cm^{-1}; nmr (CCl_4) δ 7.45 (m); mass spectrum, molecular ion *m/e* 238] in 65–70% yield.

Treatment of a stirred solution of a primary amine or amino acid tetramethylammonium salt (20 mmol) in 20 ml of dimethylformamide with 4.76 g (20 mmol) of **1** produces an intense yellow color which rapidly fades. After stirring for 0.5 hr,[9] the mixture is acidified to pH 1 with 1 *N* hydrochloric acid and extracted with 100 ml of ethyl acetate, and the organic layer is thoroughly washed with water. Drying and solvent removal under reduced pressure give a diastereomeric mixture of hydroxyoxazolidinones (**2**) (ir 1750–1760 cm^{-1}). The mixture may be quantitatively dehydrated to the desired Ox derivative in 20 ml of trifluoroacetic acid over 1–2 hr. Removal of trifluoroacetic acid under reduced pressure and crystallization of the crude product affords pure Ox derivatives in overall yields of 75–85% (Table I). Ox derivatives [ir (KBr) 1750–1760, 1360–1380 cm^{-1}; nmr ($CDCl_3$) δ 7.1–7.3 (s, 5), 7.3–7.5 (m, 5); uv λ_{max} (EtOH) 286–288 mμ, ϵ 1.5 × 10^4; fluorescence spectrum, λ_{max} (EtOH) 390–400 mμ] are stable to aqueous base, refluxing ethanolic hydrazine, ethanolic hydrogen chloride, hydrogen bromide in acetic acid, refluxing trifluoroacetic acid, and anhydrous hydrogen fluoride.[10]

Table I

Ox derivative[a]	Mp, °C[b]	Optical rotation (MeOH)
$OxCH_2CH_2Ph$	123.5–124.5[c]	
Ox-L-Ala	202–204[d]	$[\alpha]^{26}D$ −31.5° (*c* 1.02)
Ox-L-Phe	196–197[d]	$[\alpha]^{25}D$ −176° (*c* 1.02)
Ox-L-Val	234–236[d]	$[\alpha]^{24}D$ −69.3° (*c* 0.99)
Ox-L-Ala-GlyOEt	129.5–130[d]	$[\alpha]^{26}D$ +3.4° (*c* 0.99)

[a] Satisfactory elemental analyses have been obtained for all new compounds. [b] All melting points are uncorrected. [c] Crystallized from 95% ethanol. [d] Crystallized from ethyl acetate–pentane.

The Ox group may be considered as a "protected" *N*-carbobenzoxy-*N*-benzylamine group. It may be removed quantitatively by low-pressure (Parr) catalytic hydrogenation in an organic solvent containing 1 equiv of aqueous acid. Reductions are generally complete within 24 hr using 50 mg of 10% palladium on charcoal for each equivalent of Ox blocked derivative. Similarly the Ox group may be removed in 75–85% isolated yield using sodium in liquid ammonia.

Alternatively the Ox group may be cleaved under oxidative conditions. Oxidation of the oxazolinone double bond to a species equivalent to a dihydroxyoxazolidinone, followed by mild solvolysis, should free the amine function. Treatment of an Ox derivative in trifluoroacetic acid with excess *m*-chloroperbenzoic acid, followed by hydrolytic work-up, affords the free amine in 70% yield.

Simple Ox dipeptide derivatives have been prepared without difficulty using the water-soluble 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride.[11] Removal of the protecting group followed by hydrolysis[12] affords the free peptides in high yield. No racemization has been observed in the preparation of Ox derivatives, stability studies, or coupling or deblocking reactions.[13]

The properties of the 4,5-diphenyl-4-oxazolin-2-ones may lead to alternate applications for the ring system. The fluorescence and stability of Ox derivatives under solvolytic conditions suggest a possible method of peptide N-terminal residue analysis. The N-alkylation of the parent 4,5-diphenyl-4-oxazolin-2-one system under basic conditions[14] may lead to a phthalimide-like method of introducing a nitrogen function. Investigations into these areas and into the scope and limitations of the Ox protecting group are currently in progress.

Acknowledgments. We gratefully acknowledge fellowship support for one of us (F. S. G.) under National Institutes of Health Predoctoral Fellowship 5 F01 GM 43911-03 from the General Medical Sciences Unit and the continued support of the Sloan Basic Research Fund.

(9) The reaction may be conveniently monitored by observing the disappearance of the 1820-cm^{-1} band of the carbonate in the infrared spectrum.

(10) Stability experiments were carried out using Ox-L-Ala as a model. Recovered yields were greater than 95%. Melting point, spectra, and optical rotation were unchanged.

(11) J. C. Sheehan, P. A. Cruickshank, and G. L. Boshart, *J. Org. Chem.*, 26, 2525 (1961).

(12) Hydantoin formation has been noted in the alkaline hydrolysis of Ox peptide esters.

(13) Two-spot method: E. Taschner, A. Chimiak, J. F. Biernat, T. Sokolowska, Cz. Wasilewski, and B. Rzeszotarska, *Peptides, Proc. Eur. Symp., 5th, 1962*, 109 (1963).

(14) R. Gompper, *Chem. Ber.*, **89**, 1748 (1956).

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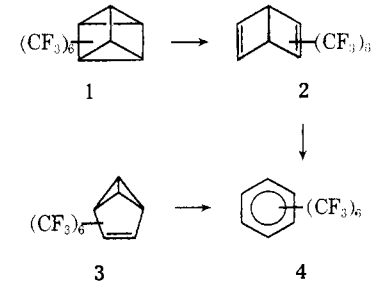
Kinetics and Thermodynamics of $(CCF_3)_6$ Valence Isomer Interconversions

Sir:

As the most complete set[1] of pure benzene valence isomers, the benzene, Dewar benzene, benzvalene, and prismane having the composition $(CCF_3)_6$[2,3] provide a unique opportunity to investigate interrelationships among the four skeletons. Accordingly, the heats of reaction and kinetic parameters have been measured for the thermal isomerizations which connect them, shown in Chart I.

Chart I. Thermal Interconversions of $(CCF_3)_6$ Isomers



(1) Though often ignored in discussions of benzene valence isomers, 3,3′-biscyclopropenyls rightfully belong in this group. An excellent review on $(CH)_n$ valence isomers has just appeared (L. T. Scott and M. Jones, Jr., *Chem. Rev.*, 72, 181 (1972)).

(2) M. G. Barlow, R. N. Haszeldine, and R. Hubbard, *Chem. Commun.*, 202 (1969); *J. Chem. Soc. C*, 1232 (1970). These authors present rate data at 170° for the reactions shown in Chart I.

(3) D. M. Lemal, J. V. Staros, and V. Austel, *J. Amer. Chem. Soc.*, 91, 3373 (1969).

Table I. Kinetic and Thermodynamic Data for Benzene Valence Isomer Interconversions

Reaction	Temp, °C	k, sec^{-1}	ΔH, kcal/mol	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu	E_a, kcal/mol	Log A
1 → **2**	225	$8.43 \pm 0.10 \times 10^{-4}$	-31.0 ± 3.9[a]	42.1 ± 0.6	10.9 ± 1.3	43.1 ± 0.6	15.41 ± 0.3
2 → **4**	225	$1.49 \pm 0.05 \times 10^{-4}$	-28.0 ± 1.4[a]	37.4 ± 1.2	-1.9 ± 2	38.4 ± 1.2	12.59 ± 0.5
3 → **4**	225	$1.12 \pm 0.05 \times 10^{-3}$	-34.4 ± 0.7[a]	38.0 ± 1.3	3.9 ± 3	39.3 ± 1.3	13.86 ± 0.6
5 → **6**[b]	150	1.06×10^{-3}	-31.7	33.0	5.1	33.8	14.50
6 → **7**[b]	150	6.57×10^{-5}	-59.5	36.4	7.5	37.2	15.03

[a] Errors are average deviations from the mean of six or more runs. [b] Values are taken from ref 11. Compound **5** also isomerizes to **7** *via* the benzvalene.

Differential scanning calorimetry (DSC) was chosen for this study since that technique yields thermodynamic and kinetic information simultaneously.[4,5] Neat reactants were sealed in aluminum sample pans (shown to have no catalytic effect) and heated according to a linear temperature program under external nitrogen pressures up to 500 psi (to prevent pan rupture). Differential power required to keep sample and reference matched in temperature was plotted *vs.* time, and thus temperature. The area under such a plot, appropriately calibrated, gave the heat of reaction. Since the shape of the power/temperature curve constituted a record of rate as a function of temperature, a simple computer analysis yielded activation parameters for these first-order isomerizations.[6] Considerably better rate data were obtained by "classical" techniques, however: isothermal reaction in Pyrex capillaries, with analysis by glc.

Because thermal decomposition of the prismane entails a pair of concurrent consecutive reactions, the heat of reaction of the prismane → Dewar benzene (**1** → **2**) transformation was obtained as the difference between the observed enthalpies of their conversion to **4**. The results of the thermodynamic (DSC) and kinetic (conventional) measurements are summarized in Table I and presented diagrammatically in Figure 1.

The uniformly high activation energies despite large negative heats of reaction are reasonable on the basis that all of the reactions are orbital symmetry forbidden to occur concertedly.[7] The finding that aromatization of the benzvalene **3** is substantially more exothermic than that of Dewar benzene **2**[8] is consistent both with our observation that hexamethylbenzvalene isomerizes to its Dewar counterpart **6** (but not *vice versa*)[9] and with MINDO/2 ground-state energy calculations on the unsubstituted skeletons.[10]

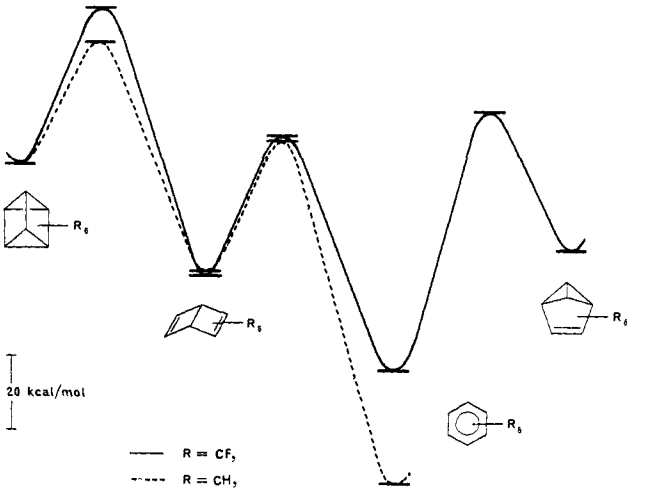
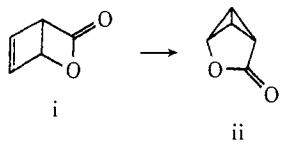


Figure 1. Energy profile for benzene valence isomer interconversions.

The data for the fluorinated prismane and Dewar benzene make possible some interesting comparisons with corresponding information obtained by Oth[11] on hexamethylprismane (**5**) and hexamethyl (Dewar benzene) (**6**) (also shown in Table I and Figure 1). The heat of reaction for the prismane → Dewar benzene transformation is similar in the two series, but ring opening of Dewar benzene **6** to hexamethylbenzene (**7**) is more than *twice as exothermic* as its fluorocarbon analog. Calculations using the point-dipole approximation of the dipole–dipole interactions among the 18 C–F bonds of **1**–**4** show clearly that the absolute energies of these structures are affected importantly by dipole–dipole repulsion, but that their relative energies are influenced only very slightly (on the order of 1 kcal/mol). Estimates of F–F and C–F nonbonded interactions in **1**–**4** and H–H and C–H interactions in their hydrocarbon counterparts have been made using Buckingham potential functions.[12] In all structures except the benzenes, the substituent groups are separated well enough that steric repulsion among them is negligible, consistent with the similar heats found for the prismane → Dewar benzene reactions. Nonbonded interactions are important in hexamethylbenzene, however, and really large in its fluorinated counterpart.[13] The ob-



i ii

(4) R. S. Porter and J. F. Johnson, Ed., "Analytical Calorimetry," Vol. 1, Plenum Press, New York, N. Y., 1968; Vol. 2, 1970.

(5) W. Adam and J. C. Chang have studied interconversions of hexamethylbenzene valence isomers by DSC (*Int. J. Chem. Kinet.*, 1, 487 (1969)).

(6) A discussion of errors in such analyses is given by H. M. Heuvel and K. C. J. B. Lind, *Anal. Chem.*, **42**, 1044 (1970).

(7) R. Hoffmann and R. B. Woodward, *Accounts Chem. Res.*, **1**, 17 (1968); R. B. Woodward and R. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, **8**, 781 (1969).

(8) This result was not a foregone conclusion, as the spontaneous conversion of i to ii illustrates (E. J. Corey and W. H. Pirkel, *Tetrahedron Lett.*, 5255 (1967)).

(9) H. Ertl and J. P. Lokensgard, unpublished results from our laboratory.

(10) N. C. Baird and M. J. S. Dewar, *J. Amer. Chem. Soc.*, **91**, 352 (1969).

(11) J. F. M. Oth, *Recl. Trav. Chim. Pays-Bas*, **87**, 1185 (1968). Oth's data, obtained by a temperature-programmed direct calorimetric method, are presumably more accurate than the DSC data of ref 5.

(12) A. Abe, R. L. Jernigan, and P. J. Flory, *J. Amer. Chem. Soc.*, **88**, 631 (1966); R. A. Scott and H. A. Scheraga, *J. Chem. Phys.*, **42**, 2209 (1965); **44**, 3054 (1966); T. W. Bates, *Trans. Faraday Soc.*, **63**, 1825 (1967).

(13) In the $(CC_2F_5)_6$ series, the Dewar form is actually stabler than the benzene at high temperatures, due to the bulkiness of the substi-

served ~30 kcal/mol difference between the enthalpies of aromatization for the Dewar benzenes is accounted for by even a conservative choice of Buckingham function parameters.

The activation parameters in the hydrocarbon and fluorocarbon series present striking contrasts. In both the prismane → Dewar benzene and Dewar benzene → benzene transformations the fluorocarbons are very much slower, but for different reasons. The fluorinated Dewar benzene depends principally upon a surprisingly low activation entropy for its great stability relative to the hydrocarbon, but the fluorinated prismane is protected by an activation enthalpy ~9 kcal/mol higher than that for hexamethylprismane. The low $\Delta S^{\ddagger}$ may signify that the six trifluoromethyl groups, which have considerable torsional freedom in the Dewar benzene, become rigidly interlocked in the transition state for aromatization. The large difference in $\Delta H^{\ddagger}$ for the prismanes cannot convincingly be attributed to labilization of the skeleton by methyl substituents: though the parent prismane is not available for comparison, hexamethyl (Dewar benzene) is thermally very much stabler than Dewar benzene itself.[14] We conclude that perfluoroalkyl groups strongly destabilize the transition state for prismane ring opening in a manner not yet adequately understood.

Finally, by virtue of their electron-withdrawing power, perfluoroalkyl substituents stoutly protect strained carbon skeletons against decomposition catalyzed by electrophiles. As an illustration, hexamethylbenzvalene is isomerized at room temperature by a clean glass surface,[9] but its fluorinated counterpart is very stable indeed.

We propose to designate as the "perfluoroalkyl (R_f) effect" the composite of stabilizing influences which perfluoroalkyl groups confer upon highly strained carbon frameworks. The R_f effect thus comprises both thermodynamic (steric in origin) and kinetic elements, where the latter include stabilization against both catalyzed and unimolecular destruction. We believe that the perfluoroalkyl effect can be of great value in the synthesis of exceedingly strained carbon skeletons.

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tuents (E. D. Clifton, W. T. Flowers, and R. N. Haszeldine, *Chem. Commun.*, 1216 (1969)).

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Book Reviews

Oxonium Ions in Organic Chemistry. By HARTWIG PERST (Institut für Organishe Chemie, Marburg, Germany). Verlag Chemie, Weinheim, Germany, and Academic Press, New York, N. Y. 1971. xii + 202 pp. $15.00.

Until quite recently most organic chemists seemed unaware of the existence and synthetic utility of oxonium salts or regarded their preparation as too involved and stability too questionable for handling ease. The surge of interest in this area was no doubt caused by the recognition of the powerful alkylating ability of the trialkyl oxonium ions. The fact that a very large number of important contributions to this area appeared in the German literature was most probably a factor in the slow uptake of interest and lack of awareness in this country. In fact, it is an English translation of a German text. This book should do much to alleviate the problem and generate further interest. The author covered the literature well through October 1969, but this is not an all inclusive review. Though much has been done since and further volumes on this topic will doubtlessly be needed in the future, this reasonably short review is an excellent beginning.

The author puts well-defined limits on his area of coverage and still surveys the field well with one exception. He chooses to omit discussion of acyl cations since the amount of oxonium contribution is judged quite small. This is most certainly true, but some examples of the contrasting chemistry may have been useful. The material is quite well documented and well organized. The author discusses in the order: the classification, stability, formation, reactions, intermediacy in chemical reactions, and preparative applications of oxonium salts. An appendix also discusses the structure of various oxonium ions. The logical presentation is enhanced by the obvious effort to generalize reactions where possible and the very liberal and strategic sprinkling of structural formulas throughout. The volume also contains an author index and good subject index. All the above points sum to a very readable work with a definite place in the organic chemist's library.

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Macromolecules: Structure and Function. By FINN WOLD (University of Minnesota). Prentice-Hall, Inc., Englewood, N. J. 1971. xiii + 305 pp. $8.75 cloth; $3.50 paper.

This book is one of four in the Foundation of Modern Biochemistry series, which includes "Organic Chemistry of Biological Compounds," "Physical Biochemistry," and "Intermediary Metabolism and its Regulation." The series covers the major topics of basic biochemistry and provides an alternative to a single comprehensive text. Each volume has extensive cross references to the other three for the purpose of integrating the series, but some duplication of material is inevitable. This volume on the structure and function of macromolecules covers proteins and nucleic acids. In addition, the structure and function of membranes are discussed. References to original literature and pertinent review articles are given. The book is devoted mainly to a description of selected model systems and the experimental basis for these models. The section on enzyme kinetics is reasonably comprehensive, but it appears to the reviewers that students without previous exposure to the subject would have some difficulty in following this section. A major lack in the book would appear to be the absence of a section on polysaccharides, which are an important class of macromolecules.

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