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REVERSAL OF THE EFFECT OF PRESSURE ON THE PRODUCT RATIO IN THE ALKYLATION OF AN AMBIDENT ANION AS A RESULT OF ION-PAIRING[1]

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One of the more useful generalizations that can be employed to interpret the effect of numerous variables on the rates and product ratios of ambident anion alkylations is that free anions tend to be attacked at the more electronegative position, and that their association with either counterions or protic solvent molecules tends to change the alkylation ratios in the opposite direction. Numerous references can be cited to other chemists who have made similar suggestions and to the various experimental facts supporting them.[3] We now wish to call attention to the following recent developments which in conjunction allow an unusual prediction to be made to test the basic concept.

One of these is that hydrostatic pressure tends to favor alkylation at the less electronegative site in protic solvents,[4] presumably because hydrogen bonding is characterized by a volume decrease,[5] so that the most highly charged site becomes more tightly bound by the solvent[6] at high pressure.

A development of great interest in this connection is a paper by Smith and Milligan,[7] who found, in support of the general concept, that ion-pairing tended to decrease the O/N product ratio in the methylation of sodium fluorenone oximate. Both conductance and rate measurements were made, and a quantitative correlation was deduced on the basis of which it could be calculated that the O/N ratio should be 1.85 for the free anion and 0.43 for the sodium oximate ion-pair. Recently Smith and Hanson[8] strengthened this interpretation by showing that in the presence of large cyclic polyether molecules (which effectively remove the cations) the O/N ratio becomes equal to 1.85, whereas in the presence of sodium tetraphenylborate (which strongly suppresses the dissociation), the ratio can be decreased to as little as 0.67.

A third development has been the recent finding that electrostatic pressure causes a very large shift in the ion-pair - free ion equilibrium in organic solvents, in favor of dissociation.[9]

A combination of these findings suggests that hydrostatic pressure should have an effect on the O/N ratio in the methylation of sodium fluorenone oximate under the Smith-Milligan conditions opposite to that hitherto observed in all other ambident anion alkylations in protic solvents.

Because of its rapid rate, the reaction was carried out under pressure in a vessel similar to that designed by Eckert,[10] which permits the mixing of reagents after they have been compressed and allowed to reach thermal equilibrium. Furthermore, because the solvent is a *t*-butanol-acetonitrile mixture (2:1 volume ratio) solidifying at about 1500 atm at 25.0°, we were limited to this rather small pressure range. Our pressure apparatus has been described previously.[4b] In each experiment the reaction was allowed to go to completion, as was easily shown by titration with standard acid. The analysis was similar to the UV method used by Smith;[7] since nitrones are known[11] to be light sensitive, care was taken to reduce exposure of the solutions to light to a minimum. All experiments were carried out at least in duplicate; the product ratios given in the Table are accurate and reproducible to ±1% with the exception of the experiment involving the oximate at its lowest concentration, which is a little less precise.

The results obtained are in excellent agreement with those predicted. Our atmospheric pressure data are in good agreement with those of Smith and Milligan:[7] at high dilution the limiting value is reached, and at higher concentration or in the presence of sodium iodide, ion-pairing decreases the O/N ratio. The free ion value is

THE O/N RATIO IN THE
ALKYLATION OF SODIUM FLUORENONE OXIMATE AT 25.0°
AT VARIOUS PRESSURES

- - - Concentrations in moles/l - - -			- - - Pressures in Kbar - - -			
"Oximate"	CH_3I	NaI (init.)	0.001	0.483	0.966	1.380
0.00098	0.0063	0	1.94	---	---	1.75
0.042	0.22	0	0.96	0.98	0.99	1.05
0.065	0.22	0	0.93	0.94	0.97	1.00
0.065	0.13	0	0.93	0.97	0.97	1.01
0.069	0.13	0	0.93	---	---	1.00
0.069	0.22	0	0.92	---	---	1.00
0.083	0.22	0	0.90	0.92	0.93	0.96
0.083	0.13	0	0.90	---	---	0.96
0.087	0.22	.094	0.79	---	---	0.89
0.087	0.22	.063	0.83	---	---	0.90

decreased by the application of pressure in the normal manner;[4] yet, *at those concentrations at which ion-pairing is important, the ratio is increased under pressure.* The only reasonable interpretation of this observation is that pressure results in a shift from paired to free ions, and as a result the O/N ratio becomes larger rather than smaller as has been observed in all other instances recorded to date in protic solvents.[12] This effect of pressure therefore is consistent with the proposition that *free* ambident anions tend to be alkylated at the site of the most electronegative atom.

The effect of pressure on the product ratio in the presence of sodium iodide is also predictable; which way it goes depends on the volume changes involved in the association of sodium ions with the two negative ions present. The data suggest that pressure affects the O/N ratio somewhat more when sodium iodide is present than in its absence, hence that it affects the association constant for sodium iodide somewhat less than that of the oximate. This is undoubtedly due to the large radius of the iodide ion.[13]

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