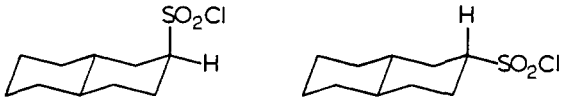
ination (E2 mechanism), (b) slow formation of the conjugate base of the sulfonyl halide[5] followed by rapid loss of Cl^- (E1cb mechanism), (c) substitution of chlorine by the tertiary amine in the slow step followed by rapid Hofmann-like elimination[6] of the elements of Et_3N^+H ("SN2 followed by E" mechanism).

The E1cb mechanism is excluded on the following grounds. The rates of formation of $PhC\bar{H}SO_2Z$ from a number of compounds of the type $PhCH_2SO_2Z$, where Z = Ph, $OCH(CH_3)_2$, CF_3, and NMePh, with triethylamine in dimethoxyethane–D_2O were measured by following the rate of exchange of deuterium for hydrogen. These rates were found to vary over a range of less than 10^2, and even the fastest of these reactions was about 10^8 times slower than the reaction of $PhCH_2SO_2Cl$ under the same conditions. Such a disproportionately large effect is only interpretable in terms of a different mechanism of reaction, *i.e.*, $PhC\bar{H}SO_2Cl$ formation cannot be involved in formation of $PhCH{=}SO_2$ from $PhCH_2SO_2Cl$.

To distinguish between the remaining two possibilities given above, namely the E2 and "SN2 followed by E" mechanisms, compounds **1** and **2** were synthesized



1 2

in order to determine their relative ease of sulfene formation. From conformational considerations it can be predicted that direct E2 elimination of HCl from **1** to give the sulfene would be faster than the same reaction of **2**, owing to (a) lowering of the relatively greater nonbonding interaction energy[7] in **1** and perhaps also (b) the existence of greater nonbonding repulsions in the transition state from **2** between the attacking triethylamine and groups adjacent to the hydrogen being removed as compared with that from **1**. Such a prediction finds support in the faster rate of reaction of axial *vs.* equatorial epimers in (a) chromic acid oxidation of cyclohexanols[8a] and (b) formation of 1-*t*-butyl-4-methylenecyclohexane either by thermolysis of the corresponding axial and equatorial phenyl sulfoxides or elimination of HBr from the 4-*t*-butylcyclohexanemethyl bromides with potassium *t*-butoxide in *t*-butyl alcohol.[9] On the other hand, if the rate-determining step is a SN2 displacement on the sulfur of the SO_2Cl group, the reaction would be expected to be slower for **1** than for **2**. This may be argued by analogy with the rates of (a) hydrolysis of esters[8b] and (b) the reaction of the 4-*t*-butylcyclohexanemethyl *p*-nitrobenzenesulfonates with lithium bromide,[9] but is most clearly indicated by the simple solvolysis of **1** and **2** in the absence of added base (a reaction which does not proceed *via* the sulfene[10]), in which **2** reacts roughly 15 times faster than **1**. It was found that **1** forms the sulfene 71 times faster than **2** with triethylamine at −25° in dimethoxyethane, clearly excluding the "SN2 followed by E" mechanism and therefore leaving the direct E2 mechanism as the only route compatible with the available data. As confirmation of the intermediacy of the sulfene in the triethylamine-induced reactions of **1** and **2**, it was found that essentially the same mixture of 2-decalinsulfonate salts was obtained by treating either **1** or **2** with triethylamine in dimethoxyethane–water.

Further definition of the nature of the transition state is provided by the following. (a) A reasonable correlation with σ^- was obtained for the rates of reaction of $XC_6H_4CH_2SO_2Cl$ with pyridine in dimethoxyethane and aniline, $\rho^- = 2.35$. (b) Deuterium isotope effects (k_H/k_D, obtained by determining product ratios) for the reaction of $PhCHDSO_2Cl$ with base in the presence of water are: pyridine 2.0,[11] triethylamine 2.6,[11] and sodium hydroxide 4.0. (c) A rate difference of $\sim 2 \times 10^5$ was found between triethylamine and pyridine with methanesulfonyl chloride. These data are entirely consistent with the E2 mechanism and suggest a transition state in which the transfer of the proton from carbon to base is nearing completion and a partial negative charge has developed on the carbon as well as on the chlorine.

Acknowledgment. This work was supported by grants from the National Research Council of Canada, the Alfred P. Sloan Foundation, and the Petroleum Research Fund administered by the American Chemical Society.

(4) The data summarized here also permit the exclusion of the considerable number of less likely mechanisms that come to light in a systematic search for alternatives to the ones given here. These will be discussed in the full paper.

(5) Rapid and reversible formation of the conjugate base followed by slow loss of Cl^- is precluded by deuterium labeling experiments,[1] in which exchange of one and only one hydrogen of a methyl or methylene group was observed.

(6) If the elimination were the slow step the reaction would have to be *second* order in Et_3N.

(7) Comparison of the nmr spectra of cyclohexanesulfonyl chloride and **1** and **2** shows that cyclohexanesulfonyl chloride exists almost entirely in the equatorial form. There seems to be no reported determination of the conformational energy of the SO_2Cl group, but that of the SO_2Ph group has been estimated to be 2.5 kcal/mole by E. L. Eliel, E. W. Della, and M. Rogic, *J. Org. Chem.*, 30, 855 (1965).

(8) For a summary see E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, New York, N. Y., 1965: (a) pp 81–84; (b) pp 72–78.

(9) J. F. King and M. J. Coppen, unpublished results.

(10) J. F. King and T. Durst, *J. Amer. Chem. Soc.*, 87, 5684 (1965).

(11) Determined by Mr. B. G. Peterson.

(12) Holder of a Province of Ontario Graduate Fellowship, 1966–1969.

J. F. King, T. W. S. Lee[12]
Department of Chemistry, University of Western Ontario
London, Ontario, Canada
Received June 30, 1969

Reaction of Oxepin–Benzene Oxide with Nucleophiles

Sir:

The metabolic products of aromatic compounds are often observed to be the corresponding 1,2-dihydroxy-1,2-dihydrobenzene or derivatives thereof.[1] Other metabolic products containing oxygen and nitrogen functions on the saturated carbon atoms of a 1,3-cyclohexadiene have been reported.[5] Chorismic acid, the

(1) For example, in mammalian systems chlorobenzene is metabolized to 4-chloro-*trans*-1,2-dihydroxy-1,2-dihydrobenzene,[2] naphthalene to *trans*-1,2-dihydroxy-1,2-dihydronaphthalene,[3] and phenanthrene to 1,2-hydroxy-1,2-dihydrophenanthrene.[4]

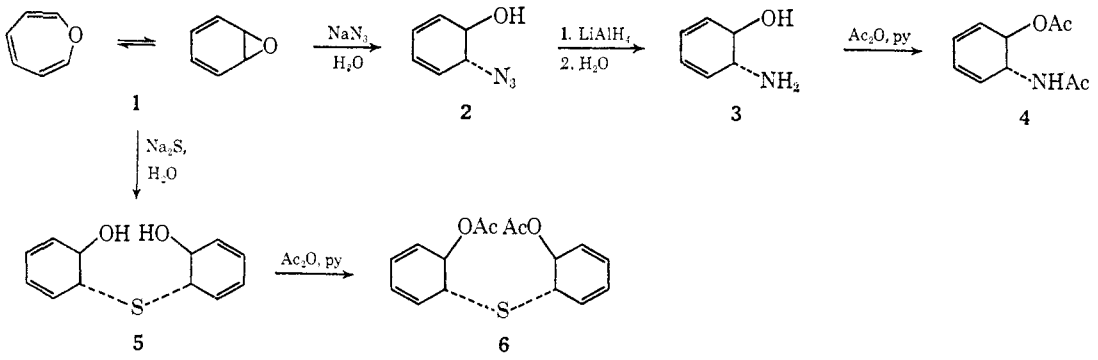
(2) J. N. Smith, B. Spencer, and R. T. Williams, *Biochem. J.*, 47, 284 (1950).

(3) J. Holtzman, J. R. Gillette, and G. W. A. Milne, *J. Amer. Chem. Soc.*, 89, 6341 (1967), and references cited therein.

(4) E. Boyland and G. Wolf, *Biochem. J.*, 42, XXXII (1948).

(5) They include *trans*-3-hydroxy-2,3-dihydroanthranilic acid,[6] *trans*-2,3-dihydroxy-2,3-dihydrobenzoic acid,[7] isochorismic acid,[8] and the antibiotic gliotoxin.[9]

(6) J. R. D. McCormick, *et al.*, *J. Amer. Chem. Soc.*, 84, 3711 (1962).



branch-point intermediate in the biosynthesis of aromatic amino acids and growth factors,[10] is the 3-enol pyruvyl ester of *trans*-3,4-dihydroxy-3,4-dihydrobenzoic acid.

Due to the importance of substituted 1,3-cyclohexadienes in nature and the suggested role of arene oxide–oxepin systems in their formation,[11] we have investigated nonenzymatic ring-opening reactions of oxepin–benzene oxide (**1**) with nucleophilic reagents.[12,13] Although no reaction was observed with **1** and $NaNH_2$ in liquid NH_3, **1** did react with NaN_3 in H_2O at room temperature for 3 hr to give *trans*-5-azido-6-hydroxy-1,3-cyclohexadiene[16] (**2**) as a pale yellow liquid in 55% yield. Reduction of **2** with $LiAlH_4$ in ether at 0° for 1 hr gave *trans*-5-amino-6-hydroxy-1,3-cyclohexadiene[16] (**3**) as white needles (60%, mp 62.0–63.5° from ether–pentane). Diacetate **4**[16] was formed in 59% yield from **3** and acetic anhydride in pyridine at 0° but could not be obtained free of acetanilide. The assignment of *trans* stereochemistry in **2** and **3** is based on the H_5–H_6 coupling in the nmr spectrum: $J_{H_5-H_6}$ in **2** = 9 Hz (CCl_4); in **3**, 12 Hz ($CDCl_3$). The values are in agreement with previous studies[17] and indicate the ring assumes the twist conformation in which the hydroxyl and azido or amino substituents are quasi-equatorial due to intramolecular hydrogen bonding.

Reaction of **1** with excess $Na_2S \cdot 9H_2O$ in H_2O at 0° for 45 min gave bis(*trans*-2-hydroxy-3,5-cyclohexadienyl) sulfide[16] (**5**) in 37% yield: mp 75–79°. This diol sulfide readily decomposed to phenol and diphenyl sulfide. Diacetate **6**[16] (mp 115.5–116.5° from ether–hexane) was prepared in 67% yield by the reaction of **5** with acetic anhydride in pyridine at 0° for 3 hr. The H_5–H_6 coupling in the nmr spectrum of **5** and **6** is 3.5 Hz (acetone-d_6) in **5** and 4.5 Hz ($CDCl_3$) in **6**. The coupling constants are in agreement with assignment of *trans* stereochemistry in which the rings assume the twist conformation with quasi-axial hydroxyl and sulfide substituents.[17]

Reaction of oxepin–benzene oxide systems with nucleophiles appears to be a useful route for the nonenzymatic synthesis of heteroatom-substituted 1,3-cyclohexadienes.[18]

(7) J. G. Young, L. M. Jackman, and F. Gibson, *Biochim. Biophys. Acta*, 148, 313 (1967).
(8) T. J. Batterham and J. G. Young, *Tetrahedron Letters*, 945 (1969).
(9) M. R. Bell, *et al.*, *J. Amer. Chem. Soc.*, 80, 1001 (1958).
(10) J. M. Edwards and L. M. Jackman, *Aust. J. Chem.*, 18, 1227 (1965), and references cited therein.
(11) D. M. Jerina, J. W. Daly, and B. Witkop, *J. Am. Chem. Soc.*, 90, 6523 (1968); D. M. Jerina, *et al.*, *ibid.*, 90, 6525 (1968); and references cited therein.
(12) Vogel[14] has reported that **1** reacts with CH_3Li to give a mixture of *cis*- and *trans*-5-hydroxy-6-methyl-1,3-cyclohexadiene and with $LiAlH_4$ to give 1,2-dihydrophenol which aromatized on attempted isolation.
(13) Jerina, *et al.*,[15] have reported enzyme-catalyzed ring opening of **1** to *trans*-5,6-dihydroxy-1,3-cyclohexadiene with rabbit liver microsomes and that incubation of **1** with rat liver supernatant and glutathione gave the premercapturic acid, S-(1,2-dihydro-2-hydroxyphenyl)-glutathione. The reaction of glutathione with **1** in the absence of enzyme occurs at one-fifth the rate of the enzyme-catalyzed reaction.[15]
(14) E. Vogel and H. Günther, *Angew. Chem.*, 79, 429 (1967).
(15) D. Jerina, *et al.*, *Arch. Biochem. Biophys.*, 128, 176 (1968).
(16) Satisfactory analytical data have been obtained for all new compounds except 4. Satisfactory spectroscopic data have been obtained for all new compounds.
(17) T. J. Batterham and J. G. Young, *Tetrahedron Letters*, 945 (1968).
(18) *cis*- and *trans*-5,6-dihydroxy-1,3-cyclohexadiene have been prepared from difficultly available starting materials.[19]
(19) M. Nakajima, I. Tomida, and S. Takei, *Chem. Ber.*, 92, 163 (1959); N. Nakajima, *et al.*, *Ber.*, 89, 2224 (1956).

Robert M. DeMarinis, Glenn A. Berchtold

Department of Chemistry, Massachusetts Institute of Technology
Cambridge, Massachusetts 02139

Received July 14, 1969

A "Normal" Temperature-Induced Helix–Coil Transition of Poly-γ-N-carbobenzoxy-L-α,γ-diaminobutyric Acid in Mixed Organic Solvents[1]

Sir:

The discovery that poly-γ-benzyl-L-glutamate (PBLG) can undergo the helix–coil transition as a function of both solvent composition and temperature[2] has prompted numerous studies of such a transition for various poly-α-amino acids (for a review, see ref 3). PBLG is known to display an "inverse" transition in mixed solvents, that is, its helical form is stable at higher temperatures and its coiled form at lower ones than room temperature. This is also true for several structurally related polypeptides in mixed organic solvents. We now wish to report a "normal" reversible temperature-induced helix–coil transition of poly-γ-N-carbobenzoxy-L-α,γ-diaminobutyric acid (PCLB), as contrasted with its higher homologs, poly-δ-N-carbobenzoxy-L-ornithine (PCLO) and poly-ε-N-carbobenzoxy-L-lysine (PCLL) (Table I). In analogy to protein denaturation, PCLB becomes helical at low temperature and disordered at high temperature.

We synthesized a high molecular weight PCLB[4] having a degree of polymerization of 470, as determined from high-speed equilibrium sedimentation,[5,6] and fol-

(1) This work was supported by grants from the U. S. Public Health Service (GM-10880, HE-06285, and GM-K3-3441).
(2) P. Doty and J. T. Yang, *J. Am. Chem. Soc.*, 78, 498 (1956).
(3) G. D. Fasman in "Poly-α-Amino Acids," G. D. Fasman, Ed., Marcel Dekker, Inc., New York, N. Y., 1967, Chapter 11.
(4) S. Kubota, J. Noguchi, and J. T. Yang, submitted for publication; lot SK-0667.
(5) D. Yphantis, *Biochemistry*, 3, 297 (1964).