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(*Z*)-3-Chloro-3-(2-naphthyl)prop-2-enal in the Synthesis of Naphthyl-Substituted Thiophene and Quinolines

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Abstract—2-(2-Naphthyl)thiophene was synthesized by condensation of 3-chloro-3-(2-naphthyl)prop-2-enal with sulfanylacetic acid. A modified procedure was proposed for the synthesis of 2-(2-naphthyl)- and 2-(2-naphthyl)-6-nitroquinolines from 3-chloro-3-(2-naphthyl)prop-2-enal.

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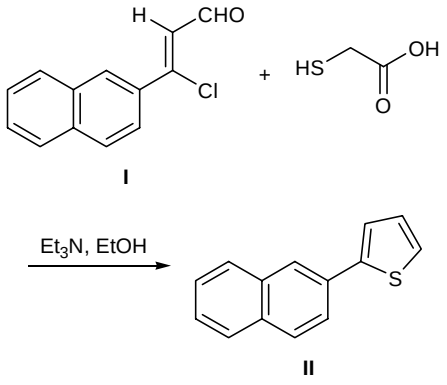
While performing systematic studies on chemical transformations of (*Z*)-3-chloro-3-(2-naphthyl)prop-2-enal, which was synthesized from 2-acetylnaphthalene by the Vilsmeier–Haak reaction [1], we showed that the high reactivity of the exocyclic chloropropene fragment makes this compound a convenient synthon for the preparation of naphthalene derivatives having various side-chain functional groups, such as enamino, iminium, hydroxyimino, peroxy, acetylenic, and nitrohalodiene moieties, as well as of a large number of heterocyclic compounds [2–4].

The goal of the present work was to synthesize a naphthyl-substituted thiophene from (*Z*)-3-chloro-3-(2-naphthyl)prop-2-enal and modify the procedure developed by us previously for the preparation of quinoline derivatives.

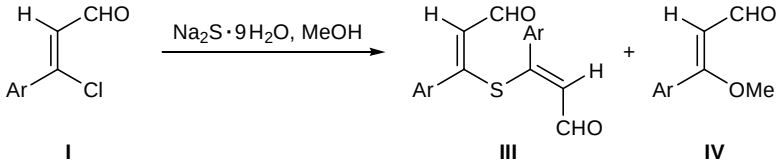
It is known that sulfanylacetic acid reacts with 3-(1-adamantyl)-3-chloropropen-2-al to give a mixture of adamantyl-substituted thiophene-2-carboxylic acid and thiophene [5]; it was also shown that the overall yield of the products increases when the reaction is performed in DMF rather than in ethanol. We found that the condensation of 3-chloro-3-(2-naphpthyl)prop-2-enal (**I**) with sulfanylacetic acid in boiling ethanol in the presence of triethylamine is complete in 5 h to give 2-(2-naphthyl)thiophene (**II**) in 34% yield (Scheme 1). The process was accompanied by considerable tarring. The reaction mixture contained no 5-(2-naphthyl)thiophene-2-carboxylic acid whose formation could be expected by analogy with the reaction with adamantylchloropropenal. When the reaction was performed in DMF as solvent, an inseparable mixture of products was obtained; its main component was triethylamine hydrochloride. The structure of compound **II** was confirmed by the analytical and spectral data (IR, ^{1}H NMR, and mass spectra). The IR spectrum of **II** contained absorption bands at 1340, 1425, and 1536 cm^{-1}, corresponding to stretching vibrations of the thiopene ring; these bands are typical of 2-substituted thiophene derivatives [6]. Compound **II** showed in the ^{1}H NMR spectrum a doublet at δ 7.10 ppm (^3J = 4 Hz) from 3-H in the thiophene ring and multiplets in the region δ 7.44–8.00 ppm, the latter belonging to protons in the naphthalene and thiophene rings. In the electron-impact mass spectrum of **II** we observed the molecular ion peak and fragment ion peaks resulting from loss of hydrogen atoms and naphthyl residue.

Unlike known methods for the synthesis of 2-(2-naphthyl)thiophene, which are based on palla-

Scheme 1.



Scheme 2.



I **III** **IV**

dium-catalyzed reactions of thiophene with aryl bromides [7] or of naphthyl trifluoromethanesulfonate with tributyl(thienyl)tin [8], the proposed procedure is simpler from the preparative viewpoint. Moreover, the yield of **II** is more than twice as large as that in the Friedel–Crafts alkylation of naphthalene with 2-chlorothiophene [9]; the latter gives a mixture of isomeric aryl-substituted thiophenes, and the yield of 2-(2-naphthyl)thiophene (**II**) does not exceed 13%.

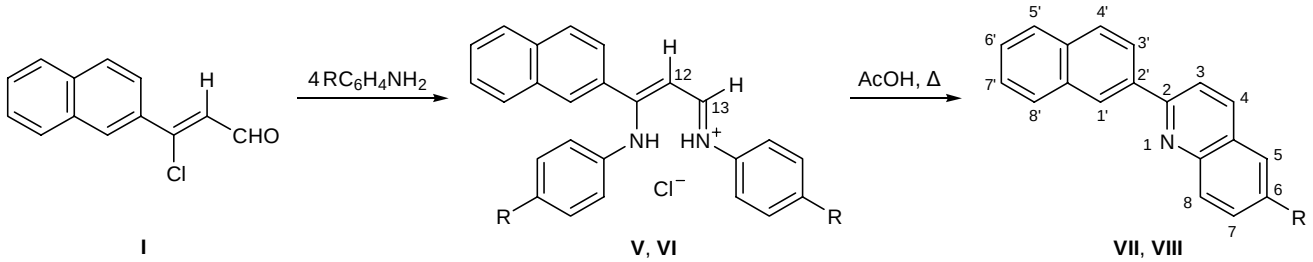
By analogy with reactions involving β-chlorovinyl aldehydes [10], we tried to obtain substituted thiopyrans by reaction of chloronaphthylpropenal **I** with sodium sulfide. However, compound **I** reacted with an equimolar amount of sodium sulfide in boiling methanol to give only acyclic products: 3,3'-thiobis-[3-(2-naphthyl)prop-2-enal] (**III**) and 3-methoxy-3-(2-naphthyl)prop-2-enal (**IV**) (53 and 22%, respectively; Scheme 2). No compounds having a thiopyran structure were detected in the reaction mixture.

As we showed previously [3, 4], propenal **I** is also a convenient starting compound for building up various nitrogen-containing heterocyclic systems, in particular 2-(2-naphthyl)quinolines. The previous procedure for the preparation of 2-(2-naphthyl)quinolines from prop-2-enal **I** includes two steps, the first of which implies the synthesis of *N*-(3-arylimino-1-(2-naphthyl)prop-1-en-1-yl)aniline hydrochlorides like **V** or **VI** from propenal **I** and 4 equiv of the corresponding aromatic amine in diethyl ether; in the second step, the isolated iminium salts are subjected to heterocyclization on heating in boiling glacial acetic acid [3] (Scheme 3).

We now describe a modified procedure for the synthesis of 2-(2-naphthyl)quinolines from propenal **I**. According to the modified procedure, 2-(2-naphthyl)- and 2-(2-naphthyl)-6-nitroquinolines **VII** and **VIII** were synthesized in one step without isolation of intermediate iminium salts **V** and **VI**. Compounds **VII** and **VIII** were obtained in 39 and 32% yield, respectively, by heating a mixture of propenal **I** and the corresponding aromatic amine (aniline or *p*-nitroaniline) at 200–210°C under solvent-free conditions. The physical constants and IR, ^{1}H NMR, and mass spectra of quinoline **VII** coincided with those reported in [3]. Previously unknown 2-(2-naphthyl)-6-nitroquinoline (**VIII**) was also synthesized in two steps as described in [3]. The reaction of propenal **I** with 4 equiv of *p*-nitroaniline in diethyl ether gave hydrochloride **VI**, and heterocyclization of the latter in boiling glacial acetic acid led to the formation of naphthylnitroquinoline **VIII** in 38% yield (calculated on the initial propenal **I**).

The structure of compounds **VI** and **VIII** was determined on the basis of their elemental compositions and IR, ^{1}H NMR, and mass spectra. In the IR spectrum of **VI**, stretching vibrations of the C=N bond appeared as a strong absorption band 1642 cm^{-1}, and bands at 1492–1537 and 1594 cm^{-1} were assigned to vibrations of C=C bonds. The NH^+ group gave rise to a broad absorption band with its maximum at 2772 cm^{-1}, and

Scheme 3.



I **V**, **VI** **VII**, **VIII**

I $\xrightarrow{4RC_6H_4NH_2,\ 200°C}$ **VII**, **VIII**

V, **VII**, R = H; **VI**, **VIII**, R = O_2N.

vibrations of the NH group were characterized by a frequency of 3300 cm^{-1}. The ^1H NMR spectrum of salt **VI** contained multiplet signals in the region δ 6.35–8.20 ppm due to aromatic protons in the naphthalene and benzene rings and olefinic protons in the $=HC^{12}–C^{13}H=N$ fragment, a broadened singlet at δ 8.55 ppm from the naphthalene 1-H proton, and a broadened singlet at δ 12.00 ppm from the NH groups. In the aromatic region we identified a doublet at δ 7.7 ppm (^3J = 6.4 Hz), which was assigned to 13-H; these data indicate conservation of the *s-cis* configuration of the side chain during the reaction [11].

In the IR spectrum of quinoline **VIII**, a strong absorption band was present at 1636 cm^{-1}; it was assigned to stretching vibrations of the C=N bond. Aromatic C=C bonds gave rise to absorption in the region 1479–1561 cm^{-1}. No NH absorption at about 3300 and 2772 cm^{-1}, which is typical of initial hydrochloride **VI**, was observed in the IR spectrum of quinoline **VIII**. The ^1H NMR spectrum of **VIII** contained multiplet signals from aromatic protons in the region δ 7.35–8.85 ppm. The molecular ion peak was present in the mass spectrum of **VIII**.

Although the yields of naphthylquinolines **VII** and **VIII** in the two-step procedure were slightly greater than those in the modified one-step synthesis (48 [3] and 38% against 39 and 32%, respectively), the latter seems to be more attractive from the preparative viewpoint, for it ensures shorter reaction time and simpler experiment and requires no solvent.

EXPERIMENTAL

The IR spectra of compounds **II–VIII** were recorded in KBr on a Nicolet Protege-460 Fourier-transform spectrometer. The ^1H NMR spectra were obtained on a Tesla BS-567A (100 MHz) instrument from solutions in acetone-d_6 (compound **II**), DMSO-d_6 (**V**, **VI**), and $CDCl_3$ (**III**, **IV**, **VII**–**VIII**); the chemical shifts were measured relative to tetramethylsilane as internal reference. The mass spectra were run on a Hewlett–Packard HP 5890/5972 GC–MS system (electron impact, 70 eV; HP-5MS capillary column, 30 m × 0.25 mm, film thickness 0.25 μm, 5% of phenylmethylsilicone; injector temperature 250°C).

2-(2-Naphthyl)thiophene (II). Sulfanylacetic acid, 1.1 g (11 mmol), and triethylamine, 2.15 g (21 mmol), were added dropwise under stirring at 0°C to a solution of 1.85 g (8.5 mmol) of compound **I** in 10 ml of ethanol. The mixture was heated for 5 h under reflux, cooled, and poured into 100 ml of 5% aqueous sodium hydroxide. The precipitate was filtered off, washed with water, and recrystallized from ethanol. Yield 0.68 g (34%), mp 101–102°C; published data: mp 102–103°C [6], 103–108°C [7]. IR spectrum, ν, cm^{-1}: 690, 744 (C–S); 1340, 1425, 1536 (C=C); 3050 (C–H). ^1H NMR spectrum, δ, ppm: 7.10 d (1H, 3-H, thiophene, ^3J = 4 Hz), 7.44–8.00 m (2H, thiophene, and 6H, naphthalene), 8.16 br.s (1H, 1-H, naphthalene). Found, %: C 80.42; H 4.35; S 15.43. $[M]^+$ 210. $C_{14}H_{10}S$. Calculated, %: C 79.96; H 4.79; S 15.25. *M* 210.28.

3,3'-Thiobis[3-(2-naphthyl)prop-2-enal] (III) and 3-methoxy-3-(2-naphthyl)prop-2-enal (IV). Compound **I**, 3.4 g (16 mmol), was added dropwise to a solution of 3.9 g (16 mmol) of $Na_2S \cdot 9H_2O$ in 25 ml of methanol under stirring at 30°C. The mixture was heated for 1 h under reflux, and the precipitate was filtered off, washed with water and diethyl ether–hexane (1:2), and dried under reduced pressure. We thus isolated 2.89 g (53%) of sulfide **III**, mp 210°C. IR spectrum, ν, cm^{-1}: 747 (C–S), 1596 (C=C), 1656 (C=O). ^1H NMR spectrum, δ, ppm: 6.65 d (1H, C=CH, ^3J = 7.7 Hz), 7.48–7.91 m (6H, naphthalene), 8.17 s (1H, 1-H, naphthalene), 9.63 d (1H, CHO, ^3J = 7.7 Hz). Found, %: C 79.57; H 4.88; S 8.53. $[M]^+$ 394. $C_{26}H_{18}O_2S$. Calculated, %: C 79.16; H 4.60; S 8.13. *M* 394.46.

The filtrate was evaporated on a rotary evaporator, the residue was treated with 50 ml of water, and the green precipitate was filtered off and washed with water and diethyl ether. Yield of compound **IV** 0.64 g (22%), mp 93–95°C. IR spectrum, ν, cm^{-1}: 729 (C–S), 1590 (C=C), 1652 (C=O). ^1H NMR spectrum, δ, ppm: 3.91 s (3H, OCH_3), 5.7 d (1H, C=CH, ^3J = 7.7 Hz), 7.50–7.84 m (6H, naphthalene), 7.85 br.s (1H, 1-H, naphthalene), 9.52 d (1H, CHO, ^3J = 7.7 Hz). Found, %: C 79.09; H 5.76. $[M]^+$ 211. $C_{14}H_{11}O_2$. Calculated, %: C 79.59; H 5.26. *M* 211.25.

***N*-(1-(2-Naphthyl)-3-(4-nitrophenylamino)prop-1-en-1-yl)-4-nitroaniline hydrochloride (VI).** A solution of 2.54 g (18.4 mmol) of *p*-nitroaniline in 3 ml of diethyl ether was added in portions under stirring to a solution of 1 g (4.6 mmol) of propenal **I** in 5 ml of diethyl ether. After 10–15 min, an intensely colored solid precipitated and was filtered off, washed with water and diethyl ether, dried under reduced pressure, and recrystallized from methanol. Yield 1.75 g (80%), mp 208–210°C. IR spectrum, cm^{-1}: 1296, 1574 (NO_2); 1492, 1514, 1537, 1594 (C=C); 1642 (C=N); 3052 (C–H); 2772 (NH^+); 3300 (NH). ^1H NMR spectrum, δ,

ppm: 6.35–8.20 m (14H, H_{arom}, and 2H, =CH–CH=N), 8.55 br.s (1H, 1-H), 12.00 br.s (2H, NH). Found, %: C 63.35; H 4.24; Cl 7.77; N 11.55. $[M]^+$ 474. $C_{25}H_{19}ClN_4O_4$. Calculated, %: C 63.23; H 4.03; Cl 7.47; N 11.79. *M* 474.88.

2-(2-Naphthyl)-6-nitroquinoline (VIII). A solution of 1.19 g (2.5 mmol) of hydrochloride **VI** in 10 ml of glacial acetic acid was heated for 3 h under reflux. The mixture was then treated with a concentrated aqueous solution of potassium hydroxide to pH 6–7, and the precipitate was filtered off, washed with water, dried under reduced pressure, and recrystallized from methanol. Yield 0.36 g (48%, calculated on **VI**, or 38%, calculated on initial propenal **I**), mp 140–142°C (from methanol). IR spectrum, ν, cm^{-1}: 1224 (C–N); 1258, 1579 (NO_2); 1479, 1506, 1561 (C=C); 1636 (C=N); 3058 (C–H). ^{1}H NMR spectrum, δ, ppm: 7.35–8.60 m (11H, H_{arom}), 8.85 br.s (1H, 1'-H). Found, %: C 75.49; H 4.24; N 9.28. $[M]^+$ 300. $C_{19}H_{12}N_2O_2$. Calculated, %: C 75.98; H 4.03; N 9.33. *M* 300.31.

2-(2-Naphthyl)- and 2-(2-naphthyl)-6-nitroquinolines VII and VIII (*general modified procedure***).** A mixture of 4.6 mmol of compound **I** and 18.4 mmol of aniline or *p*-nitroaniline was heated for 2 h at 200°C (with aniline) or fused for 20 min at 150–170°C (with *p*-nitroaniline). The resulting material was dissolved in 20 ml of hot ethanol, the solution was cooled, and the precipitate was filtered, washed with diethyl ether–hexane (1:4), recrystallized from ethanol, and dried under reduced pressure.

2-(2-Naphthyl)quinoline (VII). Yield 39%. Its physical constants and IR, ^{1}H NMR, and mass spectra were in agreement with those reported in [3].

2-(2-Naphthyl)-6-nitroquinoline (VIII). Yield 32%. Its melting point and IR, ^{1}H NMR, and mass spectra were identical to those of a sample prepared according to the procedure described in [3].

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