SYNTHESIS OF THIENO(2,3-b)QUINOLINE-2-CARBOXYLIC ESTERS FROM 3-(2-OXO-1,2-DIHYDRO-3-QUINOLYL)ACRYLIC ESTERS

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Abstract

Bromination followed by dehydroxychlorination of 3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic methyl esters yielded the trihalo compound.These afforded thieno(2, 3-b)quinoline-2- carboxylic methyl esters in good yields by boiling with thiourea in the protic solvent.

INTRODUCTION

Numerous thieno(2,3-b)quinoline derivatives are well documented for their pharmacological properties exhibiting anti-bacterial[1-3], anti-fungal[2-3], anti-anaphylactic activity[4], antiarrhythmic activity, anti-inflammatory activity[5].

Early workers from our laboratory have synthesised thieno(2, 3-b)quinolines using 3-vinylquinolin-2(1H)-ones[6-8], 3-(2′-hydroxyethyl)-2-quinolines[9], 4, 5-dihydrofuran-3-carboxanilides[10-11] and 2,3-dihydrothieno(2, 3-b)quinoline-S-oxides[12] as starting compounds. Herein we report the synthesis of thieno(2, 3-b)quinoline-2-carboxylic esters 4 from 3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic esters 2 which in turn were prepared from 2-chloro-3-formyl quinolines [13] (scheme-1)

EXPERIMENTAL

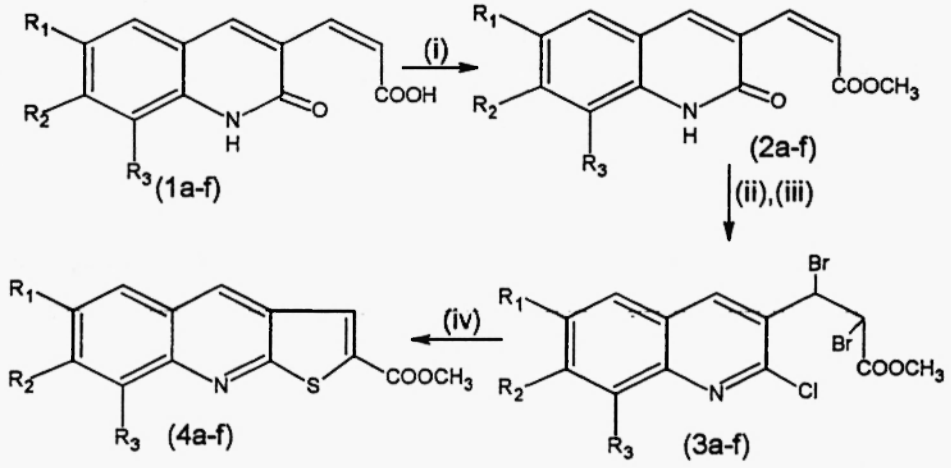
Melting points were determined using Raaga melting point apparatus and were uncorrected. The IR spectra were recorded on FTIR 8201(PC)S spectrometer as KBr pellets and the absorption frequencies are expressed in reciprocal centimeters(cm^{-1}). Proton NMR spectra were recorded on a Gemini-200MHz or on a Varian AMX 400 spectrometer in $CDCl_3$. The chemical shifts were expressed in δ(PPM) downfield from tetramethylsilane as an internal standard. Elemental analysis was performed by Perkin-Elmer model 240B CHN analyser and the values are within the permissible limits[±0.5]. The Mass spectra were recorded by EIMS technique on an Autospec mass spectrometer. The crude products were checked by thin layer chromatography and purified by column chromatography using silica gel [60-120 mesh].

3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic acids[14] **1** were synthesised according to the previously reported procedures.

Preparation of 3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic methyl esters **2**:

The methyl ester was obtained in an almost quantitative yield by boiling the 3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic acid **1** [3g] with concentrated sulphuric acid [4.5 ml] and absolute methanol [150ml]. The acid gradually passed into the solution after boiling for 5 to 6 hrs on steam bath. The solution was then allowed to cool, where a mass of needles of ester was filled within. A considerable quantity was further precipitated by dilution with two volumes of water. The whole solid was collected, washed with water, dried, recrystallised from methanol and was ready for further use.[**Table-1**]

Scheme-1



(i)conc.sulphuricacid,methanol (ii) Br_2, anhy.$CHCl_3$
(iii)$POCl_3$ (iv)Thiourea, Abs.Ethanol.

a) $R_1= R_2= R_3= H$ b) $R_1= R_3= H$, $R_2 = CH_3$ c) $R_1= R_2= H$, $R_3= CH_3$ d) $R_1= OCH_3$, $R_2= R_3= H$
e) $R_1= R_2= H$, $R_3= OCH_3$ f) R_1=H, $R_2= R_3$= -CH=CH-CH=CH-

Preparation of 2-chloro-3-(1,2-dibromo-3-quinolyl)acrylic methyl esters **3** :

The mwthyl ester **2** [0·0228 mole] was treated with freshly distilled phosphorus oxychloride [13.6ml, 0·148 mole] and kept on a steam bath for 5-6 hrs. On cooling and pouring into crushed ice the compound seperated as a creamy white solid. It was then recrystallised from petroleum ether:benzene [4:1v/v] and obtained as a creamy white coloured needles.

Preparation of Thieno(2, 3-b)quinoline-2-methyl esters :

A solution of the compound **3** [2.28g, 0.0056mole] and thiourea [0.0056 mole] in dry ethanol [30ml] was refluxed on a steam bath for 5-6 hrs. The solvent was then allowed to boil off and the residue was

mixed with chloroform and washed with water. The organic layer was separated, dried with anhydrous sodium sulphate and evaporated.Column chromatography of the residue with 100% pet.ether[60-80°C] furnished colourless crystals. This was again recrystallised from petroleum ether. **[Table-2]**

Table-1: Physical and spectroscopic data of 2a-f*

Compound	Yield	M.pt °C	IR(KBr, cm^{-1})
2a	95	218-219	1707, 3100, 3180
2b	93	143-144	1715, 3120, 3170
2c	90	236-237	1711, 3109, 3163
2d	90	139-140	1720, 3133, 3152
2e	90	130-131	1710, 3095, 3158
2f	95	148-149	1731, 3145, 3154

*recrystallised from methanol

RESULTS AND DISCUSSION

Esterification of 8-methyl-3-(2-oxo-1, 2-dihydro-3-quinolyl)acrylic methyl acid **1c** with absolute methanol and concentrated sulphuric acid at reflux temperature furnished shiny needle shaped crystals 8-methyl-3-(2-oxo-3-quinolyl)acrylic methyl ester 2c in 90% yield. This was saturated with bromine followed by dehydroxychlorination with phosphorus oxychloride resulting in a creamy white solid. This was followed by recrystallisation from pet.ether :benzene[4:1v/v] giving rise to needle shaped crystals. The spectral values of the compound was found to be as follows.

IR(KBr, cm^{-1}): appearance of prominent peaks at 1739 (-C=O), 1085(-C-Cl).

^{1}H-NMR($CDCl_3$)δ ppm: 3.94(s, 3H, CH_3 of ester), 2.77(s, 3H, CH_3), 5.15(s, 2H,-CHBr-CHBr-), 7.49(t, 1H, C_6-H, J=7.4Hz), 7.63(d, 1H, C_5-H, J=7Hz), 7.69(d, 1H, C_7-H, J=8Hz).

Thus confirming the structure of the compound as 2-chloro-3-(1,2-dibromo-3-quinolyl)acrylic methyl ester **3c**. The compound **3c** upon reaction with thiourea in dry ethanol furnished a compound in 80% yield.

IR(KBr,cm^{-1}): appearance of prominent peaks at 1715(-C=O),disappearance of 1085(-C-Cl).

^{1}H-NMR($CDCl_3$) δppm: 2.87(s, 3H, CH_3), 3.99(s, 3H, CH_3 of ester), 7.45 (t, J=7.6Hz, C_6-H), 7.64(d, J=7.6Hz, C_5-H), 7.82(d, J=7.8Hz,C_7-H), 8.10(s, C_4-H), 8.63(s, C_3-H).

The mass spectrum showed the molecular ion peak at 257(M^+). Thus the structure of the compound was identified as 8-methylthieno(2, 3-b)quinoline-2-carboxylic methyl ester 4c .The above reaction sequence was extended to synthesise the other derivatives **4a, 4b, 4d,** 4e and **4f** respectively.

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Table-2 : Physical and spectroscopic data of 4a-f[a]

Cpd[b]	M.Pt °C (yield %)	IR(KBr cm^{-1})	^{1}H-NMR($CDCl_3$) δ ppm	Mass m/z (M^+)
4a	133-134 (87)	1718	3.99(s, 3H, CH_3 of ester), 7.58(t, J=7.8Hz, C_6-H), 7.81(t, J=7.8Hz, C_7-H), 7.99(d, J=7.8Hz, C_5-H), 8.16(d, J=8.8Hz, C_8-H), 8.54(s, C_4-H), 8.68(s,C_3-H)	243
4b	154-155 (156-158)[15] (85)	1720	2.67(s, 3H, CH_3), 4.01(s, 3H, CH_3 of ester), 7.22-8.56 (m, 5H, C_3, C_4, C_5, C_6, C_8-H)	257
4c	184-185 (89)	1715	2.87(s, 3H, CH_3), 3.99(s, 3H, CH_3 of ester), 7.45 (t, J=7.6Hz, C_6-H), 7.64(d, J=7.6Hz, C_5-H), 7.82(d, J=7.8Hz,C_7-H), 8.10(s, C_4-H), 8.63(s, C_3-H).	257
4d	225-226 (84)	1724	3.99(s, 3H, OCH_3), 4.11(s, 3H, CH_3 of ester), 7.52-8.07 (m, 4H, C_4,C_5,C_7,C_8-H), 8.54(s,C_3-H).	273
4e	103-104 (45)	1729	3.95(s, 3H, CH_3), 4.01(s, 3H, CH_3 of ester), 7.25-7.99(m, 5H, C_3, C_4, C_5, C_6, C_8-H).	273
4f	161-162 (80)	1735	4.02(s, 3H, CH_3 of ester), 8.05(s, C_4-H), 8.54(s, C_3-H), 6.55-7.46(m, 6H, C_5, C_6,C_7, C_8, C_9, C_{10}-H)	293

[a]recrystallised from Pet.ether, cpd= compound

[b]The elemental analyses of all the compounds were in satisfactory agreement with the calculated values C, ±0.22; H, ±0.14; N,±0.21

REFERENCES:

1. Abdel-Rahman Abdu, E Bakhite Etify. A, Abdel-Moneam Maisa.I, Mohamed Thana.A,. Phosphorus, Sulfur Silicon Relat.Elem. **73(1-4)**, 219-27(1992).
2. Hafez A. A. Abdel, El Dean A. M. Kamal, Hassan A. A. El-Kashef H. S, Bull.Fac. Sci. **23(1)**, 93-107(1994).
3. Geies A. A, Bakhite E. A, El-Kashef H.S, Pharmazie. **53(10)**, 686-690(1998).
4. Wagner G, Vieweg H, Leistner.S, Pharmazie. **48(8)**, 576-8(1993).
5. E. A. Harrison, Jr, and K.C.Rice, J.Heterocyclic.chem. **14**, 909(1977).
6. P. Shanmugam, K.Kanakarajan, N.Soundararajan, A.Gnanasekaran, Synthesis. 253-255,(1976).
7. Periappa Shanmugam, Nachimuthu Soundararajan, Kuppusamy Kanakarajan, J.Chem.Soc. Perkin Trans I., 2O24-25, (1977).
8. Senthil.M, Shanmugam.P, Sathurappan.G, Indian J.Chem. **2b(12)**, 1017-20,(1989).
9. P.Shanmugam, T.K.Tiruvengadam, N.Soundararajan, Org.Prep.Proceed.Int. **8(b)**, 279-82(1976).
10. A.Gnanasekaran, N.Soundararajan, P.Shanmugam,. Synthesis. 612-614(1977).
11. Gnanasekaran.A, Suresh. J. R, Shanmugam. P, Sulfur lett. 15-23(1993).
12. Rajendran. S. P, Shanmugam. P, Org. Prep. Proceed. Int. **26(3)**, 349-52(1994).
13. O.Meth.Cohn, B.Narine, B.Tarnowski. J. Chem. Soc. Perkin Trans I. 1520(1981).
14. T.Tilakraj, Sarvottam Y.Ambekar. J.Indian.Chem.Soc., **Vol LXII**, 251-253(1985)
15. O.Meth.Cohn, B.Narine, B.Tarnowski and R. Hayes, A. Keyzad, S. Rhouati, A. Robinson J. Chem. Soc. Perkin Trans I,. 2509(1981).

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