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INTERCONVERSION OF NOOTKATANE AND VETISPIRANE SESQUITERPENES VIA PHOTOLYSIS OF CROSS-CONJUGATED CYCLOHEXADIENONE INTERMEDIATES[1]

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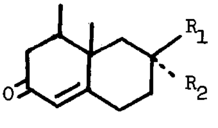
It is well known that cross-conjugated cyclohexadienones having a eudesmane skeleton are converted into guaiane derivatives on irradiation in protic solvents [2,3]. We now wish to report that the photochemical interconversion of cross-conjugated dienones of the nootkatane[4] and vetisspirane[5] type can be carried out efficiently by a two-step process involving bicyclohexenone intermediates.

Irradiation of 3,4-dehydronootkatone (2a)[6], prepared by oxidation of nootkatone[7] (1a) with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ), in dioxane for 6 hr using a 2537Å light source gave the lumiproduct 3a[bp 129–134° (bath temperature)/0.25mm; uv λ_{max}^{MeOH} 234 (ϵ 3,117) and 268 nm (ϵ 1,763); ir $\nu_{max}^{CCl_4}$ 1682 and 1610 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.15 (s, 3H, C-5CH$_3$), 1.70 (s, 3H, C($\underline{CH_3}$)=CH$_2$), 2.00(d, J=1.0Hz, 3H, C-1CH$_3$), 4.70(s, 2H, =CH$_2$), 5.52 ppm (br s, 1H, C-2H)] in 60% yield after chromatography on silica gel[8]. On irradiation of 3a in 45% aqueous acetic acid for 30 min using a 450-W Hanovia high pressure mercury lamp housed in a Pyrex probe, the starting material had completely disappeared and the spiro dienone 4a, the bicyclic dienone 5a, and 3,4-dehydronootkatone (2a) were isolated in 46, 37, and 12% yields, respectively, after chromatography on silica gel. Dienone 4a proved to be identical to anhydro-β-rotunol which has been prepared by treatment of β-rotunol with phosphorous oxychloride in pyridine[9]. Dienone 5a was found to be identical to the minor product obtained from annelation of (+)-dihydrocarvone with trans-3-penten-2-one[10] followed by oxidation of the octalone product with DDQ.

When the course of the photolysis of 3a was monitered by glc,[11] 4a and 5a were formed initially in a 7:3 ratio and this ratio approached unity and 2a began to appear on further irradiation.

When the three dienone products were irradiated separately under the conditions described for complete disappearance of **3a**, **2a** and **5a** were found to be essentially unchanged while **4a** was converted into a *ca.* 1:1 mixture of **2a** and **5a** in about 50% yield. Irradiation of **4a** in dioxane at 2537Å converted it into a mixture of four new photoproducts. The glc[11] and spectral properties of this mixture indicated that it was composed of about equal amounts of the four possible diastereomeric compounds of the type **6a**. On irradiation of this mixture in aqueous acetic acid using Pyrex filtered light, a 1:1 mixture of **2a** and **5a** was obtained. Although the 5-epimers of **2a** and **5a** are possible products of rearrangement of the mixture of isomers, no evidence for the formation of these compounds was obtained.

Dehydro-α-vetivone (**2b**)[mp 79-80°; uv λ_{max}^{MeOH} 239nm (ϵ 16,200); ir $\nu_{max}^{CCl_4}$ 1663 and 1630 cm^{-1}, nmr $\delta_{TMS}^{CCl_4}$ 1.16 (s, 3H, C-5CH$_3$), 1.77 (br s, 6H, C(CH$_3$)$_2$), 2.01 (d, J=1Hz, 3H, C-4CH$_3$), and 5.93 ppm (br s, 2H, C-1 and C-3H)] was prepared by addition of hydrogen bromide to the isolated double bond of **2a** followed by dehydrobromination of the product with tetra-*n*-butylammoninum bromide in acetone containing 2,6-lutidine[12], and irradiated for 35 min in dioxane at 2537Å to give **3b**[bp 133-138°(bath temp.)/0.2 mm; uv λ_{max}^{MeOH} 232 (ϵ 6,110) and 267 nm (ϵ 3,300); ir $\nu_{max}^{CCl_4}$ 1685 and 1609 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.16 (s, 3H, C-5 CH$_3$), 1.65 (br s, 6H, =C(CH$_3$)$_2$), 1.98 (d, J=1.3 Hz, C-1CH$_3$), and 5.47 ppm (br s, 1H, C-2H)] in 65% yield. Irradiation of **3b** under the conditions described for **3a** gave dehydro-β-vetivone (**4b**)[9] as the exclusive photoproduct in 60% yield. Irradiation of **4b** in dioxane at 2537Å gave a mixture of two products whose glc behavior[11] and spectral properties indicated that it was composed of a *ca.* 1:1 mixture of two racemic diastereomers of the type **6b**. Irradiation of this mixture in aqueous acetic acid using Pyrex filtered light gave racemic dehydro-α-vetivone (**2b**) in 50% yield from **4b**.



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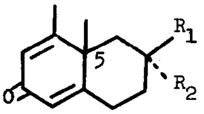

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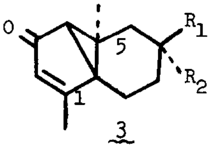

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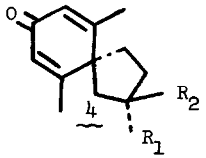

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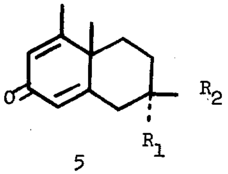

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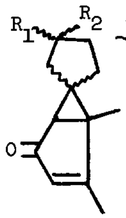

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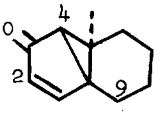

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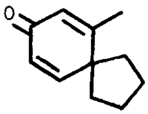

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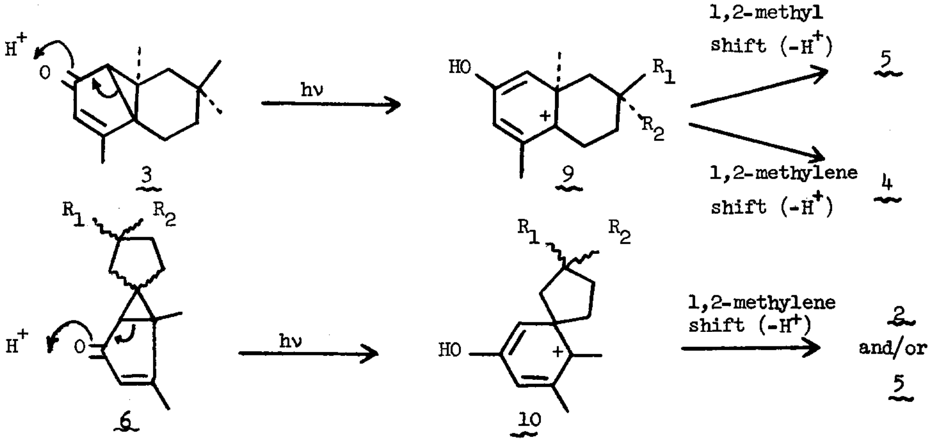
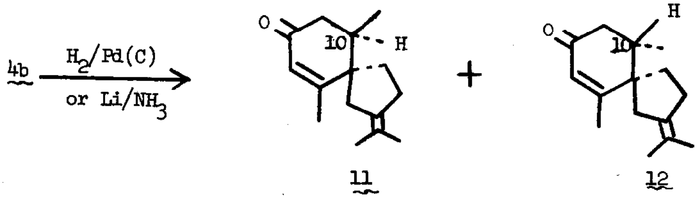
a. R_1 = H, R_2 = -C(CH$_3$)=CH$_2$ b. $R_1 R_2$ = =C(CH$_3$)$_2$

The formation of lumiproducts of the type 3 and 6 from dienones such as 2 and 4 are well known reactions[1]. Kropp has shown that irradiations of bicyclohexenones such as the 9α, 2- and 4-methyl derivatives of 7 yield new bicyclohexenones, phenols, and/or linearly conjugated dienones depending upon the location of substituents and photolysis conditions[1a,13]. It was suggested that the isolated products were formed via spiro dienone intermediates (cf. 8) but that the photolability of these species prevented their detection[1a, 13,14].

It seemed possible that the relative photostability of 4a and 4b resulted from the fact that both of the β positions of these compounds carried methyl substituents. However, we have now found that irradiation of 7 (prepared from the corresponding dienone in the usual way) under the same conditions described for 3a and 3b gives mainly 8 (bp 95-99° (bath temperature)/0.2 mm; ir $\nu_{max}^{CCl_4}$ 1667 and 1629 cm^{-1}; nmr $\delta_{TMS}^{CCl_4}$ 1.93 (d, 3H, $J \simeq 1Hz$, CH_3), 5.99 (br s, 1H, vinyl H), 5.98 and 6.91 ppm (AB quartet, J_{AB} =1 Hz, 2 vinyl H's)]. Thus the use of long wave length ultraviolet light appears to be the principal factor which allows the isolation of the spiro dienones in the above irradiations.

By analogy with previously purposed schemes irradiation of lumiproducts such as 3 and 6 in protic solvents should lead to the formation of carbonium ion intermediates such as 9 and 10, respectively. These species can yield the observed photoproducts by appropriate 1,2-methyl or ring carbon shifts to the positions para to the -OH groups. Products derived from 1,2-methyl shifts





have not been found in previous studies involving simple 6/6-fused bicyclic systems of the type 9[1a]. Thus the direct formation of 5a from 3a appears to provide the first example of a 1,2-methyl shift in a photochemically generated species on this type. The cis relationship of the methyl and isopropenyl groups would be expected to lead to a significant amount of distortion of the B ring in 9a. This factor may be responsible for the fact that the methyl and methylene migration processes are competitive (3:7). As expected, migration of the methylene group is overwhelmingly favored when it is allylic as in 9b and 10b and products 4b and 2b are obtained exclusively in these cases.

In order to complete the conversion of nootkatone into a naturally occurring vetispirane derivative, selective reductions of dehydro-β-vetivone (4b) were carried out. Catalytic hydrogenation of 4b in ethyl alcohol at atmospheric pressure using 5% palladium on carbon as the catalyst gave approximately 60% of racemic β-vetivone (11)[5] and racemic 10-epi-β-vetivone (12)[15] in a 7:3 ratio by glc[11]. Chemical reduction of 4b with two equiv. of lithium in liquid ammonia containing one equiv. t-butyl alcohol gave a mixture of 11 and 12 in ca. 80% yield. In this case the ratio of 11 to 12 was 3:7 by glc[11].

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