Bacterial Carotenoids

XXXV.* Total Synthesis of 1,2-Dihydro- and 1,2,1′,2′-Tetrahydrolycopene

H. KJØSEN and S. LIAAEN-JENSEN

Organic Chemistry Laboratories, Norwegian Institute of Technology, University of Trondheim, Trondheim, Norway

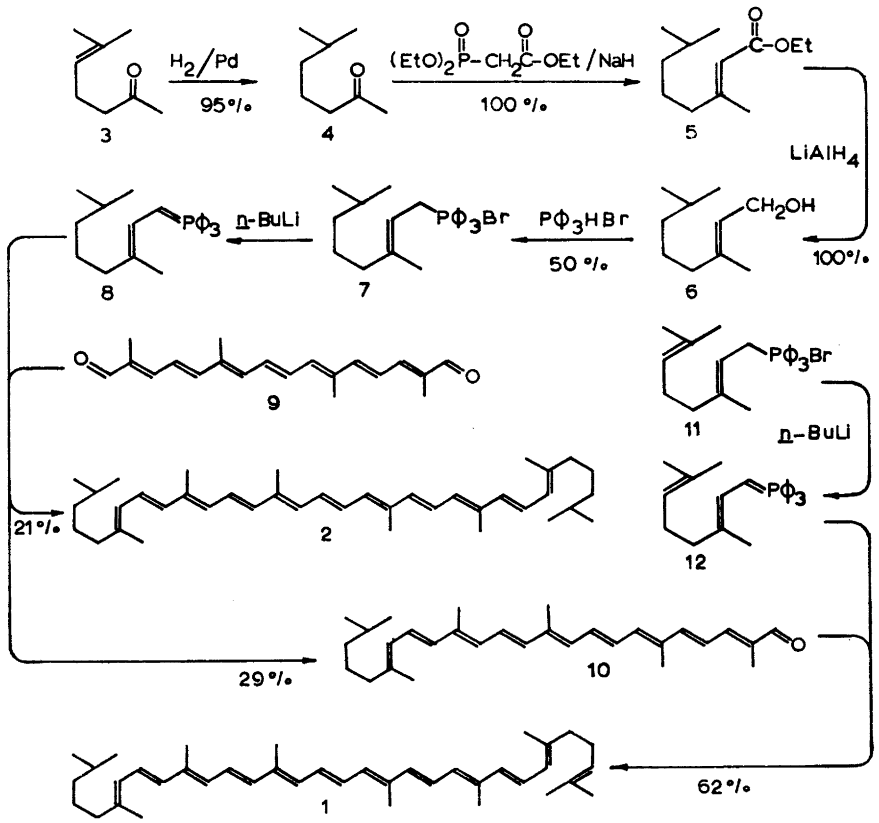
Recently Malhotra *et al.*[1] have characterised 1,2-dihydroneurosporene, 1,2-dihydrolycopene (*1*), and 1,2-dihydro-3,4-dehydrolycopene from *Rhodopseudomonas viridis*, a photosynthetic bacterium isolated by Eimhjellen.[2] Neurosporene and lycopene were also present. More recently the 1,2,1′,2′-tetrahydro analogues of neurosporene and lycopene have also been found in the same bacterium.[3] These pigments are the first carotenes to be found in nature with the 1,2-dihydro feature.

It was considered of interest to confirm the structures of these compounds by total synthesis, and we now report the synthesis of 1,2-dihydrolycopene (*1*) and 1,2,1′,2′-tetrahydrolycopene (*2*) by the route depicted in Scheme 1.

Methylheptenone (*3*) was hydrogenated in the presence of palladium catalyst to give the saturated ketone *4*. Condensation of the

* No. XXXIV. *Acta Chem. Scand.* **24** (1970) 1460.

SCHEME 1



latter ketone with ethyl diethylphosphonoacetate in a Horner reaction gave the α,β-unsaturated ester *5*. Subsequent reduction with lithium aluminium hydride afforded the alcohol *6*, which was reacted with triphenylphosphonium bromide to give the Wittig salt *7*. Treatment of the Wittig salt with butyl lithium gave the unstable phosphorane *8*, which was immediately condensed with crocetindial (*9*) to give 1,2,1',2'-tetrahydrolycopene (*2*) and 1,2-dihydro-apo-8'-lycopenal (*10*). The hydrocarbon and the monoaldehyde were separated by column chromatography on alumina. The aldehyde *10* was condensed with the phosphorane *12*, obtained from geranyltriphenylphosphonium bromide (*11*) with butyl lithium, to give 1,2-dihydrolycopene (*1*).

1,2-Dihydro- and 1,2,1',2'-tetrahydrolycopene had melting points 163–165°C and 152–154°C (uncorr.), respectively, and both compounds exhibited spectra in visible light (petroleum ether) indistinguishable from that of lycopene.

The IR spectra (KBr) differed with respect to each other and to lycopene only slightly in the 3000–2820, 1460–1440, and 1400–1350 regions caused by CH_2 and CH_3 absorptions.

The NMR spectra of both compounds showed a characteristic doublet at τ 9.12 (J=6 cps),[1] integrating for 6 H and 12 H, respectively, caused by the isopropyl end groups. In-chain and end-of-chain methyl protons gave rise to singlets at τ 8.03 and τ 8.19. In addition the dihydro compound showed singlets at τ 8.28 and τ 8.37 and a multiplet centered at τ 4.85 caused by the isopropylidene end group. The allylic methylene protons resonated at τ 7.9 and non-allylic methylene and olefinic protons gave rise to multiplets in the τ 8.4–8.9 and τ 3.0–4.25 regions, respectively.

The mass spectrum of 1,2-dihydrolycopene (*1*) showed the molecular ion at *m/e* 538 which was also the base peak. Characteristic peaks [4] associated with the following fragmentations were observed in the upper part of the spectrum: *m/e* 469 (M–69), 459 (M–79), 446 (M–92), 432 (M–106), and 380 (M–158); *m/e* 69 was abundant (88.5 %). 1,2,1',2'-Tetrahydrolycopene (*2*) showed the molecular ion at *m/e* 540 (57 %). In this case the base peak was at *m/e* 43. Characteristic fragmentations observed in the upper part of the spectrum were: *m/e* 469 (M–71), 461 (M–79), 448 (M–92), 434 (M–106), and 382 (M–158). Both mass spectra showed a number of peaks which could be associated with in-chain cleavages. M–2 peaks are occasionally observed in carotenoid mass spectra.[4,5] However, in the spectra of the di- and tetrahydrolycopenes the *m/e* 536 and *m/e* 538 ions, respectively, were negligible, thus confirming the homogeneity of the pigments.

Lycopene and the di- and tetrahydro compounds could be separated by TLC on silica G using 1 % acetone in petroleum ether as developer, but not on kieselguhr or alumina papers. This may explain why the hydrocarotenes had previously escaped detection.[6]

Spectral data and R_F-values (co-chromatography) were in complete agreement with the natural compounds.

Further details will be published. Work on the synthesis of 1,2-dihydroneurosporene, 1,2-dihydro-3,4-dehydrolycopene, and the 1,2,1',2'-tetrahydro analogues are in progress.

Acknowledgements. We are grateful to Professor T. W. Goodwin, Department of Biochemistry, the University of Liverpool, for the comparison of the natural and synthetic pigments. The crocetindial used was a gift from Dr. J. D. Surmatis, Hoffmann-La Roche, Nutley, New Jersey, USA. A maintenance grant from *Norges Almenvitenskapelige Forskningsråd* to H. K. is gratefully acknowledged.

1. Malhotra, H. C., Britton, G. and Goodwin, T. W. *Chem. Commun.* **1970** 127.
2. Eimhjellen, K. E. *Unpublished results.*
3. Malhotra, H. C., Britton, G. and Goodwin, T. W. *Intern. J. Vitaminol. In press.*
4. Enzell, C. R., Francis, G. W. and Liaaen-Jensen, S. *Acta Chem. Scand.* **23** (1969) 727.
5. Schwieter, U., Bolliger, H. R., Chopard-dit-Jean, L. H., Englert, G., Kofler, M., König, A., Planta, C. v., Rüegg, R., Vetter, W. and Isler, O. *Chimia* **19** (1965) 294.
6. Aasmundrud, O. and Eimhjellen, K. E. *Unpublished results cf.* Liaaen-Jensen, S. in Gest, H., San Pietro, A. and Vernon, L. P. *Bacterial Photosynthesis*, Antioch Press, Ohio 1963, p. 19.

Received June 25, 1970.