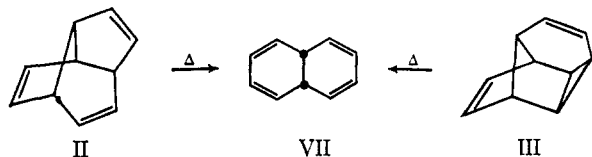


chemical rearrangements of this type are known,<sup>15</sup> and the rules of Woodward and Hoffmann<sup>16</sup> permit a concerted suprafacial shift of order [1,3]. Numerous possible paths for the production of III exist, none of them, it seems to us, attractive enough to warrant its selection over others. We will defer comment until later.

The assignment of structure to II allows identification of the last of the four photoproducts of *cis*-9,10-dihydronaphthalene reported by Doering and Rosenthal.<sup>3c,e</sup> These are bullvalene, naphthalene, V, and II.<sup>17</sup> The isolation of II from this reaction is perhaps best rationalized as the result of further photolysis of bullvalene, itself formed by irradiation of V.<sup>3d,18,19</sup> The primary product of the photolysis of *cis*-9,10-dihydronaphthalene seems to be V.<sup>3e</sup> Compound II is rapidly destroyed when it is irradiated, but small amounts of a pentacyclic hydrocarbon can be isolated.<sup>20</sup>

Both II and III can be added to the list of compounds (I-V) which are thermally converted to *cis*-9,10-dihydronaphthalene (VII). The conversion of III to VII is especially facile; heating at 120° for a few minutes suffices to complete the reaction. This finds analogy in the observation of Zimmerman<sup>14</sup> and others<sup>21</sup> that disubstituted III is rapidly converted to disubstituted naphthalenes. The reaction of II is slower, but pyrolysis in a flow system at greater than 280° yields VII cleanly. Pyrolysis of II in pentane at 100° serves to slowly destroy II, the products being naphthalene (from dehydrogenation of VII) and di- and tetrahydro-II. This provides a clue to the question



posed by Doering<sup>3c</sup> as to the fate of the hydrogen in the conversion of VII to naphthalene.<sup>22</sup>

(15) R. N. Warrener and J. B. Bremner, *Rev. Pure Appl. Chem.*, **16**, 117 (1966).

(16) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 2511 (1965).

(17) We thank these authors for spectra of the photoproducts of VII.

(18) U. Krüerke, *Angew. Chem.*, **79**, 55 (1967).

(19) P. Radlick, private communication.

(20) An indirect clue as to the structure of II appears as the pentacyclic hydrocarbon has two different vinyl hydrogens. All possible products of internal cyclization of VIII have but one kind of vinyl hydrogen. On the other hand, such a closure in II leads to XI, a structure fitting the nmr and tentatively suggested as that of the pentacyclic hydrocarbon.



(21) C. G. Krespan, B. C. McKusick, and T. L. Cairns, *J. Am. Chem. Soc.*, **83**, 3428 (1961).

(22) NOTE ADDED IN PROOF. Professor J. Meinwald and J. Labows have kindly informed us that they have found II to be one of the products formed on debromination of a mixture of dibromides obtained from the bromination of bullvalene.

Maitland Jones, Jr.

Department of Chemistry, Princeton University  
Princeton, New Jersey 08540

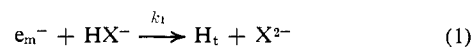
Received June 9, 1967

## Comparison of Solvated Electron Rates in Water and in Ice

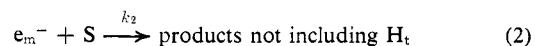
Sir:

In a recent communication the temperature dependence of solvated electron reactions with a variety of compounds was measured.<sup>1</sup> Although the specific rates for the different compounds varied over a range of 10<sup>5</sup>, the activation energy was found to be constant at 3.5 ± 0.4 kcal/mole, which is the activation energy for diffusion in water. Thus, entropic effects are responsible for the rate differences. We wish to report measurements on relative reaction rates of mobile electrons produced by  $\gamma$  irradiation of ice at 77°K. The relative reaction rates in ice at 77°K quantitatively parallel those in water at 300°K and support the conclusion that entropic effects are responsible for the rate differences.

We have previously shown<sup>2</sup> that radiation-produced mobile electrons,  $e_m^-$ , react with HSO<sub>4</sub><sup>-</sup> and H<sub>2</sub>PO<sub>4</sub><sup>-</sup> in 1 M frozen solutions at 77°K to yield trapped hydrogen atoms which can be measured by epr (eq 1). If a second



solute, S, which acts as an electron scavenger and which does not yield H<sub>t</sub> is added to the frozen solution a competition is set up (eq 2). A steady-state approximation



applied to [ $e_m^-$ ] yields the expression

$$\frac{G^0(\text{H}_t) - G(\text{H}_t)}{G(\text{H}_t)} = \frac{k_2[\text{S}]}{k_1[\text{HX}^-]} \quad (3)$$

where  $G^0(\text{H}_t)$  and  $G(\text{H}_t)$  are H<sub>t</sub> yields per 100 ev of radiation energy absorbed in the absence and presence of the scavenger. By plotting the left side of eq 3 against [S]/[HX<sup>-</sup>], a straight line through the origin is obtained with slope equal to  $k_2/k_1$ . A variety of electron scavengers, S, has been studied in this manner, and a consistent set of values is summarized in Table I.

Table I. Relative Rates of  $e_m^-$  Reactions with Solutes as Measured by Competition Kinetics of H<sub>t</sub> Yields in H<sub>2</sub>PO<sub>4</sub><sup>-</sup> or HSO<sub>4</sub><sup>-</sup> Ices

Solute (S)	Relative rates <sup>a</sup>	
	$k(e_m^- + \text{S}),$ 77°K	$k(e_{aq}^- + \text{S}),$ 300°K
Cd <sup>2+</sup>	38	52 <sup>b</sup>
Cu <sup>2+</sup>	26	27 <sup>b</sup>
CrO <sub>4</sub> <sup>3-</sup>	17	16 <sup>b</sup>
NO <sub>3</sub> <sup>-</sup>	(10)	(10) <sup>c</sup>
NO <sub>2</sub> <sup>-</sup>	5	4.2 <sup>c</sup>
CH <sub>3</sub> COCH <sub>3</sub>	3	5.3 <sup>c</sup>
Zn <sup>2+</sup>	1	1.5 <sup>b</sup>
ClCH <sub>2</sub> COO <sup>-</sup>	1	1.1 <sup>d</sup>

<sup>a</sup> All rates normalized to NO<sub>3</sub><sup>-</sup> rate = 10. <sup>b</sup> J. H. Baxendale, E. M. Fielden, and J. P. Keene, *Proc. Chem. Soc.*, 242 (1963).

<sup>c</sup> E. J. Hart, S. Gordon, and J. K. Thomas, *J. Phys. Chem.*, **68**, 1271, 1524 (1964). <sup>d</sup> M. Anbar and E. J. Hart, *ibid.*, **69**, 271 (1965).

The rates are relative to the arbitrary value of  $k = 10$  for X = NO<sub>3</sub><sup>-</sup>. Liquid-phase rates directly measured

(1) M. Anbar, Z. B. Alfassi, and H. Bregman-Reisler, *J. Am. Chem. Soc.*, **89**, 1263 (1967).

(2) L. Kevan, P. N. Moorthy, and J. J. Weiss, *ibid.*, **86**, 771 (1964); L. Kevan and C. Fine, *ibid.*, **88**, 869 (1965).

by pulse radiolysis are also given on the same relative scale. An absolute comparison of the rates in the two phases has not been made. The semiquantitative correlation of the rates for  $e_{aq}^-$  and  $e_m^-$  is extremely striking and supports the conclusion that entropic effects are responsible for the rate differences between different solutes. The correlation also implies that one may properly describe  $e_m^-$  as a mobile solvated electron in ice.

**Acknowledgment.** This research was generously supported by the Air Force Rocket Propulsion Laboratory and the U. S. Atomic Energy Commission. This is AEC Document No. C00-1528-15. We thank R. Lapple for some of the epr measurements.

Larry Kevan

Department of Chemistry, University of Kansas  
Lawrence, Kansas 66044

Received June 13, 1967

### Synthesis of Human Angiotensin I<sup>1,2</sup>

Sir:

Human angiotensin has recently been purified from the incubation mixture of human serum protein and renin.<sup>3</sup> The amino acid sequence of isolated human angiotensin appears to be identical<sup>4</sup> with that of horse angiotensin I,<sup>5</sup> *i.e.*, L-Asp-L-Arg-L-Val-L-Tyr-L-Ile-L-His-L-Pro-L-Phe-His-L-Leu, which has not been synthesized before. We wish to report the synthesis of this decapeptide and its identity with the human natural peptide in chemical and biological properties.

L-Leucine *p*-nitrobenzyl ester *p*-toluenesulfonate (I), mp 201–202°,  $[\alpha]^{22D} +10.2^\circ$  (ethanol), was prepared in 67% yield by heating a mixture of L-leucine, nitrobenzyl alcohol, toluenesulfonic acid, and benzene. *Anal.* Calcd for  $C_{20}H_{26}O_7N_2S$ : C, 54.78; H, 5.98; N, 6.39. Found: C, 54.42; H, 5.98; N, 6.41. Condensation of benzyloxycarbonyl-*im*-benzyl-L-histidine (II)<sup>6</sup> with I by the dicyclohexylcarbodiimide method<sup>7</sup> gave oily Z-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>) (III), 89%,  $R_f$  0.76.<sup>8</sup> Debonyloxycarbonylation of III with HBr in acetic acid yielded oily H-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>)·2HBr (IV), 95%,  $R_f$  0.76.<sup>8</sup> Condensation of II with H-Pro-Phe-OEt·HCl<sup>9</sup> by the dicyclohexylcarbodiimide method gave oily Z-His(*im*-Bzl)-Pro-Phe-OEt in 75% yield,  $R_f$  0.73,<sup>8</sup> which was treated with hydrazine to afford semicrystalline Z-His(*im*-Bzl)-Pro-Phe-NHNH<sub>2</sub> (V), 85%,  $R_f$  0.73.<sup>8</sup> Oily Z-His(*im*-Bzl)-Pro-Phe-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>),  $R_f$  0.84,<sup>8</sup> obtained in 46% yield from the azide derived from V with IV, was con-

verted to oily H-His(*im*-Bzl)-Pro-Phe-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>)·3HBr (VI), 95%,  $R_f$  0.76.<sup>8</sup> Condensation of benzyloxycarbonyl-O-benzyl-L-tyrosine<sup>10</sup> with L-isoleucine ethyl ester by the mixed anhydride method with isobutyl chloroformate<sup>11</sup> gave Z-Tyr(O-Bzl)-Ile-OEt (VII), 82%, mp 127–128°,  $[\alpha]^{20D} +10.7^\circ$  (acetic acid). *Anal.* Calcd for  $C_{32}H_{38}O_6N_2$ : C, 70.31; H, 7.01; N, 5.13. Found: C, 70.43; H, 7.03; N, 5.18. Hydrogenolysis of VII yielded oily H-Tyr-Ile-OEt·HCl (VIII), 94%,  $R_f$  0.77.<sup>8</sup> Condensation of benzyloxycarbonyl-L-valine with VIII by the mixed anhydride method<sup>11</sup> gave Z-Val-Tyr-Ile-OEt in 82% yield, mp 190–191°,  $[\alpha]^{22D} -20.2^\circ$  (acetic acid) (*Anal.* Calcd for  $C_{30}H_{41}O_7N_3$ : C, 64.84; H, 7.44; N, 7.56. Found: C, 64.68; H, 7.30; N, 7.75), which was converted to Z-Val-Tyr-Ile-NHNH<sub>2</sub> (IX) in 97% yield, mp 278–280°. *Anal.* Calcd for  $C_{28}H_{39}O_6H_5 \cdot 0.5H_2O$ : C, 61.07; H, 7.32; N, 12.71. Found: C, 60.98; H, 7.26; N, 12.59. Condensation of the azide derived from IX with VI yielded acyloctapeptide ester, Z-Val-Tyr-Ile-His(*im*-Bzl)-Pro-Phe-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>) (X), 34%, mp 130–134°,  $[\alpha]^{18D} -41.0^\circ$  (acetic acid). *Anal.* Calcd for  $C_{81}H_{95}O_{14}N_{13} \cdot H_2O$ : C, 65.17; H, 6.55; N, 12.20. Found: C, 65.06; H, 6.95; N, 12.05. Oily octapeptide trihydrobromide obtained from X in 97% yield,  $R_f$  0.60,<sup>8</sup> was condensed with a mixed anhydride<sup>11</sup> of benzyloxycarbonyl-nitro-L-arginine<sup>12</sup> to yield Z-Arg(NO<sub>2</sub>)-Val-Tyr-Ile-His(*im*-Bzl)-Pro-Phe-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>) (XI), 78%, mp 138–142°,  $[\alpha]^{18D} -32.5^\circ$  (acetic acid). *Anal.* Calcd for  $C_{87}H_{106}O_{17}N_{18} \cdot 6H_2O$ : C, 58.57; H, 6.67; N, 14.13. Found: C, 58.29; H, 6.57; N, 14.44. Coupling of oily nonapeptide trihydrobromide, obtained from XI in 96% yield, with a mixed anhydride<sup>11</sup> of benzyloxycarbonyl-β-benzyl-L-aspartic acid<sup>13</sup> yielded Z-Asp(β-Bzl)-Arg(NO<sub>2</sub>)-Val-Tyr-Ile-His(*im*-Bzl)-Pro-Phe-His(*im*-Bzl)-Leu-OBzl(NO<sub>2</sub>) (XII), 79%, mp 140–144°,  $[\alpha]^{18D} -30.0^\circ$  (acetic acid),  $R_f$  0.90.<sup>8</sup> *Anal.* Calcd for  $C_{98}H_{117}O_{20}N_{19} \cdot 6H_2O$ : C, 59.17; H, 6.54; N, 13.39. Found: C, 58.82; H, 6.34; N, 13.38. XII (200 mg) in a solvent of methanol-acetic acid-water (60:20:15) was hydrogenated with palladium black at room temperature for 48 hr.<sup>14</sup> The filtrate from the catalyst was evaporated, and the residue, 130 mg, was collected with the aid of a mixture of acetone and ether. This material was purified by subsequent column chromatography using carboxymethylcellulose, DEAE-Sephadex A-25, and Bio-Gel P-2 which have proved to be most effective in isolating natural human angiotensin I.<sup>4</sup> The active fractions from the Bio-Gel column with 0.1 N acetic acid as a developing solvent were lyophilized, leaving a white powder, 8.6 mg; amino acid ratios in acid hydrolysate, were Asp<sub>0.98</sub>-Arg<sub>1.03</sub>Val<sub>1.12</sub>Tyr<sub>0.88</sub>Ile<sub>0.92</sub>His<sub>1.98</sub>Pro<sub>1.10</sub>Phe<sub>1.03</sub>Leu<sub>1.06</sub>. In-

(1) This work was supported in part by U. S. Public Health Service Grant No. HE 09429-02.

(2) The abbreviation followed are from *J. Biol. Chem.*, **241**, 2491 (1966): Z, benzyloxycarbonyl; Bzl, benzyl; OBzl(NO<sub>2</sub>), *p*-nitrobenzyl ester; NHNH<sub>2</sub>, hydrazide.

(3) K. Arakawa, M. Nakatani, and M. Nakamura, *Nature*, **214**, 278 (1967).

(4) K. Arakawa, M. Nakatani, A. Minohara, and M. Nakamura, *Biochem. J.*, in press.

(5) K. E. Lentz, L. T. Skeggs, Jr., K. R. Wood, J. R. Kahn, and N. P. Shumway, *J. Exptl. Med.*, **104**, 183 (1956).

(6) B. G. Overell and V. Petrow, *J. Chem. Soc.*, 232 (1955).

(7) J. C. Sheehan and G. P. Hess, *J. Am. Chem. Soc.*, **77**, 1067 (1955).

(8) The  $R_f$  on thin layer chromatography refers to the system 1-butanol-acetic acid-pyridine-water (4:1:1:2, v/v). Compounds possessing a free amino group were detected by spraying with ninhydrin, and those with a blocked amino group by spraying with 47% hydrobromic acid and then with ninhydrin.

(9) N. Izumiya and J. Fruton, *J. Biol. Chem.*, **218**, 59 (1956).

(10) E. Wunsch, G. Fries, and A. Zwick, *Chem. Ber.*, **91**, 5421 (1958).

(11) J. R. Vaughan, Jr., and R. L. Osato, *J. Am. Chem. Soc.*, **74**, 676 (1952).

(12) M. Bergmann, L. Zervas, and H. Rinke, *Z. Physiol. Chem.*, **224**, 40 (1934).

(13) N. Izumiya, H. Uchio, and T. Yamashita, *J. Chem. Soc. Japan*, **78**, 420 (1958).

(14) The reaction was followed at various times with the chromatographic properties and the bioassay of the pressor activity, and the highest activity was observed after the hydrogenation of some 48 hr. However, chromatography indicated that the considerable part of the imidazolyl benzyl groups remained untouched, and this fact might be one of the reasons that the yield of pure product (8.6 mg) was poor. Treatment of the hydrogenated material of XII with sodium-liquid ammonia did not give a product bearing strong pressor activity.