# CONVENIENT METHOD OF PREPARING 3-SUBSTITUTED 2,2'-FURYL(THIENYL)PYRROLES

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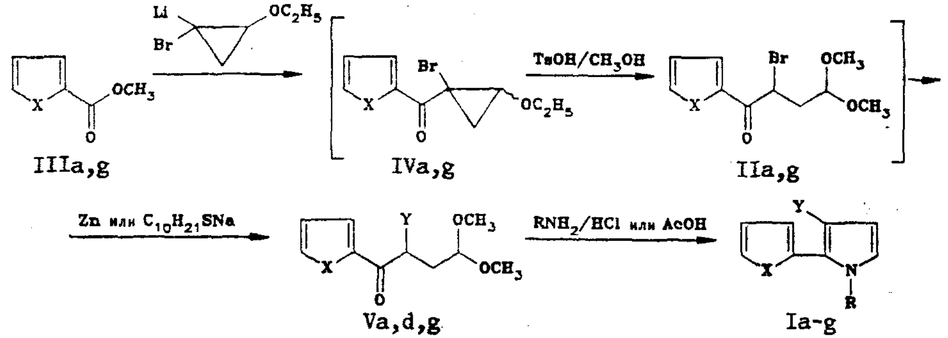
*2,2'-Furyl(thienyl)pyrroles and their 3-decylthio derivatives were synthesized by the Paal—Knorr reaction from the corresponding 3-unsubstituted or 3-decylthio-substituted dimethylacetals of 4-(2-furyl)- and 4-(2-thienyl)-4-oxobutanal. The starting materials were synthesized in three stages from methyl-2-furan- and -2-thiophenecarboxylates. The latter were treated with 1-bromo-2-ethoxycyclopropyllithium via acid-catalyzed methanolysis of the 1-bromo-2-ethoxyketones formed and further reaction with zinc powder or sodium decylthiolate.*

2,2'-Hetaroarylpyrroles are interesting as monomer precursors of conducting polymeric materials [1]. Properties of the latter, particularly their solubility in organic solvents, depend on the presence of a substituent in the 3-position of the heterocycle [2, 3]. In this work we report a convenient synthesis of the N—H, N-methyl, and N-phenyl-2,2'-furyl(thienyl)pyrroles (Ia-c) and their derivatives with decylthio groups in position 3 of the pyrrole ring Id-g (see Table 1).

The key 4-(2-furyl)- and 4-(2-thienyl)-3-bromo-1,1-dimethoxy-4-butanones (IIa, g) were obtained from methyl 2-furan- and 2-thiophenecarboxylates (IIIa, g) via the intermediate 2-furyl(thienyl)-1-bromo-2-ethoxycyclopropylketones (IVa, g) by the method reported in [4] for synthesis of 3-bromo-1,1-dimethoxy-4-alkanones. In view of their poor stability when isolated, IIa, g and IVa, g were used in further reactions without additional purification. Reduction of bromoacetal IIa with zinc in methanol by a method similar to [4] gave 4-(2-furyl)-1,1-dimethoxy-4-butanone (Va) in 81% yield (based on ether IIIa). Reaction of bromoacetals IIa, g with sodium decylthiolate in methanol gave 4-(2-furyl)- and 4-(2-thienyl)-3-decylthio-1,1-dimethoxy-4-butanones (Vd, g) in yields of 47 and 36%, respectively (based on esters IIIa, g).



I—V a,d R=H, b,e R=$CH_3$, c,f,g R=$C_6H_5$; a—f X=O, g X=S; a—c Y=H, d—g Y=$C_{10}H_{21}S$

Furylpyrrole Ia is obtained in two stages by acid hydrolysis of acetal Va to 4-(2-furyl)-2-oxobutanol (VI, 72%) and treatment of the latter with ammonium acetate in ethanol (85%). The physicochemical and spectral properties of Ia agree with those given in [5]. Pyrroles Ib-g are synthesized in 60-90% yields in a single stage by treating acetals Va, d, g with ammonium acetate, methylamine hydrochloride, or aniline in acetic acid or in a mixture of methanol—acetic acid.

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TABLE 1. Properties of the Synthesized Compounds

| Compound | Empirical formula | IR spectrum, ν, cm$^{-1}$ | PMR spectrum, δ, ppm (J, Hz) | Yield, % |
|---|---|---|---|---|
| Ia | $C_8H_7NO$ |  |  | 85 |
| Ib | $C_9H_9NO$ | 1495, 1615 | 3,3...3,5 (3H, m); 5,87 (1H, d. d $J_1=1,5$, $J_2=3,5$); 6,0...6,2 (3H, m); 6,2...6,3 (1H, m); 7,1...7,2 (1H, m) | 60 |
| Ic | $C_{14}H_{11}NO$ | 1500, 1600 | 5,4...5,5 (1H, m); 5,9...6,1 (2H, m); 6,3...6,4 (1H, m); 6,5...6,6 (1H, m); 7,0...7,3 (6H, m) | 66 |
| Id | $C_{18}H_{27}NOS$ | 1500, 1610, 3475 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 2,3...2,6 (2H, m); 6,0...6,1 (1H, m); 6,2...6,3 (1H, m); 6,4...6,5 (1H, m); 6,7...6,9 (1H, m); 7,0...7,1 (1H, m); 8,4...8,7 (1H, m) | 61 |
| Ie | $C_{19}H_{29}NOS$ | 1490, 1600 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 2,2...2,5 (2H, m); 3,56 (3H, m); 5,9...6,0 (1H, m); 6,2...6,4 (2H, m); 6,5...6,6 (1H, m); 7,2...7,3 (1H, m) | 85 |
| If | $C_{24}H_{31}NOS$ | 1500, 1600 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 2,3...2,6 (2H, m); 6,0...6,3 (3H, m); 6,6...6,7 (1H, m); 6,9...7,2 (6H, m) | 90 |
| Ig | $C_{24}H_{31}NS_2$ | 1500, 1600 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 2,3...2,6 (2H, m); 6,1...6,2 (1H, m); 6,5...6,8 (3H, m); 6,9...7,2 (6H, m) | 78 |
| Va | $C_{10}H_{14}O_4$ | 1560, 1670 | 1,6...2,0 (2H, m); 2,5...2,9 (2H, m); 3,14 (6H, s); 4,23 (1H, t, $J=6,0$); 6,36 (1H, d. d., $J_1=1,5$, $J_2=3,5$); 6,9...7,0 (1H, m); 7,4...7,5 (1H, m) | 81 |
| Vd | $C_{20}H_{34}O_4S$ | 1570, 1675 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 1,6...2,4 (4H, m); 3,04 (3H, s); 3,09 (3H, s); 3,87 (1H, d. d., $J_1=7,0$; $J_2=8,0$); 4,26 (1H, t, $J=6$); 6,3...6,4 (1H, m); 6,9...7,0 (1H, m); 7,3...7,4 (1H, m) | 47 |
| Vg | $C_{20}H_{34}O_3S_2$ | 1515, 1650, 1710 | 0,6...0,9 (3H, m); 0,9...1,3 (16H, m); 1,7...2,5 (4H, m); 3,09 (3H, s); 3,15 (3H, s); 3,93 (1H, d. d. $J_1=7,0$; $J_2=8,0$); 4,33 (1H, t, $J=6,0$); 6,8...7,1 (1H, m); 7,4...7,7 (2H, m) | 36 |
| VI | $C_8H_8O_3$ | 1570, 1680, 1735 | 2,6...3,2 (4H, m); 6,43 (1H, d. d, $J_1=1,5$; $J_2=3,5$); 7,10 (1H, d., $J=3,5$); 7,3...7,5 (1H, m); 9,71 (1H, s) | 72 |

## EXPERIMENTAL

PMR spectra were taken on a Tesla BS-467A (60 MHz) instrument with HMDS internal standard (5-10% solution in $CCl_4$) and IR spectra on a Specord IR-75 spectrophotometer. The purity of the synthesized compounds was checked by TLC on neutral $Al_2O_3$ grade II activity and also on Silufol plates with iodine vapor visualization. Column chromatography was carried out on neutral $Al_2O_3$ activity II grade and on silica gel (40-100 μm).

Elemental analytical data for C and H for these substances agreed with those calculated.

**2,2′-Furylpyrrole Ia.** A mixture of aldehyde VI (1.52 g, 10 mmoles), ammonium acetate (7.7 g, 100 mmoles), and ethanol (30 ml) was refluxed for 10 min. The ethanol was distilled off in vacuo, aqueous sodium bicarbonate solution was added (5%, 80 ml), and the product extracted with ether (3 × 25 ml). The total extract was dried with anhydrous sodium sulfate, the ether distilled off, and the residue chromatographed on an $Al_2O_3$ column (ether—hexane, 1:6) to give Ia (1.13 g) with mp 40-41°C (from hexane). According to [5], mp 44°C.

**N-Methylpyrroles Ib, e.** A mixture of acetal Va or Vd (4 mmoles), methylamine hydrochloride (5.4 g, 80 mmoles), absolute methanol (20 ml), and glacial acetic acid (40 ml) was refluxed for 4-5 h until disappearance of the starting acetal. Water (200 ml) was added to the cooled reaction mixture and the product extracted with ether (3 × 50 ml). The combined extract was washed with saturated aqueous sodium bicarbonate to neutrality and dried with anhydrous sodium sulfate. After evaporation of ether, chromatography on a silica gel column (hexane) gave compound Ib with bp 97-98°C (10 mm Hg) and $n_D^{16}$ 1.5888 or compound Ie.

**N-Phenylpyrroles Ic, f, g** are synthesized similarly to pyrroles Ib, e by refluxing a mixture of acetals Va, Vd, or Vg (4 mmoles), aniline (0.56 g, 6 mmoles), and glacial acetic acid (24 ml) for 15-50 min. Compound Ic: mp 36.5-37.5°C (hexane).

**3-Decylthio-2,2′-furylpyrrole Id** was prepared by refluxing a mixture of 3-decylthioacetal (1.48 g, 4 mmoles), ammonium acetate (3.08 g, 40 mmoles), and glacial acetic acid (15 ml) for 1 h. Standard workup and purification on an $Al_2O_3$ column (ether—hexane, 1:8) gave the product (0.75 g).

**3-Bromoacetals (IIa, g).** A solution of butyllithium in hexane (1.7 N, 66 ml) and ester IIIa or IIIg (60 mmoles) in ether (30 ml) were added sequentially to a solution of 1,1-dibromo-2-ethoxycyclopropane (22 g, 90 mmoles) in absolute tetrahydrofuran (60 ml) and absolute ether (240 ml) at —90 to —100°C over 1.5 h. The mixture was stirred at this temperature for 20 min and methanol added (15 ml). The product was heated to —20°C, poured into water (900 ml), and extracted with ether (3 × 50 ml). The combined extract was dried with sodium sulfate, the solvent removed, absolute methanol (150 ml) and p-toluenesulfonic acid (0.045 g, 0.25 mmole) added, and the solution refluxed for 10 min. The product was cooled to room temperature and used in subsequent stages without isolation.

**1,1-Dimethoxy-4-(2-furyl)-4-butanone (Va).** Zinc powder (9 g, 140 mmoles) was added to a solution of bromoacetal IIa obtained as above. The product was cooled to room temperature, aqueous sodium hydroxide (10%, 750 ml) added, and the solution extracted with ether (4 × 50 ml). Standard treatment and purification on an $Al_2O_3$ column (ether—hexane, 1:2) gives Va (14.4 g).

**3-Decylthioacetals (Vd, g).** A solution of sodium decylthiolate (from 110 mmoles sodium methylate and 100 mmoles decylmercaptan) in absolute methanol (45 ml) was added over 30 min at 15-18°C to a solution of bromoacetal IIa or IIg obtained as described above. The mixture was stirred for 20 min, water (400 ml) was added, and the product was extracted with ether (3 × 100 ml). The combined extract was washed with saturated aqueous sodium chloride, dried with anhydrous sodium sulfate, the solvent distilled off, and the residue chromatographed on an $Al_2O_3$ column (ether—hexane, 1:10) to give the thioacetal Vd or Vg.

**4-(2-Furyl)-4-oxobutanal (VI).** A mixture of acetal Va (0.8 g, 4 mmoles), ether (8 ml), and HCl (5%, 16 ml) was stirred for 1 h at room temperature. The organic layer was separated and the aqueous layer extracted with ether (3 × 5 ml). The combined extracts were combined with the organic layer, washed with saturated aqueous sodium bicarbonate (5 ml), and dried with anhydrous sodium sulfate. After distillation of solvent, crystallization of the residue (pentane—isopropanol, 10:1) gives aldehyde VI (0.44 g) with mp 59.5-60.5°C.

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