The present synthesis demonstrates the utility of a latent diene–dienophile for construction of bicyclic ketones, e.g., 5,6- and 6,6-ring systems, which are useful intermediates for the synthesis of some natural products.

(19) After our manuscript was submitted, another total synthesis of (±)-coronafacic acid by using oxy-Cope rearrangements has been reported: Jung, M. E.; Hudspeth, J. P. *J. Am. Chem. Soc.* **1980**, *102*, 2463.

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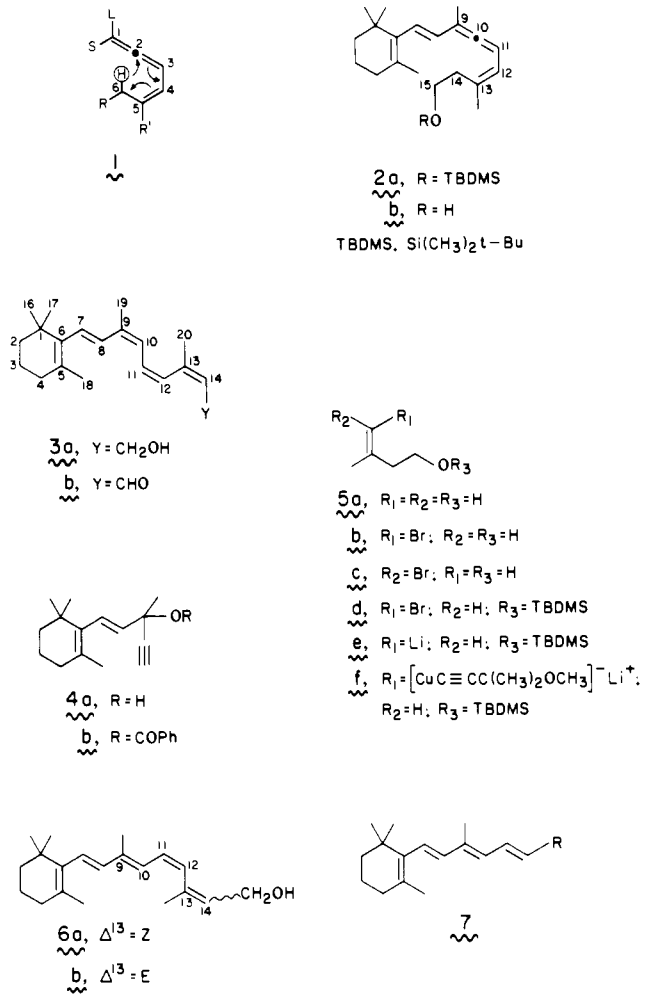
[1,5]-Sigmatropic Rearrangement of Vinylallenes: A Novel Route to Geometric Isomers of the Retinoids Possessing 11-Cis Linkages Including 9-*cis*,11-*cis*,13-*cis*-Retinal

Sir:

The thermally induced [1,5]-sigmatropic hydrogen shift of vinylallenes[1,2] of the general stereostructure **1** (Chart I) can be utilized for efficiently constructing the (3*Z*)-1,3,5-hexatriene moiety of the 1-hydroxyvitamin D system.[2] In order to examine the suitability of the vinylallene strategy for synthesizing higher order polyenes, we have directed our attention toward allenes of the vitamin A series.[3] We report the preparation and thermal studies of the 9,10-allenic retinoid **2**. The results which we wish to feature include: the first synthesis of the highly hindered 9-*cis*,11-*cis*,13-*cis*-retinol (**3a**) and -retinal (**3b**); their thermal behavior and unusual electronic spectral characteristics; the unexpected finding that the stereochemical course of the sigmatropic rearrangement of **2** is biased toward paths leading to the more hindered stereoisomeric retinols; and the gratifying observation that the 11-cis linkages of the retinols retain their stereochemical integrity under the conditions of the thermal vinylallene rearrangement.

The allene silyl ether **2a** was produced in 50% yield by the formal S_N2' coupling of propargyl benzoate **4b** with the mixed cuprate **5f**.[2,4] The sensitive propargylic benzoate **4b** was prepared by benzoylation (ether; *n*-butyllithium and then PhCOCl; 64% yield, mp 52–53 °C) of alcohol **4a**.[5] Isopentenyl alcohol (**5a**) was converted to the ~1:2 *Z*/*E* mixture **5b**–**5c**,[6] from which the pure *Z* isomer **5b** could be purified by high-pressure (Waters 500) or medium-pressure[7] liquid chromatography (LC). The bromide was subjected to protection (TBDMSCl, imidazole, DMF, 94%),[8] lithiation (2 equiv of *t*-BuLi, ether, −78 °C, 4 h),[9] and then reaction

Chart I



with $CuC{\equiv}C{-}C(CH_3)_2OCH_3$[9] to afford **5f**. The allene **2a** is a highly sensitive substance which was purified by rapid medium-pressure LC [silica gel, 2% pyridine/low-boiling petroleum ether (lbpe)][7] and then stored at −80 °C (N_2) in a low-temperature freezer. Deprotection of **2a** with *n*-Bu_4NF/THF (1 M, 3 h)[8] afforded the equally sensitive alcohol **2b** (37% yield; short silica column with 30% ether/2% pyridine in lbpe).

Thermolysis of the allenic retinol **2b** (10^{-3} M in purified skellysolve B at reflux, ~69 °C, N_2, 2 h) followed by semipreparative high-pressure LC (Waters 6000A system; Whatman M9 10/50 partisil column, 9.4 mm × 50 cm; 3% isobutyl alcohol/skellysolve B) afforded in order of elution the following absolute yields of products: 9.6% 11-*cis*,13-*cis*-retinol (**6a**), 9.1% of a new isomer, 9-*cis*,11-*cis*,13-*cis*-retinol (**3a**), and 8.7% 11-*cis*-retinol (**6b**).[10] Monitoring the thermolysis under the same conditions up to 5.5 h (2537-Å UV-detection high-pressure LC) revealed that the ratio **6a**/**3a**/**6b** remained constant (1.5:1.0:1.1, uncorrected, ±5% average deviation). Each of the three retinols retained geometric integrity when subjected to the conditions of the preparative run (~69 °C, 2 h). By comparison with authentic specimens (high-pressure LC, ^1H NMR, UV),[11] 11-*cis*,13-*cis*-retinol (**6a**) and 11-*cis*-retinol (**6b**) were positively identified while the 9-*cis*-, 9-*cis*,13-*cis*-, *all-trans*-, and 13-*cis*-retinol isomers were specifically ruled out as products of the thermolysis of **2b**, **3a**, **6a**,

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(10) Thermolysis of **2a** (10^{-3} M in purified skellysolve B, ~69 °C, 2 h, under N_2; <5% starting material remained, ^1H NMR) followed by deprotection (1 M *n*-Bu_4NF/THF, 1–3 h; filtration through silica gel with 2% pyridine/30% Et_2O in low-boiling petroleum ether) and then similar preparative high-pressure LC afforded 11.5% **6a**, 14% **3a**, and 10% **6b**.

(11) Authentic specimens or precursors to authentic specimens of the *all-trans*-, 11-*cis*-, 9-*cis*-, 13-*cis*-, 11-*cis*,13-*cis*-, and 9-*cis*,13-*cis*-retinols were made available by Dr. Gary Olson and Dr. David Coffen of the Hoffmann-La Roche Co. (Nutley, NJ).

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and **6b** under the reaction conditions. Since it is reasonable to assume that none of the eight possible 7-cis[12] isomers were present, what is described as a new isomer can only be the 9-cis,11-cis,13-cis isomer as assigned (see below) or the 9-cis,11-cis isomer. No other retinol besides **6a**, **3a**, and **6b** could be detected during high-pressure LC separation runs. The conclusion then is that **6a**, **3a**, and **6b** are primary products produced competitively. Since the three products are produced in about a 1:1:1 ratio (by weight and by integration of the RI detector trace), it is apparent that formation of 9-trans and 13-cis isomers is slightly favored. The 11-cis linkage is predetermined by the cyclic nature of these competing and presumably concerted sigmatropic shift processes.

In order to further support the stereostructure of the new retinol (**3a**), it was oxidized (MnO_2, 30-fold excess, low-boiling petroleum ether, 1 h, 4 °C; short Celite column chromatography, ether) in 82% yield to the aldehyde **3b**.[13] The ^1H NMR spectrum of the latter was clearly distinguishable from that of 9-*cis*,11-*cis*-retinal, whose spectrum was kindly provided by Professor R. S. H. Liu.[14] The ^1H NMR spectrum of **3b** is characterized by an aldehyde proton signal at τ 0.32 (d, $J \sim 7.8$ Hz); the only other retinal with such a high-field aldehyde proton chemical shift is the 11-cis,13-cis isomer: τ 0.29 (d, $J \sim 8.1$ Hz).[14] Signals assigned to H_{10} [τ 3.91 (d, $J \sim 11.7$ Hz)], H_{11} [τ 3.15 (t, $J \sim 11.7$ Hz)], and H_{12} [τ 3.98 (d, $J \sim 11.7$ Hz)][15] suggest a 10-*s*-trans conformation for **3b**. The most remarkable spectral property of **3b** is its electronic spectrum [λ_{max} (95% EtOH) 302 nm (ϵ 14 300); λ_{max} (hexane) 302 nm (ϵ 15 500)] since all other retinals absorb above 360 nm.[16] Moreover, the corresponding alcohol **3a** actually exhibits its maximum slightly to the red [λ_{max} (95% EtOH) 306 nm (ϵ 24 500)] of the aldehyde! The tetraene **7** should exhibit a maximum at 290 nm.[17] Thus, both **3a** and **3b** are probably very highly twisted about the Δ^{12} single bond.[17] When **3b** is warmed mildly, it isomerizes to 9-*cis*,13-*cis*-retinal ($t_{1/2} \sim 2$ h in $CDCl_3$ at 45 °C, by ^1H NMR)[18] through successive electrocyclic ring-closing and then ring-opening processes similar to those previously described.[12]

Although the stereoselectivity and yields of the vinylallene scheme for preparing retinoids are not high, the method is gratifyingly specific for producing the difficult-to-obtain 11-cis isomers. This feature should make it a useful method for producing these key stereoisomers of analogues in adequate quantities for vision research.

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Supplementary Material Available: Spectral and analytical data (5 pages). Ordering information is given on any current masthead page.

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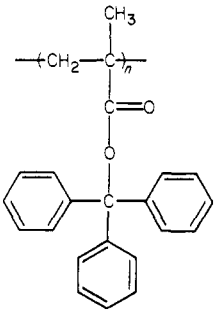
(12) For leading references, see: Kini, A.; Matsumoto, H.; Liu, R. S. H. *J. Am. Chem. Soc.* **1979**, *101*, 5078.
(13) For examples of related oxidations, see ref 3a and 12.
(14) (a) Patel, D. J. *Nature (London)* **1969**, *221*, 825: (b) Professor R. S. H. Liu has kindly provided detailed tables of ^1H NMR spectral parameters for all previously reported retinals, including unpublished data from his own laboratory.
(15) The signals attributed to H_{10} and H_{12} may be reversed.
(16) Zechmeister, L. "*Cis-Trans* Isomeric Carotenoids, Vitamins A and Arylpolyenes", Academic Press: New York, 1962; p 126.
(17) The 290-nm value was obtained from a simple Woodward's Rules calculation, assuming a base value of 255 nm for the $\Delta^{5,7,9}$ triene chromophore: Baas, J. L.; Davies-Fidder, A.; Visser, F. R.; Huisman, H. O. *Tetrahedron* **1966**, *22*, 265. The λ_{max} value of the aldehyde **3b** is significantly more highly perturbed (ref 16: 368–381 nm for other isomers) than that of the alcohol **3a** (ref 16: 312–328 nm). The aldehyde **3b** may more easily accommodate chromophore splitting(deconjugation by twisting about the Δ^{12} bond) to minimize steric congestion by virtue of added delocalization energy gained by the presence of the aldehyde and the linearly positioned (in a hyperconjugative sense) C_{13} methyl. *all-trans*- and 9-*cis*,11-*cis*,13-*cis*-retinoic acids exhibit UV maxima at 359 nm (ϵ 43 000) and 348 nm (ϵ 26 400), respectively (private communication to an anonymous referee from Dr. M. Klaus, F. Hoffmann-La Roche, Basel, Switzerland).
(18) The 11-*cis*,13-*cis*-retinal isomerizes to 13-*cis*-retinal under the same conditions with a similar half-life.

Resolution of Racemic Compounds by Optically Active Poly(triphenylmethyl methacrylate)

Sir:

We have recently reported the preparation of optically active, isotactic poly(triphenylmethyl methacrylate) (PTrMA) by chiral



PTrMA

anion catalysts such as (−)-sparteine–butyllithium complex.[1] This is the first example of the optically active vinyl polymer, the chirality of which is caused only by helicity. The polymer of high molecular weight shows high crystallinity and is insoluble in common organic solvents. This communication describes the liquid chromatographic resolution of various racemic compounds such as alcohol, ester, amine, and hydrocarbon by insoluble, optically active (+)-PTrMA.

The resolutions of racemic compounds have been achieved by column chromatography with naturally occurring or synthetic polymers as optically active adsorbents.[2] Most synthetic adsorbents were prepared either by attaching chiral molecules onto insoluble supports or by polymerizing (or binding) chiral molecules in the presence of cross-linking agents. Optically active PTrMA is a new type of synthetic chiral adsorbent and is easily prepared by a small amount of a chiral anionic catalyst.

Triphenylmethyl methacrylate (20.0 g, 60.7 mmol) was dissolved in dry toluene (400 mL) under nitrogen and cooled to −78 °C. To this solution was added a toluene solution of (−)-sparteine (0.342 g, 1.46 mmol) and butyllithium (1.21 mmol) with a syringe. After 24 h, the reaction mixture was poured into methanol (4 L), and the insoluble polymer was separated with a centrifuge. The polymer was grained and extracted with tetrahydrofuran (700 mL). The insoluble polymer was separated with a centrifuge and dried under vacuum, yield 19.4 g (96.8%). The specific rotation, $[\alpha]^{20}_D$ of this polymer is considered to be greater than +250° on the basis of the data reported previously.[1] The $\overline{DP}$ of the polymer was estimated to be 220 from a gel-permeation chromatogram of the poly(methyl methacrylate) derived from (+)-PTrMA.[1] The polymer was grained to small particles, which swelled 2–4 times

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