$C_{40}H_{72}NO_4I$: C, 63.39; H, 9.58; N, 1.85; I, 16.74. Found: C, 63.50; H, 9.62; N, 1.67; I, 16.41.

(12) Solvatochromism of the pyridinium iodide head group has previously been employed to estimate the micropolarity in the vicinity of triple ions[13] and in the Stern layer of aqueous micelles.[14,15]

(13) E. J. R. Sudhölter and J. B. F. N. Engberts, *Recl. Trav. Chim. Pays-Bas*, **96**, 86 (1977).

(14) E. J. R. Sudhölter and J. B. F. N. Engberts, *J. Phys. Chem.*, **83**, 1854 (1979).

(15) P. Mukerjee and A. Ray, *J. Phys. Chem.*, **70**, 2138: 2144, 2150 (1966).

(16) A typical procedure is as follows. Amphiphile (10 mg) is dissolved in ~1 mL of chloroform (P.A. quality, distilled from P_2O_5) in a glass tube. The chloroform is evaporated in a stream of pure nitrogen gas and 1.5 mL of Tris•NaCl buffer solution (5 mM Tris•HCl + 0.15 M NaCl, pH 7.4) is added. The thin film of amphiphile on the glass vessel is dispersed by ultrasonic irradiation using a Bransonic 220 water bath during 5 min. The turbid solution is poured into a plastic tube and is sonicated for another 30 min at 0 °C by means of a pulsed high-energy probe (Branson Sonifier Cell Disruptor B 15). After centrifugation (Hettich rotafix II, ~1000 g), a transparant supernatant is obtained which was used in all experiments.

(17) The two-step droplet method was used to prepare the specimens on Formvar and carbon coated grids. A 1% (by weight) solution of uranyl acetate was used as negative stain. Micrographs were obtained with a Philips EM 300 electron microscope (operating at 80-kV accelerating voltage) on Kodak 4463 sheets. Electron magnification was 25.000 and 50.000 times.

(18) (a) M. P. Sheets and S. I. Chan, *Biochemistry*, **11**, 4573 (1972); (b) A. D. Bangham and R. W. Horne, *J. Mol. Biol.*, **8**, 660 (1964).

(19) Similar multilayered vesicles were previously observed, for instance, by Kunitake using the same procedure.[3a]

(20) J. N. Weinstein, S. Yoshikami, P. Henkart, R. Blumenthal, and W. A. Hagins, *Science*, **195**, 489 (1977).

(21) 0.01 M Hepes + 0.135 M NaCl, pH 7.4.

(22) Perkin-Elmer MPF-43 fluorescence spectrophotometer, excitation wavelength 490 nm, emission wavelength 520 nm.

(23) The total amount of entrapped CF was determined after the experiment via destruction of the vesicles with an aqueous solution of Triton X-100 (final concentration: 1% by weight).

(24) (a) D. Chapman, *Q. Rev. Biophys.*, **2**, 185 (1975); (b) R. Lawaczeck, M. Kainosho, J. L. Girardet, and S. I. Chan, *Nature (London)*, **256**, 584 (1975); (c) R. Lawaczeck, M. Kainosho, and S. I. Chan, *Biochim. Biophys. Acta*, **443**, 313 (1976).

(25) R. A. Haberkorn, R. G. Griffin, M. D. Meadows, and E. Oldfield, *J. Am. Chem. Soc.*, **99**, 7353 (1977).

(26) Varian XL-100 FT NMR spectrometer. Vesicles generated by sonication at 0 °C in D_2O.

(27) T. Nagamura, S. Mihara, Y. Okahata, T. Kunitake, and T. Matsuo, *Ber. Bunsenges. Phys. Chem.*, **82**, 1093 (1978).

(28) Compare E. M. Kosower, "An Introduction to Physical Organic Chemistry", Wiley, New York, 1968.

(29) E_T values have been measured for **3** and **4** in solvents CH_2Cl_2, DMF, MeCN, 2-PrOH, and EtOH and for **4** also in MeOH and H_2O. For **4** in H_2O λ_m was obtained by using Mukerjee's band-match method.[15]

(30) (a) F. M. Menger, J. M. Jerkunica, and J. C. Johnston, *J. Am. Chem. Soc.*, **100**, 4676 (1978); (b) F. M. Menger, *Acc. Chem. Res.*, **12**, 111 (1979).

Ernst J. R. Sudhölter, Jan B. F. N. Engberts*
Department of Organic Chemistry, University of Groningen
Nijenborgh 16, 9747 AG Groningen, The Netherlands

Dick Hoekstra
Department of Physiological Chemistry
University of Groningen, Bloemsingel 10
9712 KZ Groningen, The Netherlands

Received November 13, 1979

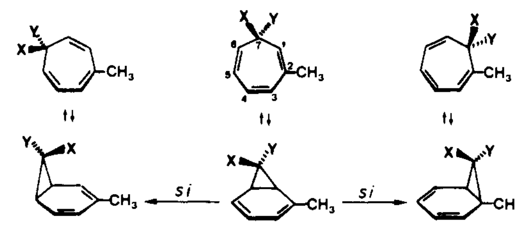
Stereochemistry of the Thermal Walk Rearrangement of Optically Active 2,7-Dimethyl-7-methoxymethyl-1,3,5-cycloheptatriene: 1,5-Carbon Migration with Inversion, *No* One-Center Epimerization at C-7

Sir:

The stereochemistry of the thermal norcaradiene walk rearrangement discovered by Berson and Willcott[1] is important for defining concerted and nonconcerted processes. Two experimental tests were reported giving conflicting results. The concern of this communication is to elucidate these discrepancies.

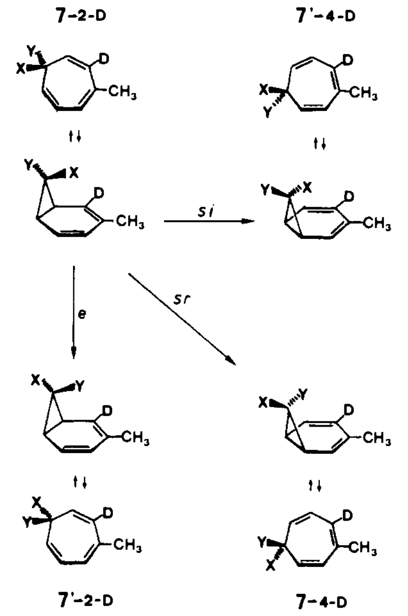
The same stereochemical course has been found for optically active ester **2** and nitrile **5** (Scheme I).[2] In both systems the thermal interconversion leading to **1** and **3**, respectively **4** and **6**, at 180 °C is highly stereoselective and proceeds with inversion at the migrating carbon, C-7 (*si*), contrary to the predictions of the Woodward-Hoffmann rules.[3]

Scheme I



X,Y = CH_3,CO_2CH_3 **1** **2** **3**
X,Y = CH_3, CN **4** **5** **6**

Scheme II



X,Y = CH_3, CH_2OCH_3

Baldwin and Broline[4] carried out a stereochemical study for the 7-methoxymethyl-substituted derivative **7**-*2-d*. In this case, however, the authors claimed three processes—one-center epimerization (*e*), rearrangement with retention (*sr*), and rearrangement with inversion (*si*)—to be responsible for racemization and deuterium scrambling in optically active **7**-*2-d* (Scheme II). The rate constants (×10^6 s) at 223.4 °C were determined to k_e = 4.5, k_{sr} = 2.9, and k_{si} = 0.5.

Surprisingly one-center epimerization is the dominating process. Neither in ester **2** nor in nitrile **5**[2] was a one-center epimerization detected. To clarify these discrepancies we repeated a stereochemical study for the 7-methoxymethyl-substituted system using optically active ether **8** (Scheme III). In the case of **7**-*2-d* the one-center epimerization as well as the inversion process leads to racemization of starting material. The experimental distinction between these two processes depends critically on the NMR analysis of the deuterium distribution in the product (Scheme II).[4] In contrast the racemization of **8** at the beginning of reaction is only affected by the one-center epimerization (Scheme III). For that reason the experimental detection of the one-center epimerization of **8** should be unambiguous.

Optically active ether **8** was prepared by reduction of optically active ester **2** with lithium aluminum hydride followed by methylation using sodium hydride and methyl iodide. Optical purity (op) and relative configuration of **2** and **8** remained

0002-7863/80/1502-2469$01.00/0 © 1980 American Chemical Society

Scheme III

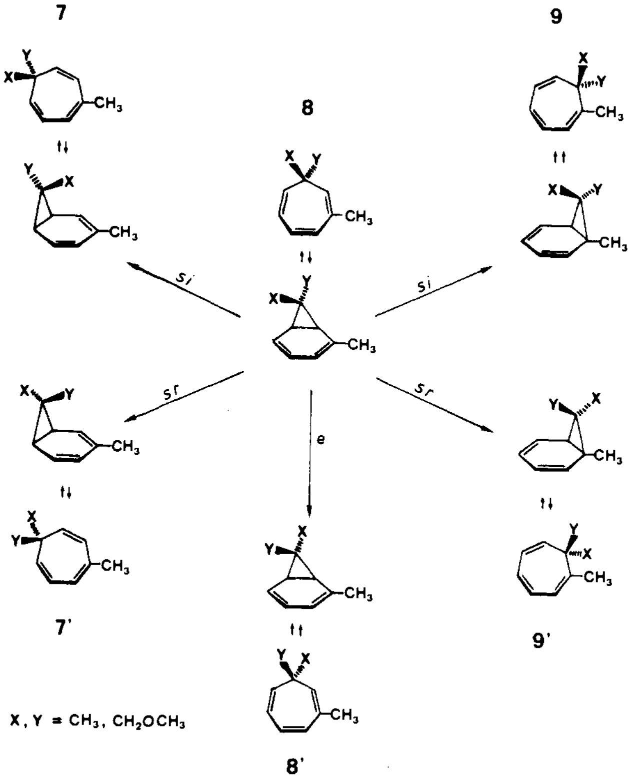


Table I. Thermolysis of Optically Active **8**[a]

product	product ratio, %	$[\alpha]^{25}{}_{404}$ (C_6D_6), deg	op, %	c,[b] %
		A. 1320 min[c]		
7	12	−30.2	38 ± 2	90
8	55	+47.1[d] +47.9	42 ± 2	≥99
9	6	−29.1	38 ± 2	90
		B. 1800 min[e]		
7	15	+62.0	75 ± 2	77
8	45	−104.6[d] −103.5	≥96	99
9	6	+70.0	≥95	98

[a] 220.0 °C, in degassed xylene, 0.5% triethylamine. The same products were obtained on thermolysis in the gas phase (227.7 °C, 2 Torr). Without triethylamine the surface-catalyzed elimination of methanol to a dimethylstyrene derivative was a major reaction. [b] $c = 100 \times \mathrm{op}/\mathrm{op}_0$. [c] (+)-**8**, $\alpha^{25}{}_{404}$ +47.1° (neat), $[\alpha]^{25}{}_{404}$ +47.9° (C_6D_6), $\mathrm{op}_0 = (42 \pm 2)\%$. [d] $\alpha^{25}{}_{404}$ (neat). [e] (−)-**8**, $\alpha^{25}{}_{404}$ −105.7° (neat), $[\alpha]^{25}{}_{404}$ −103.1° (C_6D_6), $\mathrm{op}_0 \geq 97\%$. (−)-**8** was prepared by reduction and methylation of ester (−)-**2**, $\alpha^{25}{}_{404}$ −640.0° (neat), $\mathrm{op}_0 \geq 97\%$.

Table II. Relative Configurations of Optically Active Esters **1**, **2**, and **3** and Ethers **7**, **8**, and **9**[a]

	product ratio, %	$[\alpha]^{25}{}_{404}$ (C_6D_6), deg	op, %
(−)-**1** → **7**	16	+56.5	67 ± 2
(−)-**2** → **8**	75	−101.2[b] −101.9	≥96
(−)-**3** → **9**	4	+68.6	95 ±1

[a] Thermolysis of **2**, $\alpha^{25}{}_{404}$ −640.0°, op ≥ 97% (300 min, 180.0 °C, in degassed benzene). [b] $\alpha^{25}{}_{404}$ (neat).

unchanged by this simple two-step synthesis. Thermolysis of (+)-**8** (Table IA) at 220 °C produced a mixture of **7**, **8**, and **9** and six unidentified compounds (1320 min; ratio by GC, 12:55:6:10:5:4:2:2:2).[5] Rearrangement products (−)-**7** and (−)-**9**, as well as recovered (+)-**8**, separated by preparative LC and GC, were found to be optically active. The optical purities of **7** and **9** were determined by NMR (60 MHz, C_6D_6) using a chiral shift reagent.[6] The optical activity (and hence the optical purity) of **8** was the same as that of the starting material. Analogous results were obtained by the thermolysis of (−)-**8** (Table IB).

To obtain information on the stereochemical course of the walk rearrangement the configurations of optically active ethers **7**, **8**, and **9** were correlated with the known configurations of the optically active esters **1**, **2**, and **3**. A mixture of (−)-**1**, (−)-**2**, and (−)-**3** obtained on thermolysis of (−)-**2**[2] was converted into a mixture of the corresponding ethers **7**, **8**, and **9**, as described above. Separation by preparative GC gave the optically active ethers (+)-**7**, (−)-**8**, and (+)-**9** (Table II).

The observation that (+)-**8** of undiminished optical purity was recovered from partial pyrolysis to **7** and **9** (Table I) excludes the one-center epimerization without rearrangement. According to the stereochemical correlation of optically active educts **2** (**8**) and products **1** (**7**) and **3** (**9**) (Table II), the rearrangement of **8** to **7** and **9** follows the same stereochemical route as the ester- and nitrile-substituted systems (Scheme I) and occurs predominantly with inversion at the migrating carbon, C-7. The optical purity of **7** and **9** (Table I) demonstrates that the stereoselectivity of the migration of C-7 is certainly ≥95%. Our results are well in accord with a study of Hansen[7] on similarly substituted system. We assume that the position of the vinylic substituent—methyl group at C-2 in **8** vs. at C-3 in **7**—has no significant influence on the stereochemical course. Thus, a one-center epimerization of **7**-*2-d* seems highly unlikely.

Acknowledgment. We are grateful to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

References and Notes

(1) Berson, J. A.; Willcott, M. R., III *J. Am. Chem. Soc.* **1965,** *87*, 2751, 2752; **1966,** *88*, 2494. Berson, J. A. *Acc. Chem. Res.* **1968,** *1*, 152.

(2) Klärner, F.-G. *Angew. Chem.* **1974,** *86*, 270; *Angew. Chem., Int. Ed. Engl.* **1974,** *13*, 268. Klärner, F.-G.; Yaslak, S.; Wette, M. *Chem. Ber.* **1979,** *112*, 1168.

(3) Woodward, R. B.; Hoffmann, R. *Angew. Chem.* **1969,** *81*, 797; *Angew. Chem., Int. Ed. Engl.* **1969,** *8*, 781. According to a semiempirical MO study (Schoeller, W. W. *J. Am. Chem. Soc.* **1975,** *97*, 1978), the inversion process was calculated to be favored over the retention process by some 1.4 kcal/mol.

(4) Baldwin, J. E.; Broline, B. M. *J. Am. Chem. Soc.* **1978,** *100*, 4599.

(5) The structures of 7, **8**, and **9** were determined by their spectral properties and independent synthesis starting with the esters **1**, **2**, and **3**. We thank Mr. Riemer, Max-Planck-Institut für Strahlenchemie, D-4330 Mülheim, for measuring 270-MHz ^1H NMR spectra. According to the ^1H NMR spectrum, the unknown product (10%) seems to be a 1,4-cyclohexadiene derivative which can be formed by 1,5-homodienyl hydrogen shift. The thermal behavior is very similar to that of ester **2**.[2] The occurrence of rearrangement products **7** (3%) and **9** (4%) at low conversion of **8** (12%) rules out the possibility that **7** and **9** are exclusively formed by two consecutive 1,5-homodienyl hydrogen shift.

(6) In the presence of tris[3-(heptafluoro-1-hydroxybutylidene)-(+)-camphorato]europium(III) (Goering, H. L.; Eikenberry, J. N.; Koermer, G. S. *J. Am. Chem. Soc.* **1971,** *93*, 5913. Goering, H. L.; Eikenberry, J. N.; Koermer, G. S.; Lattimer, C. J. *Ibid.* **1974,** *96*, 1493), the following enantiomeric signals were split: 7, 7-CH_3($\Delta\nu_{(+),(-)}$ = 6 Hz), *O*-CH_3 (5 Hz); **8,** 7-CH_3 (2 Hz), *O*-CH_3 (4 Hz); **9,** *O*-CH_3 (7 Hz).

(7) Hansen, R. T. Ph.D. Thesis, Yale University, 1976; *Chem. Abstr.* **1977,** *87*, 101708p; *Diss. Abstr. Int. B* **1977,** *37*, 6130. Heating optically active methyl 1-deuterio-7-methyl-7-methoxymethyl-1,3,5-cycloheptatriene-3-carboxylate at 230 °C, deuterium-scrambling isomerization (from the 1 into the 5 position), and racemization of starting material were observed to take place at approximately the same rate. A reasonable explanation for this result is a degenerate walk rearrangement of the valence-tautomeric norcaradiene with inversion at C-7.

Frank-Gerrit Klärner,* Barbara Brassel
Abteilung für Chemie der Universität Bochum
Postfach 10 21 48, D-4630 Bochum 1, West Germany

Received August 29, 1979