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ORIGINAL ARTICLE

Synthesis of 3-chloro-*N*′-(2-hydroxy-6-pentadecylbenzylidene)benzothiophene-2-carbohydrazide

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KEYWORDS

Pentadecylbenzaldehyde;
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Abstract 3-Chloro-*N*′-(2-hydroxy-6-pentadecylbenzylidene)benzothiophene-2-carbohydrazide has been synthesized by the reaction of 2-hydroxy-6-pentadecylbenzaldehyde with 3-chloro-1-benzothiophene-2-carboxylicacidhydrazide in the presence of glacial acetic acid in ethanol. The structure of this new compound was confirmed by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR and mass spectral analysis.

1. Introduction

Heterocyclic compounds containing nitrogen and sulfur exhibit a wide variety of biological activities such as antifungal (Ramesh and Maheswaran, 2003), antitumor (Silveira da et al., 2008) and anti-HIV (Pandeya et al., 1999). The thiophene ring dramatically increases the diversity of certain biological properties such as antibacterial (Shivarama Holla et al., 2003), antiviral (El-Sabbagh et al., 2009) and antitubercular (Mallikarjuna et al., 2009). In this paper, the synthesis of 3-chloro-*N*′-(2-hydroxy-6-pentadecylbenzylidene)benzothiophene-2-carbohydrazide by the condensation of 2-hydroxy-6-pentadecylbenzaldehyde and 3-chloro-1-benzo[*b*]thiophene-2-carboxylicacidhydrazide.

2. Results and discussion

Cardanol is a mixture of natural alkyl phenols obtained by vacuum distillation of cashew nut shell liquid (CNSL). The structure and composition of cardanol is given in Fig. 1. It is a mixture of saturated and unsaturated (mono-, di,- and tri-) compounds.

Cardanol is a phenolic compound with a C_{15} aliphatic chain in the meta position, obtained from cashew nut shell liquid (CNSL) and then formylation of hydrogenated cardanol

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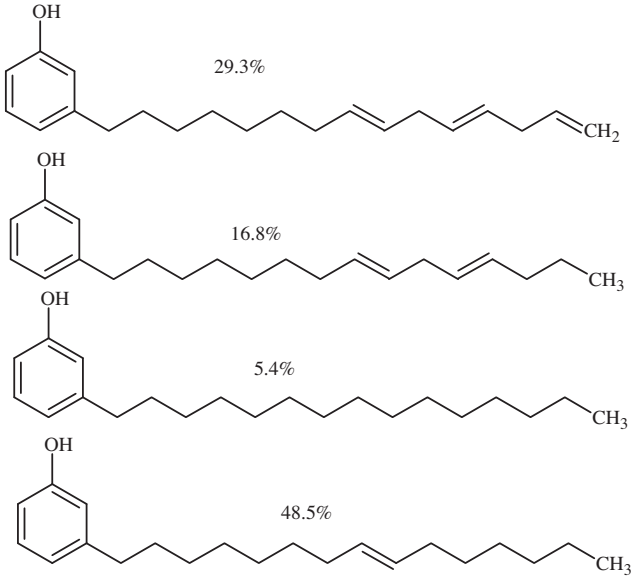


Figure 1 Structure and composition of cardanol.

using Reimer–Tiemann reaction. Following a standard procedure (Payne et al., 2006).

3-Chloro-1-benzothiophene-2-carbonylchloride was prepared by the reaction of cinnamic acid with thionylchloride in DMF and dry pyridine according to the reported method (Parkey and Castle, 1986). 3-Chloro-1-benzothiophene-2-carbonylchloride was then treated with hydrazinehydrate to obtain benzothiophene-2-carbohydrazide **2**. Compound **3** was synthesized by the reaction of 2-hydroxy-6-pentadecylbenzaldehyde with 3-chloro-1-benzo[*b*]thiophene-2-carboxylicacidhydrazide.

3. Experimental section

Melting point was determined in open capillary and is uncorrected. FT-IR spectrum was recorded on a Nicolet Fourier Transform Infrared Spectrophotometer: Impact 410 (Nicolet Instrument Technologies, Inc., WI, USA). ^{1}H NMR and ^{13}C NMR were obtained in $CDCl_3$ and DMSO-d_6 at 400 MHz for ^{1}H nuclei and 100 MHz for ^{13}C nuclei (Bruker Company, Germany). All chemical shifts were reported in parts per million (ppm) using residual proton or carbon signal in deuterated solvents as internal references. Mass spectrum was obtained using matrix-assisted laser desorption ionization mass spectrometry (MALDI-TOF) by using dithranol as a matrix. Elemental analysis (C, H, N and S) was performed on a Perkin Elmer 2400 analyzer. The purity of the compound was checked by TLC on silica gel and further purification was performed through column chromatography (silica gel, 60–120 mesh).

*3.1. Synthesis of 2-hydroxy-6-pentadecylbenzaldehyde (**1**)*

Following a previously published procedure 7, to a solution of hydrogenated cardanol (3.04 g, 0.01 mol) in toluene (20 mL) was added triethylamine (0.55 mL, 0.004 mol) and tin(IV) tetrachloride (0.001 mol). The reaction mixture was stirred for 30 min at room temperature under N_2 and then paraformaldehyde (0.66 g, 0.02 mol) was added. The reaction mixture was heated at 1000C for 8 h. After cooling down to room temperature, the reaction mixture was poured into water and acidified to pH 2 with hydrochloric acid. Then the aqueous layer was extracted with ethyl acetate. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated to dryness. The resulting crude product was purified by chromatography (silica, hexane) to give a white crystal.

Yield 65%; mp 100 °C; IR ν (cm^{-1}): 3184 (O–H st), 2958 (=C–H st), 2850, 2915 (C–H st), 1623, 1666 (C=C st); ^{1}H NMR δ ppm: 11.04 (s, ^{1}H, OH), 9.83 (s, ^{1}H, CHO), 7.44 (d, J = 7.9 Hz, ^{1}H, Ar–H), 6.83 (d, J = 6.8 Hz, ^{1}H, Ar–H), 6.80 (s, ^{1}H), 2.61 (t, J = 7.6 Hz, 2H, Ar–CH_2), 1.20–1.70 (m, 26H, $(CH_2)_{13}$), 0.87 (t, J = 6.8 Hz, 3H, CH_3); ^{13}C NMR δ ppm: 195.8, 161.8, 153.9, 133.6, 120.5, 118.4, 117.1, 36.4, 31.9, 30.7, 29.69, 29.65, 29.63, 29.5, 29.43, 29.40, 29.2, 22.7, 14.1; MS: m/z = 332.52 ($M^+ + 1$). Elemental analysis: Calculated for $C_{22}H_{36}O_2$: C, 79.46%; H, 10.91%; found: C, 79.41%; H, 10.88.

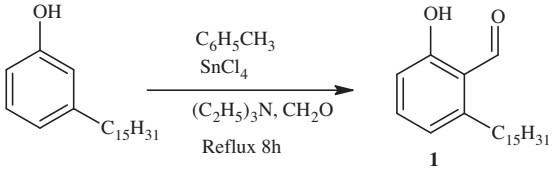
*3.2. Synthesis of 3-chloro-1-benzo[b]thiophene-2-carboxylicacidhydrazide (**2**)*

Carbonyl chloride (2.0 g, 0.0086 mol) was added to hydrazine hydrate (5.54 g, 5.33 mL, 0.17 mol) directly slowly with stirring, then the reaction mixture was stirred vigorously for about 7 h on a magnetic stirrer. The reaction mixture was cooled down to room temperature and slowly decomposed in crushed ice. The solid that separated was filtered, washed with water and recrystallized from ethanol to afford **2**.

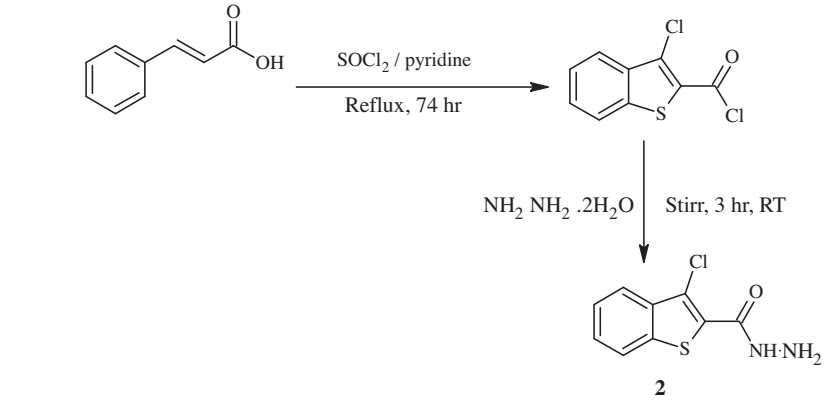
Yield 85%; mp 183 °C; IR ν (cm^{-1}): 3020 (N–H st), 1605 (C=O st), 1570 (C=C st), 1070 (=C–Cl st); ^{1}H NMR δ (ppm): 9.70 (s, ^{1}H, CONH), 8.10–7.41 (m, 4H, Ar–CH), 4.70 (2H, NH_2); ^{13}C NMR δ (ppm): 169.2, 138, 131, 129, 128, 125, 123, 122; MS, m/z: 226.68 (M^+). Anal. calcd. for $C_9H_7ClN_2OS$: C, 47.69; H, 3.11; N, 12.36; S, 14.15; found: C, 47.65; H, 3.09; N, 12.35; S, 14.12%.

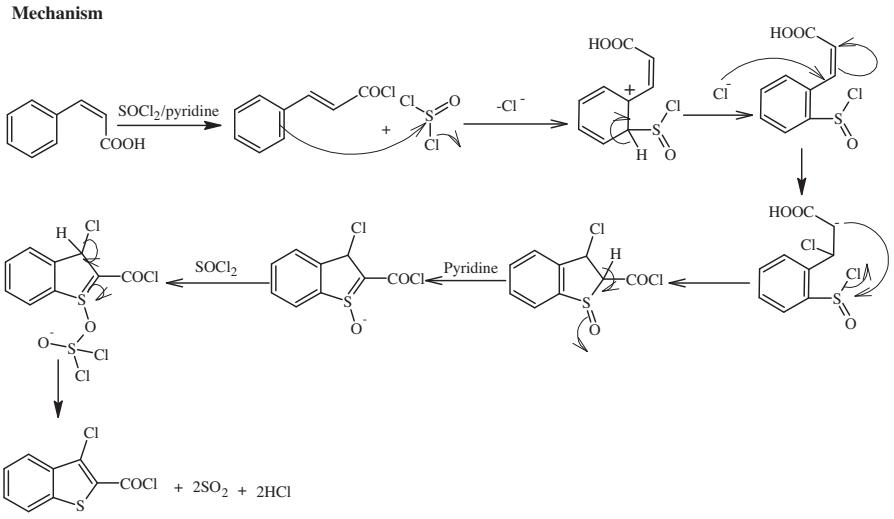
*3.3. Synthesis of 3-chloro-N′-(2-hydroxy-6-pentadecylbenzylidene)benzo[b]thiophene-2-carbohydrazide (**3**)*

A mixture of 2-hydroxy-6-pentadecylbenzaldehyde **1** (1.10 g, 3 mmol), 3-chloro-1-benzothiophene-2-carboxylicacidhydrazide **2** (0.75 g, 3 mmol) in the presence of glacial acetic acid (1 mL) in absolute ethanol (20 mL) was refluxed for 7 h. The completion of the reaction was monitored by TLC. The reaction mixture was allowed to cool down to room temperature, and then poured into crushed ice. The precipitate was filtered, dried and recrystallized from absolute ethanol. The resulting solid was further purified by column chromatography [silica,

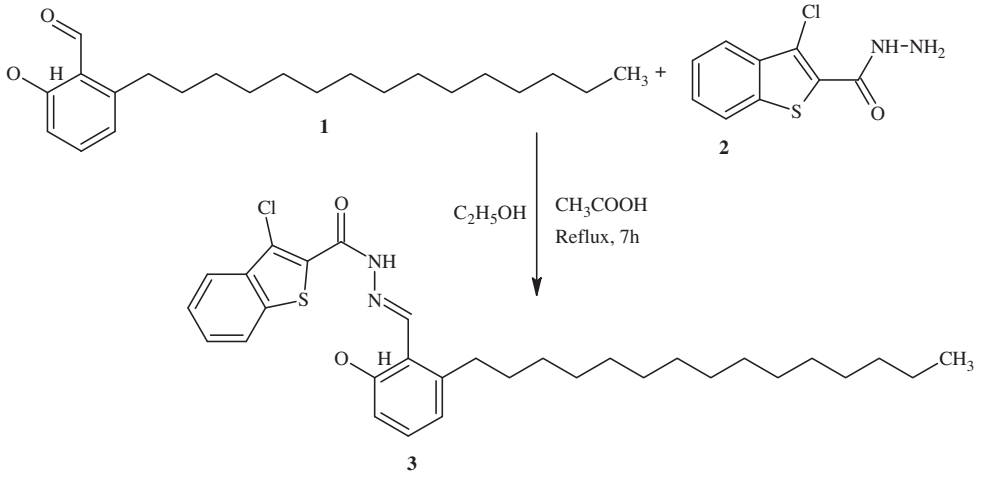


Scheme 1 Synthesis of 2-hydroxy-6-pentadecylbenzaldehyde.





Scheme 2 Synthesis of 3-chloro-1-benzo[*b*]thiophene-2-carboxylicacidhydrazide.



Scheme 3 Synthesis of 3-chloro-*N*′-(2-hydroxy-6-pentadecylbenzylidene)benzothiophene-2-carbohydrazide.

petroleum ether/ethyl acetate (70:30)], leading to compound **3** as a yellow solid.

Yield 80%; mp 291–293 °C; IR ν (cm^{-1}): 3288 (N–H), 1650 (C═O); ^{1}H NMR δ ppm: 12.11 (s, ^{1}H, OH), 10.94 (s, ^{1}H, NH), 8.61 (s, ^{1}H, CH═N), 8.15 (d, J = 7.8 Hz, ^{1}H, Ar–H), 8.06 (d, J = 7.9 Hz, ^{1}H, Ar–H), 7.94 (m, 2H, Ar–H), 7.83 (d, J = 7.8 Hz, ^{1}H, Ar–H), 6.73 (s, ^{1}H, Ar–H), 6.60 (d, J = 7.8 Hz, ^{1}H, Ar–H), 2.50 (t, J = 7.6 Hz, 2H, Ar–CH_2),

1.53–1.01 (m, 26H, $(CH_2)_{13}$), 0.83 (t, $J = 6.8$ Hz, 3H, CH_3);^{13}C NMR δ ppm: 161.3, 157.4, 156.7, 149.4, 147.0, 137.3, 136.8, 135.7, 129.2, 127.7, 125.1, 123.5, 122.3, 119.8, 116.1, 116.0, 35.1, 31.2, 30.3, 28.9, 28.9, 28.7, 28.6, 28.5, 22.0, 13.9; MS: $m/z = 540.91$ ($M^+ + 1$). Elemental analysis: Calculated for $C_{31}H_{41}ClN_2O_2S$: C, 68.80%; H, 7.64%; N, 5.18%; S, 5.92%; found: C, 69.04%; H, 8.12%; N, 5.39%; S, 6.22%. Scheme 1–3.

Acknowledgments

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