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Supporting Information

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Photoswitching Basicity

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Table of Contents

General Methods. Solvents and starting materials were used as received. Toluene and THF was distilled under an argon atmosphere over sodium prior to use. Dry DMF was purchased from Acros. All reactions were performed in an argon atmosphere. Column chromatography was carried out with 130 - 400 mesh silica gel. NMR spectra were recorded on a 400 MHz (100.6 MHz for ^{13}C) Bruker AV 400 or on a 300 MHz (75.6 MHz for ^{13}C) Bruker DPX 300 spectrometer at 27 °C using residual protonated solvent signals as internal standard (^{1}H-NMR: $\delta(CDCl_3)$ = 7.24 ppm, $\delta(CD_3CN)$ = 1.94 ppm, δ(THF-*d8*) = 3.58 ppm and ^{13}C-NMR: $\delta(CDCl_3)$ = 77.0 ppm, $\delta(CD_3CN)$ = 1.32 ppm). Mass spectrometry was performed on Thermo LTQ FT instrument (ESI, ESI-HRMS: additives of mixtures of MeOH/H_2O 75/25 + 0.5% formic acid) and MSI concept 1H (EI, 70eV ionization) as well as on a QSTARXL Applied Q-TOF with a ISV of 950 V. HPLC separations were performed with Shimadzu LC-10A systems equipped with a photodiode array detector (PAD or DAD) or with Waters Alliance systems (mixtures and gradient mixtures of acetonitrile/water) equipped with 150 x 2 mm Luna columns (3 µm, phenyl-hexyl material). The Waters systems consisted of a Waters Separations Module 2695, a Waters Diode Array detector 996 and a Waters Mass Detector ZQ 2000. Conditions are specified when describing the corresponding substances. UPLC separations were preformed with a Waters Aquiity system equipped with Acquity UPLC columns, a Water Diode Array detector, and a LCTPremierXE TOF-MS detector.

Spectroscopy. UV-visible absorption spectra were recorded, using quartz cuvettes of 1 cm length on a Cary 50 spectrophotometer equipped with a Peltier-thermostated cell holder at 25 ± 0.05 °C. All solvents employed in optical spectroscopy studies were of spectrophotometric grade. Analytical irradiation experiments (see SI Figures 1-3) were performed on degassed solutions (Ar for 5 min, 2 - $4\cdot10^{-5}$ M) of ***E*-4a-c** in CH_3CN using a LOT-Oriel 1000 W medium-pressure xenon lamp (XBO) equipped with an interference filter ($\lambda_{max\ T}$ = 365 nm @ 10% T, FWHM = 10 nm) for irradiation of ***E*-4a** and with two cut-off filters resulting in a narrow spectral window ($\lambda_{max\ T}$ = 365 nm @ 35% T, FWHM = 42 nm) for irradiation of ***E*-4b,c**. For photochemical $Z \rightarrow E$ isomerization of ***Z*-4a-c** a cut-off filter was used (λ_{max} > 400 nm @ T = 65%). Thermal $Z \rightarrow E$ isomerization of ***Z*-4a-c** was monitored by UV/vis spectroscopy (see SI Figures 4-6). Quantitative UV/vis spectra of ***Z*-4a-c** were determined combining spectroscopy and chromatography data (see SI Figures 7-9). Thermal $Z \rightarrow E$ isomerization of ***Z*-4c**-H^+ was monitored by UV/vis spectroscopy at 20 °C and 45 °C

(see SI Figures 10-11). Photochemical $E \rightarrow Z$ and $Z \rightarrow E$ isomerization of ***Z*-4c**-H^+ was monitored by UV/vis spectroscopy at 25 °C (see SI Figure 12).

Kinetic Experiments. 1 Equiv. of 4-nitrobenzaldehyde and 0.1 equiv. of catalyst **4a-c** were dissolved in THF-d_8 (c_{cat} = 0.04 M), transferred to a NMR-tube, and 12 equiv. of nitroethane were added. ^{1}H-NMR spectra (300 MHz) wre acquired at time intervals of 30 min over a period of 15 h. Plots of product formation, obtained from integration of ^{1}H-NMR spectra (exemplary shown in SI Figures 13 and 14) versus time yielded the rates of reaction (see Figures 15-17).

Single Crystal X-ray Structure Determination of *E*-4b and *Z*-4b

Definitions

$R_{int} = \Sigma \mid F_o^2 - F_o^2(\text{mean}) \mid / \Sigma [F_o^2]$

$R_1 = \Sigma \mid |F_o| - |F_c| \mid / \Sigma |F_o|$

$wR_2 = \{ \Sigma [w(F_o^2 - F_c^2)^2] / \Sigma [w(F_o^2)^2] \}^{½}$

*Crystal data for **E*-4b**:* $[C_{30}H_{41}N_3O_2]$, from acetonitrile, M_r = 475.67, orange plates, crystal size: 0.40×0.32×0.16 mm^3; a = 51.292(4), b = 13.2238(11), c = 29.023(19) Å, β = 118.50° V = 17300(6579) Å^3, T = 180 K, monoclinic, space group $C2/c$, Z = 24, ρ_{calcd} = 1.096 Mg m^{-3}, $F(000)$ = 6192, Stoe IPDS diffractometer, λ(Mo K_α) = 0.71073 Å, μ = 0.069 mm^{-1}, 35186 measured and 11173 independent reflections (R_{int} = 0.0647), 6292 with $I > 2\sigma(I)$, θ_{max} = 22.5°, apparent $T_{min/max}$ = 0.9731/0.9891, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL-97*) on F_o^2, programs from G. Sheldrick, University of Göttingen, 1997. Three independent molecules are in the crystal structure leading to an unusually large unit cell. 974 parameters, H atoms riding, R_1 = 0.0438 ($I > 2\sigma(I)$), wR_2 = 0.0949 (all data), $\Delta\rho_{max/min}$ = 0.376/-0.227 eÅ^{-3}, CCDC 686676 (see SI Figure 18).

*Crystal data for **Z*-4b**:* $[C_{30}H_{41}N_3O_2]$, from acetonitrile, M_r = 475.67, orange prisms, crystal size: 0.60×0.40×0.24 mm^3; a = 7.5388(13), b = 13.771(2), c = 14.573(2) Å, β = 102.371° V = 1446.4(4) Å^3, T = 180 K, triclinic, space group P-1, Z = 2, ρ_{calcd} = 1.092 Mg m^{-3}, $F(000)$ = 516, Stoe IPDS diffractometer, λ(Mo K_α) = 0.71073 Å, μ = 0.068 mm^{-1}, 10441 measured and 5273 independent reflections (R_{int} = 0.0678), 2397 with $I > 2\sigma(I)$, θ_{max} = 26.04°, apparent $T_{min/max}$ = 0.9601/0.9838, direct methods (*SHELXS-97*) and least-squares refinement (*SHELXL-97*) on F_o^2, programs from G. Sheldrick, University of Göttingen, 1997. 422

parameters, H atoms determined, R_1 = 0.0463 ($I > 2\sigma(I)$), wR_2 = 0.1037 (all data), $\Delta\rho_{max/min}$ = 0.363/-0.192 eÅ^{-3}, CCDC 686677 (see SI Figure 19).

pK$_a$-Determination. The pK$_a$-values were determined using a reference base (indicator) with different absorptions of the neutral (**Ind**) and the protonated form (**Ind**-H$^+$) allowing to monitor the concentration of both species spectrophotometrically.[1, 2] Neutral Red (3-amino-7-dimethylamino-2-methylphenazin) meets these requirements displaying absorption maxima at λ_{max} (**Ind**) = 441 nm and λ_{max} (**Ind**-H$^+$) = 534 nm in acetonitrile solution.[3] For further physical data, please consult Scheme 1.

Neutral red was purchased in its protonated form. The free base was obtained by dissolving few milligrams of the protonated form in water, adjusting to basic pH using aq. 1N-NaOH solution, and extraction of the free base with methylene chloride. Drying over $MgSO_4$ and removal of solvent *in vacuo* afforded the free base indicator as a dark red solid.

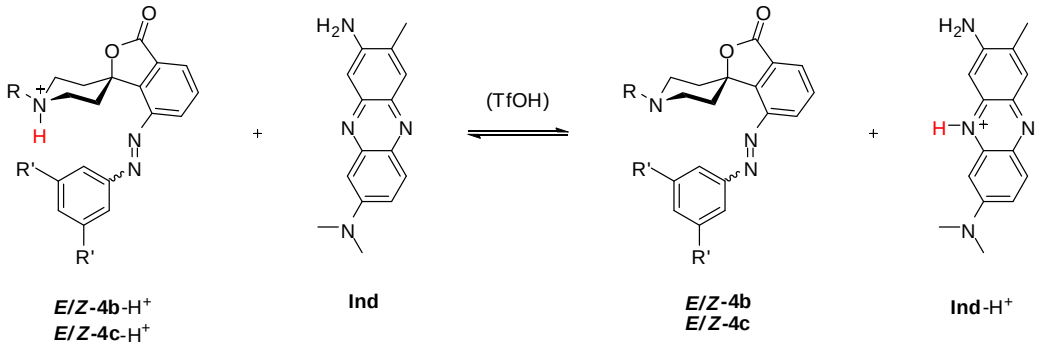
Equimolar amounts of ***E/Z*-4b** and Neutral Red were dissolved in 100 mL of acetonitrile ($c_0 = 4.1 - 4.2 \cdot 10^{-5}$ M) and a solution of trifluoromethanesulfonic acid in acetonitrile (TfOH, $c = 3.15 \cdot 10^{-3}$ M) was added in increments of 0.1 ml (V_{tot} = 1.1 mL). Concentrations of ***E/Z*-4b**, ***E/Z*-4b**-H$^+$, **Ind**, and **Ind**-H$^+$ were determined from UV/vis spectra recorded after each addition (see SI Figure 20). Finally, pK$_a$ values were obtained by applying the equations given in Scheme 1.

pK$_a$ values for ***E/Z*-4c** were determined applying a similar methodology. Equimolar amounts of ***E/Z*-4c** and Neutral Red were dissolved in 3655 µL of acetonitrile ($c_0 = 3.56 \cdot 10^{-5}$ M) and a solution of trifluoromethanesulfonic acid in acetonitrile (TfOH, $c = 5.86 \cdot 10^{-4}$ M) was added in increments of 10 µL (V_{tot} = 180 µL, see SI Figure 21). Finally, pK$_a$ values were obtained by applying the equations given in Scheme 1.

[1] I. Leito, I. Kaljurand, I. A. Koppel, L. M. Yagupolskii, V. M. Vlasov, *J. Org. Chem.*, **1998**, *63*, 7868; I. Kaljurand, T. Rodima, I. Leito, I. A. Koppel, R. Schwesinger, *J. Org. Chem.*, **2000**, *65*, 6202; M. C. Biondic, R. Erra-Balsells, *J. Chem. Soc. Perk. Trans. 2,* **1997**, *7*, 1323.

[2] For optimal results, the pK$_a$ of the reference base should not differ more than 2 pK$_a$ units from the pK$_a$ of the base to be measured.

[3] I. M. Kolthoff, M. K. Chantooni, S. Bhowmik, *Anal. Chem.*, **1967**, *39*, 315.



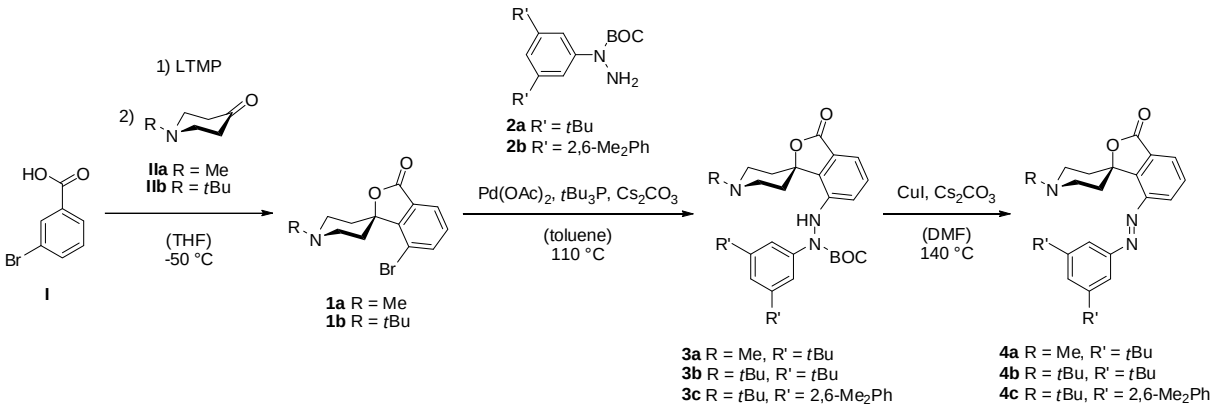
***E/Z*-4b**-H$^+$
***E/Z*-4c**-H$^+$ **Ind** ***E/Z*-4b**
***E/Z*-4c** **Ind**-H$^+$

$$K = \frac{K_a\,(\mathbf{Ind}\text{-}H^+)}{K_a\,(\boldsymbol{E/Z}\text{-}\mathbf{4b,c}\text{-}H^+)} = \frac{[\boldsymbol{E/Z}\text{-}\mathbf{4b,c}\text{-}H^+]\,[\mathbf{Ind}]}{[\boldsymbol{E/Z}\text{-}\mathbf{4b,c}]\,[\mathbf{Ind}\text{-}H^+]} \qquad K_a\,(\boldsymbol{E/Z}\text{-}\mathbf{4b,c}\text{-}H^+) = \frac{K_a\,(\mathbf{Ind}\text{-}H^+)\,[\boldsymbol{E/Z}\text{-}\mathbf{4b,c}]\,[\mathbf{Ind}\text{-}H^+]}{[\boldsymbol{E/Z}\text{-}\mathbf{4b,c}\text{-}H^+]\,[\mathbf{Ind}]}$$

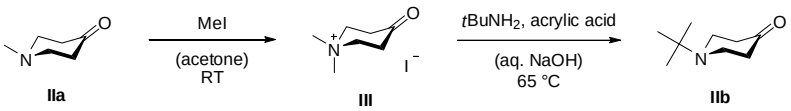
$$[\mathbf{Ind}\text{-}H^+] = \frac{Abs_{534\ nm} - c_0\,(\mathbf{Ind}) \cdot \varepsilon_{534\ nm}(\mathbf{Ind})}{\varepsilon_{534\ nm}\,(\mathbf{Ind}\text{-}H^+) - \varepsilon_{534\ nm}(\mathbf{Ind})}$$

Scheme 1. Equilibrium of ***E/Z*-4b,c**, ***E/Z*-4b,c**-H$^+$, **Ind**, and **Ind**-H$^+$ observed in titration experiment using trifluoromethanesulfonic acid in acetonitrile. pK_a values can be derived from the equation given with K_a (**Ind**-H$^+$) = 2.51 · 10^{-16}, pK_a (**Ind**-H$^+$) = 15.6,[1] $\varepsilon_{534\ nm}$ (**Ind**-H$^+$) = 33350 M^{-1} cm^{-1}, and $\varepsilon_{534\ nm}$ (**Ind**) = 420 M^{-1} cm^{-1}.

Synthesis.



Synthesis of **IIb**:



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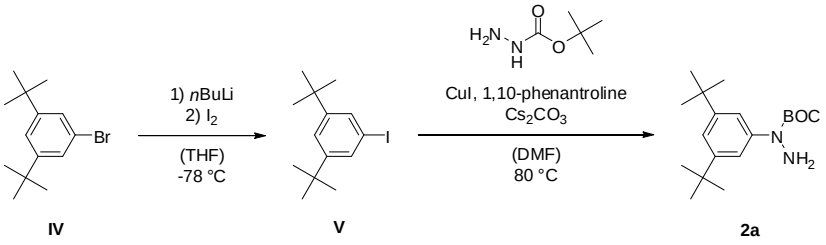
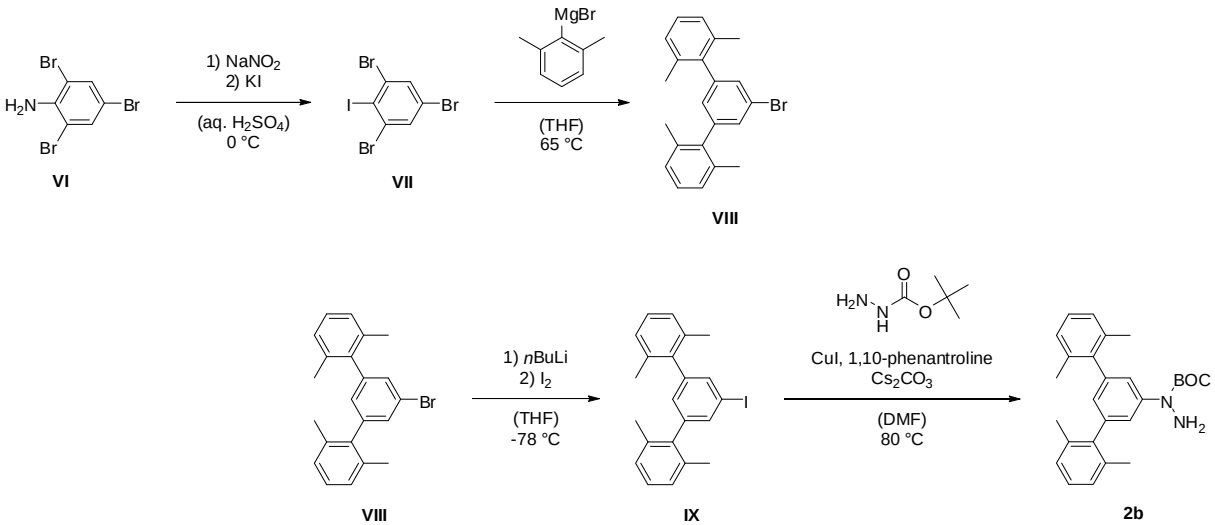


Synthesis of **2b**:



Scheme 2. Synthesis of azo-spirocompound ***E*-4a-c**.

Syntheses of Bromo-Spiro Building Blocks 1a,b

Syntheses of bromo-spiro building blocks **1a,b** were inspired by the procedures developed by Gohier et al.[4] and Parham et al.[5]

Bromo-spiro building block **1a**. 2,2,6,6-Tetramethylpiperidine (22.5 mL, 132 mmol) was dissolved in 100 mL of dry THF and cooled to -5 °C. *n*-Butyl lithium (82 mL, 1.6 M in hexane, 132 mmol) was added dropwise and stirring was continued for 1 h at -5 °C. After cooling to -50 °C, a solution of 3-bromobenzoic acid **I** (12.06 g, 60 mmol) in 30 mL of THF was added dropwise and the solution was stirred at -50 °C for 10 min. *N*-methyl-4-piperidinone **IIa (**28 mL, 240 mmol) dissolved in 25 mL of THF was added rapidly and the solution was stirred at -50 °C for 1 h. The mixture was acidified to pH ~2 using 1N aq. HCl-solution and was stirred at room temperature over night. The organic solvent was removed *in vacuo* and the remaining aqueous layer was extracted diethyl ether twice. The aqueous phase was adjusted to basic pH with solid $NaHCO_3$ and washed again with diethyl ether several times. Combined organic phases were washed with sat. aq. $NaHCO_3$-solution and water three times, respectively. Drying over $MgSO_4$ and evaporation of the solvent gave the crude product. Dissolution in methylene chloride and repetitive washing with ~800 mL of sat. aq. $NaHCO_3$-solution, followed by drying over $MgSO_4$, and evaporation of the solvent gave 2.5 g of product as nearly colorless solid (8.4 mmol, 14%). R_f (CH_2Cl_2/MeOH, 10/1) = 0.4. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.80 (dd, ^{4}J = 1 Hz, ^{3}J = 7.6 Hz, 1H, Ar-*H*), 7.78 (dd, ^{4}J = 1 Hz, ^{3}J = 7.8 Hz, 1H, Ar-*H*), 7.39 (t, ^{3}J = 7.7 Hz, 1H, Ar-*H*), 3.0 (broad m, 4H, pip-*H*), 2.62 (broad m, 2H, pip-*H*), 2.44 (s, 3H, -C*H*$_3$), 1.60 (d, 2H, ^{3}J = 16 Hz, pip-*H*). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ (ppm) = 138.8, 131.1, 128.3, 125.2, 116.4, 95.9, 51.4, 46.0, 32.3. MS (EI, 90 °C): *m/z* = 296 ([M]$^+$), 216 ([M - Br]$^+$), 129. HRMS (ESI pos.): *m/z* = 318.01004 (calc. 318.01002 for $C_{13}H_{14}N_1O_2NaBr$).

Bromo-spiro building block **1b**. 2,2,6,6-Tetramethylpiperidine (1.87 mL, 11 mmol) was dissolved in 8.4 mL of dry THF and cooled to -5 °C. *n*-Butyl lithium (6.83 mL, 1.6 M in hexane, 11 mmol) was added dropwise and stirring was continued for 1 h at -5 °C. After cooling to -50 °C, a solution of 3-bromobenzoic acid **I** (1.00 g, 5 mmol) in 2.5 mL of THF was added dropwise and the solution was stirred at -50 °C for 10 min. *N-tert*-butyl-4-piperidinone **IIb (**1.55 g, 10 mmol) dissolved in 2.1 mL of THF was added rapidly and the

[4] F. Gohier, J. Mortier, *J. Org. Chem* **2003**, *68*, 2030.

[5] W. E. Parham, D. C. Egberg, Y. A. Sayed, R. W. Thraikill, G. E. Keyser, M. Neu, W. C. Montgomery, L. D. Jones, *J. Org. Chem* **1976**, *41*, 2628.

solution was stirred at -50 °C for 1 h. The mixture was acidified to pH ~2 using 1N aq. HCl-solution and was stirred at room temperature over night. The organic solvent was removed *in vacuo* and the remaining aqueous layer was extracted with diethyl ether twice, adjusted to basic pH by addition of solid $NaHCO_3$, and extracted with diethyl ether again. Combined organic layers were washed with sat. aq. $NaHCO_3$-solution four times, three times with water, and dried over $MgSO_4$. Column chromatography (silica gel, CH_2Cl_2/MeOH, 20/1) afforded 0.45 g of product as an off-white solid (2.9 mmol, 26%). R_f (CH_2Cl_2/MeOH, 10/1) = 0.52. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.86 (dd, 1H, ^{4}J = 1 Hz, ^{3}J = 7.5 Hz, Ar-*H*), 7.81 (dd, 1H, ^{4}J = 1 Hz, ^{3}J = 7.9 Hz, Ar-*H*), 7.40 (t, 1H, ^{3}J = 7.7 Hz, Ar-*H*), 3.09 (d, 2H, ^{3}J = 8.7 Hz, pip-*H*), 2.83 (d, 2H, ^{3}J = 11.8 Hz, pip-*H*), 2.65 (t, 2H, J = 11.2 Hz, pip-*H*), 1.60 (d, 2H, ^{3}J = 12.5 Hz, pip-*H*), 1.14 (s, 9H, *N-t*-Bu-*H*)). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 138.6, 130.7, 128.6, 125.0, 116.4, 42.1, 33.6, 26.2. MS (EI, 80°C): *m/z* = 337 ($[M]^+$), 322 ($[M - CH_3]^+$). HRMS (ESI pos): *m/z* = 337.0677 (calc. 337.0677 for $C_{16}H_{20}N_1O_2Br$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 5→95% CH_3CN/H_2O): t_R = 10.58 min (97% peak area).

Synthesis of *N-tert*-butyl-4-piperidone IIb

N,N-Dimethyl-4-oxopiperidinium iodide **III**. Following a procedure developed by Amato et al.,[6] *N*-methyl-4-piperidinone **IIa** (10.4 mL, 90 mmol) was dissolved in 135 mL of acetone and cooled to 0 °C. Methyl iodide (6.7 mL, 100 mmol) was added under vigorous stirring and the resulting mixture was stirred for 10 min at 0 °C. The solution was warmed to room temperature and stirring was continued for 1 h. Isolation of the bright yellow precipitate by filtration, washing with small amounts of acetone three times, and drying over night afforded 22.3 g of product as a colorless solid (87.3 mmol, 97%). The analytical data agree with the literature.

N-tert-Butyl-4-piperidinone **IIb.** Water (40 mL) and acrylic acid (13.7 mL, 200 mmol) were mixed in a round bottom flask and 18.5 mL of a 10 M NaOH solution were added dropwise under vigorous stirring. *N*,*N*-Dimethyl-4-oxopiperidinium iodide **III** (10.2 g, 40 mmol) and *tert*-butylamine (80 mL, 755 mmol) were added and the solution was heated to reflux (65 °C) for 3 h. After cooling to 0 °C (ice/water bath), remaining *tert*-butylamine was removed quickly at 0 °C *in vacuo* using a rotary evaporator. The cold solution was extracted with ethyl

[6] J. S. Amato, J. Y. L. Chung, R. J. Cvetovich, X. Gong, M. McLaughlin, Robert A. Reamer, *J. Org. Chem* **2005**, 70, 1930.

acetate three times. Combined organic layers were washed with brine three times and dried over $MgSO_4$. Evaporation of solvent at max. 30 °C and column chromatography (silica gel, CH_2Cl_2/MeOH, 20/1, evaporation at max. 30 °C) afforded 4.67 g of product as a yellow oil (30 mmol, 75%). Alternatively, analytically pure product can be obtained by distillation of the crude material *in vacuo*. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 2.80 (t, ^{3}J = 6.1 Hz, 4H, pip-*H*), 2.38 (t, ^{3}J = 6.1 Hz, 4H, pip-*H*), 1.08 (s, 9H, *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 210, 54.1, 46.2, 42.2, 26.4. MS (ESI pos) *m/z* = 311 ($[2M + H]^+$), 188, 156 ($[M + H]^+$). HRMS (ESI pos): *m/z* = 156.1394 (calculated 156.1388 for $C_9H_{18}NO$), 311.2697 (calculated 311.2693 for $C_{18}H_{35}N_2O_2$).

Synthesis of BOC-Hydrazo Building Blocks 2a,b

BOC-protected hydrazines were synthesized according to a procedure developed by Wolter et al.[7]

3,5-Di-tert-butyliodobenzene **V.** 3,5-Di-*tert*-butylbromobenzene[8] **IV** (5.40 g, 20 mmol) was dissolved in 160 mL of THF and cooled to -78 °C. *n*-Butyl lithium (16.5 mL, 1.6 M in hexane, 26 mmol) was added and the solution was stirred at -78 °C for 1 h. Iodine (6.59 g, 26 mmol) was dissolved in THF and added at -78 °C. The cooling bath was removed and the colored solution was stirred at room temperature overnight. After washing with aq. $Na_2S_2O_3$-solution and drying over $MgSO_4$, 6.24 g of product were obtained as a colorless oil, which solidified upon standing (20 mmol, 99%). R_f (Hex/EA, 10/1) = 0.66. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.51 (d, 2H, Ar-*H*), 7.35 (s, 1H, Ar-*H*), 1.28 (s, 18H, *t*-Bu-*H*). MS (EI, 20 °C): *m/z* = 316 ($[M]^+$), 207 ($[M - CH_3]^+$). GC**:** 87.9 % peak area.

1-tert-Butoxycarbonyl-1-(3,5-di-tert-butylphenyl)hydrazine **2a**. 3,5-Di-*tert*-butyliodobenzene **V** (1.43 g, 8.25 mmol), *tert*-butyl-carbazate (1.32 g, 10 mmol), copper(I) iodide (22 mg, 0.12 mmol), 1,10-phenanthroline (170 mg, 0.9 mmol), cesium carbonate (3.72 g, 11.5 mmol), and 8.5 mL of dry DMF were mixed in a dry Schlenk tube and heated to 80 °C for 23 h. After cooling to room temperature, the solvent was evaporated and the crude mixture was purified by column chromatography (silica gel, gradient Hex/EA, 7/1 → 5/1) to afford 1.30 g of product as a yellow oil, which slowly solidified upon standing (4.01 mmol, 49%). R_f (Hex/EA, 5/1) = 0.16. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.31 (d, 2H, ^{4}J = 1.5 Hz, Ar-*H*), 7.16 (t, 1H, ^{4}J = 1.5 Hz, Ar-*H*) 1.48 (s, 9H, *t*-Bu-*H*), 1.30 (s, 18H, *t*-Bu-*H*). ^{13}C-NMR

[7] M. Wolter, A. Klapars, S. L. Buchwald, *Org. Lett.* **2001**, *3*, 3803.
[8] P. D. Bartlett, M. Roha, R.M. Stiles, *J. Am. Chem. Soc.* **1954**, *76*, 2349.

($CDCl_3$, 100 MHz): δ (ppm) = 150.9, 119.3, 118.7, 81.8, 35.3, 31.8, 28.8. MS (EI, 45 °C): *m/z* = 320 ($[M]^+$), 262 ($[M - C(CH_3)_3]^+$), 220 ($[M - CO_2C(CH_3)_3]$). HRMS (ESI pos): *m/z* = 343.2355 (calc. 343.2355 for $C_{19}H_{32}N_2O_2Na$).

2,4,6-Tribromoiodobenzene **VII.** 2,4,6-Tribromoaniline **VI** (24.7 g, 75 mmol) was dissolved in 120 mL of concentrated sulfuric acid and cooled to 0 °C. A concentrated solution of sodium nitrite (11.4 g, 165 mmol) in water was added in portions and stirring at 0 °C was continued for 3.5 h. The mixture was poured into ice/water followed by immediate addition of a mixture of potassium iodide (74.7 g, 450 mmol) with water and ice (gas evolution). The mixture was transferred to a separation funnel and extracted with ethyl acetate five times. Combined organic layers were washed with sat. aq. $NaHSO_3$-solution five times and with water and brine three times, respectively. Drying over $MgSO_4$ and removal of solvent *in vacuo* afforded a crude, reddish material which could be further purified by fractionated crystallization from ethanol/water mixtures to obtain 20.8 g of pure product (47 mmol, 63%). R_f (Hex) = 0.5. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.70 (s, 2H, Ar-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 133.7, 132.0, 123.1, 108.2. DEPT135-NMR ($CDCl_3$): δ (ppm) = 133.7 (pos.). MS (EI, 35 °C): *m/z* = 440 ($[M]^+$), 360, 312, 234, 153, 74. HRMS (EI): *m/z* = 439.6732 (calc. 439.6732 for $C_6H_2Br^{79}{}_2Br^{81}I$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 30→70% CH_3CN/H_2O): t_R = 33.32 min (100% peak area).

1-Bromo-3,5-bis(2,6-dimethylphenyl)benzene **VIII**: 1-Bromo-3,5-bis(2,6-dimethylphenyl)-benzene **VIII** was synthesized according to a procedure by Vinod and Hart.[9] A dry 3N-flask equipped with a reflux condenser and an addition funnel was charged with magnesium (1.70 g, 70 mmol) and 20 mL dry THF. A solution of bromo-2,6-dimethylbenzene (8.05 mL, 11.10g, 60 mmol) in 100 mL of dry THF was slowly added. Formation of the Grignard reagent was aided by gentle heating. The mixture was stirred for 1 h at room temperature and transferred to a second dry 3N-flask equipped with a reflux condenser and an addition funnel via a filter cannula followed by heating to reflux (65 °C). A mixture of 2,4,6-tribromoiodobenzene **VII** (8.81 g, 20 mmol) and 60 mL of dry THF was added via the addition funnel over the course of 60 min. Stirring at 65 °C was continued for 3 h. The mixture was cooled in ice/water followed by addition of 100 mL of aq. 1N-HCl solution. Phases were separated and the aqueous layer was extracted with ethyl acetate three times. Combined organic layers were washed with brine three times, dried over $MgSO_4$, and the solvent was removed *in vacuo*. The crude product was purified by column chromatography

[9] T. K. Vinod, H. Hart *J. Org. Chem.* **1991**, *56*, 5630.

(silica gel, Hex) to afford 4.28 g of pure product as a colorless oil (12 mmol, 59%). R_f (Hex) = 0.2. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.35 (d, ^{4}J = 1.5 Hz, 2H, Ar-*H*), 7.22 - 7.11 (m, 6H, Ar-*H*), 6.92 (t, ^{4}J = 1.5 Hz, 1H, Ar-*H*), 2.12 (s, 12H, C*H*$_3$). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 143.4, 140.4, 135.9, 130.4, 128.9, 127.6, 127.5, 122.7, 21.0. DEPT135-NMR ($CDCl_3$): δ (ppm) = 130.4 (pos.), 128.9 (pos.), 127.6 (pos.), 127.5 (pos.), 21.0 (pos.). MS (EI, 35 °C): *m/z* = 364 ($[M]^+$), 285 ($[M - Br]^+$), 270 ($[M - Br - CH_3]^+$), 255 ($[M - Br - 2\ CH_3]^+$). HRMS (EI): *m/z* = 364.0827 (calc. 364.0827 for $C_{22}H_{21}Br^{79}$).

1-Iodo-3,5-bis(2,6-dimethylphenyl)benzene **IX**: 1-Bromo-3,5-bis(2,6-dimethylphenyl)benzene **VII** (4.15 g, 11.4 mmol) was dissolved in 50 mL of THF and cooled to -78 °C. *n*-Butyl lithium (9.2 mL, 1.6 M in hexane, 14.8 mmol) was added and the solution was stirred at - 78 °C for 1 h. Iodine (3.75 g, 14.8 mmol) was dissolved in 10 mL of THF and added at - 78 °C. Stirring at -78 °C was continued for 1 h. The cooling bath was removed and the colored solution was quenched with sat. aq. $NaHSO_3$-solution. The organic layer was washed with sat. aq. $NaHSO_3$-solution three times and dried over $MgSO_4$. Removal of solvent *in vacuo* afforded 4.41 g of pure product as a colorless wax (10.3 mmol, 94%). R_f (Hex/EA, 9/1) = 0.8. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.56 (d, ^{4}J = 1.5 Hz, 2H, Ar-*H*), 7.22 - 7.11 (m, 6H, Ar-*H*), 6.96 (t, ^{4}J = 1.5 Hz, 1H, Ar-*H*), 2.12 (s, 12H, C*H*$_3$).). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 143.4, 140.3, 136.3, 135.9, 129.5, 127.6, 127.5, 94.7, 21.0. DEPT135-NMR ($CDCl_3$): δ (ppm) = 136.3 (pos.), 129.5 (pos.), 127.6 (pos.), 127.5 (pos.), 21.0 (pos.). MS (EI): *m/z* = 412 ($[M]^+$), 285 ($[M - I]^+$), 255 ($[M - I - 2\ CH_3]^+$), 207, 179. HRMS (EI): *m/z* = 412.0689 (calc. 412.0689 for $C_{22}H_{21}I$).

1-tert-Butoxycarbonyl-1-(3,5-bis(2,6-dimethylphenyl)phenyl)hydrazine **2b**. 1-Iodo-3,5-bis(2,6-dimethylphenyl)benzene **IX** (4.28 g, 10.37 mmol), *tert*-butyl-carbazate (1.71 g, 12.97 mmol), copper(I) iodide (198 mg, 1.04 mmol), 1,10-phenanthroline (374 mg, 2.07 mmol), cesium carbonate (4.73 g, 14.52 mmol), and 10 mL of dry DMF were mixed in a dry Schlenk tube and heated to 80 °C. Small amounts of copper(I) iodide and *tert*-butyl-carbazate were added after 16 h and heating to 80 °C was continued for additional 4 h. After cooling to room temperature, water was added and the aqueous layer was extracted with ethyl acetate three times. Combined organic layers were washed with brine three times and dried over $MgSO_4$. Removal of solvent *in vacuo* and purification of the material obtained by column chromatography (silica gel, gradient Hex/EA, 9/1 → 8/2) afforded 3.20 g of product as a colorless solid (7.25 mmol, 70%). R_f (Hex/EA, 8/2) = 0.46. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.25 (d, ^{4}J = 1.5 Hz, 2H, Ar-*H*), 7.19 - 7.09 (m, 6H, Ar-*H*), 6.72 (t, ^{4}J = 1.5 Hz, 1H,

Ar-*H*), 4.51 (broad s, 2H, N*H*$_2$), 2.12 (s, 12H, C*H*$_3$), 1.49 (s, 9H, *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 155.4, 143.5, 141.6, 141.4, 136.0, 127.4, 127.2, 126.4, 122.8, 81.9, 28.5, 21.0. DEPT135-NMR ($CDCl_3$): δ (ppm) = 127.4 (pos.), 127.2 (pos.), 126.4 (pos.), 122.8 (pos.), 28.5 (pos.), 21.0 (pos.). MS (ESI pos.): *m/z* = 439 ([M + Na]$^+$). HRMS (ESI pos.): *m/z* = 439.2357 (calc. 439.2356 for $C_{27}H_{32}O_2N_2Na$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 5→95% CH_3CN/H_2O): t_R = 24.94 min (93.5% peak area).

Synthesis of Spiro-Hydrazo Compounds 3a-c

Spiro-hydrazo building blocks were synthesized following a protocol developed by Lim et al.[10]

Spiro-hydrazo compound **3a**. Bromo-spiro building block **1a** (75 mg, 0.26 mmol), 1-*tert*-butoxycarbonyl-1-(3,5-di-*tert*-butylphenyl)hydrazine **2a** (102 mg, 0.309 mmol), palladium(II) acetate (3 mg, 0.02 mmol), cesium carbonate (138 mg, 0.4 mmol), tri-*tert*-butyl phosphine (3 mg, 0.014 mmol), and 3.2 mL of toluene were mixed under an argon atmosphere in a sealed tube and stirred at room temperature for 0.5 h followed by heating to 120 °C for 2 h. After cooling to room temperature and diluting with methylene chloride, the reaction mixture was passed through a celite plug using methylene chloride and the solvent was evaporated. Column chromatography (silica gel, CH_2Cl_2/MeOH, 30/1) afforded 77 mg of the product as a colorless oil (55%). R_f (CH_2Cl_2/MeOH, 10/1) = 0.6. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.37 (m, 2H, Ar-*H*), 7.31 (d, ^{4}J = 1.6 Hz, 2H, Ar-*H*), 7.18 (t, ^{4}J = 1.6 Hz, 1H, Ar-*H*), 7.11 (dd, ^{3}J = 7.5 Hz, ^{4}J = 1.2 Hz, 1H, Ar-*H*), 6.90 (s, 1H, N-*H*), 2.92 (broad d, ^{3}J = 8.8 Hz, pip-*H*), 2.70 (m, 2H, pip-*H*), 2.57 (broad t, ^{3}J = 10 Hz, 2H, pip-*H*), 2.4 (s, 3H, -C*H*$_3$), 1.74 (broad d, ^{3}J = 13.5 Hz, 2H, pip-*H*), 1.41 (s, 9H, *t*-Bu-*H*), 1.28 (s, 18H, *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 100.62 MHz): δ (ppm) = 169.5, 153.9, 150.9, 142.5, 141.2, 136.9, 130.6, 126.8, 119.4, 117.4, 117,2, 116.7, 83.1, 82.5, 53.3, 51.6, 46.1, 34.9, 31.3, 28.2. MS (EI, 150°C): *m/z* = 535 ([M]$^+$), 435 ([M - BOC]$^+$), 185. HRMS (ESI pos.): *m/z* = 536.34844, (calculated 536.34827 for $C_{32}H_{46}N_3O_4$).

Spiro-hydrazo compound **3b**. Bromo-spiro building block **1b** (200 mg, 0.6 mmol), 1-*tert*-butoxycarbonyl-1-(3,5-di-*tert*-butylphenyl)hydrazine **2a** (230 mg, 0.72 mmol), cesium carbonate (330 mg, 1 mmol), palladium(II) acetate (7 mg, 0.03 mmol), tri-*tert*-butylphosphine (7 mg, 0.03 mmol), and 7 mL of toluene were mixed in a sealed tube under an argon atmosphere and heated at 120 °C for 3 h. After cooling to room temperature and diluting with

[10] Y.-K. Lim, K.-S. Lee, C.-G. Cho, *Org. Lett.* **2003**, *5*, 979.

methylene chloride, the reaction mixture was passed through a celite plug using methylene chloride and the solvent was evaporated. Column chromatography (silica gel, CH_2Cl_2/MeOH, 100/1) afforded 190 mg of product as a colorless solid (0.32 mmol, 54%). R_f (CH_2Cl_2/MeOH, 50/1) = 0.24. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.39 (m, 4H, Ar-*H*), 7.20 (t, 1H, ^{4}J=1.7 Hz, Ar-*H*), 7.12 (m, 2H, Ar-*H*), 3.10 (d, 2H, ^{3}J = 9.6 Hz, pip-*H*), 2.67 (dd, 4H, ^{3}J = 13.9 Hz, ^{3}J = 25.1 Hz, pip-*H*), 1.76 (d, 2H, ^{3}J = 12.4 Hz, pip-*H*), 1.44 (s, 9H, *t*-Bu-*H*), 1.30 (s, 18H, *t*-Bu-*H*), 1.15 (s, 9H, *N*-*t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 150.9, 142.6, 130.5, 119.2, 117.2, 116.9, 84.4, 82.5, 54.4, 42.3, 34.9, 31.4, 28.2, 26.1. MS (ESI pos): *m/z* = 578 ($[M + H]^+$), 522 ($[M - C_4H_8]^+$). HRMS (ESI pos): *m/z* = 578.3948 (calc. 578.3952 for $C_{35}H_{52}N_3O_4$).

Spiro-hydrazo compound **3c**: Bromo-spiro building block **1b** (488 mg, 1.44 mmol), 3,5-bis(2,6-dimethylphenyl)-phenyl-Boc-hydrazine **2b** (721 mg, 1.73 mmol), cesium carbonate (940 mg, 2.88 mmol), palladium(II) acetate (65 mg, 0.29 mmol), tri-*tert*-butylphosphine (58 mg, 0.29 mmol), and 10 mL of toluene were mixed in a sealed tube under an argon atmosphere. The mixture was degassed by three successive freeze-pump-thaw cycles and heated at 120 °C for 12 h. After cooling to room temperature and diluting with methylene chloride, the reaction mixture was passed through a celite plug using methylene chloride and the solvent was evaporated. Column chromatography (silica gel, CH_2Cl_2/MeOH, 99/1 containing 0.1vol% NEt_3) afforded 811 mg of product as a colorless solid (1.44 mmol, 83%). R_f (CH_2Cl_2/MeOH, 99/1) = 0.18. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 7.43 - 7.28 (m, 5H, Ar-*H* + N-*H*), 7.20 - 7.06 (m, 7H, Ar-*H*), 6.74 (broad t, ^{4}J = 1.5 Hz, Ar-*H*), 3.20 - 3.05(m, 2H, pip-*H*), 2.78 - 2.63 (m, 2H, pip-*H*), 2.63 - 2.45 (m, 2H, pip-*H*), 2.11 (s, 12H, C*H*$_3$), 1.84 - 1.70 (m, 2H, pip-*H*), 1.39 (s, 9H, *t*-Bu-*H*), 1.15 (s, 9H, *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 169.7, 153.6, 142.8, 142.7, 141.7, 141.4, 136.9, 136.1, 130.7, 127.4, 127.3, 126.6, 121.2, 117.5, 117.3, 116.3, 84.4, 82.9, 54.6, 42.4, 34.4, 28.3, 26.3, 21.0. DEPT135-NMR ($CDCl_3$): δ (ppm) = 130.7 (pos.), 124.4 (pos.), 127.3 (pos.), 126.6 (pos.), 121.2 (pos.), 117.4 (pos.), 116.3 (pos.), 42.4 (neg.), 34.4 (neg.), 28.3 (pos.), 26.3 (pos.), 21.0 (pos.). MS (ESI pos): *m/z* = 674 ($[M + H]^+$), 572 ($[M - BOC]^+$). HRMS (ESI pos): *m/z* = 674.3963 (calc. 674.3958 for $C_{43}H_{52}N_3O_4$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 40→95% CH_3CN/H_2O): t_R = 12.00 min (95% peak area).

_E_-Azobenzene catalysts _E_-4a-c

Azobenzene based catalysts were synthesized adopting a procedure by Lim et al.[11]

Azobenzene catalysts ***E*-4a**. Spiro-hydrazo compound **3a** (100 mg, 0.19 mmol), copper(I) iodide (54 mg, 0.27 mmol), cesium carbonate (90 mg, 0.27 mmol), and 3 mL of dry DMF were mixed in a dry Schlenk tube and heated at 140 °C for 3 h. The mixture was diluted with methylene chloride and filtered through celite. Column chromatography (silica gel, Hex/EA, 3/1 + 0.1vol% NEt_3) afforded 48 mg of product as an orange solid (0.11 mmol, 58%). R_f (Hex/EA, 2/1 + 0.1vol% NEt_3) = 0.36. ^{1}H-NMR ($CDCl_3$, 400 MHz): δ (ppm) = 7.94 (m, 2H, Ar-*H*), 7.84 (d, ^{4}J = 1.8 Hz, 2H, Ar-*H*), 7.60 (m, 2H, Ar-*H*), 2.85 (broad m, 4H, pip-*H*), 2.53 (broad m, 2H, pip-*H*), 2.34 (s, 3H, C*H*$_3$), 1.77 (d, ^{3}J = 11Hz, 2H, pip-*H*), 1.39 (s, 18H, *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 100 MHz): δ (ppm) = 169.3, 152.8, 152.2, 146.1, 130.2, 127.7, 126.3, 120.0, 117.9, 109.8, 85.9, 51.8, 46.1, 36.0, 35.1, 31.3. MS (EI, 125 °C): *m/z* = 433 ([M]$^+$). HRMS (ESI pos.): *m/z* = 434.28009, (calc. 434.28019 for $C_{27}H_{36}N_3O_2$). HPLC (MeOH/10mmol TEAA pH 6.5 = 85/15, Nucleodur 100-5C18ec. 4 mm i.d.): t_R = 14.44 min (97% peak area).

Azobenzene catalysts ***E*-4b**. Spiro-hydrazo compound **3b** (166 mg, 0.29 mmol), copper(I) iodide (80 mg, 0.42 mmol), cesium carbonate (130 mg, 0.40 mmol), and 4.5 mL of dry DMF were mixed in a dry Schlenk tube and heated to 140 °C for 3 h. The mixture was diluted with methylene chloride and filtered through celite. Column chromatography (silica gel, PE/EA, 2/1) afforded 71 mg of product as an orange solid (0.15 mmol, 52%). R_f (PE/EA 5/1) = 0.1. ^{1}H-NMR (THF-d_8, 300 MHz): δ (ppm) = 8.05 (dd, 1H, ^{3}J = 8 Hz, ^{4}J = 0.8 Hz, Ar-*H*), 7.93 (m, 2H, Ar-*H*), 7.69 (t, 1H, ^{4}J = 1.8 Hz, Ar-*H*), 7.65 (t, 1H, ^{3}J = 7.7 Hz, Ar-*H*), 2.79 (m, 2H, pip-*H*), 3.10 (m, 2H, pip-*H*), 2.67 (m, 2H, pip-*H*), 1.83 (d, 2H, J =4.4 Hz, pip-*H*), 1.43 (s, 18H, *t*-Bu), 1.14 (s, 9H, *N*-*t*-Bu-*H*). ^{13}C-NMR (THF-d_8, 75 MHz): δ (ppm) = 167.2, 152.9, 152.2, 151.1, 146.1, 130.0, 128.6, 127.6, 126.1, 119.3, 117.9, 85.5, 53.7, 42.7, 37.7, 34.9, 30.9, 25.7. MS (ESI pos): *m/z* = 476.4 [M+H]$^+$. HRMS (ESI pos): *m/z* = 476.3274 (calculated 476.3272 for $C_{30}H_{42}N_3O_2$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 5→95% CH_3CN/H_2O): t_R = 17.14 min (96.8% peak area).

Azobenzene catalysts ***E*-4c**. Spiro-hydrazo compound **3c** (300 mg, 0.45 mmol), copper(I) iodide (127 mg, 0.67 mmol), cesium carbonate (217 mg, 0.67 mmol), and 5 mL of dry DMF were mixed in a dry Schlenk tube and heated to 140 °C for 14 h. The mixture was diluted with methylene chloride and filtered through celite. Column chromatography (silica gel, Hex/EA,

[11] Y.-K. Lim, S. Choi, K. B. Park, C.-G. Cho, *J. Org. Chem* **2004**, *69*, 2603.

9/1 + 0.1vol% NEt_3) afforded 125 mg of product as an orange solid (0.45 mmol, 49%). R_f (Hex/EA, 9/1 + 0.1vol% NEt_3) = 0.36. ^{1}H-NMR ($CDCl_3$, 300 MHz): δ (ppm) = 8.03 (d, ^{3}J = 7.9 Hz, 1H, Ar-*H*), 7.99 (d, ^{3}J = 7.9 Hz, 1H, Ar-*H*), 7.81 (d, ^{4}J = 1.6 Hz, 2H, Ar-*H*), 7.63 (t, ^{3}J = 7.9 Hz, 1H, Ar-*H*), 7.24 - 7.12 (m, 7H Ar-*H*), 2.99 (m, 2H, pip-*H*), 2.71 (m, 2H, pip-*H*), 2.58 (m, 2H, pip-*H*), 2.18 (s, 12H, C*H*$_3$), 1.82 (m, 2H, pip-*H*), 0.95 (s, 9H, , *t*-Bu-*H*). ^{13}C-NMR ($CDCl_3$, 75 MHz): δ (ppm) = 169.4, 153.3, 151.5 146.1, 142.7, 140.7, 135.8, 133.9, 130.2, 128.2, 128.0, 127.7, 127.5, 122.8, 120.1, 87.1, 53.7, 42.8, 37.8, 26.3, 21.2. DEPT135-NMR ($CDCl_3$): δ (ppm) = 130.2 (pos.), 128.2 (pos.), 127.7 (pos.), 127.5 (pos.), 122.8 (pos.), 120.1 (pos.), 42.8 (neg.), 37.8 (neg.), 26.3 (pos.), 21.2 (pos.). MS (ESI pos): *m/z* = 572 ([M + H]$^+$). HRMS (ESI pos): *m/z* = 572.3278 (calc. 572.3272 for $C_{38}H_{42}N_3O_4$). HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 40→95% CH_3CN/H_2O): t_R = 11.75 min (100% peak area).

_Z_-Azobenzene catalysts _Z_-4a-c

*Azobenzene catalysts **Z**-**4a***. Azobenzene catalysts ***E*-4a** (20 mg, 0.04 mmol) was dissolved in 100 mL of acetonitrile and degassed by bubbling argon through the solution for 10 min. Subsequently, the solution was irradiated using a LOT-Oriel 1000 W medium-pressure xenon lamp (XBO) equipped with a cut-off filter (365 nm) and a solution filter (0.31 M aqueous $CoSO_4$, 5 cm path length) for 25 min. Afterwards, the solvent was evaporated *in vacuo* at 18 °C. For scale-up purposes, this procedure was repeated five times. Column chromatography of the collected samples (neutral alumina, gradient Hex/EA, 10/1 → EA, evaporation of the solvent at 0 °C) gave 44 mg (44%) of mainly *Z* isomer ***Z*-4a** (80% ***Z*-4a** according to ^{1}H-NMR, see SI Figure 23, *E*-isomer shown in SI Figure 22 for comparison). ^{1}H-NMR (CD_3CN, 400 MHz): δ (ppm) = 7.64 (dd, ^{3}J = 7.6 Hz, ^{4}J = 0.9 Hz, 1H, Ar-*H*), 7.34 (t, ^{4}J = 1.7 Hz, 1H, Ar-*H*), 7.22 (t, ^{3}J = 7.7 Hz, 1H, Ar-*H*), 6,75 (d, ^{4}J = 1.7 Hz, 2H, Ar-*H*), 6.35 (dd, ^{3}J = 7.8 Hz, ^{4}J = 0.9 Hz, 1H, Ar-*H*), 2.87 (m, 2H, pip-*H*), 2.66 (m, 2H, pip-*H*), 2.43 (s, 2H, pip-*H*), 2.33 (s, 3H, C*H*$_3$), 1.83 (m, 2H, pip-*H*), 1.15 (s, 18H, t-Bu-*H*). HPLC (MeOH, 10mM TEAA pH 6.8 = 85/15, Nucleodur, 4 mm i.d.) = 4.25 min (90.0% peak area).

*Azobenzene catalysts **Z**-**4b***. Azobenzene catalysts ***E*-4b** (20 mg, 0.04 mmol) was dissolved in 100 mL of acetonitrile and degassed by bubbling argon through the solution for 10 min. Subsequently, the solution was irradiated at λ_{max} = 365 nm for 60 min (two cut-off filters, $\lambda_{max\ T}$ = 365 nm @ 35% T, FWHM = 42 nm). Afterwards, the solvent was evaporated *in vacuo* at 18 °C to afford ***Z*-4b** (with PSS ***Z*-4b** : ***E*-4b** 86 : 14 according to ^{1}H-NMR, see SI

Figure 25, *E*-isomer shown in SI Figure 24 for comparison). ^{1}H-NMR (CD_3CN, 400 MHz): δ (ppm) = 7.62 (dd, ^{3}J = 7.6 Hz, ^{4}J = 0.9 Hz, 1H, Ar-*H*), 7.33 (t, ^{4}J = 1.7 Hz, 1H, Ar-*H*), 7.21 (t, ^{3}J = 7.7 Hz, 1H, Ar-*H*), 6,75 (d, ^{4}J = 1.7 Hz, 2H, Ar-*H*), 6.35 (dd, ^{3}J = 7.9 Hz, ^{4}J = 0.8 Hz, 1H, Ar-*H*), 3.12 (m, 2H, pip-*H*), 2.55 (m, 4H, pip-*H*), 1.85 (m, 2H, pip-*H*), 1.15 (s, 18H, *t*-Bu-*H*), 1.11 (s, 9H, *N*-*t*-Bu-*H*). ^{13}C-NMR (CD_3CN, 75 MHz): δ (ppm) = 169.2, 153.4, 152.9, 148.9, 147.3, 130.7, 123.4, 122.2, 116.4, 86.4, 54.6, 43.3, 36.4, 35.6, 31.3, 26.4. HPLC (LUNA Phenyl-Hexyl, 3 µm, 2 x 150, gradient 20→75% CH_3CN/H_2O): t_R = 17.03 min (88.5% peak area).

Azobenzene catalysts ***Z*-4c**. Azobenzene catalysts ***E*-4c** (14 mg, 0.03 mmol) was dissolved in 100 mL of acetonitrile and degassed by bubbling argon through the solution for 10 min. Subsequently, the solution was irradiated at λ_{max} = 365 nm for 120 min (two cut-off filters, $\lambda_{max\ T}$ = 365 nm @ 35% T, FWHM = 42 nm). Afterwards, the solvent was evaporated *in vacuo* at 10 °C to afford ***Z*-4c** (with PSS ***Z*-4c** : ***Z*-4c** 91 : 9 according to ^{1}H-NMR, see SI Figure 27, *E*-isomer shown in SI Figure 26 for comparison). ^{1}H-NMR (CD_3CN, 300 MHz): δ (ppm) = 7.64 (d, ^{3}J = 7.6 Hz, 1H, Ar-*H*), 7.30 (t, ^{3}J = 7.8 Hz, 1H, Ar-*H*), 7.10 - 7.00 (m, 6H, Ar-*H*), 6.78 (t, ^{4}J = 1.5 Hz, 1H, Ar-*H*), 6.65 (d, ^{4}J = 1.5 Hz, 2H, Ar-*H*), 6.61 (d, ^{3}J = 7.6 Hz, 1H, Ar-*H*), 3.08 - 3.05 (m, 2H, pip-*H*), 2.59 - 2.5 (m, 4H, pip-*H*), 1.92 (s, 12H, C*H*$_3$), 1.68 (m, 2H, pip-*H*), 1.10 (s, 9H, *t*-Bu-*H*).

Figures

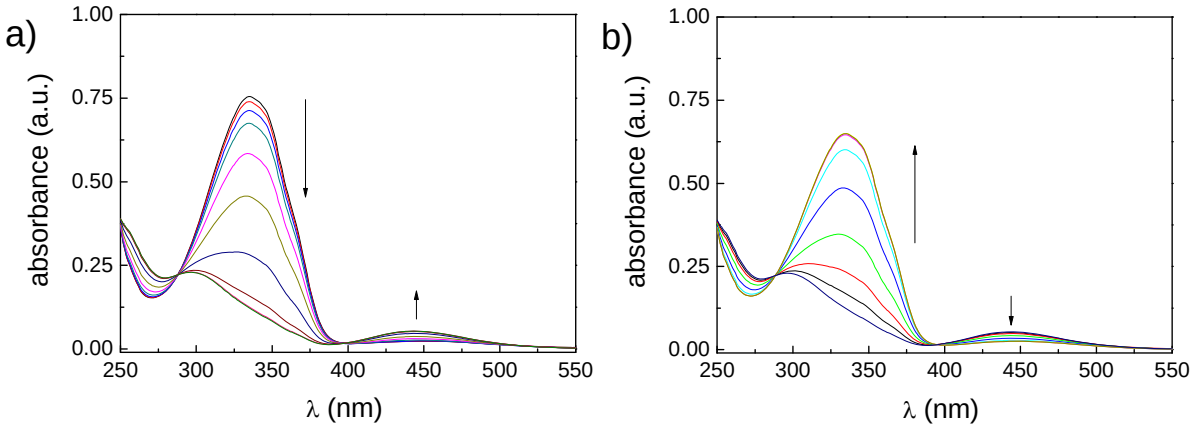


Figure 1. Irradiation of **4a** ($2.8 \cdot 10^{-5}$ M in CH_3CN): a) Isomerization ***E*-4a** → ***Z*-4a** (365 nm interference filter, 12 min 48 s irradiation time); b) Isomerization ***Z*-4a** → ***E*-4a** (400 nm cut-off filter, 4 min 15 s irradiation time).

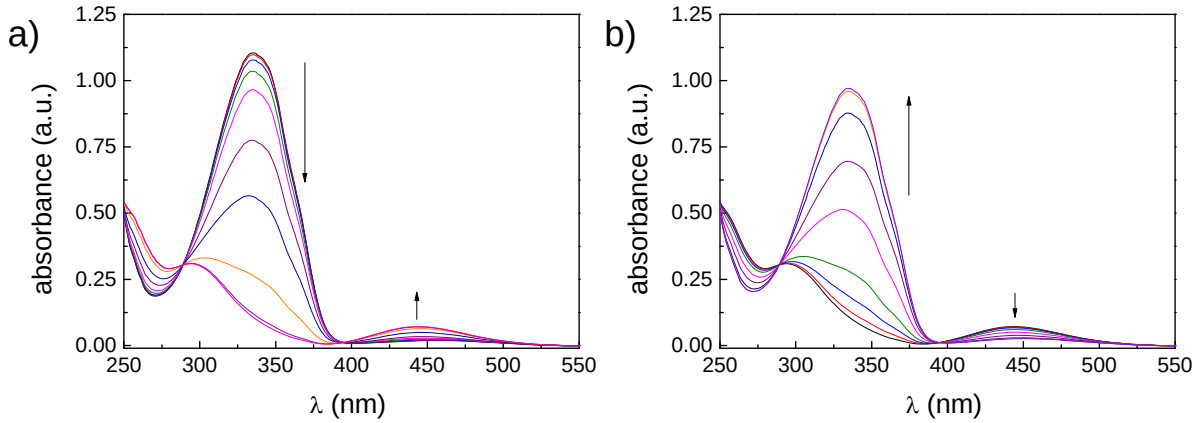


Figure 2. Irradiation of **4b** ($3.1 \cdot 10^{-5}$ M in CH_3CN): a) Isomerization ***E*-4b** → ***Z*-4b**, (λ_{irr}= 365 nm, 12 min 46 s irradiation time); b) Isomerization ***Z*-4b** → ***E*-4b** (λ_{irr} > 400 nm, 6 min 22 s irradiation time).

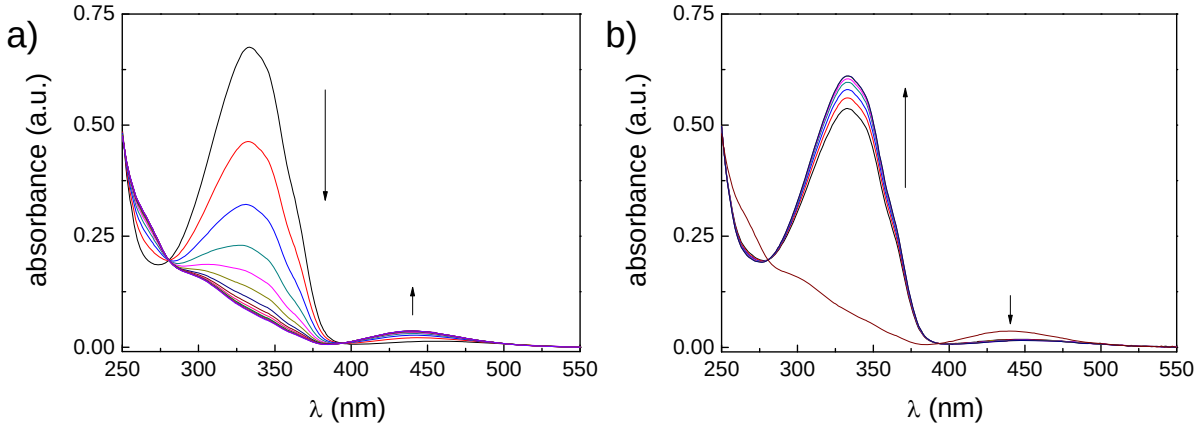


Figure 3. Irradiation of **4c** ($3.0 \cdot 10^{-5}$ M in CH_3CN): a) Isomerization ***E*-4c** → ***Z*-4c**, (λ_{irr}= 365 nm, 14 min irradiation time); b) Isomerization ***Z*-4c** → ***E*-4c** (λ_{irr} > 400 nm, 4 min irradiation time).

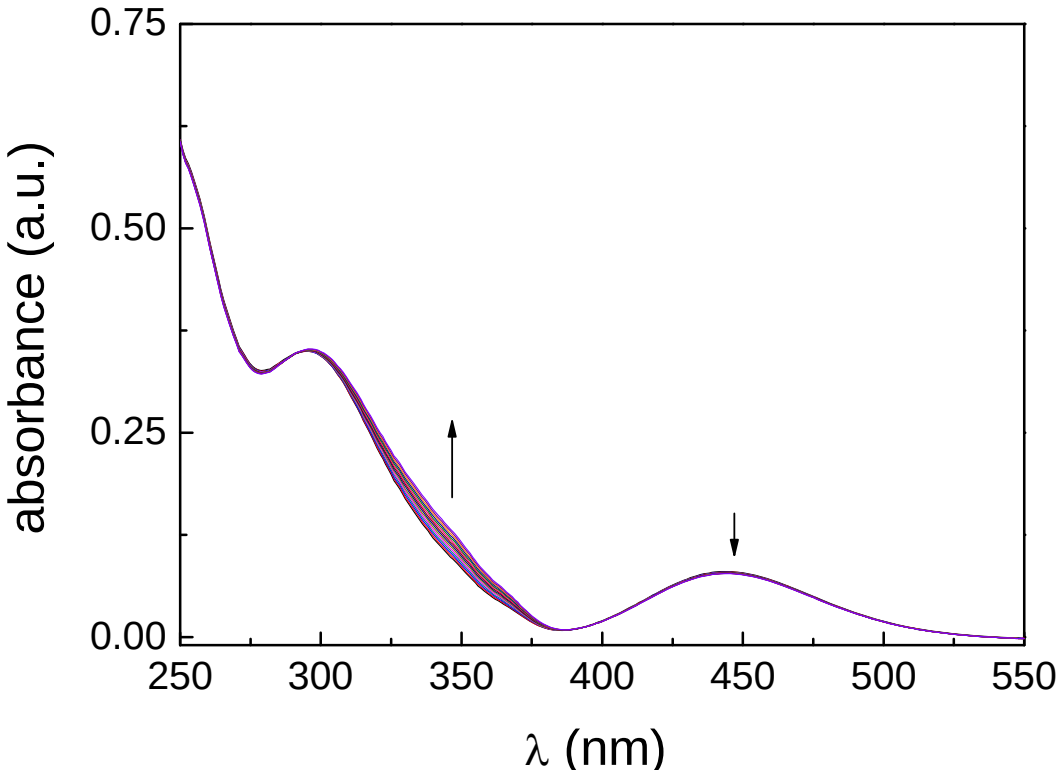


Figure 4. Thermal ***Z*-4a → *Z*-4a** isomerization at 20 °C for 13 h ($4.51 \cdot 10^{-5}$ M in CH_3CN).

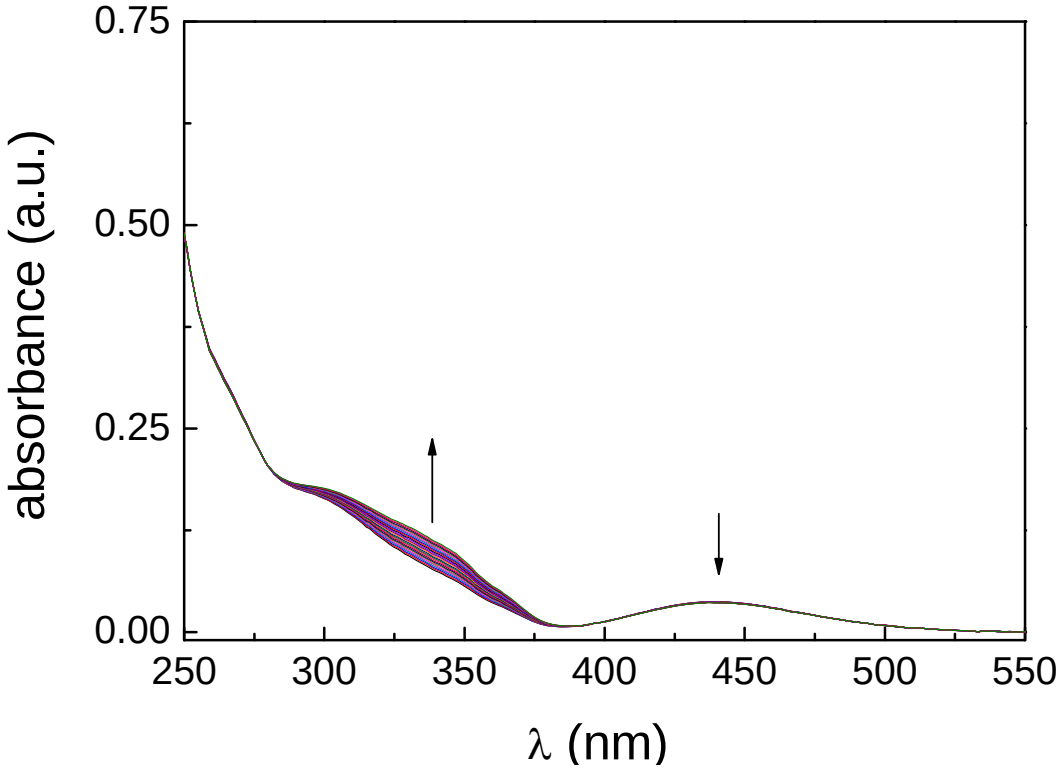


Figure 5. Thermal ***Z*-4b → *E*-4b** isomerization at 20 °C for 14 h ($3.02 \cdot 10^{-5}$ M in CH_3CN).

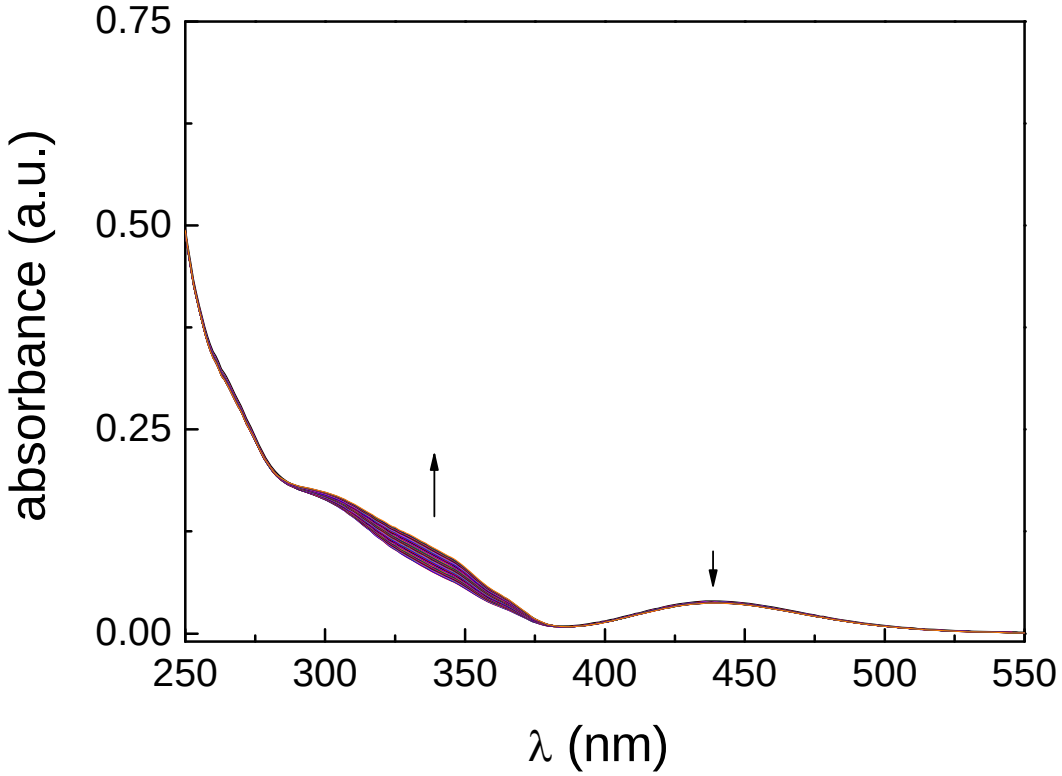


Figure 6. Thermal ***Z*-4c → *E*-4c** isomerization at 20 °C for 40 h ($2.98 \cdot 10^{-5}$ M in CH_3CN).

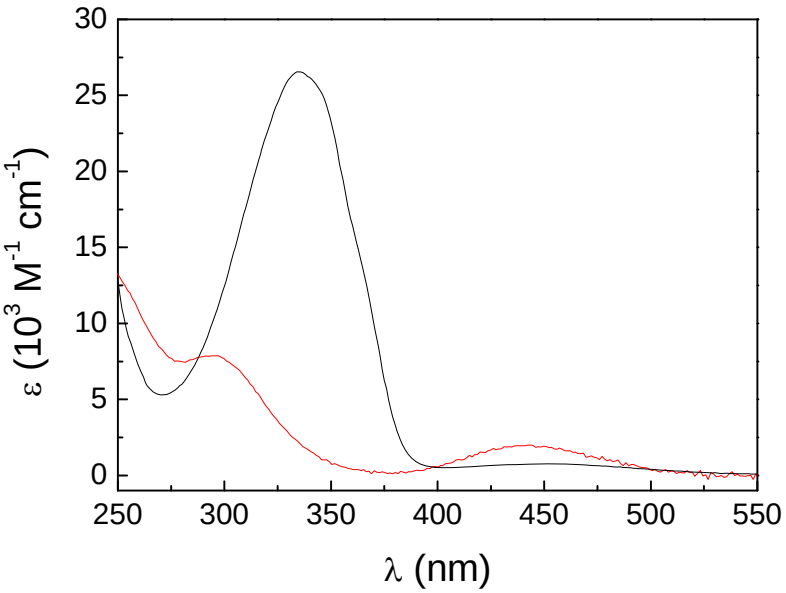


Figure 7. UV/vis-spectra of ***E*-4a** (black, c = $2.8 \cdot 10^{-5}$ M, $\varepsilon_{335\ nm}$ = 26600 $M^{-1}cm^{-1}$) and ***Z*-4a** (red, ε_{296nm} = 7900 $M^{-1}cm^{-1}$) in CH_3CN. The spectrum of ***E*-4a** was acquired using HPLC separation (125 mm Nucleodur, 2.0 mm i.d. in CH_3CN/10 mmol TEAA, pH 6.8, 0 85/15, 0.8 mL/min) coupled to a diode array detector and normalized at the isosbestic point (λ_{iso} = 288 nm).

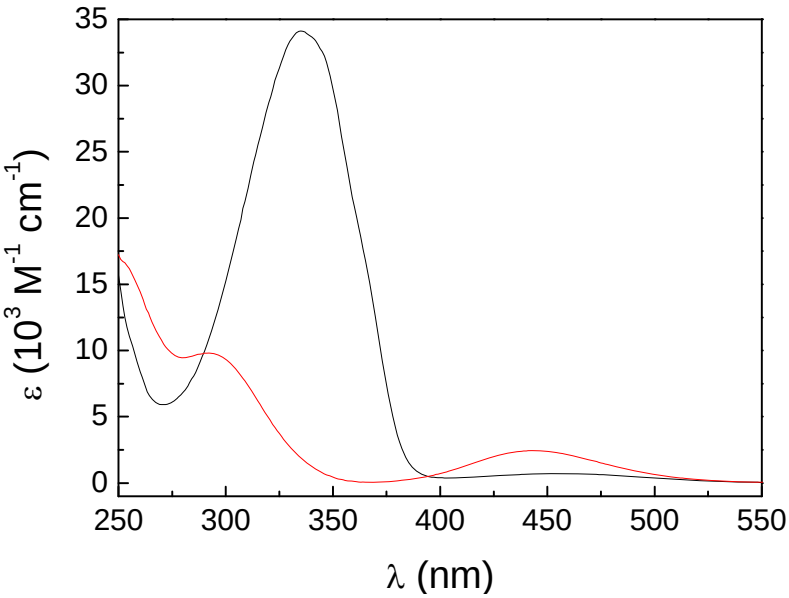


Figure 8. UV/vis-spectra of ***E*-4b** (black, c = $3.1 \cdot 10^{-5}$ M, $\varepsilon_{335\ nm} = 34100\ M^{-1}cm^{-1}$) and ***Z*-4b** (red, $\varepsilon_{292\ nm} = 9800\ M^{-1}cm^{-1}$) in CH_3CN. The spectrum of ***Z*-4b** was calculated from the UV/vis spectra of pure ***E*-4b** and the cis : trans mixture at the photostationary state, for which the cis : trans ratio was determined by HPLC separation.

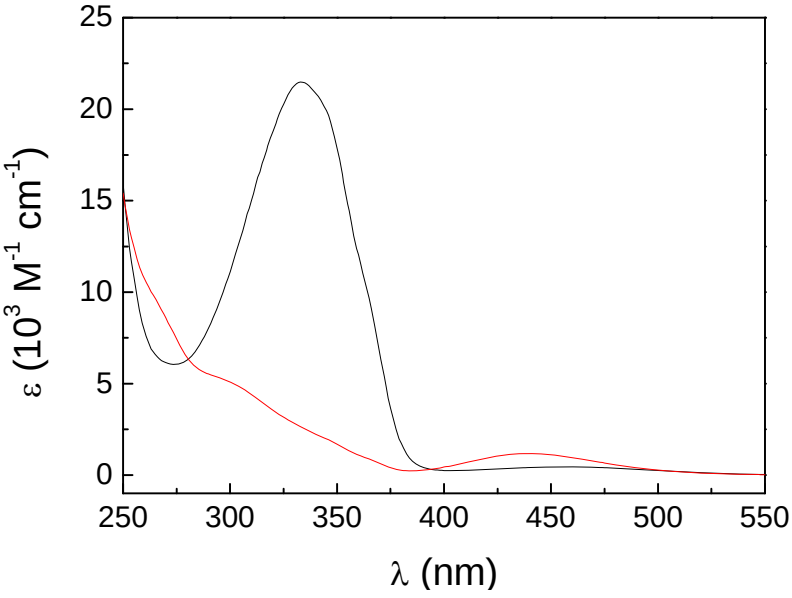


Figure 9. UV/vis-spectra of ***E*-4c** (black, c = $3.0 \cdot 10^{-5}$ M, CH_3CN, $\varepsilon_{333\ nm} = 21484\ M^{-1}cm^{-1}$) and ***Z*-4c** (red, $3.0 \cdot 10^{-5}$ M, CH_3CN, $\varepsilon_{440\ nm} = 1181\ M^{-1}cm^{-1}$) in CH_3CN. Spectra of ***Z*-4c** was obtained after analytical irradiation of a ***E*-4c** leading to quantitative conversion as indicated by UPLC analysis of the irradiated mixture showing no residual *E*-isomer.

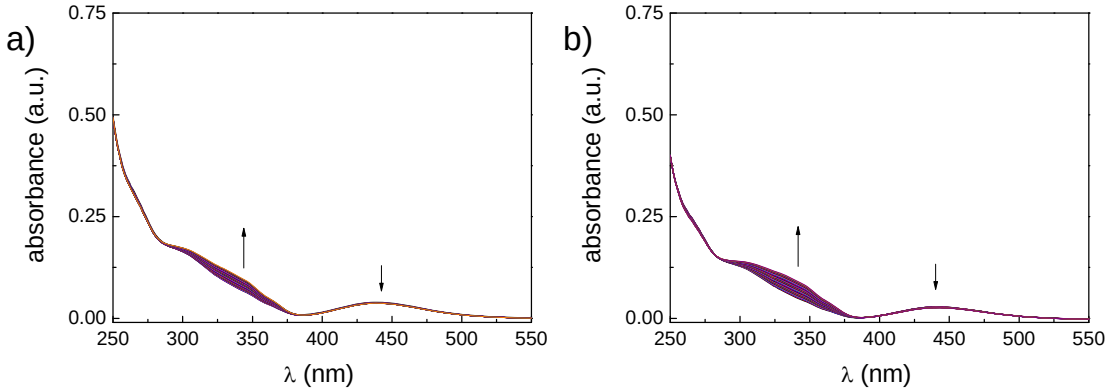


Figure 10. Thermal ***Z*** → ***E*** isomerization of base **4c** and corresponding acid **4c**-H^+ at 20 °C for 40 h: a) **4c** ($2.98 \cdot 10^{-5}$ M in CH_3CN), b) **4c**-H^+ ($2.75 \cdot 10^{-5}$ M in CH_3CN, obtained by addition of 1.2 equiv. of trifluoromethanesulfonic acid to a solution of **4c** in acetonitrile).

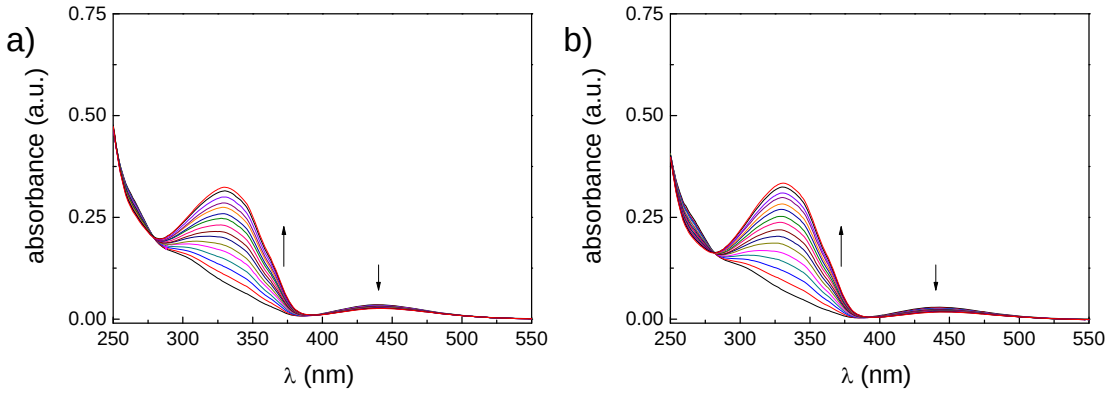


Figure 11. Thermal ***Z*** → ***E*** isomerization base **4c** and corresponding acid **4c**-H^+ at 45 °C for 16 h: a) **4c** ($2.98 \cdot 10^{-5}$ M in CH_3CN), b) **4c**-H^+ ($2.75 \cdot 10^{-5}$ M in CH_3CN, obtained by addition of 1.2 equiv. of trifluoromethanesulfonic acid to a solution of **4c** in acetonitrile).

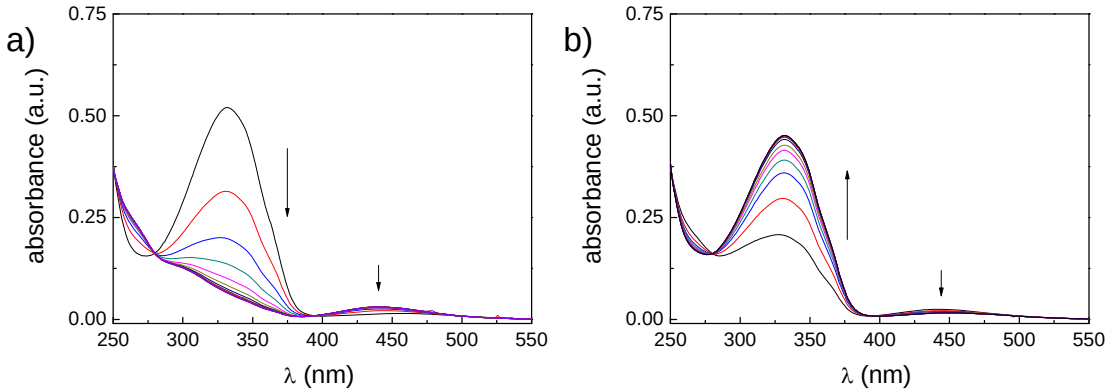


Figure 12. Irradiation of **4c**-H^+ ($2.75 \cdot 10^{-5}$ M in CH_3CN, obtained by addition of 1.2 equiv. of trifluoromethanesulfonic acid to a solution of **4c** in acetonitrile): a) Isomerization ***E*-4c**-H^+ → ***Z*-4c**-H^+, (λ_{irr}= 365 nm, 16 min irradiation time); b) Isomerization ***Z*-4c**-H^+ → ***E*-4**-H^+**c** (λ_{irr} > 400 nm, 4 min irradiation time).

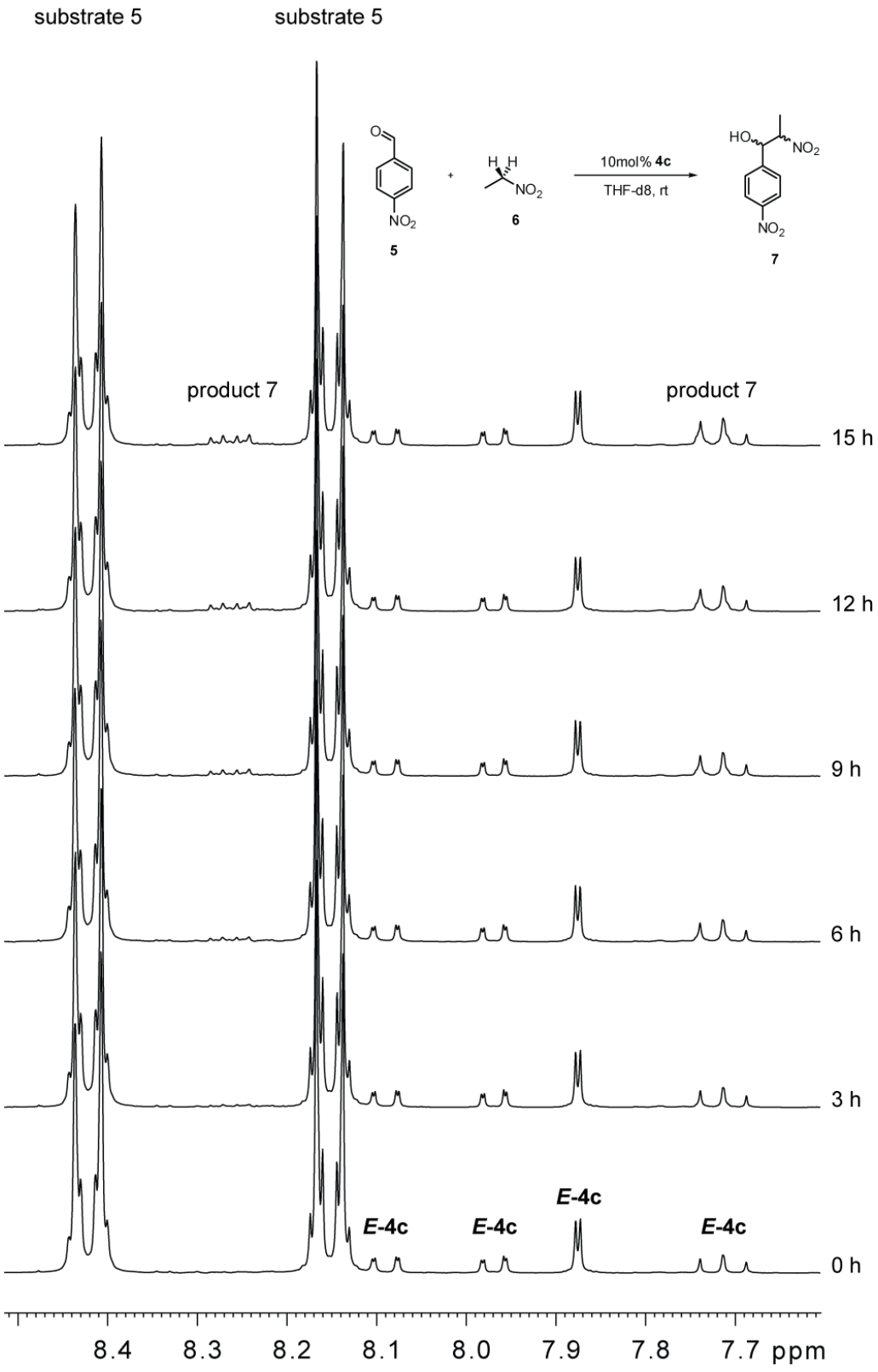


Figure 13. Monitoring of the Henry reaction of 1 equiv. of 4-nitrobenzaldehyde with 12 equiv. of nitroethane in the presence of 10 mol% ***E*-4c** by ^{1}H-NMR spectroscopy.

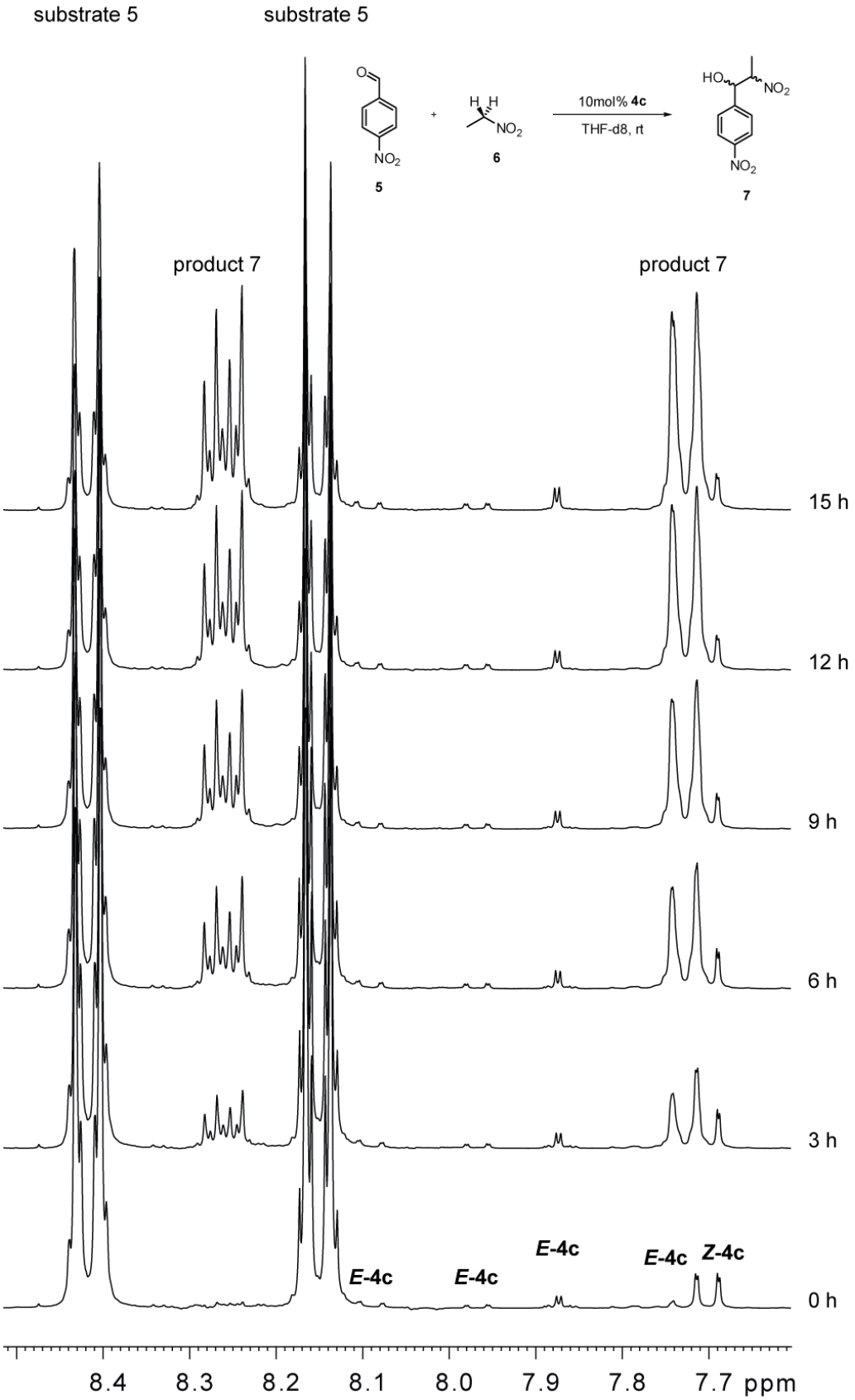
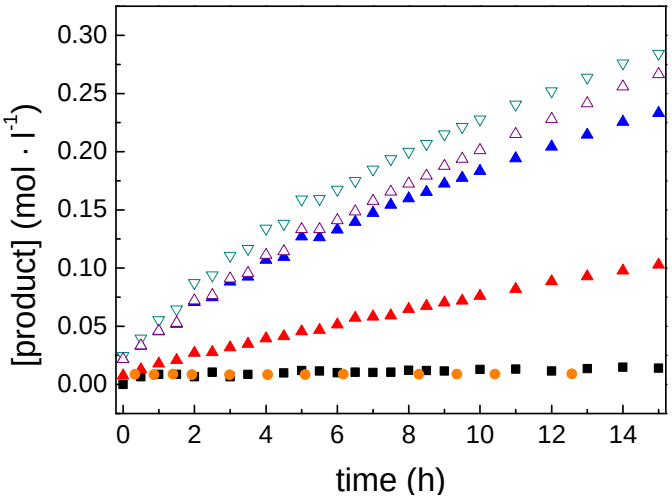
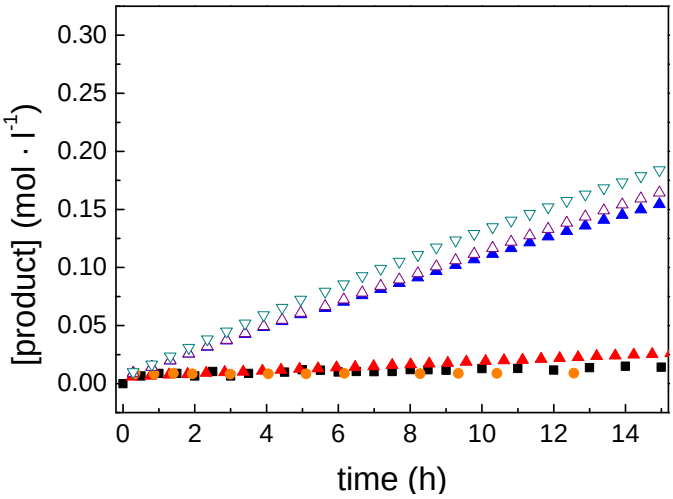


Figure 14. Monitoring of the Henry reaction of 1 equiv. of 4-nitrobenzaldehyde with 12 equiv. of nitroethane in the presence of 10 mol% ***Z*-4c : *E*-4c** (9 : 1) by ^{1}H-NMR spectroscopy.



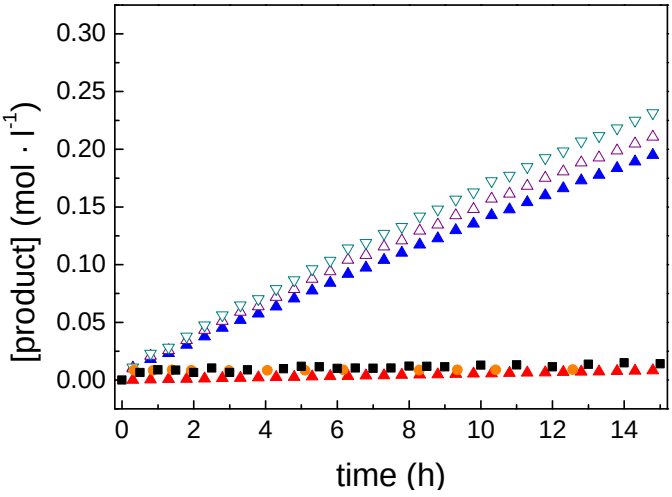
catalyst (10mol%)	k [10^{-5} s^{-1}]	k_{rel}
▽ extrapol. 100% ***Z*-4a**	2.2	4.4
△ thermal corr. PSS	1.8	3.6
▲ PSS ***Z*-4a : *E*-4a = 8 : 2**	1.5	3.0
▲ ***E*-4a**	0.50	1
● *E*-azobenzene	0.0024	0.0048
■ no catalyst	0.039	0.078

Figure 15. Catalytic performance of **4a** in the Henry reaction calculated from product concentrations determined from NMR measurements.



catalyst (10mol%)	k [10^{-5} s^{-1}]	k_{rel}
▽ extrapol. 100% ***Z*-4b**	1.3	13.5
△ thermal corr. PSS	1.0	10.4
▲ PSS ***Z*-4b : *E*-4b = 9 : 1**	0.89	9.3
▲ ***E*-4b**	0.096	1
● *E*-azobenzene	0.0024	0.025
■ no catalyst	0.039	0.41

Figure 16. Catalytic performance of **4b** in the Henry reaction calculated from product concentrations determined from NMR measurements.



catalyst (10mol%)	k [10^{-5} s^{-1}]	k_{rel}
▽ extrapol. 100% ***Z*-4c**	1.4	35.9
△ thermal corr. PSS	1.2	30.8
▲ PSS ***Z*-4c : *E*-4c = 9 : 1**	1.1	28.2
▲ ***E*-4c**	0.039	1
● *E*-azobenzene	0.0024	0.062
■ no catalyst	0.039	1.0

Figure 17. Catalytic performance of **4c** in the Henry reaction calculated from product concentrations determined from NMR measurements (SI Figures 10 and 11).

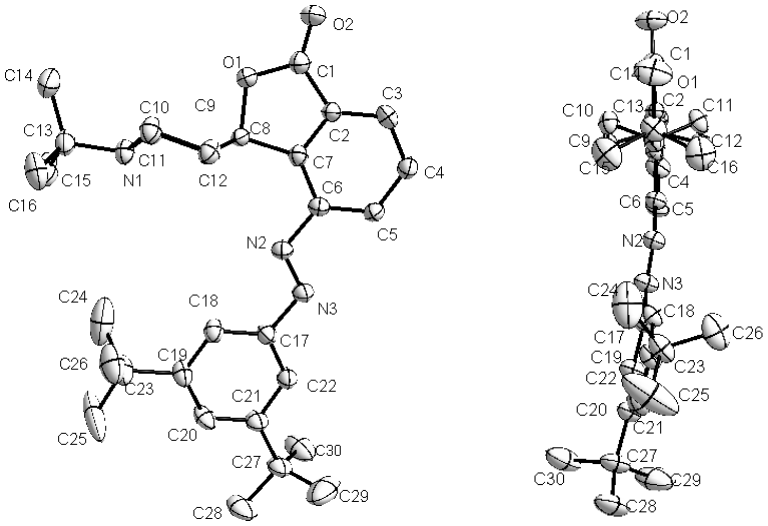


Figure 18. The single crystal X-ray structure analysis of ***E*-4b** showing the relative orientation of the 3,5-di-*tert*-butylphenylazo fragment to the piperidine ring (left) and its slight deviation from co-planarity to the isobenzofuran-1-one ring system (right).

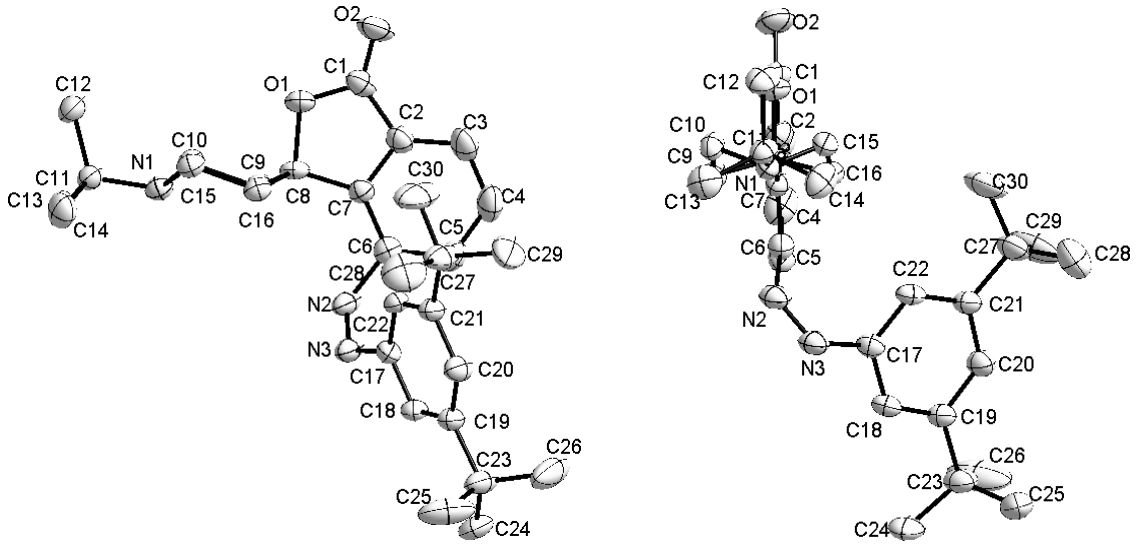


Figure 19. The single crystal X-ray structure analysis of ***Z*-4b** showing the large geometrical change upon isomerization of the azobenzene unit and the resulting open access to the basic/ nucleophilic site

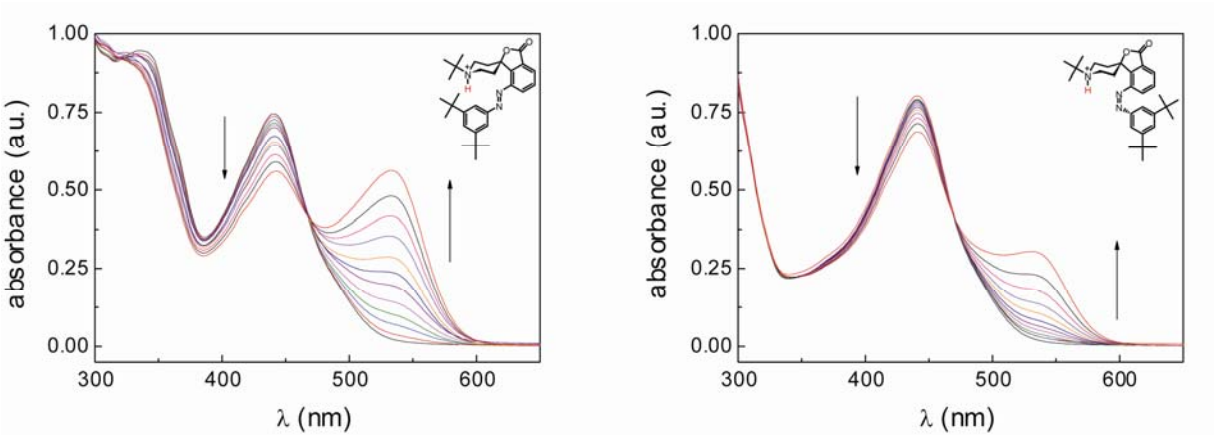


Figure 20. UV/vis titration of a solution of **4b** and neutral red as indicator. The formation of the protonated form (**Ind**-H^+) of neutral red was followed upon addition of overall 1.1 mL (0.1 mL increment) of TfOH ($c = 3.15 \cdot 10^{-6}$ M). a) ***E*-4b** and neutral red (c_0 (***E*-4b**) = c_0 (**Ind**) = $4.1 \cdot 10^{-5}$ M) resulted in a pK_a (***E*-4b**) = 15.9 ± 0.1 and b) ***Z*-4b** and neutral red (c_0 (***Z*-4b**) = c_0 (**Ind**) = $4.2 \cdot 10^{-5}$ M) resulted in pK_a (***Z*-4b**) = 16.7 ± 0.1. ***Z*-4b** was used as mixture stated at the photostationary state (***Z*-4b : *E*-4b** = 9 : 1).

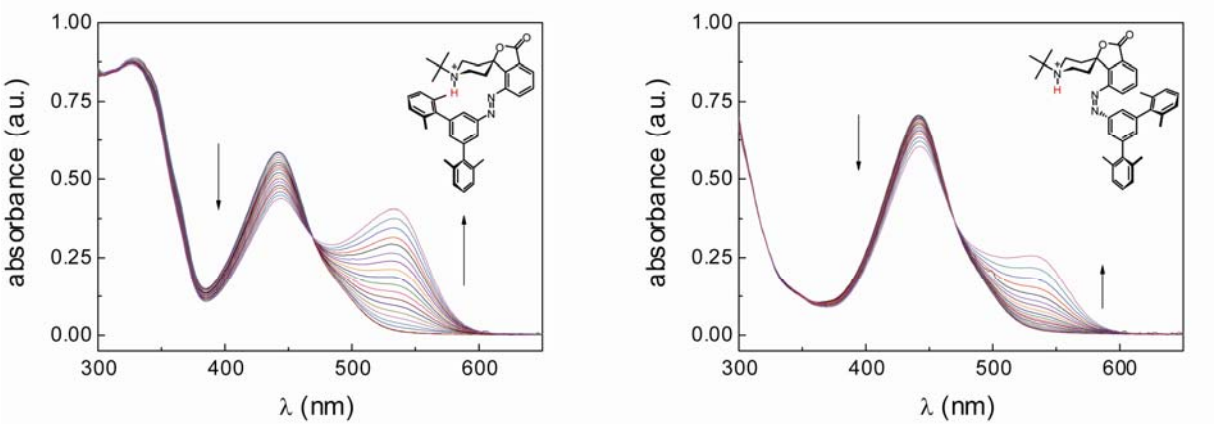


Figure 21. UV/vis titration of a solution of **4c** and neutral red as indicator. The formation of the protonated form (**Ind**-H^+) of neutral red was followed upon addition of overall 180 µL (10 µL increment) of TfOH ($c = 5.86 \cdot 10^{-4}$ M). a) ***E*-4c** and neutral red (c_0 (***E*-4c**) = c_0 (**Ind**) = $3.56 \cdot 10^{-5}$ M) resulted in a pK_a (***E*-4c**) = 16.0 ± 0.1 and b) ***Z*-4c** and neutral red (c_0 (***Z*-4c**) = c_0 (**Ind**) = $4.2 \cdot 10^{-5}$ M) resulted in pK_a (***Z*-4c**) = 16.7 ± 0.1.

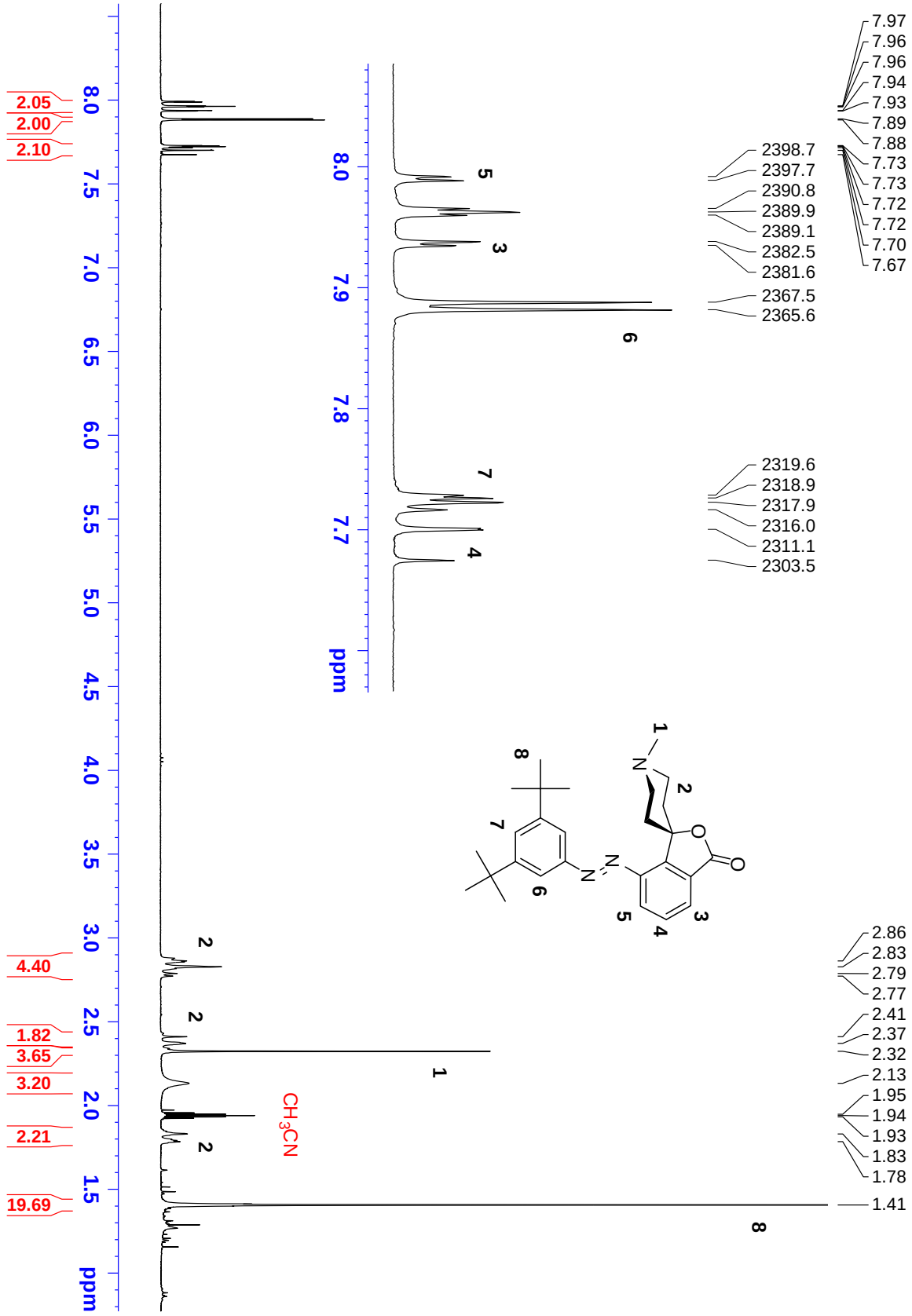


Figure 22. ^{1}H-NMR spectrum of ***E*-4a** (CD_3CN, 25 °C).

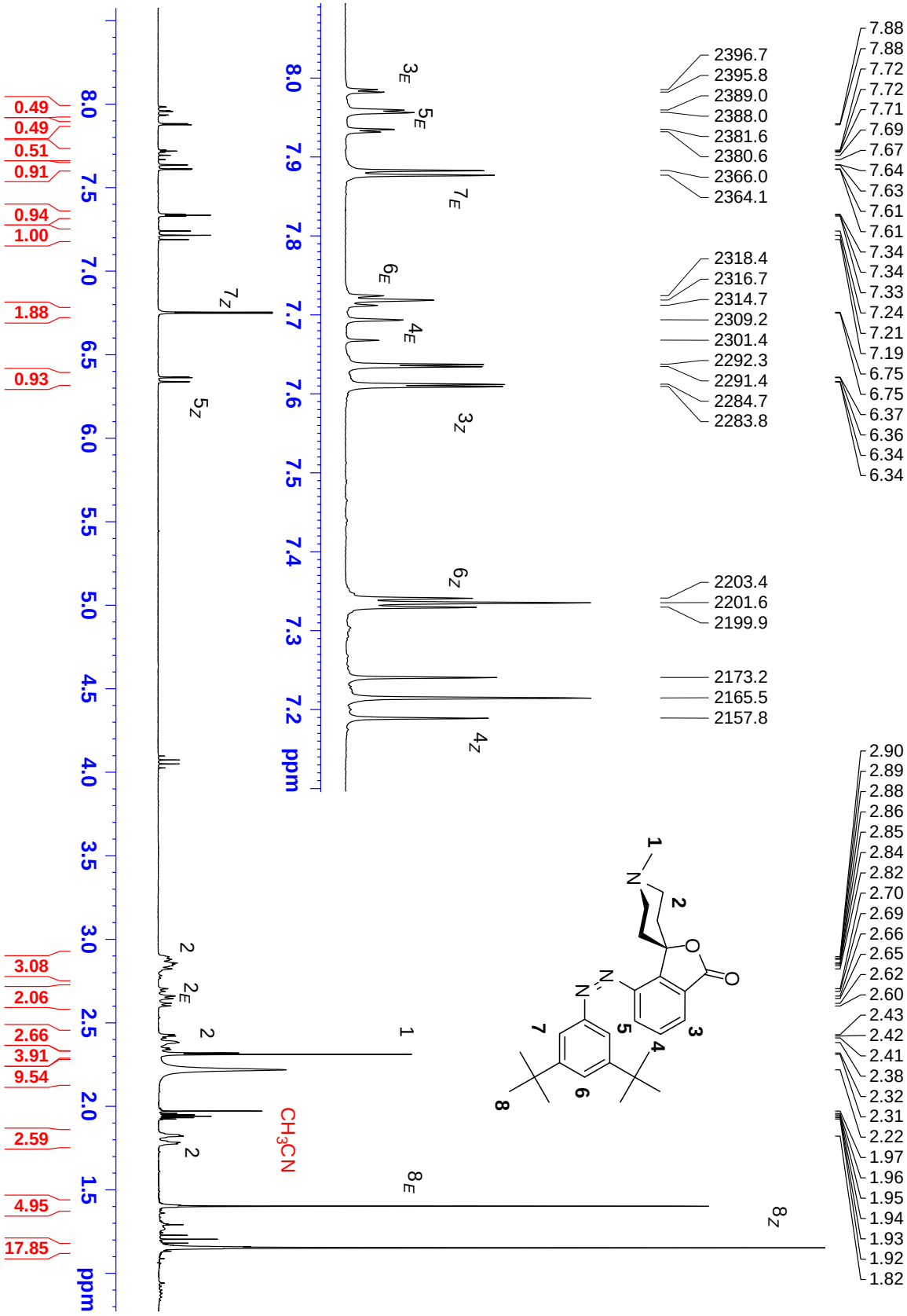


Figure 23. ^{1}H-NMR spectrum of ***Z*-4a** containing residual ~20 % ***E*-4a** (CD_3CN, 25 °C).

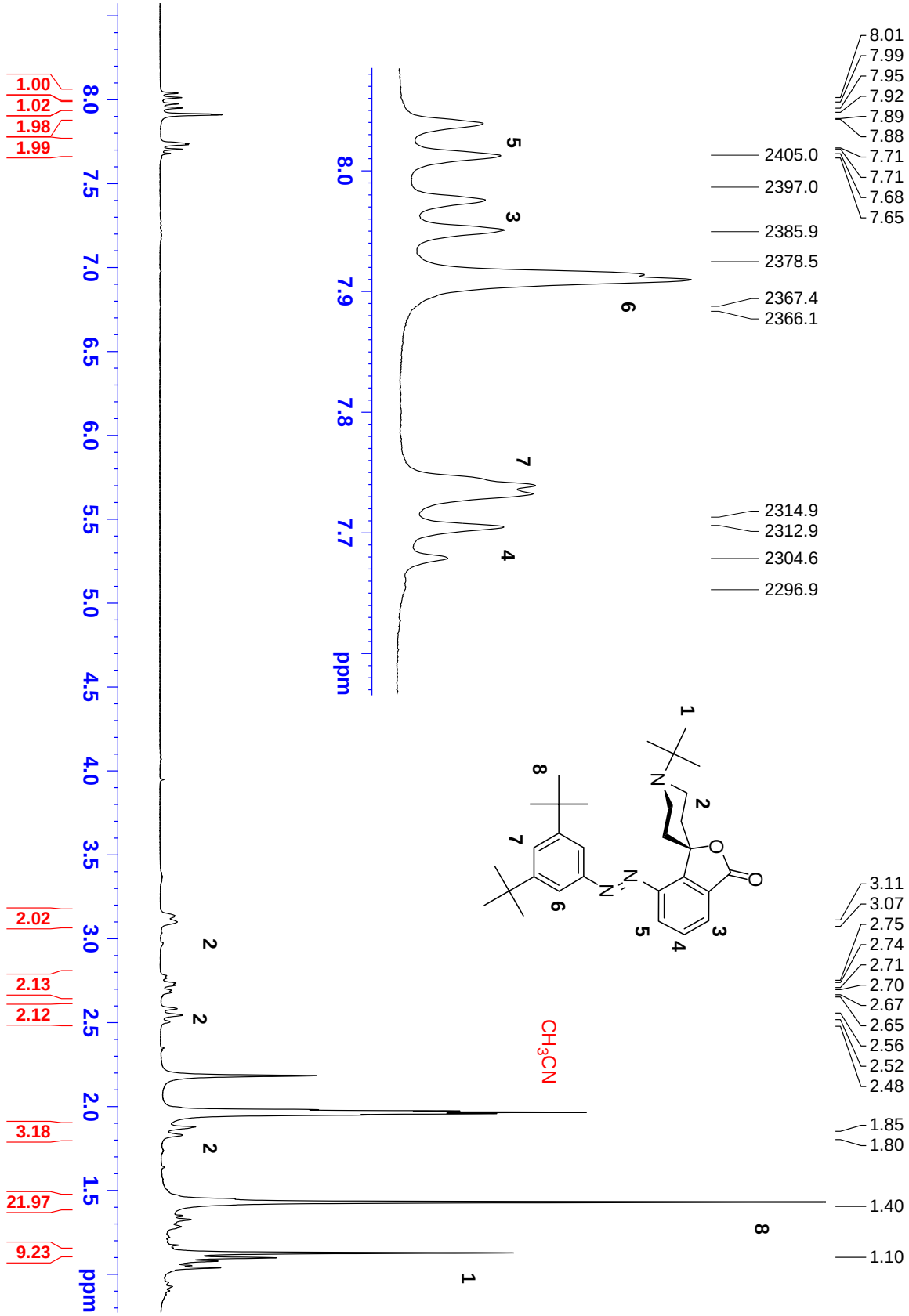


Figure 24. ^{1}H-NMR spectrum of ***E*-4b** (CD_3CN, 25 °C).

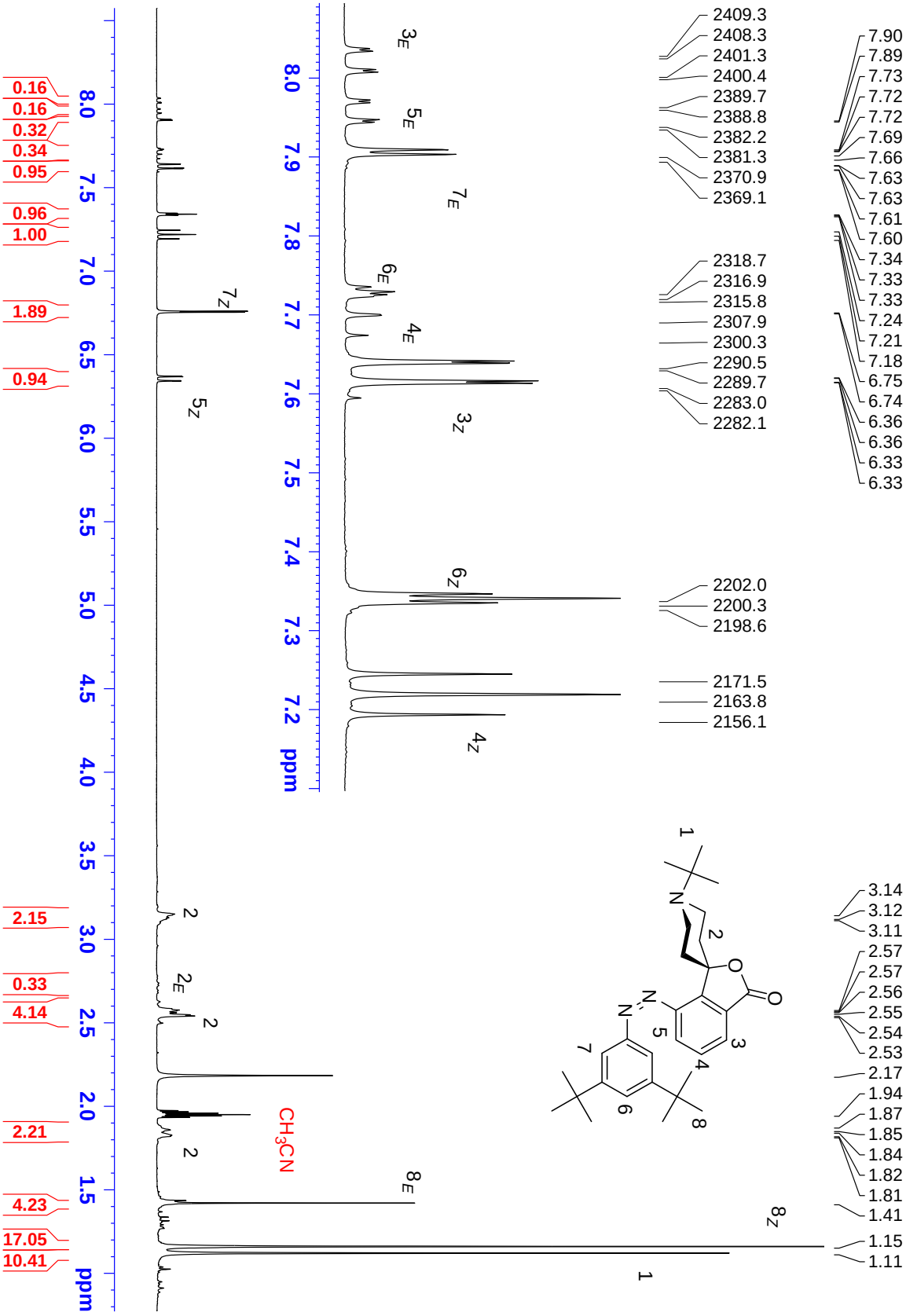


Figure 25. ^{1}H-NMR spectrum of ***Z*-4b** containing residual ~14 % ***E*-4b** (CD_3CN, 25 °C).

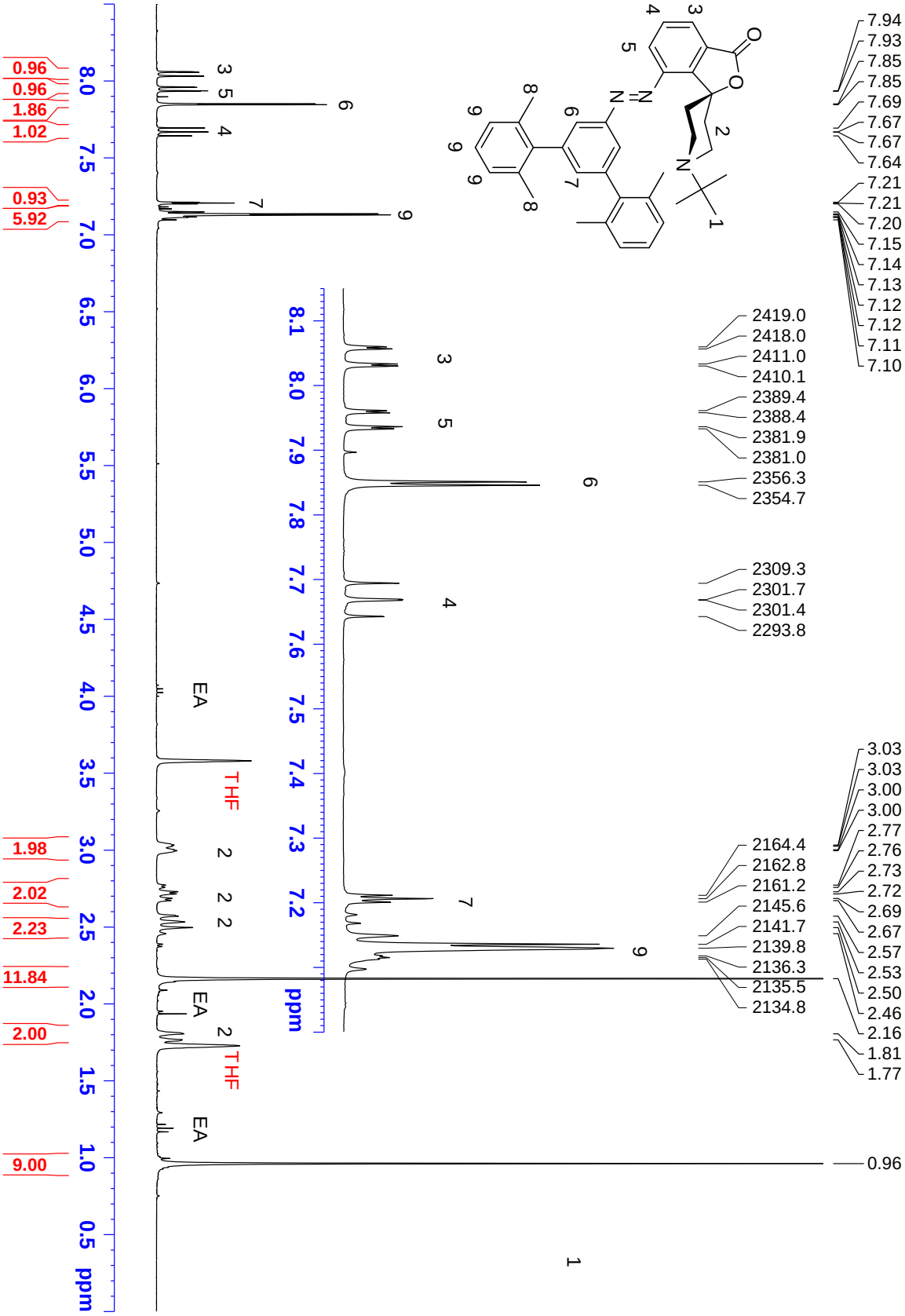


Figure 26. ^{1}H-NMR spectrum of ***E*-4c** (THF-*d8*, 25 °C).

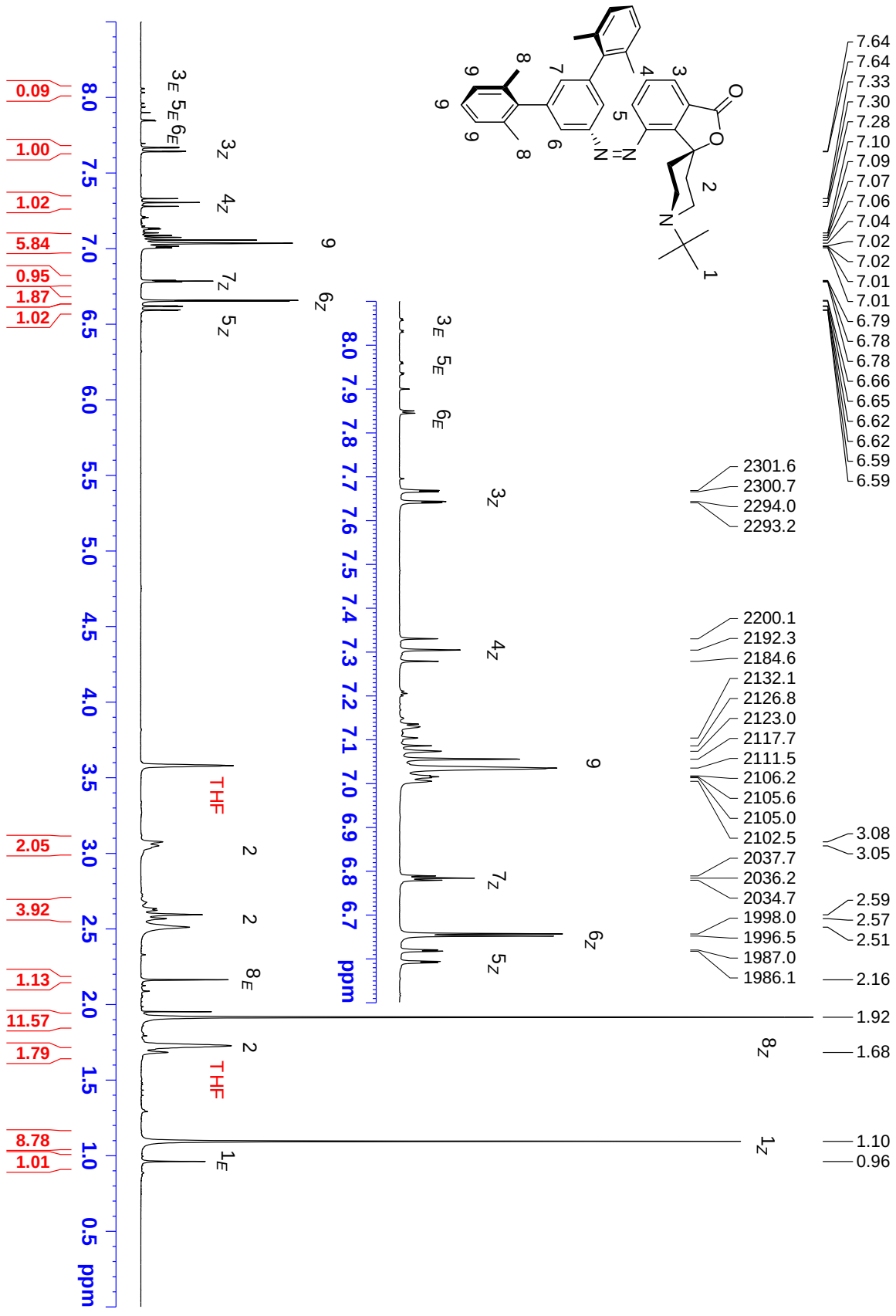


Figure 27. ^{1}H-NMR spectrum of ***Z*-4c** containing residual ~9 % ***E*-4c** (THF-*d8*, 25 °C).