icaloid characteristics so that they do not require concerted characters as badly as intramolecular electron transfer process. If there were no character differences between $T$, and $S$, potentials, electron transfer would be faster than proton transfer in both $T$, and $S$, admitting that the potential of QNH, compared with that of QNH+, is expected to be less unstable in $T$, than in $S$. We attribute the faster relaxation of the lowest triplet state of HQNH species, compared with the relaxation of the lowest triplet state of QN species, to the enhanced inter-system crossing rate of the lowest triplet state into the ground state by the vibrations of the O-H and N-H groups that exist exclusively in HQNH+ species. The observation of transient absorption due to ground state QNH+ species indicates that the very weak fluorescence and unobservable ground state absorption of QNH+ species are attributable to the energetically unfavorable potentials rather than to the unfavorable transition between $S$ and $S$.

In the this short and preliminary report we have tried to reveal that both the reverse electron and proton transfer reactions take place in the lowest triplet state potential of 6HQN as well as in its ground state potential. Further extensive studies, the results of which we will report later, on the consecutive electron and proton transfer reactions in 1, of simple 6HQN and its derivative molecular systems would shed light on the currently barely understood roles of the lowest triplet state potential in proton and electron transfer processes in general.

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References

Nucleophilic Addition on Nitrogen: Azophilic Addition of Grignard Reagent to 1-Benzyl Tetrazole Substituted Imine

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Tetrazole have been the primary choice for medicinal chemists as a carboxylic acid isoster because of their similar acidities $\rho pK_a \approx 5$ to that of the parent carboxylic acid and their stability against metabolism. Recently, particularly in connection with the development of nonpeptide receptor antagonists of the vasocactive octapeptide angiotensin II, there has been renewed interest in the chemistry of tetrazoles. In connection with our research programs of designing enzyme inhibitors and receptor antagonists, we needed various tetrazole analogs as amino acid isolaters. To this end, we have examined a synthetic methodology based on a nucleophilic addition of the Grignard reagents to imines and herein we would like to report unexpected findings regarding the regioselectivity in the addition reaction. There are numerous literature precedents on this type of reactions and it has been known that in most cases the organometallic addition to imines proceeds with a nucleophile attack normally on the carbon atom (carbonophile addition) instead of the nitrogen atom (azophile addition). This type of the reaction, particularly, the reaction of organometallic
reagents with chiral imines has been successfully used for the preparation of various nitrogen containing natural products and bioactive compounds.

Accordingly our synthetic strategy for the preparation of the azamethylytetrazole derivatives was planned as depicted in Scheme 1.

The key intermediate 6 was prepared from cyanamidomethane as shown in Scheme 2. Vinyltetrazole 4, obtained from cyanamidomethane and sodium azide, was protected with a benzyl group. Two benzylated isomers, purified chromatographically, were ozonolyzed to give the corresponding aldehydes 5 which were reacted immediately with optically pure phenethylamine to give tetrazole imines 6.

We then examined the addition reaction on imine 6 with various Grignard reagents. The addition of methylmagnesium bromide on 6 proceeded smoothly to give exclusively the addition product on the carbon atom 7b (the carbophilic addition). In contrast the reaction with ethylmagnesium bromide produced 7a exclusively in which the addition occurs on the nitrogen atom (the azophilic addition). The same azophilic product was also obtained with isopropyl and benzyl magnesium chloride. This result indicates that the reacting site is determined by the type of the Grignard reagent being used. This azophilic addition is quite unusual although there are a few examples known for nucleophile attacks on certain electrophilic nitrogen derivatives such as oximes or oxime tosyliates. Another known cases for the azophilic addition are when the imine carbon atom is much more hindered than the imine nitrogen atom or when imines were substituted with strong electron withdrawing groups as in the case of fluoromimines and N-alkyltetraphenyl-cyclopropenimines. It was also known that the reaction of the imino ester with simple Grignard reagents such as ethyl, i-propyl and benzyl magnesium halides gave the azophilic products.

The reason for the azophilic addition is probably due to the aminon stabilizing ability of the tetrazole group (Scheme 3).

We also examined the addition reaction of imines 6 with other organometallic nucleophiles such as alkyl lithiums and cuprates. However, we failed to obtain neither of carbophilic or azophilic products indicating that this unusual azophilic addition seems to be unique for the Grignard reagent. It is not clear at this moment why this unusual reaction is unique for the Grignard reagent type nucleophiles. A scope of this reaction and a possible mechanism for the reaction are subjects for our current study.

A typical reaction condition is as follows: To a solution of imine 6 (0.10 g, 0.34 mmole) in dry ethyl ether (8 mL) was added ethylmagnesium bromide (0.25 mL of 5 M solution, 0.75 mmole) at 0 °C. After 30 min, the reaction mixture was quenched with saturated aqueous NH₄Cl solution and then extracted with ethyl acetate. The organic layer was dried over MgSO₄ and concentrated to give the crude product which was purified by preparative-TLC (silica gel, hexane/ethyl acetate 3:1) to give the azophilic addition product 7a (91.7 mg, 85%).

### Table 1. Nucleophilic addition of Grignard reagent to 1-Benzyltetrazole imine

<table>
<thead>
<tr>
<th>Entry</th>
<th>R'MgX</th>
<th>7a/7b Yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MeMgBr</td>
<td>0.100</td>
</tr>
<tr>
<td>2</td>
<td>EtMgBr</td>
<td>0.090</td>
</tr>
<tr>
<td>3</td>
<td>i-PrMgCl</td>
<td>0.090</td>
</tr>
<tr>
<td>4</td>
<td>BnMgCl</td>
<td>0.090</td>
</tr>
<tr>
<td>5</td>
<td>MgBr</td>
<td>0.55</td>
</tr>
</tbody>
</table>

*Yields after purification by chromatography on silica gel preparative-TLC. The ratio of two diastereomers is 2:1.*

### References


5. N-(R)-α-Methylbenzyl-1-Benzyl 5-Tetrazole Imine (6): 1H NMR δ=7.67 (11, br-d, J=7.2 Hz imine H), 7.45-7.26 (10H, m, aromatic), 5.94 (2H, dd, J=14.0, 14.0 Hz benzyl), 5.24 (1H, quin, J=7.2 Hz chiral benzyl 1H), 1.59 (2H, d, J=7.2 Hz chiral benzyl CH). 13C NMR δ=154.08, 146.44, 141.68, 133.83, 128.92, 128.79, 127.90, 126.09, 52.58, 49.61, 21.74, 17.77. IR (cm⁻¹): 1659, 1563, 1716. M/S(M⁺): 292
11. Spectroscopic data for 9a (R'-Et): 1H NMR δ=7.32-7.23 (8H, m, aromatic), 6.96-6.92 (2H, m, aromatic). 3.45 (2H, dd, J=15.2, 15.2 Hz benzyl), 3.88 (11, q, J=6.8 Hz chiral benzyl 1H), 3.78 (21H, dd, J=14.2, 14.2 Hz.

Controlling Factors Governing Catalytic Process : Asymmetric Allylation Reaction Promoted by BINOL-Zr(IV) Catalyst with Synergetic Reagent

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As one of fundamental asymmetric bond forming reactions, allyl transfer reactions from chiral reagents to the carbonyl functionality in forming enantioenriched rich homochiral alcohols attract considerable attention from the synthetic community because the resulting products serve as chiral building blocks for multistep synthesis. The exceptional power of the allylation reaction has been enhanced by newly developed enantioselective versions, especially chiral Lewis acid catalysed allyl transfer reactions. The development of synthetic methods for achieving absolute stereoselection by the utilization of chiral catalysts increasingly requires precise control of the reaction pathway based on mechanistic behavior. Recently, we demonstrated that the utilization of molecular accelerator for the catalytic asymmetric allylation reaction promoted by BINOL-Ti(IV) complex 1 resulted in not only significantly increasing reaction rate but also reducing dosage of chiral catalyst. Described herein is an extension of the concept concerning molecular accelerating strategy to find new catalytic systems and to realize useful and practical asymmetric synthesis. There have been quite limited reports which appeared with chiral Zr species for the catalytic asymmetric synthesis; especially allylic transfer reaction. In the present research, two major progress have been made in this field for the enantioselective synthesis of homochiral alcohols: (1) the system employing BINOL-Zr(IV) catalyst with an accelerator exhibited dramatical increasing of catalytic capability (up to 5 mol %); (2) reduced side reaction significantly.

(S)-BINOL-Zr(IV) complex 2 was prepared from the reaction of (S)-BINOL with Zr(O-i-Pr)₄ in the presence of activated 4A molecular sieves. Treatment of 3 (R=C11H11Ph) with 4 in the presence of chiral catalyst 2 (5 mol %) in C11Cl3 at -20 °C for 24 h afforded product 5 (R=C11H11Ph) in 41% yield with 87% ee. We have subsequently observed that synergetic reagents can also be employed for this purpose. After surveying a series of alkylthioalkanes and alkylthiolanes for the allylation promoted by chiral catalyst 2, several key findings emerged: (1) i-PrSBEt, was generally superior to other reagents including i-PrSSiMe₂; (2) a 1:1 mixture of BINOL/ZrO(O-i-Pr) complex was proved to be most effective; (3) the new system exhibited sig-