273. Absolute Configuration of Actinioerythrin

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(2.X.78)

Summary

The CD. correlation of (3*S*,3′*S*)- and (3*R*,3′*R*)-actinioerythrol diacetate, obtained by total synthesis from β-ionone, with actinioerythrin isolated from the sea anemone *Actinia equina* L. shows that the natural compound has the (3*S*,3′*S*)-configuration.

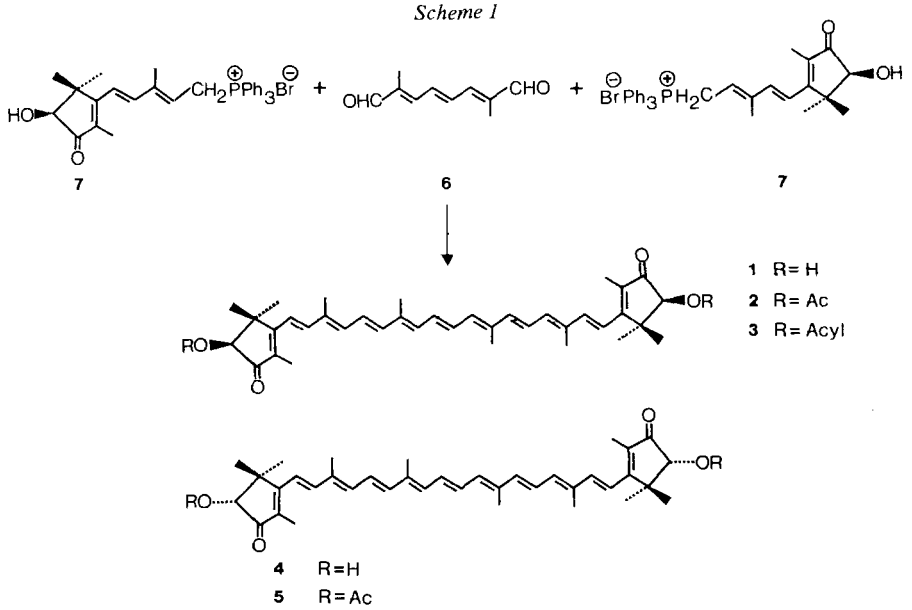
The constitution of a 2,2′-dinor-3,3′-dihydroxy-β,β-carotene-4,4′-dione has been assigned to actinioerythrin from spectroscopic and chemical evidence [1] [2]. A qualitative CD. spectrum was later reported, but no stereochemical conclusions could be made [3]. The biosynthetic mechanism suggested for the formation of actinioerythrin from (3*S*,3′*S*)-astaxanthin [1] [3] by benzilic acid rearrangement of a hypothetic intermediary triketo end group allows no prediction of the absolute configuration.

The synthesis of the parent compound actinioerythrol in racemic form (3*RS*,3′*RS*)-actinioerythrol accompanied by equal amounts of *meso*-actinioerythrol)[1]) was recently reported by *Kienzle & Minder* [4]. In order to determine the absolute configuration of actinioerythrin, we have synthesized (3*S*,3′*S*)-actinioerythrol (**1**), (3*R*,3′*R*)-actinioerythrol (**4**), and the corresponding diacetates **2** and **5** *(Scheme 1)*. The synthesis was accomplished by a *Wittig* reaction according to the building principle $C_{14}+C_{10}+C_{14}=C_{38}$, using the C_{10}-dialdehyde **6** as the central component.

The key intermediate **7** was prepared by the route outlined in *Scheme 2*. Oxidation of β-ionone (**8**) to the diketone **9** was performed in 55% yield with 3.0 equivalents of pyridinium chlorochromate in dimethyl sulfoxide at 105° for three hours. Treatment of **9** with 1.2 equivalents of ethyl orthoformate and 1.5 equivalents of ethylene glycol in the presence of a catalytic amount of *p*-toluene sulfonic acid gave

[1]) For an analytical method for the determination of (3*S*,3′*S*)-, (3*R*,3′*R*)- and (3*R*,3′*S*)-actinioerythrol by separation of the corresponding (−)-camphanic acid diesters see: *M. Vecchi & R.K. Müller*, Journal of High Resolution Chromatography and Chromatography Communications, in press.

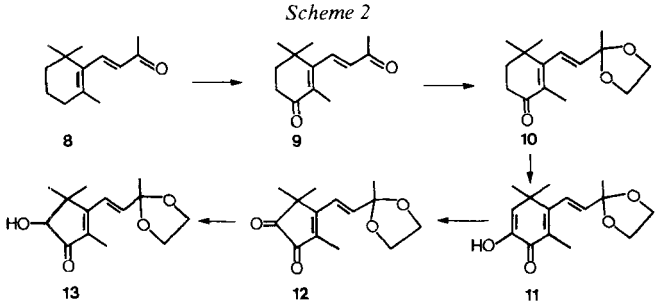
Scheme 1

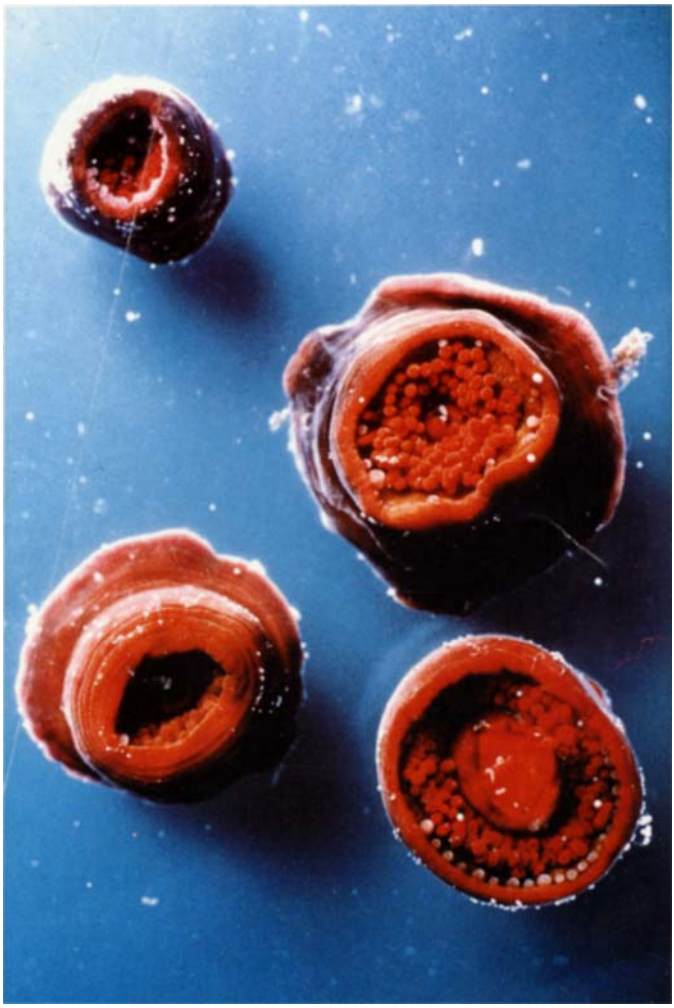


more than 50% of the monoacetal **10** (m.p. 36–37°). Subsequent oxidation of **10** by air at room temperature in *t*-butyl alcohol/potassium *t*-butyl alcoholate/toluene [5] provided the enolized diketone **11** (m.p. 107.5–108°) in 80% yield. Exposure of **11** to a large excess of manganese dioxide gave the orange five-membered acetal **12** (m.p. 110.5–112.5°) in 40% yield, subsequently reduced with 0.26 equivalents of sodium borohydride in methanol at −5° to produce the pure *α*-ketol **13** (m.p. 58–60°) in nearly quantitative yield.

Optical resolution of the hydroxy acetal **13** was accomplished by esterification of **13** with (−)-camphanic acid chloride (CpCl) of known absolute configuration [6] according to *Gerlach et al.* [7]. A mixture of the diastereomeric esters **14** and **15** in more than 90% yield *(Scheme 3)* was obtained. Separation into **14** (m.p. 139.5–140°) and **15** (m.p. 99–100°) was effected by fractional crystallization or column chromatography on silica gel. The purity of **14** and **15** used for further synthesis was more than 99.95% according to HPLC. analysis. The structure and relative configuration of the ester acetal **14** was determined by X-ray analysis. The

Scheme 2

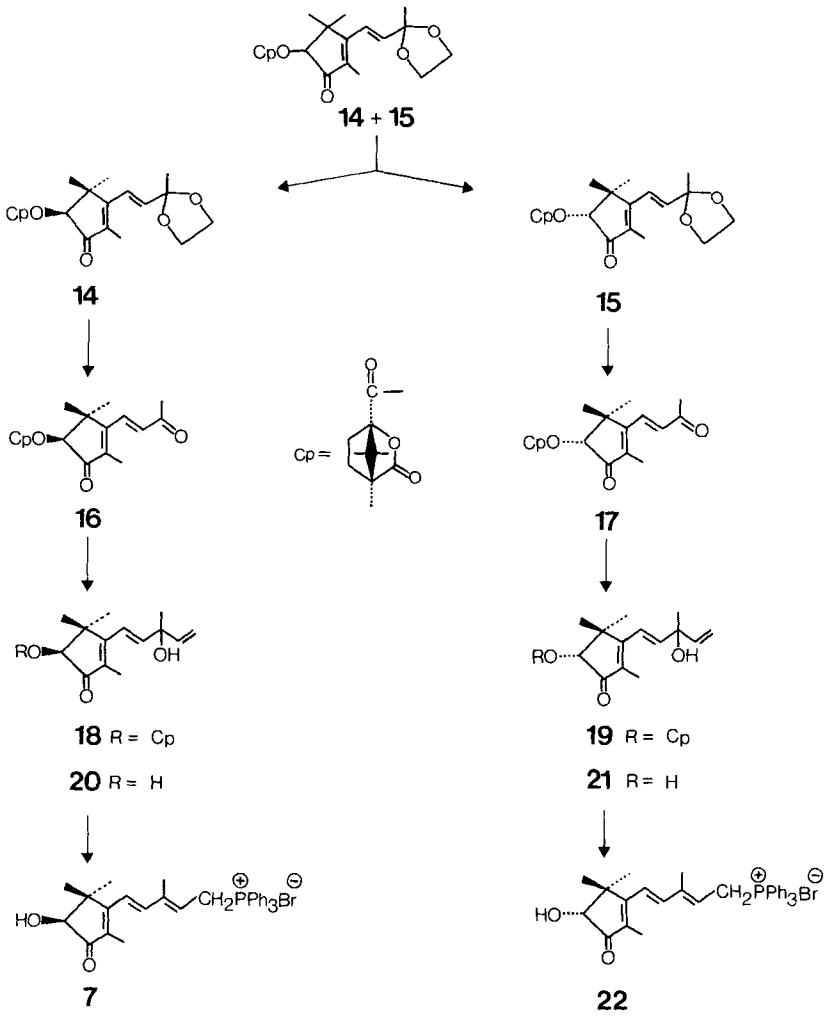




Photograph by M. Beck

Fig. 1. *Actinia equina* L.

Scheme 3



ketone **16** (m.p. 129–130°) was obtained by hydrolysis of the acetal in methanol/aqueous hydrochloric acid. Reaction of **16** with vinyl magnesium chloride in tetrahydrofurane at −70° gave the *α*-vinyl alcohol **18** (m.p. 128–132°) which was transformed into the crude C_{14}-phosphonium salt **7** (m.p. 116–118°) *via* **20** by known procedures [4]. The enantiomeric phosphonium salt **22** was prepared in the same manner from **15** *via* **17**, **19** and **21**.

The all-*trans*-configuration of the polyene chain of the diacetates **2** and **5** was unequivocally deduced from their ^{1}H- and ^{13}C-NMR. spectra at 270 and 68 MHz, respectively [8].

Actinioerythrin was isolated from *Actinia equina* L. (collected at Alnes, Godöy Island, West Norway) *(Fig. 1)* by solvent extraction as previously described [2], followed by purification on TLC. (silica) and crystallization.

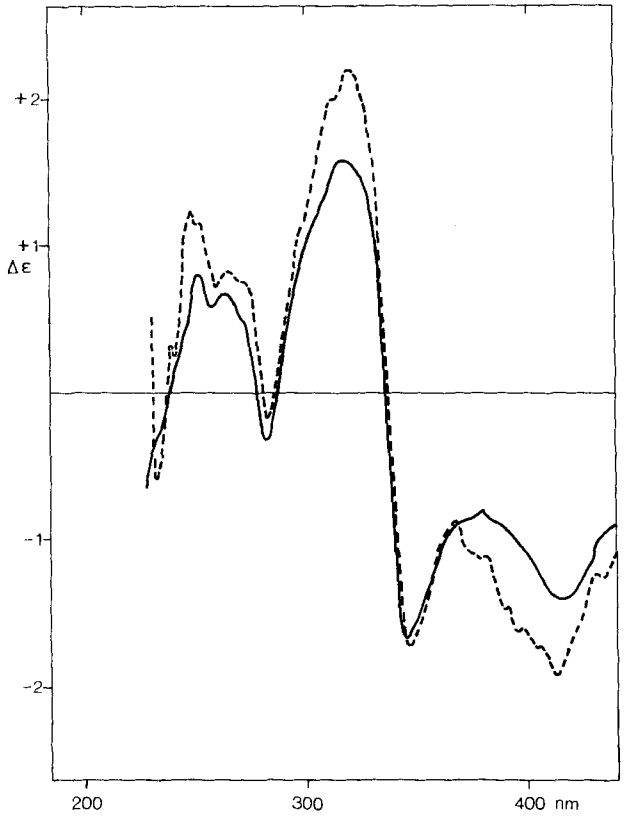


Fig. 2. *CD. spectra of actinioerythrin isolated from* Actinia equina L. (———) *and (3S,3'S)-actinioerythrol diacetate* (**2**) (– – – –) *in methylene chloride*

Identical electronic spectra of the synthetic all-*trans*-diacetates **2** and **5** and actinioerythrin confirmed the all-*trans*-configuration for the natural compound. ^{1}H-NMR. spectra supported this assignment. Comparison of the CD. spectra of (3*S*,3'*S*)-actinioerythrol diacetate (**2**) and actinioerythrin *(Fig. 2)* shows that the natural compound has the (3*S*,3'*S*)-configuration [9]. Further details on the total syntheses and the spectroscopic data will be published [8].

After completion of this project we have been informed by Dr. *R. W. Rickards* of a parallel study [10] on the absolute configuration of actinioerythrin ex *Actinia tenebrosa*. On the basis of oxidative degradation of actinioerythrin to (+)-(*S*)-dimethyl 3,3-dimethyl-malate they also assigned the (3*S*,3'*S*)-configuration to the natural compound.

We wish to thank Dr. *G. Englert* for his advice and help in the interpretation of the NMR. spectra. Prof. *H. Gerlach* readily gave us much useful advice and Mr. *H. Schneider*'s diligence made a real contribution to this work. *Sjur Liaaen-Jensen* collected the biological material. *J. D. Tauber* was on sabbatical leave from the Chemistry Department of McNeese State University, Louisiana, U.S.A.

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274. Photochemistry of 3-Substituted 1-Iminopyridinium Ylides[1]). Regiospecific *versus* Non-regiospecific Photoisomerization Patterns [1]

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Summary

3-Substituted 1-iminopyridinium ylides **1** undergo photo-induced ring enlargement to 1 *H*-1,2-diazepines. With strongly electron-withdrawing substituents the ring expansion process is regiospecific and leads exclusively to 4-substituted 1 *H*-1,2-diazepines. Weak electron-donating substituents, like a methyl group and halogen atoms, do not have any directing effect since both 4- and 6-substituted 1 *H*-1,2-diazepines are obtained. With strong electron-donating substituents no diazepines are formed; instead one observes photo-induced isomerization to the 2-aminopyridine derivatives, the process being non-regiospecific. Regiospecific photo-induced ring expansion processes are explained in terms of a simple HMO model.

Introduction. – The photo-induced ring enlargement of 1-iminopyridinium ylides **1**, which leads to the isomeric 1 *H*-1,2-diazepines **3**, is a well established ring transformation [2]. The scope and limitation of this rearrangement have not been studied in great detail so far. Therefore, we have investigated directing effects of substituents, attached to C(3) of the ylides **1**, on the ring enlargement process.

[1]) Part 10 of the series 'Photochemical Synthesis of 1,2-Diazepines'. Part 9: [17].
[2]) Basel.
[3]) Darmstadt.
[4]) Mulhouse.