The Synthesis of 4-Ethyl-2-propyl-3-substituted-pyrrolo[3,4-b]quinoline-1,9-dione Derivatives from 3,3-Dichloro-4-ethyl-thieno[3,4-b]quinoline-1,9-dione and Propylamine

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ABSTRACT

The preparation, spectral properties and structure elucidations of the hitherto undocumented 3-oxo-, 3-thioxo-, 3-propylimino-, 3-imino-, and 3-propylamino- derivatives of 4-ethyl-2-propyl-2,3-dihydro-pyrrolo[3,4-b]quinoline-1,9-dione are described. Mechanistic aspects relating particularly to the formation of the latter two unprecedented products are considered. Magnetic anisotropic effects (deshielding/line broadening of signals) are exhibited by the α-methylene protons of the 4-ethyl moiety in the ^{1}H NMR spectra of the first four of the above, and in several 3,3-dichloro-thieno[3,4-b]quinoline-1,9-diones and intramolecular H-bonded, 1,2-dialkyl-4-oxo-3-quinolinecarboxylic acid precursor substrates.

KEYWORDS

3-Imino-, 3-propylamino-, 3-propylimino-, 3-oxo-, 3-thioxo-substituted 4-ethyl-2-propyl-2,3-dihydro-pyrrolo[3,4-b]quinoline-1,9-diones, 4-methyl-, 4-propyl-substituted-3,3-dichloro-thieno[3,4-b]quinoline-1,9-diones, intramolecular H-bonding, magnetic anisotropic effects.

1. Introduction

It was earlier shown[1] that thionyl chloride acts on 1-ethyl-2-methyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid **1a** (Scheme 1)[2] to form 3,3-dichloro-4-ethyl-thieno[3,4-b] quinoline-1,9-dione **2a** at room temperature, which converts to end-product 3,3,9-trichloro-thieno[3,4-b]quinolin-1-one **3** on heating. It was also shown[3] that the aminolysis of **3** with an aliphatic primary amine RNH_2 furnishes, *inter alia*, a 4-chloro-*N*-alkyl-2-(alkylamino)thioxomethyl-3-quinolinecarboxamide **4**, such as **4a**, a 2-alkyl-3-alkylimino-9-thioxo-pyrrolo[3,4-b] quinoline derivative **5**[4], such as **5a**, and a 9-chloro-2-alkyl-3-alkylimino-pyrroloquinoline **5b**. Compound **5a** was envisaged[3] to arise *via* hydrosulphide ion, generated *in situ*, substituting the 9-chlorine atom in **5b** in a novel (overall) sulphur rearrangement reaction. Amine salts of **5a**, *viz.* **6**, exhibited significant antimicrobial properties[5]. Here we report: (i) assigning the two D_2O-exchangeable signals in representative diamide **4a**, and by extension, in other **4**; (ii) confirming the potential and utility of the aminolysis methodology to synthesize a variety of hitherto undocumented and novel pyrrolo[3,4-b]quinoline derivatives; (iii) isolating and establishing the structures of the various propylaminolysis products, including the atypical 3-imino- and 3-propylamino-substituted pyrrolo[3,4-b]quinolines **8** and **11**, respectively; (iv) demonstrating and discussing the anisotropic (deshielding/line-broadening) phenomena in the ^{1}H NMR spectra of certain of the 3-substituted pyrrolo[3,4-b]quinoline and 4-alkyl-3,3-dichloro-thieno[3,4-b]quinoline derivatives, and in several precursor intramolecular H-bonded 1,2-dialkyl-4-oxo-3-quinolinecarboxylic acids; and (v) offering possible mechanistic pathways leading to the various products.

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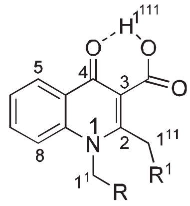
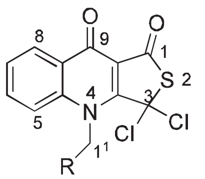
2. Results and Discussion

The ^{1}H NMR spectra of the previously[3] derived **4**, *viz.* **4a**, **4b** and **4c** (Scheme 1) each displayed two D_2O-exchangeable signals for the respective amide protons, one near δ_H 6 and the other near δ_H 9. These assignments have now been determined in representative amide **4a** R=*iso*Pr) (as were also those of ^{1}H- and ^{13}C-NMR peaks in the other currently prepared structures) by means of connectivity information from homo- and hetero-atom scalar couplings). Thus in **4a**, COSY established coupling between the δ_H 4.25 (methine, H-3^{11}) and δ_H 6.1 (H-2^{11}) protons, and between the δ_H 4.75 (methine, H-3^1) and δ_H 8.93 (H-2^{11}) protons, while HMBC correlated the δ_H 4.25 proton with the δ_C 163.5 carbonyl carbon (C-1^{11}) and the δ_H 4.75 proton with the δ_C 192 thiocarbonyl carbon (C-1^1), thereby establishing the thiocarbonyl amide proton at δ_H 8.93.

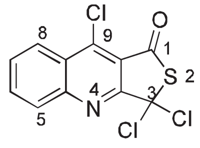
The like conclusion was reached from a NOE[6] and a ROESY experiment (in $CDCl_3$ solvent) and the assumption that in structure **4a** only the carbothioamide proton (H-2^1) could align itself sufficiently close to an aromatic proton (H-8) to elicit a positive response. In the event, exemplified in the ROESY experiment, irradiation of the δ_H 8.93 (H-2^1) (carbothioamide) proton led to enhancement of the signals at δ_H 8.07 (H-8), δ_H 4.75 (H-3^1) and δ_H 1.41 (H-4^1); in confirmation, irradiation of the δ_H 8.07 (H-8, aromatic proton) enhanced, *inter alia*, that of the δ_H 8.93 (H-2^1) signal. This outcome was not evident in DMSO-*d6* solvent,



1a R=Me, R^1=H
1b R=Et, R^1=H
1c R=R^1=Me
1d R=Me, R^1=Et
1e R=R^1=H



2a R=Me
2b R=Et
2c R=H



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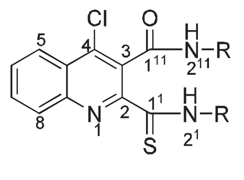
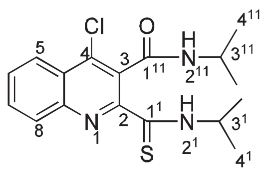
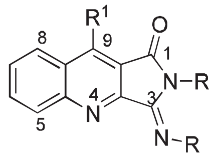


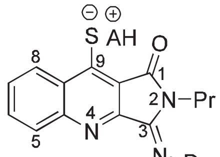
4a R=*iso*Pr
4b R=Pr
4c R=*tert*-Bu



4a



5a R^1=SH
5b R^1=Cl
5c R^1=H



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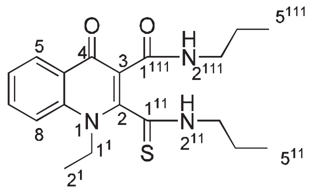
A=$EtNH_2$, $PrNH_2$, *i*$PrNH_2$, *t*-$BuNH_2$, Et_2NH, Et_3N



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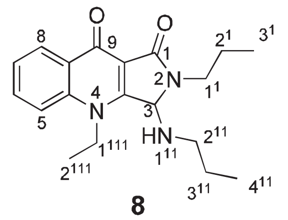

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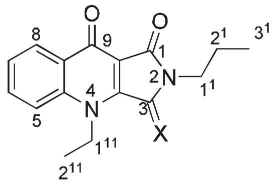
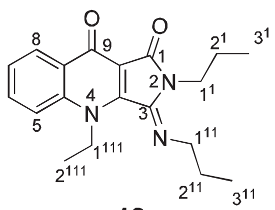


9 X=S
10 X=O
11 X=NH



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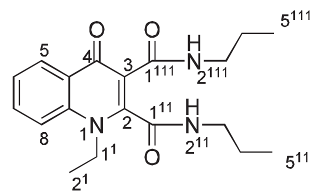

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Scheme 1
Exact stereochemistry not specified.

possibly owing to the formation of a bulkier collision[7] complex.

The rate of D_2O-exchange of the amido protons in amide **4** was seemingly influenced by steric and/or electronic factors. Thus, in **4b** (R=Pr) (in $CDCl_3$ at room temperature), both amido protons exchanged completely within minutes, whereas in **4c** (R=*tert*-Bu) each one of the corresponding two required a significantly longer time. This inference was supported with a ^{1}H NMR (DMSO-d_6, room temperature) monitoring experiment with (currently prepared) amide **7** (*vide infra*) in which the carbothioamide (δ_H 10.8) proton exchanged significantly faster (within 10 min) than did the carboxamido (δ_H 9.52) proton (>60 min).

Turning now to the application of the aminolysis methodology[3,4] to title substrate **2a**: a mixture of substrate **2a** and propylamine (in large excess) was stirred at room temperature with a combination of TLC and HPLC monitoring[8] of the progress of the reaction. Carbothioamide **7** was revealed to be an initial product, its yield reaching an (estimated) optimum value (*ca.* 70%) in 15-20 min, also formed at an early stage (as evidenced from TLC) was an unexpected reduction product, *viz.* 4-ethyl-2,3-dihydro-2-propyl-3-(*N*-propylamino)-pyrrolo[3,4-b] quinoline-1,9-dione **8** (*vide infra*). The amounts of these and of several other pyrroloquinoline reaction products decreased in the course of reaction owing to subsequent transformation by solvent (propylamine) or reagents generated *in situ* ($PrNH_3^+Cl^-$, H_2S; *vide infra*). The formation of 1-ethyl-*N*-propyl-

Table 1 NMR-derived atom connectivity and related information for 4-ethyl-2,3-dihydro-2-propyl-3-(N-propylamino)-pyrrolo[3,4-b]quinoline-1,9-dione (**8**).

Atom	δ ^{1}H /ppm – J /Hz	Integral	δ ^{13}C /ppm	COSY	HMBC
1	–	–	164.5	–	1^{1}, 3
1^{1}(a)	3.50 (m)	1	38.9	2^{1}	1, 2^{1}, 3, 3^{1}
1^{1}(b)	2.95 (m)	1	38.9	2^{1}	1, 2^{1}, 3, 3^{1}
1^{111}(a)	4.81 (bs)	1	41.3	2^{111}	–
1^{111}(b)	4.43 (m)	1	41.3	2^{111}	2^{111}, 3a, 4a
1^{11}	3.52 (bs)	1	–	2^{11}, 3	3a
2^{1}(a)	1.58 (m)	1	21.0	1^{1}, 3^{1}	1^{1}, 3^{1}
2^{1}(b)	1.50 (m)	1	21.0	1^{1}, 3^{1}	1^{1}, 3^{1}
2^{11}(a)	2.19 (m)	1	41.9	1^{11}, 3^{11}	3^{1}, 3^{11}, 4
2^{11}(b)	1.86 (m)	1	41.9	1^{11}, 3^{11}	3^{1}, 3^{11}, 4
2^{111}	1.38 (t; 7.1)	3	13.6	1^{111}	1^{111}
3	5.61 (d; 5.8)	1	69.2	1^{11}	1, 2^{11}, 3a, 9a
3a	–	–	159.6	–	1^{11}, 1^{111}, 3
3^{1}	0.85 (t; 7.2)	3	11.1	2^{1}	1^{1}, 2^{1}
3^{11}	1.32 (m)	2	22.3	2^{11}, 4^{11}	2^{11}, 4^{11}
4a	–	–	139.4	–	1^{111}, 6, 8
4^{11}	0.76 (t; 7.5)	3	11.6	3^{11}	2^{11}, 3^{11}
5	7.88 (d; 8.7)	1	116.8	6	6, 7, 8a
6	7.79 (δ; 8.7, 7.6, 1.6)	1	132.4	5, 7, 8	4a, 8
7	7.46 (dd; 8.0, 7.6)	1	124.2	6, 8	5, 8a
8	8.26 (dd; 8.0, 1.6)	1	126.0	6, 7	4a, 6, 9
8a	–	–	128.5	–	5, 7
9	–	–	170.8	–	8
9a	–	–	109.0	–	3

2-(*N*-propylaminocarbonyl)-4-oxo-3-quinolinecarboxamide **13** as a major end-product is currently attributed to the presence of water in the propylamine reactant/solvent.

The following compounds produced in the propylaminolysis reaction(s) were separated and purified, and their structures were determined from spectral and elemental analysis:

The structure of carbothioamide **7** was assigned from its NMR spectral properties (including connectivity information) and elemental analysis ($C_{19}H_{25}N_3O_2S$). Of the two amido D_2O-exchangeable signals (DMSO-d_6) at δ_H 9.52 and δ_H 10.8, respectively), the latter was shown to be due to the carbothioamide proton (H-2^{11}, Scheme 1). Amide **7** (like its analogue **4b**),[3] when treated with glacial acetic acid, underwent cyclization-*cum*-elimination of propylamine, to give 4-ethyl-2-propyl-3-thioxo-pyrroloquinoline-1,9-dione **9**. Modified acid hydrolysis (aqueous HCl, ~90°C) of amide **7** initially yielded **9** and finally, 4-ethyl-2-propyl-pyrrolo[3,4-b]quinoline-1,3,9-trione **10**. The ^{1}H NMR spectra of **9** and **10** were noteworthy in that each displayed the α-methylene protons of the 4-ethyl group as a broad and deshielded signal stemming from the anisotropic effect of a proximate hetero atom (*vide infra*).

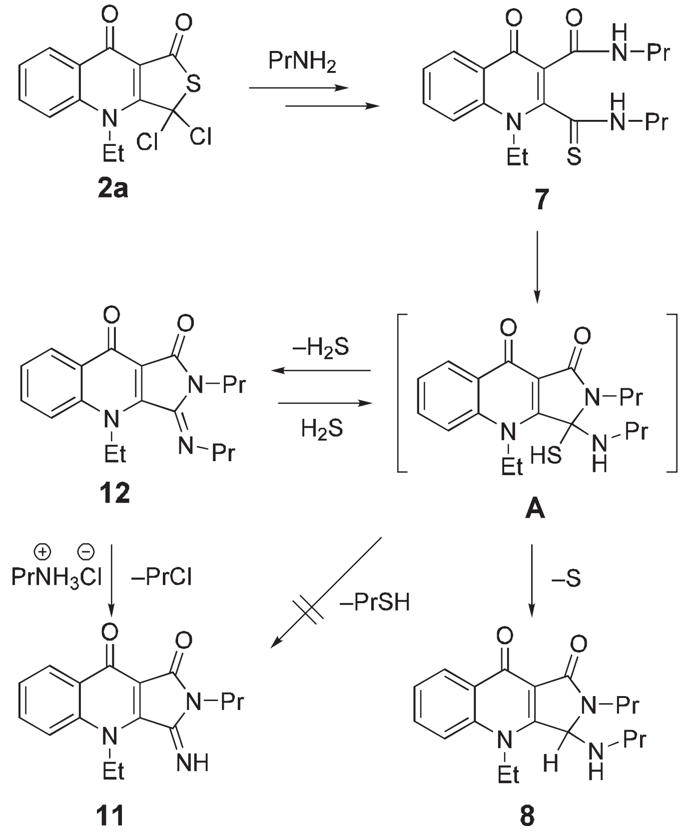
Also formed along with amide **7** in the reaction was a novel, i.e. reduction product, 4-ethyl-2,3-dihydro-2-propyl-3- (*N*-propylamino)-pyrrolo[3,4-b]quinoline-1,9-dione **8**, the structure of which was established from a comprehensive NMR study (Table 1) and elemental analysis ($C_{19}H_{25}N_3O_2$). Currently, its formation is tentatively assumed to involve elimination of sulphur from a reaction intermediate (**A**, Scheme 2, *vide infra*). The ^{1}H NMR spectrum of **8** featured, *inter alia*, four pairs of non-equivalent geminal protons (H-1^{1}, H-1^{111}, H-2^{1} and H-2^{11}; Scheme 1), respectively. The amino proton (δ_H 3.52, H-1^{11}) signal, which overlapped one of the H-1^{1} peaks, was removed by D_2O. Acid hydrolysis converted compound **8** to 4-ethyl-2-propyl-pyrroloquinoline-1,3,9-trione **10**. The reaction pathways whereby intermediate **A** is converted to reduction product **8**, and whereby acid hydrolysis transforms **8** to trione **10** remain to be clarified.

The ^{1}H NMR spectrum ($CDCl_3$) of another atypical aminolysis product, *viz.* 2-propyl-3-imino-pyrroloquinoline product **11**, $C_{16}H_{17}N_3O_2$, closely resembled those of the 3-thioxo-, and 3-oxo-derivatives, **9** and **10**, in exhibiting the α-methylene protons of the 4-ethyl moiety as a deshielded/very broad absorption near δ_H 5 (*vide infra*). The signal for the imino proton (near δ_H 8.5), overlapped that of an aromatic proton, but was well separated (δ_H 10.13) in DMSO-d_6 solvent, and readily removed by D_2O. HMBC-coupling correlations (in $CDCl_3$) observed from the proton resonance at δ_H 3.62 (H-1^{1}) located carbon resonances at δ_C 155.0 (C-3) and δ_C 164.5 (C-1), respectively, thereby unequivocally distinguishing product **11** from thione **9** [δ_C 166.5 (C-1), δ_C 188.5 (C-3)] and oxo-derivative **10** [δ_C 164 (C-1 or C-3), δ_C 165 (C-3 or C-1)]. Structure **11** was chemically substantiated by acid hydrolysis to pyrroloquinoline-1,3,9-trione **10**. The formation of imine **11** is considered to arise from propylammonium chloride (generated *in situ*) acting on 3-(*N*-propylimino)-pyrroloquinoline derivative **12** (*vide infra*).

3-Alkylimino-substituted pyrroloquinoline derivatives **5** are normally obtained in good yield from the alkylaminolysis of 3,3,9-trichloro-thienoquinoline-1-one **3**.[3] However, the analogous sterically hindered[9] and seemingly more reactive 4-ethyl-2-propyl-3-propylimino-pyrroloquinoline-1,9-dione **12** was prepared from 4-ethyl-9-oxo-3,3-dichloro-thienoquinoline-1,9-dione **2a** and propylamine by conducting the propylaminolysis reaction of substrate **2a** in the presence of lead diacetate (to remove interfering H_2S generated *in situ*).

2.1. Mechanistic Aspects

A number of tentative proposals are required to rationalize the formation of several of the aminolysis products, especially of the 3-propylamino- **8** and 3-imino-**11** derivatives, and are based on the following experimental and literature evidence: (i) As



Scheme 2
Outline of propylaminolysis reaction events/sequences. Exact stereochemistry not specified.

judged from TLC/HPLC estimations[8] thioamide **7** and 3-propyl-amino-pyrroloquinoline **8** are among the first products formed in the propylaminolysis reaction; also generated at an early stage are H_2S and $PrNH_3^+Cl^-$; (ii) 3-propylimino-pyrroloquinoline **12** appears to be an early, if not the first, non S-containing compound produced in the reaction mixture; (iii) as found experimentally, $PrNH_3^+Cl^-$ reacts with **12** to give 3-imine **11** and diamide **13**; (iv) PrSH, [in the form of its oxidation product, *viz.* dipropyl disulphide, $(PrS)_2$] was not formed (in detectable amount) in the course of the propylaminolysis reaction.

Taking cognisance of the above and knowledge of the susceptibility of several of the products to react with propylamine, it is likely that the events/sequences leading to the current pyrroloquinoline derivatives are as follows (Scheme 2):

Thioamide **7** (like its analogue **5b** from substrate **3**)[3], spontaneously cyclizes to provide the sterically[9] destabilzed intermediate **A** (Scheme 2). Competitive eliminations from **A** then occur to result in a mixture of some or all of the following products: Elimination (i) of H_2S[3] provides 3-propylimino-pyrroloquinoline (**12**); (ii) of propanethiol gives 3-imino-pyrroloquinolne **11**; and (iii) of sulphur yields reduction product 3-propylamino-pyrroloquinoline (**8**); the latter compound can be envisaged to arise from H_2S acting on the π-bond in **12** as in a Willgerodt-Kindler reaction[10], and involves a sulphur elimination as in (iii).

Experiments in support of, or otherwise to invalidate, the aforementioned suggestions were initiated: (a) It was established that propanethiol in propylamine solution in the presence of air rapidly oxidizes to dipropyl disulphide $(PrS)_2$, and that $(PrS)_2$ in propylamine solution could be detected by TLC (silica gel, benzene, iodine vapour) at a concentration of 0.3-0.4 mg/mL. At no time during the monitoring of the propylaminolysis of **2a** (involving stirring and atmospheric exposure) was $(PrS)_2$ detected (although its production would have amounted to well within the limits of detection for the amount of **11** formed). From this observation it is concluded that imine **11** does not arise from intermediate **A** by elimination of propanethiol. (b) Subsequent investigation indicated that another entity present in the reaction mixture, *viz.* propylammonium chloride, is most likely the agent responsible for 3-imine **11** production (from 3-propylimino-derivative **12**). Experiments showed that 3-propylimino-pyrroloquinoline **12** reacted with propylamine (only) to give diamide **13**, and with propylamine containing $PrNH_3^+Cl^-$ to yield both diamide **13** and 3-imine **11**.

2.2. Magnetic Anisotropic Effects

There are many examples in the literature[7,11] of the deshielding and line-broadening of ^{1}H NMR signals of protons by the presence in their vicinity of a magnetically anisotropic atom, e.g. halogen, or group, e.g. C=O, C=S and C=N-R. We report the phenomena in the currently prepared 3-thioxo-, 3-oxo-, 3-imino- and 3-propylimino-pyrrolo[3,4-b]quinolines **9**, **10**, **11** and **12**, respectively, and in their appropriate precursor compounds, *viz.* the 4-ethyl-, 4-propyl-, and 4-methyl-3,3-dichloro-thieno[3,4-b]quinoline-1,9-diones **2a**, **2b** and **2c**, and the intramolecularly[12] H-bonded 1,2-dialkyl-4-oxo-3-quinolinecarboxylic acids **1a**, **1b**, **1c**, **1d** and **1e**.

In all of the aforementioned pyrroloquinoline derivatives the α-methylene protons (H-1[1]) of the 4-ethyl group lie close to and in the deshielding region of a proximate hetero atom thereby resulting in a broad absorption near δ_H 5.0. In the thienoquinolines **2a** and **2b** the corresponding pair (H-1[1]) are likewise effected by the neighbouring chlorine atoms and resonate as a broad peak (*ca.* 2H) near δ_H 5.0 (**2a**), and near δ_H 4.8 (**2b**), respectively, while those of the 4-methyl protons in **2c** appear as a singlet (3H) at δ_H 4.35. Geometrical constraints resulting from the

H-bonding in acid **1** place the relevant (H-1^{11}) methylenes close to, and in the nodal plane, of the carbonyl oxygen of the carboxyl group as is evidenced from the broad and deshielded absorptions (*ca.* 2H) near δ_H 3.5 (**1c** and **1d**), and the singlet (3H) at δ_H 3.19 for the 2-methyl protons of **1b**.

The reality of the anisotropic effects described for the aforementioned current compounds receives support from the following comparative δ_H-values: (i) As opposed to the very broad and deshielded signal near δ_H 5.2 (*ca.* 2H) in 3-propyliminoquinoline **11**, the comparable methylene protons (1^{111}) in 3-propylamino pyrroloquinoline **8** absorb as a doublet [δ_H 4.81 (1H) and δ_H 4.43 (1H). (ii) In the representative quinoline derivatives (a) 1,2-diethyl-, and (b) 1,2-dimethyl-4(1H)-quinolinones, the δ_H-values of the non-deshielded comparable protons in (a) are: 4.25 (2H, q, *J* 7.2 Hz, H-1^{1}) and 2.75 (2H, q, *J* 7.4 Hz, H-1^{11}), and in (b)[13] are: 3.63 (3H, s, H-1^{1}) and 2.37 (3H, s, H-1^{11}), respectively. (iii) The H-bonding geometry requisite for the exhibition of broadening/deshielding effects in 1,2-dialkyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acids **1** (*vide supra*) is absent in their esters,[3] and is disrupted on forming the acid **1** anion. This latter aspect was demonstrated with 1,2-diethyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid **1c** (in $CDCl_3$): the broad absorption (*ca.* 2H) near δ_H 3.6 of the anisotropically deshielded α-methylene protons (H-1^{11}) was transformed, after addition of Na_2CO_3/D_2O, to a normal quartet (2H, q, *J* 7.5 Hz) at δ_H 2.76.

In each of the above anisotropically-effected structures the α-proton of an appropriate methylene group at any instant is situated in a different molecular environment[7], one of which is the deshielding zone of the hetero atom. Rotation about the N-C and/or C-C bond(s) exchanges the environment so that the broadening and deshielding phenomena vary with the temperature[7]. In the current work, the latter effect was shown with representative 3,3-dichloro-4-propyl-thieno[3,4-b]quinoline-1,9-dione **2b**: *inter alia*, the broad doublet [δ_H 5.2 (*ca.* 1H) and δ_H 4.35 (*ca.* 1H)] for the proton pair (2H, H-1^{1}) at 260 K, had become a very broad absorption (*ca.* 2H, centred near δ_H 4.7) at 290 K, and a less broadened signal [δ_H 4.76 (*ca.* 2H)] at 320 K, arising from an increase in rotation rate. In the instance of 3,3-dichloro-4-methyl-thieno[3,4-b]quinoline-1,9-dione **2c**, the rotation of the relatively small and sterically less hindered methyl group (H-1^{1}) was sufficiently fast on the ^{1}H NMR time scale to result in a (deshielded) signal (3H, s) at δ_H 4.35, at both 293 K and 320 K.

In summary, the accessing of a variety of hitherto undocumented 4-ethyl-2-propyl-3-substituted-pyrrolo[3,4-b]quinoline-1,9-dione derivatives, including a reduction and an elimination product, has further demonstrated the utility of the aminolysis methodology in synthesis. Mechanistic routes leading to the products are outlined. Anisotropic (deshielding/line broadening) effects which feature in the ^{1}H NMR spectra of certain of the 3-substituted pyrrolo[3,4-b]quinoline derivatives, 3,3-dichloro-thieno-[3,4-b]quinoline-1,9-diones, and intramolecularly H-bonded 1,2-dialkyl-4-oxo-3-quinolinecarboxylic acids are discussed.

3. Experimental

3.1. General Methods

Melting points were recorded on a hot-stage microscope apparatus and are uncorrected. TLC was performed on aluminium-backed plates, precoated with 0.25 mm silica gel 60. Column chromatography was carried out on silica gel 60. HPLC solvent generally used to elute: hexane: isopropyl alcohol; 450:50. NMR spectra were recorded on a Bruker AC-200 (200.13 MHz for ^{1}H), a Bruker DPX (399.900 MHz for ^{1}H) or a Bruker DRX (600.18 MHz for ^{1}H) spectrometer. $CDCl_3$ was used as solvent unless otherwise noted, and TMS as internal standard. COSY-, HSQC- and HMBC-correlated spectra were routinely used for assignments of signals, supplemented on occasion when warranted by ROESY and NOE experiments. HRMS spectra were recorded at 70 eV on a VG 70 SEQ mass spectrometer. Propylamine refers to *n*-propylamine unless otherwise indicated. Several of the compounds formed in the propylaminolysis reaction(s) were very similar by TLC while analytical HPLC showed a number of compounds to have similar retention times. Therefore the compounds were very difficult to separate cleanly by column (silica gel) chromatography. Even semi-preparative HPLC (on a 1 cm diameter column) was unsuccessful because of overlap of peaks. Moreover, several of the products such as thioamide **7** and pyrroloquinoline-1,3,9-trione **10** reacted further with propylamine (and at different rates). Therefore, in order to isolate a specific product, reaction conditions such as time, temperature, concentration, or presence of lead diacetate (*vide infra*) (or an appropriate combination) had to be manipulated to afford the desired compound in satisfactory yield.

3.2. Starting Materials

Acids **1a**, **1b**, **1c**, **1d** and **1e** were prepared by hydrolysis of the respective appropriate 1,2-dialkyl-1,4-dihydro-4-alkylimino-3-quinolinecarboxylates.[12a] The 3,3-dichloro-thieno[3,4-b]-quinolines **2b** and **2c** were obtained from the appropriate acid **1** and $SOCl_2$ at room temperature as described[1] for **2a**.

Assignment of D_2O-exchangeable protons in 4-chloro-N-(1-methylethyl)-2-[(1-methylethyl)amino)thioxomethyl]-3-quinolinecarboxamide **4a** [3]

δ_H (400 MHz, $CDCl_3$) 1.29 (3H, d, *J* 6.6 Hz, H-4^{11}), 1.40 (3H, d, *J* 6.6 Hz, H-4^{1}), 4.25 (1H, m, H-3^{11}), 4.75 (1H, m, H-3^{1}), 6.1 (1H, m, removed by D_2O, H-2^{11}), 7.63 (1H, m), 7.78 (1H, m), 8.07 (1H, d, *J* 8.4 Hz, H-8), 8.10 (1H, dd, *J* 1.4 and 8.4 Hz, H-5), 8.9 (1H, broad signal, removed by D_2O, H-2^{1}). δ_C (100 MHz, $CDCl_3$) 21.0 (C-4^{1}), 22.2 (C-4^{11}), 42.5 (C-3^{11}), 47.5 (C-3^{1}), 124.5 (C-5), 129.0 (C-6 or C-7), 129.5 (C-8), 132.0 (C-7 or C-6), 163.5 (C-1^{11}), 192.0 (C-1^{1}). HMBC ($CDCl_3$): δ_H 4.25 (H-3^{11}) correlates with δ_C 163.5 (C-1^{11}); δ_H 4.75 (H-3^{1}) with δ_C 192.0 (C-1^{1}). COSY ($CDCl_3$) correlates δ_H 4.25 (H-3^{11}) with δ_H 6.1 (H-2^{11}); δ_H 4.75 (H-3^{1}) with δ_H 8.9 (H-2^{1}). Gradient ROESY ($CDCl_3$): Irradiate: δ_H 8.93 (H-2^{1}): Observe: δ_H 8.07 (H-8), 4.75 (H-3^{1}), 1.41 (H-4^{1}). Irradiate: δ_H 8.07 (H-8). Observe: δ_H 8.93 (weak, H-2^{1}). In DMSO-d_6 (600 MHz) the two D_2O-exchangeable proton signals in **4a** are shifted downfield: δ_H 8.40 (H-2^{11}) and δ_H 10.45 (H-2^{1}), while some other signals are shifted upfield. e.g. δ_H 4.01 (H-3^{11}) and δ_H 4.59 (H-3^{1}). Gradient ROESY (DMSO-d_6): Irradiate δ_H 4.01 (3^{11}): Observe δ_H 8.40 (H-2^{11}) and δ_H 1.13 (H-4^{11}). Irradiate δ_H 4.59 (H-3^{1}): Observe: δ_H 10.46 (H-2^{1}), δ_H 4.01 (weak; H-3^{11}) and δ_H 1.24 (H-4^{1}). Irradiate δ_H 8.41 (H-2^{11}): Observe δ_H 4.01 (H-3^{11}) and δ_H 1.13 (H-4^{11}).

1-Ethyl-1,4-dihydro-N-propyl-2-[N-(propylamino)thioxomethyl]-3-quinolinecarboxamide 7 and 4-Ethyl-2,3-dihydro-2-propyl-3-(N-propylamino) pyrrolo[3,4-b]quinoline-1,9-dione **8**

3,3-Dichloro-4-ethyl-thieno[3,4-b]quinoline-1,9 dione **2a** (1.97 g; 6.27 mmol) was added portionwise (over ~5 min) with stirring to ice-cold propylamine (~10 mL, large excess). The reaction mixture was kept overnight at room temperature and treated with H_2O and $CHCl_3$. The $CHCl_3$ extract was dried (anhydrous $MgSO_4$) and evaporated under reduced pressure and temperature to a syrup which was taken up in a minimum of warm MeOH; excess EtOAc was added and the solution was stored overnight in the freezer. Crystals (775 mg), consisting principally of a mixture of products **7** and **8,** were filtered off and the mother liquor was evaporated to a syrup (1.26 g). The crystals (775 mg) were applied to a column of silica gel using acetone-benzene (3:7) containing ~5% triethylamine. Based on TLC of the fractions and consolidation, there was obtained slightly impure thioamide **7** (520 mg) and compound **8** (250 mg). The 1.26 g syrup (*vide supra*) was similarly chromatographed to provide crude thioamide **7** (570 mg; total yield: 1546 mg; ~69%) (*vide infra*) and compound **8** (69 mg; total yield: 374 mg; ~18%) (*vide infra*).

1-Ethyl-1,4-dihydro-N-propyl-2-[N-(propylamino)thioxomethyl]-3-quinolinecarboxamide **7**

Crystals (from ethyl acetate), m.p. 164°C. δ_H (600 MHz, DMSO-d_6) 0.89 (3H, t, *J* 7.4 Hz, H-5^{111}), 0.97 (3H, t, *J* 7.4 Hz, H-5^{11}), 1.35 (3H, t, *J* 7.0 Hz, H-2^{1}), 1.45 (2H, sextet, *J* 7.2 Hz, H-4^{111}), 1.69 (2H, sextet, *J* 7.3 Hz, H-4^{11}), 3.13 (2H, m, H-3^{111}), 3.52 (1H, m, H-3^{11}(a)), 3.70 (1H, m, 3^{11}(b)), 4.31 (1H, m, H-1^{1}(a)), 4.47 (1H, m, H-1^{1}(b)), 7.50 (1H, m, H-6), 7.85 (1H, m, H-7), 7.90 (1H, d, *J* 8.7 Hz, H-8), 8.33 (1H, dd, *J* 1.4 and 8.0 Hz, H-5), 9.52 (1H, bt, H-2^{111}, removed by D_2O), 10.8 (1H, bs, H-2^{11}, removed by D_2O). δ_C (150 MHz, DMSO-d_6) 11.3 (C-5^{111}), 11.5 (C-5^{11}), 14.5 (C-2^{1}), 19.8 (C-4^{11}), 22.2 (C-4^{111}), 40.1 (C-3^{111}), 42.8 (C-1^{1}), 46.5 (C-3^{11}), 117.5 (C-8), 124.5 (C-6), 126.0 (C-5), 133.0 (C-7), 138.0 (C-8a), 163.5 (C-1^{111}), 175.0 (C-4), 192.0 (C-1^{11}). (Found: C, 63.24; H, 7.01; N, 11.44. Calc. for $C_{19}H_{25}N_3O_2S$: C, 63.48; H, 7.01; N, 11.69). Monitoring of the D_2O-exchange at room temperature showed the δ_H 10.8 signal (H-2^{11}) as absent within 10 min and the δ_H 9.5 (H-2^{111}) signal still evident (*ca.* 20%) after 60 min.

4-Ethyl-2,3-dihydro-2-propyl-3-(N-propylamino)-pyrrolo[3,4-b]quinoline-1,9-dione **8**

Needles (from ethyl acetate), mp 208–211°C; Lassaigne sodium fusion test negative for Cl and S. The ^{1}H (600 MHz, $CDCl_3$) and ^{13}C (150 MHz, $CDCl_3$)-NMR data establishing structure **8** are listed in Table 1. ESI *m/z* 328 ([M+H]$^+$) (Found: C, 69.96; H, 7.39; N, 12.41. Calc. for $C_{19}H_{25}N_3O_2$: C, 69.70; H, 7.70; N. 12.84).

4-Ethyl-2,3-dihydro-2-propyl-3-thioxo-pyrrolo[3,4-b]quinoline-1,9-dione **9**

A solution of thioamide **7** (78 mg, 0.22 mmol) in glacial acetic acid (2 mL) was kept at ~50°C for ~24 h, diluted with ice-water, and the sparingly soluble crude title compound **9** was collected by filtration (67 mg, 0.22 mmol). Electrostatically-charged reddish crystals (from acetic acid), mp 258–260°C. δ_H (600 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4 Hz, H-3^{1}), 1.55 (3H, t, *J* 7.1 Hz, H-2^{11}), 1.71 (2H, sextet, *J* 7.5 Hz, H-2^{1}), 3.96 (2H, t, *J* 7.5 H-1^{1}), ~5.0 (*ca.* 2H, very broad signal, H-1^{11}), 7.52 (1H, m. H-7), 7.79 (1H, m, H-6), 7.82 (1H, d, *J* 8.5 Hz, H-5), 8.57 (1H, dd, *J* 1.4 and 8.5 Hz, H-8). δ_C (150 MHz, $CDCl_3$) 11.2 (C-3^{1}), 14.2 (C-2^{11}), 20.5 (C-2^{1}), 42.6 (C-1^{1}), 117.3 (C-5), 126.2 (C-7), 127.5 (C-8), 131 (C-8a), 133.5 (C-6), 141.0 (C-4a), 166.8 (C-1), 171.5 (C-9), 188.5 (C-3). ESI *m/z* 301 ([M+H]$^+$) (Found: C, 63.86; H, 5.60; N, 9.43. Calc. for $C_{16}H_{16}N_2O_2S$: C, 63.98; H, 5.37; N, 9.33).

4-Ethyl-2,3-dihydro-2-propyl-pyrrolo[3,4-b]quinoline-1,3,9-trione **10**

A solution of 3-thioxo-pyrroloquinoline **9** (12 mg) in 2-propanol (1 mL) containing aqueous 2 M HCl (2 mL) was kept at ~90°C overnight. After cooling, the reaction was diluted with H_2O and extracted with $CHCl_3$. Evaporation of the extract gave crude title compound **10** (9 mg). Needles (from EtOAc), mp 220–222°C. δ_H (600 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4 Hz, H-3^{1}), 1.55 (3H, t, *J* 7.2 Hz, H-2^{11}), 1.69 (2H, sextet, *J* 7.4 Hz, H-2^{1}), 3.62 (2H, t, *J* 7.3 Hz, H-1^{1}), 4.95 (*ca.* 2H, very broad signal, H-1^{11}), 7.53 (1H, t, *J* 8.0 Hz, H-7), 7.73 (1H, d, *J* 8.6 Hz, H-5), 7.79 (1H, m, H-6), 8.58 (1H, dd, *J* 1.4 and 8.5, H-8). δ_C (150 MHz, $CDCl_3$) 11.2 (C-3^{1}), 14.2 (C-2^{11}), 21.7 (C-2^{1}), 39.6 (C-1^{1}), 41.5 (C-1^{11}), 116.5 (C-5), 126.5 (C-7), 127.8 (C-8), 131.5 (C-8a), 133.3 (C-6), 140.0 (C-4a), 164.0 (C-1 or C-3), 165.5 (C-3 or C-1), 171.0 (C-9). ESI *m/z* 285 ([M+H]$^+$) (Found: C, 67.01; H, 5.78; N, 9.65. Calc. for $C_{16}H_{16}N_2O_3$: C, 67.59; H, 5.67; N, 9.85).

4-Ethyl-2,3-dihydro-3-imino-2-propyl-pyrrolo[3,4-b]quinoline-1,9-dione **11** *and 4-Ethyl-2,3-dihydro-2-propyl-3-propylimino-pyrrolo[3,4-b]quinoline-1,9-dione* **12**

3,3-Dichloro-4-ethyl-thieno[3,4-b]quinoline-1,9-dione **2a** (650 mg; 2.07 mmol) was added over ~5 min to ice-cold propylamine (5 mL; large mmol excess). The reaction mixture was kept at room temp. for a further 20 min (to ensure the complete formation of thioamide **7**). A solution (6 mL) of $Pb(OAc)_2$ in propylamine (saturated at room temp., 10 mL containing ~1.4 g $Pb(OAc)_2$) was added after which PbS immediately began to separate. HPLC evaluation showed that after ~1 h the mixture contained (estimated yields) thioamide **7** (27%), 3-propylimino derivative **12** (66%), compound **10** (5%) and 3-imino derivative **11** (2%). After ~5 h the amount of **12** present was much reduced while that of **11** was significantly increased.

4-Ethyl-2,3-dihydro-3-imino-2-propyl-pyrrolo[3,4-b]quinoline-1,9-dione **11**

To obtain **11,** the aforementioned ~5 h reaction mixture (from 650 mg **2a**) was diluted with $CHCl_3$, the PbS removed by filtration, and the washed (H_2O) and dried ($MgSO_4$) $CHCl_3$ extract was evaporated. The residual syrup (0.70 g) was applied to a column of silica gel with $CHCl_3$/acetone (4:1). Eluted fractions were examined by TLC, and by consolidation of appropriate fractions and re-chromatography there was provided imine **11** (240 mg; 0.85 mmol; 41%). Crystals, mp 181–184°C (from EtOAc). δ_H (600 MHz, $CDCl_3$) 0.97 (3H, t, *J* 7.4 Hz, H-3^{1}), 1.52 (3H, t, *J* 7.1 Hz, H-2^{111}), 1.65 (2H, sextet, *J* 7.4, H-2^{1}), 3.62 (2H, t, *J* 7.4 Hz, H-1^{1}), ~5.2 (*ca.* 2H, very broad signal, H-1^{111}), 7.49 (1H, t, *J* 7.0 Hz, H-7), 7.74 (1H, d, *J* 8.5 Hz, H-5), 7.78 (1H, m, H-6), ~8.55 (*ca.* 1H, broad signal, removed by D_2O, H-1^{11}), 8.59 (1H, dd, *J* 1.5 and 8.0 Hz, H-8). δ_C (150 MHz, $CDCl_3$) 11.2 (C-3^{1}), 14.0 (C-2^{111}), 21.5 (C-2^{1}), 38.5 (C-1^{1}), 116.3 (C-5), 125.2 (C-7), 127.7 (C-8), 130.5 (C-8a), 133.0 (C-6), 140.5 (C-4a), 155.0 (C-3), 164.5 (C-1), 171.5 (C-9). ESI *m/z* 284 ([M+H]$^+$) (Found: C, 67.77; H, 6.14; N, 14.60. Calc. for $C_{16}H_{17}N_3O_2$: C, 67.82; H, 6.05; N, 14.83). The ^{1}H NMR in DMSO-d_6 solvent showed, *inter alia*, the D_2O-exchangeable proton (1H, H-1^{11}, s) at δ_H 10.13. HMBC ($CDCl_3$) correlations: δ_H 3.62 (H-1^{1}) with δ_C 155.0 (C-3) and δ_C 164.5 (C-1). δ_H 7.5 (H-7) with δ_C 116.5 (C-5) and δ_C 130.5 (C-8a); δ_H 7.78 (H-6) with δ_C 127.7 (C-8) and δ_C 140.5 (C-4a); δ_H 8.59 (H-8) with δ_C 133.0 (C-6), δ_C 140.5 (C-4a) and δ_C 171.5 (C-9).

4-Ethyl-2,3-dihydro-2-propyl-3-propylimino-pyrrolo[3,4-b]quinoline-1,9-dione **12**

To obtain **12**, a 1 h reaction mixture (*vide supra*) from substrate **2a** (650 mg; 2.07 mmol) was treated as for **11**. The residual syrup (~630 mg) was columned [silica gel; $CHCl_3$-acetone (9:1)] to give title compound **12** (243 mg, 0.75 mmol, 36%). Crystals (from EtOAc), mp 177–178°C. δ_H (600 MHz, $CDCl_3$) 0.95 (3H, t, *J* 7.4 Hz, H-3^{1}), 1.09 (3H, t, *J* 7.4 Hz, H-3^{11}), 1.47 (3H, t, *J* 7.0 Hz, H-2^{111}), 1.66 (2H, sextet, *J* 7.5 Hz, H-2^{1}), 1.84 (2H, m, H-2^{11}), 3.85 (4H, m, H-1^{1} and H-1^{11}), ~5 (*ca.* 2H, very broad signal, 1^{111}), 7.46 (1H, m, H-7), 7.73 (2H, m, H-5 and H-6), 8.58 (1H, d, *J* 8.0 Hz, H-8). In DMSO-d_6, the aforementioned multiplet at δ_H 3.85 was well separated at 400 MHz: δ_H 3.70 (1H, t, *J* 7.4 Hz) and δ_H 3.82 (1H, t, *J* 6.4 Hz); also well separated were the aromatic protons H-5 and

H-6. δ_C 11.0 (C-3^{1}), 12.0 (C-3^{11}), 14.0 (C-2^{111}), 23.9 (C-2^{1}), 25.0 (C-2^{11}), 42.3 (C-1^{1}), 51.0 (C-1^{11}), 115.7 (C-5), 125.0 (C-7), 127.5 (C-8), 132.9 (C-6), 141.0 (C-4a), 144.0 (C-3), 166.5 (C-1), 172 (C-9). ESI *m/z* 326 ($[M+H]^+$) (Found: C, 70.18; H, 6.88; N, 12.85. Calc. for $C_{19}H_{23}N_3O_2$: C, 70.13; H, 7.12; N, 12.92).

Acid hydrolysis of compounds **8**, **11** *and* **12** *to give 4-ethyl-2-propyl-pyrrolo[3,4-b]quinoline-1,3,9-trione* **10**

(i) A mixture of 3-propylamino-pyrroloquinoline derivative **8** (22 mg), isopropyl alcohol (1.5 mL) and 2 M HCl (1.0 mL) was refluxed for ~10 h. After cooling and extracting with $CHCl_3$, evaporation of solvent gave a residue of crude title product **10**, crystals (from EtOH-H_2O), mp 216–221°C.

(ii) A mixture of imine **11** (50 mg), MeOH (10 mL) and 2 M HCl (0.5 mL) was kept at 50°C for 3 h; needles of **10** had started to separate after ~0.5 h. Cooling and filtration gave compound **10** (45 mg), mp 219–220°C.

(iii) Imine **12** (25 mg) treated as in (ii) gave **10** (16 mg), mp 221–2°C.

Each product was identified by mixture mp comparison with authentic compound **10** (*vide supra*).

1-Ethyl-1,4-dihydro-N-propyl 2-(N-propylaminocarbonyl)-4-oxo-3-quinolinecarboxamide **13**

(i) Pyrroloquinoline-1,3,9-trione **10** (67 mg) was stirred with propylamine (3 mL) at room temperature. TLC monitoring indicated that substrate **10** had all reacted in 2 h. Evaporation of the reaction and crystallization of the residue (from EtOAc/hexane) gave diamide **13**. Crystals, mp 164–165°C. δ_H (600 MHz, $CDCl_3$) 0.96 (3H, t, *J* 7.4 Hz, H-5^{111}), 1.06 (3H, t, *J* 7.4 Hz, H-5^{11}), 1.50 (3H, t, *J* 7.1 Hz, H-2^{1}), 1.60 (2H, sextet, *J* 7.3 Hz, H-4^{111}), 1.77 (2H, m, H-4^{11}), 3.45 (4H, overlapping m, H-3^{11} and H-3^{111}), 4.27 (2H, broad m, H-1^{1}), 6.81 (1H, broad signal, removed by D_2O, H-2^{11} or H-2^{111}), 7.39 (1H, d, *J* 8.7 Hz, H-8), 7.43 (1H, t, *J* 7.5 Hz, H-6), 7.64 (1H, m, H-7), 8.35 (1H, dd, *J* 1.3 and 8.1 Hz, H-5), ~9.7 (~1H, very broad signal, removed by D_2O, H-2^{111} or H-2^{11}). δ_C (150 MHz, $CDCl_3$) 11.5 (C-5^{11} and C-5^{111}), 15.0 (C-2^{1}), 22.0 (C-4^{11}), 22.5 (C-4^{111}), 41.0 (C-3^{111}), 42.0 (C-3^{11}), 44.6 (C-1^{1}), 116.2 (C-8), 124.8 (C-6), 127.0 (C-5), 133.0 (C-7), 138.7 (C-8a), 151.0 (C-2), 183.5 (C-4). ESI *m/z* 344 ($[M+H]^+$) (Found: C, 66.18; H, 6.81; N, 12.13. Calc for $C_{19}H_{25}N_3O_3$: C, 66.45; H, 7.34: N, 12.24).

(ii) Similarly, imine **12** (30 mg) after ~48 h gave diamide **13** (91%).

(iii) Similarly, 3-propylamino-pyrroloquinoline **8** (60 mg) with propylamine (3 mL) for 5-6 h gave (40 mg) diamide **13**; mp 163–164°C (from EtOAc-hexane).

The product in each instance was identified by comparison (mixture mp) with authentic diamide **13** [from (i)].

3.3. Detection of PrSH [as $(PrS)_2$] in Propylamine

It was established that PrSH in $PrNH_2$ solution is rapidly oxidized in air to dipropyl disulphide $(PrS)_2$. Also, that $(PrS)_2$ in $PrNH_2$ was detectable by TLC (silica gel, benzene, iodine) at concentrations of 0.3-0.4 mg/mL. A mixture of 3,3-dichloro-thieno[3,4-b]quinolin-1-one **2a** (38 mg) in $PrNH_2$ (0.5 mL), exposed to the atmosphere, was stirred and examined by TLC at 17, 23, 48 and 72 h; at no time was $(PrS)_2$ detected. This observation indicated that production of PrSH in the reaction is very unlikely as the amount of $(PrS)_2$ corresponding to the amount of imine **11** formed would have been detected. It was concluded that imine **11** does not arise from intermediate **A** (Scheme 2) by elimination of PrSH. The following experiment showed that the $PrNH_3^+Cl^-$ generated *in situ* is the probable agent responsible (at least to some extent) for the imine **12** → imine **11** reaction (*cf.* Scheme 2).

3.4. Conversion of Imine 12 into Imine 11 with $PrNH_2/PrNH_3^+Cl^-$

Imine **12** (10 mg) was added to a stirred solution (0.3 mL) of $PrNH_2$ containing $PrNH_3^+Cl^-$ (~24 mg). HPLC analysis indicated that the reaction mixture after 1.5 h contained (estimated amounts) imine **12** (67%), diamide **13** (14%) and imine **11** (19%); after 5.5 h: imine **12** (7%), diamide **13** (44%) and imine **11** (49%), and after 24 h: imine **12** (not detected), diamide **13** (45%) and imine **11** (39%).

1,4-Dihydro-2-methyl-4-oxo-1-propyl-3-quinolinecarboxylic acid **1b** [6]

mp 208–209°C (*ex* EtOAc) δ_H (600 MHz, $CDCl_3$) 1.15 (3H, t, *J* 7.4 Hz, H-3^{1}), 1.93 (2H, m, H-2^{1}), 3.19 (3H, s, H-1^{11}), 4.31 (2H, t, *J* 8.4 Hz, H-1^{1}), 7.53 (1H, m, H-6), 7.62 (1H, d, H-8), 7.82 (1H, m, H-7), 8.49 (1H, dd, *J* 1.4 and 8.1 Hz, H-5), 16.2 (1H, very broad signal, removed by D_2O, H-1^{111}). δ_C (150 MHz, $CDCl_3$) 11.0 (C-3^{1}), 18.5 (C-1^{11}), 22.0 (C-2^{1}), 49.5 (C-1^{1}), 116.2 (C-8), 125.0 (C-4a), 126.0 (C-6), 127.0 (C-5), 134.0 (C-7), 139.0 (C-8a), 178 (C-4).

1,2-Diethyl-1,4-dihydro-4-oxo-3-quinolinecarboxylic acid **1c**[6]

mp 167–168°C (*ex* EtOAc). δ_H (600 MHz, $CDCl_3$) 1.44 (3H, t, *J* 7.4 Hz, H-2^{11}), 1.59 (3H, t, *J* 7.2 Hz, H-2^{1}), ~3.6 (*ca.* 2H, very broad signal, H-1^{11}), 4.50 (2H, q, *J* 7.2 Hz, H-1^{1}), 7.55 (1H, m, H-6), 7.71 (1H, d, *J* 8.8 Hz, H-8), 7.83 (1H, m, H-7), 8.57 (1H, dd, *J* 1.4 and 8.1 Hz, H-5), ~16.5 (1H, broad signal, removed by D_2O, H-1^{111}). δ_C (150 MHz, $CDCl_3$) 13.3 (C-2^{11}), 14.5 (C-2^{1}), 24.0 (C-1^{11}), 42.5 (C-1^{1}), 116.2 (C-8), 125.0 (C-4a), 125.6 (C-6), 127.4 (C-5), 134.0 (C-7), 139.0 (C-8a), 165.0 (C-2), 178.5 (C-4). The anion of **1c** was formed by adding a solution of Na_2CO_3 in D_2O to **1c** in $CDCl_3$. δ_H (600 MHz, $CDCl_3$) 1.19 (6H, two overlapping triplets, H-2^{1} and H-2^{11}), 2.76 (2H, q, *J* 7.5 Hz, H-1^{11}), 4.22 (2H, q, *J* 7.2 Hz, H-1^{1}), 7.27 (1H, m, H-6), 7.56 (1H, m, H-7), 7.60 (1H, d, *J* 8.8 Hz, H-8), 8.04 (1H, d, *J* 8.1 Hz, H-5).

1,4-Dihydro-1-ethyl-4-oxo-2-propyl-3-quinolinecarboxylic acid **1d** [6]

Crystals (from EtOAc), mp 156–157°C. δ_H (200 MHz, $CDCl_3$) 1.19 (3H, t, *J* 7.3 Hz, H-3^{11}), 1.60 (3H, t, *J* 7.2 Hz, H-2^{1}), 1.68 (2H, m, H-2^{11}), ~3.5 (*ca.* 2H, very broad signal, H-1^{11}), 4.48 (2H, q, *J* 7.2 Hz, H-1^{1}), 7.55 (1H, m, H-6), 7.71 (1H, d, *J* 8.5 Hz, H-8), 7.85 (1H, m, H-7), 8.55 (1H, dd, *J* 1.5 and 8.1 Hz, H-5), 16.8 (1H, removed by D_2O, H-1^{111}).

3,3-Dichloro-4-propyl-thieno[3,4-b]quinoline-1,9-dione **2b** [6]

From acid **1b** and $SOCl_2$ at room temp. as described[1] for **2a**. Crystals (from EtOAc), mp 166–168°C. δ_H (600 MHz, $CDCl_3$) 1.13 (3H, t, *J* 7.4 Hz, H-3^{1}), 2.04 (2H, m, H-2^{1}), 4.75 (*ca.* 2H, very broad signal, H-1^{1}), 7.54 (1H, t, *J* 7.3 Hz, H-7), 7.69 (1H, d, *J* 8.7 Hz, H-5), 7.83 (1H, m, H-6), 8.53 (1H, dd, *J* 1.5 and 8.0 Hz, H-8). δ_C (150 MHz, $CDCl_3$) 10.6 (C-3^{1}), 22.3 (C-2^{1}), 49.5 (C-1^{1}), 117.5 (C-5), 126.3 (C-7), 128.0 (C-8), 129.0 (C-8a), 134.0 (C-6), 139.5 (C-4a), 172.0 (C-9). ESI *m/z* 328 ($[M+H]^+$) (Calc for $C_{14}H_{11}Cl_2NO_2S$: M, 327). Temperature dependence study: At 260 K, the (H-1^{1}) methylene protons absorbed as a doublet (δ_H 5.20, br, *ca.* 1H and δ_H 4.35, br, *ca.* 1H) centred near δ_H 4.8, and likewise those of the (H-2^{1}) methylene protons (δ_H 2.1, br, *ca.* 1H and δ_H 1.95, br, *ca.* 1H) centred near δ_H 2.05. With increase in temp. the two broad signals in each doublet began to merge, so that at 320 K the H-1^{1} protons showed as a broad peak (*ca.* 2H) near δ_H 4.75, and those of the H-2^{1} pair as a complex multiplet (2H) at δ_H 2.05.

3,3-Dichloro-4-methyl-thieno[3,4-b]quinoline-1,9-dione **2c** [6]

From acid **1e** and $SOCl_2$ at room temp. as described[1] for **2a**. Crystals (from EtOAc), mp 166–168°C. δ_H (600 MHz, $CDCl_3$) 4.35 (3H, s, H-1^{1}), 7.57 (1H, t, *J* 7.6 Hz, H-7), 7.76 (1H, d, *J* 8.6 Hz, H-5), 7.84 (1H, m, H-6), 8.52 (1H, dd, *J* 1.5 and 8.0 Hz, H-8). δ_C (150 MHz, $CDCl_3$) 37.0 (C-1^{1}), 116.3 (C-5), 126.7 (C-7), 127.3 (C-8), 129.0 (C-8a), 134.2 (C-6), 140.8 (C-4a), 161.5 (C-3a), 172.0 (C-9).

1,2-Diethyl-4(1H)-quinolinone [6]

Prepared by decarboxylation of acid **1c**. Crystals (from EtOAc-hexane), mp 114°C. δ_H (600 MHz, $CDCl_3$) 1.35 (3H, t, *J* 7.4 Hz, H-2^{11}), 1.43 (3H, t, *J* 7.1 Hz, H-2^{1}), 2.75 (2H, q, *J* 7.4 Hz, H-1^{11}), 4.25 (2H, q, *J* 7.2 Hz, H-1^{1}), 6.32 (1H, s, H-3), 7.35 (1H, m, H-6), 7.52 (1H, d, *J* 8.7 Hz, H-8), 7.64 (1H, m, H-7), 8.45 (1H, dd, *J* 1.4 and 8.0 Hz, H-5). δ_C (150 MHz, $CDCl_3$) 13.0 (C-2^{11}), 14.2 (C-2^{1}), 26.5 (C-1^{11}), 41.0 (C-1^{1}), 115.2 (C-8), 123.0 (C-6), 126.8 (C-5), 132 (C-7), 155.0 (C-2), 177.0 (C-4).

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