HYDRO-PERFLUOROALKYL PYRIMIDINYL NITROXIDES

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Abstract—Twenty-two polysubstituted 2-aminopyrimidines dissolved in F113 (CCIF2-CCl2F) solutions containing ([H(CF2CF2)nCO2I2, n = 1,2] and H(CF2CF2)nNO [-> H(CF2CF2)n* + NO] have been oxidized into detectable α-H-perfluoroalkyl pyrimidinyl nitroxides along with neutral products. A mechanism involving H-abstraction from the amino groups by H(CF2CF2)nN(O')(CF2CF2).H and the subsequent radical steps was suggested for the generation of the nitroxides. Some relationships between a_n values and the nature of the ring substituents are discussed.

INTRODUCTION

Highly biologically active substituted 2-aminopyrimidines are widely used as intermediates in the synthesis of pyrimidinyl sulfa-drugs and thiophenesulfonyleurea herbicides. In the last few years, Xue and coworkers have synthesized a large number of polysubstituted 2-aminopyrimidines via condensation of guanine with dicarbonyl compounds and nucleophilic substitution at pyrimidine nucleus [1].

Though the polysubstituted 2-aminopyrimidines are similar to the substituted anilines, these two kinds of aromatic amines behave quite differently in the oxidation by per(poly)fluorodiacyl peroxides (R_xCO_2)(FAP) in F113 solutions. In the case of p-substituted anilines, α-hydro-p-substituted phenyl nitroxides Y-C_6H_4N(O')H were generated along with the major neutral products Y-C_6H_4NHR and R_xCO_2H [2]. Apparently, all evidence supports an electron transfer mechanism. The EPR parameters of the nitroxides [Y-C_6H_4N(O')H] agree with those recorded in other reaction systems such as the reduction of nitrobenzene by LiAlH_4 [3].

Differing from our expectation, in F113 solutions of FAP, polysubstituted 2-aminopyrimidines were not converted into α-hydro polysubstituted pyrimidinyl nitroxides as the
EPR detectable products: instead they have been oxidized by F113 solutions containing the most reactive nitroxides R_N(O')_R, the spin trap R_fNO and molecular oxygen. Now we report our EPR studies of these radical processes.

RESULTS AND DISCUSSION

The twenty-two polysubstituted 2-aminopyrimidines studied are generally represented by the following formula:

\[
\begin{align*}
\text{H}_2\text{N} & \quad \text{N} \quad \text{X} \\
& \quad \text{N} \quad \Downarrow \quad \text{Z}
\end{align*}
\]

In a typical experiment, about 10 mg of crystalline polysubstituted 2-aminopyrimidine was dissolved in ~0.2 ml of F113 in an EPR tube. A 0.2 ml blue solution containing R_fN(O')_R and R_fNO in F113 was dropped into the tube; after shaking for several minutes, the tube was inserted into an EPR cavity maintained at room temperature (about 10 °C). Well resolved EPR spectra and their stick diagrams of two representative nitroxides 17 and 21 are shown in Figure 1. The structures of 22 newly observed fluorinated nitroxides are characterized by the numbers of the various equivalent magnetic nuclei, i.e., 1N(nitroxyl), 2F(at b-carbon), 2N(pyrimidinyl ring) and 2F(at g-carbon) and their respective hyperfine splitting constants, a_N(nitroxyl), a_F^b, a_N^ring, a_F^g. Their general structure should be:

\[
\begin{align*}
\text{H(CF}_2\text{CF}_2)_n \text{N(O')} & \quad \text{N} \quad \text{X} \\
& \quad \text{N} \quad \Downarrow \quad \text{Z}
\end{align*}
\]

As seen from the stick diagrams and Table 1, the nitroxides bearing the H(CF_2CF_2)_2 group possess a_N(nitroxyl)(9.26 ~ 10.08 G) and a_F^b(2F, 14.64 ~ 16.74 G) values characteristic of aryl polyfluoroalkyl nitroxides [4]. Compared to the nonfluorinated analogues (with a_N about 10.5 - 13.5 G [5]), their much reduced a_N values are due to the significant electron-withdrawing effect from nitroxy N-atoms by the strongly electronegative R_f groups.

The interaction of two b-F atoms with the unpaired spin does not much effect the structures of the pyrimidinyl rings on the other side, so that, the a_F^b(2F) values are very similar to those of the nitroxides R_fN(O')Ar reported in our previous work [6].

Interestingly, the two nitroxides bearing HCF_2CF_2 groups, have particularly high a_N(nitroxyl) values, 11.63 and 11.71 G, respectively. As we have rationalized previously [7],