Molecular Modeling: Cycloaddition

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1 Introduction

1.1 Purpose

Determine the favored product of a 1,3-dipolar cycloaddition of benzonitrile oxide (BNO) and styrene if the reaction was under thermodynamic control and if the reaction was under kinetic control using Spartan Student Version 9.
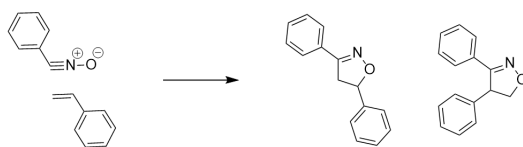

Figure 1: Net reaction of BNO and styrene and the possible product, 3,5 diphenylisoxazoline and 3,4 diphenylisoxazoline.

1.2 References

McQuarrie, D. A.; Simon, J. D. *Physical Chemistry: A Molecular Approach*; University Science Books: Sausalito, CA, **1997**.

Wiser, D.; *Determining regioselectivity of a 1,3-dipolar cycloaddition using molecular modeling*; Lake Forest College: Lake Forest, IL, **2020**; pp 1-3.

Spartan Student Ver. 9. Wavefunction: 18401 Von Karman Ave Irvine, CA, 2025. `https://store.wavefun.com/product_p/spstudent.htm`

1.3 Safety Information

There are no safety risks associated with this experiment.

2 Methods

The reactants, BNO and styrene, and the two possible products, 3,4 diphenylisoxazoline and 3,5 diphenylisoxazoline, were modeled using the Spartan Student Version 9 software. The energies of diphenylisoxazoline and 3,5 diphenylisoxazoline, as determined by a Hartree-Fock calculation with a 6-31G* base set in Spartan Student Version 9, were compared. This was used to simulate a reaction under thermodynamic control. Highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) surfaces were added to BNO and styrene. The molecules were aligned in a reaction position and the overlap HOMOs and LUMOs were observed.

3 Results/Data

3.1 Thermodynamics

Table 1: Energy and energy differences of optimized 3,4 diphenylisoxazoline and 3,5 diphenylisoxazoline.

	Energy (HF)	Energy (kcal/mol)	Ratio (%)
3,4	-704.84782	-	0
3,5	-704.854349	-	100
ΔE	0.006574	4.125	-

The change in enthalpy was assumed to be the same for forming each product ($\Delta S = 0$), so $\Delta H \approx \Delta E$. The difference seemed to be small in HF so the units were converted using the 1 HF = 627.5 kcal/mol. $\Delta E > 2.5$ kcal/mol, indicating that the 3,5 product, would be the only one formed.

3.2 Kinetics

There was better overlap between the HOMO and LUMO in the configuration that led to the 3,5 product (Fig. 2). There was also steric hindrance between the phenyl rings in the configuration that would lead to the 3,4 product.
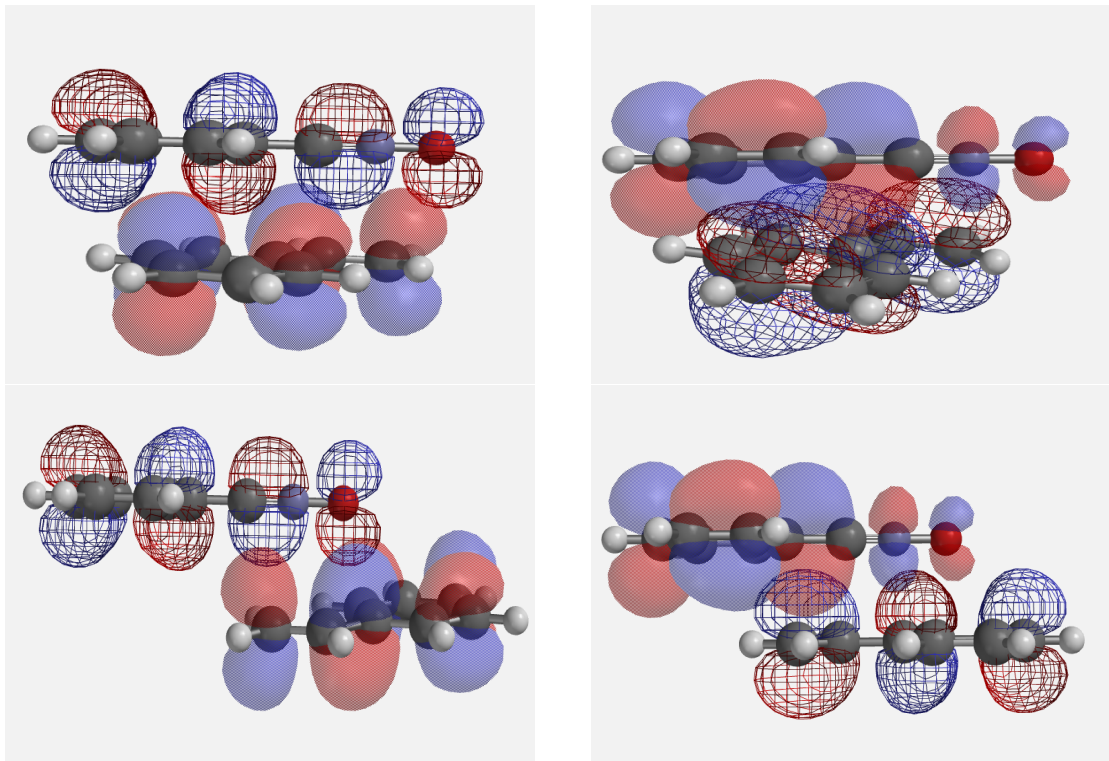

Figure 2: HOMO (mesh) and LUMO (transparent) overlap of BNO and sytrene in the formation of the 3,4 product (top) and the 3,5 product (bottom).

4 Conclusion

In a 1,3-dipolar cycloaddition of BNO and styrene, 3,5 diphenylisoxazoline is favored over 3,4 diphenylisoxazoline when the reaction is under thermodynamic control and when the reaction is under kinetic control. Under thermodynamic control, 3,5 product was lower in energy and under kinetic control, the HOMO-LUMO overlap was better and the steric effects were reduced.