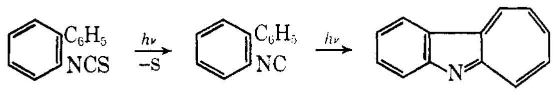
the first example of an aromatic ring expansion brought about by an insertion of an isocyanide carbon atom.



3 1 2

The isocyanide **1**, obtained from the corresponding formamidobiphenyl by dehydration,[4] is a colorless liquid,[5] bp 113–114° (1.5 mm), $n^{22}\text{D}$ 1.6115, ir (neat) 2130 cm^{-1} (NC). *Anal.* Calcd for $C_{13}H_9N$: C, 87.15; H, 5.03; N, 7.82; mol wt, 179. Found: C, 87.17, H, 5.32; N, 7.88; M^+ 179. After irradiation at 2537 Å for 19 hr, **1** in cyclohexane is transformed into 1-azabenz[*b*]azulene (**2**) in 62% yield based on recovered **1**. The product **2** is obtained as a dark red-purple solid, mp 134.5–136° (sealed tube), methiodide mp 232°.[2,6,7]

Formation of the azulene **2** from the isocyanide **1** was first revealed when both **1** and **2** were found to be produced from *o*-biphenylyl isothiocyanate (**3**).[8] After irradiation of **3** in cyclohexane at 2537 Å for 64 hr, *o*-biphenylyl isocyanide (**1**), 1-azabenz[*b*]azulene (**2**), and sulfur were obtained in corresponding yields of 25, 28, and 24% based on recovered **3**.

It appears that irradiation may develop electrophilic carbenoid properties in an isocyanide function. In addition to theoretical interest in this carbenoid species, there is potential value in synthetic work insofar as the isocyanide may be prepared *in situ* from the corresponding isothiocyanate, thereby minimizing exposure to an isocyanide, which may be malodorous and/or toxic. Other electrophilic carbenoid reactions of isocyanides are under investigation.

N. Y., 1964, p 203) attributes to resonance a certain stability for isocyanides "which display no electrophilic reactivity and behave more or less actively as nucleophiles."

(4) By adapting a general procedure reported by I. Ugi and R. Meyer, *Chem. Ber.*, **93**, 239 (1960), dehydration with phosphorus oxychloride gave the isocyanide **1** in 65% yield.

(5) I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer, and K. Offermann [*Angew. Chem.*, **77**, 492 (1965); *Angew. Chem. Intern. Ed. Engl.*, **4**, 472 (1965)] reported **1** as a solid, mp 116–118°, apparently in error.

(6) W. Treibs, R. Steinert, and W. Kirchof, *Ann.*, **581**, 54 (1953).

(7) Elemental analyses and molecular weight determinations were in agreement with structure **2**. Uv and ir absorption data were in complete agreement with previously reported data.[2,6]

(8) According to a general procedure described by J. C. Jochims, *Chem. Ber.*, **101**, 1746 (1968), the isothiocyanate **3** was prepared from *o*-biphenylylamine, dicyclohexylcarbodiimide, and carbon disulfide in 75% yield as a colorless liquid, bp 130–132 (0.25 mm), $n^{26}\text{D}$ 1.6805. *Anal.* Calcd for $C_{13}H_9NS$: C, 73.90; H, 4.29; N, 6.63; S, 15.13; mol wt, 211. Found: C, 74.25; H, 4.49; N, 6.75; S, 15.00; M^+ 211.

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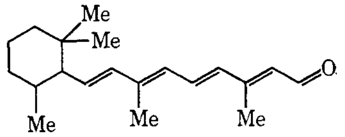
A New Series of Synthetic Visual Pigments from Cattle Opsin and Homologs of Retinal

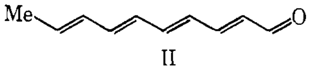
Sir:

We have already reported the synthesis of 5,6-dihydroretinal (I)[1] and the successful coupling of an irradiated sample of I with cattle opsin to yield a synthetic visual pigment, $\lambda_{\max}$ 465 mμ.[2] Since then we have characterized this to be a mixture of pigments derived from 9-*cis*-I and 11-*cis*-I. The details are being published elsewhere.[3] In continuation of our efforts to map the activity of the visual pigment chromophores, we have synthesized a number of polyene aldehydes and examined their reactivity toward cattle opsin.

Compounds I–VII were synthesized using suitable procedures. I was obtained as described earlier:[1] low-melting solid; uv $\lambda_{\max}^{\text{EtOH}}$ 363 mμ; ir (neat) 2720, 1648, 1585, 965 cm^{-1}; mass spectrum, molecular ion at *m/e* 286 ($C_{20}H_{30}O$, 286). II (mp 104–106°; uv $\lambda_{\max}^{\text{EtOH}}$ 349 mμ (lit.[4] mp 107–108°) was obtained by Wittig reaction of *all*-*trans*-2,4,6-octatrienal with triethyl phosphonoacetate followed by reduction ($LiAlH_4$) and oxidation (MnO_2).[5] III was synthesized by self-condensation of crotonaldehyde, mp 164–166° (lit.[6] mp 159–161°); $\lambda_{\max}^{\text{MeOH}}$ 382 mμ. IV was prepared[7] from β-ionone: bp 104–105° (0.08 mm). V was prepared as described earlier. The reaction of V with triethyl phosphonoacetate followed by reduction ($LiAlH_4$) afforded 7-(2,2,6-trimethylcyclohexyl)-5-methyl-2,4,6-heptatrien-1-ol as a pale yellow oil: uv



I



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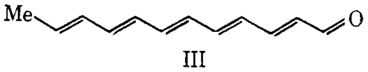

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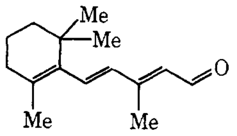
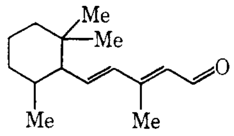
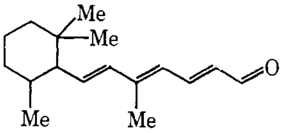


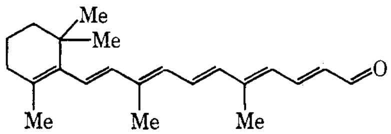
IV



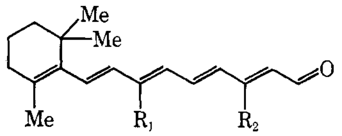
V



VI



VII



VIIIa, $R_1 = H; R_2 = CH_3$
b, $R_1 = CH_3; R_2 = H$
c, $R_1 = R_2 = H$

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(1) P. E. Blatz, P. Balasubramaniyan, and V. Balasubramaniyan, *J. Am. Chem. Soc.*, **90**, 3282 (1968).

(2) P. E. Blatz, P. B. Dewhurst, P. Balasubramaniyan, and V. Balasubramaniyan, *Nature*, **219**, 169 (1968).

(3) P. E. Blatz, P. B. Dewhurst, P. Balasubramaniyan, V. Balasubramaniyan, and M. Lin, *Photochem. Photobiol.*, in press.

(4) R. Kuhn, W. Badstubner, and C. Grundmann, *Chem. Ber.*, **69**, 98 (1936).

(5) Obtained from General Metallic Oxide Co., Jersey City, N. J.

(6) I. N. Nazarov and Zh. A. Krasnaia, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 224 (1958).

(7) Y. Ishikawa, *Bull. Chem. Soc. Japan*, **36**, 1527 (1963).

$\lambda_{\max}^{\text{EtOH}}$ 283, 273, 264, mμ; ir (neat) 3600–3000, 1630–1620, 960 cm^{-1}; mass spectrum, molecular ion at *m/e* 248 ($C_{17}H_{28}O$; 248); nmr τ 3.32 (1 H, quartet), 3.51 (1 H, doublet, J = 15 cps), 4.17 (1 H, doublet, J = 12 cps), 4.1–4.4 (1 H, multiplet), 4.49 (1 H, quartet), 5.86 (2 H, doublet, J = 6.5 cps), 7.76 (1 H, broad singlet), 8.15 (3 H, singlet), 8.1–9.0 (8 H, complex region), 9.17 (6 H, singlet), 9.24 (3 H, doublet, J = 7 cps). Oxidation (MnO_2) of the foregoing alcohol gave VI: uv $\lambda_{\max}^{\text{EtOH}}$ 328 mμ. Condensation of *all-trans*-retinal with triethyl phosphonoacetate gave ethyl 11-(2,6,6-trimethylcyclohexen-1-yl)-2,4,6,8,10-undecapentaenoate: mp 54–56°; uv $\lambda_{\max}^{\text{EtOH}}$ 386, 262 mμ; ir (neat) 1705, 1650, 970 cm^{-1}; mass spectrum, molecular ion at *m/e* 354 ($C_{24}H_{34}O_2$, 354). Reduction ($LiAlH_4$) of this ester gave the alcohol; mp 83–85°; uv $\lambda_{\max}^{\text{MeOH}}$ 356, 345, 328 (I), 312 (I) mμ; ir (KBr) 3600–3100, 1680–1550, 957 cm^{-1}; mass spectrum, molecular ion at *m/e* 312 ($C_{22}H_{32}O$, 312); nmr τ 3.20–4.05 (6 H, complex region), 3.60 (1 H, doublet, J = 16.0 cps), 4.18 (1 H, doublet, J = 15 cps), 5.81 (2 H, doublet, J = 6.0 cps), 7.46 (1 H, broad singlet), 8.08 (6 H, singlet), 8.32 (3 H, singlet), 8.00–8.85 (6 H, complex region), 9.00 (6 H, singlet). Oxidation (MnO_2) of this alcohol gave VII: $\lambda_{\max}^{\text{EtOH}}$ 400 mμ.

The opsin coupling experiments were conducted as follows: the all-*trans* aldehyde was irradiated at the corresponding absorption maximum for periods of up to 1 hr. Thin layer chromatographic (tlc) analysis of the irradiated mixture indicated the formation of one or more *cis* isomers to be present as evidenced by their slightly blue-shifted and less intense uv spectra. No other identifiable products were observed by tlc analysis. On incubation with cattle opsin for several hours, none of the isomers (all-*trans* or -*cis*) showed any opsin activity. We then synthesized the all-*trans* isomer of 9-desmethylretinal (VIIIa), 13-desmethylretinal (VIIIb), and 9,13-desmethylretinal (VIIIc). All three corresponding retinols were prepared[8] by reduction ($LiAlH_4$) of the appropriate methyl retinoate. Oxidation (MnO_2) of the retinol gave the corresponding all-*trans* aldehyde: VIIa, uv $\lambda_{\max}^{\text{EtOH}}$ 369 mμ; ir (neat) 2720, 1660, 1578, 995 cm^{-1}; mass spectrum, molecular ion at *m/e* 270 ($C_{19}H_{26}O$, 270); VIIIb, low melting solid, uv $\lambda_{\max}^{\text{EtOH}}$ 377 mμ; ir (neat) 2722, 1670, 1608, 980 cm^{-1}; mass spectrum, molecular ion at *m/e* 270 ($C_{19}H_{26}O$, 270); VIIIc, oil; uv $\lambda_{\max}^{\text{EtOH}}$ 370 mμ; ir (neat) 2710, 1675, 1572, 992 cm^{-1}; mass spectrum, molecular ion at *m/e* 256 ($C_{18}H_{24}O$, 256). Incubation of any of these all-*trans* isomers with cattle opsin did not result in photopigment formation. When an ethanolic solution of each of these aldehydes was irradiated (425 mμ) and the irradiated mixture incubated with opsin, long-wavelength absorption developed. In order to identify the active components, the irradiated mixture was applied to thin layer chromatograms (silica gel G) and the tlc patterns and the uv spectra of the different spots were compared with those obtained for different geometric isomers of retinal. This enabled a meaningful structural assignment to the different isomers, especially the 9-*cis* and 11-*cis* isomers which presumably were responsible for the opsin activity. This was established by individually coupling the pure isomers (tlc) with cattle opsin. Confirmation of these configurational assignments must await unequivocal synthesis of the separate isomers. Table I includes the spectral data on the pigments obtained from several of these derivatives and cattle opsin. The fact that we obtained genuine photopigments in these cases was checked by examining them with regard to their bleaching behavior and resistance to reaction with sodium borohydride or hydroxylamine in the dark. *Outside of retinal and 3-dehydroretinal, these compounds (I, VIIIa, VIIIb, and VIIIc) represent the first series of aldehydes that are found to combine with cattle opsin to give rise to photosensitive pigments. As of now, none of these pigments has been identified in nature and should be considered as artifacts, like the isopigments derived from 9-cis-retinal and 9-cis-3-dehydroretinal.*

Table I. Absorption Maxima (mμ) of Visual Pigments from Cattle Opsin

Compound	All *trans*	9-*cis*	9-*cis* pigment	11-*cis*	11-*cis* pigment
Retinal[a]	381	373	487	377	498
3-Dehydroretinal	401[b]	391[b]	501[d]	396[c]	517[d]
5,6-Dihydroretinal (I)[a]	363	356	465	360	465
9-Desmethylretinal (VIIIa)[a]	373	367	462	370	465
13-Desmethylretinal (VIIIb)[a]	379	369	488	377	500
9,13-Desmethylretinal (VIIIc)[a]	370	363	481	368	483

[a] Present work. All $\lambda_{\max}$ values for the aldehydes are in ethanol and for the pigments in 2% aqueous digitonin (23°, pH 6.8). [b] U. Schwieter, C. v. Planta, R. Ruegg, and O. Isler, *Helv. Chim. Acta*, **45**, 528 (1962). [c] U. Schwieter, G. Saucy, M. Montovon, C. v. Planta, R. Ruegg, and O. Isler, *ibid.*, **45**, 517 (1962). [d] H. J. A. Dartnall in "The Eye," Vol. 2, H. Davson, Ed., Academic Press, New York, N. Y., 1962, p 443.

A careful examination of the data in Table I leads us to several important conclusions. (1) It appears possible to incorporate a few more structurally related polyene aldehydes with opsin, yielding photosensitive pigments. (2) The length of the polyene side chain seems to be a significant factor in controlling the reactivity of the aldehyde. Thus, while I and VIII couple with opsin, extension (VII) or contraction (II, IV, V, or VI) of the polyenic chromophore prevents the coupling. (3) The role of the ring double bond or the in-chain methyl groups does not seem to be very critical in determining opsin activity. This is illustrated by the successful reaction of opsin with I and VIII. It is conceivable, however, that presence of these steric features enhances the activity of the chromogens. (4) The above generalizations seem to have their limits of validity. Thus failure of any noticeable reactivity of II and III suggests that there is more involved than just the polyene chain length. Apparently the alicyclic residues provide the requisite steric features. Thus, while the visual proteins seem to tolerate a mild mutation of the prosthetic chromophore, drastic changes do result in their rejection by the visual proteins.

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[8] P. J. van den Tempel and H. O. Huisman, *Tetrahedron*, **22**, 293 (1966). However, attempts to obtain analytical specimens of these alcohols or the aldehydes have not been fruitful.