Reactions of 1-Methyl-4-quinolone with 2-Lithio-1,3-dithianes

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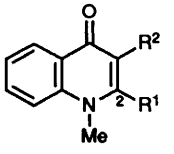
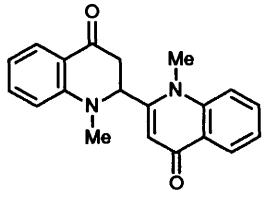
Nucleophiles, including lithiated 1,3-dithianes, add to 1-methyl-4-quinolone at the 2-position; in some cases initial adducts were subsequently trapped with added electrophile.

In the course of our studies on the 2-lithiation of 1-methyl-4-pyridone[1] and 1-methyl-4-quinolone **1a**,[2] we observed that the



	R^1	R^2
1 a	H	H
b	Li	H
c	Me	H
d	H	COPh
e	$CHS(CH_2)_3S$	CH(OH)Ph
f	$COC_6H_4CS(CH_2)_3S$-*o*	H

use of 0.5 mol equivalent of the base lithium diisopropylamide (LDA) led to the formation, in good yield, of the dimer **2** from



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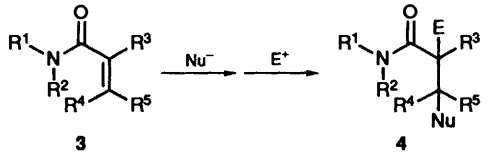
1a. This was interpreted as Michael-type addition of the lithiated species to the neutral starting material, *i.e.* addition of **1b** to the 2-position of **1a**, despite the consequent loss of aromaticity in the heterocyclic ring. In searching for precedents for this process we were surprised to find that nucleophilic additions to 4-quinolones have not apparently been previously reported. A number of similar additions have been described: alkyllithiums to 2-pyridone itself (at C-6)[3] and to 1-benzyl-2-pyridone (at C-4);[4] enamines to 3,5-dinitro-2-pyridone (at C-4);[5] and organocuprates (at C-2) to thiin-4-ones.[6]

Further related precedents are the well established nucleophilic conjugate additions to acrylamides[7] (both secondary and tertiary, with both alkyl and aryl groups on nitrogen) and to thioacrylamides.[8] The work with acyclic acrylamides and thioacrylamides also demonstrated[7,8] the trapping of the initial enolate with a subsequently added electrophile (tandem-conjugate-addition-α-alkylation) **3** ⟶ **4** (Scheme 1). It seemed to us



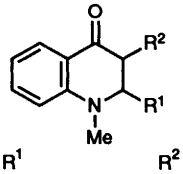
3 **4**

Scheme 1

that this concept, applied to quinolones, might provide an entry to the types of poly-heterocyclic ring systems found in many quinoline containing sea alkaloids,[9] particularly if nucleophilic and electrophilic centres could be incorporated into the same molecule. Dithioacetal-stabilised anions have been used in tandem-conjugate-addition-alkylations of butenolides[10] and with a ketone carbonyl[11] and an ester carbonyl[12] as the intramolecular electrophilic centres for trapping, in additions to butenolide and an aromatic aldehyde respectively. We describe here investigations into the interaction of some 1,3-dithiane anions with 1-methyl-4-quinolone.

Results

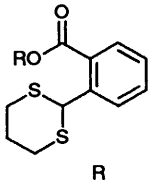
The addition of butyllithium to 1-methyl-4-quinolone, producing the quinolone **5a**, was observed in our earlier studies[2] and



	R^1	R^2
5 a	Bu	H
b	Me	H
c	$CHS(CH_2)_3S$	H
d	$CHS(CH_2)_3S$	Me
e	$CHS(CH_2)_3S$	COPh
f	Me	COPh
g	$CHS(CH_2)_3S$	CH(OH)Ph

made it necessary to effect lithiation of **1a** using LDA. In attempting to extend this observation **1a** was treated with methyllithium affording mainly the anticipated dihydro-adduct **5b** in moderate yield, and in addition quinolone **1c**, which we presume to be an autoxidation product.

Our synthetic aspirations rested on the concept of adding functionalised nucleophiles, such as an anion to be derived by deprotonation of **6**, to the quinolone, the hope being that an

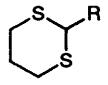


	R
6 a	Et
b	Me

initial anionic Michael intermediate would be trapped in an intramolecular fashion by the electrophilic ester function.

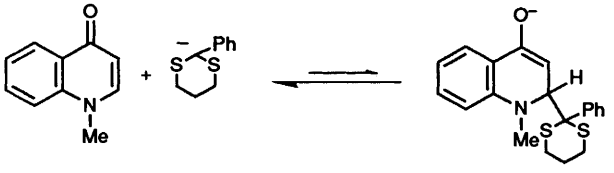
We began by assessing the viability of the first stage of the

planned tandem process by studying the reactions of the anions of 1,3-dithianes **7**. The carbanion of unsubstituted dithiane **7a**,



	R
7 a	H
b	Ph
c	3-pyridyl

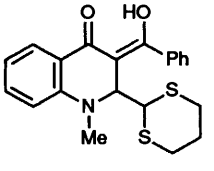
added in high yield to 1-methyl-4-quinolone to give quinolone **5c**, however with the anions derived from the phenyl and 3-pyridyl analogues, **7b** and **7c**, no reaction with quinolone **1a** took place. We interpret this as meaning that the dithiane anion addition is reversible (see also below) and that the equilibrium, for the dithiane anions further stabilised by their benzylic and pyridylic character, lies on the side of starting materials (Scheme 2).



Scheme 2

Turning to the possibility of tandem addition and α-alkylation we repeated the reaction of dithiane **7a**, but now with subsequent addition of iodomethane before work-up, and were able to isolate an adduct **5d** in which the desired sequence had indeed been realised. The 2- and 3-substituents in **5d** are *cis* as illustrated by the small (1.7 Hz) coupling between 2-H and 3-H. From a comparable experiment in which benzoyl chloride was added as an electrophilic trap, only a 60% yield of 3-benzoyl-4-quinolone **1d** was obtained. This must represent the net result of (i) nucleophilic addition at C-2, (ii) electrophilic trapping by the acid chloride, and (iii) final loss of the dithiane as its anion, initiated by base abstraction of an acidic 3-H in putative 'product' **5e**. Confirmation for this interpretation came from the reaction of the quinolone with methyllithium followed by benzoyl chloride which gave the expected **5f** as a mixture of *cis*- and *trans*-isomers.

In the light of this result we next examined the possibility of trapping, after dithiane anion addition, with benzaldehyde, expecting that in the predicted product **5g** no elimination of dithiane anion would occur, the 3-H being less acidic. In fact a separable mixture of substituted quinolone, **1e**, and its tautomer **8** was obtained. The 'non-aromatic' tautomer **8** was



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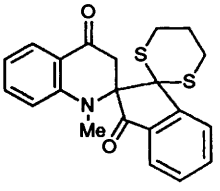
quantitatively transformed into **1e** on dissolution in methanol. Clearly both of these are autoxidation products, but they clearly demonstrate the operation of the desired tandem-addition-alkylation process in an intermolecular sense.

Having demonstrated both the dithiane addition, and the possibility of subsequent electrophilic trapping in an intermolecular sense, we treated the quinolone with ethyl 2-(1,3-dithian-2-yl)benzoate **6a** which was prepared in the usual way from the corresponding ester aldehyde.* To our surprise the product, obtained in 10% yield along with recovered starting material, was the 2-substituted quinolone ketone **1f**. The formation of this ketone can be best rationalised by postulating 2-lithiation of the quinolone,[2] with the dithiane anion acting as a base, followed by acylation, possibly in one intramolecular process, *via* the ester.

Even more intriguingly, when the same conditions were applied to the methyl ester **6b**,[13] in addition to 25% of ketone **1f**, there was isolated in 37% yield, a spiro ketone **9**, clearly deriving



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from **1f** by intramolecular dithiane anionic addition to the quinolone C-2. In a separate experiment, ketone **1f** was shown to be converted into spiro ketone **9** on treatment with butyllithium–HMPA.† The structural assignment rests on the geminal signals at δ 2.85 and 3.15, *J* 15 Hz, for the C-3 protons and on the corresponding triplet ^{13}C signal at 48.06 for C-3. Also, the chemical shift of the 1-methyl, 3.20, is typical for a 2,3-dihydroquinolone, being *ca.* 0.5–0.8 ppm more shielded than in a quinolone.

Experimental

General.—All reagents and solvents were commercially available and used without purification unless otherwise stated. All reactions were conducted under nitrogen or argon. Organic solutions were dried over anhydrous sodium sulfate or magnesium sulfate and evaporated under reduced pressure. Flash chromatography was effected on silica 60 A CC and column chromatography on silica 60H. ^1H NMR and ^{13}C NMR spectra were measured in $CDCl_3$ on a Varian XL-200 spectrometer (*J* values in Hz). UV spectra were measured on Perkin-Elmer Lambda 5 and IR spectra on Perkin-Elmer 1430 spectrometers. Mass spectra were measured on a VG MS-9 spectrometer.

1,2-Dimethyl-2,3-dihydroquinolin-4(1H)-one **5b** *and 1,2-Dimethylquinolin-4-one* **1c**.—A solution of 1-methylquinolin-4-one (100 mg, 0.63 mmol) in tetrahydrofuran (THF) (10 cm^3) was added slowly under nitrogen to a solution of MeLi (1.6 mol dm^{-3}; 2 cm^3) in THF (10 cm^3) at −78 °C. The reaction mixture was stirred for 30 min at −78 °C and then for 1 h at room temp. Aqueous NH_4Cl was added and the organic solvent was removed under reduced pressure. The resulting aqueous solution was extracted with CH_2Cl_2 and the organic solution dried and evaporated to afford a residue which was purified by column chromatography. On elution with hexane–CH_2Cl_2 (4:6) the *quinolin-4-one*, **5b** (33 mg, 30%) was obtained as an oil; $\nu_{max}(CHCl_3)/cm^{-1}$ 1620; δ_H 1.16 (3 H, d, *J* 6.6, CCH_3), 2.50 (1 H, dd, *J* 16.1, 3.0, 3-H), 2.98 (3 H, s, NCH_3), 2.99 (1 H, dd, *J* 16.1, 2.8, 3-H), 3.72 (1 H, m, 2-H), 6.63 (1 H, dd, *J* 8.4, 1.0, 8-H), 6.70 (1 H, ddd, *J* 7.9, 7.5, 1.0, 6-H), 7.40 (1 H, ddd, *J* 8.4, 7.5, 1.8, 7-H) and 7.87 (1 H, dd, *J* 7.9, 1.8, 5-H); δ_C(200 MHz) 14.09 (CCH_3), 37.15 (NCH_3), 44.32 (C-3), 56.58 (C-2), 113.27 (C-8), 116.36 (C-6), 127.66 (C-5), 135.93 (C-7) and 193.89 (C-4); *m/z* (EI, %) 175 (M^+, 4), 160 (14), 77 (20), 41 (25) and 29 (100);

* Prepared from the acid by reaction with $Et_3O^+BF_4^-$ – Et_3N.
† HMPA = Hexamethylphosphoramide.

picrate, m.p. 189–190 °C MeOH) (Found: C, 50.6; H, 3.95; N, 13.5. $C_{17}H_{16}N_4O_8$ requires C, 50.49; H, 3.98; N, 13.86%) and on elution with hexane–CH_2Cl_2 (3:7) the *quinolin-4-one*, **1c** (10 mg, 9%) was obtained; $\nu_{max}(CHCl_3)/cm^{-1}$ 1640 and 1580; δ_H 2.48 (3 H, s, CCH_3), 3.72 (3 H, s, NCH_3), 6.63 (1 H, s, 3-H), 7.24 (1 H, ddd, *J* 8.0, 7.8, 1.1, 6-H), 7.39 (1 H, dd, *J* 8.1, 1.1, 8-H), 7.59 (1 H, ddd, *J* 8.1, 7.8, 1.5, 7-H) and 7.72 (1 H, dd, *J* 8.0, 1.5, 5-H); δ_C(200 MHz) 18.79 (CCH_3), 29.07 (NCH_3), 114.52 (C-3), 121.22 (C-8), 122.04 (C-5), 125.34 (C-6), 130.60 (C-7), 146.62 (C-2) and 178.82 (C-4); *m/z* (EI, %) 174 (7), 173 (M^+, 62), 145 (17), 144 (60), 130 (46), 115 (19), 77 (24), 63 (27), 51 (32), 50 (25) and 29 (100); picrate, m.p. 182–185 °C (MeOH–Pr^i_2O) (Found: C, 50.7; H, 3.75; N, 13.9. $C_{17}H_{14}N_4O_8$ requires C, 50.74; H, 3.51; N, 13.93%).

2-(1,3-*Dithian*-2-*yl*)-1-*methyl*-2,3-*dihydroquinolin*-4(1H)-*one* **5c**.—BuLi (1.6 mol dm^{-3}; 0.43 cm^3). was added to a solution of 1,3-dithiane (76 mg, 0.63 mmol) in THF (5 cm^3) cooled at −78 °C and the mixture was stirred for 15 min at this temperature and for a further 1 h at −20 °C. The reaction mixture was cooled to −78 °C and HMPA (0.22 cm^3, 1.26 mmol) was added. After 10 min of stirring at −78 °C a solution of 1-methylquinolin-4-one (100 mg, 0.63 mmol) in THF (15 cm^3) was added. The reaction mixture was stirred for 15 min at −78 °C, then for 1 h at room temp. Aqueous NH_4Cl was added and the resulting mixture was extracted with Et_2O. The organic solution was washed several times with water, dried and evaporated to give the *quinolin*-4-*one* **5c** (160 mg, 91%), m.p. 85–87 °C ($CHCl_3$); ν_{max}(KBr)/cm^{-1} 1665 and 1600; δ_H 1.75 (1 H, m, 5′-H), 2.0 (1 H, m, 5′-H), 2.73 (4 H, m, 4′-H, 6′-H), 2.95 (2 H, m, 3-H), 3.14 (3 H, s, NCH_3), 3.70 (1 H, m, 2-H), 4.43 (1 H, d, *J* 8.0, 2′-H), 6.57 (1 H, d, *J* 8.4, 8-H), 6.65 (1 H, dd, *J* 7.8, 7.7, 6-H), 7.35 (1 H, ddd, 8.4, 7.7, 1.5, 7-H) and 7.78 (1 H, dd, *J* 7.8, 1.5, 5-H); δ_C(200 MHz) 24.97 (C-5′), 29.57 (C-4′ and C-6′), 39.78 (C-3), 40.04 (NCH_3), 49.25 (C-2′), 63.90 (C-2), 112.78 (C-8), 116.54 (C-6), 127.36 (C-5), 136.04 (C-7) and 192.02 (C-4); *m/z* (EI, %) 279 (M^+, 2), 160 (100), 119 (20) and 44 (58) (Found: C, 59.9; H, 6.15; N, 5.0; S, 22.9. $C_{14}H_{17}NOS_2$ requires C, 60.18; H, 6.13; N, 5.01; S, 22.95%).

cis-2-(1,3-*Dithian*-2-*yl*)-1,3-*dimethyl*-2,3-*dihydroquinolin*-4-(1H)-*one* **5d**.—BuLi (1.6 mol dm^{-3}; 0.43 cm^3) was added to a solution of 1,3-dithiane (76 mg, 0.63 mmol) in THF (5 cm^3) cooled at −78 °C and the mixture was stirred for 15 min then for 1 h at −20 °C. The reaction mixture was cooled at −78 °C and HMPA (0.22 cm^3, 1.26 mmol) was added. The mixture was then stirred for 10 min at −78 °C after which a solution of 1-methylquinolin-4-one (100 mg, 0.63 mmol) in THF (15 cm^3) was added. The reaction mixture was stirred for 15 min at −78 °C then for 1 h at room temp. After recooling to −78 °C, iodomethane (0.06 cm^3, 0.94 mmol) was added and the whole stirred for 15 min at −78 °C and for 1 h at room temp. Aqueous NH_4Cl was added and the resulting mixture extracted first with Et_2O and then with $CHCl_3$. The organic solutions were washed several times with water, dried and evaporated. From the $CHCl_3$ extract 15 mg of starting quinolinone were recovered. The residue from the ethereal solution was purified by column chromatography. Elution with $CHCl_3$ gave the *quinolin*-4-*one* **5d** (100 mg, 54%); ν_{max}(KBr)/cm^{-1} 1670 and 1600; δ_H 1.26 (3 H, d, *J*. 7.3, CCH_3), 1.85 (1 H, m, 5′-H), 2.05 (1 H, m, 5′-H), 2.76 (4 H, m, 4′-H, 6′-H), 3.05 (1 H, dd, *J* 7.3, 1.7, 3-H), 3.25 (3 H, s, NCH_3), 3.40 (1 H, dd, *J* 8.6, 1.7, 2-H), 4.46 (1 H, d, *J* 8.6, 2′-H), 6.64 (1 H, d, *J* 8.4, 8-H), 6.74 (1 H, dd, *J* 7.9, 7.1, 6-H), 7.44 (1 H, ddd, *J* 8.4, 7.1, 1.8, 7-H) and 7.87 (1 H, dd, *J* 7.9, 1.8, 5-H); δ_C(200 MHz) 16.66 (CCH_3), 25.20 (C-5′), 29.89 (C-4′ and C-6′), 41.01 (NCH_3), 42.73 (C-3), 49.52 (C-2′), 70.30 (C-2), 112.76 (C-8), 117.07 (C-6), 128.10 (C-5), 136.14 (C-7) and 196.16 (C-4); *m/z* (CI, %) 311 (M + 1 + NH_3, 17), 295 (19), 294 (100) and 173 (3) (Found: C, 61.1; H, 6.4; N, 4.5. $C_{15}H_{19}NOS_2$ requires: C, 61.4; H, 6.5; 4.8%).

3-*Benzoyl*-1-*methylquinolin*-4-*one* **1d**.—BuLi (1.6 mol dm^{-3}; 0.43 cm^3) was added to a solution of 1,3-dithiane (76 mg, 0.63 mmol) in THF (10 cm^3) cooled at −78 °C and the mixture was stirred for 15 min at this temperature and then for 1 h at −20 °C. The mixture was cooled to −78 °C and HMPA (0.22 cm^3, 1.26 mmol) was added. After 10 min a solution of 1-methylquinolin-4-one (100 mg, 0.63 mmol) in THF (15 cm^3) was added and the reaction mixture was stirred for 15 min at −78 °C and then for 1 h at room temp. After the mixture had been cooled again to −78 °C, benzoyl chloride (0.07 cm^3, freshly distilled, 0.63 mmol) was added. The reaction mixture was then stirred for 30 min at −78 °C and for 1 h at room temp. Aqueous NH_4Cl was added and the organic solvent was removed under reduced pressure. The resulting aqueous solution was extracted with $CHCl_3$ and the organic solution was dried and evaporated to give a residue which was purified by column chromatography. On elution with $CHCl_3$ and $CHCl_3$–MeOH (9.7:0.3) the quinolin-4-one **1d** (100 mg, 60%) was obtained; $\nu_{max}(CHCl_3)/cm^{-1}$ 1680, 1620, 1590, 1570 and 1520; δ_H 3.93 (3 H, s, NCH_3), 7.35–7.60 (5 H, m, 3′-H, 4′-H, 6-H, 8-H), 7.70–7.90 (3 H, m, 2′-H, 6′-H, 7-H), 8.23 (1 H, s, 2-H) and 8.50 (1 H, dd, *J* 8.3, 1.9, 5-H); $\delta_C(CDCl_3)$ 41.15 (NCH_3), 115.87 (C-8), 125.29 (C-5), 127.70 (C-6), 128.08 (C-3′, C-5′), 129.37 (C-2′, C-6′), 132.50 (C-7), 132.97 (C-4′), 148.59 (C-2), 175.17 (C-4) and 194.86 (C=O); λ_{max}(MeOH)/nm 380, 320 and 225 (log ε 3.01, 4.14 and 4.38); *m/z* (EI, %) 263 (M^+, 21), 262 (52), 235 (16), 234 (78), 105 (21), 77 (100) and 51 (37) (Found: C, 72.3; H, 5.1; N, 4.7. $C_{17}H_{13}NO_2{\cdot}H_2O$ requires C, 72.6; H, 5.4; N, 5.0%).

2-(1,3-*Dithian*-2-*yl*)-2-(α-*hydroxybenzylidene*)-1-*methyl*-2,3-*dihydroquinolin*-4(1H)-*one* **8** *and* 2-(1,3-*Dithian*-2-*yl*)-3-(α-*hydroxybenzyl*)-1-*methylquinolin*-4-*one* **1e**.—Using the reaction procedure and isolation sequence described for **1d**, and butyllithium (1.6 mol dm^{-3}; 1.72 cm^3), 1,3-dithiane (304 mg, 1.26 mmol), HMPA (0.22 cm^3, 1.26 mmol), quinoline **1a** (200 mg, 1.26 mmol) and benzaldehyde (133 mg, 1.26 mmol) and purification by chromatography over silica (eluting with hexane–CH_2Cl_2) the dihydroquinolinone **8** (80 mg) was obtained as a gum; $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 1660 and 1600; δ_H 1.85 (1 H, m, 5″-H), 2.00 (1 H, m, 5″-H), 2.70 (4 H, m, 3″-H and 6″-H), 3.24 (3 H, s, NCH_3), 4.57 (1 H, d, *J* 6.8, 2″-H), 4.86 (1 H, d, *J* 6.8, 2-H), 6.65 (1 H, d, *J* 8, 8-H), 6.80 (1 H, dd, *J* 6.8, 7, 6-H), 7.20–7.58 (6 H, m, 7-H and ArH) and 8.02 (1 H, dd, *J* 7, 1.2, 5-H); δ_C 25.70 (C-5″), 30.38 (C-4″ and C-6″), 40.75 (NCH_3), 49.36 (C-2″), 51.12 (C-2), 115.17 (C-8), 123.77 (C-6), 127.30 (C-4′), 128.44 (C-3′ and C-5′), 128.88 (C-2′ and C-6′), 132.15 (C-5), 143.24 (C-7) and 207.40 (C-4); *m/z* (EI, %) 383 (M^+, 0.1), 367 (3), 249 (19), 248 (100), 232 (10), 119 (30), 115 (13), 91 (10), 77 (24), 69 (13), 57 (17) and 55 (17).

Subsequent fractions afforded the quinolone **1e** (70 mg) as a gum; $\nu_{max}(CHCl_3)/cm^{-1}$ 3400, 1620 and 1570; δ_H 1.70–2.20 (2 H, m, C-5″), 2.90 (4 H, m, 4″-H and 6″-H), 3.80 (3 H, s, NCH_3), 4.40 (1 H, d, *J* 10, 2″-H), 5.48 (1 H, d, *J* 10, C*H*OH), 7.20–7.70 (8 H, m, 6-H, 7-H, 8-H, ArH) and 8.52 (1 H, dd, *J* 7.4, 1.1, 5-H); δ_C 25.65 (C-4″), 30.16 (C-4″ and C-6″), 41.37 (NCH_3), 49.25 (CH), 50.10 (CH), 115.55 (C-8), 126.77 (C-6), 127.33 (C-4′), 128.50 (C-3′ and C-5′), 128.92 (C-2′ and C-6′), 132.59 (C-5), 144.73 (C-7) and 175.80 (C-4); λ_{max}(MeOH)/nm 326, 311, 287 and 214 (log ε 3.72, 3.72, 3.61 and 4.28); *m/z* (EI %) 383 (M^+, 0.03), 260 (14), 249 (22), 248 (100), 119 (28), 115 (12), 98 (10), 97 (15), 91 (14), 83 (34), 77 (27), 69 (36) and 57 (51).

3-*Benzoyl*-1,2-*dimethyl*-2,3-*dihydroquinolin*-4(1H)-*one* **5f**.—Using the reaction procedure and isolation sequence as

described for **1d** and methyllithium (1.6 mol dm^{-3}; 2 cm^3), HMPA (0.2 cm^3, 1.26 mmol), quinolone, **1a** (100 mg, 0.63 mmol) and benzoyl chloride (0.07 cm^3, 0.63 mmol) and purification by silica chromatography, eluting with $CHCl_3$ gave the ketone, **5f** (70 mg, 40%) as a mixture of stereoisomers; δ_H 1.09 and 1.30 (3 H, 2 × d, *J* 6.8, CCH_3), 2.92 and 3.00 (3 H, 2 × s, NCH_3), 3.80–4.40 (2 H, m, 2-H and 3-H), 6.50–8.20 (9 H, m, ArH); δ_C 17.80 (CH_3), 36.40 (NCH_3), 56.22 (CH), 112.77 (C-8), 117.09 (C-6), 127.48 (C-4'), 128.33 (C-3' and C-5'), 128.70 (C-2' and C-6'), 133.57 (C-5), 135.29 (C-7) and 170.49 (C-4); *m/z* (CI, %) 297 (M + 1 + NH_3, 68), 296 (15), 281 (20), 280 (100), 279 (8), 195 (10) and 181 (11).

Ethyl 2-(1,3-*Dithian*-2-*yl*)*benzoate* **6a**.—A solution of 2-formylbenzoic acid (5 g, 33 mmol) in CH_2Cl_2 (20 cm^3) was added to triethylamine (5.75 cm^3, 41 mmol), the mixture was stirred for 10 min, triethyloxonium tetrafluoroborate (6 g, 33 mmol) was added, and the resulting mixture was stirred at room temp for 2 h. The resulting organic solution was washed with saturated aqueous sodium hydrogen carbonate and with water, dried and evaporated to give an oil which was purified by disillation to give ethyl 2-formylbenzoate (3.5 g, 60%), b.p. 110 °C (1 mmHg); ν_{max}(KBr)/cm^{-1} 1720; δ_H 1.35 (3 H, t, CH_2CH_3), 4.35 (2 H, q, CH_2CH_3), 7.30–7.70 (4 H, m, ArH) and 10.60 (1 H, s, CHO). A solution of ethyl 2-formylbenzoate (1 g, 5.3 mmol), propane-1,3-dithiol (0.6 g, 5.3 mmol) and TsOH (0.1 mg, 0.11 mmol) in benzene (15 cm^3) was heated at reflux for 12 h with azeotropic removal of water. The cooled solution was washed with aqueous NaOH (2 mol dm^{-3}), then with water. The organic solution was dried and evaporated to give the benzoate **6a** which was purified by disillation, b.p. 210–215 °C (3 mmHg) (0.6 g, 42%), m.p. 79–81 °C ($CHCl_3$); ν_{max}($CHCl_3$)/cm^{-1} 1690, 1590 and 1550; δ_H 1.41 (3 H, t, *J* 7.1, CH_2CH_3), 1.90 (1 H, m, 5'-H), 2.20 (1 H, m, 5'-H), 2.70–3.20 (4 H, m, 4'-H and 6'-H), 4.39 (2 H, q, *J* 7.1, CH_2CH_3), 6.43 (1 H, s, 2'-H), 7.34 (1 H, ddd, *J* 7.9, 7.5, 1.3, 5-H), 7.53 (1 H, ddd, *J* 7.7, 1.5, 4-H), 7.82 (1 H, dd, *J* 7.7, 1.4, 3-H) and 7.92 (1 H, dd, *J* 7.9, 1.5, 6-H); δ_C 14.64 (CCH_3), 25.73 (C-5'), 32.84 (C-4', C-6'), 47.91 (C-2'), 61.74 (CH_2O), 128.70 (C-5), 130.42 (C-6), 131.45 (C-4) and 133.31 (C-3); *m/z* [CI (NH_3), %] 287 (M + 1 + NH_3, 16), 286 (M + NH_3, 100), 269 (M, 9), 136 (10) and 69 (30) (Found: C, 58.0; H, 6.2; S, 23.7. $C_{13}H_{17}O_2S_2$ requires C, 57.96; H, 6.36; S, 23.80%).

Methyl 2-(1,3-*Dithian*-2-*yl*)*benzoate* **6b**.—This compound was prepared as described for the ethyl ester, but using trimethyloxonium tetrafluoroborate, distillation giving methyl 2-formylbenzoate (2.5 g, 45%), b.p. 110 °C (1 mmHg) [lit.,[14] 86–88 °C (0.3 mmHg)]; ν_{max}/cm^{-1} 1720; δ_H(80 MHz) 4.00 (3 H, s, CH_3), 7.50–8.00 (4 H, m, ArH) and 10.60 (1 H, s, CHO). Reaction of methyl 2-formylbenzoate (2 g, 11 mmol) with propane-1,3-dithiol (1.2 g, 11 mmol) and TsOH (0.1 mg, 0.11 mmol) in benzene (15 cm^3) was conducted as for the ethyl ester to give the *benzoate* **6b** (1.5 g, 54%) which was purified by distillation, b.p. 210–215 °C (2 mmHg); δ_H 1.95 (1 H, m, 4'-H), 2.20 (1 H, m, 5'-H), 2.80–3.20 (4 H, m, 4'-H, 6'-H), 3.92 (3 H, s, OCH_3), 6.43 (1 H, s, 2'-H), 7.33 (1 H, dd, *J* 7.8, 7.6, 4-H), 7.53 (1 H, dd, *J* 7.9, 7.6, 5-H), 7.82 (1 H, d, *J* 7.8, 3-H) and 7.91 (1 H, d, *J* 7.9, 6-H); δ_C(200 MHz) 25.10 (C-5'), 32.20 (C-4', C-6'), 47.25 (C-2'), 52.13 (CH_3), 128.09 (C-5), 129.85 (C-6), 130.85 (C-4), 132.81 (C-3) and 167.36 (C=O); *m/z* (EI, %) 254 (M^+, 27), 224 (14), 179 (31), 165 (32), 120 (36) and 77 (41) (Found: C, 56.5; H, 5.65; S, 25.2. $C_{12}H_{14}O_2S_2$ requires C, 56.66; H, 5.55; S, 25.21%).

1-*Methyl*-(2,3-*dihydroquinoline*)-2-*spiro*-2-*indan*-3'-*spiro*-2''-(1'',3''-*dithiane*)-4(1H),1'-*dione* **9** *and* 2-[2-(1,3-*Dithian*-2-*yl*)*benzoyl*]-1-*methylquinolin*-4-*one* **1f**.—Diisopropylamine (0.26 cm^3, 1.88 mmol) was added to a solution of BuLi (1.6 mol dm^{-3}; 1.2 cm^3), in THF (15 cm^3) at −78 °C and the solution was stirred at this temperature for 30 min. A solution of methyl 2-(1,3-dithian-2-yl)benzoate (320 mg, 1.26 mmol) in THF (10 cm^3) was added and the reaction was stirred for 15 min. HMPA (0.36 cm^3, 2 mmol) was added and the mixture was stirred for a further 15 min at the same temperature. A solution of 1-methylquinolin-4-one (200 mg, 1.26 mmol) in THF (15 cm^3) was slowly added at −78 °C, and after 1 h at this temperature and a further 1 h at room temp the solution was cooled at −78 °C and LDA (1.26 mmol) was added. The mixture was stirred for 30 min at −78 °C and 1 h at room temp. Aqueous NH_4Cl was added and the organic solvent was removed under reduced pressure. The resulting aqueous solution was extracted with $CHCl_3$ and the organic extract dried and evaporated to give crude material which was purified by flash column chromatography with hexane–CH_2Cl_2 (10:90). The first fractions gave the *dispiro dione* **9** (177 mg, 37%), m.p. 149–151 °C (MeOH–Me_2CO); ν_{max}(KBr)/cm^{-1} 1720, 1670 and 1600; δ_H 1.65–1.95 (2 H, m, 5''-H), 2.20–2.70 (4 H, m, 4''-H, 6''-H), 2.85 (1 H, d, *J* 15.0, 3-H), 3.15 (1 H, d, *J* 15.0, 3-H), 3.20 (3 H, s, NCH_3), 6.80 (2 H, m, 6-H, 8-H), 7.50 (2 H, m, 3'-H, 7-H), 7.80 (2 H, m, 4'-H, 5'-H) and 8.00 (2 H, m, 5-H, 6-H); δ_C 22.60 (C-5''), 28.76 (C-4'' or C-6''), 29.14 (C-6'' or C-4''), 38.70 ($3H_3$), 48.06 (C-3), 112.54 (C-8), 117.21 (C-4'), 124.44 (C-6'), 127.48 (C-6), 127.95 (C-7'), 130.36 (C-5), 136.31 (C-7 and C-7'), 190.79 (4-C=O) and 201.42 (C=O); *m/z* (EI, %) 381 (M^+, 18), 348 (11), 306 (26), 275 (24), 274 (29), 246 (36), 232 (23), 218 (26), 204 (20), 159 (30), 147 (20), 134 (22), 130 (38), 121 (30) and 77 (100) (Found: C, 65.8; H, 5.2; N, 3.5; S, 16.6. $C_{21}H_{19}NO_2S_2$ requires C, 66.11; H, 5.02; N, 3.67; S, 16.81%).

The subsequent fractions gave the *quinolin*-4-*one* **1f** (116 mg, 25%), m.p. 163–165 °C (MeOH–Me_2CO); ν_{max}(KBr)/cm^{-1} 1670, 1620 and 1600; δ_H 1.75–2.25 (2 H, m, 5''-H), 2.80–3.20 (4 H, m, 4''-H and 6''-H), 3.74 (3 H, s, NCH_3), 6.19 (1 H, s, 3-H), 6.36 (1 H, s, 2''-H), 7.21–7.96 (7 H, m, 6-H, 7-H, 8-H, 2'-H, 3'-H, 4'-H, 5'-H), 8.48 (1 H, dd, *J* 8.1, 1.7 5-H); δ_C 24.76 (C-5''), 31.94 (C-6'', C-4''), 36.89 (CH_3), 46.65 (C-2''), 112.04 (C-3), 115.76 (C-8), 124.29 (C-5), 126.79 (C-6), 128.22 (C-5'), 130.38 (C-6'), 132.16 (C-4'), 177.83 (C-4) and 192.72 (C=O); λ_{max}(MeOH)/nm 371, 336, 250 and 218 (log ε 3.28, 3.65, 4.08 and 4.29); *m/z* (EI, %) 382 (11), 381 (M^+, 43), 348 (20), 306 (39), 276 (45), 275 (39), 274 (35), 260 (28), 247 (22), 246 (42), 232 (31), 218 (39), 217 (26), 159 (21), 149 (21), 132 (25), 121 (36), 120 (29), 115 (25), 106 (29), 105 (23), 104 (24), 102 (26), 89 (53), 83 (31) and 77 (100) (Found: C, 63.3; H, 5.4; N, 3.2; S, 16.1. $C_{21}H_{19}NO_2S_2 \cdot H_2O$ requires C, 63.2; H, 5.3; N, 3.5; S, 16.0%).

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