Electronic Supplementary Material (ESI) for ChemComm.

Supporting Information for:

A Straightforward synthesis of 2,5,8-alkoxyheptazines: Application to photoredox catalyzed transformations

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List of Abbreviations

ACN	Acetonitrile
DCM	Dichloromethane
DMAP	4-Dimethylaminopyridine
EtOAc	Ethyl acetate
P.E	Petroleum Ether
TFE	1,1,1-trifluoroethanol

1. General Remarks

Unless otherwise stated, all reagents were obtained from commercial suppliers and used without further purification.

Analytical thin layer chromatography (TLC) plates were purchased from Merck KGaA (silica gel 60 F_{254}). Visualization was accomplished by irradiation with a UV light at 254 nm. Chromatography was performed using silica gel 60 (40–63 μm) from Merck.

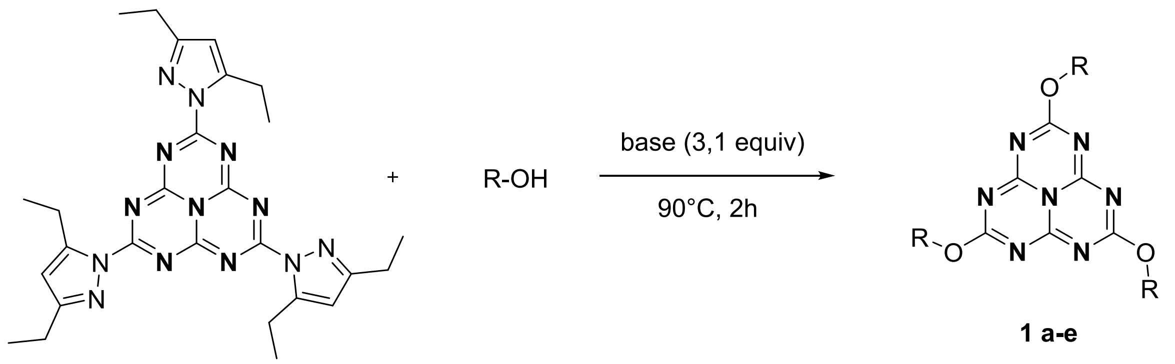
Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on Bruker spectrometers: Avance 300 MHz (QNP - ^{13}C, ^{31}P, ^{19}F - probe or Dual ^{13}C probe) and Avance 500 MHz (BB0 - ATM probe or BBI - ATM probe). Proton chemical shifts (δ) are reported in parts per million (ppm) relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ δ 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, s = sextet, h = heptet, m = multiplet, br = broad), coupling constants (*J*) and integration. Coupling constants (*J*) are reported in Hertz (Hz). Carbon chemical shifts are reported in ppm from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ δ 77.0 ppm).

Infrared spectra were recorded on Perkin Elmer Spectrum 100 FT-IR spectrometer and absorption frequencies were reported in reciprocal centimeters (cm-1).

Melting points, measured in capillary tubes on a Büchi B-540 apparatus, are uncorrected.

Mass spectra were obtained from a AEI MS-9 using electron spray ionization (ESI).

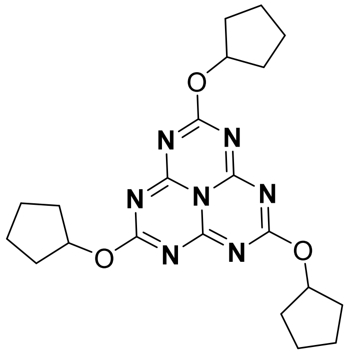
2. General Procedure for synthesis of compounds 1a to 1e



General procedure: In an Ace pressure tube (15 mL) was placed 2,5,8-tris(3,5-diethyl-pyrazolyl)-heptazine (0.56 mmol, 1 equiv). Then alcohol (5 mL, excess) and base (3.1 equiv) were added and the solution was stirred at 90°C for 2 hours. The reaction was quenched by careful addition of a solution 1M of HCl. The solution was extracted with DCM (3 times) and the combined organic phases were dried with $MgSO_4$, filtered and concentrated under vacuum. The residue was purified by silica gel flash chromatography (P.E/EtOAc gradient).

3. Synthesis and analytical data for compounds 1a to 1e

2,5,8-tricyclopentyloxy-heptazine **1a**



General procedure with DMAP as base, white solid, 43%.

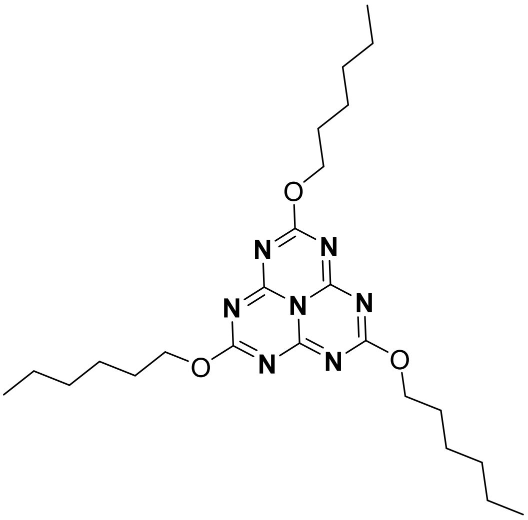
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 5.56-5.52 (m, 3H), 1.95-1.59 (m, 24H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.3 (3C), 159.3 (3C), 83.1 (3C), 32.8 (6C), 23.6 (6C).

IR (neat) ν (cm^{-1}): 2960, 1633, 1524, 1421, 1340, 1261, 1155, 1015, 958, 819, 734.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{21}H_{28}N_7O_3$ 426.2254, found 426.2250. **Mp**: 184±2 °C

2,5,8-trihexyloxy-heptazine **1b**



General procedure with 2,4,6-collidine as base, colourless liquid, 47%.

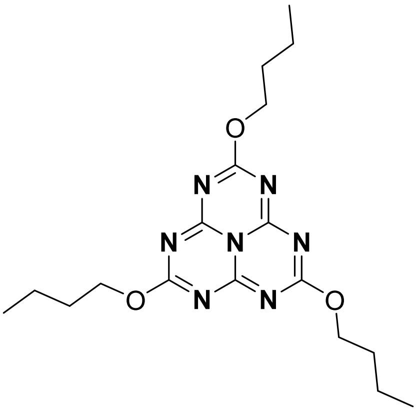
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.43 (t, *J* = 6.6 Hz, 6H), 1.77-1.72 (m, 6H), 1.42-1.28 (m, 18H), 0.87 (t, J = 6.6 Hz, 9H),

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.8 (3C), 159.5 (3C), 70.2 (3C), 31.3 (3C), 28.5 (3C), 25.3 (3C), 22.5 (3C), 14.0 (3C).

IR (neat) ν (cm^{-1}): 2928, 1636, 1531, 1428, 1343, 1261, 1025, 820, 735.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{24}H_{40}N_7O_3$ 474.3193, found 474.3183. **Mp**: 58±2 °C

2,5,8-tributoxy-heptazine **1c**



General procedure with 2,4,6-collidine as base, white solid, 95%.

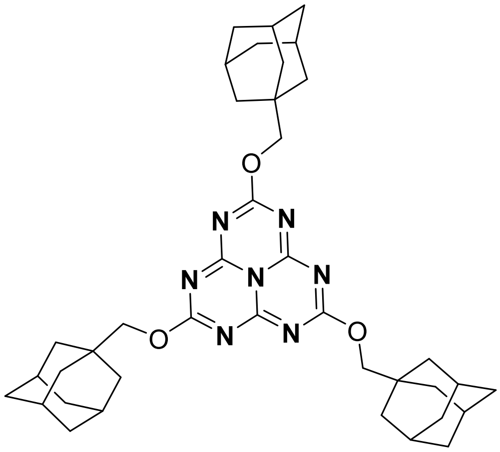
^{1}H NMR (300 MHz, $CDCl_3$) δ (ppm): 4.36 (t, *J* = 6.6 Hz, 6H), 1.68-1.63 (m, 6H), 1.39-1.32 (m, 6H), 0.85 (t, *J* = 7.3 Hz, 9H).

^{13}C NMR (75 MHz, $CDCl_3$) δ (ppm): 170.7 (3C), 159.5 (3C), 69.8 (3C), 30.4 (3C), 18.8 (3C), 13.5 (3C).

IR (neat) ν (cm^{-1}): 2960, 1635, 1534, 1427, 1364, 1264, 1063, 1032, 966, 819, 754.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{18}H_{28}N_7O_3$ 390.2254, found 390.2245. **Mp**: 124±2 °C

2,5,8-tris((adamantan-1-yl)methoxy)-heptazine **1d**



General procedure with DMAP as base, white solid, 40%.

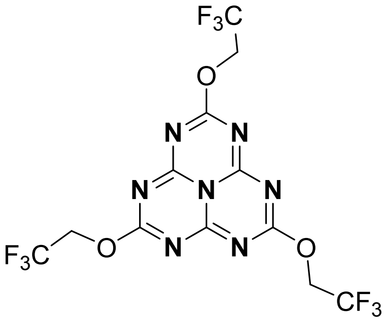
^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 4.07 (s, 6H), 2.00 (s, 9H), 1.65-1.71 (m, 36H).

^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm): 171.1 (3C), 159.4 (3C), 79.5 (3C), 39 (9C), 36.9 (9C), 33.6 (3C), 28 (9C).

IR (neat) ν (cm^{-1}): 2901, 2848, 1631, 1528, 1466, 1421, 1347, 1314, 1265, 1157, 1026, 821, 734.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{39}H_{52}N_7O_3$ 665.4053, found 666,4133. Mp: 320±2 °C

2,5,8-tris(2,2,2-trifluoroethoxy)-heptazine **1e**



General procedure with 2,4,6-collidine as base, white solid, 57%.

^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 4.85 (q, *J* = 8.1 Hz, 6H).

^{19}F NMR (282 MHz, CDCl$_3$) δ (ppm): -73.7.

^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm): 170.3 (3C), 160.3 (3C), 122.2 (q, *J* = 277.6 Hz, 3C), 64.6 (q, *J* = 37.4 Hz, 3C).

IR (neat) ν (cm^{-1}): 2925, 1634, 1543, 1422, 1244, 1155, 1070, 956, 823, 738.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{12}H_7F_9N_7O_3$ 468.0467, found 468.0439. **Mp**: 100±2 °C

Melting points of heptazines:

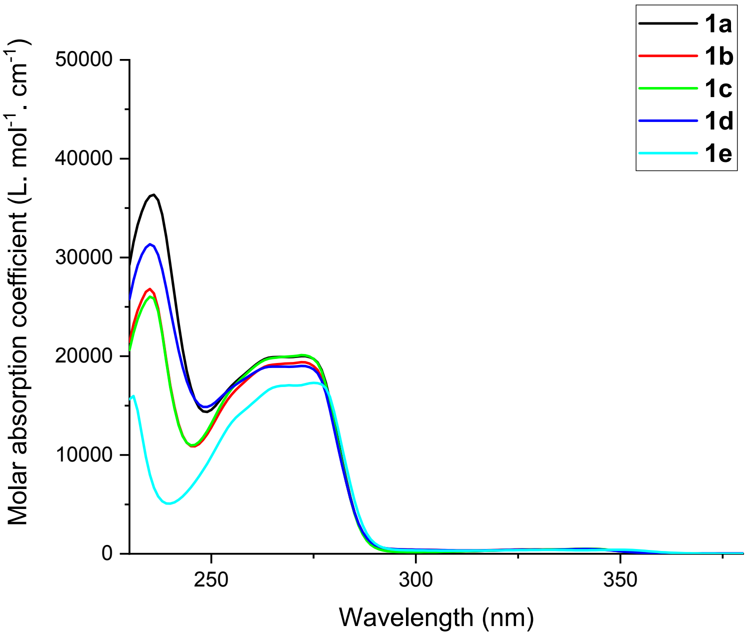
1a	184±2 °C
1b	58±2 °C
1c	124±2 °C
1d	320±2 °C
1e	100±2 °C

4. UV-vis absorption and fluorescence for compounds 1a to 1e

Spectroscopic measurements: UV-visible absorption spectra were recorded on a Cary 100 spectrophotometer in 1 cm optical length quartz cuvettes. Corrected emission spectra were obtained on a Jobin-Yvon Horiba Spex FluoroMax-3 spectrofluorometer. Dichloromethane (Aldrich, spectrometric grade or SDS, spectrometric grade) was employed as solvents for absorption and fluorescence measurements. The fluorescence quantum yields were determined by using quinine sulfate in H_2SO_4 0.1M as a standard (ΦF=0.545). The estimated experimental error is less than 10%. For the emission measurements, a right-angle configuration was used and the absorbance at the excitation wavelength are kept below 0.1 in order to avoid reabsorption artefacts.

Fluorescence decay profiles were obtained by time-correlated single-photon counting (TCSPC) method with titanium:sapphire laser (Tsunami, Spectra-Physics) pumped by a doubled Nd:YVO_4 laser (Millennia Xs, Spectra-Physics). Light pulses at 900 nm, were selected by an acousto-optic crystal at a repetition rate of 0.8 MHz, and then tripled at 300 nm by nonlinear crystals. Fluorescence photons were detected at 90˚ through a polarizer at the magic angle and monochromator, by means of a Hamamatsu MCP R3809U photomultiplier, connected to a SPC-630 TCSPC module from Becker&Hickl. The fluorescence data were analyzed using a tail-fit routine as implemented in the Origin software.

Fig.S1 Uv-vis absorption spectra of heptazines 1a to 1d in DCM (top: entire spectrum, bottom: zoom on the low energy absorption band >300 nm)



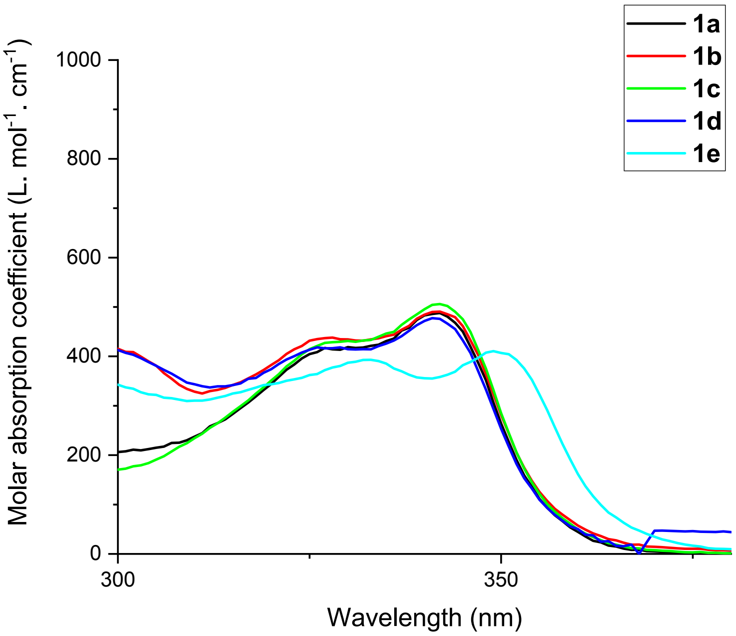


Fig.S2 Fluorescence emission spectra of compounds 1a to 1d in CH_2Cl_2.

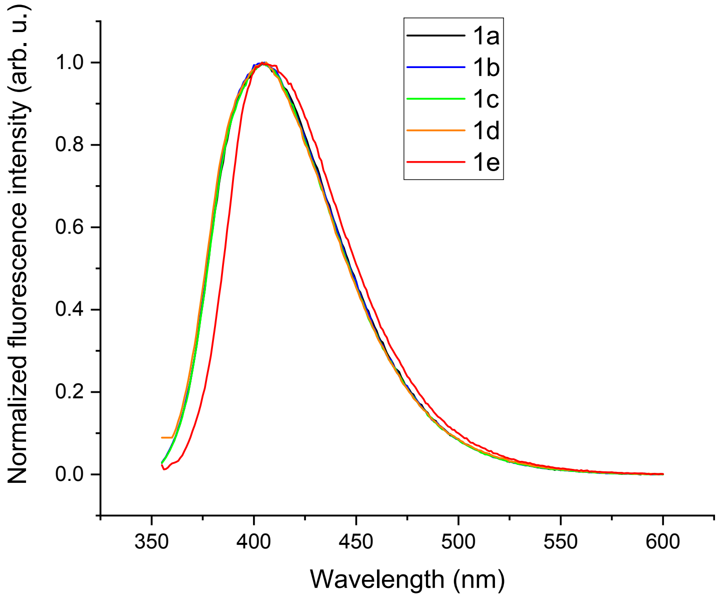


Fig. S3: Absorbance (low-energy band) in different solvents

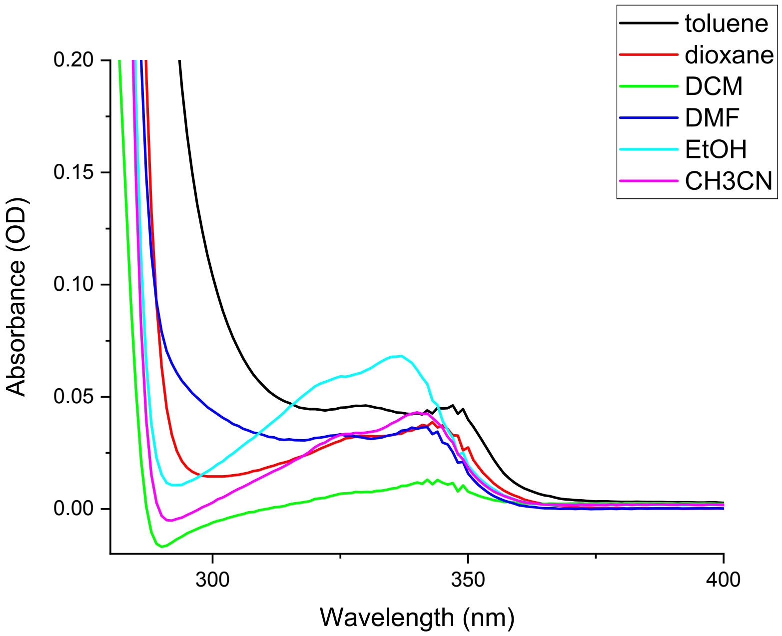
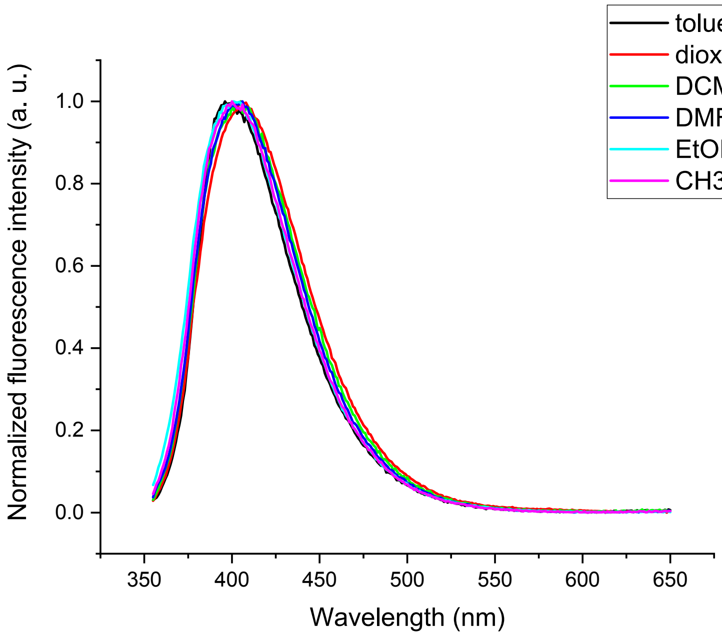


Fig. S4 Fluorescence emission in different solvents



5. Spectroscopic data for the photocatalysis of the oxidation of 5 by heptazine 1e

Fig. S5: Steady-state fluorescence emission spectra for heptazine **1e** in solution in DCM, aerated (black curve) then degassed (red curve), and degassed with increasing amounts of compound **5** (see legend in the insert)

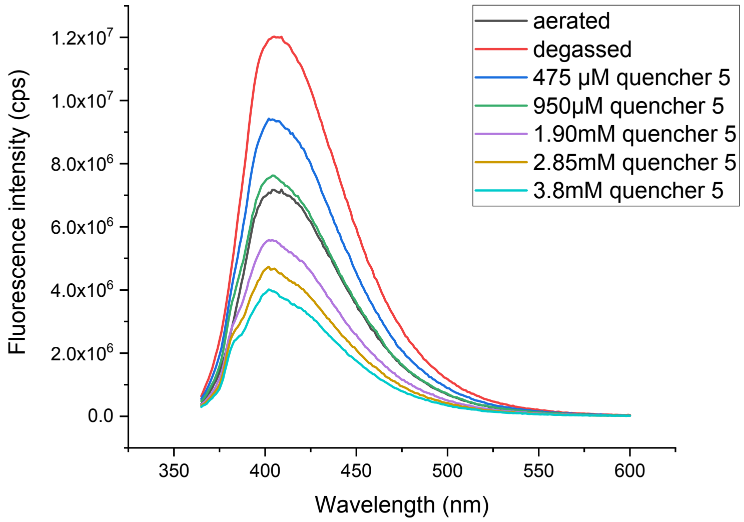
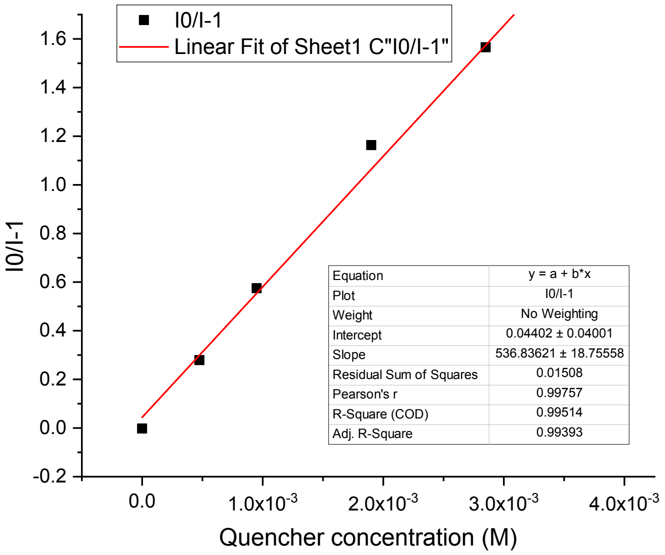


Fig. S6 Stern-Volmer analysis corresponding to the curves on Fig. 3 allowing to determine K_{sv1} = 537 L.mol^{-1}.



Equation	y = a + b*x
Plot	I0/I-1
Weight	No Weighting
Intercept	0.04402 ± 0.04001
Slope	536.83621 ± 18.75558
Residual Sum of Squares	0.01508
Pearson's r	0.99757
R-Square (COD)	0.99514
Adj. R-Square	0.99393

Fig. S7: Steady-state fluorescence emission spectra for heptazine **1e** in solution in DCM, aerated (black curve) then with increasing amounts of compound 5 (see legend in the insert)

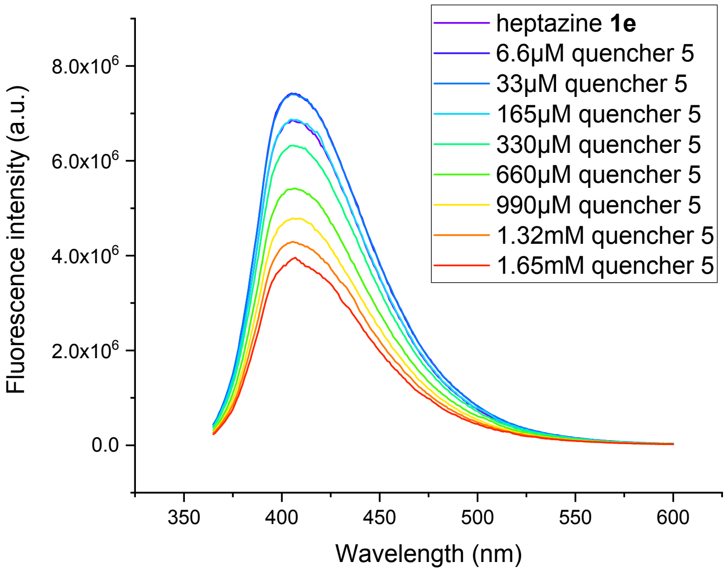
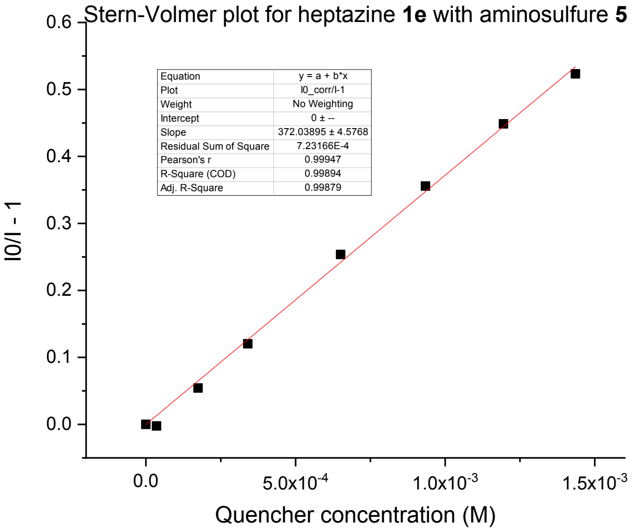


Fig. S8: Stern-Volmer analysis corresponding to the curves on Fig. S5 allowing to determine K_{sv1} = 372L.mol^{-1}.



Equation	y = a + b*x
Plot	I0_corr/I-1
Weight	No Weighting
Intercept	0 ± --
Slope	372.03895 ± 4.5768
Residual Sum of Square	7.23166E-4
Pearson's r	0.99947
R-Square (COD)	0.99894
Adj. R-Square	0.99879

6. Electrochemical data for compounds 1a to 1e, 2a and 5

Electrochemical study of all compounds were performed by cyclic voltammetry, scan rate 200 mV/s, using CH_2Cl_2 as a solvent, tetrabutylammonium tetrafluoroborate (Fluka, puriss) as electrolyte salt, with a substrate concentration $C \approx 10^{-3}$ M

Cyclic voltammetry curves :

Fig. S9: Cyclic voltammogram Heptazine 1a (2,5,8-tricyclopentanoxyheptazine)

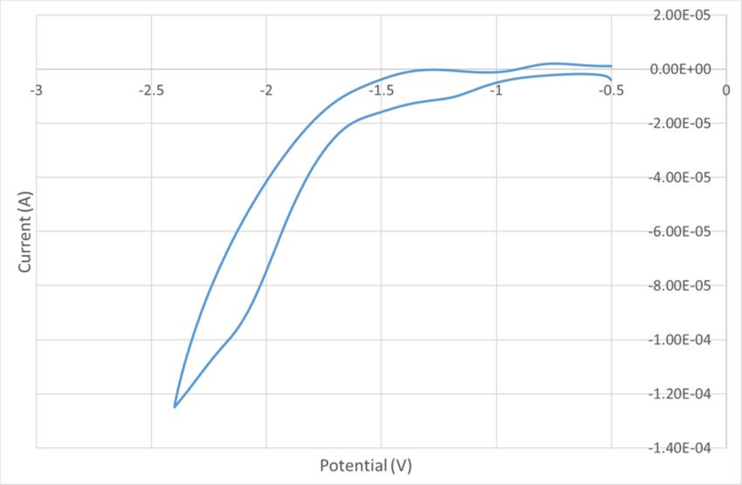
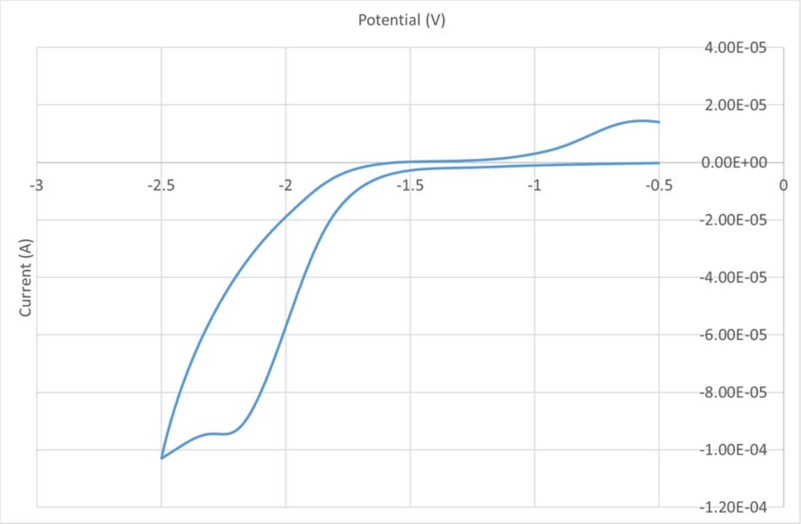
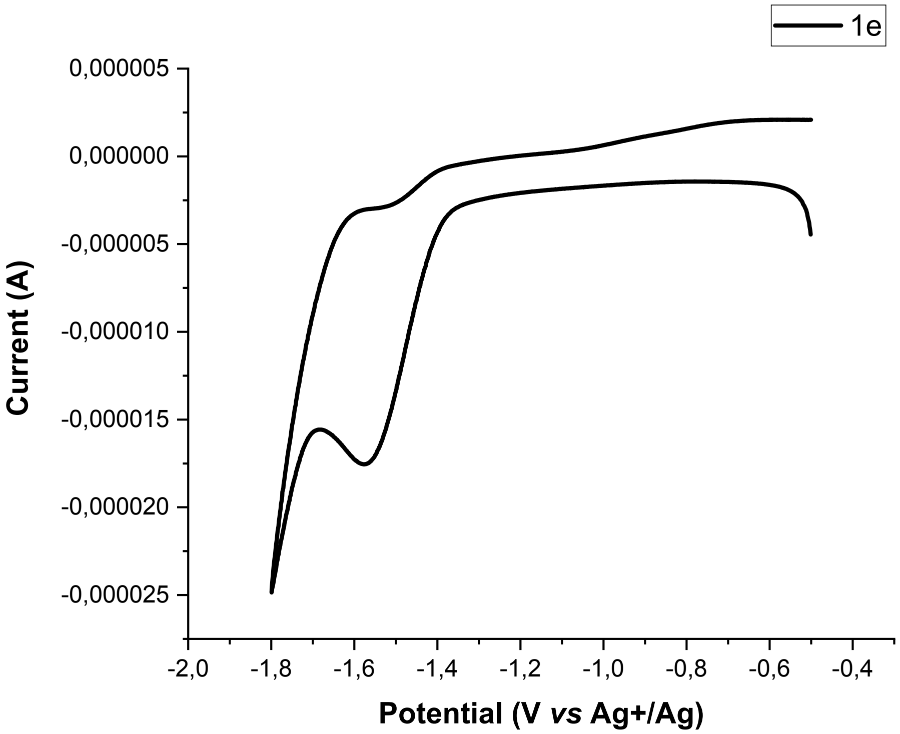


Fig. S10: Cyclic voltammogram of heptazine 1b (2,5,8-trihexyloxyheptazine) ()



Curves corresponding to compounds 1c and 1d were absolutely identical to 1b and were not registered.

Fig.S11 Cyclic voltammogram of heptazine 1e in CH_2Cl_2.



Electrochemical studies of substrates **2a** and **5** were performed using acetonitrile as a solvent, with N-tetrabutylammonium hexafluorophosphate (Fluka, puriss) as the supporting electrolyte. The substrate concentration was ca. 1mM. A 2 mm platinum electrode was used as the working electrode, along with an Ag^+/Ag (10^{-2} M) reference electrode and a Pt wire counter electrode. The cell was connected to a PAR 273A potentiostat. The reference electrode was checked vs. ferrocene as recommended by IUPAC: the oxidation potential of ferrocene was measured at +0.15 V. As a consequence, the values of oxidation potential are given *vs* Fc^+/Fc, corresponding to the measured values – 0.15V. The oxidation of the compounds reported herein are uniformly irreversible processes and the oxidation potentials were then measured by taking the input of the curves.

Fig.S12 Cyclic voltammogram of compound 2a in CH_3CN.

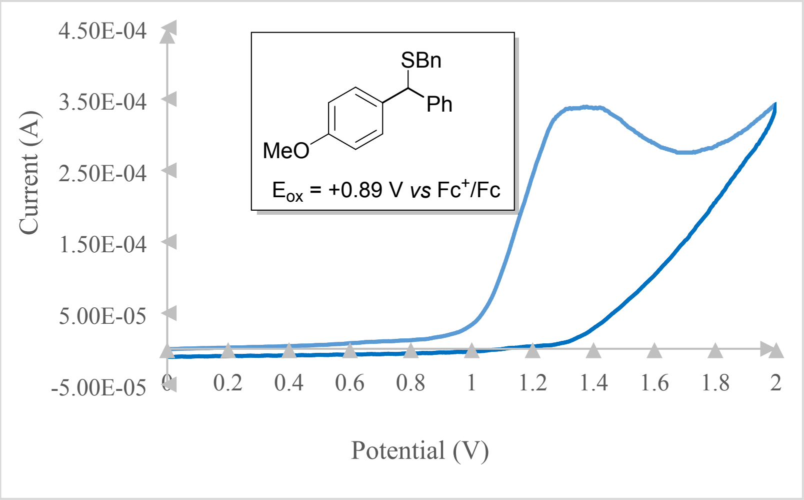
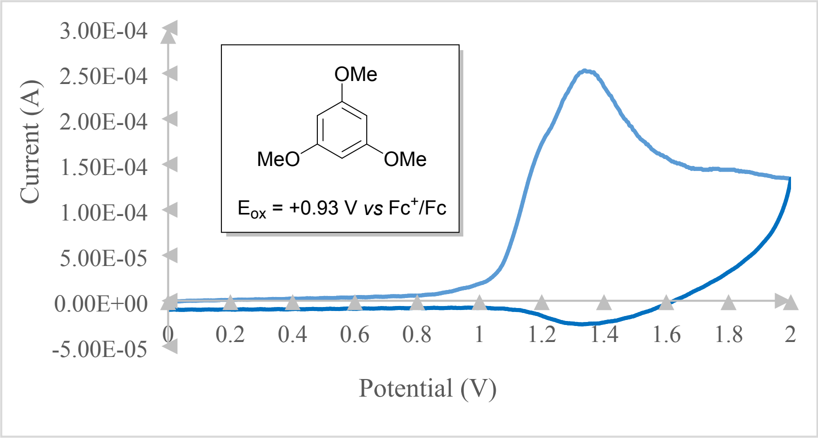


Fig.S13 Cyclic voltammogram of compound 3 in CH3CN.



7. DFT and TD-DFT calculations

Calculations were performed using the hybrid B3LYP functional, as implemented in Gaussian 16 software package. For geometry optimizations, a 6-31+G(d,p) basis set was used. All minima were verified via a calculation of vibrational frequencies, ensuring that no imaginary frequencies were present. For TD-DFT calculations, a 6-311+G(d,p) basis set was used, and an implicit solvent model (iefpcm) was used for dichloromethane.

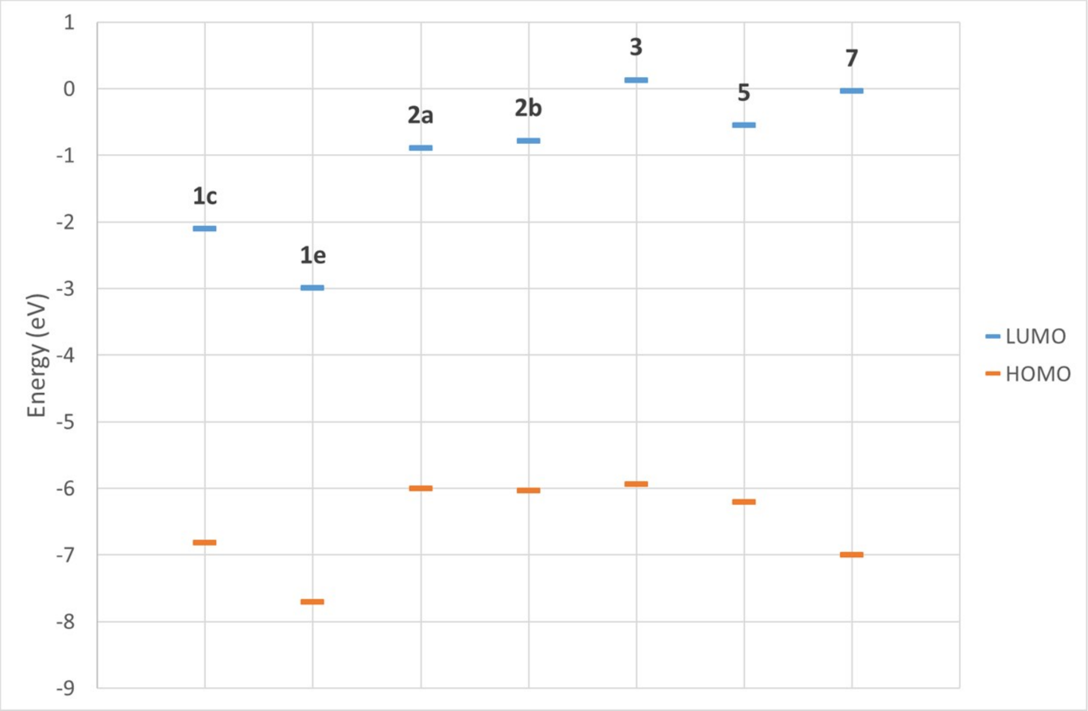


Fig S14. HOMO and LUMO energy levels (B3LYP 6-31G+(d,p)) for heptazine **1e** and the various substrates tested for photocatalytic reactions.

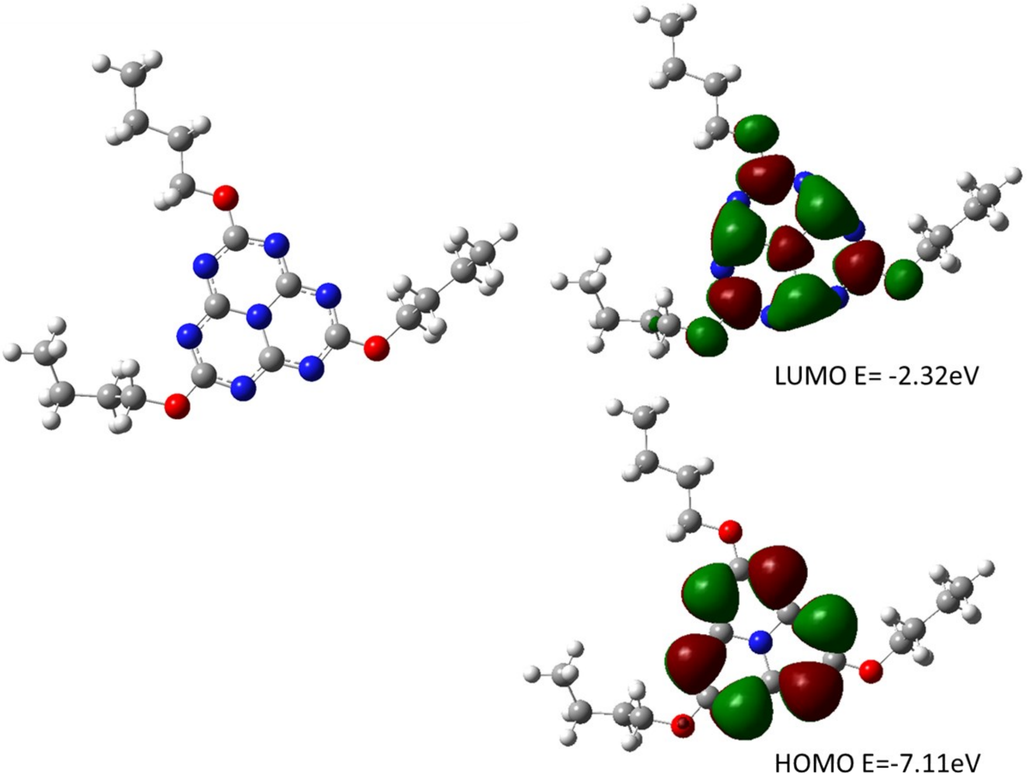


Fig.S15: Optimized geometry (B3LYP 6-31G+(d,p)) together with the representation and energy levels of HOMO and LUMO orbitals of 2,5,8-tris(butoxy)-heptazine **1c** (B3LYP 6.311G+(d,p)).

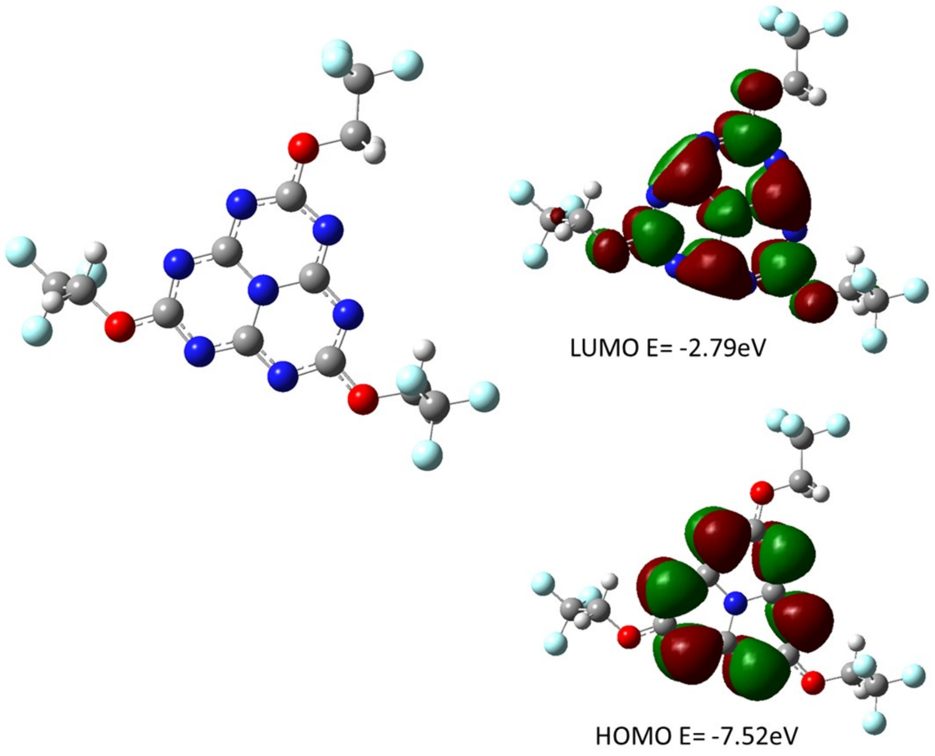


Fig.S16 Optimized geometry (B3LYP 6-31G+(d,p)) together with the representation and energy levels of HOMO and LUO orbitals of 2,5,8-tris(fluoroethoxy)-heptazine **1e** (B3LYP 6.311G+(d,p)).

transition	energy	Oscillator strength	Orbitals involved
1	332nm (3.73eV)	$f=5.10^{-4}$	HOMO-LUMO
2	264nm (4.69eV)	$f=7.10^{-4}$	HOMO-4-LUMO HOMO-3-LUMO HOMO-2-LUMO HOMO-1-LUMO+1
3	258nm (4.81eV)	f=0.1854	HOMO-LUMO+1
4	253nm (4.91eV)	f=0.1895	HOMO-2-LUMO HOMO-LUMO+2

Table 2: vertical absorption transitions computed by TD-DFT for heptazine **1c**

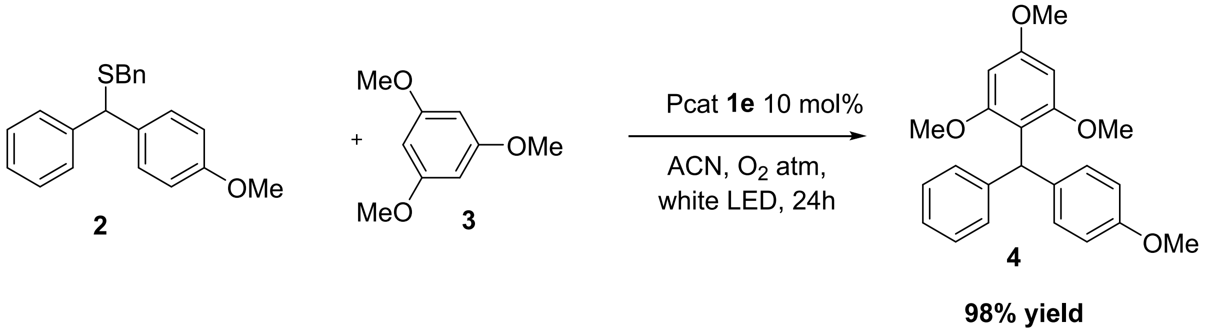
transition	energy	Oscillator strength	Orbitals involved
1	338nm (3.67eV)	$f=4.10^{-4}$	HOMO-LUMO
2	273nm (4.54eV)	$f=1.10^{-4}$	HOMO-2-LUMO+1 HOMO-1-LUMO
3	258nm (4.81eV)	f=0.1984	HOMO-LUMO+1
4	254nm 4.89(eV)	f=0.2100	HOMO-4-LUMO HOMO-LUMO+2

Table 3: vertical absorption transitions computed by TD-DFT for heptazine **1e**

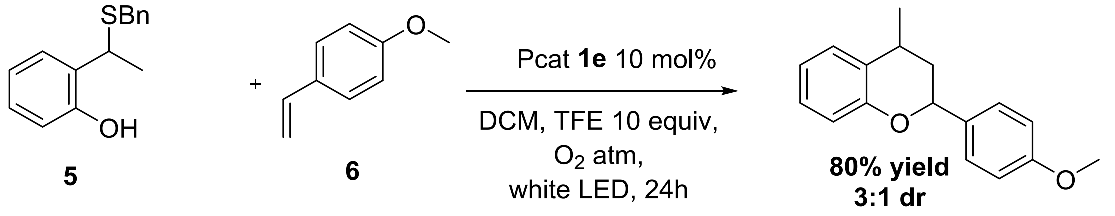
transition	energy	Oscillator strength	Orbitals involved
1	402nm (3.08eV)	$f=1.10^{-4}$	HOMO-LUMO

Table 4: calculated first singlet state computed by TD-DFT (B3LYP 6-31+G(d,p)) for heptazine **1e** in S1 state geometry using DCM as an implicit solvent.

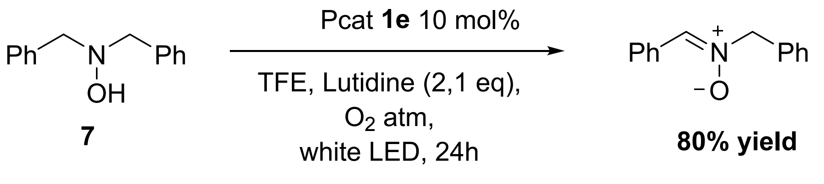
8. Selected examples of photocatalyzed transformations with heptazine 1e



In a flame-dried tube (Ø = 10 mm) were placed thioether **2** (0.1 mmol, 1 equiv) and 1,3,5-trimethoxybenzen **3** (0.15 mmol, 1.5 equiv). CH$_3$CN (1 mL) and heptazine **1e** (4.7 mg, 10 mol%) were successively added and the solution was degassed with O$_2$ for 1 minute. The balloon was left on the top of the tube to maintain the O$_2$ atmosphere and the solution was stirred under white LED irradiation at rt for 24 h. The solvent was then removed under reduced pressure and the residue was purified by silica gel flash chromatography (P.E/EtOAc 90/10) to give the triphenylmethane **4** in virtually quantitative yield.

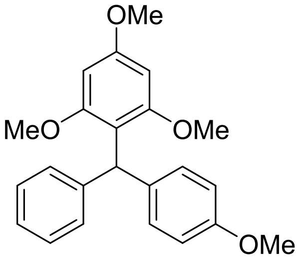


In a flame-dried tube (Ø = 10 mm) were placed thioether **5** (0.1 mmol, 1 equiv) and 4-methoxystyrene **6** (0.6 mmol, 6 equiv). DCM (1 mL), TFE (72 μL, 10 equiv) and heptazine **1e** (4.7 mg, 10 mol%) were successively added and the solution was degassed with O$_2$ for 1 minute. The balloon was left on the top of the tube to maintain the O$_2$ atmosphere and the solution was stirred under white LED irradiation at rt for 24 h. The solvent was then removed under reduced pressure and the residue was purified by silica gel flash chromatography (P.E/EtOAc gradient). An inseparable mixture of diastereoisomers (due to the 2 asymmetry centers) is obtained, which explains the complexity of the NMR spectra.



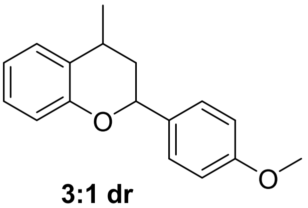
In a flame-dried tube (Ø = 10 mm) were placed N,N-dibenzylhydroxylamine **7** (0.1 mmol, 1 equiv). TFE (1 mL), lutidine (25 μL, 2.1 equiv) and heptazine **1e** (4.7 mg, 10 mol%) were successively added and the solution was degassed with O$_2$ for 1 minute. The balloon was left on the top of the tube to maintain the O$_2$ atmosphere and the solution was stirred under white LED irradiation at rt for 24 h. The solvent was then removed under reduced pressure and the residue was purified by silica gel flash chromatography (P.E/EtOAc 70/30).

1,3,5-trimethoxy-2-((4-methoxyphenyl)(phenyl)methyl)benzene



^{1}H NMR (500 MHz, CDCl$_3$) δ (ppm): 7.23-7.14 (m, 7H), 6.79 (d, *J* = 8.8 Hz, 2H), 6.16 (s, 2H), 6.01 (s, 1H), 3.81 (s, 3H), 3.78 (s, 3H), 3.60 (s, 6H). According to literature data.[1]

2-(4-methoxyphenyl)-4-metylchromane



3:1 dr

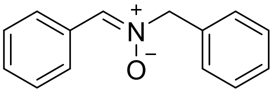
^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 7.31-7.25 (m, 2H), 7.20-7.16 (m, 1H), 7.06-7.01 (m, 1H), 6.86-6.72 (m, 4H), [5.01-4.97, 4.96-4.92 (m, 1H)], [3.74, 3.70 (s, 3H)], [3.14-3.06, 2.94-2.92 (m, 1H)], 2.18-2.07 (m, 1H), 1.82-1.69 (m, 1H), [1.34-1.32, 1.30-1.28 (d, *J* = 6.8 Hz, 3H)].

^{13}C NMR (75 MHz, CDCl$_3$) δ (ppm): 159.4 (1C), 155.0 (1C), 133.9 (1C), 129.3 (1C), 127.5 (2C), 127.3 (1C), 127.1 (1C), 120.5 (1C), 117.0 (1C), 114.0 (2C), [77.7, 73.1 (1C)], [55.3, 47.8 (1C)], [39.8, 37.0 (1C)], [30.2, 26.0 (1C)], [24.0-20.2 (1C)].

IR (neat) ν (cm^{-1}): 2959, 1612, 1579, 1515, 1486, 1297, 1247, 1175, 1115, 1036, 979, 894, 823, 754.

HRMS (ESI$^+$, m/z): [M+H$^+$] calculated for $C_{17}H_{19}O_2$ 255.1385, found 255.1379.

(Z)-*N*-benzyl-1-phenylmethanimine oxide



^{1}H NMR (300 MHz, CDCl$_3$) δ (ppm): 8.23-8.19 (m, 2H), 7.48-7.45 (m, 2H), 7.42-7.39 (m, 7H), 5.06 (s, 2H). According to literature data.[2]

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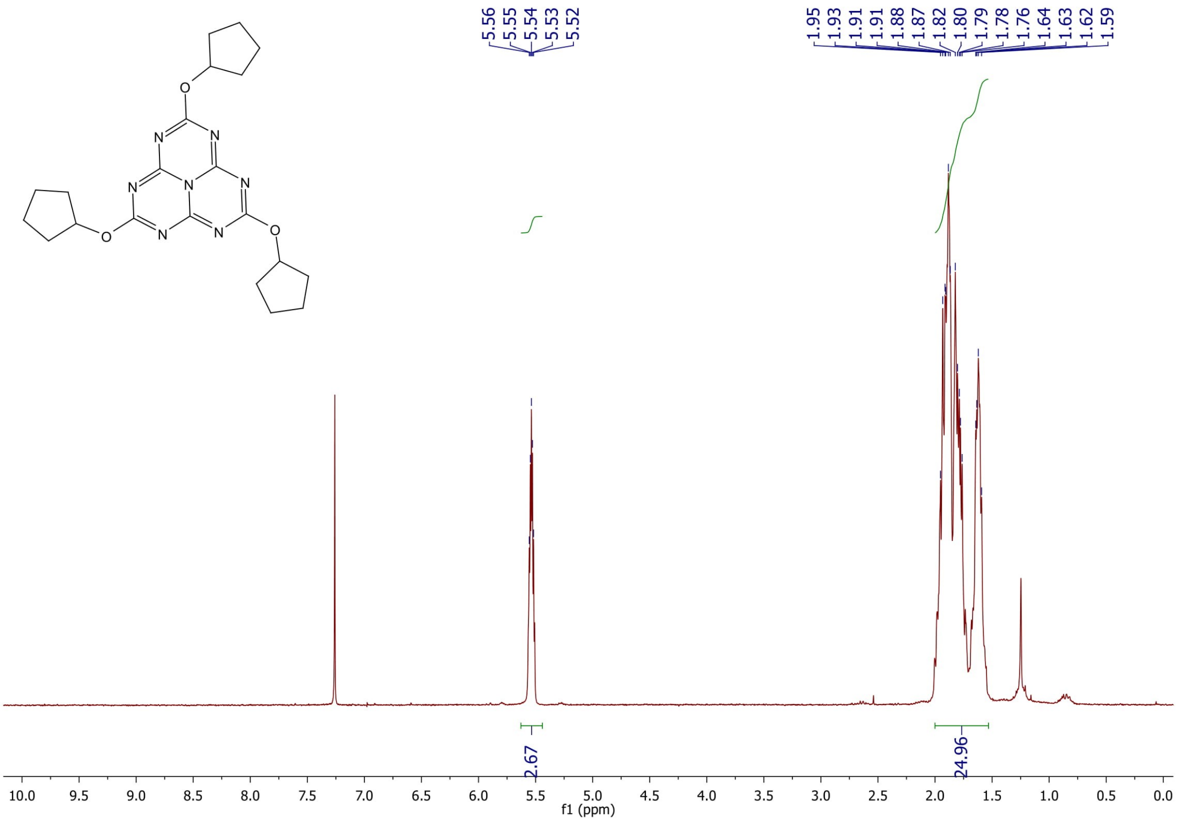
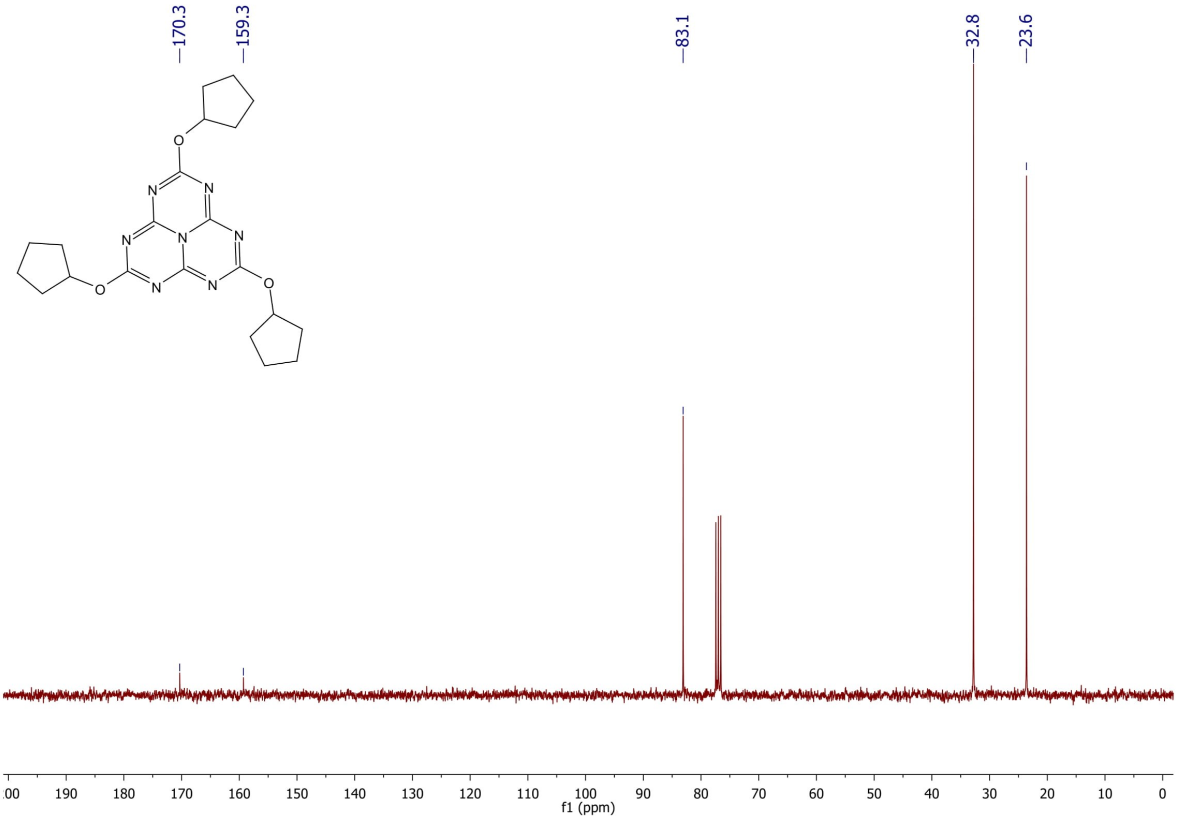
[1] M. Lanzi, J. Merad, D. V. Boyarskaya, G. Maestri, C. Allain and G. Masson, *Org. Lett.* **2018**, 20, *17*, 5247-5250.

[2] K. Yanai, H. Togo, *Tetrahedron* **2019**, 75, *25*, 3523-3529.

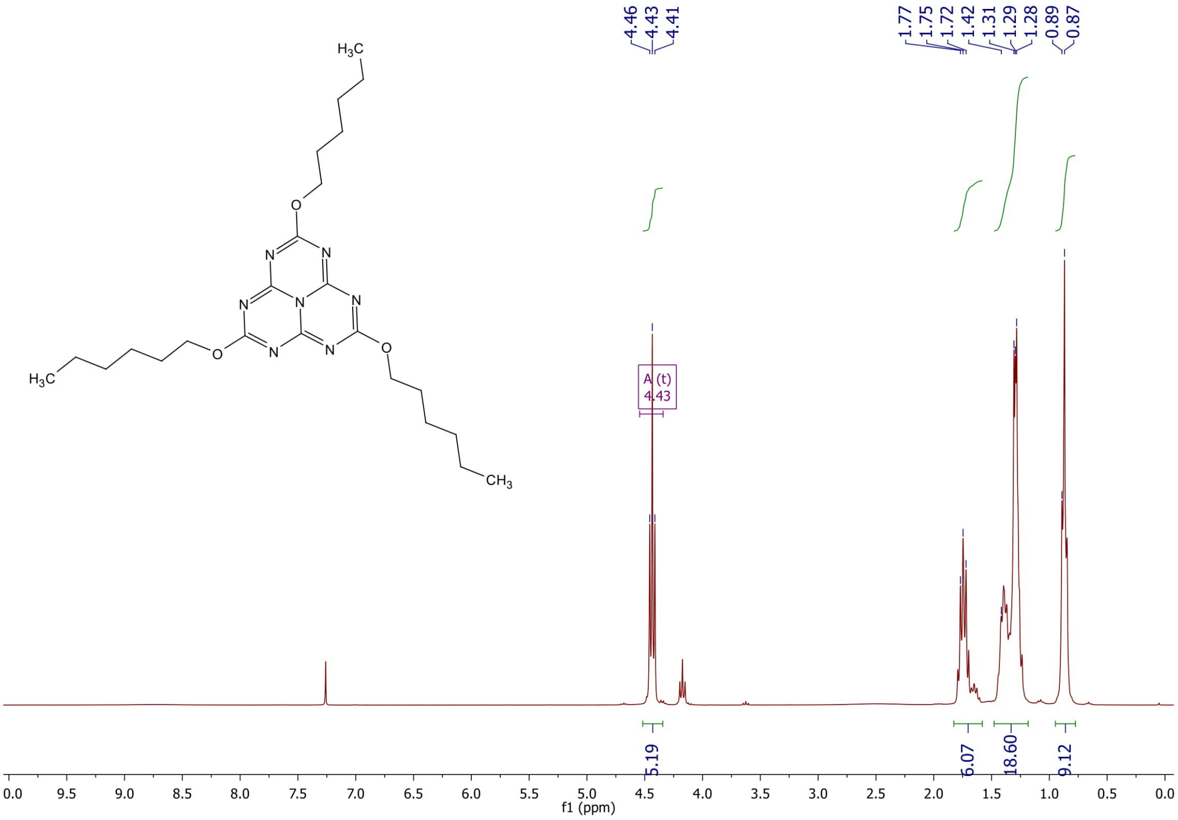
9. 1H and 13C NMR spectra of compounds 1a-e

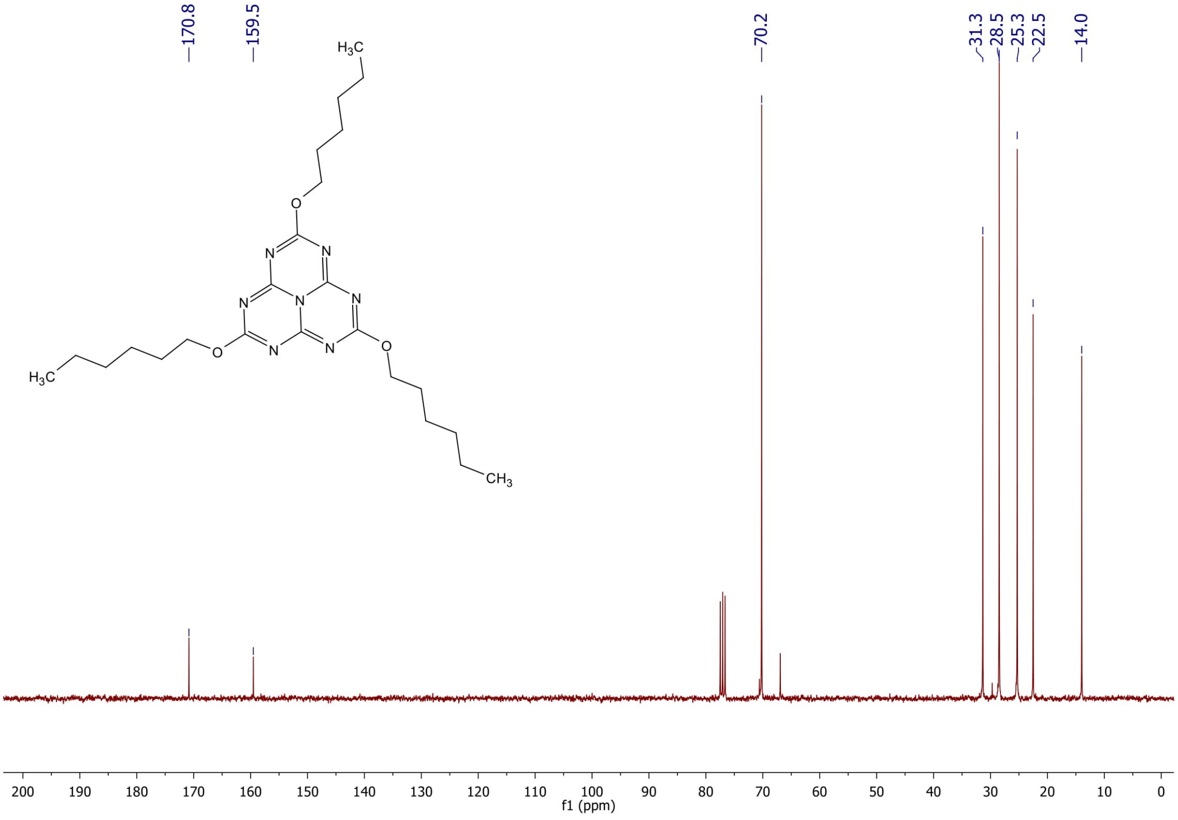
2,5,8-tris(cyclopentyloxy)-heptazine **1a**

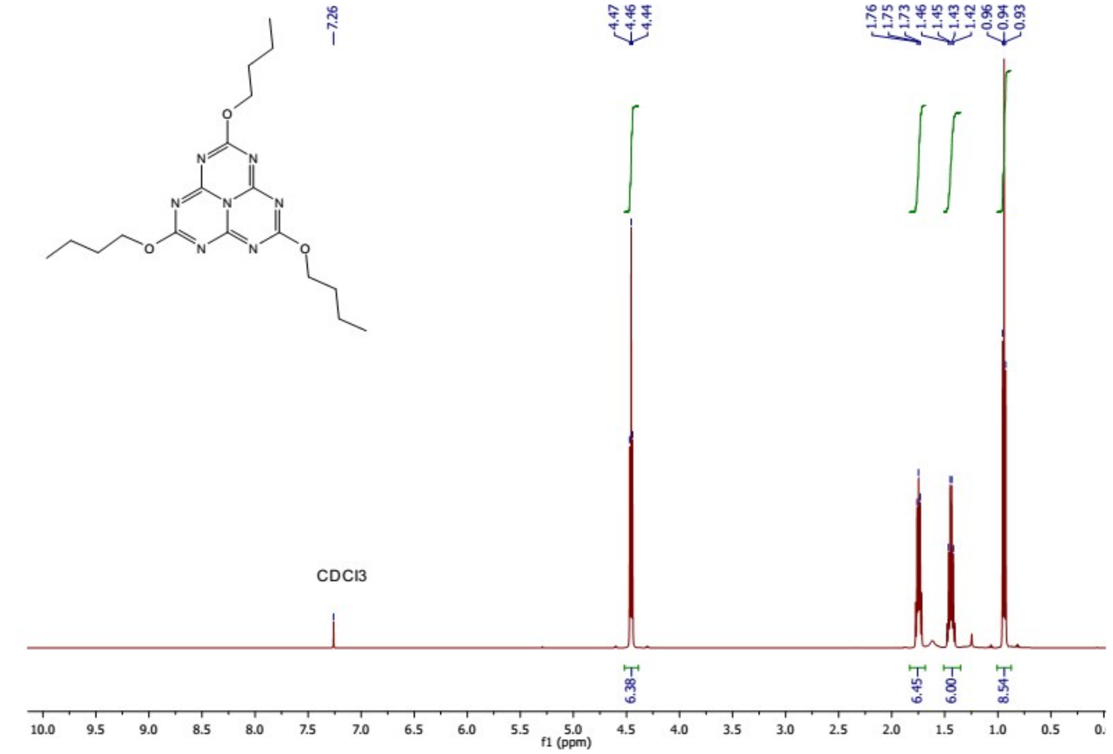




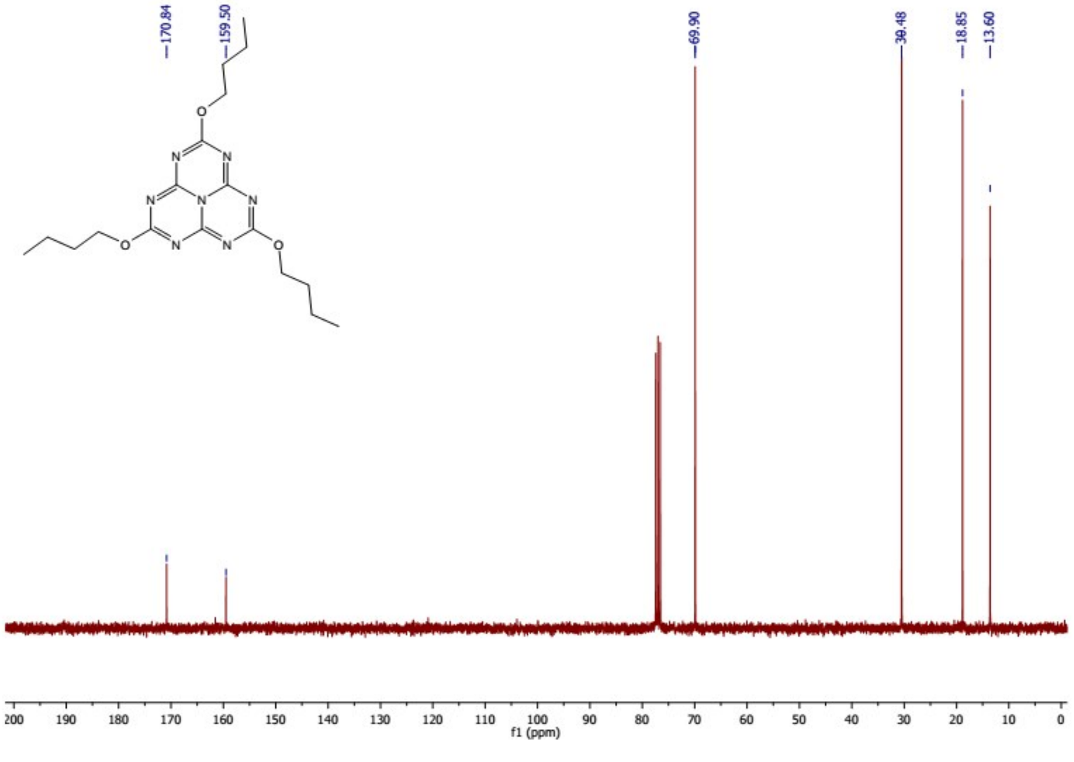
2,5,8-tris(hexyloxy)-heptazine **1b**



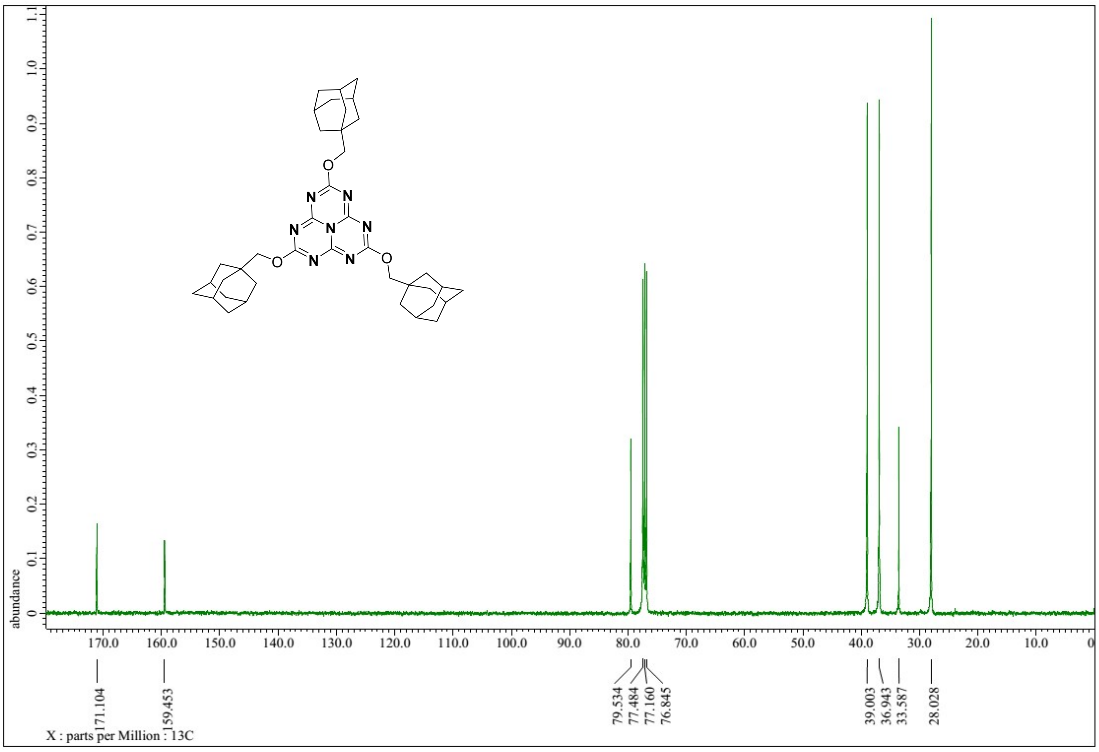


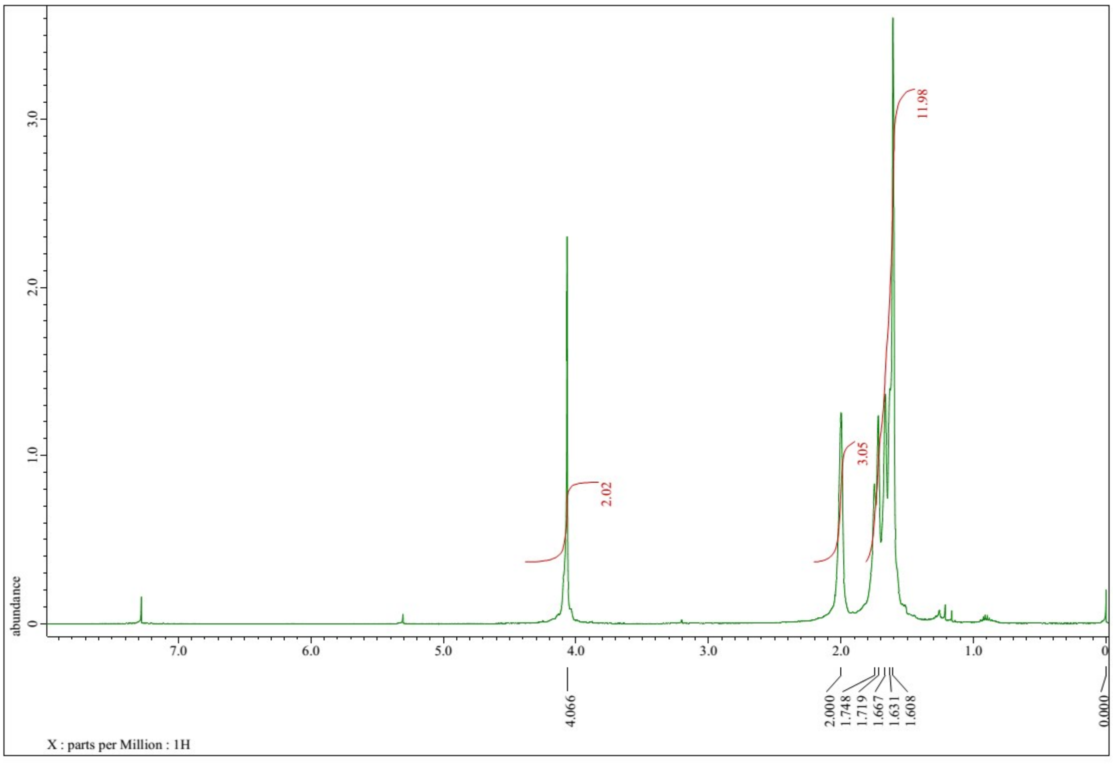


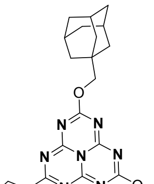
2,5,8-tributoxy-heptazine **1c**



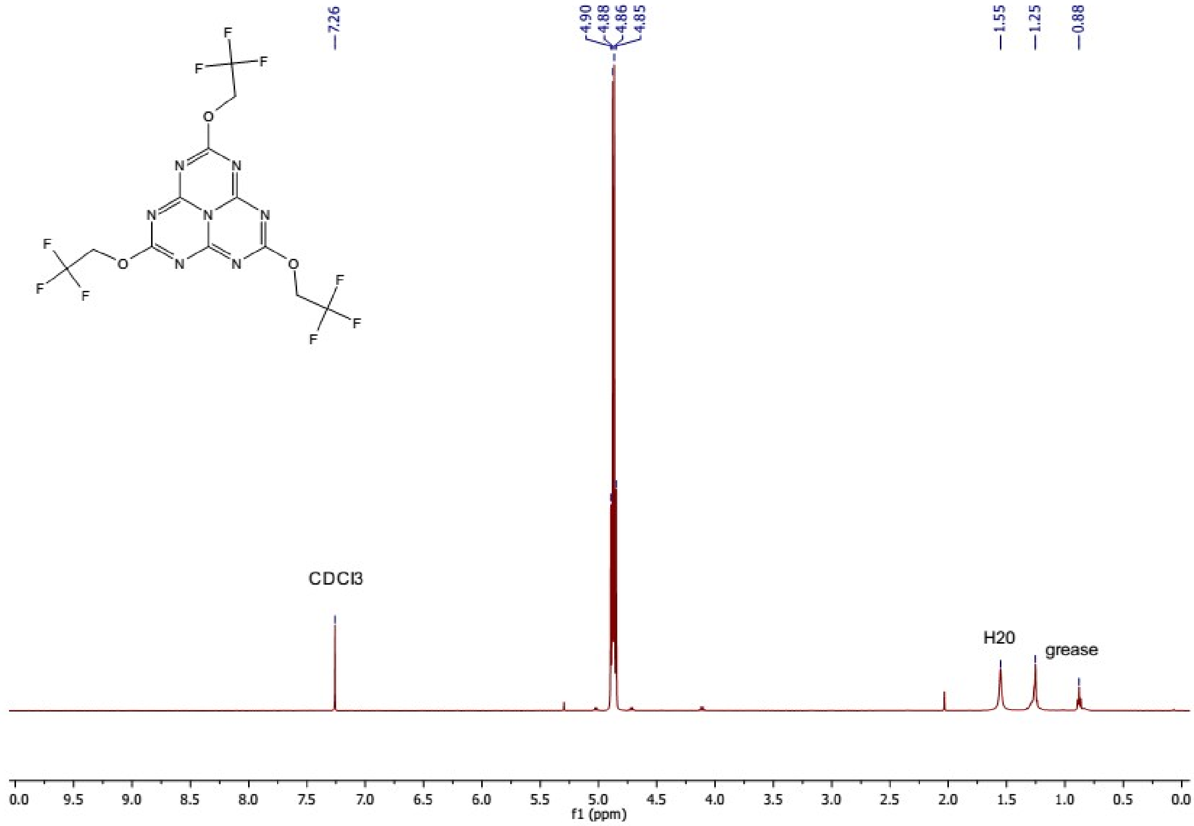
2,5,8-tris((adamantan-1-yl)methoxy)-heptazine **1d**

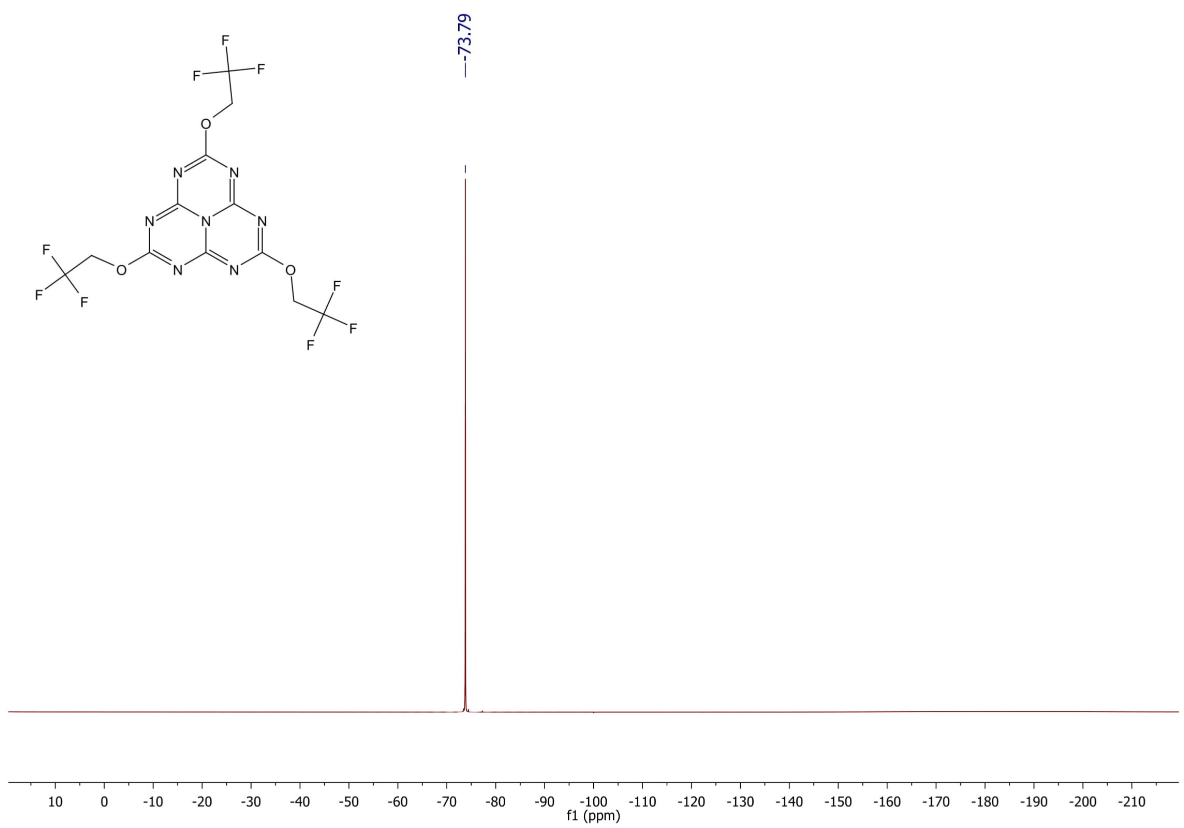


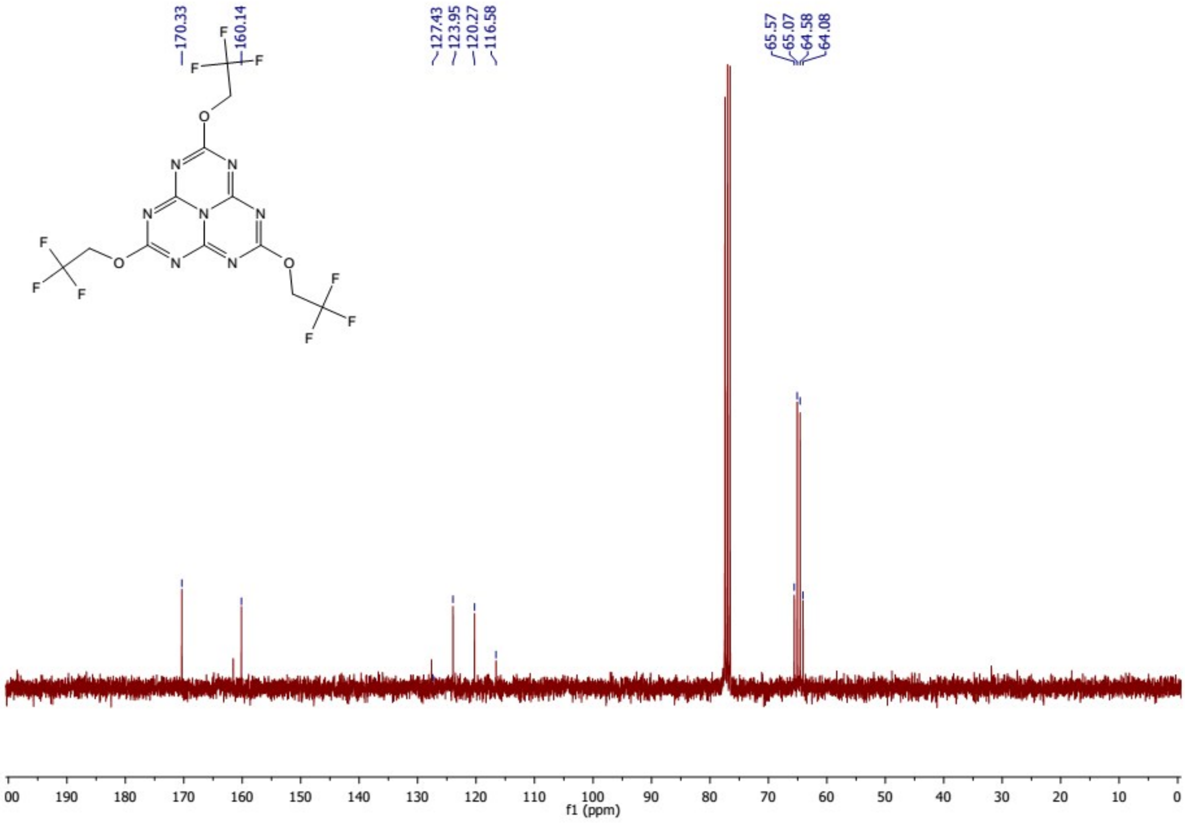




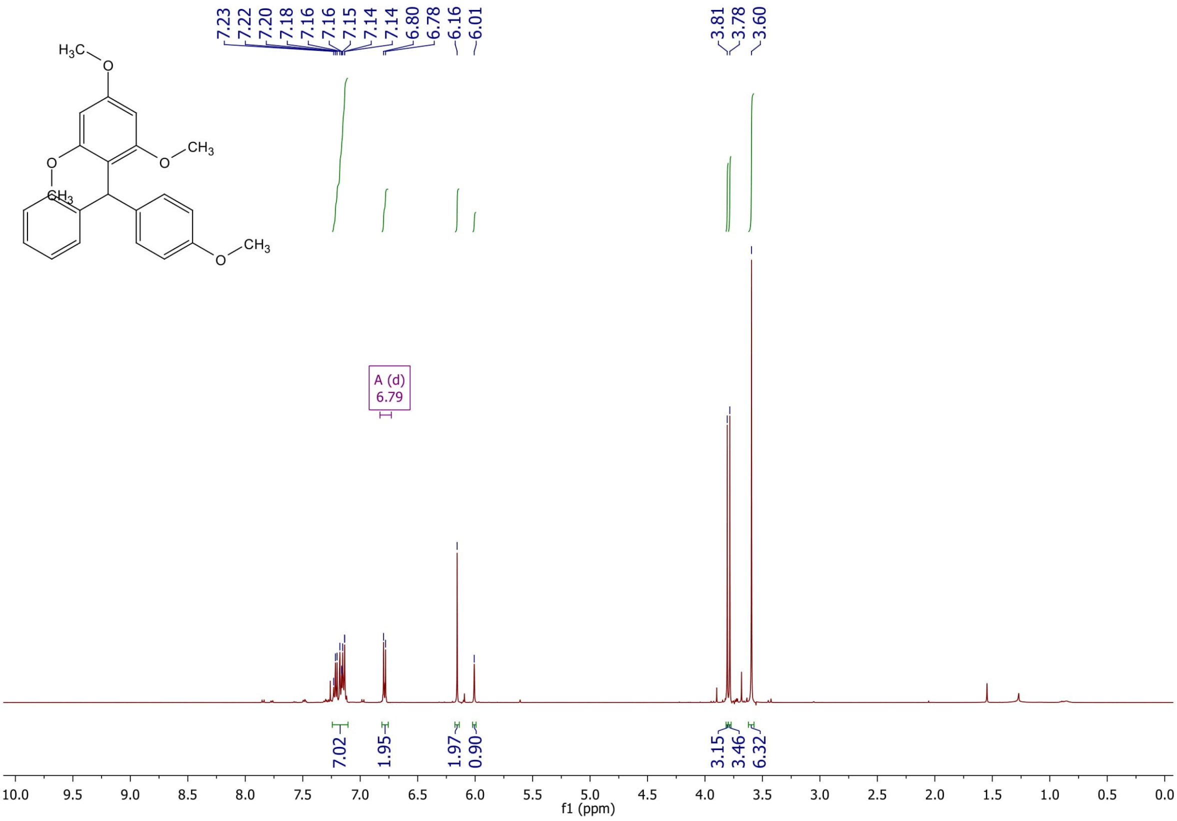
2,5,8-tris(2,2,2-trifluoroethoxy)-heptazine **1e**



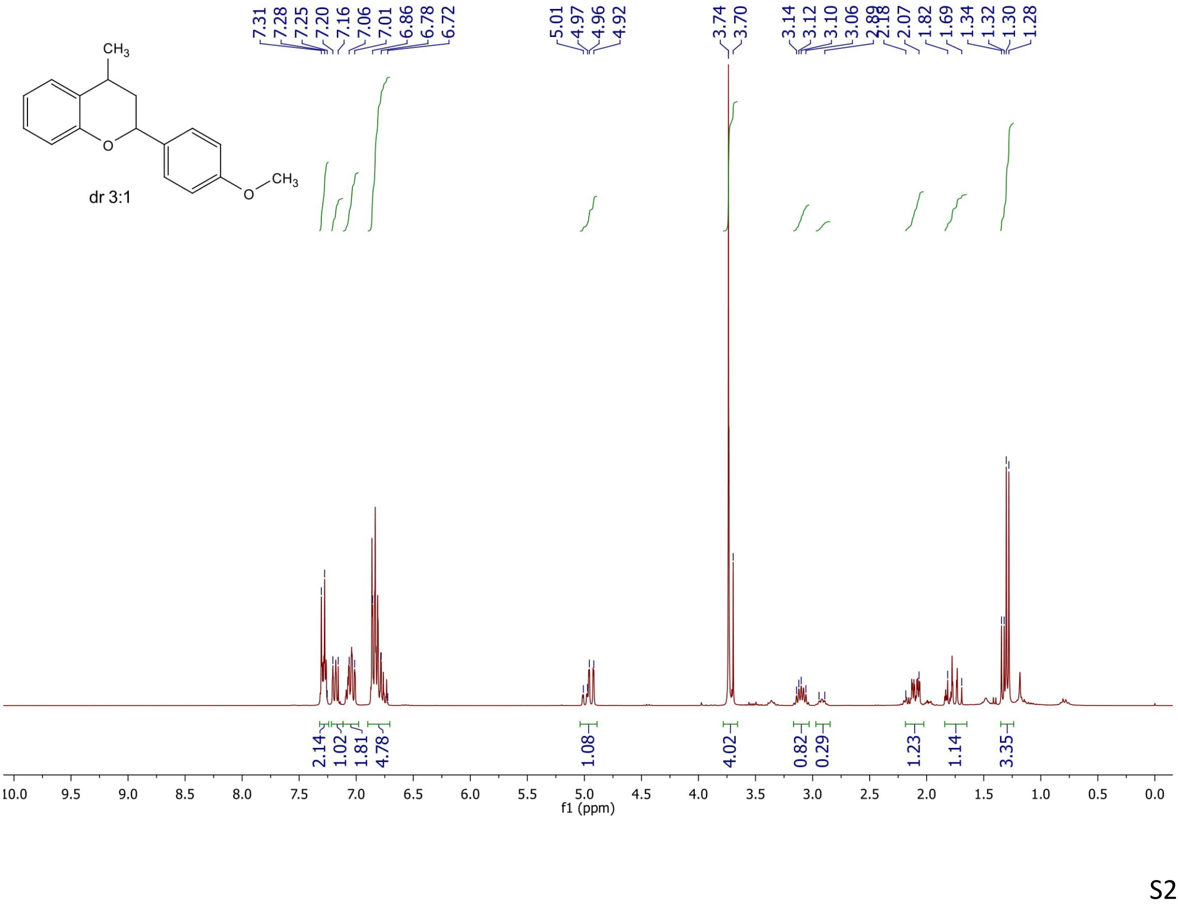


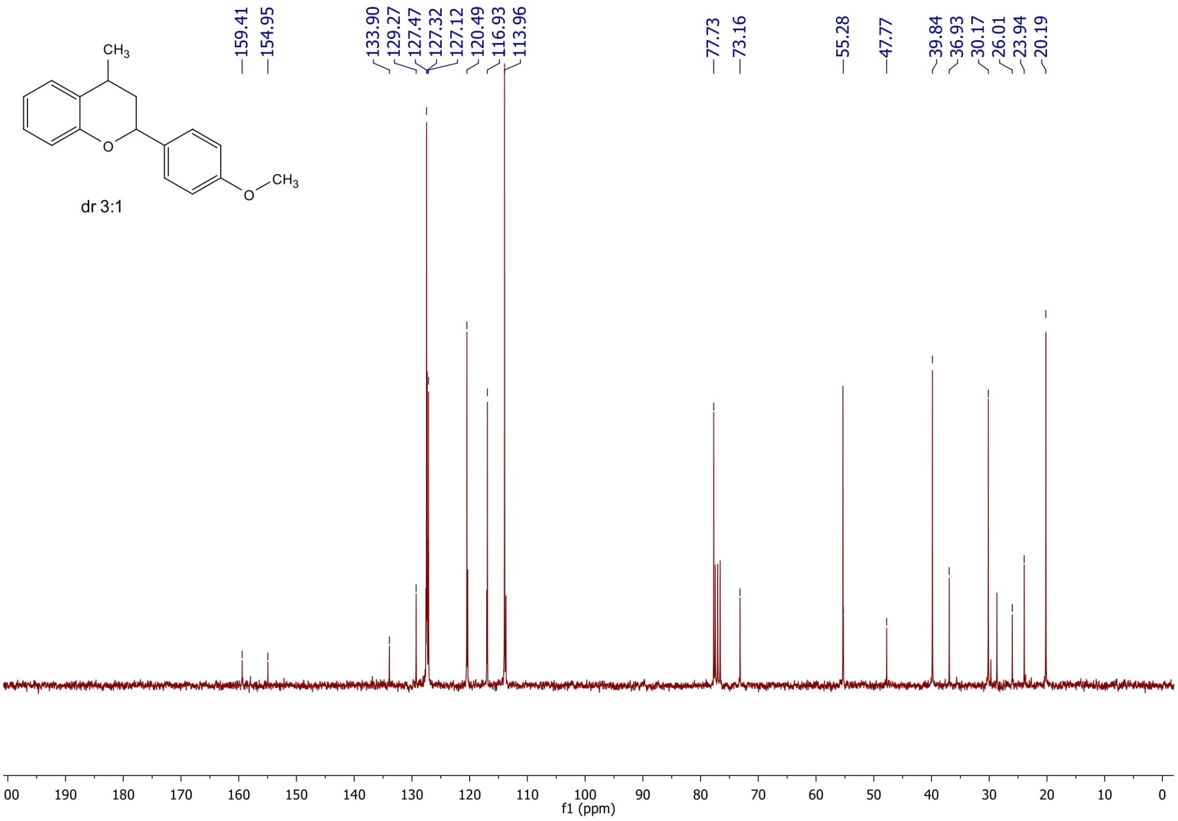


1,3,5-trimethoxy-2-((4-methoxyphenyl)(phenyl)methyl)benzene **4**



2-(4-methoxyphenyl)-4-metylchromane

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O
O
CH3
dr 3:1
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154.95
133.90
129.27
127.47
127.32
127.12
120.49
116.93
113.96
77.73
73.16
55.28
47.77
39.84
36.93
30.17
26.01
23.94
20.19
00
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

(Z)-*N*-benzyl-1-phenylmethanimine oxide