Electronic Supplementary Material (ESI) for Chemical Communications

Supporting Information

Palladium-Catalyzed Oxidative Direct C-H/C-H Cross Coupling of Anilides with β-Keto Esters

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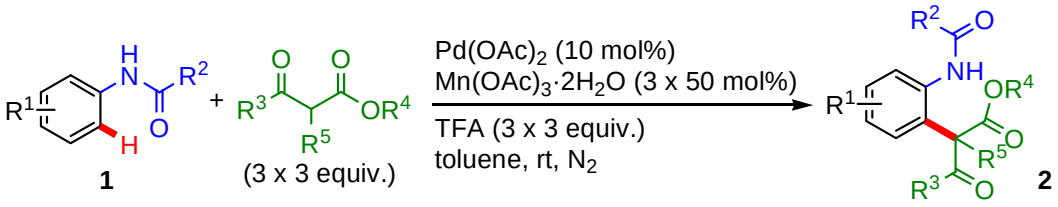
1. General Experimental Section

All the reactions were performed under a nitrogen atmosphere. All the solvents were freshly distilled and dried according to the standard methods prior to use. Anilines, 1,3-dicarbonyl compounds, $Pd(OAc)_2$, $Mn(OAc)_3 \cdot 2H_2O$ and trifluoroacetic acid (TFA) were obtained from commercial source. *N*-pivalanilides and *N*-acetanilides were prepared by the coupling reaction of corresponding anilines with pivaloyl or acetyl chlorides.[1]

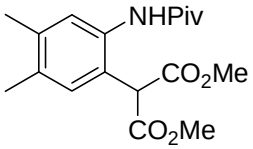
Thin layer chromatography was performed on silica gel plates. Flash column chromatography was performed on silica gel (Merck, 230-400 mesh). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 MHz spectrometer. The chemical shift (δ) values are given in ppm and are referenced to residual solvent peaks, carbon multiplicities were determined by DEPT-135 and DEPT-90 experiments. Coupling constants (*J*) were reported in hertz (Hz). Multiplicity abbreviations are: s = singlet, d= doublet, t = triplet, q = quartet, m = multiplet, dt = doublet of triplets, td = triplet of doublets, and br = broad. Mass spectra and high resolution mass spectra (HRMS) were obtained on a VG MICROMASS Fison VG platform, a Finnigan Model Mat 95 ST instrument, or a Bruker APEX 47e FT-ICR mass spectrometer. Infra-red spectra were obtained by a Bruker Vector 22 FT-IR spectrometer. Optical rotations were recorded on a Perkin-Elmer 341 polarimeter in a 10 mm cell. Melting points were measured on a BUCHI Melting Point B-545 machine. X-ray crystallographic study was preformed by a Brüker CCD area detector diffractometer.

2. General Procedure and Physical Characterization

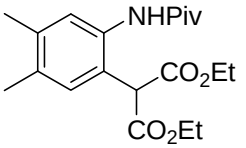


A 10 mL Schlenk test-tube (with a Quick-fit stopper and side arm) equipped with a magnetic stir bar was charged with the anilides (0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and $Mn(OAc)_3 \cdot 2H_2O$ (0.0268 g, 50 mol%). The Schlenk tube was evacuated and refilled with nitrogen for three times. Then the glass stopper was replaced by rubber septa. Dry toluene (1.5 mL), 1,3-dicarbonyl compound (0.6 mmol) and TFA (46.1 μL, 0.6 mmol) was added under a flow of nitrogen. The reaction mixture was stirred at room temperature. After 4 h, a batch of reagents [$Mn(OAc)_3 \cdot 2H_2O$ (50 mol%), 1,3-dicarbonyl compound (0.6 mmol), TFA (0.6 mmol)] was added to the

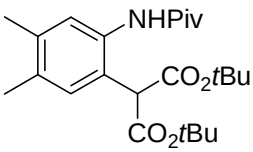
mixture. The batchwise addition was preformed again after further 4 h. The reaction was subsequently allowed to stir for overnight. Then the reaction mixture was filtered over a plug of Celite® and then concentrated. The residue was purified by flash chromatography to give the desired product.



Dimethyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)malonate (2a). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as colorless oil (85% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.85 (s, 1H, NH), 7.55 (s, 1H, ArH), 6.96 (s, 1H, ArH), 4.58 (s, 1H, CH), 3.73 (s, 6H, $2CH_3$), 2.24 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 1.29 (s, 9H, 3 CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.6 (C=O), 170.0 (C=O), 138.3 (C), 134.7 (C), 134.2 (C), 132.8 (CH), 128.0 (CH), 123.5 (C), 56.8 (CH_3), 53.4 (CH_3), 39.8 (C), 27.9 (CH), 19.9 (CH_3), 19.5 (CH_3). IR (neat, cm^{-1}): 3348.2, 2971.1, 2864.3, 1739.6, 1634.5, 1571.3, 1526.7, 1150.0. HRMS (ESI): calcd. for $C_{18}H_{25}NO_5H^+$: 336.1811, found: 336.1802.

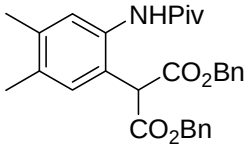


Diethyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)malonate (2b). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as colorless oil (75% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.91 (s, 1H, NH), 7.56 (s, 1H, ArH), 6.95 (s, 1H, ArH), 4.53 (s, 1H, CH), 4.27 – 4.19 (m, 2H, CH_2), 4.17 – 4.09 (m, 2H, CH_2), 2.23 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.28 (s, 9H, $3CH_3$), 1.24 – 1.21 (m, 6H, $2CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.5 (C=O), 169.6 (C=O), 138.0 (C), 134.8 (C), 133.8 (C), 132.9 (CH), 127.8 (CH), 123.5 (C), 62.5 (CH_2), 57.2 (CH_3), 39.8 (C), 27.8 (CH_3), 19.9 (CH_3), 19.5 (CH_3), 14.3 (CH_3). IR (neat, cm^{-1}): 3353.2, 2965.9, 2869.7, 1738.6, 1721.3, 1680.8, 1579.12, 1518.5, 1152.2. HRMS (ESI): calcd. for $C_{20}H_{29}NO_5H^+$: 364.2124, found: 364.2137.

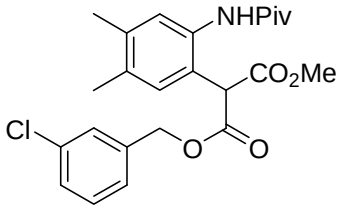


Di-*tert*-butyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)malonate (2c). Eluent: 80% *n*-hexane / 20% acetone. The product was obtained as white solid (81% yield), mp

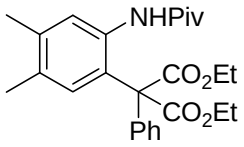
130 – 131 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.96 (s, 1H, NH), 7.64 (s, 1H, ArH), 6.93 (s, 1H, ArH), 4.39 (s, 1H, CH), 2.22 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.43 (s, 18H, 2 x $3CH_3$), 1.29 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.4 (C=O), 168.7 (C=O), 137.5 (C), 134.9 (C), 133.3 (CH), 132.9 (C), 126.8 (CH), 123.6 (C), 83.0 (C), 58.9 (CH), 39.9 (C), 28.2 (CH_3), 27.9 (CH_3), 19.9 (CH_3), 19.5 (CH_3). IR (neat, cm^{-1}): 3362.3, 2964.5, 2850.5, 1742.5, 1646.5, 1529.3, 1433.3, 1151.2. HRMS (ESI): calcd. for $C_{24}H_{37}NO_5Na^+$: 442.2569, found: 442.2562.



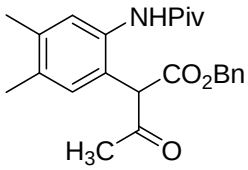
Dibenzyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)malonate (2d). Eluent: 50% *n*-hexane / 50% diethyl ether. The product was obtained as colorless oil (94% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.79 (s, 1H, NH), 7.58 (s, 1H, ArH), 7.33 – 7.29 (m, 10H), 6.96 (s, 1H, ArH), 5.26 – 5.23 (d, J = 12.0 Hz, 2H, CH_2Ph), 5.09 – 5.06 (d, J = 12.0 Hz, 2H, CH_2Ph), 4.66 (s, 1H, CH), 2.54 (s, 3H, CH_3), 2.19 (s, 3H, CH_3), 1.27 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.8 (C=O), 169.2 (C=O), 138.2 (C), 135.3 (C), 134.7 (C), 134.2 (C), 132.9 (CH), 128.9 (CH), 128.8 (CH), 128.7 (CH), 127.9 (CH), 123.4 (C), 68.2 (CH_2), 56.9 (CH), 39.8 (C), 27.8 (CH_3), 19.9 (CH_3), 19.5 (CH_3). IR (neat, cm^{-1}): 3361.2, 2961.3, 2866.5, 1739.1, 1676.5, 1517.7, 1455.6, 1148.0. HRMS (ESI): calcd. for $C_{30}H_{33}NO_5H^+$: 488.2437, found: 488.2461.



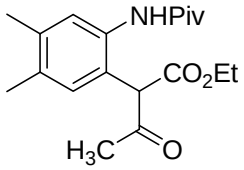
1-(3-Chlorobenzyl) 3-methyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)malonate (2e). Eluent: 50% *n*-hexane / 50% diethyl ether. The product was obtained as colorless oil (93% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.74 (s, 1H, NH), 7.54 (s, 1H, ArH), 7.28 – 7.26 (m, 3H, ArH), 7.18 – 7.16 (m, 1H, ArH), 6.97 (s, 1H, ArH), 5.23 – 5.20 (d, J = 12.0 Hz, 1H, CH_2Ph), 5.05 – 5.02 (d, J = 12.0 Hz, 1H, CH_2Ph), 4.63 (s, 1H, CH), 3.72 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.21 (s, 3H, CH_3), 1.27 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.6 (C=O), 169.7 (C=O), 169.3 (C=O), 138.3 (C), 137.3 (C), 134.8 (C), 134.7 (C), 134.3 (C), 132.8 (CH), 130.3 (CH), 129.0 (CH), 128.6 (CH), 128.1 (CH), 126.7 (CH), 123.4, 67.2 (CH_2), 56.7 (CH), 53.4 (CH_3), 39.8 (C), 27.8 (CH_3), 19.9 (CH_3), 19.5 (CH_3). IR (neat, cm^{-1}): 3367.3, 2958.4, 2866.5, 1742.5, 1676.7, 1578.5, 1517.5, 1150.8. HRMS (ESI): calcd. for $C_{24}H_{28}NO_5ClH^+$: 446.1734, found: 446.1727.



Diethyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)-2-phenylmalonate (2f). Eluent: 70% *n*-hexane / 30% diethyl ether. The product was obtained as colorless oil (52% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 7.62 (s, 1H, ArH), 7.42 – 7.40 (m, 3H, ArH & NH), 7.31 – 7.30 (m, 3H, ArH), 7.23 (s, 1H, ArH), 4.26 – 4.19 (m, 4H, $2CH_2$), 2.26 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 1.20 – 1.17 (m, 2 x 3H, $2CH_3$), 0.90 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 176.5 (C=O), 170.4 (C=O), 137.6 (C), 136.9 (C), 134.4 (C), 133.4 (C), 131.2 (CH), 129.6 (CH), 128.4 (CH), 127.7 (CH), 126.8 (CH), 67.8 (C), 62.6 (CH_2), 39.6 (C), 27.3 (CH_3), 20.0 (CH_3), 19.8 (CH_3), 14.1 (CH_3). IR (neat, cm^{-1}): 3421.4, 2977.3, 2866.5, 1729.32, 1685.3, 1517.0, 1448.3, 1242.2, 1161.8. HRMS (ESI): calcd. for $C_{26}H_{33}NO_5H^+$: 440.2437, found: 440.2444.

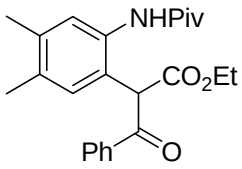


Benzyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxobutanoate (2g). The crude was purified by column chromatography twice. Eluent for the 1st: 70% *n*-hexane / 30% ethyl acetate. Eluent for the 2nd: 50% *n*-hexane / 50% diethyl ether. The product was obtained as colorless oil (69% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.22 (s, 1H, NH), 7.58 (s, 1H, ArH), 7.37 (m, 5H, ArH), 6.98 (s, 1H, ArH), 5.32 (s, 2H, CH_2Ph), 4.57 (s, 1H, CH), 2.24 (s, 3H, CH_3), 2.13 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 1.15 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 205.3 (C=O), 177.4 (C=O), 170.3 (C=O), 138.9 (C), 134.6 (C), 134.1 (C), 133.8 (C), 129.4 (CH), 129.2 (CH), 128.5 (CH), 127.5 (CH), 126.1 (C), 84.8 (C), 69.1 (CH_2), 39.7 (C), 27.5 (CH_3), 25.9 (CH_3), 19.9 (CH_3), 19.7 (CH_3). IR (neat, cm^{-1}): 3372.3, 3293.9, 2961.5, 2917.1, 1725.4, 1655.1, 1571.5, 1260.5. HRMS (ESI): calcd. for $C_{24}H_{29}NO_4H^+$: 396.2175, found: 396.2171.

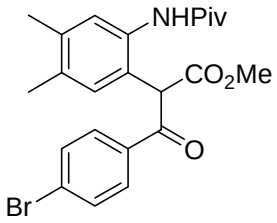


Ethyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxobutanoate (2h). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as colorless oil (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.36 (s, 1H, NH), 7.59 (s, 1H, ArH), 7.23 (s, 1H, ArH), 4.57 (s, 1H, CH), 4.40 – 4.33 (m, 2H, CO_2CH_2), 2.25 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.11 (s, 3H, $COCH_3$), 1.36 – 1.33 (t, J = 7.2 Hz, 3H, CH_3), 1.23 (s, 9H, $3CH_3$).

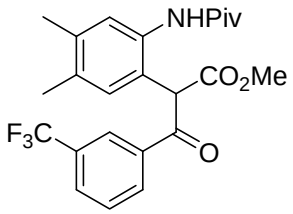
^{13}C NMR (100 MHz, $CDCl_3$): δ_C 205.3 (C=O), 177.4 (C=O), 170.5 (C=O), 138.8 (C), 134.1 (C), 133.8 (C), 128.3 (CH), 127.5 (CH), 126.2 (C), 84.7 (C), 63.7 (CH_2), 39.8 (CH), 27.6 (CH_3), 25.7 (CH_3), 19.9 (CH_3), 19.8 (CH_3), 14.4 (CH_3). IR (neat, cm^{-1}): 3345.3, 3221.1, 2961.5, 2900.3, 1608.4, 1634.1, 1491.5, 1232.5. HRMS (ESI): calcd. for $C_{19}H_{27}NO_4H^+$: 333.4256, found: 333.4260.



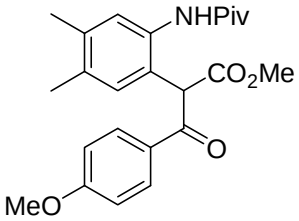
Ethyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxo-3-phenylpropanoate (2i). Eluent: 50% *n*-hexane / 50% diethyl ether. The product was obtained as white solid (48% yield), mp 157 – 159 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 13.9 (s, 0.01, enol OH), 8.60 (s, 1H, NH), 7.87 – 7.85 (d, J = 8.0 Hz, 2H, ArH), 7.53 – 7.48 (m, 2H, ArH), 7.39 – 7.35 (m, 2H, ArH), 7.04 (s, 1H, ArH), 5.47 (s, 1H, CH), 4.31 – 4.21 (m, 2H, CH_2), 2.21 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.28 (s, 9H, 3CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 195.3 (C=O), 177.4 (C=O), 170.5 (C=O), 138.1 (C), 135.8 (C), 135.1 (C), 134.4 (C), 134.0 (CH), 132.7 (CH), 129.3 (CH), 129.0 (CH), 127.9 (CH), 124.4 (C), 62.4 (CH_2), 60.3 (CH_3), 39.8 (C), 27.7 (CH_3), 19.9 (CH_3), 19.6 (CH_3), 14.4 (CH_3). IR (neat, cm^{-1}): 3379.3, 2977.5, 2866.5, 1725.0, 1676.2, 1578.0, 1518.2, 1182.7. HRMS (ESI): calcd. for $C_{24}H_{29}NO_4H^+$: 396.2175, found: 396.2177.



Methyl 3-(4-bromophenyl)-2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxopropanoate (2j). Eluent: 50% *n*-hexane / 50% diethyl ether. The product was obtained as white solid (51% yield), mp 165 – 167 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.42 (s, 1H, NH), 7.71 – 7.69 (d, J = 8 Hz, 2H, ArH), 7.65 (s, 1H, ArH), 7.44 – 7.42 (d, J = 8 Hz, 2H, ArH), 7.18 (s, 1H, ArH), 4.88 (s, 1H, CH), 3.87 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.20 (s, 3H, CH_3), 1.18 (s, 9H, 3CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 194.9 (C=O), 176.7 (C=O), 172.3 (C=O), 138.9 (C), 134.2 (C), 133.7 (C), 132.4 (CH), 131.9 (CH), 131.8 (C), 129.6 (C), 128.1 (CH), 126.9 (CH), 126.1 (C), 84.6 (C), 54.5 (CH_3), 39.8 (C), 27.6 (CH_3), 20.0 (CH_3), 19.8 (CH_3). IR (neat, cm^{-1}): 3401.9, 3251.6, 2958.8, 2917.2, 1745.8, 1717.9, 1686.8, 1661.1, 1584.5, 1518.4, 1248.9, 1177.9. HRMS (ESI): calcd. for $C_{23}H_{25}BrNO_4H^+$: 459.1045, found: 459.1041.

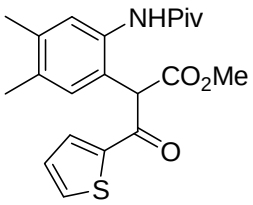


Methyl 3-(3-(Trifluoromethyl)phenyl)-2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxopropanoate (2k). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as colorless oil (42% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 8.35 (s, 1H, NH), 8.16 (s, 1H, ArH), 7.92 – 7.90 (d, J = 8.0 Hz, 1H, ArH), 7.72 – 7.70 (d, J = 8.0 Hz, 1H, ArH), 7.58 (s, 1H, ArH), 7.41 – 7.37 (t, J = 8.0 Hz, 1H, ArH), 4.82 (s, 1H, CH), 3.92 (s, 3H, CH_3), 2.24 (s, 3H, CH_3), 2.23 (s, 3H, CH_3), 1.17 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 194.6 (C=O), 176.7 (C=O), 172.1 (C=O), 139.1 (C), 134.1 (CH), 134.0 (C), 133.6 (CH), 130.7 (q, CF_3), 129.0 (CH), 127.8 (C), 127.6 (CH), 127.5 (CH), 127.2 (CH), 126.2 (C), 125.2 (C), 122.5 (C), 84.4 (CH), 54.6 (CH_3), 39.8 (C), 27.6 (CH_3), 19.9 (CH_3), 19.8 (CH_3). ^{19}F NMR (376 MHz, $CDCl_3$): -63.1 (CF_3). IR (neat, cm^{-1}): 3366.9, 2960.1, 2920.3, 1745.1, 1686.4, 1515.5, 1453.5, 1332.0, 1227.9, 1130.5. HRMS (ESI): calcd. for $C_{24}H_{24}NO_4F_3H^+$: 448.1736, found: 448.1739.

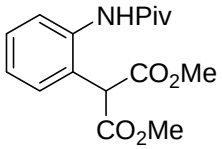


Methyl 3-(4-methoxyphenyl)-2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxopropanoate (2l). The crude was purified by column chromatography twice. Eluent for the 1st: 70% *n*-hexane / 30% ethyl acetate. Eluent for the 2nd: 70% *n*-hexane / 30% acetone. The product was obtained as colorless oil (34% yield) and existed in keto:enol (~3:1) form at room temperature, which could not be separated by the column. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 13.87 (s, 0.04, enol OH), 8.64 (s, 1H, NH, keto- form), 8.47 (s, 0.34H, NH, enol- form), 7.87 – 7.84 (m, 2.93H, ArH, mix of keto- and enol- form) 7.71 (s, 1H, ArH, enol- form), 7.53 (s, 1H, ArH, keto- form), 7.18 (s, 1H, ArH, enol- form), 7.02 (s, 1H, ArH, keto- form), 6.85 – 6.83 (d, J = 8.0 Hz, 2.15H, ArH, keto- form), 6.78 – 6.76 (d, J = 8.0 Hz, 0.78H, ArH, enol- form), 5.46 (s, 1H, CH, keto-form), 4.91 (s, 0.35H, enol- form), 3.85 (s, 1.16H, OCH_3, enol-form), 3.81 (s, 3H, OCH_3, keto- form), 3.79 (s, 1.13H, OCH_3, enol- form), 3.76 (s, 3H, OCH_3, keto- form), 2.24 (s, 1.10H, CH_3, enol- form), 2.20 (s, 6H, $2CH_3$, keto- form), 2.19 (s, 1.16H, CH_3, enol- form), 1.28 (s, 9H, $3CH_3$, keto- form), 1.19 (s, 3.34H, $3CH_3$, keto- form). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 194.5, 193.8, 177.6, 176.7, 172.6,

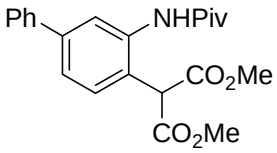
170.9, 164.4, 164.3, 138.6, 138.0, 135.1, 134.4, 134.3, 133.6, 133.3, 132.6, 131.8, 131.0, 128.6, 128.4, 127.9, 126.6, 126.5, 125.9, 124.8, 114.3, 113.8, 84.7, 59.6, 55.8, 55.7, 54.3, 53.2, 39.8, 27.8, 27.6, 20.0, 19.9, 19.8, 19.6. Totally 40 peaks were found in ^{13}C NMR analysis; however due to the high complexity of spectrum the signal cannot be assigned. IR (neat, cm^{-1}): 3369.1, 2958.3, 2866.5, 1736.3, 1672.3, 1600.2, 1513.2, 1259.7, 1171.6. HRMS (ESI): calcd. for $C_{24}H_{28}NO_5Na^+$: 434.1943, found: 434.1942.



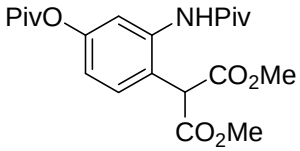
Methyl 2-(4,5-dimethyl-2-(pivalamido)phenyl)-3-oxo-3-(thiophen-2-yl)propane-ate (2m). The crude was purified by column chromatography twice. Eluent for the 1st: 70% *n*-hexane / 30% ethyl acetate. Eluent for the 2nd: 70% *n*-hexane / 30% acetone. The product was obtained as white solid (20% yield), mp 163 – 165 ^{o}C, and existed in keto:enol (~4:1) form at room temperature, which could not be separated by the column.. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 13.76 (s, 0.21H, enol OH), 8.78 (s, 1H, NH, keto- from), 8.15 (s, 1H, NH, enol- form), 7.61 – 7.60 (d, J = 4.0 Hz, 1H, thiophen-H, keto- form), 7.57 (s, 1H, ArH, keto- form), 7.55 – 7.54 (d, J = 4.0 Hz, 1H, thiophen-H, keto- form), 7.38 – 7.36 (m, 0.44H, thiophen-H & ArH, enol- form), 7.11 – 7.10 (d, J = 4.0 Hz, 0.23H, thiophen-H, enol- form), 7.06 (s, 1H, ArH, keto- form), 7.03 – 7.01 (t, J = 4.0 Hz, 1H, thiophen-H, keto- form), 6.93 (s, 0.22 H, ArH, enol- form), 6.91 – 6.89 (t, J = 4.0 Hz, 0.23H, thiophen-H, enol- form), 5.28 (s, 1H, CH, keto- form), 3.78 (s, 3H, CH_3, keto- form), 3.74 (s, 0.74H, CH_3, enol- form), 2.33 (s, 0.69H, CH_3, enol- form), 2.24 (s, 6H, $2CH_3$, keto- form), 2.22 (s, 0.78H, CH_3, enol- form), 1.26 (s, 9H, $3CH_3$, keto- form), 1.10 (s, 2.09H, $3CH_3$, enol- form). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 188.0 (C=O), 177.6 (C=O), 170.5 (C=O), 142.3 (C), 138.4 (C), 135.5 (CH), 135.2 (C), 134.4 (CH), 134.3 (C), 132.8 (CH), 128.7 (CH), 128.1 (CH), 124.4 (C), 61.1 (CH), 53.3 (CH_3), 39.8 (C), 27.8 (CH_3), 19.9 (CH_3), 19.6 (CH_3). In the ^{13}C NMR analysis, 19 peaks were identified and assigned for the keto- form. Due to the low concentration of product with enol- form, its ^{13}C NMR could not be clarified. IR (neat, cm^{-1}): 3347.8, 2967.8, 2913.9, 1735.5, 1655.1, 1516.9, 1416.9, 1173.0. HRMS (ESI): calcd. for $C_{21}H_{25}NO_4SH^+$: 388.1583, found: 388.1570.



Dimethyl 2-(2-(pivalamido)phenyl)malonate (2n). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as yellow oil (47% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.01 (s, 1H, NH), 7.81 – 7.79 (d, J = 8.0 Hz, 1H, ArH), 7.38 – 7.34 (t, J = 8.0 Hz, 1H, ArH), 7.22 – 7.20 (d, J = 8.0 Hz, 1H, ArH), 7.15 – 7.11 (t, J = 8.0 Hz, 1H, ArH), 4.65 (s, 1H, CH), 3.74 (s, 6H, $2CH_3$), 1.30 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.7 (C=O), 169.8 (C=O), 137.4 (C), 131.9 (CH), 129.6 (CH), 126.9 (CH), 126.1 (C), 125.6 (CH), 57.2 (CH_3), 53.4 (CH_3), 39.9 (CH_3), 27.8 (CH_3). IR (neat, cm^{-1}): 3350.2, 2960.4, 1742.5, 1721.9, 1677.9, 1566.2, 1526.8, 1477.9, 1305.7, 1150.5. HRMS (ESI): calcd. for $C_{16}H_{21}NO_5H^+$: 308.1498, found: 308.1483.

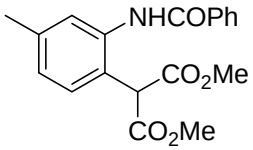


Dimethyl 2-(4-phenyl-2-(pivalamido)phenyl)malonate (2o). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as white solid (63% yield), mp 135 – 136 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9.11 (s, 1H, NH), 8.10 (s, 1H, ArH), 7.62 – 7.60 (d, J = 8.0 Hz, 2H, ArH), 7.43 – 7.39 (t, J = 8.0 Hz, 2H, ArH), 7.37 – 7.33 (t, J = 8.0 Hz, 1H, ArH), 7.28 – 7.26 (d, J = 8.0 Hz, 2H, ArH), 4.70 (s, 1H, CH), 3.78 (s, 6H, $2CH_3$), 1.33 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.8 (C=O), 169.8 (C=O), 142.8 (C), 140.4 (C), 137.7 (C), 132.3 (CH), 129.0 (CH), 128.0 (CH), 127.7 (CH), 125.5 (CH), 124.7 (C), 124.1 (CH), 56.9 (CH), 53.6 (CH_3), 40.0 (CH_3), 27.9 (CH_3). IR (neat, cm^{-1}): 3369.9, 2961.5, 2875.9, 1735.9, 1723.7, 1682.8, 1592.0, 1517.2, 1480.2, 1167.2. HRMS (ESI): calcd. for $C_{22}H_{25}NO_5H^+$: 384.1811, found: 384.1796.

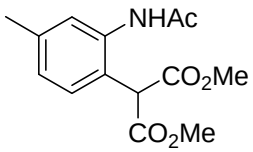


Dimethyl 2-(2-(pivalamido)-4-(pivaloyloxy)phenyl)malonate (2p). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as white solid (25% yield), mp 126 – 128 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$): δ_H 9,18 (s, 1H, NH), 7.66 (s, 1H, ArH), 7.20 – 7.18 (d, J = 8.0 Hz, 1H, ArH), 6.88 – 6.86 (d, J = 8.0 Hz, 1H, ArH), 4.64 (s, 1H, CH), 3.74 (s, 6H, $2CH_3$), 1.33 (s, 9H, $3CH_3$), 1.29 (s, 9H, $3CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 177.7 (C=O), 177.1 (C=O), 169.6 (CH), 151.9 (C), 138.6 (C),

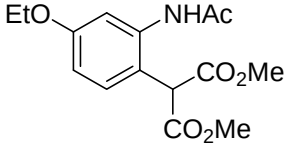
132.6 (CH), 122.7 (C), 119.4 (CH), 118.6 (CH), 56.8 (CH), 53.5 (CH_3), 40.0 (C), 39.5 (C), 27.8 (CH_3), 27.5 (CH_3). IR (neat, cm^{-1}): 3320.3, 2953.2, 2912.2, 1740.5, 1710.2, 1670.2, 1541.4, 1482.3, 1146.3. HRMS (ESI): calcd. for $C_{21}H_{28}NO_7H^+$: 430.1842, found: 430.1833.



Dimethyl 2-(2-(benzamido)-4-methylphenyl)malonate (2q). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as white solid (60% yield), mp 133 – 135 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ_H 9.69 (s, 1H, NH), 8.00 – 7.98 (d, J = 8.0 Hz, 2H, ArH), 7.54 (m, 3H, ArH), 7.16 – 7.14 (d, J = 8.0 Hz, 1H, ArH), 7.02 – 7.00 (d, J = 8.0 Hz, 1H, ArH), 4.68 (s, 1H, CH), 3.68 (s, 6H, $2CH_3$), 2.39 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.2 (C=O), 165.8 (C=O), 140.0 (C), 136.8 (C), 134.4 (C), 132.2 (CH), 131.7 (CH), 129.1 (CH), 127.8 (CH), 127.6 (CH), 126.9 (CH), 123.8 (C), 56.9 (CH), 53.6 (CH_3), 21.6 (CH_3). IR (neat, cm^{-1}): 3325.6, 2948.8, 2926.7, 1741.4, 1713.2, 1663.3, 1534.5, 1479.3, 1156.3. HRMS (ESI): calcd. for $C_{19}H_{19}NO_5H^+$: 342.1341, found: 342.1330.



Dimethyl 2-(2-acetamido-4-methylphenyl)malonate (2r). Eluent: 50% *n*-hexane / 50% ethyl acetate. The product was obtained as brown solid (51% yield), mp 139 – 140 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.7 (s, 1H, NH), 7.51 (s, 1H, ArH), 7.11 – 7.09 (d, J = 8.0 Hz, 1H, ArH), 6.98 – 6.96 (d, J = 8.0 Hz, 1H, ArH), 4.61 (s, 1H, CH), 3.74 (s, 6H, $2CH_3$), 2.34 (s, 3H, CH_3), 2.12 (s, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.1 (C=O), 169.2 (C=O), 140.0 (C), 136.5 (C), 131.6 (CH), 127.8 (CH), 127.0 (CH), 123.7 (C), 56.6 (CH), 53.5 (CH_3), 24.3 (CH_3), 21.6 (CH_3). IR (neat, cm^{-1}): 3235.5, 2955.2, 1760.9, 1744.2, 1661.3, 1582.3, 1298.4, 1149.7. HRMS (ESI): calcd. for $C_{14}H_{17}NO_5H^+$: 280.1185, found: 280.1175.

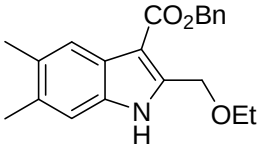


Dimethyl 2-(2-acetamido-4-ethoxyphenyl)malonate (2s). Eluent: 50% *n*-hexane / 50% ethyl acetate. The product was obtained as pale yellow solid (48% yield), mp 121 – 122 ^oC. ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.9 (s, 1H, NH), 7.32 (s, 1H, ArH),

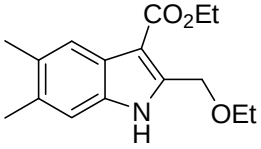
7.10 – 7.08 (d, J = 8.0 Hz, 1H, ArH), 6.70 – 6.68 (d, J = 8.0 Hz, 1H, ArH), 4.58 (s, 1H, CH), 4.05 – 4.00 (q, J = 6.8 Hz, 2H, OCH_2), 3.75 (s, 6H, $2CH_3$), 2.14 (s, 3H, CH_3), 1.41 – 1.37 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 170.3 (C=O), 160.0 (C=O), 137.7 (C), 132.5 (CH), 117.9 (C), 112.8 (CH), 112.4 (CH), 64.0 (CH_2), 56.4 (CH), 53.5 (CH_3), 24.3 (CH_3), 15.0 (CH_3). IR (neat, cm^{-1}): 3183.1, 3135.6, 3002.6, 1749.5, 1734.2, 1653.9, 1501.8, 1195.8, 1157.5. HRMS (ESI): calcd. for $C_{15}H_{19}NO_6H^+$: 310.1291, found: 310.1283.

3. Procedure for Cyclization Reaction of 2g and 2h

To a solution of **2g** or **2h** (0.2 mmol) in EtOH (5 mL), conc. HCl solution (0.1 mL) was added and the mixture was stirred at reflux for 0.5 h. Then the reaction was cooled to room temperature and concentrated. The residue was diluted with ethyl acetate (10 mL). The mixture was washed with saturated sodium bicarbonate solution, dried with Na_2SO_4 and concentrated under reduced pressure. The residue was then purified by flash column chromatography to give the free indole **3**.



Benzyl 2-(ethoxymethyl)-5,6-dimethyl-1H-indole-3-carboxylate (3g). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as pale yellow solid (73% yield), mp 120 – 123 °C. ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.98 (br, s, 1H, NH), 7.91 (s, 1H, ArH), 7.52 – 7.50 (d, J = 8.0 Hz, 2H, ArH), 7.43 – 7.33 (m, 3H, ArH), 7.16 (s, 1H, ArH), 5.42 (s, 2H, CH_2), 5.05 (s, 2H, CH_2), 3.71 – 3.66 (q, J = 6.8 Hz, 2H, OCH_2), 2.37 (s, 6H, $3CH_3$), 1.33 – 1.29 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 165.8 (C=O), 144.7 (C), 137.4 (C), 133.8 (C), 131.9 (C), 131.0 (C), 128.9 (CH), 128.3 (CH), 125.7 (C), 121.9 (CH), 111.9 (CH), 102.5 (C), 67.3 (CH_2), 66.5 (CH_2), 65.7 (CH_2), 20.7 (CH_3), 20.6 (CH_3), 15.6 (CH_3). IR (KBr, cm^{-1}): 3102.1, 2891.6, 1782.3, 1646.1, 1598.2, 1390.2. HRMS (ESI): calcd. for $C_{21}H_{23}NO_3Na^+$: 360.1576, found: 360.1570.

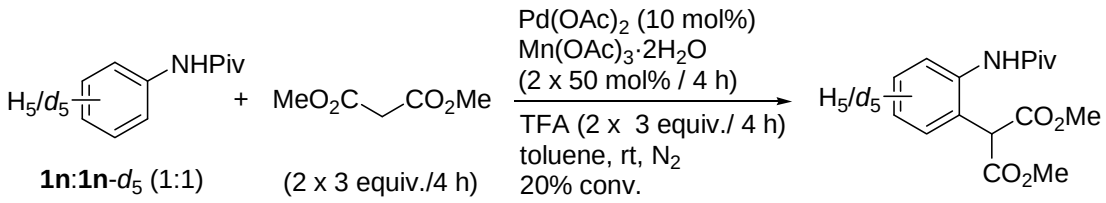


Ethyl 2-(ethoxymethyl)-5,6-dimethyl-1H-indole-3-carboxylate (3h). Eluent: 70% *n*-hexane / 30% ethyl acetate. The product was obtained as white solid (69% yield), mp 113 – 115 °C. ^1H NMR (400 MHz, $CDCl_3$): δ_H 8.90 (br, s, 1H, NH), 7.87 (s, 1H,

ArH), 7.15 (s, 1H, ArH), 5.05 (s, 2H, CH_2), 4.42 – 4.36 (q, J = 6.8 Hz, 2H, OCH_2), 3.72 – 3.67 (q, J = 6.8 Hz, 2H, OCH_2), 2.38 (s, 3H, CH_3), 2.36 (s, 3H, CH_3), 1.46 – 1.43 (t, J = 6.8 Hz, 3H, CH_3), 1.33 – 1.30 (t, J = 6.8 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ_C 166.2 (C=O), 144.3 (C), 133.8 (C), 131.9 (C), 130.9 (C), 125.7 (C), 121.8 (CH), 111.8 (CH), 102.8 (C), 67.3 (CH_2), 66.4 (CH_2), 59.9 (CH_2), 20.7 (CH_3), 20.6 (CH_3), 15.6 (CH_3), 15.0 (CH_3). IR (neat, cm^{-1}): 3012.1, 2953.6, 1713.4, 1604.1, 1451.2, 1392.1. HRMS (ESI): calcd. for $C_{16}H_{21}NO_3Na^+$: 298.1419, found: 298.1414.

4. KIE Experiment

Intermolecular competitive experiment was designed to determine the primary KIE (k_H/k_D) value of the Pd-catalyzed arene C-H functionalizations.



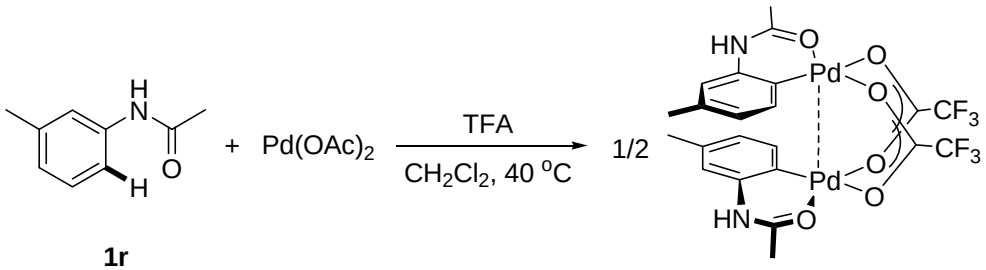
To a mixture of **1n** (0.1 mmol), **1n**-d_5 (0.1 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%) and $Mn(OAc)_3{\cdot}2H_2O$ (0.0268 g, 50 mol%), dry toluene (1.5 mL), dimethyl malonate (0.6 mmol) and TFA (46.1 μL, 0.6 mmol) was added under a N_2 atmosphere. The mixture was stirred at room temperature. After 4 h, a batch of reagents [$Mn(OAc)_3{\cdot}2H_2O$ (50 mol%), dimethyl malonate (0.6 mmol), TFA (0.6 mmol)] was added to the mixture and the reaction was stirred for further 4 h. Then the reaction mixture was filtered over a plug of Celite® and then concentrated. The substrate conversion of **1n** and **1n**-d_5 was determined by ^{1}H NMR analysis using CH_2Br_2 as the internal standard. The KIE values were calculated by the ratio of substrate conversions of **1n** and **1n**-d_5. The KIE experiment was repeated three times and the average value (k_H/k_D = 3.3) was obtained.

Calculation of KIE value:

$$KIE = \frac{k_H}{k_D} = \frac{\%\ \text{conv. of 1n}}{\%\ \text{conv. of } (1n\text{-}d_5)}$$

run	KIE value
1	3.43
2	3.21
3	3.28
Average	3.31

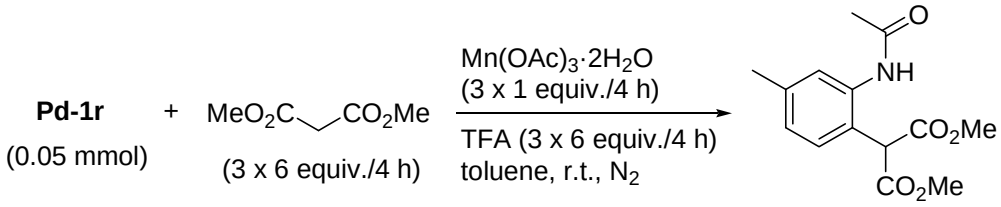
5. Synthesis of Cyclopalladated Complex Pd-1r



1r **Pd-1r**, 61%

The cyclopalladated complex was prepared according to the literature.[2] A 25 mL Schlenk test-tube (with a Quick-fit stopper and side arm) was charged with [$Pd(OAc)_2$] (0.0224g, 0.1 mmol), *N*-(*m*-tolyl)acetamide (**1r**, 0.0149 g, 0.1 mmol), TFA (0.0137g, 0.12 mmol). The Schlenk tube was evacuated and refilled with nitrogen for three times. Then the glass stopper was replaced by rubber septa. Dry DCM (5 mL), and TFA (0.0137g, 0.12 mmol) was added under a flow of nitrogen. The mixture was stirred at 40 °C for 3 h. The solution was then concentrated under reduced pressure and the residue was suspended in *n*-hexanes (5 mL). The suspension was filtered through Celite® and washed with *n*-hexanes (3 × 2 mL). The residue was then washed with DCM (5 mL), and the filtrate solution was collected and concentrated under reduced pressure to afford the cyclopalladated complex **Pd-1r** as a yellow solid (61% yield).

6. Stoichiometric Reaction of Pd-1r and Dimethyl Malonate



2r, 44%

A 10 mL Schlenk test-tube was charged with **Pd-1r** (0.05 mmol) and $Mn(OAc)_3 \cdot 2H_2O$ (0.0268 g, 50 mol%). The Schlenk tube was evacuated and refilled with nitrogen for three times. Then the glass stopper was replaced by rubber septa. Dry toluene (1.5 mL), dimethyl malonate (0.6 mmol) and TFA (46.1 μL, 0.6 mmol) was added under a flow of nitrogen. The reaction mixture was stirred at room temperature. After 4 h, a batch of reagents [$Mn(OAc)_3 \cdot 2H_2O$ (50 mol%), 1,3-dicarbonyl compound (0.6 mmol), TFA (0.6 mmol)] was added to the mixture. The batchwise addition was preformed again after further 4 h. The reaction was

subsequently allowed to stir for overnight. Then the reaction mixture was filtered over a plug of Celite® and then concentrated. The residue was purified by flash chromatography to give the desired product **2r** in 44% yield.

7. References

1. C.-W. Chan, Z. Zhou and W.-Y. Yu, *Adv. Synth. Catal.*, 2011, **353**, 2999.
2. C. S. Yeung, X. Zhao, N. Borduas and V. M. Dong, *Chem. Sci.*, 2010, **1**, 331.

8. ^{1}H and ^{13}C NMR Spectra

Figure S1. ^{1}H NMR spectrum of **2a**

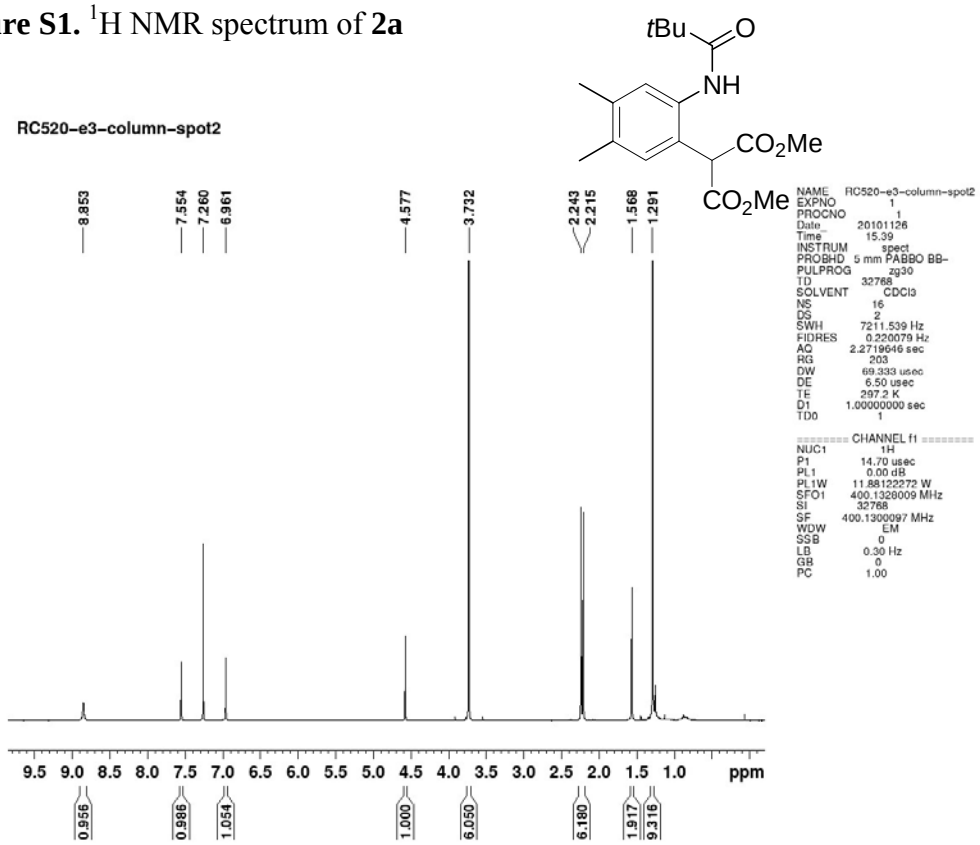


Figure S2. ^{13}C NMR spectrum of **2a**

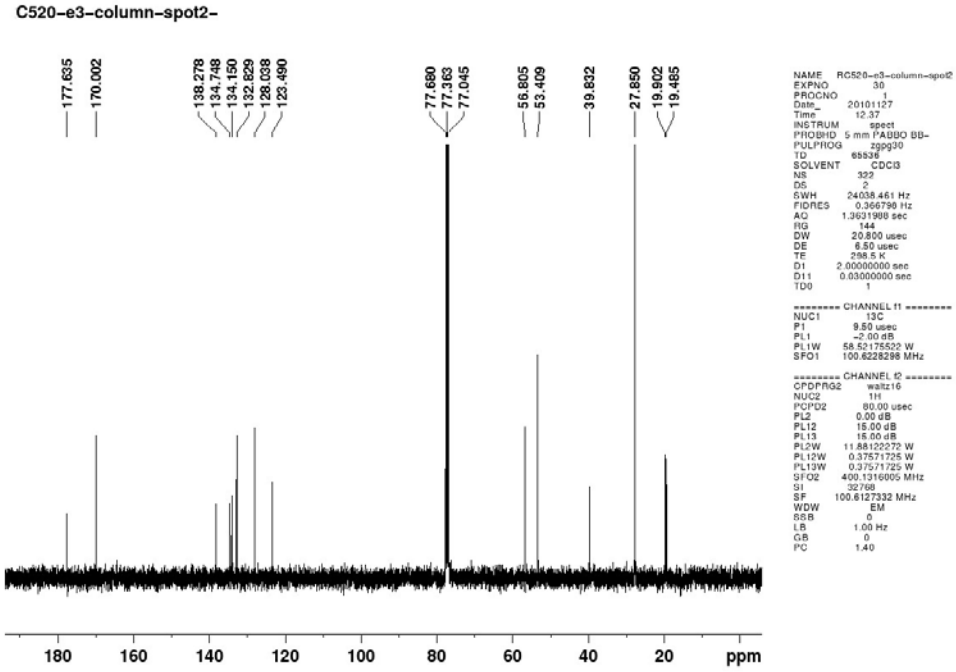


Figure S3. ^{1}H NMR spectrum of **8b**

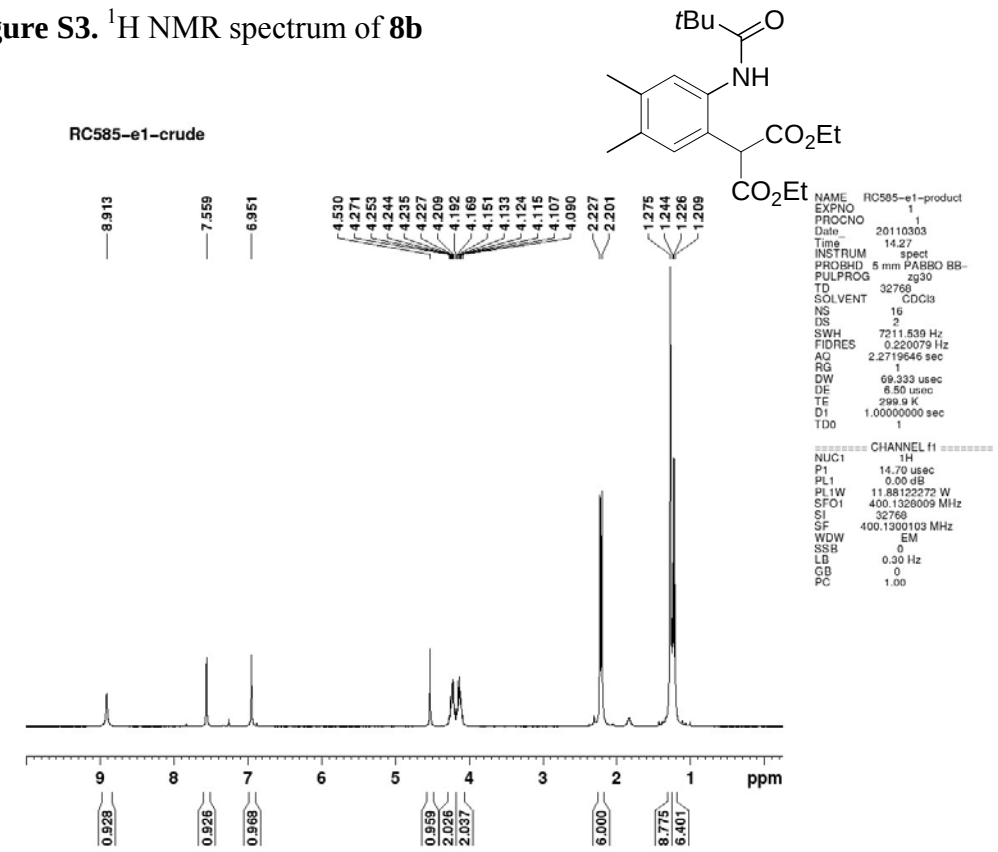


Figure S4. ^{13}C NMR spectrum of **2b**

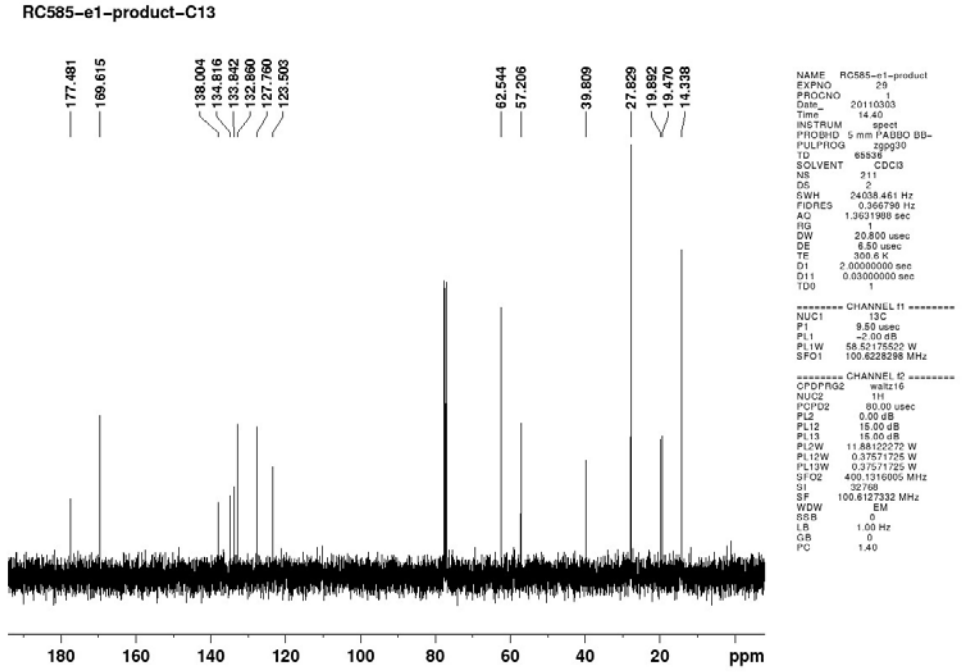


Figure S5. ^{1}H NMR spectrum of **2c**

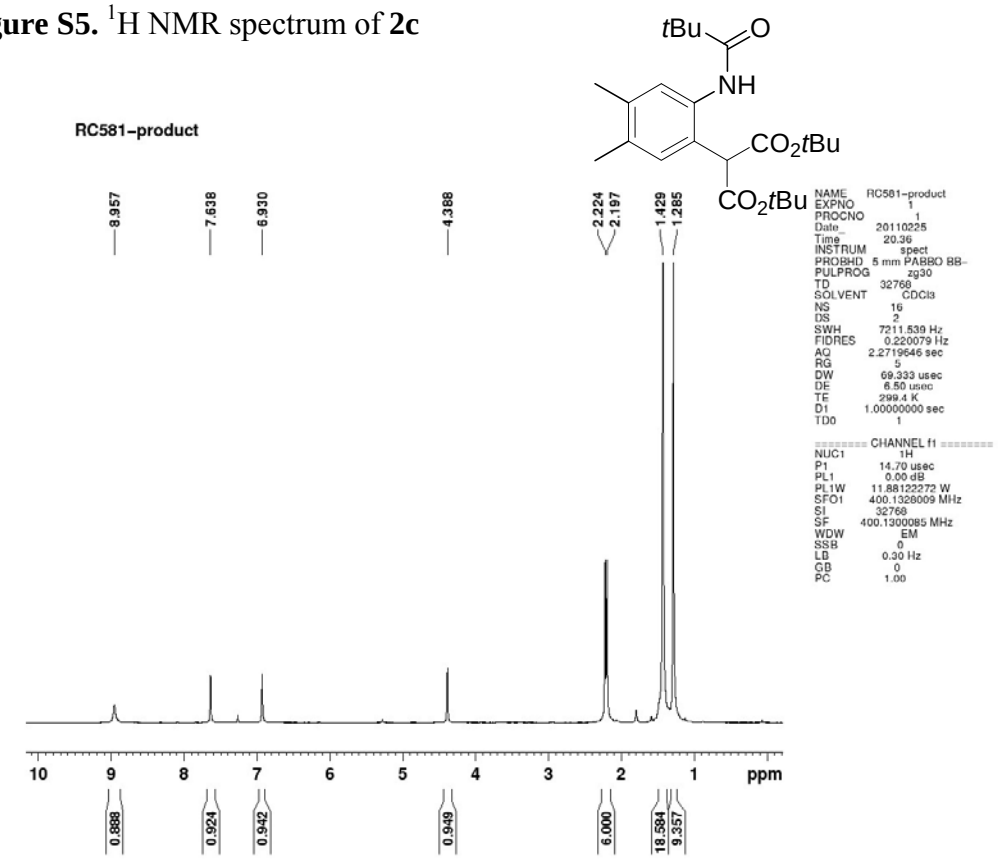


Figure S6. ^{13}C NMR spectrum of **2c**

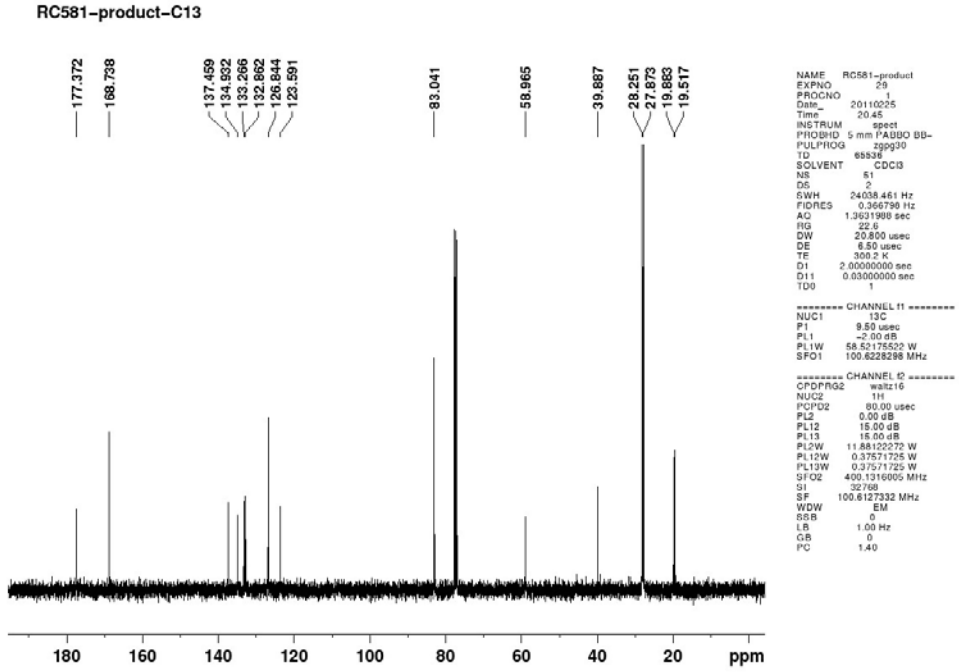


Figure S7. ^{1}H NMR spectrum of **2d**

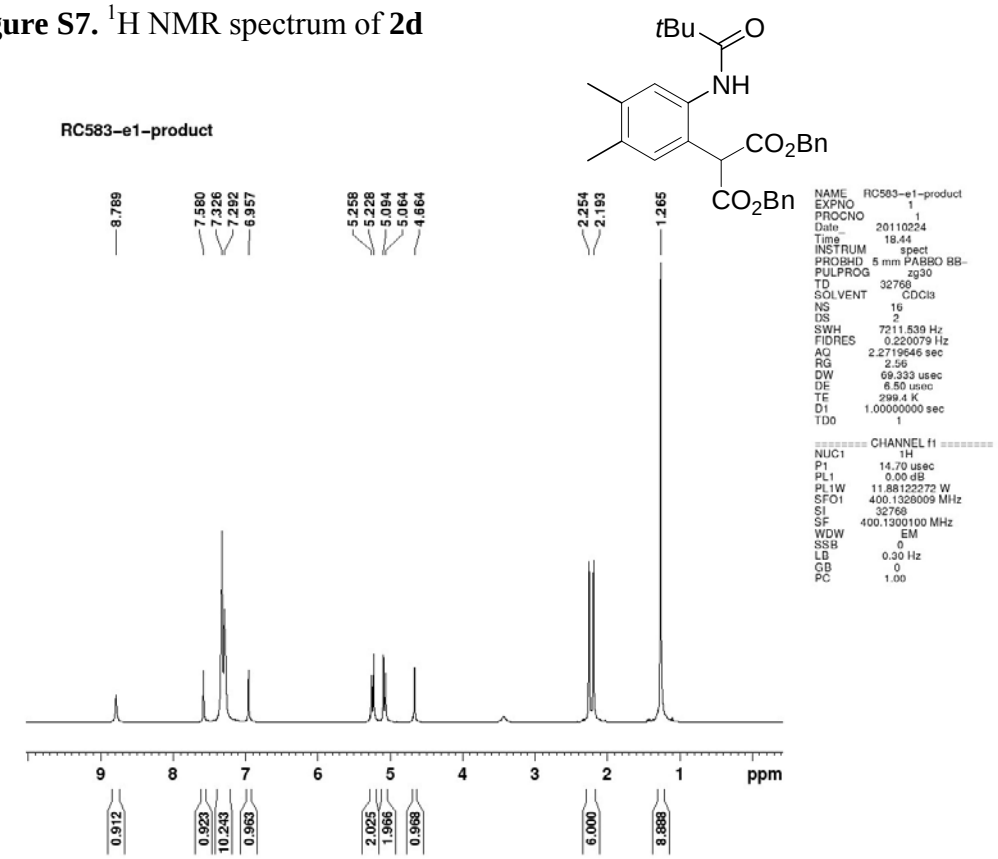


Figure S8. ^{13}C NMR spectrum of **2d**

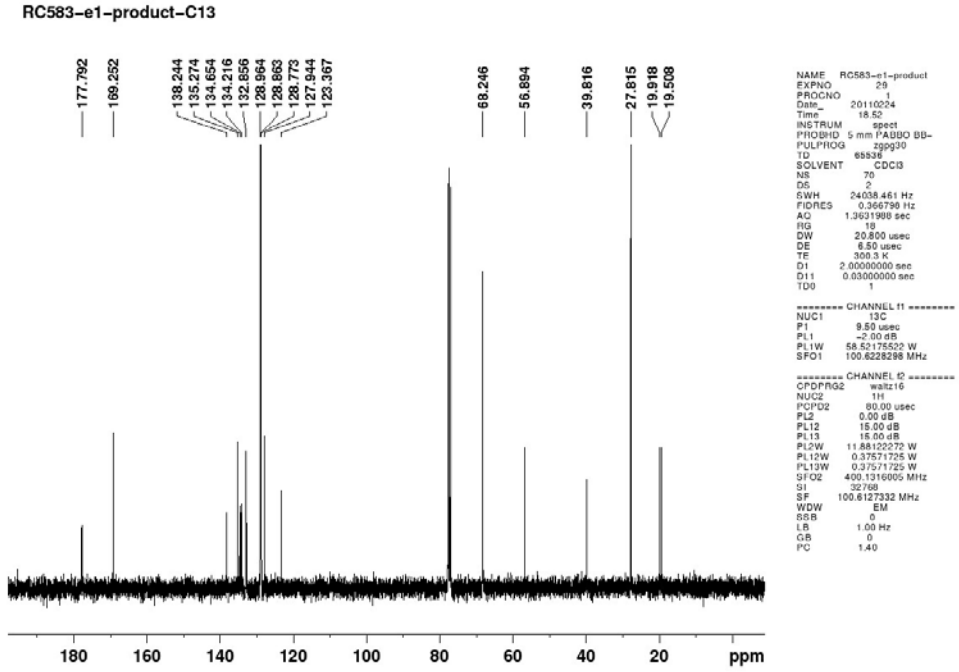


Figure S9. ^{1}H NMR spectrum of **2e**

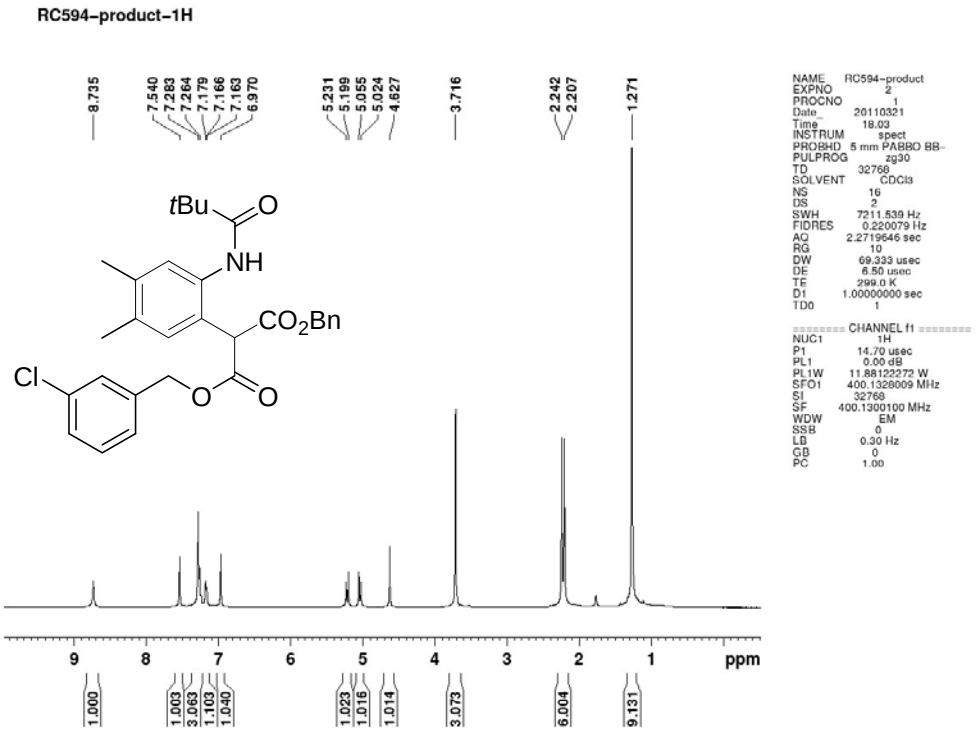


Figure S10. ^{13}C NMR spectrum of **2e**

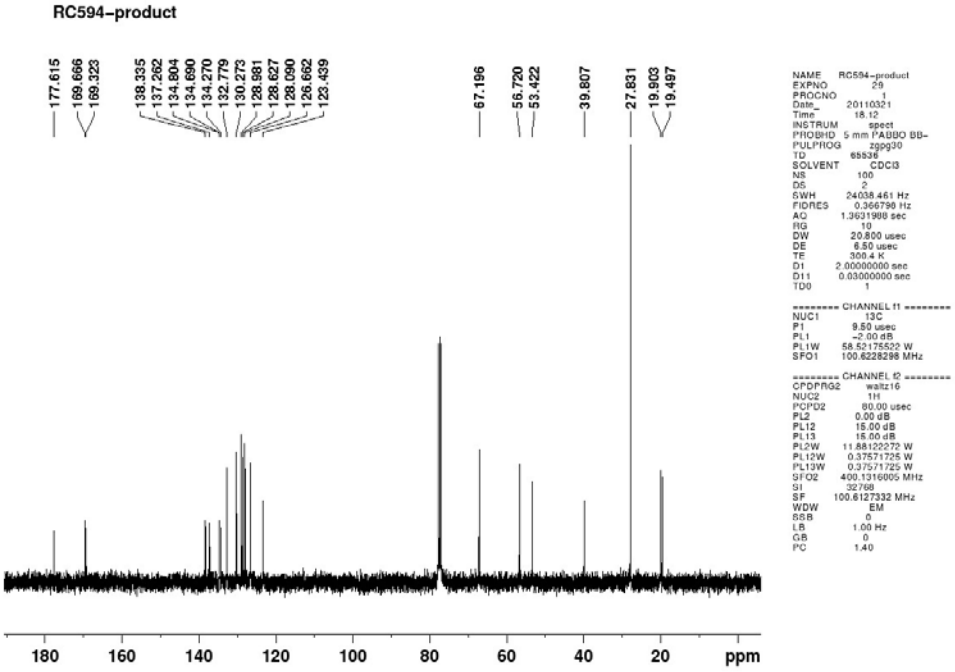


Figure S11. ^{1}H NMR spectrum of **2f**

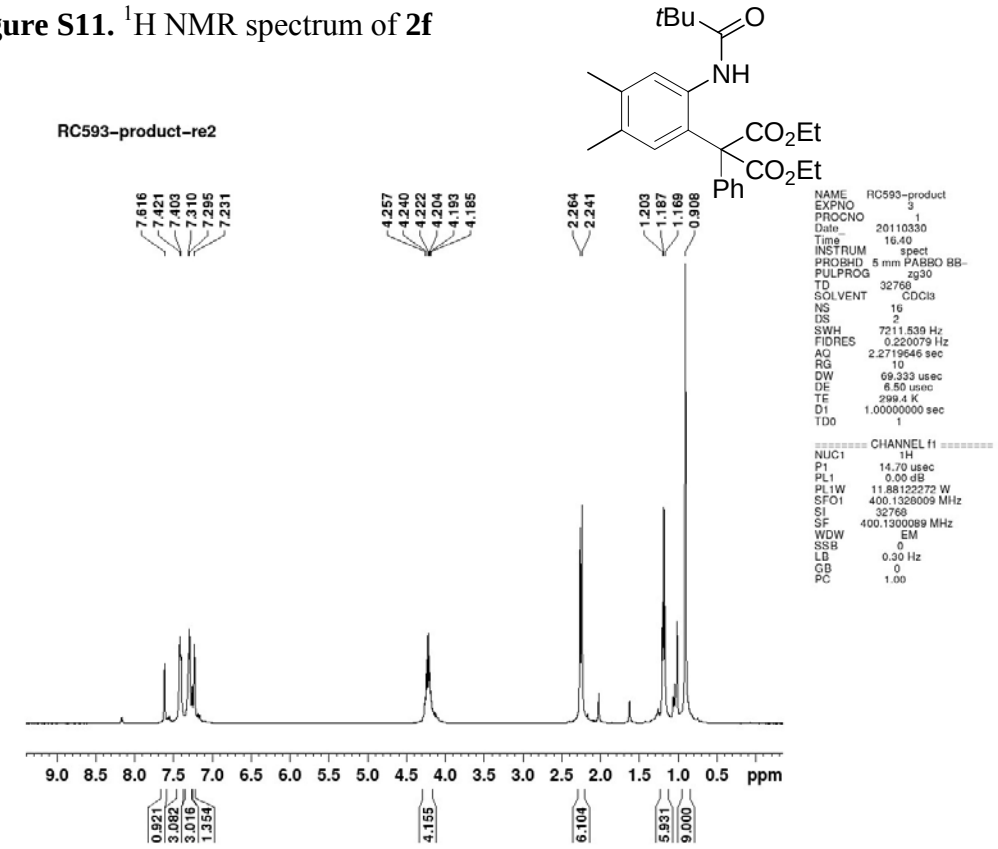


Figure S12. ^{13}C NMR spectrum of **2f**

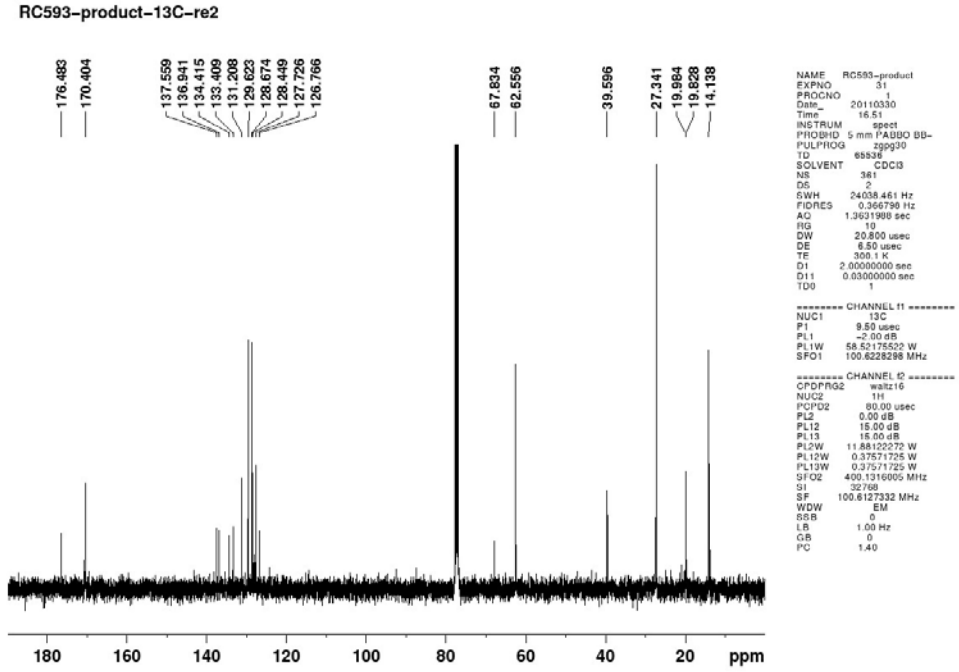


Figure S13. ^{1}H NMR spectrum of **2g**

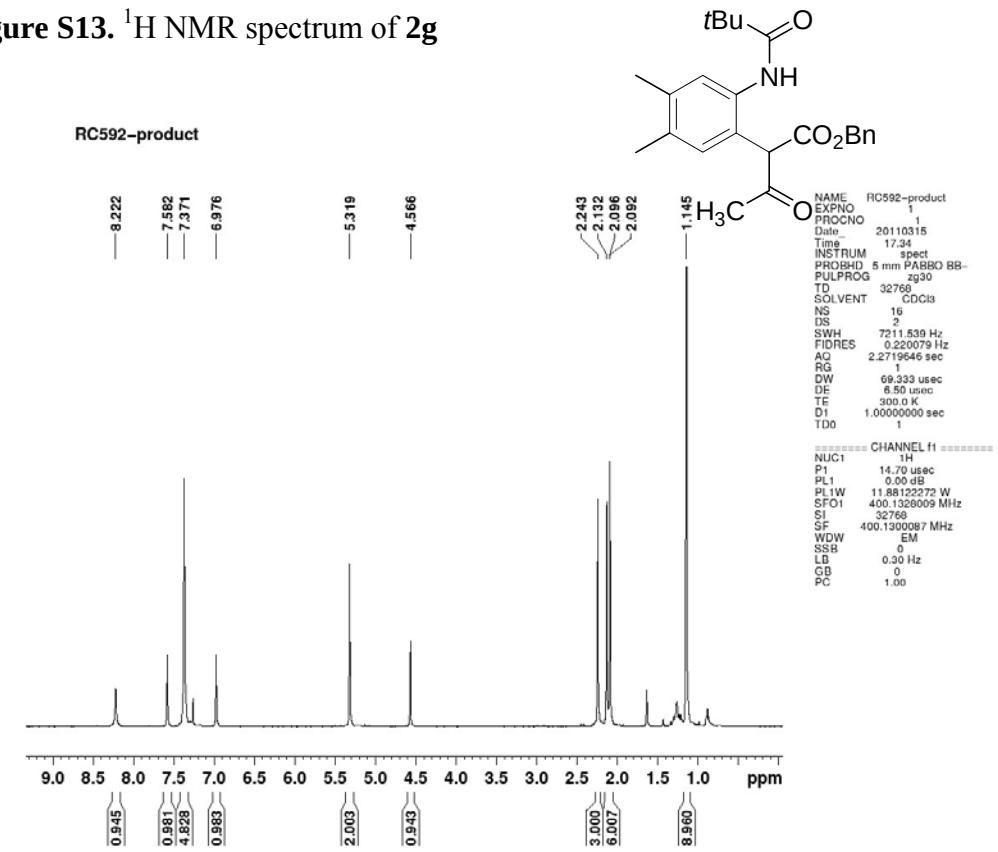


Figure S14. ^{13}C NMR spectrum of **2g**

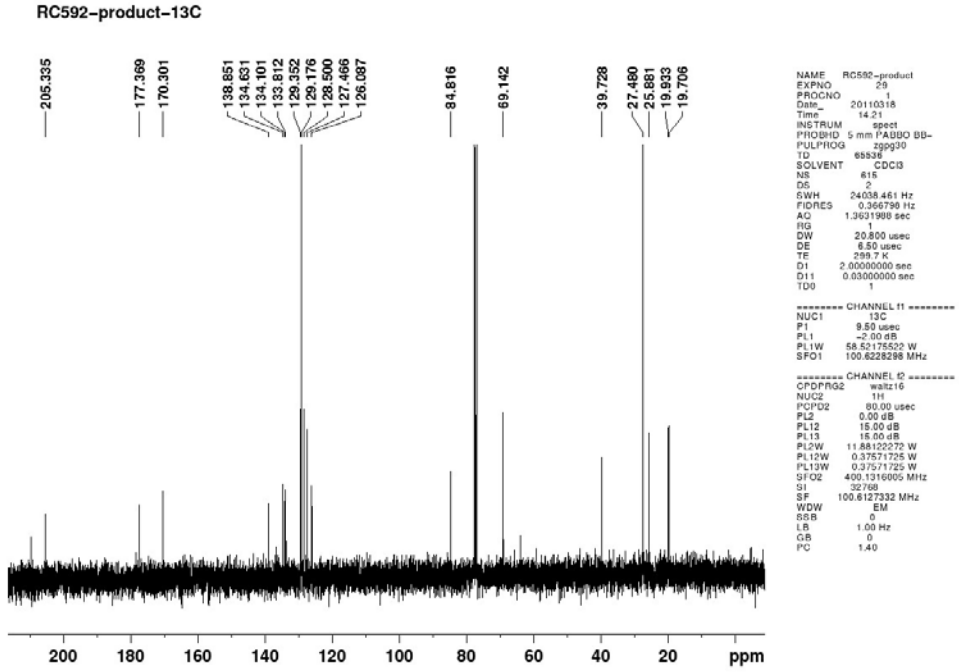


Figure S15. ^{1}H NMR spectrum of **2h**

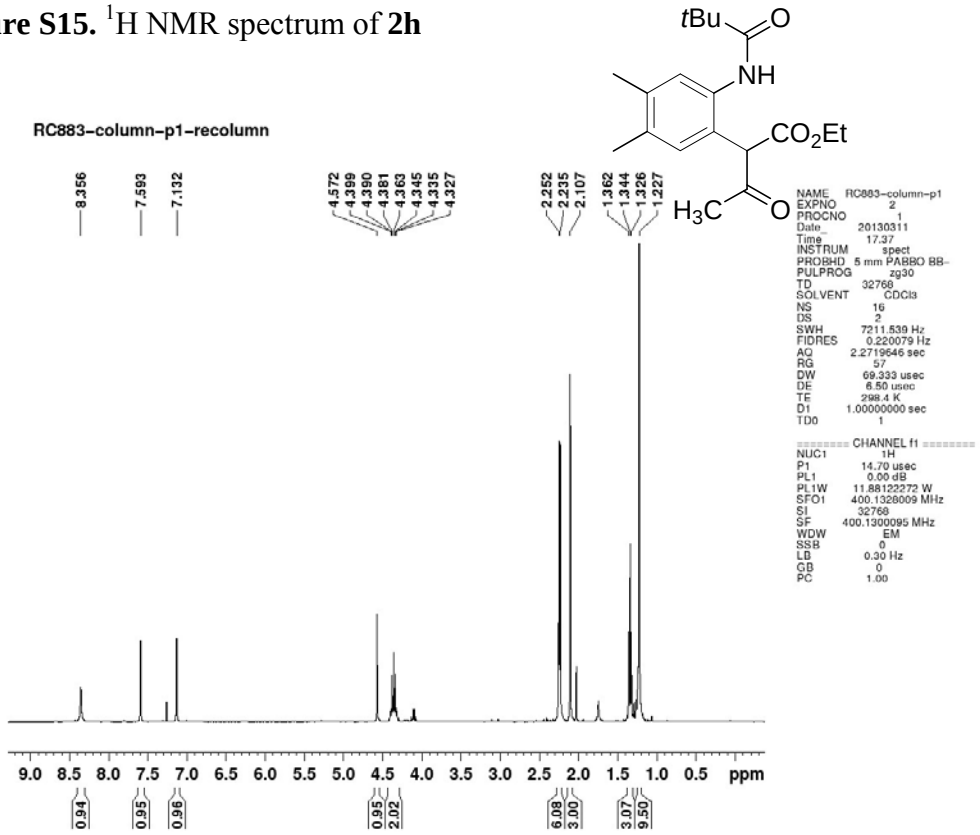


Figure S16. ^{13}C NMR spectrum of **2h**

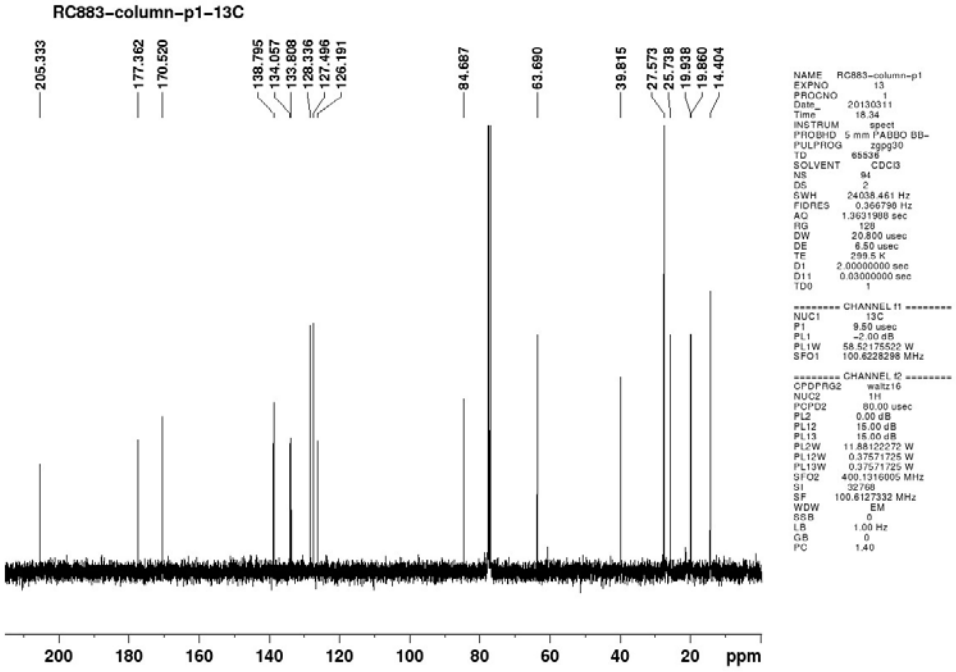


Figure S17. ^{1}H NMR spectrum of **2i**

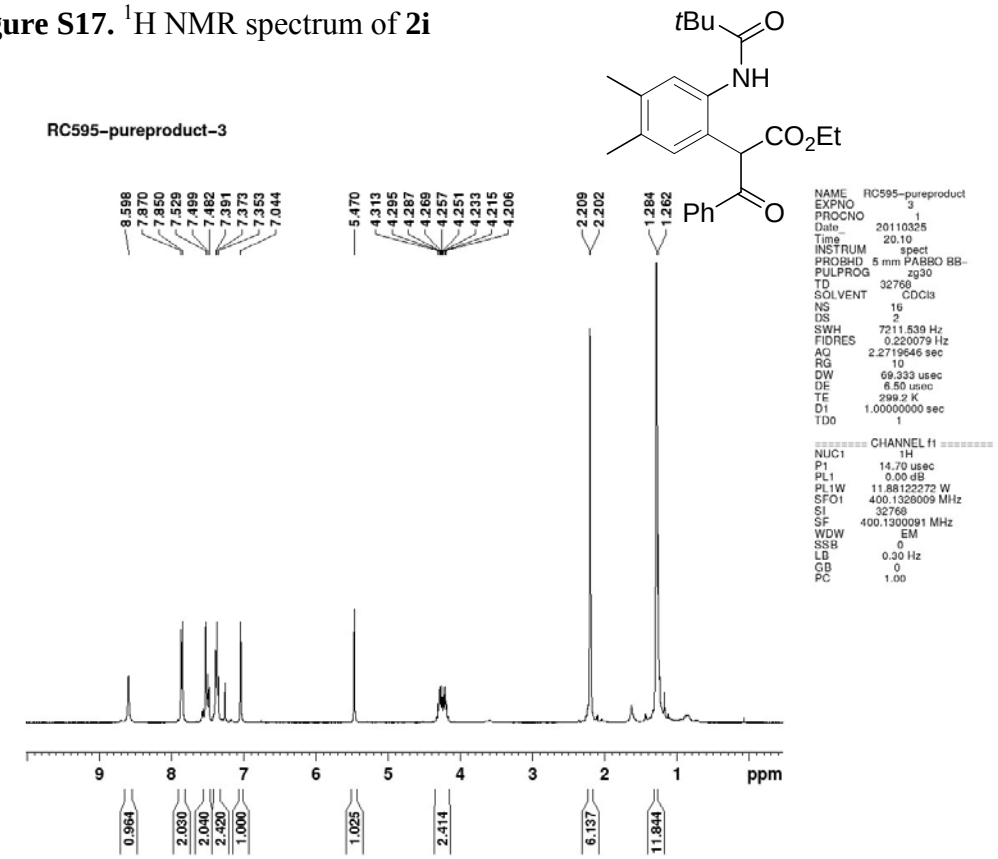


Figure S18. ^{13}C NMR spectrum of **2i**

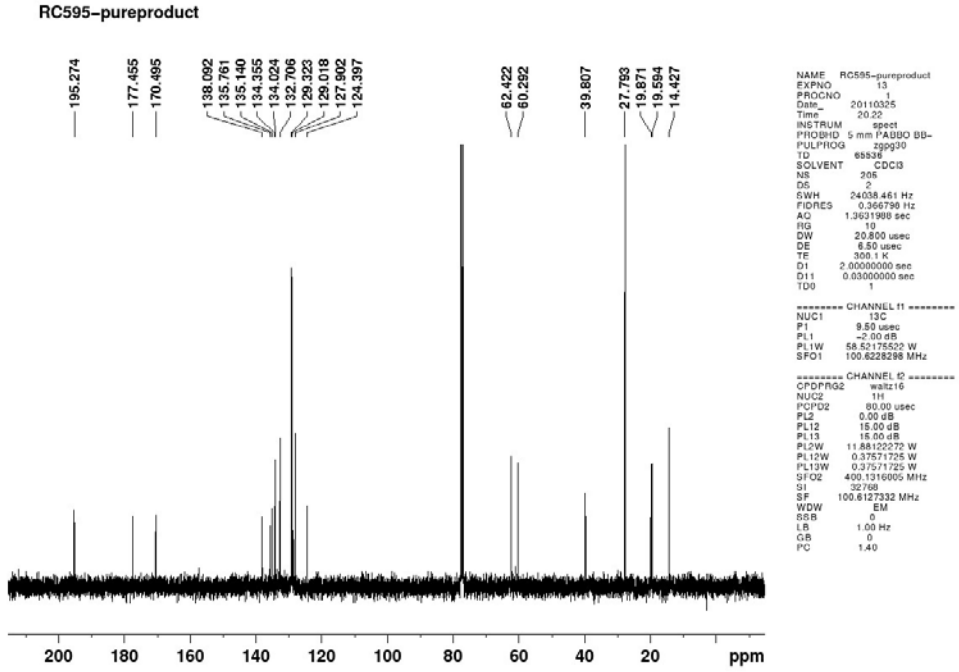


Figure S19. ^{1}H NMR spectrum of **2j**

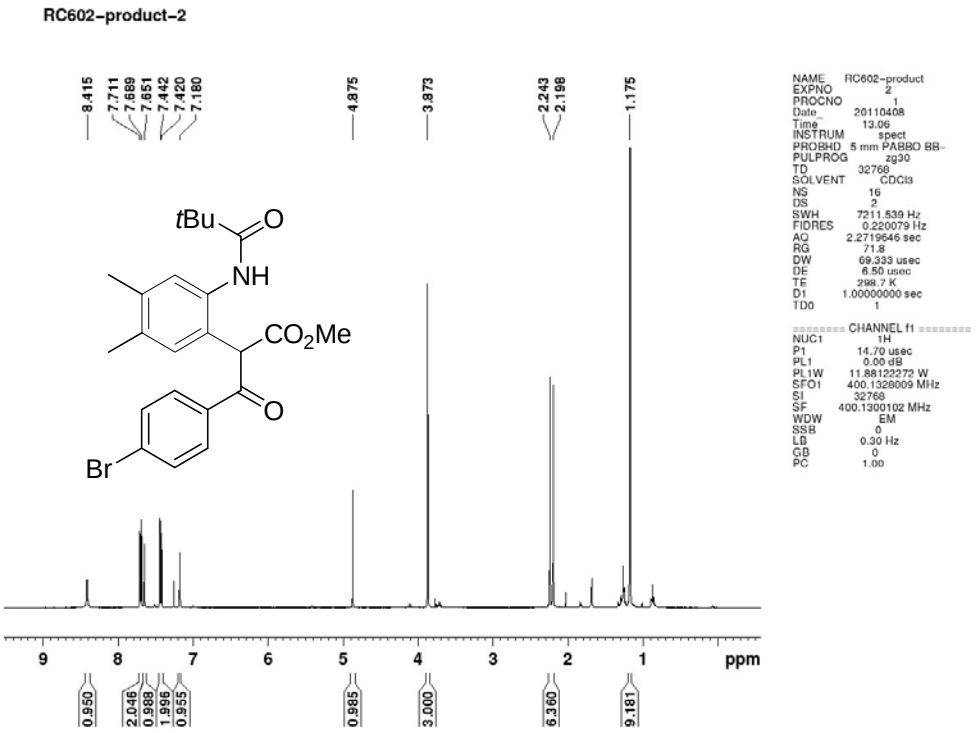


Figure S20. ^{13}C NMR spectrum of **2j**

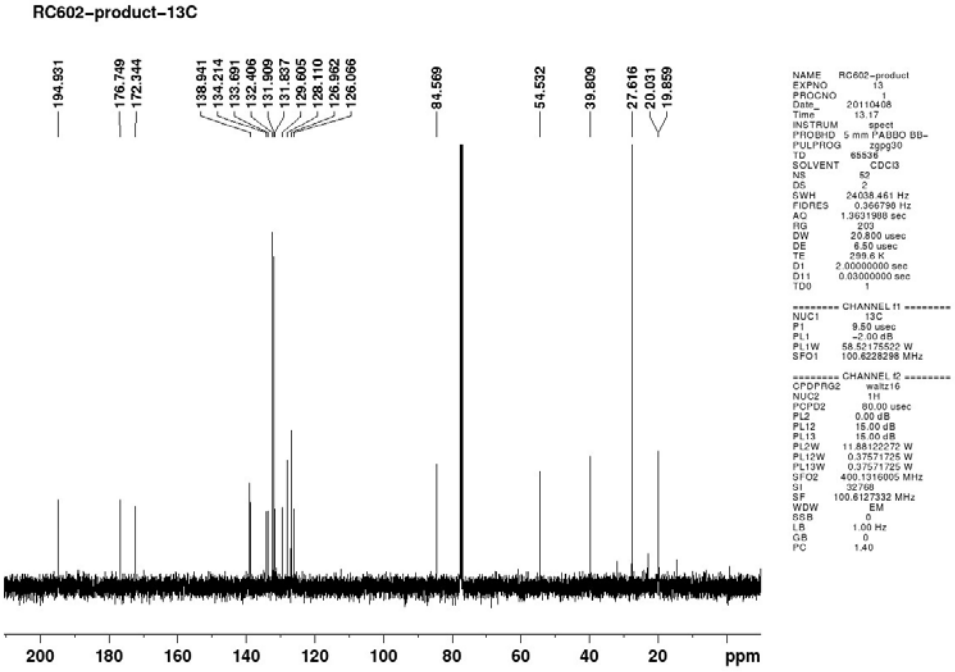
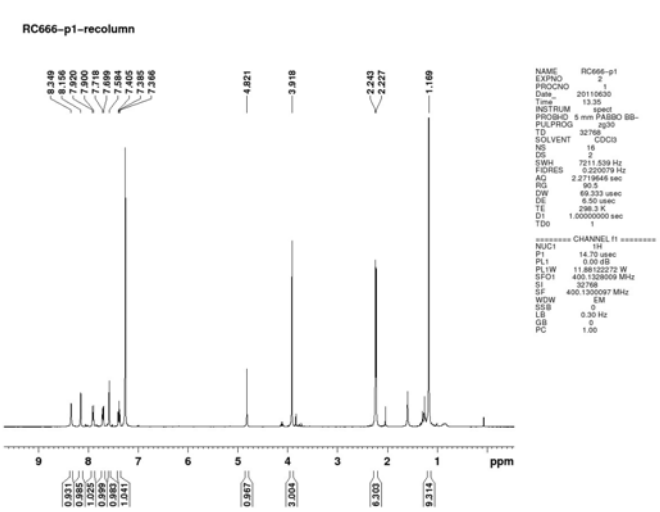


Figure S21. ^{1}H NMR spectrum of **2k**



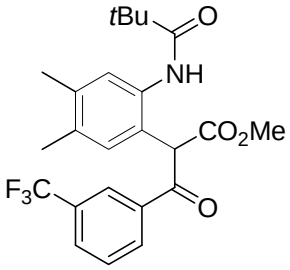


Figure S22. ^{13}C NMR spectrum of **2k**

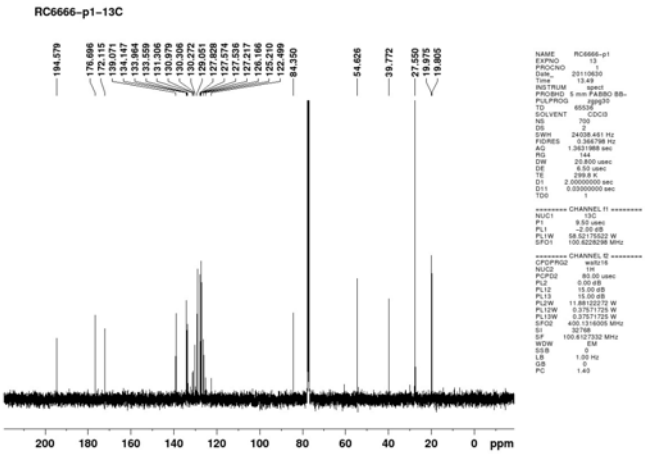


Figure S23. ^{19}F NMR spectrum of **2k**

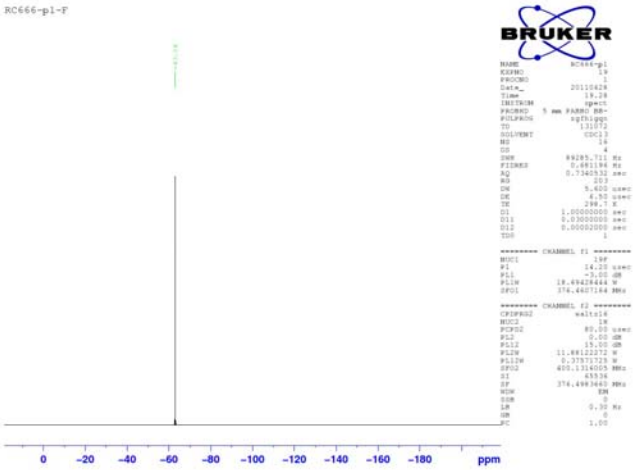


Figure S24. ^{1}H NMR spectrum of **2l**

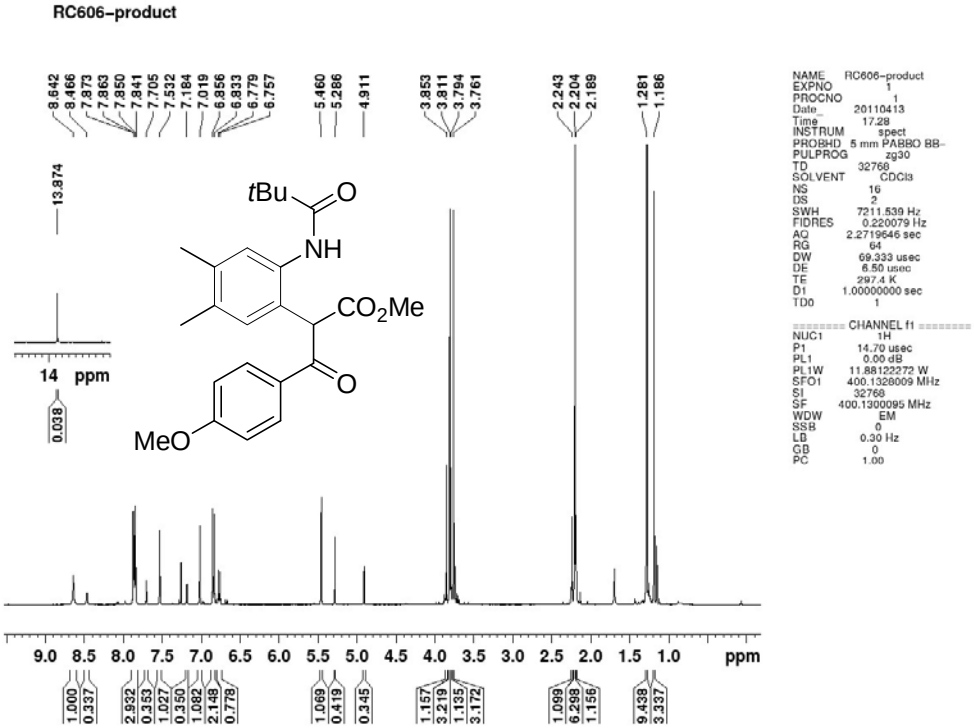


Figure S25. ^{13}C NMR spectrum of **2l**

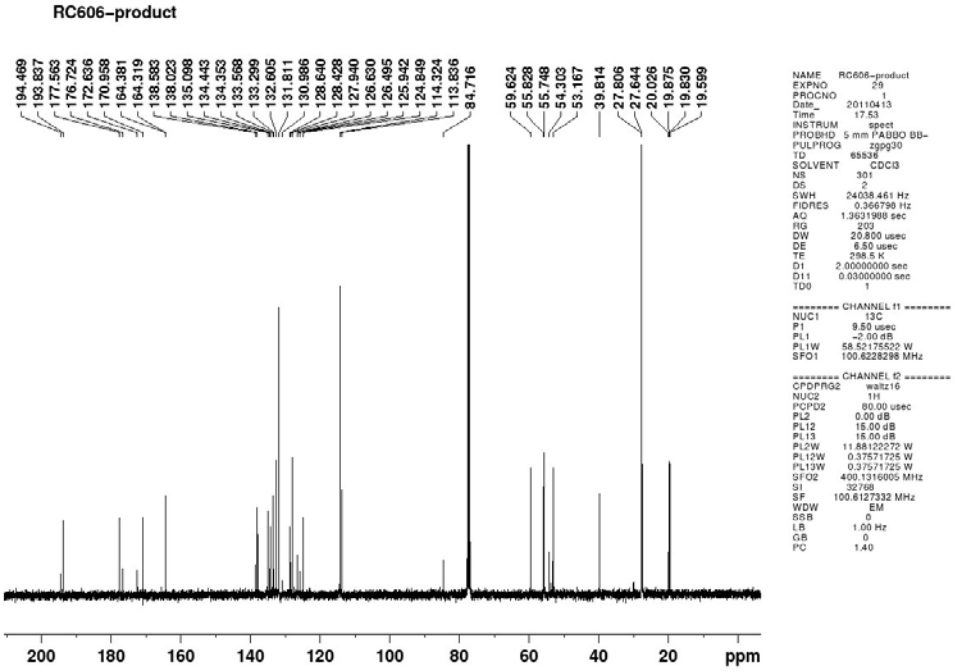


Figure S26. ^{1}H NMR spectrum of **2m**

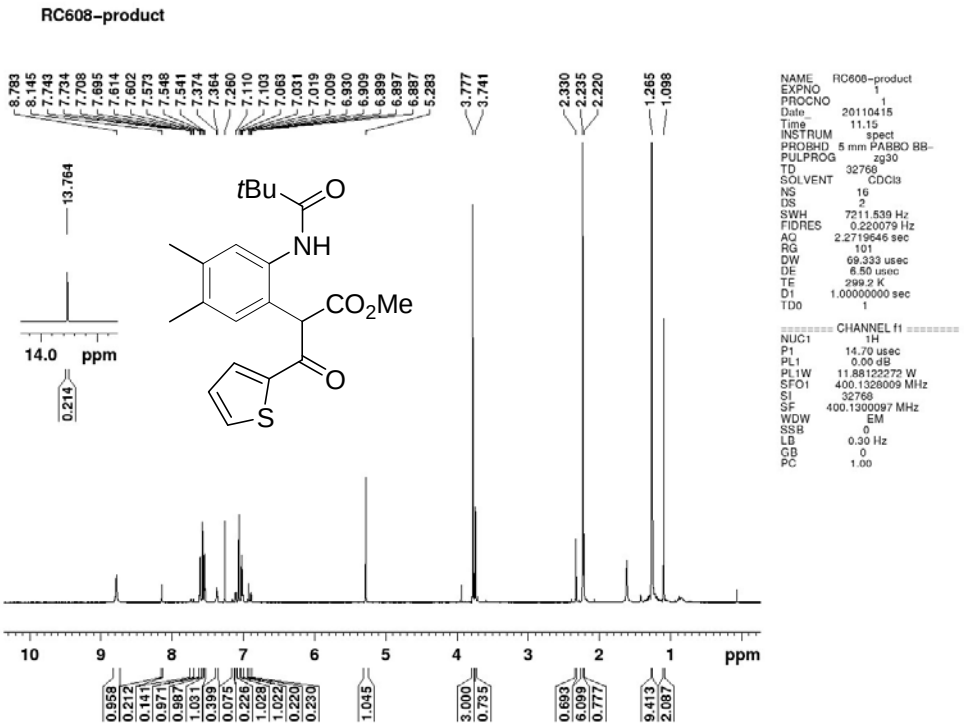


Figure S27. ^{13}C NMR spectrum of **2m**

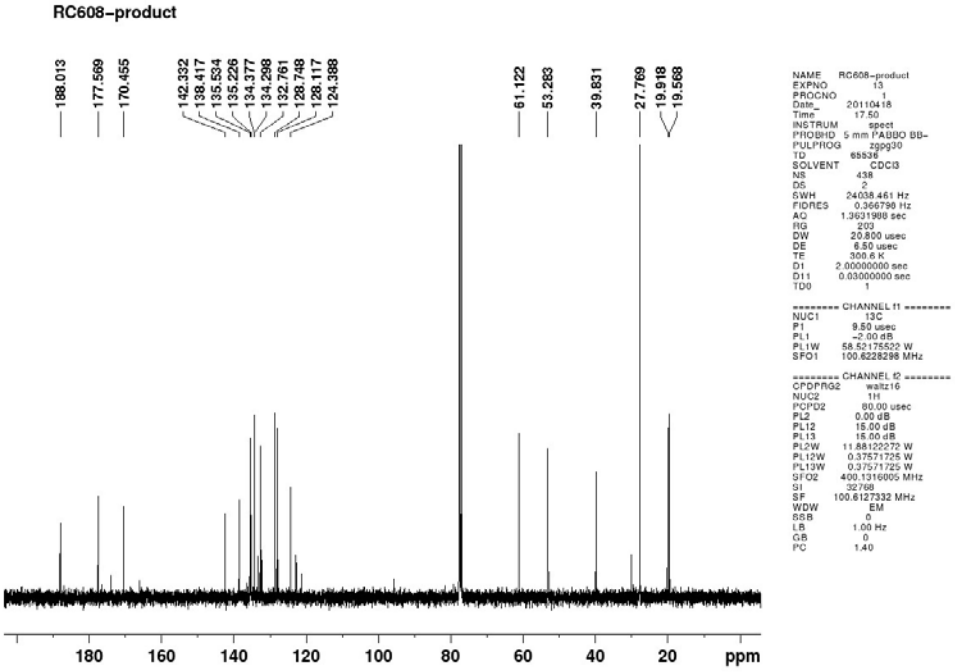


Figure S28. ^{1}H NMR spectrum of **2n**

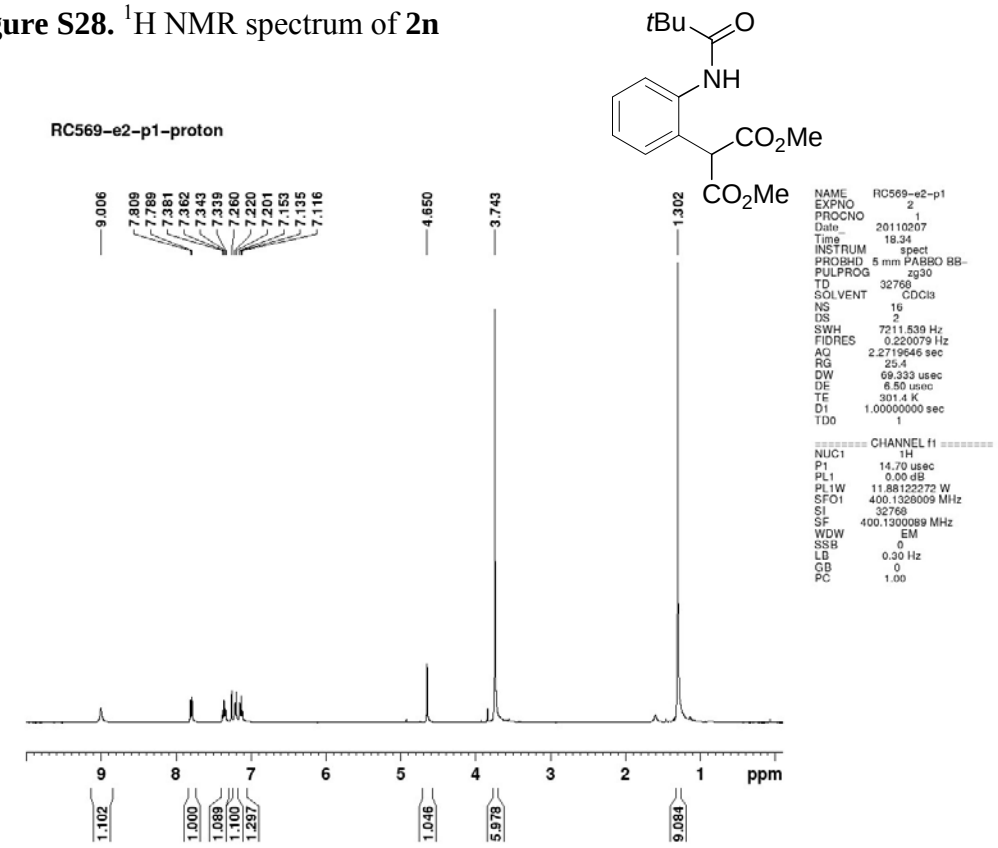


Figure S29. ^{13}C NMR spectrum of **2n**

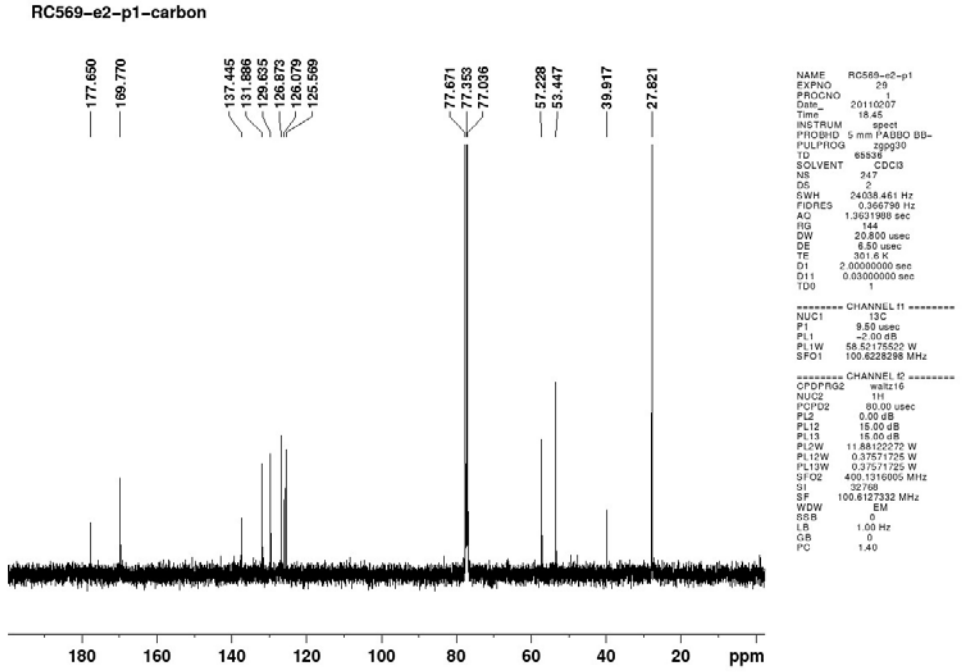


Figure S30. ^{1}H NMR spectrum of **2o**

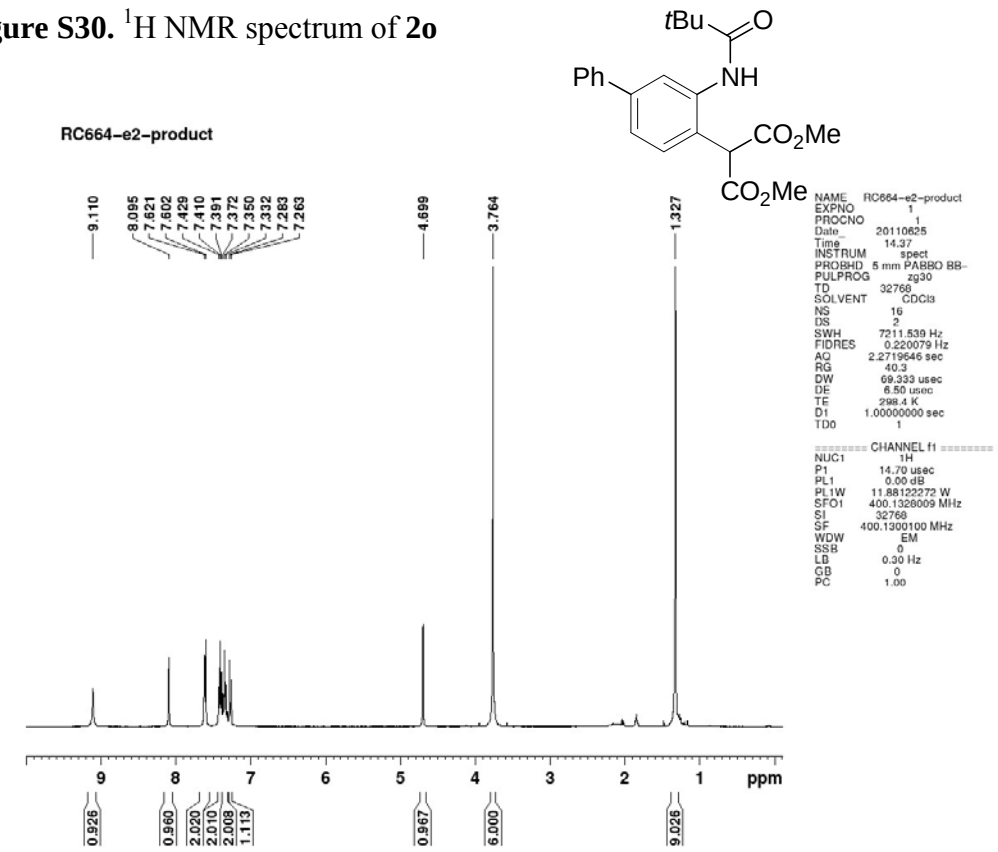


Figure S31. ^{13}C NMR spectrum of **2o**

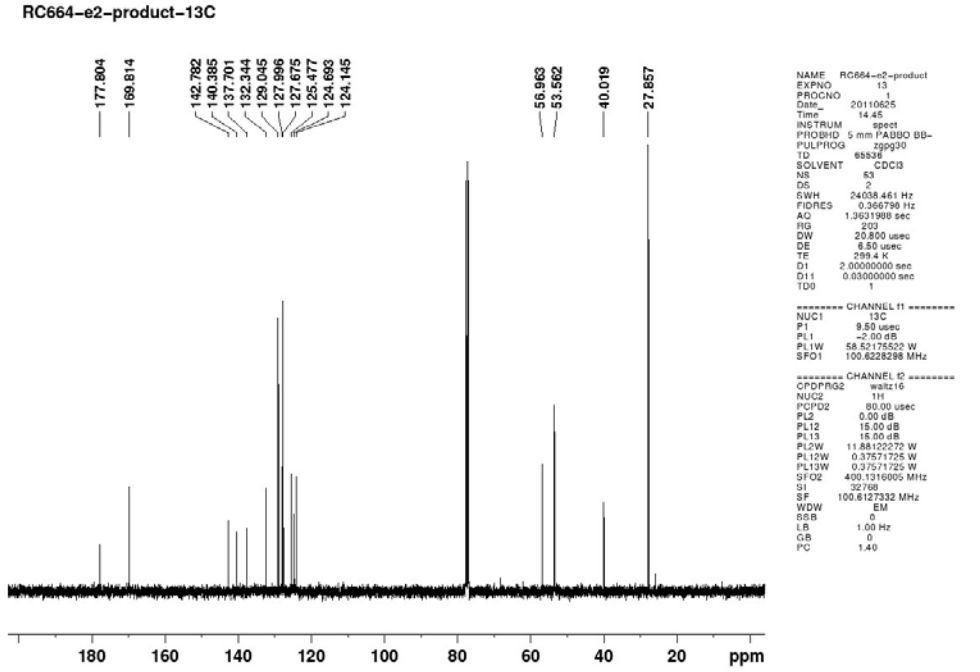


Figure S32. ^{1}H NMR spectrum of **2p**

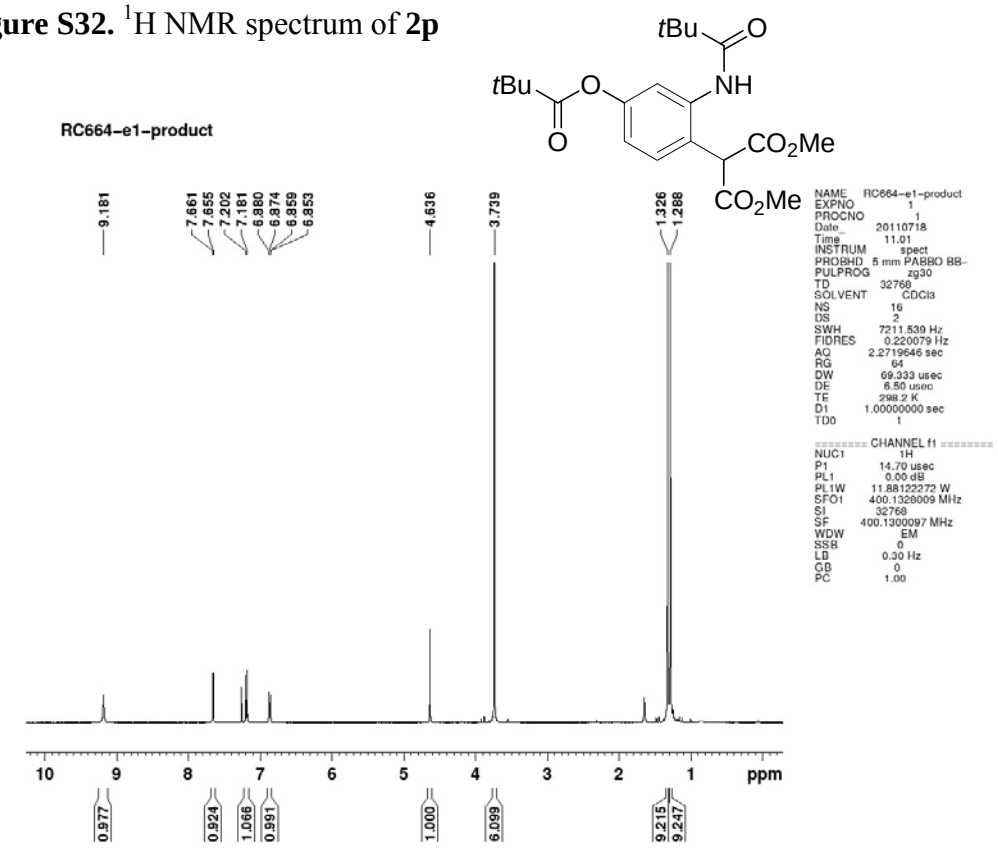


Figure S33. ^{13}C NMR spectrum of **2p**

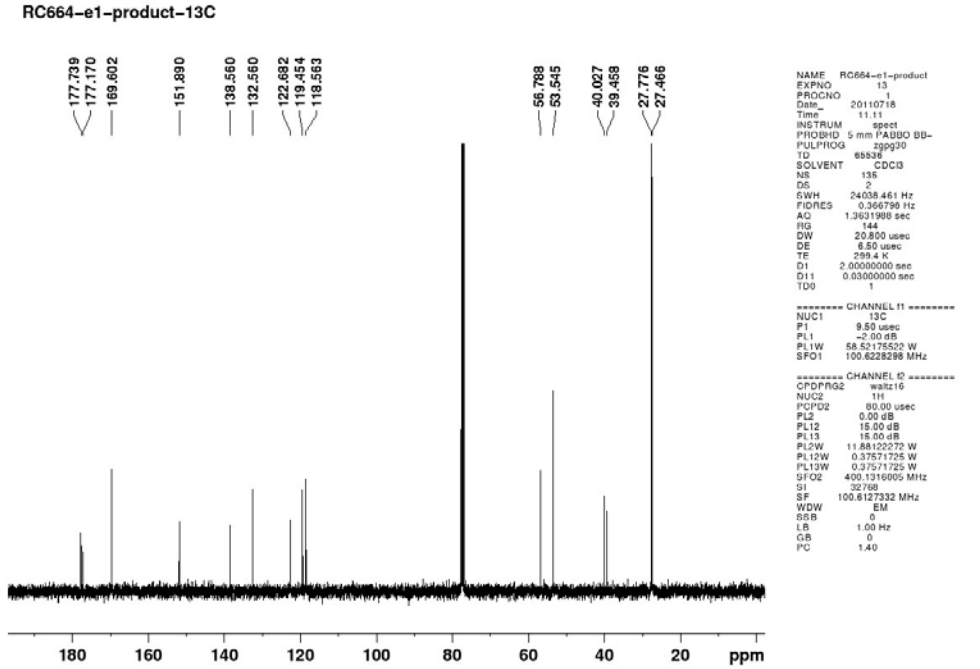


Figure S34. ^{1}H NMR spectrum of **2q**

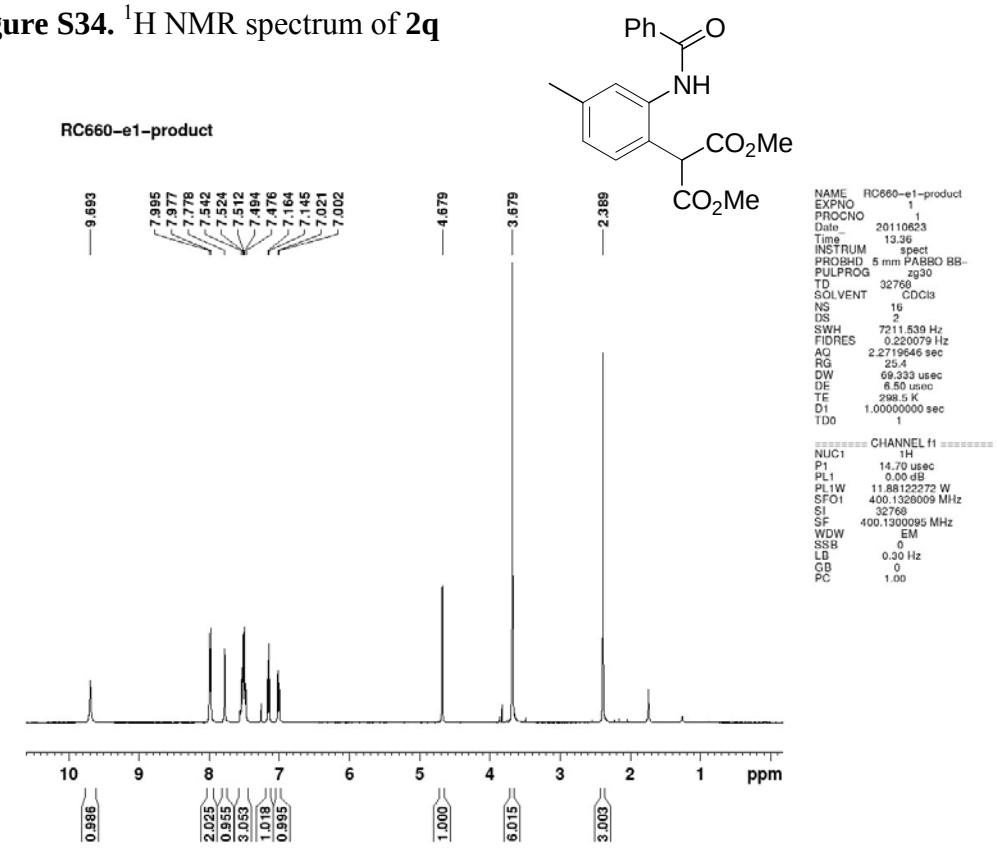


Figure S35. ^{13}C NMR spectrum of **2q**

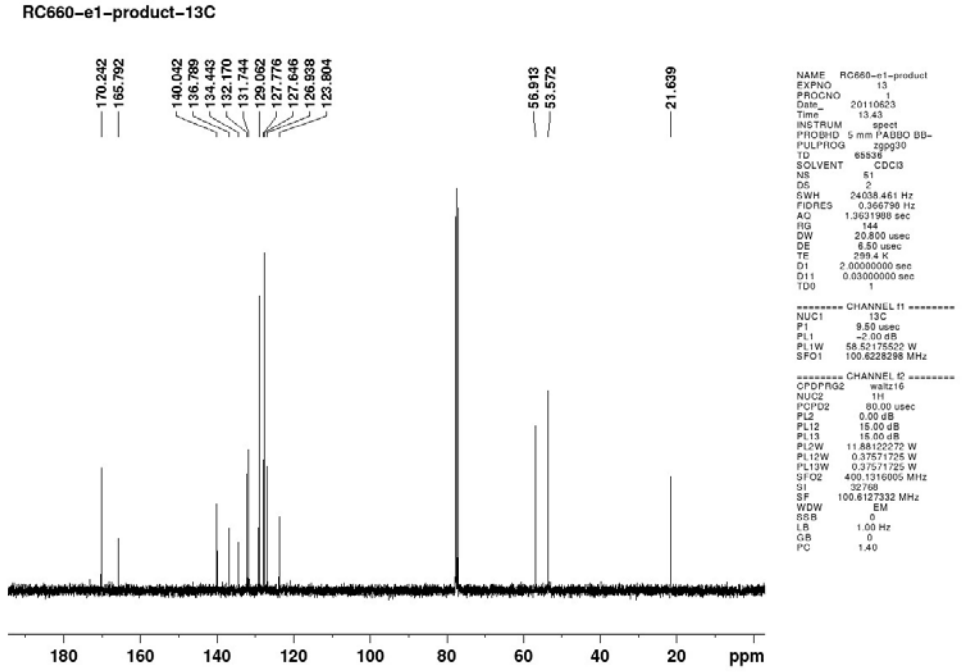


Figure S36. ^{1}H NMR spectrum of **2r**

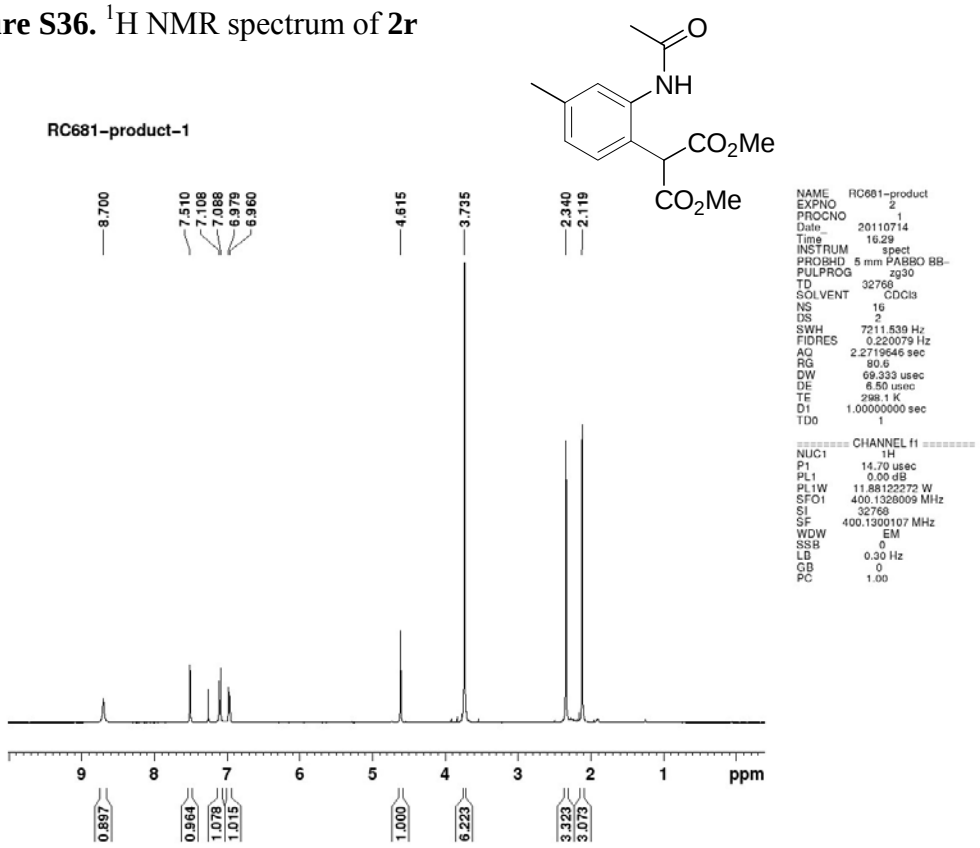


Figure S37. ^{13}C NMR spectrum of **2r**

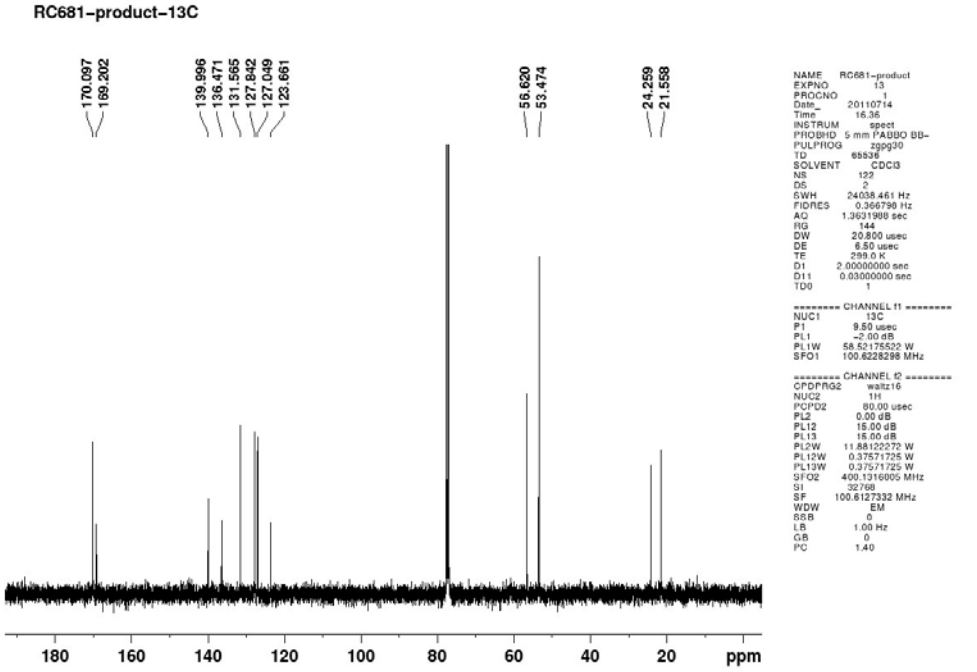


Figure S38. ^{1}H NMR spectrum of **2s**

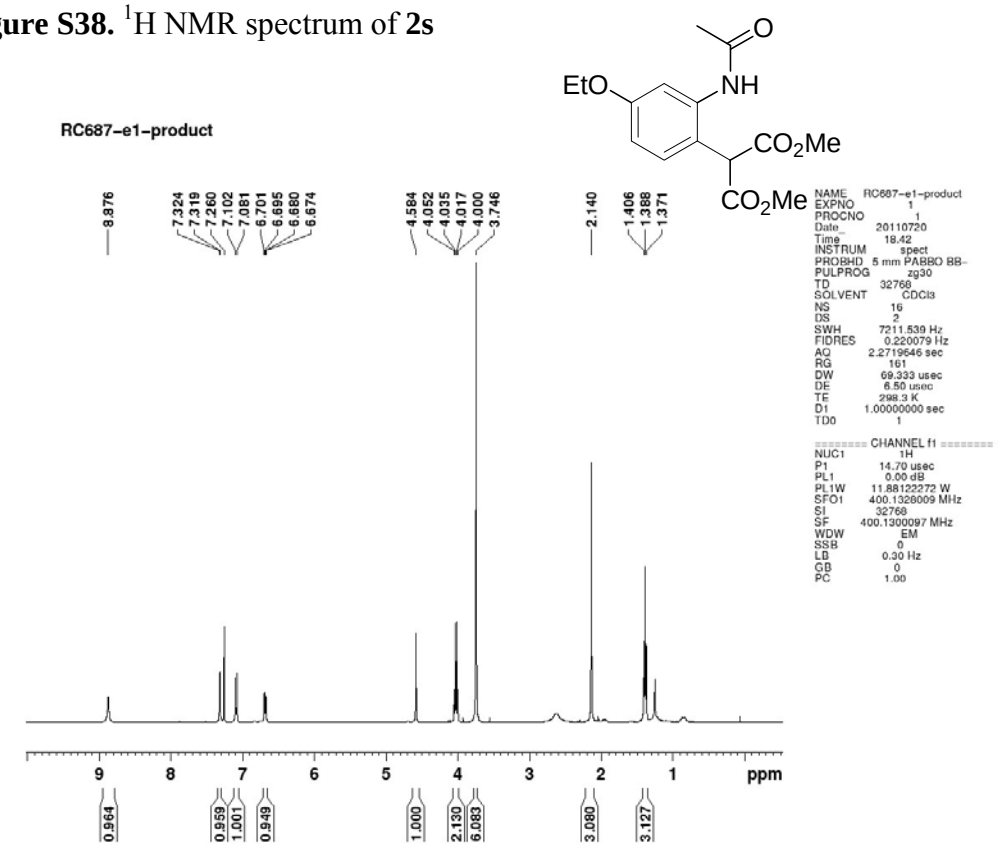


Figure S39. ^{13}C NMR spectrum of **2s**

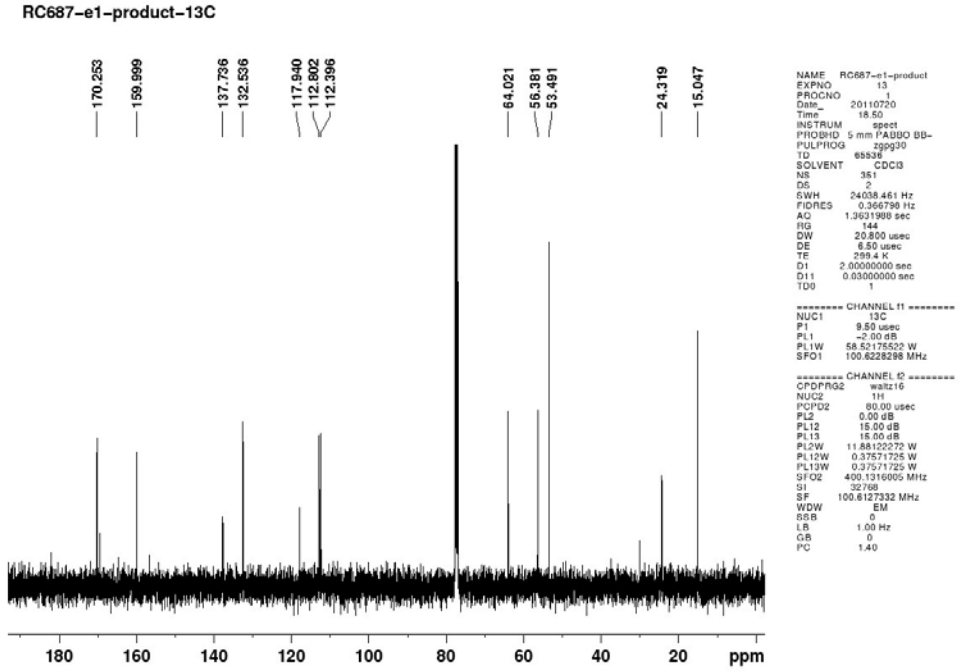


Figure S40. ^{1}H NMR spectrum of **3g**

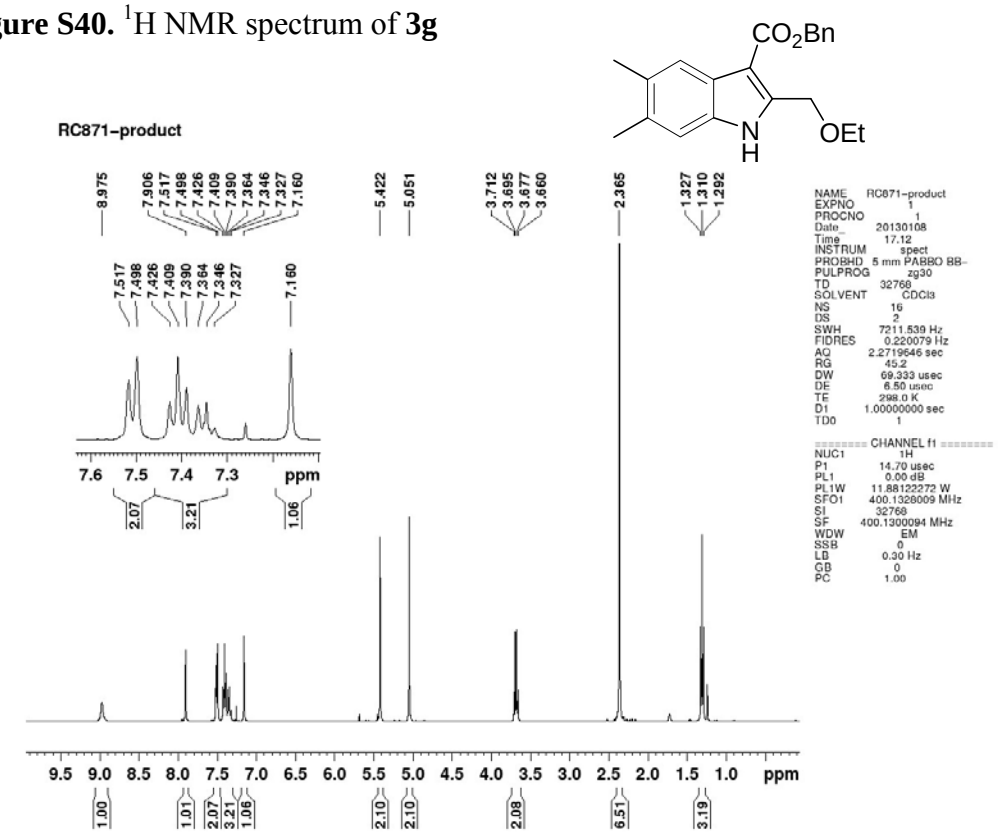


Figure S41. ^{13}C NMR spectrum of **3g**

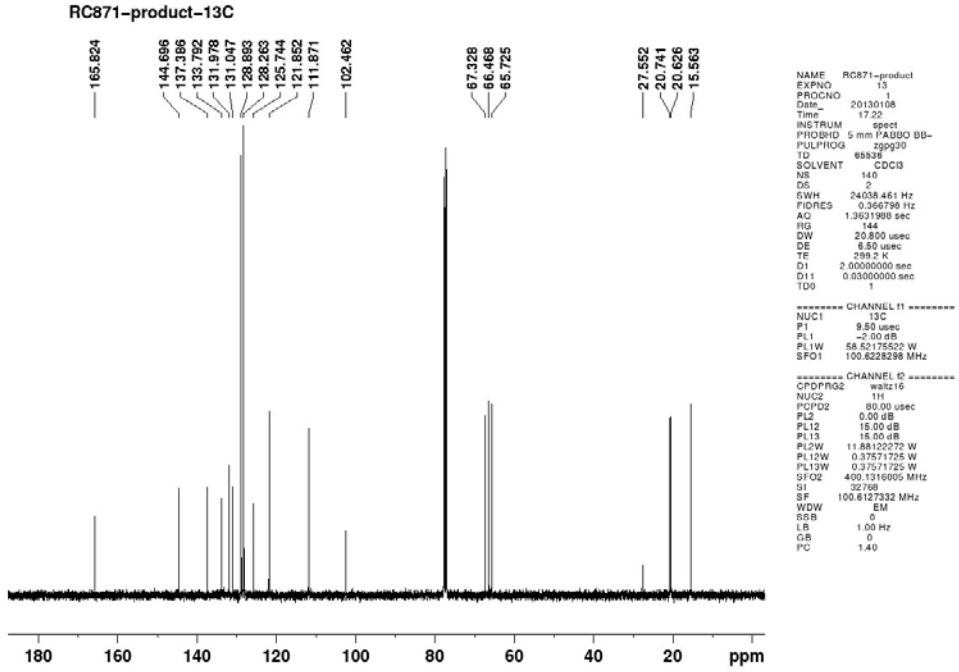


Figure S42. ^{1}H NMR spectrum of **3h**

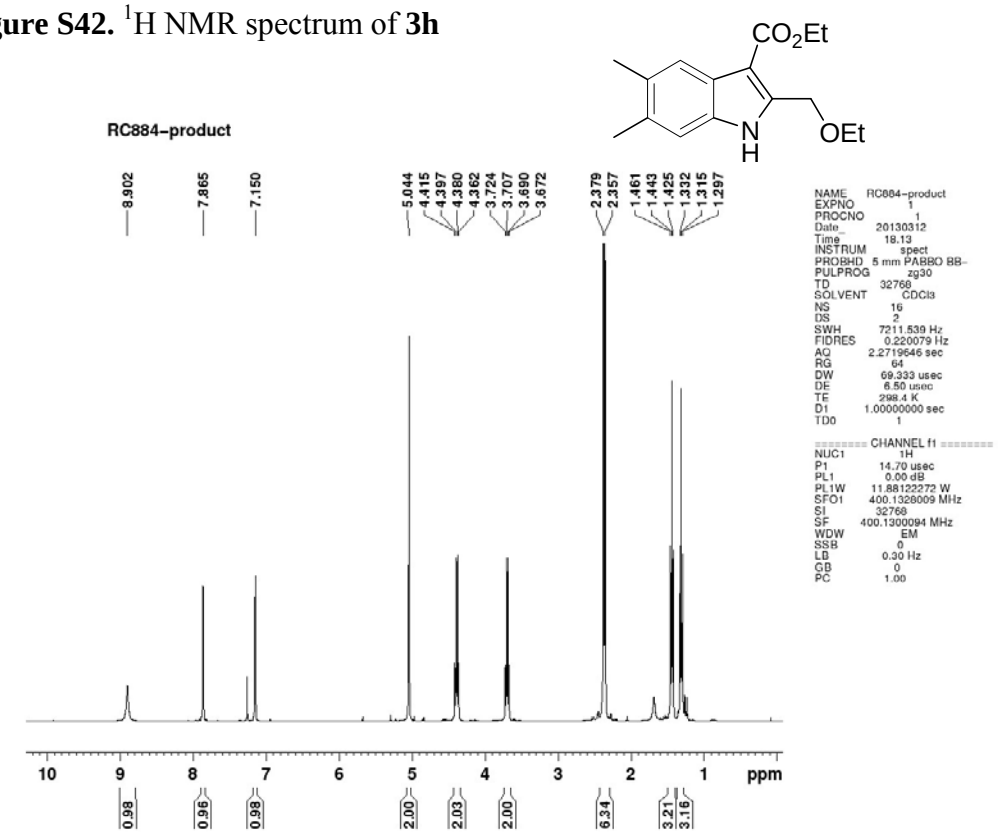
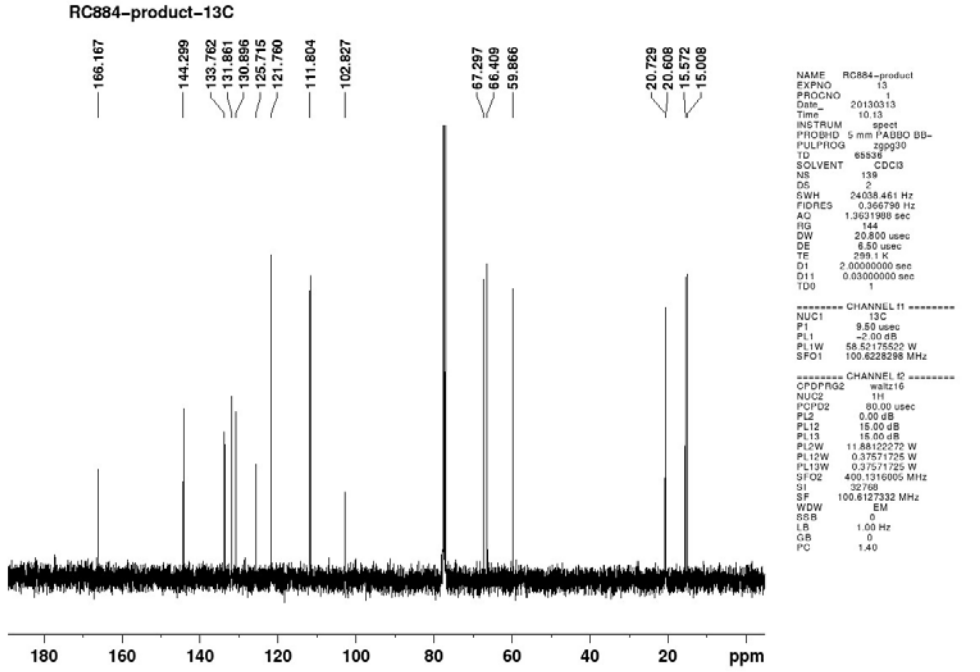


Figure S43. ^{13}C NMR spectrum of **3h**



9. X-ray Crystallographic Data of 2c

Figure S44. Molecular Structure of **2c**

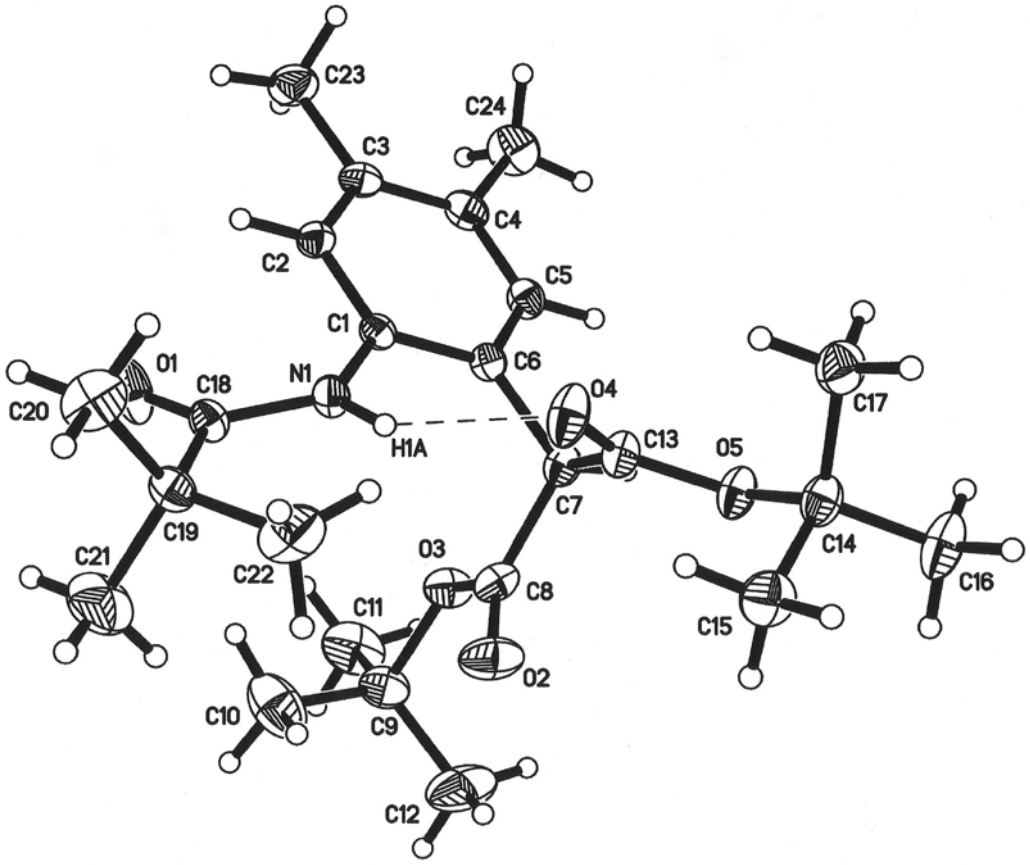


Table S1. Crystal data and structure refinement for **2c**.

Identification code	cww6	
Empirical formula	$C_{24}\ H_{37}\ N\ O_5$	
Formula weight	419.55	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 9.8535(3) Å	= 90°.
	b = 12.5734(4) Å	= 103.496(2)°.
	c = 10.7133(3) Å	= 90°.
Volume	1290.64(7) $Å^3$	
Z	2	
Density (calculated)	1.080 Mg/m^3	
Absorption coefficient	0.075 mm^{-1}	

F(000)	456
Crystal size	0.46 x 0.30 x 0.28 mm^3
Theta range for data collection	1.95 to 27.51°.
Index ranges	-12<=h<=12, -16<=k<=16, -13<=l<=13
Reflections collected	16024
Independent reflections	5730 [R(int) = 0.0363]
Completeness to theta = 27.51°	99.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.745 and 0.628
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5730 / 13 / 294
Goodness-of-fit on F^2	1.003
Final R indices [I>2sigma(I)]	R1 = 0.0515, wR2 = 0.1232
R indices (all data)	R1 = 0.0931, wR2 = 0.1471
Absolute structure parameter	1.2(12)
Largest diff. peak and hole	0.216 and -0.175 e.$Å^{-3}$

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **2c**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	1953(2)	5775(1)	8321(1)	91(1)
O(2)	5122(1)	5688(1)	5370(1)	89(1)
O(3)	5662(1)	4396(1)	6855(1)	67(1)
O(4)	2061(1)	5086(1)	3737(1)	79(1)
O(5)	3624(1)	4268(1)	2835(1)	64(1)
N(1)	2109(1)	5268(1)	6349(1)	50(1)
C(1)	2182(1)	4155(1)	6531(1)	43(1)
C(2)	1445(2)	3649(1)	7313(2)	50(1)
C(3)	1465(2)	2554(1)	7473(2)	54(1)
C(4)	2271(2)	1934(1)	6829(2)	61(1)
C(5)	3013(2)	2450(1)	6061(2)	55(1)
C(6)	2995(2)	3542(1)	5884(1)	46(1)
C(7)	3892(2)	4014(1)	5051(1)	52(1)
C(8)	4959(2)	4815(2)	5762(2)	59(1)

C(9)	6798(2)	4961(2)	7743(2)	74(1)
C(10)	6223(3)	5942(3)	8227(3)	125(1)
C(11)	7222(3)	4163(2)	8816(2)	112(1)
C(12)	7957(2)	5175(3)	7082(3)	134(1)
C(13)	3071(2)	4520(2)	3815(1)	58(1)
C(14)	3069(2)	4725(2)	1529(1)	62(1)
C(15)	3270(2)	5913(2)	1591(2)	81(1)
C(16)	3981(2)	4202(2)	757(2)	93(1)
C(17)	1567(2)	4393(2)	1032(2)	82(1)
C(18)	1956(2)	6017(1)	7224(2)	53(1)
C(19)	1776(2)	7164(1)	6768(2)	58(1)
C(20)	334(4)	7519(4)	6734(5)	89(1)
C(21)	2854(6)	7793(6)	7672(6)	127(2)
C(22)	1980(6)	7333(4)	5393(5)	100(2)
C(20')	571(7)	7229(5)	5635(5)	168(3)
C(21')	1560(10)	7809(5)	7892(6)	262(4)
C(22')	3038(5)	7549(4)	6338(8)	215(4)
C(23)	626(2)	2045(2)	8318(2)	79(1)
C(24)	2304(3)	747(2)	6941(3)	93(1)

Table S3. Bond lengths [Å] and angles [°] for **2c**.

O(1)-C(18)	1.2155(19)
O(2)-C(8)	1.199(2)
O(3)-C(8)	1.3228(19)
O(3)-C(9)	1.472(2)
O(4)-C(13)	1.210(2)
O(5)-C(13)	1.3284(19)
O(5)-C(14)	1.4933(18)
N(1)-C(18)	1.362(2)
N(1)-C(1)	1.412(2)
N(1)-H(1A)	0.8600
C(1)-C(2)	1.386(2)
C(1)-C(6)	1.405(2)
C(2)-C(3)	1.387(2)
C(2)-H(2A)	0.9300
C(3)-C(4)	1.402(3)
C(3)-C(23)	1.505(3)
C(4)-C(5)	1.384(3)
C(4)-C(24)	1.497(3)
C(5)-C(6)	1.385(2)
C(5)-H(5A)	0.9300
C(6)-C(7)	1.516(2)
C(7)-C(13)	1.521(2)
C(7)-C(8)	1.525(2)
C(7)-H(7A)	0.9800
C(9)-C(10)	1.499(4)
C(9)-C(12)	1.503(3)
C(9)-C(11)	1.509(3)
C(10)-H(10A)	0.9600
C(10)-H(10B)	0.9600
C(10)-H(10C)	0.9600
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
C(12)-H(12A)	0.9600
C(12)-H(12B)	0.9600
C(12)-H(12C)	0.9600

C(14)-C(15)	1.506(3)
C(14)-C(16)	1.507(3)
C(14)-C(17)	1.510(3)
C(15)-H(15A)	0.9600
C(15)-H(15B)	0.9600
C(15)-H(15C)	0.9600
C(16)-H(16A)	0.9600
C(16)-H(16B)	0.9600
C(16)-H(16C)	0.9600
C(17)-H(17A)	0.9600
C(17)-H(17B)	0.9600
C(17)-H(17C)	0.9600
C(18)-C(19)	1.520(2)
C(19)-C(20)	1.482(5)
C(19)-C(21)	1.487(6)
C(19)-C(20')	1.489(5)
C(19)-C(22')	1.503(5)
C(19)-C(21')	1.507(6)
C(19)-C(22)	1.547(5)
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600
C(21)-H(21A)	0.9600
C(21)-H(21B)	0.9600
C(21)-H(21C)	0.9600
C(22)-H(22A)	0.9600
C(22)-H(22B)	0.9600
C(22)-H(22C)	0.9600
C(20')-H(20D)	0.9600
C(20')-H(20E)	0.9600
C(20')-H(20F)	0.9600
C(21')-H(21D)	0.9600
C(21')-H(21E)	0.9600
C(21')-H(21F)	0.9600
C(22')-H(22D)	0.9600
C(22')-H(22E)	0.9600
C(22')-H(22F)	0.9600
C(23)-H(23A)	0.9600

C(23)-H(23B)	0.9600
C(23)-H(23C)	0.9600
C(24)-H(24A)	0.9600
C(24)-H(24B)	0.9600
C(24)-H(24C)	0.9600

C(8)-O(3)-C(9)	122.81(15)
C(13)-O(5)-C(14)	121.35(13)
C(18)-N(1)-C(1)	126.92(13)
C(18)-N(1)-H(1A)	116.5
C(1)-N(1)-H(1A)	116.5
C(2)-C(1)-C(6)	119.09(14)
C(2)-C(1)-N(1)	121.43(14)
C(6)-C(1)-N(1)	119.46(13)
C(1)-C(2)-C(3)	122.40(15)
C(1)-C(2)-H(2A)	118.8
C(3)-C(2)-H(2A)	118.8
C(2)-C(3)-C(4)	118.99(16)
C(2)-C(3)-C(23)	120.12(17)
C(4)-C(3)-C(23)	120.88(17)
C(5)-C(4)-C(3)	118.05(16)
C(5)-C(4)-C(24)	120.67(18)
C(3)-C(4)-C(24)	121.26(18)
C(4)-C(5)-C(6)	123.67(16)
C(4)-C(5)-H(5A)	118.2
C(6)-C(5)-H(5A)	118.2
C(5)-C(6)-C(1)	117.79(15)
C(5)-C(6)-C(7)	118.57(14)
C(1)-C(6)-C(7)	123.60(14)
C(6)-C(7)-C(13)	114.31(13)
C(6)-C(7)-C(8)	113.13(12)
C(13)-C(7)-C(8)	108.90(15)
C(6)-C(7)-H(7A)	106.7
C(13)-C(7)-H(7A)	106.7
C(8)-C(7)-H(7A)	106.7
O(2)-C(8)-O(3)	126.12(16)
O(2)-C(8)-C(7)	124.22(14)
O(3)-C(8)-C(7)	109.66(16)

O(3)-C(9)-C(10)	109.24(16)
O(3)-C(9)-C(12)	109.17(18)
C(10)-C(9)-C(12)	113.9(2)
O(3)-C(9)-C(11)	101.86(18)
C(10)-C(9)-C(11)	110.1(2)
C(12)-C(9)-C(11)	111.8(2)
C(9)-C(10)-H(10A)	109.5
C(9)-C(10)-H(10B)	109.5
H(10A)-C(10)-H(10B)	109.5
C(9)-C(10)-H(10C)	109.5
H(10A)-C(10)-H(10C)	109.5
H(10B)-C(10)-H(10C)	109.5
C(9)-C(11)-H(11A)	109.5
C(9)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(9)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
C(9)-C(12)-H(12A)	109.5
C(9)-C(12)-H(12B)	109.5
H(12A)-C(12)-H(12B)	109.5
C(9)-C(12)-H(12C)	109.5
H(12A)-C(12)-H(12C)	109.5
H(12B)-C(12)-H(12C)	109.5
O(4)-C(13)-O(5)	124.63(14)
O(4)-C(13)-C(7)	124.58(15)
O(5)-C(13)-C(7)	110.79(14)
O(5)-C(14)-C(15)	108.95(14)
O(5)-C(14)-C(16)	102.23(14)
C(15)-C(14)-C(16)	111.53(18)
O(5)-C(14)-C(17)	109.79(15)
C(15)-C(14)-C(17)	113.47(17)
C(16)-C(14)-C(17)	110.26(16)
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5

H(15B)-C(15)-H(15C)	109.5
C(14)-C(16)-H(16A)	109.5
C(14)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(14)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5
C(14)-C(17)-H(17A)	109.5
C(14)-C(17)-H(17B)	109.5
H(17A)-C(17)-H(17B)	109.5
C(14)-C(17)-H(17C)	109.5
H(17A)-C(17)-H(17C)	109.5
H(17B)-C(17)-H(17C)	109.5
O(1)-C(18)-N(1)	121.21(16)
O(1)-C(18)-C(19)	121.47(16)
N(1)-C(18)-C(19)	117.32(14)
C(20)-C(19)-C(21)	113.0(4)
C(20)-C(19)-C(20')	52.1(3)
C(21)-C(19)-C(20')	144.5(4)
C(20)-C(19)-C(22')	138.8(3)
C(21)-C(19)-C(22')	60.8(4)
C(20')-C(19)-C(22')	107.0(4)
C(20)-C(19)-C(21')	62.9(4)
C(21)-C(19)-C(21')	53.6(4)
C(20')-C(19)-C(21')	112.8(4)
C(22')-C(19)-C(21')	110.6(4)
C(20)-C(19)-C(18)	109.5(2)
C(21)-C(19)-C(18)	106.4(3)
C(20')-C(19)-C(18)	109.0(2)
C(22')-C(19)-C(18)	111.1(2)
C(21')-C(19)-C(18)	106.3(3)
C(20)-C(19)-C(22)	105.8(3)
C(21)-C(19)-C(22)	108.4(4)
C(20')-C(19)-C(22)	58.2(3)
C(22')-C(19)-C(22)	50.5(3)
C(21')-C(19)-C(22)	139.5(3)
C(18)-C(19)-C(22)	113.9(2)
C(19)-C(20)-H(20A)	109.5

C(19)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(19)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5
C(19)-C(21)-H(21A)	109.5
C(19)-C(21)-H(21B)	109.5
H(21A)-C(21)-H(21B)	109.5
C(19)-C(21)-H(21C)	109.5
H(21A)-C(21)-H(21C)	109.5
H(21B)-C(21)-H(21C)	109.5
C(19)-C(22)-H(22A)	109.5
C(19)-C(22)-H(22B)	109.5
H(22A)-C(22)-H(22B)	109.5
C(19)-C(22)-H(22C)	109.5
H(22A)-C(22)-H(22C)	109.5
H(22B)-C(22)-H(22C)	109.5
C(19)-C(20')-H(20D)	109.4
C(19)-C(20')-H(20E)	109.5
H(20D)-C(20')-H(20E)	109.5
C(19)-C(20')-H(20F)	109.5
H(20D)-C(20')-H(20F)	109.5
H(20E)-C(20')-H(20F)	109.5
C(19)-C(21')-H(21D)	109.5
C(19)-C(21')-H(21E)	109.5
H(21D)-C(21')-H(21E)	109.5
C(19)-C(21')-H(21F)	109.4
H(21D)-C(21')-H(21F)	109.5
H(21E)-C(21')-H(21F)	109.5
C(19)-C(22')-H(22D)	109.5
C(19)-C(22')-H(22E)	109.5
H(22D)-C(22')-H(22E)	109.5
C(19)-C(22')-H(22F)	109.5
H(22D)-C(22')-H(22F)	109.5
H(22E)-C(22')-H(22F)	109.5
C(3)-C(23)-H(23A)	109.5
C(3)-C(23)-H(23B)	109.5
H(23A)-C(23)-H(23B)	109.5

C(3)-C(23)-H(23C)	109.5
H(23A)-C(23)-H(23C)	109.5
H(23B)-C(23)-H(23C)	109.5
C(4)-C(24)-H(24A)	109.5
C(4)-C(24)-H(24B)	109.5
H(24A)-C(24)-H(24B)	109.5
C(4)-C(24)-H(24C)	109.5
H(24A)-C(24)-H(24C)	109.5
H(24B)-C(24)-H(24C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **2c**. The anisotropic displacement factor exponent takes the form: $-2^2[\ h^2 a^{*2} U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	173(1)	54(1)	47(1)	-1(1)	28(1)	7(1)
O(2)	79(1)	88(1)	94(1)	42(1)	7(1)	-19(1)
O(3)	57(1)	73(1)	63(1)	17(1)	0(1)	-6(1)
O(4)	81(1)	110(1)	48(1)	9(1)	18(1)	41(1)
O(5)	71(1)	81(1)	44(1)	9(1)	20(1)	19(1)
N(1)	70(1)	37(1)	47(1)	3(1)	20(1)	0(1)
C(1)	47(1)	37(1)	44(1)	0(1)	7(1)	-1(1)
C(2)	52(1)	46(1)	55(1)	0(1)	17(1)	-4(1)
C(3)	52(1)	48(1)	60(1)	6(1)	8(1)	-8(1)
C(4)	67(1)	37(1)	73(1)	2(1)	7(1)	0(1)
C(5)	56(1)	49(1)	58(1)	-4(1)	10(1)	7(1)
C(6)	48(1)	44(1)	45(1)	0(1)	9(1)	2(1)
C(7)	55(1)	58(1)	46(1)	5(1)	16(1)	7(1)
C(8)	47(1)	73(1)	59(1)	17(1)	15(1)	2(1)
C(9)	54(1)	81(1)	78(1)	4(1)	-4(1)	-3(1)
C(10)	113(2)	113(2)	126(2)	-32(2)	-23(2)	16(2)
C(11)	106(2)	120(2)	88(1)	27(2)	-26(1)	-7(2)
C(12)	54(1)	197(3)	145(2)	29(2)	10(1)	-25(2)
C(13)	59(1)	68(1)	48(1)	0(1)	17(1)	10(1)
C(14)	68(1)	76(1)	45(1)	10(1)	15(1)	14(1)
C(15)	91(1)	82(2)	68(1)	20(1)	14(1)	2(1)
C(16)	103(1)	128(2)	56(1)	18(1)	35(1)	39(1)
C(17)	78(1)	107(2)	58(1)	6(1)	11(1)	-2(1)
C(18)	61(1)	44(1)	51(1)	-2(1)	9(1)	1(1)
C(19)	64(1)	40(1)	67(1)	2(1)	9(1)	3(1)
C(20)	81(3)	81(3)	102	40(3)	17(2)	28(2)
C(21)	100(4)	148	111(4)	-35(4)	-21(4)	-19(4)
C(22)	122	54(3)	141(4)	40(3)	65(3)	12(3)
C(20')	234(6)	88(4)	120	27(3)	-81(4)	9(4)
C(21')	588(11)	106	154(4)	39(3)	212(6)	142(5)
C(22')	113(3)	68(3)	495(11)	120(4)	138(5)	20(3)
C(23)	82(1)	67(1)	94(1)	10(1)	31(1)	-15(1)
C(24)	114(2)	44(1)	124(2)	8(1)	31(1)	9(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for **2c**.

	x	y	z	U(eq)
H(1A)	2166	5496	5606	60
H(2A)	916	4058	7747	60
H(5A)	3554	2041	5639	66
H(7A)	4422	3425	4800	63
H(10A)	5963	6446	7539	188
H(10B)	6921	6250	8908	188
H(10C)	5418	5759	8542	188
H(11A)	6458	4047	9215	169
H(11B)	8010	4431	9441	169
H(11C)	7469	3504	8475	169
H(12A)	7646	5677	6400	201
H(12B)	8219	4523	6734	201
H(12C)	8748	5460	7689	201
H(15A)	2672	6221	2083	122
H(15B)	3043	6201	738	122
H(15C)	4225	6073	1992	122
H(16A)	4930	4427	1074	139
H(16B)	3668	4403	-128	139
H(16C)	3925	3444	833	139
H(17A)	994	4745	1517	122
H(17B)	1489	3637	1119	122
H(17C)	1263	4586	143	122
H(20A)	159	7456	7576	133
H(20B)	-317	7084	6144	133
H(20C)	224	8248	6461	133
H(21A)	2766	7674	8535	191
H(21B)	2726	8535	7469	191
H(21C)	3765	7576	7596	191
H(22A)	1960	6658	4971	150
H(22B)	2863	7672	5435	150
H(22C)	1244	7776	4919	150
H(20D)	-284	7150	5911	251

H(20E)	641	6673	5040	251
H(20F)	577	7907	5225	251
H(21D)	1492	7340	8582	394
H(21E)	715	8215	7637	394
H(21F)	2336	8282	8172	394
H(22D)	3783	7684	7076	322
H(22E)	2812	8193	5853	322
H(22F)	3325	7016	5812	322
H(23A)	152	2587	8685	119
H(23B)	1237	1656	8993	119
H(23C)	-47	1569	7817	119
H(24A)	2898	461	6430	140
H(24B)	1377	470	6642	140
H(24C)	2658	549	7822	140

Table S6. Torsion angles [°] for **2c**.

C(18)-N(1)-C(1)-C(2)	33.4(2)
C(18)-N(1)-C(1)-C(6)	-148.04(15)
C(6)-C(1)-C(2)-C(3)	-0.7(2)
N(1)-C(1)-C(2)-C(3)	177.83(13)
C(1)-C(2)-C(3)-C(4)	0.6(2)
C(1)-C(2)-C(3)-C(23)	-179.06(14)
C(2)-C(3)-C(4)-C(5)	0.0(2)
C(23)-C(3)-C(4)-C(5)	179.67(15)
C(2)-C(3)-C(4)-C(24)	-178.48(17)
C(23)-C(3)-C(4)-C(24)	1.1(3)
C(3)-C(4)-C(5)-C(6)	-0.5(2)
C(24)-C(4)-C(5)-C(6)	178.00(17)
C(4)-C(5)-C(6)-C(1)	0.4(2)
C(4)-C(5)-C(6)-C(7)	178.05(14)
C(2)-C(1)-C(6)-C(5)	0.21(19)
N(1)-C(1)-C(6)-C(5)	-178.35(12)
C(2)-C(1)-C(6)-C(7)	-177.30(13)
N(1)-C(1)-C(6)-C(7)	4.1(2)
C(5)-C(6)-C(7)-C(13)	113.85(16)
C(1)-C(6)-C(7)-C(13)	-68.66(19)
C(5)-C(6)-C(7)-C(8)	-120.74(16)
C(1)-C(6)-C(7)-C(8)	56.75(19)
C(9)-O(3)-C(8)-O(2)	-1.6(3)
C(9)-O(3)-C(8)-C(7)	178.17(15)
C(6)-C(7)-C(8)-O(2)	-129.86(18)
C(13)-C(7)-C(8)-O(2)	-1.6(2)
C(6)-C(7)-C(8)-O(3)	50.34(19)
C(13)-C(7)-C(8)-O(3)	178.61(13)
C(8)-O(3)-C(9)-C(10)	62.8(2)
C(8)-O(3)-C(9)-C(12)	-62.4(2)
C(8)-O(3)-C(9)-C(11)	179.21(17)
C(14)-O(5)-C(13)-O(4)	3.4(3)
C(14)-O(5)-C(13)-C(7)	-175.76(14)
C(6)-C(7)-C(13)-O(4)	43.3(2)
C(8)-C(7)-C(13)-O(4)	-84.3(2)
C(6)-C(7)-C(13)-O(5)	-137.52(15)

C(8)-C(7)-C(13)-O(5)	94.88(17)
C(13)-O(5)-C(14)-C(15)	63.1(2)
C(13)-O(5)-C(14)-C(16)	-178.81(17)
C(13)-O(5)-C(14)-C(17)	-61.8(2)
C(1)-N(1)-C(18)-O(1)	4.6(3)
C(1)-N(1)-C(18)-C(19)	-174.78(13)
O(1)-C(18)-C(19)-C(20)	-68.5(3)
N(1)-C(18)-C(19)-C(20)	110.9(3)
O(1)-C(18)-C(19)-C(21)	53.9(3)
N(1)-C(18)-C(19)-C(21)	-126.7(3)
O(1)-C(18)-C(19)-C(20')	-124.0(3)
N(1)-C(18)-C(19)-C(20')	55.4(4)
O(1)-C(18)-C(19)-C(22')	118.3(4)
N(1)-C(18)-C(19)-C(22')	-62.3(4)
O(1)-C(18)-C(19)-C(21')	-2.1(4)
N(1)-C(18)-C(19)-C(21')	177.3(4)
O(1)-C(18)-C(19)-C(22)	173.2(3)
N(1)-C(18)-C(19)-C(22)	-7.4(3)

Symmetry transformations used to generate equivalent atoms:

Table S7. Hydrogen bonds for **2c** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(1)-H(1A)...O(4)	0.86	2.05	2.7968(17)	145.2

Symmetry transformations used to generate equivalent atoms: