icaloid characteristically so that they do not require concerted characters as badly as intramolecular electron transfer process. If there were no character differences between T_1 and S_0 potentials, electron transfer would be faster than proton transfer in both T_1 and S_0, admitting that the potential of $^1QNH^+$, compared with that of $^1QNH^+$, is expected to be less unstable in T_1 than in S_0. We attribute the faster relaxation of the lowest triplet state of $HQNH^+$ species, compared with the relaxation of the lowest triplet state of ^1QN species, to the enhanced intersystem 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 $^1QNH^+$ species indicates that the very weak fluorescence[3] and unobservable ground state absorption of $^1QNH^+$ species are attributable to the energetically unfavorable potentials rather than to its unfavorable transition[14] between S_1 and S_0.

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

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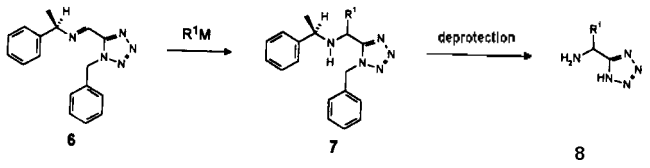
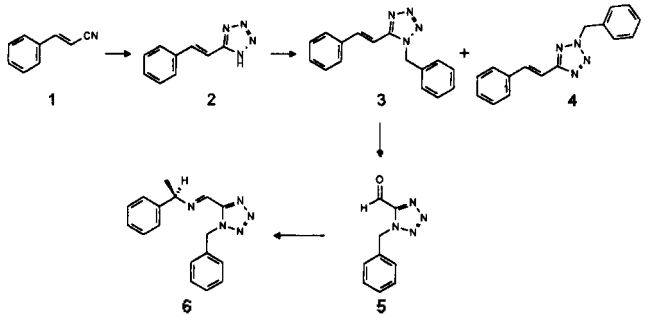
Tetrazole have been the primary choice for medicinal chemists as a carboxylic acid isostere because of their similar acidity ($pK_a \simeq 5$) to that of the parent carboxylic acid and their stability against metabolism.[1] Recently, particularly in connection with the development of nonpeptidic receptor antagonists of the vasoactive octapeptide angiotensin II, there has been renewed interest in the chemistry of tetrazoles.[2] In connection with our research programs of designing enzyme inhibitors and receptor antagonists, we needed various tetrazole analogs as amino acid isosteres.[3] To this end, we have examined a synthetic methodology based on a nucleophilic addition of the Grignard reagents on 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 (carbophilic addition) instead of the nitrogen atom (azophilic addition).[4] This type of the reaction, particularly, the reaction of organometallic



Scheme 1.



Scheme 2.

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 aminomethyltetrazole derivatives was planned as depicted in Scheme 1.

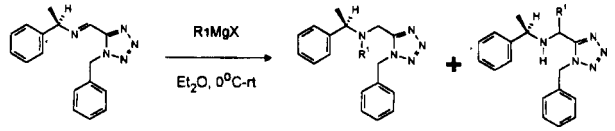
The key intermediates **6** was prepared from cinnamonitrile as shown in Scheme 2. Vinyltetrazole **2,** obtained from cinnamonitrile and sodium azide, was protected with a benzyl group. Two benzylated isomers, purified chromatographically, were ozonolyzed to give the corresponding aldehydes **5** which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

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 few examples known for nucleophile attacks on certain electrophilic nitrogen derivatives such as oximes[6] or oxime tosylates.[7] 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 fluorenimines and N-alkyltetraphenyl cyclopenta-dienimines.[8] It was also known that the reaction of the α-imino ester with simple Grignard reagents such as ethyl, *i*-propyl and benzyl magnesium halides gave the azophilic products.[9,10]

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

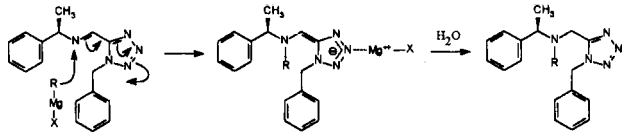
We also examined the addition reaction of imines 6 with other organometallic nucleophiles such as alkyl lithiums and cuprates. However, we failed to obtain neither of carbophilic or azophilic products indicating that this unusual azophilic addition seems to be unique for the Grignard reagent. It is not 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.

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



Entry	R¹MgX	7a:7b	Yield [a] (%)
1	MeMgBr	0:100	51 [b]
2	EtMgBr	100:0	85
3	*i*-PrMgCl	100:0	81
4	BnMgCl	100:0	76
5	MgBr	45:55	72

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



Scheme 3.

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 3 M solution, 0.75 mmole) at 0 °C. After 30 min., the reaction mixture was quenched with saturated aqueous NH_4Cl solution and then extracted with ethyl acetate. The organic layer was dried over $MgSO_4$ and concentrated to give the crude product which was purified by prep-TLC (silica gel, hexane/ethyl acetate (3/1)) to give the azophilic addition product **7a** (91.7 mg, 85%).[11]

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5. **N-(R)- α-Methylbenzyl-1-Benzyl 5-Tetrazole Imine (6):** ^{1}H NMR δ=7.67 (1H, b-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 H), 1.59 (2H, d, *J* =7.2 Hz, chiral benzyl CH_3). ^{13}C 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, 716. M/S(M^+): 292
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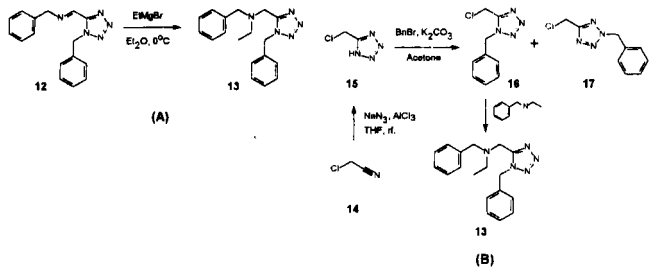
11. **Spectroscopic data for 9a (R'=Et):** H NMR δ=7.32-7.23 (8H, m, aromatic), 6.96-6.92 (2H, m, aromatic), 5.45 (2H, dd, *J* =15.2, 15.2 Hz, benzyl), 3.88 (1H, q, *J* =6.8 Hz, chiral benzyl H), 3.78 (2H, dd, *J* =14.2, 14.2 Hz, α-tetrazole), 2.65 (1H, hex, *J* =6.6 Hz, N-ethyl CH_2), 2.39 (1H, hexe, *J* =6.6 Hz, N-ethyl CH_2), 1.35 (3H, d, *J* =6.7 Hz, N-ethyl CH_3), 0.96 (3H, t, *J* =6.8 Hz, chiral benzyl CH_3). ^{13}C NMR δ=152.98, 142.23, 133.66, 128.85, 128.43, 127.79, 127.41, 127.39, 58.53, 50.39, 43.95, 42.51, 15.14, 11.69). IR (cm^{-1})=1459, 731.

The N-addition product **13** obtained under the same reaction condition from **12** was found to be identical to the compound prepared by a different synthetic method (route B) in ^{1}H, ^{13}C NMR and M/S.



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

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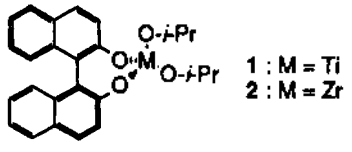
As one of fundamental asymmetric bond forming reactions, allyl transfer reactions from chiral reagents to the carbonyl functionality in forming enantiomerically rich homoallylic alcohols attract considerable attention from the synthetic community because the resulting products serve as chiral building block for multistep synthesis.[1] The exceptional power of the allylation reaction has been enhanced by newly developed enantioselective versions, especially chiral Lewis acid catalysed allyl transfer reactions.[2] 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.[3] 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.[4] Described herein is an extension of the conception 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.[5] In the present research, two major progress have been made in this field for the enantioselective synthesis of homoallylic 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 4 Å molecular sieves. Treatment of **3** (R=CH_2CH_2Ph) with **4** in the presence of chiral catalyst **2** (5 mol %) in CH_2Cl_2 at – 20 °C for 24 h afforded product **5** (R=CH_2CH_2 Ph) 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 alkylthioboranes and alkylthiosilanes for the allylation promoted by chiral catalyst **2,** several key findings emerged: (1) *i* -PrSBEt$_2$[6] was generally superior to other reagents including *i* -PrSSiMe$_3$; (2) a 1 : 1 mixture of BINOL/Zr(O- *i*- Pr)$_4$ complex was proved to be most effective; (3) the new system exhibited sig-