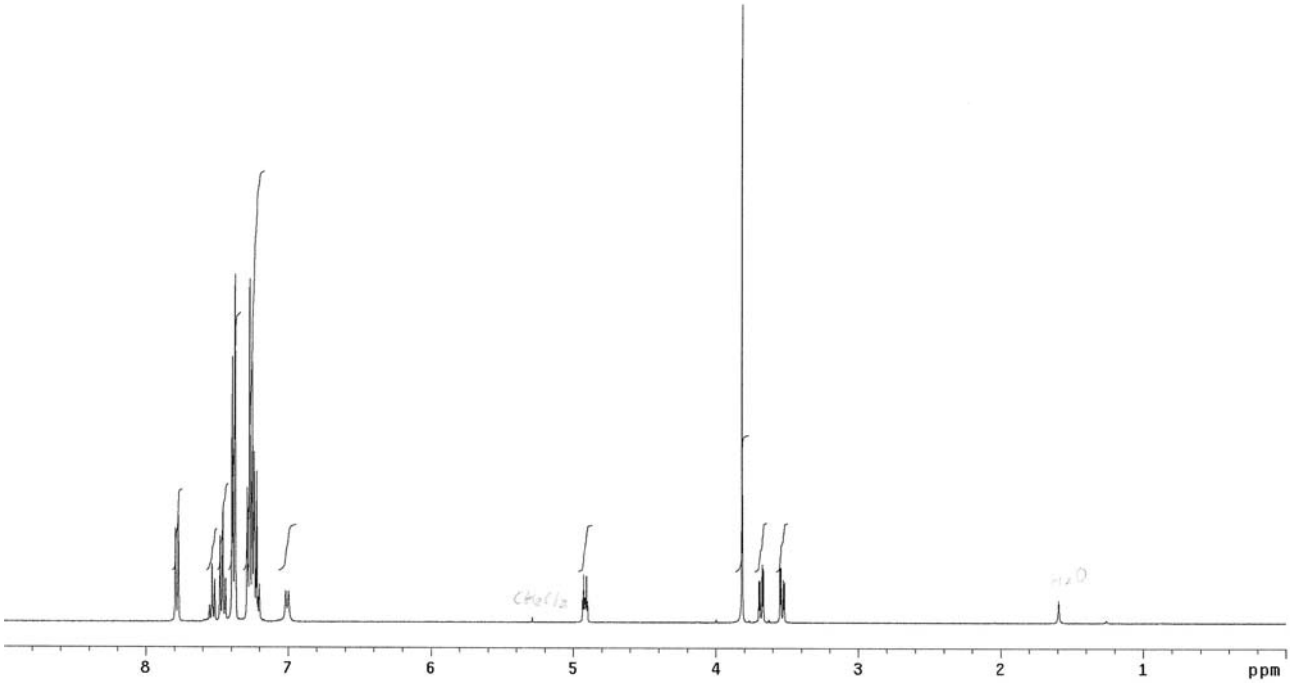

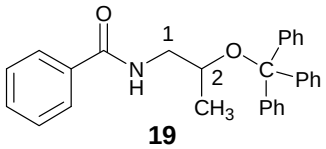

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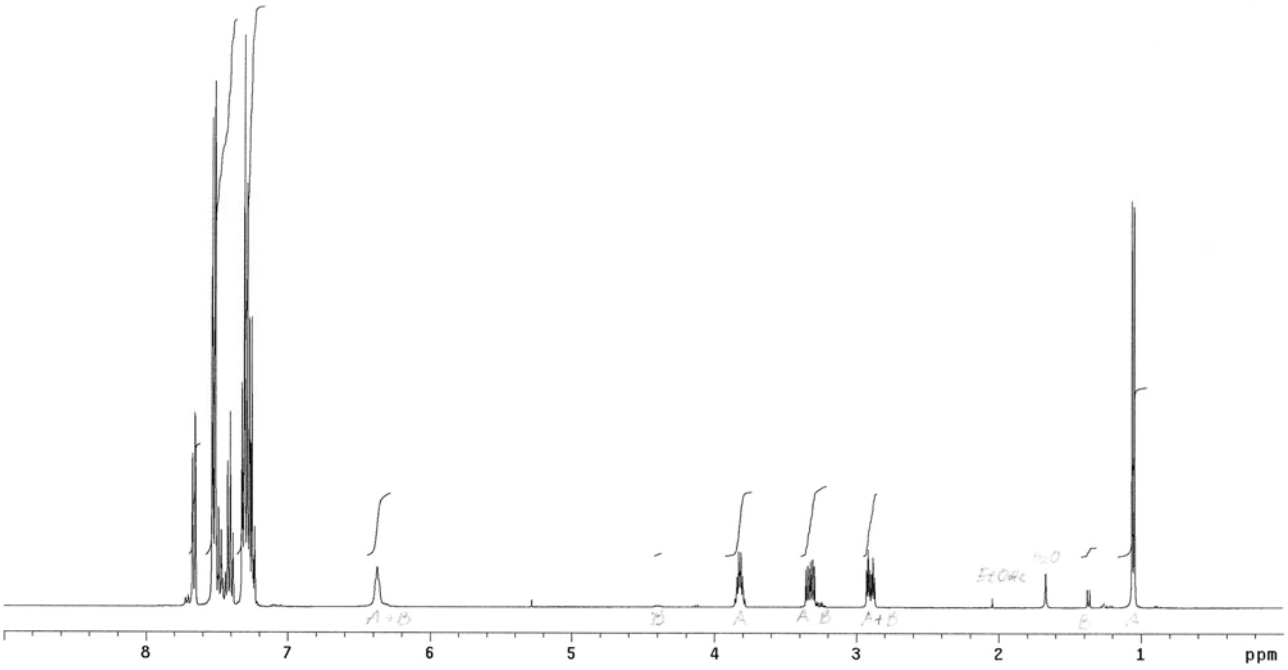
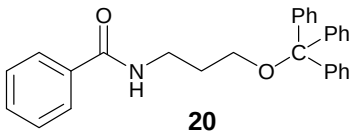


A = methyl epimer at C2
B = methyl epimer at C1 (inseparable)



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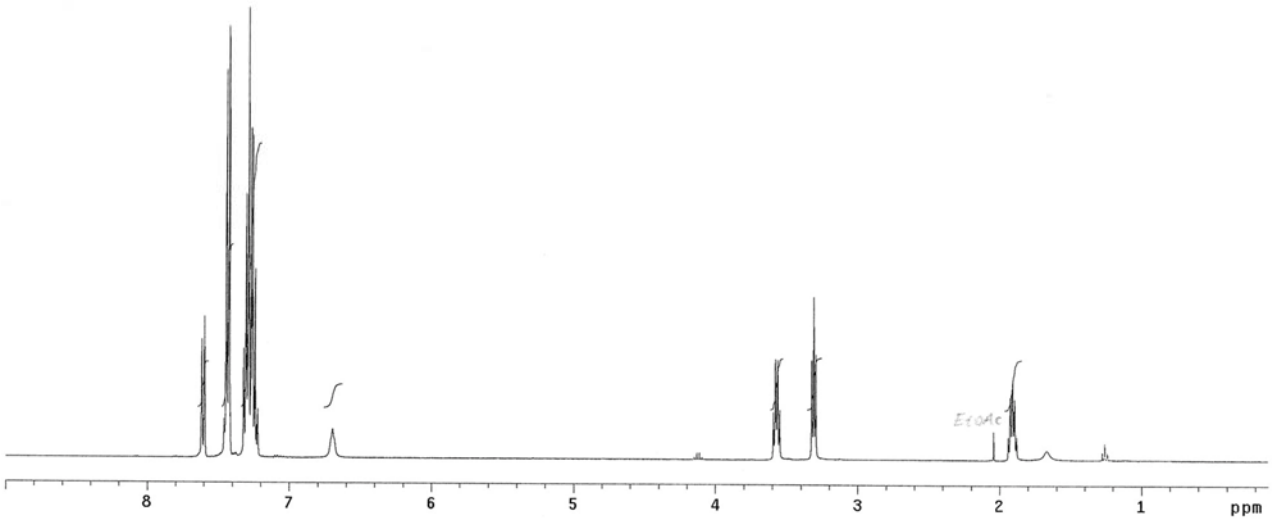

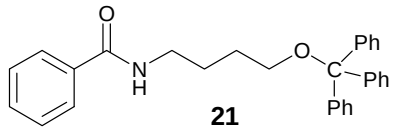

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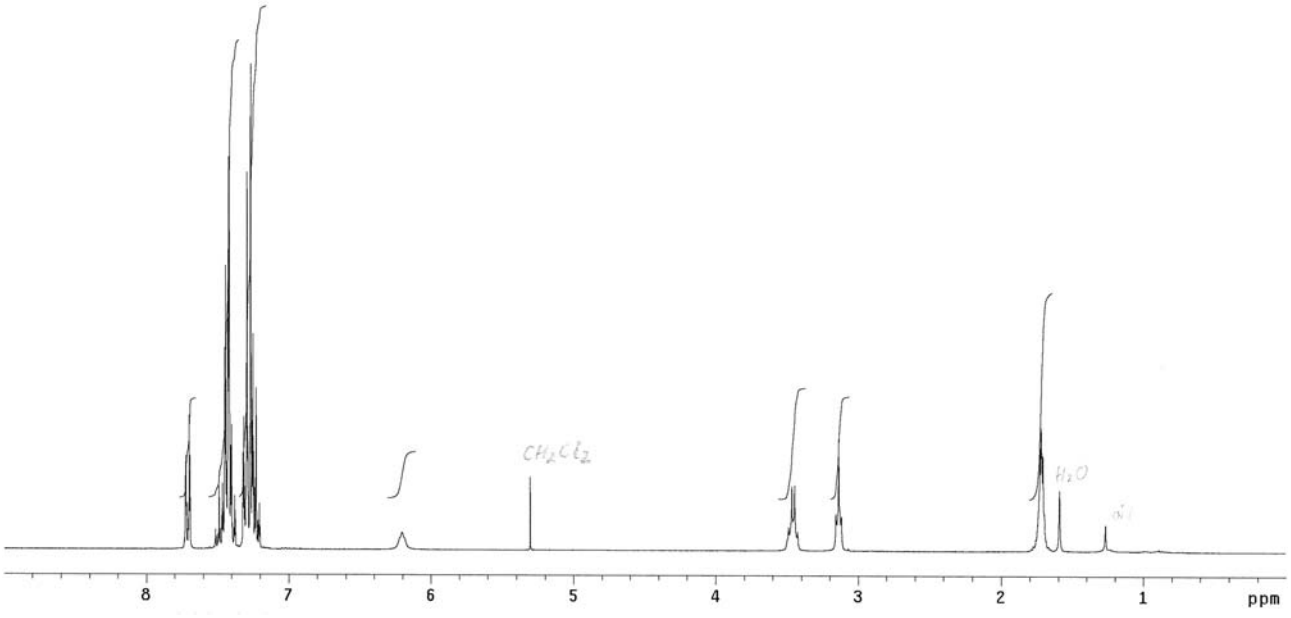

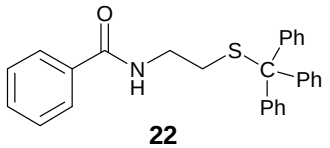

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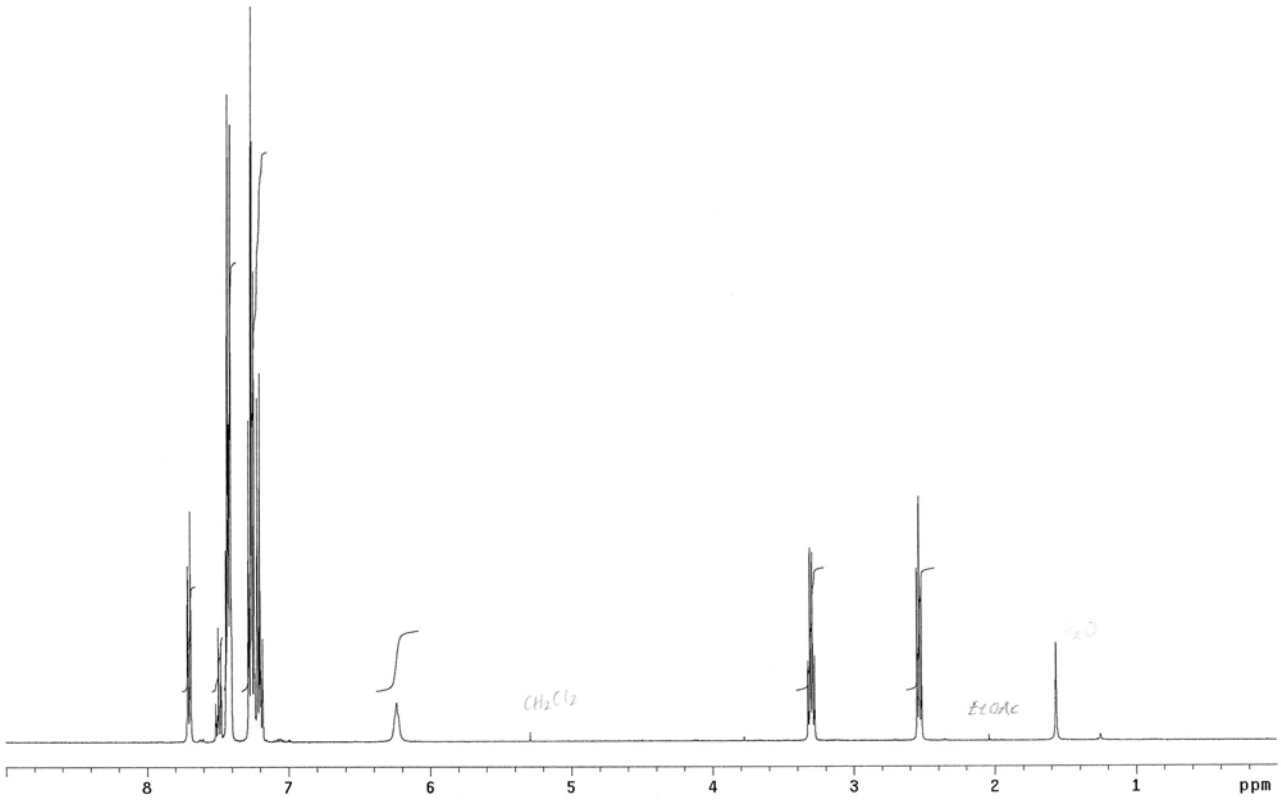

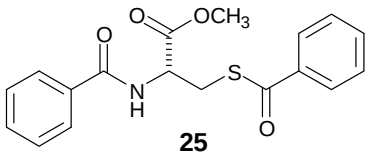

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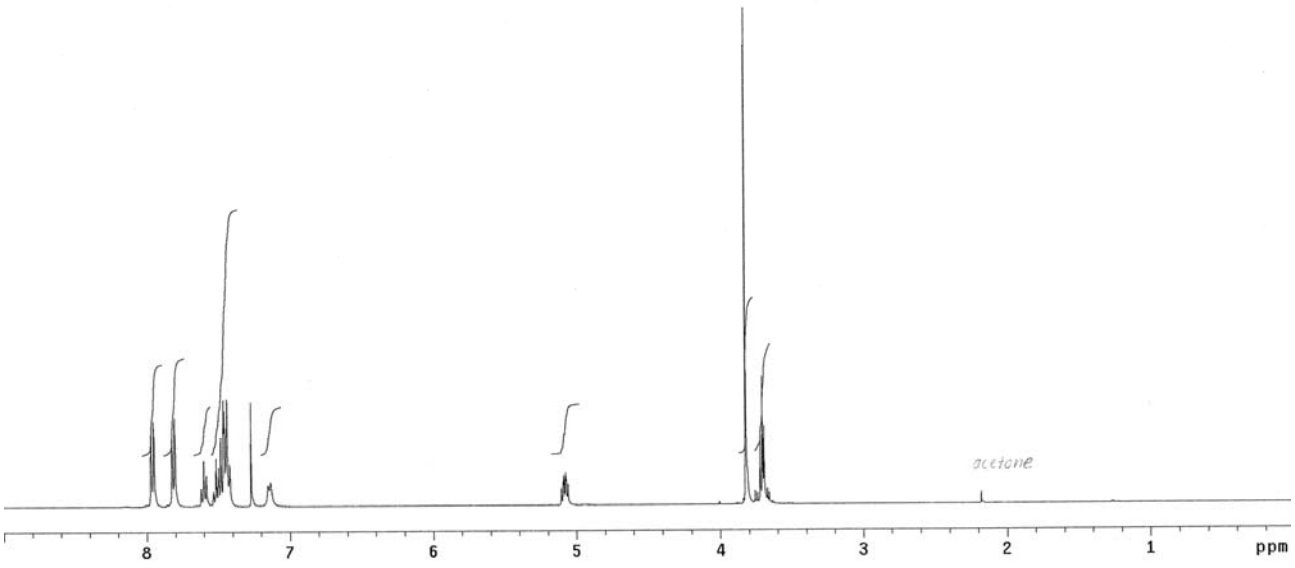

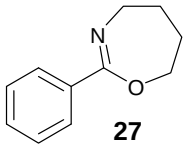

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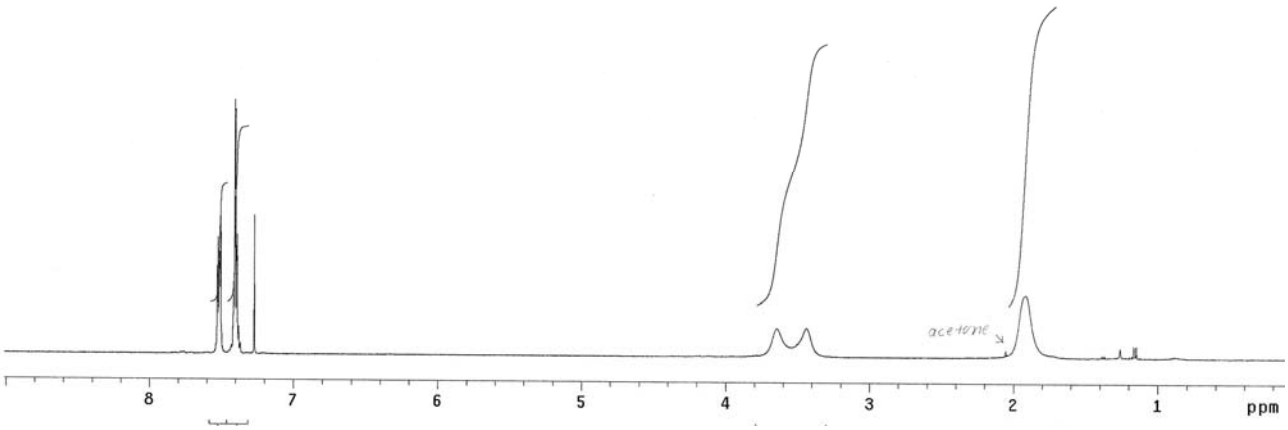

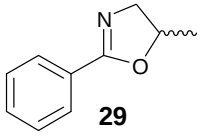

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