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Model Studies of the Hydrophobic Interaction: Water-Methane*

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ABSTRACT

The hydrophobic effect is crucial to the understanding of a number of biochemical processes, including membrane formation. A theoretical study of a model hydrophobic interaction, the water-methane system, has been carried out. A series of *ab initio* self-consistent-field calculations were performed to discern some features of the H_2O-CH_4 potential energy surface. The equilibrium configuration corresponds to a linear O - H - C arrangement, with r(C-O) = 3.85 Å, and a binding energy of 0.5 kcal/mole. Potential curves are presented for a number of other approaches. Using a double zeta basis set, several calculations were also carried out for CH_4-$(H_2O)_2$. With one water fixed at its equilibrium separation with respect to methane, the approach of a second H_2O in an analogous manner yields a repulsive interaction energy. This result is qualitatively explained by a pairwise additive model of the three molecule potential surface. Finally, a qualitative discussion is given in terms of Mulliken atomic populations.

INTRODUCTION

The hydrophobic effect has often been considered[1] the most significant factor in the organization of the constituent molecules of living matter into complex structural entities such as cell membranes and micelles. Although hydrophobic molecules may be soluble in many nonpolar solvents (e.g., alcohols or ethers), they are at best sparingly soluble in water. In contrast, the term hydrophilic is reserved for molecules that are soluble in water. The formation of cell membranes relies on molecules having both hydrophobic and hydrophilic characteristics. Tanford[1] has designated such dual-characteristic molecules as amphiphiles. A simple example of such an amphiphile would be $CH_3CH_2NH_3^+C\ell^-$, where the ionic $C\ell^-$ end is referred to as the head and the ethyl chain as the tail.

The present paper begins with the simplest hydrophopic interaction, the interaction between a single water molecule and a single methane molecule. One's first inclination might be to assume that the biological systems mentioned in the previous paragraph are so much more complex than the H_2O-CH_4 model that such a model is not particularly relevant to an understanding of the hydrophobic effect. However, in his review Tanford[1] concludes that the hydrocarbon tail of an amphiphile should have thermodynamic properties similar to those of a hydrocarbon molecule in water solution. Since it is clear that the water-methane interaction potential plays a crucial role in determining the latter

thermodynamic properties, the relevance of the present study to the hydrophobic effect is indirectly established. For physical chemists, of course, the H_2O-CH_4 interaction is of inherent interest, and would probably be estimated to be intermediate between a van der Waals attraction (e.g., Ne-Ne, $\sim$ 0.09 kcal/mole[2]) and a true hydrogen bond (e.g., H_2O-H_2O, $\sim$ 5 kcal/mole[3]).

Despite the large number of hydrogen bonded systems for which ab initio electronic structure studies have been undertaken,[4] we have been able to find only one such calculation for the H_2O-CH_4 system. This calculation, by Lathan et. al.,[5] was carried out as part of a comprehensive study of the equilibrium geometries of all molecules of the form H_mABH_n, where A and B are first row atoms C,N,O, and F. They performed self-consistent-field computations with a miminum basis set of Slater functions, each expanded as a linear combination of three gaussian functions. Lathan et. al. predict the equilibrium structure, seen in Figure 1, to be bound by 0.8 kcal/mole relative to separated CH_4 and H_2O.

The relative dearth of H_2O-CH_4 theoretical studies has in part been motivated by some skepticism as to the validity of the Hartree-Fock approximation for describing potential surfaces of this type. The qualitative suitability of single configuration wave functions for the descriptions of systems such as H_2O-H_2O and HF-HF seems well established.[4] However, the failure of Hartree-Fock to predict any attraction at all for He-He, Ne-Ne, and Ar-Ar, is equally well established.[6] It should be noted that

for the He-He[7] and Ne-Ne[8] systems, studies explicitly including correlation effects have yielded qualitatively correct potential energy curves. Thus the inherent inability of the Hartree-Fock model to describe dispersion forces does raise serious questions as to the suitability of this model for describing the CH_4-H_2O interaction. The same questions have been noted by Losonczy, Moskowitz, and Stillinger,[9] whose H_2O-Ne Hartree-Fock calculations predict a binding energy of only 0.17 kcal/mole. On the other hand, if Pople's prediction[5] of an 0.8 kcal/mole attraction is qualitatively correct, then the dispersion contribution (which we can guess to be $\sim$ 0.1 kcal/mole from the Ne-Ne molecular beam results[2]) will be relatively unimportant.

The purpose of the present study, then, is to carefully study the H_2O-CH_4 interaction at the self-consistent-field level of theory using several different basis sets. A variety of different approaches of H_2O to CH_4 have been considered. Finally, a number of calculations are reported for the H_2O-CH_4-H_2O system.

COMPARISON OF BASIS SETS

Four different basis sets of contracted gaussian functions[7] have been used in the present work:

A. Minimum Basis. 1s, 2s, $2p_x$, $2p_y$, and $2p_z$ Slater functions on carbon and oxygen were each expanded as a linear combination of four guassian functions.[10] Orbital exponents were taken from Clementi and Raimondi.[11] Similarly a 1s Slater function on hydrogen (orbital exponent 1.2) was fit as a linear combination of four gaussians. Although this basis set yields significantly lower total energies than the STO-3G set of Lathan et. al.,[5] both are minimum basis sets and one expects qualitatively similar geometry predictions and energy differences.

B. Double Zeta Basis. Twice as large as the minimum basis, this is Dunning's C,O(4s 2p), H(2s) contraction[12] of Huzinaga's C,O(9s 5p), H(4s) primitive gaussian basis sets.[13]

C. This third basis set is identical to the double zeta set above, except that the primitive (5p) set is more flexibly contracted, to (3p).

D. Double Zeta Plus Polarization. To basis B, we add a set (d_{xx}, d_{yy}, d_{zz}, d_{xy}, d_{xz}, d_{yz}) of d-like functions to carbon (α = 0.75) and oxygen (α = 0.8).

To allow a comparison of the different basis sets, the simplest linear O - H - C arrangement, designated geometry A and seen in Figure 2, was studied first. The H_2O and CH_4 geometries are held fixed at their

experimental values:[14,15] r(OH) = 1.808846 bohrs = 0.957 Å, θ(HOH) = 104.52°; and for tetrahedral CH_4, r(CH) = 2.067361 bohrs = 1.094 Å.

The results of this comparison are seen in Table I. There it is seen that our minimum basis set yields an H_2O-CH_4 bond energy of 1.81 kcal/mole, large enough to be considered a true hydrogen bond. This result is surprisingly different from the minimum basis work of Lathan et. al.,[5] who found only 0.8 kcal/mole of binding. The source of this difference probably lies not with the fact that we used a 4 gaussian expansion (as opposed to their 3 gaussians), but rather with their use of orbital exponents optimal for molecules, not atoms. In any case, it is seen clearly that all minimum basis sets are not alike. We should note, however, that the Lathan calculation predicted a C-O separation of 3.27 Å, only 0.16 Å longer than obtained from the present minimum basis.

The double zeta calculation yields a much longer C-O distance (3.85 Å) and much weaker attractive energy (0.49 kcal/mole). Basis set C yields an almost identical result, indicating clearly that the additional flexibility in the carbon and oxygen 2p functions is unnecessary.

Our final calculation, that using the double zeta plus polarization basis, yields an even longer C-O bond distance (4.01 Å) and smaller attraction (0.34 kcal/mole). This same trend, toward smaller binding energy with increasing basis set size, occurs for the water dimer.[7] In fact the near Hartree-Fock

calculations of Popkie, Kistenmacher, and Clementi[3] yield a hydrogen bond energy which is almost certainly less than the correct (unknown) value. Thus it appears that the correlation energy will be of the order of one kcal/mole greater for the water dimer than for two separated H_2O molecules. In light of these facts, it is by no means clear whether the double zeta or double zeta plus polarization results are closer to reality. We do tend to conclude that the minimum basis results are unreliable.

Given the uncertainties involved, we decided to use the double zeta basis in the remaining phases of the study. In addition to the obvious economic advantages, there would seem to be a substantial probability that the basis set and correlation errors would cancel with respect to this frame of reference.

THE DIFFERENT ORIENTATIONS OF APPROACH

In addition to geometry A, we have considered four other approaches B,C,D, and E, depicted in Figure 2. These results are summarized in Table II and Figure 7, both of which indicate that approaches B,C, and E are repulsive in nature. This is not particularly surprising when one considers the many statements in the literature[1] concerning the lack of affinity between hydrocarbons and water.

A few qualitative comments can be made concerning the repulsive interactions B,C, and E. First, the fact that C is by far the most repulsive is understood in terms of the highly unfavorable H-H interaction. That is, in a simple picture, the H atoms in H_2O and CH_4 are positively charged, and these effective charges repel via Coulomb's law. The similarity of the mildly repulsive interactions B and E is readily understood by comparison of Figures 2b and 2e. These two conformations share the undesirable feature of placing a large number of atoms in the same region of physical space.

The second most attractive conformation is geometry D, with binding energy 0.17 kcal/mole and C-O equilibrium separation 4.16 Å. Like geometry A, this conformation involves a linear O - H - C arrangement, a result consistent with the many earlier theoretical studies of hydrogen bonded systems.[4]

As well as the basic arrangements A-E, we have considered rotations (about the various C-O axes) of one molecule relative

to the other. For geometries A and D, these rotations were done at the equilibrium geometries, i.e., $r_e(CO)$. The barrier to rotation for geometry A is so small, less than 0.0001 kcal/mole, as to lie in the noise level of the present calculations. For geometry D, however, the dependence on angle of rotation was significant. If we let $\gamma = 0°$ correspond to the geometry seen in Figure 2d, then the following additional results were found: $\gamma = 0°$, 0.172 kcal/mole; $\gamma = 10°$, 0.173 kcal/mole; $\gamma = 20°$, 0.176 kcal/mole; $\gamma = 40°$, 0.188 kcal/mole; $\gamma = 60°$, 0.201 kcal/mole; $\gamma = 75°$, 0.208 kcal/mole; and $\gamma = 90°$, 0.211 kcal/mole. Thus it is seen that the binding energy goes up monotonically from 0.17 to 0.21 kcal/mole as γ goes from 0° to 90°. Energies for other values of γ are related by symmetry to those in the range 0-90°. Note finally that the $\gamma = 90°$ geometry allows the left most (in Figure 2d) H atom to "avoid" the two nearest methane hydrogens.

Although geometry B yields a completely repulsive interaction potential, by rotating the H_2O molecule by 90°, a weak attraction of 0.05 kcal/mole was found. This rotated geometry is referred to as B' in Table II. As is reasonable, this more favorable conformation corresponds to the maximum separation of water protons from the two nearest methane protons.

Approach of a Second Water Molecule

In a dilute solution, each hydrocarbon molecule will be surrounded by several water molecules. Clearly a purely *ab initio* attack on a completely realistic liquid is not practical.

However, by assuming a pairwise additive potential, it is possible to simulate the liquid via molecular dynamics. Thus it is of interest to investigate the potential surfaces involving more than two molecules and check the deviations from the pairwise model. For the water trimer such calculations have already been reported.[18,19]

The equilibrium geometry of $CH_4(H_2O)_2$ will of course be that of a methane molecule loosely bound to the water dimer. However, given our interest in the hydrophobic effect, this is not the conformation of primary concern here. Rather, we have considered a $CH_4(H_2O)_2$ structure with two O - H - C hydrophobic interactions. Since geometry A yielded the lowest CH_4-H_2O energy, this dimer structure was fixed at $r_1(CO) = 3.85$ Å. Then a second water molecule was brought up in an analogous manner. Note that when the second C-O distance, $r_2(CO)$, is 3.85 Å the three molecule complex has C_{2v} point group symmetry.

A rather surprising result was found at this latter geometry, namely that the energy with respect to separated $CH_4 + H_2O + H_2O$ is only -0.132 kcal/mole. That is, when one CH_4-H_2O dimer is fixed at its equilibrium geometry, the second CH_4-H_2O interaction becomes repulsive. Other results obtained with $r_1(CO) = 3.85$ Å were the following: $r_2(CO) = 4.0$ Å, E = -0.175 kcal/mole; $r_2(CO) = 5.0$ Å, E = -0.157 kcal/mole; and $r_2(CO) = 7.5$ Å, E = -0.305 kcal/mole. All these results are seen to lie above the -0.494 kcal/mole result obtained for $r_1(CO) = 3.85$ Å, $r_2(CO) = \infty$.

In a pairwise additive picture, the potential energy of the

$r_1 = r_2 = 3.85$ Å structure is 2 (-0.494 kcal/mole) plus the potential energy of two H_2O molecules as they remain when the CH_4 is removed to infinity. It is seen, then, that this H_2O-H_2O interaction should be repulsive by 0.856 kcal/mole to satisfy pairwise additivity. We have carried out this H_2O-H_2O calculation, r(O-O) = 6.287 Å, and find an energy of 0.695 kcal/mole relative to separated $H_2O + H_2O$. Thus it is seen that the assumption of pairwise additivity is qualitatively reasonable in this case.

POPULATION ANALYSES

Table III shows Mulliken populations for infinitely separated $H_2O + CH_4$, for the equilibrium positions of geometries A and D, and for $CH_4(H_2O)_2$ with $r_1(CO) = r_2(CO) = 3.85$ Å. Although one is correctly hesitant to assign any significance to the precise values of these atomic populations, we can at least hope that population comparisons will be chemically meaningful.

We first note that, consistent with any simple picture of electronegativity, the H atoms in H_2O are substantially more positively charged than those in methane. For geometry A, the bridging H atom in the linear O----H—C structure is labeled H_1 in Table III. At the equilibrium of geometry A, the positive charge on this bridging hydrogen is significantly increased with respect to that of isolated methane. This loss of electron density is counteracted by increases at the neighboring O and C atoms. Thus we confirm the expected picture $\overset{\delta^-}{O}$---$\overset{\delta^+}{H}$—$\overset{\delta^-}{C}$.

For structure D, the H atom in the O—H----C bridge is labeled H_2 in Table III. Again we see an increase in positive charge, 0.004 here, at the bridging hydrogen. As before, electron density flows to some degree to the neighboring more electronegative O and C atoms.

The Mulliken populations for the trimer show that the two water molecules have very similar charge distributions to isolated H_2O. However, these waters significantly distort the central methane charge distribution. The C atoms is more negatively charged by 0.054 electrons, and a very large difference in the two sets of

equivalent H atoms develops. The bridging H's (H_1 and H_2 on methane in Table III) become 0.046 electrons more positively charged than in CH_4, while the terminal hydrogens are more negatively charged, by 0.021 electrons. We conclude that these Mulliken populations present a picture of the electronic charge distribution which is consistent with both chemical intuition and the ab initio predictions made here.

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This problem was suggested to us by Robert W. Hand of the Yale Medical School. Mr. Hand carried out preliminary CNDO calculations[20] which guided our thinking about the CH_4-H_2O potential surface. We are grateful to Mr. Hand and to Professor Peter A. Kollman for many stimulating and helpful discussions. Dr. Oleh Weres also made valuable suggestions during the course of this work.

REFERENCES

1. C. Tanford, The Hydrophobic Effect (Wiley-Interscience, New York, 1973).
2. P. E. Siska, J. M. Parson, T. P. Schafer, and Y. T. Lee, J. Chem. Phys. 55, 5762 (1971).
3. H. Popkie, H. Kistenmacher, and E. Clementi, J. Chem. Phys. 59, 1325 (1973).
4. P. A. Kollman and L. C. Allen, Chem. Rev. 72, 283 (1972).
5. W. A. Lathan, L. A. Curtiss, W. J. Hehre, J. B. Lisle, and J. A. Pople, Progress in Physical Organic Chemistry, in press.
6. H. Margenau and N. R. Kestner, Theory of Intermolecular Forces (Pergamon Press, Oxford, 1971).
7. H. F. Schaefer, The Electronic Structure of Atoms and Molecules: A Survey of Rigorous Quantum Mechanical Results (Addison-Wesley, Reading, Mass., 1972).
8. W. J. Stevens, A. C. Wahl, M. A. Gardner, and A. Karo, J. Chem. Phys. 60, 2195 (1974).
9. M. Losonczy, J. W. Moskowitz, and F. H. Stillinger, J. Chem. Phys. 59, 3264 (1973).
10. W. J. Hehre, R. F. Stewart, and J. A. Pople, Symp. Faraday Soc. 2, 15 (1968).
11. E. Clementi and D. L. Raimondi, J. Chem. Phys. 38, 2686 (1963).
12. T. H. Dunning, J. Chem. Phys. 53, 2823 (1970).

13. S. Huzinaga, J. Chem. Phys. 42, 1293 (1965).

14. W. S. Benedict, N. Gailar, and E. K. Plyler, J. Chem. Phys. 24, 1139 (1956).

15. G. Herzberg, Electronic Spectra of Polyatomic Molecules (Van Nostrand Reinhold, New York, 1966).

16. B. J. Alder and T. E. Wainwright, J. Chem. Phys. 33, 1439 (1960).

17. F. H. Stillinger and A. Rahman, J. Chem. Phys. 60, 1545 (1974).

18. J. Del Bene and J. A. Pople, J. Chem. Phys. 52, 4858 (1970).

19. D. Hankins, J. W. Moskowitz, and F. H. Stillinger, J. Chem. Phys. 53, 4544 (1970).

20. J. A. Pople and D. L. Beveridge, Approximate Molecular Orbital Theory (McGraw-Hill, New York, 1970).

Table I. Summary of calculations using various basis sets for H_2O-CH_4. Results in this table refer only to geometry A, determined to lie lower energetically than the other geometries investigated. See text for a further description of the different basis sets.

Basis	R_e (C-O), Å	E (hartrees)	Binding Energy (kcal/mole)
A. Minimum Basis	3.11	-115.27652	1.810
B. Double Zeta C,O (9s 5p/4s 2p) H (4s/2s)	3.85	-116.19539	0.494
C. C,O (9s 5p/4s 3p) H (4s/2s)	3.88	-116.19663	0.485
D. Double Zeta Plus Polarization C,O (9s 5p 1d/4s 2p 1d) H (4s /2s)	4.01	-116.23600	0.339

Table II. Equilibrium bond distances and relative energies of the different H_2O-CH_4 geometrical approaches. All calculations were carried out with the double zeta basis set described in the text.

Geometry	R_e (C-O), Å	Binding Energy (kcal/mole)
A	3.85	0.494
B	Repulsive Interaction	
B'	4.22	0.050
C	Repulsive Interaction	
D	4.16	0.172
E	Repulsive Interaction	

Table III. Mulliken populations for the water-methane interaction.

System \ Populations	H_2O			CH_4				
	H_1	H_2	O	H_1	H_2	H_3	H_4	C
Separated Molecules	0.613	0.613	8.773	0.807	0.807	0.807	0.807	6.772
Equilibrium Geometry A	0.610	0.610	8.776	0.752	0.817	0.818	0.818	6.798
Equilibrium Geometry D	0.615	0.609	8.778	0.825	0.807	0.798	0.798	6.771
$CH_4\ (H_2O)_2$	0.612	0.612	8.774	0.761	0.761	0.828	0.828	6.826

FIGURE CAPTIONS

Figure 1. Qualitative view of the equilibrium geometry predicted by Lathan et. al.[5] using a minimum basis set. Note that the O---H separation is not to scale, being 3.27 Å in reality, as opposed to ∿ 1 Å for the intramolecular OH and CH distances in water and methane.

Figure 2. Schematic view of the various approaches of water to methane.

Figure 3. Potential curves for the one-dimensional interactions depicted in Figure 2. Note that the results obtained from geometry E are not plotted, as this potential curve is quite similar to curve B. For example, at R(C-O) = 4.0 and 5.0 Å, curve E lies 0.03 and 0.04 kcal/mole above curve B. At R(C-O) = 3.5 Å, curve E lies 0.09 kcal/mole below curve B.

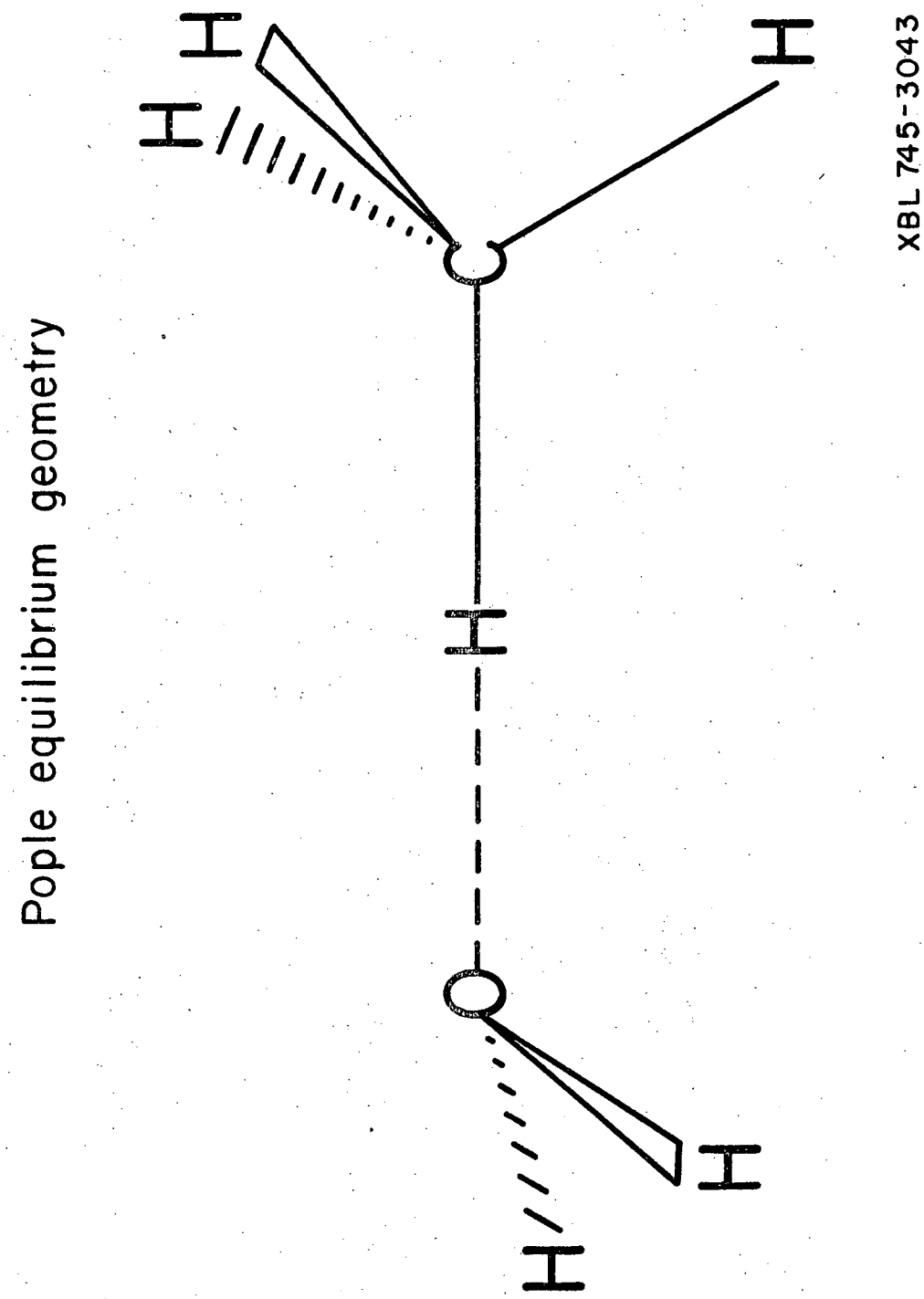


Fig. 1

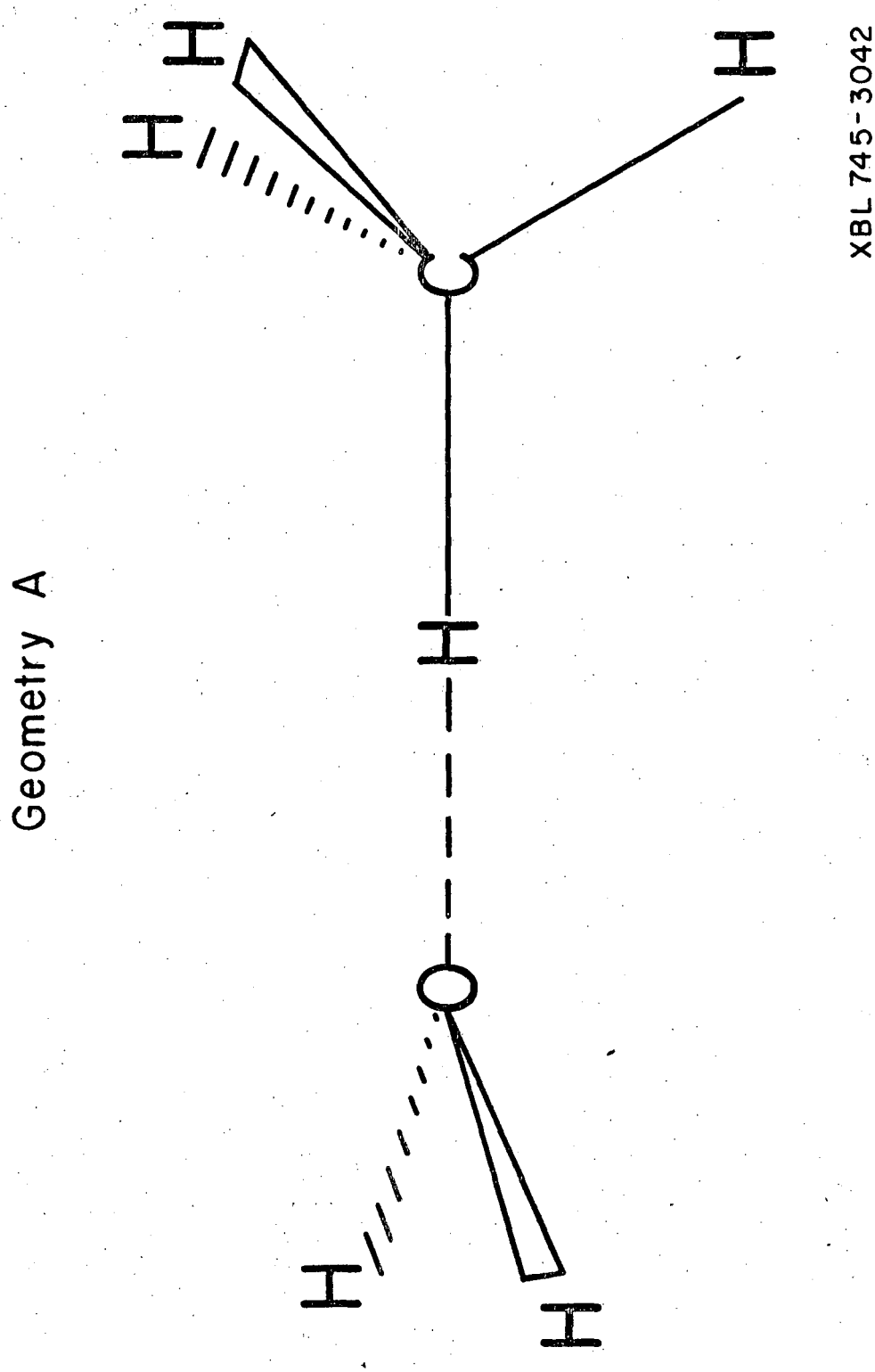


Fig. 2a

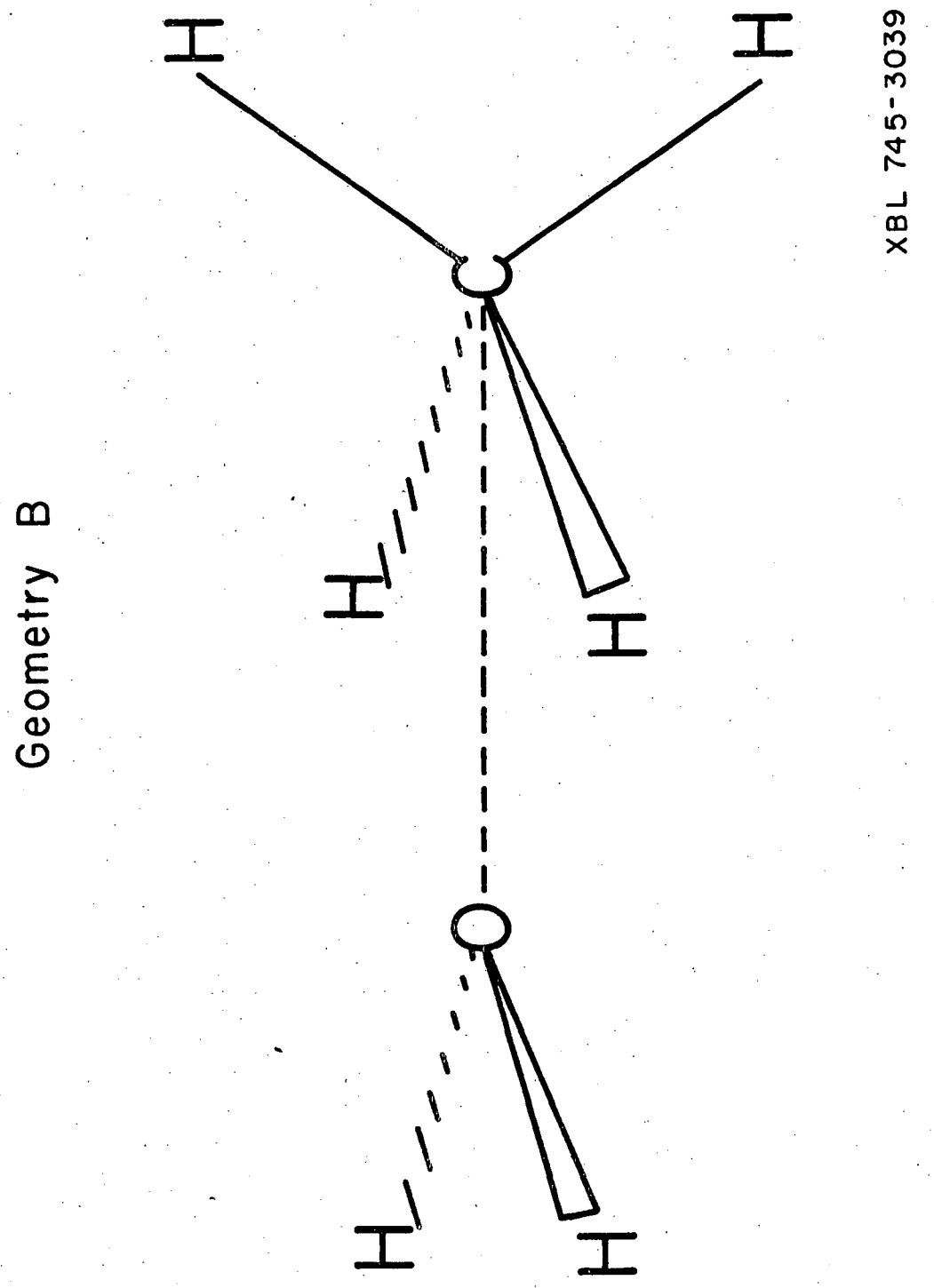
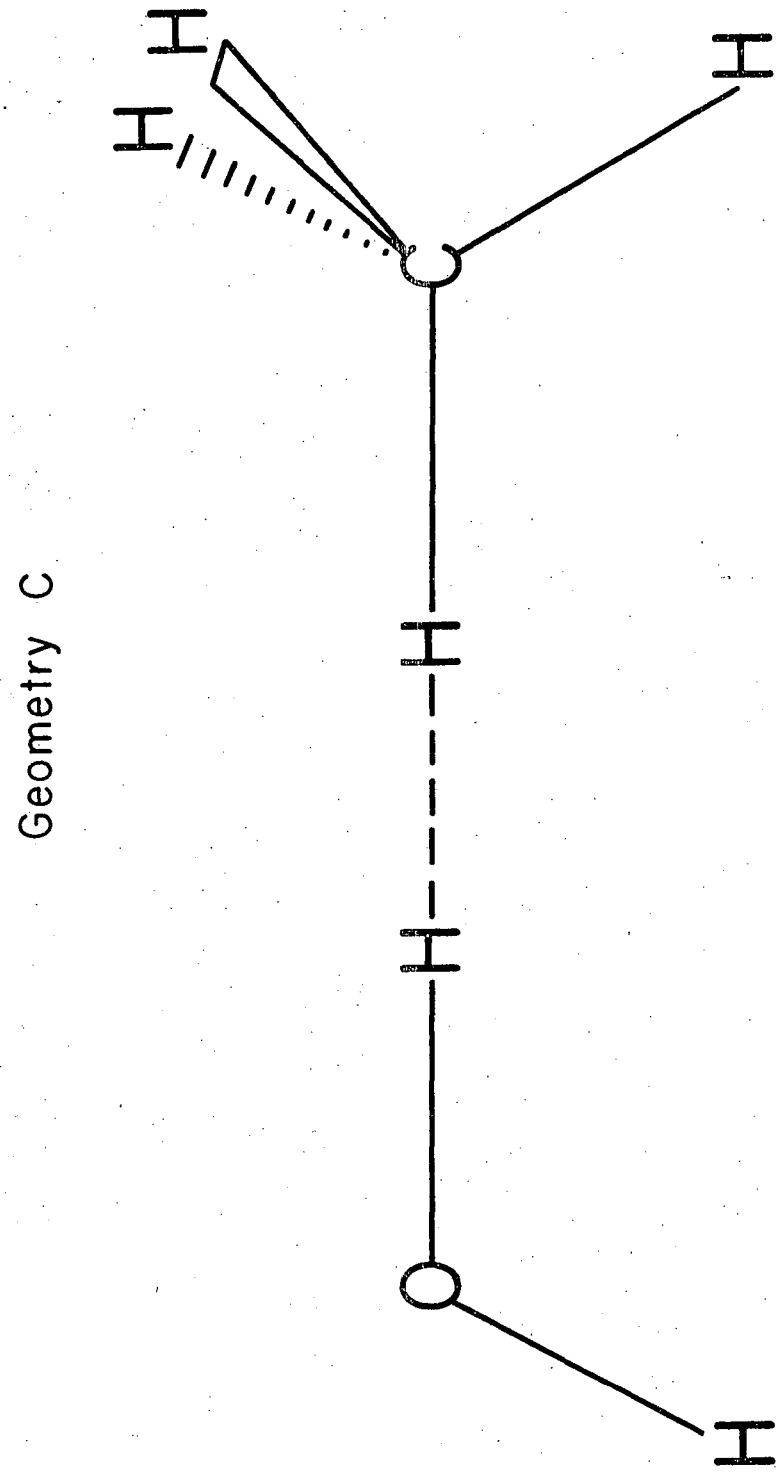


Fig. 2b



XBL 745-3040

Fig. 2c

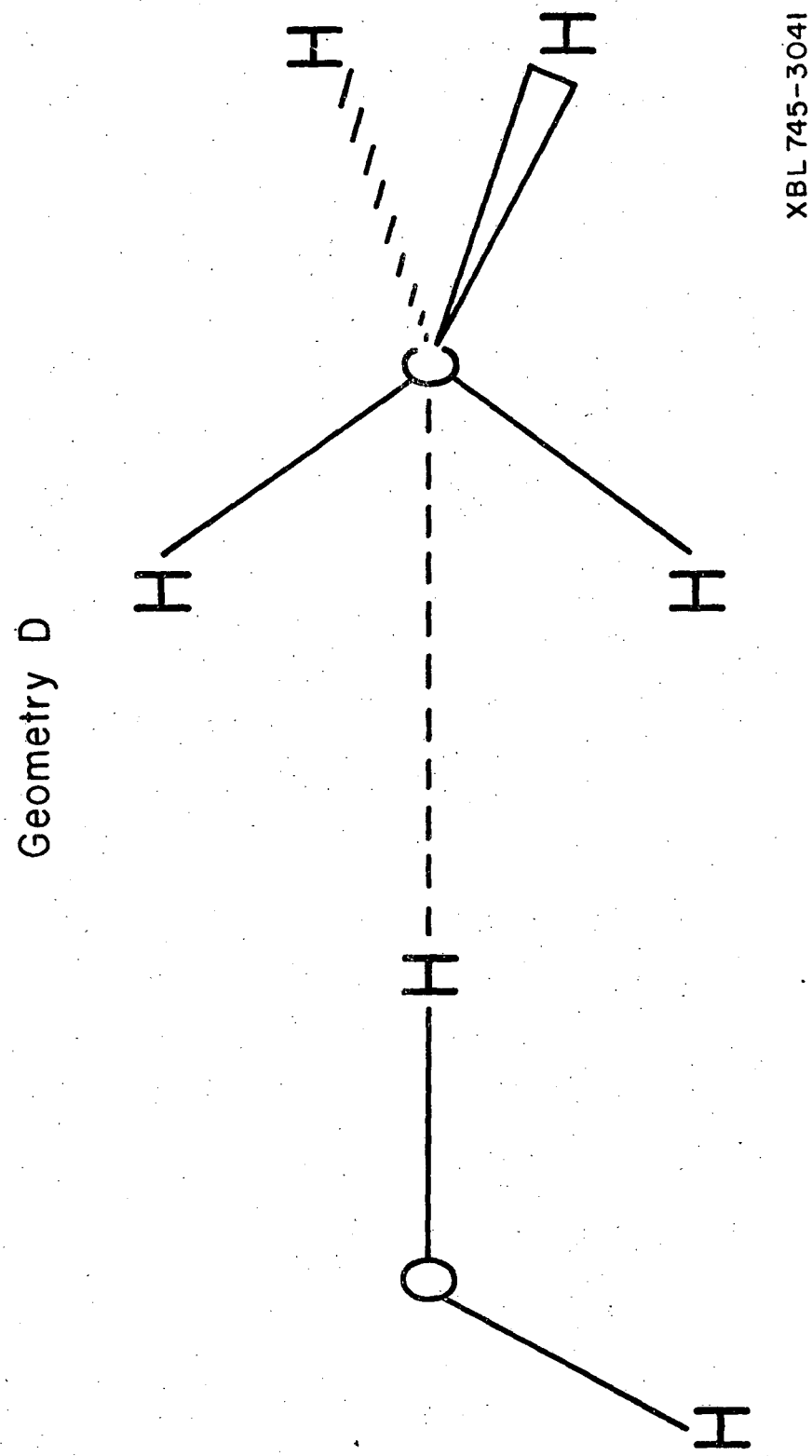


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Fig. 2d

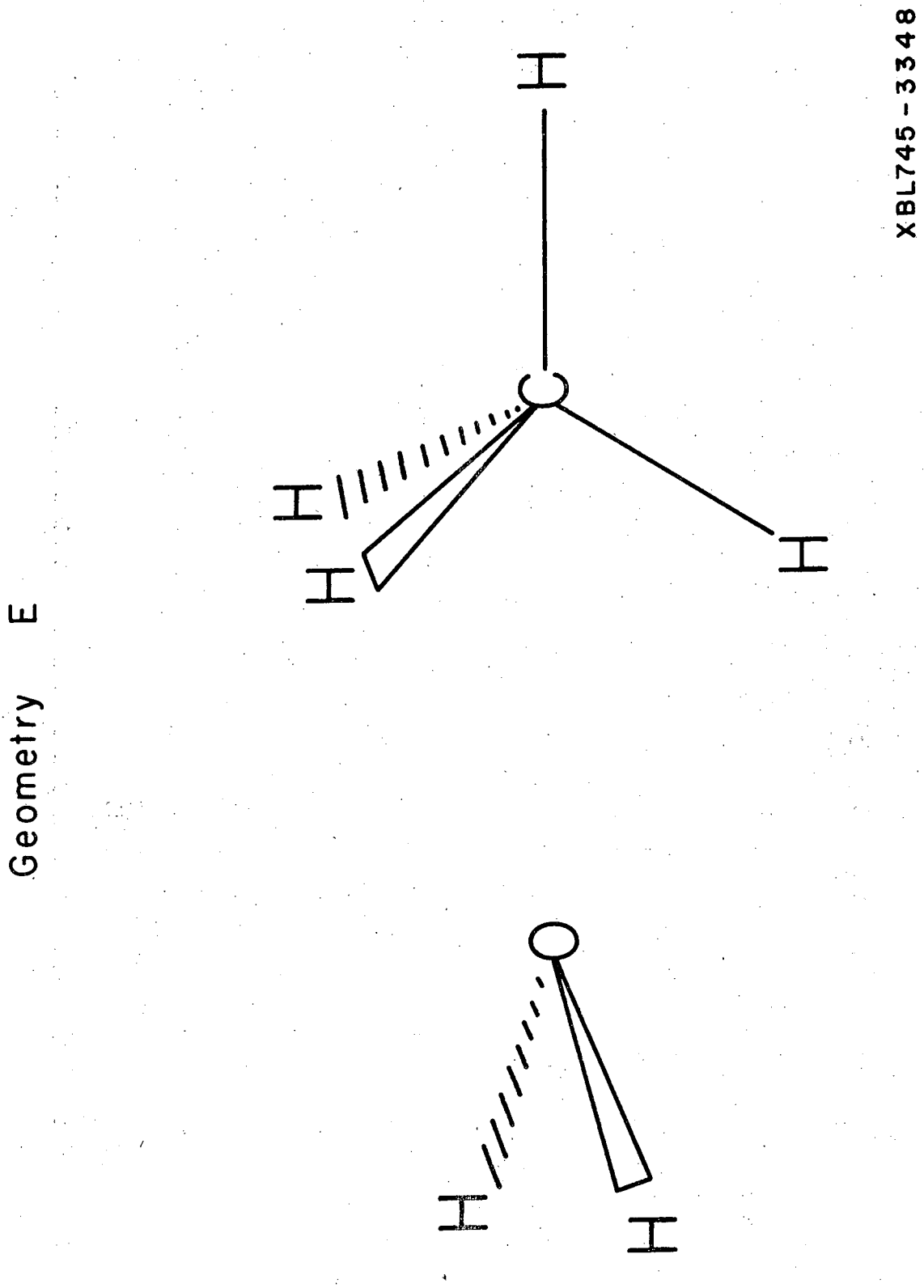

Fig. 2e

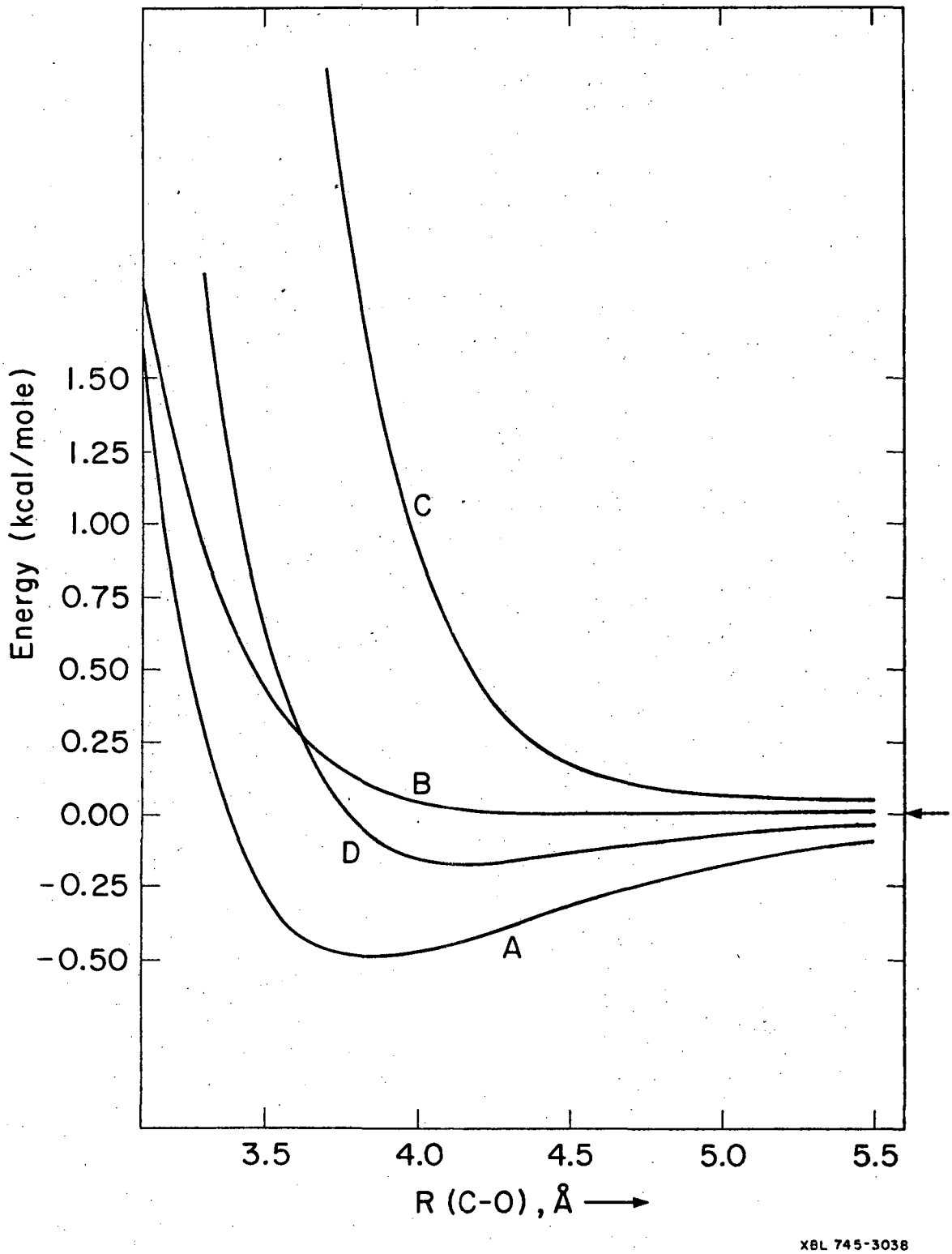
Energy (kcal/mole)
1.50
1.25
1.00
0.75
0.50
0.25
0.00
-0.25
-0.50
C
B
D
A
3.5
4.0
4.5
5.0
5.5
R (C-O), Å
XBL 745-3038

Fig. 3

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