Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information

Aluminum Oxide Mediated C-F Bond Activation in Trifluoromethylated Arenes

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Experimental section

NMR spectra were measured on Bruker Avance 300 and Bruker Avance 400 spectrometers at 20 °C. HPLC analyses were carried out using Cosmosil 5-PYE (4.6 mm x 250 mm) column (UV-Vis detection). Chromatographic purifications were carried out with flash grade silica gel Kieselgel 60 (0.06-0.2 mm). HF elimination experiments were carried out using commercially available aluminium oxide (activated, neutral, 50-200 micron). The aluminium oxides obtained from different suppliers have shown similar activity in condensation.

General procedure for synthesis of *ortho*-substituted trifluoromethylarenes

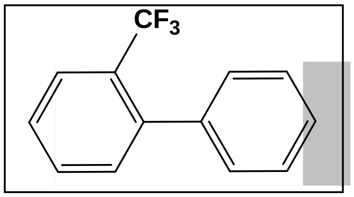
Phenylboronic acid (22.0 mmol) and 2-bromobenzotrifluoride (20.0 mmol) or 2-trifluoromethyl arylboronic acid (22.0 mmol) and arylbromide (20.0 mmol) were dissolved in the mixture of 40 mL toluene and 20 mL of methanol. Afterwards K_2CO_3 (44.0 mmol) and 50 mg of $Pd(PPh_3)_4$ were added. The reaction mixture was degassed under dynamic vacuum and refluxed for 12 h under argon atmosphere. After cooling to the room temperature mixture was washed three times with 100 mL of water. The organic layer was dried over sodium sulfate, filtered through a silica plug and solvent was removed under reduced pressure. Products were purified by column chromatography on silica using hexane as an eluent.

General procedure for Al_2O_3 mediated condensation

Typically 2-3 g of γ-Al_2O_3 were placed in a glass ampoule and activated by annealing in vacuum (10^{-2} mbar). The temperature was increased gradually, and kept for 30 min at 600 °C. After cooling to room temperature, the ampoule was filled with argon. 20-30 mg of the respective trifluoromethyl arene were carefully mixed with activated aluminum oxide. For gram-scale synthesis 3-4 mmole of the substrate (0,8-1,2g) and 10g of aluminum oxide were used. The ampoule was evacuated again and sealed. The condensation was carried out without stirring at 30-250 °C. The respective condensation products were obtained after extraction with MeOH (or MeOH/AcOH mixture) and evaporation.

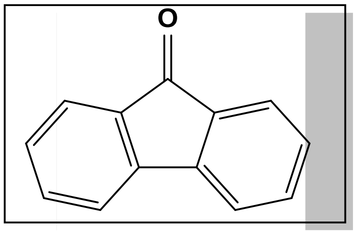
General procedure for Al_2O_3 mediated hydrolysis

Typically 1 g of γ-Al_2O_3 were mixed with 20-30 mg of the respective trifluoromethyl arene in glass ampoule under ambient atmosphere. For gram-scale synthesis 3-4 mmole of the substrate (0,8-1,2g) and 10g of aluminum oxide were used. The ampoule was heated to 100-250°C under ambient atmosphere. The hydrolysis products were obtained after extraction with MeOH/AcOH mixture and evaporation.



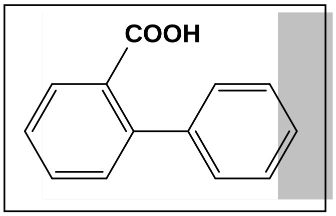
1

2-Trifluoromethyl-1,1'-biphenyl (1) was obtained according to general procedure from phenylboronic acid (22.0 mmol) and 2-bromobenzotrifluoride (20.0 mmol), Colorless liquid, yield 92%. ^{1}H NMR spectrum is in accordance with S1.



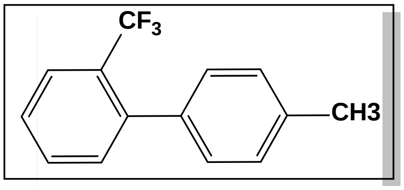
2

***9H*-Fluoren-9-one (2)** was obtained from **1** according to general procedure for Al_2O_3 mediated condensation. Yellow solid, yield 80%. ^{1}H NMR spectrum is in accordance with S2.



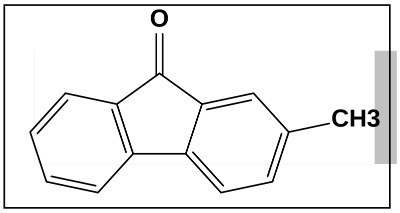
3

1,1'-Biphenyl-2-carboxylic acid (3) was obtained from **1** according to general procedure for Al_2O_3 mediated hydrolysis. White solid, quantitative yield (determined by NMR). ^{1}H NMR spectrum in agreement with S3.



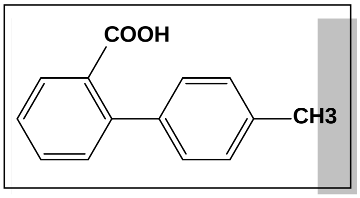
8

4'-Methyl-2-(trifluoromethyl)-1,1'-biphenyl (**8**) was obtained according to general procedure from 2-trifluoromethyl phenylboronic acid (16.0 mmol) and arylbromide (14.0 mmol). Colorless liquid, 94% yield. ^{1}H NMR spectrum is in agreement with S4.



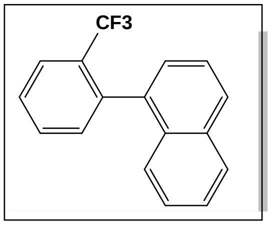
9

2-Methyl-9*H*-fluoren-9-one (9) was obtained from **8** according to general procedure for Al_2O_3 mediated condensation. Yellow liquid, yield 72%. ^{1}H NMR spectrum is in accordance with S2.



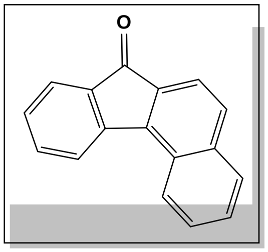
10

4-Methyl-2'-biphenylcarboxylic acid (10) was obtained following to general procedure for Al2O3 mediated hydrolysis. White solid, quantitative yield (determined by NMR). ^{1}H NMR spectrum is in agreement with S5.

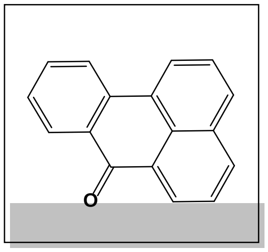


11

1-[2-(trifluoromethyl) phenyl]-naphthalene (11) was obtained according to general procedure from 1-naphthylboronic acid (16.0 mmol) and 2-bromobenzotrifluoride (14.0 mmol). Yeild 92%, white solid. ^{1}H NMR (CDCl$_3$, 400MHz) δ: 7.91 (s, 1H), 7,89 (s, 1H), 7.4 (d, J=7.81 Hz, 1H), 7.63-7.44 (m, 4H), 7.41-7.31 (m, 4H). ^{13}C NMR (CD$_2$Cl$_2$, 100MHz) δ: 139.32, 136.74, 133.25, 132.67, 132.41, 131.103, 129.6 (q), 128.18, 128.05, 127.88, 127.68, 127.02, 126.18, 126.10, 126.08, 126.02, 125.97, 124.68, 124.00 (q).

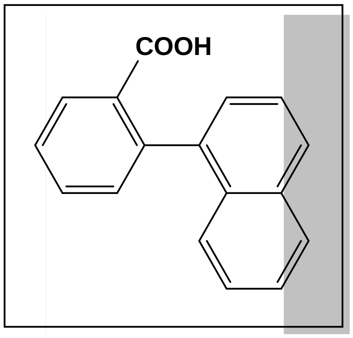


12



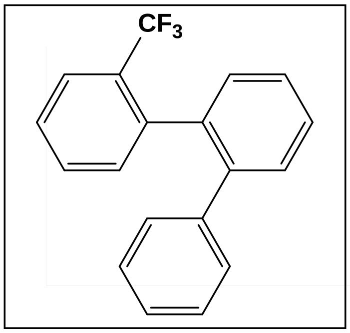
13

***7H*-Benzo[*c*]fluoren-7-one (12)** and ***7H*-Benz[*de*]anthracen-7-one (13)** were obtained from **11** according to general procedure for Al$_2$O$_3$ mediated condensation. Small amounts of **12** and **13** were separated by column chromatography for analysis. Compound **12**, orange solid, yield 18%. ^{1}H and ^{13}C NMR spectra is in accordance with S6. Compound **13**, red solid, yield 40%. ^{1}H and ^{13}C NMR spectra are in accordance with S7.



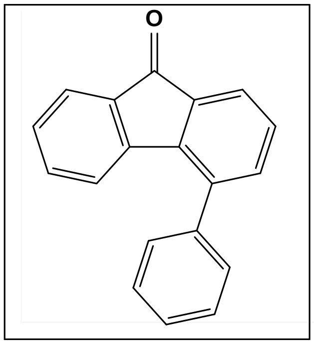
14

2-(1-Naphthalenyl)-benzoic acid (14) was obtained from **11** according to general procedure for Al_2O_3 mediated hydrolysis. White solid, quantitative yield (determined by NMR). ^1H and ^{13}C NMR spectra are in agreement with S8.

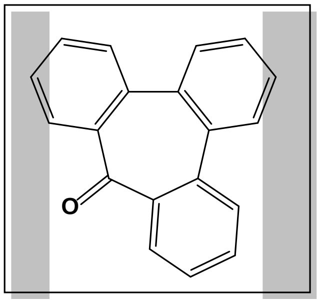


15

2-(Trifluoromethyl)-terphenyl (15) was obtained according to general procedure from 2-biphenylboronic acid (16.0 mmol) and 2-bromobenzotrifluoride (14.0 mmol). Yeild 80%, colorless oil. ^1H and ^{13}C NMR spectra are in accordance with S9.



16

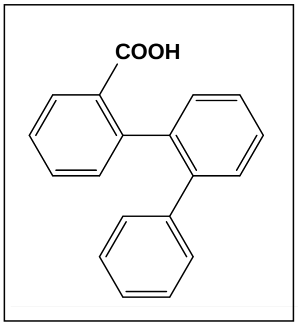


17

4-Phenyl-*9H*-fluoren-9-one (16) and ***9H*-Tribenzo[*ace*] cyclohepten-9-one (17)** were obtained from **15** according to general procedure for Al_2O_3 mediated condensation. Small amounts of 16 and 17 for NMR analysis were separated by HPLC (5PYE column, MeOH as an eluent).

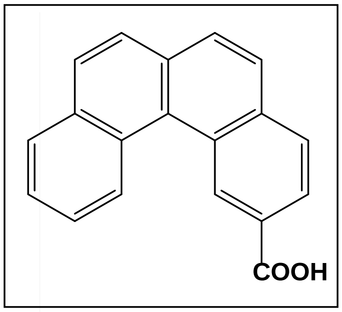
Compound **16**, orange solid, yield 8%. ^{1}H NMR (CDCl3, 300MHz) δ: 7.69-7.59 (m, 2H), 7.53-7.44 (m, 5H), 7.38-7.33 (m, 2H), 7.25-7.15 (m, 2H), 6.77 (m, 1H). ^{13}C NMR (CD2Cl2, 75MHz) δ: 193.84 (CO), 144.86, 143.36, 139.85, 137.06, 135.05, 134.80, 134.70, 129.15 (2C), 129.07 (2C), 128.49, 124.21, 123.51, 123.31. One carbon signal is not observed due to overlapping.

Compound **17**, yellow solid, yield 52%. ^{1}H and ^{13}C NMR spectra are in accordance with S10.



18

***o*-Terphenyl-2-carboxylic acid (18)** was obtained from **15** according to general procedure for Al_2O_3 mediated hydrolysis. White solid, quantitative yield (determined by NMR). ^1H NMR ($CDCl_3$, 300MHz) δ: 7.8 (d, J=7.46 Hz, 1H), 7.47-7.34 (m, 4H), 7.33-7.28 (m, 2H), 7.19-7.02 (m, 6H). ^{13}C NMR (CDCl3, 100 MHz) δ:172.05 (CO), 143.14, 141.00, 140.57, 139.93, 132.19, 131.73, 130.31, 129.80, 129.78, 129.69, 128.53, 127.72, 127.63, 126.99, 126.98, 126.81, 126.44. One carbon signal is not observed due to overlapping of signals.



20

Benzo[*c*]-phenanthrene-2-carboxylic acid (20) was obtained from **19** according to general procedure for Al_2O_3 mediated hydrolysis. White solid, yield 96 %. ^1H and ^{13}C NMR spectra are in accordance with S11.

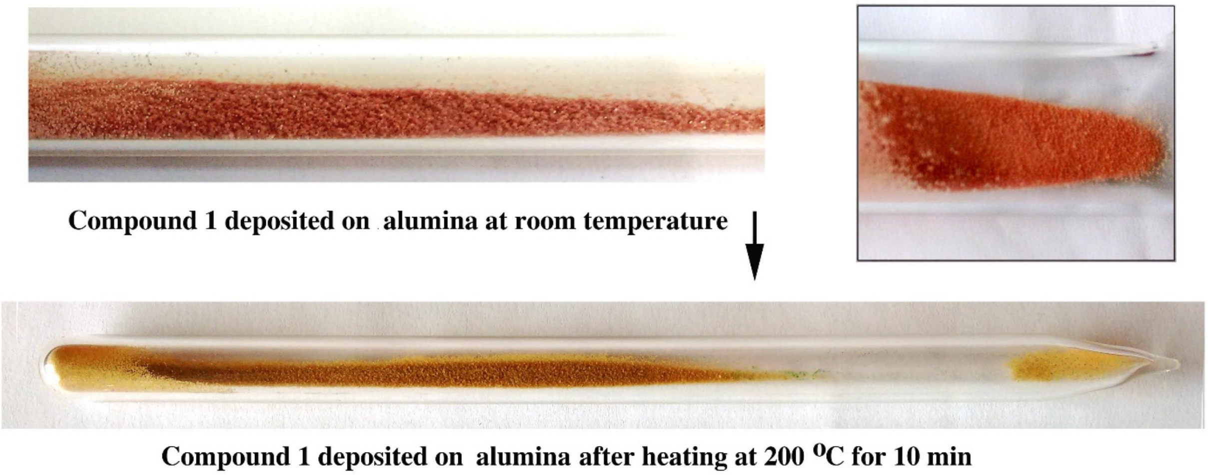


Figure S1. Condensation of compound **1** on activated alumina at room temperature (pink) and after heating at 200^{o}C for 10 minutes (yellow).

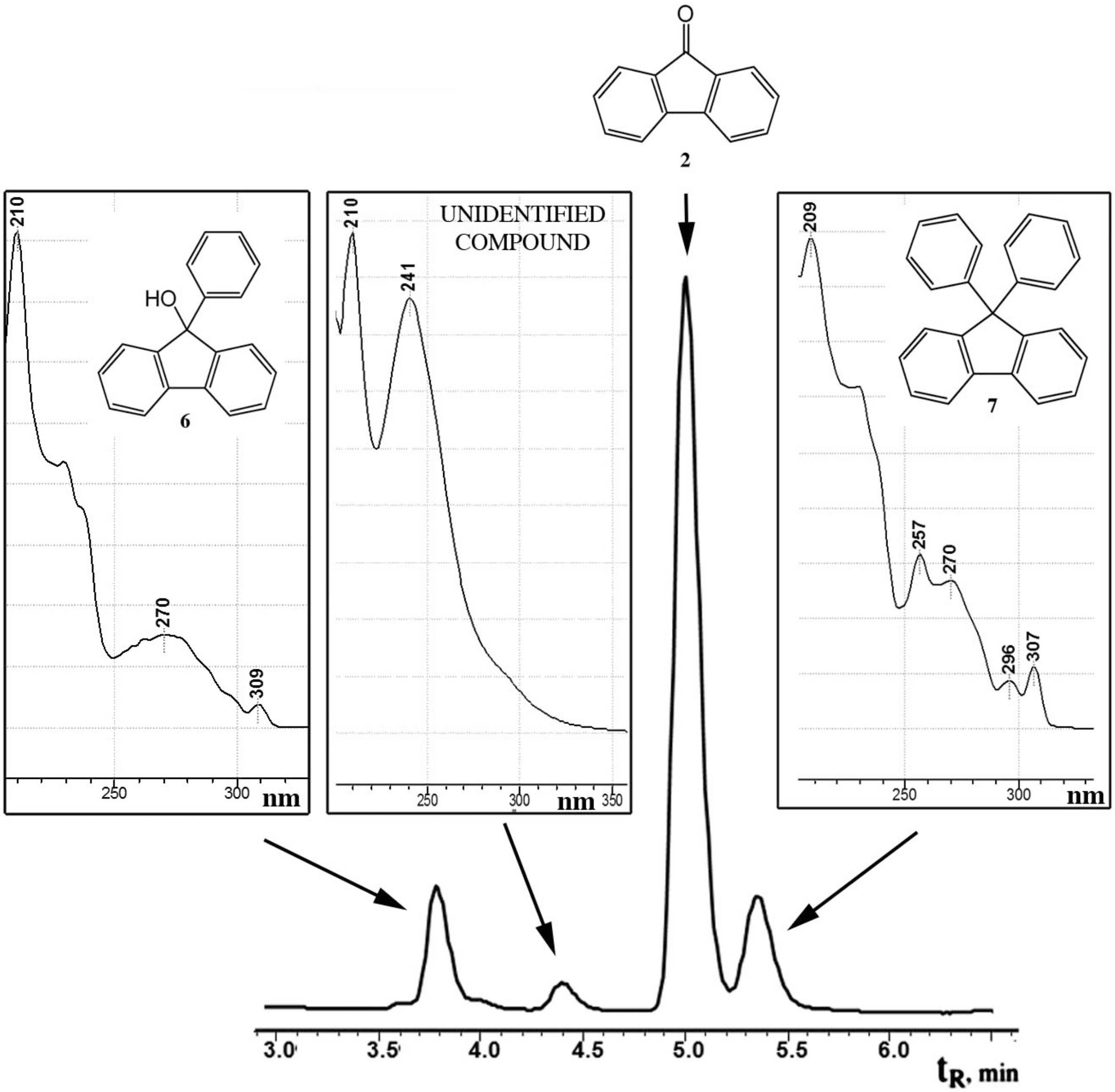


Figure S2. HPLC profile of MeOH extract (compound **2, 6** and **7**) as obtained after condensation of **1** with benzene on activated alumina at 50^{o}C for 30 minutes. HPLC conditions: 5PYE column, MeOH:cyclohexane 80:20 as eluent, 1 ml/min, 30 ^{o}C, detection 300nm. (inset) UV-Vis spectrum of **6** and **7** (MeOH:cyclohexane).

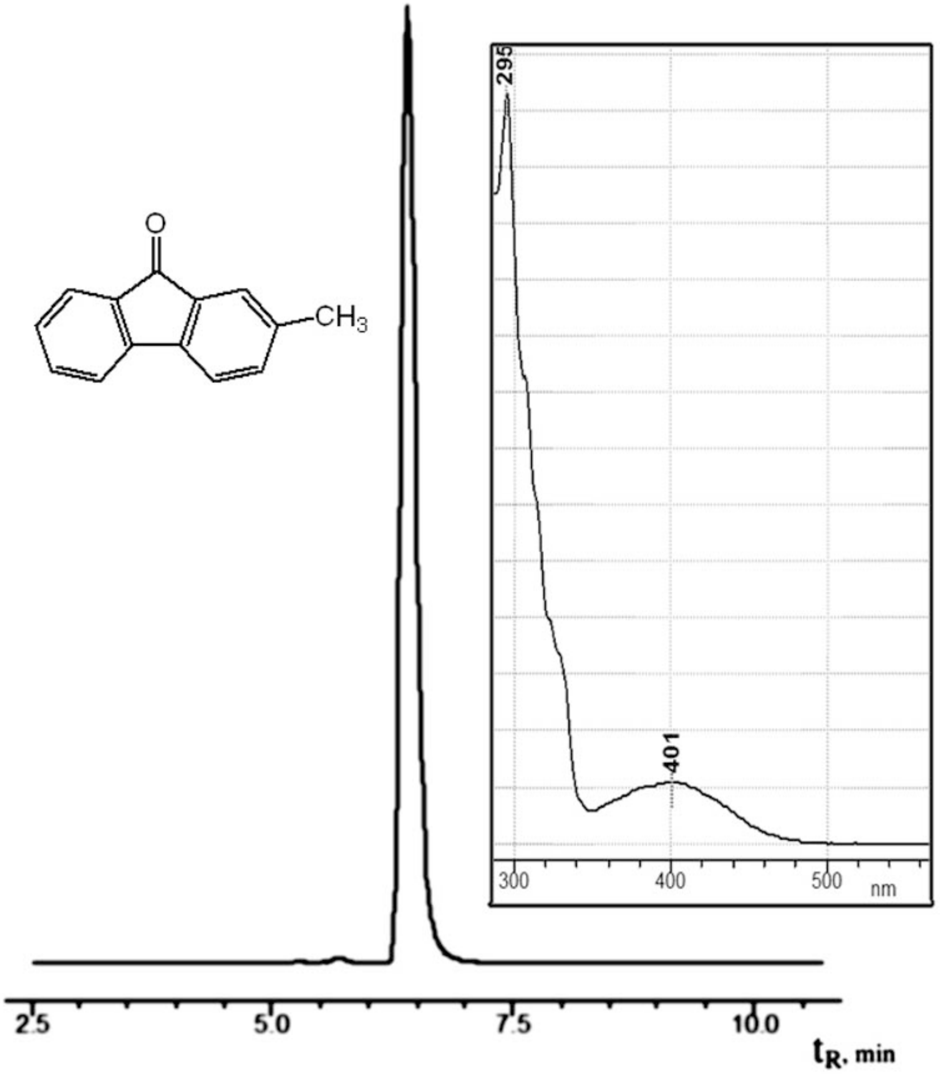


Figure S3. HPLC profile of MeOH extract (compound **9**) as obtained after condensation of **8** on activated alumina at 150^{o}C for 30 minutes. HPLC conditions: BP column, toluene:MeOH 1:9 as eluent, 1 ml/min, 30 ^{o}C, detection 300nm. (inset) UV-Vis spectrum of **8** (toluene:MeOH).

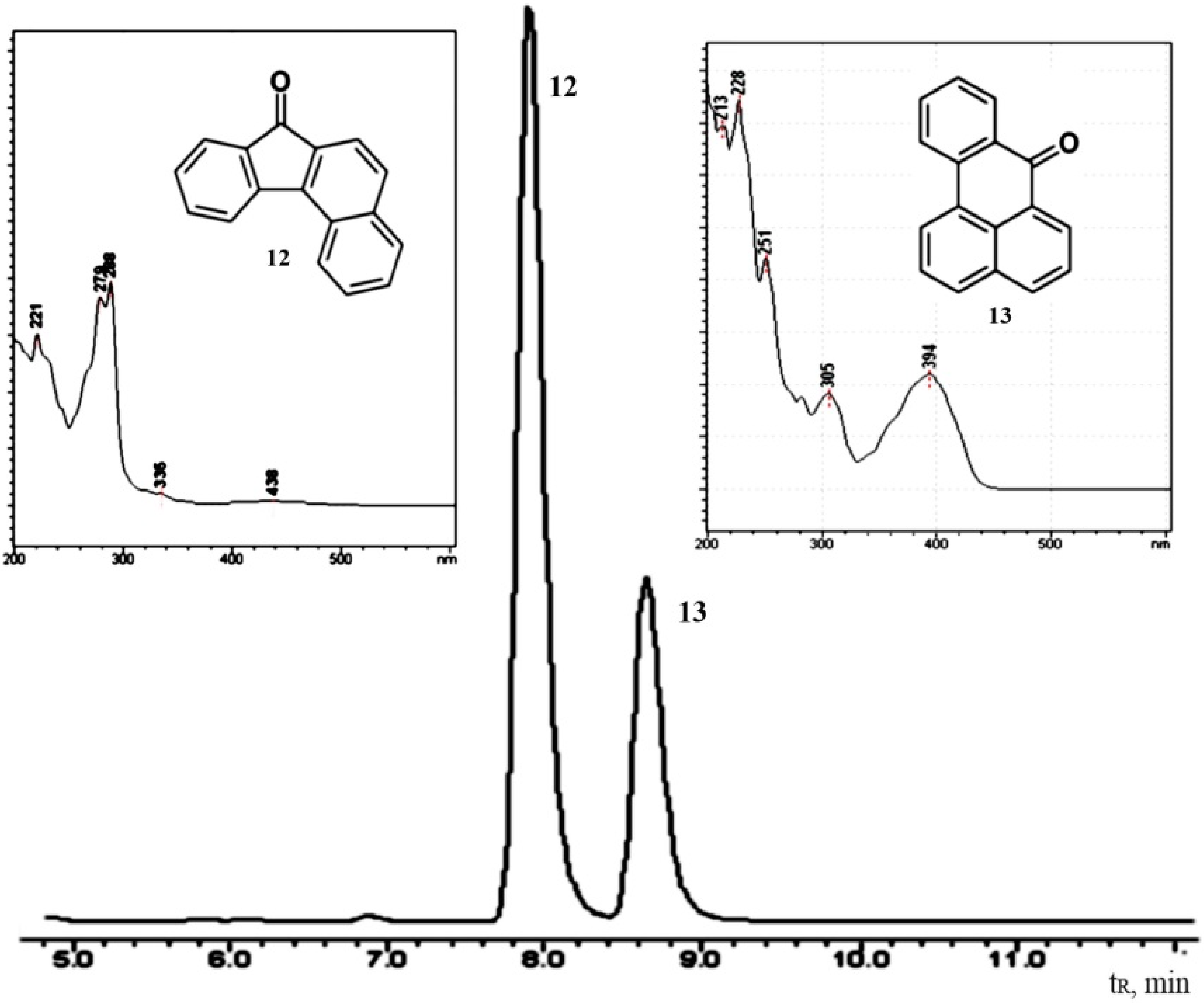


Figure S4. HPLC profile of MeOH extract as obtained after condensation of **11** on activated alumina at 150°C for 30 minutes. HPLC conditions: 5PYE column, toluene:MeOH:20:80 as eluent, 1 ml/min, 30 °C, detection 300nm. (inset) UV-Vis spectra of **12** and **13** (MeOH).

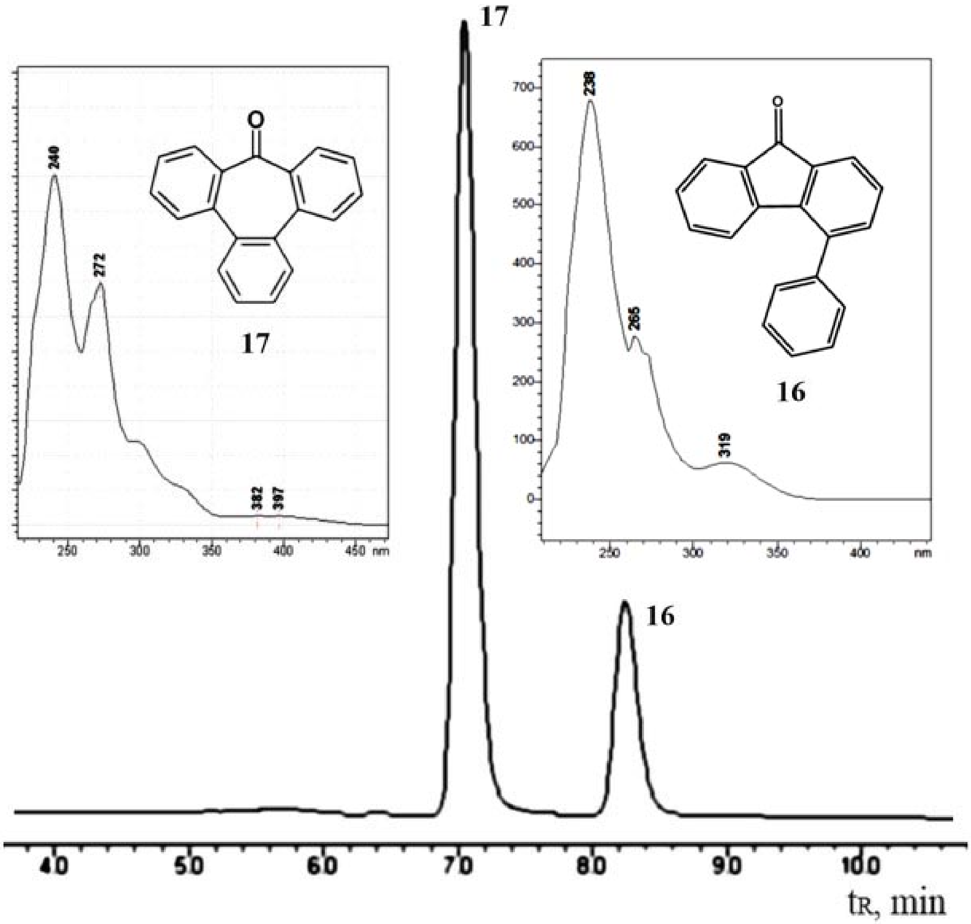


Figure S5. HPLC profile of MeOH extract (compound **16** and **17**) as obtained after condensation of **15** on activated alumina at 150^{o}C for 30 minutes. HPLC conditions: 5PYE column, MeOH as eluent, 1 ml/min, 30 ^{o}C, detection 300nm. (inset) UV-Vis spectra of **16** and **17** (MeOH).

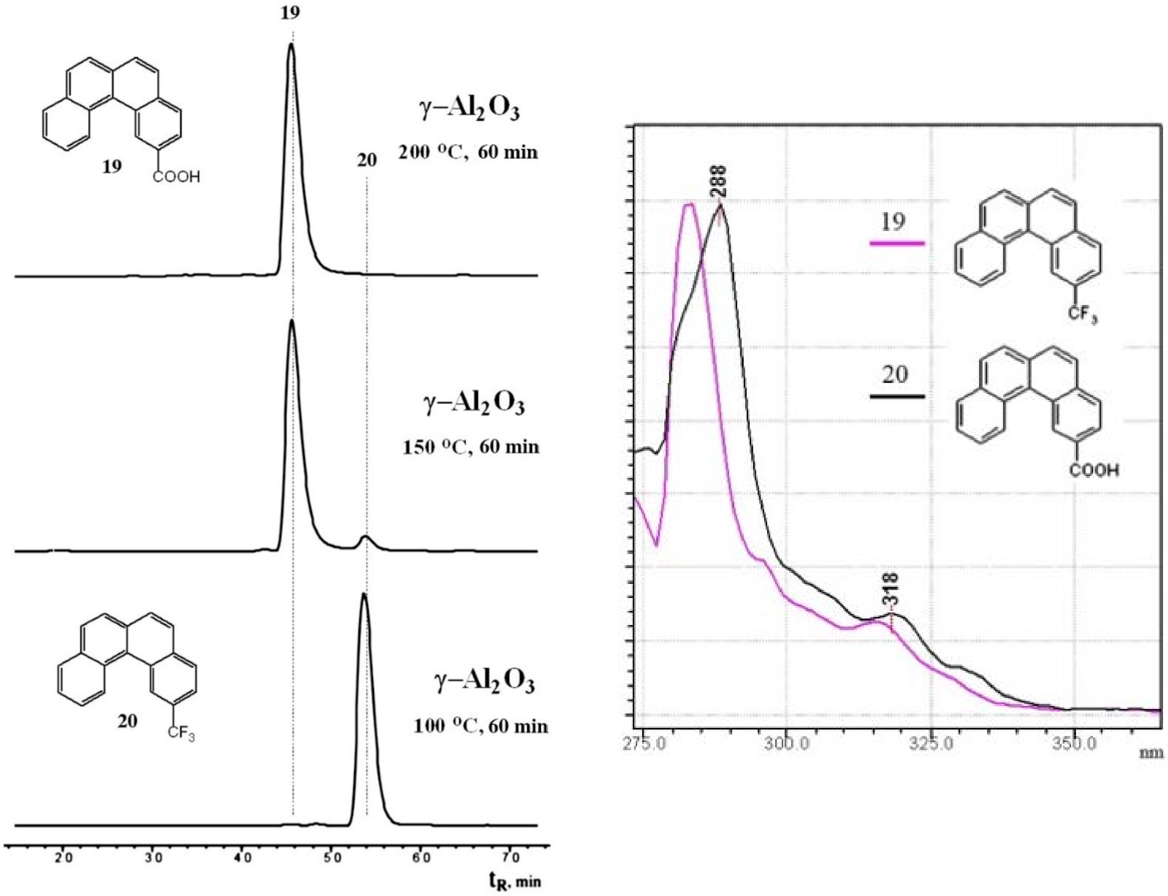


Figure S6. HPLC profile of MeOH/acetic acid extract as obtained after reaction of **19** on non-activated alumina during 60 minutes at 100°C, 150°C and 200°C. HPLC conditions: 5PYE column, toluene:MeOH (0.2% of acetic acid) 2:8 as eluent, 1 ml/min, 30°C, detection 300nm. (inset) UV-Vis spectra of **19** and **20** (toluene:MeOH 2:8).

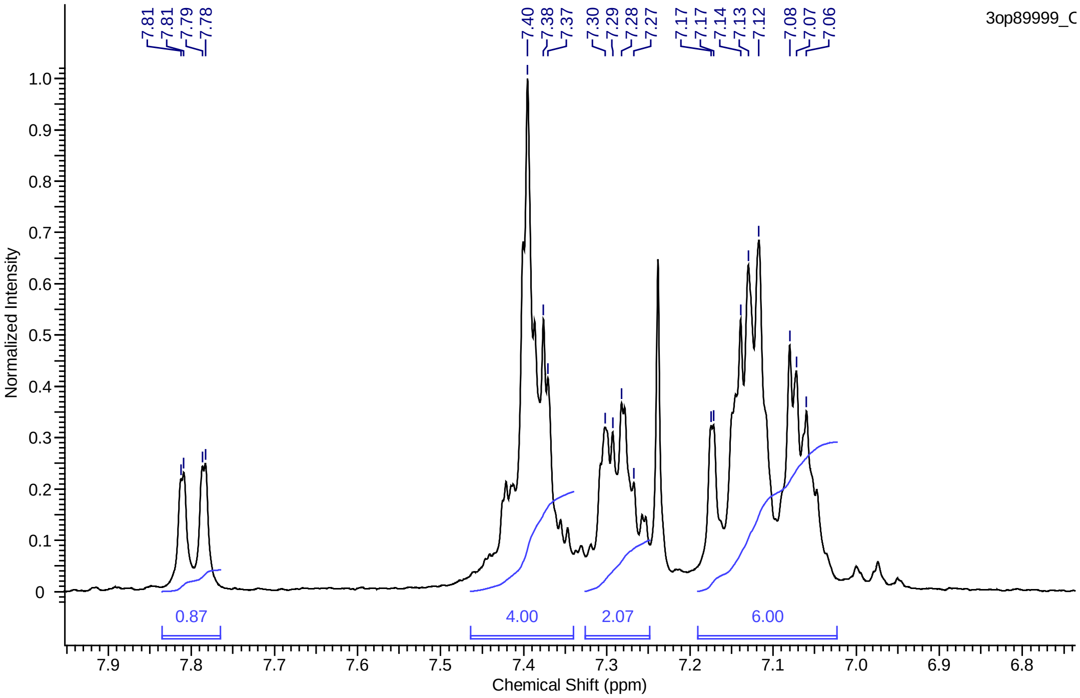


Figure S7. ^{1}H NMR ($CDCl_3$, 300MHz) spectrum of compound **18**

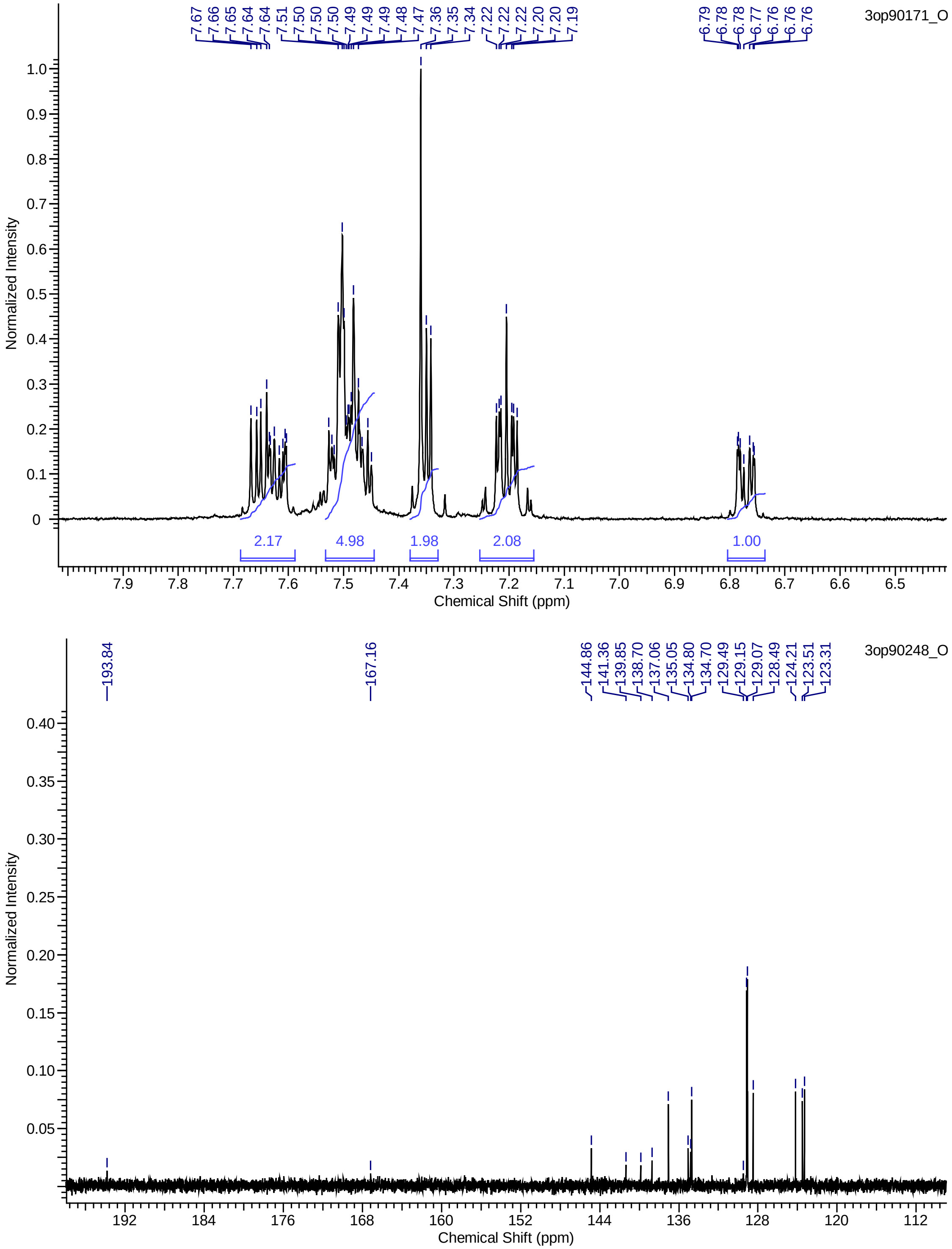


Figure S8. ^{1}H and ^{13}C NMR (CDCl3, 300MHz) spectra of compound (**16**).

References

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