A Novel Photochemical Approach to the Synthesis of DL-Pantothiolactone

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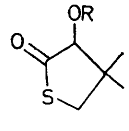
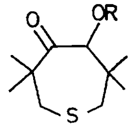
Summary A photochemical ring contraction reaction has been applied to the synthesis of pantothiolactone, a new analogue of pantolactone which is a critical intermediate in the synthesis of pantothenic acid.

As part of our studies on the use of photochemistry in the syntheses of naturally occurring materials and their derivatives, we have prepared the hitherto unknown γ-thiolactone (I, pantothiolactone) and its *O*-acetate (II) by photochemical means in good yield.

Irradiation† of the acetate (IV)[1] (2·02 g/250 ml) in degassed methanol (or t-butyl alcohol) for 11 h gave, after removal of the solvent and separation of the crude residue by column chromatography (silicic acid, elution with hexane–ether), 62% of the thiolactone (II).‡

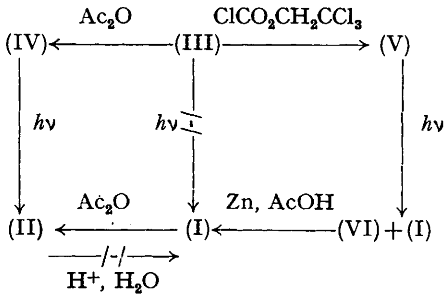


(I), R = H
(II), R = Ac
(VI), R = $\mathrm{CCl_3CH_2O\overset{\overset{O}{\|}}{C}}-$



(III), R = H
(IV), R = Ac
(V), R = $\mathrm{CCl_3CH_2O\overset{\overset{O}{\|}}{C}}-$

Irradiation of (III)[1,2] under the same conditions gave no reaction and (III) could be recovered from the reaction. We were unable to hydrolyse (II) to (I), but synthesized (I) in good yield by a nonhydrolytic route. Treatment of (III) with 2,2,2-trichloroethoxycarbonyl chloride in pyridine gave (V) in 82% yield. Compound (V) could be converted in high yield back into (III) upon treatment with zinc in acetic acid at 25°.



Irradiation of (V) in degassed methanol for 9 h gave, after removal of solvent, a mixture of products which appeared (from n.m.r. spectra), to be mainly a 2:1 mixture of (VI) and (I). Reaction of this mixture with zinc and acetic acid at 25° for 1 h gave, after separation by column chromatography, a 49% yield of DL-(I) and several minor products. The thiolactone (I) could be converted in high yield into the acetate (II) by treatment with acetic anhydride in acetic acid.

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† All photolyses were carried out using a 450 watt Hanovia apparatus and pyrex filter. Sulphides (III), (IV) and (V) show nearly identical u.v. spectra (EtOH) λ_{max} 295 (ϵ 45), 235 nm (ϵ 550).

‡ Structure assignments are supported by analytical, i.r., n.m.r., and m.s. data.

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