Reaction of β-Nitrostyrene with Diethyl Malonate in the Presence of Bispidines: The Unusual Role of the Organocatalyst

Alexander I. Dalinger [1], Sabina F. Mamedova [2], Julia V. Burykina [1], Evgeniy O. Pentsak [1] and Sergey Z. Vatsadze [1]*

[1] N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, Leninsky Prospect 47, Moscow 119991, Russia; dal1995@mail.ru (A.I.D.), ivanova@ioc.ac.ru (J.V.B), p_eugene@ioc.ac.ru (E.O.P.), zurabych@gmail.com (S.Z.V.)

[2] Department of Chemistry, Lomonosov Moscow State University, Leninskie Gory, MSU, 1-3, 119991 Moscow, Russia; sem.ms9696@gmail.com (S.F.M.)

* Correspondence: zurabych@gmail.com

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Table S1

Table S1. The results of the catalytic reaction[1] in solvents of various nature.

Solvent	Conversion of nitrostyrene 3, %[2,3]	Formation of product 5[2,3]	Side processes[2]
Toluene	100	Yes (98%[4])	No
1,4-Dioxane	100	Yes (96%[4])	No
THF	100	Yes (89%[4])	Yes
DCM	100	Yes	Yes
$CHCl_3$	100	Yes	Yes
MeCN	100	Yes	Yes
EtOH	100	Yes	Yes
n-Hexane[5]	n/a	No	n/a
H_2O[5]	n/a	No	n/a

[1] Catalytic reactions were carried out in the presence of 1 eq. *β*-nitrostyrene, 5 eq. diethyl malonate and 0.2 eq. *N*-benzylbispidine in 2 mL of corresponding solvent at room temperature for 24 hours.

[2]Determined by ^{1}H NMR of the reaction mixture.

[3]Determined by TLC analysis of the reaction mixture.

[4]The product was isolated by column chromatography.

[5] The reaction components were not soluble in these solvents.

Photos of reaction mixtures

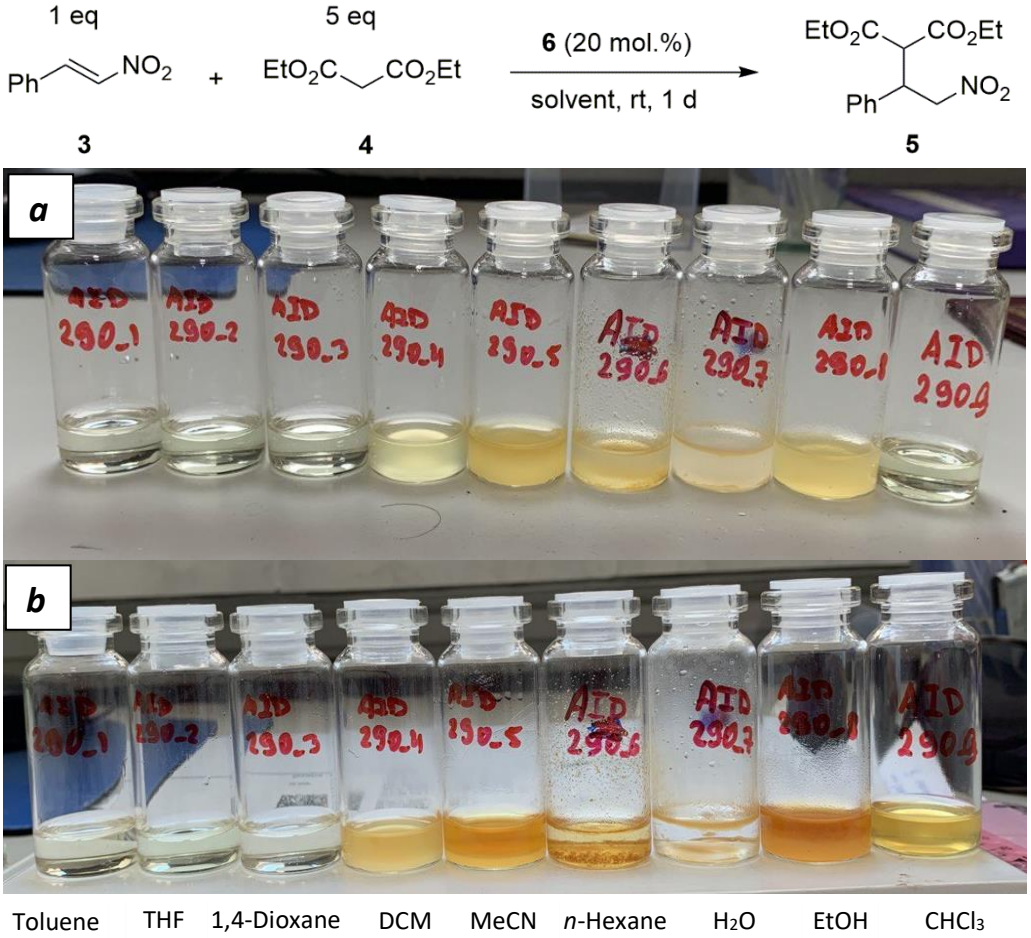


Figure S1. The reaction mixtures after the indicated time after mixing the reagents: (**a**) toluene – 1 h 15 min, THF – 1 h 10 min, 1,4-dioxane – 1 h, DCM – 50 min, MeCN – 45 min, *n*-hexane – 40 min, H_2O – 35 min, EtOH – 25 min, $CHCl_3$ – 10 min; (**b**) after 24 h.

NMR spectra

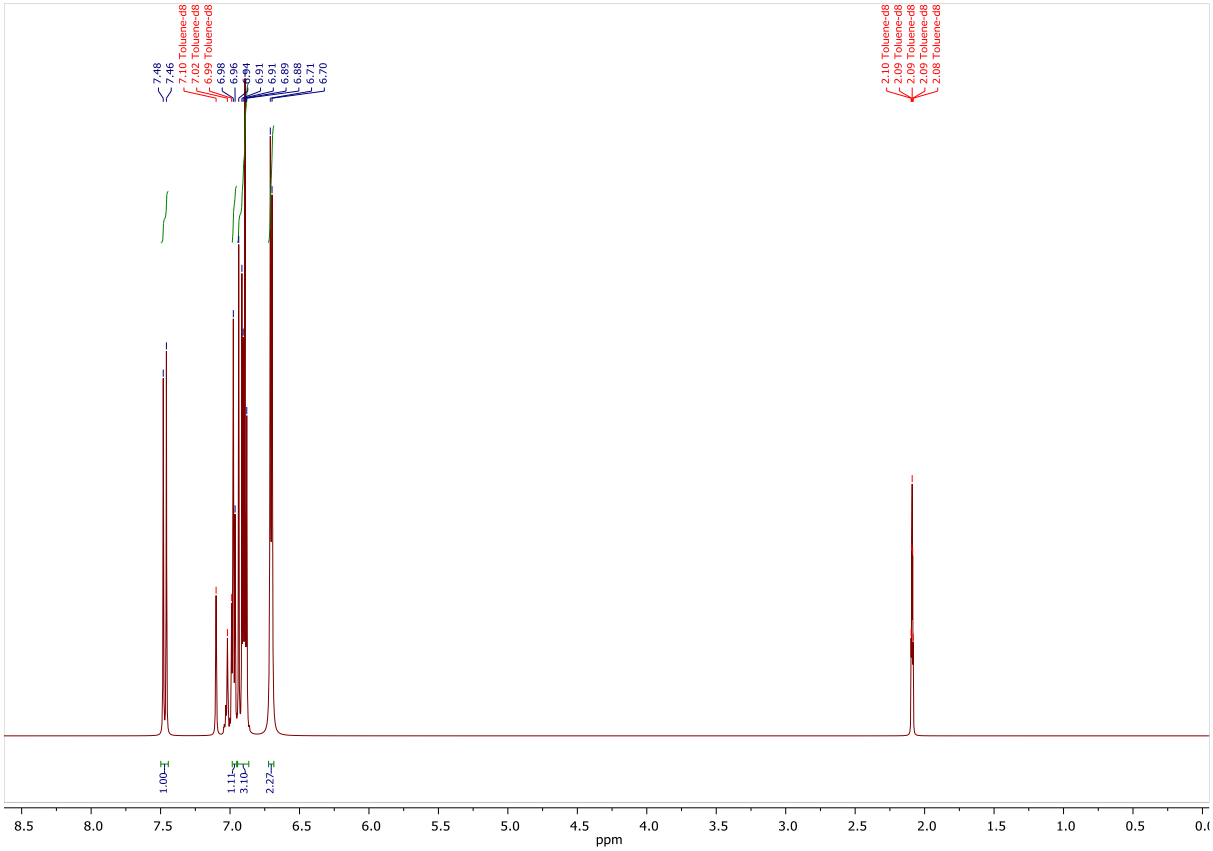


Figure S2. ^{1}H NMR spectrum of nitrostyrene **3** (600 MHz, toluene-d$_8$).

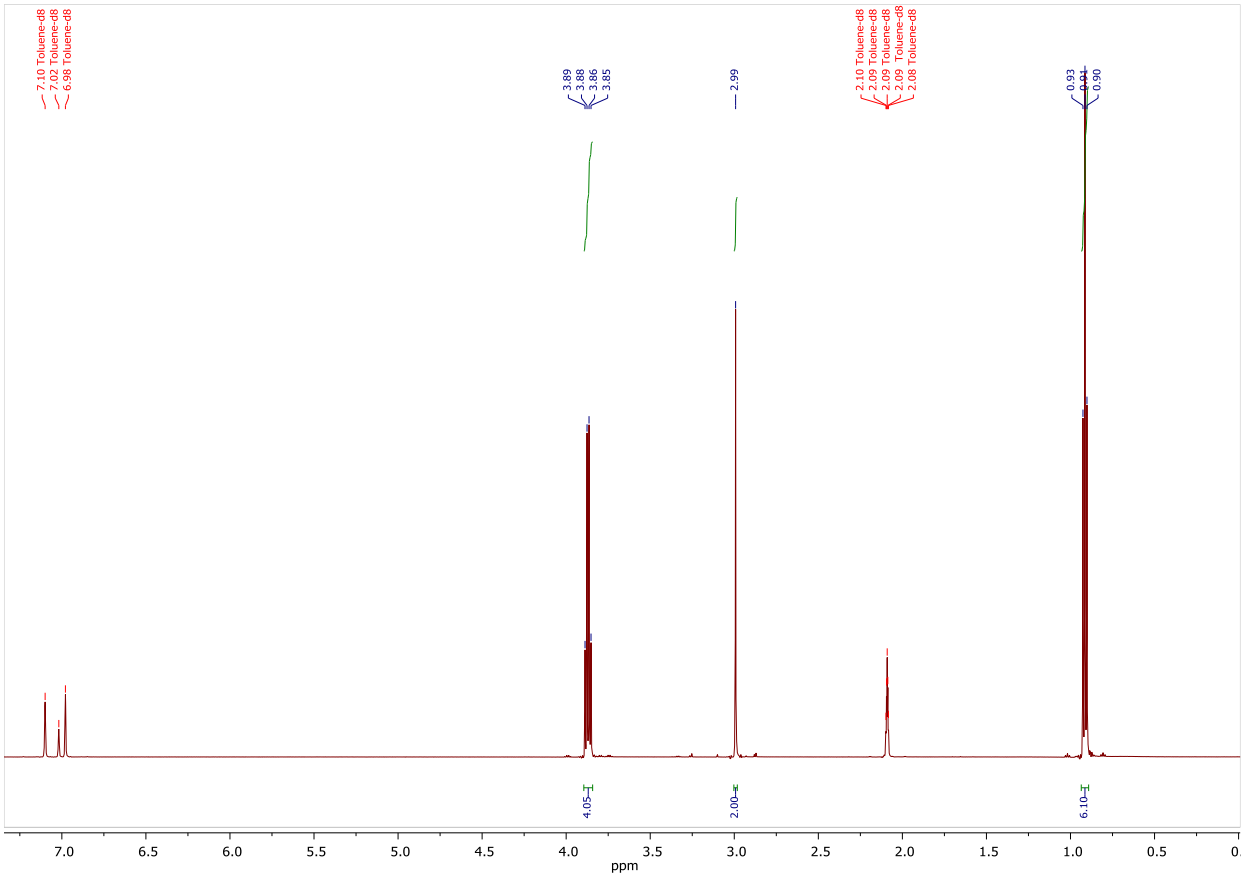


Figure S3. ^{1}H NMR spectrum of diethyl malonate **4** (600 MHz, toluene-d$_8$).

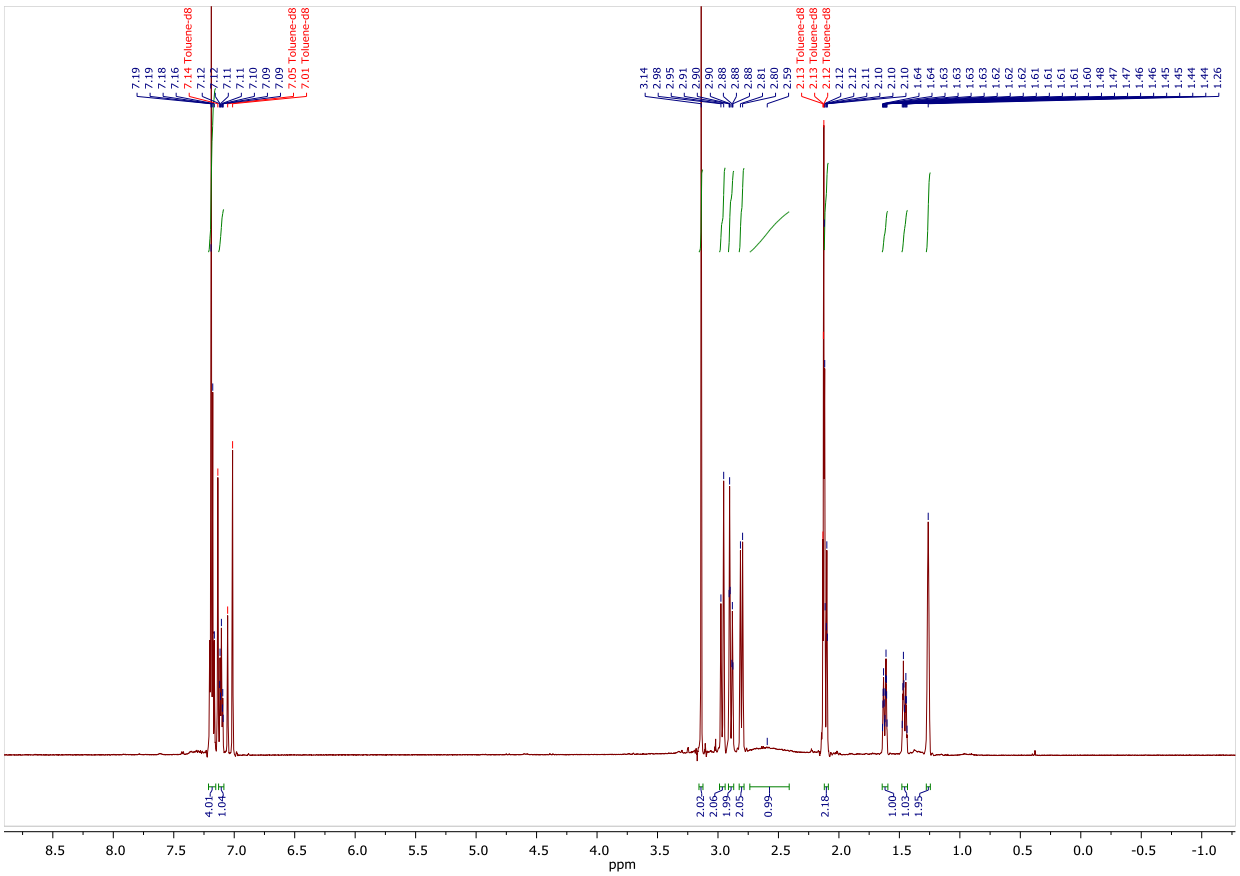


Figure S4. ^{1}H NMR spectrum of N-benzylbispidine **6** (600 MHz, toluene-d$_8$).

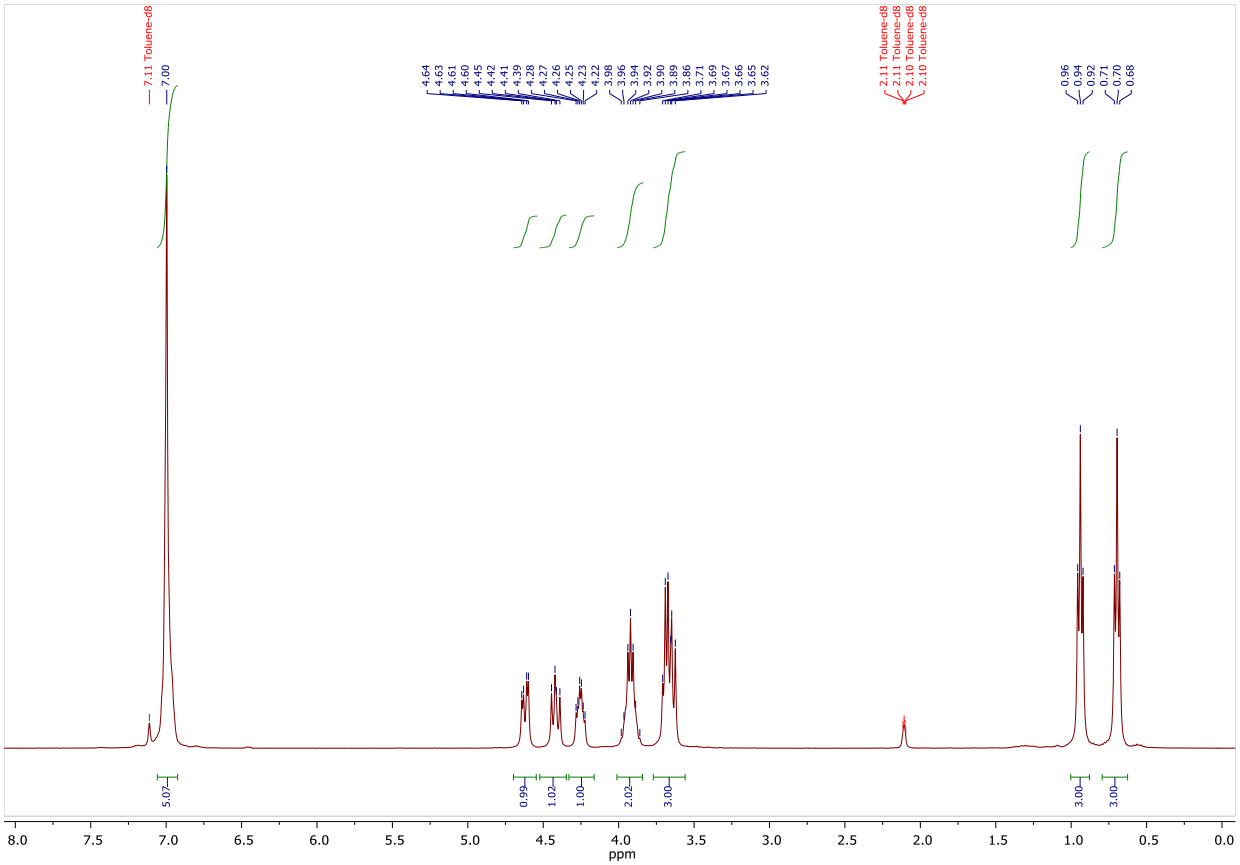


Figure S5. ^{1}H NMR spectrum of the addition product **5** (400 MHz, toluene-d$_8$).

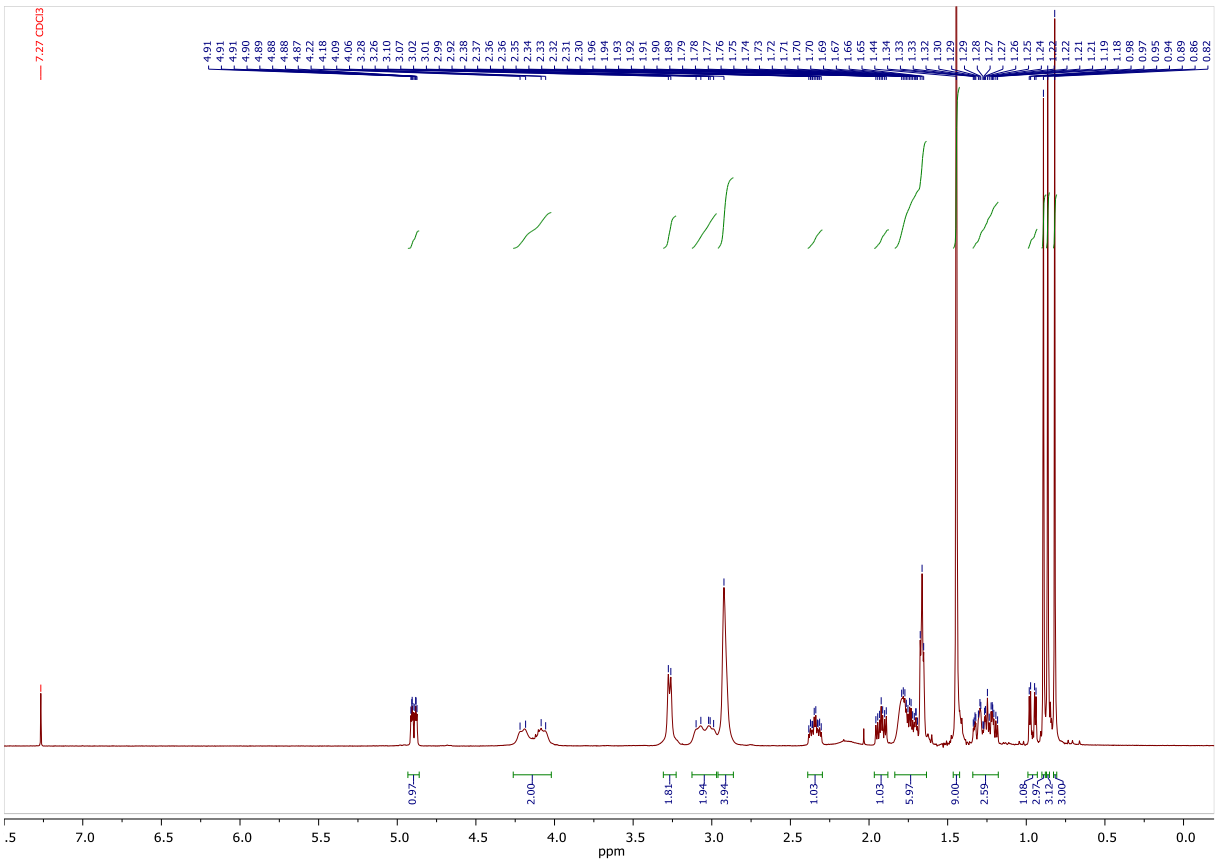


Figure S6. ^{1}H NMR spectrum of the compound **9a** (400 MHz, $CDCl_3$).

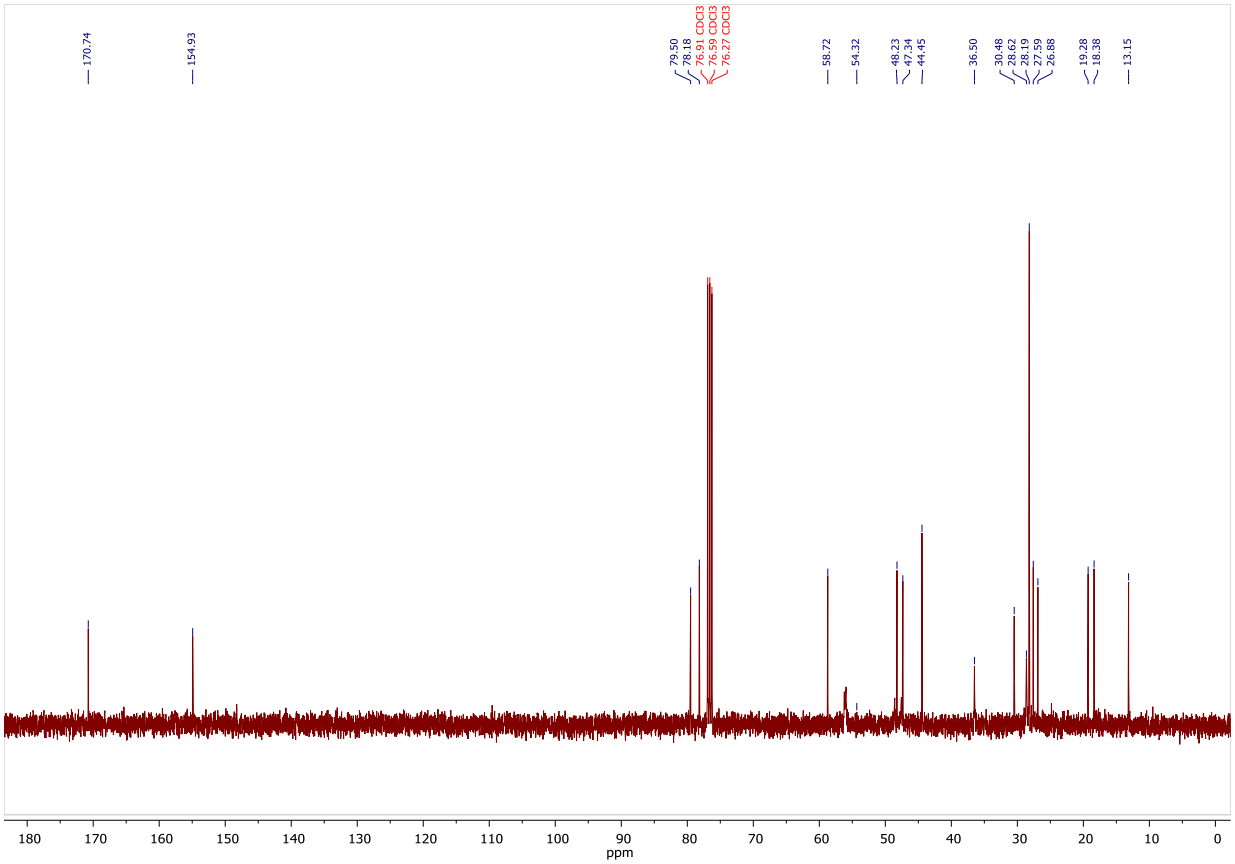


Figure S7. ^{13}C NMR spectrum of the compound **9a** (101 MHz, $CDCl_3$).

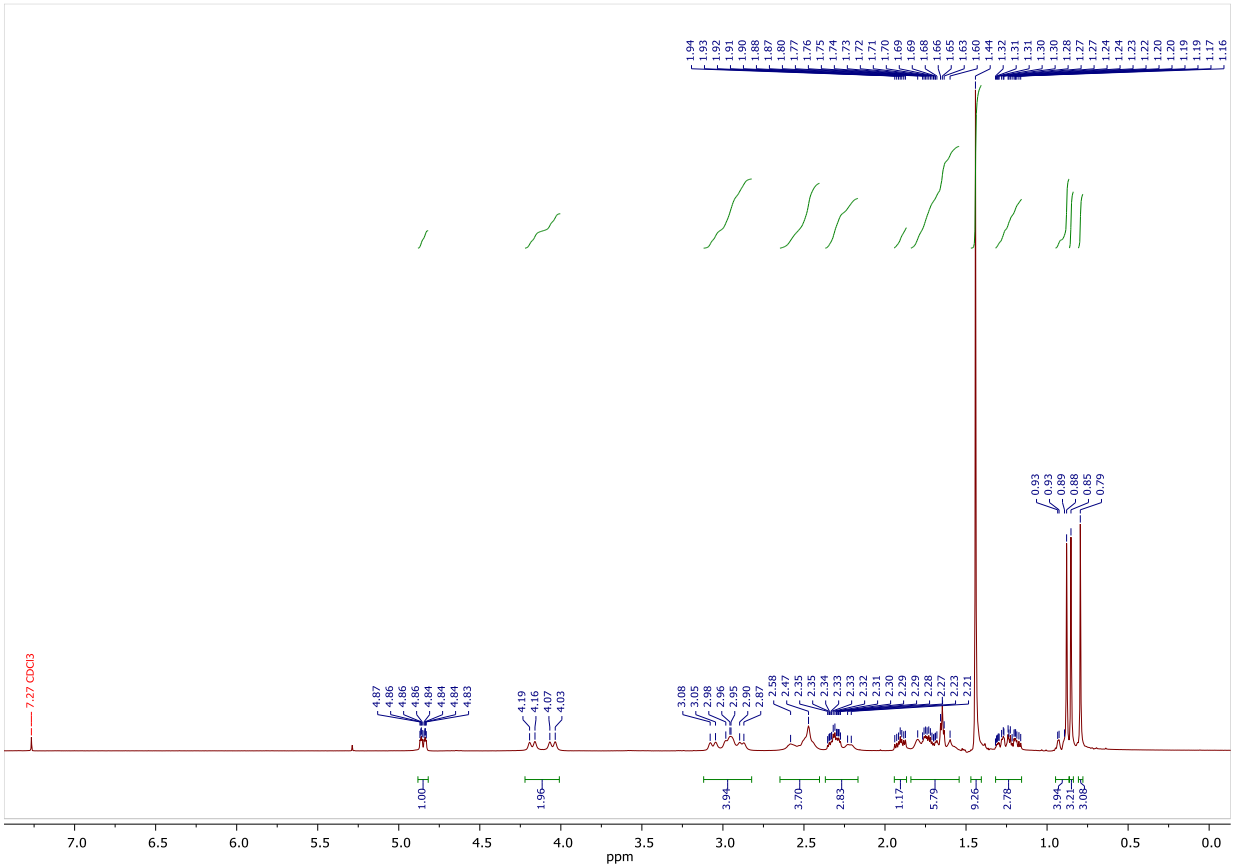


Figure S8. ^{1}H NMR spectrum of the compound **9b** (400 MHz, $CDCl_3$).

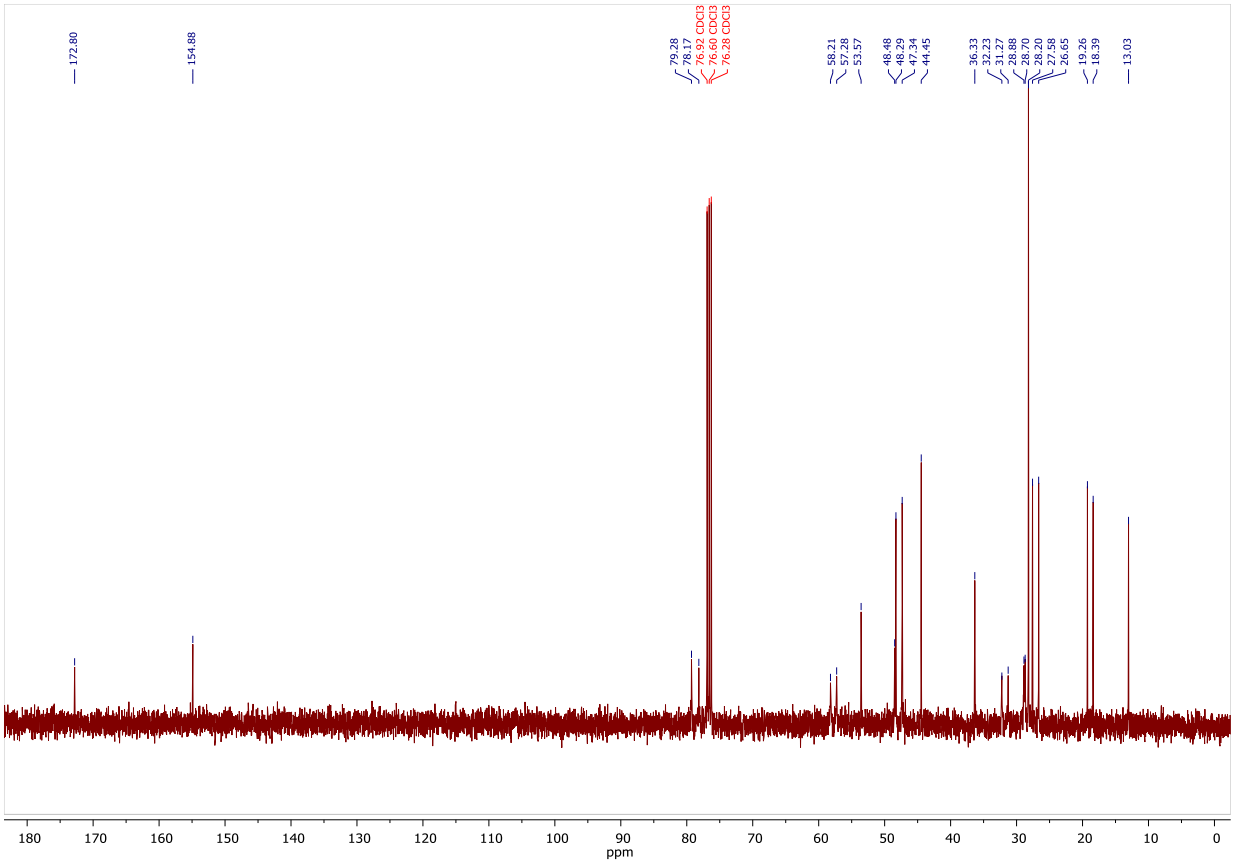


Figure S9. ^{13}C NMR spectrum of the compound **9b** (101 MHz, $CDCl_3$).

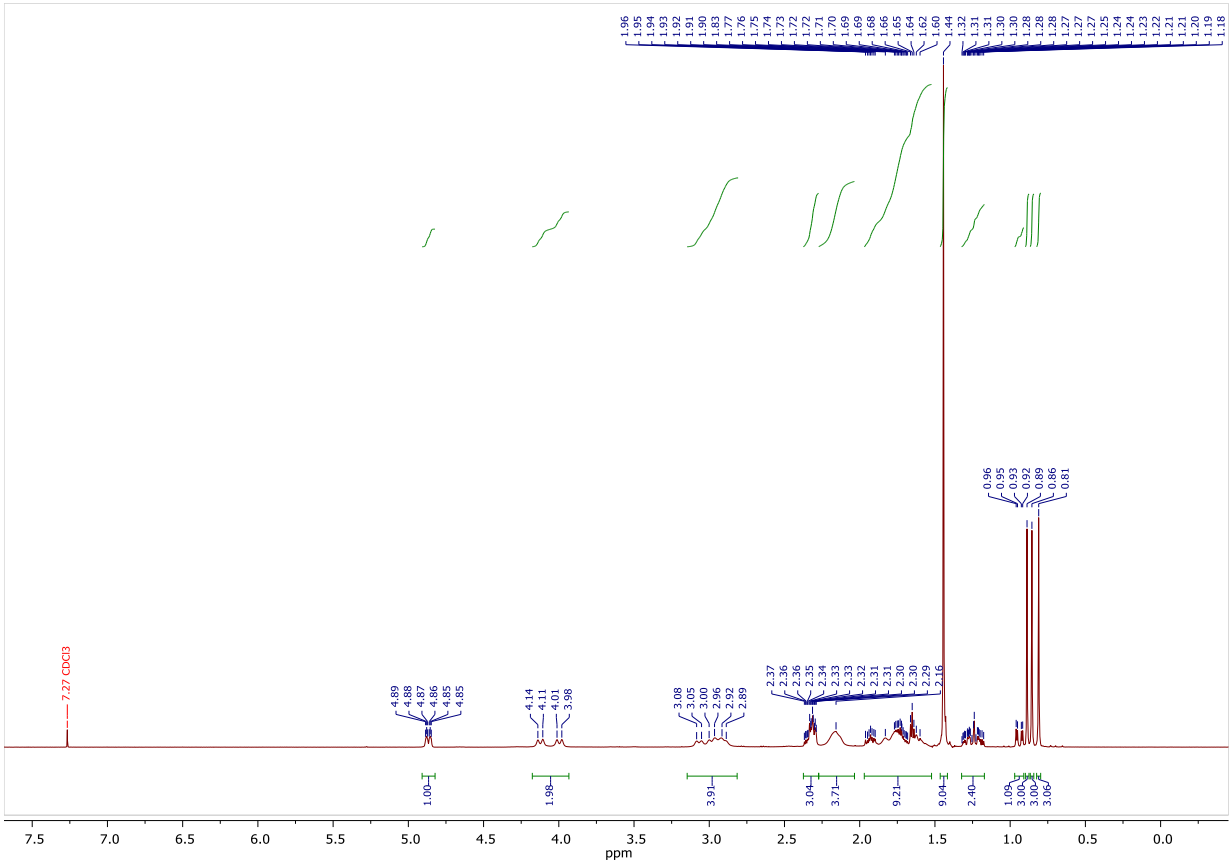


Figure S10. ^{1}H NMR spectrum of the compound **9c** (400 MHz, $CDCl_3$).

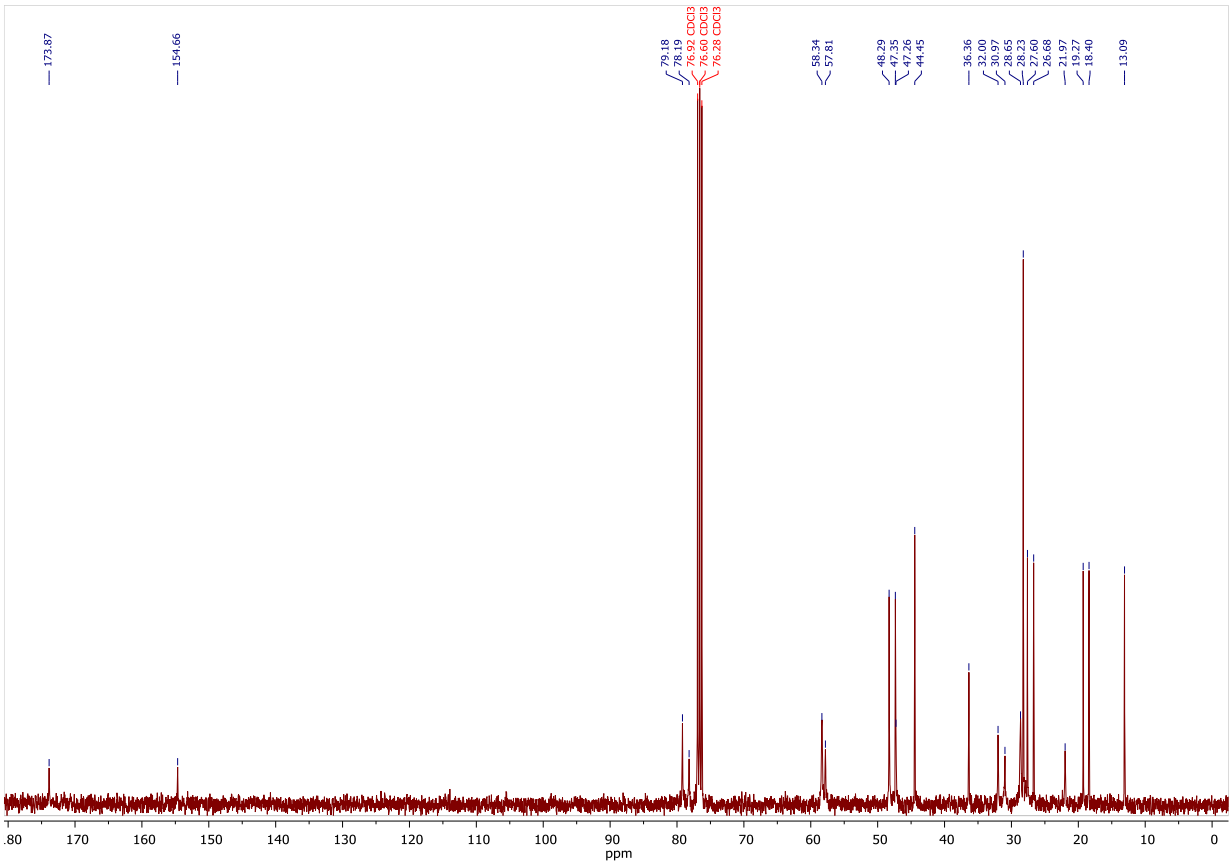


Figure S11. ^{13}C NMR spectrum of the compound **9c** (101 MHz, $CDCl_3$).

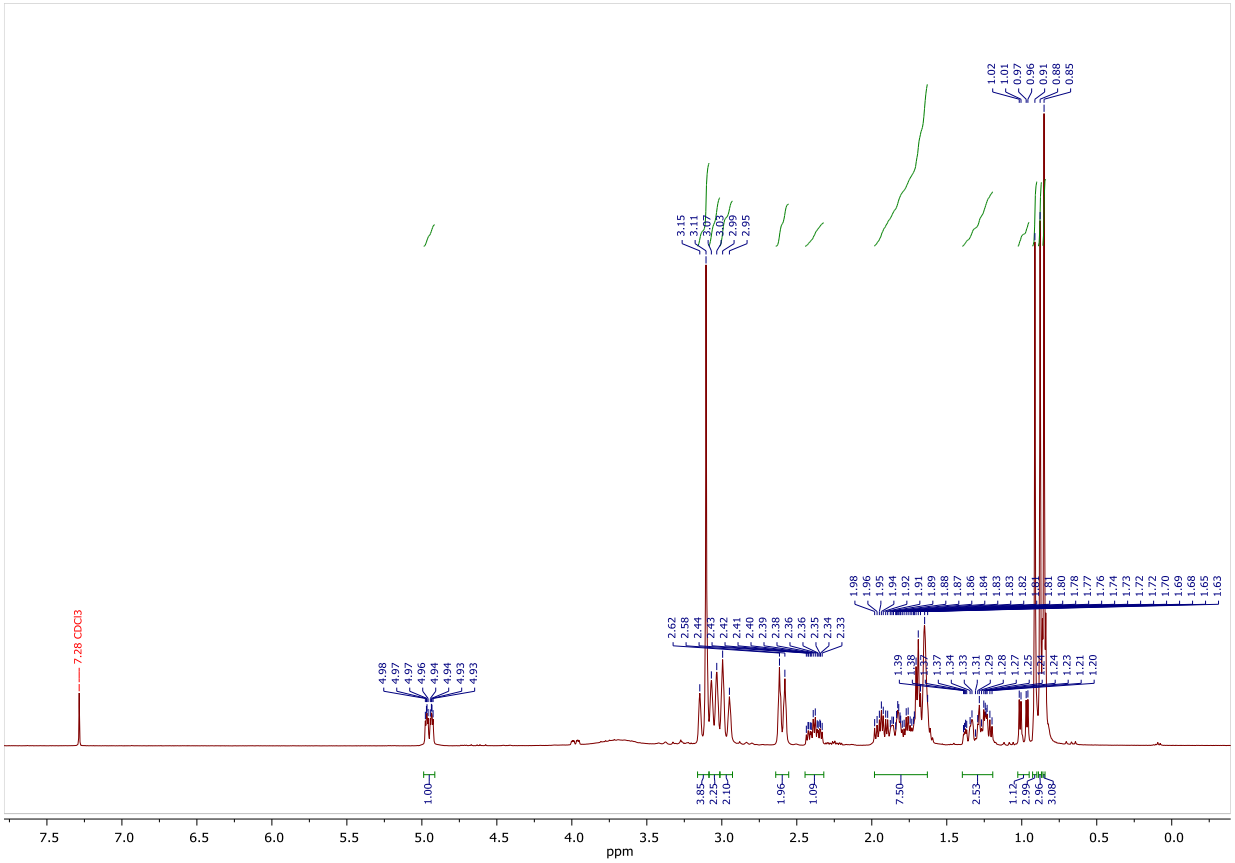


Figure S12. ^{1}H NMR spectrum of the compound **10a** (300 MHz, $CDCl_3$).

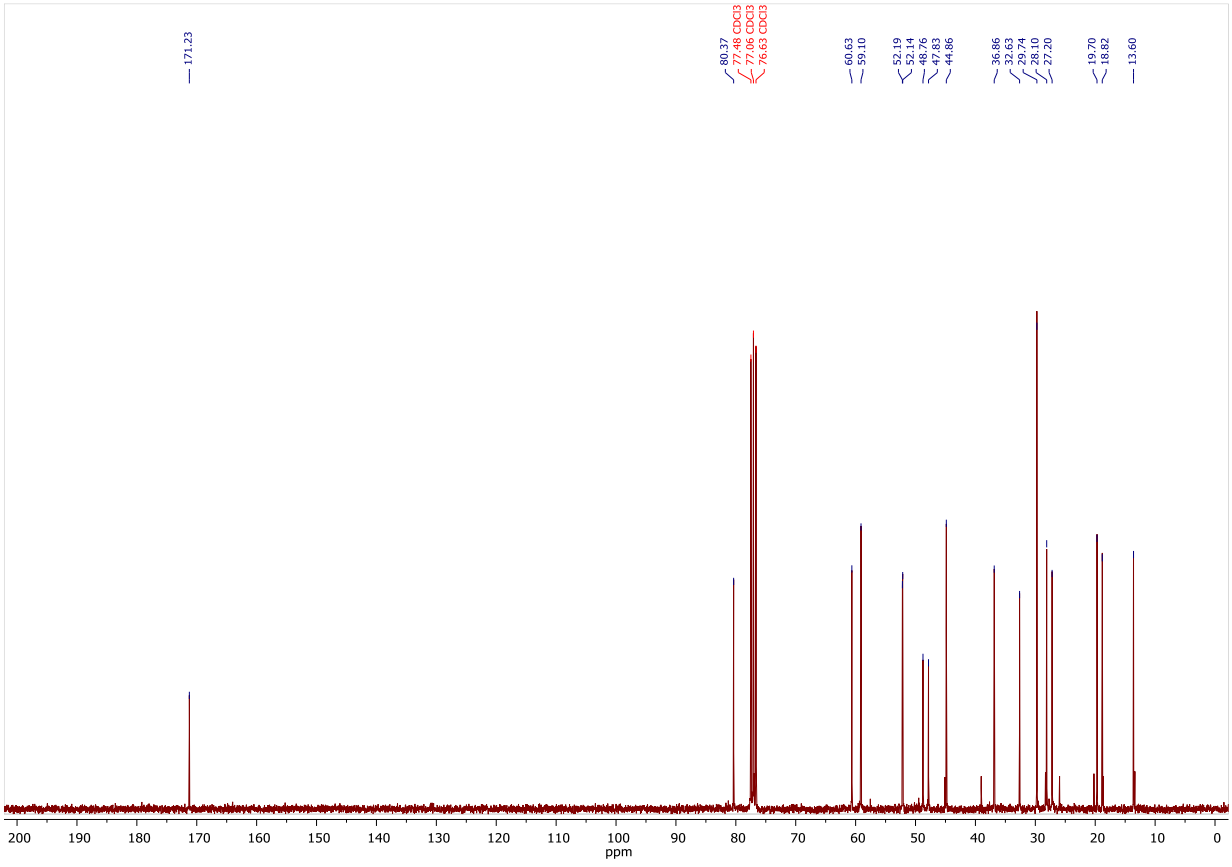


Figure S13. ^{13}C NMR spectrum of the compound **10a** (76 MHz, $CDCl_3$).

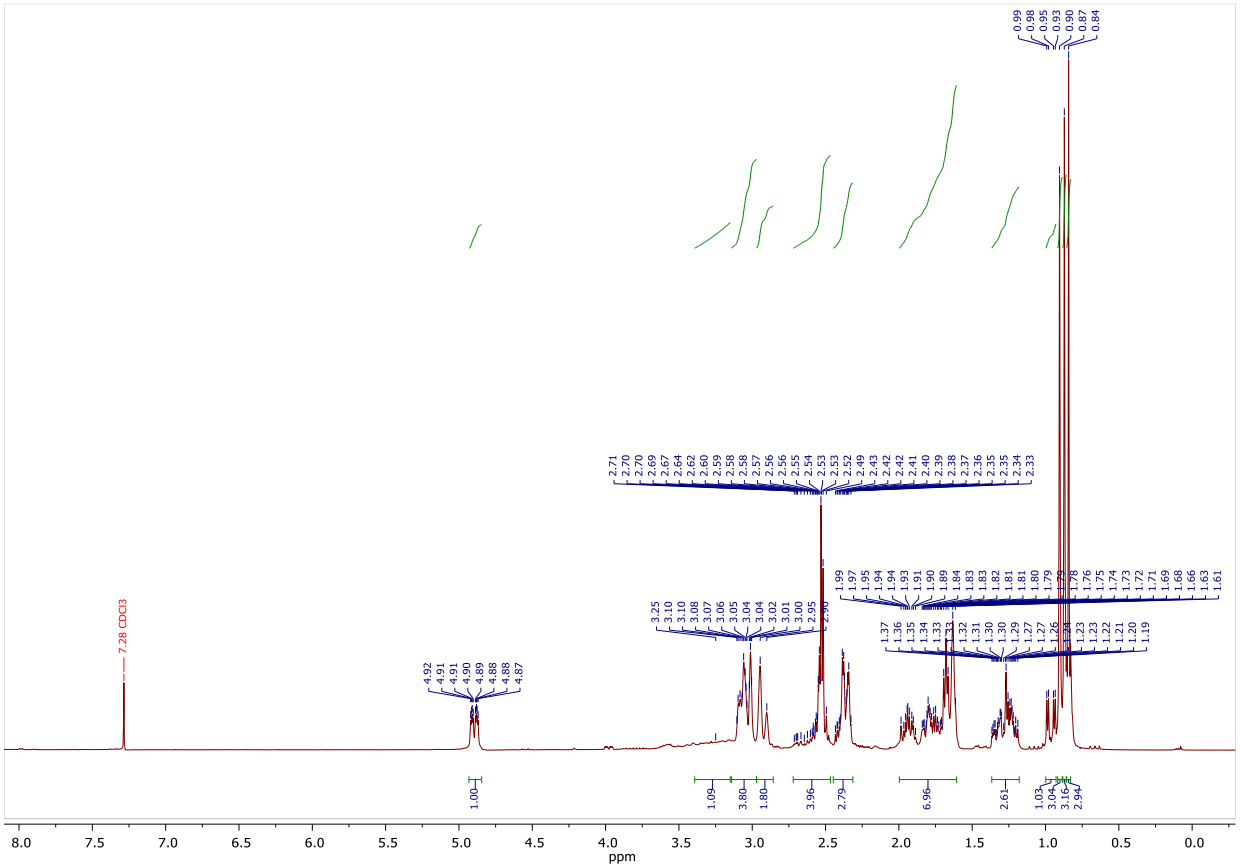


Figure S14. ^{1}H NMR spectrum of the compound **10b** (300 MHz, $CDCl_3$).

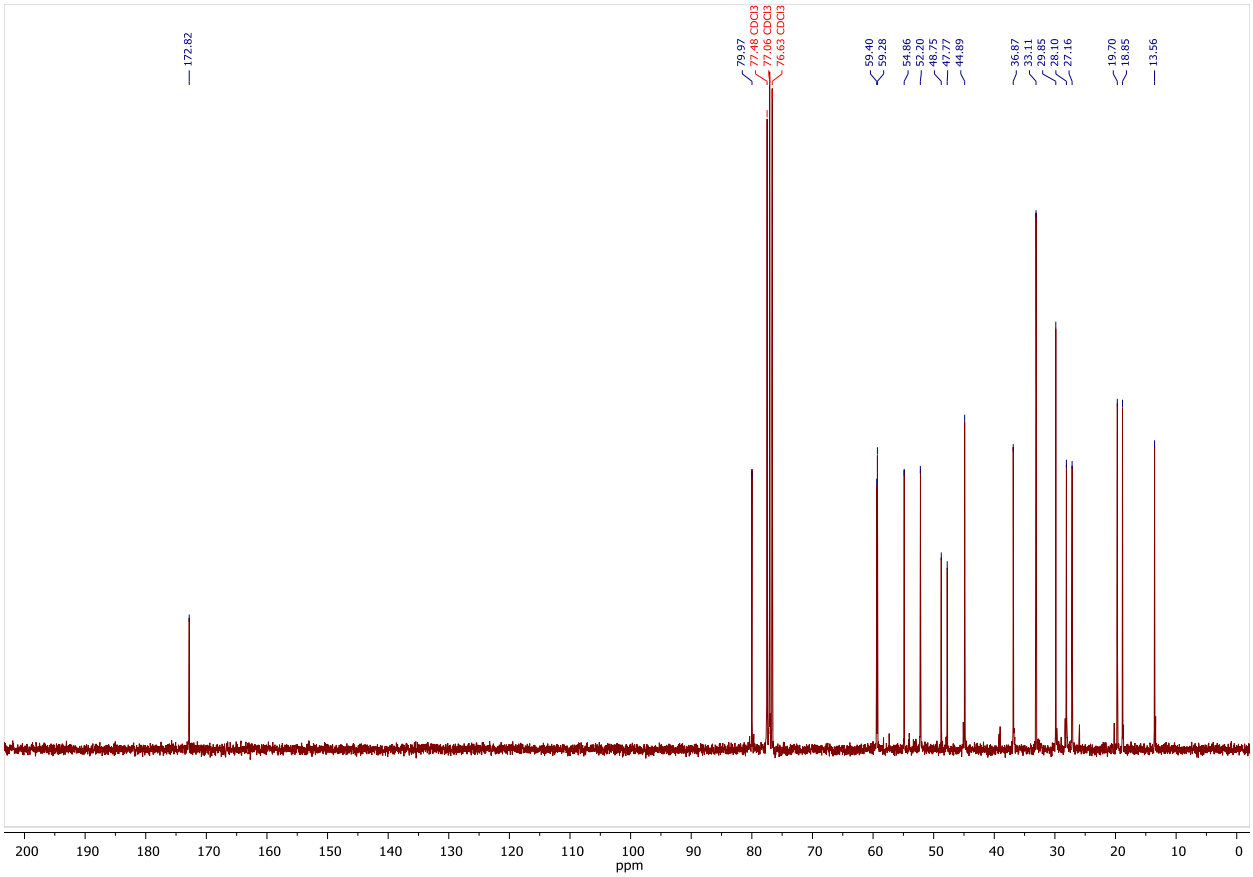


Figure S15. ^{13}C NMR spectrum of the compound **10b** (76 MHz, $CDCl_3$).

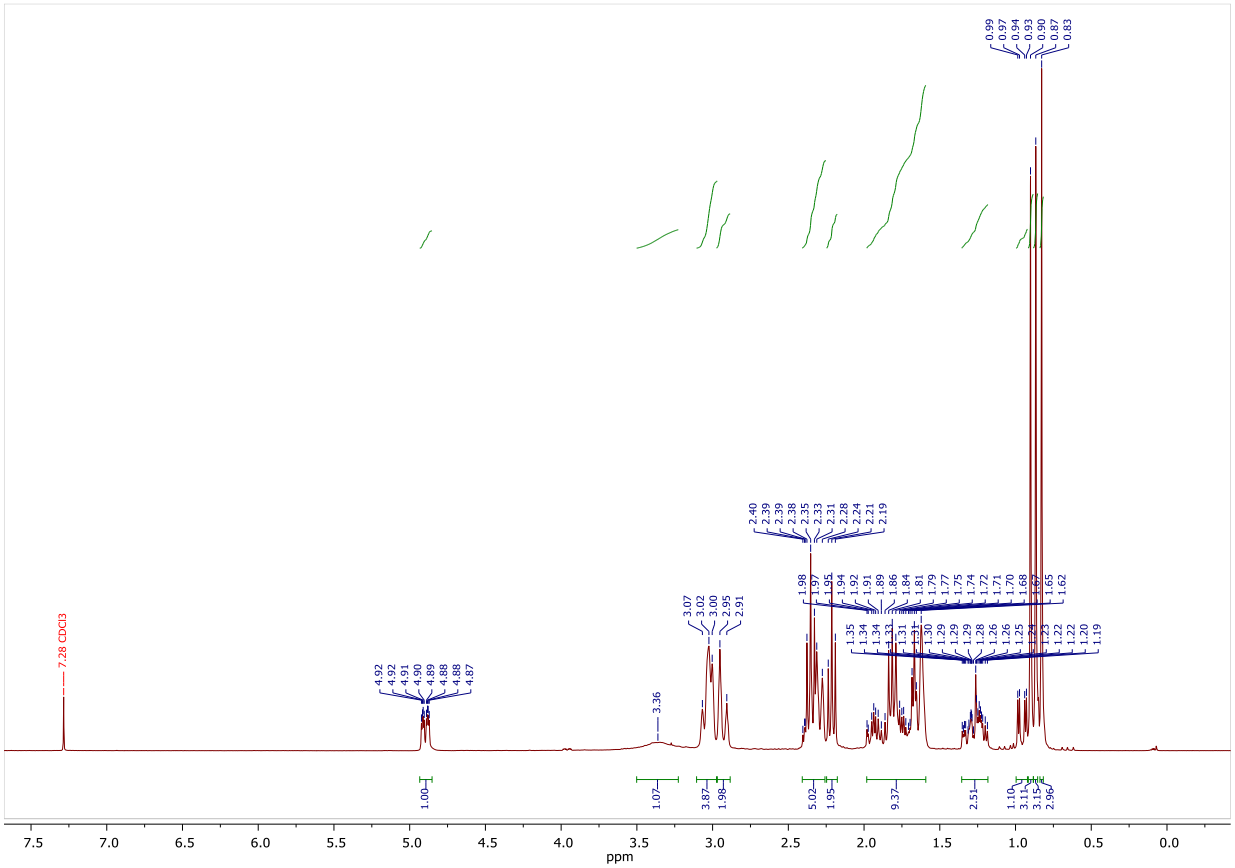


Figure S16. ^{1}H NMR spectrum of the compound **10c** (300 MHz, $CDCl_3$).

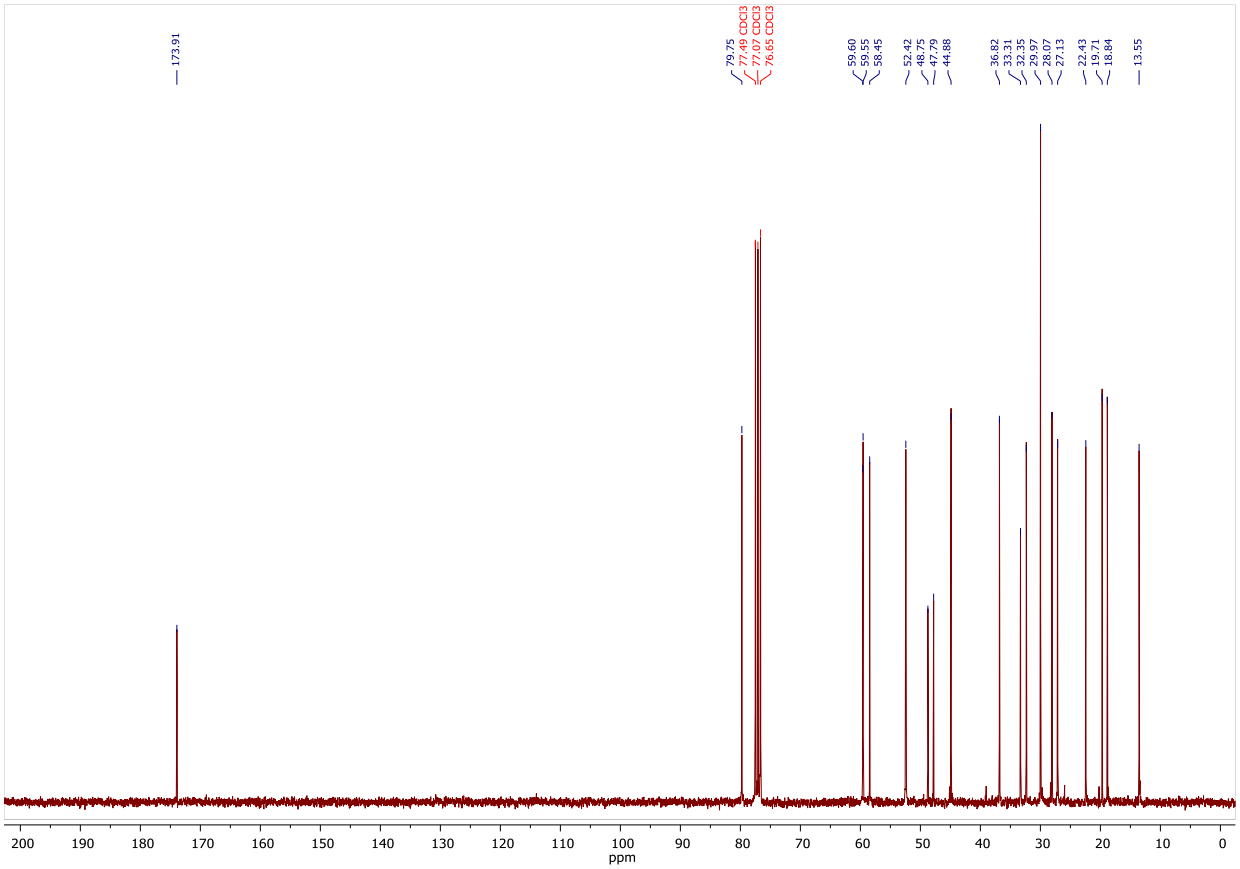
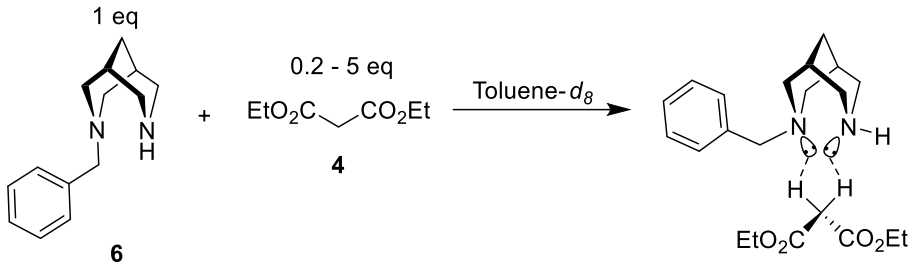


Figure S17. ^{13}C NMR spectrum of the compound **10c** (76 MHz, $CDCl_3$).



Scheme S1. Proposed formation of a supramolecular complex between *N*-benzylbispidine **6** and diethyl malonate (**4**).

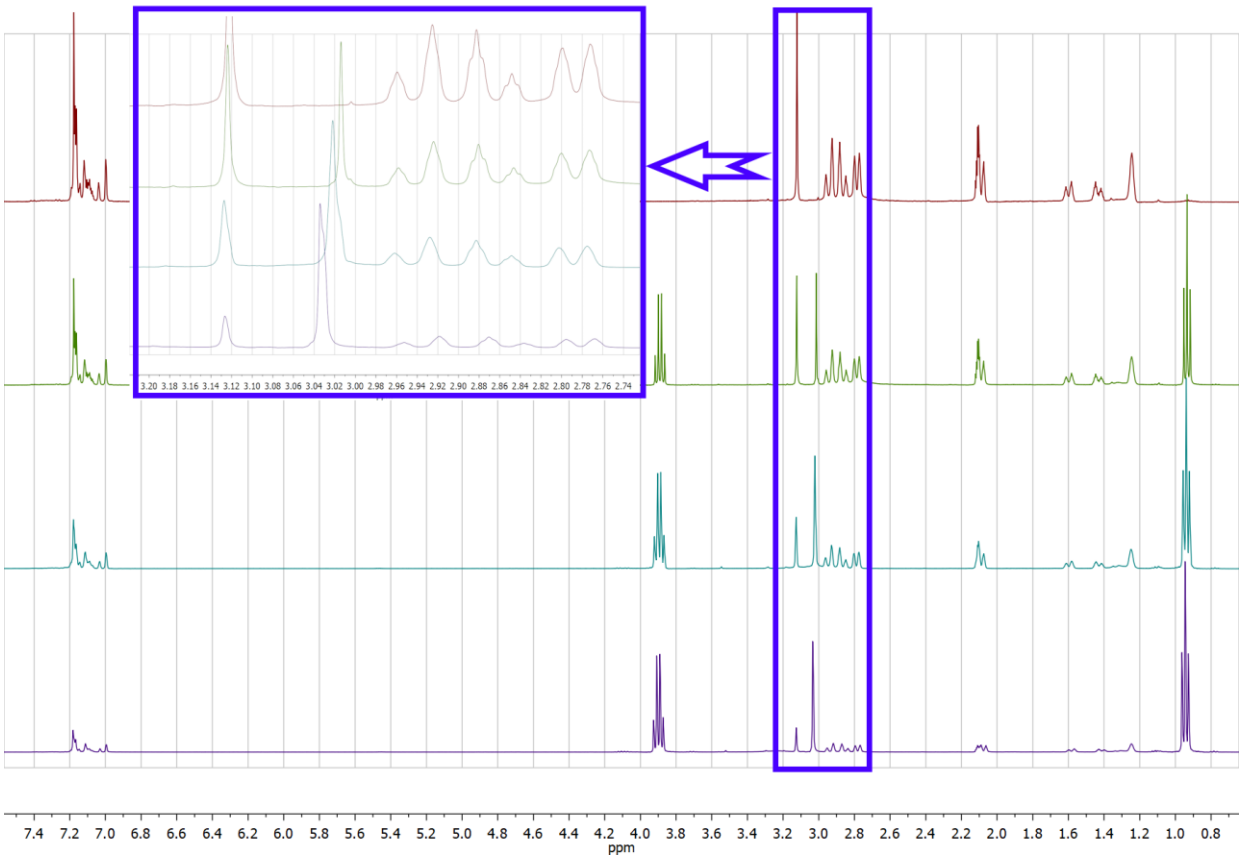


Figure S18. ^{1}H NMR spectra (400 MHz, toluene-d$_8$) of the binary mixtures of bispidine **6** and diethyl malonate in ratios: 1:0; 1:1; 1:3 and 1:5 (top to bottom).

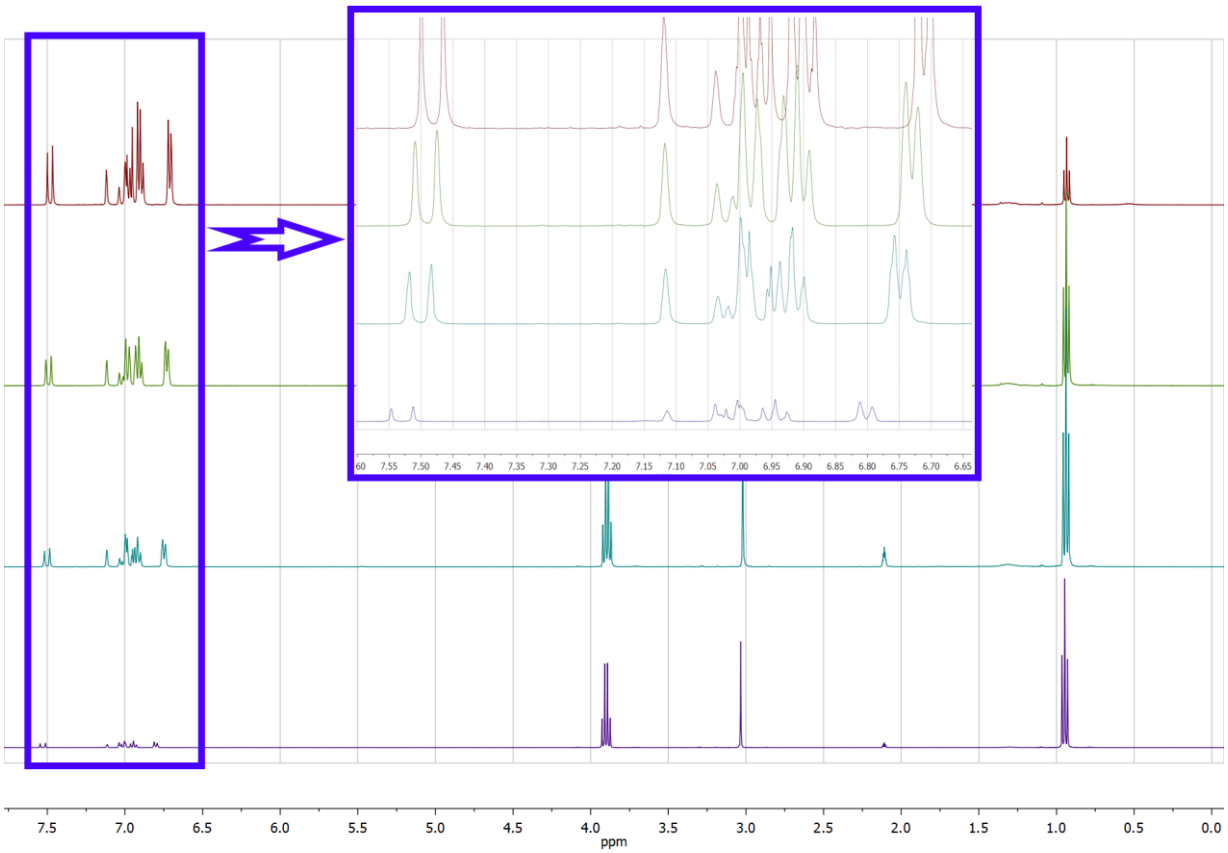


Figure S19. ^{1}H NMR spectra (400 MHz, toluene-d$_8$) of the binary mixtures of *β*-nitrostyrene and diethyl malonate in ratios: 1:0.2, 1:1, 1:2, 1:5 (top to bottom).

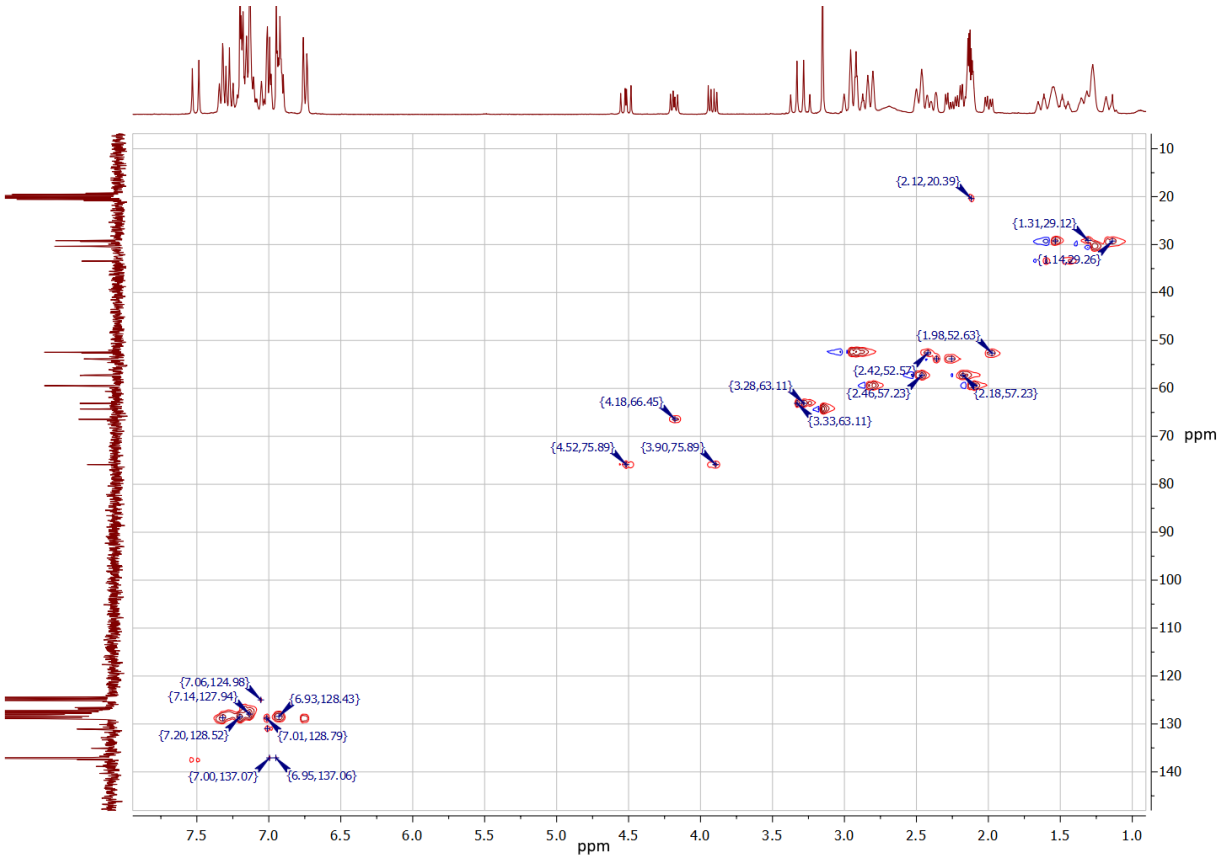


Figure S20. 2D NMR ^{1}H-^{13}C HSQC (toluene-d_8) spectrum of the binary mixture of *β*-nitrostyrene and bispidine **6** (1:1). Only the cross-peaks associated with the new reaction product are marked. The cross-peaks within the aromatic region are related to the phenyl groups of all three of the components in the mixture, although no clear correlation can be made.

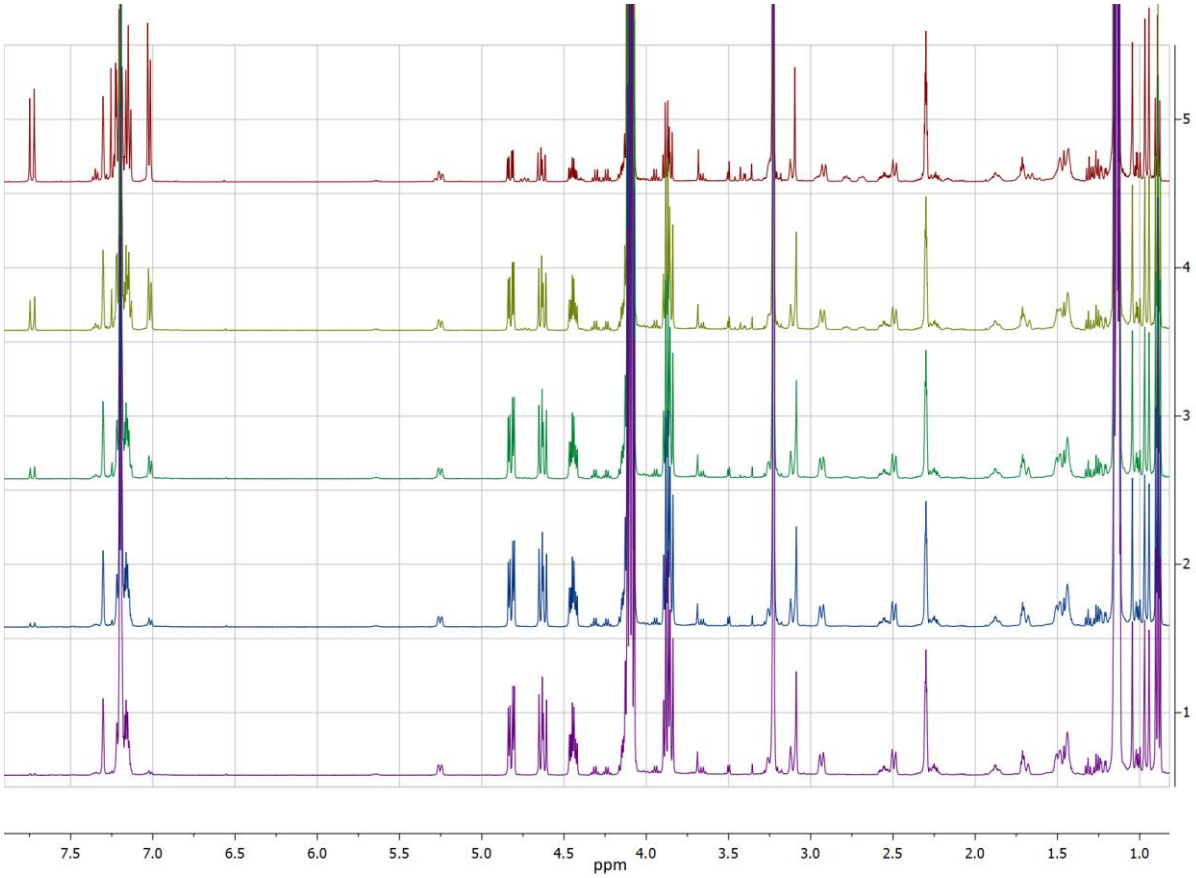


Figure S21. ^{1}H NMR spectra (600 MHz, toluene-d_8) of the catalytic reaction using bispidine **10a** as a catalyst at 0, 60, 120, 180 and 240 min after the start of the reaction (top to bottom).

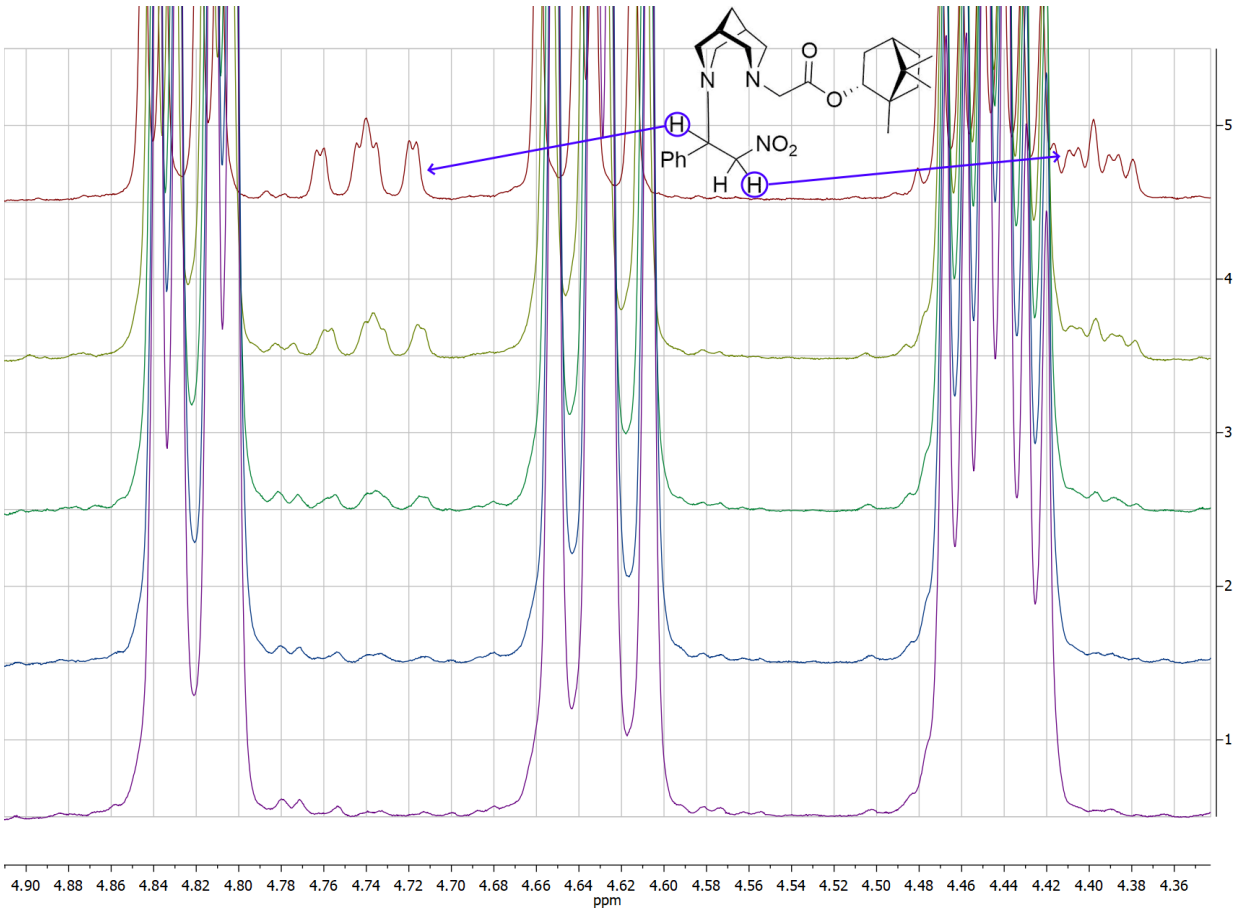


Figure S22. ^{1}H NMR spectra (600 MHz, toluene-d$_8$) of the catalytic reaction using bispidine **10a** as a catalyst at 0, 60, 120, 180 and 240 min after the start of the reaction in the region of 4.34 – 4.92 ppm (top to bottom)

HRMS spectra

Experimental

High-resolution mass spectra (HRMS) were obtained on Bruker maXis Q-TOF instrument (Bruker Daltonik GmbH, Germany) equipped with an electrospray ionization (ESI) ion source. The experiments were performed in positive (+) MS ion mode (HV Capillary: +4500 V; HV End Plate Offset: -500 V); with a scan range of *m*/*z* 50–1500. External calibration of the mass spectrometer was performed using a low-concentration tuning mix solution (Agilent Technologies). Direct syringe injection was applied for the analyzed reaction solutions in THF (flow rate: 3 μLmin^{-1}) for analytical characterization. Nitrogen was applied as nebulizer gas (1 bar) and dry gas (4.0 L/min, 200 °C). All data visualization was processed using Data Analysis 5.1 software package from Bruker Daltonics.

High-resolution mass spectra of (**11-7**, **11-8** and **11-9**) was recorded on a SolariX XR FT/ICR mass spectrometer equipped with a 15 T superconducting magnet, a ParaCell analyzer cell and an ESI Apollo II and MALDI SmartBeam-II ion source. External calibration of the mass spectrometer was performed using a low-concentration sodium trifluoroacetate solution (0.1 mg/ml in acetonitrile/water, 1:1). The data set size was 4M

with 64 scans. All MALDI-FT-ICR-MS measurements were recorded in positive ion mode with MTP 384 ground steel target plate (trans-2-[3-(4-tert-Butylphenyl)-2-methyl-2-propenylidene]malononitrile (DCTB) matrix, with a scan range of *m/z* 150 – 3000). All data visualization was processed using Data Analysis 5.1 software package from Bruker Daltonics.

Sample preparation for MALDI measurements

20 µl of sample (10 µg/mL in THF) was mixed with 20 µl of DCTB (saturated solution in THF) using a pipette and placed onto a MTP 384 ground steel target plate (Bruker Daltonics, Bremen, Germany) and allow to dry at room temperature.

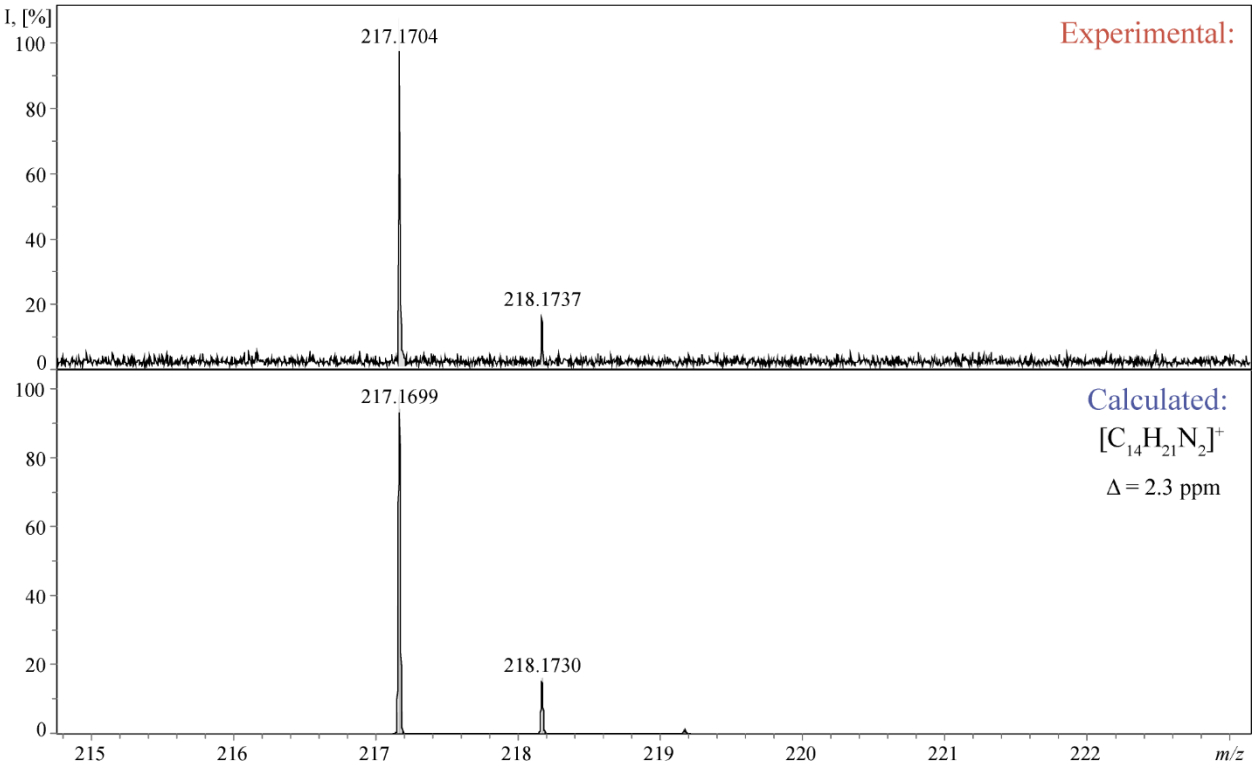


Figure S23. Experimentally detected and theoretical ESI-(+)MS spectrum of bispidine **6** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 217.1704 Da, calculated for $C_{14}H_{21}N_2$ = 217.1699 Da, Δ = 2.3 ppm.

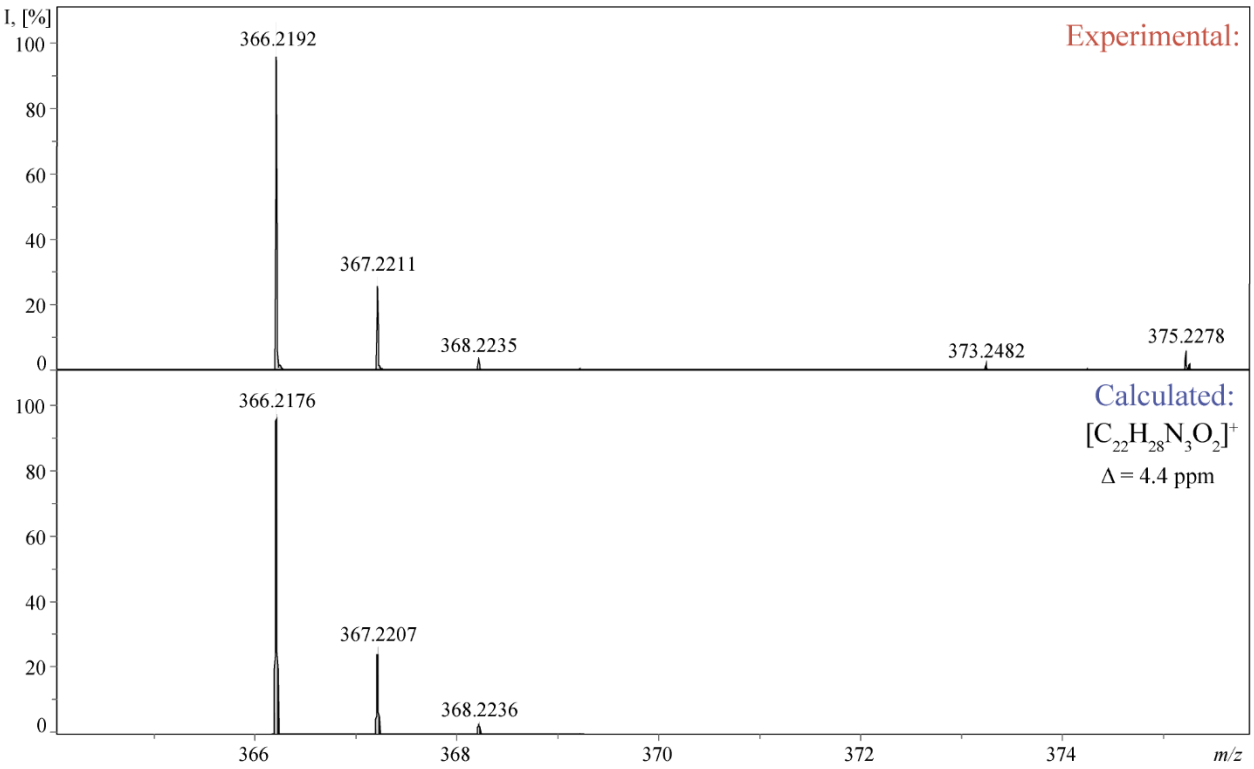


Figure S24. Experimentally detected and theoretical ESI-(+)MS spectrum of **11-1** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 366.2192 Da, calculated for $C_{22}H_{28}N_3O_2$ = 366.2176 Da, Δ = 4.4 ppm.

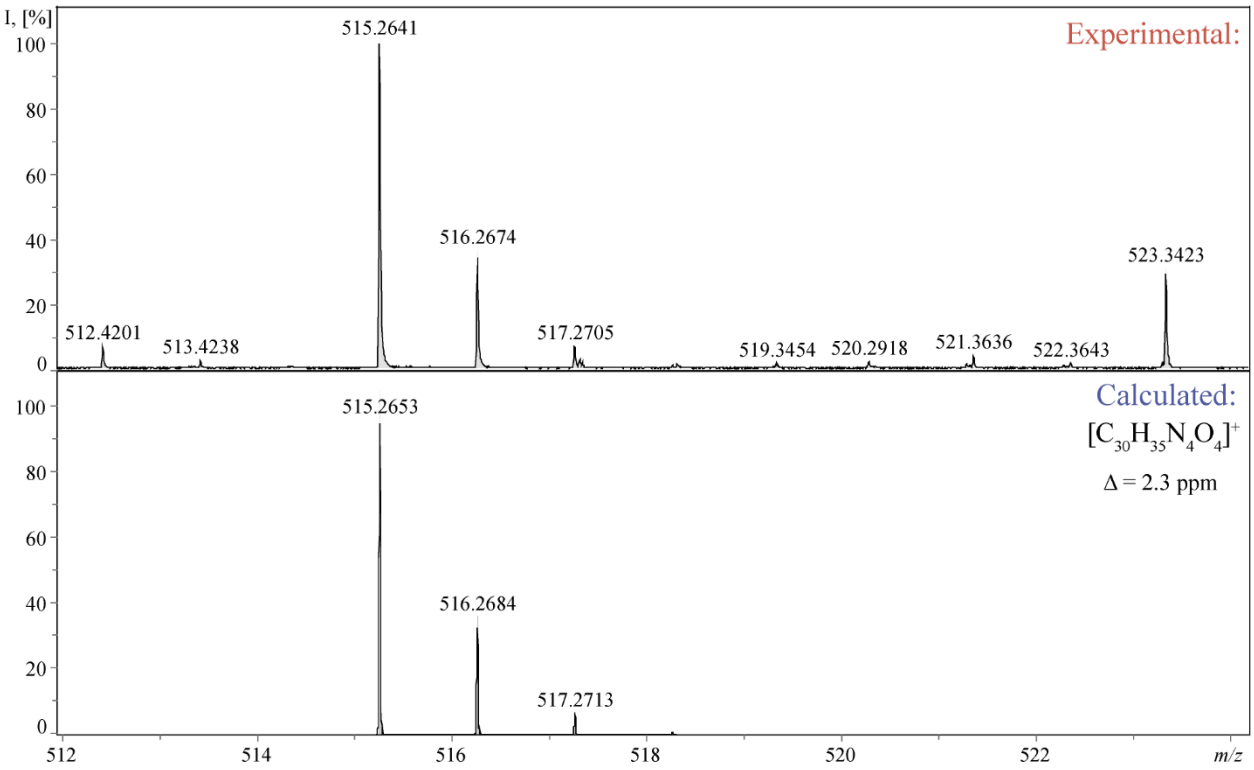


Figure S25. Experimentally detected and theoretical ESI-(+)MS spectrum of **11-2** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 515.2641 Da, calculated for $C_{30}H_{35}N_4O_4$ = 515.2653 Da, Δ = 2.3 ppm.

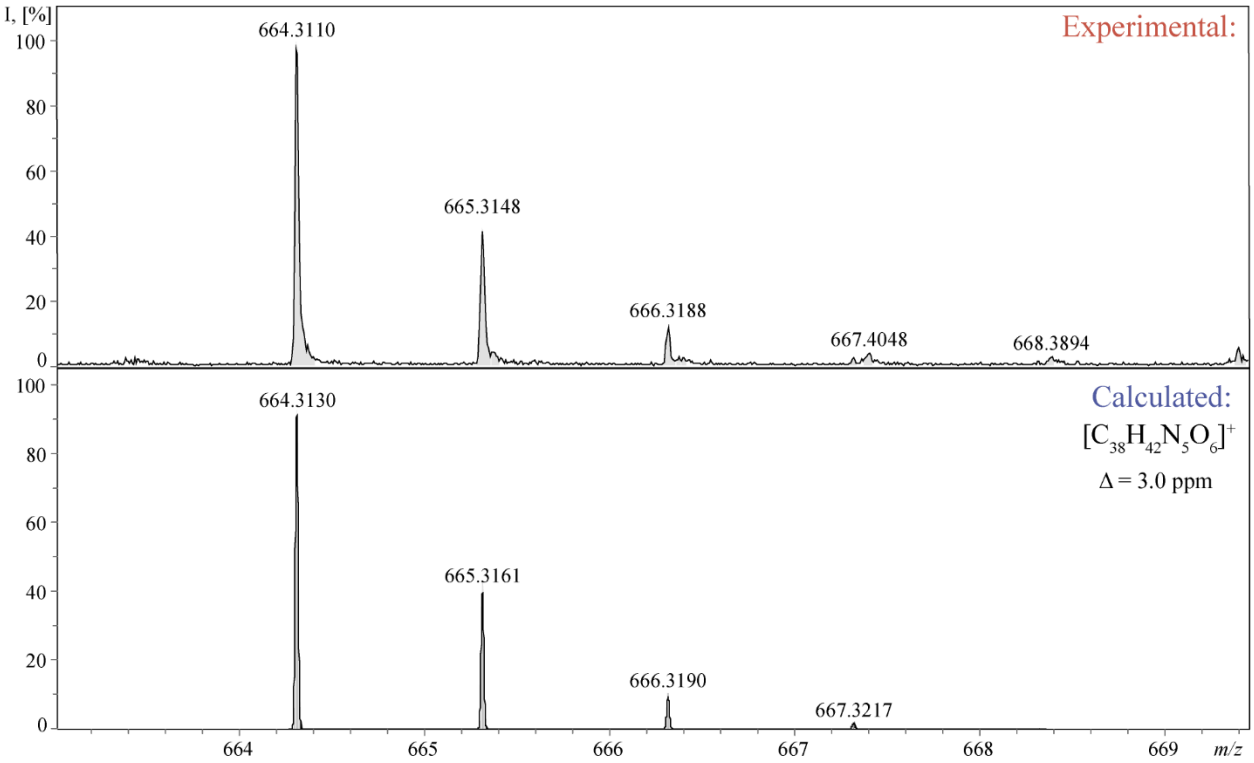


Figure S26. Experimentally detected and theoretical ESI-(+)MS spectrum of **11-3** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 664.3110 Da, calculated for $C_{38}H_{42}N_5O_6$ = 664.3130 Da, Δ = 3.0 ppm.

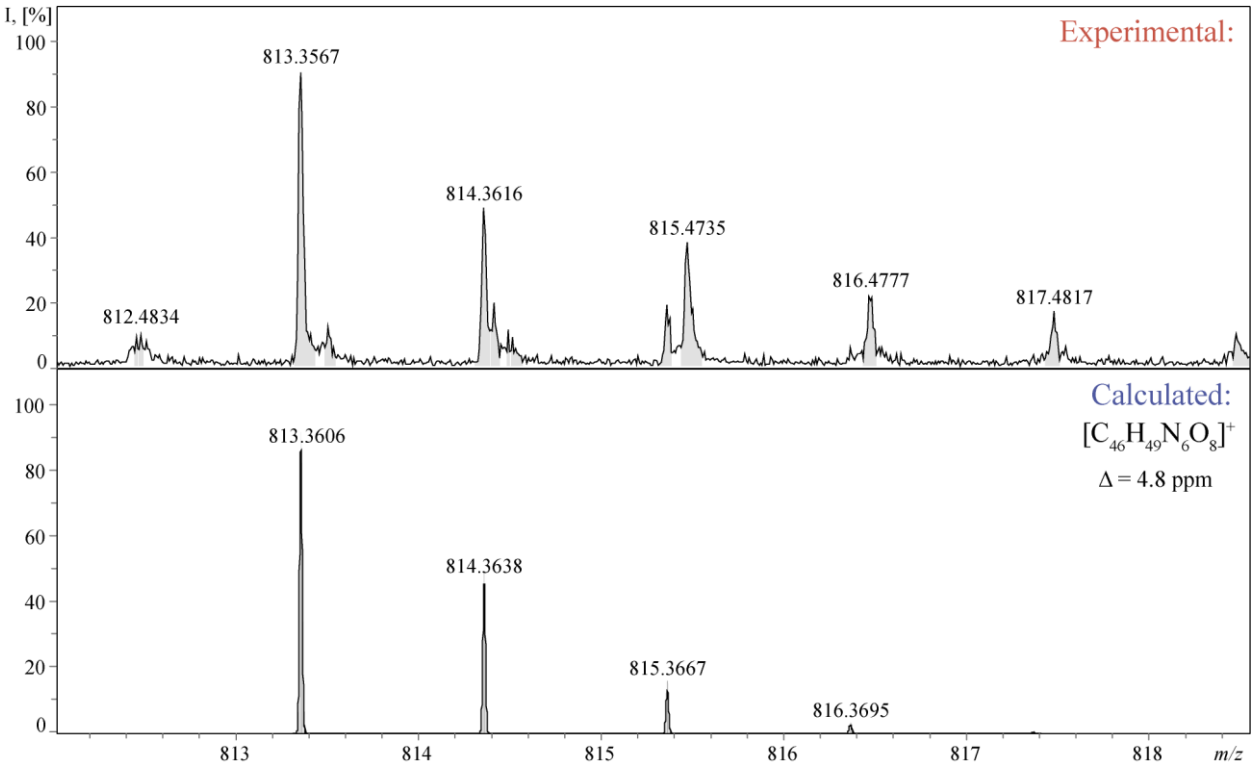


Figure S27. Experimentally detected and theoretical ESI-(+)MS spectrum of **11-4** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 813.3567 Da, calculated for $C_{46}H_{49}N_6O_8$ = 813.3606 Da, Δ = 4.8 ppm.

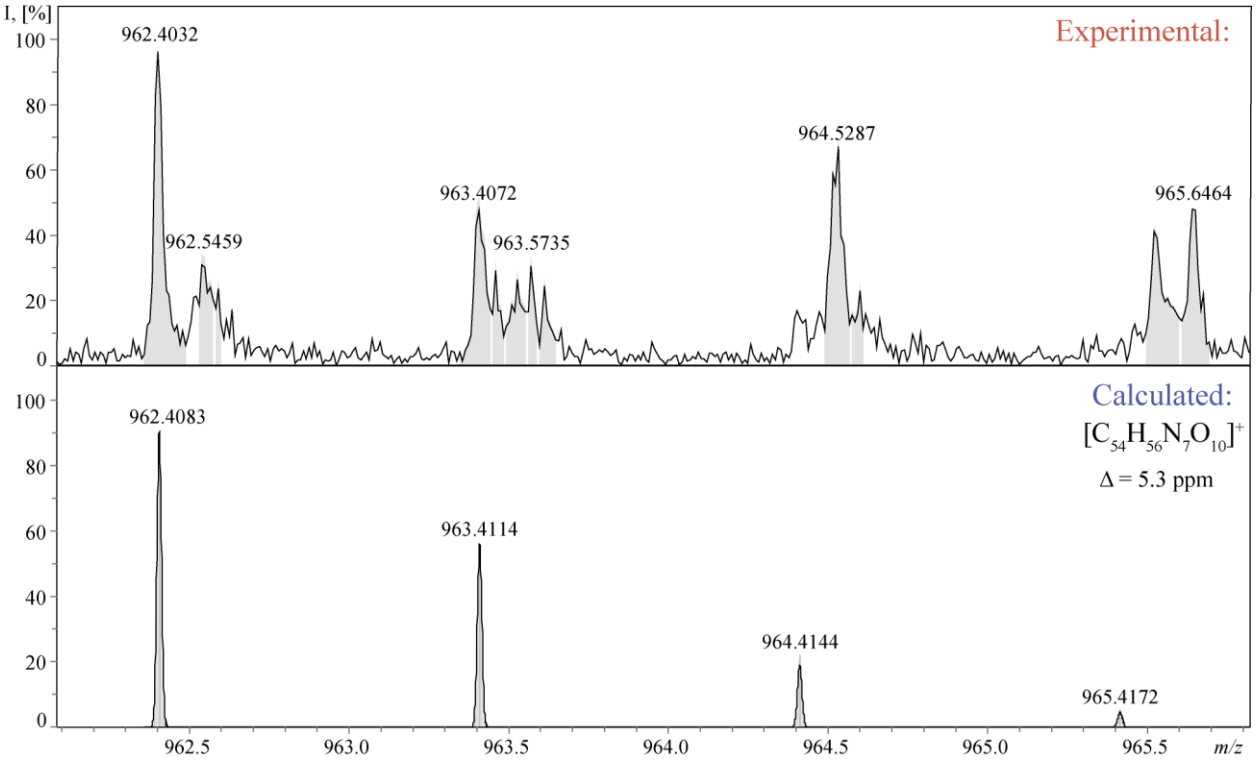


Figure S28. Experimentally detected and theoretical ESI-(+)MS spectrum of **11-5** from the reaction mixture after 2 hours; main experimental peak $[M+H]^+$ = 962.4032 Da, calculated for $C_{54}H_{56}N_7O_{10}$ = 962.4083 Da, Δ = 5.3 ppm.

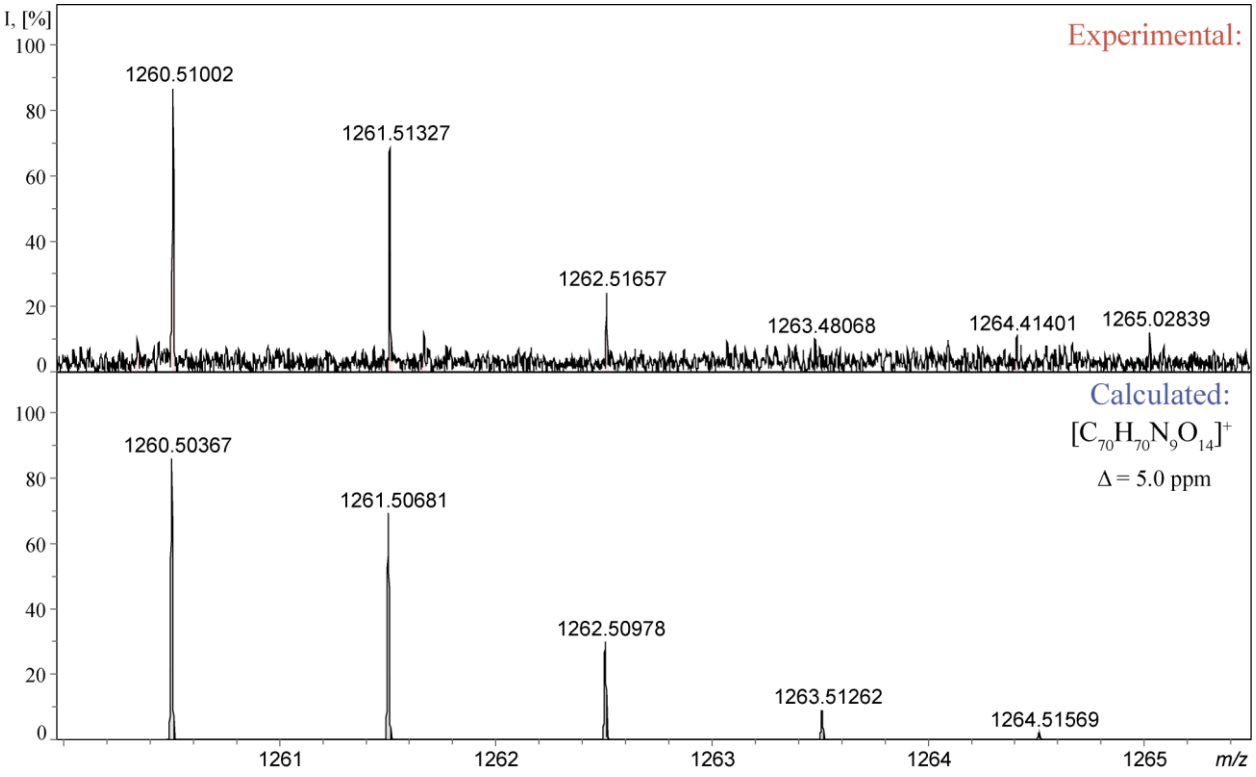


Figure S29. Experimentally detected and theoretical MALDI-(+)MS spectrum of **11-7** from the binary reaction mixture (nitrostyrene **3** + bispidine **6**) after 24 hours; main

experimental peak $[M+H]^+$ = 1260.51002 Da, calculated for $C_{70}H_{70}N_9O_{14}$ = 1260.50367 Da, Δ = 5.0 ppm.

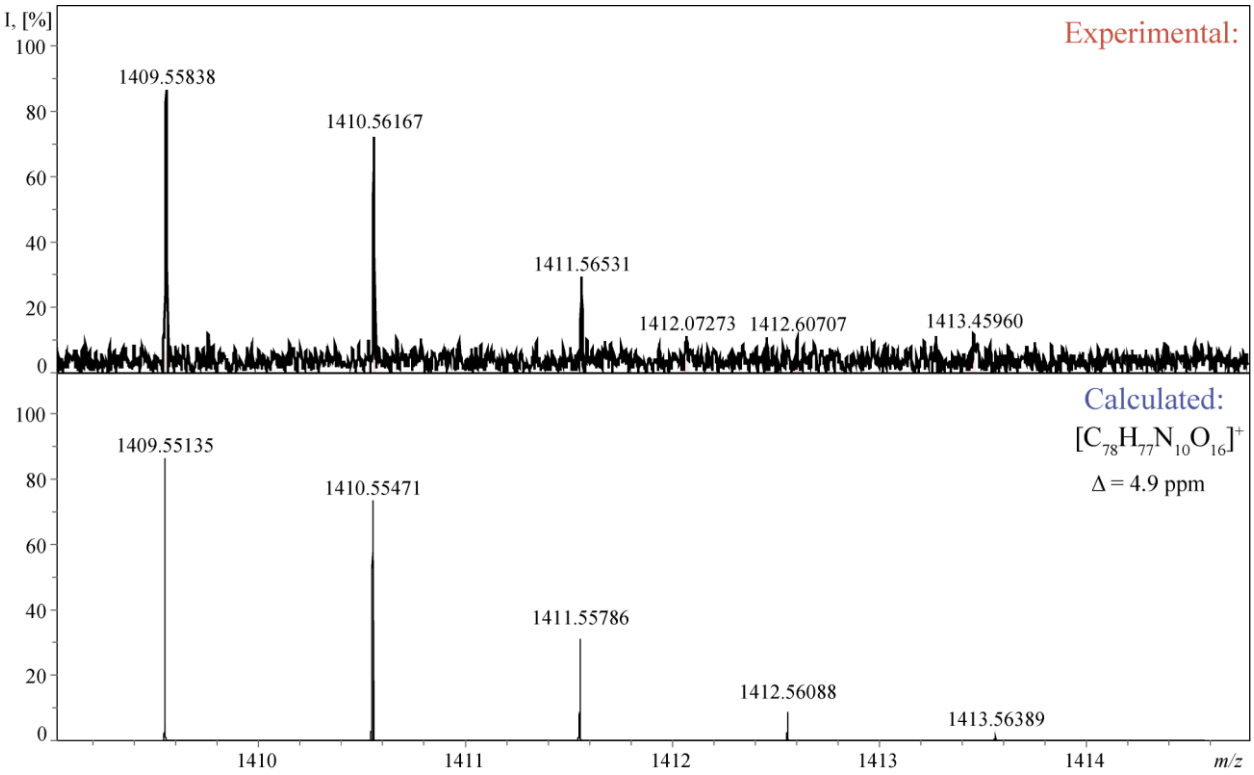


Figure S30. Experimentally detected and theoretical MALDI-(+)MS spectrum of **11-8** from the binary reaction mixture (nitrostyrene **3** + bispidine **6**) after 24 hours; main experimental peak $[M+H]^+$ = 1409.55838 Da, calculated for $C_{78}H_{77}N_{10}O_{16}$ = 1409.55135 Da, Δ = 4.9 ppm.

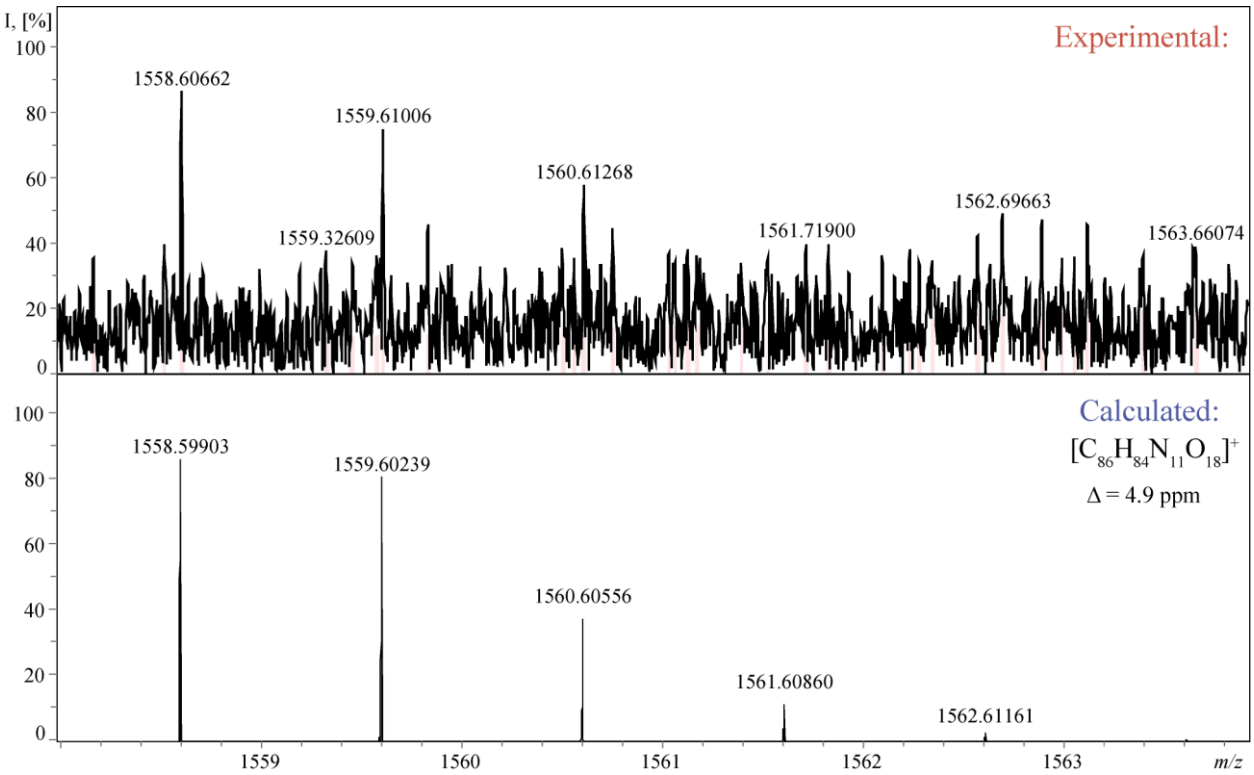


Figure S31. Experimentally detected and theoretical MALDI-(+)MS spectrum of **11-9** from the binary reaction mixture (nitrostyrene **3** + bispidine **6**) after 24 hours; main experimental peak $[M+H]^+$ = 1558.60662 Da, calculated for $C_{86}H_{84}N_{11}O_{18}$ = 1558.59903 Da, Δ = 4.9 ppm.

IR spectra

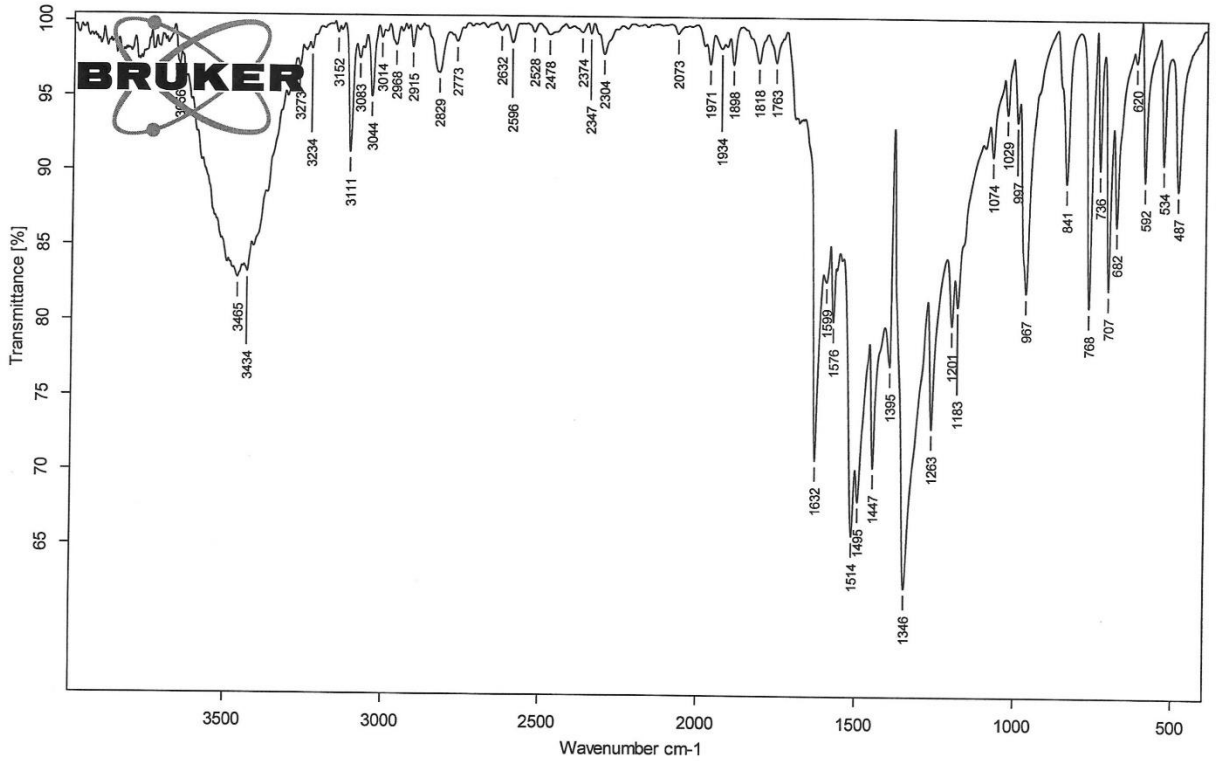


Figure S32. IR spectrum (KBr) of nitrostyrene **3**.

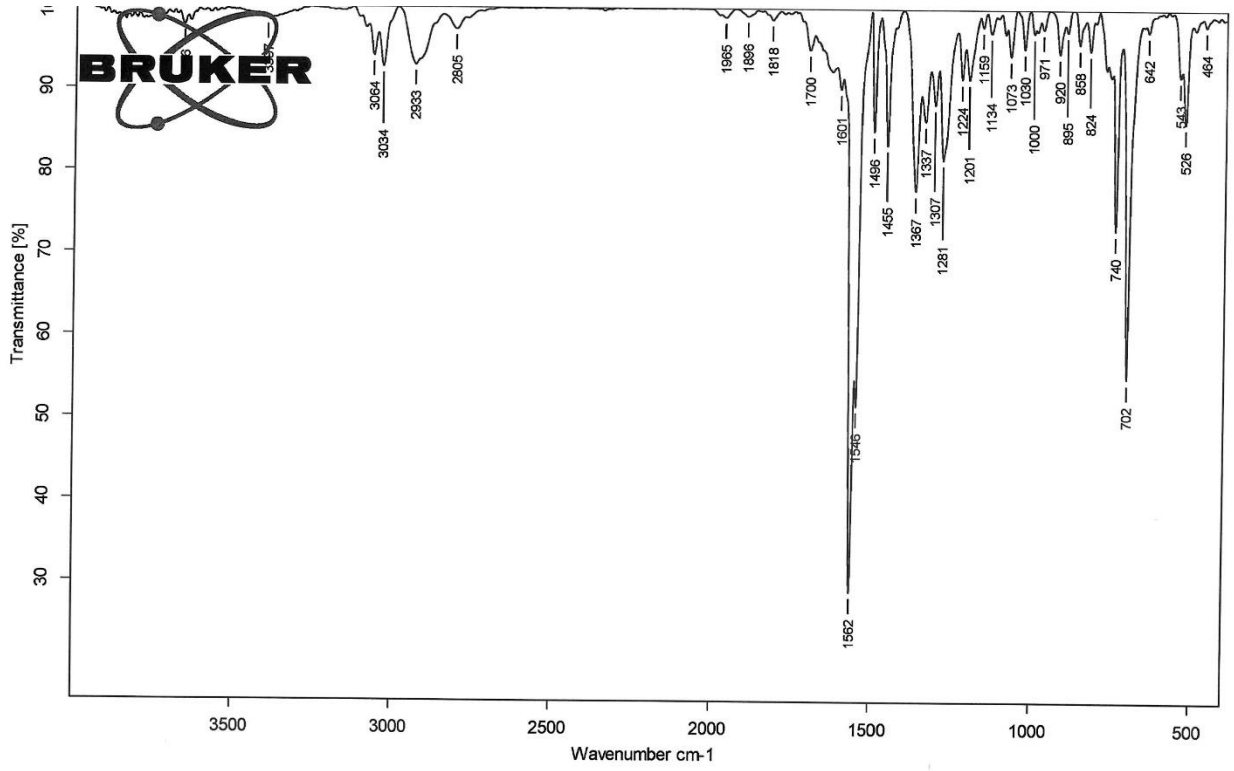


Figure S33. IR spectrum (KBr) of precipitate from binary reaction between nitrostyrene **3** and bispidine **6** in toluene.

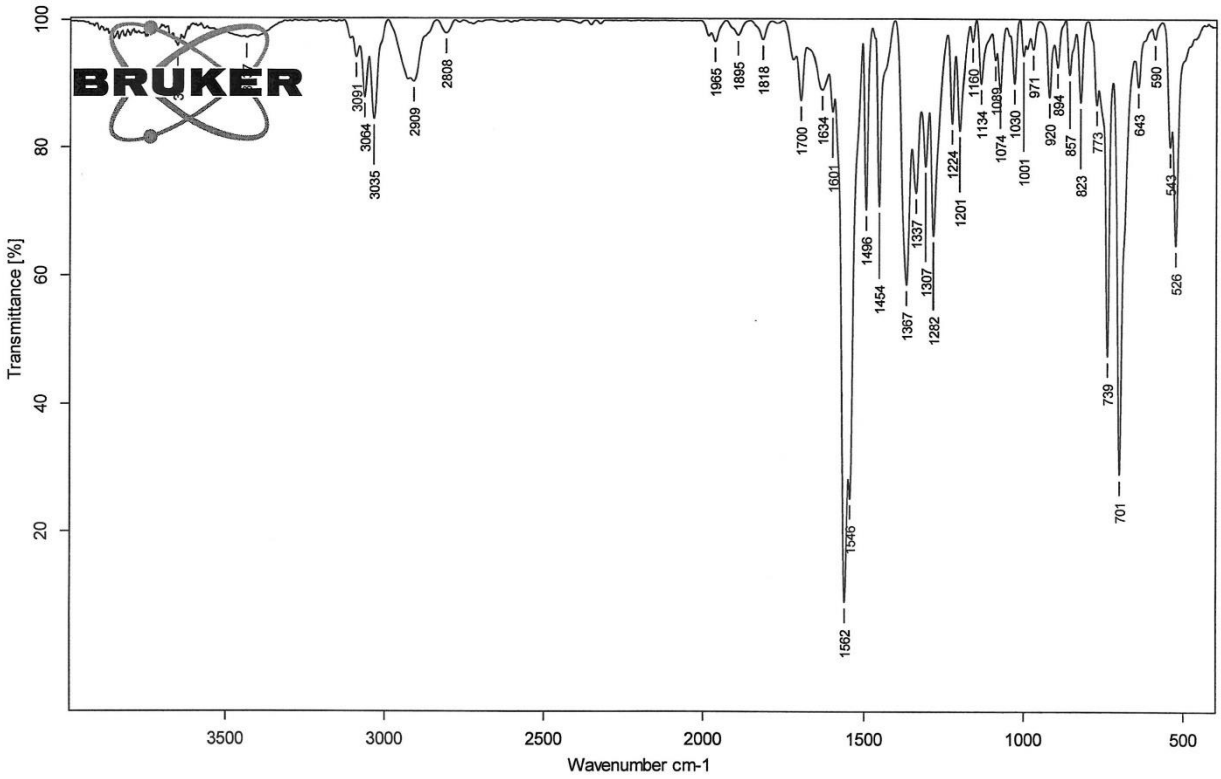


Figure S34. IR spectrum (KBr) of precipitate from binary reaction between nitrostyrene **3** and bispidine **6** in $CHCl_3$.

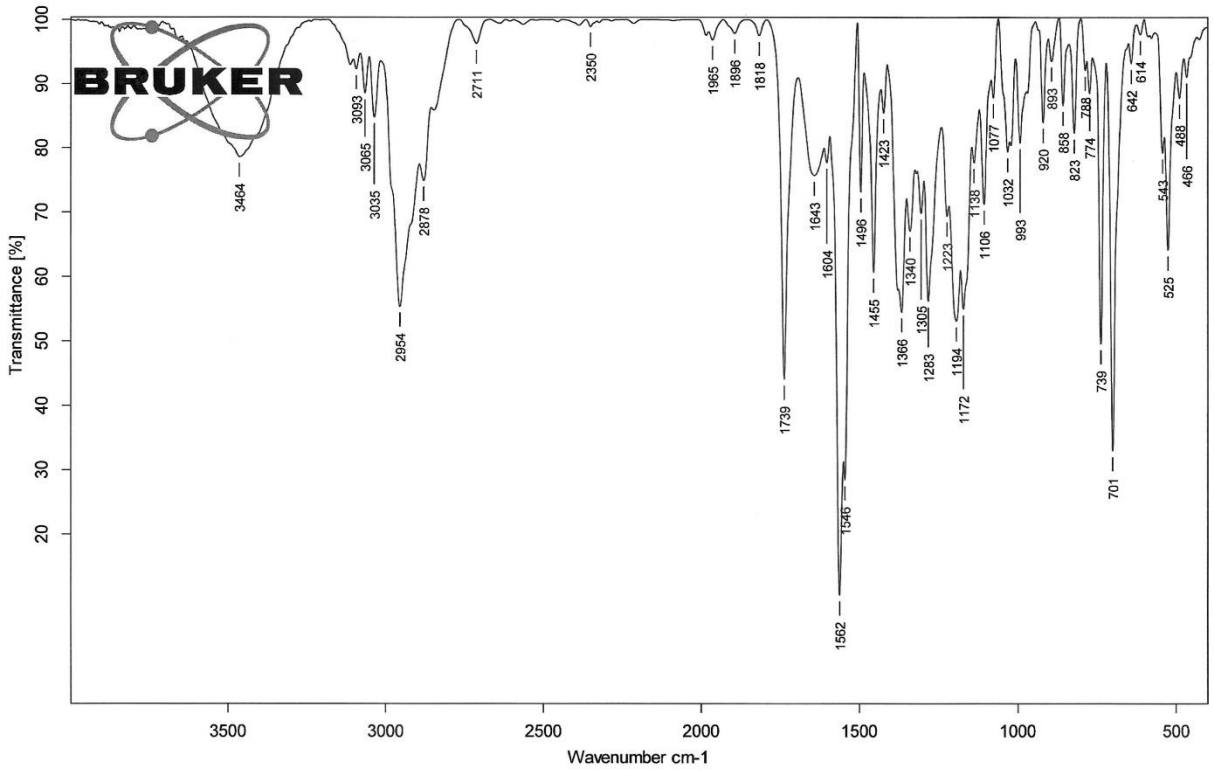


Figure S35. IR spectrum (KBr) of precipitate from binary reaction between nitrostyrene **3** and bispidine **10a** in toluene.

TGA/DSC-analysis

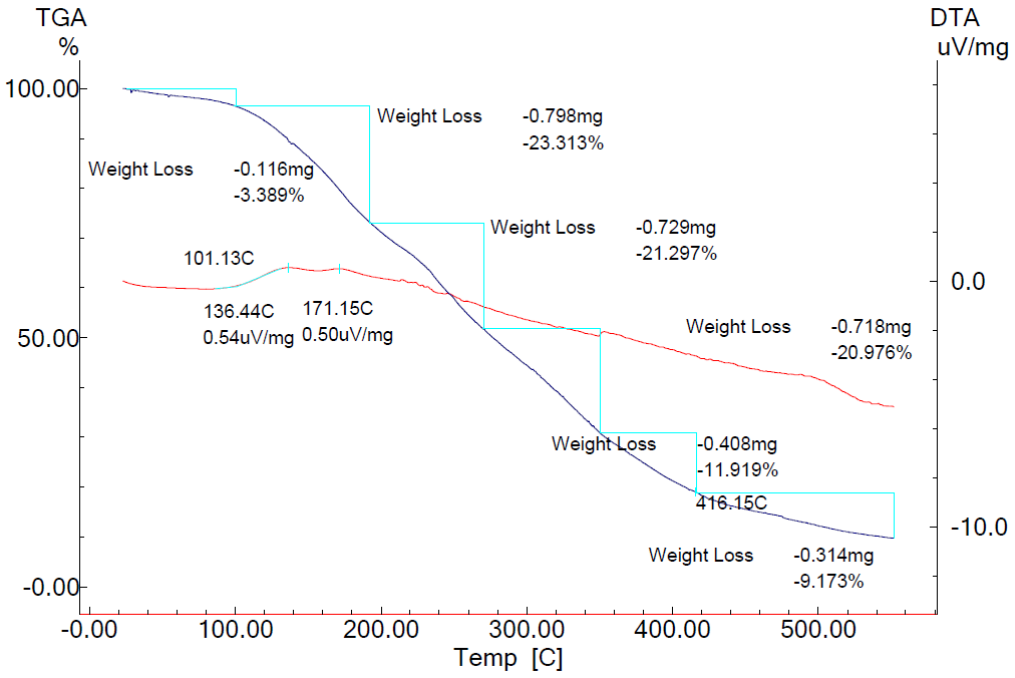


Figure S36. TGA-DSC analysis of the precipitate from the reaction between nitrostyrene **3** and bispidine **6** in toluene.

SEM-EDX study

Methodology of scanning electron microscopy and energy dispersive X-ray spectroscopy of precipitate

Target-oriented approach was utilized for the optimization of the analytic measurements [1]. Before measurements the samples were mounted on a 25 mm aluminum specimen stub and fixed by graphite adhesive tape. Metal coating with a thin film (10 nm) of chromium was performed using magnetron sputtering method as described earlier [2]. The observations were carried out using Hitachi SU8000 field-emission scanning electron microscope (FE-SEM). Images were acquired in secondary electron mode at 30 kV accelerating voltage and at working distance 8-10 mm. Morphology of the samples was studied taking into account possible influence of metal coating on the surface [2]. EDX studies were carried out using Oxford Instruments X-max EDX system before metal coating.

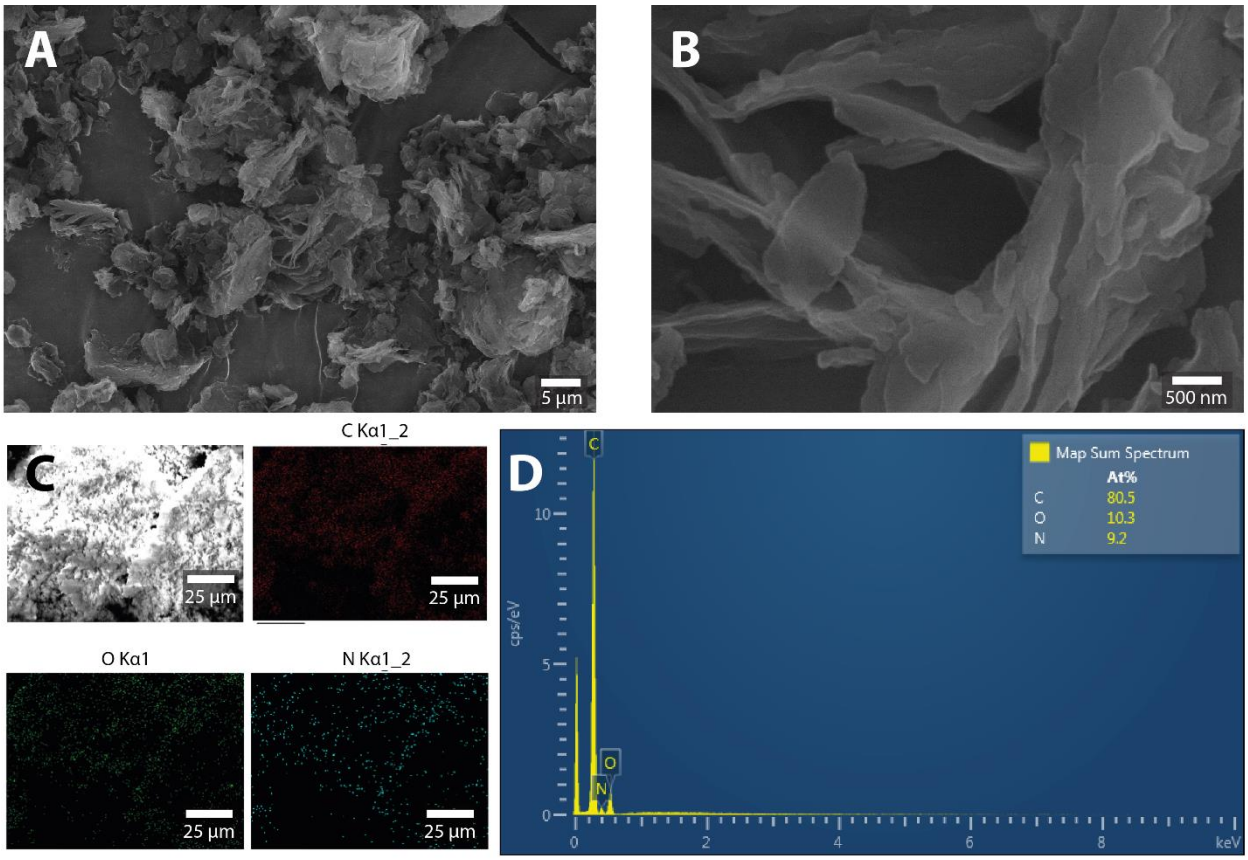
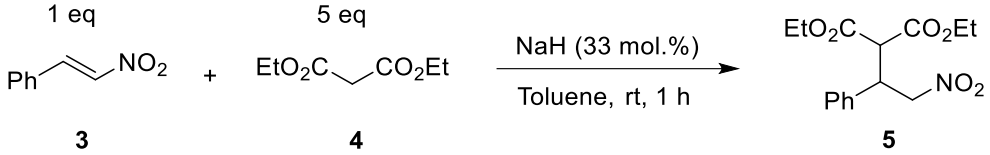


Figure S37. Results of SEM-EDX study of precipitate from binary reaction mixture between nitrostyrene **3** and bispidine **6** in toluene. A, B – scanning electron microscopy images with 5 000x and 50 000x magnifications; C - element distribution maps obtained by energy dispersive spectroscopy; D - EDX spectrum of precipitate.

The particle size ranged from 1 to 10 μm. The particles had an irregular shape and layered morphology; the thickness of individual layers could vary from 100 to 500 nm. EDX data showed a uniform distribution of carbon, nitrogen and oxygen in the sample without impurities of other elements within the sensitivity of the method. The C : O : N ratio was 8 : 1 : 1.

The addition of diethyl malonate to *β*-nitrostyrene in the presence of catalytic amounts of NaH



To a solution of 50 mg (0.34 mmol) of *β*-nitrostyrene (**3**) in 3 mL of dry toluene was added 2.7 mg (0.11 mmol, 33 mol. %) of NaH and 255 μL (268 mg, 1.7 mmol) of diethyl malonate (**4**); the mixture was stirred for 1 h at room temperature. TLC analysis showed complete conversion of nitrostyrene **3**. The reaction mixture was then diluted with water, the organic phase was separated, dried over anhydrous Na_2SO_4 and evaporated in vacuo. The residue obtained without further purification was analyzed by ^1H NMR spectroscopy in $CDCl_3$.

The complete conversion of *β*-nitrostyrene (**3**) with the formation of the addition product (**5**) was confirmed by analysis of the ^1H NMR spectrum (fig. S38).

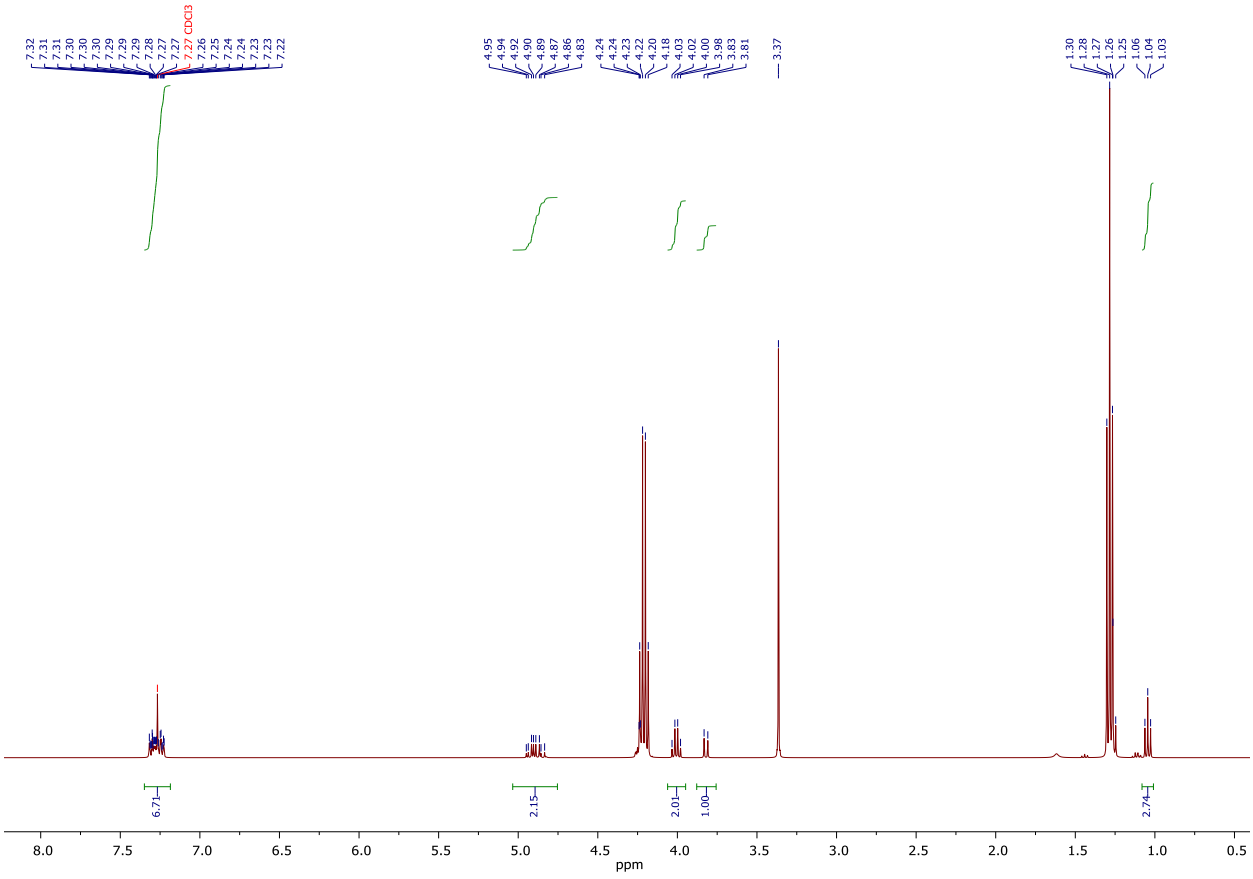


Figure S38. ^{1}H NMR (400 MHz, $CDCl_3$) spectrum of the addition reaction of diethyl malonate **4** with nitrostyrene **3** in the presence of NaH. The signals corresponding to the reaction product **5** are marked in the figure.

References

1. Kachala, V. V; Khemchyan, L.L.; Kashin, A.S.; Orlov, N. V; Grachev, A.A.; Zalesskiy, S.S.; Ananikov, V.P. Target-oriented analysis of gaseous, liquid and solid chemical systems by mass spectrometry, nuclear magnetic resonance spectroscopy and electron microscopy. *Russ. Chem. Rev.* **2013**, *82*, 648–685.
2. Kashin, A.S.; Ananikov, V.P. A SEM study of nanosized metal films and metal nanoparticles obtained by magnetron sputtering. *Russ. Chem. Bull.* **2011**, *60*, 2602–2607.