Supporting Information

Aqueous and Biphasic Nitrile Hydration Catalyzed by a Recyclable Ru(II) Complex under Atmospheric Conditions

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Experimental Section

Materials and Methods.

All manipulations were performed in air. Solvents (water, *tert*-amyl alcohol, toluene) were used as received without further purification or degassing. Benzonitrile, *o*-tolunitrile, *m*-tolunitrile, *p*-tolunitrile, *p*-methoxybenzonitrile, *p*-cyanophenol, *p*-nitrobenzonitrile, *p*-bromobenzonitrile, *p*-cyanobenzaldehyde, *2*-cyanopyridine, *4*-methylbenzyl cyanide, heptyl cyanide, pivalonitrile, acrylonitrile, ruthenium trichloride trihydrate, and deuterated NMR solvents were obtained from commercial sources and used as received. 1,3,5-Triaza-7-phosphaadamantane (PTA),[1] $[RuCl_2(\eta^6\text{-toluene})]_2$,[2] and $[RuCl_2(PTA)_4]$[3] were synthesized as reported in the literature. GC/MS analyses were obtained using a Varian CP 3800 GC (DB5 column) equipped with a Saturn 2200 MS and a CP 8410 auto-injector or an Agilent 7890A GC equipped with an Agilent 5975C inert MSD with triple axis detector and an Agilent 7693 autosampler. NMR spectra were recorded on a Varian NMR System 400 spectrometer with chemical shifts reported in ppm. ^1H and ^{13}C NMR spectra were referenced to residual solvent relative to tetramethylsilane (TMS). Phosphorus chemical shifts are relative to an external reference of 85% H_3PO_4 in D_2O with positive values downfield of the reference. The inductively coupled plasma atomic emission spectroscopy (ICP-AES) analysis was determined by Nevada Analytical Services (Reno, NV).

General Procedure for the Catalytic Nitrile Hydration.

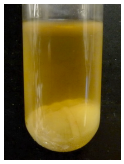
Under air, 1 mmol nitrile, 3 mL water, and 5 mol% $[RuCl_2(PTA)_4]$ (40 mg) were added to a Telfon-sealed screw-cap culture tube and stirred at 100 °C for 7 h. The GC yields were obtained by taking a small aliquot (~50 μL) from the hot solution and extracting with CH_2Cl_2 (2 mL × 3) and analysing by GC-MS. Isolated yields were obtained by either decanting the aqueous layer from the product crystals or by evaporation of the solvent followed by column chromatography over silica gel using ethyl acetate as eluent. The identity of the resulting amides was assessed by comparison of their ^1H and $^{13}C\{^1H\}$ NMR spectroscopic data with those reported in the literature and by their retention time and fragmentation from GC/MS with that of an authentic sample.

Most of the product amides crystallized out from water after hydration. However, in some cases the product did not precipitate out of aqueous solution in appreciable quantity. In the cases where isolated yield by decantation was < 60% the reaction mixture was evaporated to dryness and purified by column chromatography. Purification by column chromatography: Benzamide (a), *m*-toluamide (c), *p*-hydroxybenzamide, *p*-nitrobenzamide (f), *4*-formylbenzamide (h), picolinamide, octamide, pivalamide, acrylamide. After the general procedure, the solvent was removed under reduced pressure. The resulting crude product was purified by column chromatography over silica gel using ethyl acetate as eluent yielding a white solid. Purification by decantation: *o*-Toluamide (b), *p*-toluamide (d), *p*-methoxybenzamide (e), *p*-bromobenzamide (g), *2*-(*p*-tolyl)-acetamide (i). After the general procedure, the reaction tube was cooled to RT and placed in fridge for one hour. The amide crystals were filtered and washed with cold water (5 mL × 3) to give a white solid.

Figure 1-S. Photographs of the reaction tubes after hydration, showing different amounts of amide crystals precipitated from the aqueous solution.

(a) Hydration of benzonitrile

(b) Hydration of *o*-tolunitrile

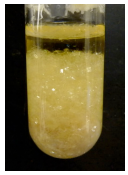


(c) Hydration of *m*-tolunitrile

(d) Hydration of *p*-tolunitrile

(e) Hydration of *p*-methoxybenzonitrile

(f) Hydration of *p*-nitrobenzonitrile



(g) Hydration of *p*-bromobenzonitrile

(h) Hydration of *p*-formyl-benzonitrile

(i) Hydration of 4-methylbenzyl cyanide

Catalyst Recycling Experiments in Water.

Under air, the corresponding nitrile (1 mmol), water (3 mL), and the ruthenium catalyst [$RuCl_2(PTA)_4$] (5 mol%) were introduced into a Telfon-sealed screw-cap culture tube, and the reaction mixture was stirred at 100 °C for 7 hours. The conversion (GC yield) was obtained by taking a small aliquot (~50 µL) from the hot solution, which after extraction with CH_2Cl_2 (2 mL × 3) was analyzed by GC-MS. After reaction completion, the solution was allowed to cool to room temperature and then placed in a refrigerator overnight, during which time the amide precipitated from solution. The aqueous supernatant containing catalyst was transferred to another reaction tube by syringe fresh nitrile was added and the tube heated to 100 °C for the next hydration cycle. A small amount of cold water (~0.3 mL) was used to rinse the benzamide crystals and was transferred to the new tube to maximize catalyst recovery.

Figure 2-S. Photographs of recycling 4-methylbenzyl cyanide in water. In the case of 4-methylbenzyl cyanide a slight decrease in activity was observed after the fifth run attributed to incomplete catalyst recovery during transfer of the aqueous supernatant indicated by a faint yellow color observed in the product after the sixth run**.** The fine solid product made complete transfer of the aqueous catalyst supernatant difficult, resulting in the lower conversion.

Catalyst Recycling Experiments in an Aqueous/Organic Biphasic System.

Under air, the corresponding nitrile (1 mmol), water (1.5 mL), *tert*-amyl alcohol (1.5 mL), and the ruthenium catalyst [$RuCl_2(PTA)_4$] (5 mol%) were introduced into a Telfon-sealed screw-cap culture tube, and the reaction mixture was stirred at 100 °C for 24 hours and allowed to cool to room temperature and placed in a refrigerator for one hour. The reaction was monitored by taking aliquots from the organic layer followed by dilution with CH_2Cl_2 and analysis by GC-MS. After reaction completion, toluene (2 mL) was added to this biphasic media followed by cooling the tube to ~0 °C for one hour. The isolation of benzamide was performed by decanting the organic layer and evaporating to dryness to afford clean product. The organic layers of runs 1, 4 and 7 were examined by ICP-AES analysis. The results are shown in Table 1-S.

Table 1-S. Biphasic hydration of benzonitrile with [$RuCl_2(PTA)_4$] recycling experiments and leaching of ruthenium into the organic layer determined by ICP-AES.[a]

Substrate	Trial	Recycling experiment[b]						
		1	2	3	4	5	6	7
	1[c]	99	99	99	98	98	89	88
	2[c]	99 (2.9)[e]	99	99	98 (24.5)[e]	90	88	82 (77.2)[e]
	3[d]	99 (58.3)[e]	99	99	94 (150.7)[e]	83	78	76 (125.2)[e]

[a] Conditions: nitrile (1 mmol), [$RuCl_2(PTA)_4$] (5 mol%), H_2O (1.5 mL), *tert*-amyl alcohol (1.5 mL), 100 °C, 24 h, in air. [b] % conversion determined by GC. [c] With addition of toluene. [d] Without addition of toluene. [e] [Ru] (in ppm) in organic layer determined by ICP-AES.

Reference

1. (a) Daigle, D. J.; Pepperman, A. B., Jr.; Vail, S. L. *J. Heterocycl. Chem.* **1974**, *11*, 407-408. (b) Daigle, D. J. *Inorg. Synth.* **1998**, *32*, 40-45.

2. Bennett, M. A.; Smith, A. K. *J. Chem. Soc., Dalton. Trans.* **1974**, 233-241.

3. (a) D. J. Darensbourg, F. Joó, M. Kannisto, A. Katho, J. H. Reibenspies and D. J. Daigle, *Inorg. Chem.*, **1994**, *13*, 200-208. (b) D. J. Darensbourg, F. Joó, M. Kannisto, A. Katho and J. H. Reibenspies, *Organometallics*, **1992**, *11*, 1990-1993. (c) C. A. Mebi and B. J. Frost, *Inorg. Chem.*, **2007**, *46*, 7115-7120.

Table 2-S. Benzonitrile hydration catalyzed by $[RuCl_2(PTA)_4]$ at various catalyst loading.[a]

Entry	Catalyst (mol%)	Time (h)	Conv.[b] (%)	TON[c]	TOF[d] (h^{-1})
1	5	0.5	13	2.6	5.2
2	5	1	32	6.4	6.4
3	5	1.5	53	10.6	7.1
4	5	2	67	13.4	6.7
5	5	3	80	16	5.3
6	5	4	90	18	4.5
7	5	5	97	19.4	3.9
8	5	6	98	19.6	3.3
9	5	7	99	19.8	2.8
10	1	7	87	87	12.4
11	1	24	99	99	4.1
12	0.1	70	99	990	14.1
13[e]	0.1	31	98(93)[f]	930[g]	30[g]
14	0.01	504	66	6600	13.1
15	0.01	1415	79	7900	5.6
16[h]	0.01	528	(83)[i]	8300[g]	15.7[g]
17[j]	0.001	864	(12)[i]	12000[g]	13.9[g]
18	0.001	1680	(17)[i]	17000[g]	10.3[g]
19	0.001	2328	(22)[i]	22000[g]	9.5[g]

[a] Conditions: nitrile (1 mmol, 0.33 M), H_2O (3 mL), 100 °C, in air. [b] Determined by GC (isolated yields in parentheses). [c] TON defined as (mol product)/(mol catalyst). [d] TOF defined as (mol product)/(mol catalyst)/h. [e] Nitrile (20 mmol, 6.66 M in water), $[RuCl_2(PTA)_4]$ (0.1 mol%, 0.02 mmol), H_2O (3 mL). [f] Isolated yield obtained by recrystallization from water (2.12 g, 88%) and purification of the filtrate by chromatography providing an additional 0.13 g (5%) benzamide. [g] Based on isolated yield. [h] Nitrile (20 mmol, 6.66 M in water), $[RuCl_2(PTA)_4]$ (0.01 mol%, 0.002 mmol), H_2O (3 mL). [i] Isolated yield by column chromatography. [j] Nitrile (20 mmol, 6.66 M in water), $[RuCl_2(PTA)_4]$ (0.001 mol%, 0.0002 mmol), H_2O (3 mL).

Figure 3-S. Photographs of gram scale benzonitrile hydration (entry 13 in Table 2-S). (a) Before hydration, two phases were observed (upper: 2 mL benzonitrile; bottom: catalyst in 3 mL water). (b) During hydration. (c) After hydration was complete (31 hours), a homogeneous solution was observed while hot. (d) After cooling to room temperature, benzamide crystals precipitated out from water. (e) Isolated benzamide by recrystallization from water.

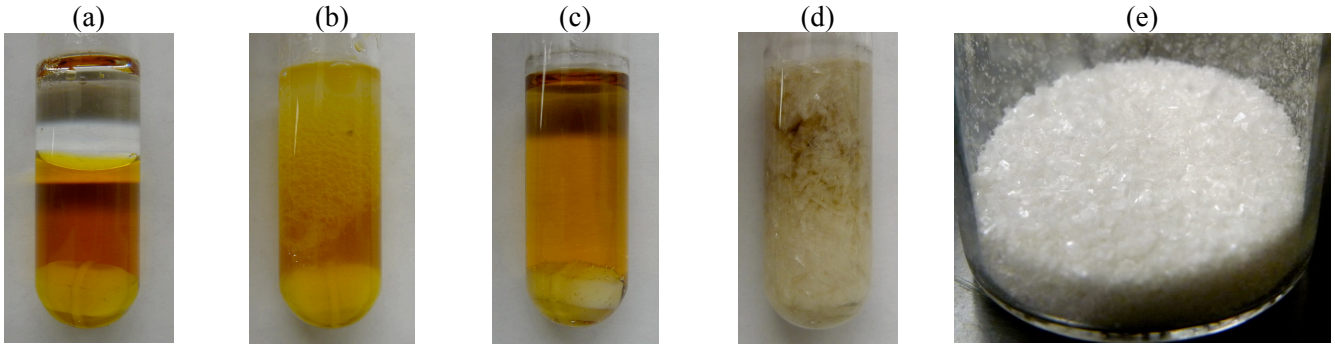


Figure 4-S. $^{31}P\{^{1}H\}$ NMR spectrum of the reaction mixture from benzonitrile hydration catalyzed by $[RuCl_2(PTA)_4]$ after 2 hours of heating.

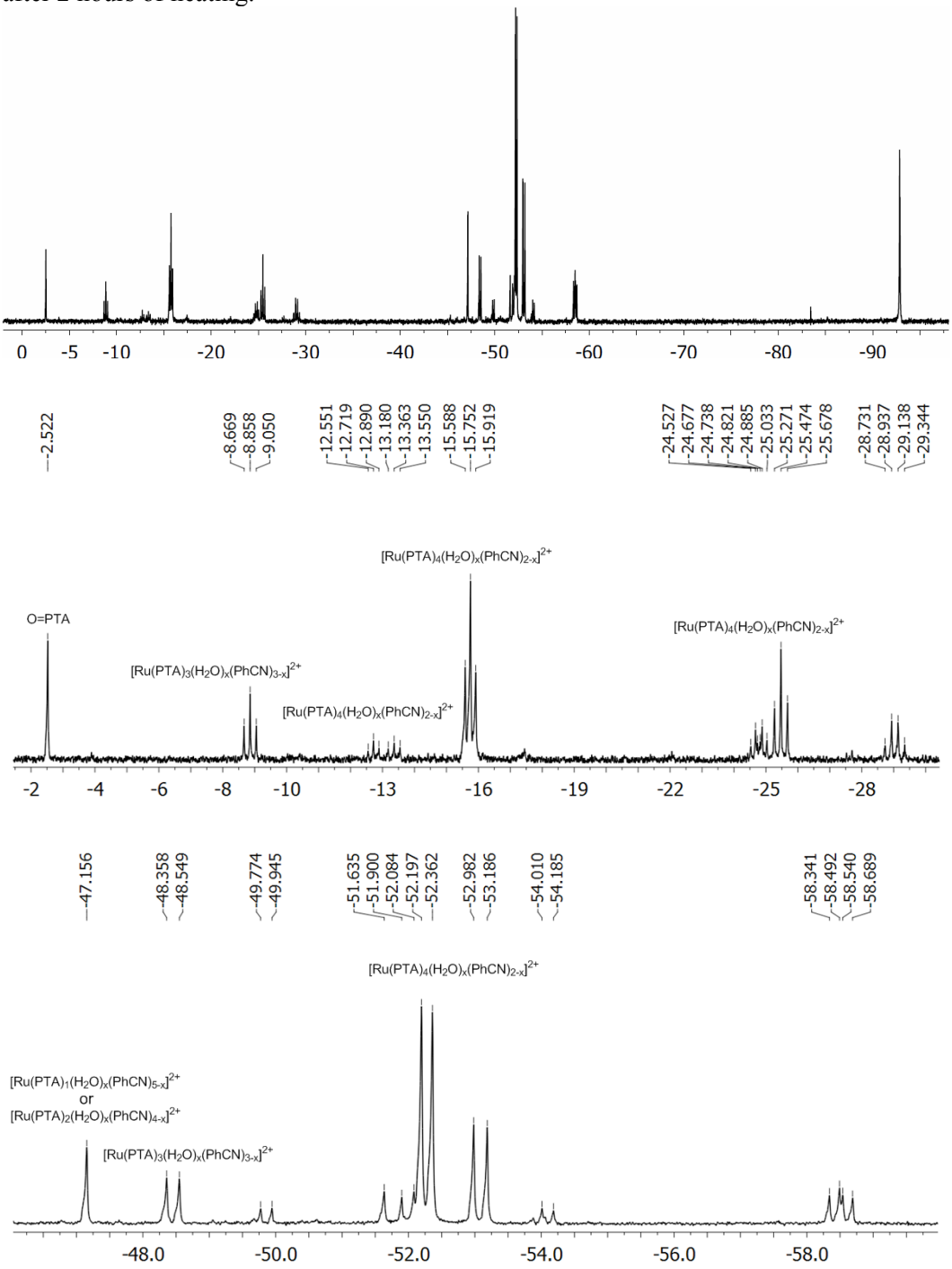


Figure 5-S. ESI-MS spectrum of $[RuCl_2(PTA)_4]$ in water.

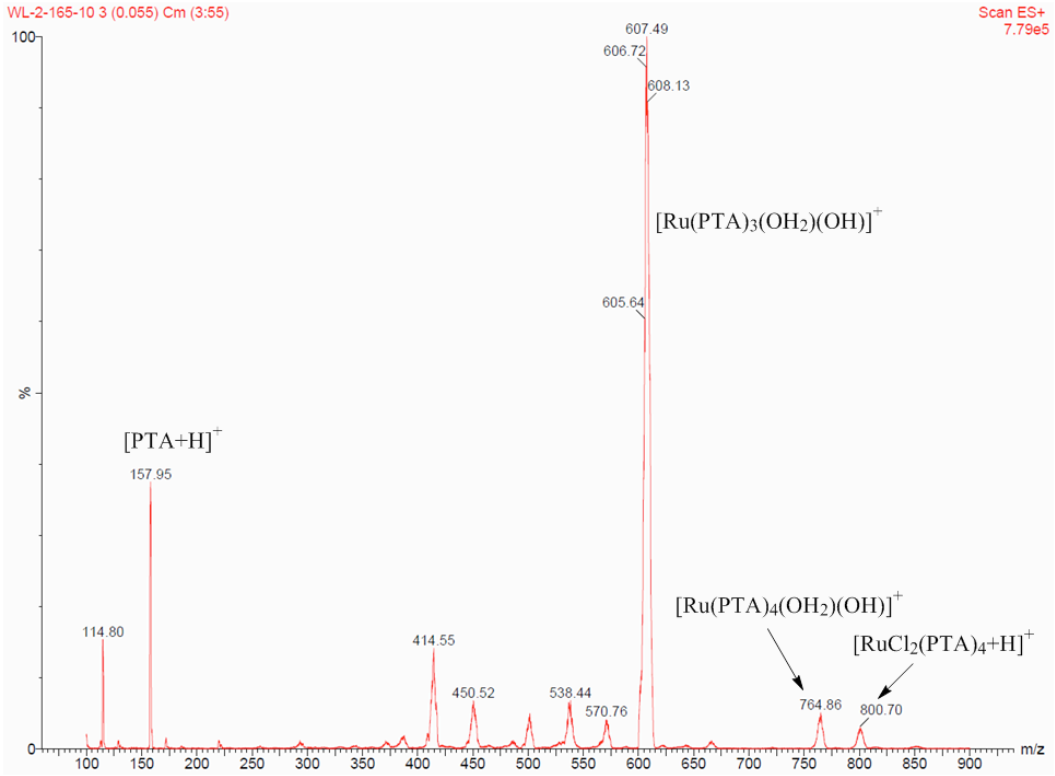


Figure 6-S. ESI-MS spectrum of $[RuCl_2(PTA)_4]$ in 0.1 M NaCl solution.

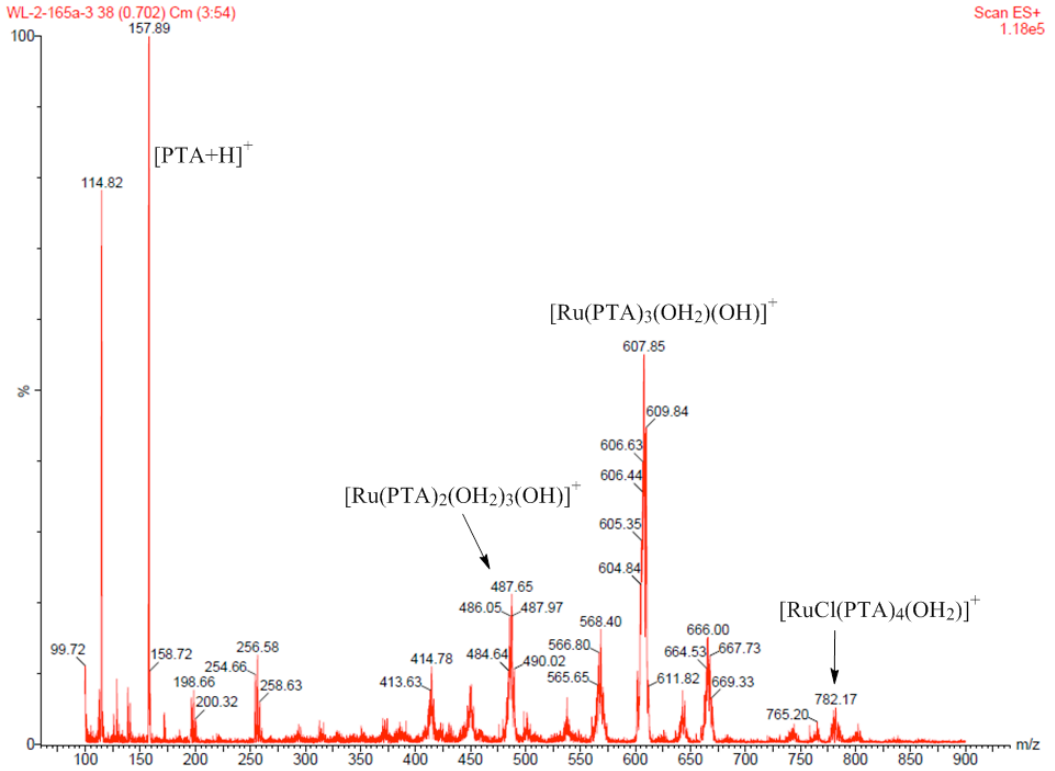


Figure 7-S. GC chromatogram for hydration of benzonitrile after 7 hours. (benzamide 5.059 min).

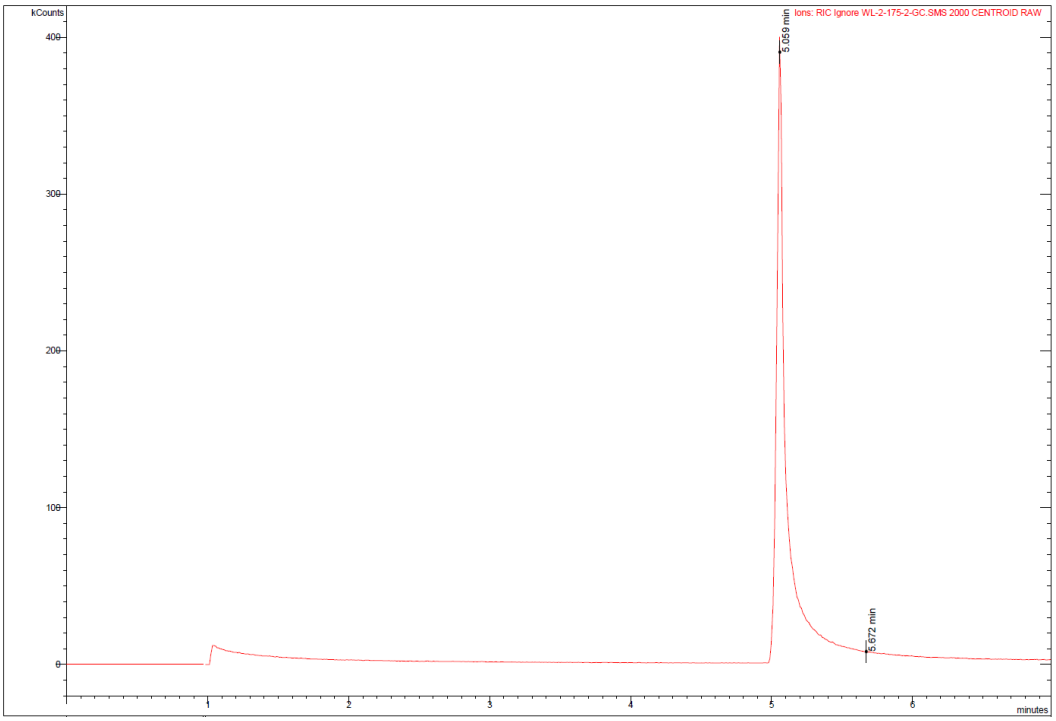


Figure 8-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of benzamide in $CDCl_3$.

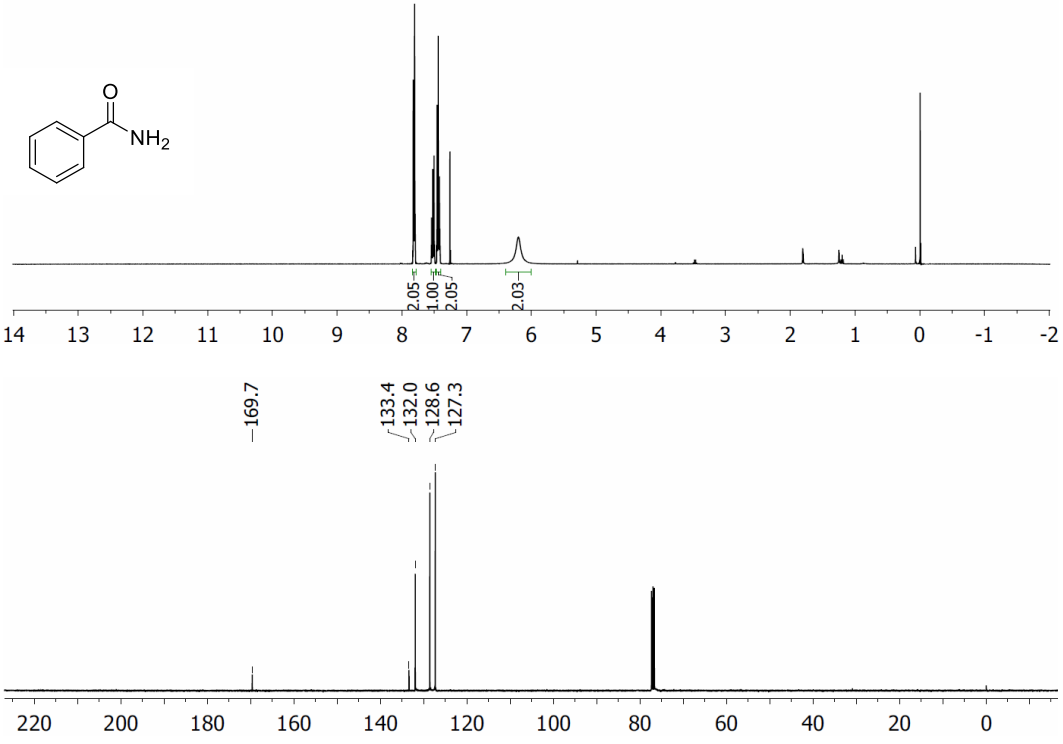


Figure 9-S. GC chromatogram for hydration of *o*-tolunitrile after 7 hours. (*o*-tolunitrile 2.683 min; *o*-toluamide 5.546 min)

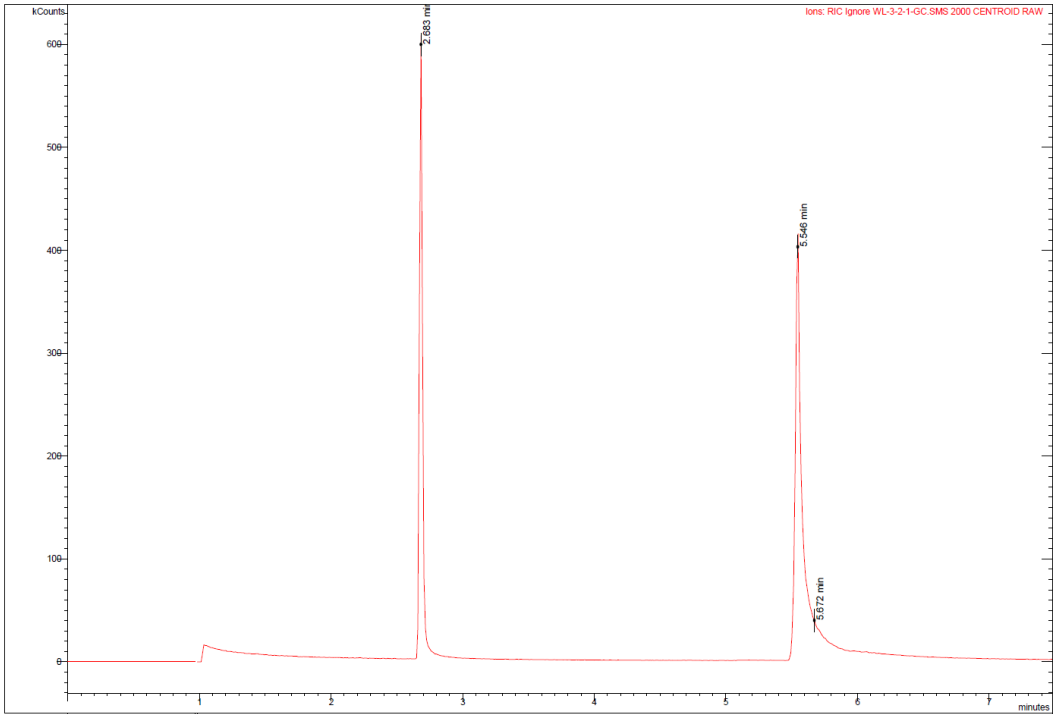


Figure 10-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *o*-toluamide in $CDCl_3$.

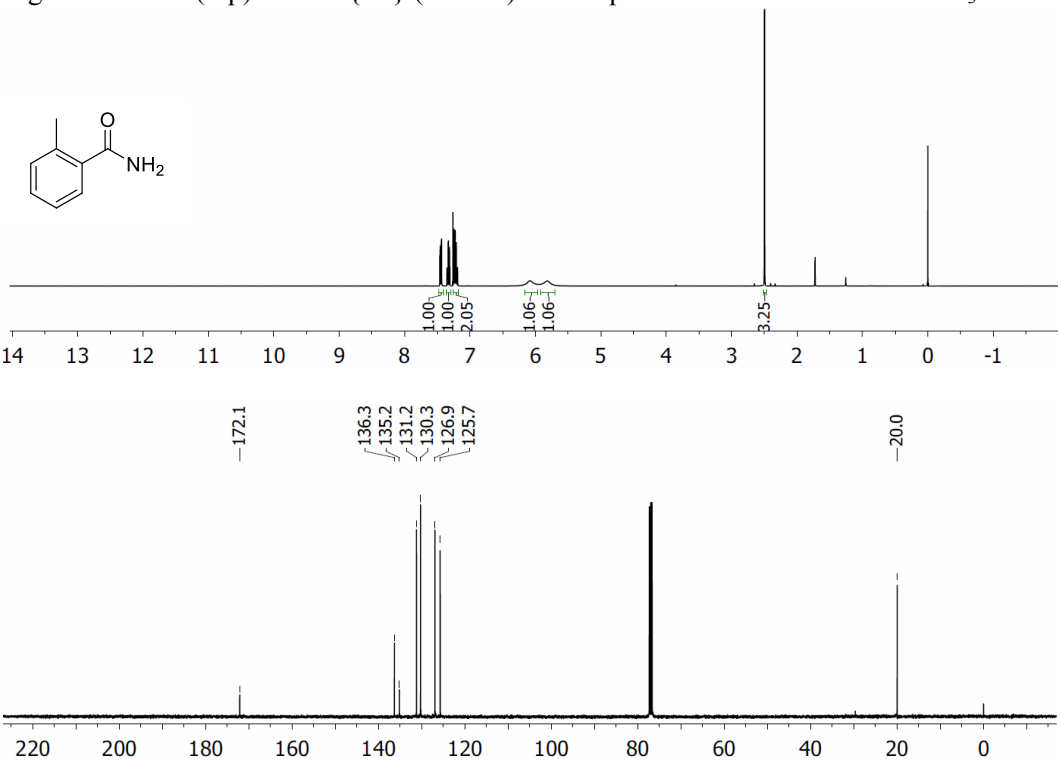


Figure 11-S. GC chromatogram for hydration of *m*-tolunitrile after 7 hours. (*m*-tolunitrile 2.869 min; *m*-toluamide 6.004 min)

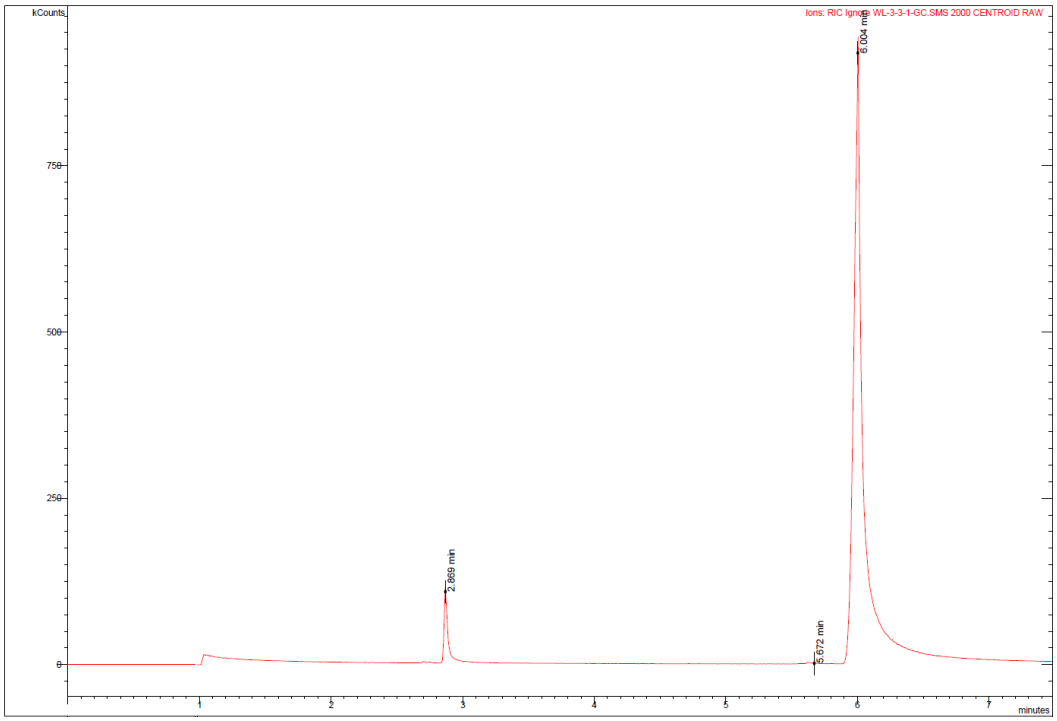


Figure 12-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *m*-toluamide in $CDCl_3$.

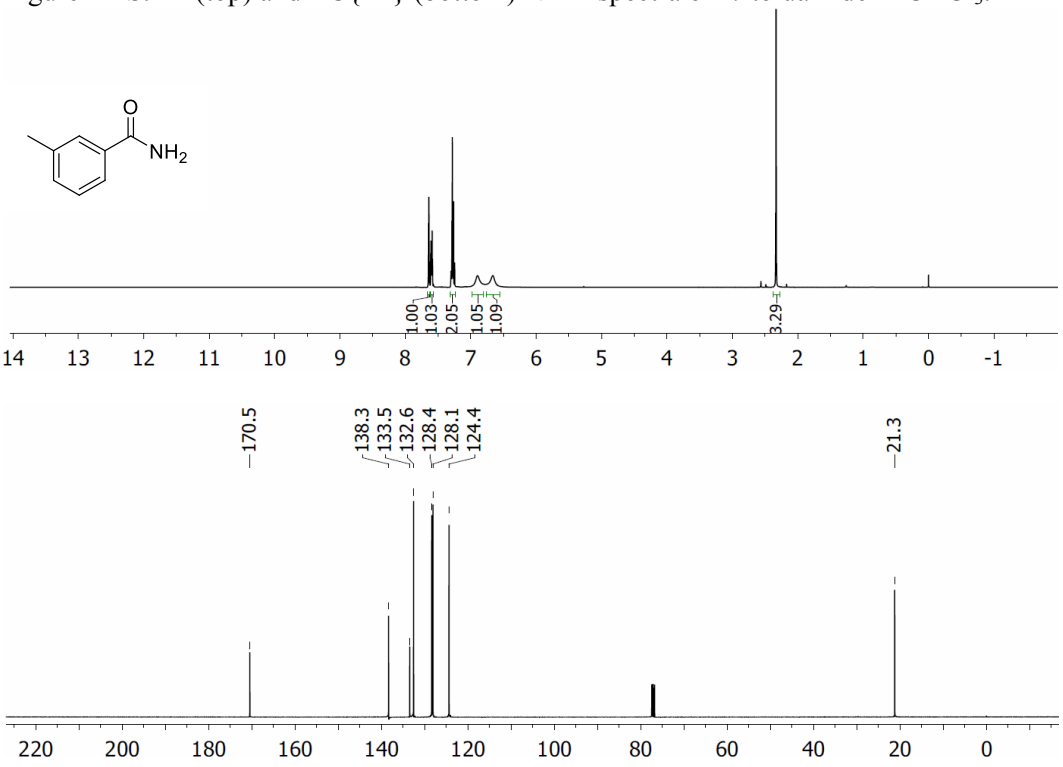


Figure 13-S. GC chromatogram for hydration of *p*-tolunitrile after 7 hours. (*p*-tolunitrile 2.993 min; *p*-toluamide 6.084 min)

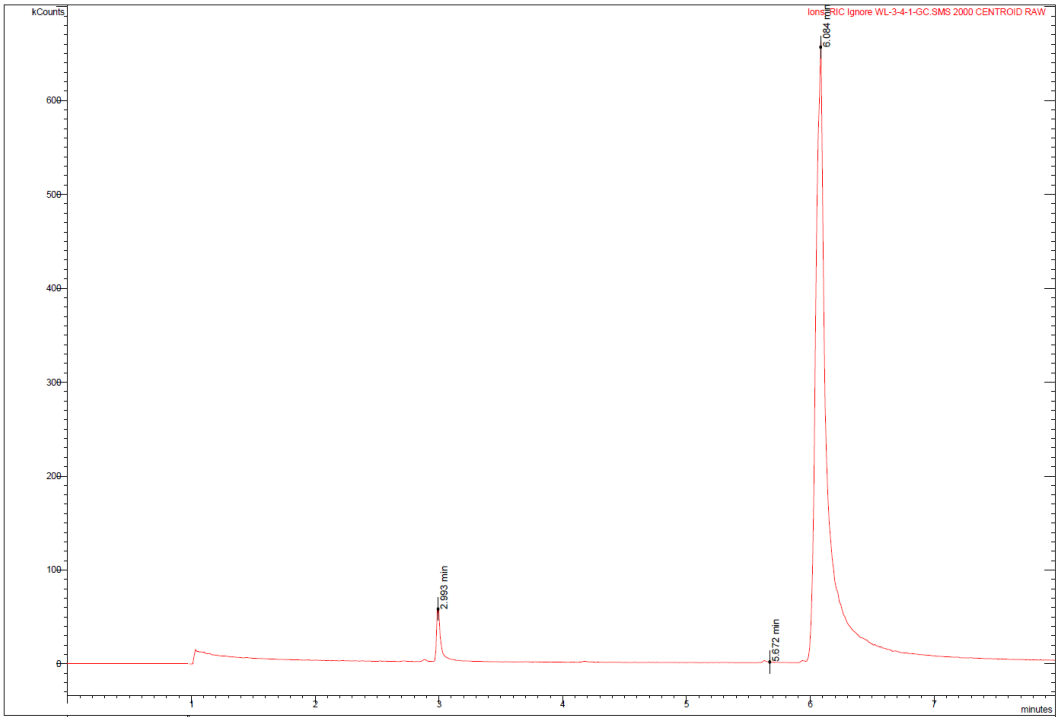


Figure 14-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *p*-toluamide in $CDCl_3$.

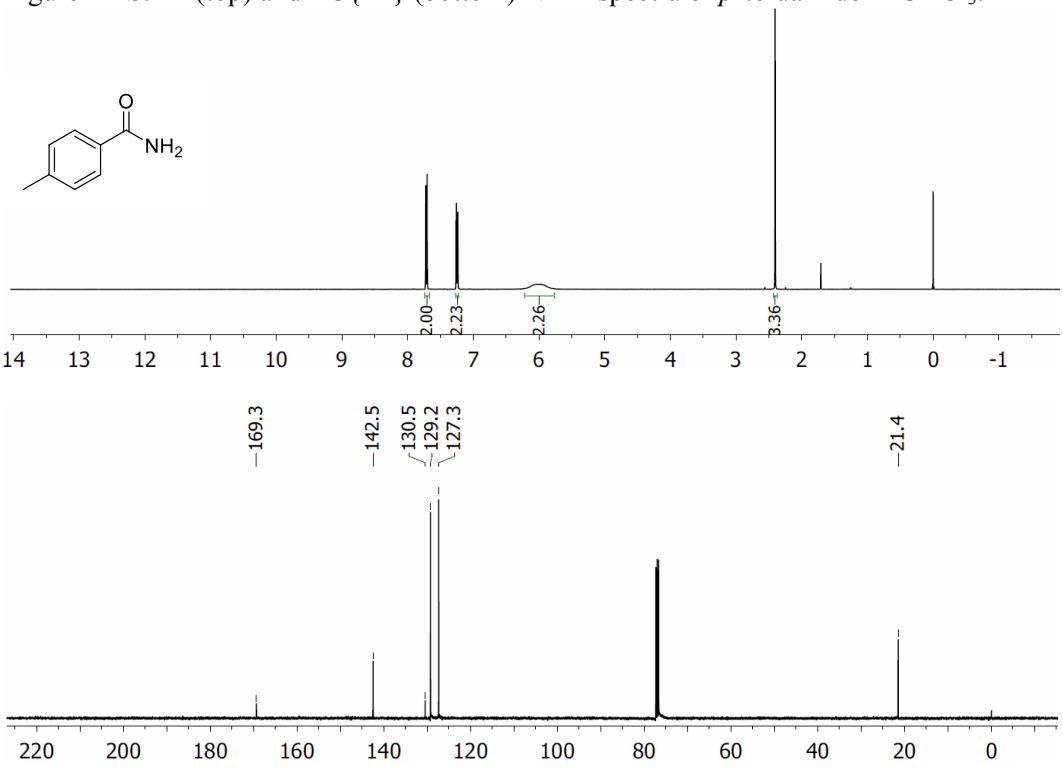


Figure 15-S. GC chromatogram for hydration of *p*-methoxybenzonitrile after 7 hours. (*p*-methoxybenzonitrile 4.481 min; *p*-methoxybenzamide 7.384 min)

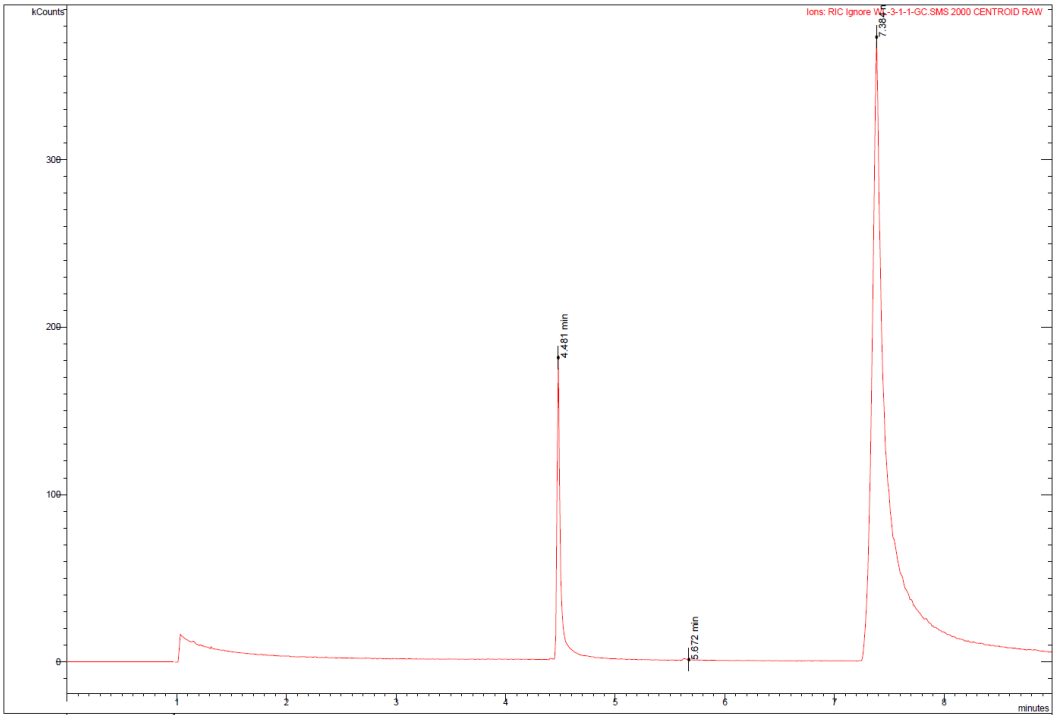


Figure 16-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *p*-methoxybenzamide in $CDCl_3$.

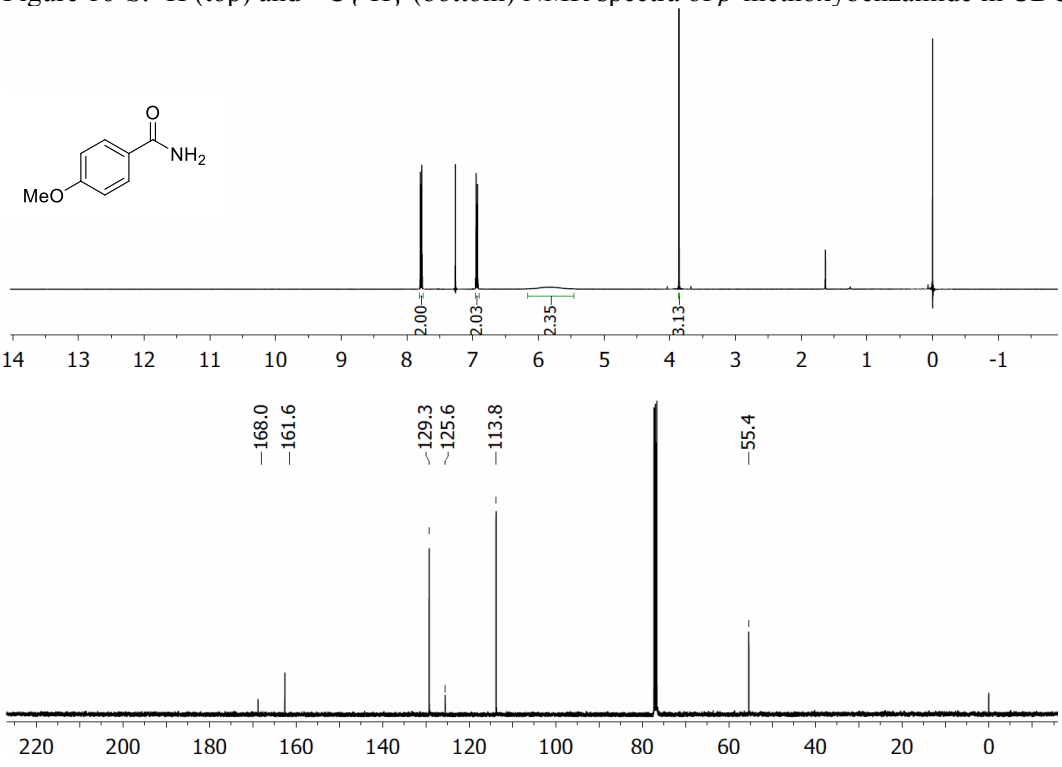


Figure 17-S. GC chromatogram for hydration of *p*-hydroxybenzonitrile after 7 hours. (*p*-hydroxybenzonitrile 6.284 min; *p*-hydroxybenzamide t 8.310 min; others: DCM at 1.449 min, toluene at 1.793 min, PTA at 6.364 min)

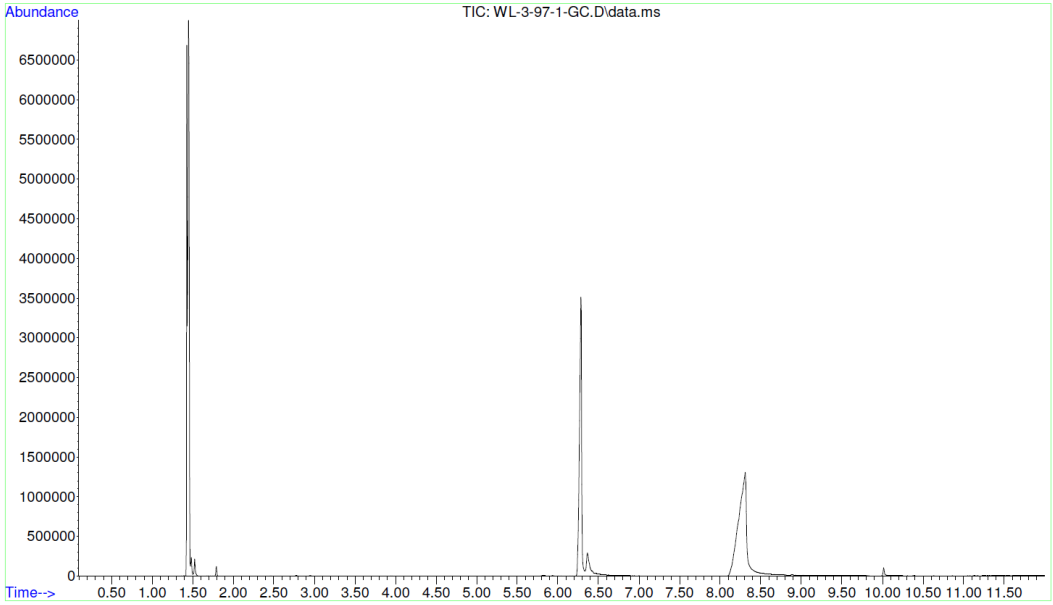


Figure 18-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *p*-hydroxybenzamide in $CDCl_3$ + DMSO-d6.

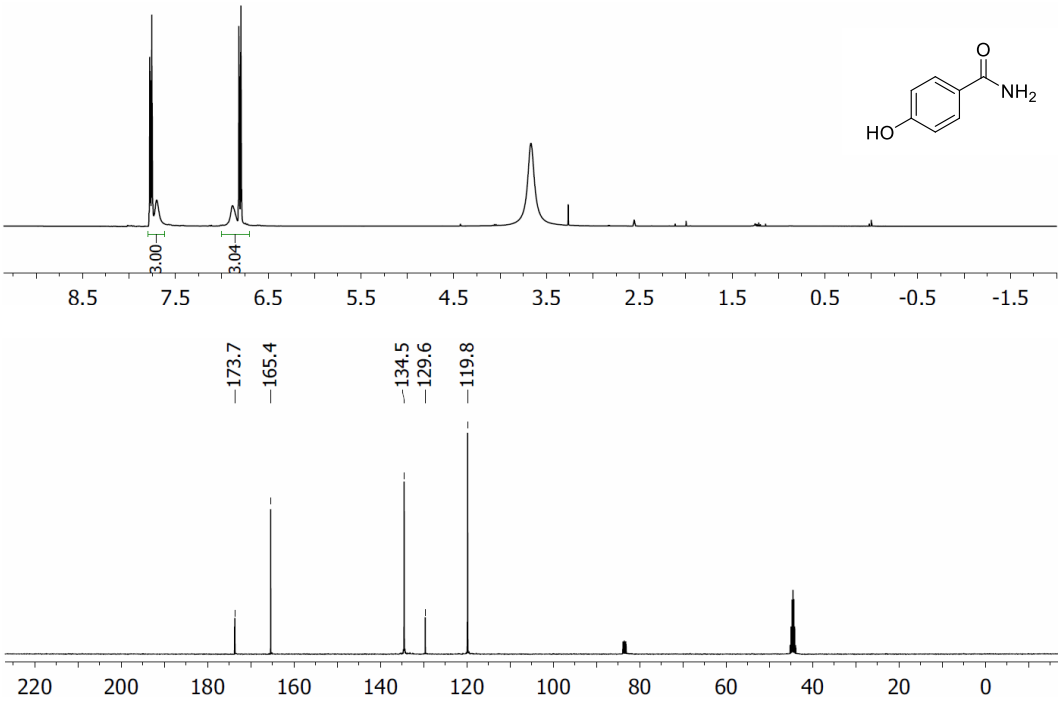


Figure 19-S. GC chromatogram for hydration of *p*-nitrobenzonitrile after 7 hours (*p*-nitrobenzamide 8.398 min).

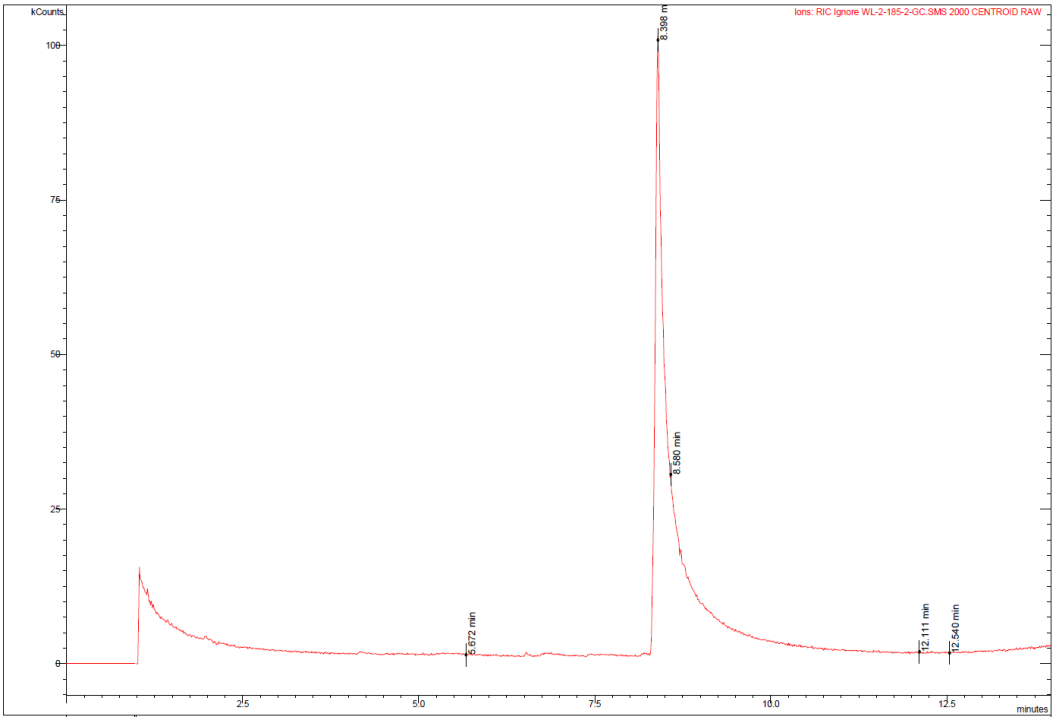


Figure 20-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *p*-nitrobenzamide in acetone-d6.

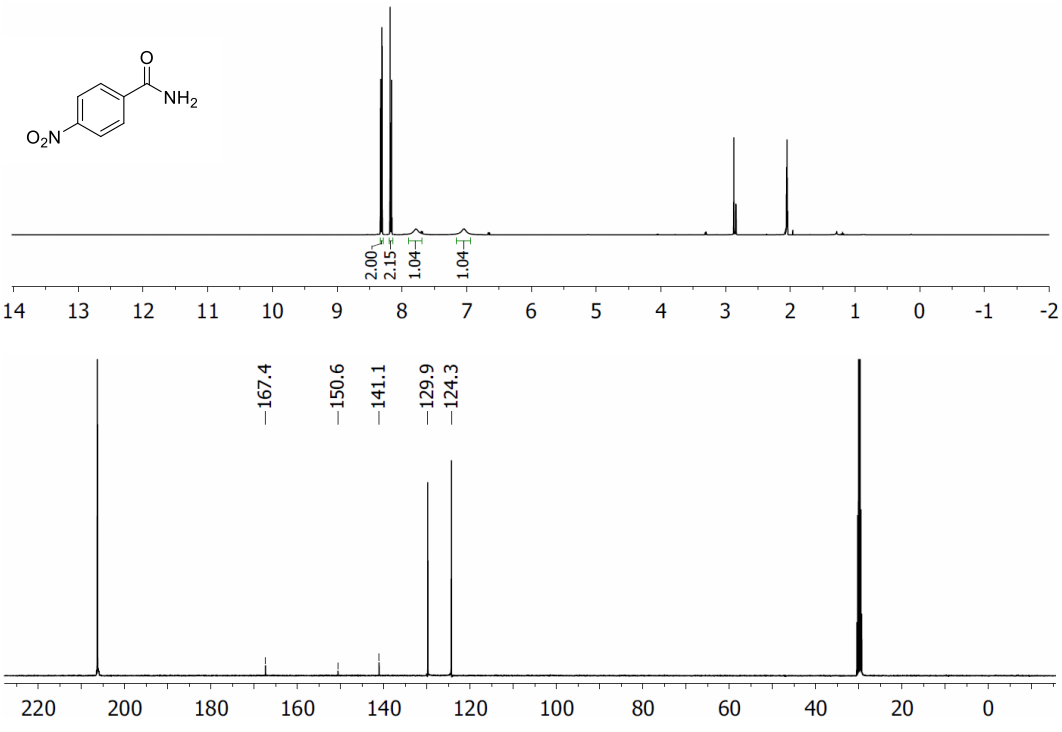


Figure 21-S. GC chromatogram for hydration of *p*-bromobenzonitrile after 7 hours (*p*-bromobenzamide 7.402 min).

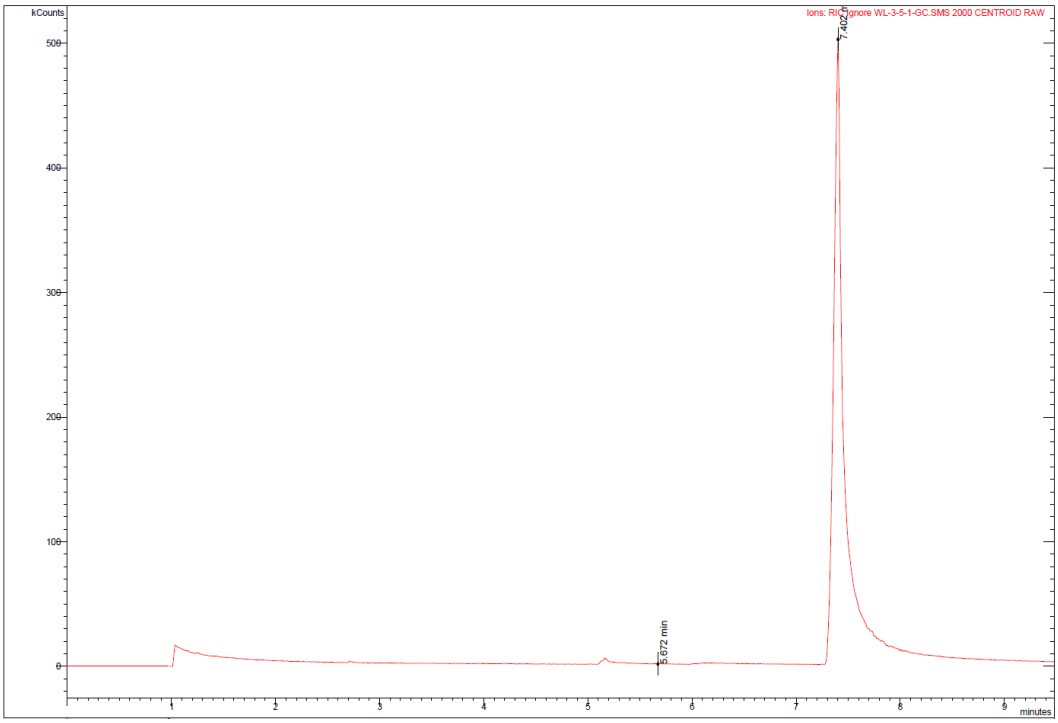


Figure 22-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *p*-bromobenzamide in $CDCl_3$.

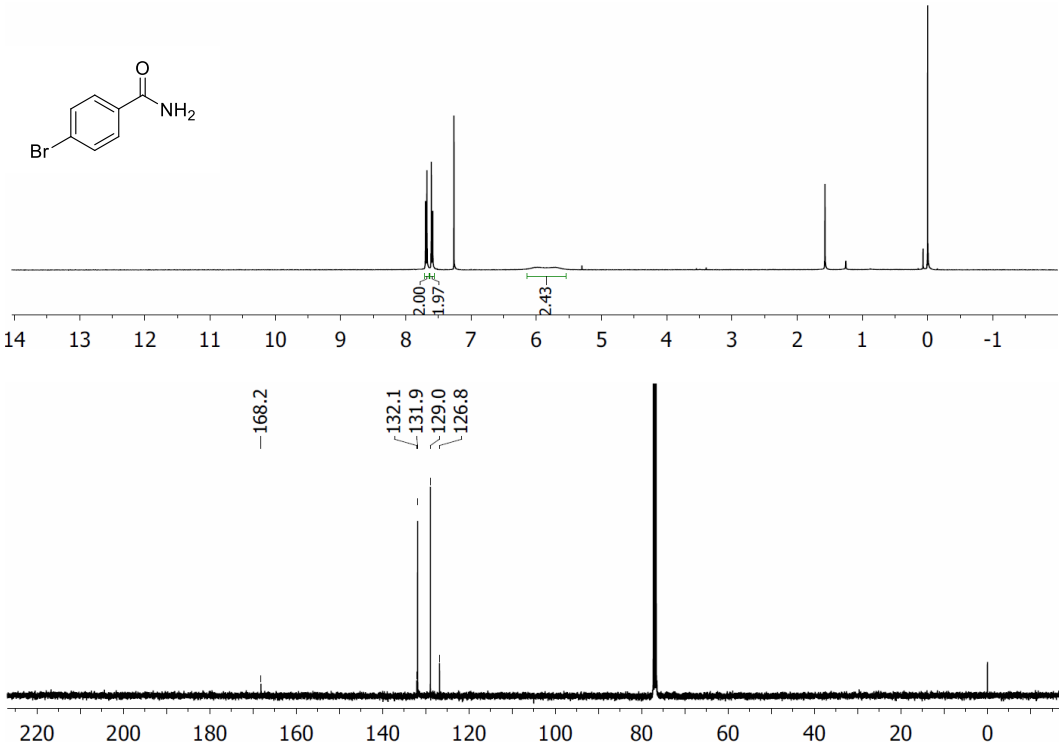


Figure 23-S. GC chromatogram for hydration of *4*-formylbenzonitrile after 7 hours (*4*-formylbenzamide 7.512 min).

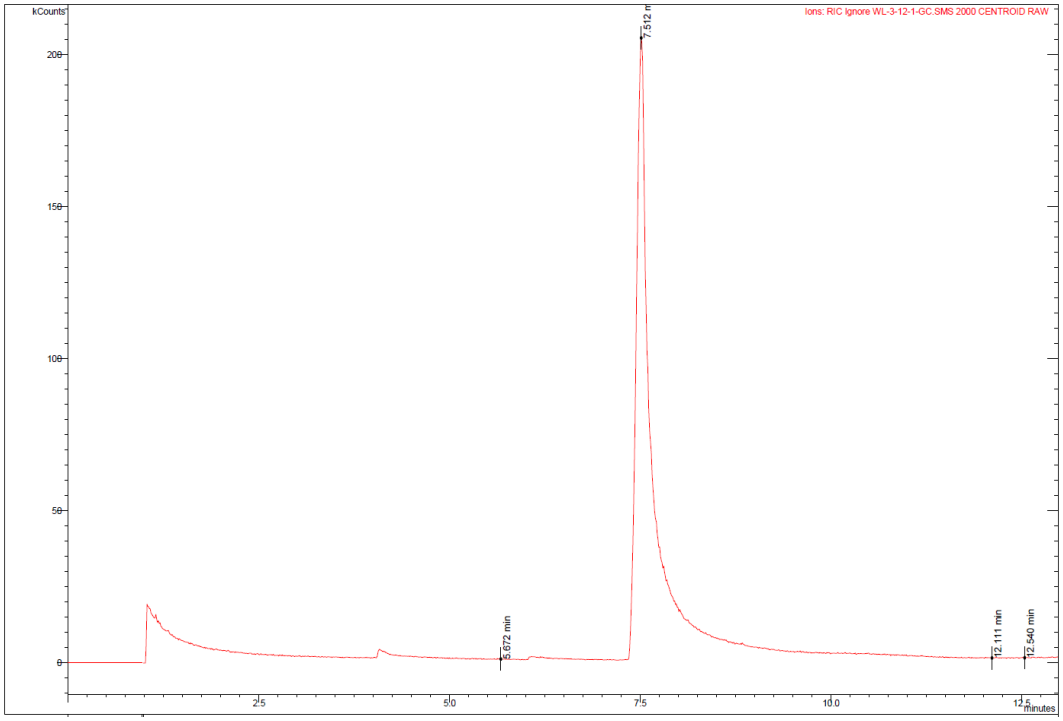


Figure 24-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *4*-formylbenzamide in $CDCl_3$.

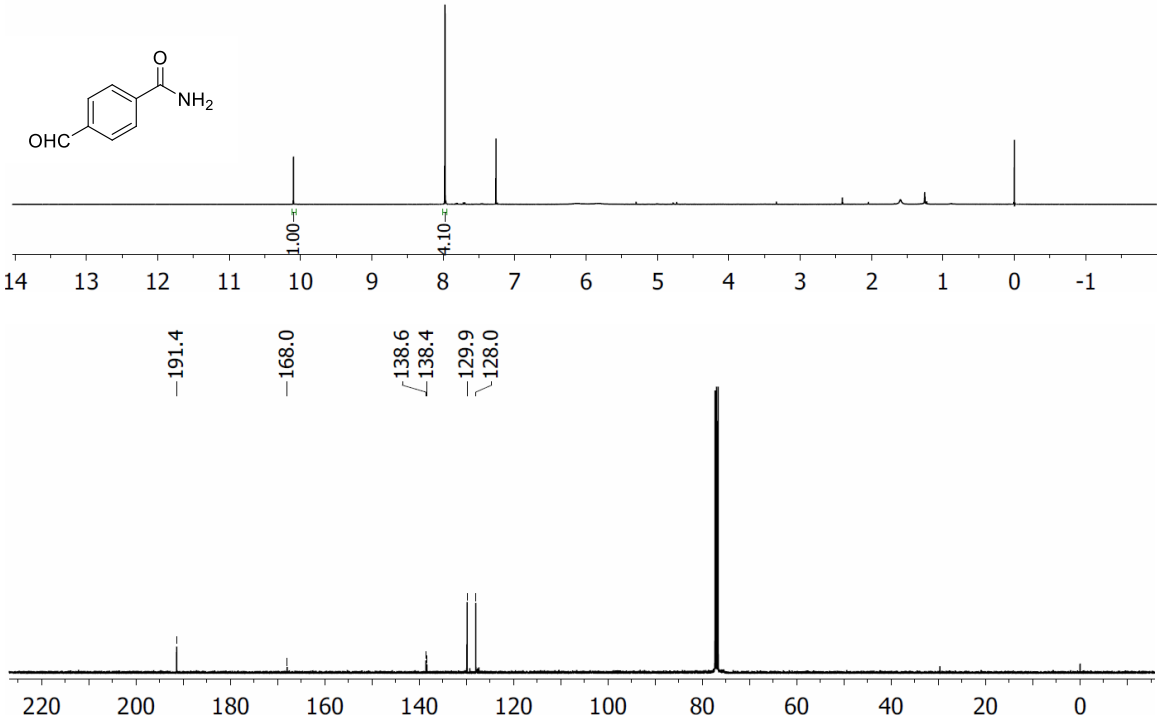


Figure 25-S. GC chromatogram for hydration of *2*-cyanopyridine after 7 hours. (*2*-cyanopyridine 2.516 min; picolinamide 4.377 min; others: PTA at 5.672 min)

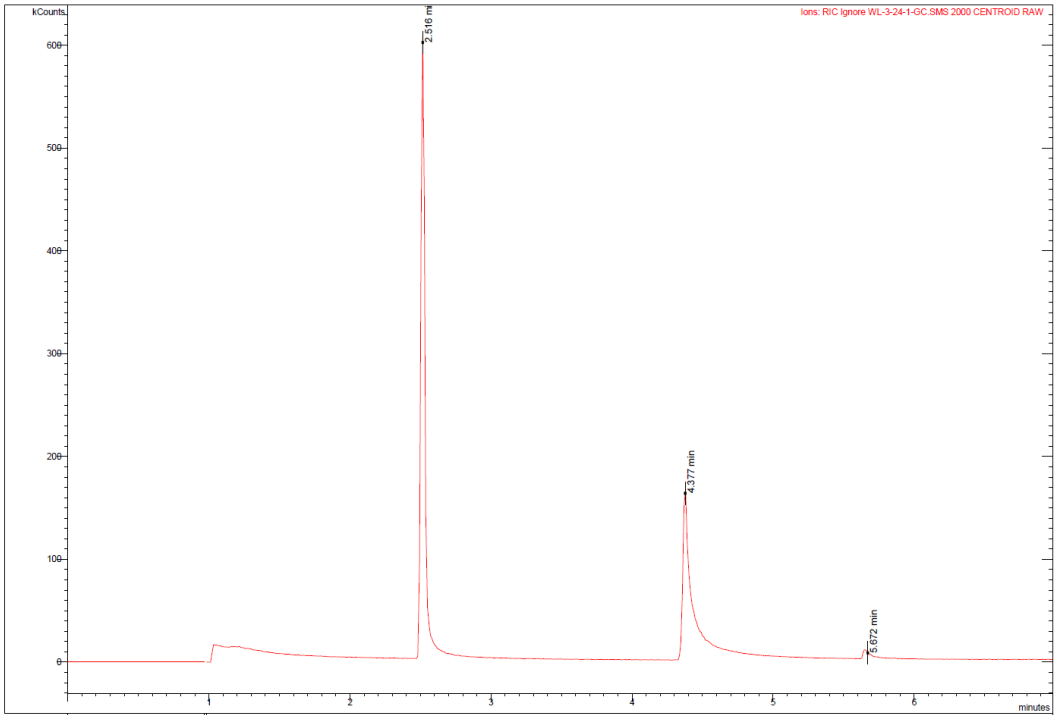


Figure 26-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of picolinamide in $CDCl_3$.

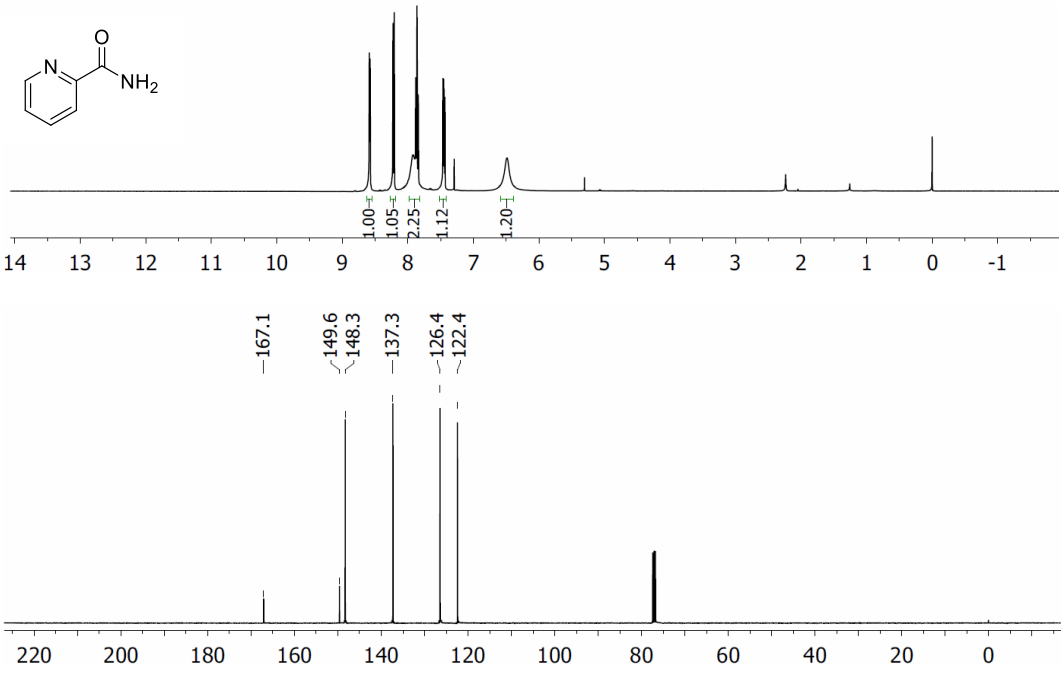


Figure 27-S. GC chromatogram for hydration of *4*-methylbenzyl cyanide after 7 hours. (*4*-methylbenzyl cyanide 4.271 min; *4*-(*p*-tolyl)-acetamide 6.512 min)

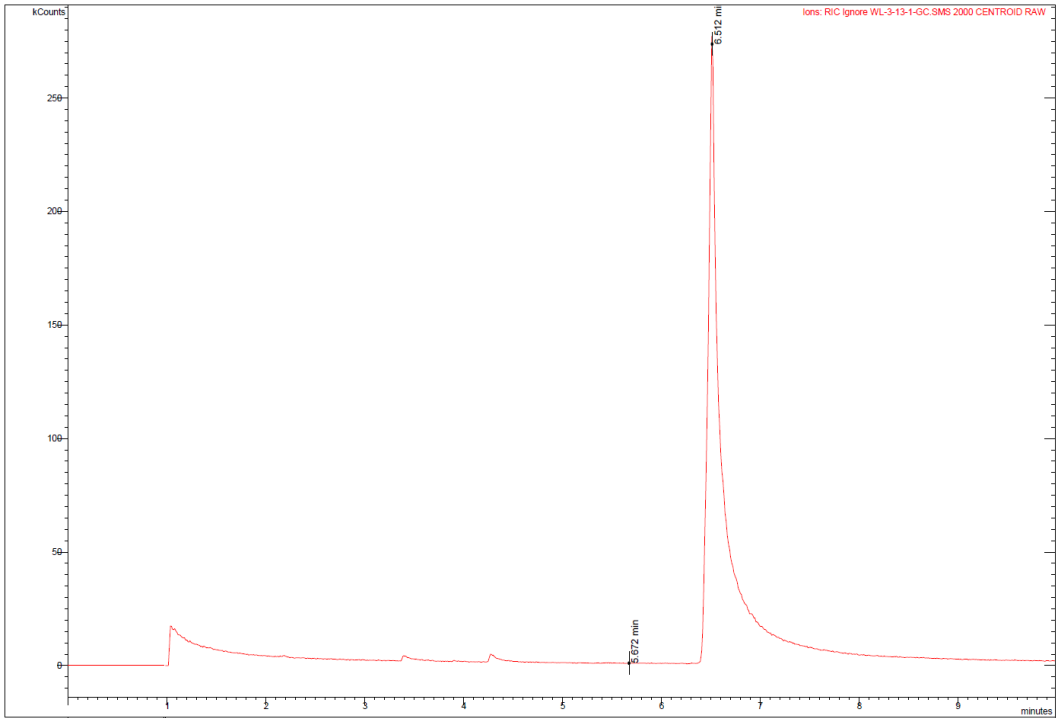


Figure 28-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of *4*-(*p*-tolyl)-acetamide in $CDCl_3$.

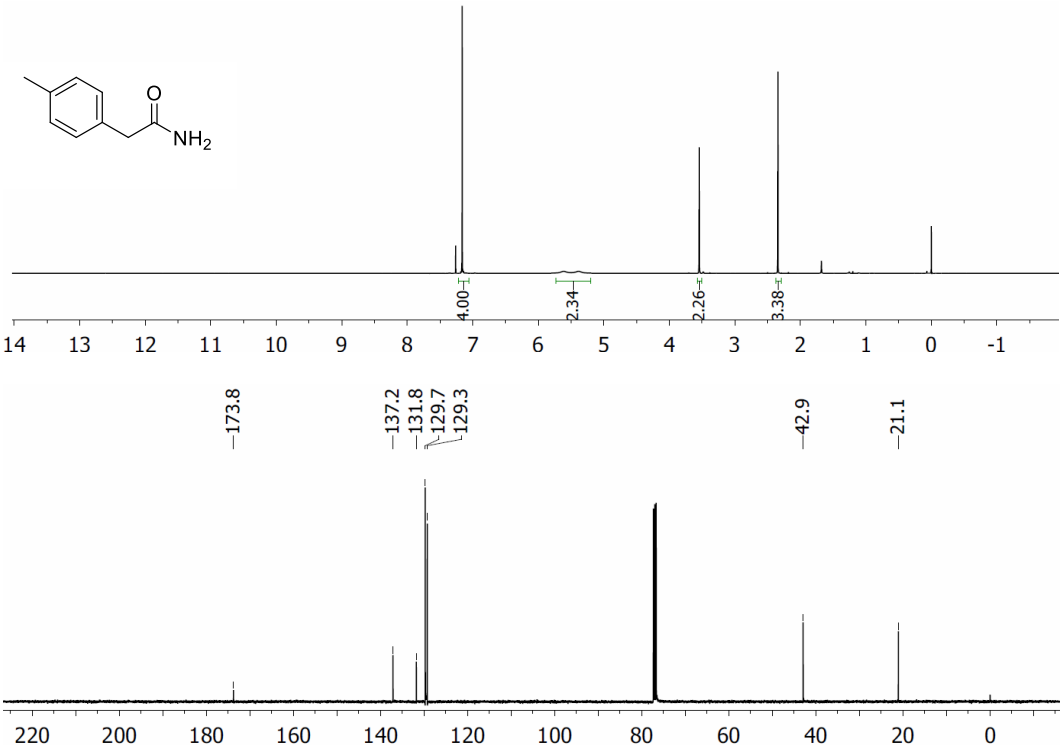


Figure 29-S. GC chromatogram for hydration of heptyl cyanide after 7 hours. (heptyl cyanide 2.816 min; octamide 5.338 min)

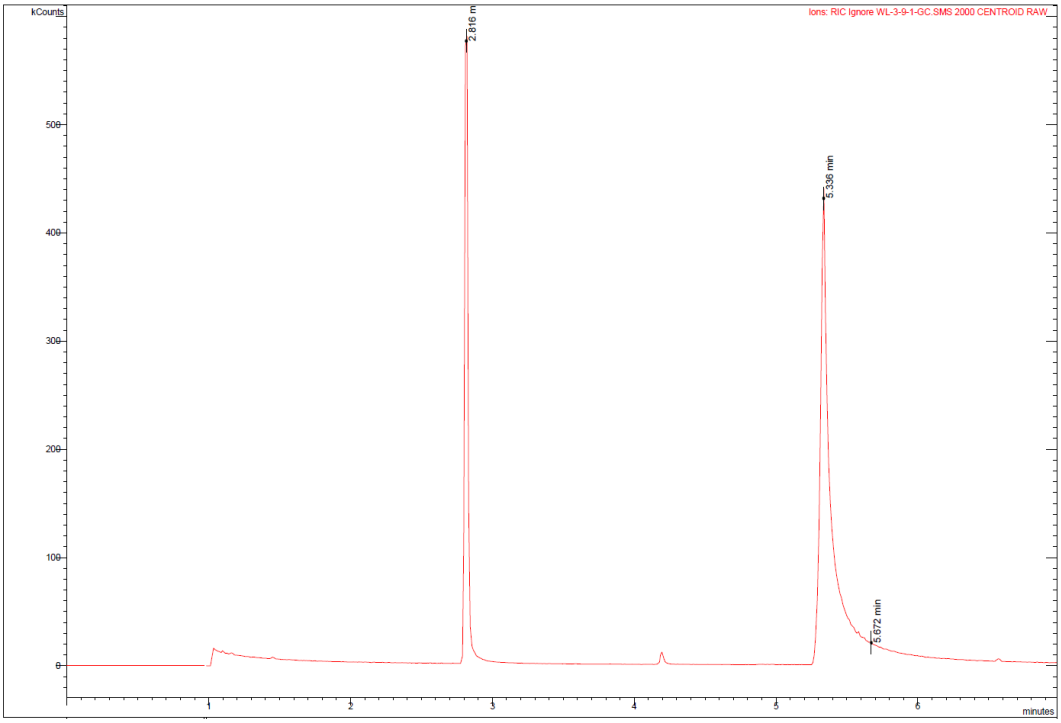


Figure 30-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of octamide in $CDCl_3$.

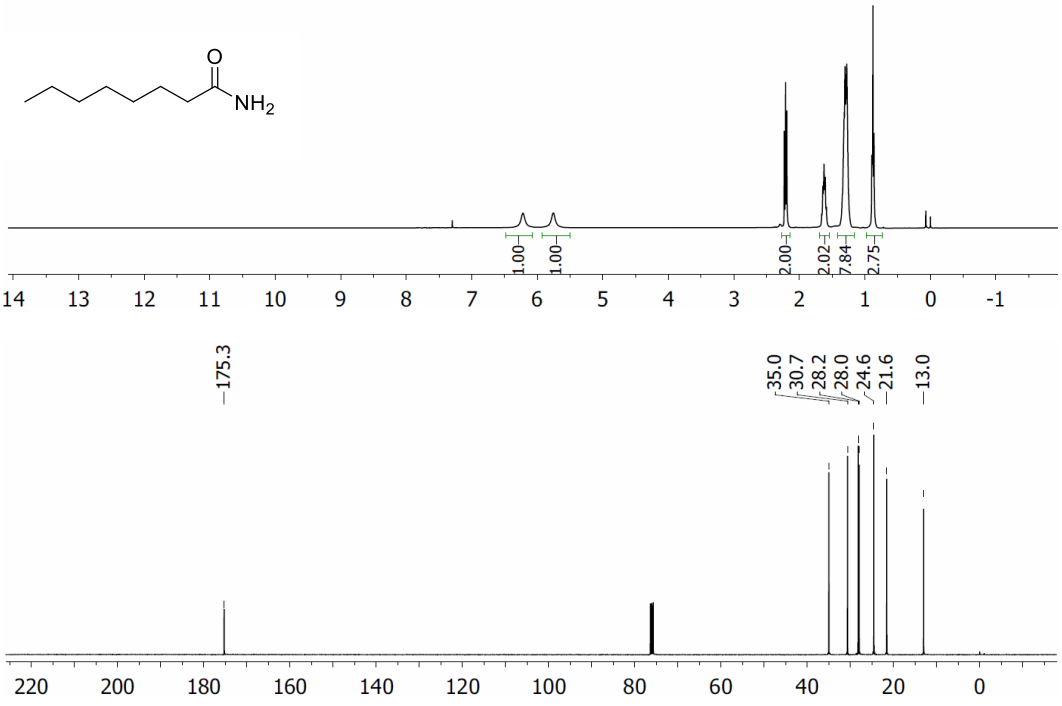


Figure 31-S. GC chromatogram for hydration of pivalonitrile after 7 hours. (pivalonitrile 1.541 min; pivalamide 2.451 min; others: DCM at 1.449 min, toluene at 1.793 min, PTA at 6.342 min)

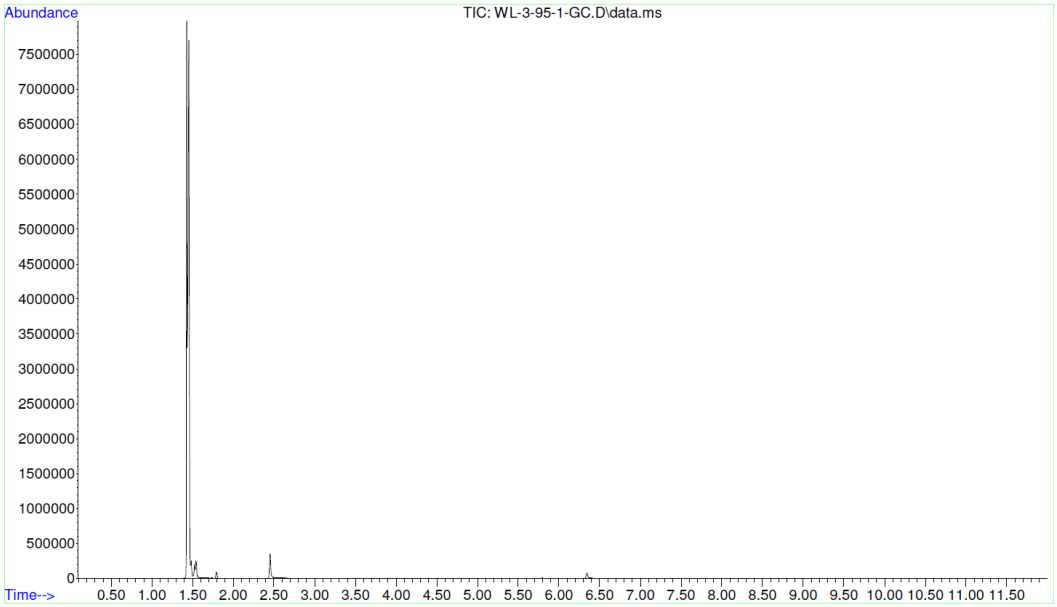


Figure 32-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of pivalamide in $CDCl_3$.

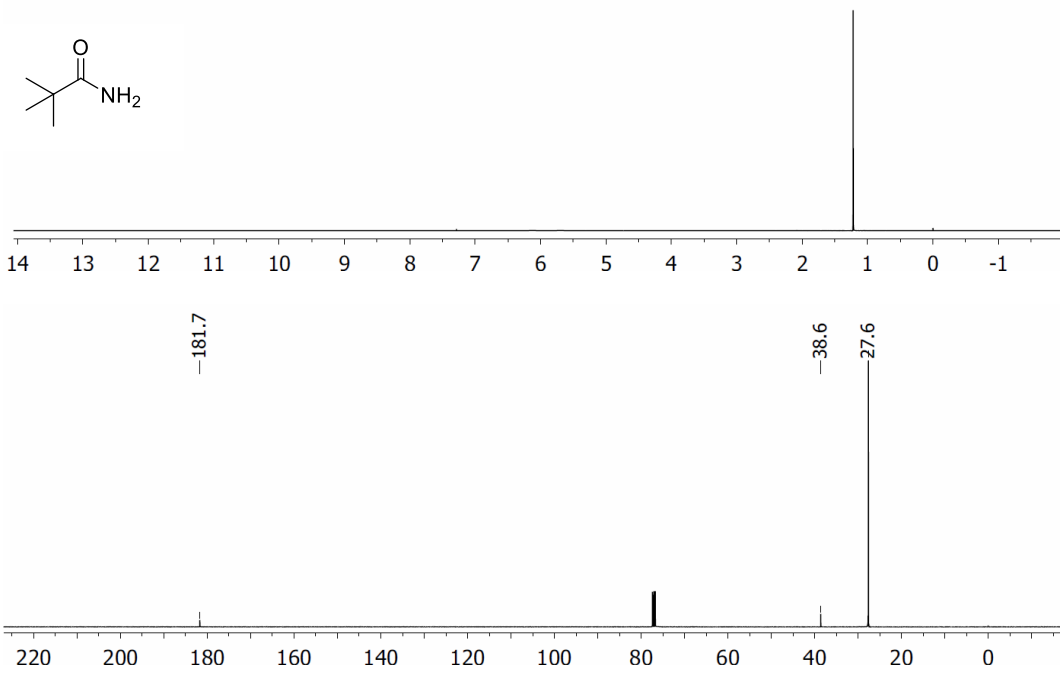


Figure 33-S. GC chromatogram for hydration of acrylonitrile after 7 hours. (acrylamide 2.044 min; others: DCM at 1.449 min, toluene 1.793 min)

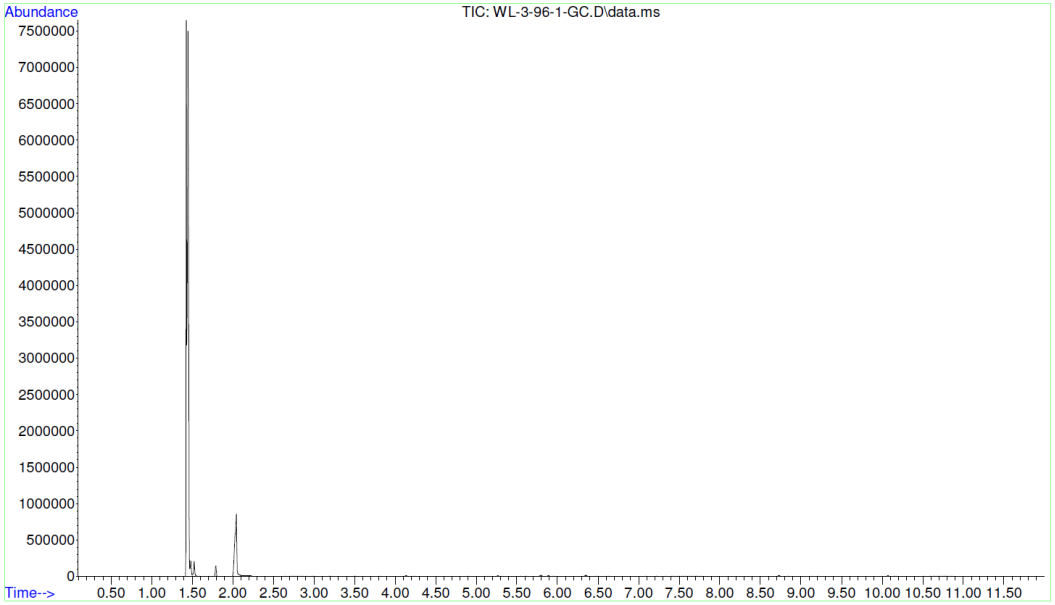


Figure 34-S. ^{1}H (top) and $^{13}C\{^{1}H\}$ (bottom) NMR spectra of acrylamide in $CDCl_3$.