Supporting Information

Tandem Reaction Progress Analysis as a Means for Dissecting Catalytic Reactions: Application to the Aza-Piancatelli Rearrangement

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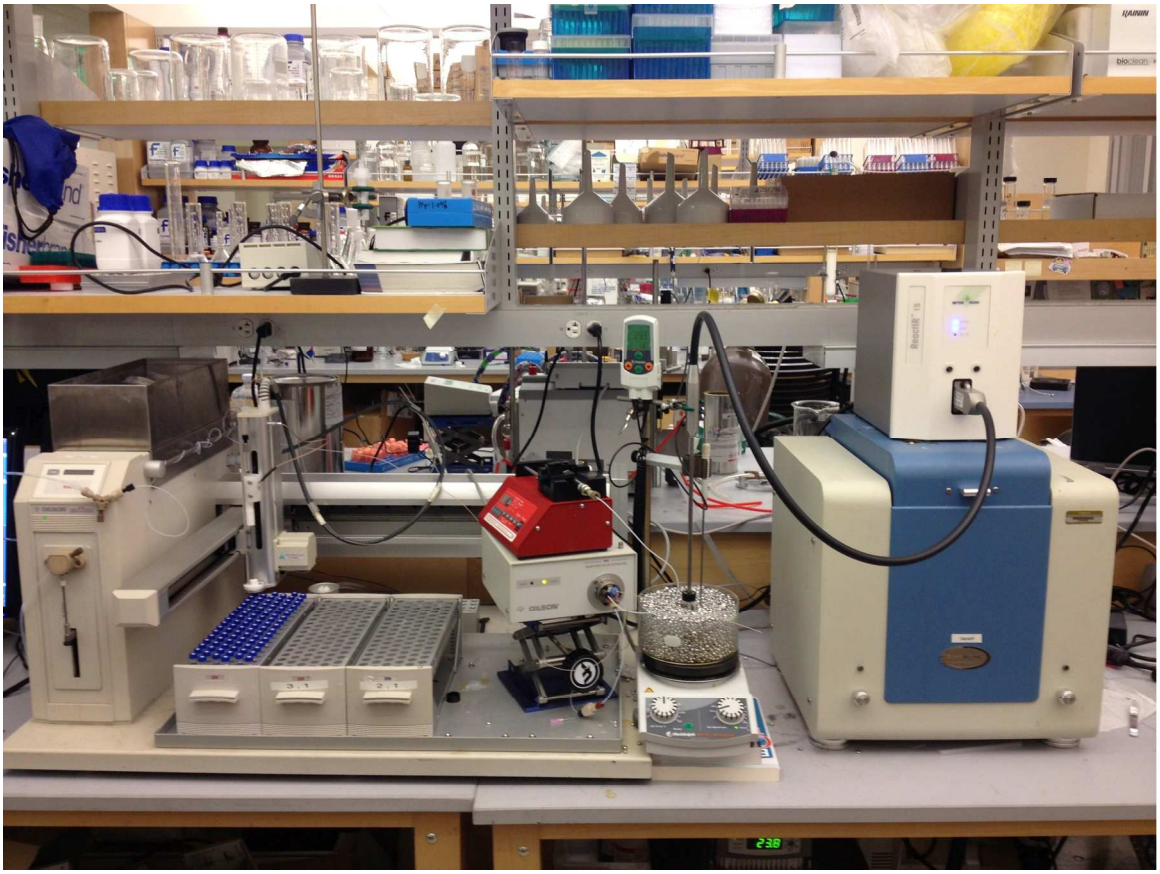
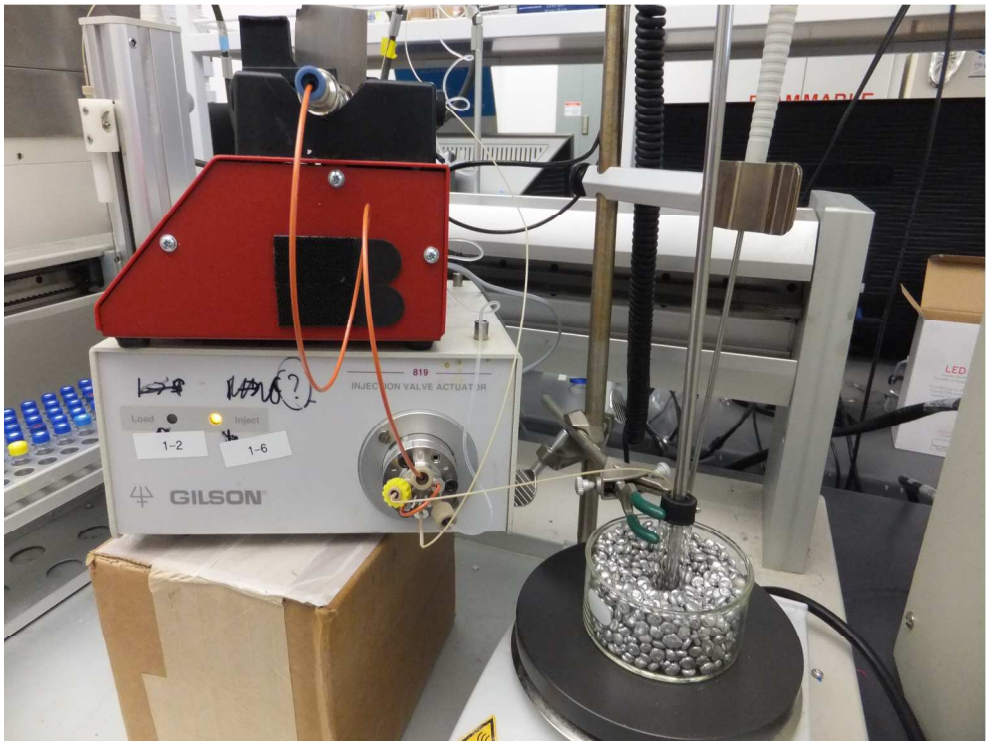
1 General Remarks

Furan-2-yl(phenyl)methanol was prepared by reacting freshly distilled furfural with phenylmagnesium bromide in a similar fashion to the literature precedent.[1] Dysprosium(III) trifluoromethanesulfonate ($Dy(OTf)_3$) was obtained from Strem Chemicals Inc. and used as received. *N,O*-dibenzylhydroxylamine was prepared as previously described.[2] Acetonitrile was purified using an Innovative Technologies PS-Micro solvent system. Flash chromatography was carried out using Fisher Chemical silica gel 60 Å (230 x 400 mesh). Analytical thin-layer chromatography (TLC) was performed on Sorbtech glass pre-coated silica gel plates and was visualized with UV light or staining with potassium permanganate. All other materials were purchased from conventional suppliers and used as received.

All kinetic experiments were conducted with automated sampling with a custom-built apparatus. From the reaction vial, 15 μL samples were automatically taken by a programmable syringe pump at defined time points through a PEEK capillary (1/32" outer diameter, 0.15 mm inner diameter). Samples were rerouted with a Gilson 918 Injection Valve Actuator (rheodyne) to a Gilson 215 automated liquid handler robot, which allowed for the dilution of the samples with 1 mL of methanol directly into LC vials. The timing and synchronization of the liquid sampling technology was governed by the pump that removed the timed aliquot, triggered the actuation of the rheodyne, and activated the subsequent sample dilution and quenching. These samples were manually transferred to the HPLC-MS for analysis as they were prepared or upon completion of the sampling period.

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INJECTION VALVE ACTUATOR
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Figure S1: Set up for Tandem reaction progress monitoring. Above: Total set up showing automatic liquid handling robot coupled to ReactIR; Below: Reactor set-up showing the ReactIR probe for in situ IR analysis and Rheodyne/syringe pump for liquid sampling

The LC samples were analyzed by HPLC/MS conducted on an Agilent 1260 Infinity apparatus under the one of the following conditions:

(1) Poroshell 120 SB-C18, 3.0 x 100 mm, 2.7-Micron Column; Temperature = 25 ºC; Solvent A = water, 0.05 % formic acid; Solvent B = acetonitrile, 0.05 % formic acid; Flow Rate = 0.425 mL/min; Starting Conditions = 70 % A, 30 % B; 0.1–4.8 min, 30 % B; 4.9–8.9 min = 85 % B; 9–10 min, B = 100 %.

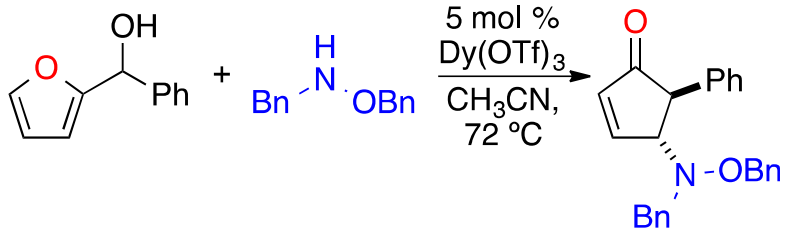
(2) Poroshell 120 EC-C8, 2.1 x 50 mm, 2.7-Micron Column; Temperature = 25 ºC; Solvent A = water, 0.05 % formic acid; Solvent B = acetonitrile, 0.05 % formic acid; Flow Rate = 0.650 mL/min; Starting Conditions = 80 % A, 20 % B; 0.1–2.8 min, 30 % B; 2.9–6 min, 85 % B; 6.01–6.50 min, 100% B.

In situ FT-IR monitoring was conducted with a Mettler-Toledo ReactIR 15 equipped with a DiComp (Diamond) ATR probe connected via an AgX (silver halide) 6 mm x 1.5 m fiber and inserted through a PTFE-lined septum fitted on the reaction vial. Reaction temperatures were monitored using an internal thermistor in the IR probe. Sampling was carried out over 2000-800 cm^{-1} at 4 wavenumber resolution with 1x gain.

^{1}H-NMR spectra were recorded on Varian NMR spectrometers (400, 500, or 600 MHz). Data for ^{1}H-NMR spectra are listed as follows: chemical shift (δ, ppm), multiplicity, coupling constant (Hz), integration, and are referenced to the residual solvent peak (7.26 ppm for $CDCl_3$). Abbreviations are as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet. ^{13}C-NMR spectra were recorded on Varian spectrometers (125 MHz), are listed in terms of chemical shift and are referenced to the residual solvent peak (77.16 ppm for $CDCl_3$).

2 Experimental Procedures

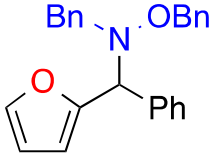
2.1 Synthesis of 4-(Benzyl(benzyloxy)amino)-5-phenylcyclopent-2-en-1-one (9a)



7 **8** **9a**

Furan-2-yl(phenyl)methanol (38.2 mg, 0.220 mmol) and *N*,*O*-dibenzylhydroxylamine (2) (46.8 mg, 0.220 mmol) were treated with $Dy(OTf)_3$ (6.7 mg, 0.011 mmol) in $MeNO_2$ (2.2 mL). The resulting reaction mixture was heated to 80 ºC for 30 min. The reaction was then quenched at 23 ºC with saturated aqueous $NaHCO_3$ (5 mL) and extracted with ethyl acetate (3 × 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and then concentrated *in vacuo*. The residue was purified by flash column chromatography to afford cyclopentenone **3** (71.6 mg, 88%) as a light orange/yellow solid. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.36 – 7.20 (m, 9H), 7.15 – 7.04 (m, 6H), 6.33 (dd, *J* = 5.8, 1.9 Hz, 1H), 4.43 (d, *J* = 11.9 Hz, 1H), 4.41 (d, *J* = 10.2 Hz, 1H), 4.24 (ddd, *J* = 2.3, 2.3, 2.3 Hz, 1H), 4.01 (d, *J* = 12.6 Hz, 1H), 3.93 (s, 1H), 3.80 (d, *J* = 12.6 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 207.1, 162.4, 139.0, 136.7, 136.6, 134.9, 129.9, 129.2, 129.1, 128.5, 128.4, 128.3, 128.3, 127.7, 127.2, 76.9, 73.9, 61.3, 52.7 ppm; **IR** (thin film) 3063, 3031, 2919, 1709, 1595, 1454, 1265, 1029, 975 cm^{-1}; **MS** (ESI) *m/z* 392.1636 (392.1626 calcd for $C_{25}H_{23}NNaO_2^+$ $[MNa]^+$).

2.2 Isolation of *N*,*O*-dibenzyl-*N*-(furan-2-yl(phenyl)methyl)hydroxylamine (9b)

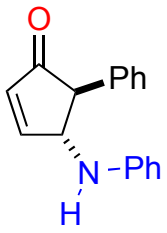


9b

Two reactions were conducted and combined to yield the product. For the first reaction, a 16 mL glass vial equipped with PTFE-silicon septum, open top screw cap, and magnetic stir bar was charged with 10 mL acetonitrile, furan-2-yl(phenyl)methanol (0.174 g, 1 mmol) and *N*,*O*-dibenzylhydroxylamine (0.213 g, 1 mmol), and $Dy(OTf)_3$ (0.030 g, 0.05 mmol, 5% catalyst). For

the second reaction, a 20 mL glass vial was charged with 15 mL acetonitrile, furan-2-yl(phenyl)methanol) (0.261 g, 1.5 mmol) and *N*,*O*-dibenzylhydroxylamine (0.320 g, 1.500 mmol), and $Dy(OTf)_3$ (0.027 g, 0.045 mmol, 3% catalyst). Both reactions were stirred and heated at 65 °C for two hours. The reactions were separately quenched at 23 ºC with saturated aqueous $NaHCO_3$ and extracted with dichloromethane (4 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated *in vacuo*. The crude gel from both reactions was purified by flash column chromatography with a gradient starting with hexanes with increasing ethyl acetate. The intermediate *N*,*O*-dibenzyl-*N*-(furan-2-yl(phenyl)methyl)hydroxylamine is collected from fractions with compounds with high R_f values and concentrated to afford a clear gel, which upon freezing solidifies as a white solid (combined yield 0.319 g, 0.864 mmol, 34.6%). The compound remains solid at room temperature. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.65 – 7.61 (m, 2H), 7.44 – 7.27 (m, 9H), 7.21 – 7.12 (m, 2H), 7.19 – 7.13 (m, 3H), 6.71 (d, J = 6.1 Hz, 2H), 6.39 – 6.35 (m, 2H), 4.95 (s, 1H), 3.97 (d, J = 9.3 Hz, 1H), 3.94 (d, J = 9.3 Hz, 1H), 3.84 (d, J = 13.0 Hz, 1H), 3.76 (d, J = 12.7 Hz, 1H) ppm; **^{13}C NMR** (125 MHz, $CDCl_3$) δ 153.8, 142.0, 139.3, 138.1, 136.6, 130.2, 129.4, 129.1, 128.5, 128.2, 128.2, 127.9, 127.4, 110.6, 109.1, 76.9, 69.8, 61.3 ppm; **HRMS** (ESI) *m/z* 392.1609 (392.1626 calcd for $C_{25}H_{23}NNaO_2$ $[MNa]^+$).

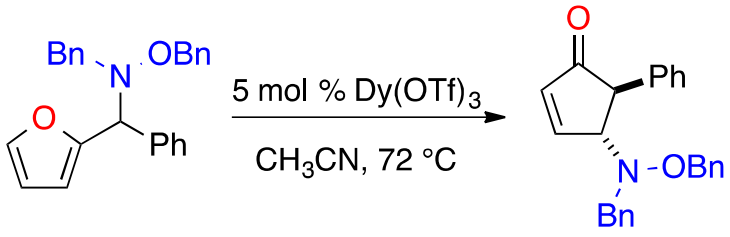
2.3 Synthesis of 4-(phenylamino)-5-phenylcyclopent-2-en-1-one (13)



13

Compound was synthesized and characterized according to the procedure previously reported in reference 3.[3]

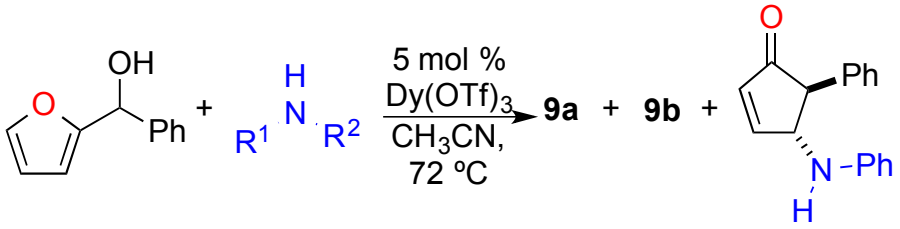
2.4 Conversion of Intermediate 9b to Cyclopentenone 9a



9b **9a**

To a 4 mL glass vial equipped with PTFE-silicon septum, open-top screw cap, and magnetic stir bar was added 2 mL of acetonitrile and *N,O*-dibenzyl-N-(furan-2-yl(phenyl)methyl)hydroxylamine (74.26 mg, 0.201 mmol). The vial was placed in a pre-heated bath of aluminum beads at 70 ºC and allowed to reach thermal equilibrium. Dy $(OTf)_3$ (6.23 mg, 0.0102 mmol, 5.1 mol % catalyst) was then added. For HPLC/MS analysis, sampling of the reaction began before addition of the catalyst. The first 20 samples were collected every 3 min while the remaining 25 samples were collected every 12 min.

2.5 Competition Experiment between Aniline and *N,O*-dibenzylhydroxylamine



7 **8**: R^1 = Bn, R^2 = OBn *and* **12**: R^1 = H, R^2 = Ph **13**

To a 10 mL glass vial equipped with PTFE-silicon septum, open-top screw cap, and magnetic stir bar was added 4.5 mL of acetonitrile, furan-2-yl(phenyl)methanol (87.0 mg, 0.5 mmol), *N,O*-dibenzylhydroxylamine (53.0 mg, 0.25 mmol), and aniline (23.0 mg, 0.25 mmol). The vial was placed in a pre-heated bath of aluminum beads at 72 ºC and allowed to reach thermal equilibrium. The in situ FT-IR instrument was blanked in hot solvent (72 ºC) contained in a separate vial. The probe was then immediately fitted onto the reaction vial. After a stable FT-IR signal was observed, Dy$(OTf)_3$ (15.0 mg, 0.025 mmol, 5 mol % catalyst) dissolved in 0.5 mL of acetonitrile was injected via syringe. For HPLC/MS analysis, sampling of the reaction

began immediately after injection of the catalyst. The first 60 samples were collected every 2 min while the remaining 36 samples were collected every 4 min.

2.6 Late Addition of Aniline

To a 10 mL glass vial equipped with PTFE-silicon septum, open-top screw cap, and magnetic stir bar was added 4.5 mL of acetonitrile, furan-2-yl(phenyl)methanol (87.0 mg, 0.5 mmol), and *N,O*-dibenzylhydroxylamine (107.0 mg, 0.5 mmol). The vial was placed in a pre-heated bath of aluminum beads at 72 ºC and allowed to reach thermal equilibrium. The in situ FT-IR instrument was blanked in hot solvent (72 ºC) contained in a separate vial. The probe was then immediately fitted onto the reaction vial. After a stable FT-IR signal was observed, $Dy(OTf)_3$ (15.0 mg, 0.025 mmol, 5 mol % catalyst) dissolved in 0.5 mL of acetonitrile was injected via syringe. The reaction was allowed to proceed for 20 min. Aniline (47.0 mg, 0.5 mmol) was injected into the reaction vial neat via a syringe. For HPLC/MS analysis, sampling of the reaction began immediately after injection of the catalyst. The first 30 samples were collected every 2 min while the remaining 30 samples were collected every 4 min.

2.7 Calibration Curves

To find relative absorptivity constants of all observable reactants, products, and intermediates (except aniline), stock solutions of each compound were made. Varying volumes of each stock solution were placed into LC vials, and the subsequent mixtures were analyzed by HPLC-MS under the second analytical method. Integrations were taken at 210 nm. Concentrations were calculated for mixtures of all compounds in LC vials for the same injection volume as detailed previously.

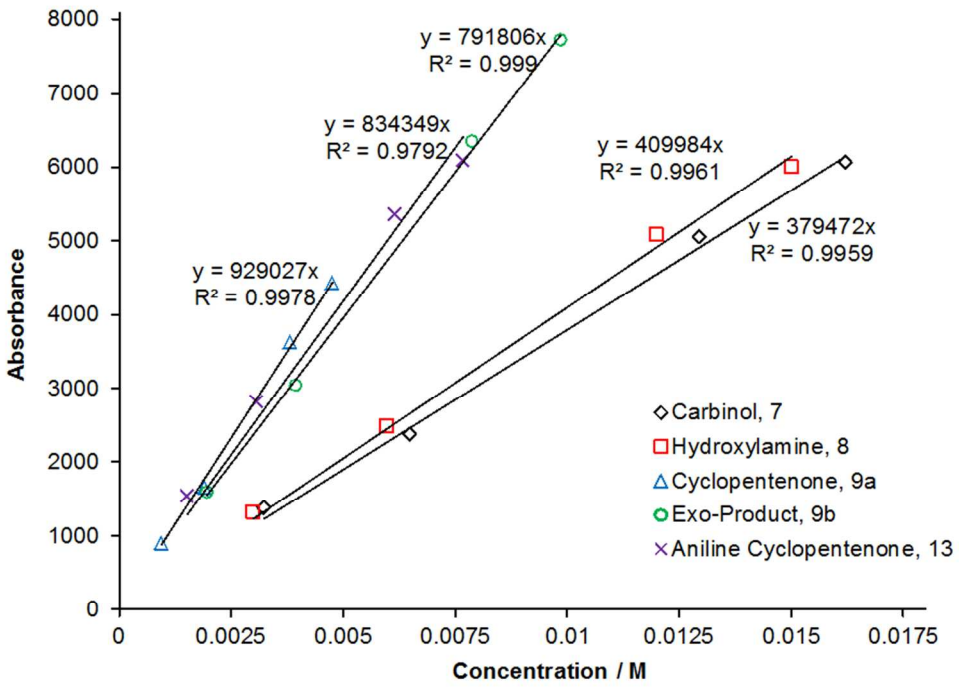
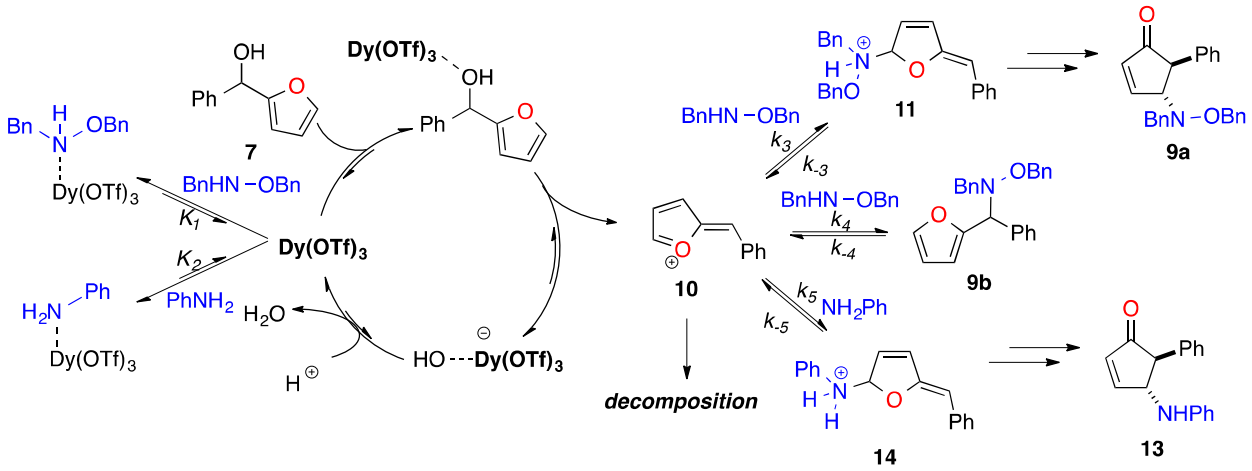


Figure S2: Calibration curves for all pertinent chemical species.

3 Kinetic Simulation Using COPASI



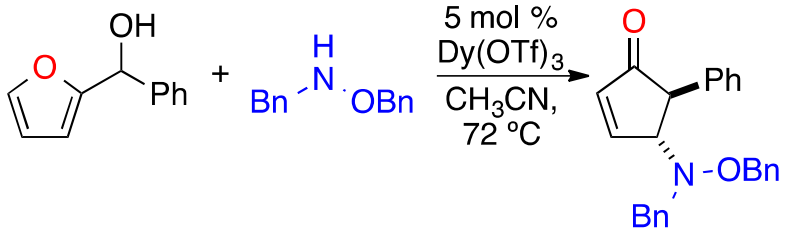
Simulation of the kinetic model was performed using Complex Pathway Simulator (COPASI).[4] The competitive mechanism was created using an input reaction array as follows:

Table S1: COPASI input reaction array.

Name	Reaction	Rate Law
01	Dy + Carbinol = Dy-OH + oxocarbenium	Mass action (reversible)
02	Dy-OH + H = Dy + H2O	Mass action (reversible)
03	oxocarbenium + aniline = aminal	Mass action (reversible)
04	aminal -> prod-1-H	Mass action (irreversible)
05	prod-1-H = prod-1 + H	Mass action (reversible)
06	Dy + aniline = Dy-aniline	Mass action (reversible)
07	Dy + hydroxylamine = Dy-hydroxylamine	Mass action (reversible)
08	oxocarbenium + hydroxylamine = exo	Mass action (reversible)
09	oxocarbenium + hydroxylamine = aminal2	Mass action (reversible)
10	aminal2 -> prod-2-H	Mass action (irreversible)
11	prod-2-H = prod-2 + H	Mass action (reversible)
12	H2O = H + OH	Mass action (reversible)
13	oxocarbenium -> decomp	Mass action (irreversible)
14	oxocarbenium + prod-1 -> decomp2	Mass action (irreversible)

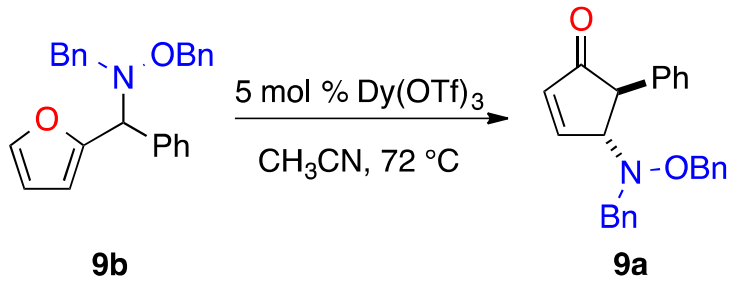
Product forming reactions involving the cationic rearrangement (Reactions 04 and 10) and decomposition of oxocarbenium (Reactions 13 and 14) were designated as irreversible. The water dissociation equilibria (Reaction 12) was fixed at a standard values of K = 1 x 10^{-14}. Concentration data from three independent experiments (shown below) were then loaded as experimental reference data.

(1)



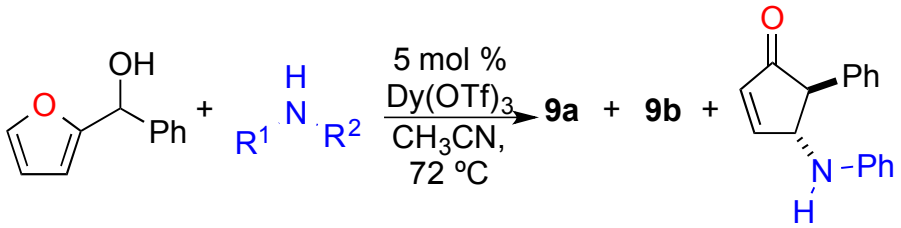
7 **8** **9a**

(2)



9b **9a**

(3)



7 **8**: R^1 = Bn, R^2 = OBn *and* **12**: R^1 = H, R^2 = Ph **13**

Initial values for the rate constants were randomized and then optimized using a generic algorithm (20000 generation, population size = 400). Optimization was run until the RMS error was constant for 1000 generations. Parameter estimation was completed for a total of 14 independent runs, each with differently randomized starting values for the rate constants. Data is tabulated in Table S2 and graphed against experimental results (Figure S2).

Table S2: Optimized rate constants from 15 independent, randomly selected initial values. Equilibrium constants (K = k1/k2) shown in red.

			1	2	3	4	5	6	7	8
1	Dy + carbinol = Dy-OH + oxo	k1 mL/(mmol*s)	0.423079	0.388353	0.462764	0.470454	0.429522	0.449669	0.456067	0.451212
1	Dy + carbinol = Dy-OH + oxo	k2 mL/(mmol*s)	3.73E-05	7.39E-06	0.00103787	0.000924324	0.000180924	0.000924324	0.00363596	3.73E-05
			1.13E+04	5.25E+04	4.46E+02	5.09E+02	2.37E+03	4.86E+02	1.25E+02	1.21E+04
2	Dy-OH + H = Dy + H2O	k1 mL/(mmol*s)	3941.42	4121.13	331.295	414.447	4927.73	11960.3	6252.12	11008.5
2	Dy-OH + H = Dy + H2O	k2 mL/(mmol*s)	0.00278094	7.99E-06	1.00E-06	83070.7	1.61513	1.47094	1.05081	4.04363
			1417297.748	516008789.8	331295000	0.004989088	3050.980416	8131.059051	5949.810146	2722.430094
3	oxo + aniline = aminal	k1 mL/(mmol*s)	33723.2	26200.9	160.664	103.665	7.83507	7.61663	8.89785	10.8931
3	oxo + aniline = aminal	k2 1/s	493.011	1942.81	0.299548	0.156787	0.000786365	7.43E-06	8.32E-06	7.34E-06
			68.40253057	13.48608459	536.3547745	661.1836441	9963.655554	1025146.034	1069666.544	1484720.859
4	aminal -> prod-1 + H	k1 1/s	0.134847	0.672922	0.0329074	0.0168579	0.0227665	0.0453752	0.00850771	0.00779717
5	prod-1-H = prod-1 + H	k1 1/s	0.00970599	0.00779483	39217.2	42718	40283.9	94373.3	205286	1.76354
5	prod-1-H = prod-1 + H	k2 mL/(mmol*s)	9.15E-06	1.68E-05	0.00196433	0.00156582	0.0535592	0.00579858	3.96E-06	0.000121367
			1060.368759	464.364947	19964669.89	27281552.16	752137.8213	16275243.25	51868714943	14530.63848
6	Dy + aniline = Dy-aniline	k1 mL/(mmol*s)	1.40634	11.3263	6.82147	3.58626	6.97168	8.47339	1.22695	1.28098
6	Dy + aniline = Dy-aniline	k2 1/s	0.00848513	0.0844557	0.0349503	0.0203852	0.0442657	0.050508	0.00663909	0.00691265
			165.7417152	134.1093615	195.1762932	175.9246905	157.4962104	167.7633246	184.806954	185.3095412
7	Dy + hydroxylamine = Dy-hydroxylamine	k1 mL/(mmol*s)	1.07E-05	0.000242082	1.63E-05	1.60E-06	1.55E-06	5.45E-06	2.22E-06	7.15061
7	Dy + hydroxylamine = Dy-hydroxylamine	k2 1/s	4.75063	4994.91	0.0969946	0.158756	0.0803651	1124.19	0.140438	14980.502
			2.24642E-06	4.84657E-08	0.000168099	1.00915E-05	1.93168E-05	4.84994E-09	1.58312E-05	0.000477328
8	oxo + hydorxylamine = exo	k1 mL/(mmol*s)	0.178373	0.251893	0.239076	0.242843	0.233771	0.208012	0.173237	0.181822
8	oxo + hydroxylamine = exo	k2 1/s	0.000670566	0.000704753	0.000661611	0.000675304	0.000694308	0.000684716	0.000668365	0.000664125
			266.0036447	357.4202593	361.3543306	359.6054518	336.6963941	303.7931055	259.1952002	273.776774
9	oxo + hydroxylamine = exo	k1 mL/(mmol*s)	0.351862	0.475541	0.506439	0.517185	0.433407	0.387698	0.341995	0.38383
9	oxo + hydroxylamine = exo	k2 1/s	1.32E-05	1.15238	1.83E-05	1.36E-05	4.66E-05	0.000128352	11.5118	0.0280269
			26735.40563	0.412659886	27731.39199	38131.20701	9302.136409	3020.584019	0.029708212	13.69505725
10	aminal2 -> prod-2-H	k1 1/s	20.492	81.896	0.529079	0.627673	0.422242	18887	13585	12825
11	prod-2-H = prod-2 + H	k1 mL/(mmol*s)	2.56928	28.8064	19.4799	16.1875	4.47133	3.9026	8.3218	11.281
11	prod-2-H = prod-2 + H	k2 1/s	8.25002	108.406	67.9771	52.8885	13.2975	11.778	26.0182	34.3124
			0.311427124	0.265726989	0.286565623	0.306068427	0.336253431	0.331346578	0.319845339	0.328773271
13	oxo -> decomp	k1 1/s	0.00173522	0.00171787	0.00205585	0.00223343	0.00221444	0.0021401	0.00161751	0.00192485
14	oxo + prod-1 -> decomp2	k1 mL/(mmol*s)	0.0976205	0.150314	0.138834	0.1531	0.130901	0.104427	0.10103	0.113242

Table S2 cont.: Optimized rate constants from 15 independent, randomly selected initial values. Equilibrium constants (K = k1/k2) shown in red.

			9	10	11	12	13	14	Average
1	Dy + carbinol = Dy-OH + oxo	k1 mL/(mmol*s)	0.419858	0.401651	0.417911	0.433061	0.423729	0.424481	0.432272214
1	Dy + carbinol = Dy-OH + oxo	k2 mL/(mmol*s)	7.39E-06	1.82E-06	2.95E-06	1.73E-05	0.00577188	2.95E-06	0.000899266
			5.68E+04	2.21E+05	1.42E+05	2.51E+04	7.34E+01	1.44E+05	47729.52471
2	Dy-OH + H = Dy + H2O	k1 mL/(mmol*s)	3022.95	2090	48976.8	2885.42	4161.17	4716.17	7772.103714
2	Dy-OH + H = Dy + H2O	k2 mL/(mmol*s)	0.0104257	0.00595734	0.494587	3.85588	1.34574	3.0304	5934.830449
			2.90E+05	3.51E+05	9.90E+04	7.48E+02	3.09E+03	1.56E+03	60677581.69
3	oxo + aniline = aminal	k1 mL/(mmol*s)	2156.66	39.39	29.0385	20.2563	13.2669	14.6637	4464.067646
3	oxo + aniline = aminal	k2 1/s	5910.07	0.010477	0.000164416	0.000113109	1.06E-05	0.000264065	596.1685124
			3.65E-01	3.76E+03	1.77E+05	1.79E+05	1.25E+06	5.55E+04	375633.2466
4	aminal -> prod-1 + H	k1 1/s	108.591	0.0163404	0.00646191	0.0088925	0.00884748	0.424852	7.857026798
5	prod-1-H = prod-1 + H	k1 1/s	0.0148288	340.888	332.94	9606	0.3069	0.0184305	30868.59637
5	prod-1-H = prod-1 + H	k2 mL/(mmol*s)	2.87E-05	1.85E-05	5.74E-05	3.25E-06	4.75E-06	1.27E-06	0.004510929
			5.17E+02	1.85E+07	5.80E+06	2.95E+09	6.46E+04	1.45E+04	3922181957
6	Dy + aniline = Dy-aniline	k1 mL/(mmol*s)	16791.3	8276.7	1.22102	7290.14	1.12263	10645.2	3074.769787
6	Dy + aniline = Dy-aniline	k2 1/s	106.059	58.1036	0.00741595	44.9384	0.00661856	66.0629	19.67389545
			1.58E+02	1.42E+02	1.65E+02	1.62E+02	1.70E+02	1.61E+02	166.0517535
7	Dy + hydroxylamine = Dy-hydroxylamine	k1 mL/(mmol*s)	1.23E-06	0.000370169	6.48E-05	0.000103527	8.10829	3.31E-06	1.089980209
7	Dy + hydroxylamine = Dy-hydroxylamine	k2 1/s	7749.29	276.769	6788.83	1.99011	287941	160056	34565.62202
			1.59E-10	1.34E-06	9.55E-09	5.20E-05	2.82E-05	2.07E-11	5.5321E-05
8	oxo + hydorxylamine = exo	k1 mL/(mmol*s)	0.80564	0.689853	0.538116	0.497792	0.226905	0.37715	0.3460345
8	oxo + hydroxylamine = exo	k2 1/s	0.00066719	0.000665256	0.000682974	0.00066007	0.000691708	0.000701466	0.000678029
			1.21E+03	1.04E+03	7.88E+02	7.54E+02	3.28E+02	5.38E+02	512.1484276
9	oxo + hydroxylamine = exo	k1 mL/(mmol*s)	1.64432	1.39453	1.02294	0.982561	0.140042	0.679105	0.6615325
9	oxo + hydroxylamine = exo	k2 1/s	0.000170939	2.02E-05	0.0172069	0.000187889	2.00E-06	0.000137252	0.907868002
			9.62E+03	6.90E+04	5.94E+01	5.23E+03	6.99E+04	4.95E+03	18836.86274
10	aminal2 -> prod-2-H	k1 1/s	4965.02	1269.54	599.178	14855	635.769	24353	6577.033857
11	prod-2-H = prod-2 + H	k1 mL/(mmol*s)	1393.51	2684.48	3906.54	3588.69	66656.4	2539.02	5775.975701
11	prod-2-H = prod-2 + H	k2 1/s	4410.41	8816.39	11769	11766.7	186968	8045.86	16578.52055
			3.16E-01	3.04E-01	3.32E-01	3.05E-01	3.57E-01	3.16E-01	0.315389718
13	oxo -> decomp	k1 1/s	0.0072574	0.00505505	0.0042028	0.00437532	0.00214536	0.00333003	0.003000374
14	oxo + prod-1 -> decomp2	k1 mL/(mmol*s)	0.476556	0.426624	0.315038	0.294277	0.127071	0.202429	0.202247393

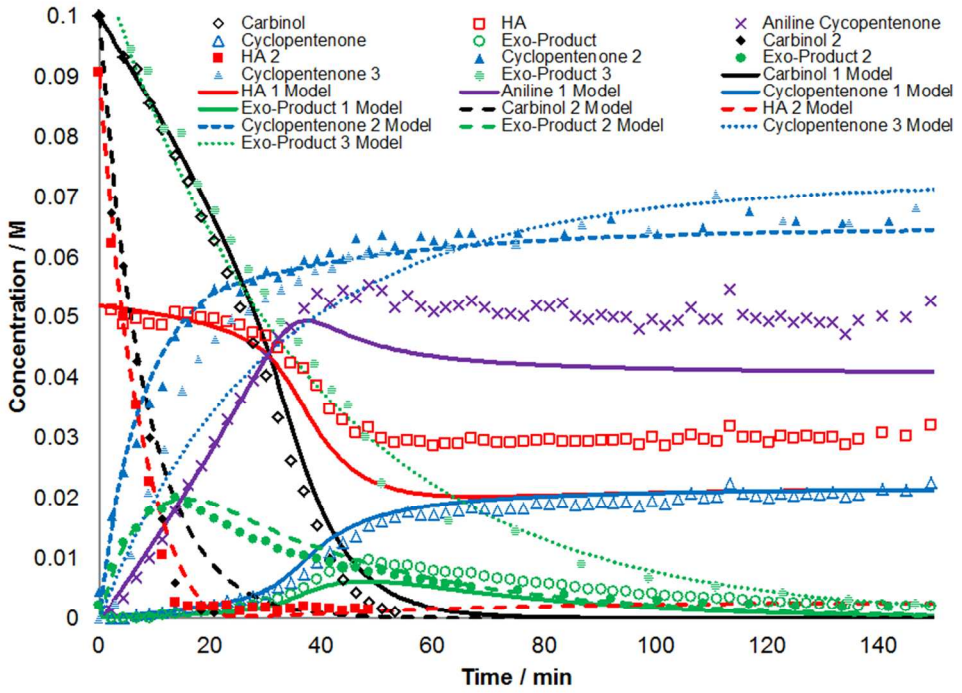


Figure S3: Overlay of all experimental data and simulated reaction progress data.

4 Reaction Progress Curves

4.1 Synthesis of 4-(Benzyl(benzyloxy)amino)-5-phenylcyclopent-2-en-1-one (9a)

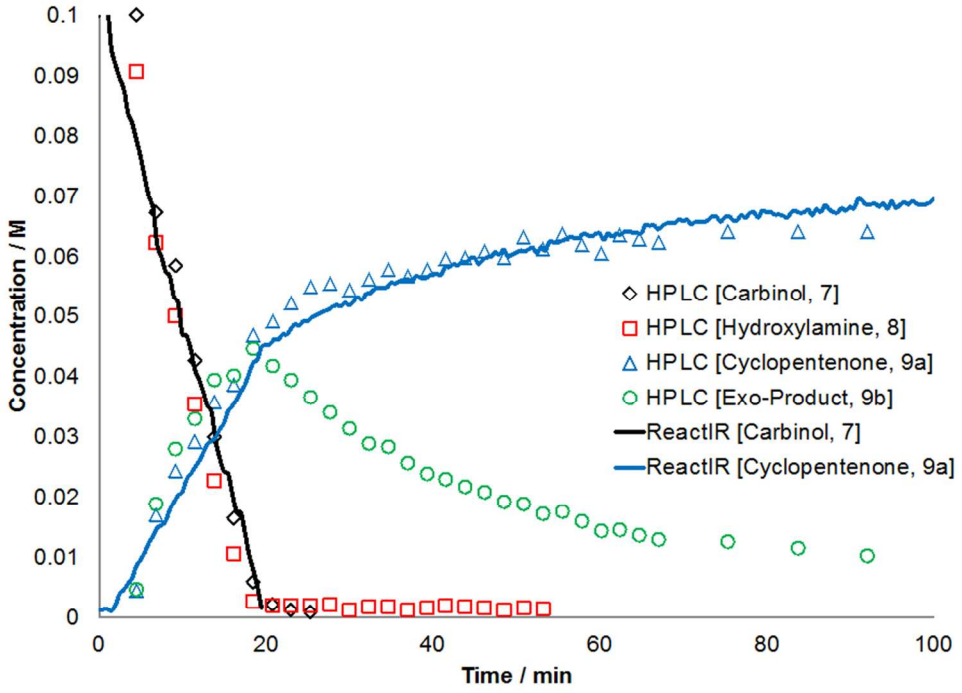


Figure S4: Reaction progress data from both HPLC-MS and IR instruments show good agreement for aza-Piancatelli rearrangement with *N*,*O*-dibenzylhydroxylamine.

4.2 Conversion of Intermediate 9b to Cyclopentenone 9a

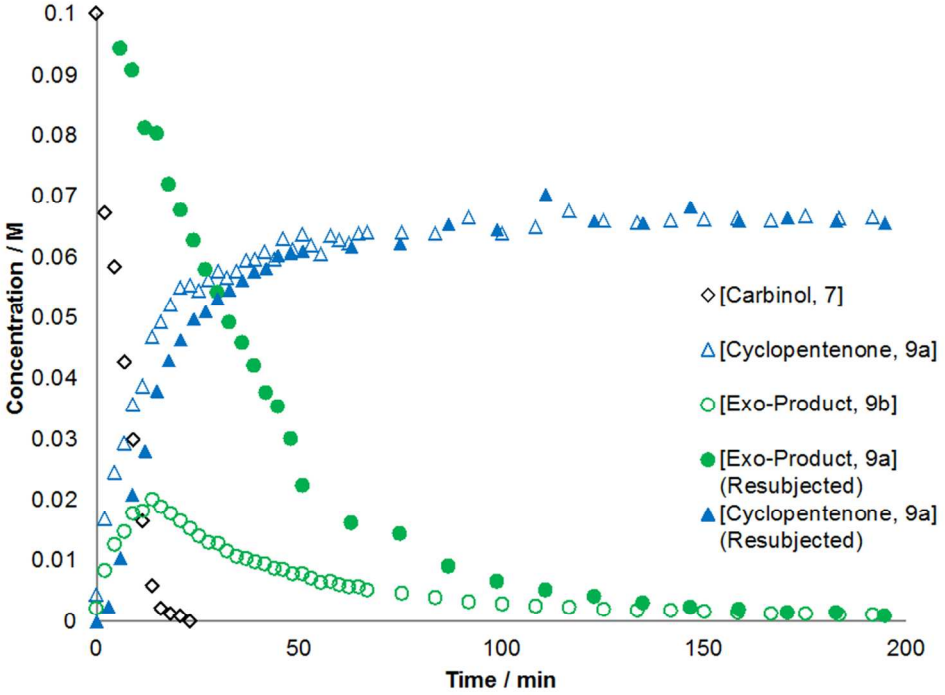


Figure S5: Reaction progress data from both HPLC-MS and IR instruments show good agreement for aza-Piancatelli rearrangement with *N*,*O*-dibenzylhydroxylamine.

4.3 Competition Reaction between Aniline and *N*,*O*-dibenzylhydroxylamine

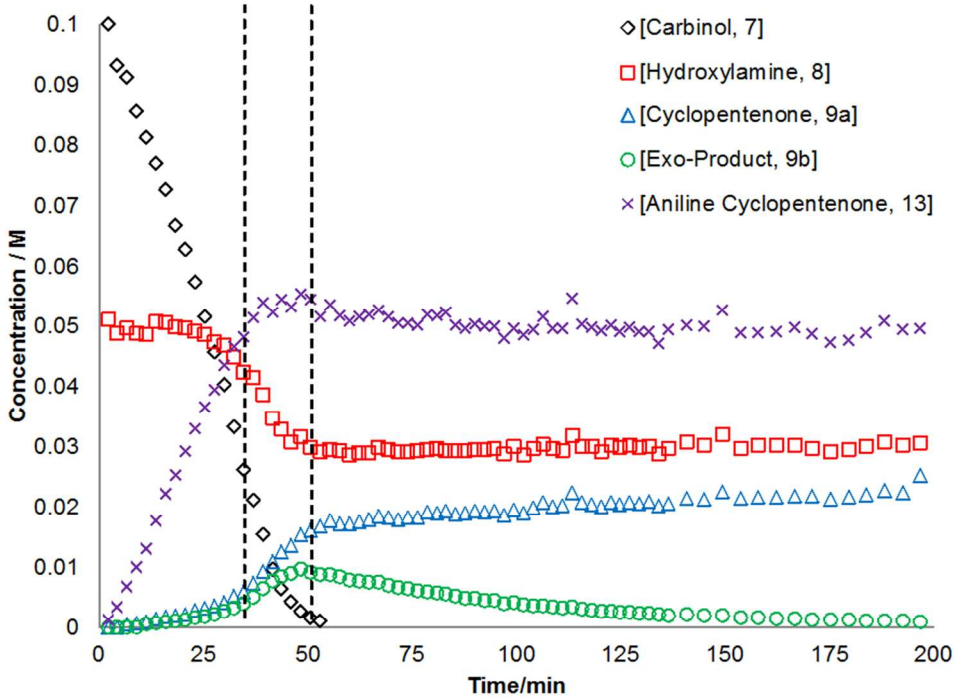


Figure S6: Aniline **10** in competition with *N*,*O*-dibenzylhydroxylamine **8** for rearrangement with furylcarbinol **7** shows a significant chemoselectivity towards the aniline cyclopentenone **13**.

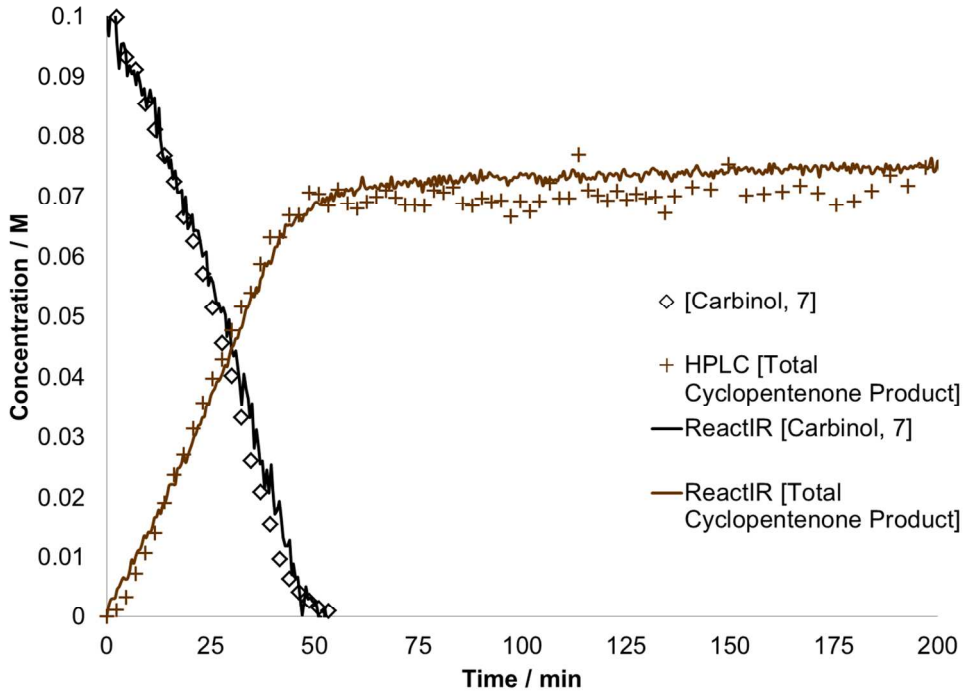


Figure S7: Overlay of ReactIR and HPLC-MS data of total cyclopentenone product for the competition reaction of *N*,*O*-dibenzylhydroxylamine and aniline shows excellent agreement.

4.4 Late Addition of Aniline Experiment

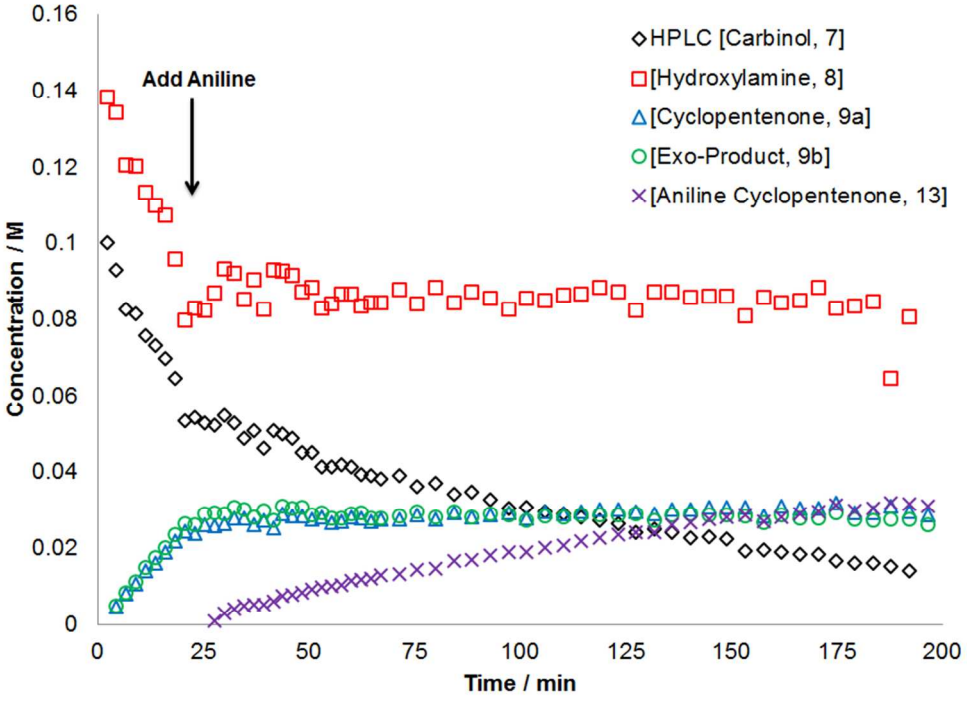


Figure S8: Late addition aniline changes the course of the on-going reaction between 2-furyl(phenyl)carbinol, N,O-dibenzylhydroxylamine to favor the aniline cyclopentenone.

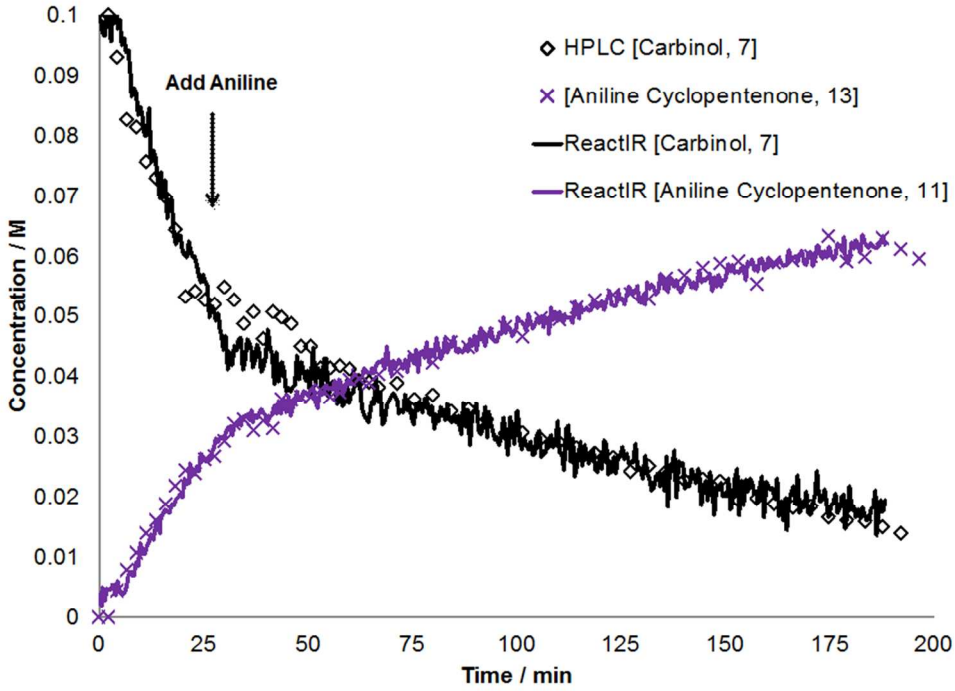


Figure S9: Overlay of HPLC-MS and ReactIR data for late aniline addition experiment also shows good agreement.

5 References

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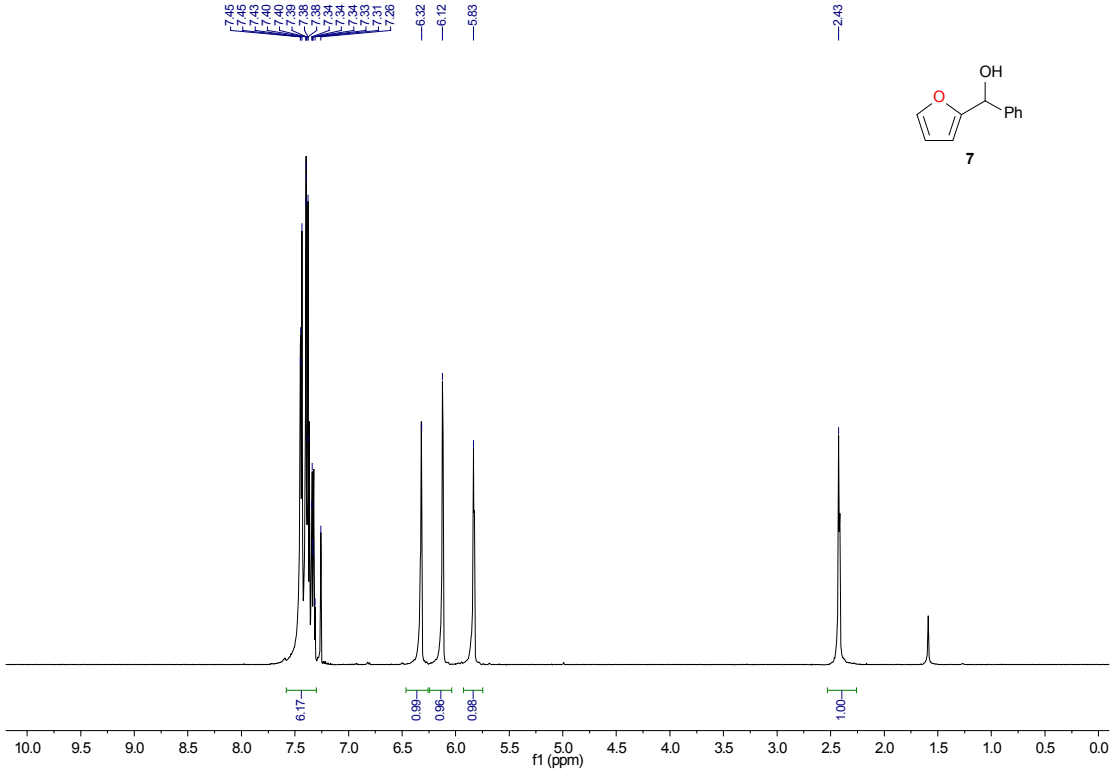
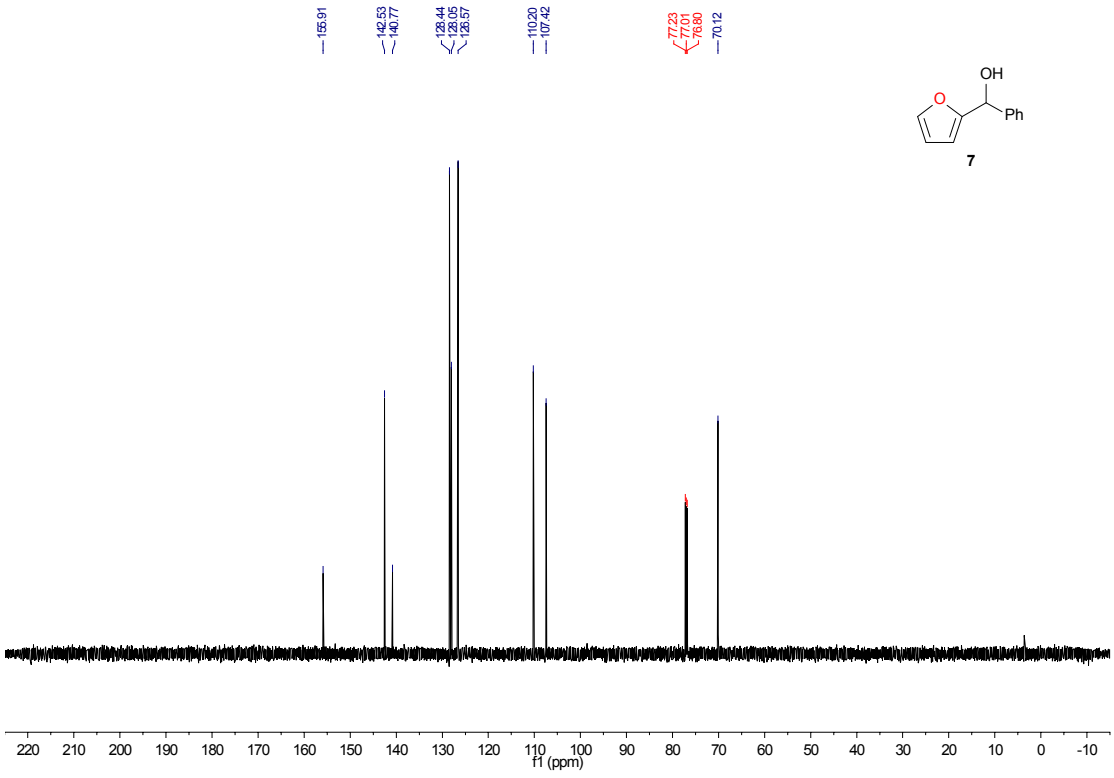
(2) Gantt; R. W.; Peltier-Pain, P.; Cournoyer, W. J.; Thorson, J. S. *Nat. Chem. Biol.*, **2011**, *7*, 685–691.

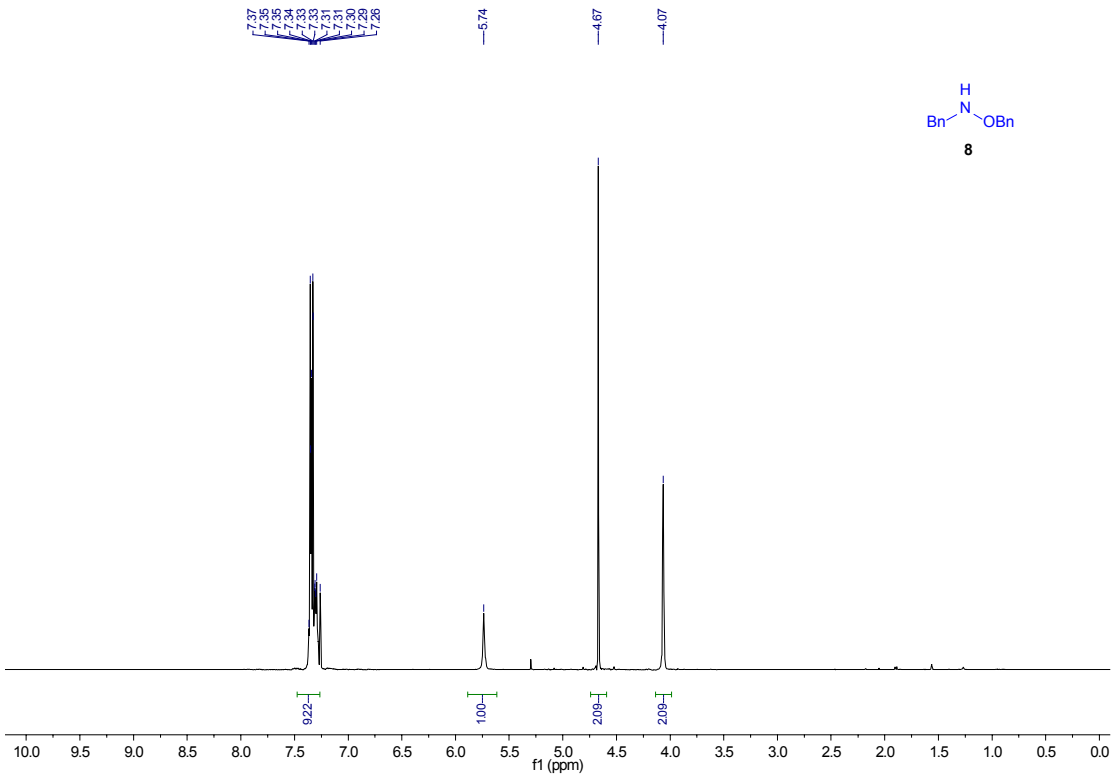
(3) Veits, G. K.; Wenz, D. R.; Palmer, L. I.; Read de Alaniz, J. *Angew. Chem. Int. Ed.*, **2010**, *49*, 9484–9487.

(4) Hoops, S.; Sahle, S.; Gauges, R.; Lee, C.; Pahle, J.; Simus, N.; Singhal, M.; Xu, L.; Mendes, P.; Kummer, U. *Bioinformatics*, **2006**, *22*, 3067–3074.

6 NMR Spectra



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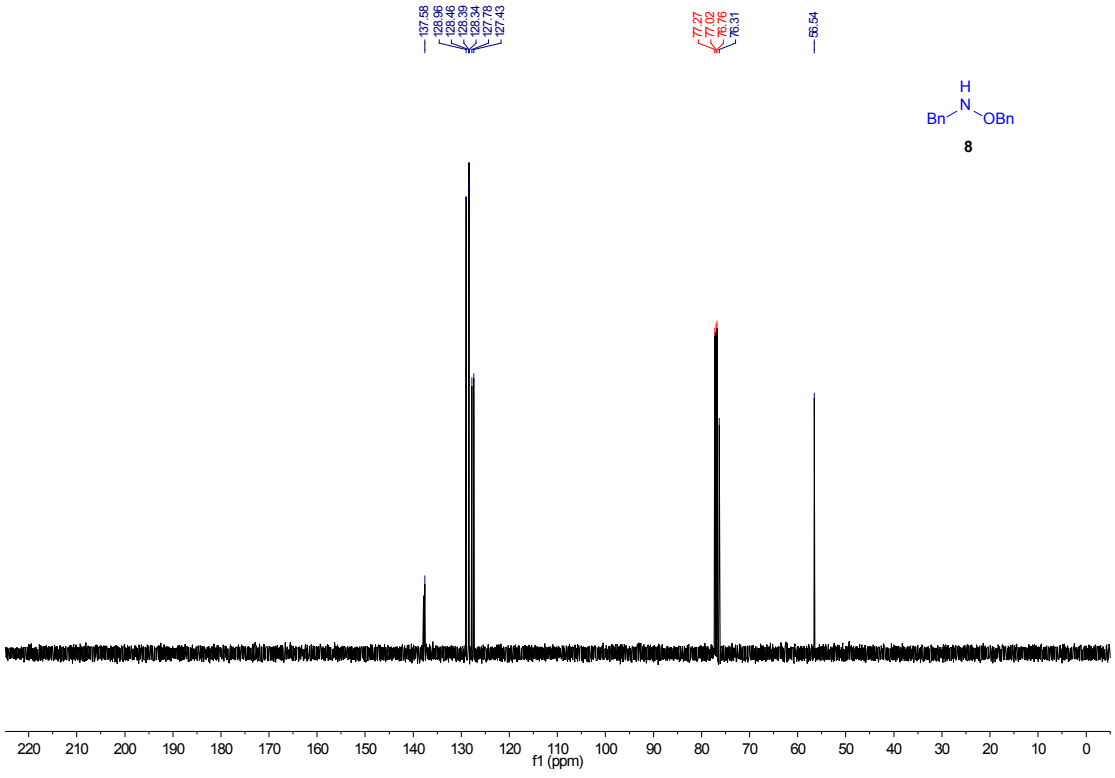
7.35
7.35
7.34
7.33
7.33
7.31
7.31
7.30
7.29
7.26
5.74
4.67
4.07
H
N
Bn
OBn
8
9.22
1.00
2.09
2.09
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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128.39
128.34
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127.43
77.27
77.02
76.76
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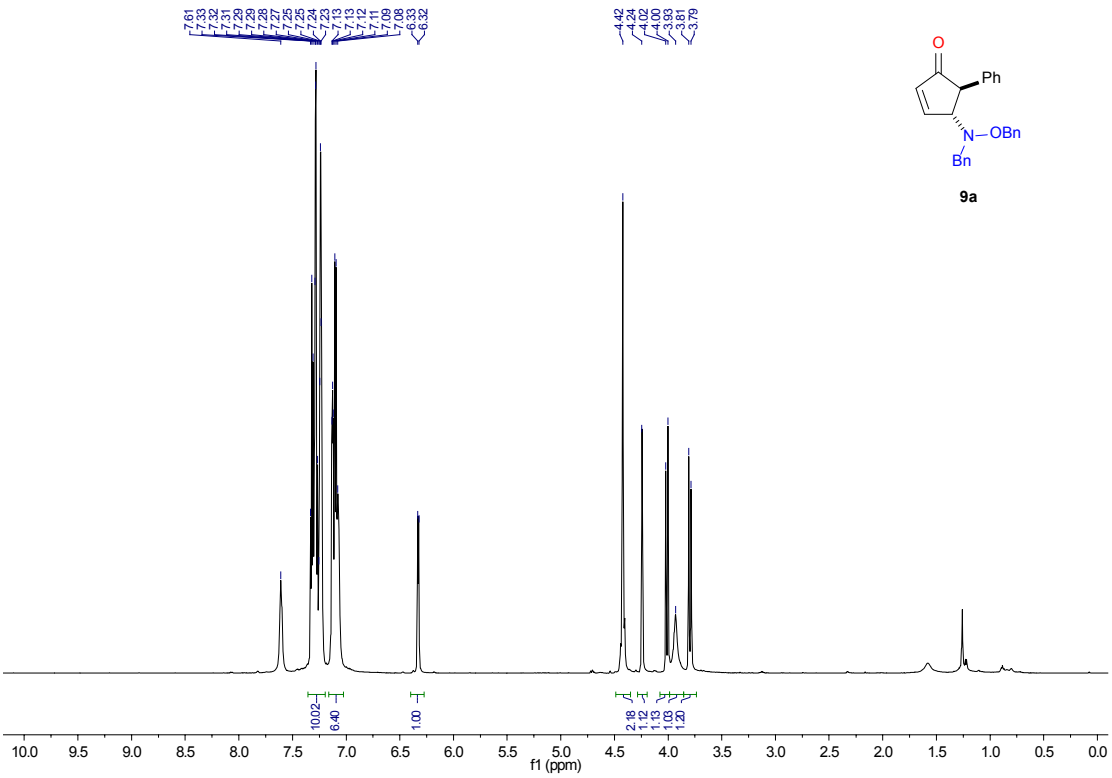
H
N
Bn
OBn
8
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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7.32
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7.29
7.28
7.27
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7.25
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7.23
7.13
7.12
7.11
7.09
7.08
6.33
6.32
4.42
4.24
4.02
4.00
3.93
3.81
3.79
10.02
6.40
1.00
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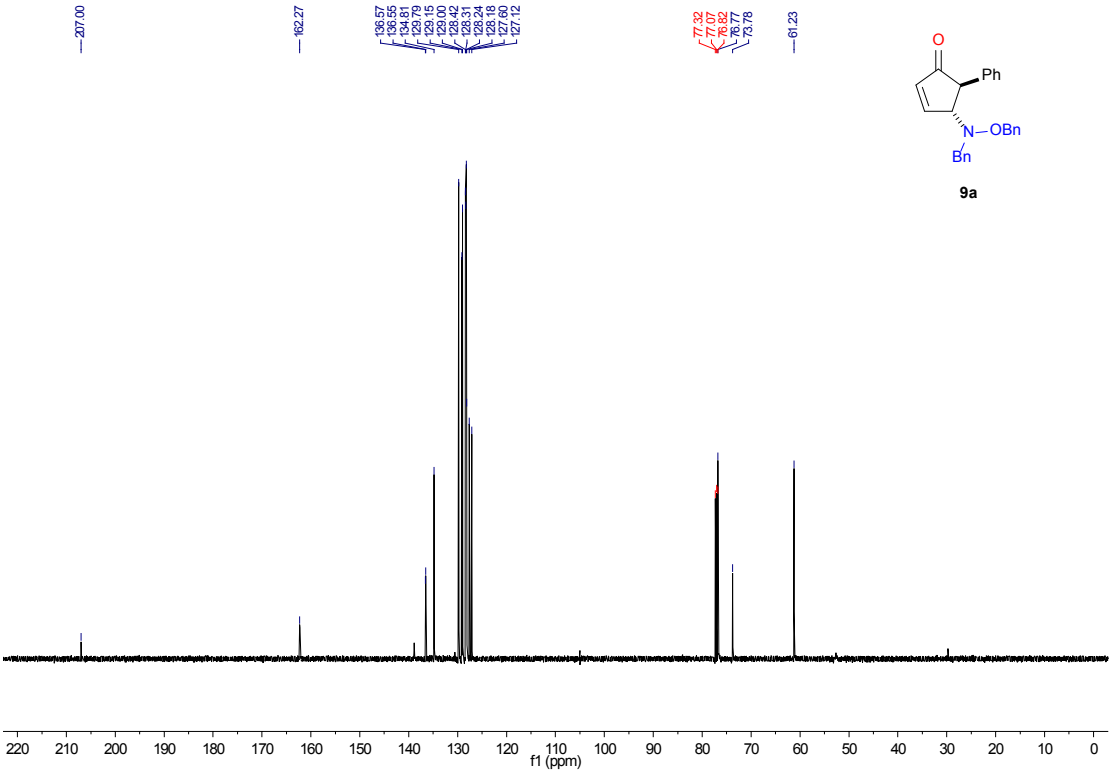
1.12
1.13
1.03
1.20
f1 (ppm)
O
Ph
N—OBn
Bn
9a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134.81
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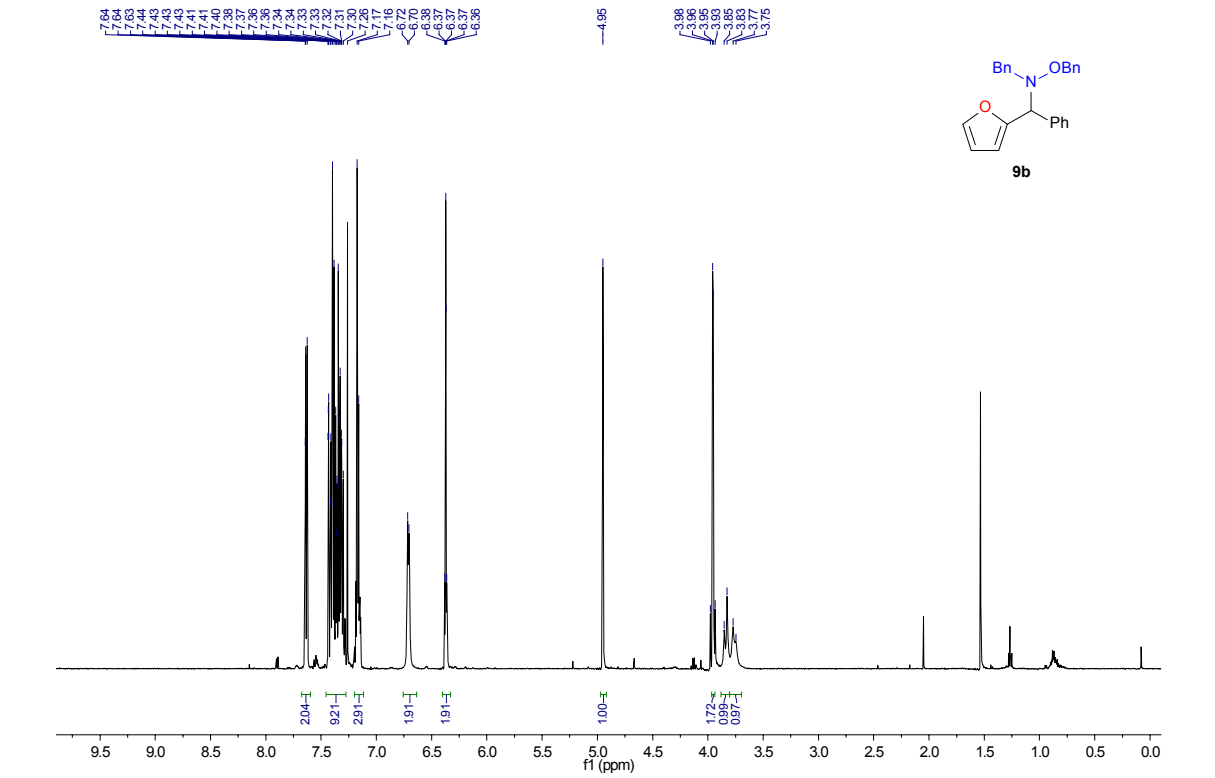
128.31
128.24
128.18
127.60
127.12
77.32
77.07
76.82
76.77
73.78
61.23
f1 (ppm)
O
Ph
N—OBn
Bn
9a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7.64
7.63
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7.43
7.43
7.43
7.41
7.41
7.40
7.38
7.37
7.36
7.36
7.34
7.34
7.33
7.33
7.32
7.31
7.30
7.26
7.17
7.16
6.72
6.70
6.38
6.37
6.37
6.37
6.36
4.95
3.98
3.96
3.95
3.93
3.85
3.83
3.77
3.75
Bn
N
OBn
O
Ph
9b
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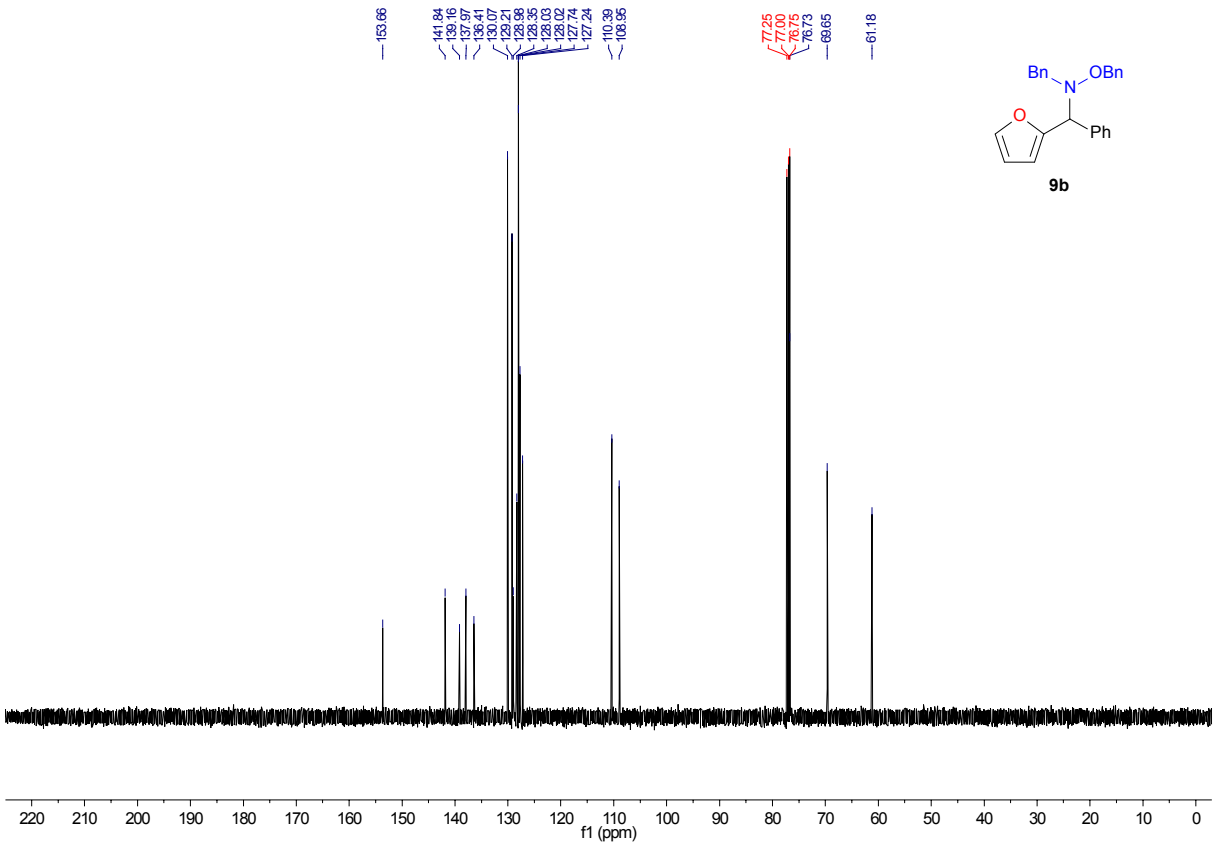
1.91
1.00
1.72
0.99
0.97
f1 (ppm)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128.03
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108.95
77.25
77.00
76.75
76.73
69.65
61.18
Bn
N
OBn
O
Ph
9b
f1 (ppm)