

Supporting Information

for

A Straightforward Modular Approach to NLO-active β -Amino Vinyl Nitrothiophenes

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General Considerations. Reagents and solvents were purchased reagent grade and used without further purification. Toluene and THF were dried and distilled according to standard procedures.¹ The 2-bromo-5-nitrothiophene was prepared according to literature.² – Column chromatography: silica gel 60 (Merck, Darmstadt), mesh 70–230. TLC: silica gel plates (60 F₂₅₄ Merck, Darmstadt). Melting points (uncorrected values): Büchi B-540. – ¹H and ¹³C NMR spectra: Bruker ARX 300, Varian VXR 400S [D₆]DMSO. The assignments of quaternary C, CH, CH₂ and CH₃ has been made by using DEPT spectra. – IR: Perkin Elmer Lambda 3. – UV/vis: Perkin Elmer Models Lambda 16. - Fluorescence spectra: Perkin-Elmer LS 50 B (irradiation at approximately 20 nm less in energy than the longest wave length absorption maximum). - MS: Finnigan MAT 90 and MAT 95 Q. – Elemental analysis were carried out in the Microanalytical Laboratory of the Institut für Organische Chemie, Ludwig-Maximilians-Universität München.

HRS-Measurements of the Hyperpolarizabilities of the Compounds 3a and 3b. The HRS experiments were carried out in chloroform. The HRS cell consisted of a 12 cm long glass tube of 1 cm diameter filled with the solution under investigation. A tunable optical parametric oscillator (OPO)-based HRS apparatus was used for the measurements at 1500 nm.³ To determine the β -values, the external reference method was used. Here, the intensity of the second harmonic $I(2\omega)$ is measured for a dilution series of the chromophore under

investigation and for a reference chromophore with a known hyperpolarizability in the same solvent. Both are plotted as a function of chromophore number density N and, in absence of absorption, the ratio of the two slopes is directly proportional to ratio of the orientational averages of the square of the first hyperpolarizabilities:

$$\frac{\text{slope}_{\text{sample}}}{\text{slope}_{\text{reference}}} = \frac{dI(2\omega)_{\text{sample}}/dN_{\text{sample}}}{dI(2\omega)_{\text{reference}}/dN_{\text{reference}}} = \frac{\langle \beta_{\text{HRS}}^2 \rangle_{\text{sample}}}{\langle \beta_{\text{HRS}}^2 \rangle_{\text{reference}}} \quad (1).$$

Chromophores with a CT along the molecule axis can be assumed to be rodlike, and all β tensor elements except β_{333} can be neglected. In this case the relation between β_{333} and the orientational averages is given by Equation 2:

$$\langle \beta_{\text{HRS}}^2 \rangle = \frac{6}{35} \cdot \beta_{333}^2 \quad (2).$$

As reference chromophore *p*-dimethylamino cinnamic aldehyde ($\beta_{333} = 35 \times 10^{-30}$ esu at 1500 nm in chloroform) was used.⁴ A more detailed description of the HRS experiment and the data evaluation can be found in reference 3.

General Procedure for the Reaction of 2-Ethynyl-5-nitrothiophene (1) and Secondary Amines 2. To a magnetically stirred solution of 1 equivalent of 2-ethynyl-5-nitrothiophene (**1**) in 5 to 10 mL of THF or dichloromethane under nitrogen the amount of amine **2** indicated in Table 1 was added dropwise at room temperature. After the reaction time indicated the reaction mixture was filtered through a short plug of celite and the solvents were evaporated *in vacuo* and the residue dried under high vacuum to give analytically pure **3** as violet microcrystals.

2-[(5-Nitro-thien-2-yl)-vinyl] pyrrolidine (3a). Mp: 115 °C. - ^1H NMR (CDCl_3 , 200 MHz): δ = 1.98 (m_c , 4 H, CH_2), 3.33 (m_c , 4 H, CH_2), 5.22 (d, $^3J_{(\text{H,H})} = 13.4$ Hz, 1 H, CH), 6.44 (d, $^3J_{(\text{H,H})} = 4.6$ Hz, 1 H, CH), 7.29 (d, $^3J_{(\text{H,H})} = 13.4$ Hz, 1 H, CH), 7.70 (d, $^3J_{(\text{H,H})} = 4.6$ Hz, 1 H, CH). - ^{13}C NMR (CDCl_3 , 75 MHz): δ = 25.2 (CH_2), 49.4 (CH_2), 91.2 (CH), 117.4 (CH), 131.8 (CH), 141.1 (2 signals: C_{quat} , CH), 158.3 (C_{quat}). - MS (70 eV) m/z : 224 (M^+), 208, 194, 178, 166, 145, 134, 120, 109, 97, 77, 71, 65, 51, 41. - IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3065 (w), 2968 (w), 2868 (w), 1607 (ss), 1502 (w), 1454 (m), 1425 (s), 1375 (m), 1326 (ss), 1309 (ss), 1266 (s), 1240 (s), 1230 (s), 1207 (s), 1139 (s), 1127 (s), 1097 (ss), 1023 (m), 965 (w), 872 (m), 791 (m), 774 (m), 725 (m), 613 (m). - UV/VIS: λ_{max} (pentane) (ϵ): 267 nm (3760), 450 (14530); λ_{max} (acetonitrile) (ϵ): 209 nm (9880), 279 (5650), 529 (36650). - Anal. Calcd. for $\text{C}_{10}\text{H}_{12}\text{N}_2\text{O}_2\text{S}$ (224.28): N, 12.49; C, 53.55; S, 14.30; H, 5.39. Found: N, 12.27; C, 53.46; S, 14.00; H, 5.43.

2-[(5-Nitro-thien-2-yl)-vinyl] piperidine (3b). Mp: 104 °C. - ^1H NMR (CDCl_3 , 200 MHz): δ = 1.64 (m_c , 6 H, CH_2), 3.22 (m_c , 4 H, CH_2), 5.39 (d, $^3J_{(\text{H,H})} = 13.3$ Hz, 1 H, CH), 6.44 (d, $^3J_{(\text{H,H})} = 4.5$ Hz, 1 H, CH), 6.95 (d, $^3J_{(\text{H,H})} = 13.3$ Hz, 1 H, CH), 7.72 (d, $^3J_{(\text{H,H})} = 4.5$ Hz, 1 H, CH). - ^{13}C NMR (CDCl_3 , 75 MHz): δ = 24.0 (CH_2), 25.4 (CH_2), 49.9 (CH_2), 90.6 (CH), 117.7 (CH), 131.6 (CH), 141.8 (C_{quat}), 144.4 (CH), 157.8 (C_{quat}). - MS (70 eV) m/z : 240, 238 (M^+), 222, 208, 192, 190, 173, 158, 149, 134, 120, 109, 97, 83, 71, 55, 41. - IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3100 (w), 2938 (m), 2851 (w), 1609 (ss), 1474 (m), 1449 (s), 1386 (m), 1347 (s), 1320 (ss), 1269 (ss), 1256 (ss), 1216 (ss), 1200 (ss), 1102 (ss), 1023 (m), 997 (m), 964 (s), 911 (w), 869 (w), 851 (w), 823 (w), 791 (m), 777 (m). - UV/VIS: λ_{max} (pentane) (ϵ): 268 nm (2310), 443 (6120); λ_{max} (acetonitrile) (ϵ): 210 nm (10460), 278 (6860), 523 (32440). - Anal. Calcd. for $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_2\text{S}$ (238.31): N, 11.76; C, 55.44; S, 13.45; H, 5.92. Found: N, 11.70; C, 55.62; S, 13.23; H, 5.97.

1-[(5-Nitro-thien-2-yl)-vinyl] morpholine (3c). Mp: 165 °C. - ^1H NMR (CDCl_3 , 200 MHz): δ = 3.21 (m_c , 4 H, CH_2), 3.72 (m_c , 4 H, CH_2), 5.45 (d, $^3J_{(\text{H,H})} = 13.5$ Hz, 1 H), 6.52 (d, $^3J_{(\text{H,H})} = 4.4$ Hz, 1 H, CH), 6.87 (d, $^3J_{(\text{H,H})} = 13.5$ Hz, 1 H, CH), 7.73 (d, $^3J_{(\text{H,H})} = 4.4$ Hz, 1 H, CH). - ^{13}C NMR (CDCl_3 , 75 MHz): δ = 48.6 (CH_2), 66.1 (CH_2), 92.3 (CH), 118.7 (CH), 131.0 (CH), 143.5 (2 signals: C_{quat} , CH), 155.6 (C_{quat}). - MS (70 eV) m/z : 240 (M^+), 224, 210, 194, 182, 160, 155, 136, 131, 109, 92, 79, 71, 65, 42. - IR (KBr): $\tilde{\nu}$ [cm^{-1}] = 3084 (w), 2966 (w), 2920 (w), 2861 (w), 1616 (ss), 1435 (s), 1384 (m), 1343 (ss), 1319 (ss), 1263 (ss), 1227 (ss), 1138 (s), 1105 (s), 1066 (m), 1005 (m), 948 (m), 863 (m), 796 (m), 726 (m), 614 (m). - UV/VIS: λ_{max} (pentane): 265 nm, 443; λ_{max} (acetonitrile) (ϵ): 210 nm (10460), 278 (6860), 523 (32440).

- Anal. Calcd. for C₁₀H₁₂N₂O₃S (240.28): N, 11.66; C, 49.99; S, 13.34; H, 5.03. Found: N, 11.60; C, 49.81; S, 13.52; H, 5.04.

Diisopropyl-2-[(5-nitro-thien-2-yl)-vinyl] amine (3d). Violet resin. - ¹H NMR (CDCl₃, 200 MHz): δ = 1.24 (d, ³J_(H,H) = 6.6 Hz, 12 H, CH₃), 3.73 (septet, ³J_(H,H) = 6.6 Hz, 2 H, CH), 5.44 (d, ³J_(H,H) = 13.4 Hz, 1 H, CH), 6.41 (d, ³J_(H,H) = 4.4 Hz, 1 H, CH), 7.14 (d, ³J_(H,H) = 13.4 Hz, 1 H, CH), 7.72 (d, ³J_(H,H) = 4.4 Hz, 1 H, CH). - ¹³C NMR (CDCl₃, 75 MHz): δ = 21.8 (CH₃), 48.0 (CH), 90.3 (CH), 117.1 (CH), 131.9 (CH), 139.4 (CH), 140.8 (C_{quat.}), 159.2 (C_{quat.}). - MS (70 eV) m/z (%): 254 (M⁺), 239 (45), 211 (33), 197 (44), 150 (10), 86 (10), 44 (13). - HRMS Calcd for C₁₂H₁₈N₂O₂S (254.35): 254.1089. Found: 254.1096.

(R)-(+)-2-Methoxymethyl-1-[2-(5-Nitro-thien-2-yl)-vinyl] pyrrolidine (3e). Violet resin. - ¹H NMR (CDCl₃, 200 MHz): δ = 1.6-1.8 (m, 1 H, CH), 2.02 (m_c, 3 H, CH₃), 3.3-3.4 (m, 7 H), 3.80 (m_c, 1 H, CH), 5.28 (d, ³J_(H,H) = 13.4 Hz, 1 H, CH), 6.46 (d, ³J_(H,H) = 4.4 Hz, 1 H, CH), 7.43 (d, ³J_(H,H) = 13.4 Hz 1 H, CH), 7.72 (d, ³J_(H,H) = 4.4 Hz, 1 H, CH). - ¹³C NMR (CDCl₃, 75 MHz): δ = 23.5 (CH₂), 28.2 (CH₂), 42.3 (CH₂), 59.3 (CH₃), 61.2 (CH), 75.2 (CH₂), 117.5 (CH), 131.7 (CH), 141.1 (2 signals: C_{quat.}, CH), 158.0 (C_{quat.}). - MS (70 eV) m/z (%): 268 (M⁺, 22), 236 (15), 223 (100), 191 (19), 176 (26), 175 (10). - IR (KBr): $\tilde{\nu}$ [cm⁻¹] = 3094 (m), 2925 (s), 2876 (ss), 1614 (ss), 1513 (m), 1434 (br), 1373 (s), 1257 (br), 1127 (br), 1031 (ss), 934 (s), 801 (s), 731 (s), 628 (w), 479 (m). - UV/VIS: λ_{\max} (pentane): 268 nm, 451; λ_{\max} (acetonitrile) (ε): 211 nm (8750), 279 (6030), 523 (33220). - Anal. Calcd. for C₁₂H₁₆N₂O₃S (268.34): C, 53.71; H, 6.01; N, 10.44; S, 11.95. Found: C, 53.92; H, 6.01; N, 10.29; S, 12.36.

(S)-(+)-1-[2-(5-Nitro-thien-2-yl)-vinyl] pyrrolidine 2-carbacid benzyl ester (3f). Violet oil. - ¹H NMR (CDCl₃, 300 MHz): δ = 1.9-2.3 (m, 4 H, CH₂), 3.2-3.6 (m, 2 H, CH₂), 4.20 (dd, ³J_(H,H) = 8.6 Hz, ³J_(H,H) = 8.1 Hz, 1 H, CH), 5.19 (s, 2 H, CH₂), 5.26 (d, ³J_(H,H) = 13.5 Hz, 1 H, CH), 6.43 (d, ³J_(H,H) = 4.5 Hz, 1 H, CH), 7.16 (d, ³J_(H,H) = 13.5 Hz, 1 H, CH), 7.35 (s, 5 H, CH), 7.71 (d, ³J_(H,H) = 4.5 Hz, 1 H, CH). - ¹³C NMR (CDCl₃, 75 MHz): δ = 23.8 (CH₂), 29.7 (CH₂), 30.1 (CH₂), 62.5 (CH), 67.3 (CH), 93.1 (CH), 118.4 (CH), 128.3 (CH), 128.7 (CH), 128.8 (CH), 131.2 (CH), 135.3 (C_{quat.}), 139.5 (2 signals: C_{quat.}, CH), 156.1 (C_{quat.}), 171.9 (C_{quat.}). - MS (70 eV) m/z (%): 358 (M⁺, 47), 224 (12), 223 (100), 176 (16), 91 (13). - HRMS Calcd. for C₁₈H₁₈N₂O₄S (358.42): 358.0987. Found: 358.0984.

1,4-Bis-2-[(5-nitro-thien-2-yl)-vinyl] piperazine (4). Mp: >200 °C (dec.). - ¹H NMR (D₆-DMSO, 600 MHz): δ = 3.26 (m_c, 8 H, CH₂), 5.60 (d, ³J_(H,H) = 13.2 Hz, 1 H, CH), 5.68 (d, ³J_(H,H) = 13.2 Hz, 1 H, CH), 6.63 (d, ³J_(H,H) = 4.2 Hz, 1 H, CH), 6.67 (d, ³J_(H,H) = 4.2 Hz, 1 H, CH), 7.38 (d, ³J_(H,H) = 13.2 Hz, 1 H, CH), 7.43 (d, ³J_(H,H) = 13.2 Hz, 1 H, CH), 7.74 (d, ³J_(H,H) = 4.2 Hz, 1 H, CH), 7.77 (d, ³J_(H,H) = 4.2 Hz, 1 H, CH). - ¹³C NMR (D₆-DMSO, 150 MHz): δ = 45.9 (CH₂), 92.3 (CH), 119.1 (CH), 133.5 (CH), 141.0 (C_{quat.}), 147.3 (CH), 159.6 (C_{quat.}). - MS (70 eV) m/z: 392 (M⁺), 376, 250, 239, 209, 171, 168, 136, 122, 112, 96, 80, 57, 56. - IR (KBr): $\tilde{\nu}$ [cm⁻¹] = 3084 (w), 2966 (w), 2920 (w), 2861 (w), 1616 (ss), 1435 (s), 1384 (m), 1343 (ss), 1319 (ss), 1263 (ss), 1227 (ss), 1138 (s), 1105 (s), 1066 (m), 1005 (m), 948 (m), 863 (m), 796 (m), 726 (m), 614 (m). - UV/VIS: λ_{max} (pentane): 272 nm, 439; λ_{max} (acetonitrile) (ε): 215 nm (5260), 279 (6050), 522 (36300). - Anal. Calcd. for C₁₆H₁₆N₄O₄S₂ (392.46): N, 14.28; C, 48.97; S, 16.34; H, 4.11. Found: N, 13.99; C, 48.92; S, 15.92; H, 4.42.

***N,N*-Diethyl-[2-(5-nitro-thien-2-yl)-1-phenyl]-vinyl amine (7).** To a degassed suspension of 208 mg (1.00 mmol) 2-bromo-5-nitrothiophene, 21.0 mg (0.03 mmol) of bis(triphenylphosphane) palladium(II) dichloride, and 2.0 mg (0.01 mmol) of copper (I) iodide in a mixture of 20 mL of THF and 10 mL of diethylamine were added dropwise a solution of 132 mg (1.30 mmol) of phenylacetylene in 1 mL of THF. Then the reaction mixture was heated to reflux temperature for 9 h. After cooling to room temperature 50 mL of diethylether were added and the suspension was filtered over a short pad of celite. The solvents of the filtrate were evaporated in vacuo at 35 °C and the resulting black oily residue was flash chromatographed on silica gel (ethyl acetate/hexanes 1 : 10) to give 131 mg (43 %; R_f = 0.25) of **7** as a violet microcrystalline solid. - ¹H NMR (CDCl₃, 300 MHz): δ = 1.15 (t, ³J_(H,H) = 7.2 Hz, 6 H, CH₃), 3.21 (d, ³J_(H,H) = 7.2 Hz, 4 H, CH₂), 5.64 (s, 1 H, CH), 6.20 (dd, ³J_(H,H) = 4.5 Hz, ⁴J_(H,H) = 0.3 Hz, 1 H, CH), 7.24 (m_c, 2 H), 7.55 (m_c, 3 H, CH). - ¹³C NMR (CDCl₃, 75 MHz): δ = 13.3 (CH₃), 44.1 (CH₂), 93.1 (CH), 120.8 (CH), 129.0 (CH), 130.0 (CH), 130.3 (2 signals, CH), 134.6 (C_{quat.}), 143.1 (C_{quat.}), 154.5 (C_{quat.}), 156.9 (C_{quat.}). - MS (70 eV) m/z (%): 302 (M⁺, 100), 273 (12), 256 (26), 240 (22), 237 (12), 212 (10), 185 (11), 184 (26), 152 (12), 132 (15), 105 (12), 104 (38), 77 (10). - HRMS Calcd. for C₁₆H₁₈N₂O₂S (302.40): 302.1089. Found: 302.1095.

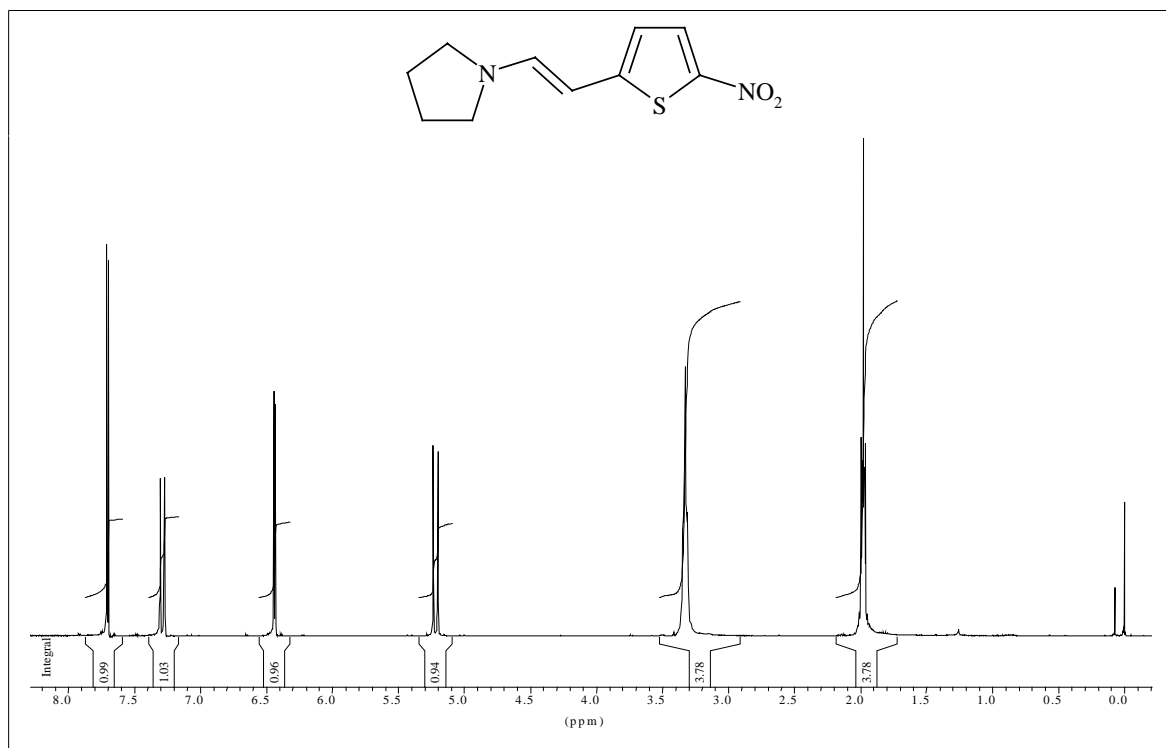
Table 1. Experimental details on the vinyl aminations of **1**.

Entry	1 mg, (mmol)	Amine 2 g, (mmol)	Solvent	Reaction time	3, 4 Yield mg, (%)
1	200, (1.3)	1.7 (24) of pyrrolidine (2a)	5 mL of THF	5 min	290 (99) of 3a
2	200, (1.3)	1.7 (20) of piperidine (2b)	10 mL of THF	30 min	290 (93) of 3b
3	200, (1.3)	0.6, (6.9) of morpholine (2c)	5 mL of THF	15 min	300 (96) of 3c
4	200, (1.3)	2.2 (21) of diisopropyl amine (2d)	5 mL of THF	15 h	280 (85) of 3d ^c
5	153, (1.0)	0.13 (1.1) of (<i>R</i>)-(+)-2-methoxymethyl pyrrolidine (2e)	3 mL of THF	1 h ^[45]	235 (82) of 3e
6	122, (0.8)	0.24 (1.0) of (<i>S</i>)-proline benzyl ester ^a (2f)	10 mL of CH ₂ Cl ₂	15 h	278 (97) of 3f ^d
7	153, (1.0)	0.04, (0.5) of piperazine ^b	10 mL of THF	16 h	160 (43) of 4

^aThe free base of the proline benzyl ester is generated by washing of a dichloromethane solution of the corresponding hydrochloride with a saturated solution of sodium bicarbonate. ^b1.5 mL of *Hünig's base* were added as auxiliary base. ^cChromatography on silica gel (hexanes/ethyl acetate 10:1).

^dChromatography on silica gel (hexanes/ethyl acetate 2:1).

Scheme 1. ^1H NMR-spectrum (CDCl_3 , 300 MHz, 20 °C) of **3a**.



Scheme 2. NOESY spectrum (CDCl_3 , 400 MHz, 25 °C) of **3a**.

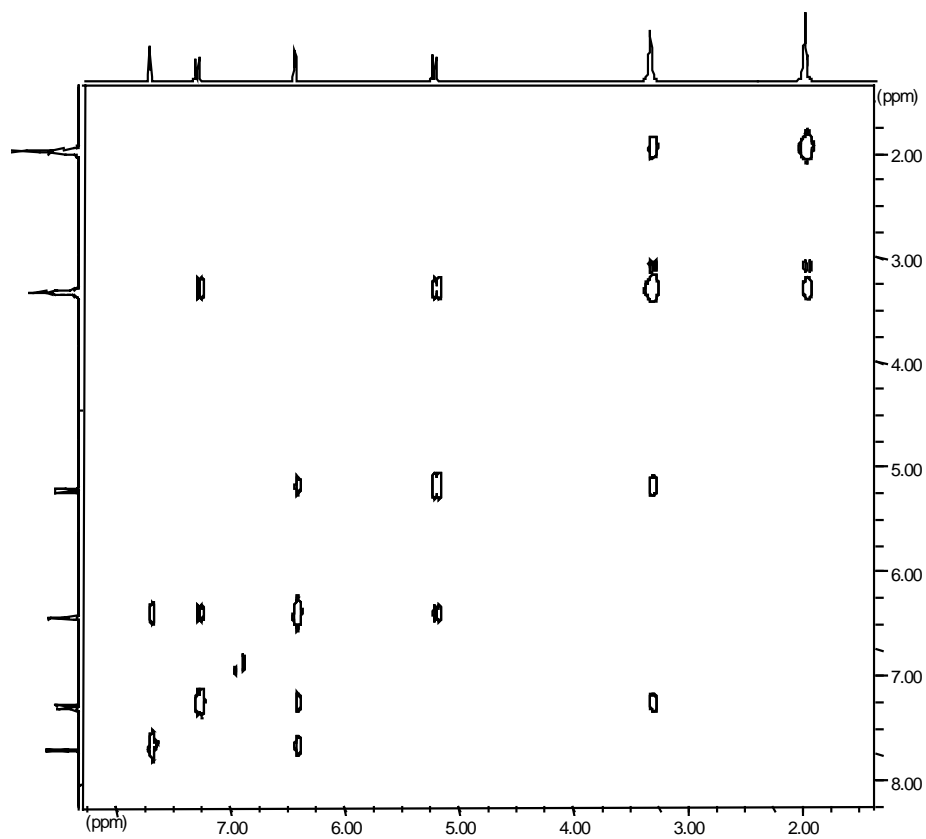
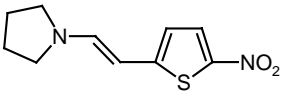
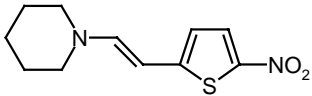
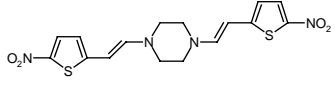
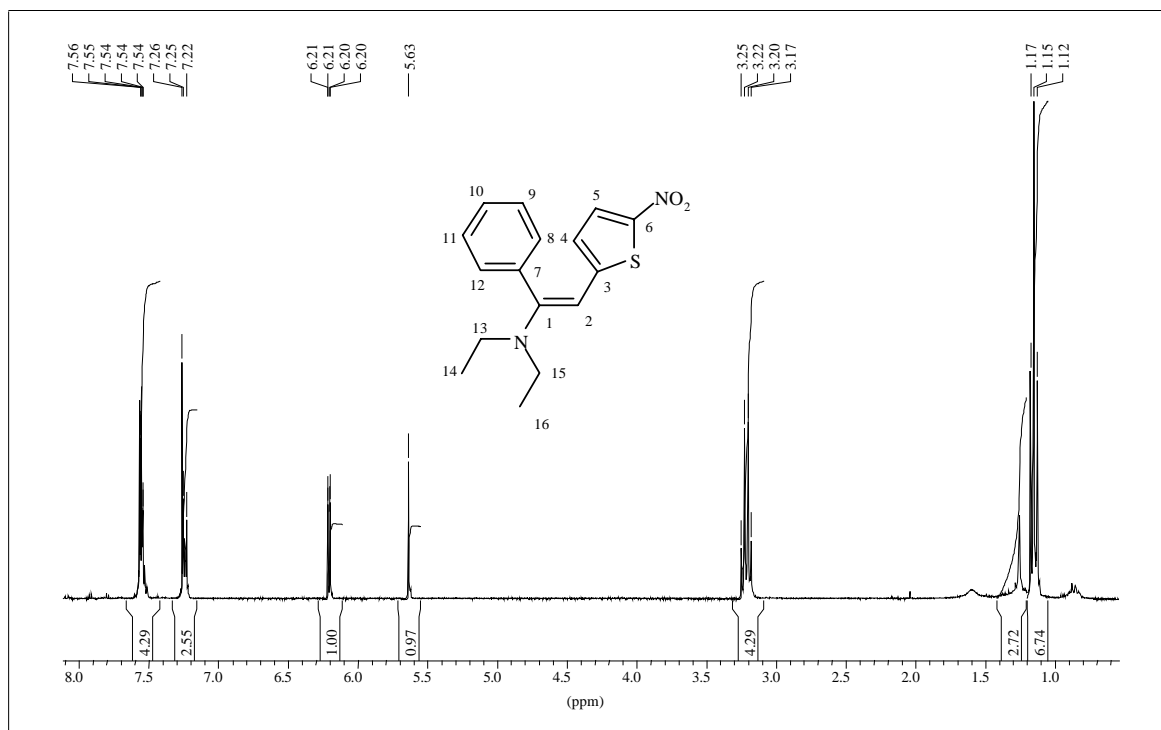


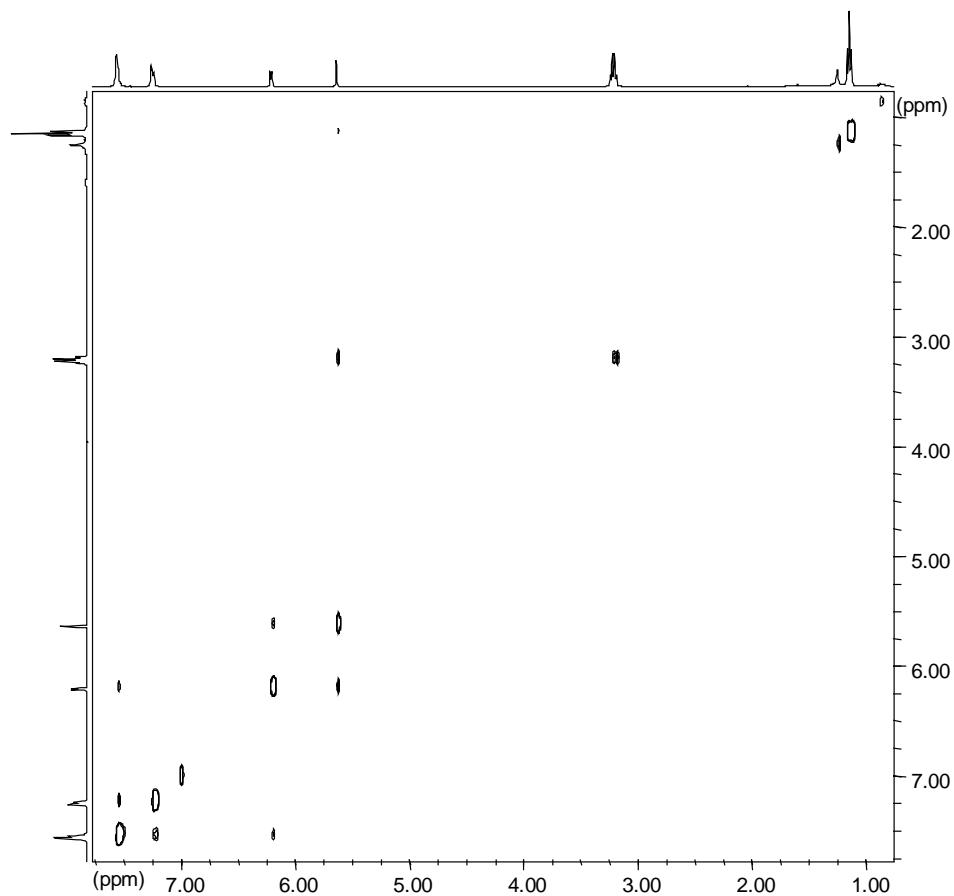
Table 2. Absorptions λ_{\max} ($\tilde{\nu}_{\max}$) and solvochromicities of the β -amino vinyl nitrothiophenes **3a**, **3b**, and **4**.

			
	3a	3b	4
pentane	450 nm (22200 cm ⁻¹)	443 nm (22600 cm ⁻¹)	439 nm (22800 cm ⁻¹)
diethylether	484 nm (20700 cm ⁻¹)	472 nm (21200 cm ⁻¹)	470 nm (21300 cm ⁻¹)
THF	506 nm (19800 cm ⁻¹)	499 nm (20000 cm ⁻¹)	498 nm (20100 cm ⁻¹)
acetone	520 nm (19200 cm ⁻¹)	514 nm (19450 cm ⁻¹)	514 nm (19450 cm ⁻¹)
chloroform	520 nm (19200 cm ⁻¹)	513 nm (19500 cm ⁻¹)	491 nm (20400 cm ⁻¹)
dichloromethane	523 nm (19100 cm ⁻¹)	515 nm (19400 cm ⁻¹)	501 nm (19960 cm ⁻¹)
acetonitrile	529 nm (18900 cm ⁻¹)	523 nm (19100 cm ⁻¹)	522 nm (19200 cm ⁻¹)
methanol	530 nm (18870 cm ⁻¹)	523 nm (19100 cm ⁻¹)	509 nm (19600 cm ⁻¹)
$\Delta\tilde{\nu}$ (pentane-acetonitrile)	3300 cm ⁻¹	3500 cm ⁻¹	3600 cm ⁻¹

Scheme 3: ¹H NMR-spectrum (CDCl₃, 300 MHz, 20 °C) of **6**.



Scheme 2. NOESY spectrum (CDCl₃, 400 MHz, 25 °C) of **6**.



References

- (1) Various editors, *Organikum*, 14th edition, VEB Deutscher Verlag der Wissenschaften, Berlin, **1993**.
- (2) Hurd, C. D., Kreuz, K. L. *J. Am. Chem. Soc.* **1952**, *74*, 2965.
- (3) Stadler, S.; Dietrich, R.; Bourhill, G.; Bräuchle, C. *Opt. Lett.* **1996**, *21*, 251.
- (4) Schmäzlin, E.; Meerholz, K.; Stadler, S.; Bräuchle, C.; Patzelt, H.; Oesterheld, D.; *Chem. Phys. Lett.* **1997**, *280*, 551.