(23) (a) Yoshifuji, M.; Gell, K. I.; Schwartz, J. *J. Organomet. Chem.* **1978**, *153*, C15-C18. (b) Rausch, M. D.; Boon, W. H.; Alt, H. G. *Ibid.* **1977**, *141*, 299-312. (c) Sonogashira, K.; Hagihara, N. *Bull. Chem. Soc. Jpn.* **1966**, *39*, 1178-1182.
(24) Camille and Henry Dreyfus Teacher-Scholar.

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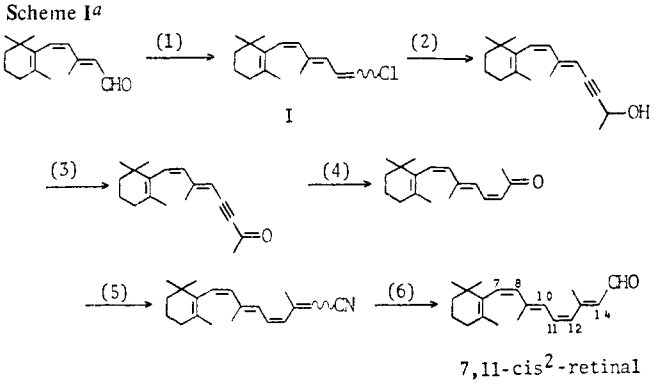
Scheme I[a]




[a] (1) $Ph_3PCH_2ClBr$, *n*-BuLi; (2) 2 mol equiv of *n*-BuLi, $CH_3CHO$; (3) $MnO_2$; (4) $H_2$/Lindlar; (5) $(EtO)_2POCH_2CN$–NaH; (6) Dibah.

## Doubly Hindered 7,11-Dicis Isomers of Retinal. Synthesis, Properties, and Interaction with Cattle Opsin[1]

*Sir:*

With the preparation of four geometric isomers of vitamin A containing the hindered 7-cis geometry,[2] only 6 of the possible 16 isomers are still unknown. Among these are the 4 containing the doubly hindered 7,11-dicis geometry (7,11-dicis, 7,9,11-tricis, 7,11,13-tricis, and all-cis).[3] Considering the relative instability of isomers containing either the 7-cis or the 11-cis geometry, one might reasonably question the possible existence of the doubly hindered isomers. In this paper we report preliminary results on studies of such isomers.

The pathway that led to successful synthesis of 7,11-*cis*$^2$-retinal is shown in Scheme I.

The starting triene was prepared according to the procedure reported earlier.[4] It was separated from the 7,9-dicis isomer by repeated passage through two silica gel columns on a Waters Prep-500 HPLC unit. Most of the reactions are adapted from those already in the literature for the synthesis of the 7-trans isomers.[5] All steps resulted in yields >50%. We might comment that step 4 of the sequence (hydrogenation over Lindlar catalyst) proceeded cleanly with no side reactions. Reaction 5 when conducted in benzene-DMF mixture (15:1) resulted in high trans stereoselectivity of the newly formed 13,14 double bond (>90%). The major isomer was readily purified on a silica gel column. Partial reduction with diisobutylaluminum hydride gave 95% yield of 7,11-*cis*$^2$-retinal.[6] The geometry of the new retinal isomer was characterized by its $^1$H NMR data: $J_{7,8}$ = 12.0 and $J_{11,12}$ = 11.3 Hz (both cis geometry).[7] The complete spectrum is shown in Figure 1.

A slight modification of Scheme I led to a mixture containing predominantly 7,13-*cis*$^2$-11,12-dehydroretinal (II) (Scheme II). The preference for 13-cis isomer in cases involving adjacent triple bonds is well documented.[8] Hydrogenation over Lindlar catalyst, however, gave a rather complex mixture of which we only succeeded in isolating one identifiable product: 7,13-*cis*$^2$-retinal.[9] We suspect that it was formed by way of 7,11,13-*cis*$^3$-retinal involving two consecutive steps of 6e electrocyclization in a manner suggested by Kluge and Lillya.[10] This result suggests that this tricis and other unknown isomers of retinal containing the 11,13-dicis geometry (9,11,13-tricis and all-cis) are probably not stable at room temperature. A certainly related observation is the reported thermal instability of 11,13-*cis*$^2$-retinal.[11a] The isomer crystallized from a solution of purified 11,13-*cis*$^2$-retinal was in fact reassigned with the 13-cis geometry.[11b]

The UV absorption spectrum of 7,11-*cis*$^2$-retinal along with those of 7-cis, 11-cis, and all-trans isomers is shown in Figure 2. It is clear that the characteristic cis band in 11-*cis*-retinal is retained in the dicis isomer and at the same time the extinction coefficient of the main band is much lower presumably owing to nonplanarity of the polyene chain as a result of the doubly hindered geometry.

7,11-*cis*$^2$-Retinal, when incubated with cattle opsin in a manner similar to the procedures used in studies of other retinal isomers,[12] was found to form a stable pigment analogue at a

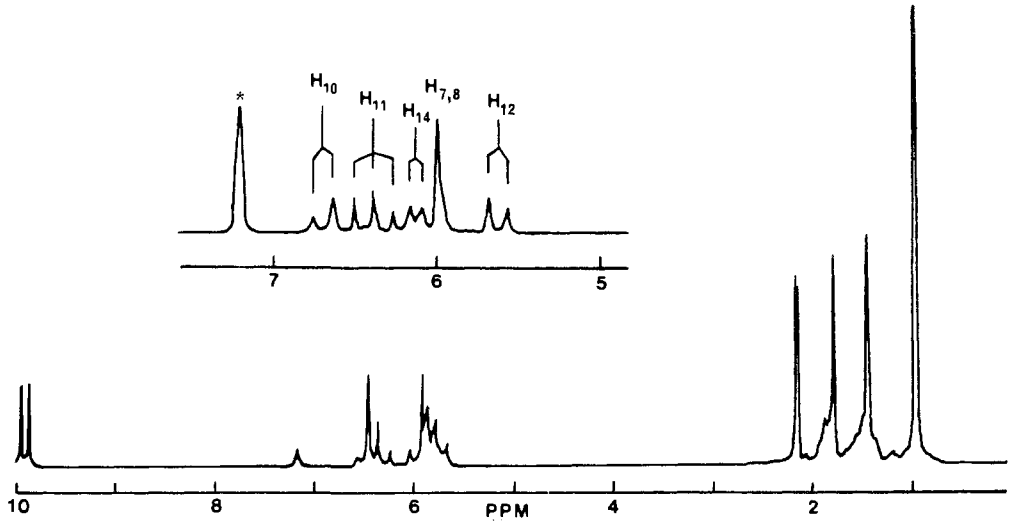



**Figure 1.** $^1$H NMR spectrum (Varian XL-100) of 7,11-cis$^2$-retinal in $CCl_4$ (containing 5% of $C_6D_6$ for locking). Insert: expanded vinyl region of the same compound taken in $C_6D_6$. The peaks marked with * are due to isotopic impurities of solvent.

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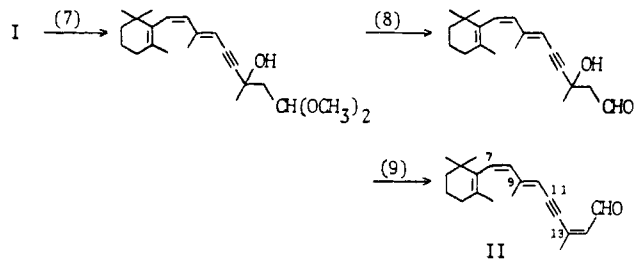
Scheme II[a]




[a] (7) 2 mol equiv of *n*-BuLi, $CH_3COCH_2CH(OCH_3)_2$; (8) *p*-TsOH · $H_2O$–acetone; (9) $CH_3SO_2Cl$–$Et_3N$, $CH_2Cl_2$.

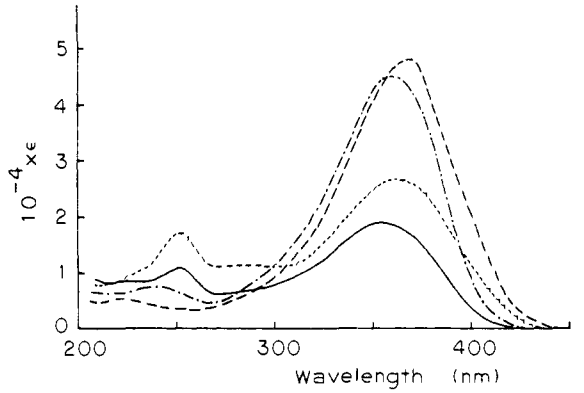



**Figure 2.** Absorption spectrum of 7,11-*cis*[2]-retinal in hexane (—) along with those of all-trans (- - -), 7-cis (-·-), and 11-cis (· · ·). Data of all-trans and 7-cis (in heptane) were taken from ref 13. Data of 11-cis were obtained for this work but are essentially identical with those reported in ref 11: 7,11-dicis, $\lambda_{max}$ 355 nm ($\epsilon$ 18 800); all-trans, 368 (48 000); 7-cis, 359 (44 100); 11-cis, 363 (26 400).

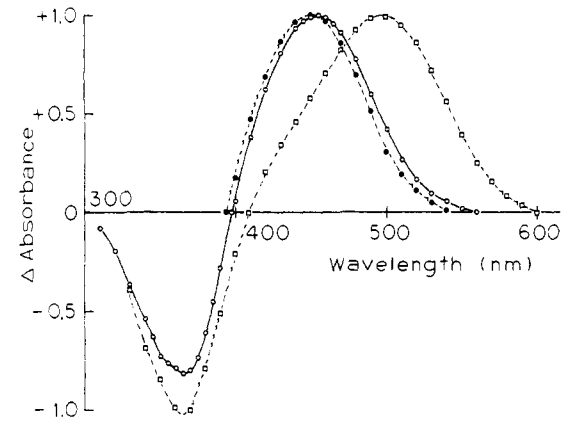



**Figure 3.** The normalized difference spectrum of digitonin solutions of 7,11-*cis*[2]-rhodopsin (—○) along with those of rhodopsin (- -□) and 7-*cis*-rhodopsin (· · ·●), obtained by subtracting the spectrum of the bleached from those of the unbleached pigment in the presence of 92 mM hydroxylamine. The data of rhodopsin and 7-*cis*-rhodopsin were obtained in our laboratory but are identical with those reported in ref 11 and 13.

rate ($k_2 \approx 1 \times 10^{-2}$ $M^{-1}$ $s^{-1}$, in 2% digitonin dissolved in 10 mM Hepes buffer (pH 7.0) at 25 °C) considerably slower than that of 11-*cis*-retinal but comparable with those of the 7-cis,11-trans isomers.[13] The pigment is moderately stable in an excess of hydroxylamine. The difference spectrum of the pigment is shown in Figure 3 along with those of 7-*cis*-rhodopsin and rhodopsin. The absorption maximum is at 455 nm, only slightly red shifted from that of 7-*cis*-rhodopsin (450 nm). Although we have yet done the detailed experiment exploring properties of this new pigment analogue, in a preliminary experiment we showed that the pigment is bleachable by yellow light (≥450 nm). Experiments are underway to examine this photobleaching process. The question whether it takes place by one-photon two-bond isomerization[14] or via intermediacy of rhodopsin and 7-*cis*-rhodopsin is most intriguing.

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## References and Notes

(1) New Geometric Isomers of Vitamin A and Carotenoids. 7. For part 6, see ref 7a.
(2) (a) Ramamurthy, V.; Liu, R. S. H. *Tetrahedron* **1975**, *31*, 201–206. (b) Asato, A. E.; Liu, R. S. H. *J. Am. Chem. Soc.* **1975**, *97*, 4128–4130.
(3) The remaining two isomers are 9,11-dicis and 9,11,13-tricis.
(4) Ramamurthy, V.; Tustin, G.; Yau, C. C.; Liu, R. S. H. *Tetrahedron* **1975**, *31*, 193–199.
(5) See, e.g., Mayer H.; Isler, O. In "Carotenoids", Isler, O., Ed.; Verlag Chemie: Weinheim/Bergstr.: Germany, 1971; pp 325–575.
(6) To achieve consistently high yield of the aldehyde, the use of a modified workup procedure involving wet silica gel in benzene was found necessary.
(7) For a discussion of the NMR data characteristic of the polyene geometry, see: (a) Asato, A. E.; Matsumoto, H.; Denny, M.; Liu, R. S. H. *J. Am. Chem. Soc.* **1978**, *100*, 5957–5960. (b) Patel, D. *Nature (London)* **1969**, *221*, 825–828.
(8) See p 273, ref 5
(9) $^1H$ NMR ($CDCl_3$): 1.06, 1.54, 1.94, 2.10 (methyls), 5.98 ($H_7$), 6.11 ($H_8$), 6.36 ($H_{10}$), 6.92 ($H_{11}$), 7.22 ($H_{12}$), 5.80 ($H_{14}$), 10.10 ppm ($H_{15}$) ($J_{7,8}$ = 11.5, $J_{11,12}$ = 15.5 Hz). 7,13-*cis*[2]-Retinal was previously isolated as a mixture with 7,9,13-*cis*[3]-retinal (see ref 2).
(10) Kluge, A. F.; Lillya, C. P. *J. Am. Chem. Soc.*, **1971**, *93*, 4458–4463.
(11) (a) Wald, G.; Brown, P. K.; Hubbard, R.; Oroshnik, W. *Proc. Natl. Acad. Sci. U.S.A.* **1955**, *41*, 438–451. (b) Oroshnik, W.; Brown, P. K.; Hubbard, R.; Wald, G. *Ibid.* **1956**, *42*, 578–590.
(12) Matsumoto, H.; Horiuchi, K.; Yoshizawa, T. *Biochim. Biophys. Acta* **1978**, *501*, 257–268.
(13) deGrip, W.; Liu, R. S. H.; Asato, A. E.; Ramamurthy, V. *Nature (London)* **1976**, *262*, 416–418.
(14) Crouch, R.; Purvin, V., Nakanishi, K.; Ebrey, T. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 1538–1542.

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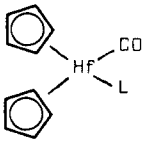
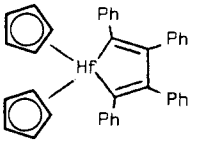
## Structure and Reactivity of the First Hafnium Carbonyl, $(\eta^5\text{-}C_5H_5)_2Hf(CO)_2$

*Sir:*

In contrast to the rich and varied chemistry displayed by the more abundant members of group 4b, titanium and zirconium, the organometallic chemistry of hafnium has only recently begun to develop.[1] Earlier joint studies in our laboratories have been concerned with the formation, structure, and reactivity of compounds containing organohafnium $\sigma$ bonds[2] and with hafnium-containing metallocycles.[3] We now report on the crystal and molecular structure of the first hafnium carbonyl, $(\eta^5\text{-}C_5H_5)_2Hf(CO)_2$ (**1**),[4,5] as well as on some thermally and photochemically induced reactions of this compound.




**1** L = CO
**2** L = $PPh_3$
**3** L = $PMe_3$
**4** L = $Ph_2PCH_2CH_2PPh_2$
**5** L = $PF_3$

**6**

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