3 with alkanes and alkenes strongly suggest that similar functionalization mechanisms are operable for both types of complexes.[8]

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Registry No. 3, 85282-35-5; $Mn^{III}TPP(OAc)$, 58356-65-3; PPh_3, 603-35-0; bicyclo[2.2.1]hept-2-ene, 498-66-8; cyclohexene, 110-83-8; *cis*-stilbene, 645-49-8; *trans*-stilbene, 103-30-0; cyclohexane, 110-82-7; isobutane, 75-28-5.

New Probes for Electron-Transfer Processes. Evidence Supporting the Single-Electron-Transfer Mechanism in Additions of Carbanions to Dienones

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The question of whether carbanion additions to carbonyl compounds proceed via a single-electron-transfer (SET) pathway or a polar pathway has received much attention in recent years. Many of the studies in this area have sought to determine the operability of the SET pathway via the use of a variety of internal probes. These include, inter alia, cis–trans isomerizations of bulky enones[2] and the incorporation of "free radical clocks" in the carbanion.[3] In this communication we report on the development of a new probe for detecting SET processes and the use of this probe in elucidating the mechanism of carbanion additions to dienones.

The internal probe that we have used is the ethylenedioxy group. By placing this functional group on the α-carbon of a ketyl (radical anion), one introduces the possibility of carbon–oxygen bond scission. If the α-ethylenedioxyketyl in question is generated by a single electron transfer from a carbanion to an α-ethylenedioxy carbonyl compound, radical–radical anion combination is forced to compete with carbon–oxygen bond scission[4] (Scheme I). Since in direct carbanion additions to these substrates carbon–oxygen bond scission cannot be a competitive process, *the direct observation of products derived from carbon–oxygen bond scission in carbanion additions to α-ethylenedioxy carbonyl compounds would implicate the presence of a ketyl intermediate and would thereby provide strong support for the operability of the SET mechanism.*

In this regard we have studied the reactions of **1** with a variety of organometallics (see Table I). The most obvious fact that emerged from our studies is that significant amounts of **4** were produced in *all* of the cases investigated. This observation is, of course, completely consistent with the SET mechanism proposed in Scheme I. Similarly, the results obtained from the series *n*-butyllithium, *sec*-butyllithium, and *tert*-butyllithium are also compatible with the SET pathway, i.e., while the magnitude of k_3 is expected to decrease as the size of R· increases, the magnitude of k_2 has no direct relationship with R.

Unfortunately, although both of these observations are consistent with the SET mechanism, they do not rule out the possibility that the addition products (**6**) are formed by competitive direct carbanion addition. In order to answer this question, we examined the reaction of **1**[5] with 1-lithio-5-hexene (−78 → 25 °C). Since we have independently shown that this lithiate does not undergo any structural rearrangements,[6] the fact that *all* of the observed addition product, **6**, had R = cyclopentylcarbinyl clearly indicates the intermediacy of the 5-hexenyl radical,[7] which then undergoes a well-precedented rearrangement to the cyclopentylcarbinyl radical.[8] Radical/radical anion coupling produces **5**, which, upon quenching with a proton source, produces **6**. *These results taken as a whole not only demonstrate the operability of the SET mechanism with dienones but also rule out the possibility of any competitive direct carbanion addition.*

One additional point should be made. We had previously shown that quinols possessing general structure **7** could be produced by

Scheme I

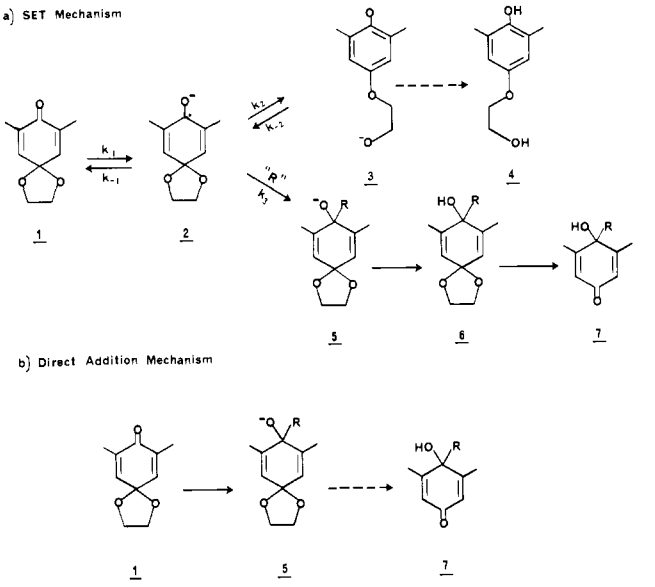

Table I

reagent	R	solvent	temp, °C	% 1[a]	% 6[a]	% 4[a]
$(CH_3)_2Cu\ Li$	CH_3^-	Et_2O	−78	15		85
CH_3Li	CH_3^-	Et_2O	−78 → 25	10	88	2
		THF	−78 → 25	7	90	3
		THF	−78		95	5
CH_3MgBr	CH_3^-	THF	−78 → 25	7	90	3
		THF	−78	2	95	3
n-C_4H_9Li	n-$C_4H_9^-$	Et_2O	−78 → 25	5	90	5
		THF	−78 → 25	4	95	1
		THF	0 → 25	8	46	46
n-C_4H_9MgBr	n-$C_4H_9^-$	THF	0	10	40	50
sec-C_4H_9Li	s-$C_4H_9^-$	THF	−78	30	26[b]	44
t-C_4H_9Li	t-$C_4H_9^-$	THF/	−78	10		90
		TMEDA[c]	−78 → 25	5	25[b]	70
sec-C_4H_9Li	s-$C_4H_9^-$	THF/ TMEDA[c]	−78 → 25	10	52	38

[a] Obtained via NMR spectroscopy. [b] Some ketal hydrolysis occurred during workup. Yield indicates the total amount of 6 and 7 that were produced. [c] Tetramethylethylenediamine (3 mol equiv equiv).

(1) Fellow of the Alfred P. Sloan Foundation, 1980–1984. Recipient of a Camille and Henry Dreyfus Teacher–Scholar Fellowship, 1981–1986.

(2) For example see: Ashby, E. C.; Wiesemann, T. L. *J. Am. Chem. Soc.* **1978**, *100*, 310.

(3) For example, see: (a) Smith, J. G.; Irwin, D. C. *J. Am. Chem. Soc.* **1980**, *102*, 2757. (b) Ashby, E. C.; Bowers, J. S. *Ibid.* **1977**, *99*, 8504. See also: Griller, D.; Ingold, K. U. *Acc. Chem. Res.* **1980**, *13*, 317.

(4) Electron-transfer reactions involving γ-alkoxyenones rarely result in expulsion of the γ-alkoxy group from the intermediate radical anion. For example, see: Ruden, R. A.; Letterer, W. E. *Tetrahedron Lett.* **1975**, 2043. For an exception to this, see: Nilsson, A.; Ronlan, A.; Parker, V. D. *Ibid.* **1975**, 1107.

(5) A general method for the synthesis of quinone ketals, such as **1**, will be the subject of future reports.

(6) This lithiate was generated via a lithium–halogen exchange reaction involving 1-bromo-5-hexene, 2 equiv of *tert*-butyllithium, and 3 equiv of TMEDA in THF. If this mixture is quenched with trimethylsilyl chloride, 5-hexenyltrimethylsilane is cleanly produced.

(7) Because of the lack of radical byproducts observed, it is unlikely that this reaction produces a "free" 5-hexenyl radical. Instead, the radical is probably bound to a hexenyllithium aggregate and therefore less prone to participate in radical/radical or radical/molecule reactions.

(8) Walling, C.; Cioffari, A. *J. Am. Chem. Soc.* **1972**, *94*, 6059.

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direct carbanion addition to 2,6-dimethylbenzoquinone under conditions where the anion was unaggregated, weakly solvated and had a small counterion.[9] However, in that study we noted that when the inherent steric requirements of the carbanion become very large (e.g., secondary carbanions), selective attack at the more hindered carbonyl carbon is no longer possible. Our mechanistic studies with **1** had led us to a simple solution to this problem. Since the ring-opening reaction (**2** → **3**) exhibits a much larger temperature dependence than the competing addition process (**2** → **5**), secondary carbanions can be cleanly added to **1** at very low temperatures (see last entry in Table I) to produce (after quenching and ketal hydrolysis) **7** in good yield.[10]

Acknowledgment. This work was supported by a grant from the National Institutes of Health and, in part, by the McCandless Fund (Emory University).

Registry No. 1, 85268-20-8; **4**, 85268-21-9; **6** (R = Me), 85268-22-0; **6** (R = Bu), 85268-23-1; **6** (R = *sec*-Bu), 85268-24-2; **6** (R = *t*-Bu), 85268-25-3; $(CH_3)_2Cu{\cdot}Li$, 15681-48-8; CH_3Li, 917-54-4; CH_3MgBr, 75-16-1; *n*-C_4H_9Li, 109-72-8; *n*-C_4H_9MgBr, 693-03-8; *sec*-C_4H_9Li, 598-30-1; *t*-C_4H_9Li, 594-19-4; 1-lithio-5-hexene, 85268-26-4.

(9) Liotta, D.; Saindane, M.; Barnum, C. *J. Org. Chem.* **1981**, *46*, 3369.
(10) **4** can be easily separated from **6** by simple base extraction.

7-*cis*,9-cis,11-*cis*-Retinal, *all*-*cis*-Vitamin A, and 7-*cis*,9-*cis*,11-*cis*-12-Fluororetinal. New Geometric Isomers of Vitamin A and Carotenoids. 12[1]

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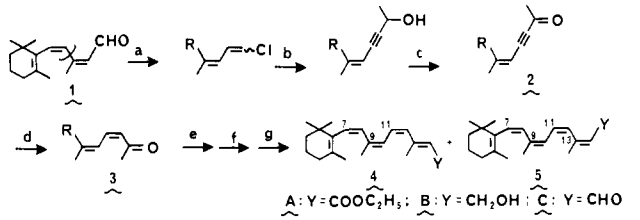
The geometric isomers of vitamin A occupy an important chapter in studies of stereospecificity of the binding site of the visual protein opsin.[2] Of its 16 possible geometric isomers, 14 are known. They are the six earlier reported 7-trans isomers (*all-trans*; 9-*cis*; 11-*cis*; 13-*cis*; 9-*cis*,13-*cis*; 11-*cis*,13-*cis*)[3] and the eight more recently reported hindered isomers (7-*cis*; 7-*cis*,9-*cis*; 7-*cis*,13-*cis*; 7-*cis*,9-*cis*,13-*cis*;[4] 7-*cis*,11-*cis*; 7-*cis*,11-*cis*,13-*cis*;[5] 9-*cis*,11-cis;[6] 9-*cis*,11-*cis*,13-*cis*[7]). Now we report the synthesis of the last two remaining isomers: 7-*cis*,9-*cis*,11-*cis* and the interesting all-*cis*.

The synthetic sequence used in the synthesis of the missing isomers of vitamin A was similar to that recently reported for the doubly hindered 7-*cis*,11-*cis* isomer[5] but with 7-*cis*,9-*cis*-β-ionylideneacetaldehyde (**1**)[4b,c] as the starting material (see Scheme I). Partial hydrogenation of the 11-dehydro-C_{18}-ketone **2** was the key step in the synthetic sequence because hydrogenation at later stages invariably led to complex mixtures. Even at the C_{18} stage, in order to avoid over hydrogenation, the reaction was carried out to only 70–80% completion. Since the 11-dehydro compounds were found more easily separated at a later stage, the *all-cis*-C_{18}-ketone **3** mixed with small amounts of the dehydro ketone was used in the chain-extension reaction. Ethyl lithio(trimethylsilyl)acetate, **6**, was chosen as the reagent because of its demonstrated higher reactivity and the concomitant lack of stereospecificity.[8] The crude condensation product mixture was partially separated by flash column chromatography. The early fractions were the 11-dehydro esters. The later fractions contained two components, subsequently separated by preparative HPLC. Their structures were readily deduced from their 300-MHz ^1H NMR spectra (see supplemental material).[9] The early eluting fraction was ethyl 7-*cis*,9-*cis*,11-*cis*-retinoate (**4A**) with the 13-trans geometry indicated by the low-field CH_3-13 signal, the 7-cis and the 11-cis geometry by the small coupling constants, and the 9-cis geometry by the low-field H_8 signal.[10] For similar reasons, the principal of the later eluting fraction was identified to be ethyl *all-cis*-retinoate (**5A**). The UV–vis absorption spectra of both compounds with the much blue shifted absorption maxima (328 and 330 nm in hexane) are consistent with the expected nonplanar conformation of these severely crowded isomers.

A mixture of the two C_{20} esters was converted to the corresponding aldehydes[4a] and separated by preparative HPLC with the mixtures of isomeric 11-dehydroretinals conveniently eluted in early fractions. The first eluted retinal isomer was 7-*cis*,9-*cis*,13-*cis*-retinal, identified by comparison of ^1H NMR spectra.[4b] Since all operations were carried out at room temperature, this was an expected isomer from facile thermal isomerization of

Scheme I



[a] Ph_3PCH_2Cl, X; BuLi. [b] 2BuLi; CH_3CHO. [c] MnO_2. [d] H_2–Lindlar catalyst. [e] $Me_3SiCHCO_2EtLi$, 6. [f] Dibal-H. [g] MnO_2 (R = *cis*-$C_{11}H_{17}$ (see structure 1)).

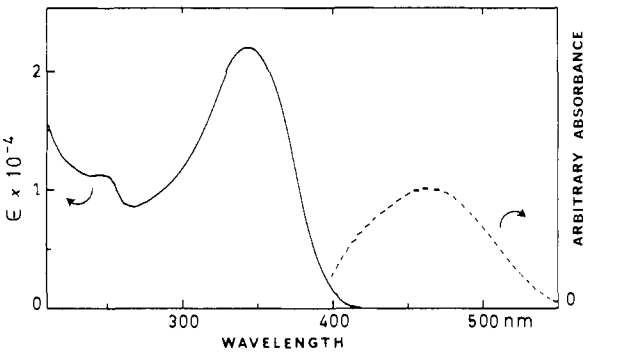


Figure 1. UV–vis absorption spectrum of 7-*cis*,9-*cis*,11-*cis*-retinal in cyclohexane (solid line), λ_{max} 345 nm (ε 22 000), and difference absorption spectrum of 7-*cis*,9-*cis*,11-*cis*-rhodopsin (dashed line) in 1% digitonin, obtained after taking the difference between the spectra of the pigment in an excess of hydroxylamine before and after photobleaching with yellow light.

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(2) (a) Wald, G. *Science* (*Washington*, D.C.) **1968**, *162*, 230–239. (b) Liu, R. S. H. In "Carotenoid Chemistry and Biochemistry"; Britton, G., Goodwin, T. W., Eds.; Pergamon Press: New York, 1982; pp 253–264.
(3) Wald, G.; Brown, P. K.; Hubbard, R.; Oroshnik, W. *Natl. Acad. Sci. U.S.A.* **1955**, *41*, 438–450; **1956**, *42*, 578–580.
(4) (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. (c) Liu, R. S. H.; Asato, A. E. *Methods Enzymol.* **1982**, *88*, 506–516.
(5) Kini, A.; Matsumoto, H.; Liu, R. S. H. *J. Am. Chem. Soc.* **1979**, *101*, 5078–5079.
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(7) Knudsen, C. G.; Carey, S. C.; Okamura, W. H. *J. Am. Chem. Soc.* **1980**, *102*, 6355–6356.
(8) Taguchi, H.; Shimoji, K.; Yamamoto, H.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1974**, *47*, 2529–2529.
(9) Recorded on a Nicolet NT-300 spectrometer acquired through a grant by the National Science Foundation (CHE 8100240) and the University of Hawaii.
(10) For ^1H NMR data of geometric isomers of retinoids, see: (a) Patel, D. *Nature* (*London*) **1969**, *221*, 825–827. (b) Vetter, W.; Englert, G.; Rigassi, N.; Schwieter, U. In "Carotenoids"t; Isler, O., Ed.; Birkhäuser Verlag: Basel, 1971; p 213–225. (c) Reference 4c.

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