Scheme I
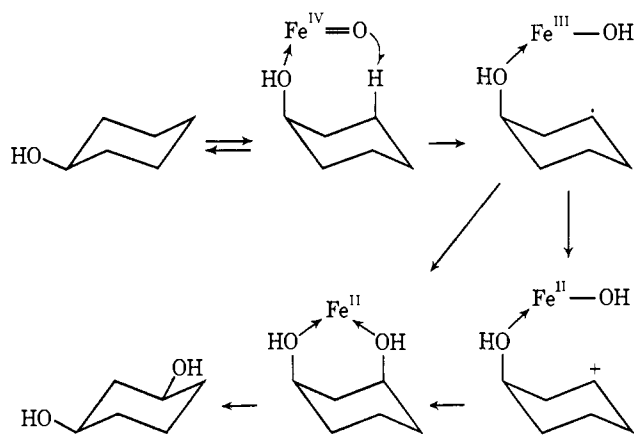

If bond lengths and angles are appropriate, collinearity of the C···H···O moiety, a requisite in other free radical hydrogen abstractions,[11] may be more easily obtained by attack at C-3 although it is not apparent from models that a trans-diequitorial attack at C-2 should be disfavored strictly on this geometrical basis. Indeed, there appears to be a small but significant increase in the proportion of 1,2-diol when iron salts are used. The near-exclusive formation of cis-1,3-cyclohexanediol can be economically explained by directed oxidation of the incipient alkyl radical by the proximate iron(III) by either an electron transfer or ligand transfer process.[12] Competition for the intermediate cyclohexyl carbonium ion by solvent can account for the loss of stereoselectivity upon addition of water.

The operation of this mechanism requires a stereospecific removal of the C-3 hydrogen cis to the hydroxyl group. That cis-hydrogen abstraction does indeed predominate was determined by examination of hydroxylation products of trans-3-trans-5-cyclohexanol-d_2 (1).[13] The deuterium content of 1 was found to be 2.0 from its mass spectrum while integration of the Eu-(fod)$_3$-shifted pmr spectrum[14] indicated that 88.5% of the deuterium content was trans at C-3 and C-5, the remainder being cis.

Oxidation of 1 again afforded cis-1,3-cyclohexanediol as the major hydroxylation product, the mass spectrum of which indicated a 3:1 ratio of dideuterated to mono-deuterated diol.[15]

While it is clear that much of the deuterium at C-3 has been retained in this oxidation, an accurate determination of the stereoselectivity for hydrogen abstraction requires the measurement of the hydrogen isotope effect for this reaction. This value was determined by a competitive oxidation of cyclohexane and cyclohexane-d_{12} which leads to k_H/k_D = 1.26 for cyclohexane → cyclohexanol and k_H/k_D = 1.75 for cyclohexanol → cyclo hexanone.

The hydrogen isotope effect for oxidation of cyclo-

hexanol to cyclohexanone observed here is in close accord with the value determined by Walling[1e] for isopropyl alcohol in an aqueous medium with Fenton's reagent, suggesting a similar mechanism. The hydroxylation of cyclohexane, however, shows an anomalously small hydrogen isotope effect, and we interpret this low value as an indication of a change in the nature of the oxidant from that in water solution.

With the value of the hydrogen isotope effect, k_H/k_D = 1.26, and the known stereochemical integrity of 1, one must conclude that hydrogen abstraction from C-3 occurs cis to the hydroxyl group of cyclohexanol 80% of the time. Thus, in accord with the proposed mechanism (Scheme I), the conversion of cyclohexanol to cis-1,3-cyclohexane diol occurs with net retention at C-3.[16] Further elaboration of the nature of this iron-derived oxidant and its relationship to intermediates involved in enzymatic hydroxylation are currently under way.

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Influence of Solvent on the Mobility of Molecules Covalently Bound to Polystyrene Matrices

Sir:

Despite the growing body of knowledge relating to chemical reactions occurring on polymer supports, there still exists only a primitive level of understanding of the physical and chemical nature of "immobilized" substrates and the role which the solvent plays in these heterogeneous systems.[1]

We wish to report the use of the spin-labeling technique in examining the mobility of a nitroxide bound to cross-linked polystyrene in the solvent-swelled state.[2] Our results establish (1) the choice of swelling solvent has a substantial influence on the physical nature of the resin-bound nitroxide and (2) the dominant role of solvent is to define the degree of swelling of the polymer lattice.

The nitroxide 2,2,6,6-tetramethyl-4-piperidinol-1-oxyl (1) was covalently attached to polystyrene by reaction with 2% cross-linked chloromethylated polystyrene (2)

(11) (a) E. J. Corey and W. R. Hertler, *J. Amer. Chem. Soc.*, **80**, 2903 (1958); (b) *ibid.*, **81**, 5209 (1959); (c) *ibid.*, **82**, 1657 (1960).

(12) J. K. Kochi, A. Bemis, and C. L. Jenkins, *J. Amer. Chem. Soc.*, **90**, 4616 (1968), and references to earlier work therein.

(13) M. M. Green, R. J. Cook, *J. Amer. Chem. Soc.*, **91**, 2129 (1969).

(14) R. E. Rondeau and R. E. Sievers, *J. Amer. Chem. Soc.*, **93**, 1524 (1971).

(15) (a) cis-1,3-Cyclohexanediol, m/e (relative intensity) 117 (7.2), 116 (100.0), 115 (4.3), 114 (5.3); cis-1,3-cyclohexanediol-d_n, m/e (relative intensity) 119 (18.0), 118 (100.0), 117 (36.9), 116 (10.7). (b) Similar oxidation of cyclohexanol deuterated at C-4 afforded cis-1,3-cyclohexanediol with *complete* retention of the label.

(1) J. M. Stewart and J. D. Young, "Solid Phase Peptide Synthesis," W. H. Freeman, San Francisco, Calif., 1969; J. I. Crowley and H. Rapoport, *J. Amer. Chem. Soc.*, **92**, 6363 (1970); M. A. Kraus and A. Patchornik, *ibid.*, **93**, 7325 (1971); J. P. Collman, L. S. Hegedus, M. P. Cooke, J. R. Norton, G. Dolcetti, and D. N. Marquardt, *ibid.*, **94**, 1789 (1972); R. H. Grubbs, C. Gibbons, L. C. Kroll, W. D. Bonds, Jr., and C. H. Brubaker, *ibid.*, **95**, 2373 (1973); E. C. Blossey, D. C. Neckers, A. L. Thayer, and A. P. Schaap, *ibid.* **95**, 5820 (1973).

(2) C. L. Hamilton and H. M. McConnell, "Structural Chemistry and Molecular Biology," A. Rich and N. Davidson, Ed., W. H. Freeman, San Francisco, Calif., 1968, p 115; O. H. Griffith and A. S. Waggoner, *Accounts Chem. Res.*, **2**, 17 (1969).
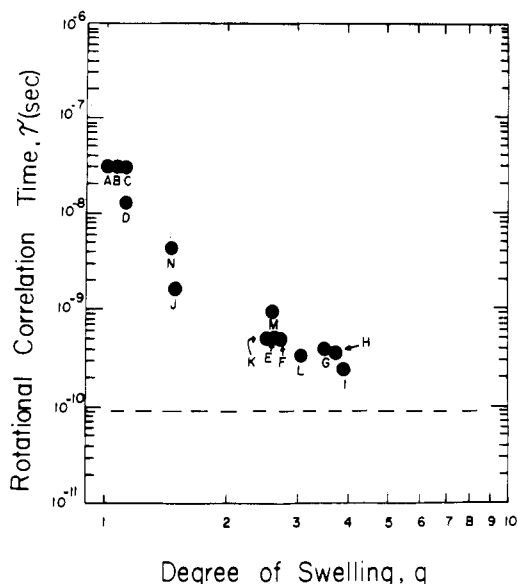
Figure 1. Plot of τ as a function of q for **3** swelled in (A) no solvent, (B) ethanol, (C) 2-propanol, (D) acetonitrile, (E) ethyl acetate, (F) N,N-dimethylformamide, (G) carbon tetrachloride, (H) dichloromethane, (I) benzene, (J) ethanol in benzene (67% v/v), (K) ethanol in benzene (33% v/v), (L) ethanol in benzene (17% v/v), (M) **4** swelled in benzene, and (N) **5** swelled in benzene; the dashed line (----) represents the value of τ measured for a benzene *solution* of nitroxide polymer **6**.

(0.2 mmol of chlorine/gram of polymer), swelled in N,N-dimethylformamide (DMF) in the presence of base.[3] Analysis of the resulting nitroxide polymer, **3**,
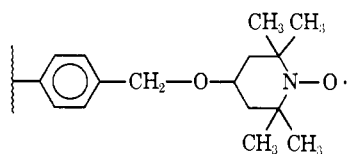
3, 0.2 mmol of nitroxide/gram of polymer; 2% ring substitution

indicated complete replacement of the chloride ion by the spin label.[4,5] Rotational correlation times, τ, were calculated from observed room temperature electron paramagnetic resonance (epr) spectra.[6-9] The degree of swelling values, q (swelled volume/dry volume), were

(3) J. S. Brimacombe, B. D. Jones, M. Stacey, and J. J. Willard, *Carbohyd. Res.*, 2, 167 (1966). The polymer product was filtered, washed with water, ethanol, and ether, and dried under vacuum.

(4) Nitrogen was determined by microanalysis (Midwest Microlab, Indianapolis, Ind.).

(5) Chloromethylation of the polystyrene occurs uniformly, requiring a uniform distribution of the nitroxide along the polymer: R. B. Merrifield and V. Littau in E. Bricas, "Peptides 1968," North Holland Publishing Co., Amsterdam, 1968, p 179.

(6) Each polymer sample was swelled with a given solvent for 24 hr in an epr tube, sealed with a No-Air stopper, and then purged with nitrogen for 10 min.

(7) D. Kivelson, *J. Chem. Phys.*, 27, 1087 (1957); J. H. Freed and G. K. Fraenkel, *ibid.*, 39, 326 (1963); S. A. Goldman, G. V. Bruno, and J. H. Freed, *J. Phys. Chem.*, 76, 1858 (1972); A. T. Bullock, G. G. Cameron and P. M. Smith, *J. Polym. Sci., Part A-2*, 11, 1263 (1973).

(8) The rigid lattice value of the anisotropic ^{14}N hyperfine splitting used was 32.3 G; this was determined experimentally from **3** in the dry state at 77°K.

(9) Those spectra which appeared as three sharp lines were further analyzed and found to be well behaved; *i.e.*, the quantity (line width)$^2 \times$ (amplitude) was constant for all three lines ($\pm 1\%$): G. K. Fraenkel, *J. Phys. Chem.*, 71, 139 (1967). Correlation times calculated for polystyryl nitroxides containing less than 0.2×10^{-4} mmol of nitroxide/gram of polymer differed from those calculated for **3** by less than a factor of two.

determined from the measured density of the dry resin and the weight of imbibed solvent.[10,11]

Data obtained for nitroxide polymer **3** swelled in a variety of solvents are presented in Figure 1. A distinct trend can be noted; as the degree of swelling of the polymer increases, the rotational correlation time of the spin-label decreases. In order to ensure the absence of any special solvent effects, we measured the mobility of the label in **3** swelled in different mixtures of benzene and ethanol. Here again, we detected the same trend. Incremental replacement of ethanol by benzene led to both a higher degree of swelling and a correspondingly smaller correlation time. We also found that by increasing the crosslink density of the polystyryl nitroxide to 4%, **4**, and 12%, **5**, the degree of swelling decreased and the correlation time increased.[12] All of the data obtained fall along a smooth curve which asymptotically approaches the value of τ measured for a benzene *solution* of an analogous noncross-linked polystyryl nitroxide, **6**.[12] This plot clearly demonstrates that the rotational motion of the covalently bound spin-label is primarily dependent upon the degree of swelling of the polymer lattice. Although the precise relationship between q and τ has not yet been determined, the results cited here establish that *those solvents which swell polystyrene matrices the most will allow for the greatest mobility of the substrates bound to them.*

Our observation that the physical nature of resin-bound molecules varies substantially with the degree of swelling of the polymer lattice suggests that the chemical nature of such species may be similarly influenced.[13] We are presently carrying out experiments designed to test this hypothesis.

(10) Swelling measurements were made after the nitroxide polymers were equilibrated with a given solvent for at least 24 hr; swelling equilibrium was usually attained within a 2-hr period. Reproducibility was $\pm 5\%$.

(11) In this calculation it was assumed that the volumes of the polymer and the solvent are additive. The density of **3** was experimentally found to be 0.95 ± 0.03 g/cm^3.

(12) Prepared from the corresponding chloromethylated polymer containing 0.2 mmol of chlorine/gram of polymer.

(13) A recent study dealing with a polystyrene-bound hydrogenation catalyst revealed a marked dependency of the catalyst's activity on the choice of solvent used to swell the polymer: W. Dumont, J. C. Poulin, T. P. Dang, and H. B. Kagan, *J. Amer. Chem. Soc.*, 95, 8295 (1973).

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8-Azaadenosine. Crystallographic Evidence for a "High-Anti" Conformation around a Shortened Glycosidic Linkage

Sir:

We wish to report the results of our X-ray structural investigation of 8-azadenosine and discuss the effects of the 8-aza substitution on both the glycosidic C–N bond and the torsion angle χ around the glycosidic bond. The structure of this nucleoside is of particular signifi-