Table I. The Fractional Population of Various Amino Acids in Different Ionization States (at room temperature)

Amino acid (β-substituent)	pD	Ionization state	$J_{\alpha\beta_1}$	$J_{\alpha\beta_2}$	P_I	P_{II}	P_{III}
Ser	0.4	+	4.20	3.40	0.15	0.07	0.78
(OH)	7.5	+−	5.70	3.64	0.28	0.10	0.62
	12.2	−	5.91	4.25	0.30	0.15	0.55
Asp	0.4	+	6.37	4.16	0.34	0.16	0.50
(COOH)	5.8	+−−	8.75	3.83	0.56	0.09	0.35
	12.3	−−	9.85	3.99	0.66	0.12	0.22
Asn	1.1	+	6.91	4.20	0.39	0.15	0.46
($CONH_2$)	5.0	+−	8.03	3.97	0.50	0.13	0.38
	12.3	−	9.05	4.65	0.59	0.19	0.22
AspOMe	0.4	+	6.48	4.52	0.36	0.17	0.47
($COOCH_3$)	6.9	+−	7.06	4.44	0.41	0.17	0.43
	12.1	−	7.55	5.37	0.45	0.25	0.30
Phe	0.4	+	7.65	5.65	0.46	0.28	0.26
(phenyl)	7.1	+−	7.90	5.20	0.48	0.24	0.28
	12.5	−	7.53	5.42	0.45	0.26	0.29
Tyr	0.2	+	7.65	5.45	0.46	0.26	0.28
(hydroxy	5.2	+−	8.01	4.89	0.49	0.21	0.30
phenyl)	11.9	−−	7.63	4.97	0.46	0.22	0.33

uents into the same spatial area.[10] This effect is clearest for Ser, in which about 80% of the molecules exist in III at low pD.[8] However, in the case of Phe and Tyr, P_{III} is not the largest, presumably because the strong steric hindrance between the bulky phenyl or the hydroxyphenyl group and the carboxylate and/or amino group become more important.[11]

A marked increase of P_I was observed for Asp, Asn, and AspOMe, accompanied by the decrease of P_{III}, at higher pD's. These changes occurred in two steps, which correspond to the ionization state changes. From a closer look at the data we might conclude that the first change corresponds to the coulombic repulsion between the α-carboxylate anion and either the β-carboxylate anion (Asp), the carboxyamide (Asn), or the carboxymethyl (AspOMe) group. A further increase of I in alkaline solutions can be explained by a favorable coulombic interaction in III between the ammonium cation and the β-substituents at neutral pD, this is eliminated by the deprotonation of the ammonium group. The appreciable differences in P_I for these three compounds in alkaline solutions might indicate that the electrostatic repulsion between the α-carboxylate and the β-substituents decrease in the following order: $COO^- > CONH_2 > COOMe$.

The same arguments can be made for Ser. In this case, however, a charge repulsion between the α-carboxylate and the hydroxyl group is not strong enough to be an overwhelming factor for determining the population of each rotamer. The population profiles of Phe and Tyr are very similar, and do not greatly depend on pD's as expected for steric repulsion.

The above discussions about the factors responsible for the conformational energy in aqueous solution can be summarized as follows: (I) a tendency for large groups to be close, due to the water structure, (II) coulombic interactions (possibly including hydrogen bonding) among charged (polar) groups, either attractive or repulsive, (III) steric hindrance arising from large substituents. Which of these dominates strongly depends on the pD, temperature, ionic strength, and presumably many other parameters. Obviously the population changes must not in general be analyzed based on a single one of these factors.

This preliminary account of the conformational analysis of amino acids clearly demonstrates that by specific deuteration a better understanding of the intra- and inter (solute-solvent, solute-solute) molecular interactions which determine the structure in solution can be obtained. A full account of these and further results will be published shortly.

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(7) A racemic mixture of (2*S*,3*S*)- and (2*R*,3*R*)-[3-^{2}H]Ser was prepared by a previously reported method for [^{15}N]Ser (P. Stetter, Jr., *J. Biol. Chem.*, **144**, 501 (1942)). We employed a catalytic hydrogenation for reducing the precursor olefin, of which geometry was deduced by comparing the $J_{H-^{13}C}$ (H—C═C—C) value with those from model compounds.
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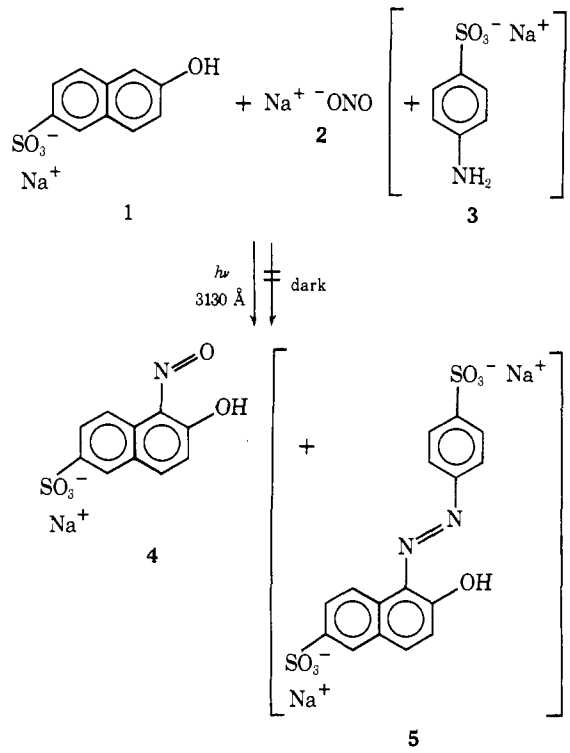
Utilization of Excited State p*K*'s to Initiate a Ground State Chemical Reaction

Sir:

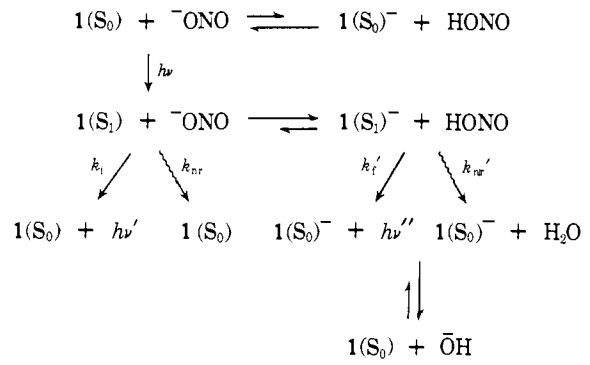
The physicochemical properties of molecular photoexcited states are often quite different from those of the ground state due to a change in electron distribution upon electronic excitation.[1] Acidity constants, for example, for electronically excited molecules[2-5] have been observed to vary considerably from that of the molecular ground state. In the case of 2-naphthol an increase in acidity of six orders of magnitude has been observed[4,6] as a result of electronic excitation. To date, however, the utilization of this enhanced acidity of excited state species to initiate a bimolecular ground state chemical reaction has not been reported.

We have now observed the initiation of a ground state chemical reaction as a direct consequence, we believe, of the enhanced acidity of the excited singlet state of several hydroxy aromatic compounds. Nitrosation and diazo coupling reactions of sodium 2-naphthol-6-sulfonate (1- and 2-naphthol, as well as phenols) in neutral aqueous solution (EtOH-H_2O for naphthols) have been initiated photochemically in the presence of sodium nitrite. The reaction sequence (aqueous solution, pH 7.0) is presented in Scheme I. The nitrosation and diazo coupling reaction, which do not take place in the dark at constant pH, require the presence of nitrous acid (pK = 3.37 (12.5°) H_2O) which reacts with **1** to produce **4**. Sodium nitrite serves both to increase the rate of deprotonation of the naphthol excited state[7] by means of general acid-base catalysis as well as being a reactant. In the presence of the aromatic amine (**3**) an arylazonaphthol (**5**) is formed either by the direct reaction of **3** on **4** or the

Scheme I



Scheme II



diazotization of **3** and subsequent reaction with **1**. The photochemically induced nitrosation and arylazonaphthol formation have been achieved both in solution (i.e., H_2O, EtOH-H_2O) in quartz optical cells (in the presence of O_2 and in N_2 purged samples) as well as in polymer films (e.g., polyvinylpyrrolidone) using a variety of 4-substituted phenylanilines (i.e., Br, CN, NO_2) and 6-substituted 2-naphthols (i.e., $SO_3^-Na^+$, $CO_2^-Na^+$) either with sodium nitrite or isopentyl nitrite. The naphthol derivative is selectively excited with either 3000 Å light using a Rayonet photochemical reactor or 3130 Å light using a high pressure Hg arc with an interference filter (Jena Glass, Mainz, Germany). The 1-arylazo-2-naphthols and 1-nitroso-2-naphthols formed photochemically were characterized by comparison of their physical constants (i.e., melting point and ir and uv spectra) with the literature values.[8-11] Photonitrosation of 1-naphthol, phenol, and phenol derivatives has also been observed. In the case of phenol 2537 Å light was employed as the exciting irradiation. The photoreactions were normally carried to only 10–20% completion due to interference from light absorption by the photoproduct(s).

Scheme II describes schematically in a more specific manner the photochemically induced production of acid in H_2O (pH 7.0). As a consequence of electronic excitation compound **1**, which exists predominantly in its protonated form in its ground state, **1** (S_0), is rapidly deprotonated in the presence of nitrite ion producing a local increase in the concentration of nitrous acid. Deactivation of the excited singlet by radiative (k_f) and nonradiative processes (k_{nr}) as well as intersystem crossing to the excited triplet state competes with protonation of **2**. Deactivation of the singlet state naphtholate anion **1** (S_1) by radiative or nonradiative processes to the more basic ground state anion results in proton abstraction from water and production of hydroxide anion when H^+ in the form of H_3O^+ or HONO has been consumed by chemical reaction. The pH of an unbuffered reaction mixture has been observed to increase as the photochemical reaction proceeds and the process becomes self-limiting.

The quantum efficiency (ϕ) for the production of **4** in K_2HPO_4-NaOH buffered aqueous solution (pH 7.0) at 25° with **1** and **2** in 1.0×10^{-3} *M* concentration was found to be $\sim 10^{-4}$. Radiative and nonradiative decay modes of the excited singlet state of **1** appear to compete effectively with proton transfer under these conditions.

The position of nitrosation on the naphthol and phenol derivatives was that typically found for the reaction of nitrous acid with the ground state of the hydroxy aromatic. That is to say that 1-nitroso-2-naphthol and 4-nitrosophenol were the primary photoproducts formed when 2-naphthol and phenol were photolyzed in the presence of sodium nitrite, respectively. The position of nitrosation indicates to us that the increase in nitrous acid concentration and not the increase in naphtholate anion concentration is primarily responsible for the observed photoreaction. Chemical reactions involving the electronically excited naphtholate anion would be expected to occur mainly at positions other than the 1 position.[12]

We conclude then that the photochemical induced nitrosation and azo coupling are a direct consequence of the enhanced acidity of the 2-naphthol, for example, derivative upon photoexcitation from the ground state ($pK(S_0) \simeq 9.5$)[4] to the excited singlet state ($pK(S_1) \simeq 3.1$)[4] producing a local increase in acidity which allows protonation of nitrite ion. The much lower acidity of the lowest triplet state of 2-naphthol ($pK(T_1) \simeq 8.1$)[4] as well as the absence of oxygen quenching suggests that the triplet state does not contribute significantly to the photonitrosation process.[4,5b]

In summary, we have demonstrated an excited state acid catalyzed bimolecular reaction. We believe that this is the first report of such a reaction sequence and consider that extension of the principle could develop into a fruitful and exciting research area.

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