Selective Thiylation of 1-Vinylpyrrole-2-carbaldehydes: Synthesis of the Novel Pyrrole Synthons 2-[Bis(ethylsulfanyl)methyl]-1-vinylpyrroles and 1-(2-Ethylthioethyl)pyrrole-2-carbaldehydes

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Abstract: 1-Vinylpyrrole-2-carbaldehydes have been selectively thiylated with ethanethiol either at the aldehyde (acid catalysis) or at the *N*-vinyl group (free-radical initiation) to afford 1-vinylpyrrole-2-carbaldehyde thioacetals (88–99% yield) or 1-(2-ethylthioethyl)pyrrole-2-carbaldehydes (68–89% yield), respectively. Both derivatives constitute important new families of pyrrole building blocks. Exhaustive thiylation at both the aldehyde and vinyl functionalities was achieved by acid-catalyzed reaction of the ethylthioethyl derivative of pyrrole-2-carbaldehyde with ethane thiol. An unexpected reduction of the ethylthioacetal group by ethanethiol to give the ethylthiomethyl group under free-radical initiation was also observed and is discussed.

Key words: 1-vinylpyrrole-2-carbaldehydes, ethanethiol, thiylation, thioacetals, sulfides, radical initiation, acid catalysis

The recent synthesis of 1-vinylpyrrole-2-carbaldehydes[1] has allowed access to a number of new families of potent pyrrolic building blocks. Among these synthons are 1-vinylpyrrole-2-carbaldehyde thioacetals **2** and 1-(2-alkylthioethyl)pyrrole-2-carbaldehydes **3**. Thioacetals are known to be both classic synthons for the aldehyde 'umpolung' strategy of synthesis[2] and is a commonly used protecting group.[3] Recently, thioacetals have attracted increasing attention as auxiliaries in the synthesis of natural porphirins and related pigments,[4] olefins and acetylenes,[5] pyrrolidines and pyrroles,[6] 2-thiosubstituted furans,[7] benzofuranes,[8,9] indoles and indenes.[10] Thioacetals of 2-formylpyrrolidines are key intermediates in the synthesis of pyrrolo[2,1*c*][1,4]benzodiazepines which are capable of sequence-selective binding to DNA. Such benzodiazepines form part of a group of naturally occurring antitumor antibiotics produced by various *Streptomyces* species such as anthramycin, tomaymycin, sibiromycin and DC-81.[11,12] The use of a thioacetal functionality as a means of protecting a pyrrole derived molecule during the preparation of otherwise inaccessible dipyrrolylmethane derivatives, was described in an earlier work.[13] The use of pyrroles with alkyl-sulfide substituents in the synthesis of complex pyrrolic structures, have also been investigated.[14,15]

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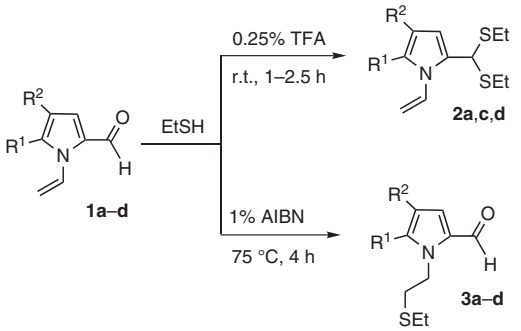
These achievements notwithstanding, selective aldehyde- or N-vinyl-thiylation of the pyrroles **1** still represents a challenge since both functionalities might be expected to participate in the reaction.

In this paper, we report a selective thiylation of pyrroles **1** that allows a clean synthesis of both 1-vinylpyrrole-2-carbaldehyde thioacetals **2** and 1-(2-alkylthioethyl)pyrrole-2-carbaldehydes **3** in good to excellent yields (Scheme 1).



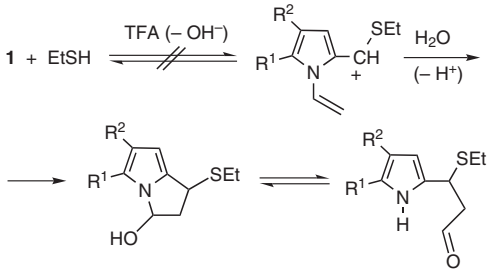
Pyrrole	R^1	R^2	Yield (%)	
1			**2**	**3**
a	H	H	90	87
b	$(CH_2)_4$		–*	68
c	Ph	H	91	77
d	2-thienyl	H	99	89

*Complex mixture of products

Scheme 1

Pyrroles **1**, when allowed to stand with a slight excess of ethanethiol in the presence of catalytic amounts of trifluoroacetic acid (TFA), in benzene, at room temperature, were found to afford thioacetals **2a**, **2c** and **2d** in 90–99% yield. Neither Markovnikov adducts to the *N*-vinyl group, nor oligomers, commonly formed from 1-vinylpyrroles under the action of acids,[16,17] were detected in the reaction mixtures. Furthermore, though cyclization via the nucleophilic *N*-vinyl group could have been expected (Scheme 2), no such products were observed.

Apparently, the above processes only take place in the case of tetrahydroindole **1b**, resulting in the formation of a complex mixture of products under the same conditions. Presumably, this behavior stems from the higher nucleophilicity of its *N*-vinyl group, caused by a donor effect of the cyclohexane fragment.

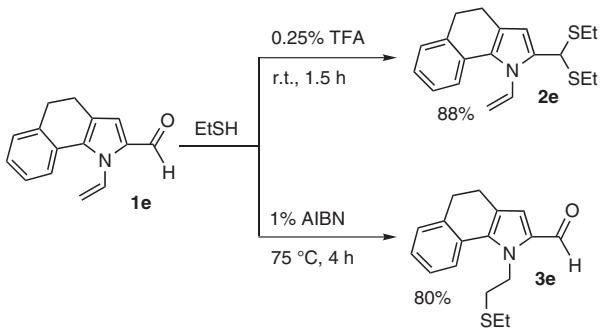


Scheme 2

In the presence of catalytic amounts of the free-radical initiator 2,2′-azobisisobutyronitrile (AIBN), at 75 °C in benzene, the same reactants (equimolar ratio) cleanly furnished anti-Markovnikov adducts to the double bond **3a–d** in 68–89% yield, leaving the aldehyde function unaffected (Scheme 1). It is worth noting that free-radical polymerization, which is known to take place with 1-vinylpyrroles under similar conditions,[16,17] was not observed.

The double bond of pyrroles **1** proved to be more reactive towards thiol addition under AIBN initiation than 1-vinylpyrroles lacking the formyl substituent,[16,17] since the latter required significantly longer (18–25 hours) for the reaction to reach completion under similar conditions.[18]

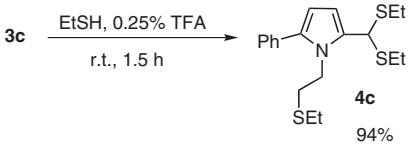
The same conditions could be applied to the thiylation of structurally more complex 1-vinyl-4,5-dihydrobenzo[*g*]indole-2-carbaldehyde **1e** which, when treated with ethanethiol according to the above protocols, selectively afforded both vinylpyrrole **2e** and aldehyde **3e** in 88% and 80% yields, respectively (Scheme 3).



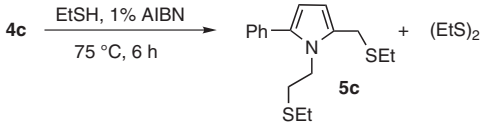
Scheme 3

Exhaustive thiylation of pyrroles **1** was achieved in two steps through treatment of the adducts **3** with the thiol under the conditions described for the synthesis of thioacetals **2** (Scheme 4).

Interestingly, when the trisulfide **4c** or the aldehyde **1c** and excess ethanethiol were submitted to the AIBN-initiated free-radical conditions described above, an unexpected reduction of the thioacetal function to the ethylthiomethyl derivative **5c** (up to the 80% in the product mixture) and diethyl disulfide (identified by GLC) took place (Scheme 5).

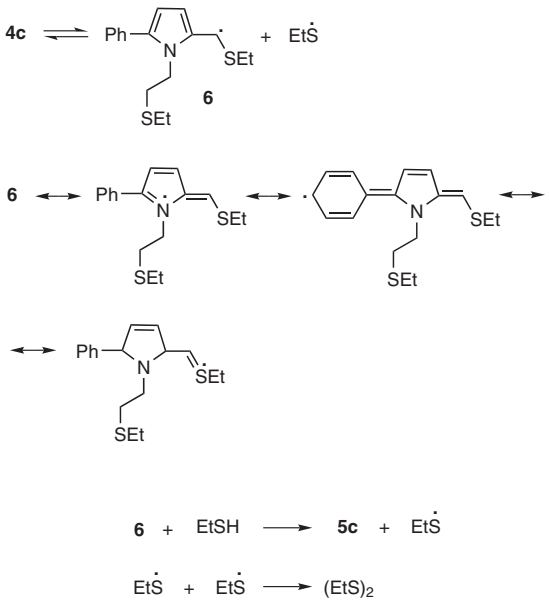


Scheme 4



Scheme 5

It could be envisaged that this unusual reaction pathway for thioacetal reduction could proceed via the intermediate radical **6**, which would be stabilized by extensive resonance interaction with both the neighboring phenyl pyrrole moiety and the sulfur atom (Scheme 6). Such stabilization could considerably decrease the C–S bond dissociation energy.



Scheme 6

In conclusion, an efficient, selective thiylation of available[1] 1-vinylpyrrole-2-carbaldehydes **1** at either the aldehyde or the vinyl functionalities, as well as their exhaustive thiylation, has been accomplished. These advances have provided for a general synthetic approach to 1-vinylpyrrole-2-carbaldehyde thioacetals, 1-(2-alkylthioethyl)pyrrole-2-carbaldehydes and 1-(2-alkylthioethyl)pyrrole-2-carbaldehyde thioacetals, all of which constitute novel families of promising pyrrole synthons.

IR spectra were recorded using a Bruker IFS 25 spectrometer. ^{1}H NMR and ^{13}C NMR spectra were measured using an AV-400 spectrometer in $CDCl_3$ solutions with HMDS as the internal standard. Gas chromatographic analyses were performed using an Agi-

lent 6890N instrument. 1-Vinylpyrrole-2-carbaldehydes were prepared by a known literature procedure.[1] Organic solvents were dried by standard methods. Commercially obtained reagents were used without further purification.

Synthesis of Thioacetals; Typical Procedure

A solution of pyrrole **1c** (0.20 g, 1 mmol), ethanethiol (0.20 g, 3 mmol) and TFA (0.005 g, 0.25% with respect to total mass) in benzene (2 mL) was kept at r.t. until consumption of **1c** was complete (~1 h; monitored by GLC). $NaHCO_3$ (0.10 g) was added and the mixture was shaken before the liquid phase was decanted off and the solid residue was washed with benzene (3 × 0.5 mL). Purification of the crude product by column chromatography (Al_2O_3; *n*-hexane–Et_2O, 2:1) gave the pure product **2c** (0.28 g, 91%).

2-[Bis(ethylsulfanyl)methyl]-1-vinylpyrrole (2a)

Red viscous oil; n_D^{20} 1.4640.

IR (KBr): 3113, 3089, 3035, 2968, 2926, 2870, 1685, 1670, 1640, 1563, 1544, 1523, 1507, 1475, 1449, 1422, 1375, 1358, 1310, 1290, 1265, 1219, 1200, 1156, 1122, 1093, 1072, 1054, 1036, 1014, 969, 883, 865, 792, 772, 742, 719, 679, 654, 594, 520 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.31 (dd, J_{B-X} = 15.4 Hz, J_{A-X} = 8.8 Hz, 1 H, H_X), 6.97 (dd, *J* = 3.2, 1.7 Hz, 1 H, H-5), 6.21 (dd, *J* = 3.4, 1.7 Hz, 1 H, H-3), 6.08 (dd, *J* = 3.4, 3.2 Hz, 1 H, H-4), 5.11 (d, J_{B-X} = 15.4 Hz, 1 H, H_B), 6.06 (s, 1 H, CH), 4.74 (d, J_{A-X} = 8.8 Hz, 1 H, H_A), 2.61 (m, 2 H, CH_2), 2.53 (m, 2 H, CH_2), 1.22 (t, 6 H, *J* = 7.3 Hz, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 131.42 (C-α), 128.52 (C-2), 118.65 (C-5), 111.36 (C-3), 109.18 (C-4), 99.00 (C-β), 44.86 (CH), 25.83 (CH_2), 14.49 (CH_3).

Anal. Calcd for $C_{11}H_{17}NS_2$: C, 58.11; H, 7.54; N, 6.16; S, 28.20. Found: C, 58.17; H, 7.43; N, 6.12; S, 28.29.

2-[Bis(ethylsulfanyl)methyl]-5-phenyl-1-vinylpyrrole (2c)

Orange-red viscous oil; n_D^{20} 1.4857.

IR (KBr): 3106, 3057, 3014, 2968, 2926, 2869, 2837, 2725, 1653, 1639, 1602, 1552, 1541, 1497, 1480, 1452, 1438, 1416, 1377, 1337, 1296, 1260, 1209, 1193, 1162, 1134, 1119, 1099, 1050, 1009, 970, 935, 912, 870, 836, 813, 785, 759, 736, 706, 669, 652, 602, 474 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (m, 2 H, H_{ortho}), 7.34 (m, 2 H, H_{meta}), 7.25 (m, 1 H, H_{para}), 6.93 (dd, J_{B-X} = 15.7 Hz, J_{A-X} = 8.6 Hz, 1 H, H_X), 6.41 (d, *J* = 3.7 Hz, 1 H, H-3), 6.20 (d, *J* = 3.7 Hz, 1 H, H-4), 5.21 (d, J_{B-X} = 15.7 Hz, 1 H, H_B), 5.18 (s, 1 H, CH), 5.16 (d, J_{A-X} = 8.6 Hz, 1 H, H_A), 2.71 (m, 2 H, CH_2), 2.60 (m, 2 H, CH_2), 1.27 (t, *J* = 7.3 Hz, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 134.87 (C-5), 133.37 (C_{ipso}), 131.66 (C-α), 131.11 (C-2), 128.97 (C_{ortho}), 128.25 (C_{meta}), 126.88 (C_{para}), 111.15 (C-β), 110.86 (C-3), 109.77 (C-4), 44.10 (CH), 25.47 (CH_2), 14.40 (CH_3).

Anal. Calcd for $C_{17}H_{21}NS_2$: C, 67.28; H, 6.97; N, 4.62; S, 21.13. Found: C, 67.17; H, 7.11; N, 4.74; S, 21.28.

2-[Bis(ethylsulfanyl)methyl]-5-thienyl-1-vinylpyrrole (2d)

Red viscous oil; n_D^{20} 1.4998.

IR (KBr): 3106, 3065, 3030, 2967, 2926, 2869, 1667, 1641, 1603, 1559, 1507, 1470, 1448, 1412, 1399, 1374, 1359, 1325, 1298, 1263, 1217, 1188, 1156, 1074, 1050, 1029, 970, 911, 782, 757, 727, 699, 658, 617, 605, 513, 492 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.18 (dd, *J* = 4.9 Hz, *J* = 1.2 Hz, 1 H, H-5′), 7.00 (dd, *J* = 3.4 Hz, *J* = 1.2 Hz, 1 H, H-3′), 6.97 (dd, *J* = 4.9 Hz, *J* = 3.4 Hz, 1 H, H-4′), 6.88 (dd, J_{B-X} = 15.7 Hz, J_{A-X} = 8.7 Hz, 1 H, H_X), 6.34 (d, *J* = 3.7 Hz, 1 H, H-3), 6.24 (d, *J* = 3.7 Hz, 1 H, H-4), 5.41 (d, J_{B-X} = 15.5 Hz, 1 H, H_B), 5.40 (s, 1 H, CH), 5.26 (d, J_{A-X} = 8.7 Hz, 1 H, H_A), 2.66 (m, 2 H, CH_2), 2.53 (m, 2 H, CH_2), 1.22 (t, *J* = 7.3 Hz, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.04 (C-2′), 131.59 (C-α), 131.58 (C-2), 128.19 (C-4′), 127.68 (C-5), 125.74 (C-3′), 124.74 (C-5′), 113.17 (C-β), 110.80 (C-3), 110.39 (C-4), 44.84 (CH), 25.45 (CH_2), 14.37 (CH_3).

Anal. Calcd for $C_{15}H_{19}NS_3$: C, 58.21; H, 6.19; N, 4.53; S, 31.08. Found: C, 58.08; H, 6.26; N, 4.62; S, 31.14.

2-[Bis(ethylsulfanyl)methyl]-1-vinyl-4,5-dihydrobenz[*g*]indole (2e)

Orange-red viscous oil; n_D^{20} 1.4586.

IR (KBr): 3106, 3057, 3014, 2968, 2926, 2869, 2837, 2725, 1653, 1639, 1602, 1552, 1541, 1497, 1480, 1452, 1438, 1416, 1377, 1337, 1296, 1260, 1209, 1193, 1162, 1134, 1119, 1099, 1050, 1009, 970, 935, 912, 870, 836, 813, 785, 759, 736, 706, 669, 652, 602, 474 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.50 (m, 1 H, H-9), 7.13 (m, 1 H, H-6), 7.08 (m, 1 H, H-8), 7.06 (dd, J_{B-X} = 15.7 Hz, J_{A-X} = 8.3 Hz, 1 H, H_X), 6.97 (m, 1 H, H-7), 6.22 (s, 1 H, H-3), 5.48 (d, J_{B-X} = 15.7 Hz, 1 H, H_B), 5.35 (d, J_{A-X} = 8.3 Hz, 1 H, H_A), 5.10 (s, 1 H, CH), 2.83 (m, 2 H, H-5), 2.65 (m, 2 H, CH_2), 2.59 (m, 2 H, H-4), 2.53 (m, 2 H, CH_2), 1.22 (t, *J* = 7.3 Hz, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 136.15 (C-5a), 132.70 (C-α), 131.66 (C-2), 129.70 (C-9a), 129.08 (C-9b), 128.38 (C-6), 126.24 (C-8), 125.05 (C-7), 122.97 (C-3a), 121.72 (C-9), 112.79 (C-β), 109.42 (C-3), 44.73 (CH), 30.85 (C-5), 22.51 (CH_2), 22.47 (C-4), 14.40 (CH_3).

Anal. Calcd for $C_{19}H_{23}NS_2$: C, 69.26; H, 7.04; N, 4.25; S, 19.46. Found: C, 69.13; H, 7.19; N, 4.12; S, 19.39.

Synthesis of 1-(2-Ethylthioethyl)pyrrole-2-carbaldehydes; Typical Procedure

A mixture of pyrrole **1c** (0.20 g, 1 mmol), ethanethiol (0.07 g, 1 mmol) and AIBN (0.02 g, 1% with respect to total mass) in benzene (2 mL) was placed to a glass ampule under argon. The ampoule was sealed and kept at 75 °C for 4 h. After carefully opening the vial, the solvent and ethanethiol were removed under vacuum and the crude product was purified by column chromatography (Al_2O_3; *n*-hexane–Et_2O, 2:1) to afford the adduct **3c** (0.20 g, 77%).

1-(2-Ethylthioethyl)pyrrole-2-carbaldehyde (3a)

Light-yellow viscous oil; n_D^{20} 1.3840.

IR (KBr): 3132, 3109, 3035, 2966, 2927, 2871, 2851, 2806, 2770, 2722, 1528, 1479, 1440, 1405, 1370, 1322, 1282, 1267, 1233, 1219, 1177, 1139, 1077, 1058, 1031, 978, 943, 884, 767, 747, 710, 682, 608 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.47 (s, 1 H, CHO), 6.94 (m, 1 H, H-5), 6.88 (dd, *J* = 4.2 Hz, *J* = 1.7 Hz, 1 H, H-3), 6.16 (dd, *J* = 4.2 Hz, *J* = 2.7 Hz, 1 H, H-4), 4.40 (m, 2 H, H-α), 2.80 (m, 2 H, H-β), 2.40 (q, *J* = 7.3 Hz, 2 H, CH_2), 1.19 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.83 (CHO), 131.66 (C-5), 130.98 (C-2), 124.93 (C-3), 109.58 (C-4), 49.50 (C-α), 32.41 (C-β), 25.94 (CH_2), 14.84 (CH_3).

Anal. Calcd for $C_9H_{13}NOS$: C, 58.98; H, 7.15; N, 7.64; S, 17.49. Found: C, 59.07; H, 7.10; N, 7.48; S, 17.81.

1-(2-Ethylthioethyl)-4,5,6,7-tetrahydroindole-2-carbaldehyde (3b)

Yellow viscous oil; n_D^{20} 1.3712.

IR (KBr): 2996, 2928, 2871, 2852, 1654, 1514, 1490, 1468, 1460, 1448, 1441, 1421, 1380, 1366, 1344, 1322, 1286, 1266, 1229, 1175,

1132, 1108, 1057, 1020, 950, 852, 829, 816, 744, 706, 593, 481, 458 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1 H, CHO), 6.63 (s, 1 H, H-3), 4.32 (m, 2 H, H-α), 2.78 (m, 2 H, H-β), 2.64 (m, 2 H, H-7), 2.52 (q, *J* = 7.3 Hz, 2 H, CH_2), 2.50 (m, 2 H, H-5), 1.85 (m, 2 H, H-6), 1.76 (m, 2 H, H-4), 1.26 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 177.97 (CHO), 139.90 (C-7a), 130.35 (C-2), 123.64 (C-3), 120.33 (C-3a), 45.52 (C-α), 32.04 (C-β), 26.17 (CH_2), 23.35 (C-7), 22.96 (C-6), 22.83 (C-4), 22.29 (C-5), 15.06 (CH_3).

Anal. Calcd for $C_{13}H_{19}NOS$: C, 65.78; H, 8.07; N, 5.90; S, 13.51. Found: C, 65.48; H, 8.13; N, 6.16; S, 13.57.

1-(2-Ethylthioethyl)-5-phenylpyrrole-2-carbaldehyde (3c)
Orange-red viscous oil; n_D^{20} 1.4113.

IR (KBr): 3114, 3061, 3029, 2968, 2926, 2870, 2803, 2755, 2721, 1671, 1654, 1638, 1605, 1578, 1532, 1502, 1460, 1424, 1395, 1368, 1336, 1289, 1267, 1219, 1158, 1099, 1074, 1039, 1001, 979, 921, 789, 759, 700, 671, 632, 538, 505, 457 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.32 (s, 1 H, CHO), 7.45 (m, 2 H, H_{ortho}), 7.37 (m, 2 H, H_{meta}), 7.29 (m, 1 H, H_{para}), 6.98 (d, *J* = 4.0 Hz, 1 H, H-3), 6.28 (d, *J* = 4.0 Hz, 1 H, H-4), 4.45 (m, 2 H, H-α), 2.78 (m, 2 H, H-β), 2.51 (q, *J* = 7.3 Hz, 2 H, CH_2), 1.25 (t, *J* = 7.3 Hz, 6 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.31 (CHO), 144.50 (C-5), 132.05 (C-2), 131.33 (C_{ipso}), 128.77 (C_{ortho}), 128.25 (C_{meta}), 126.88 (C_{para}), 125.58 (C-3), 111.37 (C-4), 44.79 (C-α), 31.98 (C-β), 25.59 (CH_2), 14.77 (CH_3).

Anal. Calcd for $C_{15}H_{17}NOS$: C, 69.46; H, 6.61; N, 5.40; S, 12.36. Found: C, 69.62; H, 6.70; N, 5.53; S, 12.44.

1-(2-Ethylthioethyl)-5-thienylpyrrole-2-carbaldehyde (3d)
Dark-orange crystals; mp 23–25 °C.

IR (KBr): 3103, 3080, 2997, 2963, 2926, 2870, 2812, 2724, 1672, 1654, 1638, 1560, 1510, 1473, 1457, 1434, 1418, 1395, 1369, 1347, 1314, 1285, 1230, 1195, 1177, 1072, 1039, 969, 951, 898, 847, 779, 746, 706, 629, 593, 500, 481, 458 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.51 (s, 1 H, COH), 7.41 (dd, *J* = 5.2 Hz, *J* = 1.2 Hz, 1 H, H-5′), 7.16 (dd, *J* = 3.7 Hz, *J* = 1.2 Hz, 1 H, H-3′), 7.11 (dd, *J* = 5.2 Hz, *J* = 3.7 Hz, 1 H, H-4′), 6.91 (d, *J* = 4.2 Hz, 1 H, H-3), 6.35 (d, *J* = 4.2 Hz, 1 H, H-4), 4.57 (m, 2 H, H-α), 2.79 (m, 2 H, H-β), 2.51 (q, *J* = 7.3 Hz, 2 H, CH_2), 1.23 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 179.00 (COH), 136.54 (C-5), 132.69 (C-2), 132.07 (C-2′), 127.99 (C-3′), 127.85 (C-4′), 127.44 (C-5′), 124.97 (C-3), 112.50 (C-4), 46.31 (C-α), 32.00 (C-β), 25.90 (CH_2), 15.07 (CH_3).

Anal. Calcd for $C_{13}H_{15}NOS_2$: C, 58.84; H, 5.70; N, 5.28; S, 24.16. Found: C, 58.98; H, 5.65; N, 5.31; S, 24.23.

1-(2-Ethylthioethyl)-4,5-dihydrobenz[*g*]indole-2-carbaldehyde (3e)
Lilac crystals; mp 56–58 °C.

IR (KBr): 3102, 3052, 2998, 2972, 2957, 2929, 1653, 1640, 1536, 1506, 1471, 1463, 1452, 1436, 1425, 1414, 1383, 1367, 1306, 1292, 1282, 1239, 1228, 1205, 1183, 1143, 1114, 1090, 1053, 988, 974, 905, 864, 849, 823, 797, 765, 744, 703, 481 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 9.46 (s, 1 H, COH), 7.50 (m, 1 H, H-9), 7.31 (m, 1 H, H-8), 7.29 (m, 1 H, H-6), 7.22 (m, 1 H, H-7), 6.76 (s, 1 H, H-3), 4.78 (m, 2 H, H-α), 3.00 (m, 2 H, H-β), 2.80 (q, *J* = 7.3 Hz, 2 H, CH_2), 2.67 (m, 2 H, H-4), 1.23 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 178.39 (COH), 139.11 (C-5a), 137.84 (C-9b), 131.96 (C-2), 129.20 (C-9a), 128.05 (C-6), 127.93 (C-8), 127.33 (C-7), 123.82 (C-3a), 123.05 (C-9), 122.61 (C-3), 47.34 (C-α), 31.51 (C-β), 31.16 (C-5), 25.89 (CH_2), 22.19 (C-4), 15.26 (CH_3).

Anal. Calcd for $C_{17}H_{19}NOS$: C, 71.54; H, 6.71; N, 4.91; S, 11.23. Found: C, 71.45; H, 6.68; N, 4.99; S, 11.11.

2-[Bis(ethylsulfanyl)methyl]-1-(2-ethylthioethyl)-5-phenylpyrrole (4c)
A solution of formylpyrrole **3c** (0.2 g, 0.8 mmol), ethanethiol (0.2 g, 3 mmol) and TFA (0.005 g) in benzene (2 mL) was kept at r.t. for 1.5 h, until consumption of **3c** was complete (monitored by GC). The mixture was shaken with $NaHCO_3$ (0.10 g) and the residue was decanted and washed with benzene (3 × 0.5 mL). After the removal of benzene and ethanethiol under vacuum, the crude product was purified by column chromatography (Al_2O_3; *n*-hexane–Et_2O, 2:1) to give thioacetal **4c** (0.27 g, 94%).

Yellow-orange viscous oil; n_D^{20} 1.5101.

IR (KBr): 3103, 3061, 3028, 2966, 2925, 2869, 2828, 1575, 1550, 1505, 1467, 1456, 1415, 1375, 1349, 1314, 1265, 1232, 1196, 1178, 1155, 1073, 1052, 1026, 972, 916, 855, 782, 756, 661, 607, 549, 480 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.40 (m, 2 H, H_{ortho}), 7.39 (m, 2 H, H_{meta}), 7.32 (m, 1 H, H_{para}), 6.30 (d, *J* = 3.7 Hz, 1 H, H-3), 6.07 (d, *J* = 3.7 Hz, 1 H, H-4), 4.29 (m, 2 H, H-α), 2.72 (m, 2 H, CH_2), 2.60 (m, 2 H, CH_2), 2.56 (m, 2 H, H-β), 2.24 (q, *J* = 7.3 Hz, 2 H, CH_2), 1.28 (t, *J* = 7.3 Hz, 6 H, CH_3), 1.07 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.33 (C-5), 133.69 (C_{ipso}), 129.51 (C-2), 129.21 (C_{ortho}), 128.43 (C_{meta}), 127.32 (C_{para}), 108.73 (C-4), 109.93 (C-3), 44.61 (CH), 44.61 (C-α), 31.50 (C-β), 25.59 (CH_2), 25.44 (CH_2), 14.83 (CH_3), 14.44 (CH_3).

Anal. Calcd for $C_{19}H_{27}NS_3$: C, 62.42; H, 7.44; N, 3.83; S, 26.31. Found: C, 62.54; H, 7.37; N, 4.00; S, 26.48.

1-(2-Ethylthioethyl)-2-ethylthiomethylpyrrole (5c)
A mixture of thioacetal **4c** (0.20 g, 0.6 mmol), ethanethiol (0.20 g, 3.0 mmol) and AIBN (0.02 g, 1% with respect to total mass) in benzene (2 mL) was sealed in ampoule and heated at 75 °C for 6 h. After cooling, the ampoule was carefully opened and the volatile components (ethanethiol, diethyldisulfide and benzene) were removed under vacuum (3 mm Hg). GC analysis of the resulting mixture showed it to contain **4c** (15%), **5c** (80%) and unidentified impurities (5%).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.42 (m, 2 H, H_{ortho}), 7.34 (m, 2 H, H_{meta}), 7.25 (m, 1 H, H_{para}), 6.08 (d, *J* = 3.7 Hz, 1 H, H-3), 6.06 (d, *J* = 3.7 Hz, 1 H, H-4), 4.26 (m, 2 H, H-α), 3.90 (s, 2 H, CH_2SEt), 2.60 (m, 2 H, H-β), 2.51 (q, *J* = 7.3 Hz, 2 H, CH_2), 2.24 (q, *J* = 7.3 Hz, 2 H, CH_2), 1.19 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.17 (t, *J* = 7.3 Hz, 3 H, CH_3).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.50 (C-5), 133.71 (C_{ipso}), 129.21 (C_{ortho}), 128.70 (C-2), 128.43 (C_{meta}), 127.32 (C_{para}), 109.90 (C-3), 108.91 (C-4), 44.77 (C-α), 32.02 (C-β), 27.70 (CH_2SEt), 25.60 (CH_2), 25.55 (CH_2), 14.77 (CH_3), 14.47 (CH_3).

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