SYNTHESIS OF XANTHONES BY DAYLIGHT PHOTOOXIDATIVE CYCLIZATION OF (*E*)-2-STYRYLCHROMONES

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Abstract

The synthesis of 12*H*-benzo[a]xanthene-12-ones induced by daylight photooxidative cyclization of (*E*)-2-styrylchromones is reported. This transformation involves the (*E*) to (*Z*) photoisomerization of 2-styrylchromones, followed by electrocyclic and oxidative processes, and was followed by ^{1}H NMR spectroscopy.

INTRODUCTION

During the last three decades, a large number of xanthones have been isolated from both higher plants and microorganisms. The growing interest in these compounds is easily accounted for their pharmacological and microbiological activities (1,2).

The synthesis of xanthones by photooxidative cyclization of styrylchromones has been reported by two research groups (3,4). However, in each case the process was always carried out by irradiation of benzene solutions of 2-styrylchromones, in quartz vessels, with UV light; the claimed yields of the obtained xanthones were in the range 1-31 %.

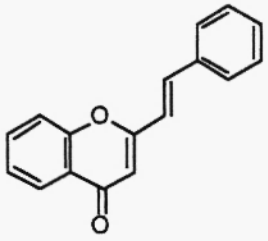
In this communication the synthesis of xanthones is reported, in 50-60 % yields, induced by day light photooxidative cyclization of chloroform solutions of (*E*)-2-styrylchromones in borosilicate glass vessels. It involves the (*E*) to (*Z*) photoisomerization of 2-styrylchromones, and then electrocyclic and oxidative processes. These latter transformations were followed by ^{1}H NMR spectroscopy.

RESULTS AND DISCUSSION

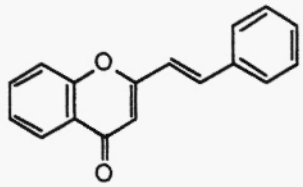
We have already reported the synthesis of 2-styrylchromones by the oxidative cyclization of 2'-hydroxy-2-cinnamylideneacetophenones, at reflux in DMSO, with a catalytic amount of iodine (5). In this work it was established that (*E*) is the stereochemistry of the vinylic system of 2-styrylchromones, unsubstituted in the double bond; also of the two possible species, 1 and 2, only 1 is present. However, in the present work, the synthesis of 2-α-alkylstyrylchromones, from the corresponding 2'-hydroxy-2-cinnamylideneacetophenones **3** was carried out. In this case it was observed that both the (*E*), **4**, and (*Z*), **5** (6), isomers were formed, the (*E*) in higher proportions. The yields, after tlc separation, were 76-83 % for (*E*) and 11-15 % for (*Z*) isomers.

The most noticeable features in the ^{1}H NMR spectra of (*E*), **4**, and (*Z*), **5**, isomers are the signals corresponding to the resonances of H-3 and H-β protons which appear as singlets, respectively at δ 6.50-6.56 and 7.52-7.66 ppm for the

(*E*) and at δ 6.24-6.30 and 6.72-6.86 ppm for the (*Z*) isomer. NOE experiments with (*E*)-2-α-methylstyrylchromone **4a** have indicated a close proximity between CH_3 and H-3 and H-2', thus allowing us to establish the stereochemistry of their vinylic system, as shown in **4a**. In the case of (*Z*)-2-α-methylstyrylchromone **5a**, proximity between CH_3 and H-3 and H-β was also shown; also no NOE effect on H-2' was observed upon irradiation of the H-3 resonance. These findings indicate that of the possible structures, **5a** and **6**, only **5a** was detected by NMR.



1



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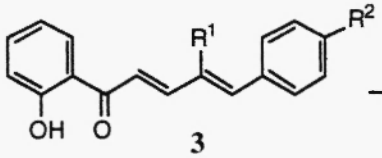
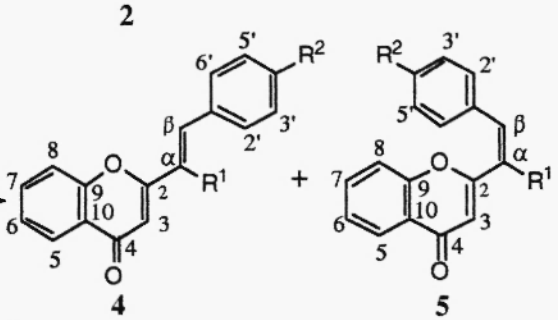


3

DMSO/I_2

Reflux, 30 min.

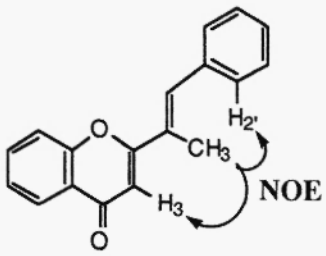


4 **5**

a) R^1 = Me; R^2 = H

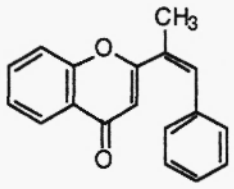
b) R^1 = Hexyl; R^2 = H c) R^1 = Me; R^2 = *t*-Butyl

d) R^1 = Me; R^2 = Cl e) R^1 = Et; R^2 = Cl

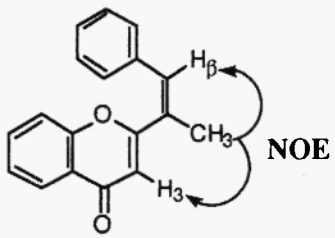


4a

Irradiation of CH_3 ---> NOE to H-3 (7 %) and H-2' (3%)



6



5a

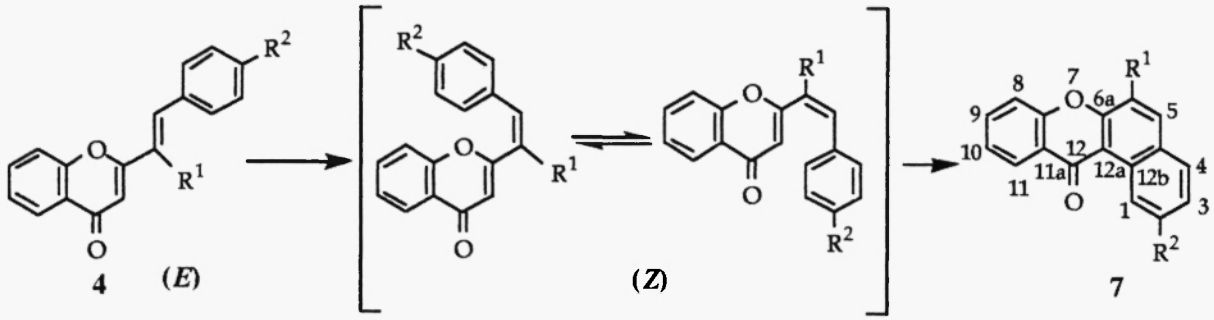
Irradiation of CH_3 ---> NOE to H-3 (7 %) and H-β (7%)

Scheme 1

A chloroform solution of each (*E*)-2-α-alkylstyrylchromones **4a-e** remains unaltered if it is kept in the dark, at room temperature or at reflux. However after exposing each solution to daylight the isomerization into the corresponding (*Z*) stereoisomer was observed.

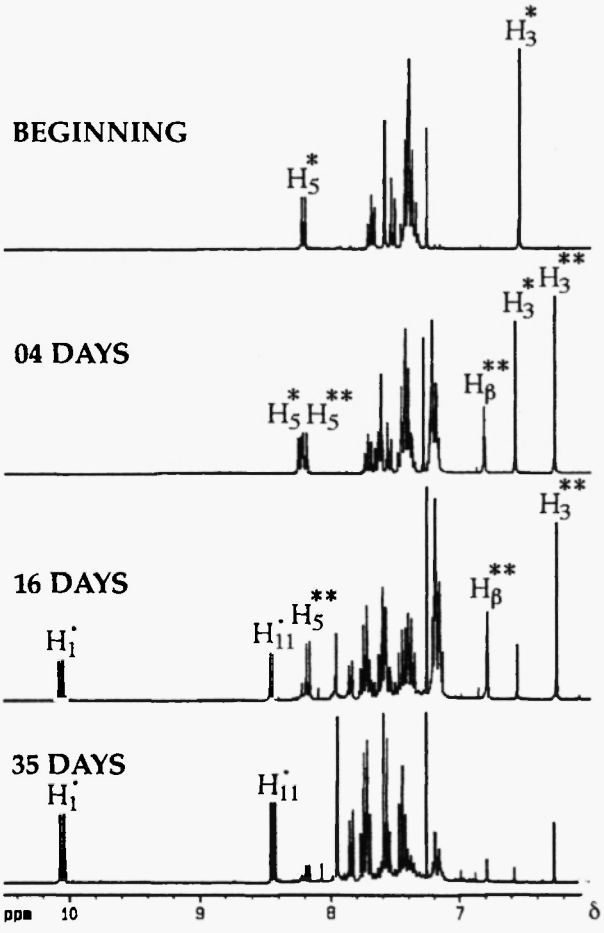
Solutions of compounds **4a-e** in deuteriochloroform, after four days under day light, gave rise to new signals, in addition to those due to the (*E*) and (*Z*) stereoisomers, in the corresponding ^1H NMR spectra. It was concluded that these signals were due to new products, the 12*H*-benzo[a]xanthene-12-ones **7a-e** (7), which were isolated in 60 % yield. The formation of these compounds is consistent with the (*E*) to (*Z*) isomerization, followed by electrocyclic and oxidative

processes (Scheme 2). Figure 1 shows the sequence of transformations, which were followed by ^{1}H NMR spectroscopy, of a deuteriochloroform solution of (*E*)-2-α-hexylstyrylchromone **4b** taken at different time intervals.



a) R^1 = Me; R^2 = H
b) R^1 = Hexyl; R^2 = H
c) R^1 = Me; R^2 = t-Butyl
d) R^1 = Me; R^2 = Cl
e) R^1 = Et; R^2 = Cl
f) R^1 = R^2 = H

Scheme 2



Only the (*E*), (*), isomer **4b** is present.

Mixture of (*E*), (*), and (*Z*), (**), isomers (~ 1:1).

Mainly (*Z*) isomer **5b**, (**), and xanthone **7b**, (·).

Mainly xanthone **7b**, (·), is present.

Figure 1 - Transformations of (*E*)-2-α-hexylstyrylchromone 4b, in deuteriochloroform, induced by day light and followed by ^{1}H NMR

It was also possible to carry out similar transformations with the unsubstituted (*E*)-2-styrylchromome; however in this case a longer period of time was necessary and the yield of the corresponding 12*H*-benzo[a]xanthene-12-one 7f was lower (~ 50 %).

In the ^{1}H NMR spectra of 12*H*-benzo[a]xanthene-12-ones 7 the main features are the signals at δ 10.05-10.12 and 8.38-8.45 ppm, which are due to the resonances of H-1 and H-11 protons. In compounds 7a,b and 7f due to the coupling of H-1 with H-2 and H-3 protons, the signal assigned to H-1 proton appears as a double doublet, whereas in the case of 7c-e it appears as a doublet due to the coupling with H-3 proton. The higher chemical shifts values of the H-1 and H-11 protons are mainly due to the deshielding anisotropic effect of the carbonyl group.

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6. Structural characterizations of 4a and 5a are considered as examples of the 2-styrylcromone (*E*), **4**, and (*Z*), **5**, stereoisomers:
   4a; Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38; Found: C, 82.69; H, 5.41; ^{1}H NMR in $CDCl_3$ (δ, ppm from TMS; J Hz) 2.19 (CH_3, s), 6.51 (H-3, s), 7.31-7.42 (H-2',3',4',5',6', m), 7.37 (H-6, dd, J 7.9 and 7.3), 7.51 (H-8, d, J 8.5), 7.66 (H-β, s broad), 7.66 (H-7, ddd, J 8.5, 7.3 and 1.5), 8.19 (H-5, dd, J 7.9 and 1.5); ^{13}C NMR in $CDCl_3$ (δ, ppm from TMS) 14.1 (CH_3), 108.1 (C-3), 117.8 (C-8), 123.6 (C-10), 124.9 (C-6), 125.5 (C-5), 128.4 (C-α), 128.1 (C-4'), 128.4 (C-3',5'), 129.5 (C-2',6'), 133.7 (C-7), 133.8 (C-β), 136.0 (C-1'), 155.9 (C-9), 164.3 (C-2), 178.7 (C-4).
   5a; ^{1}H NMR in $CDCl_3$ (δ, ppm from TMS; J Hz) 2.23 (CH_3, d, J 1.5), 6.27 (H-3, s), 6.86 (H-β, s broad), 7.00 (H-8, dd, J 8.1 and 1.2), 7.15-7.24 (H-2',3',4',5',6', m), 7.34 (H-6, ddd, J 7.8, 7.6 and 1.2), 7.55 (H-7, ddd, J 8.1, 7.6 and 1.6), 8.15 (H-5, dd, J 7.8 and 1.6); ^{13}C NMR in $CDCl_3$ (δ, ppm from TMS) 22.6 (CH_3), 111.0 (C-3), 117.9 (C-8), 123.9 (C-10), 125.0 (C-6), 125.4 (C-5), 127.6 (C-4'), 128.1 (C-3',5'), 128.4 (C-2',6'), 128.9 (C-α), 133.6 (C-7), 135.2 (C-β), 136.6 (C-1'), 155.9 (C-9), 165.1 (C-2), 178.3 (C-4).
7. Structural characterization of 7a as an example of the xanthones 7: Anal. Calcd. for $C_{18}H_{12}O_2$: C, 83.06; H, 4.65; Found: C, 82.79; H, 4.59; ^{1}H NMR in $CDCl_3$ (δ, ppm from TMS; J Hz) 2.67 (CH3, d, J 0.9), 7.45 (H-10, ddd, J 7.8, 7.5 and 1.1), 7.55 (H-3, ddd, J 7.7, 7.6 and 0.9), 7.59 (H-8, dd, J 8.1 and 1.1), 7.72 (H-2, ddd, J 8.1, 7.6 and 1.2), 7.74 (H-9, ddd, J 8.1, 7.5 and 2.1), 7.82 (H-4, dd, J 7.7 and 1.2), 7.96 (H-5, s broad), 8.44 (H-11, dd, J 7.8 and 1.2), 10.05 (H-1, dd, J 8.1 and 0.9); ^{13}C NMR in $CDCl_3$ (δ, ppm from TMS) 16.9 (CH_3), 114.4 (C-11a), 117.6 (C-8), 123.4 (C-12a), 124.3 (C-10), 126.1 (C-3), 126.6 (C-1), 126.7 (C-12b), 126.7 (C-11), 127.5 (C-4), 128.5 (C-2), 129.9 (C-4a), 130.1 (C-6), 133.8 (C-9), 136.1 (C-5), 154.5 (C-7a), 156.8 (C-6a), 178.8 (C-12).

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