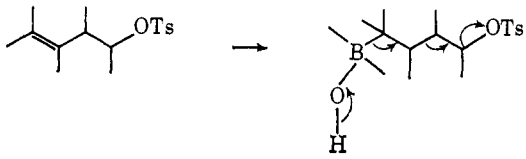
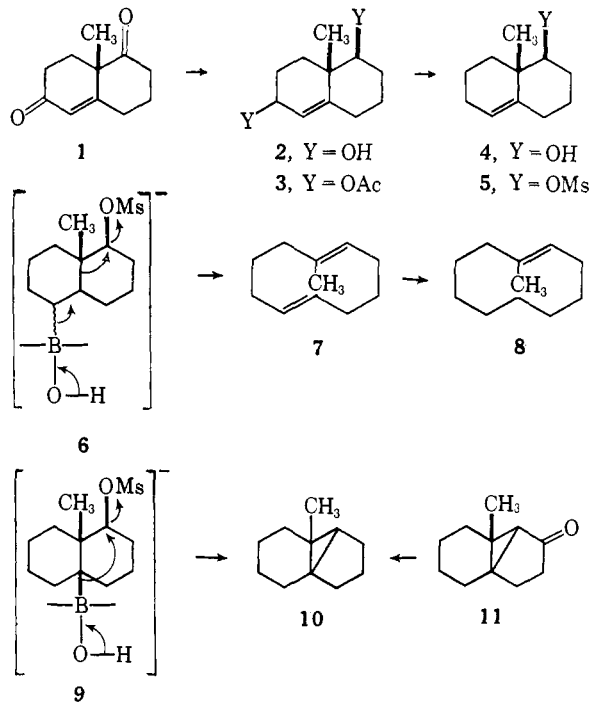
possible route to 1-methyl-*trans*,*trans*-1,6-cyclododecadiene (**7**) and related compounds.[3] The striking success of initial endeavors along these lines, plus the novelty and possible generality of the fragmentation sequence (Scheme I) to other homoallylic sulfonates (*e.g.*, cholesteryl tosylate), prompts this announcement of our preliminary findings.

Scheme I



Unsaturated dione **1**[4] was converted to the unsaturated alcohol **5** [bp 66–71° at 0.05 mm: λ_{max}^{film} 2.96 (OH), 9.45, 9.55, 10.00, and 10.62 μ; $\delta_{TMS}^{CCl_4}$ = 5.36 (C=CH), 3.45–3.05 (CHOH), and 0.97 ppm (angular CH_3)] *via* a three-step sequence involving reduction with lithium aluminum hydride, acetylation of the resulting diol **2**,[5] and hydrogenolysis of the diacetate **3** with lithium in ethylamine.[6] The methanesulfonate derivative **5** (mp 59–59.5°) was treated with an equi-



molar quantity of 0.4 *M* diborane in tetrahydrofuran, after 2 hr aqueous sodium hydroxide was added, and the mixture was heated to reflux for 1 hr. The hydrocarbons (*ca.* 90% yield after column chromatography) isolated by preparative gas chromatography consisted of an 85:15 mixture of the cyclodecadiene **7** [λ_{max}^{film} 6.94, 10.08, 10.38, 10.82, and 11.90 μ; $\delta_{TMS}^{CCl_4}$ = 5.35–4.85 (vinyl H, unresolved multiplet, 3 H) and 1.53 ppm (vinyl CH_3, 3 H)], and the tricyclodecane **10** [λ_{max}^{film} 9.90, 10.38, 10.60, and 10.95 μ; $\delta_{TMS}^{CCl_4}$ = 0.94 ppm (angular CH_3)].

(3) Several of the previously cited methods lead to medium rings containing *trans*, *trans*-1,5-dienes.[2d-f] However, no direct route to *trans*,*trans*-1,6-dienes has yet been reported.

(4) Obtained from Aldrich Chemical Co., Inc., Milwaukee, Wis.

(5) C. B. C. Boyce and J. S. Whithurst, *J. Chem. Soc.*, 2680 (1960).

(6) *Cf.* A. S. Hallsworth, H. B. Henbest, and T. I. Wrigley, *ibid.*, 1969 (1957).

The strong absorption band at 10.4 μ in the infrared spectrum of diene **7** confirms the *trans* stereochemistry assigned to the disubstituted double bond.[2a] Partial hydrogenation of this diene over platinum in ethanol afforded *trans*-1-methylcyclodecene (**8**),[7] thus establishing the nature of the trisubstituted double bond. The stereochemistry and the location of both double bonds follows from mechanistic considerations. Additional support for the latter assignment was provided by the isolation of methyl 5-oxohexanoate and dimethyl glutarate as the sole products from oxidation of diene **7** ($KMnO_4$–KIO_4)[8] followed by treatment of the acidic material with ethereal diazomethane.

An authentic sample of the minor hydrocarbon product, tricyclodecane **10**, was prepared *via* Wolff–Kishner reduction of the related ketone **11**.[9] Hydrocarbons **7** and **10** gave very similar mass spectra with prominent peaks at *m/e* = 150 (parent), P − 15, P − 57, P − 71, P − 83, and P − 109.

Scheme I depicts one possible mechanism for cleavage of the carbon–boron bond leading to the observed products. Alternatively the tetracoordinated boron species (*e.g.*, **6** and **9**) could undergo displacement on boron by hydroxide. Undoubtedly the driving force for both processes comes from partial ionization of the carbon–oxygen bond of the sulfonic ester.

Judging from analogous cases, the hydroboration of olefin **5** should not be stereoselective.[10] However, this factor would not be expected to influence the conversion of **6** to **7** since both the *cis*- and *trans*-fused isomers of **6** can meet the geometric requirements for β fragmentation.[11] Assuming inversion of configuration at the carbon attached to boron, the *cis*-decalylborane **9** should lead to hydrocarbon **10**.[12] The formation of this particular alkylborane isomer from olefin **5** finds close precedent in a related system.[13]

Acknowledgment. Support of this work through a research grant (GP-4174) from the National Science Foundation is gratefully acknowledged.

(7) *Cf.* J. G. Traynham and W. C. Baird, Jr., *J. Org. Chem.*, 27, 3189 (1962).

(8) *Cf.* R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, 33, 1701 (1955).

(9) H. E. Zimmerman, R. G. Lewis, J. J. McCullough, A. Padwa, S. W. Staley, and M. Semmelhack, *J. Am. Chem. Soc.*, 88, 1965 (1966).

(10) *Cf.* F. Sondheimer and S. Wolfe, *Can. J. Chem.*, 37, 1870 (1959).

(11) *Cf.* C. A. Grob, IUPAC Kekule Symposium, London, Sept 1958, Butterworth and Co., Ltd., London, 1959, p 114 ff.

(12) For an analogous synthesis of cyclopropanes, see M. F. Hawthorne, *J. Am. Chem. Soc.*, 82, 1886 (1960).

(13) J. A. Marshall, M. T. Pike, and R. D. Carroll, *J. Org. Chem.*, in press. For a possible explanation of the relatively high percentage of anti-Markovnikov hydroboration product obtained from these olefins, see P. Binger and R. Köster, *Tetrahedron Letters*, No. 4, 156 (1961).

(14) Public Health Service Fellow of the National Institute of General Medical Sciences, 1964–present.

James A. Marshall, Gordon L. Bundy[14]
Department of Chemistry, Northwestern University
Evanston, Illinois 60201
Received August 1, 1966

Nucleoside Phosphorothioates

Sir:

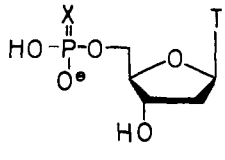
A great number of nucleotides with modifications in the sugar or base residue have been synthesized. So far, the only nucleotides modified at the phosphate residue

are nucleoside phosphites[1] and nucleoside phosphonates.[2] We tried to modify the phosphate $\geqslant P{=}O$ group into a phosphorothioate $\geqslant P{=}S$ group. For studies of the influence of the $\geqslant P{=}O$ group on chemical, biochemical, and physicochemical properties of nucleotides, nucleoside phosphorothioates should be of interest.

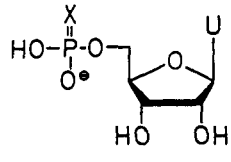
The usual procedure for the phosphorylation of nucleosides involves the condensation of a suitable phosphomonoester and a nucleoside with dicyclohexylcarbodiimide (DCC) and subsequent removal of the phosphate protecting group. It is known, however, that the reaction of phosphonothioic acid esters with DCC to pyrophosphates results in the formation of dicyclohexylthiourea.[3] We therefore looked for ways to phosphorylate nucleosides without the intermediate formation of pyrophosphate. As a suitable compound for such a phosphorylation we synthesized triimidazolyl-1-phosphinsulfide (I) [mp 145–150°; *Anal.* Calcd: N, 31.71; S, 12.10; P, 11.68. Found: N, 31.40; S, 12.01; P, 11.35; nmr ($CDCl_3$) τ 7.11, 7.31, and 7.73 (1:1:1)] in analogy to triimidazolyl-1-phosphinoxide.[4]

A pyridine solution of 3′-O-acetylthymidine (II) or 2′,3′-dimethoxybenzylideneuridine was treated with 2 equiv of I at room temperature for 12 hr, the solvent removed, and the resulting residue heated in 80% acetic acid to 100° for 10 min. The acetyl group in the reaction with II was removed with concentrated aqueous ammonium hydroxide. After purification on a DEAE-cellulose column (HCO_3^- form) and subsequent precipitation of inorganic phosphate as the barium salt, we obtained thymidine 5′-phosphorothioate (IIIa) [*Anal.* (as disodium salt) Calcd: C, 31.42; H, 3.42; N, 7.33; P, 8.10; S, 8.38. Found: C, 31.70; H, 3.93; N, 6.98; P 8.52; S, 7.78; $\lambda_{max}^{H_2O}$ 267 mμ (ϵ 9.600)] and uridine 5′-phosphorothioate (IVa) [*Anal.* (as disodium salt monohydrate). Calcd: C, 26.78; H, 3.22; N, 6.95; P, 7.68; S, 7.95. Found: C, 27.17; H, 3.11; N, 6.53; P, 7.50; S, 7.56; $\lambda_{max}^{H_2O}$ 262 mμ (ϵ 10.000)] in 25–30% yield, homogeneous by paper chromatography and electrophoresis.

The phosphorylation of 5′-tritylthymidine in the same way yielded the desired thymidine 3′-phosphorothioate only in *ca.* 3% yield.



T = thymyl
IIIa, X = S
b, X = O



U = uracilyl
IVa, X = S
b, X = S

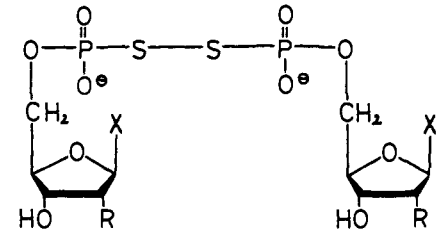
IIIa and IVa can be distinguished from their O analogs IIIb and IVb by paper chromatography but not by electrophoresis at pH 3.5 (formate buffer) or 8.0 (phosphate buffer). IIIa and IVa are completely resistant to *E. coli*[5] and calf intestinal[6] alkaline phosphatase. At least for the former these compounds are not competitive inhibitors. We used the enzymatic digestion with *E. coli* alkaline phosphatase for the analysis of mixtures of O- and S-nucleotides.

Table I. R_f Values of Compounds on Paper Chromatography

Compd	Solvent[a] A	Solvent[a] B
IIIa	0.24	0.33
IIIb	0.29	0.25
IVa	0.18	0.22
IVb	0.21	0.24
V	0.40	
VI	0.25	

[a] Solvent A: ethanol–1 *M* ammonium acetate (7:3, v/v); solvent B: 2-propanol–concentrated ammonia–water (7:1:2, v/v). Paper: Schleicher and Schüll 2043 b, washed.

Acid phosphatase from potatoes[6] degraded IIIa and IVa to nucleosides in *ca.* 15% over a period of 2 hr at 37° at pH 4.6. The sodium salts of IIIa and IVa are hydrolyzed to the corresponding nucleosides on heating in 80% acetic acid to 100° (10 μmoles in 2 ml). After 10 min IIIa is cleaved to 22% (IVa, 39%), after 40 min to 67% (IVa, 83%). The sodium salts are also hydrolyzed to the nucleosides in DMSO–pyridine (1:1, v/v) solution (10 μmoles in 0.4 ml). After 7 days at room temperature IIIa is hydrolyzed to 33% (IVa, 23%), after 11 days to 55% (IVa, 45%). The mechanism of this reaction is under investigation. Like free phosphorothioic acid[7] the sodium salts of IIIa and IVa can be oxidized quantitatively by 1 equiv of $K_3[Fe(CN)_6]$. The disulfides V and VI show the same properties as pyrophosphates on paper chromatography and electrophoresis. They are reduced to the starting materials IIIa and IVa by $NaBH_4$.



V, X = thymyl
R = H
VI, X = uracilyl
R = OH

The pyridinium salts of IIIa and IVa are desulfurized to the corresponding nucleotides IIIb and IVb in DMSO–pyridine (1:1, v/v) solution[8] (20 μmoles in 0.4 ml). After 7 days at room temperature IIIa is desulfurized completely, IVa to 90%.

In a subsequent publication we will report on the synthesis of dinucleoside phosphorothioates and polyphosphates.

(1) A. Holy and F. Šorm, *Collection Czech. Chem. Commun.*, **31**, 1562 (1966).
(2) T. C. Meyers, K. Nahamura, and A. B. Danielzadek, *J. Org. Chem.*, 30, 1517 (1965).
(3) M. Mikolajczyk, *Chem. Ber.*, **99**, 2083 (1966).
(4) F. Cramer, H. Schaller, and H. A. Staab, *Chem. Ber.*, **94**, 1612 (1961).
(5) Purchased from Sigma Chemical Co., St. Louis, Mo.
(6) Purchased from C. F. Boehringer, Mannhein, Germany.
(7) H. Neumann, J. Z. Steinberg, and E. Katchalski, *J. Am. Chem. Soc.*, **87**, 3841 (1965).
(8) M. Mikalajczyk, *Angew. Chem. Intern. Ed. Engl.*, **5**, 419 (1966); *Angew. Chem.*, **78**, 393 (1966).

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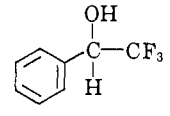
Fritz Eckstein
Max-Planck-Institut für Experimentelle Medizin
Chemische Abteilung, Göttingen, Germany
Received June 27, 1966

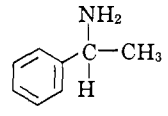
The Nonequivalence of Physical Properties of Enantiomers in Optically Active Solvents. Differences in Proton Magnetic Resonance Spectra. II

Sir:

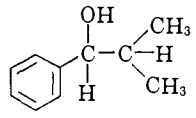
We have recently reported[1] that the fluorine nmr spectra of the enantiomers of trifluoromethylphenylcarbinol (I) are dissimilar when optically active α-phenethylamine (II) is used as solvent. We now wish to report the first examples of nonequivalence of the proton magnetic resonance spectra of enantiomers in an optically active solvent.



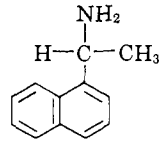
I



II



III



IV

In fluorotrichloromethane, the resonance of the carbinyl proton in racemic phenylisopropylcarbinol (III) appears as a doublet[2] ($|J_{H-H}| = 6.8$ cps) at 4.1 ppm from internal tetramethylsilane. When *d*-α-(1-naphthyl)ethylamine (IV) ($[\alpha]^{27}D$ +75.6° (neat), lit.[3] for the *levo* isomer $[\alpha]^{25}D$ −80.8° (neat)) is used as the solvent, the carbinyl proton resonances of the enantiomers have different chemical shifts and give rise to two equally intense sets of doublets ($|J_{H-H}| = 6.3$ cps).[4] At 60 Mc the sets are separated by 1.6 cps; at 100 Mc the separation is 2.5 cps.[5] The increased separation at the higher frequency rules out the possibility that the increased multiplicity arises from some unusual solvent effect causing long-range coupling which is not observed when fluorotrichloromethane is used as solvent. Further indication that the increased multiplicity has been correctly interpreted arises from the observation that replacement of the optically active amine with racemic amine causes the two sets of doublets to coalesce. This indicates that any given carbinol molecule is solvated by both optical forms of the amine solvent during the time required for nmr measurement. Because of this fast exchange, both carbinol enantiomers are in identical average magnetic environments and no longer have dissimilar spectra. An important consequence of this fast exchange is that *the solvent need not be completely optically pure* in order for one to observe spectral nonequivalence of enantiomeric solutes. The magnitude of the observed nonequivalence will simply be proportional to the optical purity of the solvent in cases where such fast exchange obtains.

The chemical shifts of the enantiomeric carbinyl proton resonances are unequally affected by changes in temperature, ratio of amine to carbinol, and extent of dilution with optically inactive solvents. Hence, the separation between the sets of carbinyl proton resonances is affected by the choice of experimental conditions as well as by the operating frequency of the spectrometer.[6]

Under similar conditions, proton spectral nonequivalence of the enantiomers of trifluoromethylphenylcarbinol, methyl-2-naphthylcarbinol, and methyl-*o*-fluorophenylcarbinol has also been noted. The ability to observe pmr spectral nonequivalence greatly enhances the scope of our previously reported nmr method for optical purity determination.[1] In all cases cited, the extent of nonequivalence is great enough to allow 60-Mc nmr optical purity determinations to be made. The use of higher frequency nmr spectrometers will facilitate these determinations.

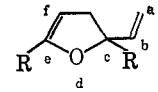
(1) W. H. Pirkle, *J. Am. Chem. Soc.*, **88**, 1837 (1966).
(2) The absence of observable coupling between the carbinyl and hydroxyl protons suggests that the hydroxyl protons are undergoing rapid intermolecular exchange.
(3) E. Samuelsson, *Svensk. Kem. Tidskr.*, **34**, 7 (1922).
(4) It has proven advantageous to use fluorotrichloromethane as a diluent in order to obtain better resolution through diminished viscosity and to shift the carbinyl proton resonance from underneath the methine proton resonance of the solvent amine.
(5) The 100-Mc spectra were obtained by Dr. N. Bhacca of Varian Associates. The 60-Mc spectra were determined by means of a Varian A56/60A spectrometer.
(6) The effect of these parameters upon the extent of enantiomeric spectral nonequivalence is being studied in order to gain a better understanding of the origin of the phenomenon.

T. G. Burlingame, W. H. Pirkle
Noyes Chemical Laboratory, University of Illinois
Urbana, Illinois
Received July 22, 1966

Thermal Rearrangement of 2,5-Dimethyl-2-vinyl-2,3-dihydrofuran to 4-Methyl-4-cycloheptenone

Sir:

Inherent in the simple 2-vinyl-2,3-dihydrofuran structure is the rearrangement-prone bisallylic system of an allyl vinyl ether (I, atoms a–f). Such furan derivatives



I, R = H
II, R = CH_3

have been observed to undergo a variety of rearrangements depending on the conditions imposed and the location and nature of substituents on the basic structure, I; thus, acylcyclopentenes,[1] 1-acyl-2-vinylcyclopropanes,[2] and acyclic dienic carbonyl compounds[3] have been reported as products.

In our continuing interest in Claisen and Cope rearrangements and with a view to exploring the geometric

(1) J. Wiemann and S. T. Thuan, *Compt. Rend.*, **241**, 503 (1955); *Bull. Soc. Chim. France*, 199 (1958).
(2) J. Wiemann, N. Thoai, and F. Weisbuch, *ibid.*, 2187 (1964).
(3) J. Wiemann, P. Casals, and N. Lefebvre, *ibid.*, 310 (1962); N. Thoai, *ibid.*, 225 (1964).