A New Xanthone Synthesis from the Diels–Alder Reaction between 2-Vinylchromen-4-ones and Cyclopentanone Enamine

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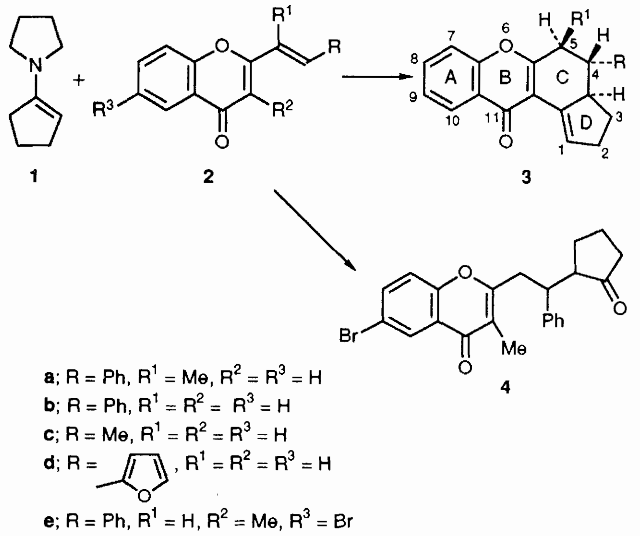
The reaction between 2-vinylchromen-4-ones and 1-pyrrolidinylcyclopentene give substituted 2,3,3a,4-tetrahydrocyclopenta[*a*]xanthen-11(5*H*)-ones; the stereochemistry of the product shows that the initial step in the reaction may be considered to be an *exo*-addition Diels–Alder with inverse electron demand.

2-Styrylchromen-4-ones have been used to synthesise xanthen-9(9*H*)-ones in very low yields *via* photochemical cyclisations,[1–3] and *via* Diels–Alder reactions with maleic anhydride and *N*-arylmaleimides.[4,5] These Diels–Alder reactions would appear to involve a diene and a dienophile which are both electron deficient. A more favourable reaction however would be expected between the electron deficient diene in 2-vinylchromen-4-ones and an electron rich dienophile such as an enamine.

We have now carried out such reactions by refluxing in 95% ethanol, equimolar amounts of the enamine 1-pyrrolidinylcyclopentene **1** and a variety of (*E*)-2-vinylchromen-4-ones **2a–d**. In each case a crystalline product with stoichiometric formula (**1** + **2**-C_4H_9N) was obtained in 50–60% yield. All products exhibited very similar spectra (*e.g.* **3a**†) showing that they have analogous structures; all showed typical IR and UV spectra for a chromone and one alkenic hydrogen (at *ca.* δ_H 7.1) in their ^1H NMR spectra. In the case of **3a** this clearly shows that the double bond is not in the position expected from an unrearranged Diels–Alder product, and is further confirmed by the methyl group (at δ_H 1.22) appearing as a doublet (*J* 6.8 Hz). In each case, structure elucidation was accomplished using 1D and 2D NMR techniques, the results of which are discussed below for **3a**. Spectral editing of the ^{13}C NMR spectra was achieved by the DEPT analysis which for the product from **1** and **2a** revealed three methines and two methylenes. The ^1H–^{13}C COSY spectrum showed that the



a; R = Ph, R^1 = Me, R^2 = R^3 = H
b; R = Ph, R^1 = R^2 = R^3 = H
c; R = Me, R^1 = R^2 = R^3 = H
d; R = , R^1 = R^2 = R^3 = H
e; R = Ph, R^1 = H, R^2 = Me, R^3 = Br

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† Satisfactory analytical and spectroscopic data have been obtained for all new compounds. *Selected data* **3a**: m.p. 189–191 °C; IR (Nujol) ν/cm^{-1} 1640; ^1H NMR (270 MHz, $CDCl_3$) δ 8.27 (dd, 1 H, *J* 7.8 and 1.3 Hz, 9-H), 7.62 (t, 1 H, *J* 7.8 Hz, ArH), 7.42–7.20 (m, 7 H, ArH), 7.11 (br s, 1 H, 1-H), 3.22 (m, 1 H, 5-H), 3.05 (m, 1 H, 3a-H), 2.45 (m, 3 H, CH_2-2 + 4-H), 1.71 (m, 1 H, 3-H_a), 1.29 (m, 1 H, 3-H_b) and 1.23 (d, 3 H, *J* 6.84 Hz, Me); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ 176.6 (CO), 167.9, 155.2, 142.3, 134.4, 123.5 and 115.0 (6 × quaternary C), 133.0, 128.7, 128.7, 128.0, 128.0, 126.9, 126.1, 124.8 and 117.6 (9 × aromatic CH), 129.4 (CH, C-1), 54.9 (CH, C-4), 50.0 (CH, C-3a), 41.4 (CH, C-5), 32.8 (CH_2, C-2), 29.0 (CH_2, C-3) and 15.4 (CH_3); *m/z* 328 (M^+, 100%), 313 (28) and 237 (18).

three methine signals, δ_c 54.9, 50.0 and 41.4, correlate with δ_H 2.44, 3.05 and 3.22, respectively; one methylene was at δ_c 32.8 (δ_H 2.46), whilst the other (δ_c 29.0) correlated with two well separated proton signals (δ_H 1.29 and 1.71). The ^{1}H–^{1}H COSY spectrum, aided by spin-decoupling experiments, revealed the following connections: Me (δ_H 1.23)–CH (δ_H 3.22)–CH (δ_H 2.44)–CH (δ_H 3.05)–CH$_2$ (δ_H 1.71 and 1.29)–CH$_2$ (δ_H 2.46)–alkenic H (δ_H 7.11). This leads unambiguously to structure **3a** for the product from **2a**, and using similar experiments and arguments, to **3b–d** for the products from **2b–d**, respectively. The stereochemistry of the cyclohexene ring was established from ^{1}H NMR spin-decoupling experiments. Irradiation of the methyl signal resulted in the multiplet at δ_H 3.22 collapsing to a doublet (with J 10.7 Hz) revealing the $J_{4,5}$ coupling constant. 4-H was similarly identified (at δ 2.44) and shown to be a triplet (superimposed on the broad C-2 CH$_2$ group) with a coupling constant approximately equal to that of $J_{4,5}$, thus revealing $J_{3a,4}$. From the Karplus equation these coupling constants indicate a large dihedral angle, or *trans*-diaxial relationship for both 5-H/4-H and 4-H/3a-H. Consequently the stereochemistry of the C-ring is established with all three substituents (at C-5, C-4 and C-3a) being in the more stable equatorial position. Furthermore, the *trans*-stereochemistry at C-3a, C-4 is consistent with a Diels–Alder reaction having occurred *via* an *exo*-addition.

These data suggest that the formation of the xanthones **3a–d** is *via* an initial Diels–Alder reaction with inverse electron demand leading to a *cis*-fused C/D ring intermediate which rearranges (1,3-hydrogen shift from C-11a to C-5) to give the chromone ring and eliminates pyrrolidine (or water if the iminium ion had hydrolysed) by presumably a *trans*-elimination involving 1-H.

In an endeavour to test the generality of the reaction with a more sterically hindered 2-vinylchromen-4-one, **2e** was treated with enamine **1**. The product was found to be quite different from **3**, and was shown to be **4** from an X-ray crystallographic structure elucidation,[6] which was needed to place unambiguously the cyclopentanone substituent on the ethyl chain. Compound **4** is presumably obtained *via* a Michael addition of the enamine giving an iminium ion which is hydrolysed. The isolation of **4** suggests a possible alternative step-wise mechanism for the formation of **3**.

The generality of this novel enamine-2-vinylchromen-4-one reaction is being studied.

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