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A series of compounds **3a-d,i-n** with two or three 1,2,3-thiadiazole rings, useful for photocrosslinking processes, was prepared from the di- or triketones **1a-d,i,n** via the corresponding hydrazones **2a-d,i,n** by applying the Hurd-Mori method. A special synthetic sequence, **1e**, **2e**, **3e**, **3f/3g**, was elaborated for the olefinic system **3h**.

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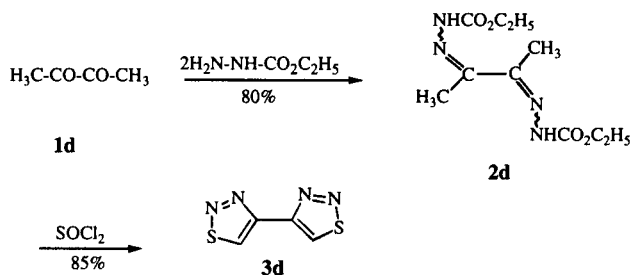
Polymers with 1,2,3-thiadiazole rings in the side chains are interesting materials for photocrosslinking processes and the generation of photoresists, X-ray resists and electron beam resists [1-6]. The 1,2,3-thiadiazole rings can either be introduced in a polymer precursor [1,2] or directly in the monomer [3-7]. The latter concept has to be confined to polymerization reactions in which all 1,2,3-thiadiazole rings are kept intact. A thermal cleavage would lead to an undesired premature crosslinking. An alternative concept is based on the admixture of compounds with two or more 1,2,3-thiadiazole rings to polymers with reactive sites (nucleophilic groups *etc.*). The photochemical denitrogenation could then lead to 1,3-diradicals and subsequently to thioketenes [8] which react with different polymer chains. Naturally a twofold reaction with the same chain cannot be excluded for a certain part of the additive.

Therefore we synthesized a few compounds with two or more 1,2,3-thiadiazole rings and different spacers. The Hurd-Mori reaction [9] represents a very convenient and plentiful procedure for these preparations. Scheme 1 shows the formation of 1,3- and 1,4-bis(1,2,3-thiadiazol-4-yl)benzene **3c** [10,11]. The diketones **1a-c** were first

transformed to the corresponding hydrazones **2a-c** which contain ethoxycarbonyl groups as good leaving groups. NOE measurements show that the (*E*)-configurations predominate largely. The *E/Z* isomerism of the CN double bonds has no influence on the cyclization process with thionyl chloride [12]; the optimized overall yields for both steps are between 86 and 89%.

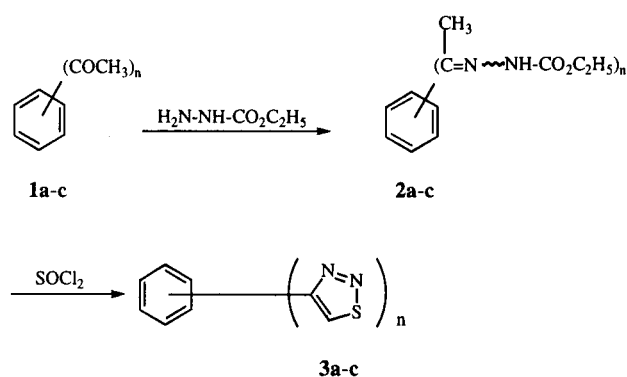
2,3-Butanedione **1d** gives in analogous reaction sequence 4,4'-bi(1,2,3-thiadiazolyl) **3d**. Multiple 1,2,3-thiadiazoles especially those with a high nitrogen content can show a vigorous decomposition (explosion) on heating. Compound **3d** eliminates nitrogen in the temperature range of the melting process at 240°.

Scheme 2



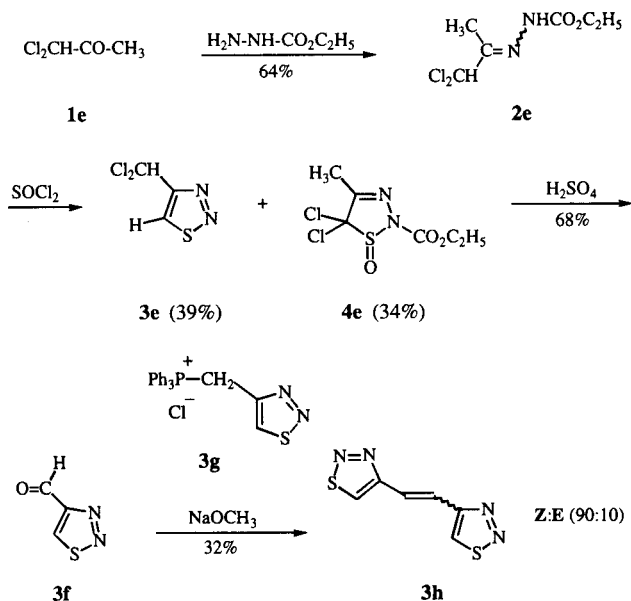
The Hurd-Mori reaction fails often for α,β -unsaturated ketones [13]; therefore we conceived for 1,2-bis(1,2,3-thiadiazol-4-yl)ethene **3h** a synthetic route in which the olefinic double bond was formed in the last reaction step. Treatment of the hydrazone **2e** of 1,1-dichloroacetone **1e** with thionyl chloride led to two ring closure products **3e** and **4e** (Scheme 3). Contrary to mono-chlorinated or -brominated acetone [14] a significant regioselectivity could not be observed. The ring closure on the side of the dichloromethyl group cannot result in the generation of a heteroaromatic 5-membered ring, the ethoxycarbonyl leaving group is not split off. Hydrolysis of **3e** yields the aldehyde **3f** [15-17]. The target compound **3h** was finally obtained by a Wittig reaction of **3f** and the phosphonium salt **3g** [7]. The assignment of the configuration *Z* (90%) or *E* (10%) was achieved by the determination of the vicinal couplings of the olefinic protons: $^3J_{H,H} = 13.3$ Hz for (*Z*)-**3h** and 16.0 Hz for (*E*)-**3h**. The ^{13}C satellites in the ^1H nmr spectrum were measured for this purpose.

Scheme 1



| 1-3 | n | Position of substitution | Yield [%] 2 | Yield [%] 3 |
|----------|---|--------------------------|--------------------|--------------------|
| a | 2 | 1,3 | ~100 | 89 |
| b | 2 | 1,4 | 93 | 95 |
| c | 3 | 1,3,5 | 95 | 91 |

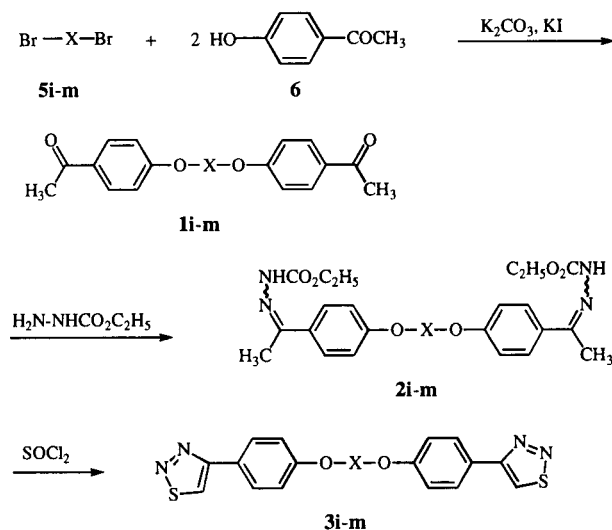
Scheme 3



The diketones **1i-m**, prepared by the reaction of **5i-m** and **6** could be subjected to a normal Hurd-Mori procedure. The dihydrazones **2i-m** as well as the 1,2,3-thiadiazoles **3i-m** were obtained in high to quantitative yields.

Compound **3n**, which contains a still longer spacer between the two 1,2,3-thiadiazole rings, was synthesized

Scheme 4



| | | Yields [%] | | |
|-------|----------------------------------|------------|----|----|
| 1-3,5 | -X- | 1 | 2 | 3 |
| i | (CH ₂) ₂ | 37 | 90 | 88 |
| j | (CH ₂) ₃ | 80 | 96 | 93 |
| k | (CH ₂) ₆ | 88 | 99 | 92 |
| l | (CH ₂) ₁₂ | 89 | 99 | 91 |
| m | | 89 | 56 | 98 |

on a route related to the preparation of **3i-m**. The diketone **1n** obtained by the reaction sequence **5k** + **6** → **7**, **7** + **8** → **1n** was transformed to the ditosylhydrazone **2n** which gave **3n** in reasonable yields.

The ¹H and ¹³C nmr data of **3a-n** are summarized in Table 1.

EXPERIMENTAL

The melting points were measured with a Büchi apparatus and were not corrected. The ¹H and ¹³C nmr spectra were recorded on Bruker AM 400 and AC 200 spectrometers in deuteriochloroform or DMSO-d₆ with TMS as internal standard. The infrared spectra were recorded on a Beckman Acculab 4 spectrometer. The EI mass spectra were obtained on a Varian MAT CH7A (70 eV ionisation energy), and the FD mass spectra on a Finnigan M 95 spectrometer.

General Procedure for the Preparation of Multiple Hydrazones **2a-d**.

A solution of di- or triketone **1a-c** (25.0 mmoles), a few drops of concentrated hydrochloric acid and 2 or 3 equivalents of ethylhydrazinecarboxylate were refluxed overnight in dry chloroform (150 ml). The water generated was continuously removed. The precipitated multiple hydrazone **2a-c** was filtered off and washed with diethyl ether. If necessary, a recrystallization from methanol or ethanol can be performed.

1,1'-(1,3-Phenylene)bisethanone Bis(ethoxycarbonylhydrazone) (**2a**).

The pale yellow powder, obtained in quantitative yield melted at 152-153° and had ¹H nmr signals in DMSO-d₆ at δ 1.29 (t, 6H, CH₃), 2.28 (s, 6H, CH₃), 4.18 (q, 4H, OCH₂), 7.42/8.08 (m, 4H, aromatic H), 10.18 (s, 2H, NH), and ¹³C nmr signals in DMSO-d₆ at δ 14.1/14.6 (CH₃), 60.6 (OCH₂), 123.6/126.6/138.5 (aromatic CH), 128.2 (aromatic Cq), 148.8 (CN), 154.2 (CO). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 334 (100).

Anal. Calcd. for C₁₆H₂₂N₄O₄: C, 57.47; H, 6.63; N, 16.76. Found: C, 57.39; H, 6.56; N, 16.62.

1,1'-(1,4-Phenylene)bisethanone Bis(ethoxycarbonylhydrazone) (**2b**).

The pale yellow powder, obtained in 93% yield melted at 237° dec and showed ¹H nmr signals in DMSO-d₆ at δ 1.26 (t, 6H, CH₃), 2.21 (s, 6H, CH₃), 4.15 (q, 4H, OCH₂), 7.76 (s, 4H, aromatic H), 10.14 (s, 2H, NH) and ¹³C nmr signals in DMSO-d₆ at δ 13.6/14.5 (CH₃), 60.5 (OCH₂), 125.8 (aromatic CH), 129.2 (aromatic Cq), 148.4 (CN), 154.1 (CO). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 334 (100).

Anal. Calcd. for C₁₆H₂₂N₄O₄: C, 57.47; H, 6.63; N, 16.76. Found: C, 57.33; H, 6.62; N, 16.78.

1,1',1''-(1,3,5-Benzenetriyl)trisethanone Tris(ethoxycarbonylhydrazone) (**2c**).

The almost colorless powder, obtained in 95% yield melted at 230° dec. The ¹H nmr signals in DMSO-d₆ were found at δ 1.28 (t, 9H, CH₃), 2.26 (s, 9H, CH₃), 4.18 (q, 6H, OCH₂), 7.99 (s, 3H, aromatic H), 10.18 (s, 3H, NH). ¹³C nmr signals were mea-

Scheme 5

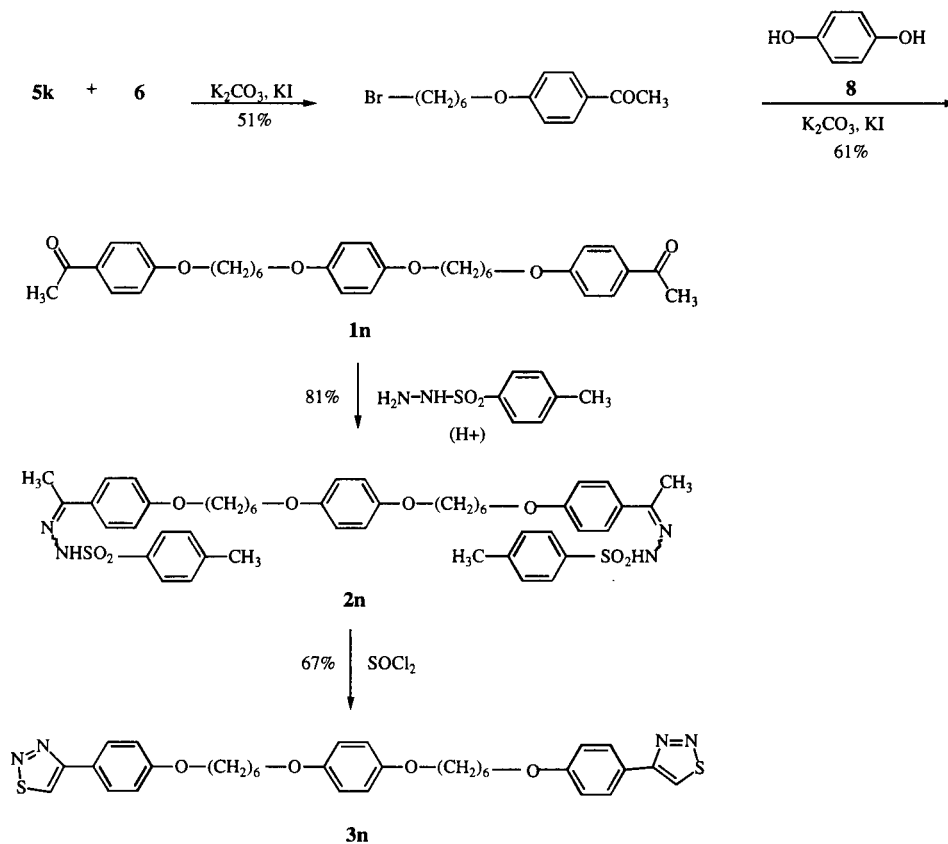


Table I

^{13}C and 1H NMR data of the 1,2,3-Thiadiazoles **3a-m** (δ values in DMSO- d_6 , TMS as internal standard)

| Compound 3 | 1,2,3-Thiadiazole ring | | Substituent on C-4 |
|----------------------------|------------------------|------------|---|
| | C-4 | C-5 / 5-H | |
| a | 161.3 | 133.9/9.80 | 131.6 (Cq), 125.7, 127.8, 130.2/8.91, 8.24, 7.73 (arom CH) |
| b | 161.2 | 133.9/9.76 | 131.4 (Cq), 127.9/8.33 (arom CH) |
| c | 160.8 | 134.5/9.89 | 132.5 (Cq), 126.1/8.95 (arom CH) |
| d | 153.6 | 136.6/9.86 | |
| e [a] | 162.3 | 135.9/8.87 | 62.8/7.27 (CHCl ₂) |
| f | 162.0 | 140.6/9.30 | 183.1/10.54 (CHO) |
| g | 150.8 | 139.9/8.70 | 22.2/5.98 (CH ₂), 118.0 (Cq), 130.0, 133.9, 135.0/7.68-7.92 (CH, Phenyl) |
| (<i>Z</i>)- h [a] | 158.7 | 136.3/9.19 | 121.0/7.19 (olef CH) |
| (<i>E</i>)- h [a] | 159.8 | 132.4/8.50 | 122.6/7.93 (olef CH) |
| i | 163.5 | 131.6/9.54 | 66.5/4.45 (OCH ₂), 159.1, 123.6 (Cq), 115.2, 128.6/7.19, 8.11 (arom CH) |
| j | 160.0 | 128.7/9.11 | 62.5/4.10 (OCH ₂), 26.9/2.14 (CH ₂), 157.3, 121.5 (Cq), 113.0, 126.6/6.91, 7.89 (arom CH) |
| k [a] | 162.8 | 128.1/8.51 | 68.0/4.05 (OCH ₂) 29.1, 25.8/1.62-1.87, 1.57 (CH ₂), 160.1, 123.5 (Cq), 115.1, 128.7/7.02, 7.96 (arom CH) |
| l [a] | 162.3 | 128.3/8.49 | 68.2/4.01 (OCH ₂) 29.5/29.5, 29.4, 29.2, 26.0/1.76-1.83, 1.23-1.45 (CH ₂), 160.2, 123.4 (Cq), 115.1, 128.7/7.00, 7.95 (arom CH) |
| m | 161.4 | 127.6/9.51 | 68.9/5.21 (OCH ₂) 136.3 (Cq central phenylene), 131.2/7.51 (CH, central phenylene) 158.9, 123.4 (Cq), 115.3, 128.4/7.15, 8.08 (arom CH) |
| n | 164.0 | 128.5/9.48 | 67.7/68.1/4.00-4.12 (OCH ₂) 28.6, 28.3, 25.2, 25.1/1.45-1.72 (CH ₂), 159.3 (Cq, central phenylene), 115.3/6.81 (CH, central phenylene) 161.9, 124.4 (Cq), 115.0, 131.9/7.09, 7.96 (arom CH) |

sured in DMSO- d_6 at δ 14.3/14.6 (CH₃), 60.6 (OCH₂), 124.1 (aromatic CH), 138.6 (aromatic Cq), 148.7 (CN), 154.2 (CO). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 462 (100).

Anal. Calcd. for C₂₁H₃₀N₆O₆: C, 54.54; H, 6.54; N, 18.17. Found: C, 54.49; H, 6.51; N, 18.19.

2,3-Butandione Bis(ethoxycarbonylhydrazone) (2d).

The colorless powder, obtained in 80% yield melted at 241° dec. The ¹H and ¹³C nmr signals were found in DMSO- d_6 at δ 1.24 (t, H, CH₃), 2.10 (s, 6H, CH₃), 4.15 (q, 4H, OCH₂), 10.12 (s, 2H, NH), and 11.4/14.4 (CH₃), 60.6 (OCH₂), 149.2 (CN), 153.8 (CO), respectively. The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 258 (100).

Anal. Calcd. for C₁₀H₁₈N₄O₄: C, 46.50; H, 7.02; N, 21.69. Found: C, 46.40; H, 6.81; N, 21.57.

1,1-Dichloroacetone Ethoxycarbonylhydrazone (2e).

Ethyl hydrazonecarboxylate (104 g, 1.0 mmole) and 127 g (1.0 mmole) 1,1-dichloroacetone (1e) were stirred in 1 l of toluene at room temperature for 5-6 hours. The concentrated solution yielded 136 g (64%) of 2e as colorless crystals which after treatment with cold methanol melted at 114°. The ¹H and ¹³C nmr signals in deuteriochloroform were measured at δ 1.30 (t, 3H, CH₃), 2.03 (s, 3H, CH₃), 4.28 (q, 2H, OCH₂), 6.37 (s, 1H, CHCl₂), 7.89 (s, 1H, NH) and δ 9.4 (CH₃), 14.3 (CH₃, ester), 62.4 (OCH₂), 73.0 (CHCl₂), 147.0 (CN), 153.8 (CO), respectively. The ei ms spectrum (70 eV) showed peaks at m/z (%) 212 (18), 214 (11), 216 (2, [M⁺, Cl₂ patten]), 177 (100), 179 (32, [M⁺-Cl]), 129 (96), 101 (75).

Anal. Calcd. for C₆H₁₀Cl₂O₂N₂: C, 33.82; H, 4.73; N, 13.15. Found: C, 33.75; H, 4.74; N, 13.13.

Reaction of 2e with Thionyl Chloride.

Dry 2e (106.5 g, 500 mmoles) was slowly added at room temperature to 300 ml (4.13 moles) of thionyl chloride. After 12 hours of stirring the remaining thionyl chloride was removed *in vacuo* and the residue distilled over a Vigreux column. 4-Dichloromethyl-1,2,3-thiadiazole (3e) (32.9 g, 39%) was obtained as the first fraction (76-80°/1 Torr) and ethyl 5,5-dichloro-2,5-dihydro-4-methyl-1-oxo-1,2,3-thiadiazol-2-carboxylate (4e) (44.0 g, 34%) as the second fraction (135-137°/1 Torr). The yellowish oil 3e had ir absorptions (film) at ν 3100, 2990, 1265, 1235, 1205, 1110, 980, 885, 825, 810, 750, 730 cm⁻¹. The ¹H and ¹³C nmr data are listed in Table 1. The ei ms spectrum (70 eV) showed peaks at m/z (%) 168 (6), 170 (3), 172 (1, [M⁺, Cl₂ pattern]), 105 (100), 107 (38, [Cl pattern]), 69 (71), 45 (99).

Anal. Calcd. for C₃H₂Cl₂N₂S: C, 21.4; H, 1.19; N, 16.67. Found: C, 21.4; H, 1.24; N, 16.53.

A film of 4e, a yellow oil showed ir absorptions at ν 2980, 1755, 1715, 1460, 1425, 1390, 1375, 1360, 1310, 1290, 1235, 1150, 1090, 1040, 990, 940, 865, 830, 780, 750, 730, 680, 665 cm⁻¹. The ¹H nmr measurement in deuteriochloroform gave signals at δ 1.34 (t, 3H, CH₃ ester), 2.28 (s, 3H, CH₃), 4.40 (q, 2H, OCH₂) and the ¹³C nmr spectrum signals at δ 11.2/14.1 (CH₃), 64.8 (OCH₂), 101.1 (C-5), 150.9 (C-4), 151.9 (CO). In the ei ms spectrum (70 eV) peaks were obtained at m/z (%) 258 (54)/260 (38)/262 (8 [M⁺, Cl₂ pattern]) 109 (100)/111 (62)/113 (10 [Cl₂ pattern]).

Anal. Calcd. for C₆H₈Cl₂N₂O₃S: C, 27.8; H, 3.11; N, 10.81. Found: C, 27.87; H, 3.12; N, 10.80.

1,2,3-Thiadiazole-4-carbaldehyde (3f).

Compound 3e (30.0 g, 180 mmoles) and 150 ml of concentrated sulfuric acid were stirred for 1 hour under nitrogen at 200 Torr and 140-145°. The mixture was poured on ice and the aqueous phase extracted with diethyl ether in a liquid-liquid extractor. Colorless crystals precipitated from the dried (magnesium sulfate) and concentrated solution. Sublimation at 80-90°/15 Torr gave 14.9 (68%) of 3f, which melted at 86°; ir absorptions (potassium bromide) were found at ν 3080, 1680, 1455, 1395, 1265, 1245, 1110, 980, 885, 850, 810 cm⁻¹. The ¹H and ¹³C nmr data are listed in Table 1. The identification was achieved by comparison with an authentic sample [17].

(Z)- and (E)-1,2-Di(1,2,3-thiadiazol-4-yl)ethene 3h.

Sodium (1.15 g, 50 mmoles) was slowly added at 0° under argon. The reaction mixture was stirred for 15 minutes at room temperature and treated with (5.7 g, 50 mmoles) of 3f in 50 ml of dry methanol. As soon as 3f could not be detected anymore by tlc, 5 ml of concentrated hydrochloric acid was added, the methanol was evaporated and the residue treated with diethyl ether/petroleum ether (30-60°) until the generated triphenylphosphine oxide precipitated. The organic layer was dried (magnesium sulfate) and concentrated. The crude product 3h was recrystallized from methanol, 3.14 g (32%) colorless crystals (mp 76°) was obtained. The ¹H nmr spectroscopy revealed a ratio Z:E = 90:80. The ir spectrum (potassium bromide) showed absorptions at ν 3100, 1385, 1265, 1250, 1220, 1190, 1110, 990, 980, 970, 900, 890, 840, 820, 790 cm⁻¹. The ei ms spectrum (70 eV) contains peaks at m/z (%) 196 (2, [M⁺]), 86 (75), 95 (56), 70 (31), 69 (100).

Anal. Calcd. for C₆H₄N₄S₂: C, 36.72; H, 2.05; N, 28.55. Found: C, 36.69; H, 2.03; N, 28.56.

General Procedure for the Preparation of the Multiple 1,2,3-Thiadiazoles 3a-d.

To a stirred solution of thionyl chloride (20.23 g, 170.0 mmoles) several portions of the hydrazones 2a-d (15.0 mmoles) were added at 0°. The reaction mixture was stirred at room temperature overnight until no more hydrogen chloride was produced. The excess thionyl chloride was evaporated *in vacuo* and the residue was washed with ether and toluene. The remaining fine powder was dried to afford the multiple 1,2,3-thiadiazoles 3a-d in good yields. A recrystallization from dimethyl sulfoxide can be performed.

1,3-Bis(1,2,3-thiadiazol-4-yl)benzene (3a).

The pale yellow powder, obtained in 89% yield melted at 141-142°; ir (potassium bromide): ν 3115, 3072, 2350, 1583, 1504, 1448, 1412, 1305, 1278, 1228, 1207, 1092, 1060, 1047, 966, 930, 920, 896, 818, 800, 783, 698, 682 cm⁻¹; ¹H and ¹³C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 246 (100).

Anal. Calcd. for C₁₀H₆N₄S₂: C, 48.76; H, 2.46; N, 22.75; S, 26.04. Found: C, 48.47; H, 2.52; N, 22.87; S, 26.40.

1,4-Bis(1,2,3-thiadiazol-4-yl)benzene (3b).

The beige powder, obtained in 95% yield melted at 212° dec; ir (potassium bromide): ν 3064, 2370, 1630, 1451, 1411, 1261, 1221, 1194, 1111, 1053, 1020, 932, 892, 848, 820, 783, 686 cm⁻¹; ¹H and ¹³C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 246 (100).

Anal. Calcd. for $C_{10}H_6N_4S_2$: C, 48.76; H, 2.46; N, 22.75; S, 26.04. Found: C, 48.72; H, 2.49; N, 22.68; S, 26.11.

1,3,5-Tris(1,2,3-thiadiazol-4-yl)benzene (**3c**) [10,11].

The yellow powder, obtained in 91% yield melted at 228° dec; ir (potassium bromide): ν 3100, 1600, 1494, 1436, 1418, 1276, 1227, 1078, 1046, 978, 900, 882, 820, 810, 788, 680 cm^{-1} ; 1H and ^{13}C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 330 (100).

Anal. Calcd. for $C_{12}H_6N_6S_3$: C, 43.62; H, 1.83; N, 25.43; S, 29.11. Found: C, 43.59; H, 1.79; N, 25.38; S, 29.10.

4,4'-Bi(1,2,3-thiadiazolyl) (**3d**) [10].

The fine powder, obtained in 85% yield melted at 208° dec; ir (potassium bromide): ν 3108, 2443, 1610, 1398, 1232, 1219, 104, 916, 908, 896, 807 cm^{-1} ; 1H and ^{13}C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ion of m/z (%) 170 (100).

Anal. Calcd. for $C_4H_2N_4S_2$: C, 28.23; H, 1.18; N, 32.92; S, 37.67. Found: C, 28.21; H, 1.22; N, 33.01; S, 37.69.

General Procedure for the Preparation of the Diketones **1i-m**.

A mixture of 4-hydroxyacetophenone (4.1 g, 30.0 mmoles), dibromoalkane **5i-m** (15.0 mmoles), potassium carbonate (2.1 g, 30.0 mmoles), potassium iodide (4.0 g, 24.0 mmoles) and a few drops of aliquate 336 in dry acetone (100 ml) was refluxed for about 40-60 hours. The reaction was followed with tlc in chloroform. After cooling the reaction mixture was stirred with water (40 ml) and extracted with dichloromethane (3 x 40 ml). The combined organic layers were dried with magnesium sulfate. Removal of the solvent *in vacuo* and recrystallization from acetone gave the diketones **1i-m** as colorless crystals.

1,1'-[1,2-Ethanedylbis(oxy-4,1-phenylene)]bisethanone (**1i**).

The colorless crystals, obtained in 37% yield melted at 163°. The 1H nmr signals in deuteriochloroform and DMSO- d_6 were found at δ 2.47 (s, 6H, CH_3), 4.39 (s, 4H, OCH_2) 6.98/7.86 (AA' BB', 8H, aromatic H). The ^{13}C nmr signals were measured in a 1:1 mixture of deuteriochloroform and DMSO- d_6 at δ 25.9 (CH_3), 66.2 (OCH_2), 113.9/130.0 (CH, phenylene), 130.0/161.8 (Cq, phenylene), 195.5 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 298 (84, M^+), 283 (100, [M^+-CH_3]), 121 (86).

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.47; H, 6.08. Found: C, 72.73; H, 6.28.

1,1'-[1,3-Propanedylbis(oxy-4,1-phenylene)]bisethanone (**1j**).

The colorless crystals, obtained in 80% yield melted at 120-121°. The 1H nmr signals in deuteriochloroform were found at δ 2.29 (m, 2H, CH_2), 2.52 (s, 6H, CH_3), 4.21 (t, 4H, OCH_2), 6.91/7.90 (AA' BB', 8H, aromatic H). The ^{13}C nmr signals were measured in deuteriochloroform at δ 26.2 (CH_3), 29.1 (CH_2), 64.5 (OCH_2), 114.2/130.6 (CH, phenylene), 130.6/162.7 (Cq, phenylene), 196.6 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 312 (47, M^+), 297 (27, [M^+-CH_3]), 177 (15), 43 (100).

Anal. Calcd. for $C_{19}H_{20}O_4$: C, 73.06; H, 6.45. Found: C, 72.81; H, 6.28.

1,1'-[1,6-Hexanedylbis(oxy-4,1-phenylene)]bisethanone (**1k**).

The colorless crystals, obtained in 88% yield melted at 122-123°. The 1H nmr signals in deuteriochloroform were found

at δ 1.53 (m, 4H, CH_2), 1.82 (m, 4H, CH_2), 2.52 (s, 6H, CH_3), 4.00 (t, 4H, OCH_2), 6.88/7.89 (AA' BB', 8H, aromatic H). The ^{13}C nmr signals were measured in deuteriochloroform at δ 25.6 (CH_3), 26.1/28.9 (CH_2), 67.9 (OCH_2), 114.0/130.4 (CH, phenylene) 130.2/162.9 (Cq, phenylene), 196.5 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 354 (78, M^+), 339 (36, [M^+-CH_3]), 121 (100).

Anal. Calcd. for $C_{22}H_{26}O_4$: C, 74.55; H, 7.39. Found: C, 74.34; H, 7.18.

1,1'-[1,12-Dodecanedylbis(oxy-4,1-phenylene)]bisethanone (**1l**).

The colorless crystals, obtained in 89% yield melted at 112-113°. The 1H nmr signals in deuteriochloroform were found at δ 1.29 (m, 16H, CH_2), 1.82 (m, 4H, CH_2), 2.54 (s, 6H, CH_3), 3.99 (t, 4H, OCH_2), 6.89/7.91 (AA' BB', 8H, aromatic H). The ^{13}C nmr signals were measured in deuteriochloroform at δ 25.9/26.2 (CH_3 , CH_2), 29.1/29.3/29.5/29.5 (CH_2), 68.2 (OCH_2), 114.1/130.5 (CH, phenylene) 130.2/163.1 (Cq, phenylene), 196.5 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 438 (8, M^+), 423 (5, [M^+-CH_3]), 121 (100).

Anal. Calcd. for $C_{28}H_{38}O_4$: C, 76.68; H, 8.73. Found: C, 76.48; H, 8.65.

1,1'-[1,4-Dimethylbenzene- α,α' -diylbis(oxy-4,1-phenylene)]bisethanone (**1m**).

The colorless crystals, obtained in 89% yield melted at 187-188°. The 1H nmr signals in deuteriochloroform were found at δ 2.53 (s, 6H, CH_3), 5.12 (s, 4H, OCH_2), 7.00/7.90 (AA' BB', 8H, aromatic H), 7.44 (s, 4H, central aromatic H). The ^{13}C nmr signals were measured in deuteriochloroform at δ 26.4 (CH_3), 69.7 (OCH_2), 114.5/130.6 (CH, phenylene), 127.8 (CH, central phenylene) 130.6/162.4 (Cq, phenylene), 136.2 (Cq, central phenylene), 196.7 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 374 (3, M^+), 359 (1, [M^+-CH_3]), 240 (100), 104 (80).

Anal. Calcd. for $C_{24}H_{22}O_4$: C, 76.99; H, 5.92. Found: C, 76.78; H, 5.81.

Preparation of the Dihydrazones **2i-m**.

These compounds have been prepared from the diketones **1i-m** by the same procedure as **2a-d**.

1,1'-[Ethanedylbis(oxy-4,1-phenylene)]bisethanone Bis(ethoxy-carbonylhydrazone) (**2i**).

The beige powder, obtained in 90% yield melted at 236-237°. The 1H nmr signals in DMSO- d_6 were found at δ 1.24 (t, 6H, CH_3), 2.17 (s, 6H, CH_3), 4.15 (m, 4H, OCH_2 of the ester), 4.35 (s, 4H, OCH_2), 6.99/7.68 (AA' BB', 8H, aromatic H), 9.96 (s, 2H, NH) and ^{13}C nmr signals in DMSO- d_6 at δ 13.7, 14.6 (CH_3), 60.4 (OCH_2 of the ester), 66.3 (OCH_2), 114.2/127.4 (CH, phenylene), 131.0/158.9 (Cq, phenylene), 148.7 (CN), 154.2 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 470 (6, M^+), 424 (3, [$M^+-OCH_2CH_3$]), 383 (5, [$M^+-HNCO_2CH_2CH_3$]), 44 (100).

Anal. Calcd. for $C_{24}H_{30}N_4O_6$: C, 61.26; H, 6.43; N, 11.91. Found: C, 61.05; H, 6.33; N, 11.93.

1,1'-[1,3-Propanedylbis(oxy-4,1-phenylene)]bisethanone Bis(ethoxycarbonylhydrazone) (**2j**).

The colorless powder, obtained in 96% yield melted at 182-183°. The 1H nmr signals in DMSO- d_6 were found at δ 1.19

(m, 2H, CH₂), 1.25 (t, 6H, CH₃), 2.17 (s, 6H, CH₃), 4.17 (m, 8H, OCH₂), 6.96/7.67 (AA' BB', 8H, aromatic H), 9.98 (s, 2H, NH) and ¹³C nmr signals in DMSO-d₆ at δ 13.6/14.5 (CH₃), 28.5 (CH₂), 60.3 (OCH₂ of the ester), 64.3 (OCH₂), 114.1/127.3 (CH, phenylene), 130.8/159.0 (Cq, phenylene), 148.7 (CN), 154.1 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 484 (23, M⁺), 438 (9, [M⁺-OCH₂CH₃]), 396 (45, [M⁺-CO₂CH₂CH₃]), 262 (74), 222 (100).

Anal. Calcd. for C₂₅H₃₂N₄O₆: C, 61.97; H, 6.66; N, 11.56. Found: C, 61.88; H, 6.48; N, 11.68.

1,1'-[1,6-Hexanediybis(oxy-4,1-phenylene)]bisethanone Bis(ethoxycarbonylhydrazone) (**2k**).

The colorless powder, obtained in quantitative yield melted at 208-209°. The ¹H nmr signals in DMSO-d₆ were found at δ 1.24 (t, 6H, CH₃), 1.46/1.72 (2m, 8H, CH₂), 2.15 (s, 6H, CH₃), 3.97 (t, 4H, OCH₂), 4.14 (m, 4H, OCH₂ of the ester), 6.91/7.65 (AA' BB', 8H, aromatic H), 9.98 (s, 2H, NH) and ¹³C nmr signals in DMSO-d₆ at δ 13.6/14.6 (CH₃), 25.2/28.5 (CH₂), 60.3 (OCH₂ of the ester), 67.3 (OCH₂), 114.0/127.3 (CH, phenylene), 130.6/159.2 (Cq, phenylene), 148.8 (CN), 154.2 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 526 (3, M⁺), 481 (1, [M⁺-OCH₂CH₃]), 438 (10, [M⁺-HNCO₂CH₂CH₃]), 134 (15), 45 (100).

Anal. Calcd. for C₂₈H₃₈N₄O₄: C, 63.86; H, 7.27; N, 10.64. Found: C, 63.66; H, 7.33; N, 10.41.

1,1'-[1,12-Dodecanediybis(oxy-4,1-phenylene)]bisethanone Bis(ethoxycarbonylhydrazone) (**2l**).

The pale yellow powder, obtained in quantitative yield melted at 185-186°. The ¹H nmr signals in deuteriochloroform were found at δ 1.28/1.59/1.69 (3m, 16H, CH₂ and CH₃ of the ester), 2.15 (s, 6H, CH₃), 3.98 (m, 4H, OCH₂), 4.28 (m, 4H, OCH₂ of the ester), 6.84/7.68 (AA' BB', 8H, aromatic H) and ¹³C nmr signals in deuteriochloroform at δ 12.6/14.6 (CH₃), 26.06/26.2/-29.2/29.4/29.5 (CH₂), 61.9 (OCH₂ of the ester), 68.1 (OCH₂), 114.3/127.7 (CH, phenylene), 130.6/160.3 (Cq, phenylene), 148.9 (CN), 154.3 (CO). The ei ms (70 eV) spectrum showed the molecular ions at m/z (%) 610 (3, M⁺), 45 (100).

Anal. Calcd. for C₃₄H₅₀N₄O₆: C, 66.86; H, 8.25; N, 9.17. Found: C, 66.97; H, 7.94; N, 9.14.

1,1'-[1,4-Dimethylbenzene-α,α'-diylbis(oxy-4,1-phenylene)]bisethanone Bis(ethoxycarbonylhydrazone) (**2m**).

The pale yellow powder, obtained in 56% yield melted at 251° dec and had ¹H nmr signals in DMSO-d₆ at δ 1.22 (t, 6H, CH₃), 2.15 (s, 6H, CH₃), 4.16 (m, 4H, OCH₂ of the ester), 6.99/7.87 (AA'BB', 8H, aromatic H), 5.10 (s, 4H, OCH₂), 7.43 (s, 4H, central phenylene), 9.99 (s, 2H, NH). The ¹³C nmr signals were measured in DMSO-d₆ at δ 13.6/14.7 (CH₃), 60.8 (OCH₂ of the ester), 67.8 (OCH₂), 114.5/127.6 (CH, phenylene), 130.5/160.1 (Cq, phenylene), 127.6 (CH, central phenylene), 136.3 (Cq, central phenylene), 148.8 (CN), 154.3 (CO). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 547 (100).

Anal. Calcd. for C₃₀H₃₄N₄O₆: C, 65.92; H, 6.27; N, 10.25. Found: C, 65.99; H, 6.18; N, 10.15.

Preparation of the Bis-1,2,3-thiadiazoles **3i-m**.

These compounds have been prepared from the dihydrazones **2i-m** by the same procedure as **3a-d**.

1,2-Bis[4-(1,2,3-thiadiazol-4-yl)phenoxy]ethane (**3i**).

The beige powder, obtained in 88% yield melted at 212° dec; ir (potassium bromide): ν 3080, 2930, 2870, 2350, 1601, 1522, 1460, 1445, 1415, 1370, 1300, 1270, 1242, 1220, 1175, 1114, 1080, 1065, 1050, 936, 890, 838, 800, 778, 655 cm⁻¹; ¹H and ¹³C nmr (Table 1). The ei ms (70 eV) spectrum showed peaks at m/z (%) 382 (2, M⁺), 354 (3, [M⁺-N₂]), 326 (1, [M⁺-2N₂]), 89 (100), 77 (64).

Anal. Calcd. for C₁₈H₁₄N₄O₂S₂: C, 56.53; H, 3.69; N, 14.65; S, 16.77. Found: C, 56.63; H, 3.88; N, 14.71; S, 16.66.

1,3-Bis[4-(1,2,3-thiadiazol-4-yl)phenoxy]propane (**3j**).

The orange powder, obtained in 93% yield melted at 145° dec; ir (potassium bromide): ν 3078, 2935, 2868, 2340, 1735, 1600, 1568, 1520, 1498, 1450, 1410, 1390, 1370, 1300, 1240, 1212, 1170, 1110, 1090, 1060, 1032, 989, 968, 930, 890, 830, 786, 750, 718, 635 cm⁻¹; ¹H and ¹³C nmr (Table 1). The ei ms (70 eV) spectrum showed peaks at m/z (%) 396 (24, M⁺), 368 (67, [M⁺-N₂]), 340 (8, [M⁺-2N₂]), 150 (100).

Anal. Calcd. for C₁₉H₁₆N₄O₂S₂: C, 57.56; H, 4.07; N, 14.13; S, 16.17. Found: C, 57.68; H, 4.17; N, 14.08; S, 16.11.

1,6-Bis[4-(1,2,3-thiadiazol-4-yl)phenoxy]hexane (**3k**).

The pale yellow powder, obtained in 92% yield melted at 201-202°; ir (potassium bromide): ν 3082, 2938, 2856, 1600, 1570, 1522, 1454, 1412, 1388, 1320, 1300, 1266, 1250, 1215, 1176, 1108, 1068, 1040, 1020, 930, 888, 832, 820, 803, 780, 725, 635 cm⁻¹; ¹H and ¹³C nmr (Table 1). The ei ms (70 eV) spectrum showed peaks at m/z (%) 438 (9, M⁺), 410 (37, [M⁺-N₂]), 382 (4, [M⁺-2N₂]), 150 (95), 55 (100).

Anal. Calcd. for C₂₂H₂₂N₄O₂S₂: C, 60.25; H, 5.06; N, 12.77; S, 14.62. Found: C, 60.28; H, 5.09; N, 12.71; S, 14.56.

1,12-Bis[4-(1,2,3-thiadiazol-4-yl)phenoxy]dodecane (**3l**).

The beige powder, obtained in 91% yield melted at 163° dec; ir (potassium bromide): ν 3065, 2910, 2836, 1740, 1600, 1568, 1518, 1495, 1452, 1406, 1382, 1294, 1245, 1211, 1170, 1103, 1028, 996, 930, 885, 832, 814, 804, 778, 720, 636 cm⁻¹; ¹H and ¹³C nmr (Table 1). The ei ms (70 eV) spectrum showed peaks at m/z (%) 522 (4, M⁺), 494 (12, [M⁺-N₂]), 466 (11, [M⁺-2N₂]), 150 (100), 55 (94).

Anal. Calcd. for C₂₈H₃₄N₄O₂S₂: C, 64.34; H, 6.56; N, 10.72; S, 12.27. Found: C, 64.43; H, 6.62; N, 10.73; S, 12.05.

1,4-Bis[4-(1,2,3-thiadiazol-4-yl)phenoxy]methyl]benzene (**3m**).

The pale brown powder, obtained in quantitative yield melted at 230° dec; ir (potassium bromide): ν 3060, 2900, 2855, 1720, 1604, 1572, 1524, 1500, 1460, 1418, 1368, 1300, 1244, 1220, 1170, 1110, 1045, 1010, 936, 890, 870, 830, 810, 788, 635 cm⁻¹; ¹H and ¹³C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ion at m/z (%) 459 (100).

Anal. Calcd. for C₂₄H₁₈N₄O₂S₂: C, 62.86; H, 3.96; N, 12.22; S, 13.98. Found: C, 62.93; H, 4.03; N, 12.25; S, 13.93.

4-(6-Bromohexyloxy)acetophenone (**7**).

A mixture of 4-hydroxyacetophenone (2.8 g, 20.5 mmoles), 1,6-dibromohexane (50.0 g, 205.1 mmoles) and potassium carbonate (20.0 g, 145.0 mmoles) in dry acetone (80 ml) was refluxed for 30 hours. The reaction was followed with tlc in chloroform. After cooling, the precipitated salts were removed and the solvent was dried *in vacuo*. The excess 1,6-dibromohex-

ane was removed *in vacuo* and the residual pale yellow oil was separated from traces of 1,6-dibromohexane on a silica gel column with petroleum ether (40-70°). The product was eluated with chloroform and the solvent was evaporated *in vacuo* to give a yellow oil which crystallized slowly at the room temperature. The colorless crystals, obtained in 51% yield melted at 38-40°. The ¹H nmr signals in deuteriochloroform were found at δ 1.47-1.48 (m, 4H, CH₂), 1.77-1.88 (m, 4H, CH₂), 2.51 (s, 3H, CH₃), 3.39 (t, 2H, CH₂Br), 3.98 (t, 2H, OCH₂), 6.87/7.88 (AA' BB', 4H, aromatic H). The ¹³C nmr signals were measured in deuteriochloroform at δ 25.2 (CH₃), 26.2-33.5 (CH₂), 67.9 (OCH₂), 114.1/130.5 (CH, phenylene), 130.2/163.0 (Cq, phenylene), 196.5 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 299 (8, M⁺), 283 (29, [M⁺-CH₃]), 163 (18, [M⁺-C₆H₁₂Br]), 121 (100).

Anal. Calcd. for C₁₄H₁₉O₂Br: C, 56.20; H, 6.40; Br, 26.71. Found: C, 56.53; H, 6.38; Br, 26.63.

1,1'-[1,4-Phenylenebis(oxy-1,6-hexanedyl-oxy-4,1-phenylene)]bisethanone (**1n**).

A mixture of **7** (8.98 g, 30.0 mmoles), 1,4-dihydroquinone (1.65 g, 16.0 mmoles), potassium carbonate (4.15 g, 30.0 mmoles) and potassium iodide (4.98 g, 30.0 mmoles) was refluxed in 120 ml of dry acetone for 40 hours. The reaction was followed with tlc in methanol/chloroform (1:3). After cooling, the reaction mixture was stirred with water (50 ml) and extracted with dichloromethane (3 x 40 ml). The combined organic layers were dried (magnesium sulfate). Removal of the solvent *in vacuo* and recrystallization from acetone gave the diketone **1n** (yield 5.3 g, 61%) as a colorless powder which melted at 143-145°. The ¹H nmr signals in deuteriochloroform were found at δ 1.50-1.53 (m, 8H, CH₂), 1.76-1.84 (m, 8H, CH₂), 2.53 (s, 3H, CH₃), 3.89 (t, 4H, central OCH₂), 4.00 (t, 4H, OCH₂), 6.80 (s, 4H, central aromatic H), 6.90/7.90 (AA' BB', 8H, aromatic H). The ¹³C nmr signals were measured in deuteriochloroform at δ 25.9 (CH₃), 25.8-29.3 (CH₂), 68.1 (central OCH₂), 68.5 (OCH₂), 114.2/130.6 (CH, phenylene), 130.3/163.1 (Cq, phenylene), 115.5 (CH, central phenylene), 153.3 (Cq, central phenylene), 196.7 (CO). The ei ms (70 eV) spectrum showed peaks at m/z (%) 546 (100, M⁺), 328 (31, [M⁺-C₁₄H₁₉O₂]), 218 (46, [M⁺-C₂₀H₁₉O₄]), 137 (68), 110 (96).

Anal. Calcd. for C₃₄H₄₂O₆: C, 74.70; H, 7.74. Found: C, 74.38; H, 7.66.

1,1'-[1,4-Phenylenebis(oxy-1,6-hexanedyl-oxy-4,1-phenylene)]bisethanone Bis(tosylhydrazone) (**2n**).

To a warm solution of toluene-4-sulfonic acid hydrazide (3.0 g, 16.0 mmoles) in 30 ml of dry ethanol the diketone **1n** (4.37 g, 8.0 mmoles) was added. The solution was refluxed for 1.0 hour and then concentrated to one-half of its original volume. After cooling the reaction mixture to room temperature, the product precipitated as a colorless powder which was washed with a small amount of cool ethanol. The dried powder was obtained in 81% yield and melted at 140-142°. The ¹H nmr signals in DMSO-d₆ were found at δ 1.44/1.69 (m, 8H, CH₂), 2.12/2.35 (2s, 6H, CH₃), 3.86 (t, 4H, central OCH₂), 4.05 (t, 4H, OCH₂), 6.81 (s, 4H, central aromatic H), 6.89/7.78 (AA' BB', 8H, aromatic H), 7.39/7.54 (AA' BB', 8H, toluene, aromatic H), 10.33 (s, 2H, NH). The ¹³C nmr signals were measured in DMSO-d₆ at δ 14.0 (CH₃), 20.9 (CH₃ of toluene), 25.2/26.2/28.4/28.6 (CH₂), 67.4 (central OCH₂), 68.8 (OCH₂), 114.1/127.3 (CH,

phenylene), 130.3/159.6 (Cq, phenylene), 115.3 (CH, central phenylene), 153.4 (Cq, central phenylene), 127.5/129.3 (CH, toluene), 136.3/143.1 (Cq, toluene), 152.6 (CN). The fd ms (5 kV) spectrum showed the molecular ions at m/z (%) 883 (100).

Anal. Calcd. for C₄₈H₅₈N₄O₈S₂: C, 65.28; H, 6.62; N, 6.34; S, 7.26. Found: C, 65.43; H, 6.76; N, 6.18; S, 7.16.

1,4-Bis[6-(4-(1,2,3-thiadiazol-4-yl)phenoxy)hexyloxy]benzene (**3n**).

The compound has been prepared from **2n** by the same procedure as described for **3a-d**. The pale brown powder, obtained in 67% yield melted at 131° dec; ir (potassium bromide): ν 2930, 2860, 1590, 1505, 1460, 1250, 1225, 1174, 1028, 840, 774 cm⁻¹; ¹H and ¹³C nmr (Table 1). The fd ms (5 kV) spectrum showed the molecular ions at m/z (%) 630 (100).

Anal. Calcd. for C₃₄H₃₈N₄O₄S₂: C, 64.74; H, 6.07; N, 8.88; S, 10.17. Found: C, 64.29; H, 6.18; N, 8.83; S, 10.09.

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REFERENCES AND NOTES

- [1] G. A. Delzenne and U. L. Laridon, *Ind. Chim. Belg.*, **34**, 395 (1969).
- [2] G. A. Delzenne (Gevaert-Agfa), U.S. Patent 3,457,073 (1969).
- [3] O. Zimmer and H. Meier, *J. Chem. Soc., Chem. Commun.*, 481 (1982).
- [4] M. Pieper and H. Meier, *Liebigs Ann. Chem.*, 1353 (1986).
- [5] W. Prass, R. Zertani, J. Lingnau, N. Hanold and H. Meier (Hoechst AG), German Offen. 3,835,039 (1990); *Chem. Abstr.*, **113**, P 241515d (1990).
- [6] W. Prass, R. Zertani, J. Lingnau, N. Hanold and H. Meier (Hoechst AG), European Patent 363,817 (1990); *Chem. Abstr.*, **113**, P 181455x (1990).
- [7] N. Hanold, H. Kalbitz, M. Al-Smadi and H. Meier, *Z. Naturforsch.*, **50b**, 1121 (1995).
- [8] H. Meier and K. P. Zeller, *Angew. Chem.*, **89**, 876 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 835 (1977).
- [9] C. D. Hurd and R. I. Mori, *J. Am. Chem. Soc.*, **77**, 5359 (1955).
- [10] H. Meier and N. Hanold in Houben-Weyl: Methoden der Organischen Chemie, Vol E **8d**, G. Thieme, Stuttgart, 1994, p 60.
- [11] G. L'abbé, B. Haelterman and W. Dehaen, *J. Chem. Soc., Perkin Trans. 1*, 2203 (1994).
- [12] O. Zimmer and H. Meier *Chem. Ber.*, **114**, 2938 (1981).
- [13] M. Pieper, W. Teichert and H. Meier, *Liebigs Ann. Chem.*, 1334 (1986).
- [14] M. Fujita, T. Kobori, T. Hiyama and K. Kondo, *Heterocycles*, **36**, 33 (1993).
- [15] See also F. T. Lee and G. P. Volpp, *J. Heterocyclic Chem.*, **7**, 415 (1970).
- [16] See also T. Kobori, M. Mikako, T. Hyama and T. Nagate, Sagami Chem. Res. Taisho Pharma Co. Ltd., Japan Kokai Tokkyo Koho, JP 05,271,209 (1993); *Chem. Abstr.*, **120**, P163820c (1994).
- [17] T. Kobori, M. Fujita, T. Hiyama and K. Kondo, *Synlett*, 95 (1992).