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SYNTHESIS OF 3,4-BIS (4'-METHYLPHENYL) THIENO [2,3-b]THIOPHENE: FIRST EXAMPLE OF PERI-DIARYL THIENOTHIOPHENE

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ABSTRACT: 3,4-bis(4'-methylphenyl) thienothiophene, the first example of peri-(3,4) diaryl thienothiophene has been synthesized by a sequence involving preparation of ketene dithioacetal, Dieckmann type cyclization, ester hydrolysis and decarboxylation.

Thieno [2,3-b] thiophene system^{1,2} is of potential interest to us with respect to i) exploring its π -excessive character in many recent applications³ and ii) developing sterically crowded molecules by placing appropriate aryl substituents at its peri- (i.e. 3 and 4) positions, for conformational analysis⁴. Though, a plethora of substituted thieno[2,3-b] thiophenes are known⁵, surprisingly not a single example of thieno [2,3-b] thiophene bearing aryl substituent both at its 3 and 4 positions could be located in the literature. This fact prompted us to develop the first synthesis of a model, 3,4- diaryl substituted thienothiophene, namely, 3,4- bis(4'- methylphenyl) thieno[2,3-b] thiophene (1)⁶ which is described in this paper.

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The synthetic sequence for the target molecule 1 utilizes the well known Dieckmann cyclization protocol⁷ and is depicted in the Scheme 1. To begin with, the condensation of the known diketone $(2)^8$ with CS₂ and ethyl bromoacetate under our recently described procedure⁹ (anhyd. DMF/KF, RT, 2 h) produced ketene dithioacetal (3) as a reddish oil in 66% yield. The structure is supported by elemental analysis and spectral data. On treatment with sodium ethoxide in absolute ethanol, compound (3) cleanly and spontaneously cyclized to provide thienothiophene diester

(4) as a colorless crystalline solid, m.p. 154-56°C in excellent yield. Though, the molecule (4) is apparently symmetric, its IR spectrum showed not one but two ester carbonyl absorptions at 1735 and 1680 cm⁻¹ which most likely arise due to anti (in and out) orientation of ester groups as shown in the structure 4. Its ¹H nmr, however, revealed a clean triplet and a quartet (δ 1.2 and δ 4.20; J = 7 Hz each) for -OCOCH₂CH₃ groups, a singlet at δ 2.1 for aromatic methyls and a singlet at δ 6.7 for aromatic protons (4 H) on account of accidental magnetic equivalence of these protons. The ¹H nmr spectrum thus displayed characteristics attributable to predominantly single conformer whereas the IR data imply higher rotational barrier around the ester - thienothiophene bonds¹⁰.

The diester (4) was submitted to hydrolysis under basic condition (aq. KOH in CH₃OH, reflux) to afford upon acidification, diacid (5) in good yield. The final step, the decarboxylation of (5) was carried out under thermal condition (250°C, 10 min.) to provide after SiO₂ column chromatographic purification of the crude, the desired product, 3,4- bis (4'-methylphenyl) thieno[2,3-b] thiophene (1) in 60 % yield. The compound (1) analyzed accurately for $C_{20}H_{16}S_2$ (M' at m/z 320) and showed in its ¹H nmr a sharp singlet at δ 2.3 due to the aromatic methyl and an overlapping double doublet (J = 6 Hz) between δ 6.9 and δ 7.0 for the aromatic protons, the proton belonging to the thienothiophene moiety appeared as a singlet at δ 7.2. These spectral data are fully consistent with highly symmetrical structural for (1).

The above synthesis of (1) thus constitutes the first example of peri-diaryl thienothiophene system and moreover the adopted methodology appears well suited to provide access to other homo- and heteroaryl peri-di substituted thienothiophenes. Our results on novel donor- acceptor 3,4- di

aryl thienothiophenes synthesized using the above methodology will be reported elsewhere.

EXPERIMENTAL

Melting points (uncorrected) were determined on a Gallenkamp melting point apparatus. IR spectra were recorded on a Shimadzu FTIR-4200 spectrophotometer as oil film or KBr discs. ¹H NMR spectra were taken on a Varian EM-360L (60 MHz) spectrometer with TMS as internal standard.

Preparation of ketene dithioacetal (3) - To a vigorously stirred solution of 1.3-bis-(4-methylphenyl) 1.3-propanedione 2⁸ (3.75 g, 15 mmol) in dry DMF (30 ml) at room temperature were added in quick succession, commercially available anhydrous KF (12 g), freshly distilled carbon disulfide (1.4 ml, ca. 20 mmol) and ethyl bromoacetate (5.1 g, 30 mmol) and stirring was maintained for 2 h. The reaction mixture was diluted with cold water and extracted with diethyl ether (3 x 100 ml). The combined organic extract was washed with 10 % NaOH, followed by water and dried over anhyd. Na₂SO₄. Removal of solvent gave a dark red oil which was purified by SiO₂ column chromatography (petroleum ether : ethyl acetate 70: 30 as eluent) to give 3 as a red oil in 66 % yield (4.95 g). IR (oil film): 2940, 1720, 1685, 1660, 1620, 1470, 1380, 1185, 1120, 1040, 950 cm^{-1} ; ¹Hnmr (CDCl₃) : δ 1.2 (3H, t, J= 8 Hz), 2.45 (3H, s), 3.12 (2H, overlapping dd, J=9 Hz), 4.1 (2 H, q, J=8 Hz), 7.2 (2 H, d, J=7 Hz). 7.9 (2H, d, J = 7 Hz). Anal. calc. for C_{26} H₂₈ O₆ S₂ : C, 62.49; H, 5.60; S, 12.80. Found : C, 62.13; H, 5.87; S, 13.09.

Formation of 3,4-bis(4'-methylphenyl) thieno(2,3-b) thiophene 2,5diethyl dicarboxylate (4)- Sodium ethoxide was prepared from sodium (460 mg, 20 mmol) in 50 ml of absolute ethyl alcohol to which, at room temperature, was rapidly added Ketene dithioacetal 3 (3.20 g, 6.4 mmol). The reaction was stirred vigorously whereupon within a minute a copious white solid precipitated out from the reaction mixture. The reaction was stirred at room temperature for a period of 45 min, poured on crushed ice and the solid allowed to settle. The white solid was filtered, washed with little chilled ethanol and finally crystallized from ethanol to provide crystals of 4, m.p. 154-56°C in 70 % yield (2.07 g). IR (KBr); 2985, 1735, 1680, 1505, 1390, 1285, 1178, 1070, 830 cm⁻¹ : ¹H nmr (CDCl₃); δ 1.2 (3H, t, J = 7 Hz), 2.1 (3H, s), 4.2 (2H, q, J= 7 Hz), 6.7 (4 H, s). Anal. cacl. for C₂₆ H₂₄ O₄ S₂ : C, 67.24; H, 5.17; S, 13.79. Found : C, 67.40; H, 4.88; S, 13.56.

Formation of diacid (5) - The diester 4 (1.0 g, 2.15 mmol) was boiled in 100 ml of methanol and 30 ml of 10 % aq. KOH was added dropwise during 20 min. The reaction was refluxed further for 48 hr, cooled to room temperature and slight insoluble residue filtered off. The clear filtrate was neutralized with conc. HCl and the precipitated acid filtered, washed with cold water and air dried to give 5 in 76 % yield (0.67 g), m.p. 245-50°C; IR (KBr): 3400, 3060, 1680, 1620, 1580, 1500, 1340, 1305, 1220, 1150, 880 cm⁻¹; Anal. calc. for C₂₂ H₁₆ O₄ S₂ : C, 64.70; H, 3.92; S, 15.68. Found : C, 64.97; H, 4.05; S, 15.31.

Formation of 3,4- bis (4'- methylphenyl) thieno[2,3-b] thiophene (1) -Diacid 5 (204 mg, 0.5 mmol) was heated in a pyrex tube by immersing in a silicon oil bath kept at 250-60°C for a period of 10 min. whereby considerable browning of the solid occurred along with evolution of CO_2 . After cooling the contents to room temperature, the crude product was dissolved in minimum of CHCl₃ and loaded on silica gel column. Elution of the column with petroleum ether (60-80°C fraction) gave product 1 as a pale yellow solid in 60 % yield (102 mg), m.p. 242-43°C; IR (KBr) : 2905, 11490, 1355, 1240, 1225, 1180, 1020, 975, 815 cm⁻¹; ¹H nmr (CDCl₃) ; δ 2.3 (3H, s), 6.9 to 7.0 (4H, dd, J = 6.0 Hz each), 7.2 (1H, s). Anal. calc. for C₂₀H₁₆S₂ : C, 75.00; H, 5.00; S, 20.00. Found : C, 75.30; H, 5.32; S, -19.75.

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