RESULTS AND DISCUSSION

Figure 2 displays the compounds used for the study. The compounds were used to determine which electrostatic charge at the N7 position is best correlated with the rate of glycosidic bond cleavage. The structural and electronic features of each compound were investigated through the implementation of the Spartan molecular volume spreadsheet function. Molecular volumes for each compound were calculated by determining the volume of the compound and then summing the volumes of its individual atoms. The molecular volume is then found to be correlated with the rate of glycosidic bond cleavage, R2 = 0.8638. These results imply that the steric environment imposed at the N7-position by molecules that impose a longer glycosidic bond might be expected to induce the depurinating event quickly. This is consistent with the notion that electrophiles cause the glycosidic bond between the base and the sugar to weaken. As bonds weaken, they grow longer in length. Thus, a larger ligand could cause a weakening of the glycosidic bond. In summary, with the compounds shown in Figure 2, the rate of glycosidic bond cleavage is best predicted by the size of the ligand at the N7-position. A larger ligand could cause a weakening of the glycosidic bond. In summary, with the compounds shown in Figure 2, the rate of glycosidic bond cleavage is best predicted by the size of the ligand at the N7-position.

CONCLUSIONS

Recent studies have highlighted the importance of N7-adducted guanines and the T1/2 for depurination in DNA of some species and is stable compared to other N-7 adducted guanines. Chemical modifications of the N7-position of guanine to electron withdrawing groups or electron donating groups help to weaken the glycosidic bond. Modifications at the N7-position can affect the rate of glycosidic bond cleavage, R2 = 0.599. These results imply that the steric environment imposed at the N7-position by molecules that impose a longer glycosidic bond might be expected to induce the depurinating event quickly. This is consistent with the notion that electrophiles cause the glycosidic bond between the base and the sugar to weaken. As bonds weaken, they grow longer in length. Thus, a larger ligand could cause a weakening of the glycosidic bond. In summary, with the compounds shown in Figure 2, the rate of glycosidic bond cleavage is best predicted by the size of the ligand at the N7-position. A larger ligand could cause a weakening of the glycosidic bond. In summary, with the compounds shown in Figure 2, the rate of glycosidic bond cleavage is best predicted by the size of the ligand at the N7-position.

ACKNOWLEDGEMENTS

Portions of this project were funded by an NSF STEP grant, NSF-0336462.