SYNTHESIS AND REACTIONS OF THIOPHENE SULFIDES. COMMUNICATION 40. AN UNUSUAL REACTION OF 2,5-BIS(METHYLTHIO)-3,4-BIS(o-HYDROXYPHENYLIMINOMETHYL)THIOPHENE

Ya. L. Gol'dfarb, M. A. Kalik, V. S. Bogdanov,
and V. K. Zav'yalova

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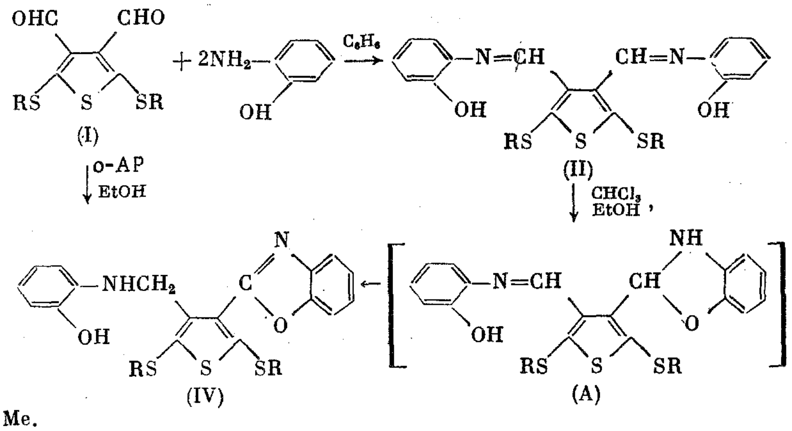
We have previously developed a convenient method for synthesis of thiophene-3,4-dialdehyde (I) substituted in the α position of the thiophene ring by two methylthio groups. An investigation of the reaction of the dialdehyde (I) with o-aminophenol (o-AP) has shown that, depending on the solvent used, isomeric compounds are formed. For example, reaction of (I) with two equivalents of o-aminophenol in benzene gives a yellow crystalline solid with mp 135-136°C, which according to its elemental analysis and IR, UV, PMR, and ^{13}C NMR spectra is 2,5-bis(methylthio)-3,4-bis(o-hydroxyphenylaminomethyl)thiophene (II):



R = Me.

The IR spectrum of the bisazomethine (II) contained bands for the associated CH group at 3420 cm⁻¹, and also (on dilution to a concentration of $6 \cdot 10^{-3}$ mole/liter) for the free OH group (3600 cm⁻¹), together with absorption for C=N (1620 cm⁻¹). The PMR spectrum in $CDCl_3$ contained two singlets (δ 2.55 and 9.26 ppm), assigned to the SMe and N=CH protons, and a multiplet for the aromatic protons in the range 6.80-7.40 ppm. The ^{13}C NMR spectrum contained 10 signals for 20 carbon atoms (δ, ppm, $J_{^{13}C, ^{1}H}$, Hz, solution in $CDCl_3$): 20.3 q (140.6) (SMe) 115.2 (160.9), 115.5 (155.4), 120.3 (161.8), 129.0 (161.8) (CH_{aromat}), 152.3 m $(=\overset{|}{C}OH)$, 135.8 m $(=\overset{|}{C}N=)$, 134.5 d (11.1) (thiophene β-C), 114.3 d.d (4.6) (thiopene α-C), and 150.9 d (163.7) (CH=N). Assignment of the signals to the appropriate carbon atoms was carried out on the basis of the δ and $J_{^{13}C, ^{1}H}$ values, and by comparison with the spectrum of a model compound (III) obtained from the dialdehyde (I) and p-anisidine: (δ, ppm, $J_{^{13}C, ^{1}H}$): 20.7 q (140.6) (SMe); 5.5 q (148.0) (OMe), 114.5 (157.2) and 122.2 m (157.2) (CH_{arom}), 158.4 m $(=\overset{|}{C}OMe)$, 145.0 m $(=\overset{|}{C}N=)$, 135.9 d.d. (11.1, 2.8) (thiophene β-C), 143.1 d.d (4.6) (thiophene α-C), 153.2 d (163.7) (CH=N), assignment of the CH=N signal being made from selective heteronuclear $^{13}C-\{^{1}H\}$ double resonance (irradiation at the frequency of the N=CH proton, δ = 9.26 ppm). In addition, high-resolution ^{13}C NMR data obtained for monosubstituted thiophenes [2] were taken into account when considering the chemical shifts and coupling constants. Thus, the ^{13}C NMR and PMR spectra confirmed the presence of all the structural fragments present, and that the structure of (II) was symmetrical.

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
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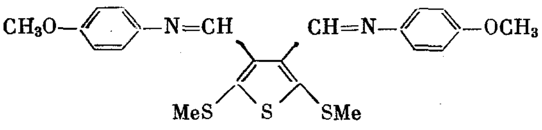

(III)

Condensation of the bisaldehyde (I) with o-aminophenol in alcohol afforded a light-colored isomeric product, mp 153-155°C. The presence of two signals (2.40 and 2.67 ppm) for the SCH_3 group in the PMR spectrum of this isomer, as opposed to one in (II), indicates that its structure is nonsymmetrical. Its IR, UV, mass, PMR, and especially its ^{13}C NMR spectra lead to the structure 2,5-bis(methylthio)-3-(2'-benzoxazolyl)-4-(o-hydroxyphenylaminomethyl)thiophene (IV). The ^{13}C NMR spectrum (in $CDCl_3$ contained 20 signals, which indicated the nonequivalence of all the carbon atoms, as would be expected for (IV) (δ, ppm) ($J_{^{13}C,\,^{1}H}$): 19.0 q (140.6) (SMe), 22.4 q (141.5) (SMe), 44.2 t (138.7) (NCH_2), 110.5 (166), 115.1 (153), 119.5 (156), 120.1 (163), 120.6 (160), 121.9 (162), 124.8 (160.9), 125 (163) ($C{-}H_{arom}$), 123.8 s, 133.2 br.s, 135.6 br.s., 141.2 br.s., 143.9 br.s., 148.3 s, 148.6 s, 149.9 m (substituted carbon atoms of the benzene and thiophene rings), 159.0 s (OC=N).

It follows from these results that changing from structure (II) to structure (I) results in the loss of the two signals for the CH=N protons, and the appearance of a signal for the two protons of the NCH_2 group (4.59 ppm) in the PMR spectrum, and correspondingly to the appearance of a singlet with δ 159.0 ppm and a triplet at 44.2 ppm (J = 138.7 Hz) in place of a doublet for the two (CH=N) carbons, all the remaining carbon atoms (Both aromatic and SMe) retaining the same multiplicities.

The structure of (IV) was also confirmed by its IR and UV spectra. Thus, the IR spectrum of (IV) in concentrations of $6 \cdot 10^{-2}$ and $6 \cdot 10^{-3}$ mole/liter contained absorption for the free OH group (3600 cm^{-1}) and a broad band at 3300 cm^{-1} assigned to the associated NH group, together with strong absorption at 1550 and 1610-1590 cm^{-1} characteristic of the benzoxazole ring. The UV spectrum of (IV), in contrast to that of (II), showed a hypsochromic shift of the long-wavelength maximum (357-365 nm) to 330 nm, and a decrease by a factor of approximately 2 in the ε value of the short-wavelength maximum (204-206 nm). These changes could be due to the formation of the cyclic benzoxazole structure and shortening of the conjugated chain as a result of the hydrogenation of one of the C=N bonds.

The bisazomethine (II) is stable on storage in the solid state or in solution benzene, whereas in solvents such as chloroform and ethanol it is gradually converted into (IV), as is well shown by PMR and ^{13}C NMR spectroscopy over a period of time.* This transition is seen in highly dilute solutions (10^{-2}-10^{-3} mole/liter), suggesting that this is an intramolecular reaction.

Although the reaction mechanism is not yet clear, it may be assumed that in polar solutions the formation of the benzoxazoline intermediate (A) is possible (see reaction sequence), this then undergoes facile conversion into the aromatic benzoxazole system with the loss of two hydrogen atoms, which, however, then adds to the azomethine group of the other half of the molecule. The ease with which this reaction takes place (absence of catalyst, 20°C) is apparently due to the spatial arrangement of the substituents in the 3 and 4 positions of the thiophene ring, facilitating proton transfer by the possible formation of N...H, N or CH...N hydrogen bonds. In addition, examination of skeletal and Stuart—Briegleb models shows that the structure (IV) thus formed, containing the aromatic benzoxazole system, is less strained.

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*After only a few hours at 20°C, the spectra of (II) in $CDCl_3$ show signals for (IV), and after 3 days the signals for each compound are of approximately equal intensity. After 5-6 days, the signals for (II) disappear completely, only the spectrum of (IV) being seen.

EXPERIMENTAL

IR spectra were obtained on UR-20 and Specord IR-75 spectrophotometers. PMR and ^{13}C NMR spectra were obtained on a Bruker WM-250 spectrometer (250 MHz) in impulse mode. Chemical shifts are given on the δ scale relative to TMS. UV spectra were obtained on Specord UV-VIS spectrometer. Molecular weights were determined by mass spectrometry on a Varian MAT CH-6 mass spectrometer, using an ionizing voltage of 70 eV, with direct introduction of the sample into the ion source.

2,5-Bis(methylthio)-3,4-bis-(N,N'-o-hydroxyphenyliminomethyl)thiophene (II). A solution of 0.46 g (2 mmoles) of (I) and 0.432 g (4 mmoles) of o-aminophenol in 20 ml of dry benzene was boiled for 30 min, the solvent removed, and the residue (0.81 g) recrystallized from bezene* to give (II), mp 136-137°C, yield 66.5%. PMR spectrum (in $CDCl_3$), δ, ppm): 2.55 s (6H, 2,5-SCH_3), 6.8-7.3 m (10H, C_6H_4OH), 9.26 s (2H, CH=N), in C_6D_6): 1.88 s (SCH_3), 6.85-7.02 m (C_6H_4OH), 9.12 s (CH=N). IR spectrum (in chloroform, ν, cm^{-1}): a) $6\cdot10^{-2}$ mole/liter: 3420 (OH), 1620 (C=N); b) at $6\cdot10^{-3}$ mole/liter: 3600, 3420 (OH), 1620-1630 (C=N); c) KBr disks: 3360 (OH), 1615 (C=N), UV spectrum [λ_{max}, nm (ε)]: a) in chloroform, $CHCl_3$, 263 (24800), 302 (18800), 365(21800); b) in ethanol, 204 (70100), 245 (25900), 290 (20900), 357 (12500). Found: C 57.93; H 4.47; N 6.31; S 23.15%. M 414. $C_{20}H_{18}N_2O_2S_3$ Calculated: C 57.94; H 4.38; N 6.76; S. 23.20. M 414.5.

2,5-Bis(methylthio)-3-(2'-benzoxazolyl)-4-(o-hydroxyphenylaminomethyl)thiophene (IV). a) A solution of 0.46 g (2 mmoles) of (I) and 0.43 g (4 mmoles) of o-aminophenol in 20 ml of absolute alcohol was boiled for 30 min, and the dark-colored solution was cooled, the solid filtered off, and washed with chloroform to give 0.43 g (52.5%) of (IV), mp 153-155°C (from ethyl acetate with decolorizing charcoal). PMR spectrum (in $CDCl_3$, δ, ppm): 2.40, 2.67 s (6H, 2.5-SCH_3), 4.59 s (2H, CH_2N), 6.82-7.90 m (10H, CH_{arom}, NH, OH); C_6H_6: 1.91, 1.99 s (SCH_3), 4.63 (CH_2N), 6.64-7.89 m (aromatic protons). IR spectrum in chloroform (ν, cm^{-1}): concentration $6\cdot10^{-2}$ and $6\cdot10^{-3}$ mole/liter: 3600 (OH), 1610 (C=N), 3300 br (NH), 1590 w, 1555s. UV spectrum [λ_{max}, nm (ε)]: $CHCl_3$—245 (24900), 256 (26500), 286 (33500), 335 (14400); and EtOH—206 (40900), 240 (17000), 253 (20400), 285 (22800), 330 (9600). Found: C 57.93; H 4.58; N 6.63; S 23.07%. M 414. $C_{20}H_{18}N_2O_2S_3$. Calculated: C 57.94; H 4.38; N 6.76; S 23.20%, M 414.5. b) a solution of 0.07 g of (II) in 1 ml of chloroform was kept at 20°C for 6 days, evaporated, and the residue recrystallized from ethyl acetate to give (IV), mp 150-151°C.

2,5-Bis(methylthio)-3,4-bis-(p-methoxyphenyliminomethyl)thiophene (III). A solution of 0.5 g (2.16 mmoles) of (I) for 0.54 g (4.34 mmoles) of p-anisidine in 15 ml of absolute alcohol was boiled for 30 min, the alcohol removed under reduced pressure, and the residue washed with hot C_7H_{16} and filtered. Recrystallization from alcohol gave 0.8 g (85%) of the Schiff's base (III), mp 105-106°C. PMR spectrum in $CDCl_3$ (δ, ppm): 2.54 s (6H, 2.5-SCH_3), 3.83 s (6H, OCH_3), 6.92-7.30 m (8H, C_6H_4), 9.26 s (CH=N); in CCl_4, 2.49 s (SCH_3), 3.71 s (OCH_3), 6.79-7.09 m (C_6H_4), 9.16 s (CH=N), IR spectrum in chloroform (ν, cm^{-1}): 1618 (C=N). UV spectrum in alcohol [λ_{max}, nm (ε)]: 880 (16600), 375 (34800), 294 (34300), 247 (70800). Found: C 59.59; H 5.21; N 6.42; S 21.57%. M 442. $C_{22}H_{22}N_2O_2S_3$. Calculated: C 59.69; H 5.01; N 6.33; S 21.73%. M 422.61.

CONCLUSIONS

In polar solvents (ethanol and chloroform), 2,5-bis(methylthio)-3,4-bis-(o-hydroxyphenyliminomethyl)thiophene undergoes intramolecular rearrangement to 2,5-bis(methylthio)-3-(2'-benzoxazolyl)-4-(o-hydroxyphenylaminomethyl)thiophene.

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*When ethyl acetate was used for recrystallization, 0.9 g of product gave 0.32 g of the bisazomethine (II) and 0.48 g of (IV).

LITERATURE CITED

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