2.

Reduction of Styrene Oxide. The following experiment illustrates the technique utilized in cases where the reaction mixture was subjected to identification of products.

Utilizing the above general procedure, the reduction of styrene oxide with LTDBA was performed for 0.5 h at 0℃. The reaction mixtrue was then hydrolyzed with 2 N HCl and the organic layer was taken up in ether. The GC analysis showed the presence of 99% of 1-phenylethanol and trace of 2-phenylethanol.

In cases where a single product in the reaction mixture was apparent, we did not perform the product identification further.

Genaral Procedure for Stereoselectivity Study. The reduction of 3,3,5-trimethylcyclohexanone is descirbed as representative. To a 10 m*l* vial capped by a rubber septum was added 2 m*l* of a solution of LTDBA in THF (1.50 M, 3 mmol). The vial was kept at 0℃, and to this was added 1 m*l* of a 2 M compound (2 mmol) in THF. The reaction mixture was stirred for 3 h at that temperature and then hydrolyzed by 3 N H_2SO_4. The aqueous layer was saturated with anhydrous magnesium sulfate, and the organic layer was subjected to GC analysis. The results are summarized in Table 3.

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Ruthenium Catalyzed Synthesis of 1-Substituted Perhydroazocines from Primary Amines and 1,7-Heptanediol

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The reaction of primary aromatic amines with 1,7-heptanediol in the presence of a catalytic amount of ruthenium complex in dioxane at 180℃ for 24 hours gave the corresponding 1-substituted perhydroazocines in moderate yield.

Introduction

A large variety of methods are known for building up pi-piperidine,[1] and perhydroazepine[2] rings, which are often present in natural products. In these methods, substrates such as 1,5- and 1,6-dihaloalkanes or 1,6-dihalogenoamines are used as the starting materials and hetero-rings are usually closed intramolecularly at the nitrogen atom.

We have previously reported the synthesis of 1-substituted pyrrolidines,[3] piperidines,[4] and perhydroazepines[5] from succinaldehyde, glutaraldehyde or adipaldehyde, and primary amines, respectively with tetracarbonylhydridoferrate, $HFe(CO)_4^-$, as a selective reducing agent. These reactions, however, required stoichiometric amounts of $HFe(CO)_4^-$.[6]

Watanabe *et al.*[7] have recently developed organic synthesis involving dehydrogenation of an alcohol by a ruthenium cata-

Table 1. Reaction Condition on the Synthesis of 1-(4-Tolyl)perhydroazocine from *p*-Toluidine and 1,7-Heptanediol[a]

Exp. No.	Catalyst $RuCl_3 \cdot nH_2O$ (mol%)[e]	PR_3 (mol%)	Molar ratio[c]	Yield (%)[d]
1	2.0	6.0(PPh_3)	2.0	25
2	2.0	6.0(PPh_3)	1.0	17
3	2.0	6.0(PPh_3)	0.5	1
4	2.0	6.0(PPh_3)	3.5	16
5	2.0	6.0($P(OEt)_3$)	2.0	5
6[f]	2.0	6.0(PPh_3)	2.0	26
7[f]	2.0	6.0(PPh_3)	2.0	13
8	2.0	6.0(PBu_3)	2.0	20
9	2.0	–	2.0	0
10	–	6.0(PPh_3)	2.0	0

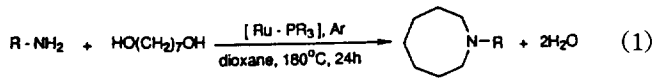
[a] *p*-Toluidine (0.27 g, 2.5 mmol), 1,7-Heptanediol (0.66 g, 5.0 mmol), $RuCl_3 \cdot nH_2O$ (0.01 g, 0.05 mmol), PPh_3 (0.04 g, 0.15 mmol), and dioxane (10 m*l*) at 180℃ for 24 h. [b] Based on an amount of *p*-Toluidine used. [c] [1,7-Heptanediol]/[*p*-Toluidine]. [d] Isolates yield. [e] For 40 h. [f] 150℃.

lyst as a key step. For example, they and we have reported that the reactions of primary amines with 1,4-butanediol,[7] 1,5-pentanediol,[8] and 1,6-hexanediol[9] gave the corresponding 1-substituted pyrrolidines, piperidines, and perhydroazepines, respectively in good yields.

This paper deals with catalytic synthesis of 1-substituted perhydroazocines from primary amines and 1,7-heptanediol.

Results and Discussion

Primary amines were reacted with 1,7-heptanediol in the presence of catalytic amounts of ruthenium complexes in dioxane at 180℃ for 24 hours to give 1-substituted perhydroazocines along with small amounts of heptanolamine derivatives (Eq. 1).



(1)

The reaction of 1,7-heptanediol with *p*-toluidine as a primary aromatic amine was utilized to establish the optimum conditions (Table 1). The catalyst system of $RuCl_3 \cdot nH_2O$ with PPh_3 or PBu_3 showed the higher activity for the synthesis of 1-(4-tolyl)perhydroazocine (Exp. Nos. 1 and 8), while the system of $RuCl_3 \cdot nH_2O$ with $P(OEt)_3$ exhibited almost no activity (Exp. No. 5). Yields were very sensitive to the type or phosphine ligand coordinated to the ruthenium catalyst. A considerable catalytic activity was maintained at 150℃ (Exp. No. 7). The longer time did not affect the yields of products (Exp. No. 6). Also it was observed that the yields depended on the molar ratio of 1,7-heptanediol over *p*-toluidine (Exp. Nos. 2, 3 and 4). In the absence of either $RuCl_3 \cdot nH_2O$ or PR_3, the substrate was recovered quantitatively (Exp. Nos. 9 and 10).

Using the optimum condition (Exp. No. 1 in Table 1), the substituted anilines such as toluidines, anisidines, and chloroanilines reacted with 1,7-heptanediol to produce the corresponding 1-tolyl-, 1-anisidyl-, and 1-(chrolophenyl)perhydroazocines, respectively. Para or meta substituted methyl, methoxy group, and chlorine atom on the aniline ring have no effect on the yields of reactions (Exp. Nos. 1, 11, 13, 14, 16, and 17). Ortho substituted anilines gave low yields because of steric hindrance (Exp. Nos. 12, 15, and 18). The reaction of aniline with 1,7-heptanediol gave 1-phenylperhydroazocine in moderate yield (Exp. No. 19). That of benzylamine with 1,7-heptanediol gave a trace amount of product along with mainly tarry materials (Exp. No. 20).

Table 2. Synthesis of 1-Substituted Perhydroazocines from Primary Amines and 1,7-Heptanediol[a]

Exp. No	Amine	Product	Yield(%)[b]
1	*p*-Toluidine	1-(4-Tolyl)perhydroazocine	25
11	*m*-Toluidine	1-(3-Tolyl)perhydroazocine	22
12	*o*-Toluidine	1-(2-Tolyl)perhydroazocine	3
13	*p*-Chloroaniline	1-(4-Chlorophenyl)perhydroazocine	22
14	*m*-Chloroaniline	1-(3-Chlorophenyl)perhydroazocine	21
15	*o*-Chloroaniline	1-(2-Chlorophenyl)perhydroazocine	6
16	*p*-Anisidine	1-(4-Anisidyl)perhydroazocine	19
17	*m*-Anisidine	1-(3-Anisidyl)perhydroazocine	17
18	*o*-Anisidine	1-(2-Anisidyl)perhydroazocine	0
19	Aniline	1-Phenylperhydroazocine	19
20	Benzylamine	1-Benzylperhydroazocine	tr

[a] Amine (2.5 mmol), 1,7-heptanediol (0.66 g, 5 mmol), $RuCl_3 \cdot nH_2O$ (0.01 g, 0.05 mmol), PPh_3 (0.04 g, 0.15 mmol), and dioxane (10 m*l*) at 180℃ for 24 h. [b] Isolated yield.

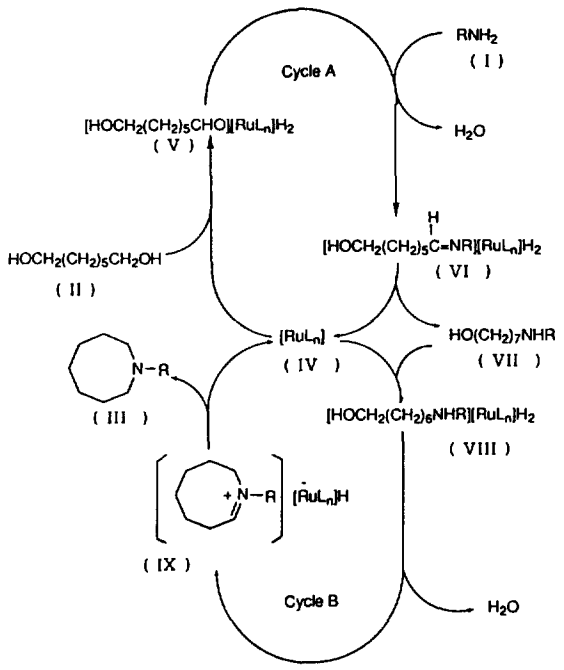
Even though the yields are low, the synthetic methods of the perhydroazocines are new and simple procedure. From these results it can be suggested that the reaction of primary aromatic amines with 1,7-heptanediol in the Ru-PR_3 catalyst is suitable for the synthesis of 1-arylperhydroazocines, but not suitable for that of 1-alkylperhydroazocines.

A possible catalytic cycle for these reactions is postulated as follows: A hydroxy group of the 1,7-heptanediol(II) oxidatively coordinates to the active catalyst center(IV). Oxidation pathway *via* alkoxohydride complexes have been proposed by several authors,[10-12] Nucleophilic attack of the amine(I) on the resulting aldehyde intermediate(V) yields the Schiff base complex(VI). The hydrogenation of the Schiff base intermediate gives aminoalcohol derivatives(VII). Successively, (VIII) is cyclized intramolecularly to give the product(III) *via* an immonium intermediate(IX) in cycle B in a simillar manner.

Experimental

All commercial solvents were purified using the standard method. 1,7-Heptanediol and amines were obtained from TCI, Aldrich, and Sigma, and used without further purification.

^{1}H-NMR spectra were obtained at 60 MHz on a Varian EM 360 or at 300 MHz on a Bruker AM 300 spectrometer. All chemical shifts were measured relative to TMS. Low resolution mass spectra were obtained using Shimadzu-QP 1000 spectrometer at 70 eV. Gas chromatography (GLC) was



Scheme 1

performed on a Shimadzu GC-3BT gas chromatograph.

A typical reaction of *p*-toluidine with 1,7-heptanediol will be described to exemplify the general reaction procedure: A stainless steel reactor (100 m*l*) containing a glass liner was used in the reaction. Under argon stream, dioxane (10 m*l*), *p*-toluidine (0.27 g, 2.5 mmol), 1,7-heptanediol (0.68 g, 5.0 mmol), $RuCl_3 \cdot nH_2O$ (0.01 g, 0.05 mmol), and PR_3 (0.15 mmol) were added with magnetic stirring bar into the glass liner set in the reactor. After sealing the reactor, an air purge was confirmed by pressurization (10 atm)-depressurization of sequence argon. The reactor was heated to 180℃ and thermostated at this temperature with stirring for 24 hours. The reaction was terminated by rapid cooling and reactor was discharged. Column chromatography of the evaporated reaction mixture on silica gel with hexane/ethyl acetate mixture (2 : 1) as an eluent gave 1-substituted perhydroazocine (25%).

Analytical data of 1-substituted perhydroazocines were as follows:

1-(4-Tolyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.52(m, 6H, CH_2), 1.70(m, 4H, CH_2), 2.22(s, 3H, CH_3), 3.37(t, J=4.3 Hz, 4H, CH_2), 6.57(d, J=8.5 Hz, 4H, aromatic-H); ^{13}C-NMR ($CDCl_3$) δ 14.07(CH_3), 26.62(CH_2), 26.95 (2CH_2), 27.01(2CH_2), 50.40(2CH_2), 110.92(2CH), 123.65(C), 129.58(2CH), 146.06(C); mass (m/e); 203(M^+), 174, 160, 134, 119, 91, 43; Calcd for $C_{14}H_{21}N$: C, 82.65; H, 10.45; N, 690. Found: C, 82.70; H, 10.41; N, 6.89.

1-(3-Tolyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.55(M, 6H, CH_2), 1.71(m, 4H, CH_2), 2.3(s, 3H, CH_3), 3.41(t, 5.6 Hz, 4H, CH_2), 6.47 (m, 3H, aromatic-H), 7.10(m, 1H, aromatic-H); ^{13}C-NMR ($CDCl_3$) δ 14.11(CH_3), 26.68(CH_2), 26.68(CH_2), 27.01(2CH_2), 27.12(2CH_2), 50.46(2CH_2), 108.30 (CH), 111.69(CH), 115.88(CH), 128.94(CH), 138.61(C), 148.29 (C); mass(m/e) 203 (M^+), 174, 160, 146, 134, 119, 91.

1-(2-Tolyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.0-2.0(m, 10H, CH_2), 2.05(s, 3H, CH_2), 3.2(m, 4H, CH_2), 6.4-7.1(m, 4H, aromatic-H); mass(m/e) 203(M^+), 174, 160, 146, 134, 119, 118, 91, 43.

1-(4-Chlorophenyl)perhydroazocine. Colorless; ^{1}H-NMR ($CDCl_3$) δ 1.57(s, 10H, CH_2), 3.40(t, J=4.3 Hz, 4H, CH_2), 6.47(d, J=9.5 Hz, 2H, aromatic-H), 7.05(d, J=9.5 Hz, 2H, aromatic-H); mass(m/e) 225, 223(M^+), 194, 180, 166, 154, 139(B), 43.

1-(3-Chlorophenyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.55(m, 6H, CH_2), 1.70(m, 4H, CH_2), 3.42(t, J=10 Hz, 4H, CH_2), 6.6(m, 3H, aromatic-H), 7.1(t, J=9 Hz, 2H, aromatic-H); ^{13}C-NMR ($CDCl_3$) δ 26.48(CH_2), 26.67(2CH_2), 26.61(2CH_2), 50.61(2CH_2), 50.61(2CH_2), 109.29(CH), 110.85 (CH), 114.67(CH), 129.93(CH), 135.00(C), 149.16(C); mass(m /e) 225, 223(M^+), 194, 180, 166, 139, 43.

1-(2-Chlorophenyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.70(s, 10H, CH_2), 3.2(b, 4H, CH_2), 7.05(m, 4H, aromatic-H); mass(m/e) 225, 223(M^+), 194, 180, 166, 154, 139(B), 43.

1-(4-Anisidyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.58(s, 10H, CH_2), 3.36(t, J=4.0 Hz, 4H, CH_2), 3.67 (s, 3H, CH_3), 6.48(d, J=10 Hz, 2H, aromatic-H), 6.70(d, J=10 Hz, 2H, aromatic-H); mass(m/e) 225, 219(M^+), 190, 176, 160, 150, 135(B), 43, 31.

1-(3-Anisidyl)perhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.56(s, 10H, CH_2), 3.39(t, J=4 Hz, 4H, CH_2), 3.68(s, 3H, CH_3), 6.03(m, 2H, CH), 6.17(d, J=2 Hz, 1H, aromatic-H), 6.92(t of d, J=8.5 Hz of 2 Hz, 1H, aromatic-H); mass(m/e) 219(M^+), 190, 176, 162, 150, 135(B), 43, 31.

1-Phenylperhydroazocine. Colorless oil; ^{1}H-NMR ($CDCl_3$) δ 1.54-1.57(m, 6H, CH_2), 1.76(m, 4H, CH_2), 3.44(t, J=5.6 Hz, 4H, CH_2), 6.66(m, 3H, aromatic-H), 7.22(m, 2H, aromatic-H); ^{13}C-NMR ($CDCl_3$) δ 26.74(CH_2), 27.01(2CH_2), 50.57(2CH_2), 111. 18(2CH), 115.02(CH), 129.13(2CH), 148.10(C); mass(m/e) 189 (M^+), 160, 146, 132, 105(B), 43.

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Infrared Multiphoton Dissociation of CF_2HCl: Laser Fluence Dependence and the Effect of Intermolecular Collisions

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The effect of intermolecular collisions in the infrared multiphoton dissociation (IRMPD) of difluorochloromethane was investigated using He, Ar, and N_2 as buffer gases. The reaction probability for IRMPD of difluorochloromethane was measured as a function of laser fluence and the buffer gas pressure under unfocused beam geometry. It was observed that the reaction probability was initially enhanced with the increase of buffer gas pressure up to about 20 torr, but showed a decline at higher pressures. The reaction probability increases monotonically with the laser fluence, but the rate of increase diminishes at higher fluences. An attempt was made to simulate the experimental results by the method of energy grained master equation (EGME). From the parameters that fit the experimental data, the average energy loss per collision, $<\Delta E>_d$, was estimated for the He, Ar, and N_2 buffer gases.

Introduction

An intense, pulsed IR laser radiation has been shown to promote molecules in the gas phase to high vibrational levels of the ground electronic state *via* the simultaneous absorption of many infrared photons. It is now well established that when a molecule is excited above a certain level by IR multiphoton absorption (IRMPA), the energy pumped into the molecule is more or less randomly distributed among all vibrational degrees of freedom before decomposition starts.[1-6] Such a highly excited molecule is not qualitatively very different from the energized molecules or transient complexes produced by inelastic and/or reactive molecular collisions, and the IRMPD technique has been widely used for the study of dynamics of unimolecular reactions.

Since the first report of IRMPD of CF_2HCl,[7] many studies have been done on the IR laser induced chemistry of this molecule. Grunwald *et al.* reported the effect of buffer gas pressure on the macroscopic absorption cross section and the dissociation yield.[7] Sudboe *et al.* investigated the three-center unimolecular elimination reaction of HCl from CF_2HCl in a molecular beam experiment, and showed that the measured translational energy distribution of the product could be explained by the statistical (RRKM) theory.[8,9] Stephenson *et al.* studied the laser intensity and Ar pressure dependence of IRMPD of CF_2HCl by monitoring the CF_2 : $(\tilde{X}^1A_1)$ carbene with the laser-induced fluorescence technique.[10-13] They reported that there existed a narrow "linear dependence" range in the log-log plot of dissociation probability *vs.* laser fluence between 5-25 MW/cm^2 of laser intensity; a smooth bending over and saturation in product formation was also observed (25-150 MW/cm^2). Increasing Ar pressure above a certain level (~50 torr) initially increased the CF_2HCl dissociation rate due to what may be called the "rotational hole-filling", but the rate soon became independent of Ar pressure up to 1 atm. They were also able to reproduce their results by a model calculation. Van den Bergh *et al.* reported a different pressure dependence feature in the IRMPD of CF_2HCl.[14-16] They used unfocussed laser pulses (2-8 J/cm^2) and observed the collisional deactivation effect of Ar buffer gas. They tried to simulate the results with a model calculation, and found that simple energy-grained master equation (EGME) was adequate to describe the IRMPD results of CF_2HCl.[14-16] Dolikov *et al.* examined the possibility of mode-selectivity of multiphoton excitation, but they found it impossible to excite a specific mode at least on the time scale of 10^{-8} sec. They observed that absorption of mere 4-5 quanta resulted in the excitation of all vibrational modes.[6]

Recent studies of the IRMPD of CF_2HCl include subjects such as deuterium separation using the difference of absorption cross section due to the isotope effect,[17] the effect of laser frequency and translational energy on the IRMPD of CF_2HCl,[18] and CF_2: carbene generation for the purpose of secondary use in bimolecular reaction chemistry with diatomic molecules.[19,20]

The laser-induced reaction of this molecule is particularly simple, being represented by

‡Deceased.