Angewandte Chemie
Eine Zeitschrift der Gesellschaft Deutscher Chemiker

Supporting Information

69451 Weinheim, Germany

Supporting Information

Direct and Waste-Free Amidations and Cycloadditions by Organocatalytic Activation of Carboxylic Acids at Room Temperature

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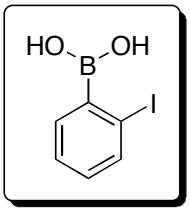
1. Experimental Details and Compound Data.

1.1) General Informations.

Unless otherwise stated, all reactions were performed under argon atmosphere using flame-dried glassware. Toluene and CH_2Cl_2 were distilled from CaH_2. THF was distilled from sodium with benzophenone as an indicator. Analytical thin layer chromatographies were performed on Merck Silica Gel 60 F254 plates. NMR spectra were recorded on Varian INOVA-300, INOVA-400 or INOVA-500 MHz instruments. The residual solvent protons (^{1}H) or the solvent carbon (^{13}C) were used as internal standards. ^{1}H NMR data are presented as follows: chemical shift in ppm (δ) downfield from tetramethylsilane (multiplicity, coupling constant, integration). The following abbreviations are used in reporting NMR data: s, singlet; br s, broad singlet; d, doublet; t, triplet; q, quartet; dd, doublet of doublets; m, multiplet; sept, septet. High-resolution mass spectra were recorded by the University of Alberta mass spectrometry service laboratory using either electron impact (EI) or electrospray ionization (ESI) techniques. Infrared spectra were obtained on a Nicolet Magna-IR 750 with frequencies expressed in cm^{-1}. X-ray crystallography was performed using a Bruker P4/RA/SMART 1000 CCD diffractometer. Powdered 4 A molecular sieves (< 5 micron, Aldrich) were dried overnight in a vacuum oven (138 ^oC) prior to use.

1.2) Preparation and Data of *ortho*-Iodophenylboronic acid (2)



To a solution of 1,2-diiodobenzene (1.02 g, 30.8 mmol) in 300 mL of a mixture of THF and Et_2O (1:1) at -78 ºC was added dropwise *iso*propyl magnesium chloride (2 M in THF, 15.4 mL, 30.8 mmol). The mixture was stirred at that temperature for 2 h and then, triisopropyl borate (17.4 g, 92.4 mmol) was added. The solution was slowly warmed to room temperature and stirred overnight. HCl (10% aq., 400 mL) was added and the resulting mixture was stirred 30 min. at

room temperature. The aqueous layer was extracted with Et_2O (3 x 500 mL). Drying of the organic phase (Na_2SO_4) and evaporation gave the crude that was purified by flash chromatography (100% hexane then hexane/EtOAc; 4:1) to yield the desired product (0.62 g, 82% yield) as a white solid.

^{1}H-NMR (400 MHz, CD_2Cl_2) δ 7.86 (dd, *J* = 1.2, 7.6 Hz, 1H), 7.77 (dd, *J* = 1.8, 7.6 Hz, 1H), 7.41 (dt, *J* = 1.2, 7.6 Hz, 1H), 7.14 (dt, *J* = 1.8, 7.6 Hz, 1H), 5.22 (s, 2 H).

^{13}C-NMR (125 MHz, CD_2Cl_2) δ 139.8, 136.9, 132.5, 128.0, 100.7, (C attached to B not seen on the NMR at 27 ^{0}C).

^{11}B NMR (128 MHz, CD_2Cl_2) δ 29.10.

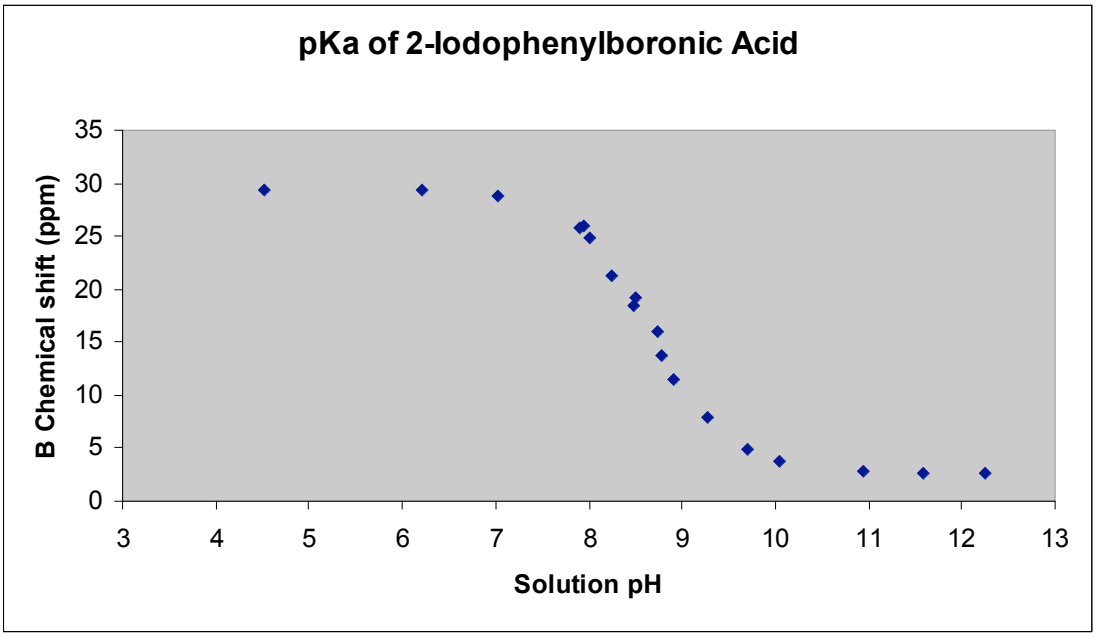
IR (Microscope, cm^{-1}) 3306, 1581, 1352, 999, 820, 752.

HRMS (EI) for $C_6H_6O_2{}^{11}BI$: calcd. 247.95056; found, 247.95068.

CCDC 664933

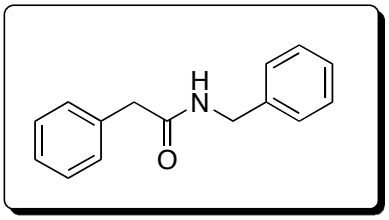
pKa (^{11}B NMR titration) 8.90.

NMR titration assay. Phosphate buffer solution: In a volumetric flask (50 mL), 690 mg of NaH_2PO_4 were placed with 5 mL of D_2O. The flask was filled to 50 mL with H_2O. Boronic acid solution: In a volumetric flask (25 mL), 99 mg of boronic acid **2** was dissolved in a minimum of DMSO. The flask was filled to 25 mL with the phosphate buffer solution (resulting solution: 16 mM of **2** in 0.1 M phosphate buffer; 90/10 H_2O/D_2O). Solution for ^{11}B NMR: 1 mL of the boronic acid solution was placed in a vial. This solution was adjusted to the desired pH with an aqueous NaOH solution. The ^{11}B NMR is made from this solution. The pKa is determined using the plot of the boron chemical shift vs. the pH of the solution.



1.3) General Procedure for Organocatalytic Amidations.

1.3.1) *N*-Benzyl-2-phenyl-acetamide (table 1, entry 1)

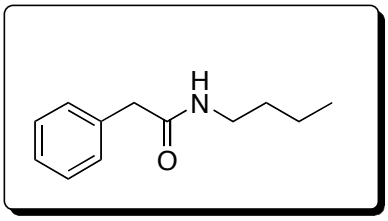


Into a 25 ml round bottom flask equipped with a stir bar was added phenyl acetic acid (0.075 g, 0.55 mmol, 1.1 eq), *ortho*-bromophenylboronic acid (10 mg, 0.05 mmol, 10 mol%) and 1g of activated 4A Molecular sieves. Dichloromethane (7 mL) was added and the mixture was stirred for 10 min. Then, benzylamine (55 μL, 0.5 mmol, 1 eq) was added (in order to get reproducible results, it is necessary to use a gas tight 100 μl syringe). The resulting mixture was stirred for 48 h at room temperature (24-25 ^{0}C). The reaction mixture was filtered through a pad of Celite ® 545, the filtrate was washed with aqueous acidic solution (pH = 4), aqueous basic solution (pH = 10-11) and brine. The organic layer was collected, dried over anhydrous Na_2SO_4 and evaporated to yield the title compound (0.123 g, 99%) as a pure product. The catalyst can be recuperated in up to 80% yield by acidification of the aqueous basic solution to pH 7 and extraction with EtOAc.

The characterization of the compound matched previous reports: (a) Wing-Kei Chan.; Chi-Ming Ho.; Man-Kin Wong.; Chi-Ming Che. *Journal of the American Chemical Society* **2006**, *128*, 14796. (b) Donald C. Dittmer.; Qun Li.; Dimitry V. Avilov. *Journal of Organic Chemistry* **2005**, *70*, 4682.

1.4) Amides Preparations and Data.

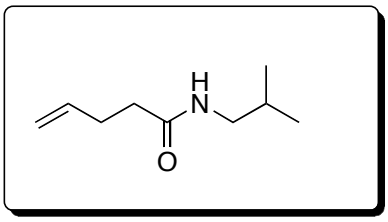
1.4.1) *N*-butyl-2-phenyl-acetamide (table 1, entry 3)



The title compound was prepared using the general procedure for the organocatalytic amidations (66% yield in DCM, 87% yield in THF).

The characterization of the compound matched previous reports: (a) Petrovic, S. D.; Stojanovic, N. D.; Stojanovic, O. K.; Kobilaov, N. L. Fac. Technol. Metall. *Journal of the Serbian Chemical Society* **1986**, *51*, 395. (b) Ram, R. N.; Ashare, R.; Mukerjee, A. K. *Chemistry & Industry* (London, United Kingdom) **1983**, *14*, 569.

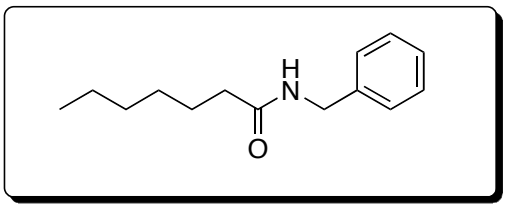
1.4.2) Pent-4-enoic acid *iso*butylamide (table 1, entry 4)



The title compound was prepared using the general procedure for the organocatalytic amidations (80% yield).

The characterization of the compound matched previous reports: (a) Gagosz, F.; Moutrille, C.; Zard, S. Z. *Organic letters*, **2002**, *4*, 2707. (b) Blakemore, P. R. *Science of Synthesis*, **2005**, *21*, 833.

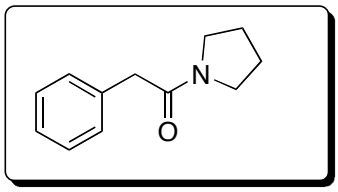
1.4.3) Heptanoic acid benzylamide (table 1, entry 5)



The title compound was prepared using the general procedure for the organocatalytic amidations. (99% yield).

The characterization of the compound matched previous reports: (a) Hoeter, J. M.; Otte, K. M.; Gellman, S. H.; Stahl S. S. *Journal of the American Chemical Society* **2006**, *128*, 5177. (b) Lee, H. L.; Aube, J. *Tetrahedron* **2007**, *63*, 9007. (c) Bell, C. M.; Kissounko, D. A.; Gellman, S. H.; Stahl S. S. *Angewandte Chemie, International Edition* **2007**, *46*, 761.

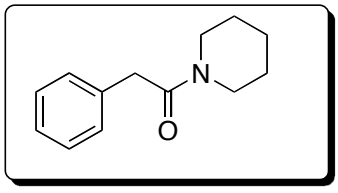
1.4.4) 2-Phenyl-1-pyrrolidin-1-yl-ethanone (table 1, entry 6)



The title compound was prepared using the general procedure for the organocatalytic amidations (41% yield, 76% yield with catalyst **2**).

The characterization of the compound matched previous reports: (a) Smitrovich, J. H.; DiMichele, L.; Qu, C.; Boice, G. N.; Nelson, T. D.; Huffman, M. A.; Murry, J. *Journal of Organic Chemistry* **2004**, *69*, 1903. (b) Karitzky, A. R.; He, H. Y.; Suzuki, K. *Journal of Organic Chemistry* **2000**, *65*, 8210. (c) Nelson, T. D. *Chirality* **2004**, *16*, 609. (d) Hackett, S. *Journal of Organic Chemistry* **1986**, *51*, 879.

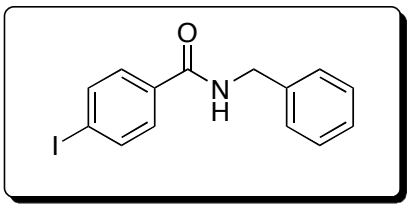
1.4.5) 2-Phenyl-1-piperdin-1-yl-ethanone (table 1, entry 7)



The title compound was prepared using the general procedure for the organocatalytic amidations. The catalyst **2** was used (52% yield in DCM, 97% yield in THF).

The characterization of the compound matched previous reports: (a) Shen, W.; Kunzer, A. *Organic Letters* **2002**, *4*, 1315. (b) Wang, W. B.; Roskamp, E. J. *Journal of Organic Chemistry* **1992**, *57*, 6101.

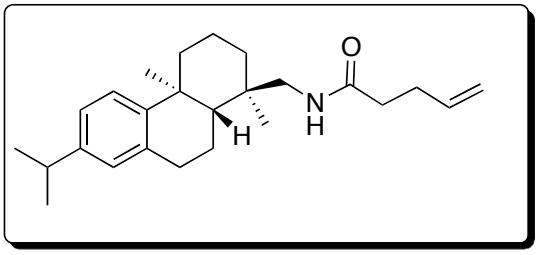
1.4.6) *N*-Benzyl-4-iodobenzamide (table 1, entry 8)



The title compound was prepared using the general procedure for the organocatalytic amidations. The solvent for the reaction was toluene, the temperature was 50 ^{o}C and catalyst **2** (20 mol%) was used (24% yield after chromatography).

The characterization of the compound matched previous reports: Klapars, A.; Antilla, J. C.; Huang, X.; Buchwald, S. L. *Journal American Chemical Society* **2001**, *123*, 7727.

1.4.7) Pent-4-enoic acid (7-*iso*propyl-1,4α-dimethyl-1,2,3,4,4α,9,10,10α-octahydro phenanthren-1-ylmethyl)-amide (table 1, entry 9)



The title compound was prepared using the general procedure for the organocatalytic amidations. The catalyst **2** was used (74% yield after chromatography).

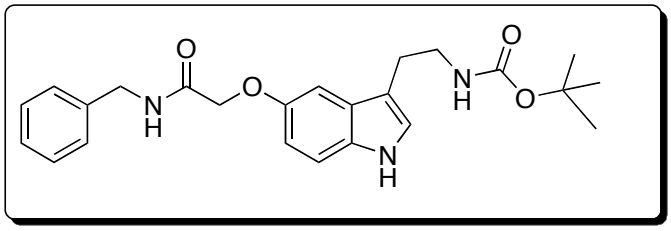
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.4 Hz, 1H), 7.00 (dd, *J* = 1.8, 8.0 Hz, 1H), 6.89 (s, 1H), 5.79 (m, 1H), 5.38 (br s, 1H), 5.00 (dd, *J* = 18.0, 18.4 Hz, 2H), 3.00 (m, 3H), 2.25 (m, 4H), 1.75-0.81 (m, 23H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 147.0, 145.5, 137.0, 134.7, 126.8, 124.0, 123.7, 115.5, 49.7, 45.2, 38.3, 37.3, 37.2, 36.1, 35.9, 33.3, 30.1, 29.6, 25.2, 23.90, 23.87, 18.9, 18.6, 18.5.

IR (Cast film, cm^{-1}) 3305, 3078, 2956, 2925, 2853, 1711, 1644, 1553, 1498.

HRMS (ESI) for $C_{25}H_{37}NONa$: calcd. 390.27674; found, 390.27689.

1.4.8) {2-[5-(Benzylcarbomoyl-methoxy)-1*H*-indol-3-yl] ethyl}-carbamic acid *tert*-butyl ester (table 1, entry 10)



The title compound was prepared using the general procedure for the organocatalytic amidations. The catalyst **2** (20 mol%) was used (95% yield).

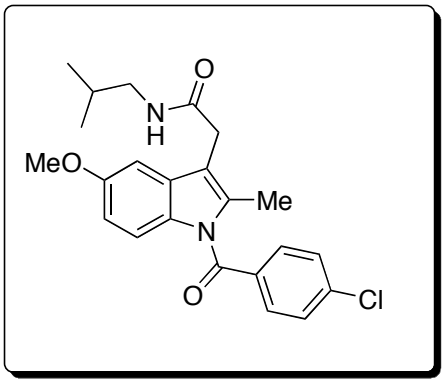
^{1}H NMR (300 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.24 (m, 6H), 7.05 (m, 1H), 6.85 (dd, *J* = 2.8, 8.7 Hz, 1H), 4.60 (s, 2H), 4.50 (d, *J* = 3.6 Hz, 2H), 3.43 (m, 2H), 2.90 (t, *J* = 6.75 Hz, 2H), 1.44 (s, 9H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 155.9, 151.4, 137.8, 132.2, 128.6, 127.7, 127.6, 127.5, 123.4, 112.8, 112.1, 111.8, 102.8, 79.1, 68.6, 42.9, 40.7, 28.3, 25.7.

IR (Cast film, cm^{-1}) 3430, 3319, 2976, 2930, 1692, 1672, 1533,1174, 733.

HRMS (ESI) for $C_{24}H_{29}N_3O_4Na$: calcd. 446.20503, found; 446.20537.

1.4.9) 2-[1-(4-Chloro-benzoyl)-5-methoxy-2-methyl-*1H-indol*-3-yl]-*N-iso*-butyl-acetamide (table 1, entry 11a)



The title compound was prepared using the general procedure for the organocatalytic amidations (73% yield).

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.8 Hz, 2H), 7.46 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 2.8 Hz, 1H), 6.88 (d, *J* = 9.2 Hz, 1H), 6.68 (d, *J* = 2.4 Hz, 1H), 5.77 (t, *J* = 5.6 Hz, 1H), 3.80 (s, 3H),

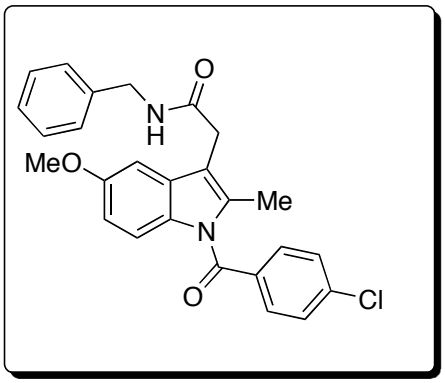
3.64 (s, 2H), 3.02 (t, *J* = 6.4 Hz, 2H), 2.37 (s, 3H), 1.67 (sept, *J* = 6.8 Hz, 1H), 0.78 (d, *J* = 6.8 Hz, 6H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 168.2, 156.2, 139.4, 136.2, 133.5, 131.0, 130.8, 130.2, 129.1, 115.0, 112.8, 112.4, 100.6, 55.6, 46.8, 32.1, 28.3, 19.8, 13.1.

IR (Cast film, cm^{-1}) 3296, 3086, 2960, 2929, 1680, 1647, 1592, 1478, 1359, 1324, 1225, 1090, 734.

HRMS (ESI) for $C_{23}H_{25}N_2O_3ClNa$: calcd. 435.14459; found 435.14489.

1.4.10) *N*-Benzyl-2-[1-(4-chloro-benzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]-acetamide (table 1, entry 11b)



The title compound was prepared using the general procedure for the organocatalytic amidations (93% yield).

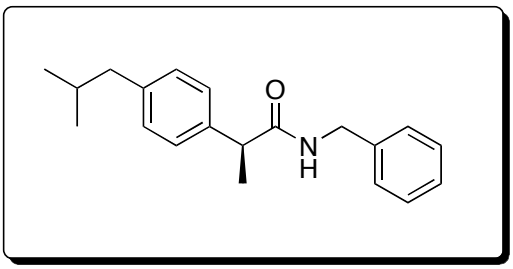
^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.25 (m, 3H), 7.18 (m, 2H), 6.90 (m, 1H), 6.85 (d, *J* = 9.0 Hz, 1H), 6.70 (d, *J* = 5.7 Hz, 1H), 6.18 (t, *J* = 5.7 Hz, 1H), 4.41 (d, *J* = 6.0 Hz, 2H), 3.78 (s, 3H), 3.70 (s, 2H), 2.34 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 168.1, 156.2, 139.4, 138.0, 136.2, 133.5, 131.0, 130.8, 130.2, 129.05, 128.97, 128.5, 127.3, 115.0, 112.7, 112.3, 100.7, 55.6, 43.4, 32.1, 13.2.

IR (Cast film, cm^{-1}) 3297, 3065, 2929, 1679, 1650, 1478, 1359, 1324, 1226, 1089, 733.

HRMS (ESI) for $C_{26}H_{23}N_2O_3ClNa$: calcd. 469.12894; found 469.12918.

1.4.11) *(S)-N*-Benzyl-2-(4-*iso*butyl-phenyl)-propionamide (table 1, entry 12a)

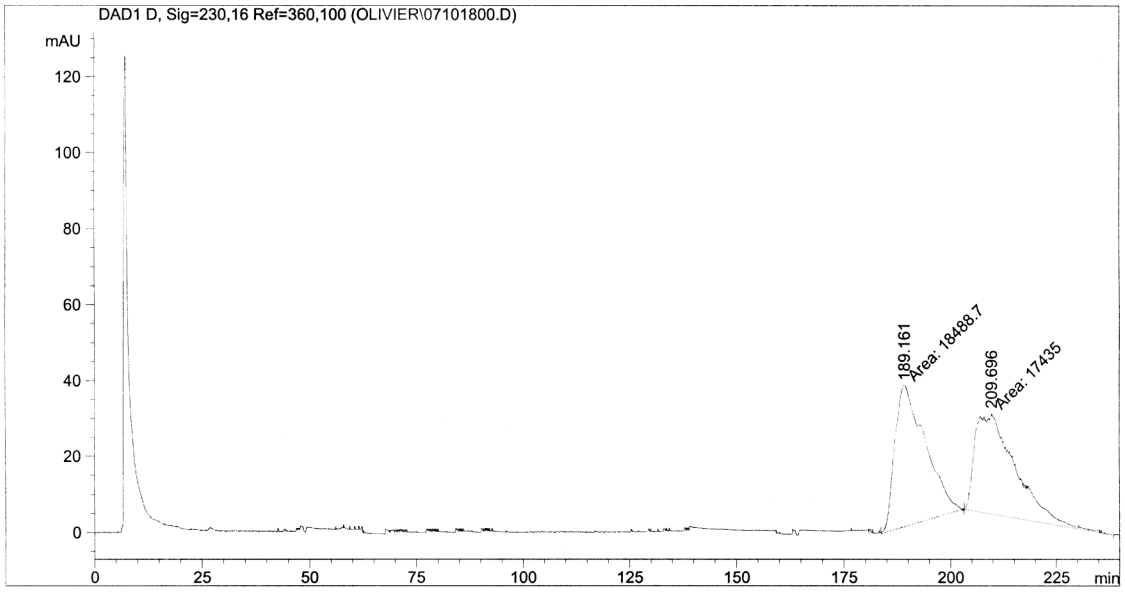


The title compound was prepared using the general procedure for the organocatalytic amidations. The solvent for the reaction was THF and catalyst **2** was used (73% yield after chromatography). Special care should be taken with the basic extraction for basic sensible substrates. A pH higher then 9 for the aqueous solution should be avoided.

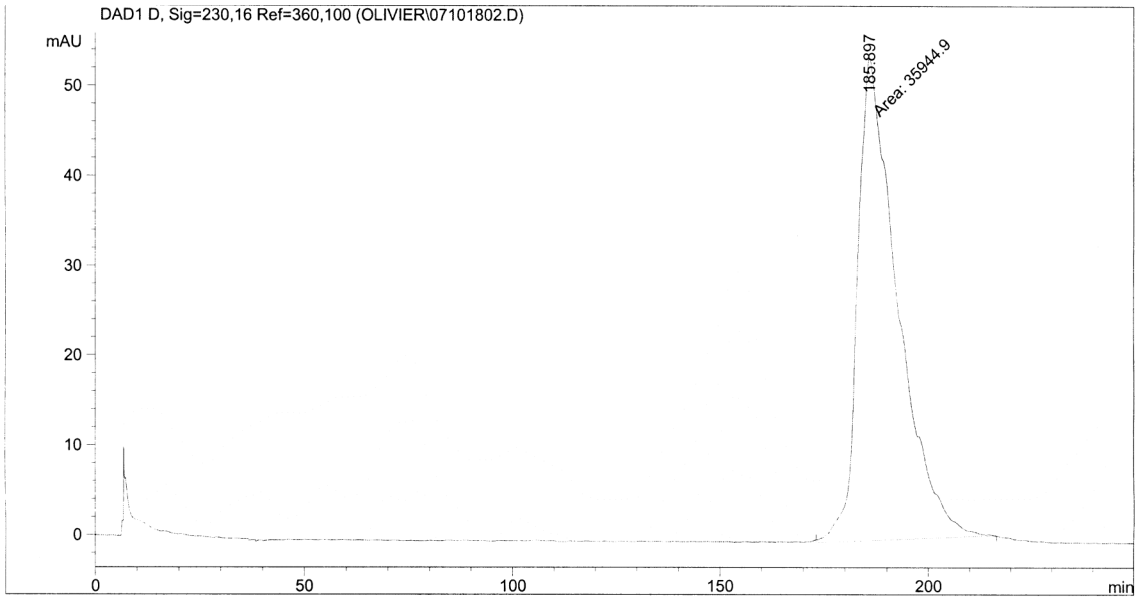
The characterization of the compound matched previous reports: Sudrik, Surendra G.; Chavan, Sambhaji P.; Chandrakumar, K. R. S.; Pal, Sourav; Date, Sadgopal K.; Chavan, Subhash P.; Sonawane, Harikisan R. *Journal of Organic Chemistry* **2002**, *67*, 1574-1579.

HPLC (Chiralcel OD column. Hexane/isopropanol 99/1. Flow rate of 0.5 mL/min. Temperature at 0.5 ^{0}C. UV detection at 230 nm)

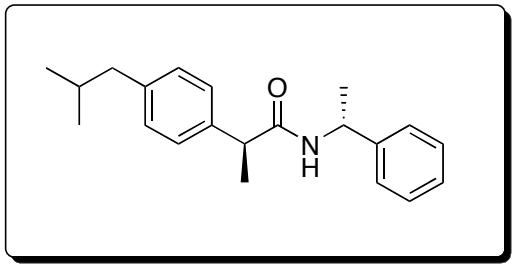
Racemic mixture (prepare from racemic ibuprofen):



Chiral product:



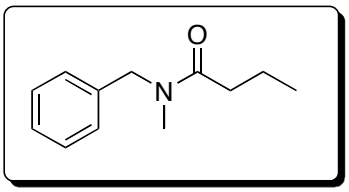
1.4.12) ***(S,R)*****-2-(4-*iso*Butyl-phenyl)-*N*-(1-phenyl-ethyl)-propionamide (table 1, entry 12b).**



The title compound was prepared using the general procedure for the organocatalytic amidations but the reaction was stopped after 16 h. The solvent for the reaction was THF and catalyst **2** (20 mol%) was used (70% yield after chromatography). Special care should be taken with the basic extraction for basic sensible substrates. A pH higher then 9 for the aqueous solution should be avoided. Some racemization has been observed when using a basic solution at pH 11.

The ^{1}H NMR of the compound matched previous report: Ebbers, Eelco J.; Ariaans, Gerry J. A.; Bruggink, Alle; Zwanenburg, Binne *Tetrahedron: Asymmetry* **1999**, *10*, 3701-3718.

1.4.13) *N*-Benzyl-*N*-methyl-butyramide (see reference 16)



The title compound was prepared using the general procedure for the organocatalytic amidations (with the boronic acid catalyst and the molecular sieves) but butyric anhydride was used instead of the acid. The reaction was stopped after 24 h (95% yield).

The title compound was reported before (Sugasawa, S.; Fujii, T. *Chem. & Pharm. Bull*. **1958**, *6*, 587) but full characterization was not given. Both amide rotamers can be observed on the ^{1}H and ^{13}C NMR at 27 ^{0}C.

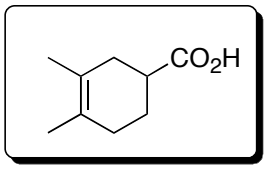
^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.29 (m, 5H), 4.58 (2xs, 2H), 2.94 (2xs, 3H), 2.37 (m, 2H), 1.72 (m, 2H), 0.97 (2xt, J = 7.2 Hz, 3H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.5 (173.2), 137.6 (136.7), 128.9 (128.5), 128.0 (127.5), 127.2 (126.3), 53.3 (50.7), 35.5 (35.1), 34.8 (33.8), 18.8 (18.6), 14.0.

IR (Cast film, cm^{-1}) 3295, 3063, 2963, 2933, 2874, 1645, 1453, 1402, 1076, 731, 699.

1.5) General Procedure for the Diels-Alder Reaction.

1.5.1) 3,4-Dimethyl-cyclohex-3-enecarboxylic acid (table 2, entry 1)



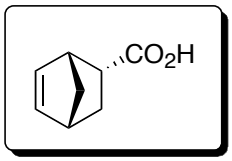
To a solution of acrylic acid (0.10 g, 1.39 mmol) in dichloromethane (2 mL) was added the *ortho*-bromophenylboronic acid (58 mg, 20 mol%) followed by the 2,3-dimethyl-1,3-butadiene (0.23 g, 2.78 mmol). This solution was stirred at 25 ^{o}C for 48 h. Upon completion, the product was directly purified by column chromatography (diethyl ether/pentane 1:1) the yield the title compound (0.19 g, 90%) as a white solid.

The characterization of the compound matched previous reports: (a) Pescarmona, P. P. *Journal of Molecular Catalysis A: Chemical* **2004**, *220*, 37. (b) Furuta, K.; Miwa, Y.; Iwanaga, K.;

Yamamoto, H. *Journal of the American Chemical Society* **1988**, *110*, 6254. (c) Bachman, G. B. *Journal of Organic Chemistry* **1939**, *4*, 493.

1.6) Cyloadducts Preparations and Data

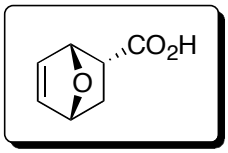
1.6.1) Bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (table 2, entry 2)



The title compound was prepared using the general procedure for the Diels-Alder reaction but the reaction was stopped after 24 h (99% yield).

The characterization of the compound matched previous reports: Akkari, R. *European Journal of Organic Chemistry* **2004**, *11*, 2441.

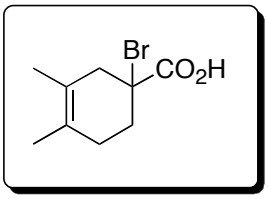
1.6.2) 7-Oxa-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (table 2, entry 3)



The title compound was prepared using the general procedure for the Diels-Alder reaction but catalyst **2** was used (20 mol%) (35% yield). Longer reaction time failed to increase the yield.

The characterization of the compound matched previous reports: Moore, J. A.; Partain, E. M., III. *Journal of Organic Chemistry* **1983**, *48*, 1105.

1.6.3) 1-Bromo-3,4-dimethyl-cyclohex-3-enecarboxylic acid (table 2, entry 4)



The title compound was prepared using the general procedure for the Diels-Alder reaction (71% yield).

^{1}H-NMR (500 MHz, $CDCl_3$) δ 11.58 (br s, 1H), 2.87 (d, *J* = 17.5 Hz, 1H), 2.67 (d, *J* = 17.5 Hz, 1H), 2.28 (m, 2 H), 2.20 (m, 2 H), 1.63 (s, 6 H).

^{13}C-NMR (125 MHz, $CDCl_3$) δ 177.3, 125.0, 122.7, 59.2, 43.0, 34.1, 30.3, 19.0, 18.6.

IR (Microscope, cm^{-1}) 2903, 2606, 1701, 1413, 1294, 1229, 934.

HRMS (EI) for $C_9H_{13}O_2{}^{81}Br$: calcd. 234.00784; found, 234.00760; for $C_9H_{13}O_2{}^{79}Br$: calcd. 232.00989; found, 232.00964

1.7) Procedure for Competition Reaction Between Carboxylic Acid and Ester Toward Diels-Alder Cycloadiition.

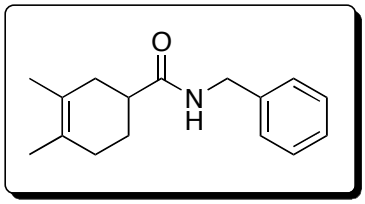
1.7.1) 3,4-Dimethyl-cyclohex-3-enecarboxylic acid and Methyl 3,4-dimethyl cyclohex-3-enecarboxylate (eq. 1)

To a solution of acrylic acid (0.10 g, 1.39 mmol) and methyl acrylate (0.12 g, 1.39 mmol) in dichloromethane (2 mL) was added the *ortho*-bromophenylboronic acid (58 mg, 20 mol%) followed by the 2,3-dimethyl-1,3-butadiene (0.12 g, 1.39 mmol). This solution was stirred at 25 ^{o}C for 48 h. Upon completion, the product was directly purified by column chromatography (diethyl ether/pentane 1:1) the yield 3,4-dimethyl-cyclohex-3-enecarboxylic acid (0.15 g, 69%) and methyl 3,4-dimethyl cyclohex-3-enecarboxylate (0.012 g, 5%).

The characterization of methyl 3,4-dimethyl cyclohex-3-enecarboxylate matched previous report: Hara, K.; Akiyama, R.; Sawamura, M. *Org. Lett.* **2005**, *7*, 5621.

1.8) Procedure for the Sequential one-pot Diels-Alder/Amidation Reaction.

1.8.1) 3,4-Dimethyl-cyclohex-3-enecarboxylic acid benzylamide (eq. 1)



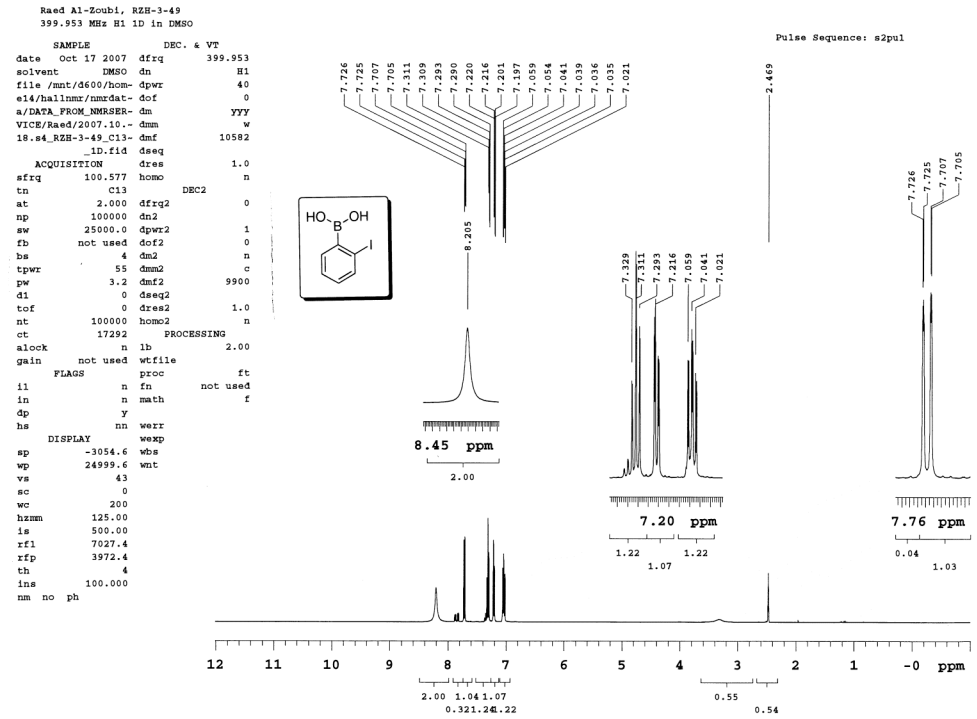
To a solution of acrylic acid (0.10 g, 1.39 mmol) in dichloromethane (2 mL) was added the *ortho*-iodophenylboronic acid (60 mg, 20 mol%) followed by the 2,3-dimethyl-1,3-butadiene (0.23 g, 2.78 mmol). This solution was stirred at 25 ^{o}C for 72 h. After this time, molecular sieves

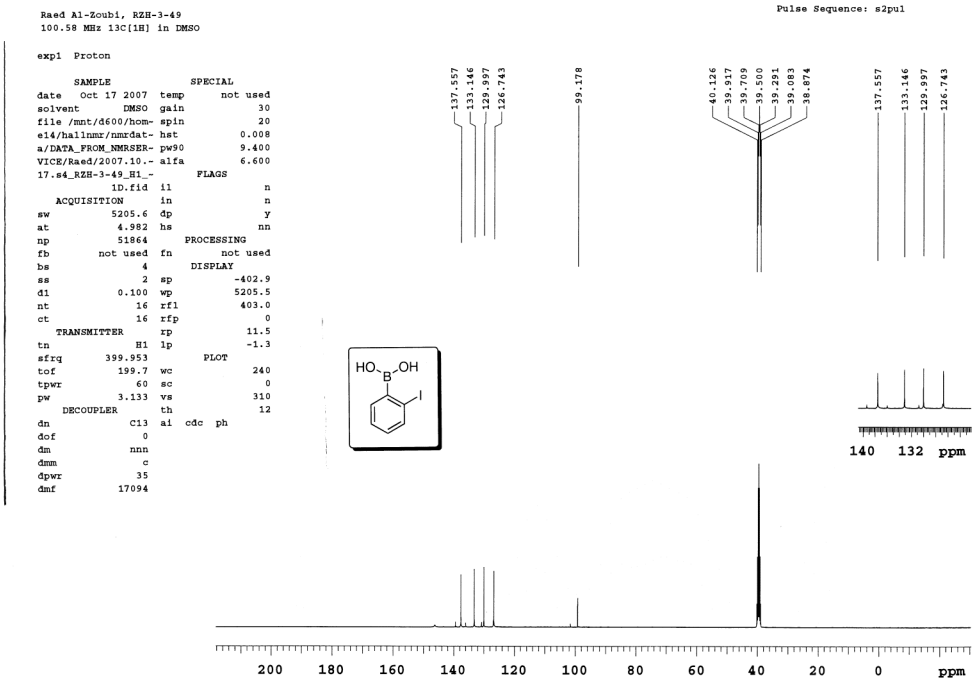
were added and the amount of solvent was increased to 8 mL. This mixture was stirred for 1 h and benzylamine (0.10 g, 1.04 mmol) was added. The reaction was stirred for 72 h at 25 ^{o}C. Upon completion, the mixture was filtered through celite and the celite was washed with dichloromethane (2x10 mL). The filtrate was then extracted with aqueous NaOH solution (pH 10-11, 2x20 mL), aqueous HCl solution (pH 4, 2x20 mL) and brine. The organic phase was dried with sodium sulphate. Concentration of the organic yielded the pure amide (0.17 g, 66%) as a white solid.

The characterization of the compound matched previous reports: Akkari, R. *Tetrahedron: Asymmetry* **2004**, *15*, 2515.

2. NMR Spectrum Data for New Compounds.

2.1) ^{1}H-, ^{13}C- & ^{11}B- NMR of o*rtho*-iodophenylboronic acid **(2)** in *D*-DMSO and CD_2Cl_2 at 27 ^{o}C.

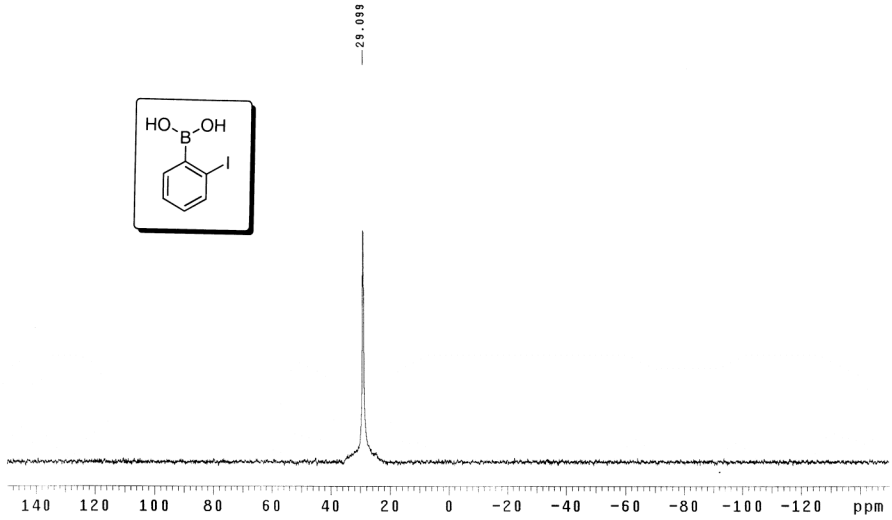




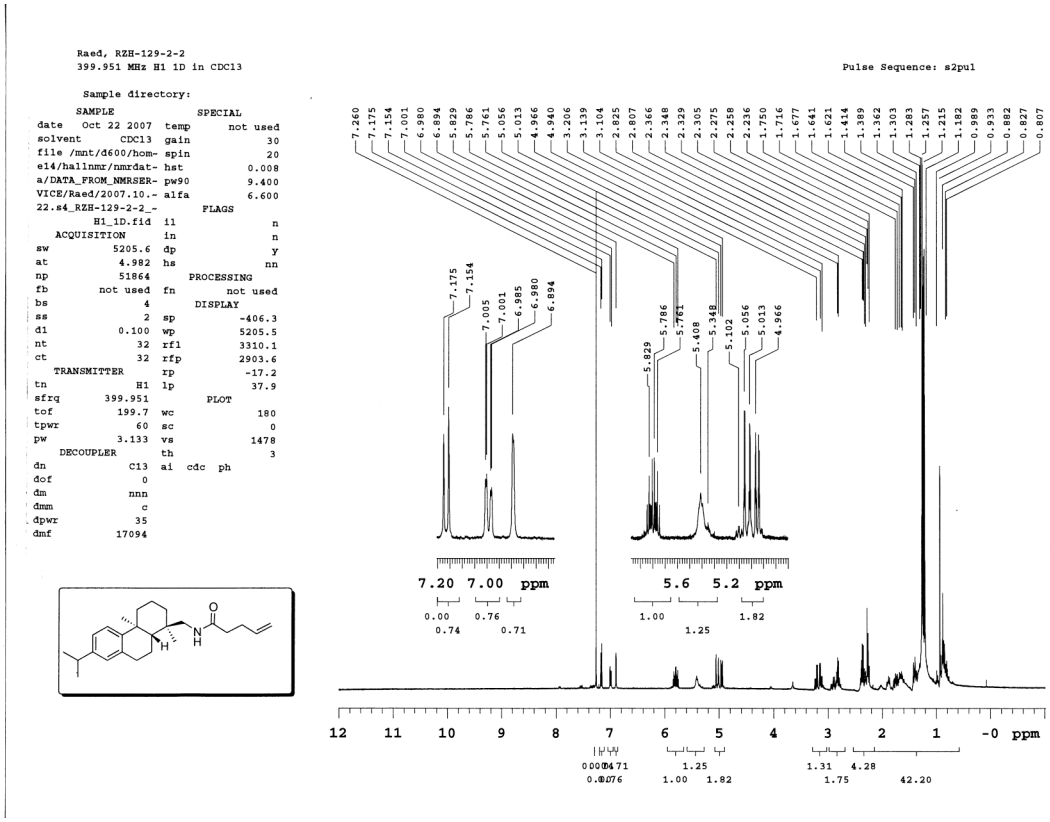
Oliver Marion, OMH4-81
128.269 MHz B11[H1] 1D in CD2Cl2

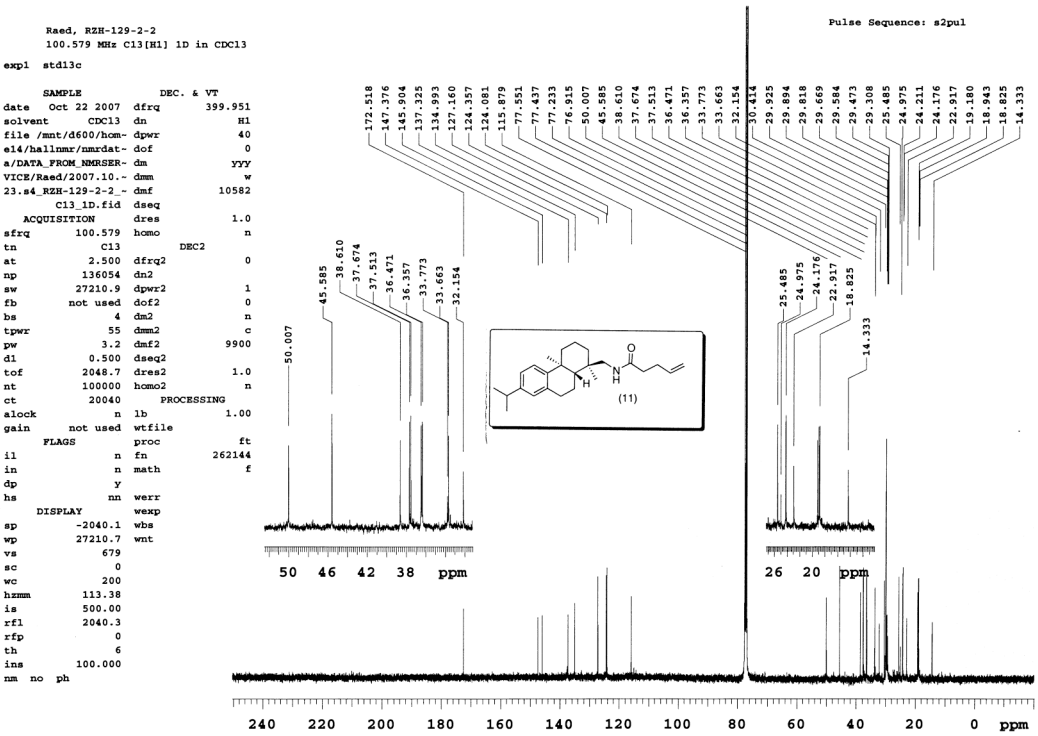
exp5 Boron

SAMPLE		SPECIAL	
date	Oct 10 2007	temp	not used
solvent	cd2cl2	gain	40
file	/mnt/d600/hom~	spin	not used
e12/gennmr/nmrdata~		hst	0.008
/HALL/Oliwier/2007~		pw90	29.125
.10/2007.10.10.14_~		alfa	10.000
OMH4-81_B11_1D.fid		FLAGS	
ACQUISITION		il	n
sw	38461.5	in	n
at	2.012	dp	y
np	154798	hs	nn
fb	not used	PROCESSING	
bs	4	lb	10.00
ss	2	fn	not used
d1	0.100	DISPLAY	
nt	1e+06	sp	-19230.5
ct	120	wp	38461.2
TRANSMITTER		rfl	19230.8
tn	B11	rfp	0
sfrq	128.270	rp	-23.3
tof	2852.8	lp	0
tpwr	60	PLOT	
pw	9.708	wc	180
DECOUPLER		sc	0
dn	H1	vs	47
dof	0	th	17
dm	yyy	nm	cdc ph
dmm	w		
dpwr	40		
dmf	11441		

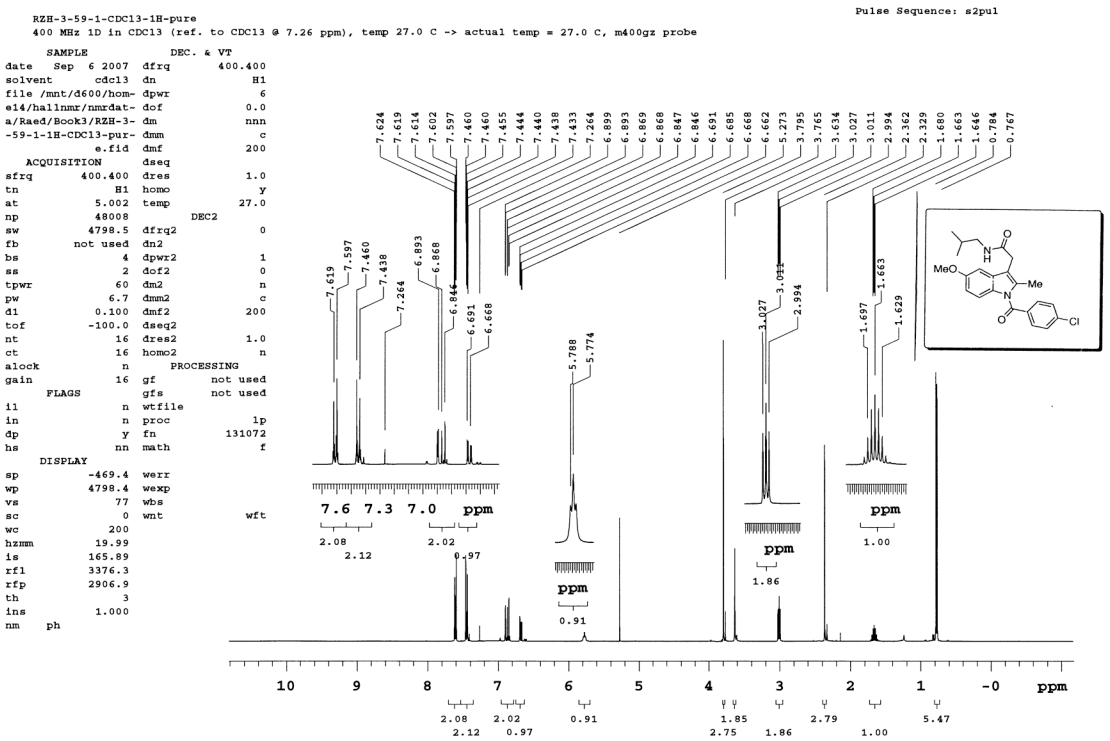


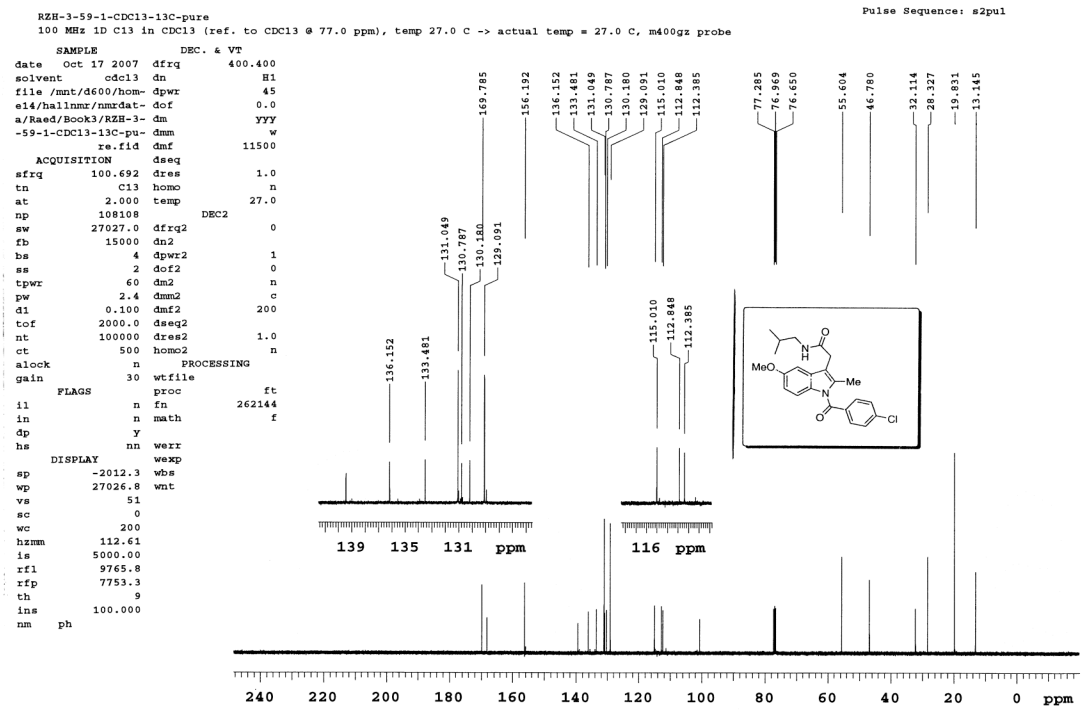
2.2) ^{1}H- & ^{13}C-NMR of Pent-4-enoic acid (7-isopropyl-1,4α-dimethyl-1,2,3,4,4α,9,10,10α-octahydro phenanthren-1-ylmethyl)-amide (**Table 1, entry 11**) in $CDCl_3$ at 27 ^{o}C.



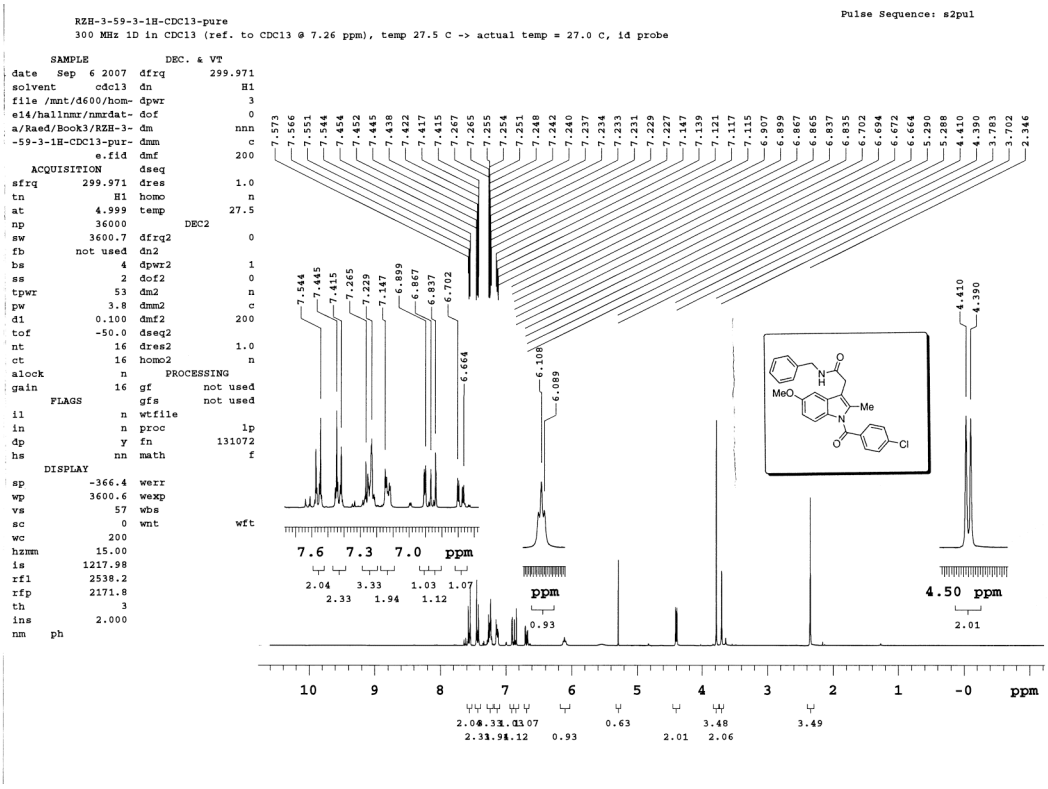


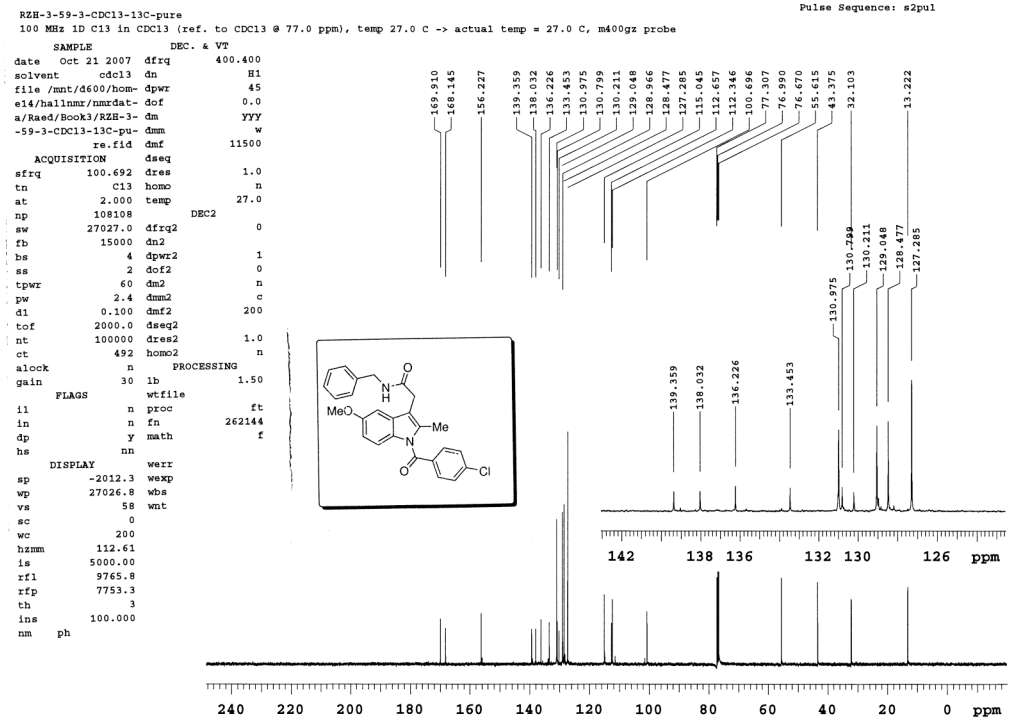
2.3) ^{1}**H- &** ^{13}**C-NMR** of 2-[1-(4-Chloro-benzoyl)-5-methoxy-2-methyl-*1H-indol*-3-yl]-*N-iso*-butyl-acetamide (**Table 1, entry 12a**) in $CDCl_3$ at 27 ^{o}C.



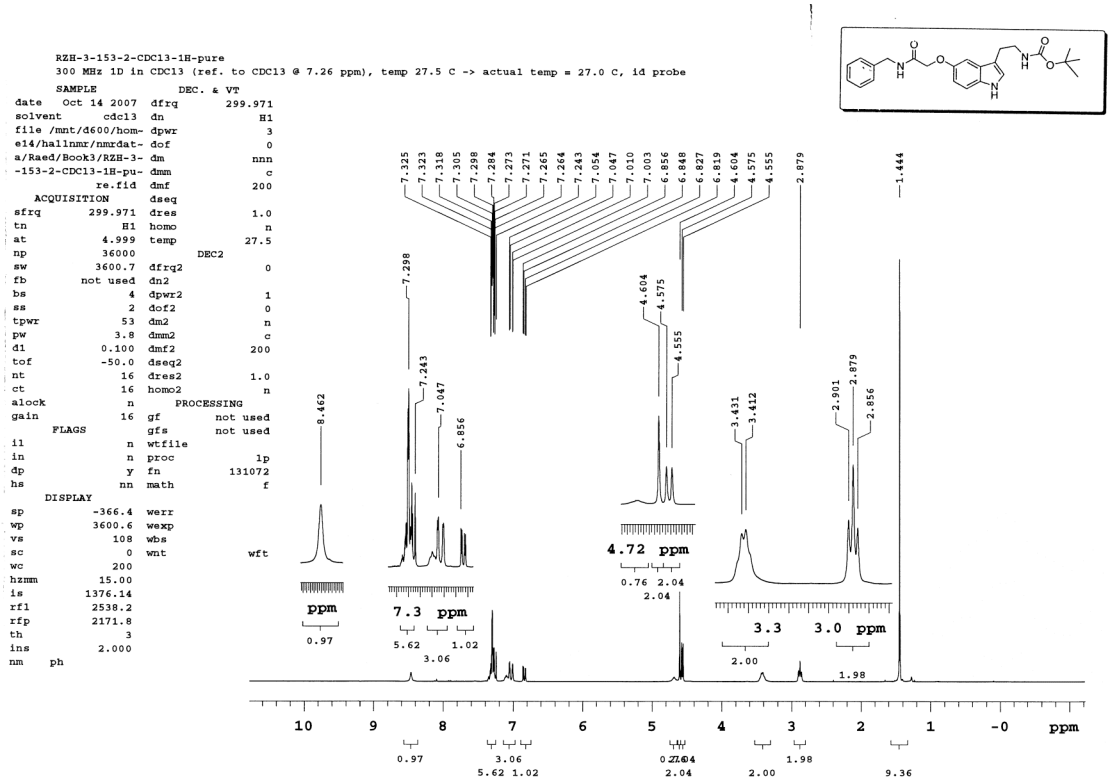


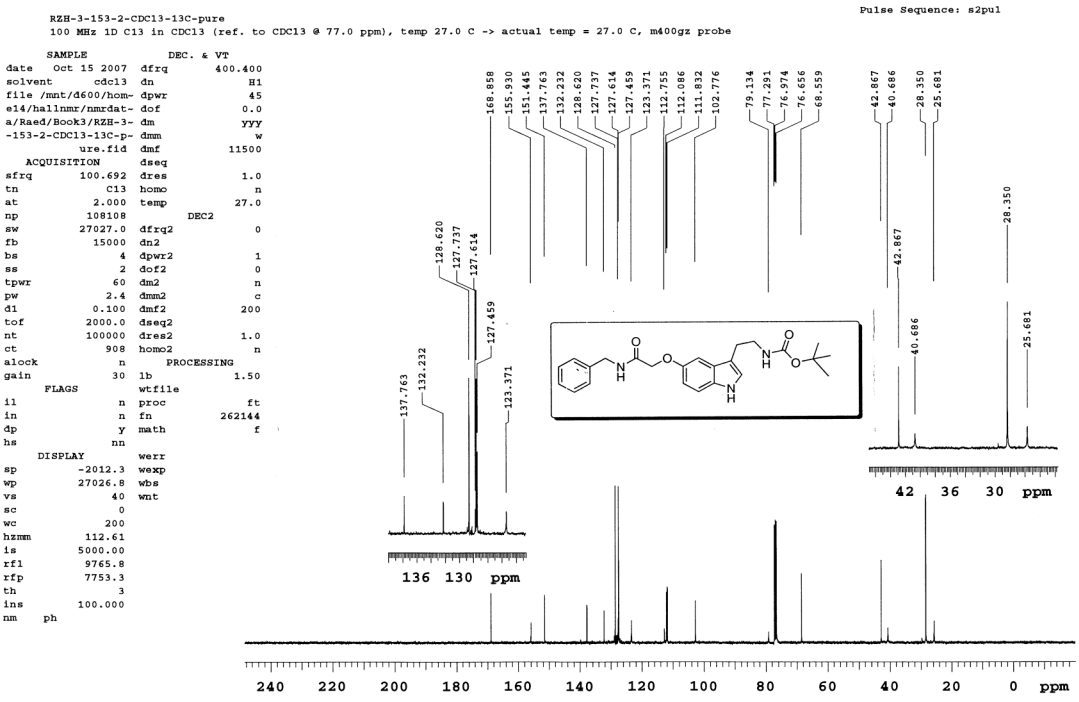
2.4) ^{1}H- & ^{13}C-NMR of *N*-Benzyl-2-[1-(4-chloro-benzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]-acetamide (**Table 1, entry 12b**) in $CDCl_3$ at 27 ^{o}C.



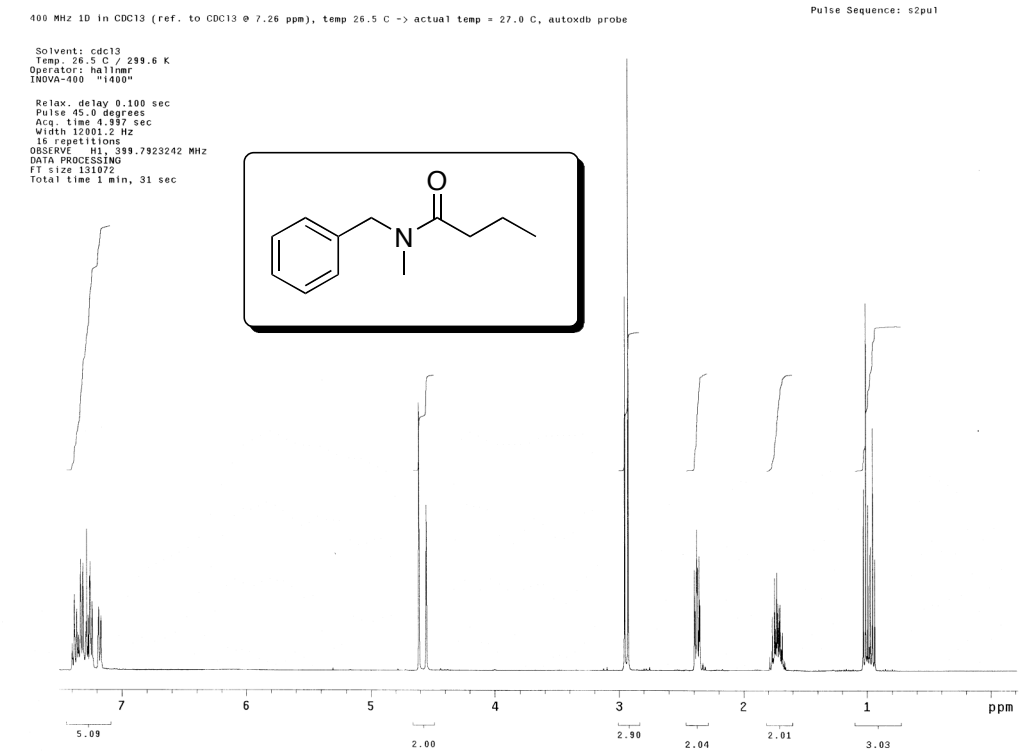


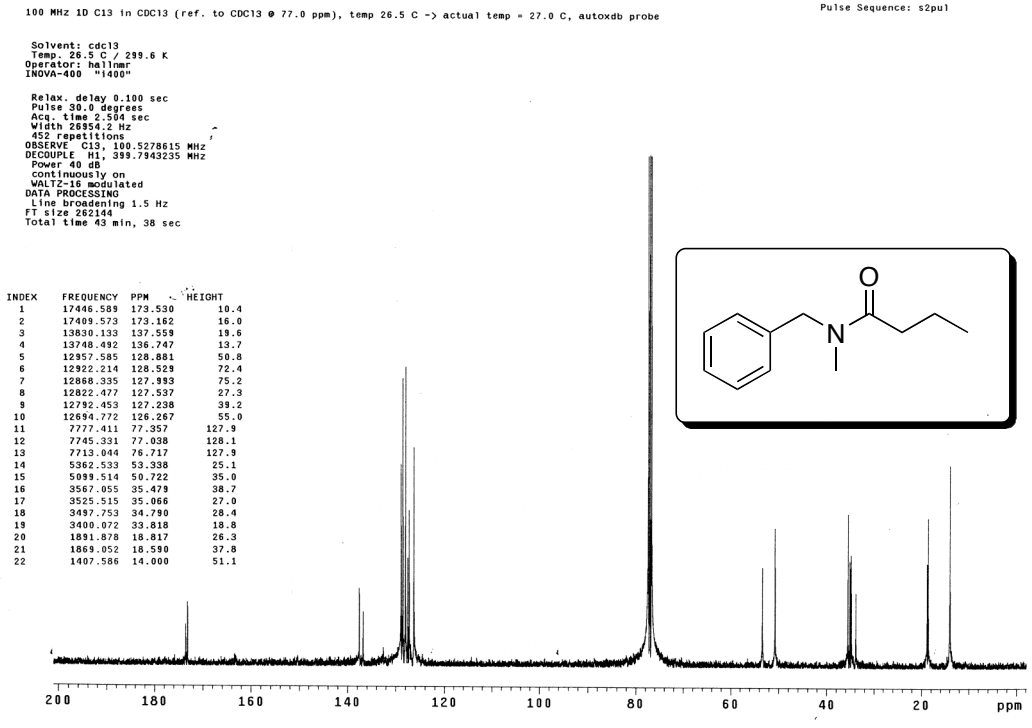
2.5) ^{1}H- & ^{13}C-NMR of *tert*-butyl 2-(5-((benzylcarbamoyl)methoxy)-1H-indol-3-yl)ethyl carbamate (**Table 1, entry 13**) in $CDCl_3$ at 27 ^{o}C.



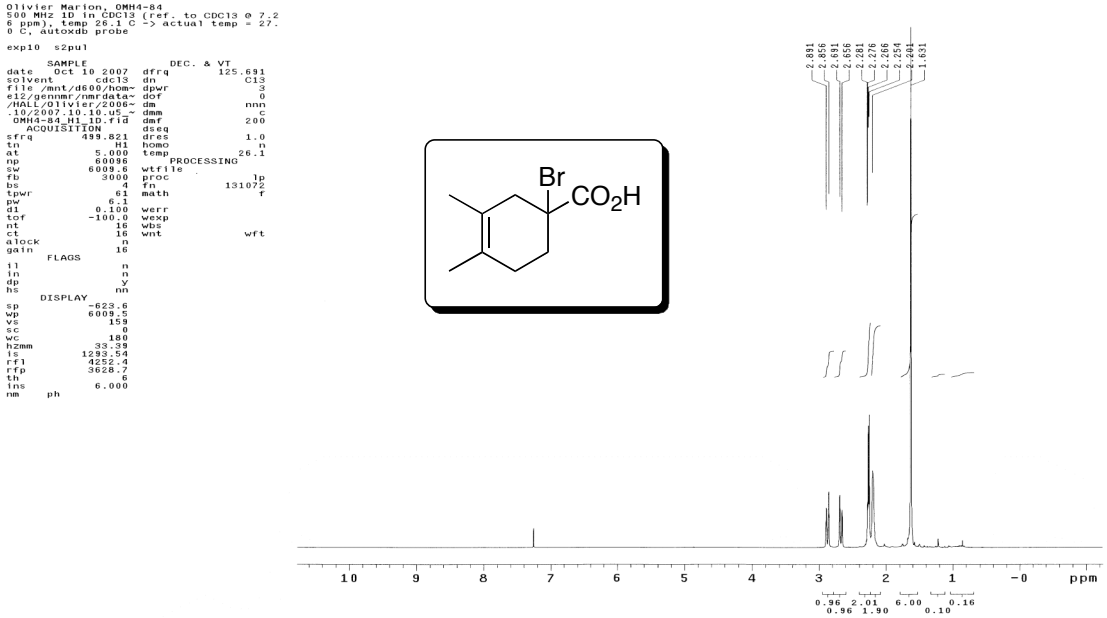


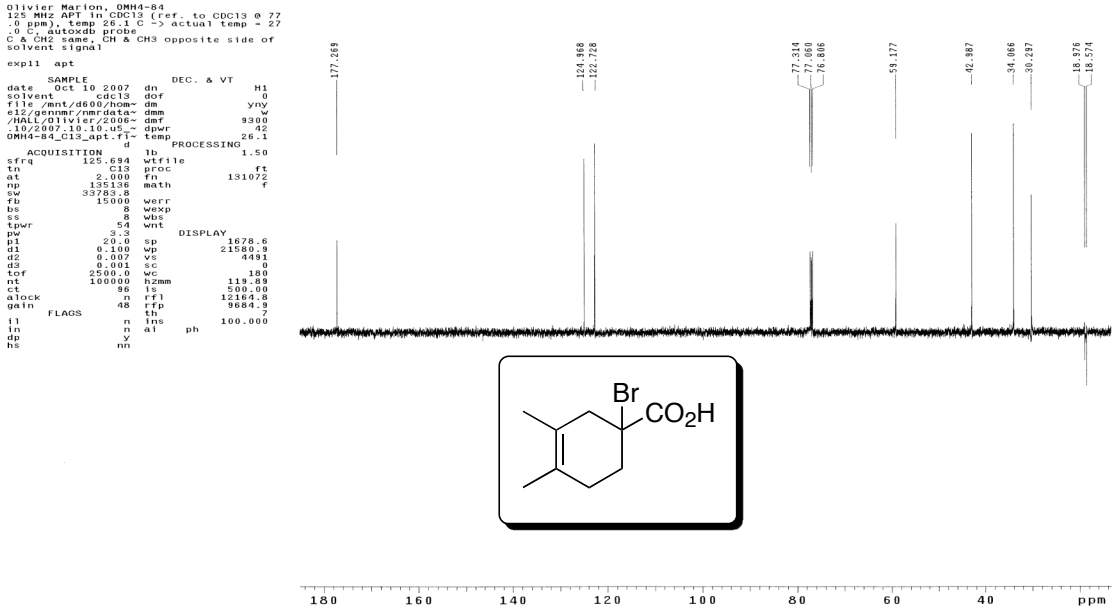
2.6) ^{1}H- & ^{13}C-NMR of N-Benzyl-N-methyl-butyramide (see reference 16) in $CDCl_3$ at 27 ^{o}C.



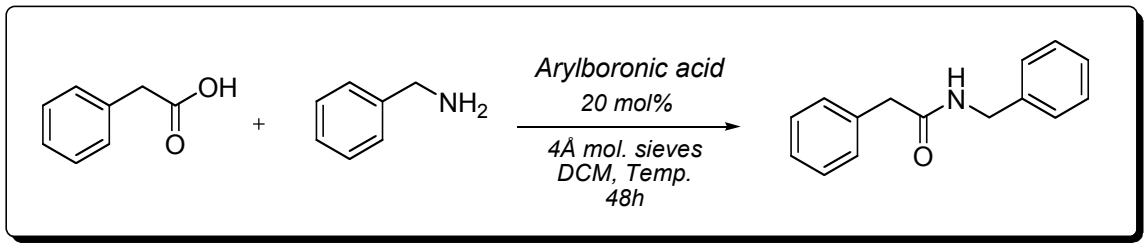


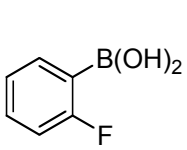
2.7) ^{1}**H- &** ^{13}**C-NMR** of 1-Bromo-3,4-dimethyl-cyclohex-3-enecarboxylic acid (**table 2, entry 4**) in $CDCl_3$ at 27 °C.



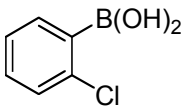


3. List of All Tested Boronic Acids.

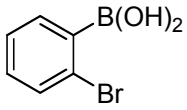




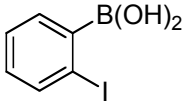
25 °C
98%



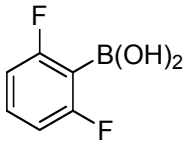
25 °C
99%



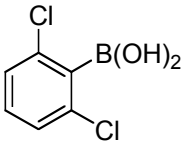
25 °C
99%



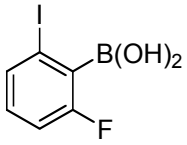
25 °C
99%



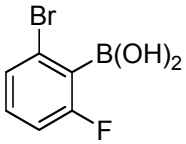
35-40°C 85%
25°C 42%



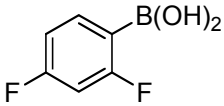
25 °C
10%



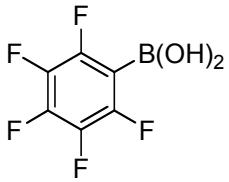
25 °C
50%



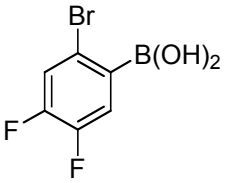
25 °C
33%



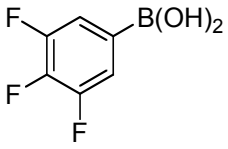
35-40°C 99%
25°C 63%



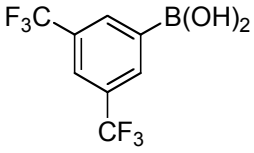
35-40°C
11%



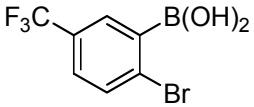
35-40°C
64%



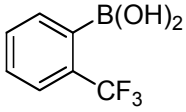
35-40°C 85%
25°C 56%



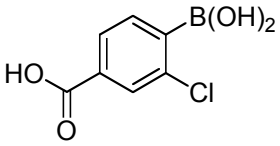
35-40°C
92%



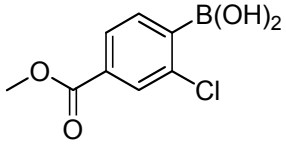
25 °C
60%



35-40°C
28%



25 °C
49%



25 °C
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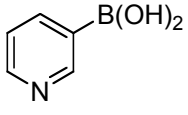
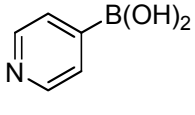
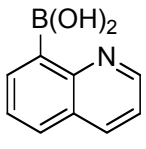


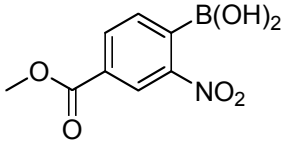
35-40 °C
0%



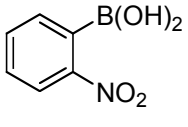
35-40 °C
0%



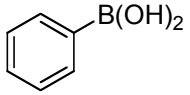
35-40 °C
0%



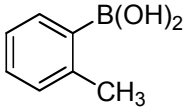
25 °C
53%



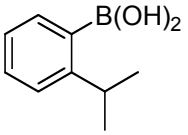
35-40 °C 99%
25 °C 72%



35-40 °C
31%



35-40 °C *75%*
25 °C *15%*



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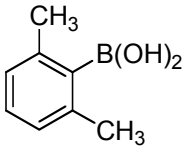
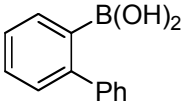
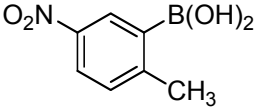
0%



35-40 °C *89%*
25 °C *21%*



35-40 °C
3%



35-40 °C
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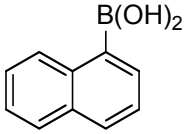
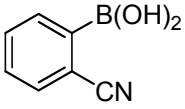
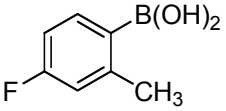


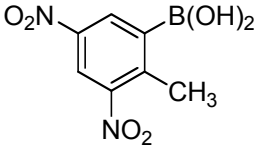
35-40 °C
0%



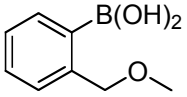
35-40 °C
86%



35-40 °C
94%



35-40 °C
0%



25 °C
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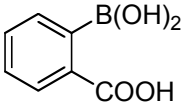

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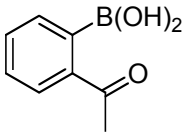
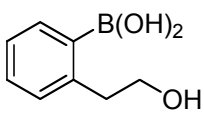
0%



35-40 °C
0%



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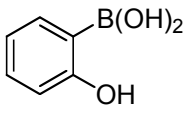
0%



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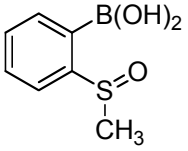
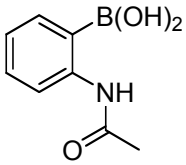
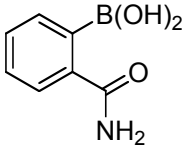
0%



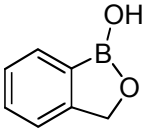
35-40 °C
65%



35-40 °C
15%



35-40 °C
16%



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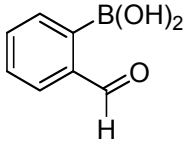

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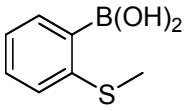
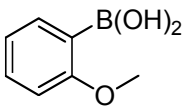
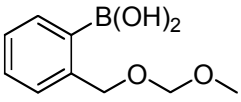
0%



25 °C
82%



35-40 °C
15%



35-40 °C
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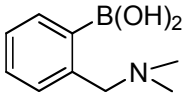

35-40 °C
0%

4. *X*-ray Data File for *ortho*-iodophenylboronic acid (2).

STRUCTURE REPORT

XCL Code: DGH0712 **Date:** 29 August 2007

Compound: 2-Iodophenylboronic acid
Formula: $C_6H_6BIO_2$

Supervisor: D. G. Hall **Crystallographer:** R. McDonald

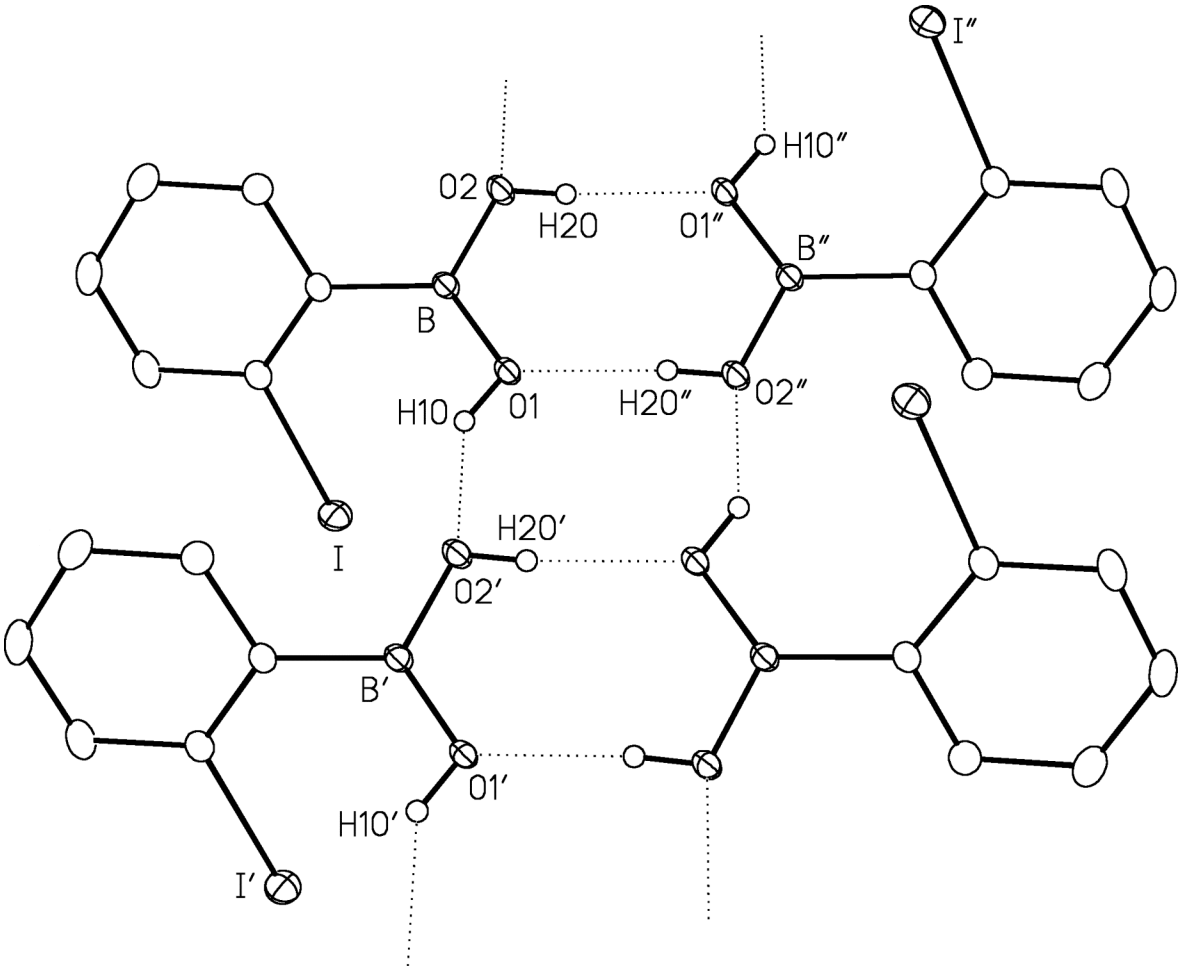

Figure Legends

Figure 1. Perspective view of the 2-iodophenylboronic acid molecule showing the atom labelling scheme. Non-hydrogen atoms are represented by Gaussian ellipsoids at the 20% probability level. Hydrogen atoms are shown with arbitrarily small thermal parameters.

Figure 2. Illustration of the hydrogen-bonded interactions bewteen adjacent 2-iodophenyl-boronic acid molecules in the crystal lattice. Primed atoms are related to unprimed ones via the crystallographic symmetry operation (-1+*x*, *y*, *z*) (translation parallel to the crystal *a* axis). Double-primed atoms are related to unprimed ones via the crystallographic inversion center ($^1/_2$, 0, $^1/_2$). The chain propagates in a direction parallel to the crystal *a* axis.

Figure 1

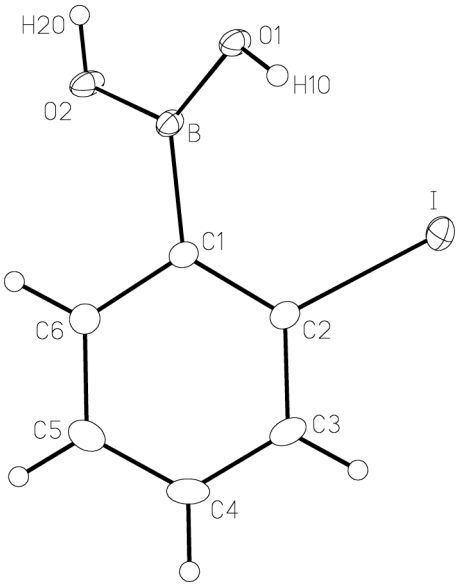

Figure 2

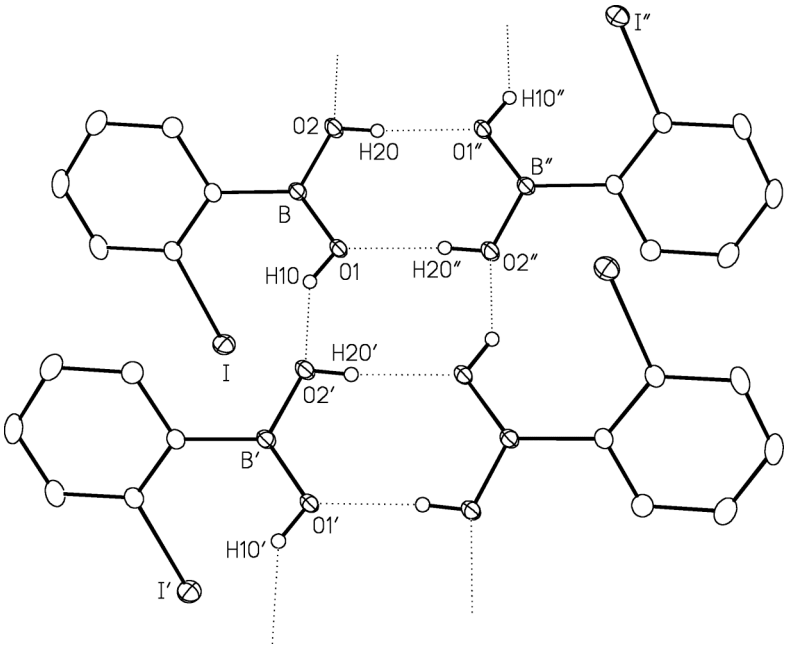

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Table 1. Crystallographic Experimental Details

A. Crystal Data	
formula	$C_6H_6BIO_2$
formula weight	247.82
crystal dimensions (mm)	0.43 × 0.34 × 0.10
crystal system	triclinic
space group	$P\bar{1}$ (No. 2)
unit cell parameters[a]	
a (Å)	4.9134 (6)
b (Å)	7.2588 (8)
c (Å)	11.1904 (12)
α (deg)	93.4364 (14)
β (deg)	92.2282 (14)
γ (deg)	95.7291 (14)
V (Å^3)	396.00 (8)
Z	2
ρ_{calcd} (g cm^{-3})	2.078
μ (mm^{-1})	3.977
B. Data Collection and Refinement Conditions	
diffractometer	Bruker PLATFORM/SMART 1000 CCD[b]
radiation (λ [Å])	graphite-monochromated Mo Kα (0.71073)
temperature (°C)	–80
scan type	ω scans (0.3°) (15 s exposures)
data collection 2θ limit (deg)	55.06
total data collected	3524 (-6 ≤ h ≤ 6, -9 ≤ k ≤ 9, -14 ≤ l ≤ 14)
independent reflections	1816 (R_{int} = 0.0162)
number of observed reflections (*NO*)	1767 [$F_o^2 \geq 2\sigma(F_o^2)$]
structure solution method	direct methods (*SHELXS–97*[c])
refinement method	full-matrix least-squares on F^2 (*SHELXL–97*[d])
absorption correction method	Gaussian integration (face-indexed)
range of transmission factors	0.6918–0.2796
data/restraints/parameters	1816 [$F_o^2 \geq -3\sigma(F_o^2)$] / 0 / 93
goodness-of-fit (S)[e]	1.114 [$F_o^2 \geq -3\sigma(F_o^2)$]
final R indices[f]	
R_1 [$F_o^2 \geq 2\sigma(F_o^2)$]	0.0257
wR_2 [$F_o^2 \geq -3\sigma(F_o^2)$]	0.0667
largest difference peak and hole	1.681 and –0.621 e Å^{-3}

[a]Obtained from least-squares refinement of 4564 reflections with 5.66° < 2θ < 55.06°.

(continued)

Table 1. Crystallographic Experimental Details (continued)

[b]Programs for diffractometer operation, data collection, data reduction and absorption correction were those supplied by Bruker.

[c]Sheldrick, G. M. *Acta Crystallogr*. **1990**, *A46*, 467–473.

[d]Sheldrick, G. M. *SHELXL-97*. Program for crystal structure determination. University of Göttingen, Germany, 1997.

[e]$S = [\Sigma w(F_o^2 - F_c^2)^2/(n - p)]^{1/2}$ (n = number of data; p = number of parameters varied; $w = [\sigma^2(F_o^2) + (0.0287P)^2 + 0.5545P]^{-1}$ where $P = [\mathrm{Max}(F_o^2, 0) + 2F_c^2]/3$).

[f]$R_1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$; $wR_2 = [\Sigma w(F_o^2 - F_c^2)^2/\Sigma w(F_o^4)]^{1/2}$.

Table 2. Atomic Coordinates and Equivalent Isotropic Displacement Parameters

Atom	*x*	*y*	*z*	U_{eq}, Å^2
I	0.08771(4)	0.18397(3)	0.127654(17)	0.04225(10)*
O1	0.2845(4)	0.1116(3)	0.4155(2)	0.0321(4)*
O2	0.7568(4)	0.1779(3)	0.4360(2)	0.0375(5)*
C1	0.5179(6)	0.3920(4)	0.3092(3)	0.0274(5)*
C2	0.3529(6)	0.4099(4)	0.2063(3)	0.0303(6)*
C3	0.3660(8)	0.5718(5)	0.1460(3)	0.0426(7)*
C4	0.5487(9)	0.7214(5)	0.1875(4)	0.0479(9)*
C5	0.7201(8)	0.7085(5)	0.2862(4)	0.0460(8)*
C6	0.7035(7)	0.5461(4)	0.3464(3)	0.0368(6)*
B	0.5134(6)	0.2193(4)	0.3874(3)	0.0266(6)*

Anisotropically-refined atoms are marked with an asterisk (*). The form of the anisotropic displacement parameter is: $\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^*c^*U_{23} + 2hla^*c^*U_{13} + 2hka^*b^*U_{12})]$.

Table 3. Selected Interatomic Distances (Å)

Atom1	Atom2	Distance	Atom1	Atom2	Distance
I	C2	2.115(3)	C1	B	1.569(4)
O1	B	1.363(4)	C2	C3	1.388(4)
O2	B	1.363(3)	C3	C4	1.383(6)
C1	C2	1.402(4)	C4	C5	1.376(6)
C1	C6	1.403(4)	C5	C6	1.390(5)

Table 4. Selected Interatomic Angles (deg)

Atom1	Atom2	Atom3	Angle	Atom1	Atom2	Atom3	Angle
C2	C1	C6	116.1(3)	C3	C4	C5	120.4(3)
C2	C1	B	126.9(3)	C4	C5	C6	119.7(3)
C6	C1	B	117.0(3)	C1	C6	C5	122.1(3)
I	C2	C1	121.5(2)	O1	B	O2	116.9(3)
I	C2	C3	116.1(2)	O1	B	C1	125.5(2)
C1	C2	C3	122.3(3)	O2	B	C1	117.6(2)
C2	C3	C4	119.4(3)				

Table 5. Hydrogen-Bonded Interactions

D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	∠D–H···A (deg)	Note
O1–H1O···O2[a]	0.84	1.98	2.700(3)	142.5	[a]At -1+*x*, *y*, *z*
O2–H2O···O1[b]	0.84	1.92	2.754(3)	169.7	[b]At 1–*x*, $\bar{y}$, 1–*z*

Table 6. Torsional Angles (deg)

Atom1	Atom2	Atom3	Atom4	Angle	Atom1	Atom2	Atom3	Atom4	Angle
C6	C1	C2	I	174.2(2)	C6	C1	B	O1	140.1(3)
C6	C1	C2	C3	-1.6(5)	C6	C1	B	O2	-36.8(4)
B	C1	C2	I	-6.6(4)	I	C2	C3	C4	-175.6(3)
B	C1	C2	C3	177.5(3)	C1	C2	C3	C4	0.4(5)
C2	C1	C6	C5	1.0(5)	C2	C3	C4	C5	1.4(6)
B	C1	C6	C5	-178.2(3)	C3	C4	C5	C6	-2.0(6)
C2	C1	B	O1	-39.0(5)	C4	C5	C6	C1	0.7(6)
C2	C1	B	O2	144.1(3)					

Table 7. Anisotropic Displacement Parameters (U_{ij}, Å^2)

Atom	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
I	0.04584(15)	0.04807(15)	0.03038(13)	0.00450(9)	-0.00965(9)	-0.00415(10)
O1	0.0217(9)	0.0377(11)	0.0386(11)	0.0177(9)	-0.0026(8)	0.0045(8)
O2	0.0209(9)	0.0484(13)	0.0462(13)	0.0259(10)	-0.0004(9)	0.0047(8)
C1	0.0262(12)	0.0288(13)	0.0283(13)	0.0073(11)	0.0011(10)	0.0050(10)
C2	0.0310(13)	0.0324(14)	0.0285(14)	0.0069(11)	-0.0003(11)	0.0052(11)
C3	0.053(2)	0.0424(17)	0.0340(16)	0.0162(14)	-0.0038(14)	0.0098(15)
C4	0.064(2)	0.0321(16)	0.050(2)	0.0185(15)	0.0084(17)	0.0055(15)
C5	0.053(2)	0.0324(16)	0.051(2)	0.0061(14)	0.0035(16)	-0.0063(14)
C6	0.0385(16)	0.0353(15)	0.0359(16)	0.0055(13)	-0.0033(13)	0.0000(12)
B	0.0237(13)	0.0315(14)	0.0252(14)	0.0068(11)	-0.0009(11)	0.0049(11)

The form of the anisotropic displacement parameter is:
$\exp[-2\pi^2(h^2a^{*2}U_{11} + k^2b^{*2}U_{22} + l^2c^{*2}U_{33} + 2klb^*c^*U_{23} + 2hla^*c^*U_{13} + 2hka^*b^*U_{12})]$

Table 8. Derived Atomic Coordinates and Displacement Parameters for Hydrogen Atoms

Atom	x	y	z	U_{eq}, Å^2
H1O	0.1450	0.1637	0.3969	0.048
H2O	0.7279	0.0959	0.4851	0.056
H3	0.2506	0.5799	0.0768	0.051
H4	0.5558	0.8337	0.1477	0.057
H5	0.8493	0.8102	0.3129	0.055
H6	0.8215	0.5393	0.4150	0.044