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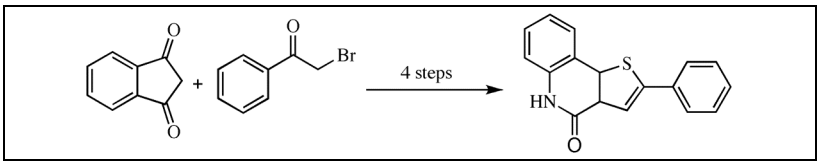
Received August 12, 2005



2-Phenacylindan-1,3-dione (**3**) was treated with Lawesson's reagent (2,4-bis(4-methoxyphenyl)-1,3-dithia-2,4-diphosphetane-2,4-disulfide) to form 2-phenyl-4*H*-indeno[1,2-*b*]thiophene-4-one (**4**). Compound **4** was subsequently reacted with hydroxyl amine to form the oxime (**5**), which, upon treatment with polyphosphoric acid, underwent ring expansion (Beckmann rearrangement) to give 2-phenylthieno[3,2-*c*]quinoline-4(5*H*)one.

J. Heterocyclic Chem., **43**, 629 (2006).

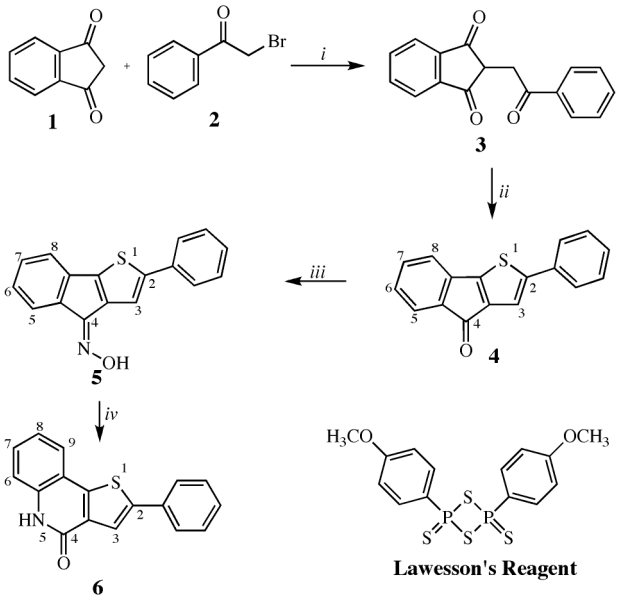
Introduction.

The indeno[1,2-*b*]thiophene ring system was first synthesized in 1967 through the conversion of 3-phenyl-2,5-thiophenedicarboxylic acid into the diacid chloride followed by cyclization using aluminum trichloride and carbon disulfide [1]. To our knowledge this work represents the only reported synthesis of this ring system. The only previously described synthesis of the thieno[*c*]-quinoline ring system was reported by Gronowitz *et al.* which involved the Pd(0)-catalyzed coupling of 2-formyl-benzeneboronic acids with *t*-butyl-*N*-(*ortho*-halothienyl)-carbamates [2].

Results and Discussion.

In the present work, we wish to describe a new method for preparing a derivative of indeno[1,2-*b*]thiophene which is transformed, by a ring expansion (Beckmann rearrangement) [3] to form a derivative of the thieno[*c*]-quinoline ring system. For this work, 2-phenacylindane-1,3-dione (**3**) was used as the starting material. Compound **3** was prepared according to a modified method of one described by Ramadas [4], who reported a yield of 60 %. Thus, **3** was prepared in 80 % yield, with higher purity than the previously described procedure [4], using a modification of the procedure which was used to prepare 2-benzoyl-5,5-dimethyl-cyclohexane-1,3-dione from dimedone and phenacyl bromide [4]. In this method, indan-1,3-dione (**1**) was allowed to react with phenacylbromide (**2**) in the presence of sodium ethoxide [5] to give **3** in 80% yield. Reaction of **3** with Lawesson's reagent (Scheme **1**) in toluene afforded the indeno[1,2-*b*]thiophene derivative **4** in good (75%) yield.

Scheme 1



i; Sodium ethoxide *ii*: Lawesson's Reagent, toluene, reflux, 6 h;
iii; NH_2OH, CH_3COONa, CH_3COOH, refulx 4 h; *iv*: PPA (P_2O_5, H_3PO_4)

Compound **4** was subsequently converted to 2-phenyl-4*H*-indeno[1,2-*b*]thiophene-4-one oxime (**5**) by reaction with hydroxyl amine in the presence of sodium acetate in acetic acid. Rearrangement of the oxime (Beckmann rearrangement) was affected with poly phosphoric acid (PPA) to give 2-phenylthieno[3,2-*c*]quinoline-4(5*H*)one (**6**) in 65% isolated yield (see Scheme 1). The structure of compounds **4**, **5** and **6** were elucidated based on ir, ^{1}H NMR and elemental analysis. The ir spectrum of **4** shows a carbonyl stretching band at 1693 cm^{-1} corresponding to and consistent with the cyclic ketone present in **4**. The ^{1}H NMR spectrum consisted of a singlet at δ 8.48 ppm corresponding to the H-3 proton

of the thiophene ring and a doublet at δ 8.92 corresponding to H-5 of the fused benzene ring as well as remaining aromatic resonances (H-6, H-7, and H-8) of the fused benzene ring protons and those of the phenyl group attached to C-2 of the thiophene ring.

The ir spectrum of **5** shows a broad peak with two maxima at 3402 and 3275 cm^{-1} corresponding to the OH absorptions for both forms of the oxime. Also, no absorption corresponding to a carbonyl group was observed. In the ^1H NMR spectrum of **5**, a singlet at δ 7.86 was observed corresponding to H-3 of the thiophene ring. Also, two singlets were observed at 12.52 and 12.50 ppm in a 1:3 ratio respectively, corresponding to the *E* and *Z* forms of the oxime. A NOESY experiment was performed to determine which diastereomer predominates. A correlation was observed between the more intense singlet resonating at δ 12.50 with the singlet resonating at δ 7.86 corresponding to H-3, indicating the major diasteriomer has the (*Z*) configuration (the configuration shown in Scheme **1**). There were no correlations observable between the less intense signal at δ 12.52 with any resonance signals associated with the fused aromatic ring. The region between δ 7.2 and δ 7.8 ppm in the ^1H spectrum consists of many overlapping resonances, which display an overly complicated spin pattern, produced by the presence of both Z / E isomers of the oxime.

The ir spectrum of **6** displayed the characteristic NH stretching absorption at 3455, and the CO stretch at 1694 cm^{-1}. The NMR spectrum was straight-forward with the observation of characteristic resonances such as the singlet at δ 8.47 corresponding to H-3, a doublet at δ 8.92 corresponding to H-9 (the bay region proton of the benzene moiety) as well as all other expected aromatic resonances.

Because **5** is formed as the *Z* isomer it is expected that the compound shown for **6** will be formed by the Beckmann rearrangement *via* ring expansion anti to the oxime. The Beckmann rearrangement product, where the amide functional group is reversed, would result from the *E* isomer. For **6**, the carbonyl resonance is observed at δ 190.0 ppm indicating that the carbonyl carbon is adjacent to the thiophene ring. For the other isomer, where the carbonyl carbon would be adjacent to benzene ring, the chemical shift is predicted to be closer to δ 165 ppm. Elemental analysis of all products was found to be in good agreement with the proposed structures.

In conclusion this work reports a novel and facile method for synthesizing derivatives of the indeno[1,2-*b*]thiophene and thieno[*c*]quinoline ring systems starting with readily available starting materials under straight forward reaction conditions and with easy workup.

EXPERIMENTAL

All melting points were obtained in open capillary tubes and are uncorrected. The ir spectra were recorded in KBr discs using a Perkin Elmer FT- spectrophotometer Model Spectrum RX1. The ^1H and ^{13}C NMR spectra were determined on a Varian Mercury 300 MHz FT-NMR 300 and 75 MHz, respectively, in DMSO-d_6 as solvent. Chemical shifts expressed in ppm (δ) relative to TMS (tetramethylsilane) as an internal standard (δ 0.00 ppm). The NOESY experiment was acquired using the standard Varian microprogram with 200 increments and with a mixing time of 200 msec. Microanlytical determinations were performed, in house, using a Perkin Elmer Series II CHNS/O Analyzer 2400. Reagents were purchased from Aldrich Chemical.

2-Phenacylindan-1,3-dione (**3**).

A mixture of (5.4 g, 100 mmoles) of sodium methoxide, (14.6 g, 100 mmoles) indan-1,3-dione and (19.9 g, 100 mmoles) of phenacyl bromide in 145 ml of ethanol was heated under reflux for 30 min. and then cooled. The sodium bromide which formed was removed by filtration, and the filtrate was concenterated *in vacuo*. The residual sirup was dissolved in a mixture of chloroform (50 ml) and 10% sodium hydroxide (50 ml). The aqueous phase was separated and re-extracted with chloroform (50 ml). The aqueous phase was cooled in ice bath, made acidic with hydrochloric acid, and extracted with chloroform (3 x 50 ml). The combined organic extracts were dried with anhydrous magnesuim Sulphate, filtered and the filtrate was evaporated *in vacuo* to dryness. Recrystallization of the crude product from ethanol gave compound **3** as yellow crystals, m.p. 188-190 °C, yield 80%, IR (KBr): 3650, 3030, 1740, 1680 cm^{-1}; ^1H-NMR (deutereochloroform): δ 3.3 (t, 1H, CH), 3.9 (d, 2H, CH_2), 7.4-7.9 (m, 9H, arom-H).

2-Phenyl-4*H*-indeno[1,2-*b*]thiophene-4-one (**4**).

A solution of 0.07 g of **3** (0.29 mmole) and 0.08 g of Lawesson's reagent (0.19 mmole) in toluene (5 ml) was heated under reflux for 6 hours. After removal of the solvent *in vacuo*, the residual solid was crystallized from ethanol/DMF to give **4** as green crystals, yield 75%; mp 252-253 °C; ir (KBr): 1699 (CO) cm^{-1}; ^1H nmr (DMSO-d_6): δ 7.24 (t, 1H), 7.48 (m, 3H), 7.68 (d, 2H), 8.48 (s, 1H, H3), 8.92 (d, 1H).

Anal. Calcd. for $C_{17}H_{10}OS$: C, 77.84; H, 3.84. Found: C, 77.34; H, 3.68.

2-Phenyl-4*H*-indeno[1,2-*b*]thiophene-4-one oxime (**5**).

To a solution 0.75 g of **4** (2.9 mmoles) dissolved in 50 ml of acetic acid was added a solution of 1.08 g (15 mmoles) of hydroxylamine hydrochloride dissolved in 5 *M* sodium acetate and the mixture was heated under reflux for 4 hours. The reaction mixture was then poured into cold water, the solid collected by filtration then crystallized from ethanol/DMF to give compound **5** as dark green crystals, yield 70%; mp 230-232 °C; ir (KBr): 3402 (OH) cm^{-1}; ^1H nmr (DMSO-d_6): δ 7.22-7.78 (m, 9H, Ar-H), 7.86 (s, 1H, H3), 12.50 (s, 1H, OH, *Z* diastereomer), 12.52 (s 0.3H, OH, *E* diastereomer).

Anal. Calcd. for $C_{17}H_{11}NOS$: C, 73.62; H, 4.00; N, 5.05. Found: C, 73.42; H, 3.86; N, 4.93.

2-Phenylthieno[3,2-*c*]quinoline-4(5*H*)one (**6**).

To a mixture of phosphrous pentoxide (1.8 g, 7.0 mmoles) and phosphoric acid (1 ml) was added 0.038 g (0.14 mmole) of **5** and the mixture was mechanically stirred at 80-100 °C for 3 hours. The mixture was treated with ice-water and the solid deposited was filtered and then crystallized from ethanol/

dichloromethane mixture to give **6** as yellowish green crystals, yield 65%, mp 220-222 °C; ir (KBr): 3455 (NH), 1694 (CO) cm^{-1}; ^1H nmr (DMSO-d_6): δ 7.22 (m, 1H), 7.36 (m, 2H), 7.48 (t, 2H), 7.67 (d 2H), 7.99 (m, 2H), 8.47 (s, 1H, H-3), 8.92 (d, 1H). ^{13}C nmr (DMSO-d_6): δ 190.0, (CO), 159.75, 159.25, 158.75, 158.24 (thiophene), 145.49, 143.07, 142.26, 138.56, 134.11, 121.60, 117.77, 113.94, 110.10 (aromatic).

Anal. Calcd. for $C_{17}H_{11}NOS$: C, 73.62; H, 4.00; N, 5.05. Found: C, 73.95; H, 3.99; N, 4.89.

Acknowledgement.

The authors thank the National Science Foundation for providing the funds for the purchase of the Varian Mercury 300 NMR (Award # 9980793) and the Fulbright commission of Egypt for providing living expensed for TAE.

REFERENCES AND NOTES

[1] D. W. H. MacDowell and T. B. Patrick, *J. Org. Chem.*, **32**, 2441 (1967).

[2] Y. Yang, A-B. Hörnfeldt and S. Gronowitz, *J. Heterocyclic Chem.*, **26**, 865 (1989).

[3] R. E. Gawly, *Org React.* **35**, 1 (1988) and references therein.

[4] P. V. Padmanabhan, D. V. Ramna and S. R. Ramadas, *Indian Journal of Chemistry*, **22B**, 1 (1983).

[5] H. J. Shaeffer and R. Vince, *J. Org. Chem.*, **27**, 4502 (1962).