Thienoquinolines, II[1]

A New and Convenient Synthesis of Thieno(2,3-b)quinoline

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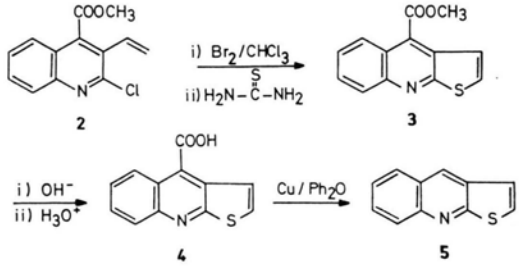
Methyl-2-chloro-3-vinylquinoline-4-carboxylate, Methyl-thieno(2,3-b)quinoline-4-carboxylate, Thieno(2,3-b)quinoline-4-carboxylic Acid, Thieno(2,3-b)quinoline

A new and convenient synthesis of thieno-(2,3-b)quinoline starting from methyl-3-vinylquinolin-2(1 H)-one-4-carboxylate is described.

Hitherto, two methods[2,3] are known for the synthesis of the parent thieno(2,3-b)quinoline (**5**). Of them, the one due to KUWAYAMA *et al.*[2] involves a five-stage process from 3-(2-hydroxyethyl)-quinolin-2(1 H)-one. HULL[3] obtained the parent compound **5** by proceeding through *o*-isothiocyanatocinnamaldehyde obtained from quinoline by ring-fission with thiophosgene and alkali.

We wish to report a new and convenient synthesis of thieno(2,3-b)quinoline (**5**) utilizing the readily accessible methyl 3-vinylquinolin-2(1 H)-one-4-carboxylate (**1**)[4] as the starting intermediate. Treatment of **1** with phosphoryl chloride yielded the chloroquinoline (**2**). Addition of bromine to **2** and subsequent treatment of the resulting trihalo compound with thiourea in boiling ethanol readily furnished methyl thieno(2,3-b)quinoline-4-carboxylate (**3**). The ester **3** was neatly converted into the parent thienoquinoline (**5**) by hydrolysis, followed by decarboxylation of the resulting acid **4** with copper powder in boiling diphenyl ether.



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The advantage of this method for the preparation of the title compound lies in its simplicity, ease of operation and good overall yield (43.5%). The compound **5**, thus obtained, was found to be identical in all respects (m.p., mixed m.p., superimposable IR, NMR, and TLC) with the authentic sample[3]*.

Experimental[5]

Methyl-3-vinylquinolin-2(1 H)-one-4-carboxylate (**1**)[4]

This ester is conveniently obtained by mixing a methanol solution of 3-vinylquinolin-2-(1 H)-one-4-carboxylic acid with ethereal diazomethane and quickly evaporating the solution when the vigorous evolution of nitrogen subsided. The residue was taken in chloroform, washed sequentially with aqueous sodium bicarbonate and water. The organic layer, after drying, was evaporated and the residue purified[4] to furnish the pure ester.

Methyl-2-chloro-3-vinylquinoline-4-carboxylate (**2**)

A mixture of **1** (2.3 g) and phosphoryl chloride (4 ml) was heated on a steam bath for 1 h. After cooling, it was poured into ice-water, basified with ammonia, and extracted with chloroform. The chloroform extract was washed with water, dried and evaporated. The residue was chromatographed over alumina in petrol (60–80 °C). Yield: 2.24 g (90%); m.p. 54–55 °C (colourless needles from petrol (40–60 °C)); ν_{max}^{KBr} 1725 (CO_2CH_3), 975 and 930 cm^{-1} ($-CH=CH_2$); δ 4.03 (s, 3 H, CO_2CH_3); 5.53, 5.79, 7.03 (each a dd, 1 H of A, B, and X parts respectively of the ABX system: $H_X\diagdown C=C\diagup^{H_B}_{H_A}$, $J_{AX}=18$, $J_{BX}=11$ and $J_{AB}=2$ Hz), 7.5–8.0 (m, 3 H, 6-, 7-, and 8-H), 8.12 (dd, 1 H, 5-H, $J=9$, 2.5 Hz).

$C_{13}H_{10}NO_2Cl$

Calcd	C 63.03	H 4.07	N 5.66,
Found	C 62.76	H 4.20	N 5.78.

Methyl-thieno(2,3-b)quinoline-4-carboxylate (**3**)

Bromine (0.8 g, 5 mmol) in dry chloroform (30 ml) was added to a stirred solution of **2** (1.2 g, 5 mmol) in dry chloroform (30 ml). Stirring was continued for 1 h and then the solution was evaporated. The residue was mixed with thiourea (0.95 g, 12.5 mmol) and absolute ethanol (30 ml) and refluxed on a steam bath for 5 h. A yellow solid separated initially from the reaction mixture which then slowly went into solution. After cooling, the reaction mixture was poured into ice water and basified with ammonia. The product was extracted with chloroform, dried and then evaporated. Chromatography of the residue over alumina in benzene gave **3**. Yield: 0.875 g (75%), m.p. 142–143 °C (petrol

* Kindly provided by Dr. R. HULL of ICI Ltd., England.

60–80 °C); ν_{max}^{KBr} 1720 cm^{-1} (CO_2CH_3); δ 4.13 (s, 3 H, CO_2CH_3), 7.75–8.33 (m, 5 H, 2-, 3-, 6-, 7-, and 8-H), 8.45 (dd, 1 H, H-5, $J = 7.5$, 2.5 Hz).

$C_{13}H_9NO_2S$

Calcd	C 64.19	H 3.73	N 5.76,
Found	C 64.38	H 3.84	N 5.94.

Thieno(2,3-b)quinoline-4-carboxylic acid (4)

The above ester (490 mg) was mixed with methanol (6 ml) and 1 N aqueous NaOH (30 ml) and heated at reflux for $1^1/_2$ h. The reaction mixture was cooled and acidified with 5 N HCl when the acid separated as crystalline solid. It was purified by dissolving in $NaHCO_3$, filtering and acidifying the clear filtrate with acetic acid. The resulting acid washed with water and alcohol had m.p., 309–310 °C (decomp.); Yield: 420 mg (92%); ν_{max}^{KBr} 1690 cm^{-1} (COOH).

$C_{12}H_7NO_2S$

Calcd	C 62.88	H 3.08,	
Found	C 62.60	H 3.16.	

Thieno(2,3-b)quinoline (5)

The acid 4 was heated with copper powder (200 mg) in diphenyl ether (20 ml) under reflux for 3 h. It was cooled and filtered and the residue was washed with ether. The washings and the filtrate were combined, diluted with more ether, and extracted with dil. HCl (5 N). The acid extract was separated, basified with ammonia, and extracted with ether. The ether extract was evaporated after drying (Na_2SO_4). Chromatography of the residue over alumina (basic) in benzene gave 5 as colourless needles. Yield: 131 mg (71%), m.p. 107–108 °C (petrol 60–80 °C) (lit.[3], m.p. 104–106 °C). δ 7.32 (d, 1 H, 3-H, $J = 6$ Hz), 7.62 (d, 1 H, 2-H, $J = 6$ Hz), 7.62–7.85 (m, 2 H, 6-, and 7-H), 7.98 (dd, 1 H, 5-H, $J = 8$, 1.5 Hz), 8.27 (dd, 1 H, 8-H, $J = 8$, 1.5 Hz), 8.52 (s, 1 H, 4 H).

$C_{11}H_7NS$

Calcd	C 71.32	H 3.81	N 7.57,
Found	C 71.15	H 3.70	N 7.50.

$M^+ = 185$. The NMR spectrum of 5 taken at 100 MHz agreed with the published data[3]. The picrate of 5 was prepared and recrystallised from alcohol m.p. 213–214 °C (lit.[2], 212–213 °C). It was found identical (m.p. mixted m.p.) with the picrate prepared from the authentic sample.

We thank Dr. R. HULL for providing us a sample of his synthetic compound 5 and obtaining a 100 Hz NMR, and mass spectra for our sample. We (K. K. and N. S.) thank the U. G. C. (India) for financial assistance.

[1] Part I: P. SHANMUGAM, K. KANAKARAJAN, N. SOUNDARARAJAN, and A. GNANASEKARAN, Synthesis 1976, 253.

[2] Y. KUWAYAMA, YAKUGAKU ZASSHI **82**, 1028 [1962]; C. A. **58**, 5687 [1963]; G. KOBAYASHI, Y. KUWAYAMA, and S. O. KAMURA, ibid. **83**, 234 [1963]; C. A. **59**, 5144 [1963].

[3] R. HULL, J. C. S. PERKIN I **1973**, 2911.

[4] P. SHANMUGAM and P. LAKSHMINARAYANA, Z. Naturforsch. **27b**, 474 [1972].

[5] Melting points were uncorrected. Infrared spectra were recorded on a Beckmann IR-20 spectrophotometer, the NMR spectra were recorded on a Varian A-60 instrument in $CDCl_3$ solution with TMS as internal standard, and mass spectra on an A. E. I. MS 9 spectrometer. (The 100 MHz NMR spectrum of 5 was taken on a Varian H. A. 100 instrument.)