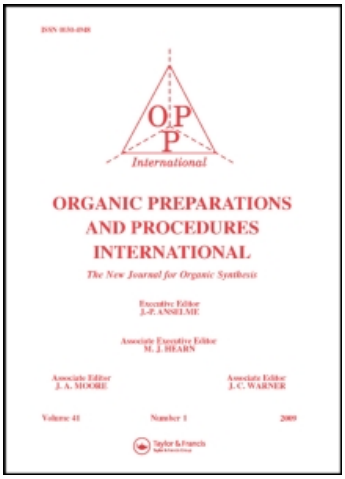

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SYNTHESIS OF SUBSTITUTED 1,3,4-THIADIAZOLES USING LAWESSON'S REAGENT

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ORGANIC PREPARATIONS AND PROCEDURES INT., 37 (3), 213-222 (2005)

SYNTHESIS OF SUBSTITUTED 1,3,4-THIADIAZOLES USING LAWESSON'S REAGENT

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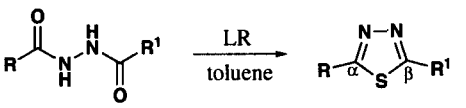
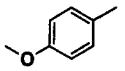
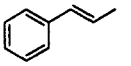
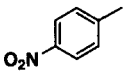
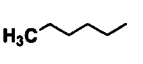
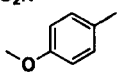
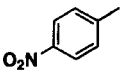
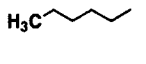
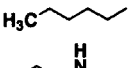
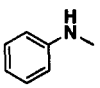
Sulfur containing compounds have many specific and unique properties, which cause them to be continued interest. Because of their extensive biological activity spectrum, 1,3,4-thiadiazoles have been examined as potential antibacterial,[1] antiviral,[2] analgesic,[3] antitumor,[4] anticonvulsant,[1] and anti-inflammatory[3,5] drugs, pesticides and fungicides. Some of them form thermotropic liquid crystals and have interesting electro-optical properties.[6] Moreover, thiadiazoles have been used as corrosion and oxidation inhibitors,[7] dyes or metal ion complexation reagents.[8,9,10,11]

The most popular method of synthesis of this class of compounds involves cyclization and dehydration of thiohydrazides or other substrates with the S-C-N-N-C-S moiety.[1,2,6] Usually phosphorus oxychloride or sulfuric acid have been used in such reactions. Another route for 1,3,4-thiadiazole ring synthesis, is *via* exchange of the oxygen atom in 1,3,4-oxadiazole to sulfur, using tetraphosphorus decasulfide or thiourea;[12] however in our experience, this method does not work in many cases. Lawesson has described the thionation of 1,2-diacylhydrazineswith 2,4-*bis*(4-methoxyphenyl)-1,2,3,4-dithiadiphosphetane (Lawesson's reagent), followed by spontaneous cyclization and dehydrosulfurization as an improved method of thiadiazole ring formation. Unfortunately, this study only dealt with a narrow group of compounds, mainly dialkyl thiadiazoles.[13] We decided to test the utility of this method for the synthesis of a broad range of 2,5-disubstituted 1,3,4-thiadiazoles. The structures of the compounds prepared are shown in *Schemes 1-3*.

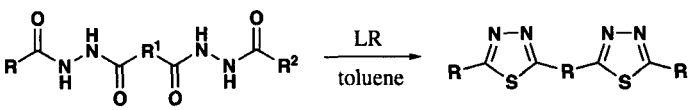
The present method is a useful route for the synthesis of different types of substituted 1,3,4-thiadiazoles. Often, their synthesis by other methods was difficult and the products were obtained in low yield. This method is especially useful for the synthesis of *bis*-thiadiazoles and polymers containing the 1,3,4-thiadiazole unit, which are interesting complexing agents and may be used as liquid crystals and conducting polymers. The mild reaction conditions permit the preparation of some sensitive compounds in good yield and purity. No by-product formation was

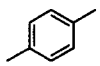


R	R^1	Cmpd	Yield [%]	R	R^1	Cmpd	Yield [%]
		**1**	96			**10**	90
		**2**	93			**11**	95
		**3, 4**	90/95			**12**	90
		**5**	85			**13**	95
		**6**	90			**14**	54
		**7**	80			**15**	75
		**8**	83			**22**	96
		**9**	80				

Synthesis of Mono and Disubstituted 1,3,4-Thiadiazoles

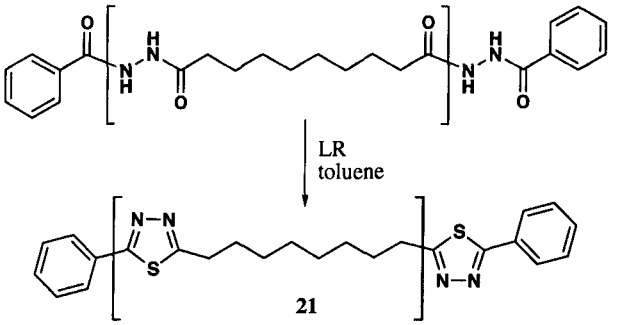
Scheme 1



R	R^1	R^2	Cmpd	Yield (%)
	----		**16**	95
			**17**	75
			**18**	95
			**19**	80
			20	92

Synthesis of *bis*(1,3,4-Thiadiazoles)

Scheme 2



Synthesis of Polymer Containing 1,3,4-Thiadiazole Units

Scheme 3

observed thus making the isolation and purification of 1,3,4-thiadiazoles from the reaction mixture simple and straightforward. The exact mechanism of this reaction is not known with certainty but probably involves thionation of both carbonyl groups followed by concurrent cyclization with the elimination of hydrogen sulfide.

EXPERIMENTAL SECTION

N,N'-Diacylhydrazines were synthesized according to the procedures described elsewhere.[14,15] All solvents were dried and distilled before use. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Varian Gemini 300 spectrometer operating at 300.072, 282.352 and 75.45 MHz respectively, using standard pulse sequences and referred to internal TMS (^{1}H and ^{13}C NMR; 0.00 ppm) and $CFCl_3$ (^{19}F NMR; 0.00 ppm); the assignments were made on the basis of ^{1}H-^{13}C HMQC spectra. Low resolution mass spectra were determined on an AMD 402 two–sector mass spectrometer (AMD Intectra, Germany) of B/E geometry. High-resolution data were obtained on the same instrument using a peak matching technique. Elemental compositions of the ions discussed were determined with an error of less than 10 ppm in relation to perfluorokerosene (Fluka, Switzerland) at a resolving power of 10000. The compounds were introduced into the mass spectrometer using a direct insertion probe in EI mode (70 eV, 0.5 mA total emission current) with an accelerating voltage of 8 kV, a source temperature of 200°C and an inlet temperature of 70-150°C. Fragmentation patterns of some of the 1,3,4-thiadiazoles studied were discussed elsewhere.[16] Elemental analyses were obtained on a Vario EL III (Elementar, USA) analyser. Melting points were measured on a Boethius apparatus and left uncorrected. Chromatographic separations were carried out on silica gel 60 (70-230 mesh, Merck) and silica gel 60 TLC plates (Merck) with fluorescent indicator, using a mixture of ether and dichloromethane. Recrystallizations were performed from ethanol.

2-Phenyl-1,3,4-thiadiazole (1).- To a suspension of 1-benzoyl-2-formylhydrazine (**1a**) (1 mmol) in 25 cm^3 of dry toluene, Lawesson's reagent was added (1.1 mmol) and the solution was refluxed over 1 h. After this time the reaction was complete (TLC: diethyl ether as eluent). The solvent was evaporated and the semi-solid residue was chromatographed on silica. First, dichloromethane was used as an eluent, to remove 2,4,6-tris(4-methoxyphenyl)-1,3,5,2,4,6-triox-

atriphosphoran-2,4,6-trisulfide and then the product was eluted with a diethyl ether - dichloromethane mixture. The solvent was evaporated and crystallization of the solid from ethanol gave 155 mg (96%) of product as white flakes, mp 50-51°C (*lit.*[17] 47-50°C). ^{1}H NMR ($CDCl_3$): δ 9.16 (s, 1H); 7.98 (m, 2H); 7.50 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 168.66; 151.57; 131.48; 129.26; 129.20; 128.14. HR-MS: Calcd. for $C_8H_6N_2S$: 162.02518. Found: 162.02682.

Anal. Calcd for $C_8H_6N_2S$: C, 59.26; H , 3.73; N, 17.27; S, 19.77

Found: C, 59.42; H, 3.68,;N, 17.47; S, 19.70

2,5-Diphenyl-1,3,4-thiadiazole (2): Obtained from 1,2-dibenzoylhydrazine (**2a**) (1 mmol) and Lawesson's reagent (1.2 mmol) according to the procedure described for **1** as white flakes in 93% (225 mg) yield, mp 141-142°C (*lit.*[17] 139-144°C). ^{1}H NMR ($CDCl_3$): δ 8.02 (m, 2H); 7.51 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 167.93; 130.98; 130.05; 129.06; 127.81. HR-MS: Calcd. for $C_{14}H_{10}N_2S$: 238.05647. Found: 238.05688.

Anal. Calcd for $C_{14}H_{10}N_2S$: C, 70.56; H, 4.23; N, 11.75; S 13.45

Found: C, 70.46; H, 4.23; N, 11.63,; S 13.48

2-(4-Methoxyphenyl)-5-phenyl-1,3,4-thiadiazole (3): Obtained from the reaction of 1-(4-methoxybenzoyl)-2-benzoylhydrazine (**3a**) (1 mmol) with Lawesson's reagent in procedure described for compound **1** as white crystals in 90% (240 mg) yield, mp 126-127°C (*lit.*[17] 133°C). ^{1}H NMR ($CDCl_3$): δ 7.99 (m, 2H); 7.94 (d; 2H; J = 7.2 Hz); 7.48 (m, 3H); 6.99 (d; 2H; J = 7.2 Hz); 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 167.85; 167.29; 161.85; 130.87; 130.26; 129.43; 129.10; 127.80; 122.82; 114.50; 55.43. HR-MS: Calcd. for $C_{15}H_{12}N_2OS$:268.06705. Found: 268.06574.

Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.14; H, 4.51; N, 10.44; S 11.95

Found: C, 67.10; H, 4.53; N, 10.36; S, 12.06

2-(4-Methoxyphenyl)-5-phenyl-1,3,4-thiadiazole-5-[^{13}C] (4): Obtained from the reaction of 1-(4-methoxy-benzoyl)-2-[^{13}C-*carboxy*]benzoylhydrazine (**4a**) (1 mmol) with Lawesson's reagent in the procedure described for compound **1** as white crystals in 95% (255 mg) yield, mp 126-127°C. ^{1}H NMR ($CDCl_3$): δ 7.99 (m, 2H); 7.94 (d; 2H; J = 7.2 Hz); 7.48 (m, 3H); 6.99 (d; 2H; J = 7.2 Hz); 3.89 (s, 3H). ^{13}C NMR ($CDCl_3$): δ 167.84; 167.27; 161.84; 130.87; 130.19; 129.42; 129.07 (d; J = 64.2 Hz); 127.77 (d; J = 5.2 Hz); 122.81; 114.48; 55.42. HR-MS: Calcd. for $^{13}CC_{14}H_{12}N_2SO$: 269.07040. Found: 269.07103.

Anal. Calcd for $C_{15}H_{12}N_2OS$: C, 67.28; H, 4.46; N, 10.40; S, 11.91

Found: C, 67.17; H, 4.49; N, 10.32; S 11.97

2-(4-Nitrophenyl)-5-phenyl-1,3,4-thiadiazole (5).- A mixture of 1-(4-nitrobenzoyl)-2-benzoyl-hydrazine (**5a**) (1 mmol) and Lawesson's reagent (1.5 mmol) in dry toluene (50 cm^3) was heated over 5 h. Then, the solvent was evaporated and the residue was extracted twice with dichloromethane (25 cm^3) and once with diethyl ether (25 cm^3). The insoluble, crude product was crystallized from ethanol to give 240 mg (85%) yellow powder of **5**, mp 273-274°C [dec.]; (*lit.*[17] 256-257°C). ^{1}H NMR ([^{2}H]- TFA): δ 8.59 (d, 2H; J = 7.8 Hz); 8.35 (d, 2H; J = 7.8 Hz);

8.14 (d, 2H; J = 7.0 Hz); 7.96 (t, 1H; J = 7.0 Hz); 7.80 (t, 2H; J = 7.0 Hz). ^{13}C NMR ([^{2}H]- TFA): δ 177.25; 168.10; 151.15; 137.42; 132.00; 130.97; 129.39; 129.20; 125.36; 122.19. HR-MS: Calcd. for $C_{14}H_9N_3O_2S$: 283.04153. Found: 283.04230.

Anal. Calcd for $C_{14}H_9N_3O_2S$: C, 59.35; H, 3.20; N, 14.83; S, 11.32

Found: C, 59.20; H, 3.28; N, 14.64; S, 11.32

2-(4-Methoxyphenyl)-5-(4-nitrophenyl)-1,3,4-thiadiazole (6): Obtained from the reaction of 1-(4-methoxybenzoyl)-2-(4-nitrobenzoyl)hydrazine (**6a**) (1 mmol) and Lawesson's reagent (1.5 mmol) in dry toluene (50 cm^3). The reaction mixture was heated over 5 h and then the solvent was evaporated. The product was separated by column chromatography as described for compound **1**, but pure diethyl ether was used for elution of **6**. Crystallization of the solid obtained after ether evaporation from ethanol gave 90% (280 mg) of **6** as a fine, bright yellow crystals, mp 259-260°C. ^{1}H NMR ([^{2}H]- TFA): δ 8.57 (d, 2H; J = 7.8 Hz); 8.31 (d, 2H; J = 7.8 Hz); 8.14 (d, 2H; J = 7.2 Hz); 7.31 (d, 2H; J = 7.2 Hz); 4.08 (s, 3H). ^{13}C NMR ([^{2}H]- TFA): δ 178.28; 170.04; 167.65; 152.80; 134.30; 133.90; 131.02; 127.20; 118.59; 115.83; 57.52. HR-MS: Calcd. for $C_{15}H_{11}N_3O_3S$: 313.05212. Found: 313.05083.

Anal. Calcd for $C_{15}H_{11}N_3O_3S$: C, 57.50; H, 3.54; N, 13.41; S, 10.23

Found: C, 57.26; H, 3.61; N, 13.44; S, 10.31

2-Phenyl-5-(3-pyridyl)-1,3,4-thiadiazole (7).- To a suspension of 1-benzoyl-2-nicotinoylhydrazine (**7a**) (1 mmol) in dry toluene (25 cm^3) was added an equivalent amount of Lawesson's reagent. After 2 h of refluxing, the solvent was evaporated and to the semisolid residue 5 M potassium hydroxide solution was added (5 cm^3). This mixture was extracted twice with dichloromethane (25 cm^3) and twice with diethyl ether (25 cm^3). The combined organic layers were washed with water (25 cm^3) and the product was reextracted to a 5 M solution of hydrochloric acid (2 x 25 cm^3). The aqueous layer was basified with 5 M potassium hydroxide solution and **7** was extracted with diethyl ether (2 x 25 cm^3). After drying by sodium sulfate and solvent evaporation, the product was recrystallized from ethanol, to give 200 mg (80%) of white crystals, mp 155-156°C (*lit.*[17] 150-155°C). ^{1}H NMR ($CDCl_3$): δ 9.19 (d, 1H; J = 1.6 Hz); 8.74 (dd, 1H; J = 6.2 Hz, 1.6 Hz); 8.37 (dt, 1H; J = 8.2 Hz, 1.6 Hz); 8.03 (m, 2H); 7.52 (m, 3H); 7.47 (ddd, 1H; J = 8.2 Hz, 6.2 Hz, 0.9 Hz). ^{13}C NMR ($CDCl_3$): δ 168.59; 164.56; 151.73; 148.84; 134.56; 131.29; 129.90; 129.17; 128.02; 126.60; 123.77. HR-MS: Calcd for $C_{13}H_9N_3S$ 239.05171. Found: 239.05204.

Anal. Calcd for $C_{13}H_9N_3S$: C, 65.25; H, 3.79; N, 17.58; S 13.40

Found: C, 65.15; H, 3.80; N, 17.25; S, 13.22

2,5-(2-Pyridyl)-1,3,4-thiadiazole (8): Obtained and purified from the reaction of 1,2-dipicolinoylhydrazine (**8a**) (1 mmol) with Lawesson's reagent according to the procedure described for compound **7** as a white powder (200 mg, 83%), mp 210-211°C [~160°C subl.] (*lit.*[17] 201-222°C). ^{1}H NMR ($CDCl_3$): δ 8.70 (ddd, 1H; J = 6.0 Hz, 1.8 Hz, 0.9 Hz); 8.42 (ddd, 1H; J = 8.8 Hz, 1.2

Hz, 0.9 Hz); 7.87 (td, 1H; J = 8.8 Hz, 1.8 Hz); 7.41 (ddd, 1H; J = 8.8 Hz, 6.0 Hz, 1.2 Hz). ^{13}C NMR ($CDCl_3$): δ 171.80; 149.92; 149.31; 137.07; 125.32; 120.95. HR-MS: Calcd for $C_{12}H_8N_4S$: 240.04697. Found: 240.04732.

Anal. Calcd for $C_{12}H_8N_4S$: C, 59.99; H, 3.36; N, 23.32; S ,13.34

Found: C, 59.67; H, 3.54; N, 23.12; S, 12.99

2,5-(3-Pyridyl)-1,3,4-thiadiazole (9): Obtained and purified as for compound **7** from the reaction of 1,2-dinicotinoylhydrazine (**9a**) (1 mmol) with Lawesson's reagent. Crystallization gave 195 mg (80%) of **9** as white crystals, mp 200-201°C [~175°C subl.] (*lit.*[17] 219°C).

^1H NMR ($CDCl_3$): δ 9.23 (s, 1H); 8.78 (d, 1H; J = 6.0 Hz); 8.40 (dt, 1H; J = 8.3 Hz, 1.7 Hz); 7.50 (dd, 1H; J = 8.3 Hz, 6.0 Hz). ^{13}C NMR ($CDCl_3$): δ 164.63; 152.77; 147.89; 134.28; 125.81; 123.92. HR-MS: Calcd. for $C_{12}H_8N_4S$: 240.04697. Found: 240.04543.

Anal. Calcd for $C_{12}H_8N_4S$: C, 59.98; H, 3.36; N, 23.32; S, 13.34

Found: C, 59.67; H, 3.35; N, 23.02; S, 13.30

2,5-(4-Pyridyl)-1,3,4-thiadiazole (10): Obtained and purified as for compound **7** from the reaction of 1,2-diisonicotinoylhydrazine (**10a**) (1 mmol) with Lawesson's reagent. Crystallization gave 216 mg (90%) of **10** as creamy white crystals, mp 220-221°C (*lit.*[17] 244-246°C). ^1H NMR ($CDCl_3$): δ 8.83 (d, 1H; J = 5.9 Hz); 7.90 (d, 1H; J = 5.9 Hz). ^{13}C NMR ($CDCl_3$): δ 167.08; 151.05; 136.56; 121.57. HR-MS: Calcd for $C_{12}H_8N_4S$: 240.04697. Found: 240.04922.

Anal. Calcd for $C_{12}H_8N_4S$: C, 59.98; H, 3.36; N, 23.32; S, 13.34

Found: C, 59.77; H, 3.47; N, 23.47; S, 12.99

2-(2-Pyridyl)-5-(4-pyridyl)-1,3,4-thiadiazole (11): The same procedure as for compound **7** synthesis was adopted, except 1-picolinoyl-2-isonicotinoylhydrazine (**11a**) (1 mmol) was used in the place of **7a**. The product was obtained as slightly yellow flakes (228 mg, 95%), mp 194-195°C. ^1H NMR ($CDCl_3$): δ 8.79 (d, 2H; J = 6.1 Hz); 8.68 (ddd, 1H; J = 6.1 Hz, 1.8 Hz, 1.0 Hz); 8.41 (ddd, 1H; J = 8.8 Hz, 1.2 Hz, 1.0 Hz); 7.91 (d, 2H; J = 6.1 Hz); 7.89 (td, 1H; J = 8.8 Hz, 1.8 Hz); 7.44 (ddd, 1H; J = 8.8 Hz, 6.1 Hz, 1.2 Hz). ^{13}C NMR ($CDCl_3$): δ 171.33; 167.48; 150.86; 149.91; 148.60; 137.22; 137.12; 125.66; 121.43; 121.10. HR-MS: Calcd for $C_{12}H_8N_4S$: 240.04697. Found: 240.04785.

Anal. Calcd for $C_{12}H_8N_4S$: C, 59.98; H, 3.36; N, 23.32; S 13.34

Found: C, 60.02; H, 3.36; N, 23.51; S, 13.62

2-Phenyl-5-(2-phenylethenyl)-1,3,4-thiadiazole (12): Obtained from 1-phenyl-2-cinnamonoylhydrazine (**12a**) (1 mmol) according to the procedure described above for compound **1**. After crystallization, compound **12** was obtained as flesh-coloured crystals (238 mg, 90%), mp 135-136°C (*lit.*[17] mp 137°C). ^1H NMR ($CDCl_3$): δ 7.99 (m, 2H); 7.2-7.6 (m, 10H). ^{13}C ($CDCl_3$): δ 167.54; 166.96; 139.01; 135.16; 131.12; 130.08; 129.61; 129.16; 128.97; 127.93; 127.29; 118.31. HR-MS: Calcd for $C_{16}H_{12}N_2S$: 264.07211. Found: 264.07360.

Anal. Calcd for $C_{16}H_{12}N_2S$: C, 72.70; H, 4.58; N, 10.60; S, 12.13

Found: C, 72.61; H, 4.64; N, 10.39; S, 12.22

2-Phenyl-5-pentyl-1,3,4-thiadiazole (13).- A mixture of 1-benzoyl-2-hexanoylhydrazine (**13a**) (1 mmol) and Lawesson's reagent (1.1 mmol) was heated under reflux in dry toluene (50 cm^3) over 5 h. The solvent was evaporated,to dryness and the residue was dissolved in dichloromethane and chromatographed on silica, using CH_2Cl_2 for elution. The combined fractions (checked by TLC) were combined and evaporated to afford **13** as a colorless oil which solidified after some time to white, waxy crystals (220 mg, 95%), mp 40-41°C. ^1H NMR ($CDCl_3$): δ 7.95 (m, 2H); 7.48 (m, 3H); 3.13 (t, 2H; J = 6.7 Hz); 1.85 (qu, 2H; J = 6.7 Hz); 1.40 (m, 4H); 0.92 (t, 3H; J = 6.6 Hz). ^{13}C NMR ($CDCl_3$): δ 170.39; 168.33; 130.80; 130.35; 129.05; 127.79; 31.10; 30.16; 29.74; 22.52; 13.87. HR-MS: Calcd for $C_{13}H_{16}N_2S$: 232.10342. Found: 232.10249.

Anal. Calcd for $C_{13}H_{16}N_2S$: C, 67.20; H, 6.94; N, 12.06; S, 13.80
Found: C, 67.31; H, 6.63; N, 11.93; S, 13.55

2-Phenyl-5-trifluoromethyl-1,3,4-thiadiazole (14): 1-Benzoyl-2-trifluoroacetylhydrazine (**14a**) (1 mmol) was converted to **14** according to the procedure described for **13**. After chromatography, 125 mg (54%) of white solid was obtained, mp 105-106°C. ^1H NMR ($CDCl_3$): δ 7.99 (m, 2H); 7.48 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 168.45; 167.44 (q; J = 26.7 Hz); 130.55; 129.93; 129.22; 127.77; 124.17 (q; J = 268.2 Hz). ^{19}F NMR ($CDCl_3$): δ 59.37 (s). HR-MS: Calcd for $C_9H_5F_3N_2S$: 230.01256. Found: 230.01342.

Anal. Calcd for $C_9H_5F_3N_2S$: C, 46.96; H, 2.19; N, 12.17; S, 13.93
Found: C, 47.08; H, 2.27; N, 12.01; S, 13.80

2,5-Dipentyl-1,3,4-thiadiazole (15): Compound **15** was synthesized from 1,2-dihexanoylhydrazine (**15a**) (1 mmol) and Lawesson's reagent (1.3 mmol) according to the procedure described above for compound **13**. The oily product obtained after chromatography was distilled using a Kugelrohr apparatus to produce 170 mg (75%) of pale yellow liquid, mp 16-18°C. ^1H NMR ($CDCl_3$): δ 2.96 (t, 2H; J = 6.7 Hz); 1.69 (qu, 2H; J = 6.7 Hz); 1.27 (m, 4H); 0.81 (t, 3H; J = 6.8 Hz). ^{13}C NMR ($CDCl_3$): δ 170.12; 30.90; 29.85; 29.46; 22.01; 13.60. HR-MS: Calcd for $C_{12}H_{22}N_2S$: 226.15038. Found 226.15111.

Anal. Calcd for $C_{12}H_{22}N_2S$: C, 63.67; H, 9.80; N, 12.37; S, 14.19
Found: C, 63.42; H, 9.95; N, 12.48; S, 14.07

5,5'-*bis*(2,2'-Diphenyl-1,3,4-thiadiazole) (16).- A suspension of 2,2'-bis(benzoyl)oxalyldihydrazide (**16a**) (1 mmol) and Lawesson's reagent (2.2 mmol) in dry toluene (50 cm^3) was heated over 3 h and then the solvent was evaporated. The semi-solid residual mixture was dissolved in dichloromethane and the product was isolated by column chromatography, as described for compound **1**. After crystallization from methanol, 305 mg (95%) of slightly cream-colored crystals were obtained, mp 258-260°C (*lit.*[17] 252°C). ^1H NMR ($CDCl_3$): δ 8.09 (m, 2H); 7.56 (m, 3H). ^{13}C NMR ($CDCl_3$): δ 170.34; 159.01; 131.97; 129.41; 128.27. HR-MS: Calcd. for $C_{16}H_{10}N_4S_2$: 322.03470. Found: 322.03195.

Anal. Calcd for $C_{16}H_{10}N_4S_2$: C, 59.61; H, 3.13; N, 17.38; S, 19.89
Found: C, 59.52; H, 3.18; N, 17.19; S, 19.87

1,4-*bis*(2-Phenyl-1,3,4-thiadiazol-5-yl)benzene (17).- A mixture of terephthalic acid *bis*(2-benzoylhydrazide) (**17a**) (1 mmol) and Lawesson's reagent (2.5 mmol) was heated in dry toluene (100 cm^3) over 24 h. After cooling, the solvent was evaporated, and the solid residue was extracted twice with diethyl ether (25 cm^3), twice with dichloromethane (25 cm^3), once with warm chloroform (25 cm^3) and once with warm ethanol (25 cm^3). The obtained, very poorly soluble, pale yellow powder (300 mg, 75%), was identified as compound **17**, mp 292-293°C (*lit.*[17] 310-311°C). ^1H NMR ([^2H]- TFA): δ 8.37 (s, 2H); 8.11 (d, 2H; J = 7.1 Hz); 7.92 (t, 1H; J = 7.1 Hz); 7.76 (t, 2H; J = 7.1 Hz). ^{13}C NMR ([^2H]- TFA): δ 176.84; 168.74; 137.36; 130.92; 129.66; 129.13; 122.19. HR-MS: Calcd for $C_{22}H_{14}N_4S_2$ 398.06598. Found: 398.06671.

Anal. Calcd for $C_{22}H_{14}N_4S_2$: C, 66.31; H, 3.54; N, 14.06; S, 16.09
Found: C, 65.95; H, 3.60; N, 13.86; S, 15.89

1,8-*bis*(2-Phenyl-1,3,4-thiadiazol-5-yl)octane (18): Generated from sebacic acid *bis*(2-benzoylhydrazide) (**18a**) (1 mmol) according to the procedure described for compound **1**, but with twice the amount of Lawesson reagent. After crystallization, 412 mg (95%) of **18** was obtained as flesh-colored leaves, mp 154-155°C. ^1H NMR ($CDCl_3$): δ 7.96 (m, 2H; 7.47 (m, 3H); 3.13 (t, 2H; J = 6.6 Hz); 1.84 (qu, 2H; J = 6.6 Hz); 1.39 (m, 4H). ^{13}C NMR ($CDCl_3$): δ 170.24; 168.35; 130.81; 130.29; 129.04; 127.78; 30.12; 29.94; 28.94; 28.83. HR-MS: Calcd for $C_{24}H_{26}N_4S_2$: 434.15988. Found: 434.16106.

Anal. Calcd for $C_{24}H_{26}N_4S_2$: C, 66.32; H, 6.03; N, 12.89; S, 14.75
Found: C, 66.18; H, 6.02; N, 12.62; S, 14.55

2,6-*bis*(2-(2-Pyridyl)-1,3,4-thiadiazol-5-yl)pyridine (19).- A mixture of 2,6-pyridinedicarboxylic acid *bis*(2-picolinylhydrazide) (**19a**) (1mmol) and Lawesson's reagent (2.2 mmol) was refluxed over 10 h. Afterwards, the solvent was evaporated to give a semi-solid residue which was basified with 5 M solution of potassium hydroxide and extracted twice with diethyl ether (50 cm^3). The product was then re-extracted to 5M hydrochloric acid and then the aqueous layer was basified with 5M KOH. After extraction with diethyl ether, the organic layer was dried over anhydrous sodium sulfate. Evaporation of the solvent followed by crystallization from ethanol gave **19** as a yellow powder (320 mg, 80%), mp 320-322°C (subl.). ^1H NMR ([^2H]- TFA): δ 9.12 (dd, 2H; J = 6.2 Hz, 2.0 Hz); 8.99 (td, 2H; J = 8.6 Hz, 2.0 Hz); 8.76 (d, 2H; J = 8.6 Hz); 8.73 (d, 2H; J = 8.0 Hz); 8.43 (t, 1H; J = 8.0 Hz); 8.39 (ddd, 2H; J = 8.6 Hz, 6.2 Hz, 0.9 Hz). ^{13}C NMR ([^2H]- TFA): δ 175.69; 161.60; 150.44; 148.12; 144.10; 141.54; 140.92; 130.31; 128.56; 125.99. HR-MS: Calcd for $C_{19}H_{11}N_7S_2$: 401.05173. Found: 401.05210.

Anal. Calcd for $C_{19}H_{11}N_7S_2$: C, 56.84; H, 2.76; N, 24.42; S, 15.97
Found: C, 56.44; H, 2.92; N, 24.09; S, 15.94

2,6-*bis*(2-Phenyl-1,3,4-thiadiazol-5-yl)pyridine (20): Synthesised from 2,6-pyridinedicarboxylic acid *bis*(benzoylhydrazide) (**20a**) (1 mmol) according to the procedure described for compound **19**. Crystallization from ethanol gave 367 mg (92%) of white, crystalline solid, mp

235.0°C (dec.). ^{1}H NMR ($CDCl_3$): δ 8.48 (d, 2H; J = 8.1 Hz); 8.11 (m, 4H); 8.07 (t, 1H; J = 8.1 Hz); 7.55 (m, 6H). ^{13}C NMR ($CDCl_3$): δ 170.48; 168.80; 149.27; 138.58; 131.44; 130.11; 129.26; 128.05; 122.24. HR-MS: Calcd for $C_{21}H_{13}N_5S_2$: 399.06128. Found: 399.06041.

Anal. Calcd for $C_{21}H_{13}N_5S_2$: C, 63.14; H, 3.28; N, 17.53; S, 16.05

Found: C, 63.27; H, 3.19; N, 17.41; S, 16.00

α-(2-Phenyl-1,3,4-thiadiazo-5-yl)-ω-phenylpoly(1,3,4-thiadiazol-2,5-diyl-octane-1,8-diyl) (21).- To a suspension of **21a** (0.1 mmol; n = 10) in dry toluene, 1.2 mmol of Lawesson's reagent was added. The mixture was heated for 10h and the solvent was evaporated *in vacuo*. The residue then was extracted twice with hot diethyl ether, twice with hot dichloromethane, once with hot methanol and then dried overnight under reduced pressure. Polymer **21** (200 mg, 90%) was obtained as a pale yellow solid with a softening temperature about 100°C. The average number of 1,3,4-thiadiazol-2,5-diyl-octane-1,8-diyl residues, determined by the ^{1}H NMR method, was about 10 and the amount of unreacted diacylhydrazinyl group determined by IR, was found to be less than 5%. ^{1}H NMR ([^{2}H]- TFA): δ 8.10 (b, 2H); 7.95 (b, 1H), 7.75 (b, 2H); 3.20-3.25 (b, 20H); 1.80-1.90 (b, 20H); 1.30-1.45 (b, 40H).

Anal. Calcd for $C_{114}H_{170}N_{22}S_{11}$ (for n = 10): C, 62.20; H, 7.78; N, 14.00; S, 16.02

Found: C, 61.86; H, 7.31; N, 13.88; S, 15.34

2-(3-Pyridyl)-5-phenylamino-1,3,4-thiadiazole (22): Obtained and purified according to the procedure described for compound **7** from 1-phenyl-2-(3-nicotinylhydrazine)carboamide (**22a**) (1 mmol) as creamy-white crystals (244 mg, 96%), mp 262-264°C. ^{1}H NMR ([^{2}H]$_6$-DMSO): δ 10.66 (s, 1H); 9.06 (d, 1H; J = 1.5 Hz); 8.68 (dd, 1H; J = 6.2 Hz, 1.5 Hz); 8.28 (dt, 1H; J = 8.2 Hz, 1.5 Hz); 7.66 (d, 2H; J = 7.4 Hz); 7.57 (d, 1H; J = 8.2 Hz); 7.39 (t, 2H; J = 7.4 Hz); 7.05 (t, 1H; J = 7.4 Hz). ^{13}C NMR ([^{2}H]$_6$-DMSO): δ 164.68; 154.58; 150.85; 147.33; 140.38; 134.03; 129.18; 126.56; 124.23; 122.26; 117.62. HR-MS: Calcd for $C_{13}H_{10}N_4S$: 254.06262. Found 254.06084.

Anal. Calcd for $C_{13}H_{10}N_4S$: C, 61.40; H, 3.96; N, 22.03; S, 12.61

Found: C, 61.34; H, 4.00; N, 21.87; S, 12.67

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17. All melting points come from Beilstein Database.

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