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Synthesis of the Enolic β-Diketone Carotenoids, Mytiloxanthin and Trikentriorhodin

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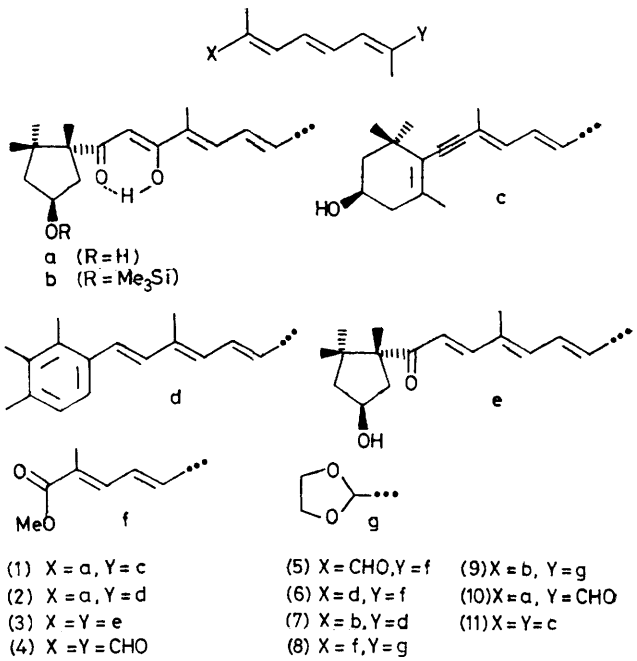
Summary Claisen type condensations between the appropriate polyene esters and methyl ketones are used to synthesise the enolic β-diketone carotenoids trikentriorhodin and the 9-*cis* isomer of mytiloxanthin.

Mytiloxanthin (**1**)[1] and trikentriorhodin (**2**)[2] are unique carotenoids owing to the presence of an enolic β-diketone system in which the carbon–carbon double bond of the enol is part of the main polyene chain. The synthesis of both of these carotenoids will be described with known absolute stereochemistry at all chiral centres; the 9-*cis* isomer of mytiloxanthin is obtained.

The close relationship between the β-diketone end group (a) and that of capsorubin (**3**)[3] suggested a synthesis *via* the intermediate methyl ketone (**14**) used in the synthesis of (**3**).[3] A new synthesis of (**14**) utilised the ester (**16**) readily prepared from (+)-camphor.[4] Hydroboration of (**16**) gave a mixture of the isomeric hydroxy esters (**12**) (29%) and (**17**) (44%). The corresponding *cis* isomers could not be detected. The ester (**12**) was converted into the corresponding methyl ketone (**14**) (51%) *via* the corresponding carboxylic acid (**13**).[6]

A Claisen type condensation[7] between a polyene ester and a methyl ketone using $LiNH_2$ in tetrahydrofuran (THF) was shown to give polyene β-diketones in high yields (up to 90%). Concomitant Michael reactions did not occur,



(1) X = a, Y = c
(2) X = a, Y = d
(3) X = Y = e
(4) X = Y = CHO
(5) X = CHO, Y = f
(6) X = d, Y = f
(7) X = b, Y = d
(8) X = f, Y = g
(9) X = b, Y = g
(10) X = a, Y = CHO
(11) X = Y = c

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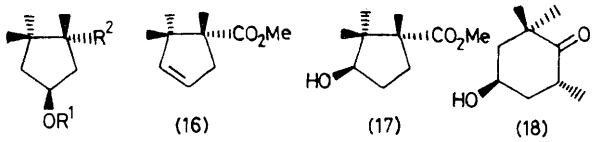
presumably owing to the extended conjugation of the polyene chain. For the two natural carotenoids (**1**) and (**2**) the required esters were synthesised by conventional methods. The dial (**4**) was converted into (**5**) (35%) by a Wittig reaction. A second Wittig reaction gave the ester (**6**) (52%) which was treated with the protected methyl ketone (**15**) to give the β-diketone (**7**) (27%). Acid treatment of (**7**) gave trikentriorhodin (**2**) (79%) which could not be separated by t.l.c. from natural material and the spectral properties (visible, i.r., n.m.r., and m.s.) were in agreement with those published.[2] The c.d. spectrum of the synthetic sample showed a very weak signal: $\Delta\epsilon$ −0·05 (262 nm), +0·06 (303 nm), and −0·06 (370 nm). The c.d. spectrum of natural trikentriorhodin has not been reported.

9-*cis* Mytiloxanthin (**1**) was prepared from the ester (**5**) by protecting the aldehyde as an acetal (**8**) (82%) before the Claisen condensation with (**15**). The acetal (**9**) produced in 55% yield was cleaved with acid (52%) and a Wittig reaction[8] on the apoaldehyde (**10**) formed gave 9-*cis* mytiloxanthin (**1**)† (9%). which was identical with a sample produced by stereomutation of natural all-*trans* mytiloxanthin. All attempts to prepare the all *trans* isomer failed. Although the acetylenic end group (c) was prepared from the optically active hydroxy ketone (**18**)[9] there was no detectable c.d. spectrum with the 9-*cis* mytiloxanthin. This result was not unexpected as natural mytiloxanthin, alloxanthin (**11**), and trikentriorhodin (see above) all have extremely weak c.d. spectra.[10]



(16) (17) (18)

(12) R^1 = H, R^2 = CO_2Me
(13) R^1 = H, R^2 = CO_2H
(14) R^1 = H, R^2 = COMe
(15) R^1 = Me_3Si, R^2 = COMe

The synthesis of related compounds, and their preparation from the corresponding acetylenic ketones or *via* aldol condensations, will be described in the full paper.

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† This stereochemistry is based on the small changes in the light absorption and ^1H n.m.r. spectra and comparison with those of authentic compounds in the alloxanthin (**11**) series.

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