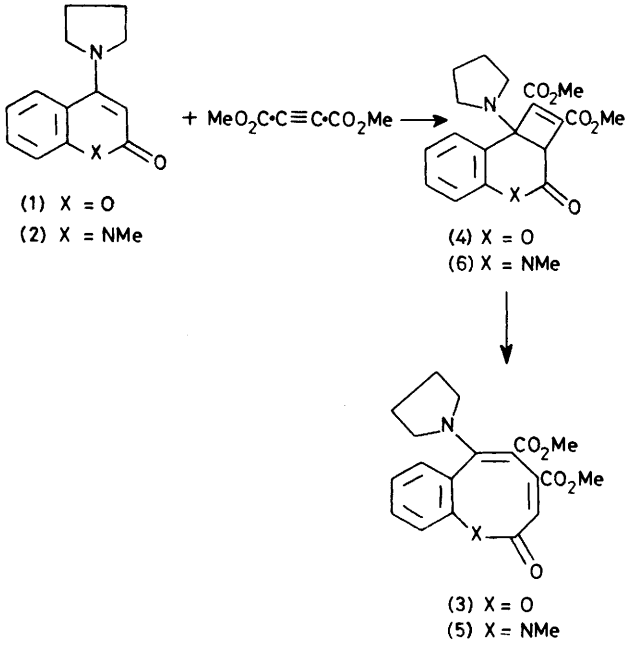
Addition of Dimethyl Acetylenedicarboxylate to 4-(Pyrrolidin-1-yl)coumarin and to 1-Methyl-4-(pyrrolidin-1-yl)quinolin-2(1*H*)-one

By **David J. Haywood** and **Stewart T. Reid,*** The Chemical Laboratory, University of Kent at Canterbury, Canterbury, Kent CT2 7NH

Addition of dimethyl acetylenedicarboxylate to 4-(pyrrolidin-1-yl)coumarin and to 1-methyl-4-(pyrrolidin-1-yl)-quinolin-2(1*H*)-one affords dimethyl 2-oxo-6-(pyrrolidin-1-yl)-1-benzoxocin-4.5-dicarboxylate and dimethyl 1.2-dihydro-1-methyl-2-oxo-6-(pyrrolidin-1-yl)-1-benzazocine-4.5-dicarboxylate, respectively, in moderate yield.

In recent years, dimethyl acetylenedicarboxylate has been widely used in the synthesis of medium-sized ring carbocycles [1] and heterocycles.[2] Cycloaddition of dimethyl acetylenedicarboxylate to a variety of cyclic alkenes provides fused cyclobutene systems which readily undergo thermal electrocyclic ring opening to yield the corresponding medium-sized ring dienes. Cyclic enamines have proved particularly valuable in this connection as reactants, and more recently the addition has been extended to include cyclic enaminoketones; in this way, dimethyl 8-hydroxy-6,6-dimethyl-4-oxocyclo-octa-1(8),2-diene-1,2-dicarboxylate has been prepared by the addition of dimethyl acetylenedicarboxylate to 5,5-dimethyl-3-(pyrrolidin-1-yl)cyclohex-2-enone.[3] In this paper, we report what to our knowledge are the first additions of dimethyl acetylenedicarboxylate to enamino-lactones and -lactams.



The systems studied were the readily available 4-(pyrrolidin-1-yl)coumarin (1) and 1-methyl-4-(pyrrolidin-1-yl)quinolin-2(1*H*)-one (2.) The coumarin (1) was prepared from 4-chlorocoumarin by a method based on that reported,[4] and the quinolin-2-one (2) was obtained by treatment of 4-chloro-1-methylquinolin-2(1*H*)-one with pyrrolidine in benzene. The structure (2) was confirmed by analytical and spectral data.

Addition of dimethyl acetylenedicarboxylate to the coumarin (1) was effected by refluxing in toluene for 48 h. The yellow crystalline adduct, obtained in 43% yield, was assigned the 1-benzoxocin structure (3) on the basis of analytical and spectral data. A singlet at δ 6.38 in the ^{1}H n.m.r. spectrum is clearly attributable to H-3 in the oxocin-2-one (3) and effectively eliminates the cyclobutene (4) as an alternative structure. The ^{13}C n.m.r. spectrum is in complete agreement with structure (3): thirteen signals in the range δ 96.3—167.0 (p.p.m. from $SiMe_4$) can be assigned tentatively to the thirteen alkene, aromatic, and carbonyl carbon atoms. The pale yellow benzazocin-2-one (5) is formed in a similar fashion in 58% yield from the quinolin-2-one (2).

In these reactions, the formation of the eight-membered heterocycles is believed to involve the intermediates (4) and (6), produced initially by cycloaddition to the 3,4-double bond of the heterocycle, which undergo thermal electrocyclic ring opening.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. I.r. spectra were recorded with a Perkin-Elmer 257 spectrophotometer, and n.m.r. spectra with a JEOL PS-100 spectrometer, with $SiMe_4$ as reference. Mass spectra were determined with an A.E.I. MS 902 instrument.

4-(*Pyrrolidin-1-yl*)*coumarin* (1).—4-(Pyrrolidin-1-yl)coumarin was prepared from 4-chlorocoumarin [5] by a method based on that previously reported.[4] Pyrrolidine (3.56 g) was added to a solution of 4-chlorocoumarin (2.70 g) in anhydrous dimethyl sulphoxide (15 ml) and the resulting solution stirred at room temperature for 24 h. The mixture was poured into water (80 ml), and the precipitate filtered off, washed with 10% hydrochloric acid, aqueous 10% sodium hydroxide, and water, dried *in vacuo*, and crystallised from methanol–diethyl ether to give 4-(pyrrolidin-1-yl)coumarin (2.70 g, 84%), m.p. 131° (lit.,[4] 130.5°), $\nu_{max.}$ (CH_2Cl_2) 1 680, 1 610, and 1 590 cm^{-1}; δ_H ($CDCl_3$) 1.9—2.1 (4 H, m), 3.5—3.7 (4 H, m), 5.2 (1 H, s), and 7.0—8.0 (4 H, m); δ_C ($CDCl_3$) 162.7 (C-2), 155.2 (C-4), 154.2 (C-8a), 131.0 (C-7), 125.7 (C-6), 122.7 (C-5), 117.8 (C-8), 116.2 (C-4a), 86.5 (C-3), and 51.9 and 25.7 (4 pyrrolidinyl carbons); *m/e* 215 (M^+, 100%).

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1-*Methyl*-4-(*pyrrolidin*-1-*yl*)*quinolin*-2(1H)-*one* (2).—Pyrrolidine (3.56 g) was added to a solution of 4-chloro-1-methylquinolin-2(1*H*)-one [6] (2.90 g) in dry benzene (20 ml) and the mixture heated under reflux for 5 h. The *quinolin*-2-*one* (2) (2.60 g, 76%) was obtained by distillation and recrystallisation of the residue from ethyl acetate; m.p. 82°; $\nu_{max.}$ (CH_2Cl_2) 1 620 and 1 580 cm^{-1}; δ_H ($CDCl_3$) 1.9—2.3 (4 H, m), 3.7—4.0 (4 H, m), 3.8 (3 H, s), 4.2 (1 H, s), and 7.3—8.6 (4 H, m); δ_C ($CDCl_3$) 163.8 (C-2), 154.1 (C-4), 140.5 (C-8a), 129.8 (C-7), 126.1 (C-5), 120.1 (C-6), 117.3 (C-4a), 114.4 (C-8), 97.2 (C-3), 51.9 and 25.7 (4 pyrrolidinyl carbons), and 29.0 (NCH_3); *m/e* 228 (M^+, 100%) (Found: C, 73.6; H, 7.0; N, 12.2. $C_{14}H_{16}N_2O$ requires C, 73.7; H, 7.1; N, 12.3%).

Dimethyl 2-*Oxo*-6-(*pyrrolidin*-1-*yl*)-1-*benzoxocin*-4,5-*dicarboxylate* (3).—Dimethyl acetylenedicarboxylate (1.00 g) was added to a solution of 4-(pyrrolidin-1-yl)coumarin (1.15 g) in dry toluene (20 ml), and the mixture was heated under reflux for 48 h. The solvent was removed by distillation under reduced pressure and the residue crystallised from methanol to give the *benzoxocin* (0.80 g, 43%), m.p. 185—186°; $\nu_{max.}$ (CH_2Cl_2) 1 760, 1 735, 1 700, and 1 535 cm^{-1}; δ_H ($CDCl_3$) 1.6—2.0 (4 H, m), 2.8—3.4 (4 H, m), 3.60 (3 H, s), 3.64 (3 H, s), 6.38 (1 H, s), and 6.9—7.4 (4 H, m); δ_C ($CDCl_3$) 167.0, 166.0, 164.9, 154.1, 149.5, 139.9, 130.8, 130.3, 128.8, 126.4, 123.9, 120.1, 96.3, 53.6 (2C), 52.5, 51.2, and 25.2 (2C); *m/e* 357 (M^+, 40%) and 282 (100) (Found: C, 64.1; H, 5.5; N, 3.8. $C_{19}H_{19}NO_6$ requires C, 63.9; H, 5.7; N, 3.9%).

Dimethyl 1,2-*Dihydro*-1-*methyl*-2-*oxo*-6-(*pyrrolidin*-1-*yl*)-1-*benzazocine*-4,5-*dicarboxylate* (5).—Dimethyl acetylenedicarboxylate (1.00 g) was added to a solution of 1-methyl-4-(pyrrolidin-1-yl)quinolin-2(1*H*)-one (1.15 g) in dry benzene (20 ml) and the mixture heated under reflux for 10 h. Distillation, followed by crystallisation of the residue from methanol, gave the *azocine* (1.10 g, 58%), m.p. 219—220°; $\nu_{max.}$ (CH_2Cl_2) 1 725, 1 690, 1 650, and 1 530 cm^{-1}; δ_C ($CDCl_3$) 1.5—2.0 (4 H, m), 2.8—3.4 (4 H, m), 3.30 (3 H, s), 3.58 (3 H, s), 3.62 (3 H, s), 6.48 (1 H, s), and 7.0—7.5 (4 H, m); δ_C 167.6 (2C), 165.1, 155.3, 141.5, 137.0, 135.7, 130.0, 129.6, 128.1, 127.5, 124.6, 96.3, 53.1 (2C), 52.2, 50.8, 34.8, and 25.6 (2C); *m/e* 370 (M^+, 35%), 355 (48), and 323 (100) (Found: C, 64.8; H, 6.2; N, 7.5. $C_{20}H_{22}N_2O_5$ requires C, 64.9; H, 6.0; N, 7.6%).

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