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A Novel Intramolecular 1,2-Arene-Alkene Photocycloaddition

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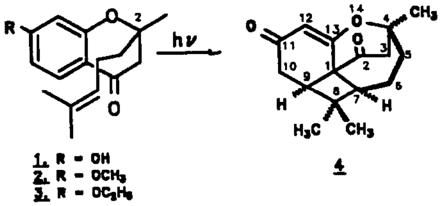
Abstract: A novel intramolecular 1,2-arene-alkene photocycloaddition of 2-alkenyl-7-hydroxy-4-chromanone(1) and its alkyl ethers (2 and 3) to (4α,7α,9α)4,8,8-trimethyl-14-oxatetracyclo(6.5.$1^{4,13}$.$0^{1,9}$)tetradeca-12-ene-2,11-dione (4) is described.

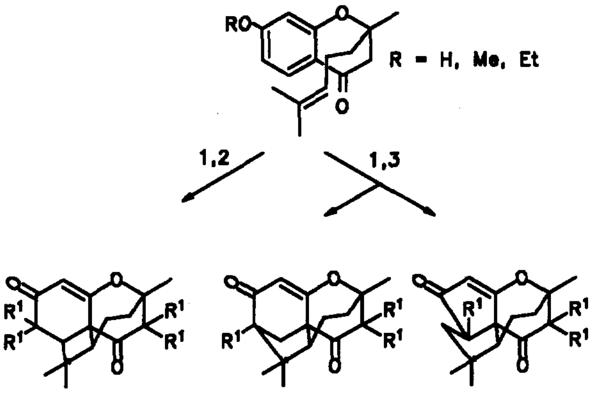
During the course of our work on cannabinoid synthons, an interesting intramolecular arene-alkene photocycloaddition was encountered. A fused multicyclic photocycloadduct, (4α,7α,9α)4,8,8-trimethyl-14-oxatetracyclo(6.5.$1^{4,13}$.$0^{1,9}$)tetradeca-12-ene-2,11-dione (4) was obtained by novel photochemical transformation of 2-methyl-2-(4-methyl- 3-pentenyl)-7-hydroxy-4-chromanone (1) and its 7-alkoxy analogs (2 and 3) (Scheme-1). This communication deals with the characterisation and possible mechanism of formation of the photoproduct (4).



Scheme-1

1 was prepared by the cross-aldol condensation of 2,4-dihydroxyacetophenone with 6-methyl-5-hepten-2-one (79% yield) followed by HMPT cyclodehydration[1] (50% yield). The product was characterised by spectral analysis[2]. Photolysis of 1 in C_6H_6 with near UV irradiation[3] (3 hr) gave a highly crystalline photoproduct **4** in 25% yield. A comparative analysis of NMR, MS, IR and UV data[2,4] of 1 and **4** suggests the involvement of an intramolecular arene-alkene photocycloaddition in the formation of **4**. There are two possible pathways[5,6] for the cycloaddition of the alkene side chain with aromatic part in 1, *viz* 1,2- (*ortho-*) pericyclic process leading to structure **4** or 1,3- (*meta-*) cycloaddition to form **5** or **6** respectively. Distinction between **4** and **5** or **6** could be made by deuterium exchange experiments.

On base-catalysed deuterium exchange (CD_3ONa/CD_3OD) of the photoproduct, the pyranone methylene protons at δ 2.62 and 2.75 and a 2H doublet at δ 2.35 disappeared due to deuterium exchange while the methine triplet at δ 3.27 collapsed into a singlet. Based on isotopic exchanges, structure **4** was assigned to the photoadduct ruling out the alternate structures **5** and **6** (Scheme-2). NOESY, ^1H-^1H COSY, and ^1H-^{13}C HETCOR spectra were also in agreement with the structure **4**.

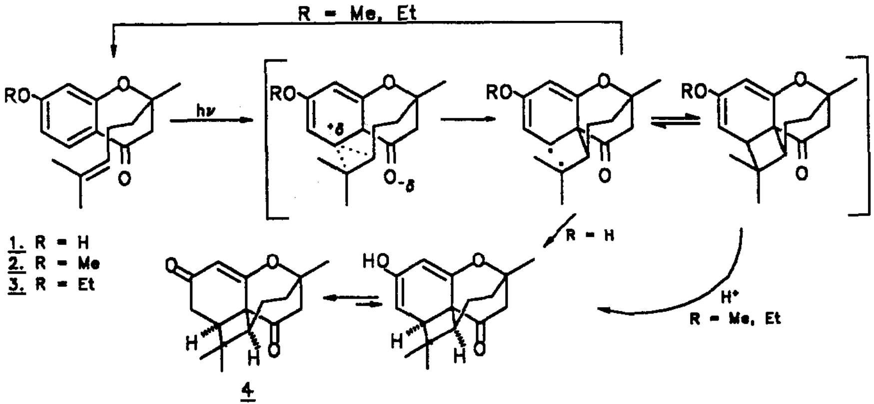


4 R1 = H 5 6

R1 = D Possible sites of deuteration

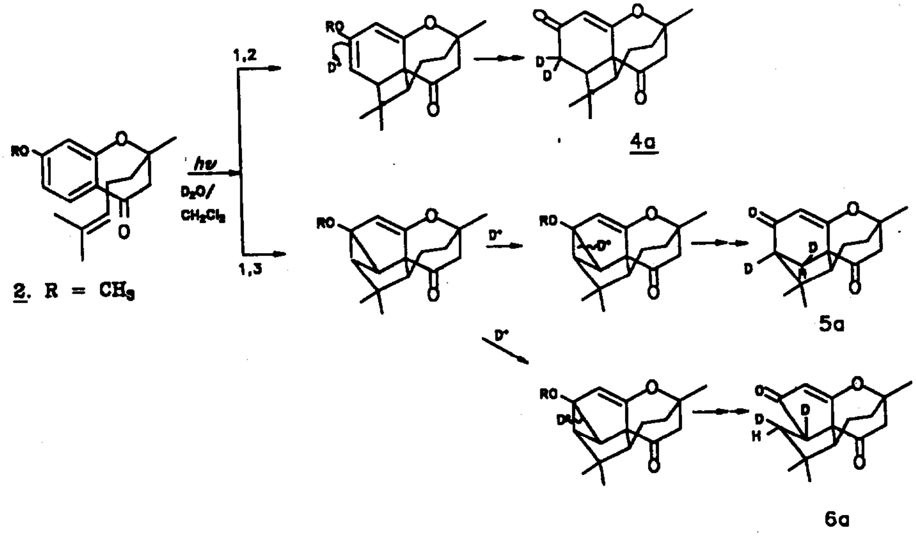
Scheme-2

The molecular model of 1 and its analogs showed the possibility of extensive overlapping of the arene with the axial alkenyl side chain which could lead to quenching of arene ketone triplet by the alkene side chain in intramolecular photochemical process.



Scheme-3

In the case of 7-hydroxychromanone (1) the intermediate diene-ol, formed by 2+2 photocycloaddition, tautomerises to the corresponding enone 4 (Scheme-3). But in contrast, irradiation of 7-alkoxy analogs (2 and 3) in C_6H_6 did not give arene-alkene cycloaddition product as in 1. It is postulated that in the case of 2 or 3, the steric strains favour the reversion of the diene-ol ether intermediate to the starting molecule. However, under acidic conditions, the diene-ol ether might cleave and tautomerise to enone 4. Based on this hypothesis the acid-catalysed photoreaction should give 4. Indeed, the photoreaction of 2 and 3 did take place readily both in C_6H_6 in the presence of p-toluenesulphonic acid[7] as well as in the chlorinated solvents like $CHCl_3$ or CH_2Cl_2 containing trace quantity of H_2O giving 4[8] . Evidence for this pathway was provided by carrying out the photolysis in the presence of D_2O. Thus, when CH_2Cl_2 solution of 3 was irradiated[8] in the presence of D_2O, the methylene protons (δ 2.35, d in 4) were absent and the methine proton (δ 3.27, t in 4) appeared as a singlet in ^1H NMR of deuterated photoproduct (4a, M^+ 262) (Scheme-4). These experiments provide further support to the structure 4 for the photoproduct. In the case of *meta* photocycloaddition (structures 5 and 6) the electrophilic mono deuteration at the methylene (δ 2.35) and the methine (δ 3.27) would have resulted in formation of 5a or 6a.



Scheme-4

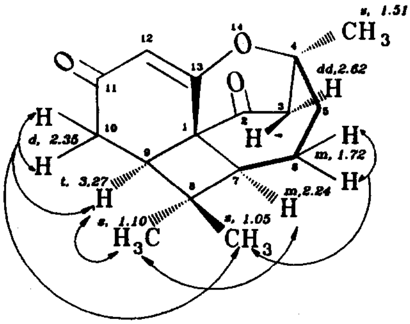


Fig. 1. Some important nOe observed in 4

The stereochemical considerations suggest that cycloaddition would occur from one stereoface because only the conformers with axial alkenyl side chain provides the necessary spatial requirements for the *ortho* arene–alkene cycloaddition. In the NOESY spectrum of **4**, the methyl group at δ 1.05 showed nOe with the methylene protons at 6 and 10- positions. The *cis*- relation between H-7 and H-9 was inferred by the nOe between both these protons with the methyl group (δ 1.10) at the lower face of the molecule (Fig. 1). Based on the above observations, the fusion between four and heterocyclic seven membered rings at C-1 and C-7 junction is *cis*. Thus, the photochemical process is governed by the stereochemistry of carbon at 2-position of the chromanones and is diastereospecific.

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1. Banerji, A.; Kalena, G. P. ***Synth. Commun.*** **1989**, 19, 159-166.
2. **1**: B.p.160^0/0.05mm; **MS** m/z 260, 179, 178, 177, 138, 137, 136, 110, 109, 108, 82, 81, 70, 69; UV (MeOH) λmax(log ε) 275 nm (4.41), 314 nm (4.16); ^{1}H **NMR** ($CDCl_3$) δ 1.40(s, 3H, CH_3), 1.56(s, 3H, CH_3), 1.65(s, 3H, CH_3), 1.76(m, 2H, CH_2), 2.08(m, 2H, CH_2), 2.62 and 2.78(AB quartet, 2H, J_{AB} = 16.7 Hz, CH_2), 5.05(m, 1H, $-CH_2-CH=C<$), 6.41(d, 1H, J = 2.25 Hz, ArH), 6.54(dd, 1H, J = 8.5 and 2.25 Hz, ArH), 7.77(d, 1H, J = 8.5 Hz, ArH), 8.6(s, 1H, OH).
3. Argon bubbled soln of **1** in anhydrous benzene(0.002 M) in Pyrex tube was irradiated in Rayonet RPR-208 apparatus at 350 nm. The photolysis in sunlight was equally effective. The reactions were monitored by vpc (OV-17, 5% ; 230^0).
4. **4**: M.p. 215^0; Analysed for $C_{16}H_{20}O_3$; **MS** m/z 260, 177, 137, 110, 109, 108, 91, 82, 81, 77, 69; **IR** 1725, 1660, 1620 cm^{-1}; UV (MeOH) λmax(log ε) 263 nm (4.14); ^{1}H **NMR** ($CDCl_3$) δ 1.05(s, 3H, 8-CH_3), 1.10(s, 3H, 8-CH_3), 1.51(s, 3H, 4-CH_3), 1.72(m, 2H, 6-CH_2), 1.92 and 2.17(m, 2H, 5-CH_2), 2.24(m, 1H, 7-H), 2.35(d, 2H, J = 4.7 Hz, 10-CH_2) 2.62 and 2.75(ABX dq, 2H, J_{AB} = 19.2 Hz, J_{AX} ≈ 0 Hz, J_{BX} = 1.36 Hz, 3-CH_2), 3.27(t, 1H, J = 4.7 Hz, 9-CH), 5.68(s, 1H, 12-CH); ^{13}C **NMR** ($CDCl_3$) δ 18.55(C-8'), 21.06(C-6), 30.7(C-4'), 31.45(C-8"), 32.25(C-10), 34.98(C-9), 37.17(C-8), 37.37(C-5), 49.57(C-3), 52.39(C-7), 52.58(C-1), 78.9(C-4), 106.54(C-12), 171(C-13), 197.15(C-11), 200.00(C-2).
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7. A soln of **2** in benzene (0.002M, 50 ml) with hydrated p-toluenesulphonic acid (5 mg) was irradiated in Rayonet apparatus. **4** was isolated by tlc.
8. The optimum concentration (0.002 M soln in $CHCl_3$ or CH_2Cl_2, sunlight, Pyrex glass, 1.5 - 2 hr) was established by vpc analysis of the reaction mixture at different intervals. In a typical experiment, a soln of **2** in CH_2Cl_2 (0.002M, 25 ml) was irradiated in sunlight in the presence of D_2O (0.05 ml) for 2 hr. The product was isolated by tlc and analysed by **MS** and **NMR**. Stirring of the **4** with DCl in CH_2Cl_2 for 24 hr did not show comparable exchange, thus excluding acid catalysed deuteration.

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