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Photocycloaddition of angelicin and its thiinone analogue to 2,3-dimethylbut-2-ene

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Abstract

On irradiation (350 nm) in benzene containing 2,3-dimethylbut-2-ene, angelicin (**2**) and thioangelicin **3** undergo selective cyclobutane formation at the six-membered heterocycle, i.e. at the pyranone and thiinone C=C double bond respectively. © 1997 Elsevier Science S.A.

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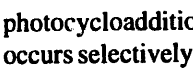
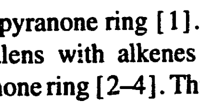
1. Introduction

Light-induced reactions of psoralens (2*H*-furo[3,2-*g*]benzopyran-2-ones, e.g. **1**) with thymine units in DNA result in the crosslinking of the two strands of the DNA helix via two consecutive (2+2)-photocycloadditions, the first occurring at the furan C=C double bond and the second at the C=C double bond in the pyranone ring [1]. In contrast, photocycloaddition of psoralens with alkenes in solution occurs selectively at the pyranone ring [2–4]. This difference in reactivity has been attributed to the fact that the photoaddition of a psoralen to a nucleic acid helix is preceded by intercalation of these linear tricyclic compounds into the DNA in a dark reaction, a process not observed for the angular "isopsoralens" (2*H*-furo[2,3-*h*]benzopyran-2-ones, e.g. **2**), which form monoadducts with DNA only [5,6]. Replacing the pyranone oxygen by sulphur improves both the dark interaction [7] and the light-induced formation of crosslinks [8,9] with DNA. In this paper, we report the results of the first comparative study of the photoreactivity of angelicin (**2**) and the corresponding thioangelicin **3** towards 2,3-dimethylbut-2-ene.



1



2: X = O
3: X = S

2. Results and discussion

Irradiation (Rayonet RPR-100 photoreactor equipped with 350 nm lamps) of an argon-degassed solution containing **2** [10] (37.2 mg, 2×10^{-4} mol) and 2,3-dimethylbut-2-ene (168 mg, 2×10^{-3} mol) in 2 ml benzene for 50 h led to about 65% conversion of the starting material to afford one new product, 4,4,5,5-tetramethyl-3α,6α-cyclobuta[*c*](2*H*-furo-[2,3-*g*]-1-benzopyran)-2-one (**4**), isolated by chromatography on SiO_2 with CH_2Cl_2 as eluent (27 mg (50%), m.p. 113 °C). Proton nuclear magnetic resonance (^{1}H-NMR) ($CDCl_3$): 7.58 (d, 2 Hz), 7.25 (d, 8 Hz), 6.95 (d, 2 Hz), 6.80 (d, 8 Hz), 3.46 (d, 10 Hz), 3.27 (d, 10 Hz), 1.29, 1.24, 1.04 and 0.75 (s, CH_3). ^{13}C-NMR ($CDCl_3$): 167 (s), 155 (s), 145 (d), 144 (s), 125 (d), 117 (s), 114 (s), 108 (d), 104 (d), 45 (s), 44 (s), 43 (d), 42 (d), 27 (q), 26 (q), 21 (q), 20 (q). Mass spectrometry (MS): 270 (M^+, 0.2%), 84 (100%).

Similarly, irradiation (Rayonet RPR-100 photoreactor equipped with 350 nm lamps and a cut-off filter (less than 340 nm)) of an argon-degassed solution containing 5*H*-thiopyrano[2,3-*e*]-1-benzofuran-5-one (**3**) [11] (40.4 mg, 2×10^{-4} mol) and 2,3-dimethylbut-2-ene (168 mg, 2×10^{-3} mol) in 2 ml benzene for 10 h led to quantitative conversion to a 1 : 4 mixture of **5** and **6** which were separated by chromatography on SiO_2 (CH_2Cl_2–hexane, 3 : 2) to give first 7,7,8,8-tetramethyl-6α,9β-cyclobuta[*h*](5*H*-thiopyrano-[2,3-*e*]-1-benzofuran)-5-one (**5**) (9 mg (15%); m.p. 103 °C; ^{1}H-NMR ($CDCl_3$): 7.54 (d, 2 Hz), 7.24 (d, 8 Hz), 7.09 (d, 8 Hz), 6.65 (d, 2 Hz), 3.46 (d, 14 Hz), 2.60 (d, 14 Hz),

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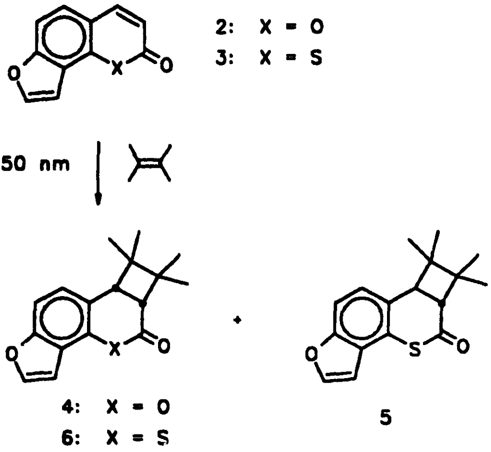
1.26, 1.18, 1.16 and 0.99 (s, CH_3); ^{13}C-NMR ($CDCl_3$): 196 (s), 152 (s), 144 (d), 131 (s), 125 (s), 124 (s), 120 (d), 107 (d), 104 (d), 52 (d), 47 (d), 42 (s), 40 (s), 23 (q), 22 (q), 19 (q), 18 (q); MS: 286 (M^+, 0.1%), 84 (100%)) and then the *cis*-fused 6α,9α-diastereoisomer **6** (40 mg (67%); m.p. 159 °C; ^{1}H-NMR ($CDCl_3$): 7.55 (d, 2 Hz), 7.23 (d, 8 Hz), 6.88 (d, 8 Hz), 6.62 (d, 2 Hz), 3.81 (d, 10 Hz), 3.03 (d, 10 Hz), 1.26, 1.09, 0.96 and 0.75 (s, CH_3); ^{13}C-NMR ($CDCl_3$): 196 (s), 152 (s), 144 (d), 125 (d), 123 (s), 122 (s), 121 (s), 108 (d), 103 (d), 51 (d), 47 (d), 46 (s), 45 (s), 26 (q), 24 (q), 20 (q), 19 (q); MS: 286 (M^+, 0.4%), 84 (100%). These data fully correlate with those of the cycloadducts of coumarin [12] and thiocoumarin [13] to the same alkene.



The photochemical reactivity of angelicin (**2**) towards simple alkenes in solution parallels that of psoralen (**1**) [2], as cycloaddition occurs exclusively at the pyranone C=C double bond and the quantum efficiency of cycloadduct formation for both furocoumarins is higher than that for coumarin [12] itself. Replacing the pyranone oxygen by sulphur (**2**→**3**) leads to the expected increase in the rate of conversion to cycloadducts due to the improved light absorption at 350 nm and the much more efficient intersystem crossing of thiocoumarins vs. coumarins. The formation of **4** : 1 mixtures of *cis*- and *trans*-fused cycloadducts at the thiinone ring has also been observed for other tricyclic [*g*]-fused thiocoumarins [14], and seems to be typical for all related molecules.

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