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SYNTHESIS OF CAROTENOID ANALOGUES HAVING PYRIDINE, FURAN, AND THIOPHENE RINGS AS TERMINAL GROUPS

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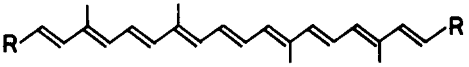
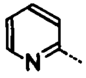
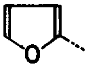
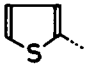
Summary: Heteroaromatic carotenoid analogues having 2-pyridyl, 3-pyridyl, 2-furyl, 3-furyl, 2-thienyl, and 3-thienyl groups at both the ends of tetramethyloctadecanonaene chain, were synthesized and their spectral properties were examined.

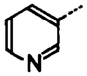
Since the discovery of carotenoids having aromatic terminal groups, an increasing number of this class of compounds have been known from nature as well as by synthesis. However, the terminal groups have so far been completely confined to benzene or naphthalene derivatives and no heteroaromatic carotenoid has been described. Here, we wish to report the synthesis and spectral properties of six such compounds (1-6).

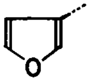


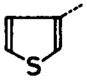
1 R = 

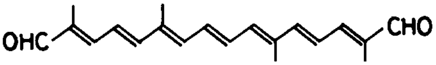
3 R = 

5 R = 

2 R = 

4 R = 

6 R = 



7

Pyridylmethylenation of 7 (crocetindialdehyde)1) was best accomplished by treating 7 with triphenylpyridylmethylphosphonium chloride hydrochlorides2) and excess sodium t-butoxide in DMF at 40°C for two days. The products were purified by TLC on silica gel. 1: Mp 219°C3) (38% based on 7); λ_{max}4) 519, 485 (ε=1.91×10^5), 459 nm; IR(KBr)5) 970 cm^{-1}; NMR (δ, $CDCl_3$) 2.00(s, 6H), 2.06(s, 6H), 5.85-7.90(m, 20H), 8.54(broad d, J=4.5 Hz, 2H). It was soluble in dilute hydrochloric acid (λ_{max} 493 nm in 10% hydrochloric acid) and reprecipitated unchanged by neutralization. On treatment with excess iodomethane, it gave an N,N'-dimethyldipyridinium salt; mp 264°C, λ_{max} (ethanol) 511 nm. It also gave a picrate;6) mp > 300°C; λ_{max} (dichloromethane) 480, 450 nm. 2: Mp 210-211°C (25%); λ_{max} 518, 483 (ε=1.42×10^5), 456 nm; IR 970 cm^{-1}; NMR 2.00(s, 6H), 2.07(s, 6H), 6.10-7.05(m, 14H), 7.29(m, 2H), 7.82(broad d, J=8 Hz, 2H), 8.46(m, 2H), 8.64(m, 2H).

For furylmethylenation or thenylenation of 7, the phosphoranes derived from furylmethyltriphenyl-7) or triphenylthenylphosphonium salts8) and phenyllithium in ether were used in dichloromethane at room temperature. To circumvent the low reactivity and apparent instability of these phosphoranes, freshly prepared phosphorane solutions were added repeatedly until all the aldehydes (7 and the intermediary half aldehyde) were consumed. 3: Mp 208-209°C (83%); λ_{max} 525, 492 ($\varepsilon=1.86\times10^5$), 464 nm; IR 965 cm^{-1}; NMR 2.00(s, 12H), 6.00-7.30(m, 18H), 7.40(m, 2H). 4: Mp 238-239°C (80%); λ_{max} 494, 468 ($\varepsilon=1.38\times10^5$) nm; IR 965 cm^{-1}; NMR 1.99(s, 12H), 6.00-7.10(m, 16H), 7.18-7.59(m, 4H). 5: Mp 236-238°C (78%); λ_{max} 528, 494 ($\varepsilon=1.62\times10^5$), 464 nm; IR 970 cm^{-1}; NMR 2.01(s, 12H), 6.10-7.30(m, 20H). 6: Mp 245°C (76%); λ_{max} 500, 472 ($\varepsilon=1.41\times10^5$) nm; IR 970 cm^{-1}; NMR 1.99(s, 6H), 2.00(s, 6H), 5.97-7.65(m, 20H).

The UV-absorption curves of 1-6 were typical of usual carotenoids.[9] Bathochromic effect of 2-pyridyl groups added to the nonaene chromophore in conjugation was almost the same as that of 3-pyridyl groups and they were comparable to that of phenyl groups.[10] On the contrary, in the furyl or thienyl series, hetero-rings of 2-substitution arose larger and those of 3-substitution smaller bathochromic shifts than that caused by phenyl groups. These can be interpreted as a reflection of partial diene character of these five-membered heteroaromatic nuclei.

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References and Notes

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1) O. Isler, H. Gutmann, H. Lindlar, M. Montavon, R. Rüegg, G. Ryser, and P. Zeller, *Helv. Chim. Acta*, 39, 463 (1956).

2) A reported procedure [B. R. Baker and M. H. Doll, *J. Med. Chem.*, 14, 793 (1971)] was used with a slight modification in which heating a mixture of chloromethylpyridine hydrochlorides and triphenylphosphine in dry DMF at 140°C for 20 h, followed by removal of solvent under diminished pressure gave the corresponding triphenyl-2-, 3-, and 4-pyridylmethylphosphonium salt hydrochlorides in almost quantitative yields. In the present synthesis, the DMF solutions were used for the next ylide-formation step without the isolation of the salts.

3) These six compounds (1-6) gave satisfactory CHN or CH analyses.

4) UV spectra were measured in benzene solutions unless otherwise specified.

5) Only the out-of-plane deformation vibration of chain hydrogens was given here. This absorption appeared in strong singlet throughout the compounds (1-6) supporting the all-trans configurations of the conjugated polyene systems.

6) Elementary analysis (C, 73.5; H, 6.2; N, 8.0%) indicated that the picrate consisted of two moles of 1 and one mole of 2,4,6-trinitrophenol (Calcd for $C_{70}H_{71}N_7O_7$: C, 74.90; H, 6.38; N, 8.74%). The entirely pure sample could not be obtained.

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