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Synthesis and Crystal Structure of 2-Methyl-3-ethyl methanoate benzo[h]quinoline

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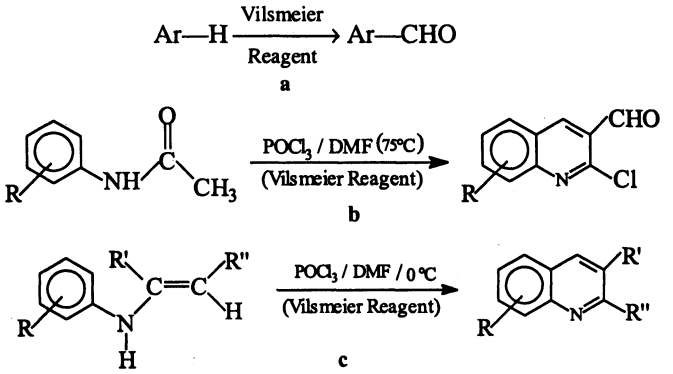
The synthesis of a new benzoquinoline derivative from an enamine using Vilsmeier reagent has been reported. The 2-methyl-3-ethyl methanoate benzo[h]quinoline obtained was identified by classic and usual spectroscopic techniques as well as X-ray structural determination.

Key Words: Benzoquinoline, Naphthopyridine, Vilsmeier, Quinoline, X-ray.

INTRODUCTION

The synthesis, chemical properties, spectroscopic and pharmacological studies of new quinoline and benzoquinoline derivatives are a vast and important domain of investigation[1-13]. Vilsmeier complexes of general formula [$>N^+$=CHCl, $^-OPOCl_2$] are much used in the synthesis strategy of this class of compounds[14]. Usually, Vilsmeier and Haack[15] have generally used their reagent to formylate aryl compounds for extending an aryl structure with a carbon atom **(Scheme-1a).** Meth-Cohn and co-workers[1,2] used the same reagent for the formylation and cyclization of activated arylamides to quinolinic derivatives **(Scheme-1b).**

From actived arylenamines, as a starting material, various researchers synthesized, by the same method, quinoline derivatives with a good yield[16,17] **(Scheme-1c):**



Scheme-1

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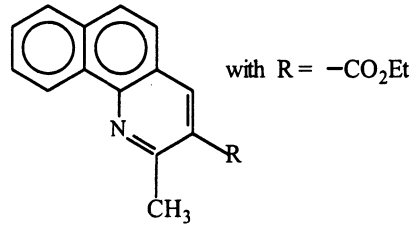
RESULTS AND DISCUSSION

Using the potential ability of the Vilsmeier-Haack reaction[14, 15], a new crystalline benzoquinoline derivative, 2-methyl-3-ethyl méthanoate benzo[h]quinoline is synthesized from arylenamine.

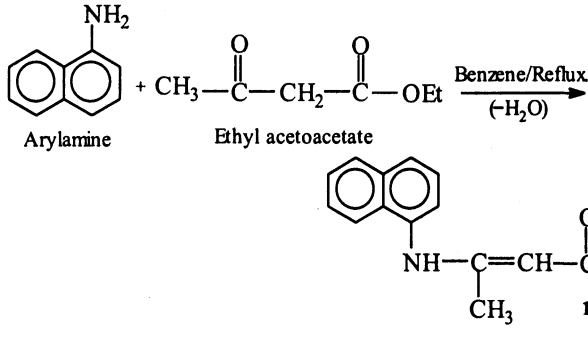


2-Methyl-3-ethyl methanoate benzo[h]quinoline

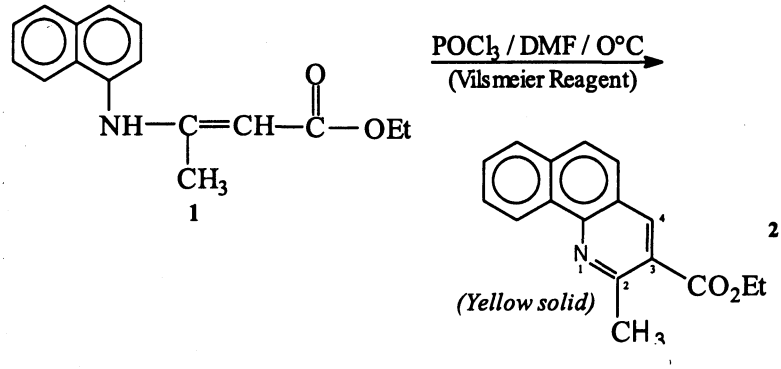
The extension and the aromatic character of the conjugated system confer to the product an important stability and it is obtained with a good yield although naphthyl residue does not contain any activated donor groups.

1. Synthesis reaction of the compound.

* Enamine préparation:



*Cyclization and isomerization:



2-Methyl-3-ethyl methanoate benzo[h] quinoline

Scheme-2

2. X-Ray crystal structure analysis

Single crystals of the title compound were obtained by slow evaporation of an Et_2O/hexane (1 : 4) solution. The ORTEP drawing of the molecular structure and selected bond lengths are given in Fig. 1[18]. These data are in agreement with the structure deduced from the classical spectroscopic techniques.

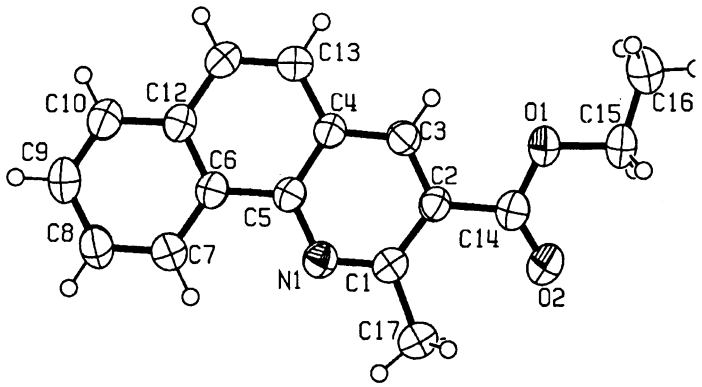


Fig. 1. ORTEP drawing of the title compound. Selected bond lengths, N1-C1: 1.329(3), N1-C5: 1.352(3), O1-C14: 1.344(3), O1-C15: 1.452(3), O2-C14: 1.201(3), C1-C2: 1.424(3), C2-C3: 1.373(3), C2-C14: 1.486(3) Å

EXPERIMENTAL

All solvents have been dried, distilled and freshly used[19, 20].

Preparation of the Vilsmeier reagent

To 0.015 mol of freshly distilled and anhydrous dimethylformamide were added dropwise at 0–5°C with continuous stirring, 0.015 mol of phosphorus oxychlorure. At the end of the addition the stirring is continued for 30 min at room temperature[15].

Synthesis of the enamine (1)

To an equimolecular mixture of naphtylamine and acetylacetoacetate dissolved in dry benzene were added 5 drops of anhydrous acetic acid as catalyst. The reaction mixture was heated under reflux for 4 h. The water formed was removed using a Dean-Starck system and the benzene solvent was eliminated. The residue was dried in a desiccator under vacuum to give enamine **1** as a purple oily product. Yield: 86%. IR (KBr, cm^{-1}): 3430 ν(NH: enamine), 1751 ν(C=O). δ_{ppm} ^{1}H NMR ($CDCl_3$/TMS/250 MHz): 8.50 (s, H, NH); 7.25–8 (m, 7H, aromatics); 4.25 (q, J = 6.32 Hz, 2H, Et); 1.75 (s, 3H, CH_3); 1.25 (t, J = 6.32 Hz 3H, Et);

Synthesis of the benzoquinoline derivative: (2)

To a freshly prepared Vilsmeier reagent is added, under inert atmosphere, 0.05 mol of enamine **1** dissolved in 25 mL of purified chloroform. The resulting

mixture is stirred at 0°C during 2 h and then allowed to stand at room temperature before its transfer to a saturated $NaHCO_3$ aqueous solution. The organic layer is extracted by chloroform, dried with anhydrous magnesium sulfate. After evaporation of $CHCl_3$ *in vacuc* the yellow solid residue is let overnight to crystallize completely, giving crude 2-methyl-3-(methanoate ethyl)benzo[h]quinoline **2**. Purification is achieved by recrystallization from a mixture of Et_2O/Hexane (1 : 4) giving plate crystals of yellow colour. Yield: 85%; melting point 78.5°C. IR (KBr, cm^{-1}): 1750 ν(C=O), 1633 ν(N=C: pyridinic); δ_{ppm} ^1H NMR ($CDCl_3$/TMS/250 MHz): 8.8 (s, H, 4-H); 7.9–7.6 (m, 6H aromatics); 4.4 (q, J = 6.31 Hz, 2H, Et); 3,1 (s, 3H, Me); 1.6 (t, J = 6.31 Hz, 3H, Et). δ_{ppm} ^{13}C NMR ($CDCl_3$/TMS/250 MHz): δ 166.42 (s); 157.89 (s); 146.74 (s); 139.56 (s); 134.63 (s); 130.11 (s); 129.21 (s); 127.88 (d); 127.31 (s); 125.25 (d); 123.88 (d); 77.52 (s); 77.11 (d); 76.50 (s); 61.42 (s); 25.45 (s); 14.33 (s). Mass: m/z 165.1 $[M]^+$ 100%.

ACKNOWLEDGEMENTS

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18. Data for X-ray structure analysis were collected at room temperature on a Nonius Kappa CCD diffractometer with MoKα radiation (λ = 0.71073 Å) and graphite monochromator. Structure was solved by direct method and refined against F^2 with the full-matrix, least-

squares methods using SHELXS-97 and SHELXL-97 respectively. Crystal data: $C_{17}H_{15}NO_2$, m.w. = 265.30, triclinic, space group P-1, a = 7.2488(4), b = 7.4137(3), c = 12.8750(8) Å, α = 104.587(2), β = 90.061(2), γ = 92.418(2)°, V = 668.96(6) Å^3, Z = 2, Dc = 1.317 g cm^{-3}, R1 = 0.0661, wR2 = 0.1530 for 2312 observed reflections with I > 2σ(I). Crystallographic data (excluding structure factors) for this structure have been deposited with the Cambridge Crystallographic Data Center as supplementary publication CCDC-229947. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax +44-(0)1223-336033, or e-mail: deposit@ccdc.cam.ac.uk).

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