Table I. Conversion of Doubly Labeled α-Tyrosine into β-Tyrosine

expt.	precursor ($^3H/^{14}C$ ratio)	$^3H/^{14}C$ for β-tyrosine	% ^3H retention
1[a]	3(*R,S*)-[3-^{3}H,3-^{14}C]-DL-α-tyrosine (8.56)	4.56	53
2[b]	3(*S*)-[3-^{3}H,3-^{14}C]-DL-α-tyrosine (5.87)	1.35	23
3[b]	3(*R*)-[3-^{3}H,3-^{14}C]-DL-α-tyrosine (2.25)	1.86	83
4[b]	[2-^{3}H,1-^{14}C]-L-α-tyrosine (4.43)	0.71	16

[a] In vivo experiment. [b] In vitro experiment.

group from C-2 of α-tyrosine to C-3 leads to loss of the 3-*pro-S* hydrogen atom of the amino acid. The lack of complete tritium loss or retention observed in these two experiments is probably due to the fact that the chirally tritiated forms of α-tyrosine are only ~85% optically pure.[4]

A complete picture of the stereospecificity of the amino group migration to C-3 requires that the absolute configuration of natural β-tyrosine be known. The absolute configuration was determined in the following way. Resolution of 3-formamido-3-(*p*-methoxyphenyl)propionic acid with (+)-cinchonine gave (*R*)-(+)-3-formamido-3-(*p*-methoxyphenyl)-propionic acid with $[\alpha]_D$ +128° (93% optically pure).[5,6] Demethylation and deformylation of the optically active formamido acid with refluxing hydrobromic acid yielded β-tyrosine which was purified by recrystallization and then converted into the hydrochloride salt. Recrystallization of the hydrochloride gave (*R*)-β-tyrosine hydrochloride which exhibited an $[\alpha]_D$ −4.15°. Since β-tyrosine hydrochloride isolated from edeine A and B exhibits an $[\alpha]_D$ +7.8°, it follows that naturally occurring β-tyrosine has the *S* configuration.[7] This information combined with the knowledge that the 3-*pro-S* hydrogen atom of α-tyrosine is lost during amino group migration leads to the conclusion that the amino group is introduced at C-3 with inversion of configuration.

The loss of the 3-*pro-S* hydrogen atom from α-tyrosine as the result of β-tyrosine formation suggested that the mechanism of the α-tyrosine mutase reaction might be related to that of the reactions catalyzed by the ammonia-lyase enzymes.[8] All of the ammonia-lyases that have been examined catalyze a loss of ammonia that involves the removal of the same hydrogen atom in an absolute sense as that removed from C-3 of α-tyrosine by the mutase enzyme. In addition, both histidine and phenylalanine ammonia-lyase are deactivated by reagents that react with carbonyl groups. Evidence has been obtained that indicates that the electrophilic group present at the active sites of these ammonia-lyases is a dehydroalanyl residue. At present, little is known regarding the nature of the electrophilic group that occurs at the active site of α-tyrosine mutase. To gain some insight into the possible nature of the electrophilic group in tyrosine mutase, an in vitro experiment was carried out with [2-^{3}H]-L-α-tyrosine.[9] The results of this experiment are shown in Table I (expt 4): the in vitro conversion of [1-^{14}C,2-^{3}H]-L-α-tyrosine into β-tyrosine proceeds with loss of most of the tritium label from C-2 of α-tyrosine.[10] This observation is compatible with the formation of a Schiff base between a carbonyl group at the active site of the mutase and the amino group of α-tyrosine. It is apparently not consistent with the formation of an adduct between the amino group of α-tyrosine and a dehydroalanyl residue since the ammonia-lyase enzymes do not catalyze exchange of the α-hydrogen atoms of their amino acid substrates. The results of expt 4 also serve to emphasize the differences between the α-tyrosine mutase enzyme and an L-lysine 2,3-aminomutase found in *Clostridium*.[11] The lysine mutase requires pyridoxal phosphate and *S*-adenosylmethionine as cofactors and it catalyzes an isomerization that proceeds without incorporation of hydrogen from the medium. The stereospecificity of the lysine mutase reaction remains to be determined.

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(7) Assuming that the rotation reported for natural β-tyrosine hydrochloride corresponds to 100% optical purity, then the synthetic (*R*)-β-tyrosine hydrochloride has an optical purity of ~53%. Apparently some racemization of the asymmetric center occurs during the hydrobromic acid treatment.
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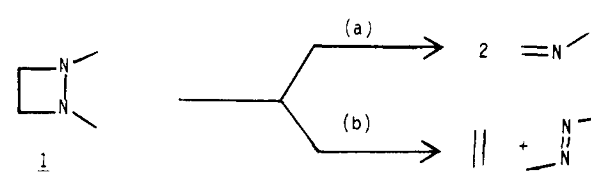
Flash Vacuum Thermolysis of 1,2-Diazetidines

Sir:

Thermolysis of unsaturated six-membered-ring hydrazines, 1,2,3,6-tetrahydropyridazine derivatives, generates dienes and azo compounds,[1] and the synthetic utility of this cycloreversion as a source of diimide has been well established.[1d] Nelsen[1a] has proposed that this cycloreversion is a concerted retro-Diels–Alder reaction. However, analogous thermolytic studies on four-membered-ring hydrazines, 1,2-diazetidines, are few.[2] For unsubstituted 1,2-diazetidines **1**,



two cycloreversions are conceivable, namely, (a) cleavage to imines and (b) fragmentation to an alkene and an azo compound. We have prepared the fused-ring 1,2-diazetidine[3] **2** for which four unique thermolytic pathways are possible: (1) a [2π + 2σ + 2σ] reversion to quadricyclane and azomethane; (2) a [2σ + 2σ] reversion to norbornadiene and azomethane; (3) a [2π + 2σ + 2σ] reversion to cyclopentadiene and Δ^3-1,2-dimethyl-1,2-diazetine (**3**); and (4) a [2σ + 2σ] cycloreversion to diimine **4**.

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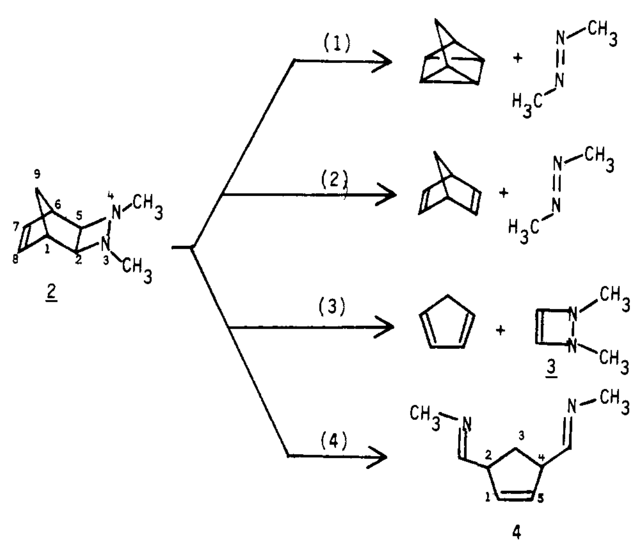
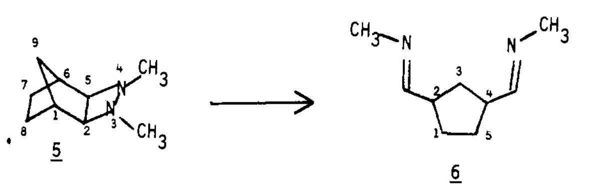


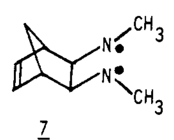
Solutions of **2** at 200 °C slowly turn black, and no characterizable product could be isolated. Since the primary product of this thermolysis was apparently unstable, **2** was then subjected to flash vacuum thermolysis[4] (FVT). FVT of **2** at 450 °C (contact time,[4b] ~0.5 s) produces diimine[5] **4** as the sole product, and thermolysis of the analogous saturated 1,2-diazetidine[3] **5** at 450 °C produces diimine **6** as the exclusive



product.[6] Integration of the ^{1}H NMR spectrum of the crude pyrolysate vs. CH_2Cl_2 added as an internal standard indicated an 86% recovery of **4**. Diimines **4** and **6** were identified on the basis of infrared and ^{1}H and ^{13}C NMR spectra.[5,6] The cis configuration at C-2, C-4 in **4** and **6**, demanded if the C-1, C-2 or C-5, C-6 bonds in **2** and **5** remain intact during the thermolysis, was indicated by spectral comparison with authentic samples of **4** and **6** prepared from the reaction of methylamine with *cis*-4-cyclopentene-1,2-dicarboxaldehyde[7] and *cis*-1,3-cyclopentanedicarboxaldehyde, respectively. The ^{1}H and ^{13}C NMR spectra of **4** and **6** show singlets for *N*-methyl absorptions, indicating either that both imines have the same configuration (anti) or that all possible syn and anti configurations are rapidly equilibrating at room temperature.

Thermolysis of **2** at 400 °C results in incomplete decomposition (~50% conversion of **2** into **4**), and at 600 °C **4** is the sole product. The thermolysis of **5** exhibits a temperature dependence similar to that shown by **2**: at 400 °C, incomplete decomposition of **5** (~60%) is observed; and at 600 °C, diimine **6** is still the sole product. The similarity of the product and temperature dependency of the thermolyses of **2** and **5** indicate the absence of participation of the double bond in the decomposition of **2**.

Two mechanistic extremes for the conversion of **2** to **4** are possible: (1) a concerted cycloreversion ($2\sigma_s + 2\sigma_a$ or $2\sigma_s + 2\sigma_s$);[9] or (2) a stepwise process involving initial rupture of the N–N bond producing biradical **7** that undergoes β scission to



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4. A concerted cycloreversion seems unlikely since the bicyclo ring in **2** prevents the four-membered ring from adopting the skewed conformation requisite for the symmetry-allowed[9] [$2\sigma_s + 2\sigma_a$] process. A [$2\sigma_s + 2\sigma_s$] cycloreversion is also possible; however, it is difficult to understand why such a symmetry-forbidden process would be observed in preference to other possible symmetry-allowed pathways available for the thermolysis of **2** [e.g., (1) and (3)]. As a result, we propose that a two-step process involving initial rupture of the weakest (N–N) bond in **2** is operative.

Research on more complete elucidation of the mechanism of thermal cycloreversion of 1,2-diazetidines is in progress.

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(6) **6**: ^{1}H NMR ($CDCl_3$) δ 7.60 (d, J = 4 Hz, 2 H), 3.26 (s, 6 H), 1.45–2.28 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 168.6 (C=N), 47.7 (*N*-CH_3), 45.4 (C-2, C-4), 33.8 (C-3), 29.2 (C-1, C-5); IR (CCl_4) 1680 cm^{-1} (C=N); mass spectrum parent peak at *m/e* 152. Like diimine **4**, **6** also slowly polymerizes at room temperature.
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Interception and Characterization of a Hydridoalkylrhodium Intermediate in a Homogeneous Catalytic Hydrogenation Reaction

Sir:

Reductive elimination of an alkane from a *cis*-hydridoalkyl metal complex (formed by olefin insertion into the corresponding dihydrido complex) has frequently been postulated as the product-forming step in the homogeneous catalytic hydrogenation of olefins.[1,2] However, failure of the proposed hydridoalkyl intermediate to accumulate in detectable concentrations generally has precluded direct observation of this step, the evidence for which has thus far been largely indirect.[3] We now report the interception and characterization of such a hydridoalkyl intermediate and the direct observation of the alkyl–hydride reductive elimination step, in a homogeneous catalytic hydrogenation reaction.

Our observations relate to the homogeneous catalytic hydrogenation of methyl (*Z*)-α-acetamidocinnamate (MAC, **1**),

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