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Effect of Reaction Media on Photoreaction of Provitamin D_3

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Abstract: The photoisomerization of provitamin D_3 is carried out in silica gel-hexane matrix, ethanol and hexane. The results show that in silica gel-hexane matrix and ethanol, the desired product of prevtamin D_3 and vitamin D_3 can be obtained in high yield, while the undesirable byproducts are greatly limited.

Keywords: Photoisomerization, vitamin D_3.

Introduction

The photochemistry of provitamin D_3 (Pro) has been studied extensively in many years[1-4]. As shown in **Scheme 1**[1], irradiation of provitamin D_3 in organic solvents results in its photoisomerization to previtamin D_3 (Pre). Previtamin D_3 can be thermally transferred into vitamin D_3 (VD_3), which is of commercial interests. However, previtamin D_3 also undergoes the photochemical back reaction leading to the regeneration of provitamin D_3 and the photoisomerization resulting in the undesired byproducts tachysterol (Tachy) and lumisterol (Lumi). The key characteristic of the photochemistry of provitamin D_3 in solution is the high selectivity of tachysterol at many photolysis wavelengths[5,6]. In recent years, much attention has been given to the photochemical reactions in microorganized media, such as micelles[7], vesicles[8], Langmuir-Blodgettt films[9], organic polymers[10], zeolites[11], in comparison with reactions in solutions and the results show good chemiselectivity, regioselectivity, and/or stereoselectivity in these microorganized media.

In this paper, we investigate the photoisomerizations of provitamin D_3 in silica-gel suspension, and solutions in ethanol and hexane. The results demonstrate that the formation of Tachy is greatly limited, while the formation of previtamin D_3 and vitamin D_3 are favored in silica gel suspension and in ethanol solution.

Experimental

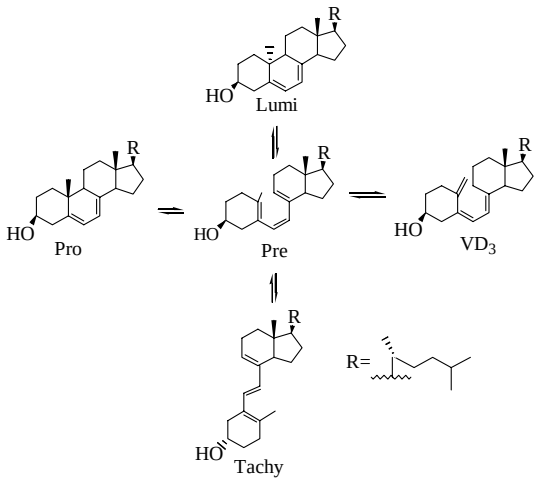
Provitamin D_3 with 99% purity was made in our lab. Hexane and ethanol (A.R) were from Beijing Chemical Industry. Silica gel was chromatographic grade from Qingdao Hai Yang Chemical Croup Co. of China. 2% of provitamin D_3 was loaded to silica gel

from a chloroform solution, then the silica gel was suspended in hexane.

The photochemical reactions were carried out using a 450 W medium pressure Hanovia lamp in a water-cooled quartz immersion well. All the samples were in quartz tubes and were bubbled with argon prior to irradiation. During irradiation, the samples were stirred with a magnetic stirring bar and bubbled with argon. After irradiation, the silica gel was washed with ethanol and the photoreaction solutions in ethanol and hexane were injected into HPLC directly.

Analysis of the products formed during the irradiation was carried out using a Perkin-Elmer HPLC system, equipped with UV/Vis detector. A Supelcosil LC-Si 5 μ m column (4.6 mm ID, 25 cm) was used with a mobile phase of 0.3% pentanol in hexane. Retention time and independent samples established peak identities.

Scheme 1 Photoreaction of provitaminD_3



Results and discussion

Figure 1 HPLC traces for the irradiation of the provitamin D_3 (a) in silica gel suspension (b) in hexane (Pre 12.0 min; Lumi 15.9 min; VD_3 22.3 min; Tachy 24.8 min; Pro 34.1 min)

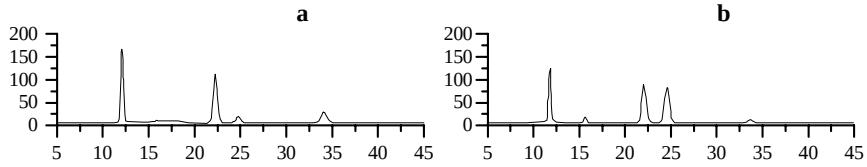


Figure 1a shows the HPLC traces obtained from the irradiation of provitamin D_3 in silica gel suspension. **Figure 1b** is the HPLC results from the irradiation of the provitamin D_3 solution in hexane. The formation of byproduct, tachysterol and lumisterol is well limited in silica gel suspension than in hexane, while the desired

products, previtamin D_3 and vitamin D_3 form in good yield. Similar results are obtained in ethanol as in silica gel suspension.

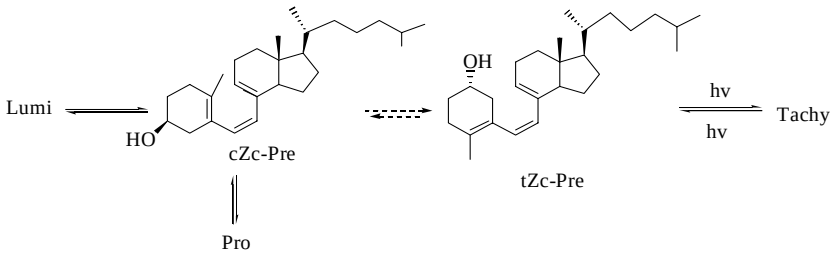
Table 1 The HPLC area percent of the Pre+VD_3 and Tachy after photolysis in different media

Reaction media	Area%		
	Pre+VD_3	Tachy	Tachy/(Pre+VD_3)
hexane	59.9	32.0	0.53
silica gel	71.0	5.3	0.074
ethanol	59.3	5.8	0.10

Table 1 shows the relative amount of Tachy compared with the previtamin D_3 and vitamin D_3 obtained after irradiation of provitamin D_3 in different media. Although the area cannot represent the absolute amount of the compounds, it could show the tendency of the change. The third column lists the data of Tachy when the same amount of product is formed. The ratios of Tachy/(Pre + VD_3) are 0.53 in hexane, 0.074 in silica gel and 0.10 in ethanol. It can be seen that, the formation of Tachy is greatly limited in silica gel, also in ethanol.

The different selectivity of the reaction can be explained by the conformational equilibrium of previtamin D_3. It is suggested that previtamin D_3 may exist as an equilibrium of cZc and tZc conformers and the formation of Tachy arises predominately from the tZc rotamer, while the cZc rotamer leads to the formation of Provitamin D_3 (as shown in **Figure 2**) [12].

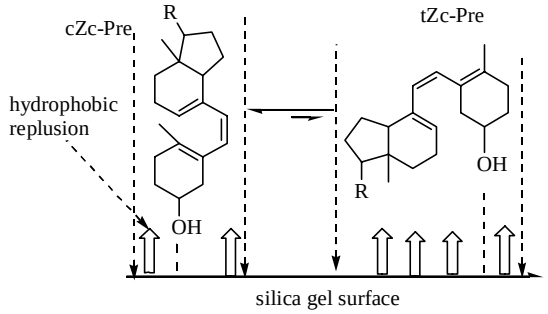
Figure 2 Simplified two-conformation scheme of previtmin D_3 reversible photoconversion



This may explain why in silica gel –hexane suspension, the formation of Tachy reduces dramatically. Provitamin D and its photoisomer can be absorbed on the surface of silica gel *via* hydrogen bonding between the C3-hydroxyl group of the steroid and surface active centers (surface water or Si-OH groups). Hydrophobic and electrostatic interactions restrict intramolecular rotation around the single bonds of previtamin D_3 and provide an orientation resulting in minimal contact of the steroids hydrophobic area surface of the silica gel. Consequently, rotation barrier increases and previtamin D_3 shifts its conformational equilibrium in favor of its cZc conformer (**Figure 3)**. The results in ethanol support the explanation in silica gel. As a poor solvent for hydrophobic previtamin D_3 molecules, the ethanol forces previtamin D_3 to form

aggregates which restrict the free rotation of previtamin D_3. This results in the depopulating the tZc forms of the previtamin D_3 and gives a good selectivity of photoisomerization of provitamin D_3 in ethanol.

Figure 3 Conformation shift caused by silica gel surface *via* hydrophobic repulsion between hydrophobic tail and skeleton of previamin D_3 and silica gel surface



Conclusion

The photoisomerization of provitamin D_3 is carried out in silica gel suspension or in ethanol solution with preferential formation of desired products, previtamin D_3 and vitamin D_3. The increasing of cZc conformer formation limits the toxic byproduct Tachy, while increases the yields of the products.

Acknowledgments

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