

the methylene halide is also a potential proton source, one might well expect formation of methane and ethyl halide, and hence ethane and propane, to be competitive. In theory, formation of ethyl halide might result either from direct displacement (eq 5) or from dissociative electron transfer followed by radical coupling (eq 6). Either mechanism predicts the following reactivity order for ethyl halide formation: $\text{CH}_2\text{I}_2 > \text{CH}_2\text{Br}_2 > \text{CH}_2\text{Cl}_2$.⁵ The ease of proton transfer from methylene halide to methyl anion (eq 7) should not, however, be particularly halogen sensitive.⁶ The halogen dependence of the relative yields of methane, ethane, and propane observed experimentally (Table I) is thus wholly consistent with the mechanism proposed in Scheme II.

The constant relative yield of ethylene generated by the three methylene halides requires that the competition between carbon-carbon bond formation and proton abstraction which characterizes the methyl anion-methylene halide interaction be inoperative during methylene radical anion-methylene halide encounters. Either this reaction does not contribute substantially to ethylene formation or, as seems more likely, the methylene radical anion is simply a far more potent reducing agent (or nucleophile) than it is a base so that each methylene radical anion-methylene halide encounter leads to carbon-carbon bond formation either by dissociative electron transfer and coupling or by direct displacement (eq 3, Scheme I). To the extent that methylene radical anion dimerization (eq 4) represents the source of ethylene, one would, of course, expect the relative yield of ethylene to be insensitive to the nature of the halide employed. The crucial step in this mechanistic postulate is the initial dimerization.⁷ Since the reduction potential of ethylene is more negative than that of naphthalene, the two subsequent one-electron transfer reactions to naphthalene might well be sufficiently rapid with respect to proton abstraction by the dianion to obviate that species as a prime source of ethane.

In summary, we believe the results reported here support our suggestion¹ that the carbenes or carbenoids generated by reaction of sodium naphthalene with alkyl geminal dihalides can be further reduced to carbene radical anions at rates competitive with those of typical carbene (carbenoid) reactions—in this case, intermolecular addition to an olefinic double bond. In addition they provide the first example(s), other than proton abstraction, of chemistry characteristic of a carbene radical anion, *i.e.*, formal nucleophilic displacement and/or dimerization to a dianion. Finally they

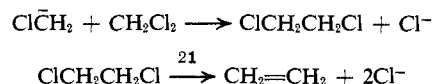
(5) The polarographic half-wave potentials (*vs.* NCE) for CH_2Cl_2 , CH_2Br_2 , and CH_2I_2 are, respectively, -2.23 , -1.48 , and -1.12 V [M. V. Stackelberg and W. Stracke, *Z. Elektrochem.*, **53**, 118 (1949)]; the relative leaving group abilities of the halides for displacement at saturated carbon are $\text{I} > \text{Br} > \text{Cl}$ [see, *e.g.*, E. M. Kosower, "An Introduction to Physical Organic Chemistry," Wiley, New York, N. Y., 1968, pp 80-81, and references therein cited].

(6) No data are available for the pK_a 's of the methylene halides, but by analogy to the behavior of the haloforms [J. Hine, N. W. Burske, M. Hine, and P. B. Langford, *J. Amer. Chem. Soc.*, **79**, 1406 (1957)] one would expect the kinetic acidities of CH_2I_2 and CH_2Br_2 to be nearly identical and only slightly greater than that of CH_2Cl_2 .

(7) Although this mechanistic postulate intrigued us from the moment the data of Table I were obtained, we were too timid to suggest formation of the ethylene dianion in the original version of this communication. We are emboldened to present this postulate here by its independent suggestion by a referee, who notes "a reader...repulsed by piling up all that negative charge...should [keep] in mind that ion aggregation factors can overcome most of that."

suggest that in reaction with a substrate which can function both as a proton source and as a substrate for nucleophilic displacement (or dissociative electron transfer), the methylene radical anion favors nucleophilic attack over proton abstraction to a greater extent than does the methyl anion (methyl sodium).

Finally, we must admit the obvious, namely, that we cannot conclusively eliminate all alternatives to the interpretation presented here. In particular, we cannot with certainty exclude the possibility that ethylene formation results from the sequence



The constancy in the relative yield of ethylene from the three methylene halides is difficult to rationalize by such a hypothesis, however, and, in general, the totality of the data, for reasons too involved to elaborate here, in our opinion, militates against the plausible alternatives to the carbene radical anion postulate.

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Relationship of Nitrogen Lone Pair Interactions to Thermodynamic Parameters Associated with Amine Basicities

Sir:

The interaction of orbitals through space and through bonds has been a topic of increasing interest in recent years,¹ stimulated largely by the development of photoelectron spectroscopy (PES).² Hoffmann¹ considers the extent of interaction to be measured by the magnitude of the one-electron energy level splitting after interaction, compared to that splitting in the (theoretical) absence of such interaction or in a model compound where that interaction is absent. While PES provides a direct measure of one-electron orbital energies,^{2,3} there are other chemical properties which may provide a measure of such interactions. We wish to report the determination of the gas-phase basicities (proton affinities) of I and II in the absence of solvation phenomena using the techniques of ion cyclotron resonance spectroscopy⁴ and delineate the relationship between nitrogen lone pair interactions and thermodynamic parameters associated with amine basicity.

Gas-phase and solution basicities of I and II along



(1) R. Hoffmann, *Accounts Chem. Res.*, **4**, 1 (1971).

(2) D. W. Turner, A. D. Baker, C. Baker, and C. R. Brundle, "Molecular Photoelectron Spectroscopy," Wiley, New York, N. Y., 1970.

(3) This assumes that Koopmans' theorem is valid.

(4) For a recent review, see J. L. Beauchamp, *Annu. Rev. Phys. Chem.*, **22**, 527 (1971). Trapped ion techniques used in the present study are described in T. B. McMahon and J. L. Beauchamp, *Rev. Sci. Instrum.*, **43**, 509 (1972).

Table I. Thermodynamic Parameters Related to Amine Basicities^a

Species (B)	Solution ^b		Gas phase			
	pK _a	-ΔH _p , ^c kcal/mol	IP _a , ^d eV	IP _v , ^d eV	PA(B), ^e kcal/mol	D(B ⁺ -H), ^f kcal/mol
(CH ₃) ₃ N	9.80	8.82	7.82	8.50	226.6	93.3
(C ₂ H ₅) ₃ N	10.72	10.32	7.50	8.18	233.3	92.6
	11.15	11.14	7.69	8.02	233.7	97.4
	8.82	7.21	7.23	7.52	230.2	83.3

^a All data at 298°K. ^b Solution data taken from the recent critical survey of F. M. Jones III, Ph.D. Thesis, University of Pittsburgh, 1970. The data for diazabicyclooctane are from the study of P. Paoletti, J. H. Stern, and A. Vacca, *J. Phys. Chem.*, **69**, 3759 (1965). ^c Enthalpy of base protonation in aqueous solution. ^d Adiabatic (IP_a) and vertical (IP_v) ionization potentials. Data from ref 11-13; K. Watanabe, T. Nakayama, and J. Mottl, *J. Quant. Spectrosc. Radiat. Transfer*, **2**, 369 (1962); S. Craddock, E. A. V. Ebsworth, W. J. Savage, and R. A. Whiteford, *J. Chem. Soc., Faraday Trans. 1*, **68**, 934 (1972). ^e Proton affinity, defined in text. Free energy data for proton transfer equilibria were converted to enthalpy differences as described in ref 6. All data relative to PA(NH₃) = 207 kcal/mol. ^f Homolytic BH⁺ bond dissociation energy.



with trimethyl- and triethylamine are summarized in Table I. The gas-phase basicities are defined by the enthalpy change for reaction 1 and are readily measured



using previously described techniques.⁴⁻⁷ We have shown that homolytic bond dissociation energies, defined by the enthalpy change for reaction 2, are useful



in correlating basicities.^{4,7-9} In particular, we have demonstrated that the homolytic BH⁺ bond dissociation energies are constant for homologous series.^{7,9,10} For example, all tertiary aliphatic amines are found to have $D(\text{B}^+-\text{H}) = 93 \pm 1$ kcal/mol.⁷ Noteworthy, then, is the observation (Table I) that the homolytic BH⁺ bond dissociation energies of the tertiary bicyclic amines I and II are significantly different from the acyclic tertiary amines. The higher value for quinuclidine (97.4 kcal/mol) can be understood in terms of the preference which radical cations derived from aliphatic amines have for planar geometry.^{2,11} In the bicyclic ring system, relaxation to this configuration is greatly restrained. Even more striking is the case of diazabicyclooctane, where $D(\text{B}^+-\text{H})$ is 14 kcal/mol less than in the model compound quinuclidine. *This difference in BH⁺ homolytic bond dissociation energies for diazabicyclooctane compared to quinuclidine is, we feel, a direct*

manifestation and thus a direct "chemical" measure of the nitrogen lone pair interactions. The enthalpies of protonation do not themselves provide an indication of the interaction. The low BH⁺ homolytic bond dissociation energy may be attributed to the orbital interactions which lead to the splitting of the lone pairs into symmetric (n₊) and antisymmetric (n₋) combinations and result in the low first ionization potential of I.¹²⁻¹⁴ More simply stated, *the diazabicyclooctane radical cation is resonance stabilized, and comparison of the BH⁺ homolytic dissociation energies of I and II provides a measure of the resonance stabilization.*¹⁵

There are other examples which can be cited to support the conjecture that BH⁺ homolytic bond dissociation energies provide a measure of lone pair interactions. Using primary amines as a model, $D(\text{B}^+-\text{H})$ for hydrazine is 10 kcal/mol lower.¹⁶ Similarly, $D(\text{B}^+-\text{H})$ for *trans*-azomethane is 34.0 kcal/mol lower than $D(\text{B}^+-\text{H})$ for model immines.¹⁷ PES studies of lone pair interactions in hydrazine¹⁸ and azomethane¹⁹ reveal n₊ - n₋ splittings of 0.73 and 3.3 eV, respectively, to be compared with the n₊ - n₋ splitting of 2.13 eV for I.

The above results can be summarized along with the interesting implications they have relating to the reactivity of radical cations.

(1) Schemes which correlate gas-phase basicities with adiabatic ionization potentials by assuming constant BH⁺ homolytic bond dissociation energies in homologous series are useful for predicting unknown basicities.^{4,7,9} Deviations from such correlations, however, provide insight into alteration of the factors which

(5) D. H. Aue, H. M. Webb, and M. T. Bowers, *J. Amer. Chem. Soc.*, **94**, 4726 (1972); M. T. Bowers, D. H. Aue, H. M. Webb, and R. T. McIver, *ibid.*, **93**, 4313 (1971).

(6) E. M. Arnett, F. M. Jones, M. Taagepera, W. G. Henderson, J. L. Beauchamp, D. Holtz, and R. W. Taft, *J. Amer. Chem. Soc.*, **94**, 4724 (1972).

(7) W. G. Henderson, M. Taagepera, D. Holtz, R. T. McIver, J. L. Beauchamp, and R. W. Taft, *J. Amer. Chem. Soc.*, **94**, 4728 (1972).

(8) J. L. Beauchamp and S. E. Buttrill, *J. Chem. Phys.*, **48**, 1783 (1968).

(9) M. C. Caserio and J. L. Beauchamp, *J. Amer. Chem. Soc.*, **94**, 2638 (1972).

(10) This breaks down when rehybridization energies are not constant: J. L. Beauchamp, Ph.D. Thesis, Harvard University, 1967. For example, $D(\text{B}^+-\text{H})$ for ethylene oxide is ~10 kcal/mol higher than for strain-free oxiranes. Similar effects have been noted by D. H. Aue, S. M. Webb, and M. T. Bowers (unpublished results) for small ring nitrogen bases.

(11) A. B. Cornford, D. C. Frost, F. G. Herring, and C. A. McDowell, *Can. J. Chem.*, **49**, 1138 (1971).

(12) P. A. Bishoff, J. A. Hashmall, E. Heilbronner, and V. Horning, *Tetrahedron Lett.*, 4025 (1969).

(13) E. Heilbronner and K. A. Muszkat, *J. Amer. Chem. Soc.*, **92**, 3878 (1970).

(14) R. Hoffmann, A. Imamura, and W. J. Hehre, *J. Amer. Chem. Soc.*, **90**, 1499 (1968).

(15) This bears a direct analogy to the comparison of primary C-H bond energies in propylene and propane, the difference being utilized as a measure of resonance stabilization in the allyl radical: see, for example, Z. B. Alfassi, D. M. Golden, and S. W. Benson, *Int. J. Chem. Kinet.*, **6**, 155 (1973).

(16) R. H. Staley and J. L. Beauchamp, unpublished results.

(17) M. S. Foster and J. L. Beauchamp, *J. Amer. Chem. Soc.*, **94**, 2425 (1972). Measurements of the proton affinity and adiabatic ionization potential of azomethane have been recently refined: M. S. Foster and J. L. Beauchamp, unpublished results.

(18) K. Osafune, S. Katsumata, and K. Kimura, *Chem. Phys. Lett.*, **19**, 369 (1973); A. W. Potts, T. A. Williams, and W. C. Price, *Discuss. Faraday Soc.*, No. 54, 104 (1972).

(19) E. Haselbach and E. Heilbronner, *Helv. Chim. Acta*, **53**, 684 (1970).

affect the stability of B^+ relative to BH^+ . Lone pair interactions are one of the more intriguing origins of such deviations.

(2) A measure of the resonance stabilization afforded radical cations by lone pair interactions may be obtained from a comparison of their BH^+ homolytic bond dissociation energies to those of model compounds in which such interactions are absent.

(3) The stabilization afforded radical cations by lone pair interactions is manifest in the chemical reactivity of these species. It is thus significant that diazabicyclooctane, ¹⁶ hydrazine, ¹⁶ and azomethane ¹⁷ radical cations are unreactive with the parent neutral. This is in direct contrast to the behavior of the majority of nitrogen bases, where the radical cation reacts rapidly to form the protonated parent ²⁰ and is a direct consequence of the reduction of $D(B^+-H)$ to a value below carbon hydrogen bond dissociation energies in the neutral molecule.

Acknowledgment. This research was supported in part by the United States Atomic Energy Commission under Grant No. AT(04-3)767-8.

(20) It is interesting to note that in solution diazabicyclooctane undergoes reversible one-electron oxidation at a platinum electrode [S. F. Nelsen and P. J. Hintz, *J. Amer. Chem. Soc.*, **94**, 7114 (1972)] and is long enough lived to give a well-resolved esr spectrum [T. M. McKinney and D. H. Geske, *ibid.*, **87**, 3013 (1965)].

(21) Camille and Henry Dreyfus Teacher-Scholar, 1971-1976.

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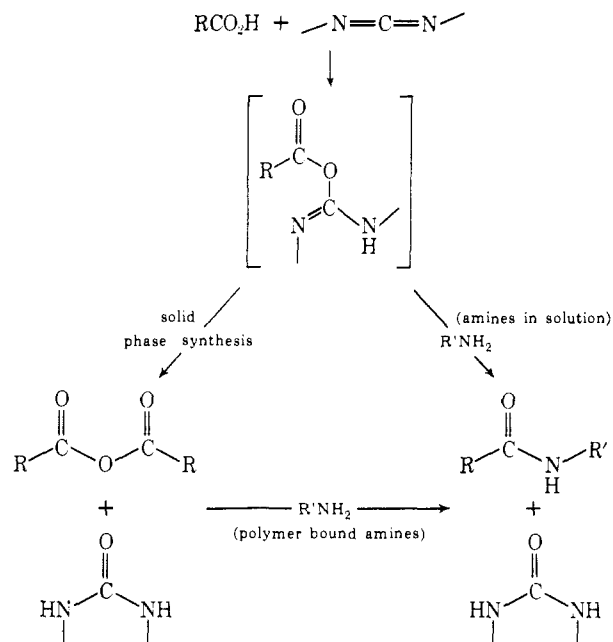
Mechanism of the Carbodiimide Reaction. II. Peptide Synthesis on the Solid Phase

Sir:

Recently we reported a mechanistic study of the reaction of carboxylic acids with amines mediated by *N,N'*-dicyclohexylcarbodiimide (DCC).¹ Our evidence indicated that the initial acylating agent in the DCC reaction was distinguishable from the carboxylic acid anhydride (Scheme I) under conditions normally encountered during peptide synthesis *in solution*. The *O*-acylisourea, as originally postulated by Khorana,² appears to be the actual acylating agent. We now present evidence that under the conditions of *solid phase* peptide synthesis³ the DCC reaction mechanism follows the alternate path and the actual acylating agent is the symmetrical anhydride.

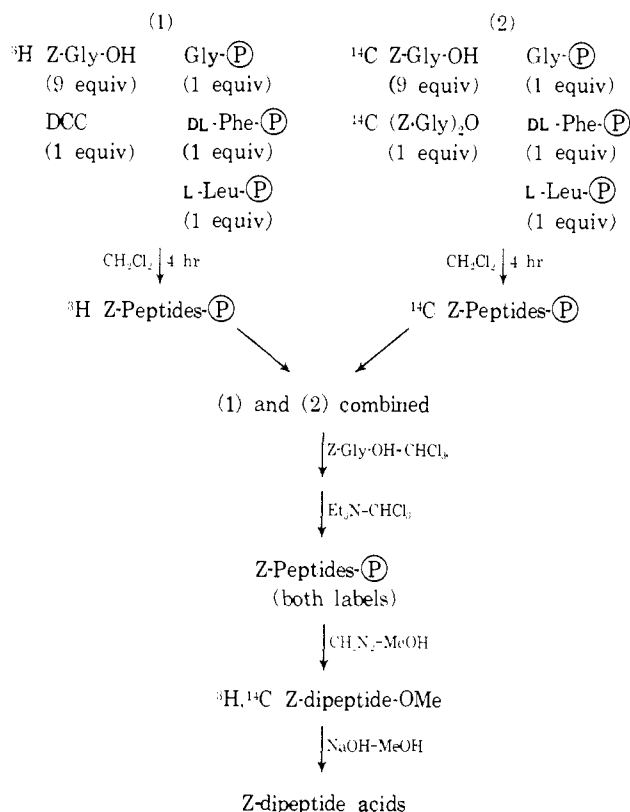
Merrifield resins⁴ were separately loaded with *tert*-butoxycarbonylglycine (0.52 mequiv/g), *tert*-butoxycarbonyl-DL-phenylalanine (0.34 mequiv/g), and *tert*-butoxycarbonyl-L-leucine (0.39 mequiv/g) then combined, N deblocked, and assayed according to standard procedures.⁵ Samples of the mixed resin were equilibrated with saturated (0.03 M) solutions of either (1) ³H or (2) ¹⁴C-labeled benzyloxycarbonylglycine (Z-Gly-

Scheme I



OH) in CH_2Cl_2 , according to the stoichiometry indicated in Scheme II. The suspensions were then treated

Scheme II



with limited amounts of DCC and anhydride, respectively, followed by shaking for 4 hr. The two resin batches were then combined, washed with $CHCl_3$ saturated with unlabeled Z-Gly-OH and 10% $Et_3N-CHCl_3$, and subjected to diazomethane catalyzed transesterification⁶ to liberate the peptides from the resin as their

(1) J. Rebeck and D. Feitler, *J. Amer. Chem. Soc.*, **95**, 4052 (1973).

(2) H. G. Khorana, *Chem. Ind. (London)*, 1087 (1955).

(3) R. B. Merrifield, *Advan. Enzymol.*, **32**, 221 (1969).

(4) Available from Calbiochem, San Diego, Calif.

(5) J. Stewart and J. Young, "Solid Phase Peptide Synthesis," W. H. Freeman, San Francisco, Calif., 1969.

(6) H. Bredereck, R. Siekeo, and L. Kamphenkel, *Chem. Ber.*, **89**, 1169 (1956). This somewhat obscure catalytic reaction is ideal for removing peptides from the polymer under essentially neutral conditions. Typically, the resin-bound peptide is over-layered with meth-