Supporting Information

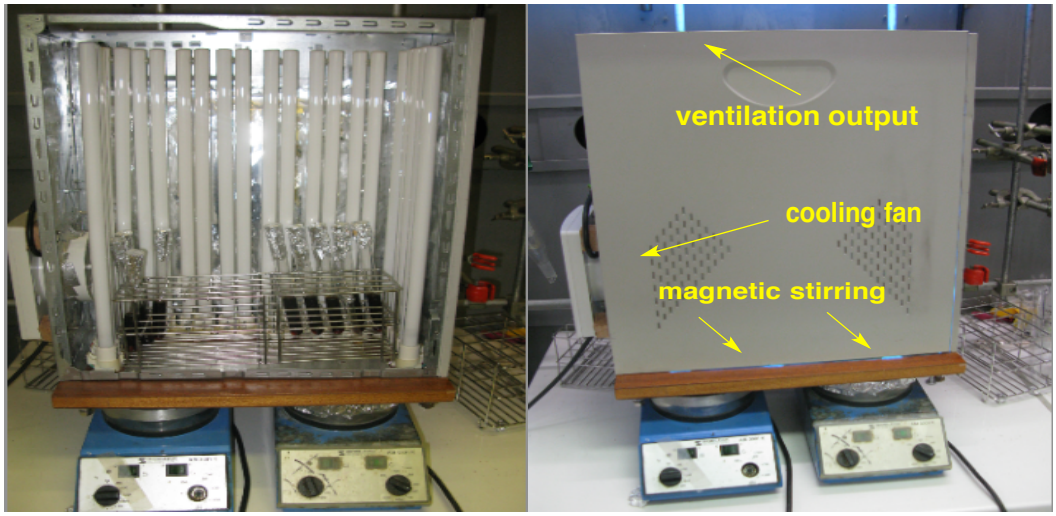
Remarkably high homoselectivity in [2+2] photodimerization of *trans*-cinnamic acids in multicomponent system

Thanh Binh Nguyen* and Ali Al-Mourabit

General information

Reagents obtained from commercial supplier were used without further purification. NMR Chemical shifts are reported in (δ) ppm relative to tetramethylsilane (TMS) with the residual solvent as internal reference (DMSO-d_6, δ 2.50 ppm, methanol-d_4, δ 3.31 ppm for ^{1}H and δ 39.5 ppm for ^{13}C. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz) and integration.

Photochemical reactions were carried out under argon with magnetic stirring in 17 mL Pyrex test tubes surrounded by 12 PL-L 36W/10/4P Philips lamps in an old computer case. The reactor is cooled by a fan (inside temperature varies from 35 to 40 °C).

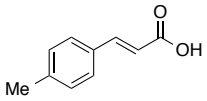


For more information about specification of the lamps, see:
http://www.lighting.philips.com/main/prof/lamps/special-lamps/medical-lamps/medical-therapy-uva-puva/uva-puva-pl-s-pl-l/927903421014_EU/product (Accessed on February 23th 2016).

Preparation of acrylic acids

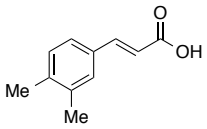
Except for *o*- and *p*-hydroxycinnamic acids (**F** and **D**) and *p*-chlorocinnamic acid (**G**) which were obtained from Fluka and used as such, acrylic acids **A**-**H** and **J** were prepared from the corresponding substituted aldehydes by condensation with malonic acid in pyridine in the presence of small amounts of piperidine (See Table 1).

(*E*)-3-(*p*-Tolyl)acrylic acid (A)



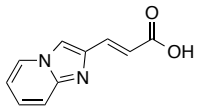
^{1}H NMR (300 MHz, DMSO-d_6) δ 12.30 (broad s, 1H), 7.56 (d, J = 7.9 Hz, 2H), 7.56 (d, J = 16.1 Hz, 1H), 7.22 (d, J = 7.9 Hz, 2H), 6.45 (d, J = 16.1 Hz, 1H), 2.32 (s, 3H).

(*E*)-3-(3,4-Dimethylphenyl)acrylic acid (B)



^{1}H NMR (300 MHz, DMSO-d_6) δ 12.27 (broad s, 1H), 7.51 (d, J = 15.9 Hz, 1H), 7.45 (d, J = 1.7 Hz, 1H), 7.38 (dd, J = 7.6, 1.7 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 6.44 (d, J = 15.9 Hz, 1H), 2.23 (s, 6H).

(*E*)-3-(Imidazo[1,2-a]pyridin-2-yl)acrylic acid (C)

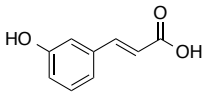


^{1}H NMR (300 MHz, DMSO-d_6) δ 11.50 (broad s, 1H), 8.52 (d, J = 6.9 Hz, 1H), 8.24 (s, 1H), 7.63 (d, J = 16.0 Hz, 1H), 7.54 (d, J = 9.0 Hz, 1H), 7.27 (dd, J = 9.0, 7.5, Hz, 1H), 6.88 (dd, J = 7.5, 6.9 Hz, 1H), 6.60 (d, J = 16.0 Hz, 1H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 167.7, 145.1, 140.4, 136.2, 127.2, 126.1, 119.7, 116.8, 115.2, 112.5.

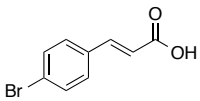
HRMS-ESI+: m/z [M + H]+ calcd for $C_{10}H_9N_2O_2$: 189.0664; found: 189.0682.

(*E*)-3-(3-Hydroxyphenyl)acrylic acid (E)



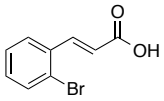
^{1}H NMR (300 MHz, DMSO-d_6) δ 12.36 (broad s, 1H), 9.60 (broad s, 1H), 7.49 (d, J = 16.1 Hz, 1H), 7.21 (t, J = 7.9 Hz, 1H), 7.09 (dd, J = 7.9, 2.0 Hz, 1H), 7.01 (t, J = 2.0 Hz, 1H), 6.82 (dd, J = 7.9, 2.0 Hz, 1H), 6.40 (d, J = 16.1 Hz, 1H).

(*E*)-3-(4-Bromophenyl)acrylic acid (H)



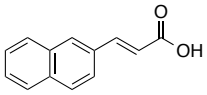
^{1}H NMR (300 MHz, CD_3OD) δ 7.62 (d, J = 16.1 Hz, 1H), 7.59-7.51 (m, 4H), 6.51 (d, J = 16.1 Hz, 1H).

(*E*)-3-(2-Bromophenyl)acrylic acid (I)



^{1}H NMR (300 MHz, CD_3OD) δ 8.04 (d, J = 16.0 Hz, 1H), 7.76 (dd, J = 7.8, 1.8 Hz, 1H), 7.65 (dd, J = 8.0, 1.1 Hz, 1H), 7.42-7.37 (m, 1H), 7.32-7.26 (m, 1H), 6.47 (d, J = 16.0 Hz, 1H).

(*E*)-3-(Naphthalen-2-yl)acrylic acid (J)

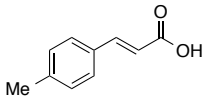
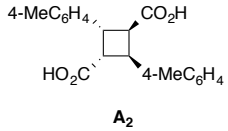
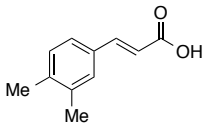
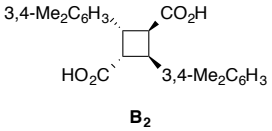
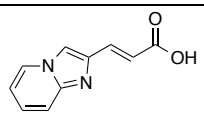
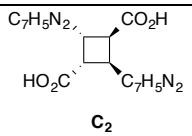
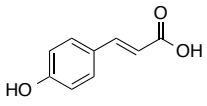
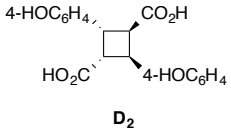
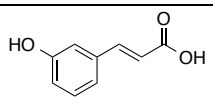
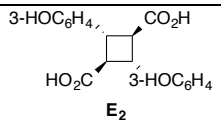


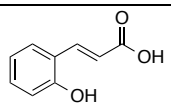
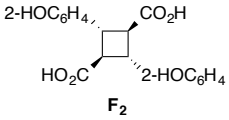
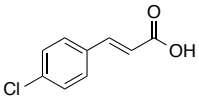
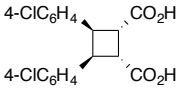
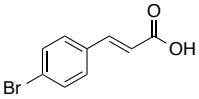
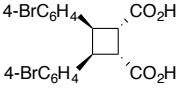
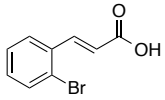
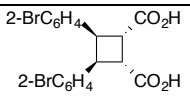
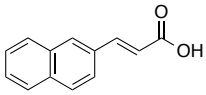
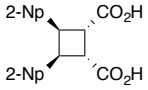
^{1}H NMR (300 MHz, DMSO-d_6) δ 12.49 (broad s, 1H), 8.18 (s, 1H), 7.96-7.86 (m, 4H), 7.74 (d, J = 16.0 Hz, 1H), 7.59-7.53 (m, 2H), 6.66 (d, J = 16.0 Hz, 1H).

General procedure for photocycloaddition

Single solid acrylic acids **A-J** (or their solid mixture) (~0.1 mmol each) dispersed in cyclohexane (2 mL) was stirred under an argon atmosphere in a 17 mL Pyrex test tube in the above-mentioned photo reactor for indicated reaction times (see Schemes 2-6 of the Manuscript and Table 1 of the Supporting information). Removal of cyclohexane afforded the single homocycloadduct (or their mixture) in virtually quantitative yields.

Table 1. Reaction time for individual case to attain full conversion

Cinnamic acid Obtention method (yield)	Structure	t (h)	Adduct
A Method 1 (65%)		40	 **A_2**
B Method 1 (63%)		40	 **B_2**
C Method 1 (96%)		24	 **C_2**
D Commercially available		24	 **D_2**
E Method 2 (81%)		24	 **E_2**

F Commercially available		24	 **F_2**
G Commercially available		20	 **G_2**
H Method 2 (95%)		24	 **H_2**
I Method 2 (90%)		12	 **I_2**
J Method 1 (67%)		6	 **J_2**

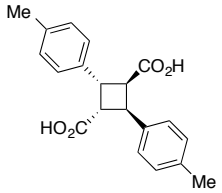
A mixture of aldehyde (10 mmol), malonic acid (1.35 g, 13 mmol) and piperidine (85 mg, 1 mmol) in pyridine (2 mL) was stirred in an open 17-mL test tube at 100 °C for 16 h. The crude mixture was treated as the following methods:

Method 1: the crude reaction mixture was diluted with cold MeOH (4-6 mL) and filtered. The solid was washed with cold MeOH (4 mL × 5) and dried *in vacuo*.

Method 2: the crude reaction mixture was diluted with H_2O (2-4 mL) and treated with concentrated HCl (3 mL). The solid was washed thoroughly with H_2O and dried in air and next in a vacuum desiccator (silica gel) for one night.

Single adduct characterization

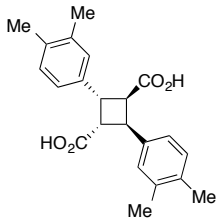
(1*R*,2*R*,3*S*,4*S*)-2,4-di-*p*-tolylcyclobutane-1,3-dicarboxylic acid (A_2)



^{1}H NMR (500 MHz, DMSO-d_6) δ 12.04 (broad s, 2H), 7.23 (d, J = 7.7 Hz, 4H), 7.13 (d, J = 7.7 Hz, 4H), 4.23 (dd, J = 10.5, 7.0 Hz, 2H), 3.75 (dd, J = 10.5, 7.0 Hz, 2H), 2.28 (s, 6H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.0, 136.4, 135.7, 128.7, 127.5, 46.3, 40.7, 20.6.

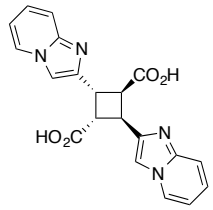
(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(3,4-dimethylphenyl)cyclobutane-1,3-dicarboxylic acid (B_2)



^{1}H NMR (500 MHz, DMSO-d_6) δ 12.01 (broad s, 2H), 7.11 (s, 2H), 7.08-7.04 (m, 4H), 4.19 (dd, J = 10.5, 7.0 Hz, 2H), 3.73 (dd, J = 10.5, 7.0 Hz, 2H), 2.21 (s, 6H), 2.19 (s, 6H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.0, 136.9, 135.7, 134.4, 129.3, 128.8, 125.0, 46.3, 40.7, 19.5, 19.0.

(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(imidazo[1,2-a]pyridin-2-yl)cyclobutane-1,3-dicarboxylic acid (C_2)

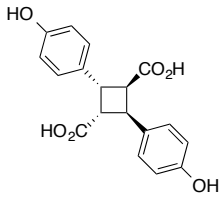


^{1}H NMR (300 MHz, DMSO-d_6) δ 12.00 (broad s, 2H), 8.49 (d, J = 6.6 Hz, 2H), 7.86 (s, 2H), 7.52 (d, J = 8.9 Hz, 2H), 7.19 (dd, J = 8.9, 6.6 Hz, 2H), 6.85 (t, J = 6.6 Hz, 1H), 4.44 (dd, J = 10.1, 7.0 Hz, 2H), 3.86 (dd, J = 10.1, 7.0 Hz, 2H).

^{13}C NMR (125 MHz, DMSO-d_6 and a drop of TFA) δ 172.0, 140.1, 135.7, 134.3, 129.7, 117.9, 113.8, 112.5, 45.1, 33.3.

HRMS-ESI+: m/z [M + H]+ calcd for $C_{20}H_{17}N_4O_4$: 377.1250; found: 377.1242.

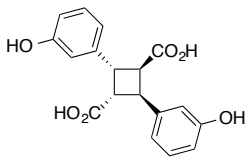
(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(4-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (D_2)



^{1}H NMR (300 MHz, DMSO-d_6) δ 11.99 (broad s, 2H), 9.28 (broad s, 2H), 7.13 (d, J = 8.5 Hz, 4H), 6.70 (d, J = 8.5 Hz, 4H), 4.13 (dd, J = 10.2, 7.1 Hz, 2H), 3.65 (dd, J = 10.2, 7.1 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.2, 156.1, 129.7, 128.8, 115.0, 46.8, 40.4.

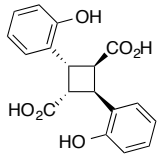
(1*R*,2*S*,3*R*,4*S*)-2,4-*bis*(3-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (E_2)



^{1}H NMR (500 MHz, DMSO-d_6) δ 12.10 (broad s, 2H), 9.31 (broad s, 2H), 7.10 (t, J = 7.9 Hz, 2H), 6.75 (d, J = 7.9 Hz, 2H), 6.71 (d, J = 2.0 Hz, 2H), 6.63 (dd, J = 7.9, 2.0 Hz, 2H), 4.13 (dd, J = 10.4, 7.3 Hz, 2H), 3.70 (dd, J = 10.4, 7.3 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 172.9, 157.2, 140.9, 129.1, 118.2, 114.4, 113.6, 46.2, 41.1.

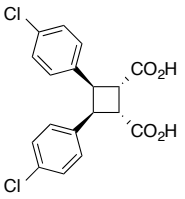
(1*R*,2*S*,3*R*,4*S*)-2,4-*bis*(2-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (F_2)



^{1}H NMR (500 MHz, DMSO-d_6) δ 11.83 (broad s, 2H), 9.41 (broad s, 2H), 7.23-7.21 (m, 2H), 7.06-7.02 (m, 2H), 6.79-6.77 (m, 4H), 4.48 (dd, J = 10.1, 7.7 Hz, 2H), 3.74 (dd, J = 10.1, 7.7 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.6, 155.2, 127.4, 127.2, 126.0, 118.6, 114.7, 44.9, 35.7.

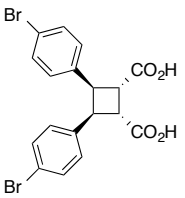
(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(4-chlorophenyl)cyclobutane-1,2-dicarboxylic acid (G_2)



^{1}H NMR (300 MHz, DMSO-d_6) δ 12.51 (broad s, 2H), 7.16 (d, J = 8.5 Hz, 4H), 7.07 (d, J = 8.5 Hz, 4H), 4.22 (d, J = 6.2 Hz, 2H), 3.80 (d, J = 6.2 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.8, 138.2, 130.6, 129.8, 127.7, 43.7, 42.4.

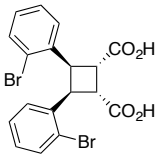
(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(4-bromophenyl)cyclobutane-1,2-dicarboxylic acid (H_2)



^{1}H NMR (300 MHz, DMSO-d_6) δ 12.51 (broad s, 2H), 7.30 (d, J = 8.5 Hz, 4H), 7.02 (d, J = 8.5 Hz, 4H), 4.20 (d, J = 6.2 Hz, 2H), 3.79 (d, J = 6.2 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.7, 138.5, 130.6, 130.1, 119.1, 43.6, 42.3.

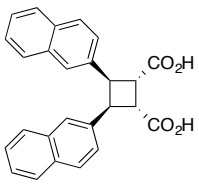
(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(2-bromophenyl)cyclobutane-1,2-dicarboxylic acid (E_2)



^{1}H NMR (500 MHz, DMSO-d_6) δ 12.59 (broad s, 2H), 7.43-7.40 (m, 2H), 7.35-7.32 (m, 2H), 7.20-7.15 (m, 2H), 7.05-7.00 (m, 2H), 4.64 (d, J = 6.4 Hz, 2H), 3.86 (d, J = 6.4 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 173.6, 137.8, 132.2, 129.1, 128.4, 127.1, 124.6, 43.9, 42.6.

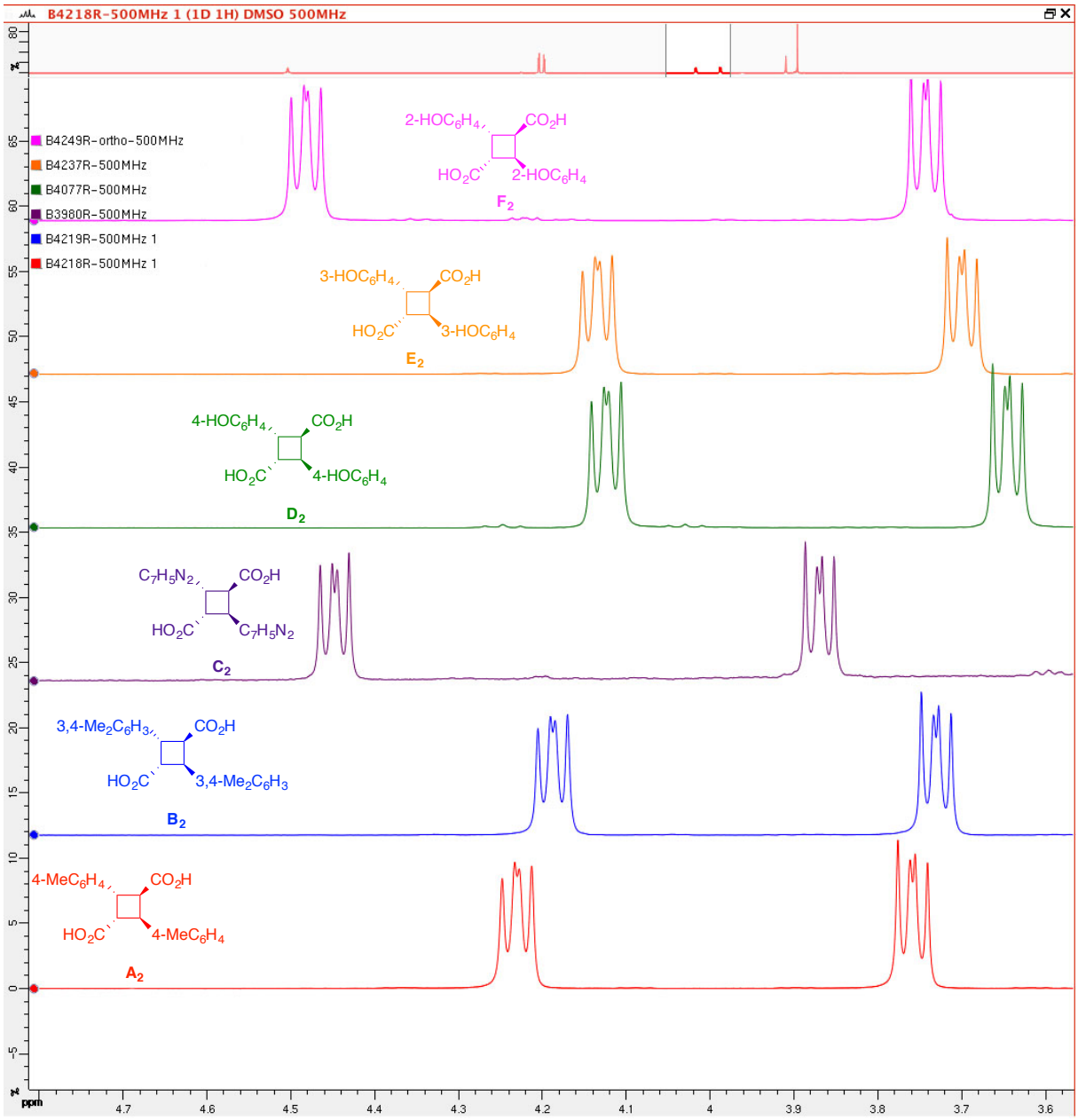
(1*R*,2*S*,3*R*,4*S*)-3,4-di(naphthalen-2-yl)cyclobutane-1,2-dicarboxylic acid (J_2)



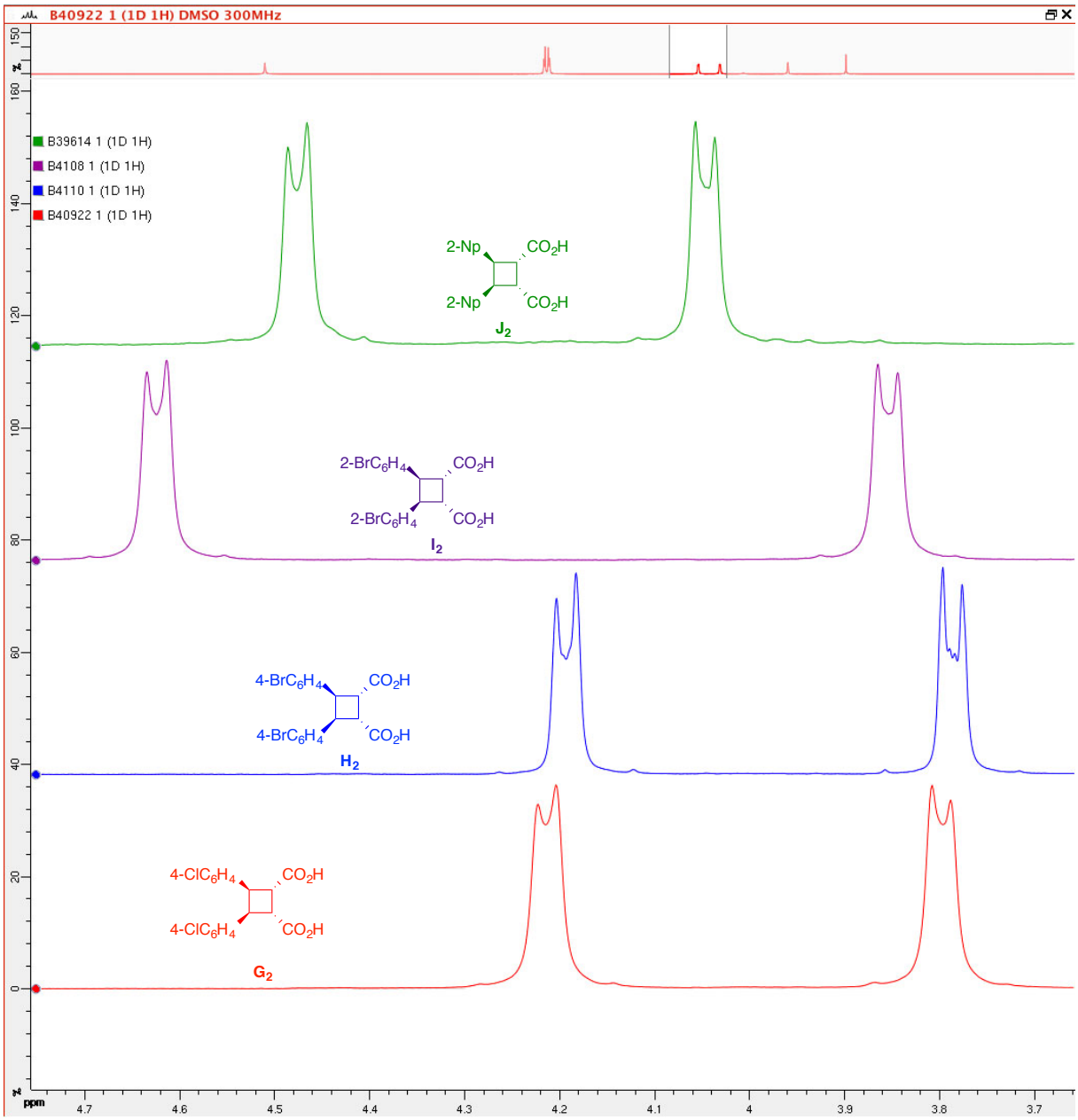
^{1}H NMR (300 MHz, DMSO-d_6) δ 13.42 (broad s, 2H), 8.56-8.53 (m, 2H), 8.46 (d, J = 7.4 Hz, 2H), 8.33 (d, J = 7.4 Hz, 2H), 8.21-8.10 (m, 4H), 8.00 (dd, J = 8.4, 1.3 Hz, 2H), 5.28 (d, J = 6.2 Hz, 2H), 4.85 (d, J = 6.2 Hz, 2H).

^{13}C NMR (75 MHz, DMSO-d_6) δ 174.0, 137.1, 132.6, 131.4, 127.4, 127.2, 127.0, 126.7, 126.0, 125.8, 125.3, 44.7, 42.7.

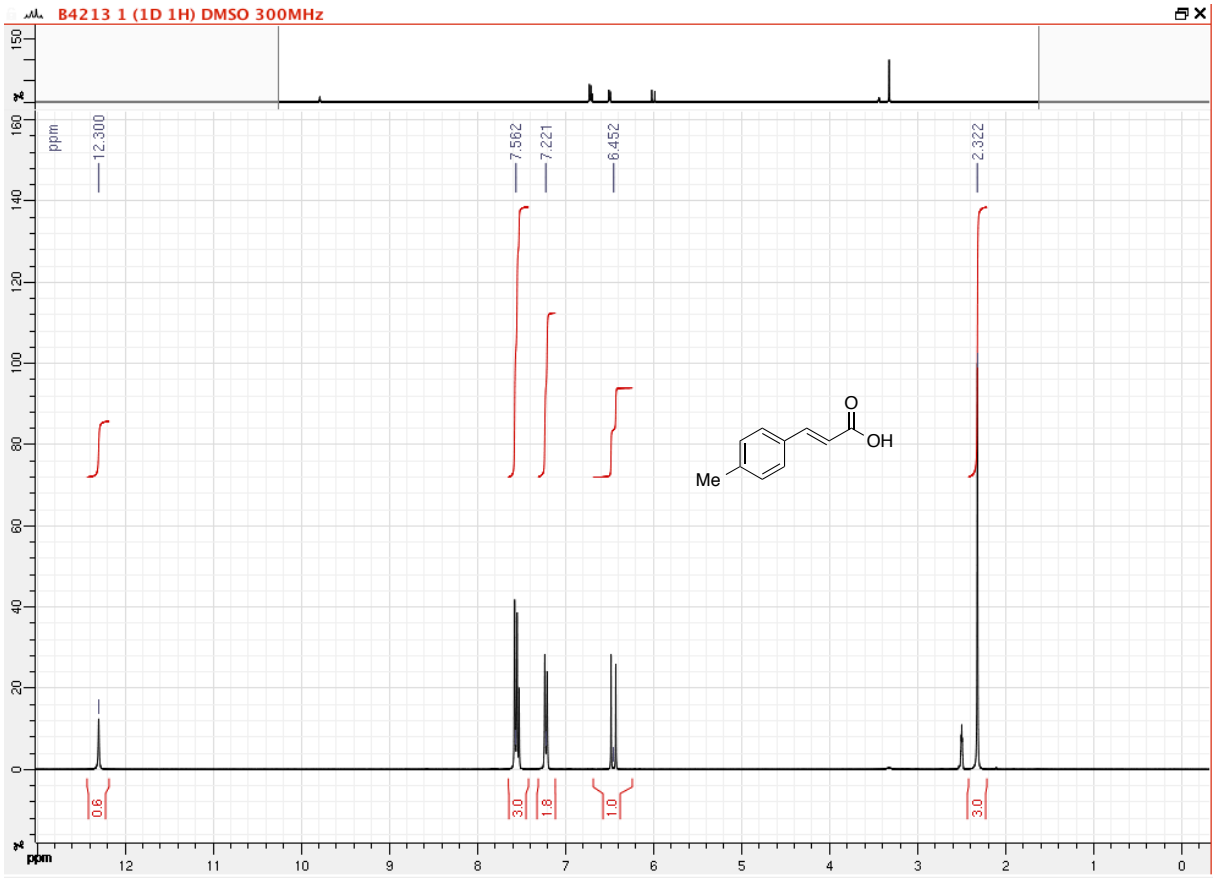
Comparison of cyclobutane signals of α-truxillic type adducts A_2-F_2



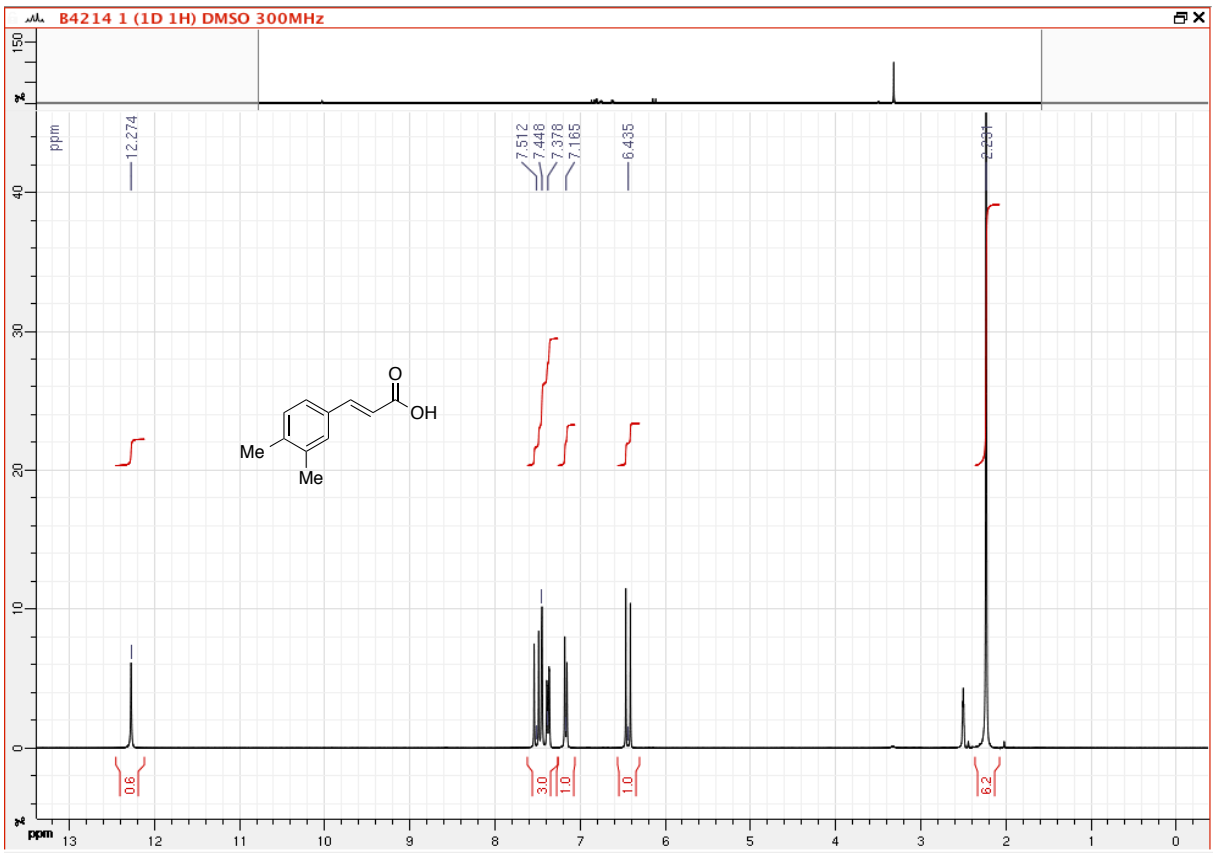
Comparison of cyclobutane signals of β-truxinic type adducts G_2-J_2



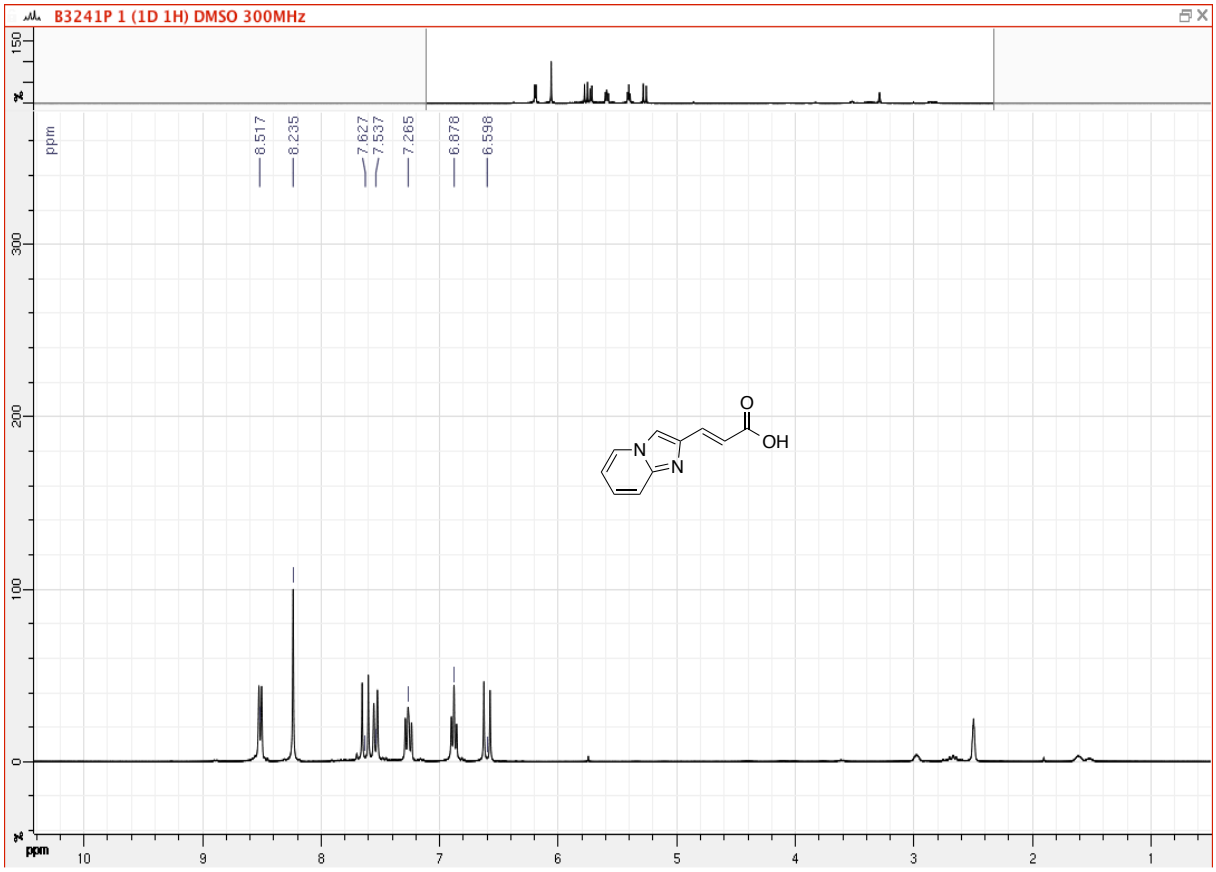
(*E*)-3-(*p*-Tolyl)acrylic acid (A)

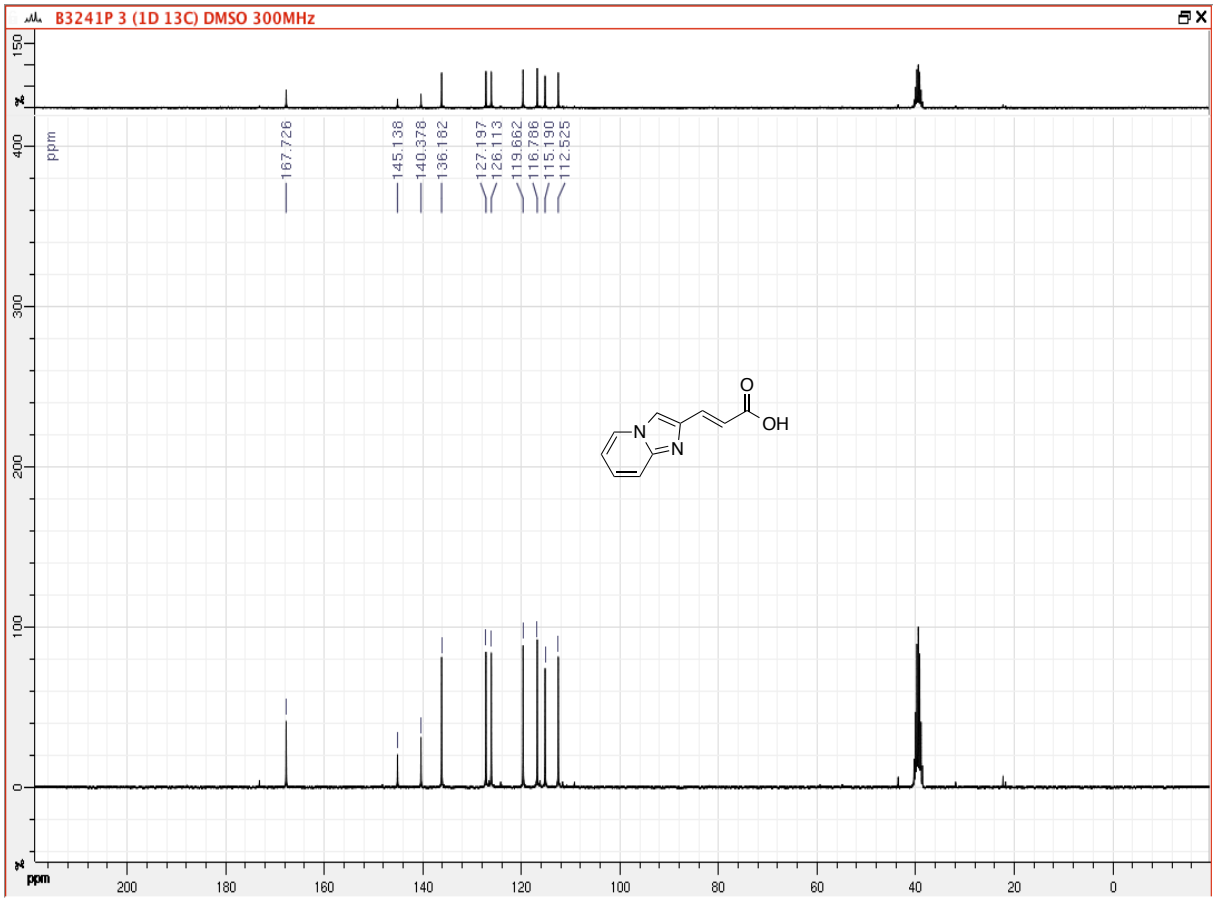


(*E*)-3-(3,4-Dimethylphenyl)acrylic acid (B)

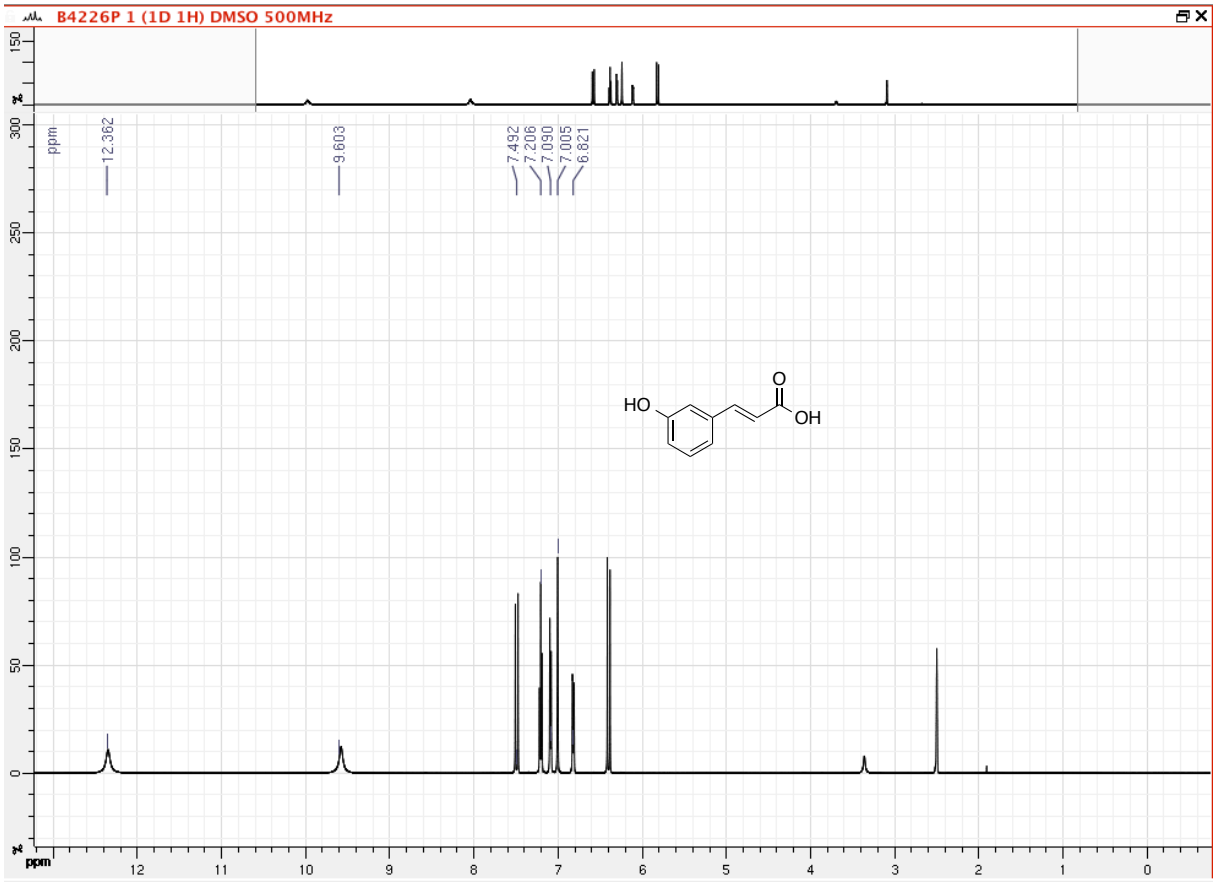


(*E*)-3-(Imidazo[1,2-a]pyridin-2-yl)acrylic acid (C)

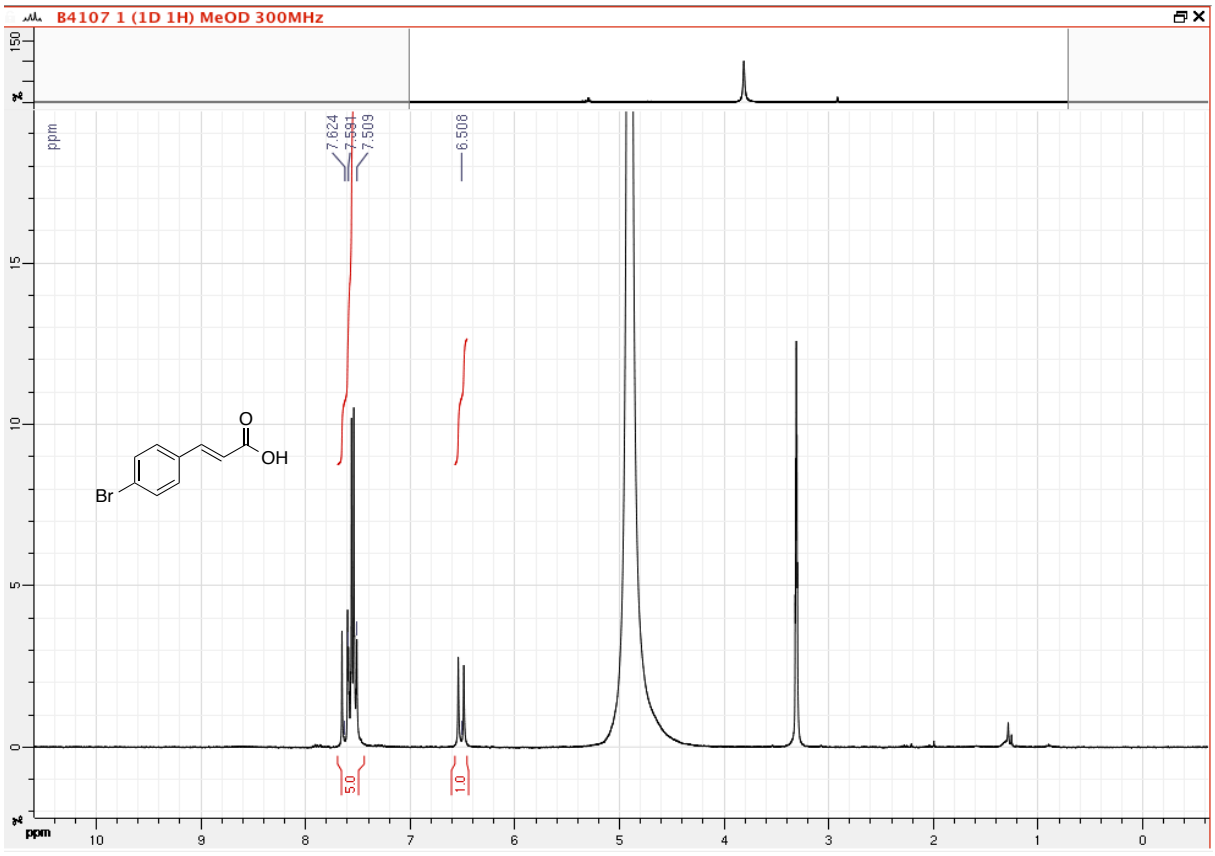




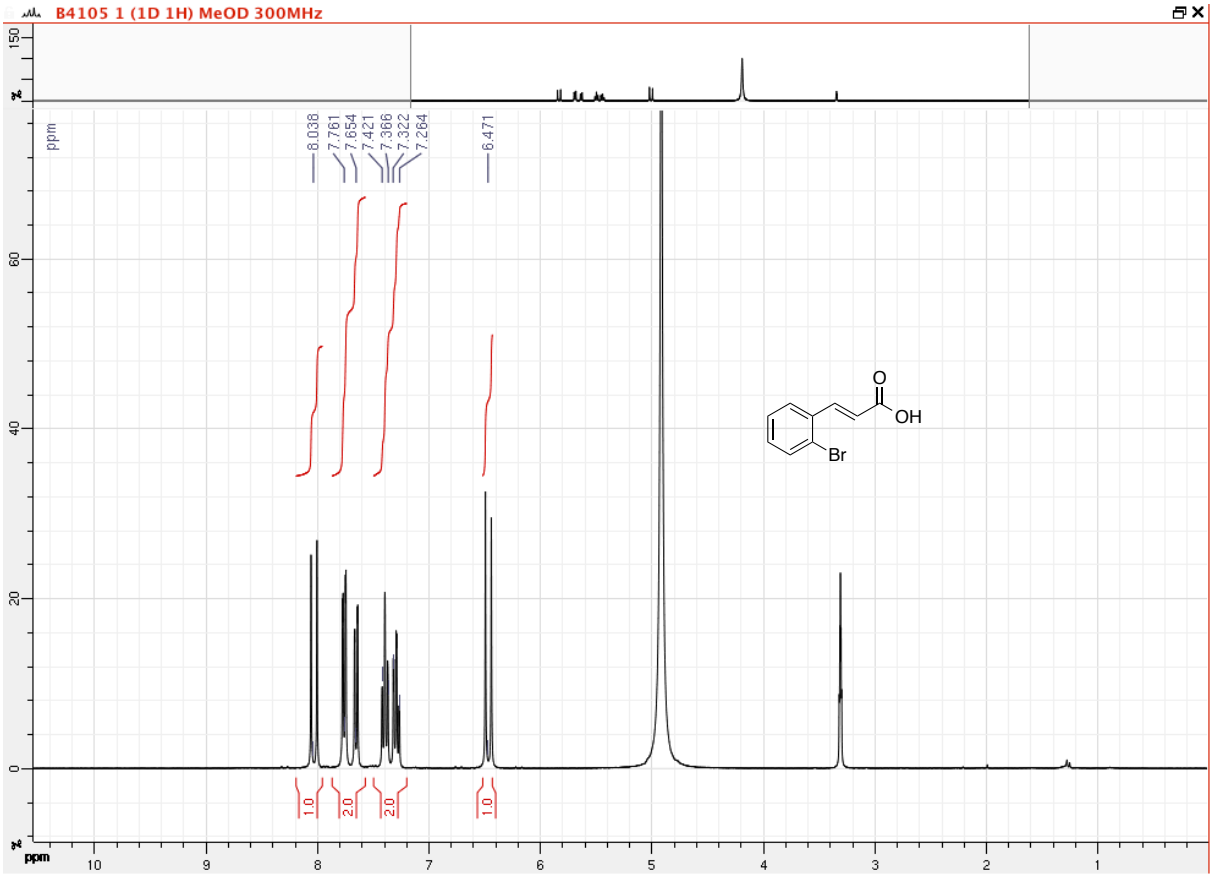
(*E*)-3-(3-Hydroxyphenyl)acrylic acid (E)



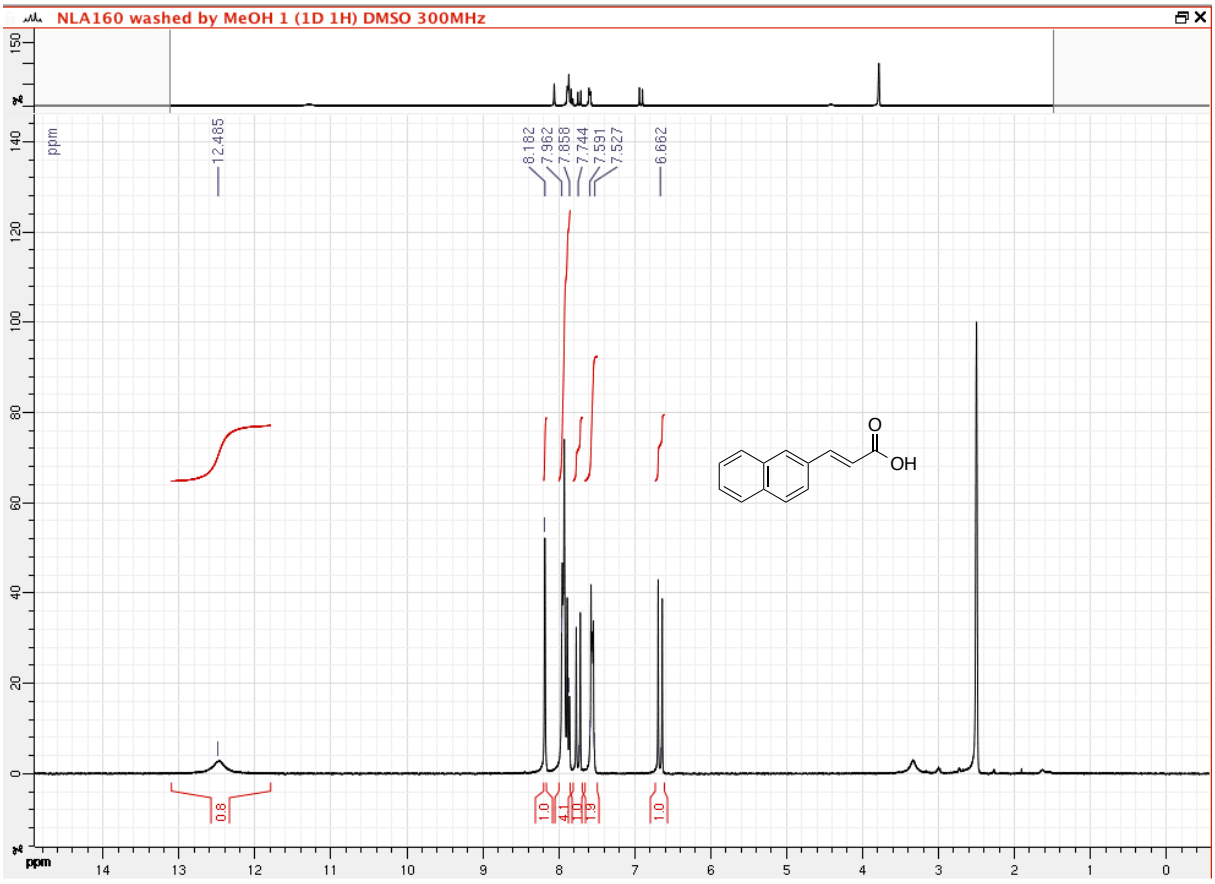
(*E*)-3-(4-Bromophenyl)acrylic acid (H)



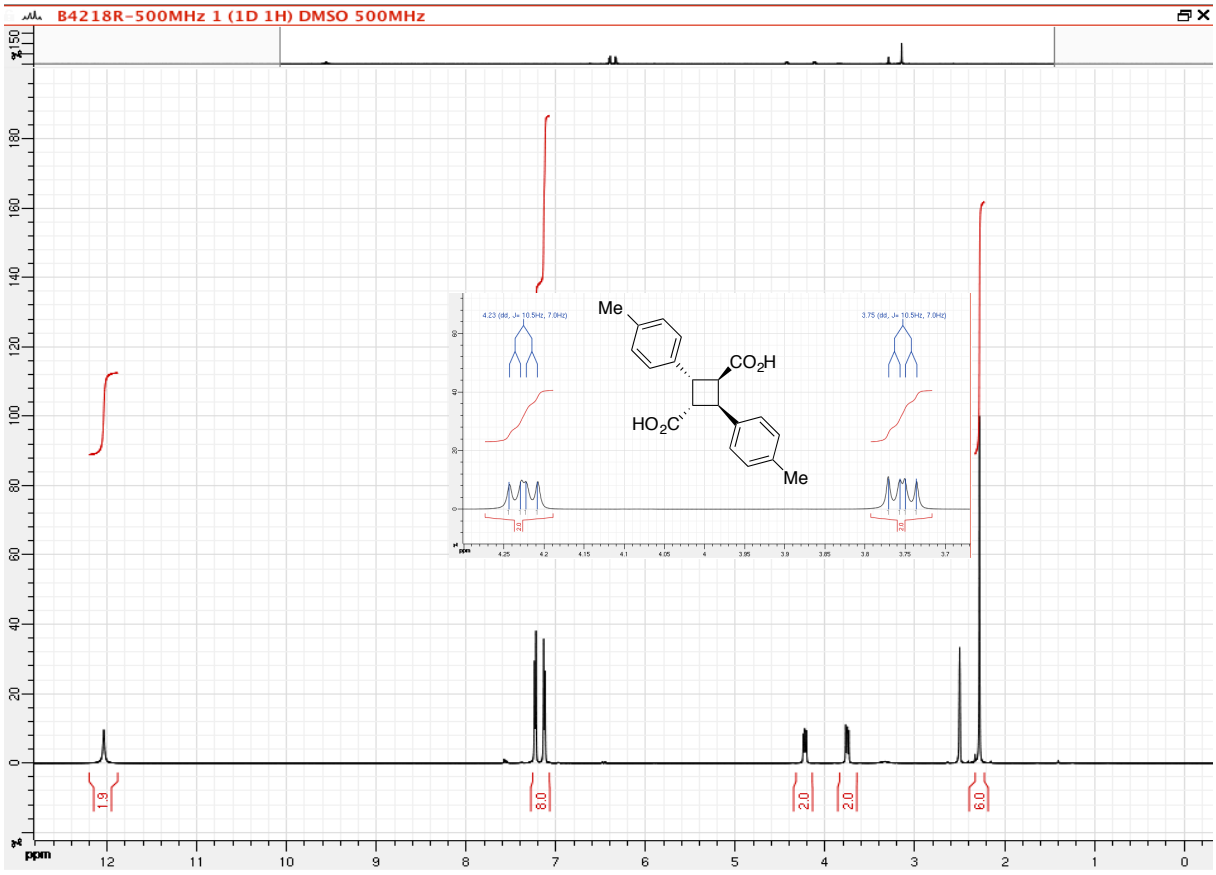
(*E*)-3-(2-Bromophenyl)acrylic acid (I)

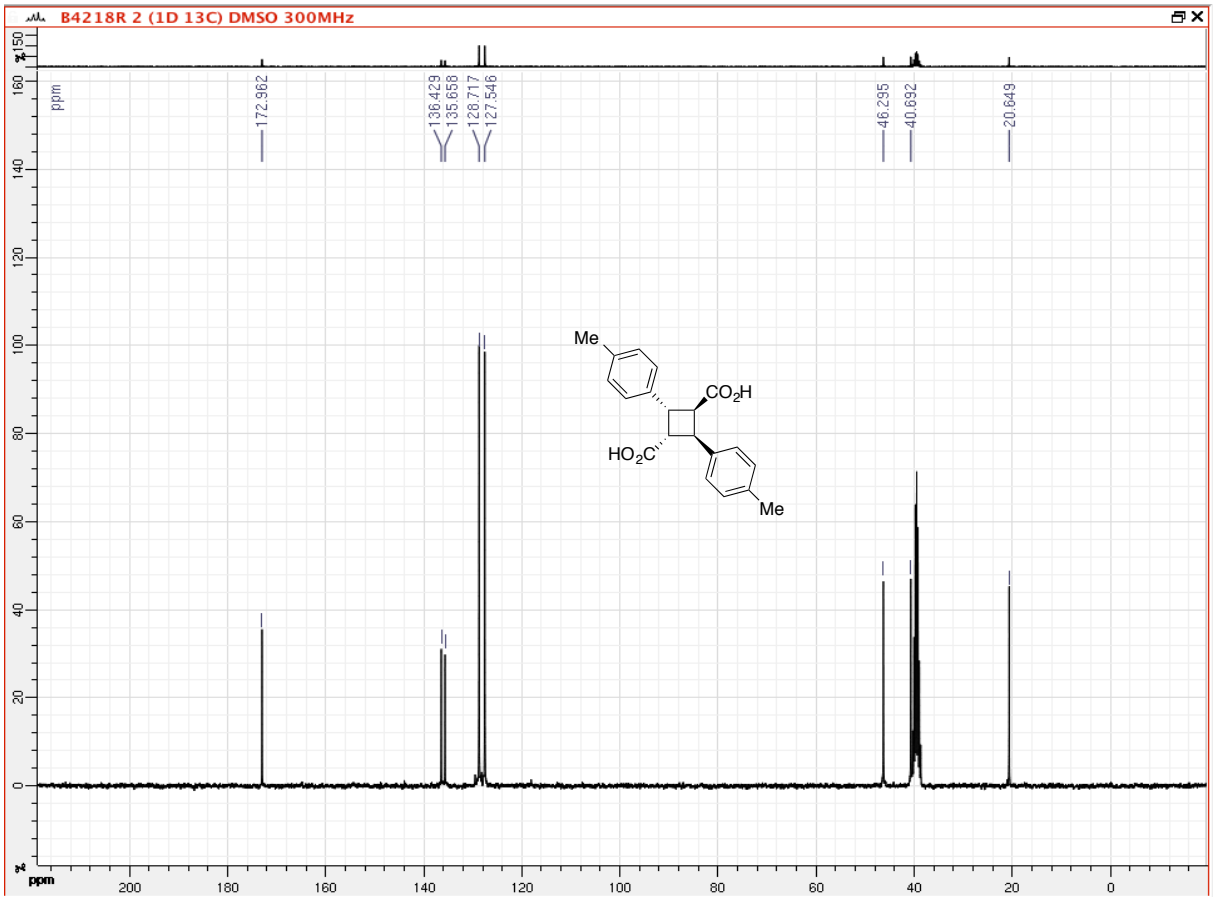


(*E*)-3-(Naphthalen-2-yl)acrylic acid (J)

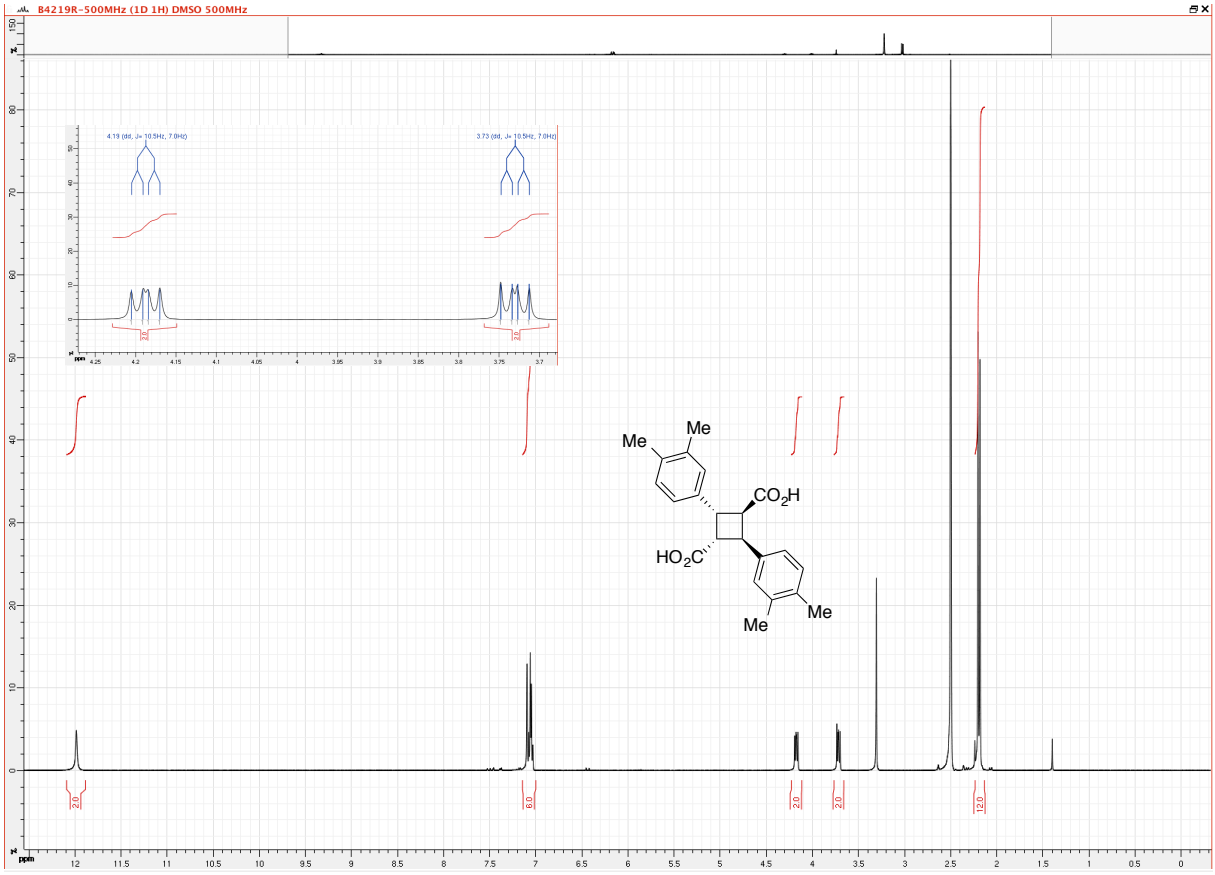


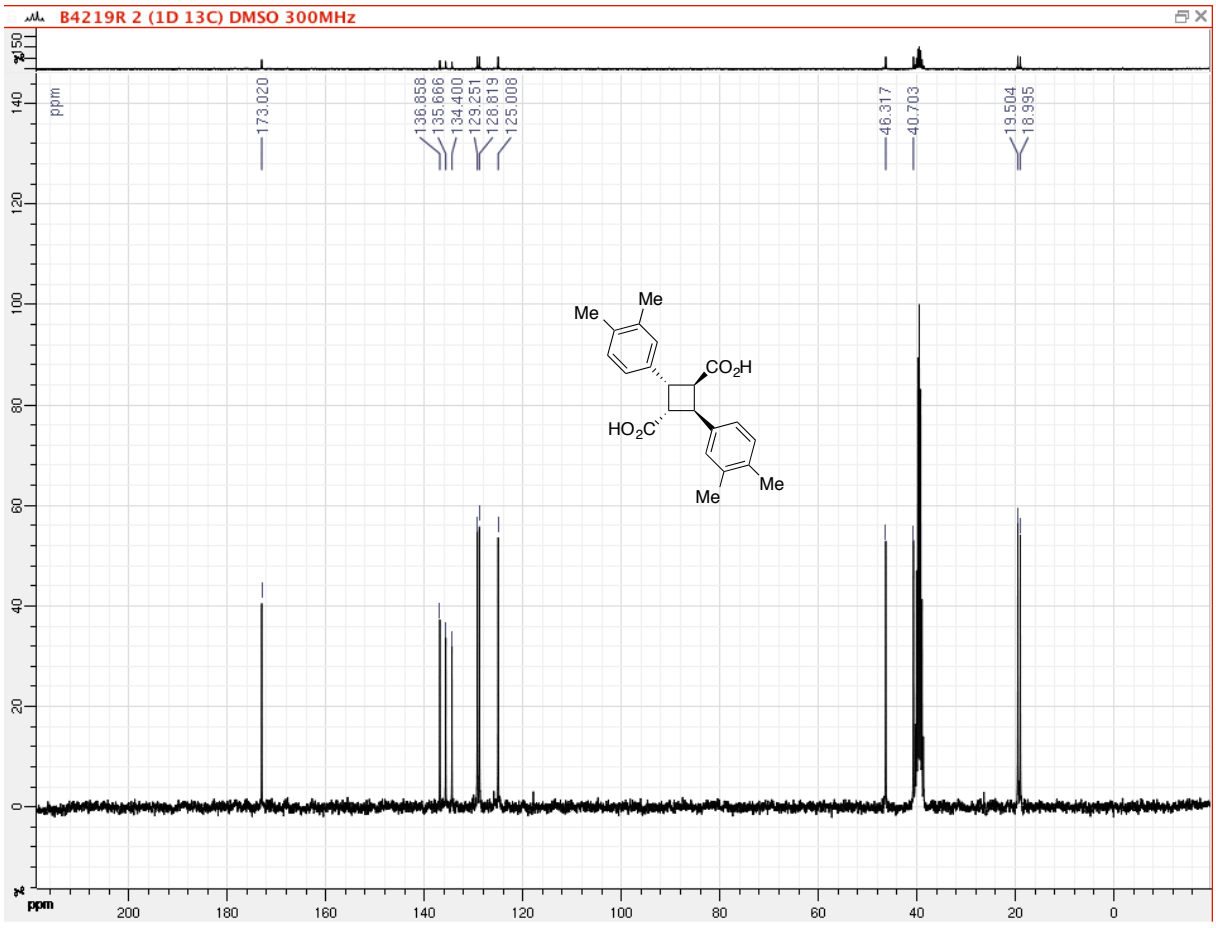
(1*R*,2*R*,3*S*,4*S*)-2,4-di-*p*-tolylcyclobutane-1,3-dicarboxylic acid (A_2)



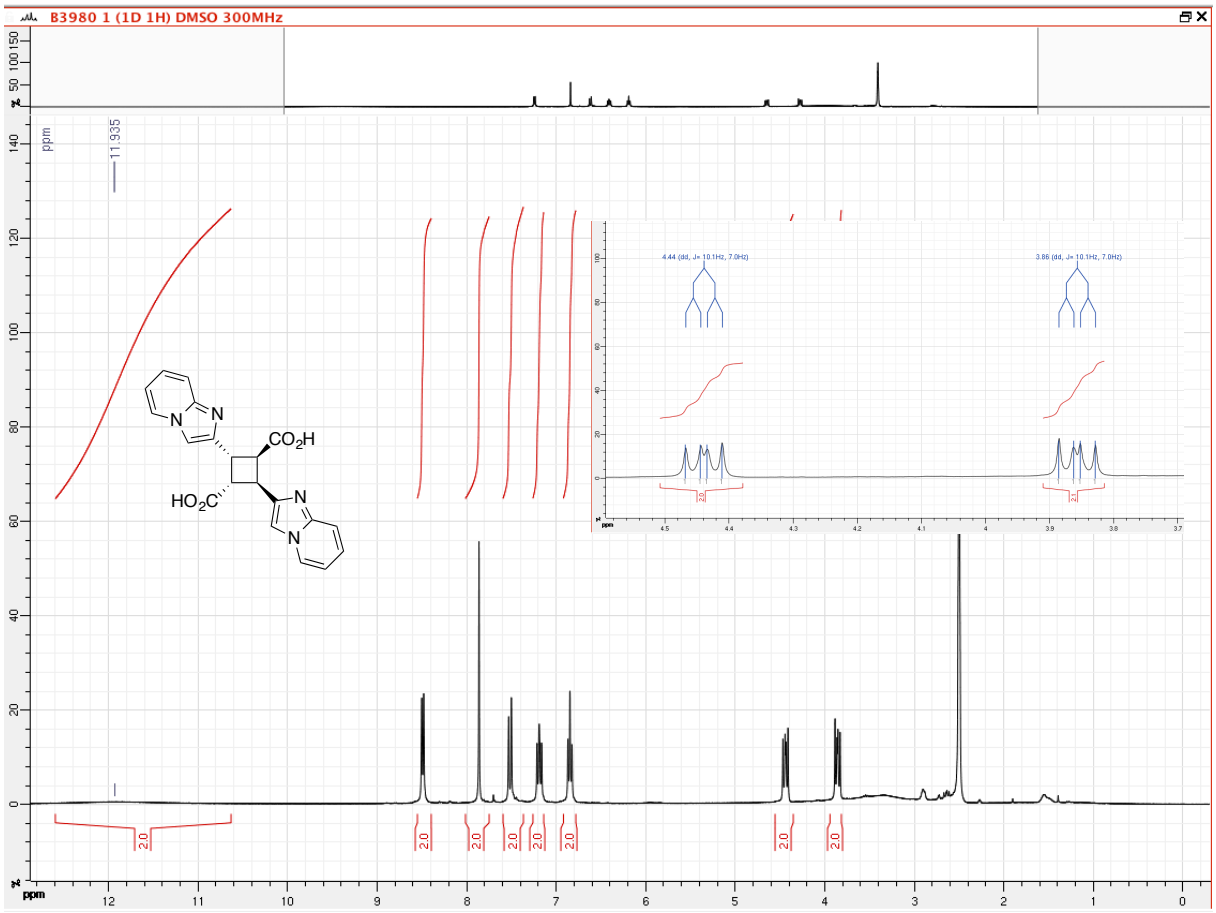


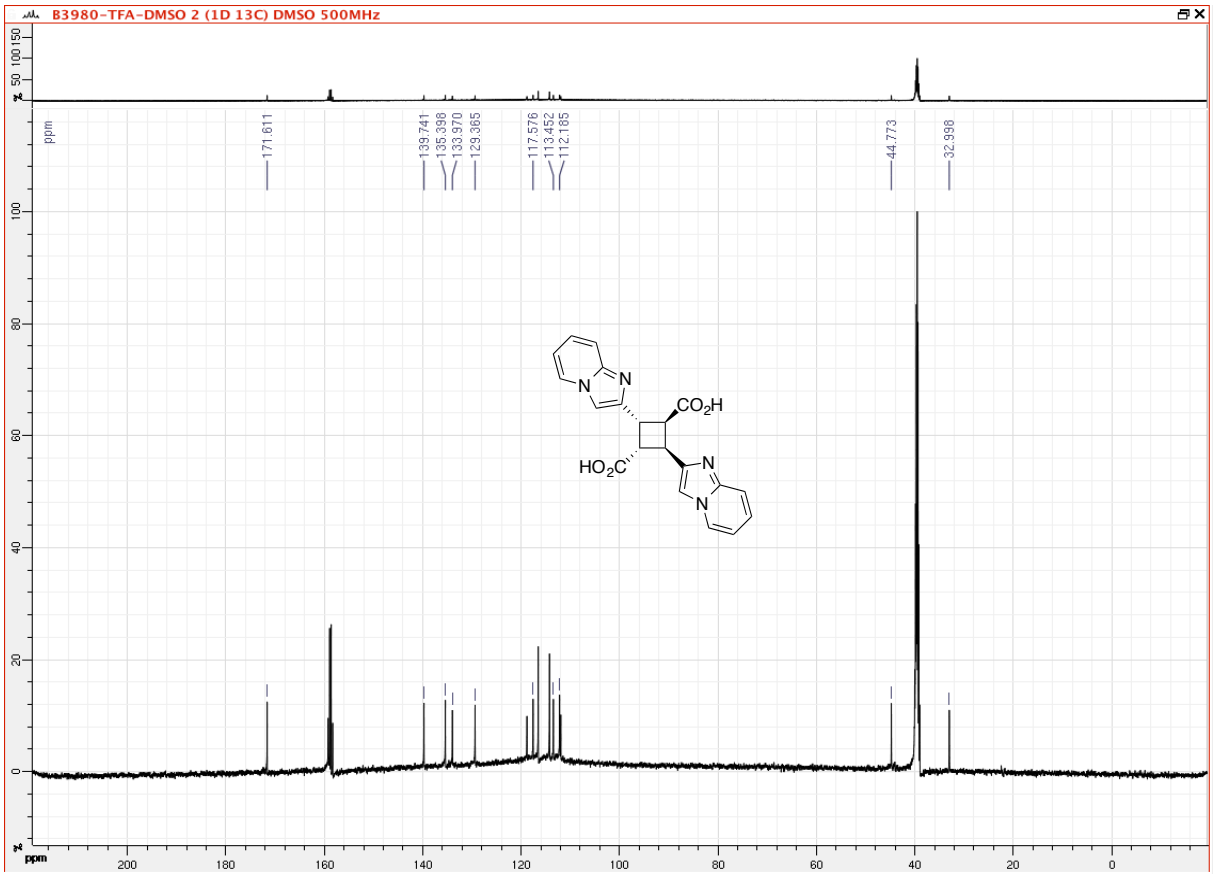
(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(3,4-dimethylphenyl)cyclobutane-1,3-dicarboxylic acid (B_2)



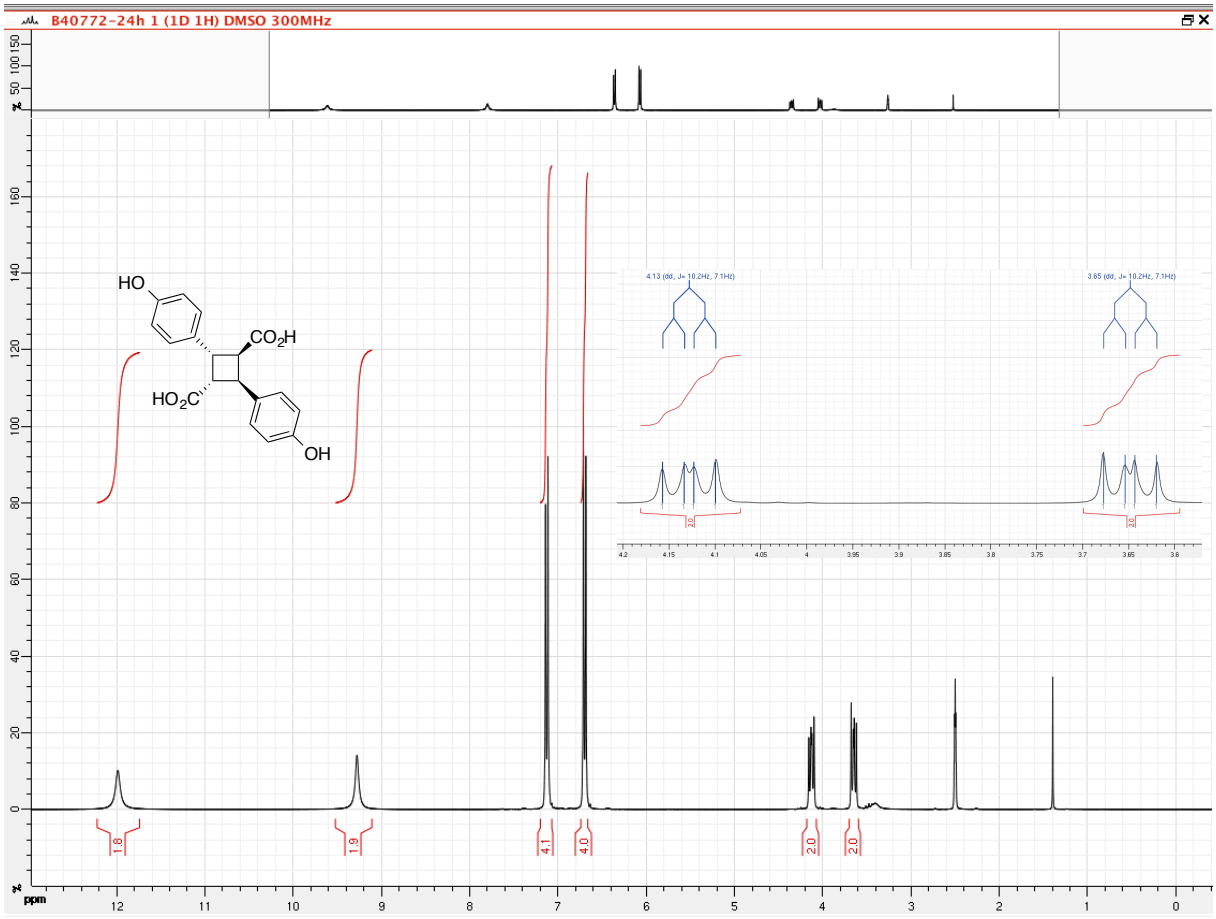


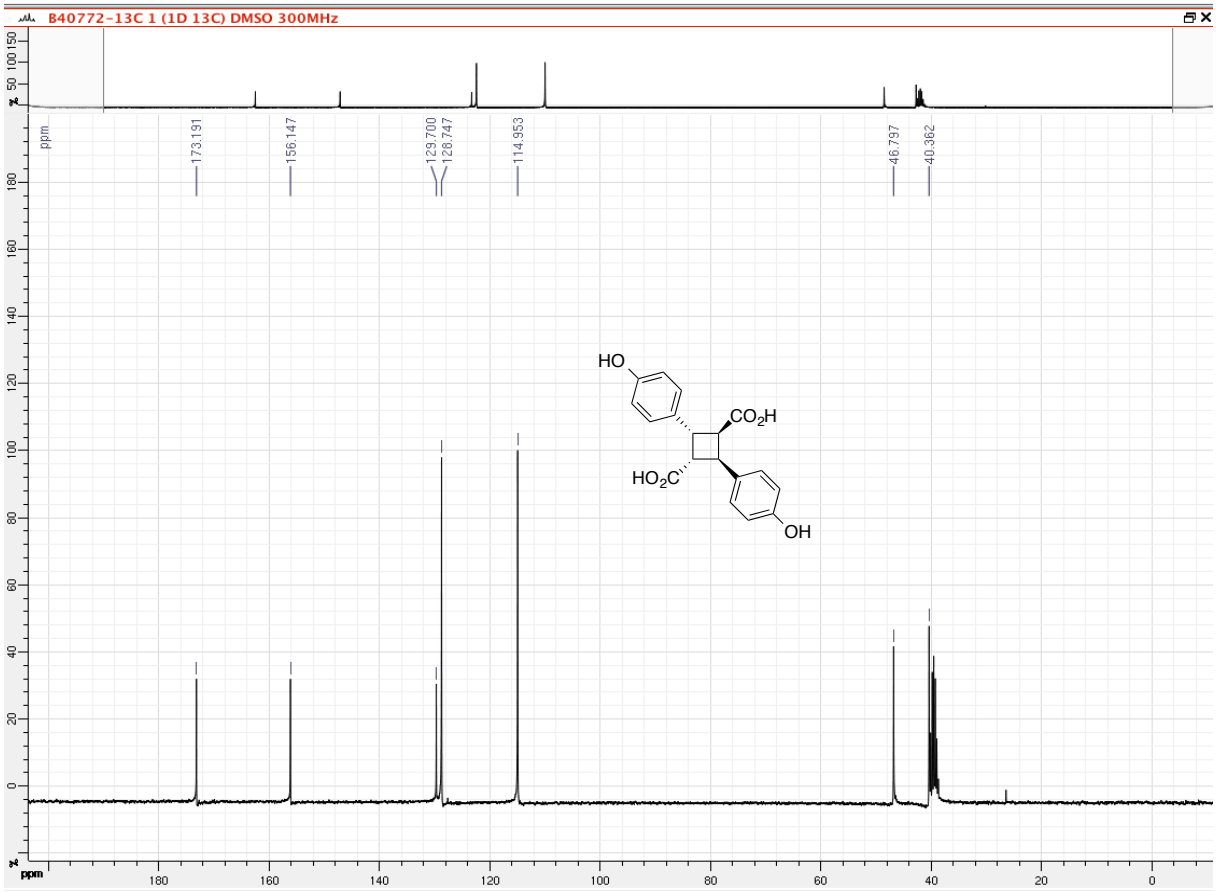
(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(imidazo[1,2-a]pyridin-2-yl)cyclobutane-1,3-dicarboxylic acid (C_2)



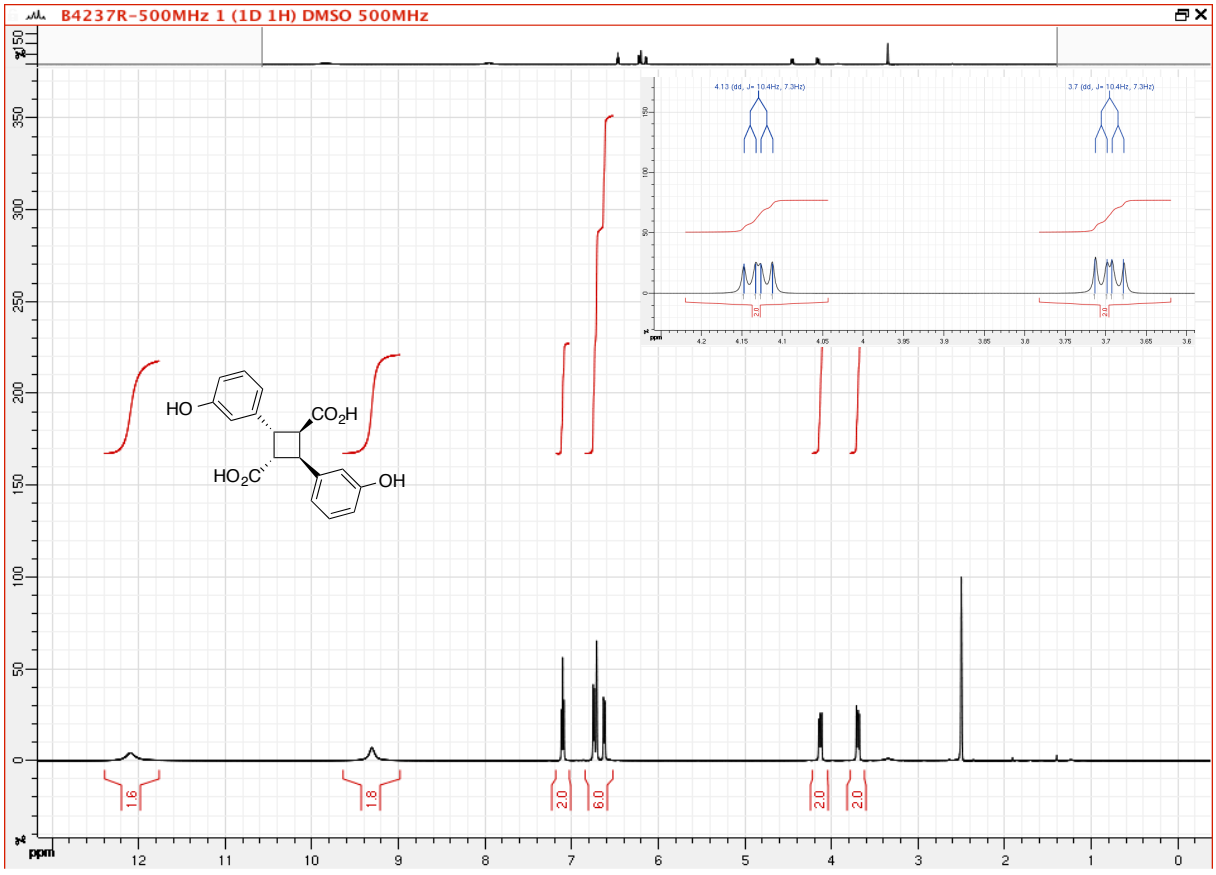


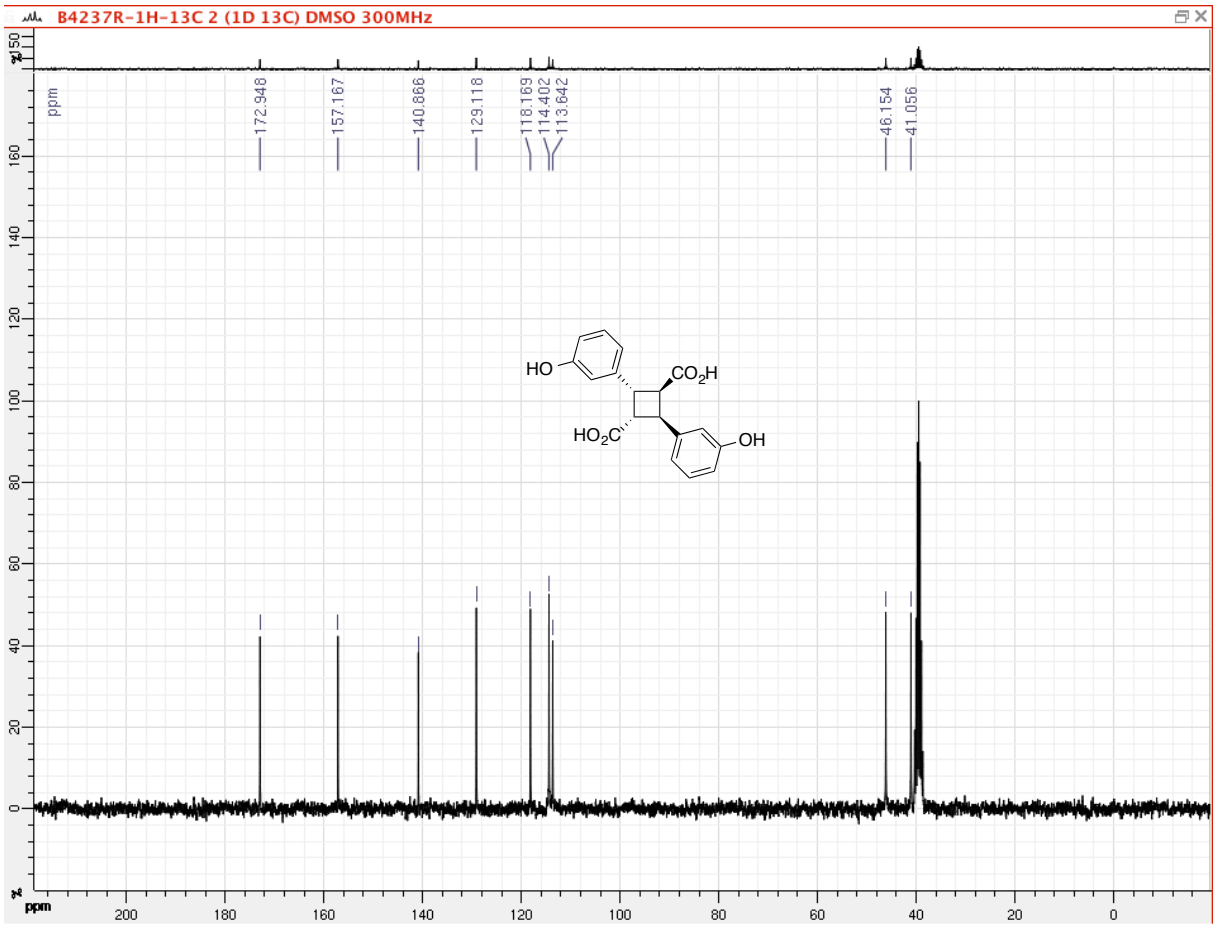
(1*R*,2*R*,3*S*,4*S*)-2,4-*bis*(4-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (D_2)



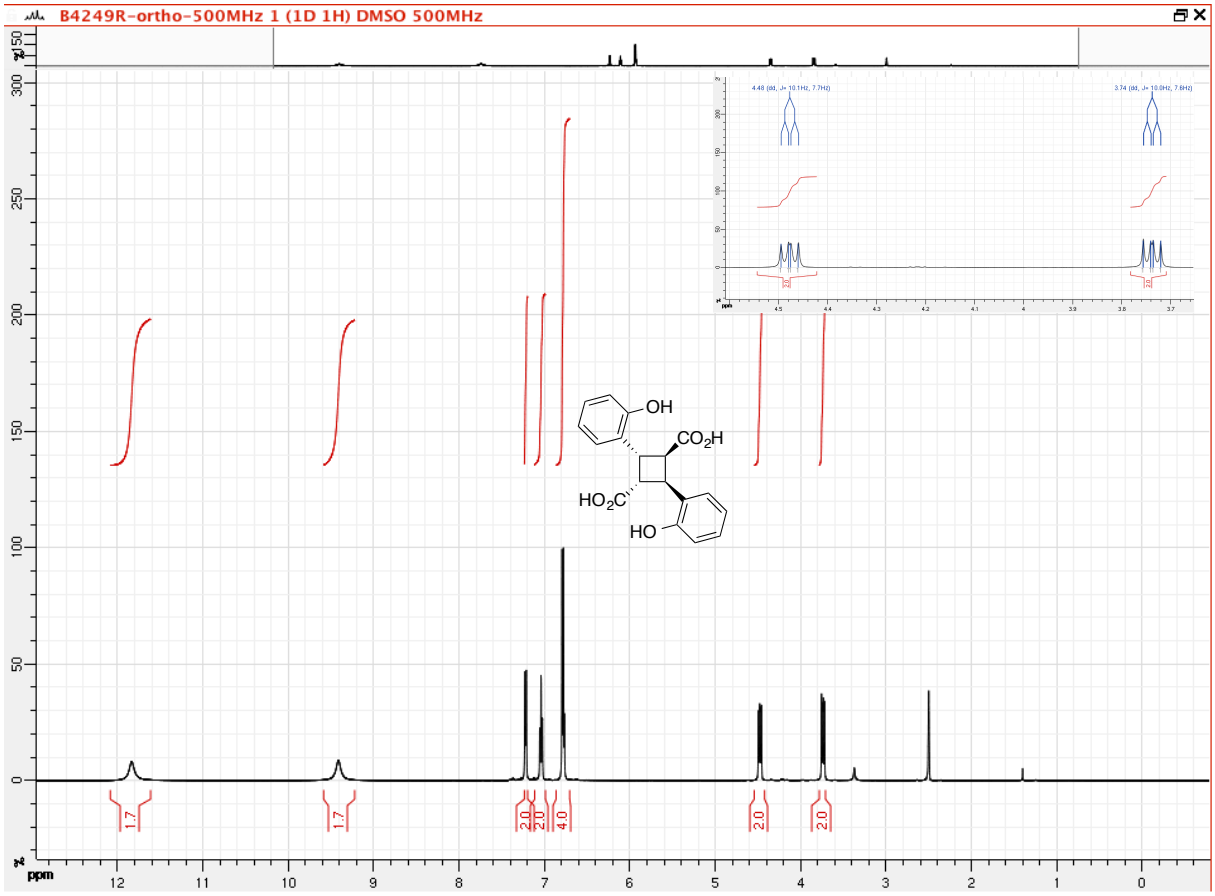


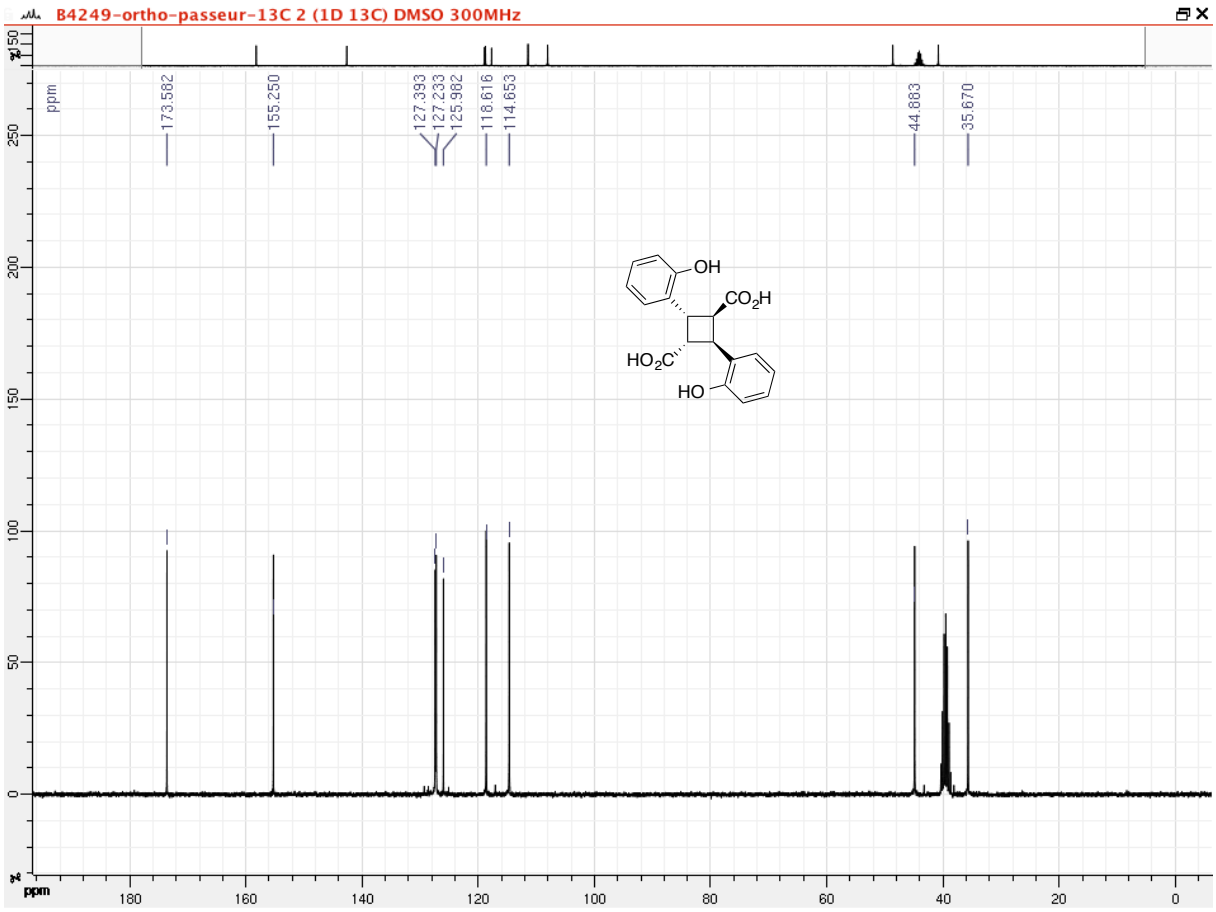
(1*R*,2*S*,3*R*,4*S*)-2,4-*bis*(3-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (E_2)



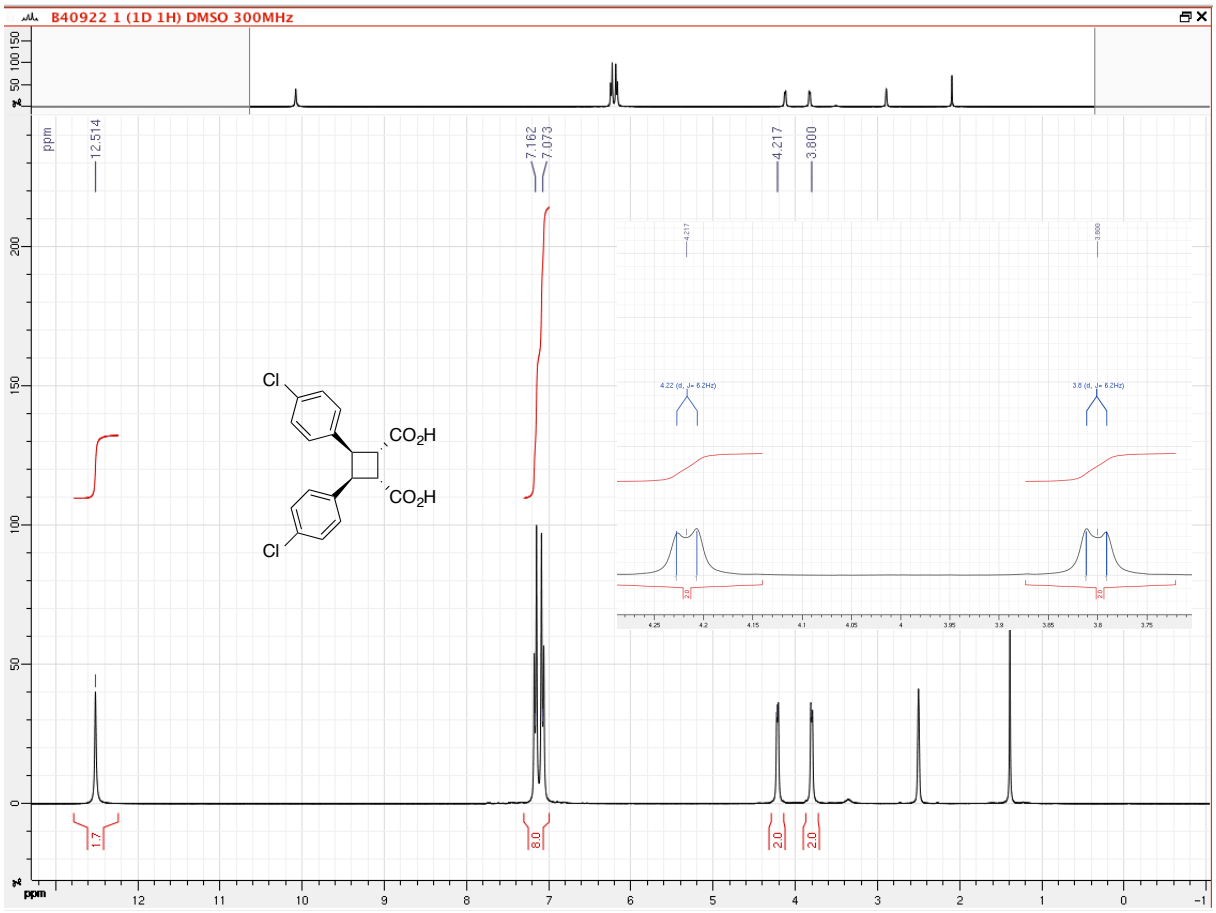


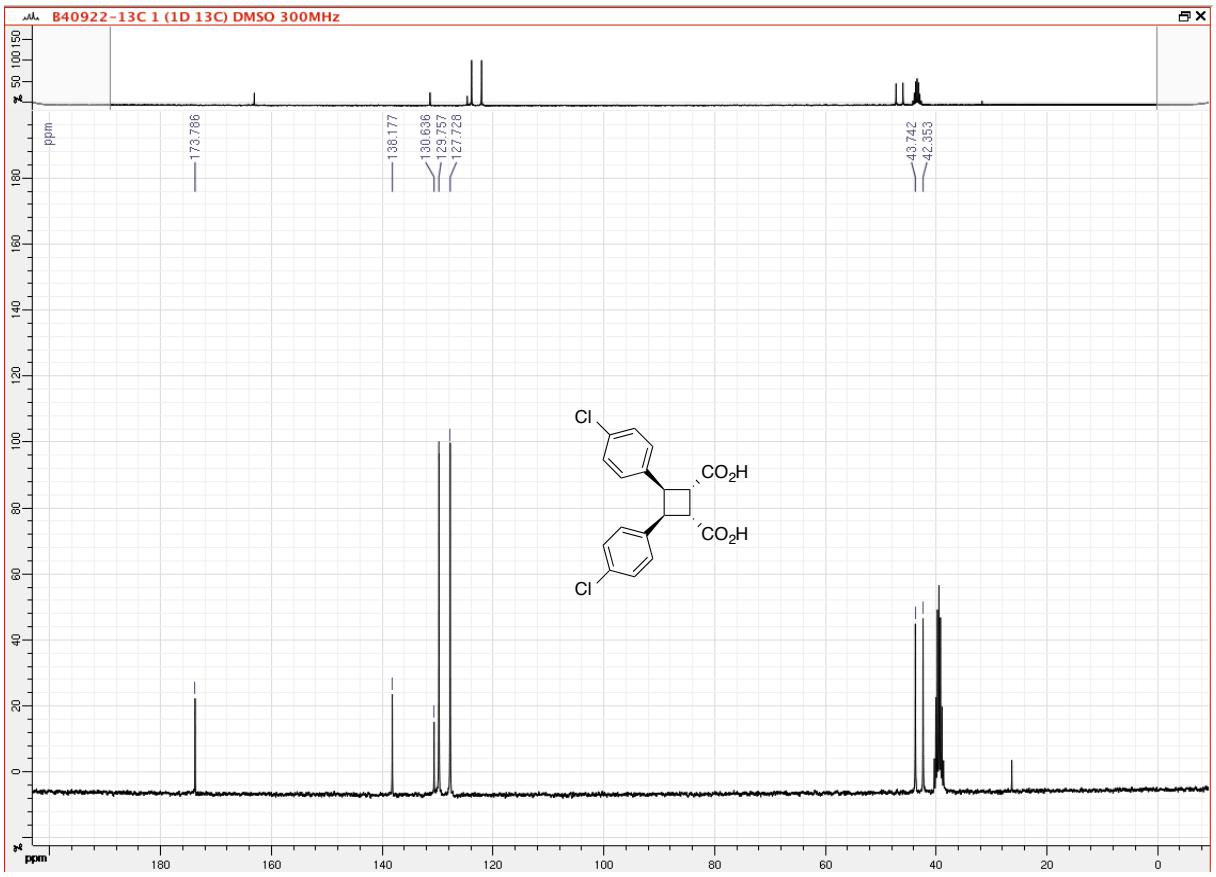
(1*R*,2*S*,3*R*,4*S*)-2,4-*bis*(2-hydroxyphenyl)cyclobutane-1,3-dicarboxylic acid (F_2)



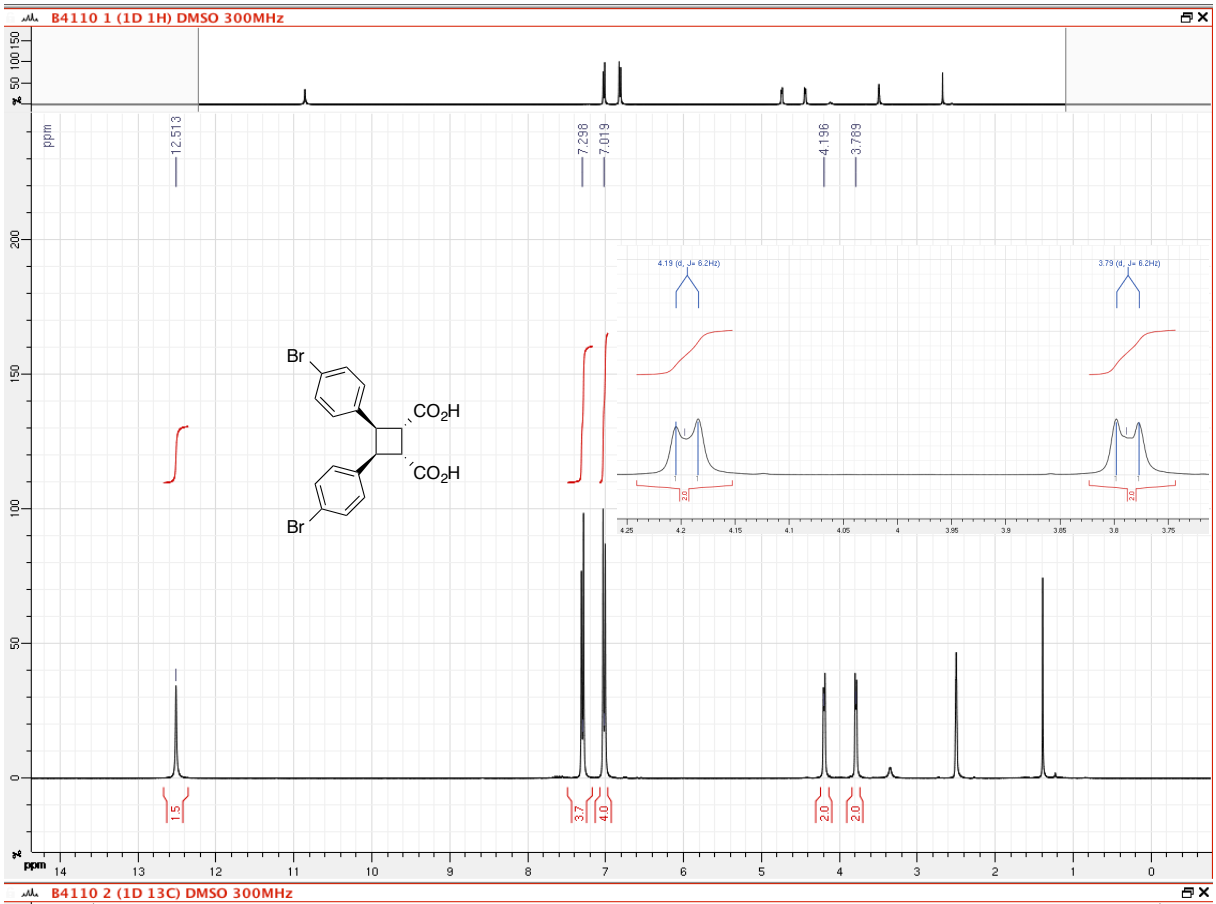


(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(4-chlorophenyl)cyclobutane-1,2-dicarboxylic acid (G_2)

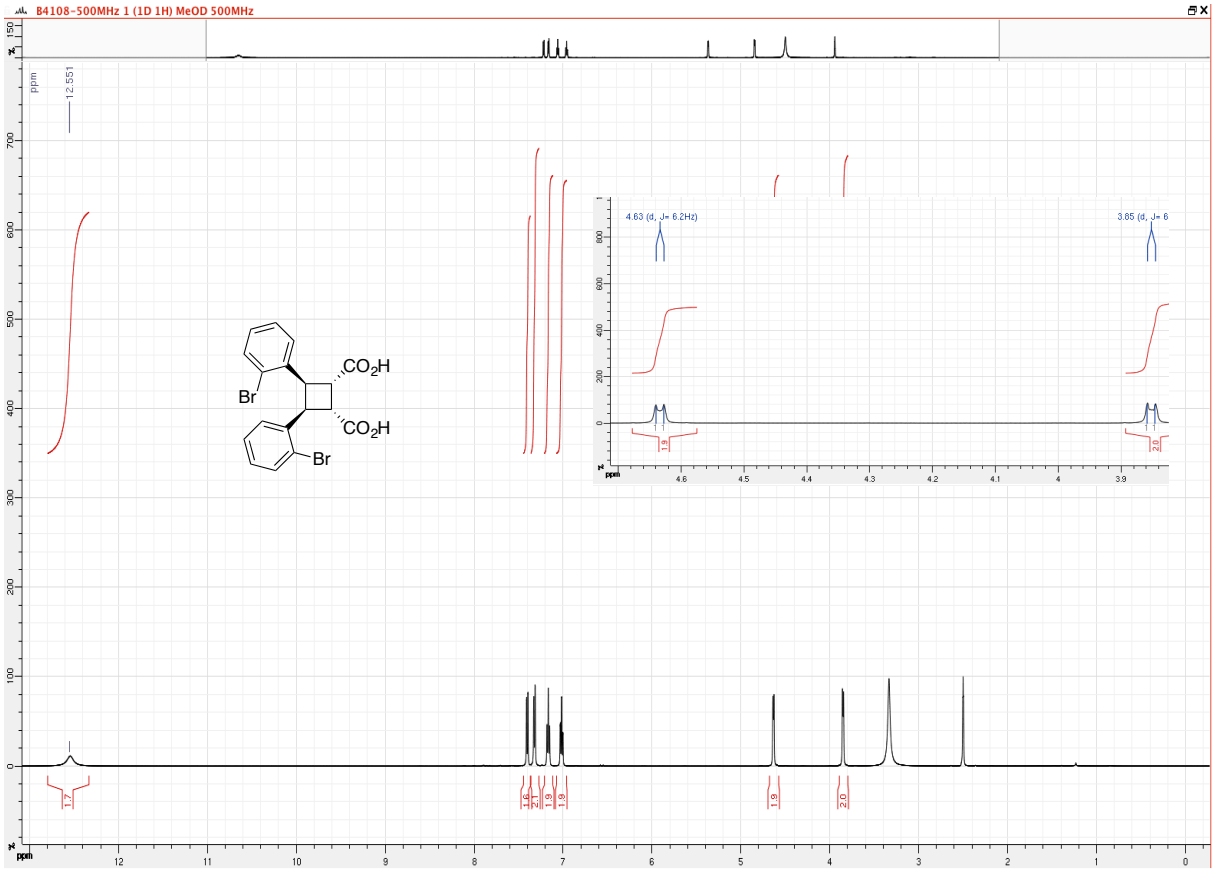


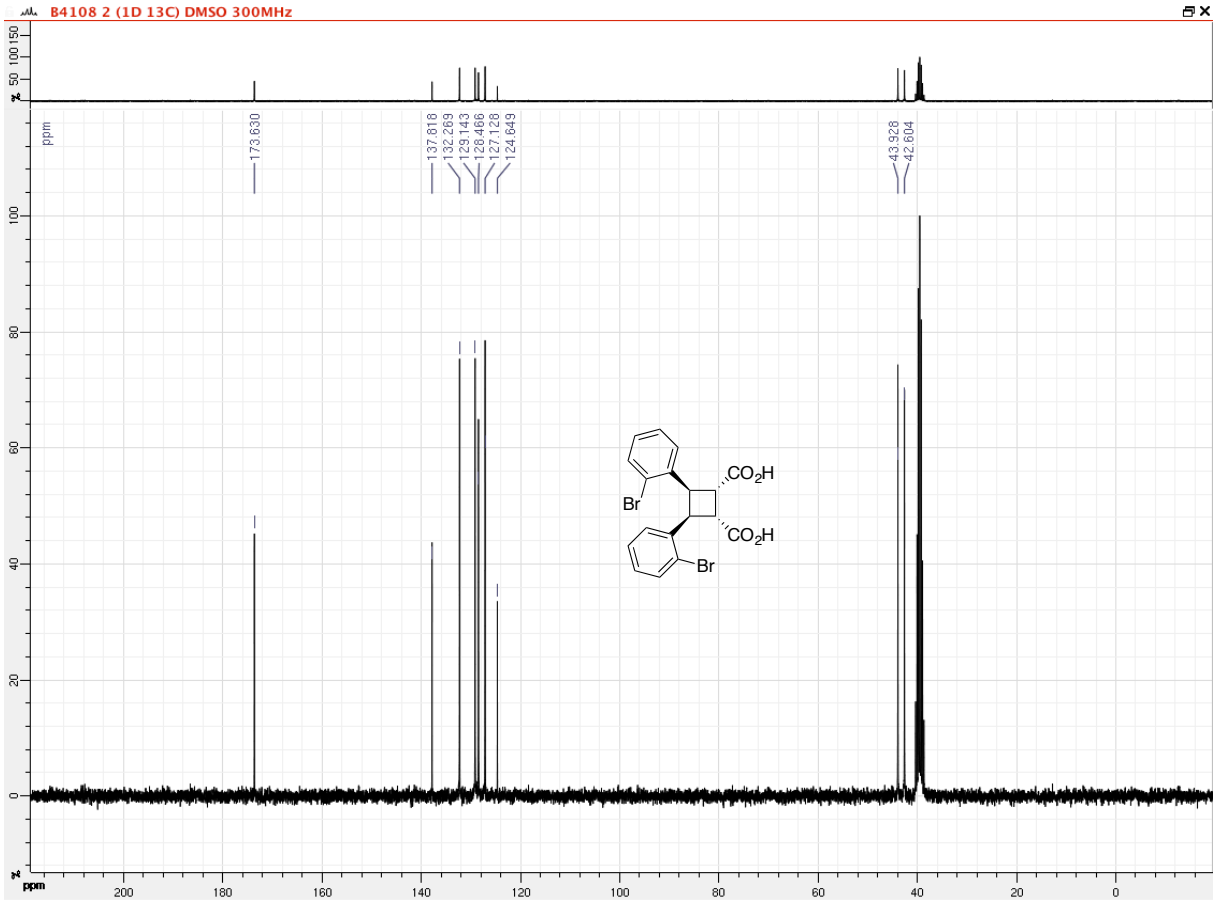


(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(4-bromophenyl)cyclobutane-1,2-dicarboxylic acid (H_2)

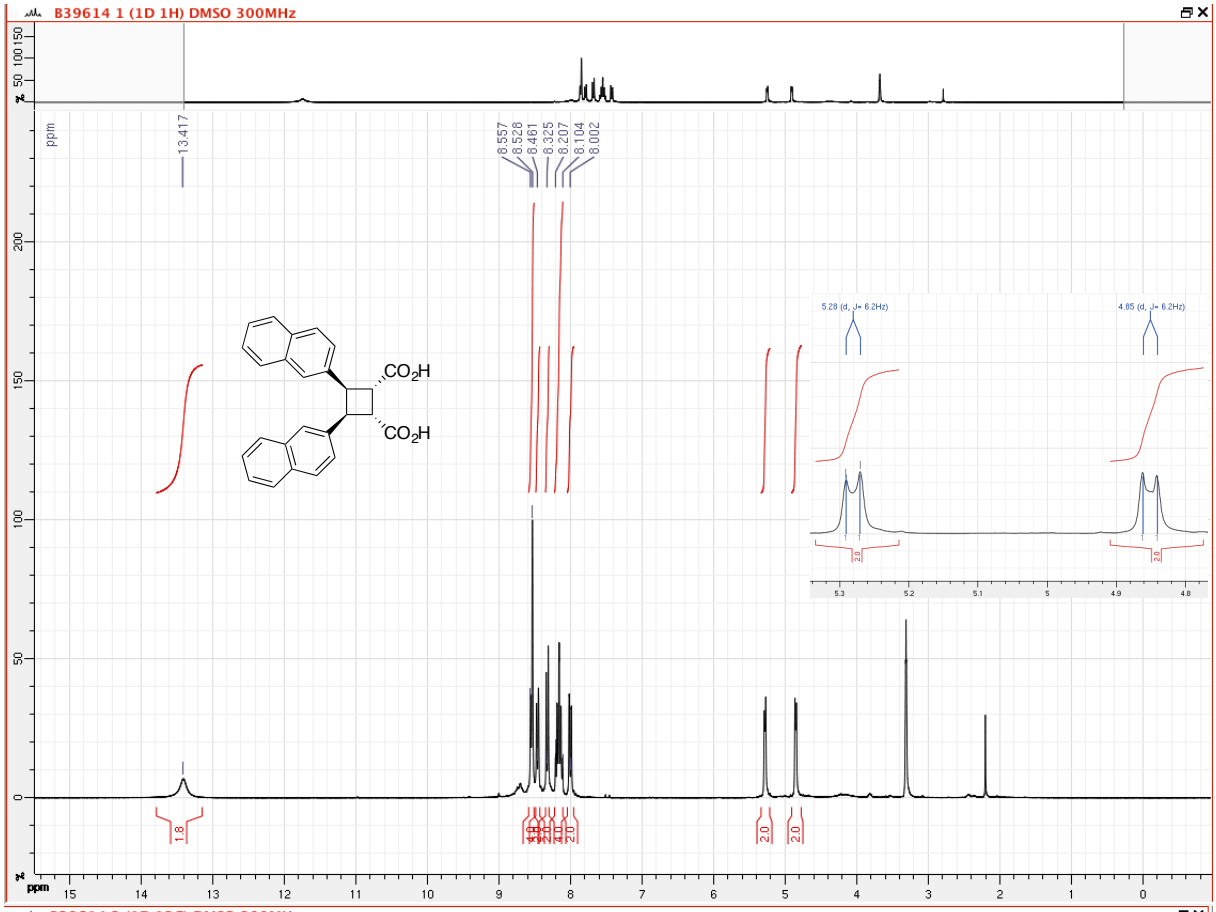


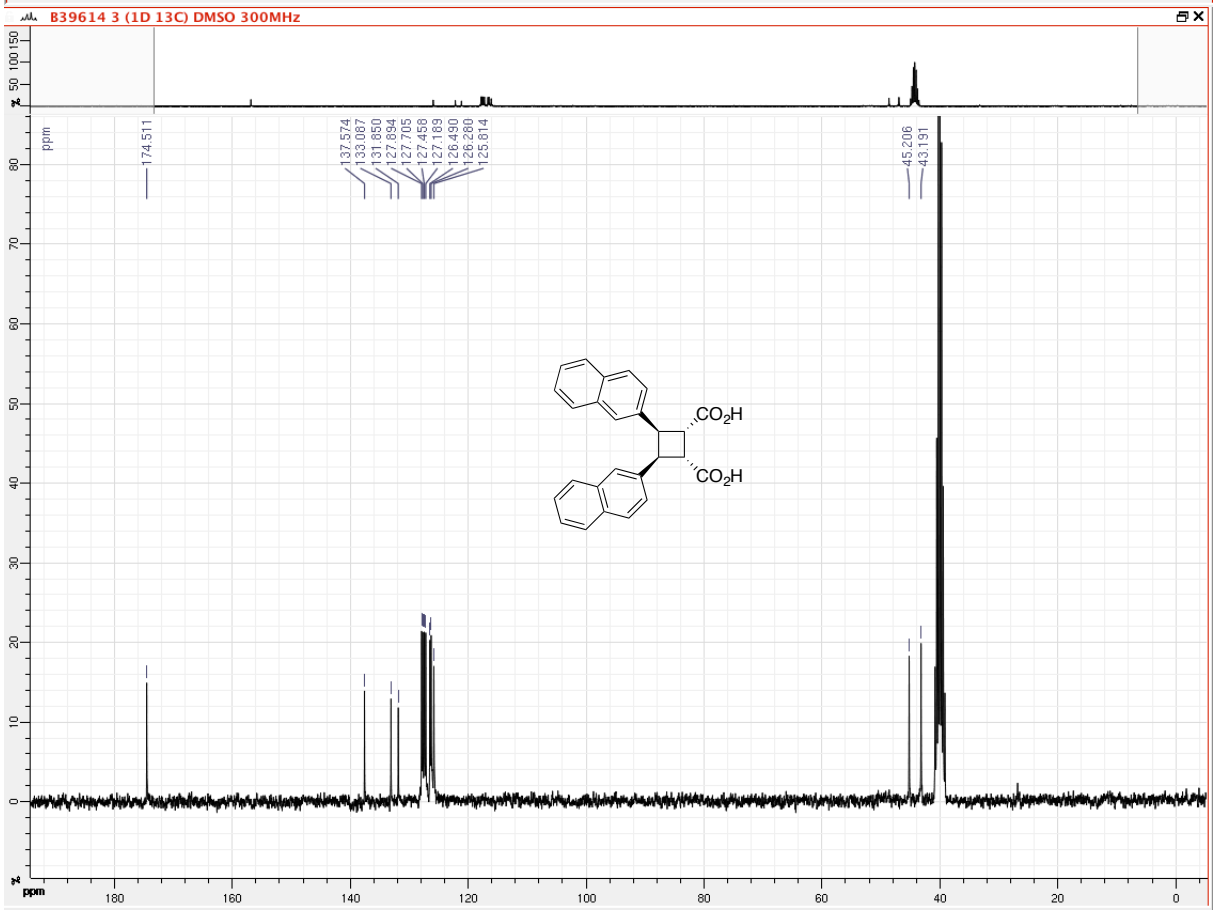
(1*R*,2*S*,3*R*,4*S*)-3,4-*bis*(2-bromophenyl)cyclobutane-1,2-dicarboxylic acid (E_2)



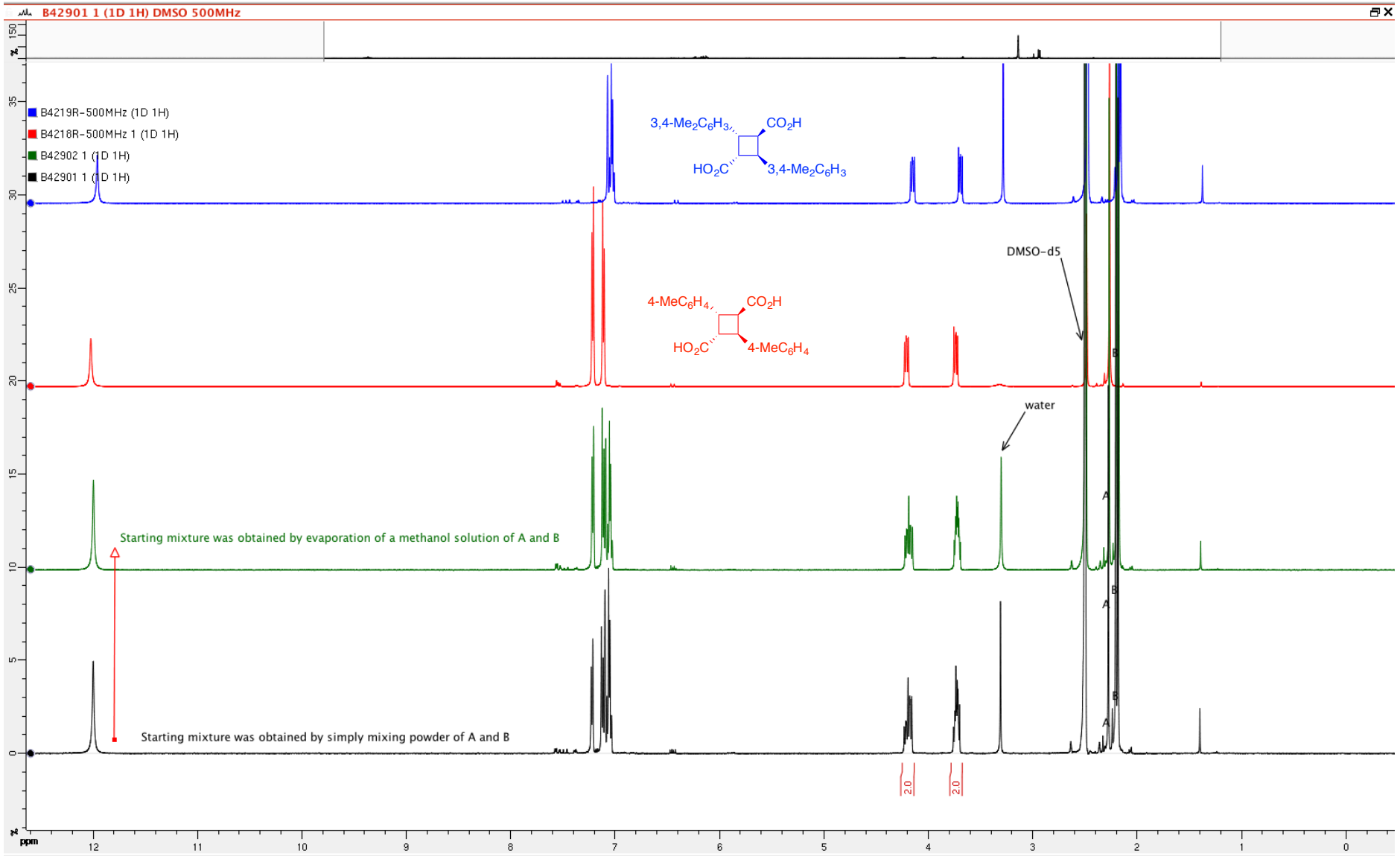


(1*R*,2*S*,3*R*,4*S*)-3,4-di(naphthalen-2-yl)cyclobutane-1,2-dicarboxylic acid (J_2)

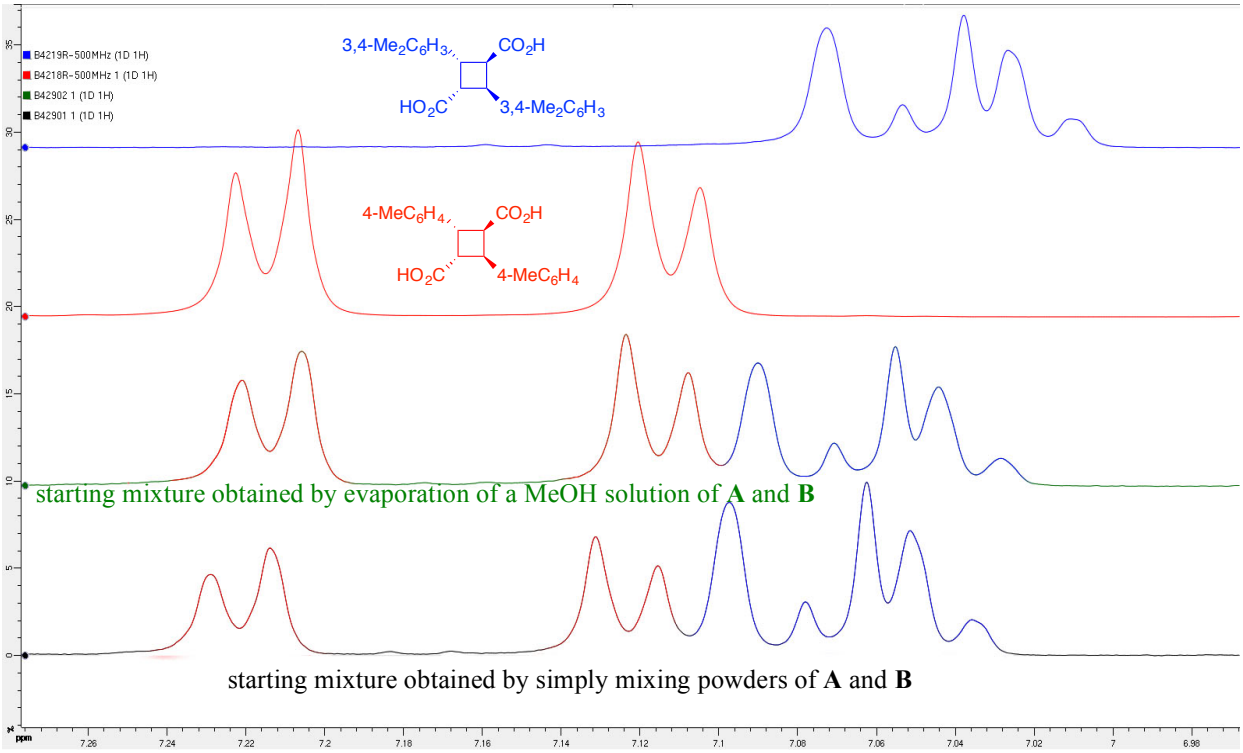




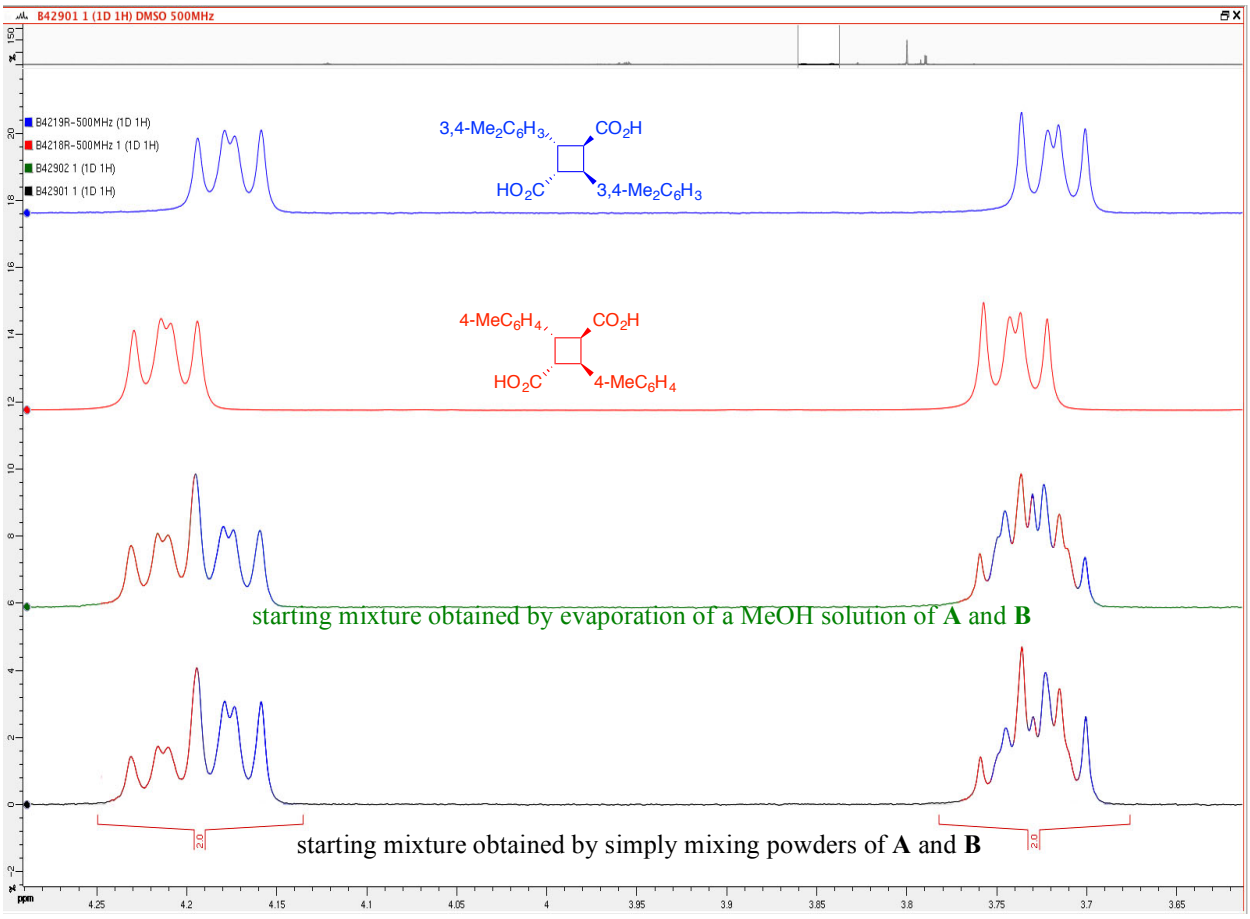
[2 + 2] Photodimerization of an equimolar solid mixture of A and B dispersed in cyclohexane (Scheme 2a)



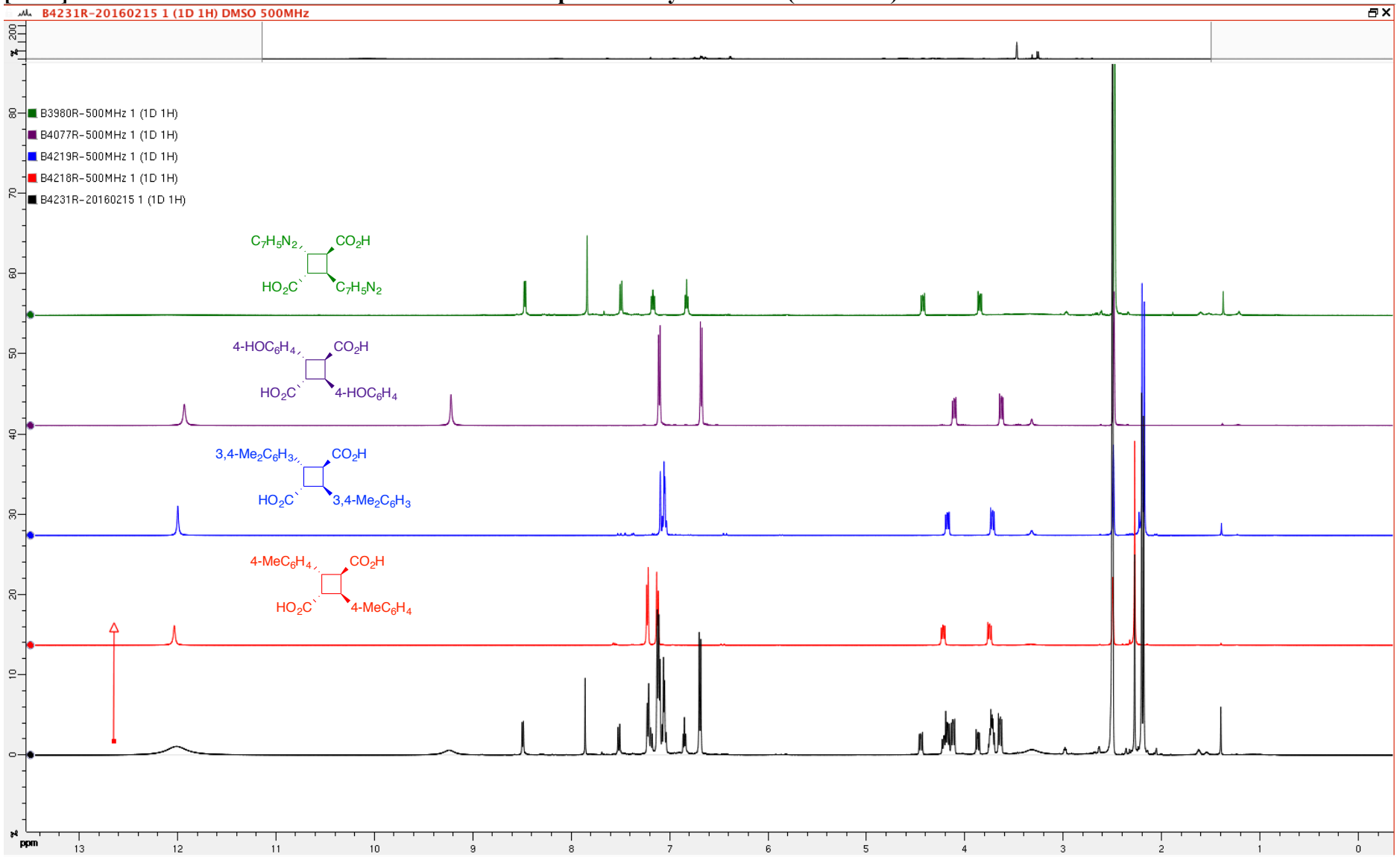
Aromatic zone (Scheme 2b)



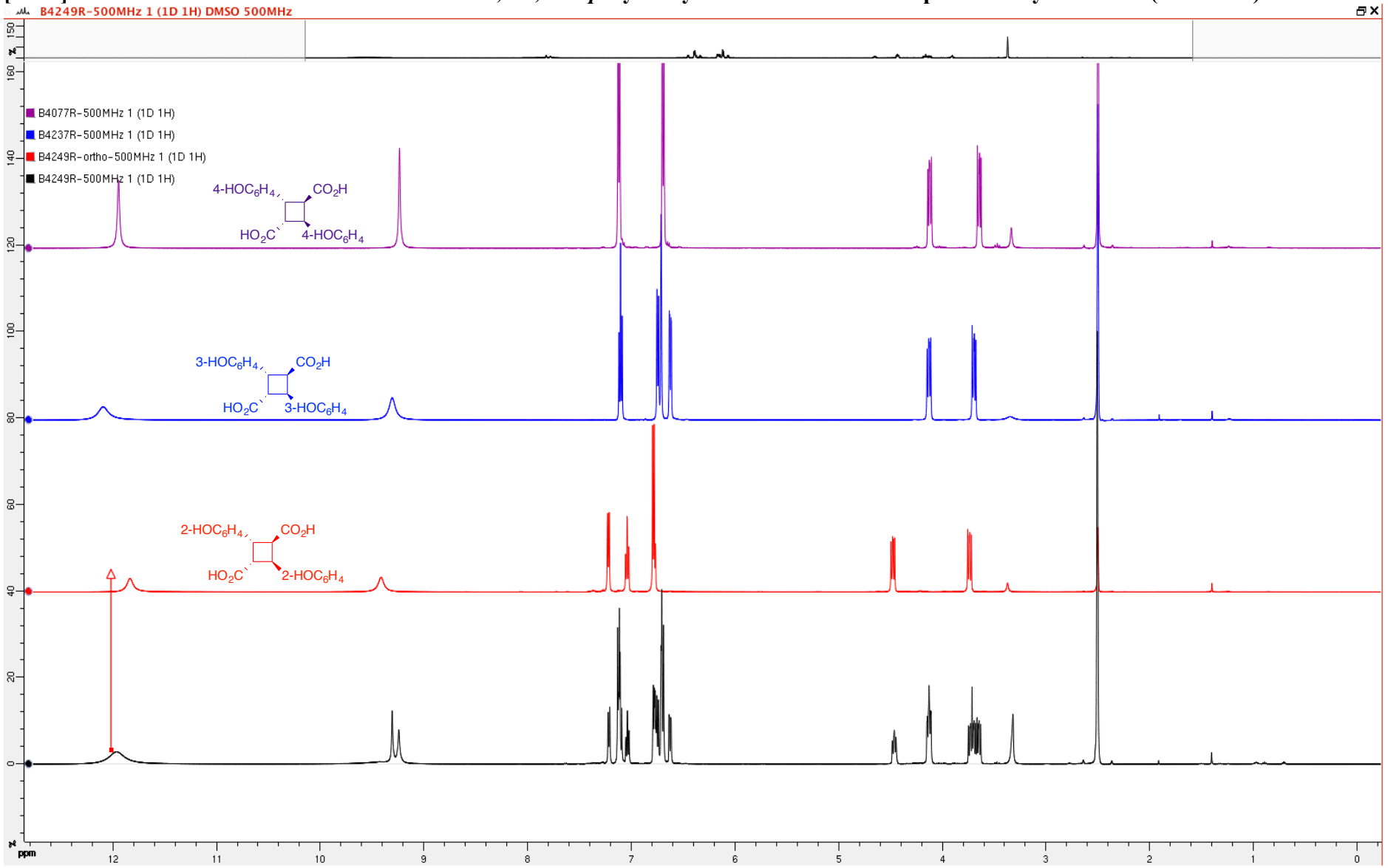
cyclobutane proton signals (Scheme 2c)



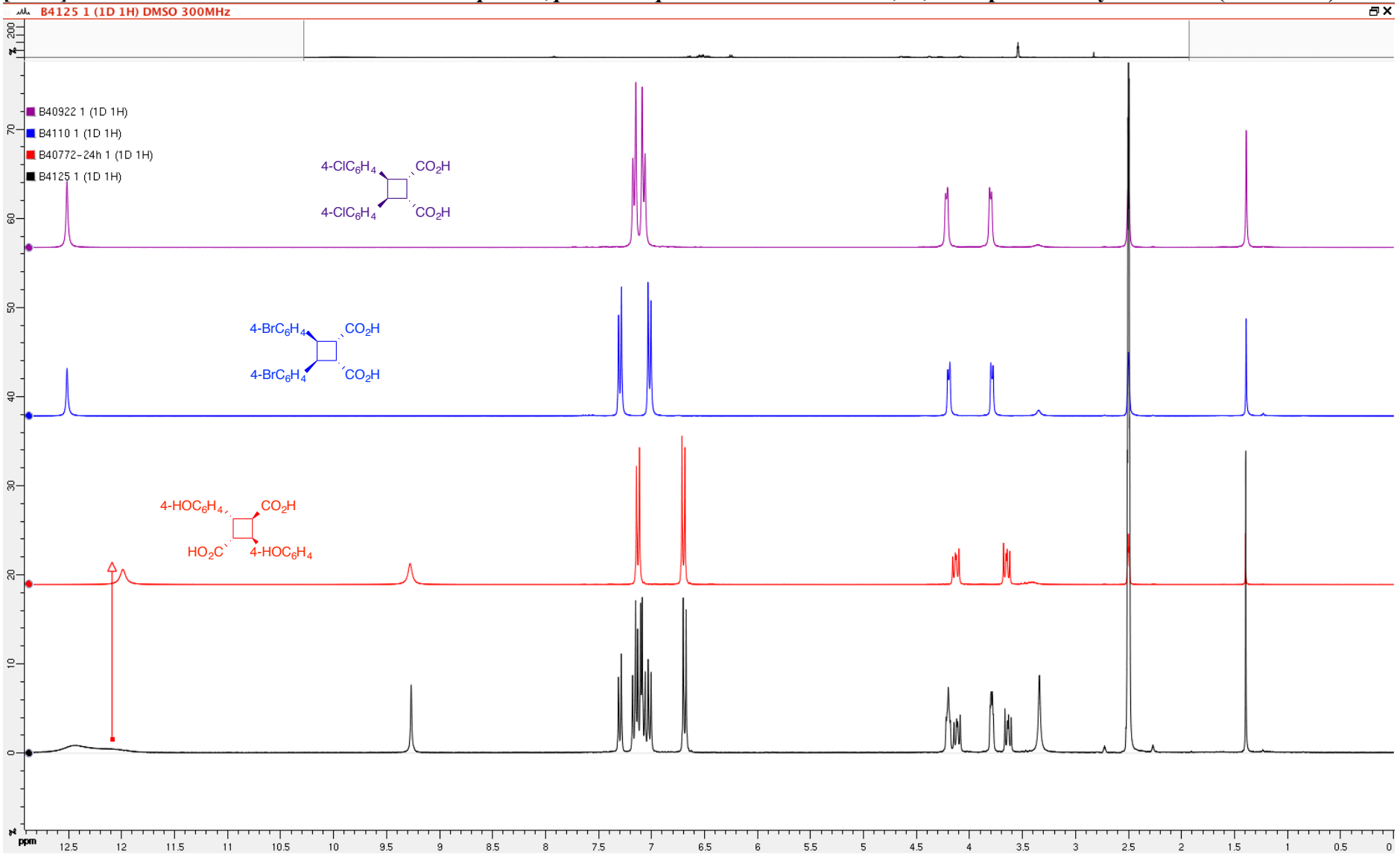
[2 + 2] Photodimerization of a solid mixture of A-D dispersed in cyclohexane (Scheme 3)



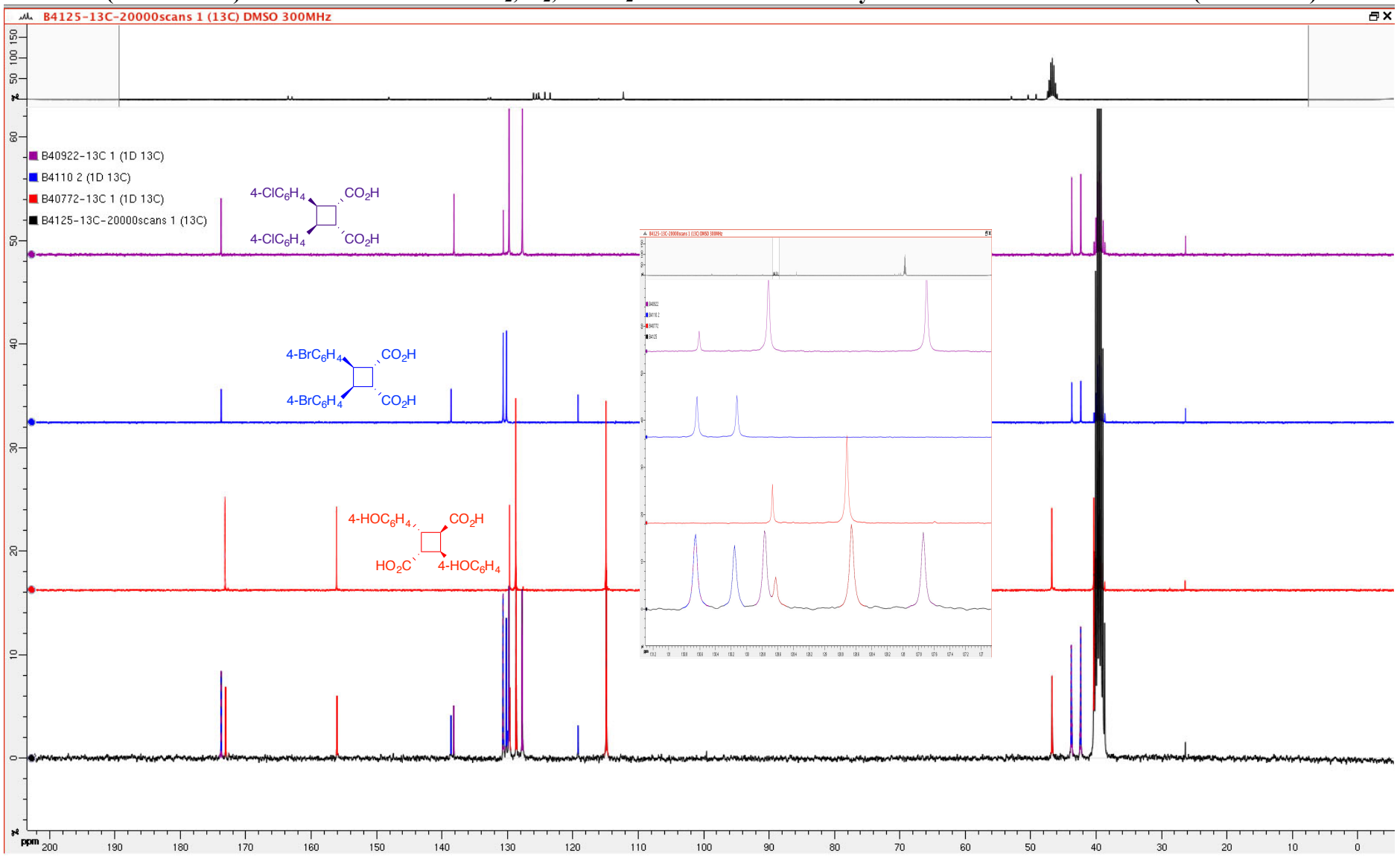
[2 + 2] Photodimerization of a solid mixture of *o*-, *m*-, and *p*-hydroxycinnamic acids D-F dispersed in cyclohexane (Scheme 4)



[2 + 2] Photodimerization of a solid mixture of *p*-HO-, *p*-Cl- and *p*-Br- cinnamic acids D, G, H dispersed in cyclohexane (scheme 5a)



^{13}C NMR (20000 scans) of the crude mixture of D_2, G_2, and H_2 showed no trace of any cross adduct could be detected (Scheme 5b)



[2 + 2] Photodimerization of a solid mixture of six cinnamic acids D-F, H-J dispersed in cyclohexane (Scheme 6)