

ACTIVE RECEPTORS IN THE NUCLEOPHILIC ADDITION OF PYRROLIDINE TO ACRYLAMIDE

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Abstract- Three amide receptors which show significant catalytic activity in the nucleophilic addition of pyrrolidine to acrylamide have been prepared. Additional hydrogen bonds and charge-transfer in the transition state are invoked to explain the catalytic effect.

Complexes in which the association constant is higher in the transition state than in the ground state should show catalytic activity, as pointed out by Pauling.¹ This is a very attractive possibility for the development of artificial enzymes because no active groups are required and, consequently, synthesis is kept easy.

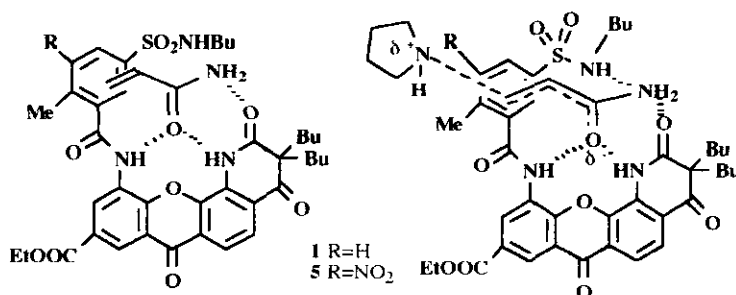


Figure 1: Proposed structures for the acrylamide complex and a possible transition state.

Amide enolates show pyramidalized nitrogen atoms in their X-ray structures² which undergo strong hydrogen bonding. An amide receptor capable of setting this kind of hydrogen bond could show catalytic activity in reactions whose transition state is enolate-like, since only during the reaction will the amide nitrogen pyramidalize, yielding a new hydrogen bond and therefore leading to a stronger complex.

The heterocyclic receptor (1) (Figure 1) is suitable for binding acrylamide ($2.8 \times 10^2 \text{ M}^{-1}$). The ground state complex is essentially formed due to three hydrogen bonds. However, if the amide nitrogen pyramidalizes an

additional hydrogen bond could be set with the sulfonamide residue in the receptor, the hydrogen bonds in the complex increasing to four. Receptor (1) is indeed able to catalyze the nucleophilic addition of pyrrolidine to acrylamide, while compound (2) (Figure 2) shows almost no activity (Table 1).

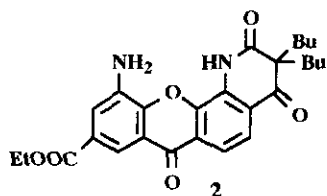


Figure 2

Receptor	K _s (M ⁻¹)	t _{1/2} (min)
1	2.8 × 10 ²	40
3	2.1 × 10 ⁴	35
5	3.0 × 10 ³	25

Table 1: Association constants of receptors with acrylamide and reaction half lives in the presence of pyrrolidine at 20 °C. Receptor 0.03 M, acrylamide 0.3 M and pyrrolidine 0.33 M. Reaction half life in the absence of receptor: 150 min

Receptor (3) (Figure 3) shows a slightly better catalytic activity in this reaction (Table 1). This compound is a far better acrylamide binder than receptor (1) (2.1 × 10⁴ M⁻¹). Probably, the sulfonamide group hinders the guest in the receptor (1) complex; however, the main advantage of 3 lies in the charge-transfer effect from the acrylamide to the dinitrotoluic residue.³

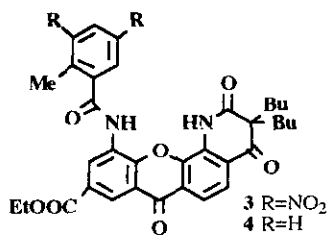


Figure 3

This effect also explains the catalytic activity of 3 since the enolate-like transition state should be electron richer than the acrylamide, making the complex stronger.⁴ In the absence of the nitro groups (receptor (4), Figure 3) almost no catalytic activity has been detected either in nucleophilic additions or in α deuteration reactions.⁵

The inclusion of a nitro group in receptor (5) (Figure 1), permits the combination of both type of catalytic effects. The higher association constant of this receptor with acrylamide (3.0 × 10³ M⁻¹), compared with receptor (1), probably shows the presence of charge-transfer. The combination of this effect with the additional hydrogen bond leads to the best catalytic activity (Table 1).

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REFERENCES

1. L. Pauling, *Chem. Eng. News*, 1946, **24**, 1375.
2. T. Laube, J. D. Dunitz, and D. Seebach, *Helv. Chim. Acta*, 1985, **68**, 1373.
3. M. Crego, C. Raposo, C. Caballero, E. García, J. Saez, and J. R. Morán, *Tetrahedron Lett.*, 1992, **33**, 7437.
4. For an interesting discussion on the effect of π complexes on reactivity see: M. L. Bender, R. J. Bergeron, and M. Komiyama, 'The Bioorganic Chemistry of Enzymatic Catalysis', ed. by J. Wiley, Sons, New York, 1984.
5. M. Crego, C. Raposo, M. L. Mussons, M.C. Caballero, and J. R. Morán, *Tetrahedron Lett.*, 1994, **35**, 1929.

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