Selective Synthesis of (Benzyl)biphenyls by Successive Suzuki-Miyaura Coupling of Phenylboronic Acids with 4-Bromobenzyl Acetate under Air Atmosphere

Masato Ohsumi*† and Nagatoshi Nishiwaki*‡§

†Kochi National College of Technology, Nankoku, Kochi 783-8508, Japan

‡School of Environmental Science and Engineering, Kochi University of Technology, Tosayamada, Kami, Kochi 782-8502, Japan

§Research Center for Material Science and Engineering, Kochi University of Technology, Tosayamada, Kami, Kochi 782-8502, Japan

*E-mail: nishiwaki.nagatoshi@kochi-tech.ac.jp.

Tel: +81-887-57-2517, Fax: +81-887-57-2520 (N.N.).

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General

All the reagents and solvents were commercially available and used as received. The ^{1}H NMR spectra were measured on a JEOL 400 spectrometer at 400 MHz with TMS as an internal standard. The ^{13}C NMR spectra were measured on a JEOL 400 spectrometer at 100 MHz. The IR spectra were recorded on a JASCO FT/IR-4100 spectrometer. The melting points were determined on an As-one melting-points apparatus ATM-02, and were uncorrected. The high resolution mass spectra were measured on a JEOL JMS-700N. Gas chromatography (GC) was performed with Shimadzu GC 8A. Flash column chromatography was performed with Wako-gel C-200 (100–200 mesh, Wako). Benzyl carbonates were prepared according to literature procedures.[1]

General procedure of the Suzuki–Miyaura coupling reaction

To a solution of $PdCl_2$ (1.8 mg, 10 μmol), DPEPhos (5.9 mg, 11 μmol), $NaHCO_3$ (50.2 mg, 0.6 mmol) and phenylboronic acid **2a** (36.6 mg, 0.3 mmol) in ethanol (1.0 mL), benzyl carbonate **1a** (33.2 mg, 0.2 mmol) was added, and the resultant mixture was heated in a screw capped sealed tube at 80 °C for 3 h. After filtration using a Celite pad, the filtrate was extracted with hexane (10 mL x 3). The combined organic layer was washed with brine (10 mL x 1), dried over $MgSO_4$, and concentrated under reduced pressure. The residue was treated with flash column chromatography (EtOAc/hexane = 90/10) to afford the coupling product **3a** (26.5 mg, 0.158 mmol, 79%).

When other conditions and substrates were employed, the experiments were conducted in a similar way.

Screening of the reaction conditions

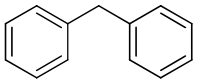
When the reaction conditions were screened, the experiments were conducted in a similar way with the last section except for the column chromatography. The yield was determined by GC by calibration curve that was prepared beforehand using naphthalene as an internal standard.

Structural confirmation of the products

All products except for **7** and **8** are known compounds. The structures of products were confirmed by comparing the ^{1}H NMR spectra with those of authentic samples. The purity of the isolated products was confirmed by gas chromatography as shown in next pages (the large peak within 1 min. retention time belongs to the solvent (AcOEt)).

GC conditions
Gas (flow rate): N_2 (60 mL/min), H_2(50 mL/min), Air (500 mL/min)
Carrier gas: N_2
Temperature: Injector 250 °C, Column 180–230 °C
Column: Glass column with 3 mm diameter and 3 m length
Packed with Silicone DC550/20%
Detection: FID

Figure S1. Compound **3a**[2]



3a

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3a**: 3.682 min

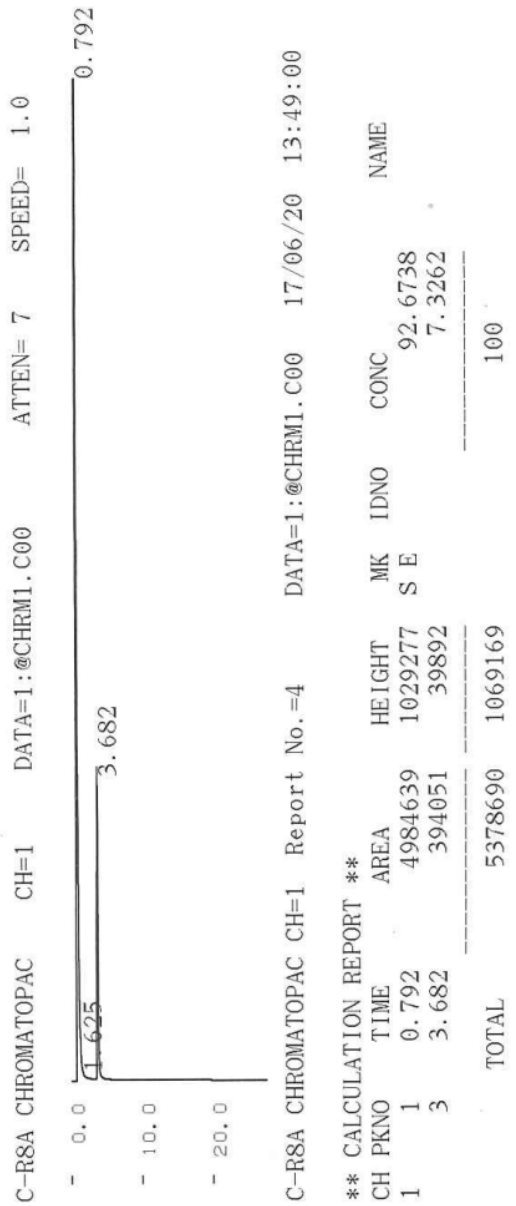
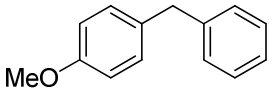


Figure S2. Compound **3b**[2]



3b

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3b**: 12.222 min

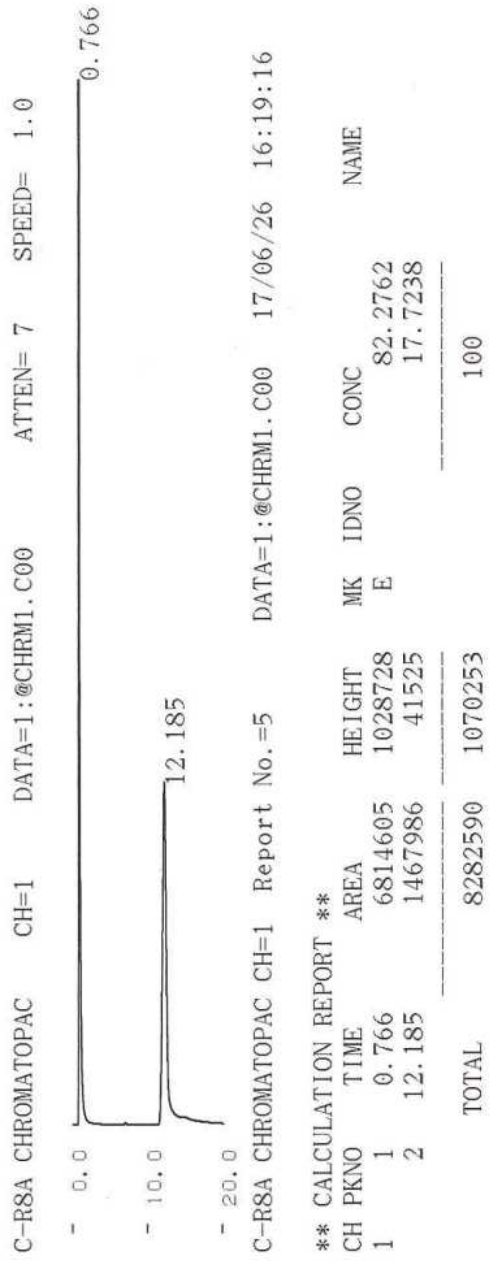
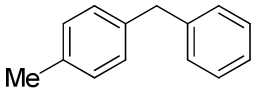


Figure S3. Compound **3c**[2]



3c

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3c**: 5.181 min

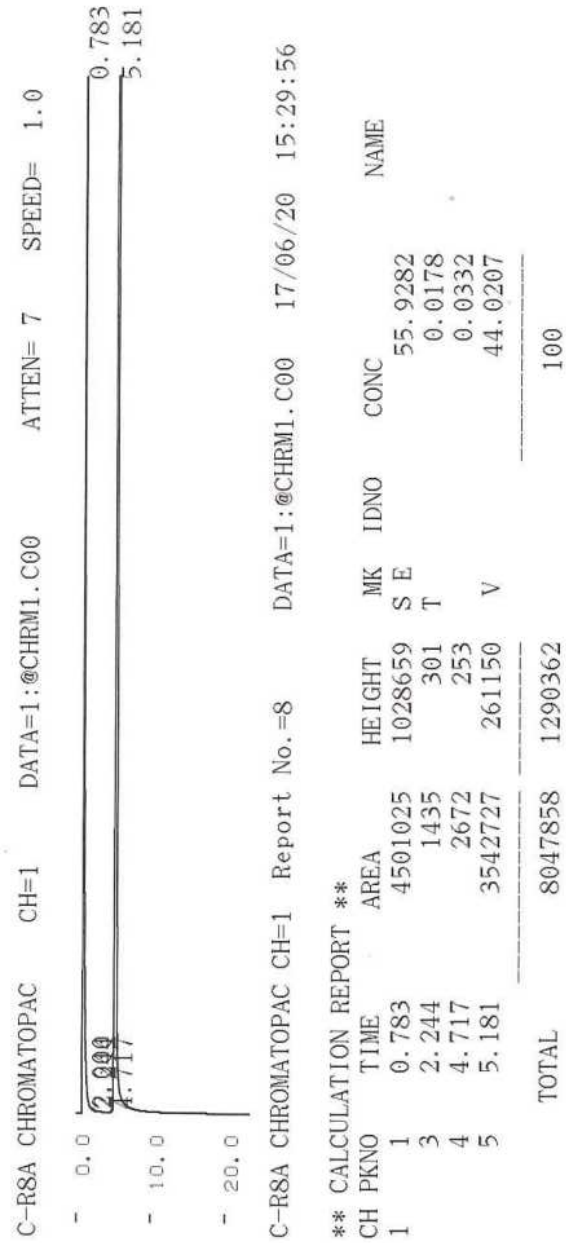
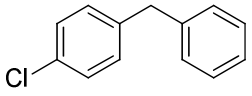


Figure S4. Compound **3d**[2]



3d

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3d**: 7.670 min

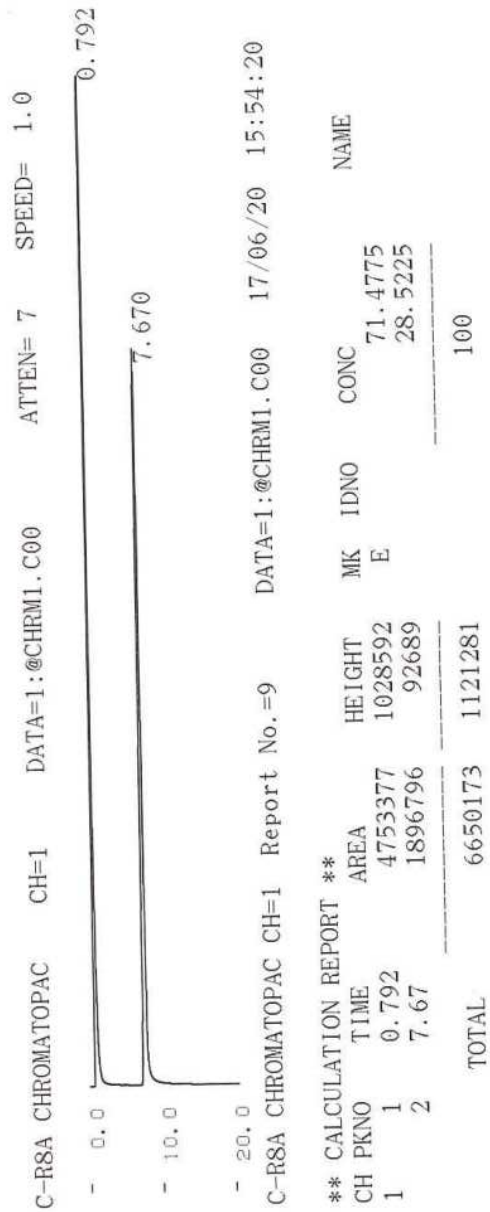
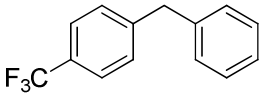


Figure S5. Compound **3e**[2]



3e

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3e**: 3.214 min

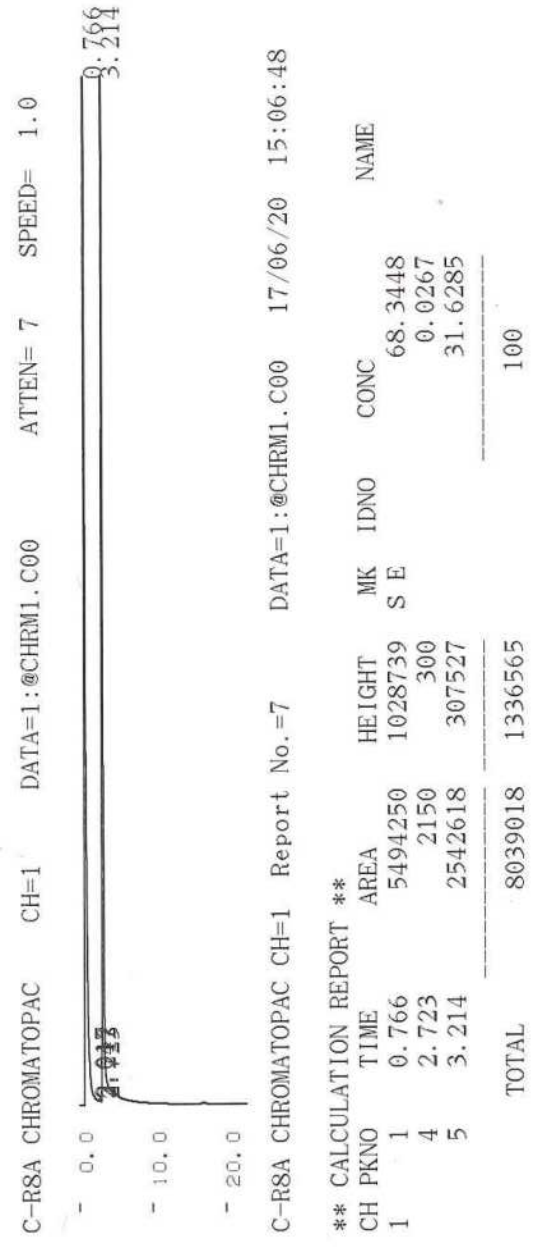
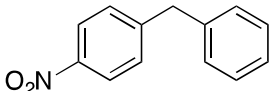


Figure S6. Compound **3f**[3]



3f

Colorless Oil

Injector 250 °C / Column 230 °C

Retention time of **3f**: 9.018 min

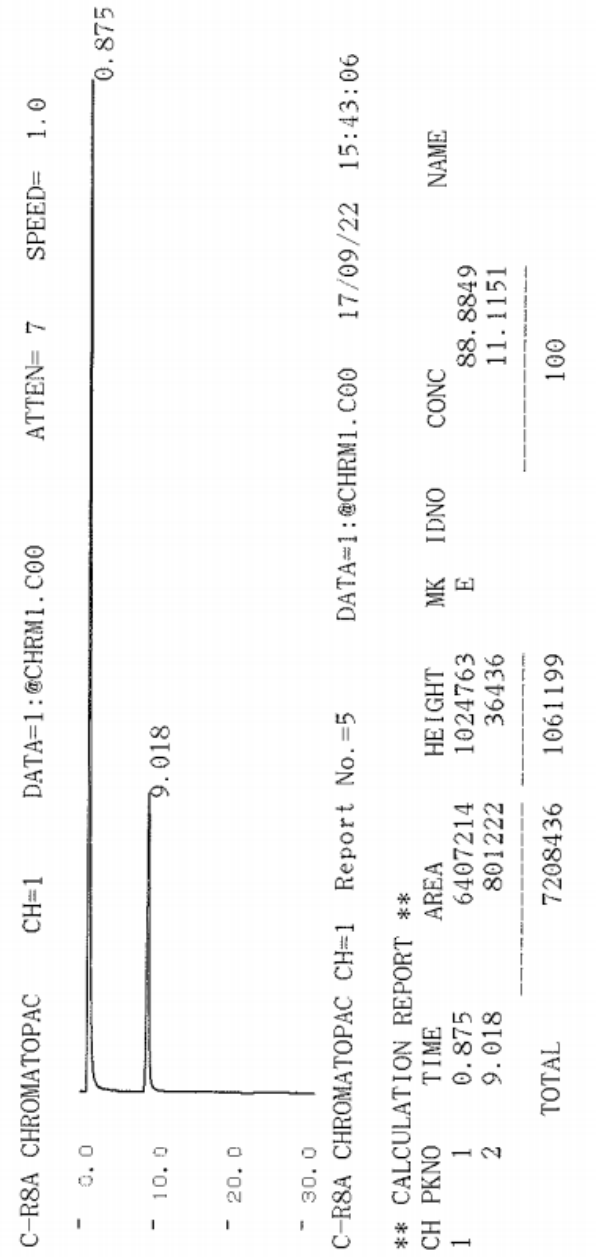
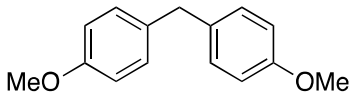


Figure S7. Compound **3g**[4]



3g

Colorless oil

Injector 250 °C / Column 200 °C

Retention time of **3f**: 14.559 min

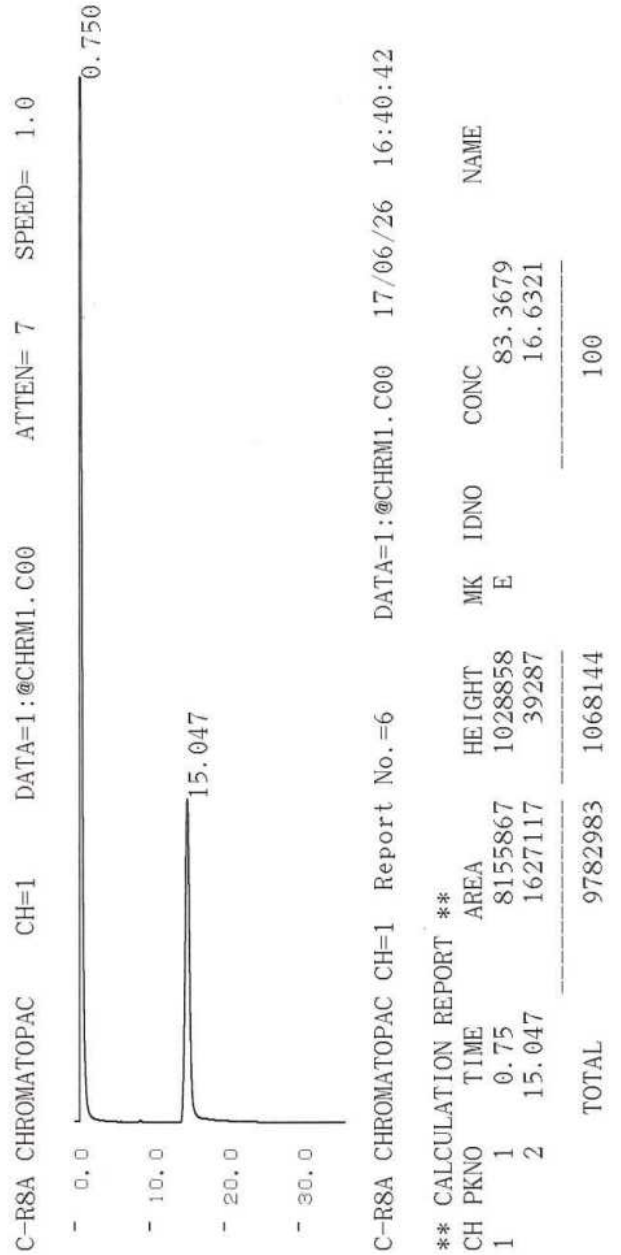
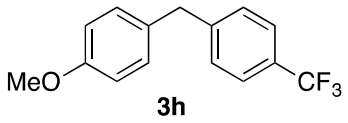


Figure S8. Compound **3h**[5]



3h

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3h**: 9.090 min

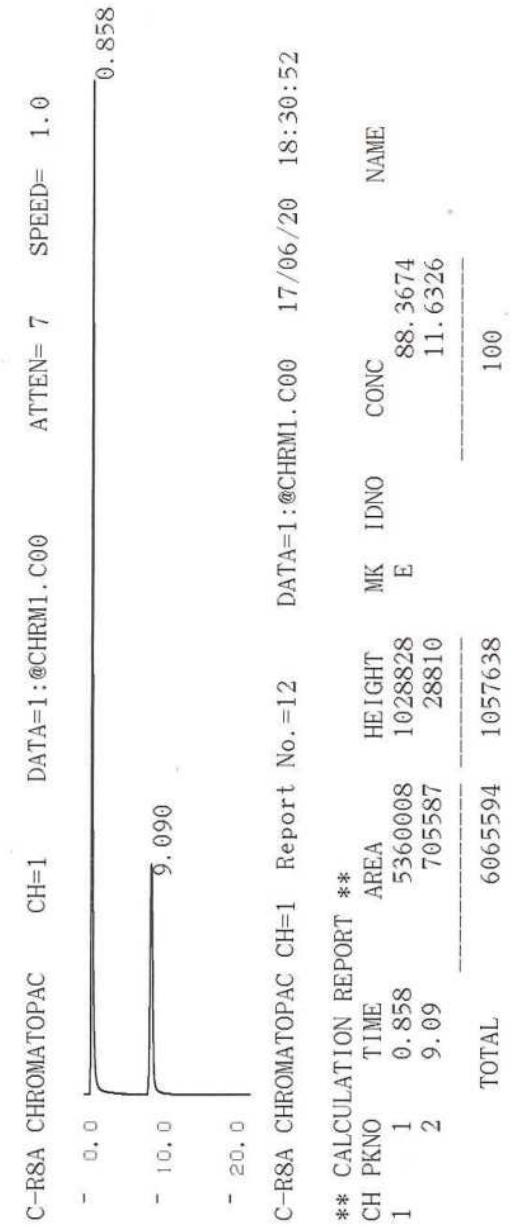
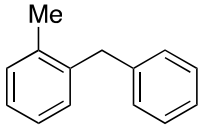


Figure S9. Compound **3i**[6]



3i

Colorless oil

Injector 250 ℃ / Column 180 ℃

Retention time of **3i**: 5.108 min

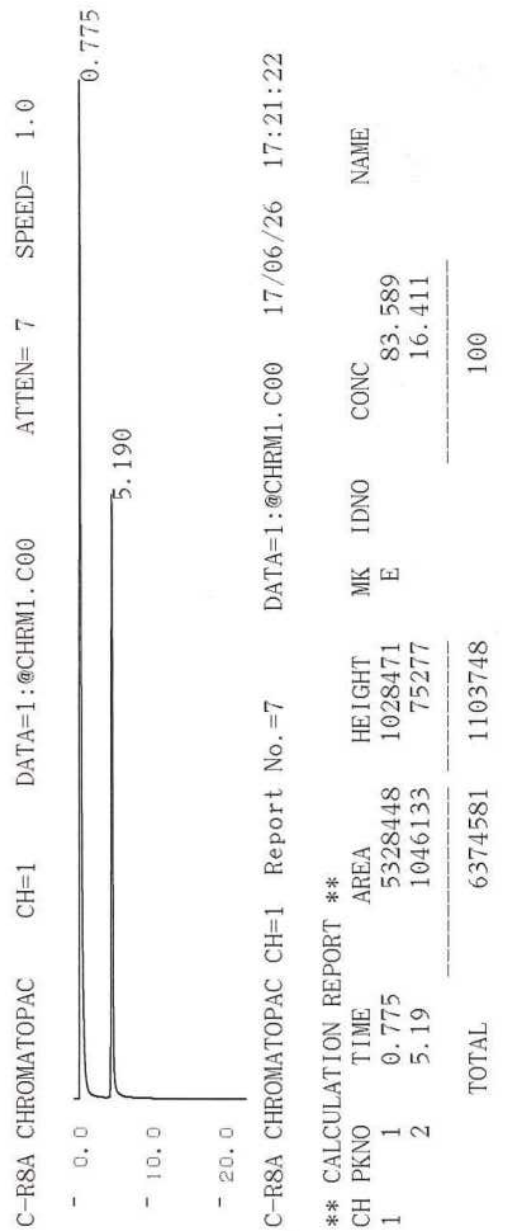
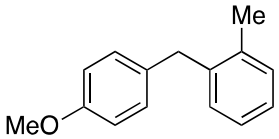


Figure S10. Compound **3j**[5]



3j

Colorless oil

Injector 250 ℃ / Column 180 ℃

Retention time of **3j**: 10.715 min

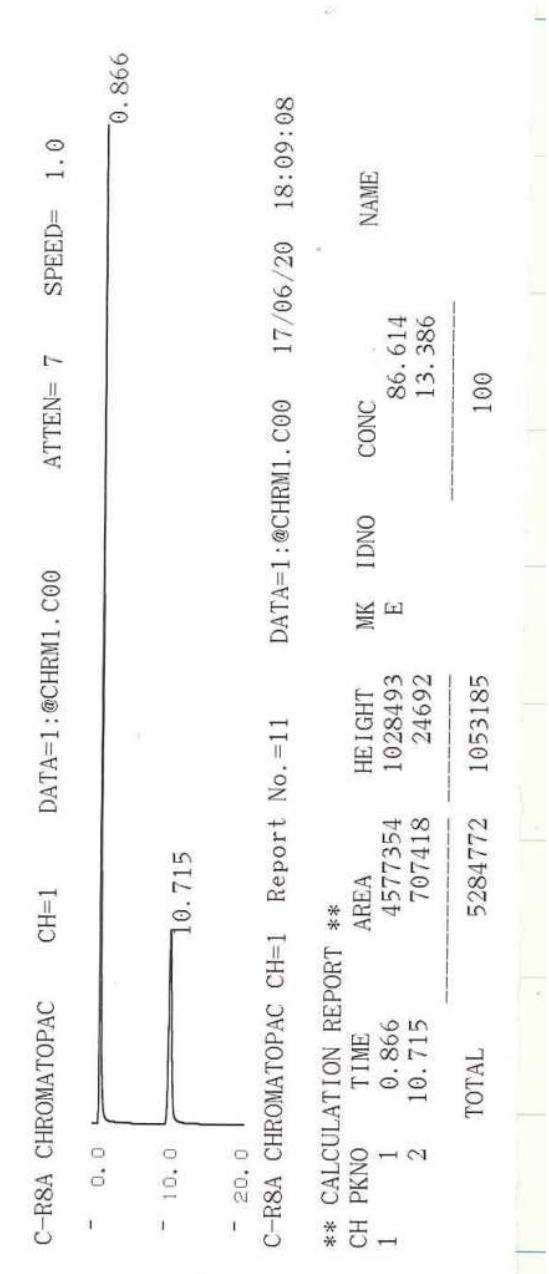
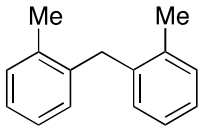


Figure S11. Compound **3k**[2]



3k

Colorless oil

Injector 250 °C / Column 180 °C

Retention time of **3k**: 6.383 min

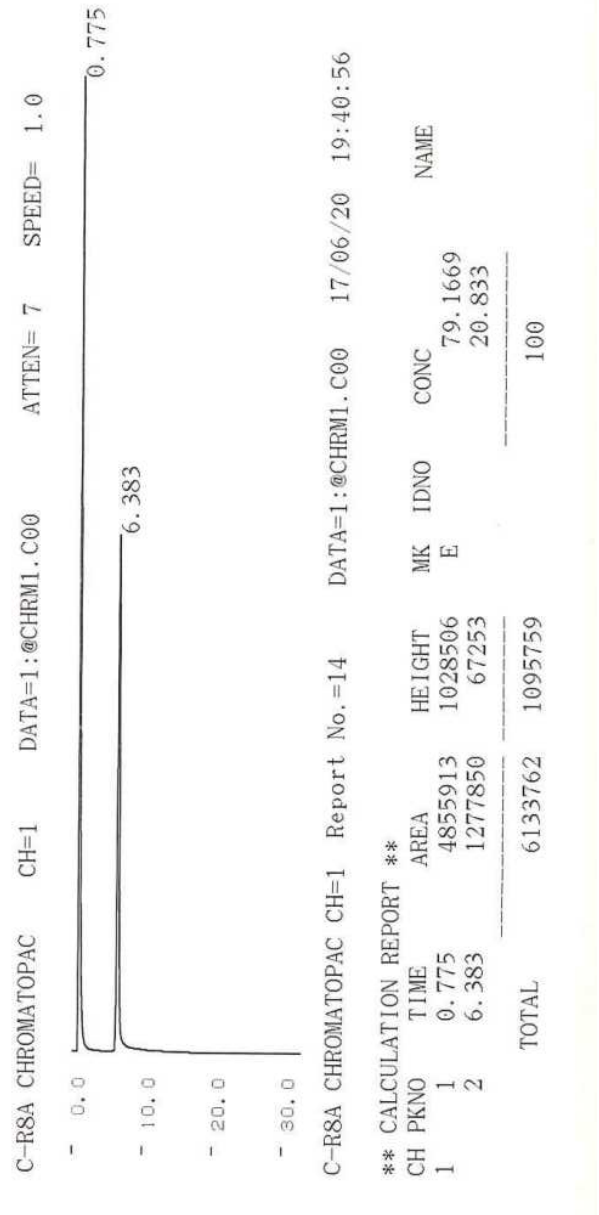
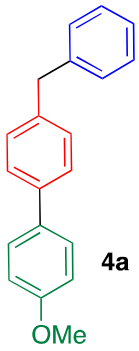


Figure S12. Compound **4a**[7]

White solid

Injector 250 ℃ / Column 240 ℃

Retention time of **4a**: 27.138 min



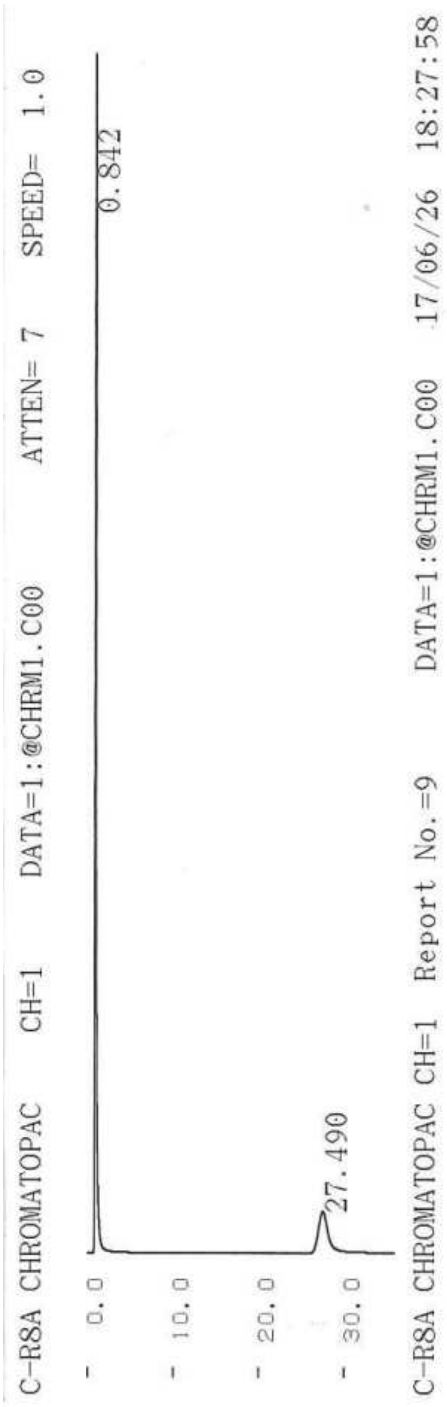
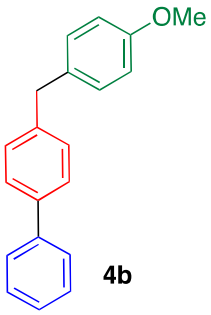


Figure S13. Compound **4b**[8]

White solid

Injector 250 ℃ / Column 240 ℃

Retention time of **4b**: 26.255 min



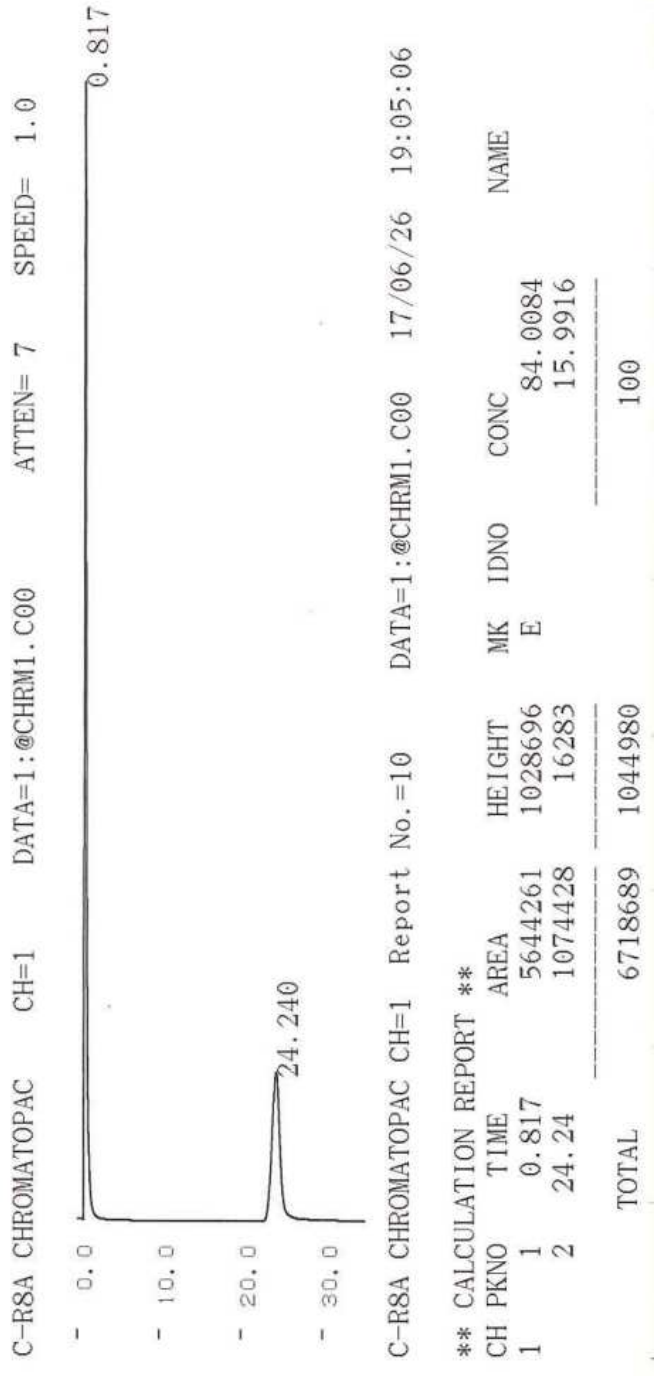
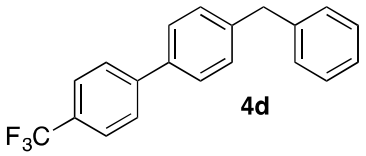


Figure S14. Compound **4d**[9]



White solid

Injector 250 °C / Column 230 °C

Retention time of **4d**: 22.662 min

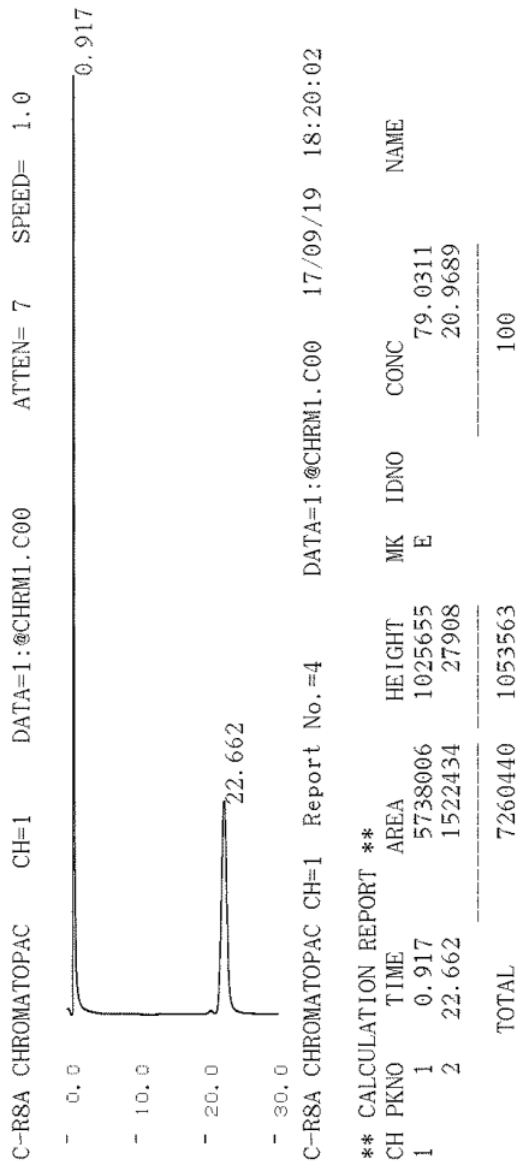
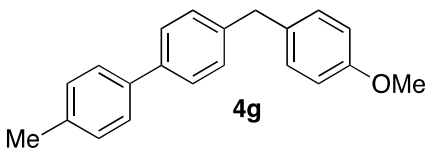
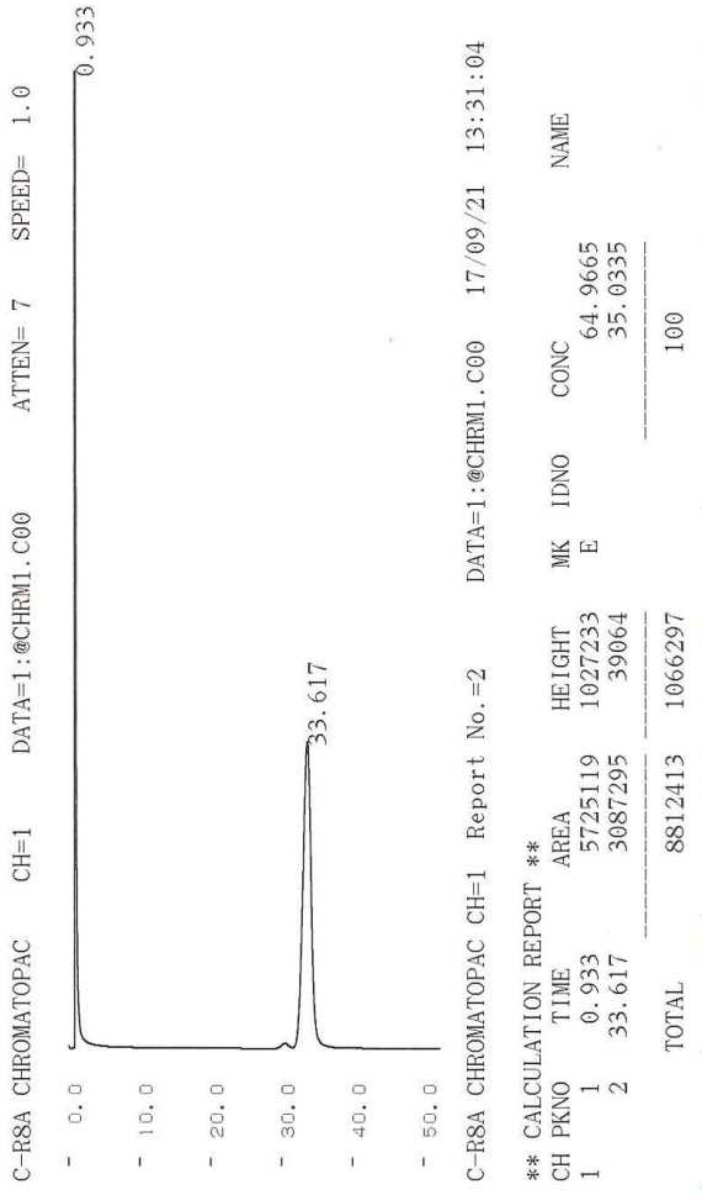


Figure S15. Compound **4g**[10]



White solid
Injector 250 °C / Column 240 °C
Retention time of **4g**: 22.662 min



References

(1) Selva, M.; Benedet, V.; Fabris, M. *Green Chem.* **2012**, *14*, 188

(2) Pal, S.; Chowdhury, S.; Rozwadowski, E.; Auffrant, A.; Gosmini, C. *Adv. Synth. Cat.* **2016**, *358*, 2431–2435.

(3) Singh, M. K.; Lakshman, M. K. *ChemCatChem* **2015**, *7*, 4156–4162.
(4) Ueda, M.; Nakakoji, D.; Kuwahara, Y.; Nishimura, K.; Ryu, I. *Tetrahedron Lett.* **2016**, *57*, 4142–4144.
(5) Zhang, J.; Gusheng, G.; Xu, J.; Sun, H.; Shen, Q. *Org. Lett.* **2016**, *18*, 2860–2863.
(6) Zhu, J.; Perez, M.; Douglas, D. W. *Angew. Chem. Int. Ed.* **2016**, *55*, 8448–8451.
(7) Ronson, T. O.; Carney, J. R.; Whitwood, A. C.; Taylor, R. J. K.; Fairlamb, I. J. S. *Chem. Commun.* **2015**, *51*, 3466–3469.
(8) Wang, X.-X.; Luo, M.-J.; Lu, J.-M. *Org. Biomol. Chem.* **2015**, *13*, 11438–11444.
(9) Kim, W.-K.; Jang, J.-H.; Jo, H.; Park, K. *ACS Comb. Sci.* **2014**, *16*, 225–231.
(10) Rao, M. L. N.; Dhanorkar, R. J. *RSC Adv.* **2013**, *3*, 6794–6798.

4’-phenyl-4-[(4-trifluoromethylphenyl)methyl]-1,1’-biphenyl (4c) ($CDCl_3$)
Figure S16.

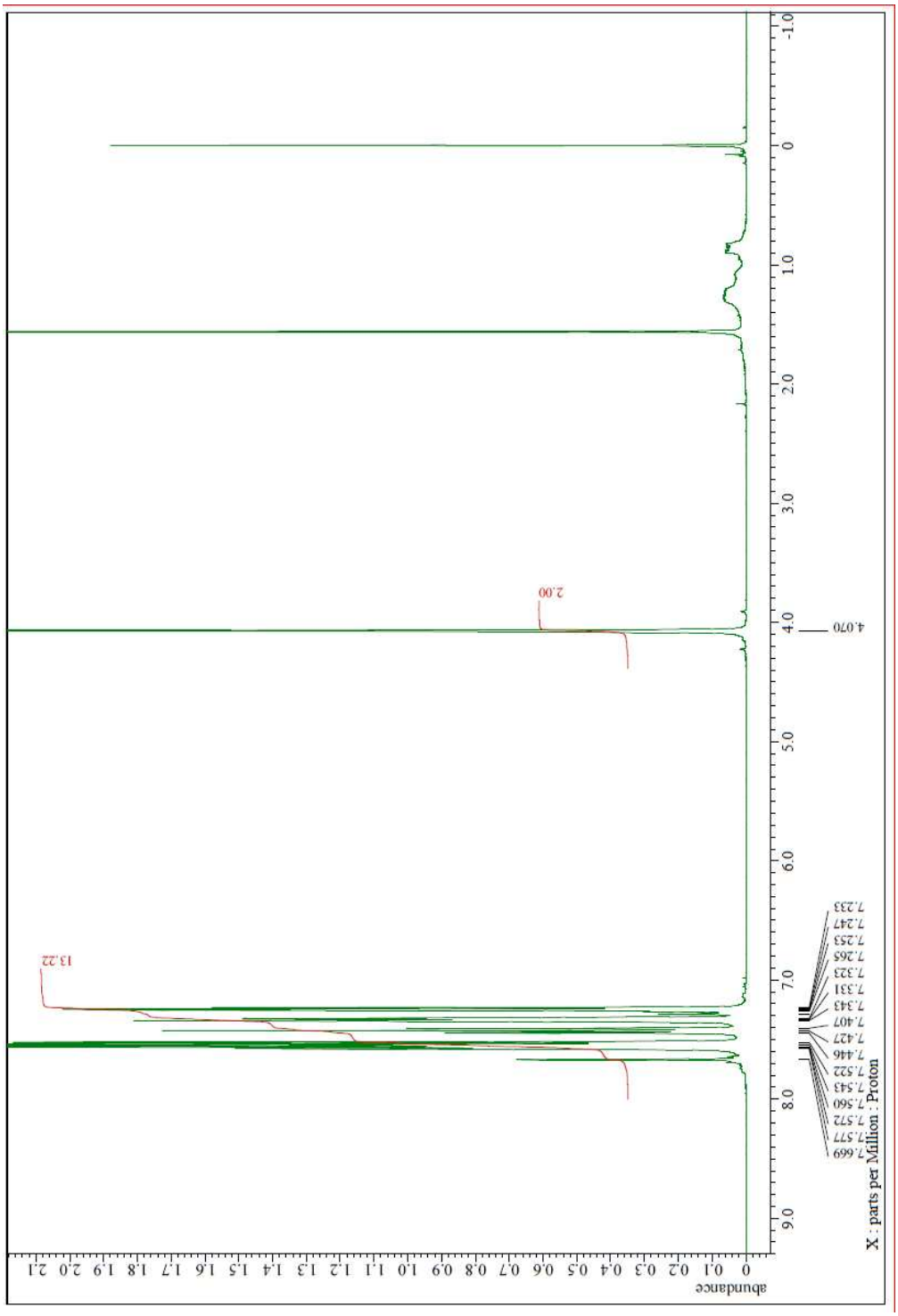


Figure S17.

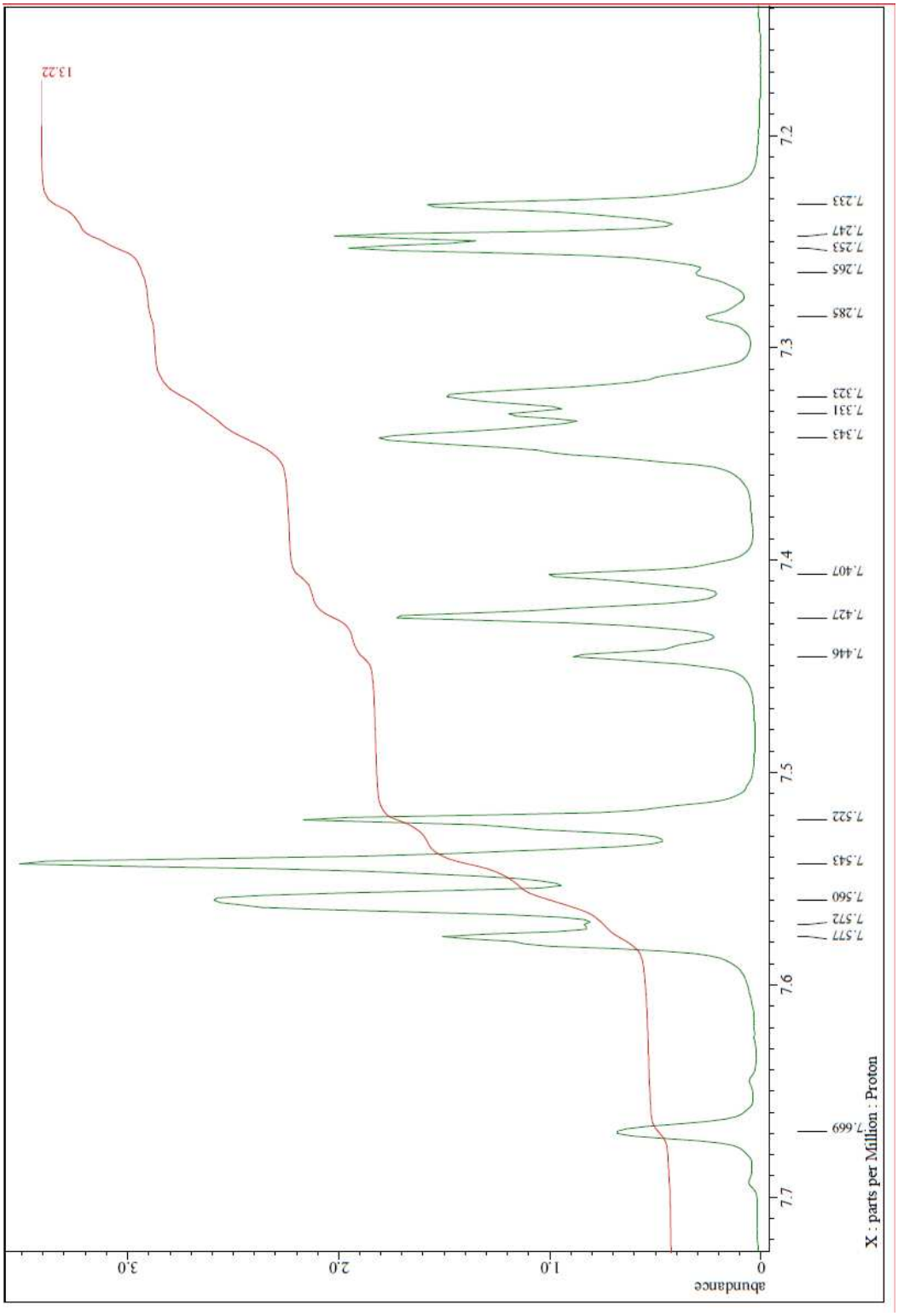
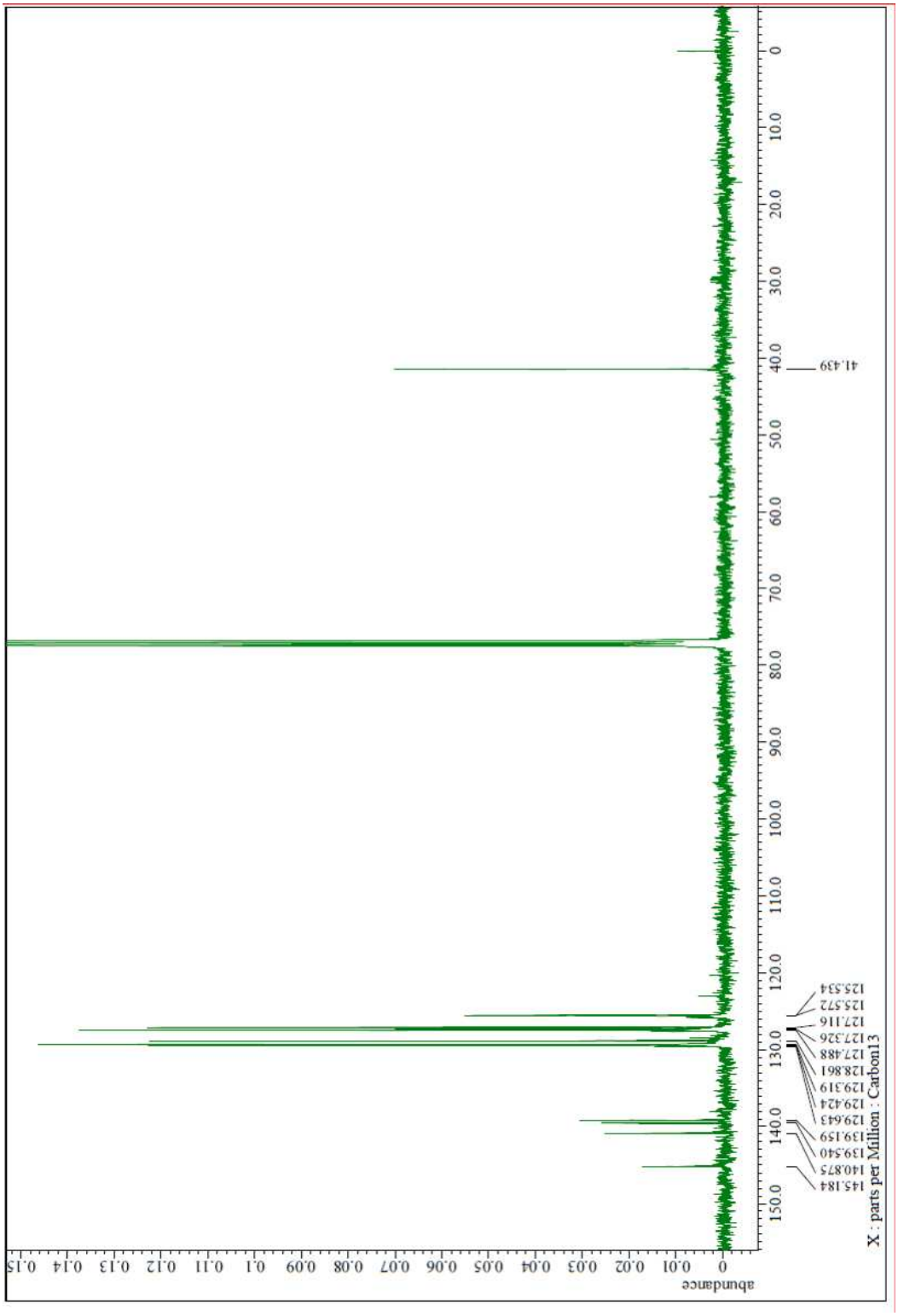

13.22
7.233
7.247
7.253
7.265
7.285
7.323
7.331
7.343
7.407
7.427
7.446
7.522
7.543
7.560
7.572
7.577
7.669
7.2
7.3
7.4
7.5
7.6
7.7
X : parts per Million : Proton
abundance
0
1.0
2.0
3.0

Figure S18.


41.439
125.534
125.572
127.116
127.326
127.488
128.861
129.319
129.424
129.643
139.159
139.540
140.875
145.184
X : parts per Million : Carbon13
abundance

4’-(4-methoxyphenyl)-4-[(4-trifluoromethylphenyl)methyl]-1,1’-biphenyl (4e)
($CDCl_3$)

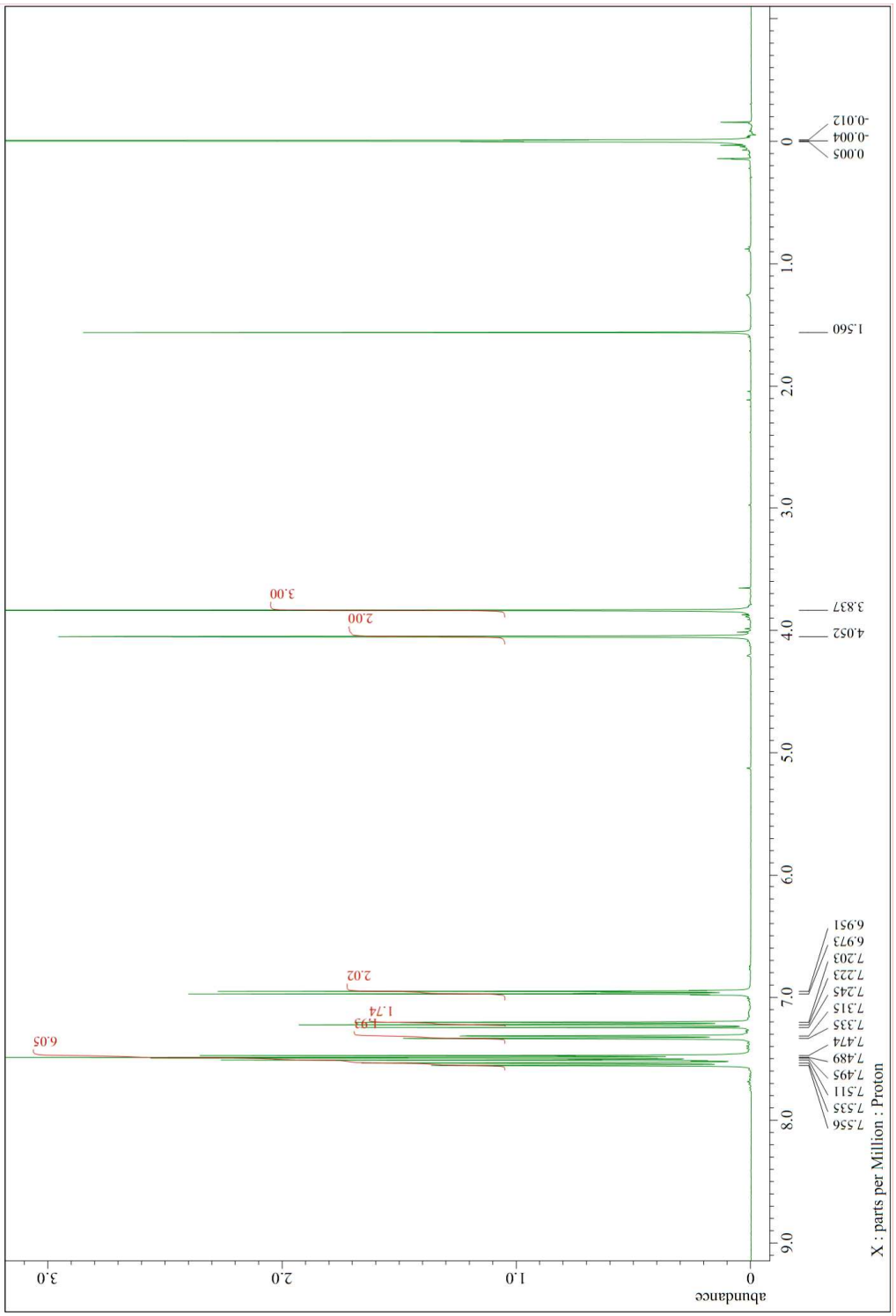


Figure S19.

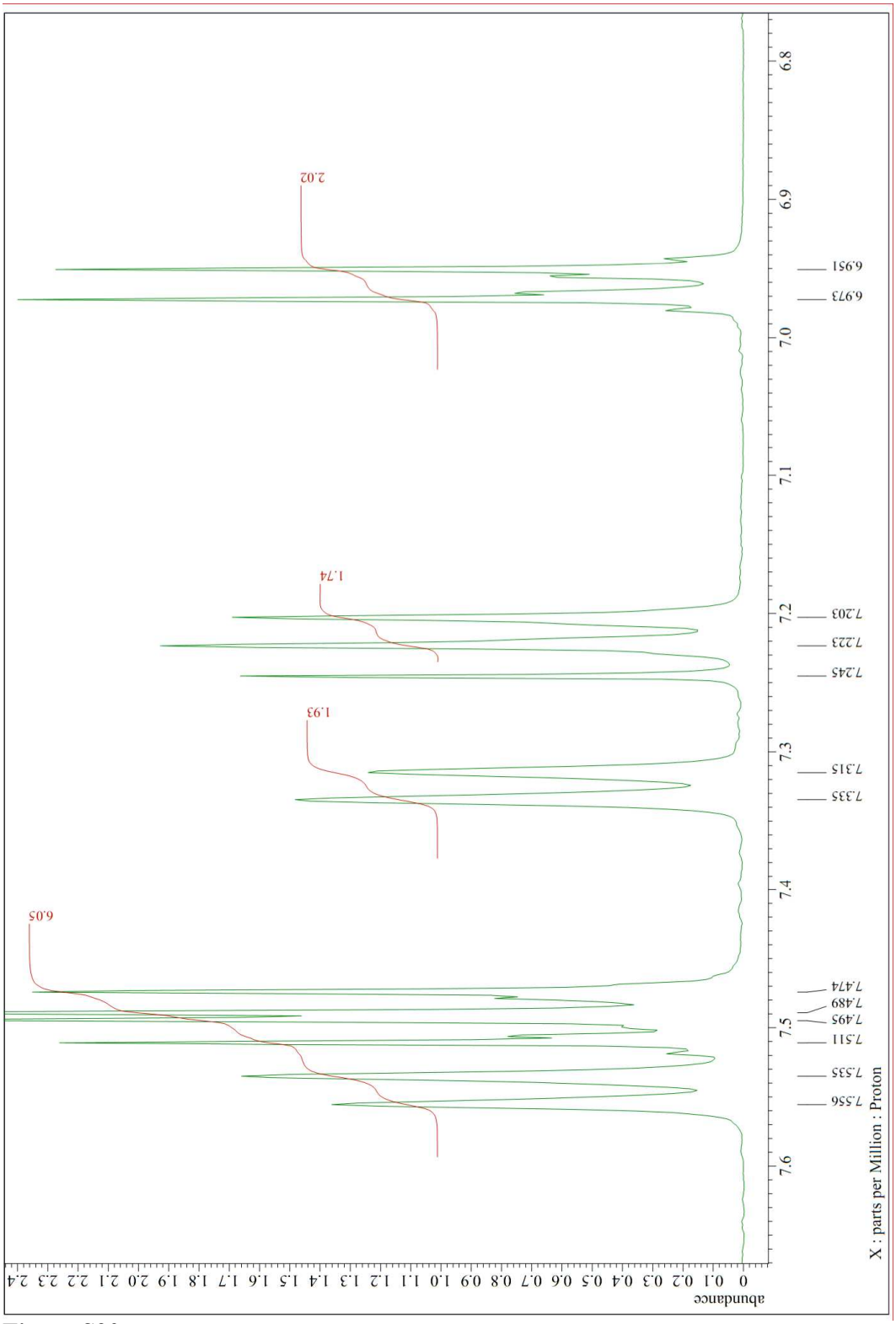

abundance
X : parts per Million : Proton
6.05
1.93
1.74
2.02
7.556
7.535
7.511
7.495
7.489
7.474
7.335
7.315
7.245
7.223
7.203
6.973
6.951

Figure S20.

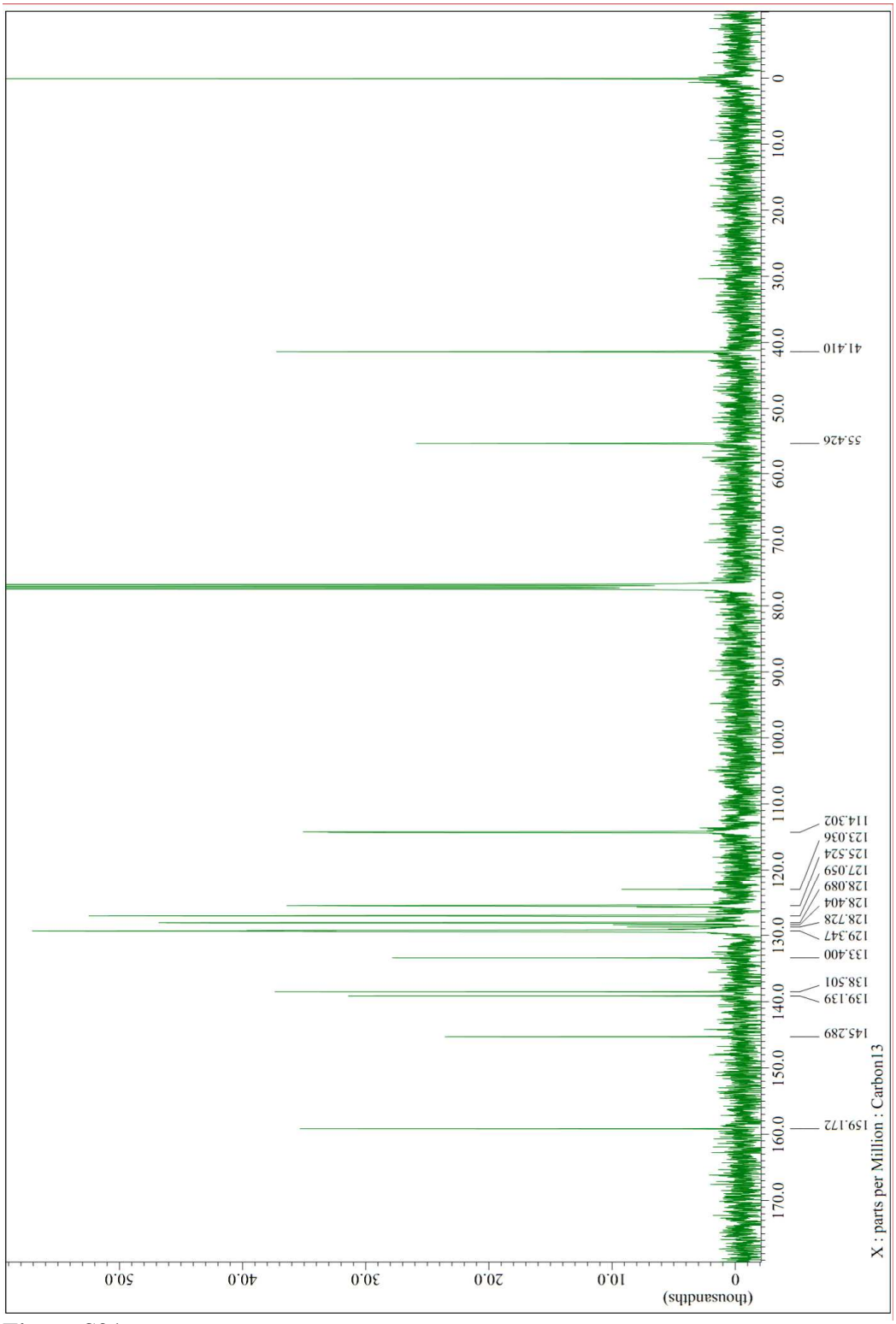
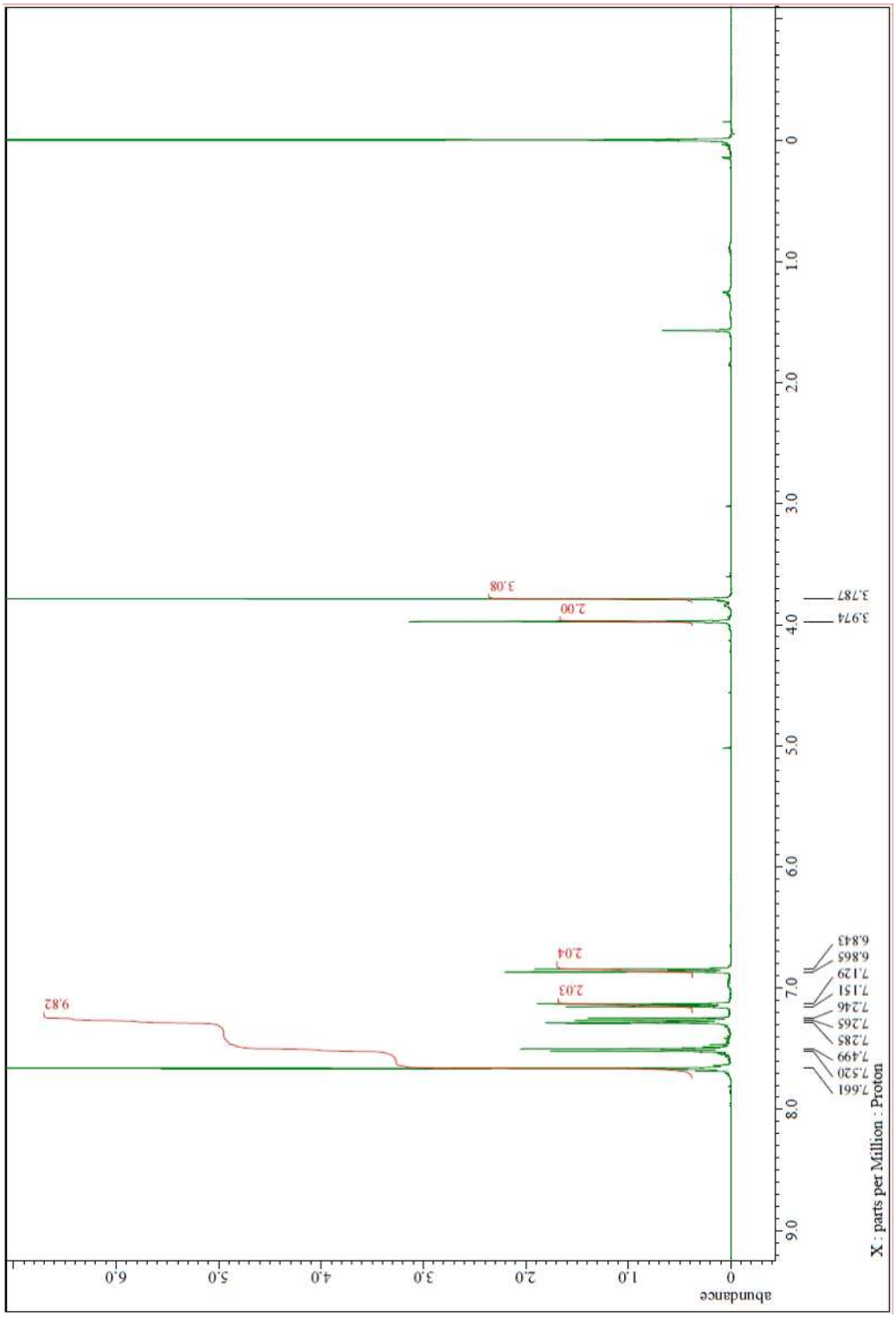

X : parts per Million : Carbon13
(thousandths)
41.410
55.426
114.302
123.036
125.524
127.059
128.089
128.404
128.728
129.347
133.400
138.501
139.139
145.289
159.172

Figure S21.

4-(4-methoxyphenyl)-4'-[(4-trifluoromethylphenyl)methyl]-1,1'-biphenyl (4f)

($CDCl_3$)

Figure S22.



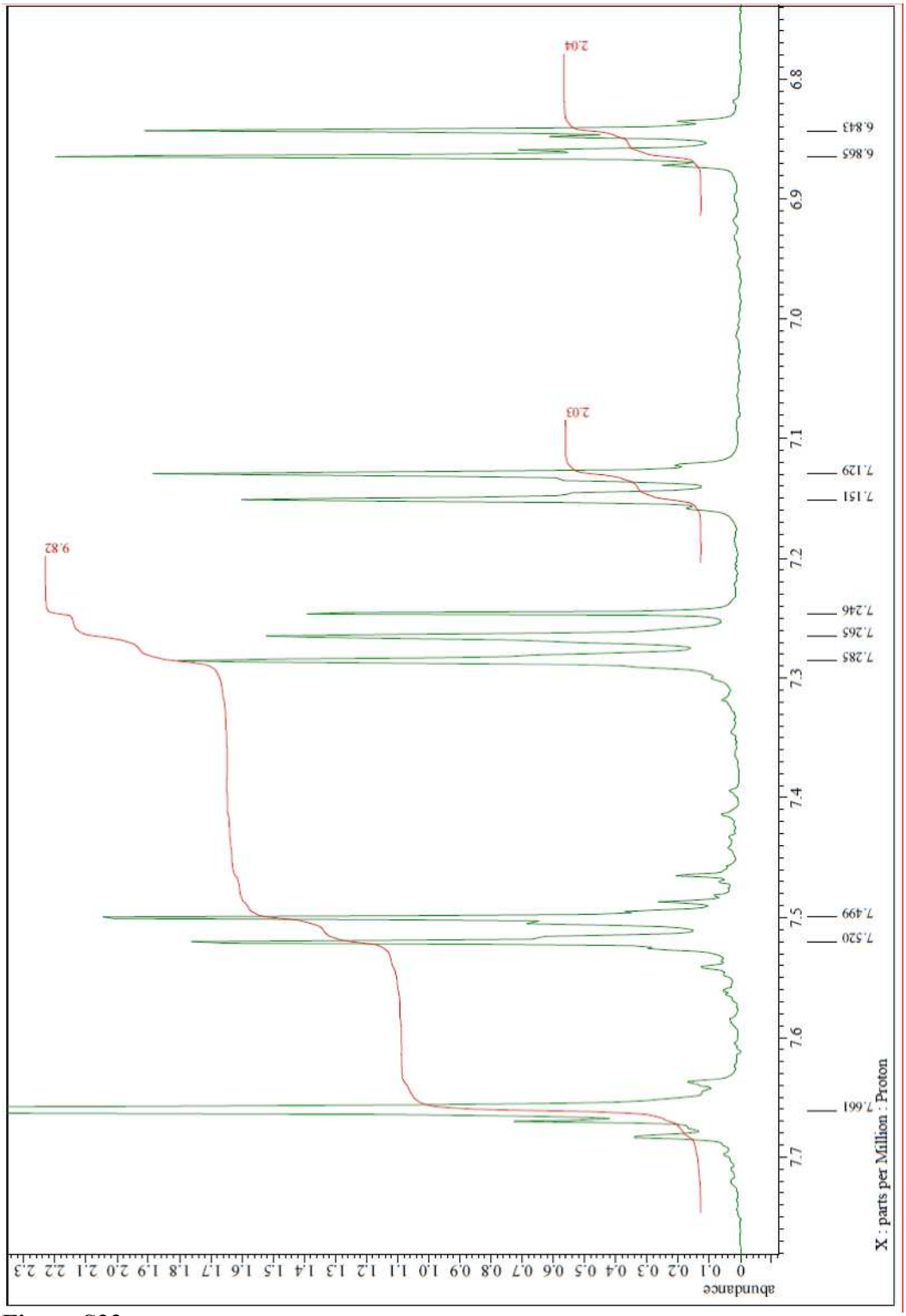
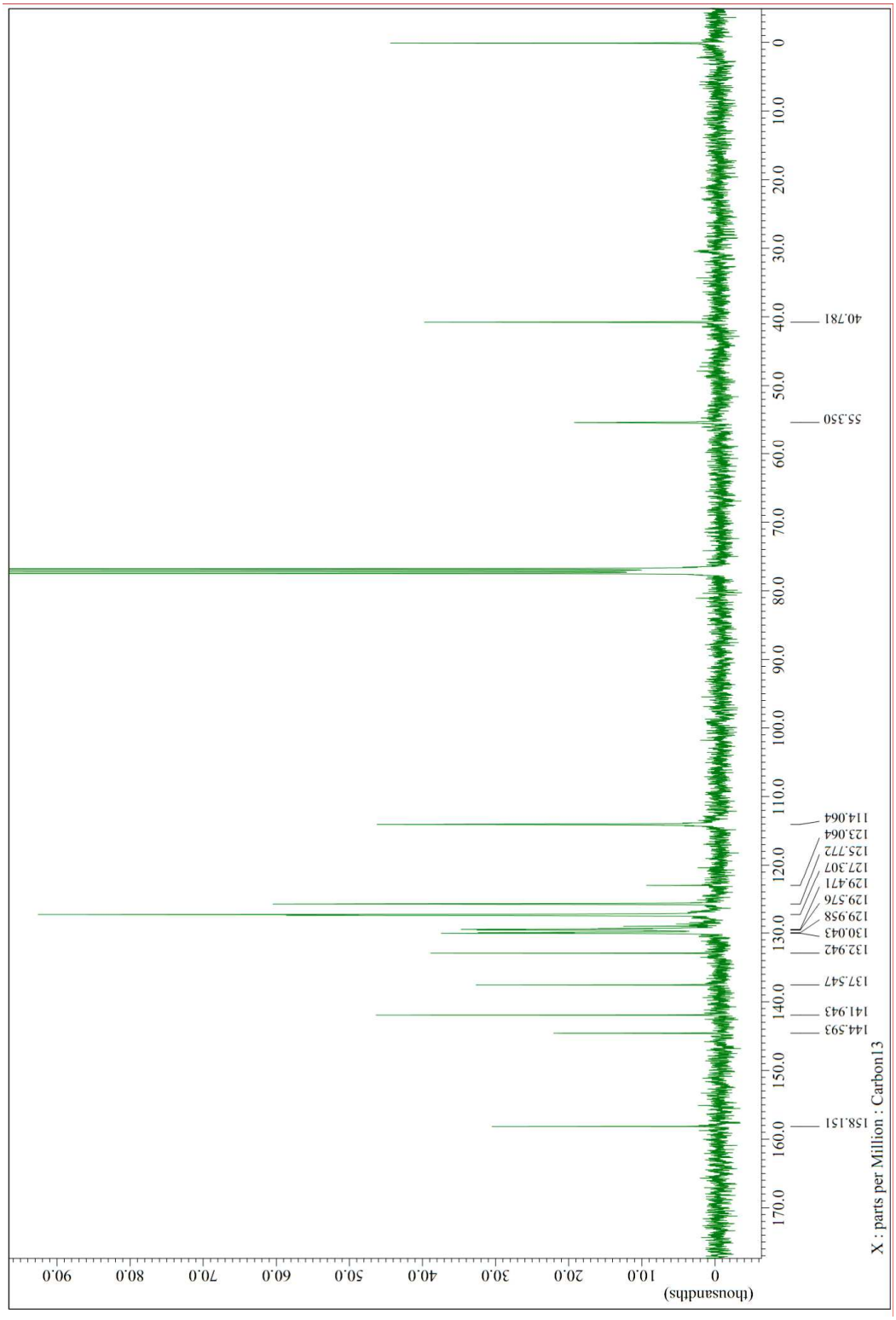

2.04
2.03
9.82
6.843
6.865
7.129
7.151
7.246
7.265
7.285
7.499
7.520
7.661
X : parts per Million : Proton
abundance

Figure S23.

Figure S24.


40.781
55.350
114.064
123.064
125.772
127.307
129.471
129.576
129.958
130.043
132.942
137.547
141.943
144.593
158.151
X : parts per Million : Carbon13
(thousandths)